

# Supporting Information

## Enantioselective Construction of Spirodihydrofuran Oxindoles via One-Pot Organo-/Iodine Sequential Catalysis

Ai-Bao Xia,<sup>1,\*</sup> Li-Sha Huang,<sup>1</sup> Chang-Ping Li,<sup>2</sup> Qing-Bo Hu,<sup>1</sup> Jin-Yao  
Zhu,<sup>1</sup> Liang Bai<sup>1</sup> and Dan-Qian Xu<sup>1,\*</sup>

*<sup>1</sup>Catalytic Hydrogenation Research Centre, State Key Laboratory  
Breeding Base of Green Chemistry-Synthesis Technology, Zhejiang  
University of Technology, Hangzhou, 310014, Zhejiang, China*

*<sup>2</sup>Hangzhou Environmental Protection Co., Ltd, Hangzhou 310063, P.R.  
China*

*Fax (+86) 0571 88320066;*

*E-mail: xiaaibao@zjut.edu.cn; chrc@zjut.edu.cn*

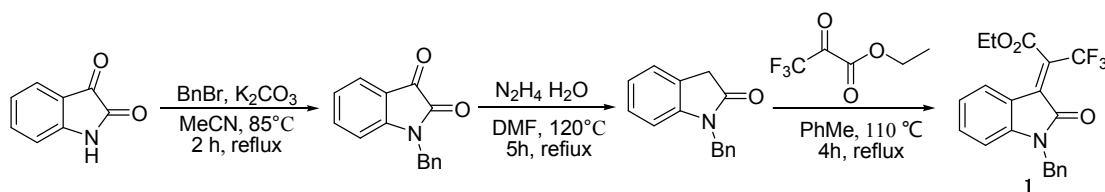
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## 1. General information

NMR data were obtained on Bruker AVANCE III for  $^1\text{H}$  at 500 MHz and for  $^{13}\text{C}$  at 125 MHz with TMS as the internal standard. HRMS data were measured on an Agilent 6545 Q-TOF LC/MS with an ESI source. In each case, enantiomeric excess was determined on a chiral column in comparison with authentic racemates by chiral HPLC, using a JASCO LC-2000 Plus system consisting of MD-2010 HPLC diode array detector or an Agilent 1260 chromatography. Column chromatography and flash chromatography experiments were conducted using silica gel GF254 (200-300 mesh) eluting with ethyl ether and petroleum ether. TLC experiments were carried out on glass-backed silica plates. Chemicals were used without purification as commercially available.

The Boc protected isatin-derived  $\alpha$ -trifluoromethylacrylate was prepared according to a previously reported procedure. For details, see: Q.-X. Lou, Y.-Y. Ding, D.-F. Xu, G.-K. Liu, J.-L. Zhao, *Adv. Synth. Catal.*, 2017, **359**, 2557.

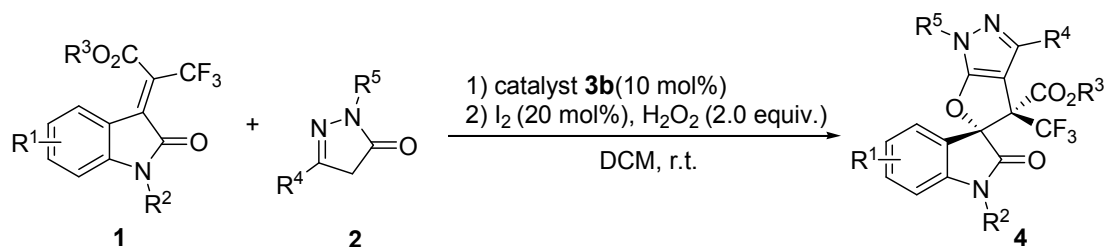
## 2. Typical experimental procedure for the preparation of substrate **1** and organo-/iodine sequential catalysis, and characterization of products **4**



Isatins (10 mmol) and benzyl bromide (12 mmol) were stirred in CH<sub>3</sub>CN (25 mL) in the presence of K<sub>2</sub>CO<sub>3</sub> (12 mmol) at 85 °C for 2 h. Reactions were monitored by TLC. After completion, the reaction mixture was concentrated under reduced pressure. The residue was added into H<sub>2</sub>O (50 mL) and extracted with EtOAc (3×20 mL), then the mixture was dried and concentrated.

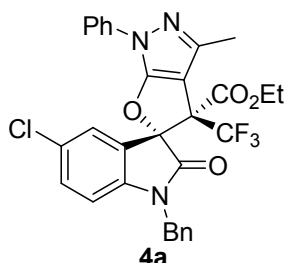
The above solid and hydrazine hydrate (10 mL) was directly added in DMF (10 mL), the mixture was stirred at 120 °C for 5 h. After completion, the reaction mixture was concentrated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate =10:1) to give the oxindole.

The oxindole, 3,3,3-trifluoromethyl pyruvic acid ethyl ester (1.98 mL, 15 mmol) and piperidine (0.27 mL, 3 mmol) were stirred in toluene (25 mL) at 110 °C for 4 h. After completion, the reaction mixture was extracted with EtOAc (3×20 mL), washed with water, dried and concentrated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate =10:1) to give **1**.

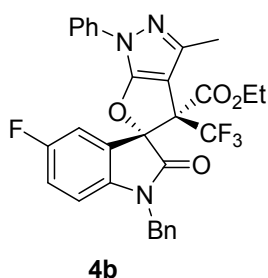


$\alpha$ -Trifluoromethyl acrylates **1** (0.4 mmol) and pyrazolones **2** (0.2 mmol) were stirred in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) in the presence of catalyst **3b** (0.02 mmol) at room temperature for 36 h, then I<sub>2</sub> (0.04 mmol) and 30% H<sub>2</sub>O<sub>2</sub> aqueous solution (0.4 mmol) were added, and the mixture was stirred for 2 h at room temperature. The reaction was

monitored by TLC. After completion, the mixture was dried and concentrated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate =10:1) to give products **4**.

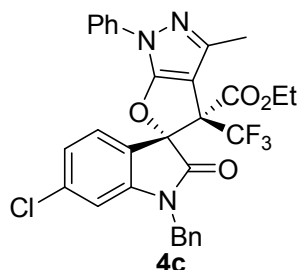


**ethyl-(4R,5R)-1'-benzyl-5'-chloro-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 178-180 °C, 90.6 mg, 78% yield, 96% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/*n*-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 14.4 min (minor), 19.1 min (major).  $[\alpha]_D^{20}$  = -70 ( $c$  = 0.56 in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 – 7.63 (m, 3H), 7.42 – 7.37 (m, 6H), 7.35 – 7.30 (m, 2H), 7.25 – 7.19 (m, 1H), 6.69 (d,  $J$  = 8.5 Hz, 1H), 5.02 (d,  $J$  = 15.9 Hz, 1H), 4.74 (d,  $J$  = 15.9 Hz, 1H), 4.50 – 3.76 (m, 2H), 2.44 (s, 3H), 1.33 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 166.0, 158.8, 145.1, 143.0, 137.5, 134.3, 132.3, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.8, 128.6, 128.0, 127.4 ( $\times 2$ ), 126.0, 123.7 ( $J$  = 286 Hz), 122.1, 118.5 ( $\times 2$ ), 111.2, 100.4, 98.2, 77.2, 63.6, 44.4, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{23}\text{ClF}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  604.1221, found 604.1224.

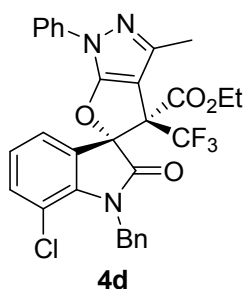


**ethyl-(4R,5R)-1'-benzyl-5'-fluoro-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 150-152 °C, 74.6 mg, 66% yield, 92% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/*n*-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 12.1 min (minor), 14.3 min (major).  $[\alpha]_D^{20}$  = -6 ( $c$  = 0.57 in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 – 7.64 (m, 2H), 7.48 – 7.45 (m, 1H), 7.43 – 7.34 (m, 6H), 7.35 – 7.30 (m, 1H), 7.25 – 7.17 (m, 1H), 7.10 – 7.05 (m, 1H), 6.71 – 6.68 (m, 1H), 5.03 (d,  $J$  = 15.9 Hz, 1H), 4.73 (d,  $J$  = 15.9 Hz, 1H), 4.32 – 4.27 (m, 2H), 2.43 (s, 3H), 1.33 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.7, 166.0, 159.1 (d,  $^1J_{\text{C-F}}$  = 241.9 Hz), 158.8, 145.0,

140.4 (d,  $^4J_{C-F} = 2.1$  Hz), 137.6, 134.4, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.0, 127.4 ( $\times 2$ ), 125.9, 123.8 ( $J = 286$  Hz), 122.6 (d,  $^3J_{C-F} = 8.82$  Hz), 118.8 (d,  $^2J_{C-F} = 23.7$  Hz), 118.5 ( $\times 2$ ), 116.3 (d,  $^2J_{C-F} = 21.4$  Hz), 110.9 (d,  $^3J_{C-F} = 8.82$  Hz), 100.4, 98.3, 77.2, 63.6, 44.4, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[C_{30}H_{23}F_4N_3O_4 + Na]^+$   $m/z$  588.1517, found 588.1521.

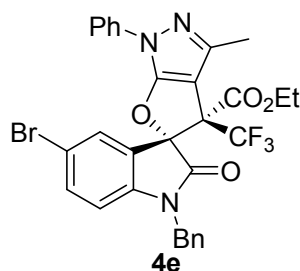


**ethyl-(4R,5R)-1'-benzyl-6'-chloro-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 162-164 °C, 95.3 mg, 82% yield, 96% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 10/90, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 5.8$  min (minor), 7.8 min (major).  $[\alpha]_D^{20} = -36$  (c = 0.53 in  $CH_2Cl_2$ ).  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.77 – 7.58 (m, 3H), 7.42 – 7.38 (m, 7H), 7.23 – 7.18 (m, 1H), 7.14 – 7.09 (m, 1H), 6.78 (d,  $J = 1.9$  Hz, 1H), 5.01 (d,  $J = 15.9$  Hz, 1H), 4.73 (d,  $J = 15.9$  Hz, 1H), 4.36 – 4.18 (m, 2H), 2.43 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  172.0, 166.0, 158.8, 145.8, 145.1, 138.5, 137.6, 134.2, 129.3, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.1, 127.4 ( $\times 2$ ), 125.9, 123.8 ( $J = 286$  Hz), 123.3, 119.7, 118.4 ( $\times 2$ ), 110.8, 100.4, 98.0, 77.2, 63.6, 44.5, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[C_{30}H_{23}ClF_3N_3O_4 + Na]^+$   $m/z$  604.1221, found 604.1229.

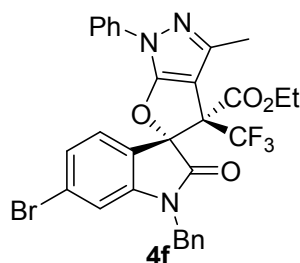


**ethyl-(4R,5R)-1'-benzyl-7'-chloro-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 142-144 °C, 93.0 mg, 80% yield, 96% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 16.1$  min (minor), 19.5 min (major).  $[\alpha]_D^{20} = -9$  (c = 0.56 in  $CH_2Cl_2$ ).  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.69 – 7.61 (m, 3H), 7.41 – 7.37 (m, 3H), 7.36 – 7.33 (m, 4H), 7.30 – 7.25 (m, 1H), 7.24 – 7.20 (m, 1H), 7.13 – 7.08 (m, 1H), 5.40 – 5.20 (m, 2H), 4.25 – 4.20 (m, 2H), 2.41 (s, 3H), 1.29 (t,  $J = 7.1$  Hz, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  172.6, 165.9, 158.8, 145.1, 140.6, 137.6, 136.6, 135.0, 129.2 ( $\times 2$ ), 128.6 ( $\times 2$ ), 127.4, 127.0, 126.7 ( $\times 2$ ),

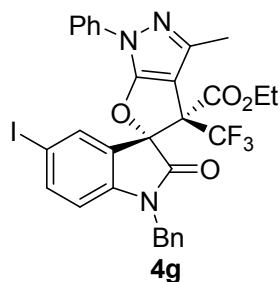
125.9, 124.2, 124.1, 123.8 ( $J = 283$  Hz), 118.4 ( $\times 2$ ), 116.2, 100.5, 97.7, 77.2, 63.6, 45.6, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[C_{30}H_{23}ClF_3N_3O_4 + Na]^+$   $m/z$  604.1221, found 604.1224.



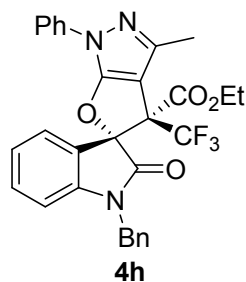
**ethyl-(4R,5R)-1'-benzyl-5'-bromo-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp182-184 °C, 86.3 mg, 69% yield, 94% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 10/90, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 6.4$  min (minor), 9.0 min (major).  $[\alpha]_D^{20} = -18$  ( $c = 0.50$  in  $CH_2Cl_2$ ).  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.82 (d,  $J = 1.9$  Hz, 1H), 7.66 (d,  $J = 8.0$  Hz, 2H), 7.49 (dd,  $J = 8.5, 1.9$  Hz, 1H), 7.42 – 7.36 (m, 6H), 7.35 – 7.30 (m, 1H), 7.25 – 7.18 (m, 1H), 6.64 (d,  $J = 8.4$  Hz, 1H), 5.02 (d,  $J = 15.9$  Hz, 1H), 4.73 (d,  $J = 15.8$  Hz, 1H), 4.33 – 4.26 (m, 2H), 2.44 (s, 3H), 1.33 (t,  $J = 7.1$  Hz, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  171.5, 166.0, 158.8, 145.0, 143.5, 137.5, 135.2, 134.2, 131.3, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.0, 127.3 ( $\times 2$ ), 125.9, 123.7 ( $J = 283$  Hz), 123.1, 118.5 ( $\times 2$ ), 115.9, 111.7, 100.4, 98.1, 77.2, 63.6, 44.4, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[C_{30}H_{23}BrF_3N_3O_4 + Na]^+$   $m/z$  648.0716, found 648.0718.



**ethyl-(4R,5R)-1'-benzyl-6'-bromo-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp195-197 °C, 98.8 mg, 79% yield, 97% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 11.6$  min (minor), 14.6 min (major).  $[\alpha]_D^{20} = -3$  ( $c = 0.54$  in  $CH_2Cl_2$ ).  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.68 – 7.62 (m, 2H), 7.58 – 7.52 (m, 1H), 7.42 – 7.36 (m, 6H), 7.31 – 7.25 (m, 2H), 7.24 – 7.21 (m, 1H), 6.93 (d,  $J = 1.8$  Hz, 1H), 5.00 (d,  $J = 15.8$  Hz, 1H), 4.73 (d,  $J = 15.8$  Hz, 1H), 4.38 – 4.09 (m, 2H), 2.42 (s, 3H), 1.31 (t,  $J = 7.1$  Hz, 3H);  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  171.9, 166.0, 158.8, 145.8, 145.1, 137.6, 134.2, 129.5, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.1, 127.4 ( $\times 2$ ), 126.6, 126.3, 125.9, 123.8 ( $J = 281$  Hz), 120.2, 118.4 ( $\times 2$ ), 113.6, 100.4, 98.1, 77.2, 63.6, 44.5, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[C_{30}H_{23}BrF_3N_3O_4 + Na]^+$   $m/z$  648.0716, found 648.0719.

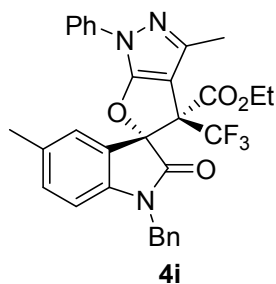


**ethyl-(4R,5R)-1'-benzyl-5'-iodo-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp181-183 °C, 91.5 mg, 68% yield, 92% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 10/90, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 6.7$  min (minor), 9.7 min (major).  $[\alpha]_D^{20} = -27$  ( $c = 0.7$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (s, 1H), 7.76 – 7.57 (m, 3H), 7.43 – 7.35 (m, 6H), 7.35 – 7.30 (m, 1H), 7.25 – 7.17 (m, 1H), 6.54 (d,  $J = 8.3$  Hz, 1H), 5.01 (d,  $J = 15.9$  Hz, 1H), 4.73 (d,  $J = 15.9$  Hz, 1H), 4.33 – 4.15 (m, 2H), 2.44 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.2, 166.0, 158.8, 145.0, 144.1, 141.1, 137.5, 136.8, 134.2, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.0, 127.3 ( $\times 2$ ), 126.0, 123.7 ( $J = 286$  Hz), 123.4, 118.5 ( $\times 2$ ), 112.2, 100.4, 97.9, 85.5, 77.3, 63.6, 44.3, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{23}\text{F}_3\text{IN}_3\text{O}_4 + \text{Na}]^+$   $m/z$  696.0578, found 696.0578.

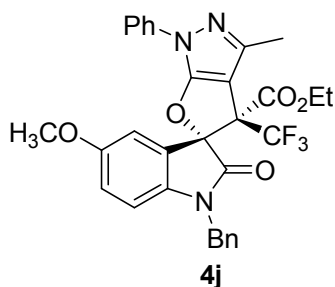


**ethyl-(4R,5R)-1'-benzyl-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp128-130 °C, 67.8 mg, 62% yield, 94% ee, >20:1 dr. HPLC (IF-H, *i*-PrOH/n-hexane = 7/93, flow rate = 0.7 mL/min,  $\lambda = 254$  nm)  $t_R = 13.8$  min (minor), 17.4 min (major).  $[\alpha]_D^{20} = -30$  ( $c = 0.56$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.76 – 7.64 (m, 3H), 7.45 – 7.29 (m, 8H), 7.24 – 7.09 (m, 2H), 6.79 (d,  $J = 8.0$  Hz, 1H), 5.04 (d,  $J = 15.8$  Hz, 1H), 4.76 (d,  $J = 15.9$  Hz, 1H), 4.42 – 4.21 (m, 2H), 2.44 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.9, 166.1, 159.0, 155.1, 145.1, 144.4, 137.7, 134.8, 132.3, 129.2 ( $\times 2$ ), 128.9 ( $\times 2$ ), 128.2, 127.8, 127.8, 127.4 ( $\times 2$ ), 124.4 ( $J = 283$  Hz), 123.2, 121.3, 118.4 ( $\times 2$ ), 110.1, 77.2, 63.4, 44.3, 29.7, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{24}\text{F}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  570.1611, found 570.1616.

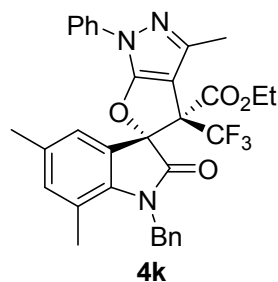




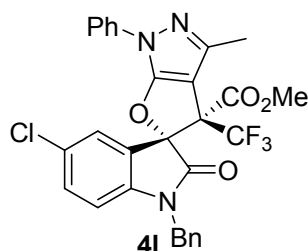
***ethyl-(4R,5R)-1'-benzyl-3,5'-dimethyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate***, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp194-196 °C, 56.1 mg, 50% yield, 90% ee, >20:1 dr. HPLC (IE-H, *i*-PrOH/n-hexane = 10/90, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 8.2$  min (minor), 11.2 min (major).  $[\alpha]_D^{20} = -27$  ( $c = 0.53$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 – 7.67 (m, 2H), 7.53 (s, 1H), 7.43 – 7.35 (m, 6H), 7.33 – 7.29 (m, 1H), 7.23 – 7.14 (m, 2H), 6.67 (d,  $J = 8.1$  Hz, 1H), 5.01 (d,  $J = 15.8$  Hz, 1H), 4.74 (d,  $J = 15.8$  Hz, 1H), 4.32 – 4.22 (m, 2H), 2.45 (s, 3H), 2.35 (s, 3H), 1.31 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.8, 166.1, 159.1, 145.1, 142.0, 137.7, 134.9, 132.9, 132.6, 129.2 ( $\times 2$ ), 128.9, 128.8 ( $\times 2$ ), 127.8, 127.4 ( $\times 2$ ), 125.8, 123.9 ( $J = 286$  Hz), 121.3, 118.4 ( $\times 2$ ), 109.9, 100.6, 99.0, 77.2, 63.4, 44.3, 21.1, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{31}\text{H}_{26}\text{F}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  584.1768, found 584.1773.



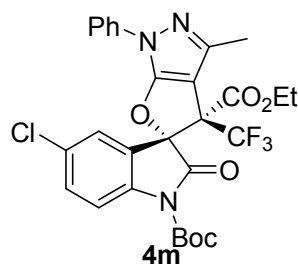
***ethyl-(4R,5R)-1'-benzyl-5'-methoxy-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate***, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp175-177 °C, 81.9 mg, 71% yield, 88% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 260$  nm)  $t_R = 17.6$  min (minor), 24.4 min (major).  $[\alpha]_D^{20} = -58$  ( $c = 0.64$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (d,  $J = 8.0$  Hz, 2H), 7.43 – 7.34 (m, 6H), 7.33 – 7.29 (m, 2H), 7.25 – 7.17 (m, 1H), 6.93 – 6.85 (m, 1H), 6.66 (d,  $J = 8.7$  Hz, 1H), 5.00 (d,  $J = 15.8$  Hz, 1H), 4.73 (d,  $J = 15.8$  Hz, 1H), 4.32-4.14 (m, 2H), 3.79 (s, 3H), 2.44 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.6, 166.0, 159.0, 156.1, 145.1, 137.7, 137.6, 134.8, 129.2 ( $\times 2$ ), 128.9 ( $\times 2$ ), 127.8, 127.4 ( $\times 2$ ), 125.8, 123.8 ( $J = 279$  Hz), 122.3, 118.5 ( $\times 2$ ), 117.2, 115.2, 110.6, 100.6, 99.0, 77.2, 63.5, 55.9, 44.3, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{31}\text{H}_{26}\text{F}_3\text{N}_3\text{O}_5 + \text{Na}]^+$   $m/z$  600.1717, found 600.1720.



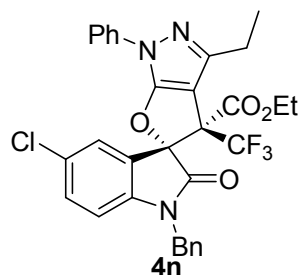
**ethyl-(4R,5R)-1'-benzyl-3,5',7'-trimethyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 178-180 °C, 70.2 mg, 61% yield, 97% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 18.8$  min (minor), 22.5 min (major).  $[\alpha]_D^{20} = -30$  ( $c = 0.52$  in  $\text{CH}_2\text{Cl}_2$ ).  **$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71 – 7.64 (m, 2H), 7.43 – 7.32 (m, 6H), 7.32 – 7.24 (m, 2H), 7.20 (t,  $J = 7.5$  Hz, 1H), 6.97 (s, 1H), 5.31 – 4.98 (m, 2H), 4.32 – 4.20 (m, 2H), 2.42 (s, 3H), 2.32 (s, 3H), 2.24 (s, 3H), 1.31 (t,  $J = 7.2$  Hz, 3H);  **$^{13}\text{C NMR}$**  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  173.2, 166.5, 159.3, 145.3, 140.2, 138.0, 137.1( $\times 2$ ), 133.1, 129.4( $\times 2$ ), 129.1( $\times 2$ ), 127.5, 127.0, 126.1, 125.9( $\times 2$ ), 124.1( $J = 286$  Hz), 122.4, 120.5, 118.6( $\times 2$ ), 100.9, 98.9, 77.5, 63.6, 45.9, 21.0, 19.0, 14.0, 13.8 ppm. HRMS (ESI+) calcd for  $[\text{C}_{32}\text{H}_{28}\text{F}_3\text{N}_3\text{O}_6 + \text{Na}]^+$   $m/z$  614.1276, found 614.1274.



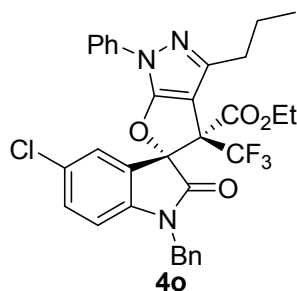
**methyl-(4R,5R)-1'-benzyl-5'-chloro-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 190-192 °C, 87.3 mg, 77% yield, 93% ee, >20:1 dr. HPLC (ID-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 17.9$  min (minor), 33.1 min (major).  $[\alpha]_D^{20} = -6$  ( $c = 0.50$  in  $\text{CH}_2\text{Cl}_2$ ).  **$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71 – 7.60 (m, 3H), 7.42 – 7.31 (m, 8H), 7.25 – 7.19 (m, 1H), 6.72 (d,  $J = 8.5$  Hz, 1H), 5.05 (d,  $J = 15.8$  Hz, 1H), 4.71 (d,  $J = 15.9$  Hz, 1H), 3.77 (s, 3H), 2.42 (s, 3H);  **$^{13}\text{C NMR}$**  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 166.3, 158.8, 145.1, 142.9, 137.5, 134.3, 132.3, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.9, 128.6, 128.1, 127.4 ( $\times 2$ ), 125.9, 123.8 ( $J = 279$  Hz), 122.8, 118.5 ( $\times 2$ ), 111.2, 100.3, 98.2, 77.2, 53.9, 44.4, 13.5 ppm. HRMS (ESI+) calcd for  $[\text{C}_{29}\text{H}_{21}\text{ClF}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  590.1065, found 590.1061.



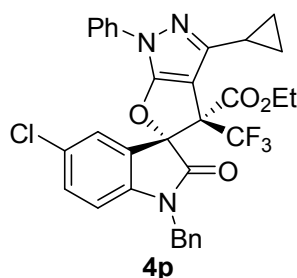
**1'-(tert-butyl)4-ethyl-(4R,5R)-5'-chloro-3-methyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-1',4-dicarboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp165-167 °C, 79.2 mg, 67% yield, 93% ee, >20:1 dr. HPLC (IC-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 9.5 min (minor), 10.9 min (major).  $[\alpha]_D^{20}$  = -21 ( $c$  = 0.50 in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (d,  $J$  = 8.9 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.68 – 7.61 (m, 2H), 7.56 – 7.50 (m, 1H), 7.42 – 7.34 (m, 2H), 7.24 – 7.17 (m, 1H), 4.41 – 4.16 (m, 2H), 2.42 (s, 3H), 1.61 (s, 9H), 1.31 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.6, 165.5, 158.8, 148.3, 145.1, 139.8, 137.4, 132.7, 130.5, 129.2 ( $\times 2$ ), 128.0, 126.0, 123.4 ( $J$  = 286 Hz), 121.7, 118.5 ( $\times 2$ ), 116.9, 99.9, 97.6, 85.5, 77.2, 63.7, 28.0 ( $\times 3$ ), 13.6, 13.5 ppm. HRMS (ESI+) calcd for  $[\text{C}_{28}\text{H}_{25}\text{ClF}_3\text{N}_3\text{O}_6 + \text{Na}]^+$   $m/z$  614.1276, found 614.1274.



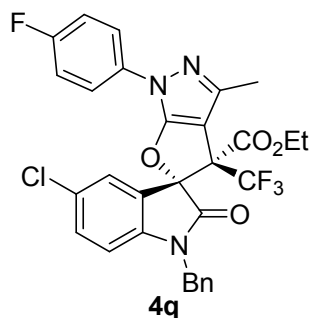
**ethyl-(4R,5R)-1'-benzyl-5'-chloro-3-ethyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp151-153 °C, 65.5 mg, 55% yield, 95% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 11.9 min (major), 14.4 min (minor).  $[\alpha]_D^{20}$  = -44 ( $c$  = 0.51 in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72 – 7.63 (m, 3H), 7.44 – 7.35 (m, 6H), 7.36 – 7.31 (m, 2H), 7.27 – 7.18 (m, 1H), 6.69 (d,  $J$  = 8.5 Hz, 1H), 5.02 (d,  $J$  = 15.9 Hz, 1H), 4.74 (d,  $J$  = 15.9 Hz, 1H), 4.28 (dd,  $J$  = 10.6, 7.1 Hz, 2H), 2.87 – 2.79 (m, 2H), 1.40 (t,  $J$  = 7.6 Hz, 3H), 1.31 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.6, 166.0, 158.6, 149.9, 142.9, 137.7, 134.3, 132.2, 129.2 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.8, 128.8, 128.0, 127.4 ( $\times 2$ ), 125.8, 123.9 ( $J$  = 285 Hz), 123.0, 118.6 ( $\times 2$ ), 111.1, 99.6, 98.1, 77.2, 63.6, 44.4, 21.1, 13.8, 12.5 ppm. HRMS (ESI+) calcd for  $[\text{C}_{31}\text{H}_{25}\text{ClF}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  618.1378, found 618.1374.



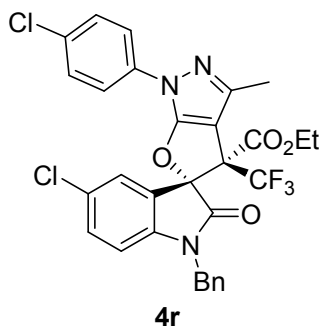
**ethyl-(4R,5R)-1'-benzyl-5'-chloro-2'-oxo-1-phenyl-3-propyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp157-159 °C, 95.0 mg, 78% yield, 95% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 12.5$  min (major), 15.2 min (minor).  $[\alpha]_D^{20} = -11$  ( $c = 0.51$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 – 7.63 (m, 3H), 7.42 – 7.30 (m, 8H), 7.21 (t,  $J = 7.4$  Hz, 1H), 6.68 (d,  $J = 8.5$  Hz, 1H), 5.02 (d,  $J = 15.8$  Hz, 1H), 4.73 (d,  $J = 15.8$  Hz, 1H), 4.28 (t,  $J = 7.2$  Hz, 2H), 2.85 – 2.65 (m, 2H), 1.87 (q,  $J = 7.6$  Hz, 2H), 1.31 (t,  $J = 7.1$  Hz, 3H), 1.08 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.7, 166.1, 158.8, 149.0, 143.1, 137.9, 134.5, 132.4, 129.4( $\times 2$ ), 129.2( $\times 2$ ), 128.9, 128.7, 128.2, 127.5( $\times 2$ ), 126.0, 123.9( $J = 286$  Hz), 123.2, 118.7( $\times 2$ ), 111.3, 100.1, 98.3, 77.5, 63.7, 44.6, 30.1, 21.8, 14.4, 14.0 ppm. HRMS (ESI+) calcd for  $[\text{C}_{32}\text{H}_{27}\text{ClF}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  632.1534, found 632.1529.



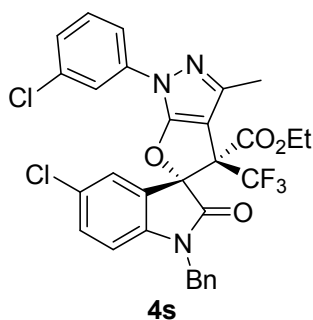
**ethyl-(4R,5R)-1'-benzyl-5'-chloro-3-cyclopropyl-2'-oxo-1-phenyl-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp164-166 °C, 99.5 mg, 82% yield, 92% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 12.9$  min (major), 15.3 min (minor).  $[\alpha]_D^{20} = -43$  ( $c = 0.54$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (s, 1H), 7.64 – 7.61 (m, 2H), 7.42 – 7.31 (m, 8H), 7.22 – 7.16 (m, 1H), 6.69 (d,  $J = 8.5$  Hz, 1H), 5.03 (d,  $J = 15.9$  Hz, 1H), 4.74 (d,  $J = 15.9$  Hz, 1H), 4.35 – 4.26 (m, 2H), 2.14 – 2.05 (m, 1H), 1.32 (t,  $J = 7.1$  Hz, 3H), 1.24 – 1.17 (m, 1H), 1.11 – 1.05 (m, 1H), 0.98 – 0.90 (m, 2H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.6, 166.1, 158.5, 149.7, 143.0, 137.7, 134.3, 132.2, 129.1 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.8, 128.6, 128.0, 127.4 ( $\times 2$ ), 125.7, 123.8 ( $J = 286$  Hz), 123.0, 118.4 ( $\times 2$ ), 111.2, 100.6, 98.1, 77.2, 63.5, 44.4, 13.8, 8.5, 8.0, 7.7 ppm. HRMS (ESI+) calcd for  $[\text{C}_{32}\text{H}_{25}\text{ClF}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  630.1378, found 630.1378.



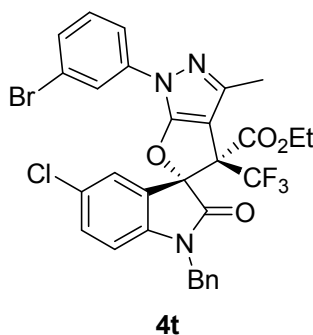
***ethyl-(4R,5R)-1'-benzyl-5'-chloro-1-(4-fluorophenyl)-3-methyl-2'-oxo-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate***, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp174-176 °C, 110.2 mg, 92% yield, 91% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 17.9 min (major), 24.3 min (minor).  $[\alpha]_D^{20}$  = -50 ( $c$  = 0.53 in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (d,  $J$  = 2.0 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.40 – 7.29 (m, 6H), 7.13-7.04 (m, 2H), 6.69 (d,  $J$  = 8.5 Hz, 1H), 5.03 (d,  $J$  = 15.8 Hz, 1H), 4.73 (d,  $J$  = 15.9 Hz, 1H), 4.37 – 4.21 (m, 2H), 2.41 (s, 3H), 1.32 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 165.9, 160.6 (d,  $^1J_{\text{C-F}}$  = 245.6 Hz), 158.6, 145.1, 143.0, 134.2, 133.8 (d,  $^4J_{\text{C-F}}$  = 2.6 Hz), 132.3, 129.0 ( $\times 2$ ), 128.8, 128.6, 128.1, 127.3 ( $\times 2$ ), 123.8 ( $J$  = 286 Hz), 122.6, 120.3 (d,  $^3J_{\text{C-F}}$  = 8.2 Hz) ( $\times 2$ ), 116.0 (d,  $^2J_{\text{C-F}}$  = 22.7 Hz) ( $\times 2$ ), 111.2, 100.4, 98.2, 77.2, 63.7, 44.4, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{22}\text{ClF}_4\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  622.1127, found 622.1123.



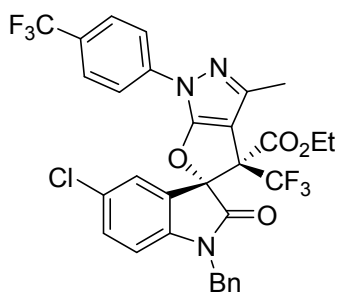
***ethyl-(4R,5R)-1'-benzyl-5'-chloro-1-(4-chlorophenyl)-3-methyl-2'-oxo-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate***, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp154-156 °C, 102.1 mg, 83% yield, 88% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 268 nm)  $t_R$  = 13.6 min (major), 18.6 min (minor).  $[\alpha]_D^{20}$  = -45 ( $c$  = 0.51 in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (d,  $J$  = 2.0 Hz, 1H), 7.60 (d,  $J$  = 8.6 Hz, 2H), 7.40 – 7.30 (m, 8H), 6.70 (d,  $J$  = 8.4 Hz, 1H), 5.02 (d,  $J$  = 15.8 Hz, 1H), 4.73 (d,  $J$  = 15.9 Hz, 1H), 4.34 – 4.23 (m, 2H), 2.42 (s, 3H), 1.32 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 165.8, 158.7, 145.4, 143.0, 136.0, 134.2, 132.4, 131.3, 129.3 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.9, 128.6, 128.1, 127.3 ( $\times 2$ ), 123.7 ( $J$  = 286 Hz), 122.6, 119.6 ( $\times 2$ ), 111.3, 100.7, 98.3, 77.2, 63.7, 44.4, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{22}\text{Cl}_2\text{F}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  638.0832, found 638.0827.



**ethyl-(4R,5R)-1'-benzyl-5'-chloro-1-(3-chlorophenyl)-3-methyl-2'-oxo-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 163-165 °C, 92.3 mg, 75% yield, 89% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 15.6$  min (major), 19.3 min (minor).  $[\alpha]_D^{20} = -16$  ( $c = 0.58$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (d,  $J = 7.9$  Hz, 2H), 7.57 (s, 1H), 7.41 – 7.31 (m, 7H), 7.19 (d,  $J = 7.5$  Hz, 1H), 6.70 (d,  $J = 8.5$  Hz, 1H), 5.04 (d,  $J = 15.9$  Hz, 1H), 4.74 (d,  $J = 15.8$  Hz, 1H), 4.34 – 4.07 (m, 2H), 2.43 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.7, 166.0, 159.1, 145.8, 143.2, 138.7, 135.3, 134.4, 132.6, 130.5, 129.2( $\times 2$ ), 129.1, 128.9, 128.3, 127.5( $\times 2$ ), 126.1, 123.9( $J = 286$  Hz), 122.8, 118.7, 116.5, 111.5, 101.0, 98.6, 77.5, 63.9, 44.7, 14.0, 13.8 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{22}\text{Cl}_2\text{F}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  638.0832, found 638.0832.

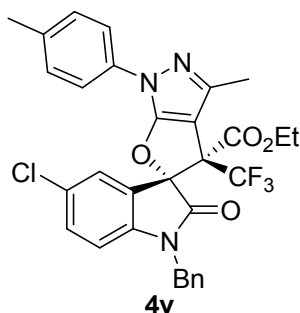


**ethyl-(4R,5R)-1'-benzyl-1-(3-bromophenyl)-5'-chloro-3-methyl-2'-oxo-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp 177-179 °C, 104.1 mg, 79% yield, 91% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda = 254$  nm)  $t_R = 13.8$  min (major), 17.6 min (minor).  $[\alpha]_D^{20} = -41$  ( $c = 0.54$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.88 – 7.82 (m, 1H), 7.72 – 7.66 (m, 1H), 7.63 – 7.58 (m, 1H), 7.42 – 7.30 (m, 7H), 7.25 (t,  $J = 8.1$  Hz, 1H), 6.70 (d,  $J = 8.5$  Hz, 1H), 5.04 (d,  $J = 15.8$  Hz, 1H), 4.74 (d,  $J = 15.9$  Hz, 1H), 4.37 – 4.21 (m, 2H), 2.42 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 165.8, 158.8, 145.6, 143.0, 138.6, 134.2, 132.4, 130.5, 129.0 ( $\times 2$ ), 128.9, 128.9, 128.6, 128.1, 127.3 ( $\times 2$ ), 123.9 ( $J = 273$  Hz), 122.9, 122.5, 121.3, 116.8, 111.3, 100.8, 98.4, 77.2, 63.7, 44.4, 13.8, 13.6 ppm. HRMS (ESI+) calcd for  $[\text{C}_{30}\text{H}_{22}\text{BrClF}_3\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  682.0327, found 682.0325.



4u

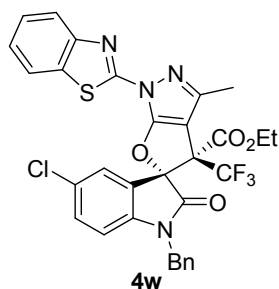
**ethyl-(4R,5R)-1'-benzyl-5'-chloro-3-methyl-2'-oxo-4-(trifluoromethyl)-1-(4-(trifluoromethyl)phenyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp147-149 °C, 92.2 mg, 71% yield, 90% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $l = 254$  nm)  $t_R = 14.6$  min (major), 19.7 min (minor).  $[\alpha]_D^{20} = -34$  ( $c = 0.50$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (d,  $J = 8.4$  Hz, 2H), 7.71 – 7.60 (m, 3H), 7.41 – 7.30 (m, 6H), 6.71 (d,  $J = 8.5$  Hz, 1H), 5.02 (d,  $J = 15.8$  Hz, 1H), 4.75 (d,  $J = 15.9$  Hz, 1H), 4.39 – 4.23 (m, 2H), 2.44 (s, 3H), 1.33 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.6, 166.0, 159.4, 146.3, 143.2, 140.4, 134.4, 132.7, 129.2( $\times 2$ ), 129.1, 128.8(q,  $^3J_{\text{CF}_3} = 5.0$  Hz), 128.3, 127.9(q,  $^2J_{\text{CF}_3} = 32.8$  Hz), 127.66( $\times 2$ ), 127.4, 126.7(q,  $^3J_{\text{CF}_3} = 3.8$  Hz), 124.1(q,  $^1J_{\text{CF}_3} = 273$  Hz), 123.9( $J = 286$  Hz), 122.7, 118.3( $\times 2$ ), 111.5, 101.4, 98.7, 77.5, 64.0, 44.7, 14.0, 13.8 ppm. HRMS (ESI+) calcd for  $[\text{C}_{31}\text{H}_{22}\text{ClF}_6\text{N}_3\text{O}_4 + \text{Na}]^+$   $m/z$  672.1095, found 672.1099.



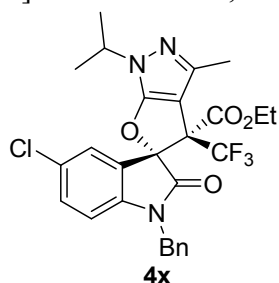
4v

**ethyl-(4R,5R)-1'-benzyl-5'-chloro-3-methyl-2'-oxo-1-(*p*-tolyl)-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp150-152°C, 77.4 mg, 65% yield, 94% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $l = 280$  nm)  $t_R = 14.1$  min (major), 17.6 min (minor).  $[\alpha]_D^{20} = -22$  ( $c = 0.53$  in  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.67 (d,  $J = 2.0$  Hz, 1H), 7.52 (d,  $J = 8.2$  Hz, 2H), 7.41 – 7.30 (m, 6H), 7.18 (d,  $J = 7.9$  Hz, 2H), 6.68 (d,  $J = 8.5$  Hz, 1H), 5.01 (d,  $J = 15.9$  Hz, 1H), 4.73 (d,  $J = 15.8$  Hz, 1H), 4.37 – 4.21 (dd,  $J = 7.1, 5.1$  Hz, 2H), 2.42 (s, 3H), 2.35 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  171.8, 166.3, 158.9, 144.9, 143.2, 135.9, 135.4, 134.5, 132.4, 129.9( $\times 2$ ), 129.2( $\times 2$ ), 129.0, 128.7, 128.2, 127.5( $\times 2$ ), 124.0( $J$

=286 Hz), 123.0, 118.7(×2), 111.4, 100.3, 98.3, 77.5, 63.8, 44.6, 21.1, 14.0, 13.8 ppm. HRMS (ESI+) calcd for [C<sub>31</sub>H<sub>25</sub>ClF<sub>3</sub>N<sub>3</sub>O<sub>4</sub> + Na]<sup>+</sup> m/z 618.1378, found 618.1373.



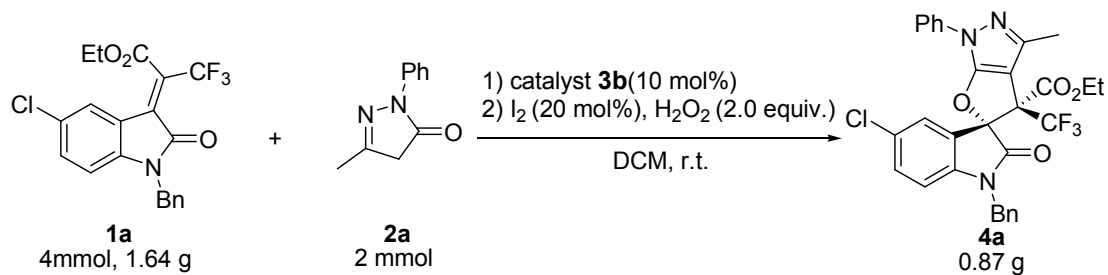
**ethyl-(4R,5R)-1-(benzo[d]thiazol-2-yl)-1'-benzyl-5'-chloro-3-methyl-2'-oxo-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp149-151°C, 85.5 mg, 67% yield, 98% ee, >20:1 dr. HPLC (AD-H, *i*-PrOH/n-hexane = 7/93, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 12.4 min (major), 17.3 min (minor).  $[\alpha]_D^{20}$  = -36 (c = 0.51 in CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.94 – 7.89 (m, 1H), 7.87 – 7.80 (m, 1H), 7.75 – 7.69 (m, 1H), 7.46 – 7.29 (m, 8H), 6.68 (d,  $J$  = 8.5 Hz, 1H), 5.09 (d,  $J$  = 15.9 Hz, 1H), 4.65 (d,  $J$  = 15.9 Hz, 1H), 4.40 – 4.23 (m, 2H), 2.45 (s, 3H), 1.32 (t,  $J$  = 7.1 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  171.4, 165.7, 159.8, 158.0, 151.4, 148.3, 143.4, 134.4, 132.8, 132.7, 129.1(×2), 129.1, 128.2, 127.6(×2), 127.5, 126.6, 125.1, 123.8( $J$  = 286 Hz), 123.0, 122.5, 121.6, 111.4, 102.6, 99.0, 77.5, 64.0, 44.8, 14.0, 13.9 ppm. HRMS (ESI+) calcd for [C<sub>31</sub>H<sub>22</sub>ClF<sub>3</sub>N<sub>4</sub>O<sub>4</sub>S + Na]<sup>+</sup> m/z 661.0895, found 661.0887.



**ethyl-(4R,5R)-1'-benzyl-5'-chloro-1-isopropyl-3-methyl-2'-oxo-4-(trifluoromethyl)-1,4-dihydrospiro[furo[2,3-c]pyrazole-5,3'-indoline]-4-carboxylate**, purified by flash chromatography on silica gel, eluting with petroleum ether/ethyl acetate 15/1 (v/v); white solid, mp153-155°C, 79.9 mg, 73% yield, 99% ee, >20:1 dr. HPLC (IB-H, *i*-PrOH/n-hexane = 20/80, flow rate = 1.0 mL/min,  $\lambda$  = 254 nm)  $t_R$  = 15.8 min (major), 19.4 min (minor).  $[\alpha]_D^{20}$  = -19 (c = 0.52 in CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.64 (s, 1H), 7.39 – 7.34 (m, 4H), 7.33 – 7.29 (m, 2H), 6.66 (d,  $J$  = 8.5 Hz, 1H), 4.98 (d,  $J$  = 15.9 Hz, 1H), 4.75 (d,  $J$  = 16.0 Hz, 1H), 4.37 – 4.29 (m, 1H), 4.25 (q,  $J$  = 7.1 Hz, 2H), 2.34 (s, 3H), 1.46 (dd,  $J$  = 6.8, 1.9 Hz, 6H), 1.30 (t,  $J$  = 7.2 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  171.8, 166.2, 158.8, 143.1, 143.0, 134.4, 132.0, 128.9 (×2), 128.6, 128.5, 128.0, 127.3 (×2), 123.8 ( $J$  = 286 Hz), 122.9, 111.1, 98.2, 97.4, 77.2, 63.4, 51.6, 44.3, 21.9, 21.6, 13.8, 13.4 ppm. HRMS (ESI+) calcd for [C<sub>27</sub>H<sub>25</sub>ClF<sub>3</sub>N<sub>3</sub>O<sub>4</sub> + Na]<sup>+</sup> m/z 570.1378, found 570.1379.



### 3. Scale-up experiment



(Z)-ethyl 2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-3,3,3-trifluoropropanoate **1a** (4 mmol) and pyrazolone **2a** (2 mmol) were stirred in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) in the presence of catalyst **3b** (0.02 mmol) at room temperature for 36 h, then I<sub>2</sub> (0.4 mmol) and 30% H<sub>2</sub>O<sub>2</sub> aqueous solution (4 mmol) were added, and the mixture was stirred for 2 h at room temperature. The reaction was monitored by TLC. After completion, the mixture was dried and concentrated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate =10:1) to give the product **4a** in 75% yield (0.87 g, > 20:1 dr and 95% ee).

## 4. ESI-MS spectrum

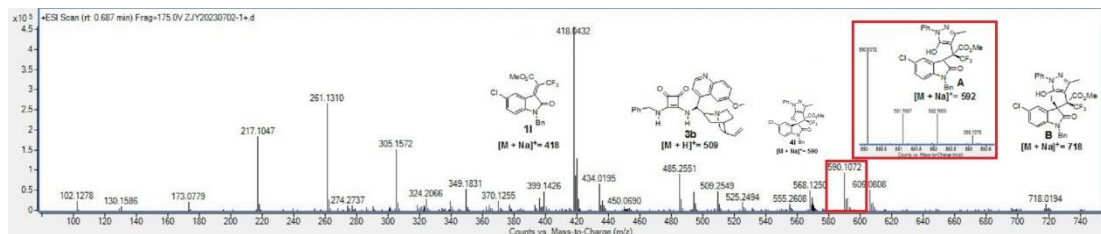
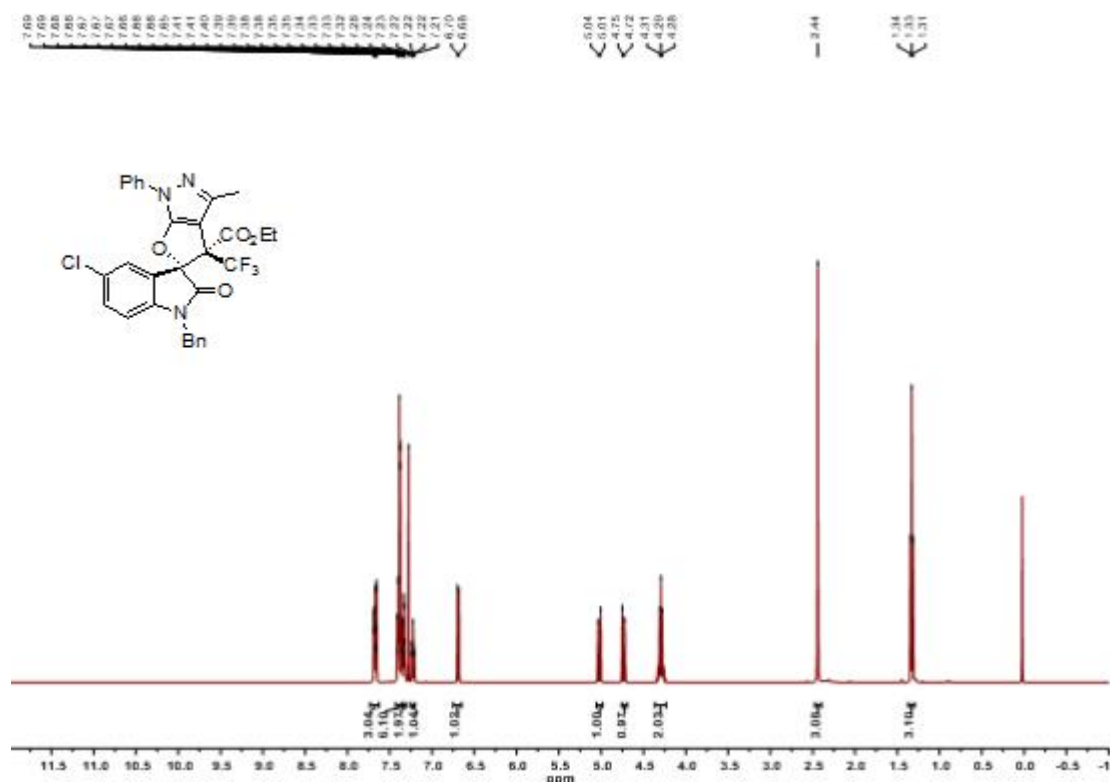


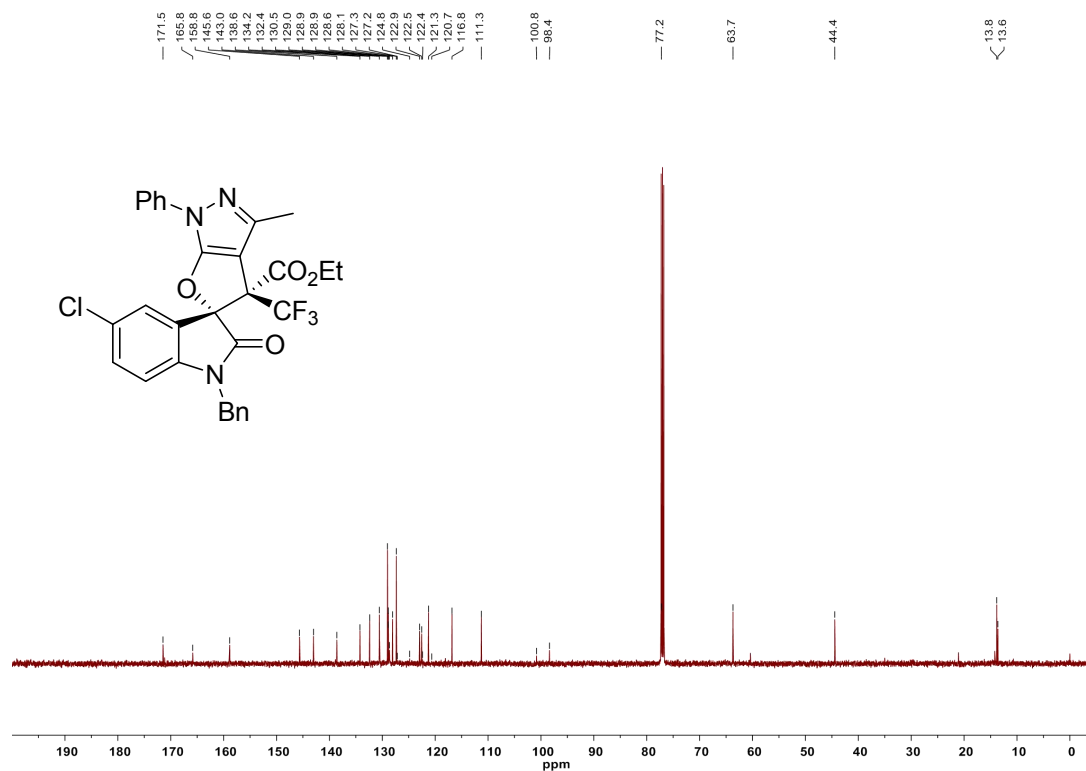
Figure S1 ESI-MS spectrum (positive mode) of the reaction

## 5. <sup>1</sup>H, <sup>13</sup>C NMR spectra and HPLC chromatograms of compounds 4a-4x

### <sup>1</sup>H NMR spectrum of 4a (CDCl<sub>3</sub>, 500 MHz)

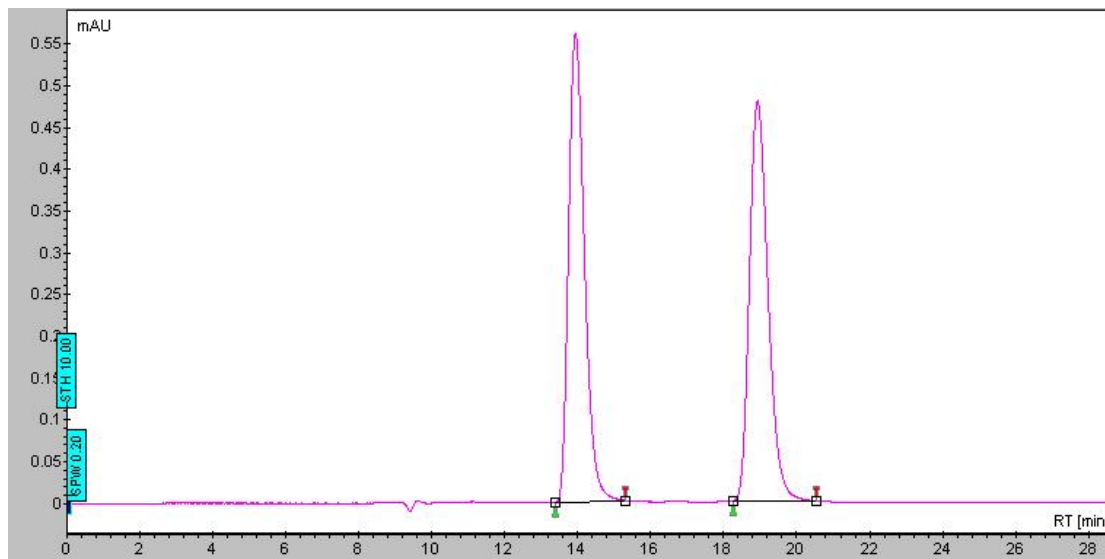


### <sup>13</sup>C NMR spectrum of 4a (CDCl<sub>3</sub>, 125 MHz)



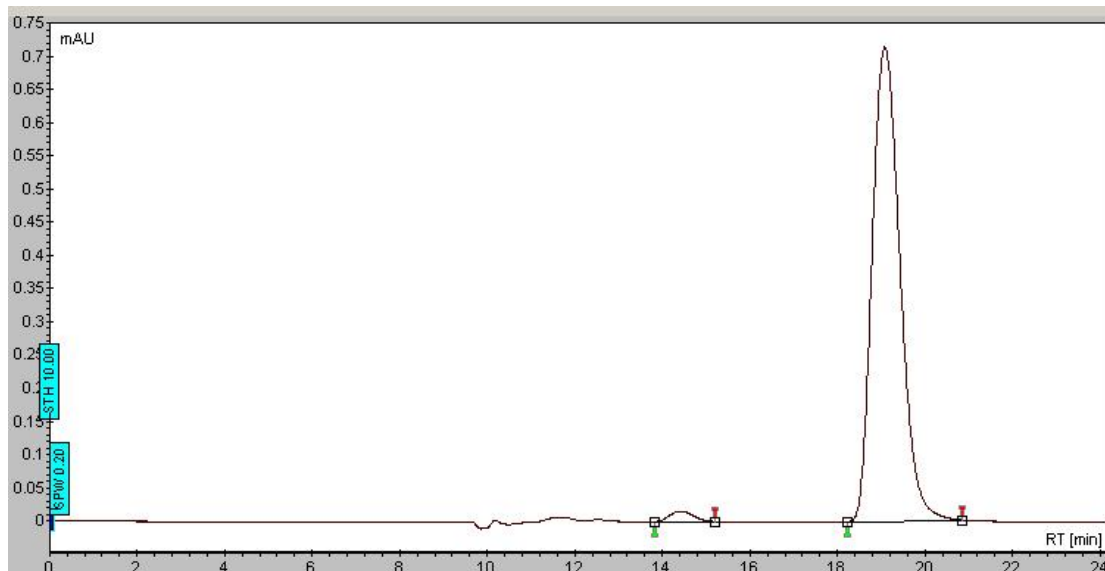
## HPLC chromatograms of 4a

### 4a-rac



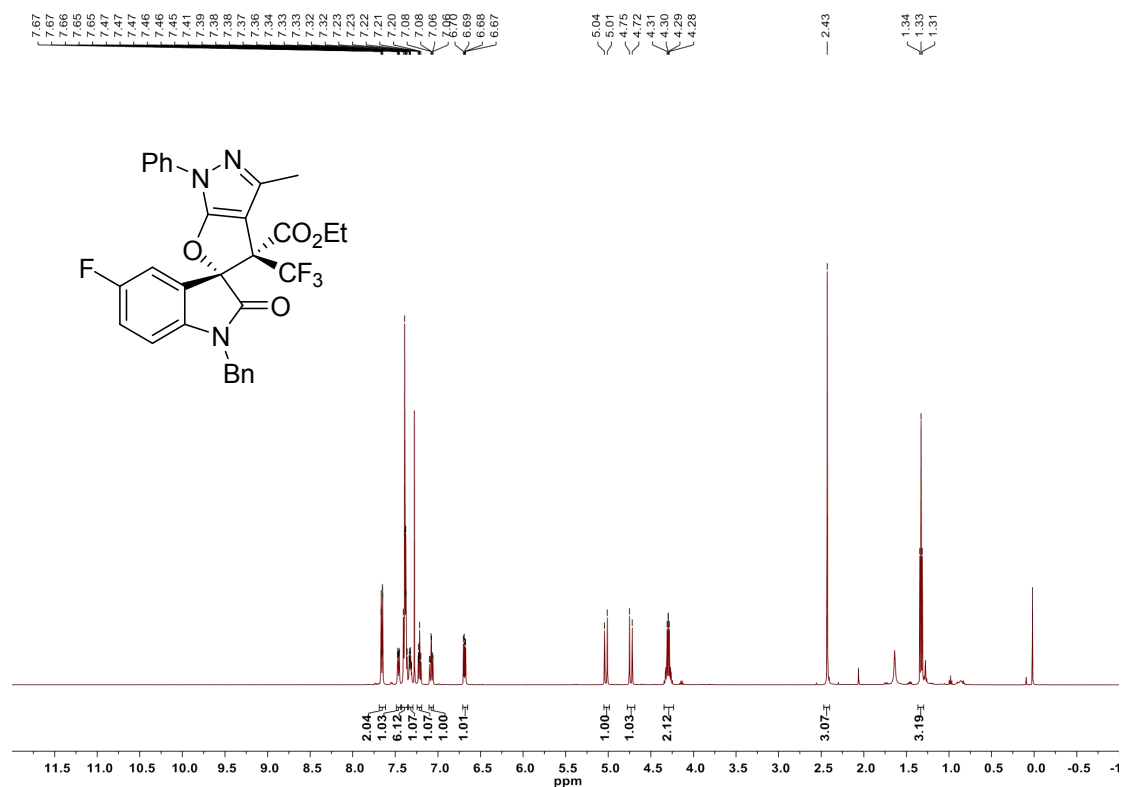
#	Start time[min]	Time[min]	End time[min]	Area%
1	13.388	13.932	15.306	50.080
2	18.263	18.932	20.541	49.920

### 4a-chr

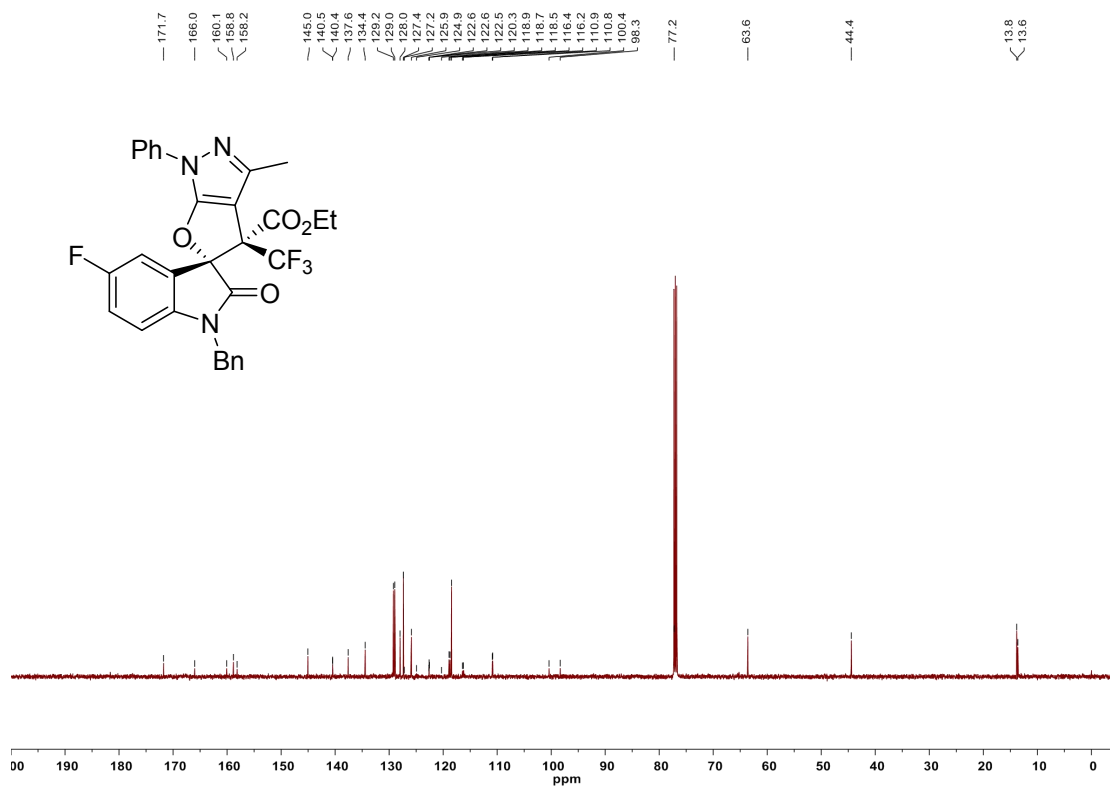


#	Start time[min]	Time[min]	End time[min]	Area%
1	13.822	14.412	15.201	1.808
2	18.228	19.079	20.851	98.192

### <sup>1</sup>H NMR spectrum of 4b (CDCl<sub>3</sub>, 500 MHz)

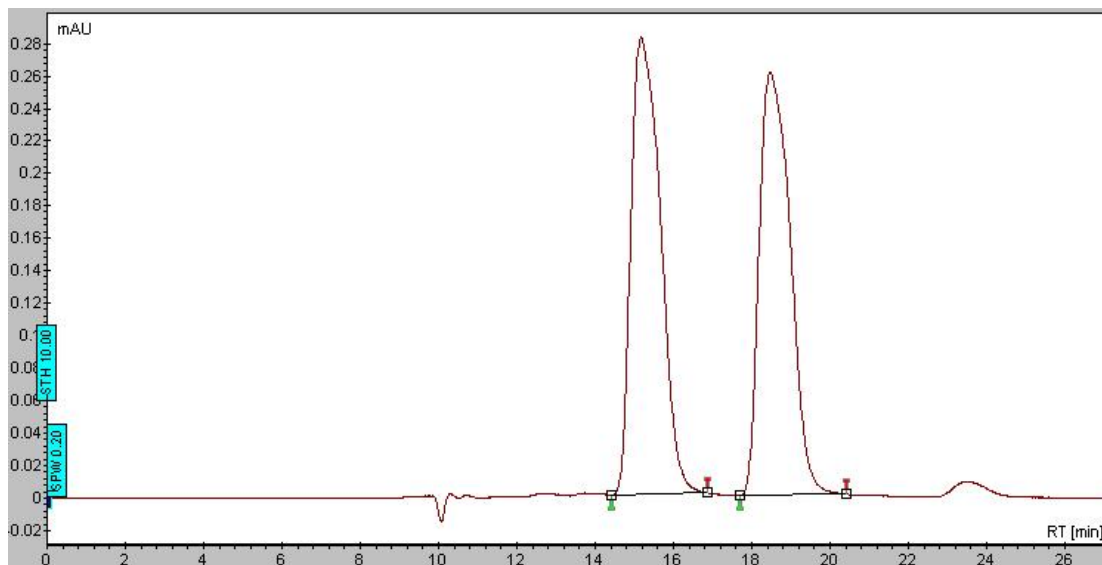


### <sup>13</sup>C NMR spectrum of 4b (CDCl<sub>3</sub>, 125 MHz)



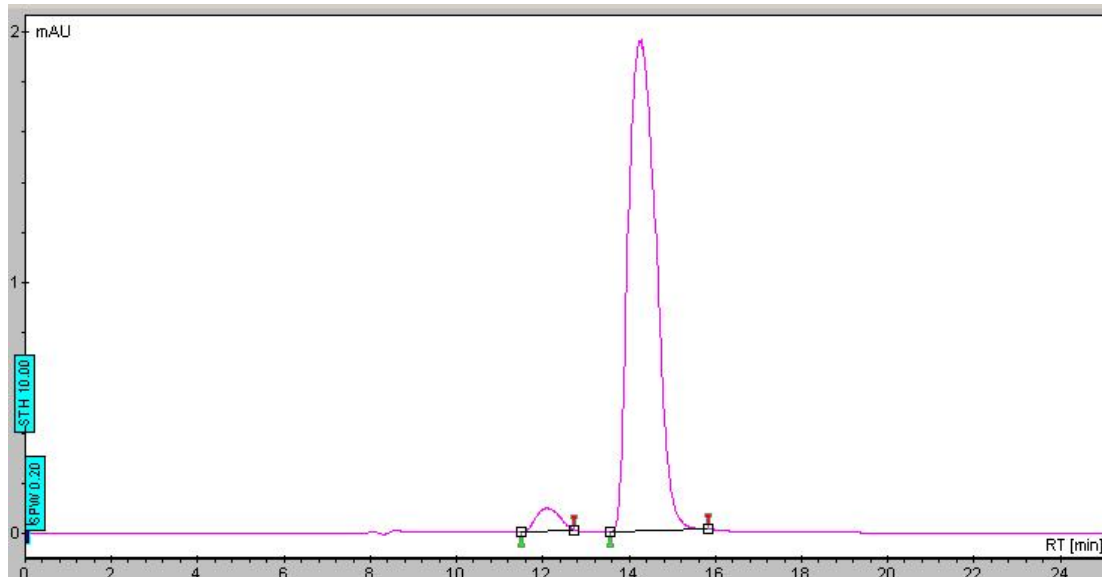
## HPLC chromatograms of 4b

### 4b-rac



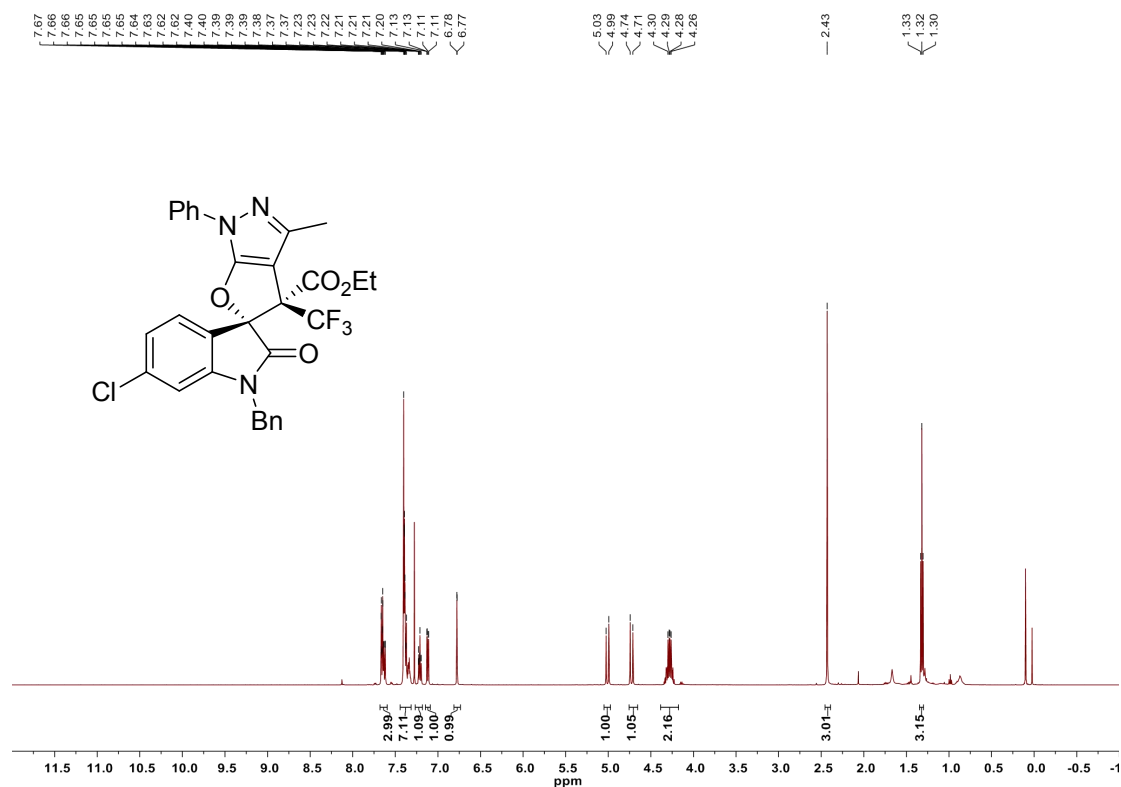
#	Start time[min]	Time[min]	End time[min]	Area%
1	14.407	15.159	16.859	50.700
2	17.689	18.465	20.404	49.300

### 4b-chr

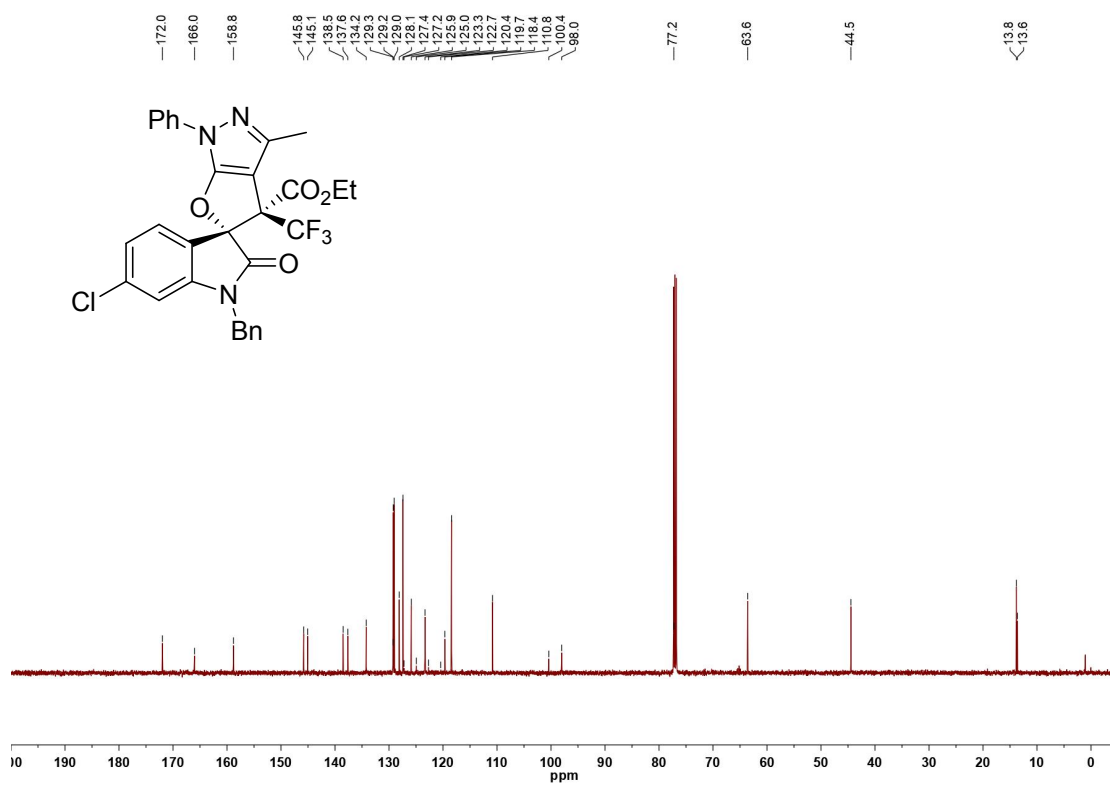


#	Start time[min]	Time[min]	End time[min]	Area%
1	11.498	12.092	12.721	3.800
2	13.560	14.279	15.832	96.200

### $^1\text{H}$ NMR spectrum of 4c ( $\text{CDCl}_3$ , 500 MHz)

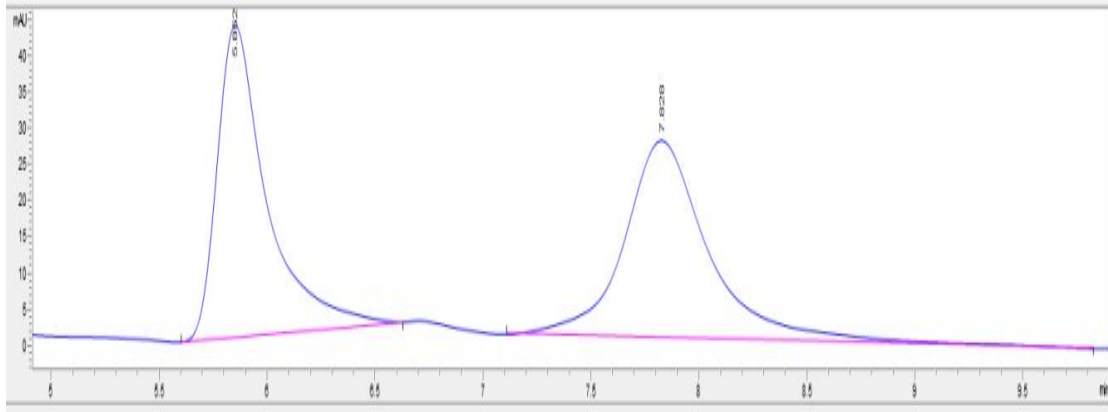


### $^{13}\text{C}$ NMR spectrum of 4c ( $\text{CDCl}_3$ , 125 MHz)



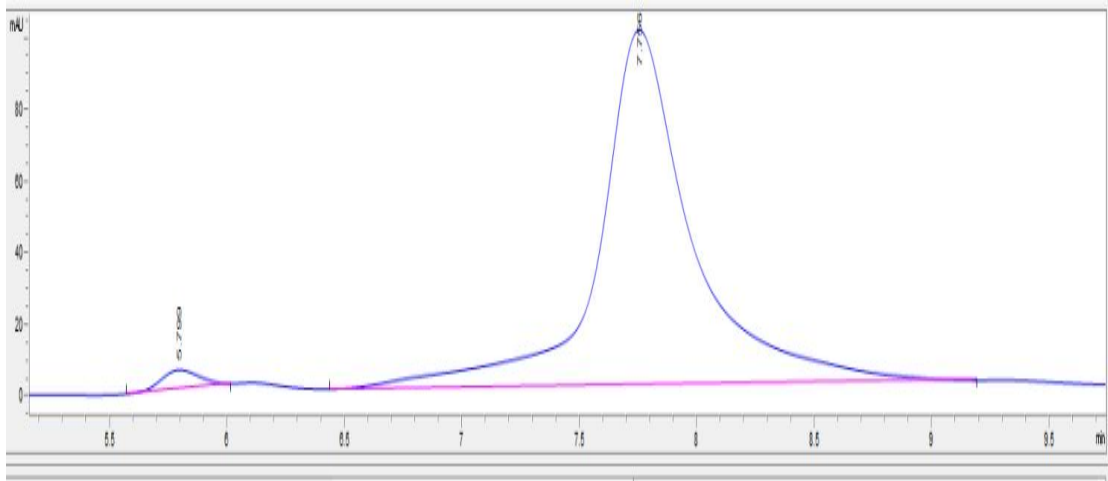
## HPLC chromatograms of 4c

### 4c-rac



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.852	689.1	43	0.2348	0.519	47.641	BB
2	7.828	757.3	27.2	0.405	0.737	52.359	BB

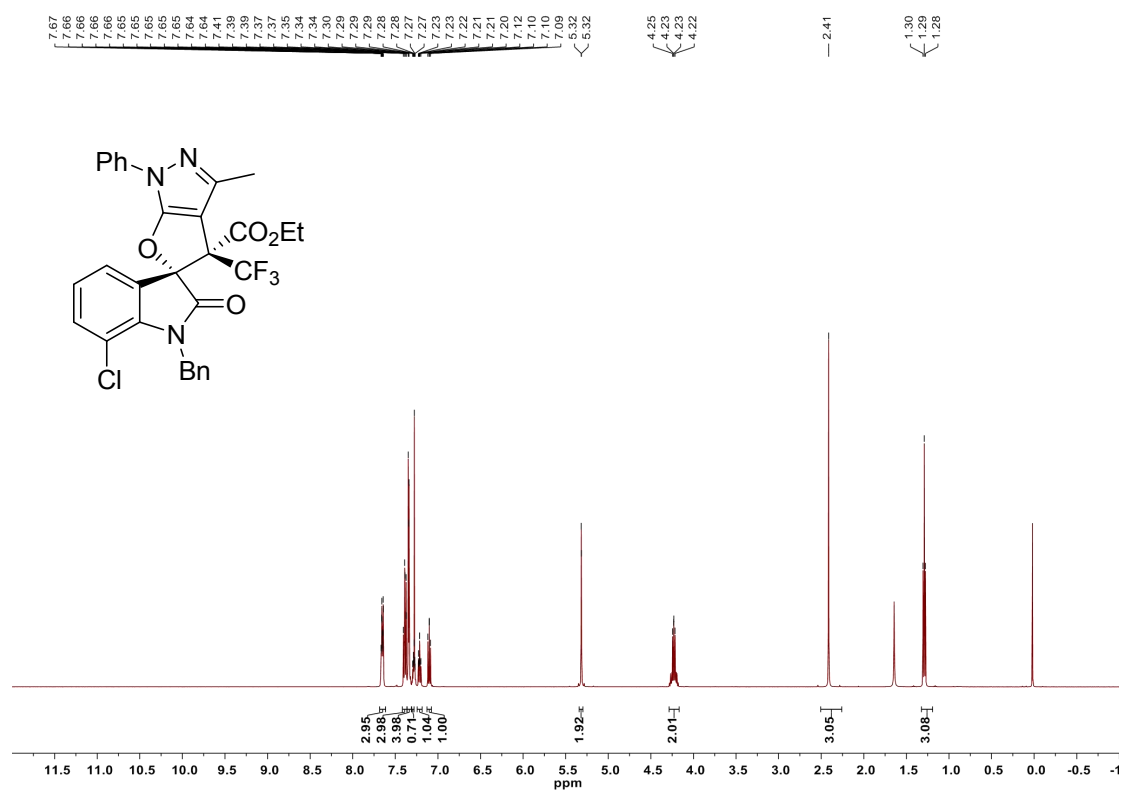
### 4c-chr



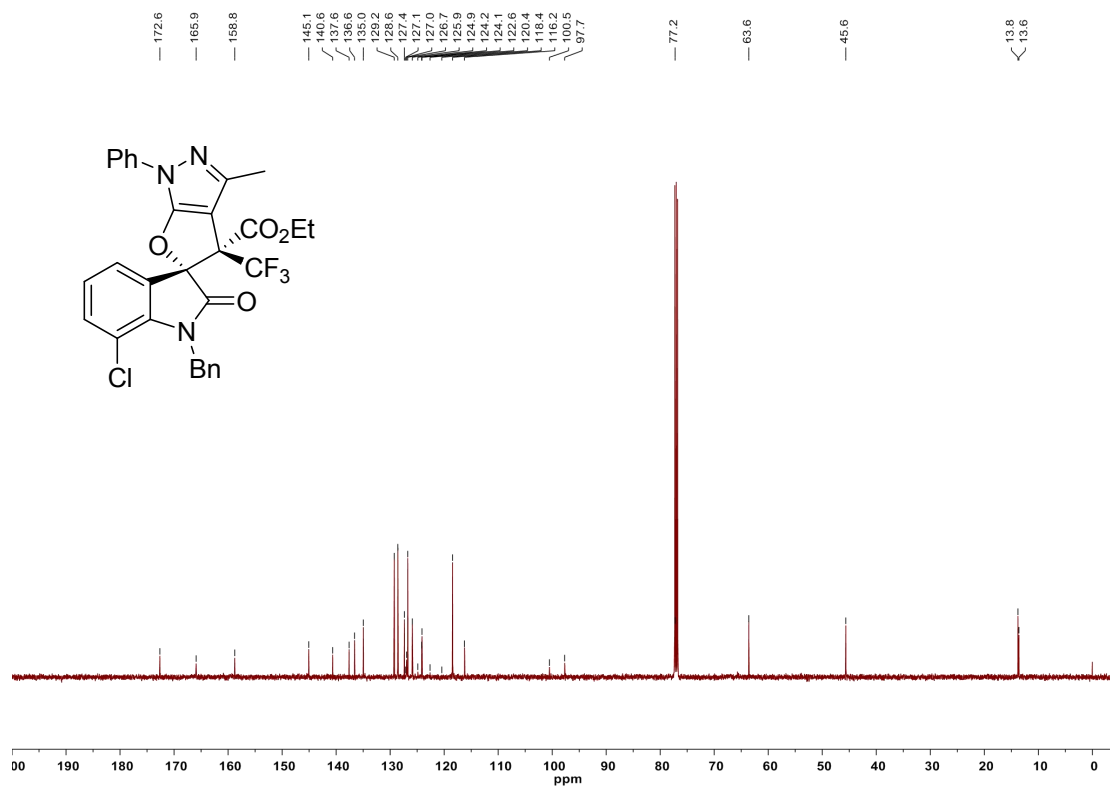
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	5.799	58.5	5.2	0.1748	0.904	2.080	BB
2	7.756	2753.3	98.4	0.3944	0.779	97.920	BB



### <sup>1</sup>H NMR spectrum of 4d (CDCl<sub>3</sub>, 500 MHz)

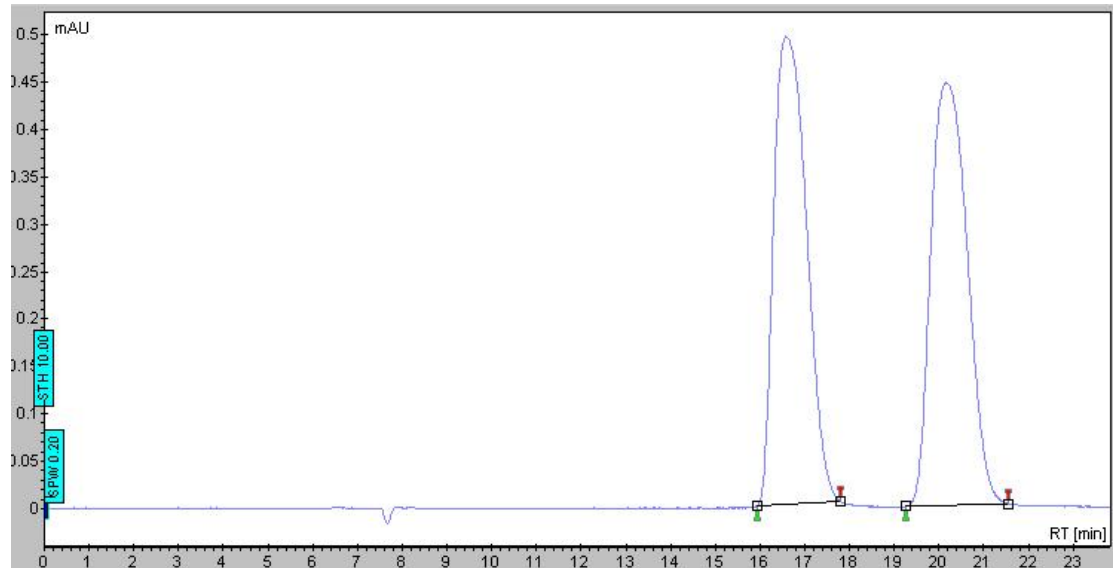


### <sup>13</sup>C NMR spectrum of 4d (CDCl<sub>3</sub>, 125 MHz)



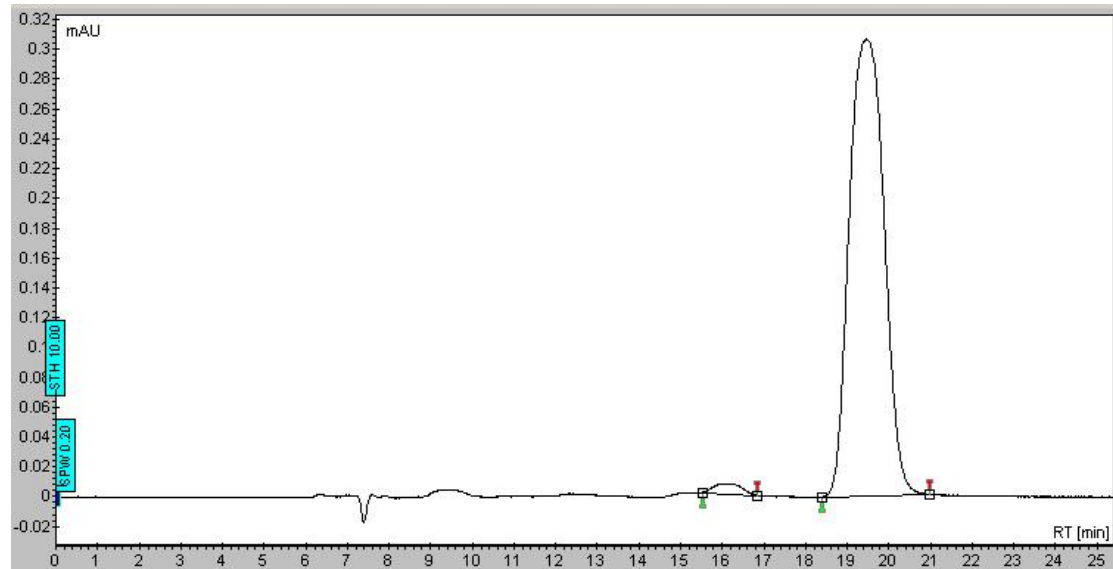
## HPLC chromatograms of 4d

### 4d-rac



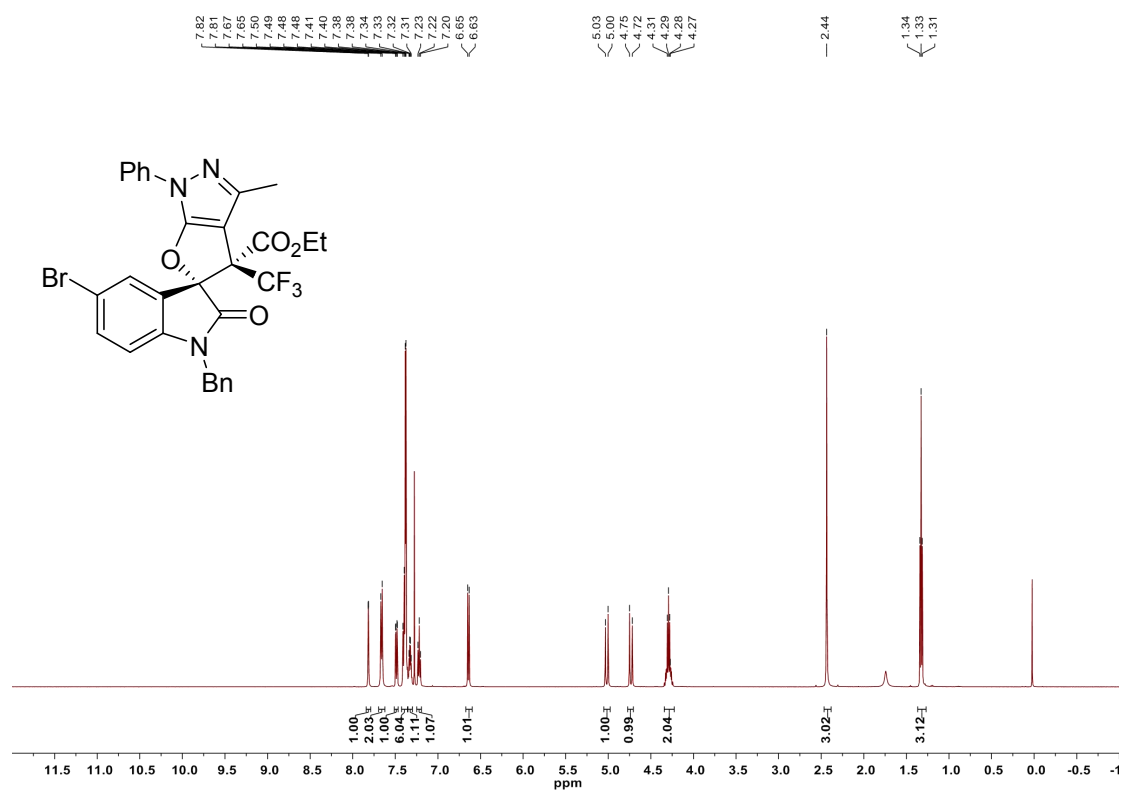
#	Start time[min]	Time[min]	End time[min]	Area%
1	15.938	16.572	17.797	49.820
2	19.258	20.145	21.549	50.180

### 4d-chr

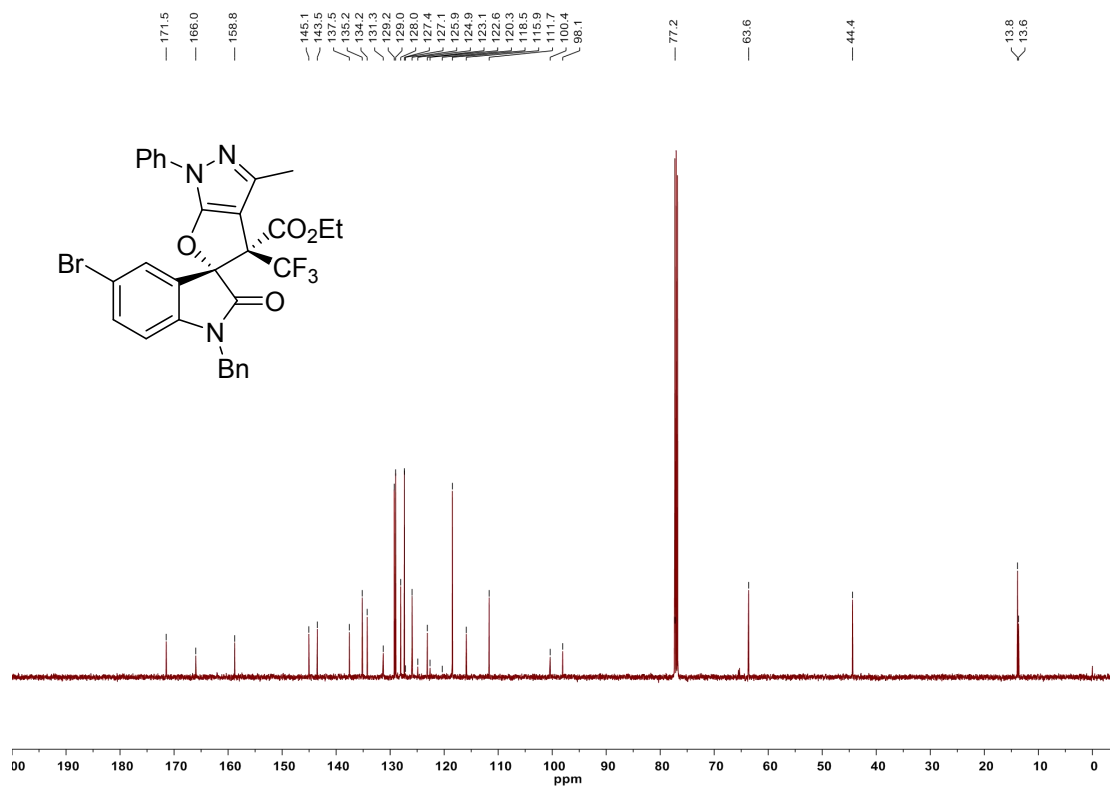


#	Start time[min]	Time[min]	End time[min]	Area%
1	15.530	16.132	16.839	1.760
2	18.396	19.452	20.978	98.240

### $^1\text{H}$ NMR spectrum of 4e ( $\text{CDCl}_3$ , 500 MHz)

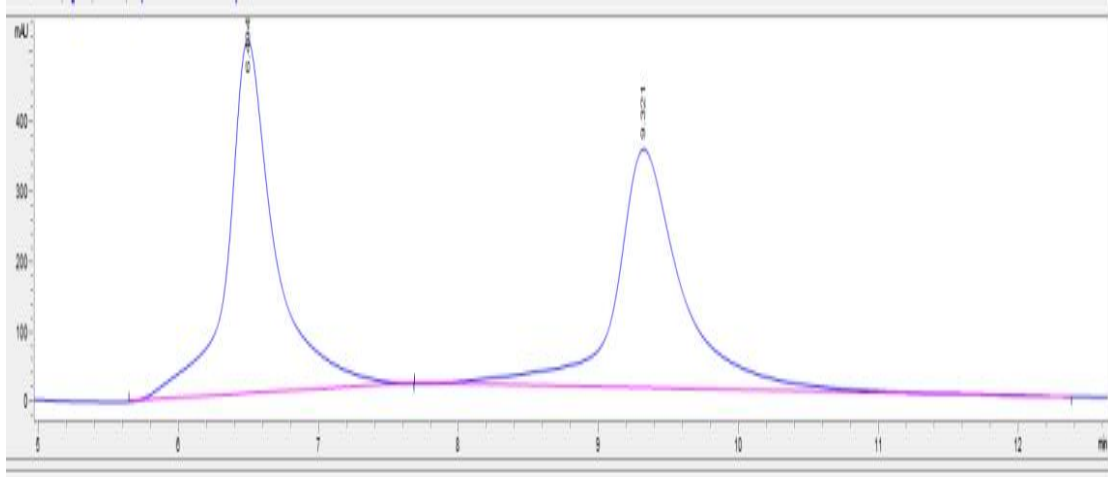


### $^{13}\text{C}$ NMR spectrum of 4e ( $\text{CDCl}_3$ , 125 MHz)



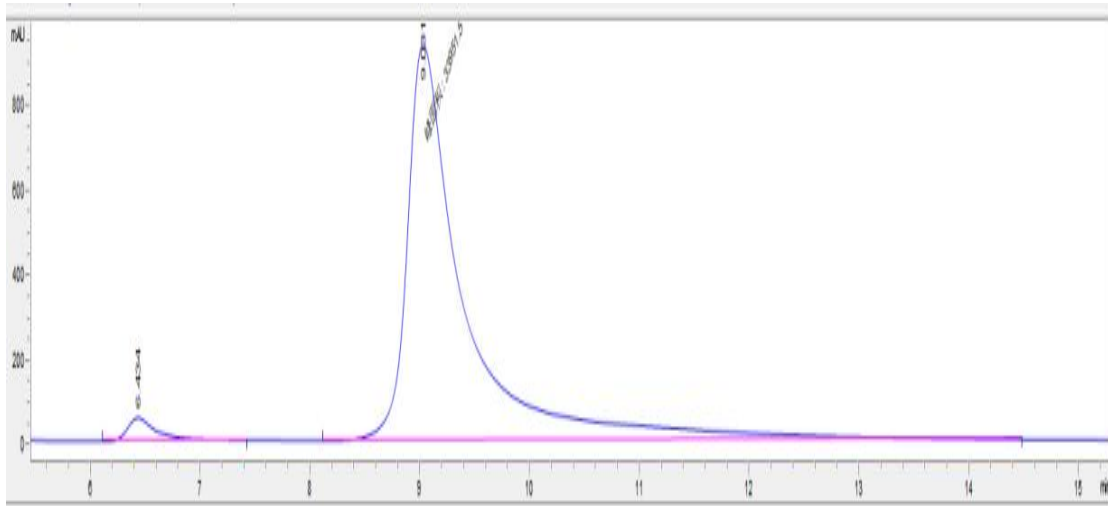
## HPLC chromatograms of 4e

### 4e-rac



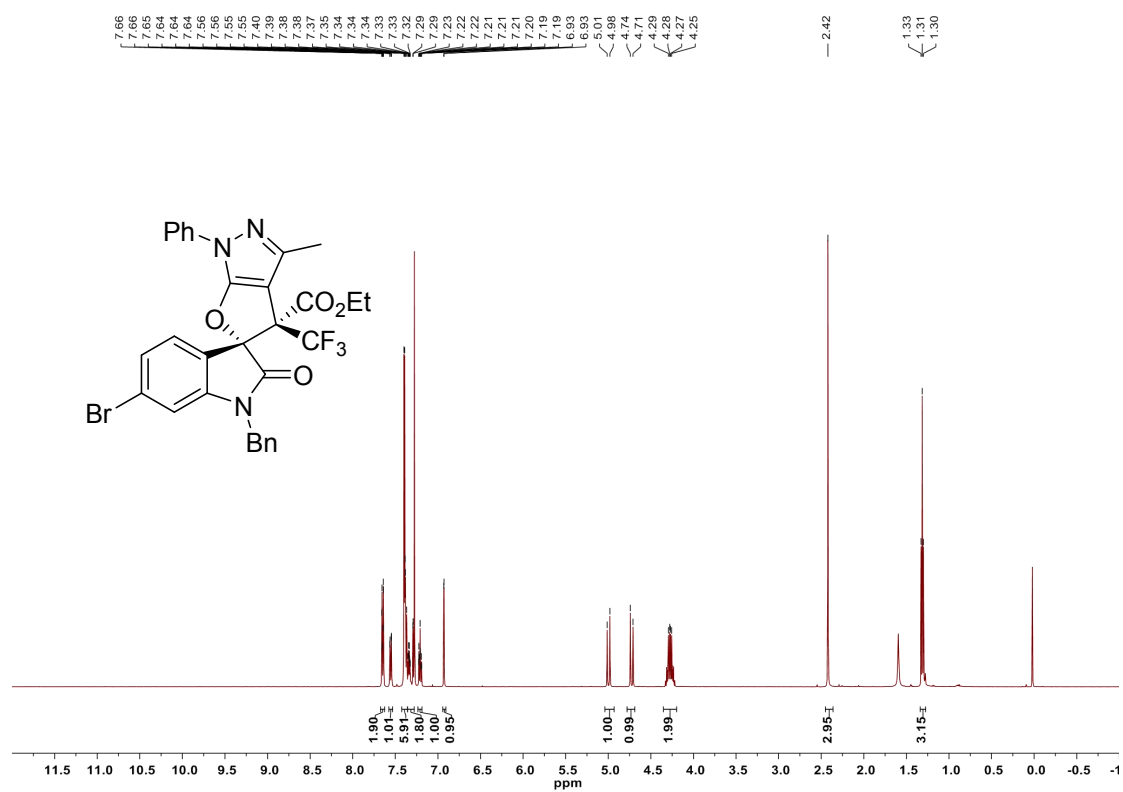
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.494	12002.7	506.6	0.3304	0.741	50.940	BB
2	9.321	11559.5	341.6	0.4788	0.746	49.060	BBA

### 4e-chr

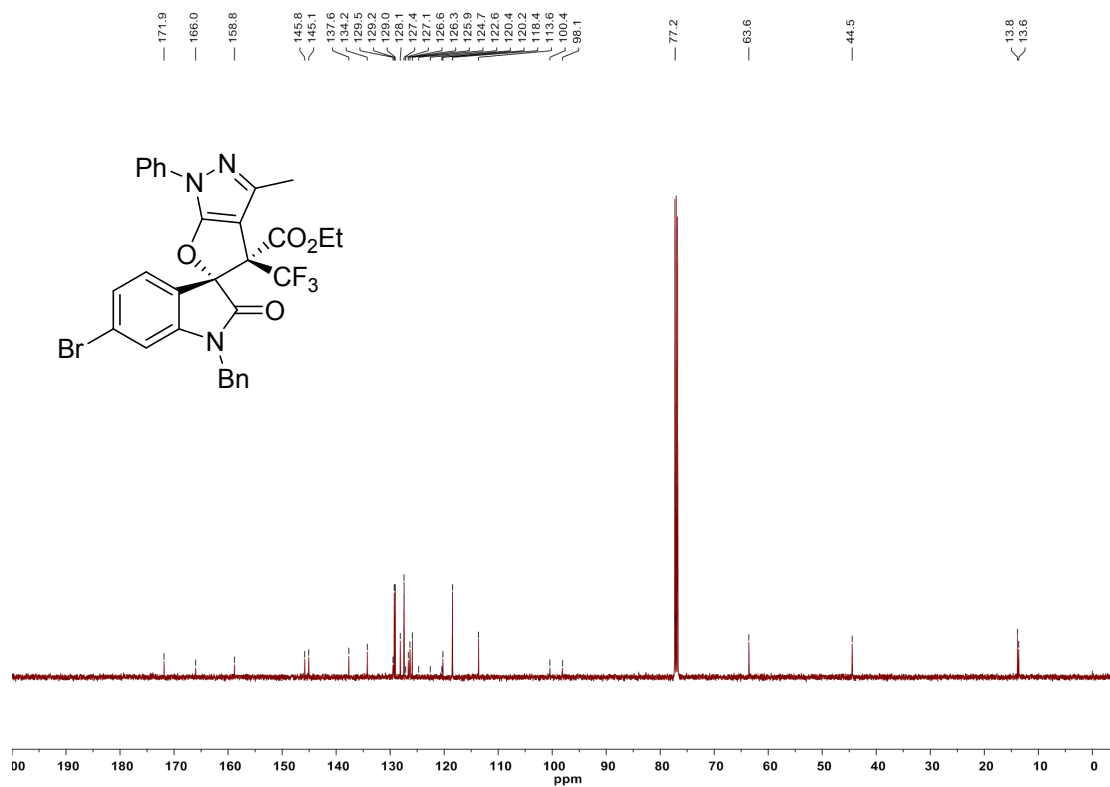


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.434	1013	54.2	0.2722	0.511	2.897	BB
2	9.031	33951.5	936.3	0.6044	0.372	97.103	MM

### $^1\text{H}$ NMR spectrum of 4f ( $\text{CDCl}_3$ , 500 MHz)

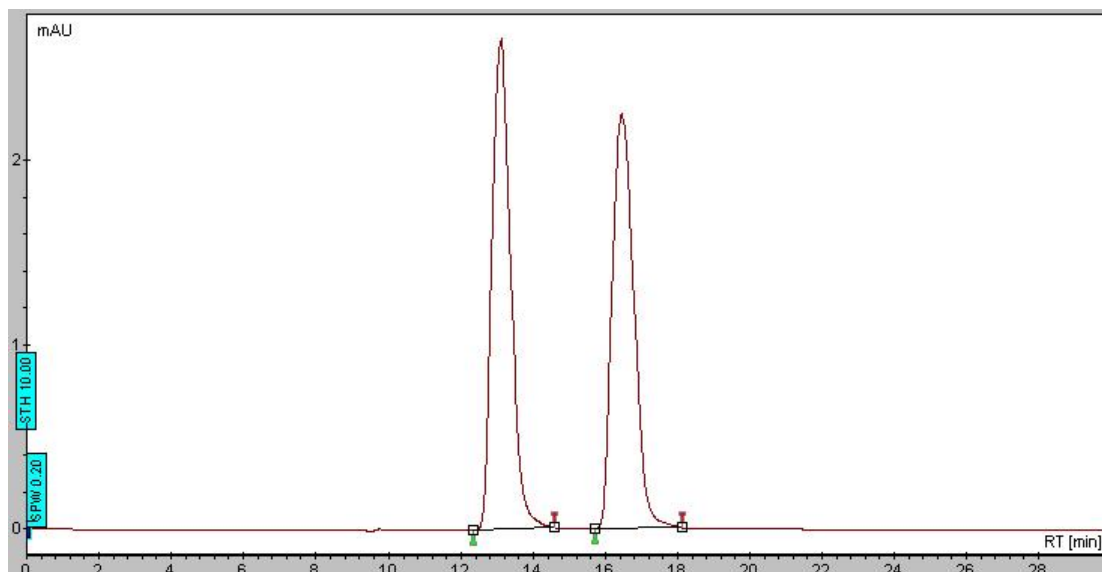


### $^{13}\text{C}$ NMR spectrum of 4f ( $\text{CDCl}_3$ , 125 MHz)



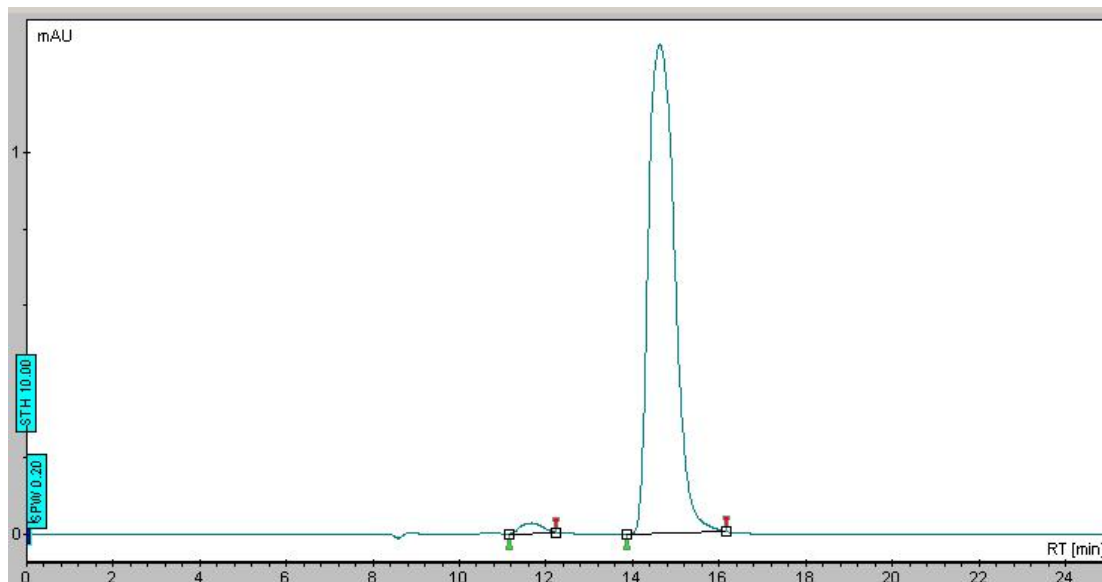
## HPLC chromatograms of 4f

### 4f-rac



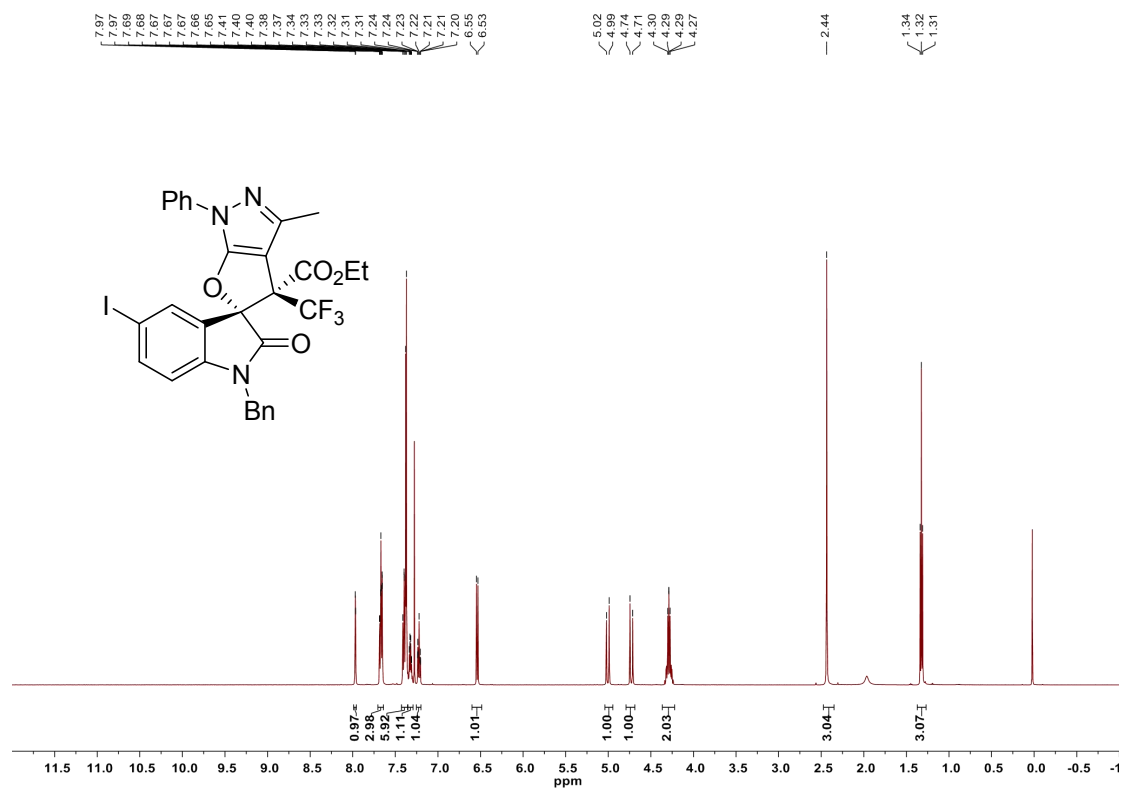
#	Start time[min]	Time[min]	End time[min]	Area%
1	12.349	13.119	14.594	50.424
2	15.717	16.465	28.128	49.576

### 4f-chr

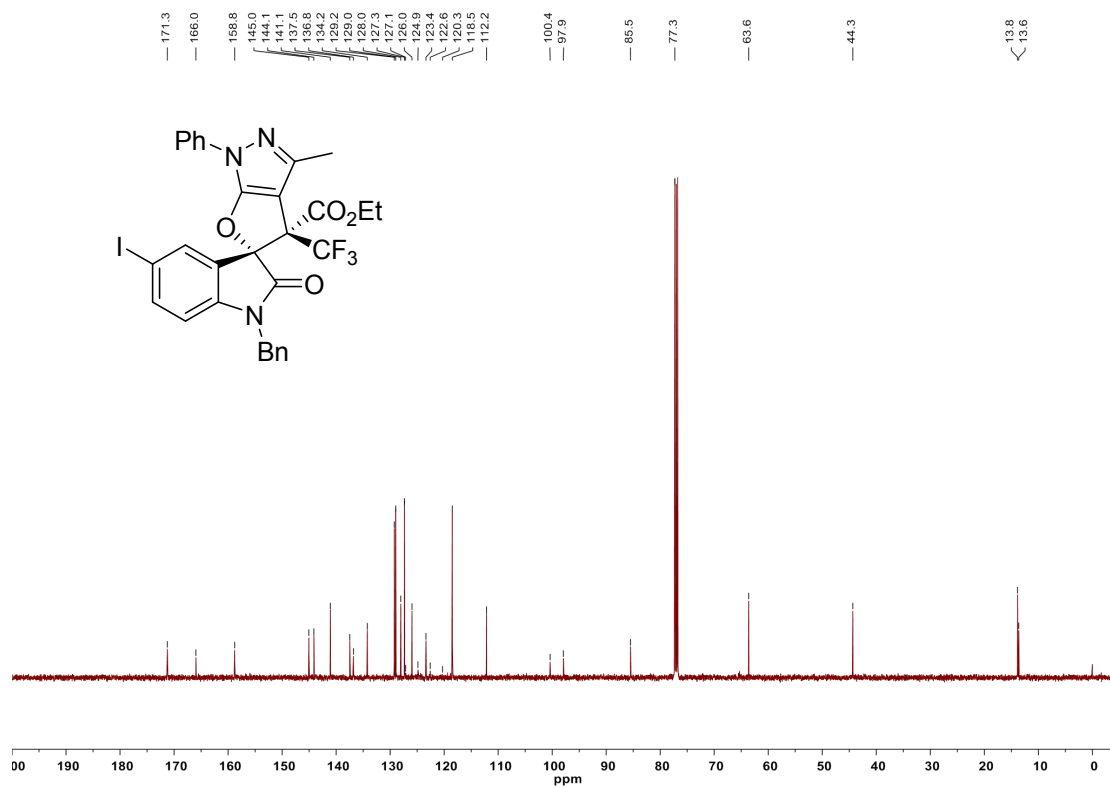


#	Start time[min]	Time[min]	End time[min]	Area%
1	11.148	11.639	12.228	1.639
2	13.865	14.626	16.165	98.307

### $^1\text{H}$ NMR spectrum of 4g ( $\text{CDCl}_3$ , 500 MHz)

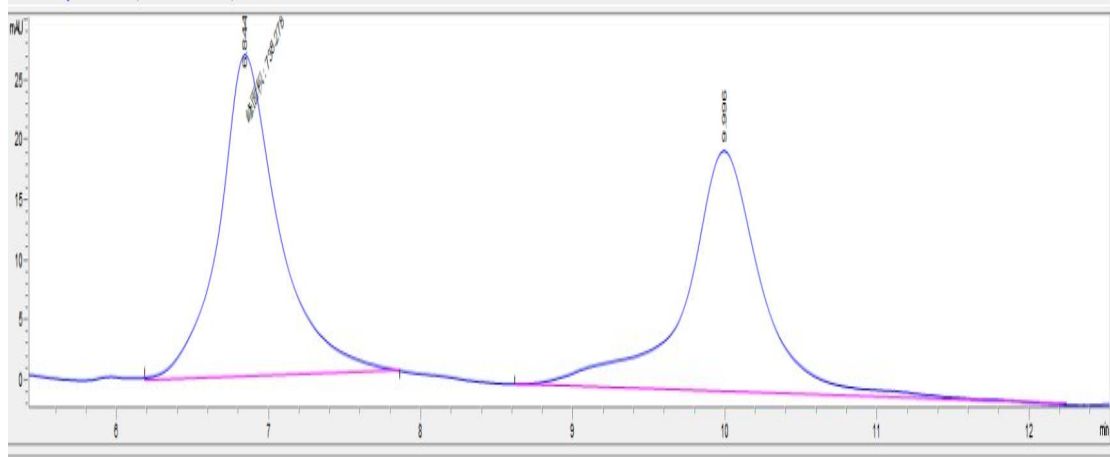


### $^{13}\text{C}$ NMR spectrum of 4g ( $\text{CDCl}_3$ , 125 MHz)



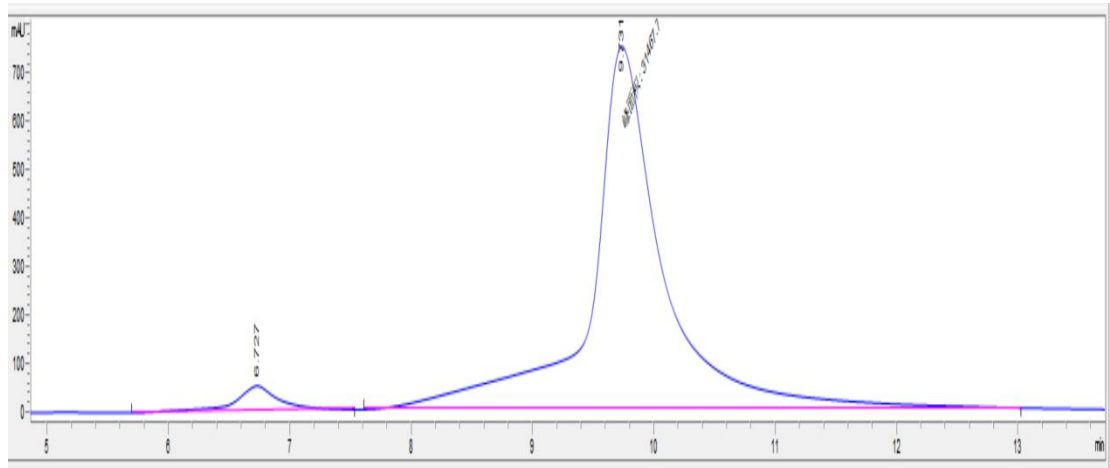
## HPLC chromatograms of 4g

### 4g-rac



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.844	738.3	26.8	0.4588	0.758	50.807	MM
2	9.996	714.8	20	0.4983	1.013	49.193	BB

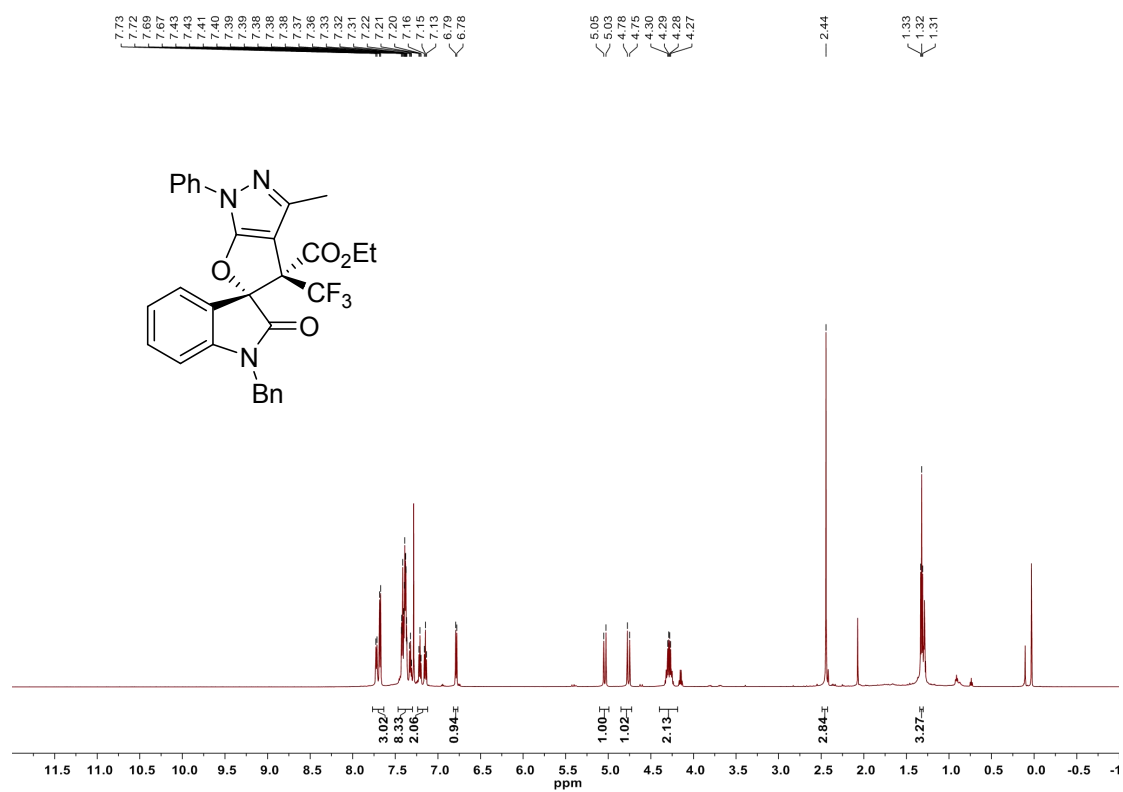
### 4g-chr



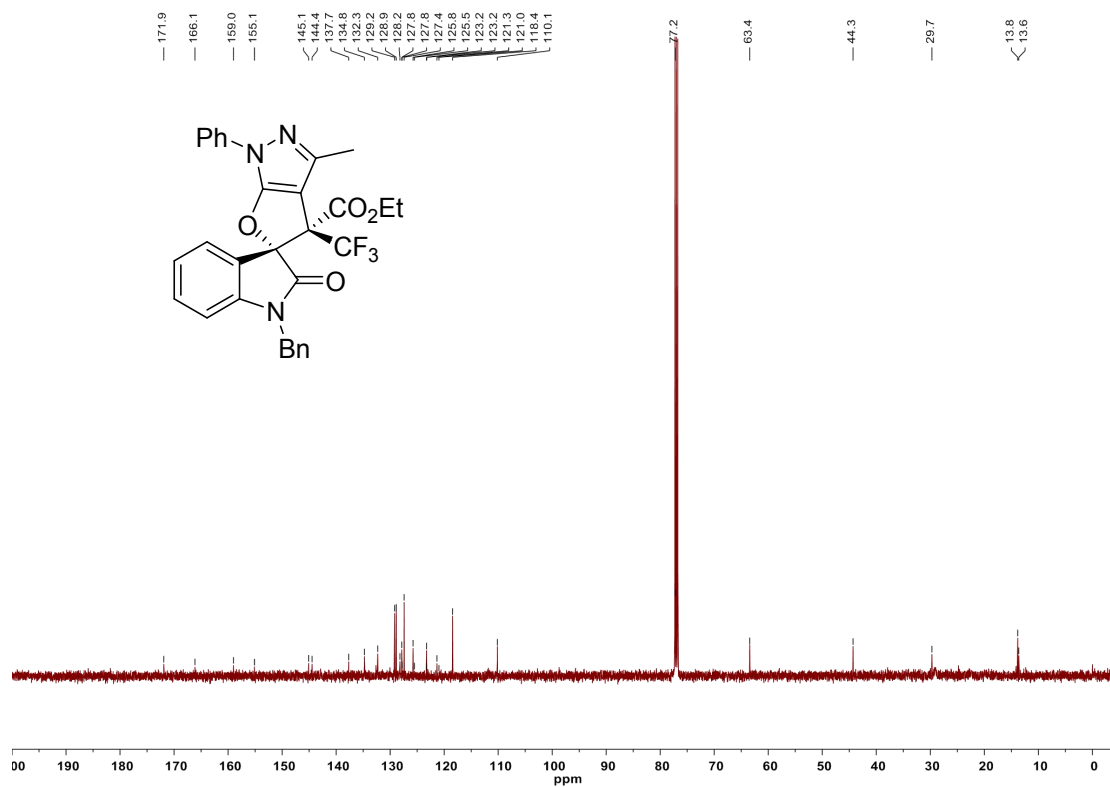
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	6.727	1329.1	51.5	0.365	1.027	4.053	BB
2	9.731	31467.7	747.9	0.7012	0.762	95.947	MM



### <sup>1</sup>H NMR spectrum of 4h (CDCl<sub>3</sub>, 500 MHz)

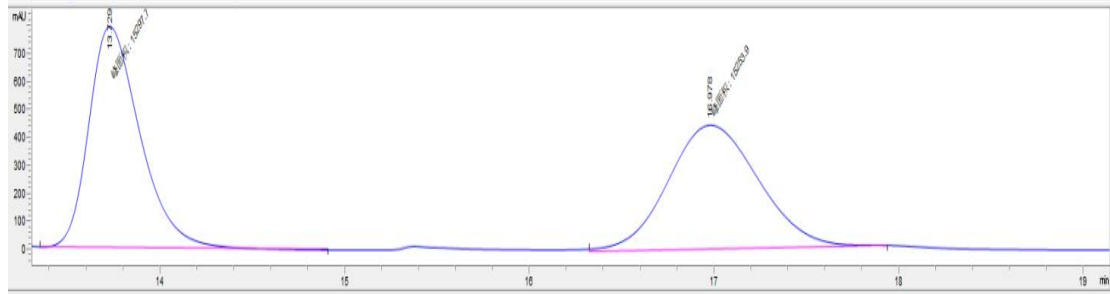


### <sup>13</sup>C NMR spectrum of 4h (CDCl<sub>3</sub>, 125 MHz)



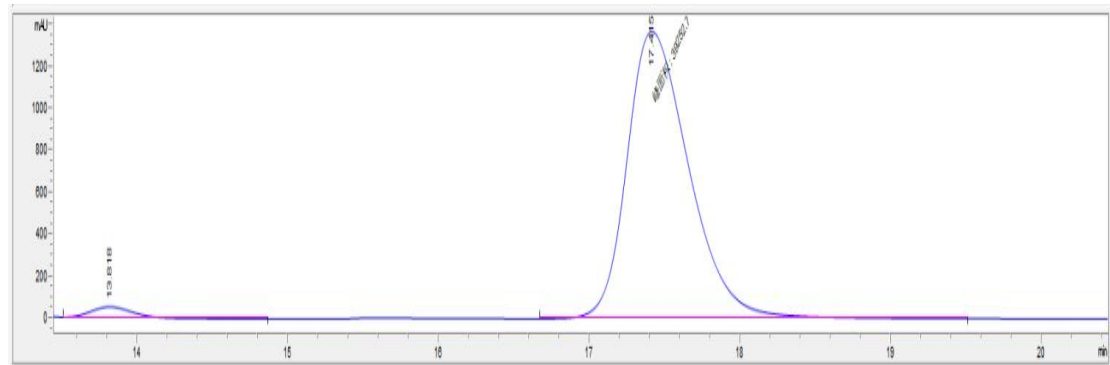
## HPLC chromatograms of 4h

### 4h-rac



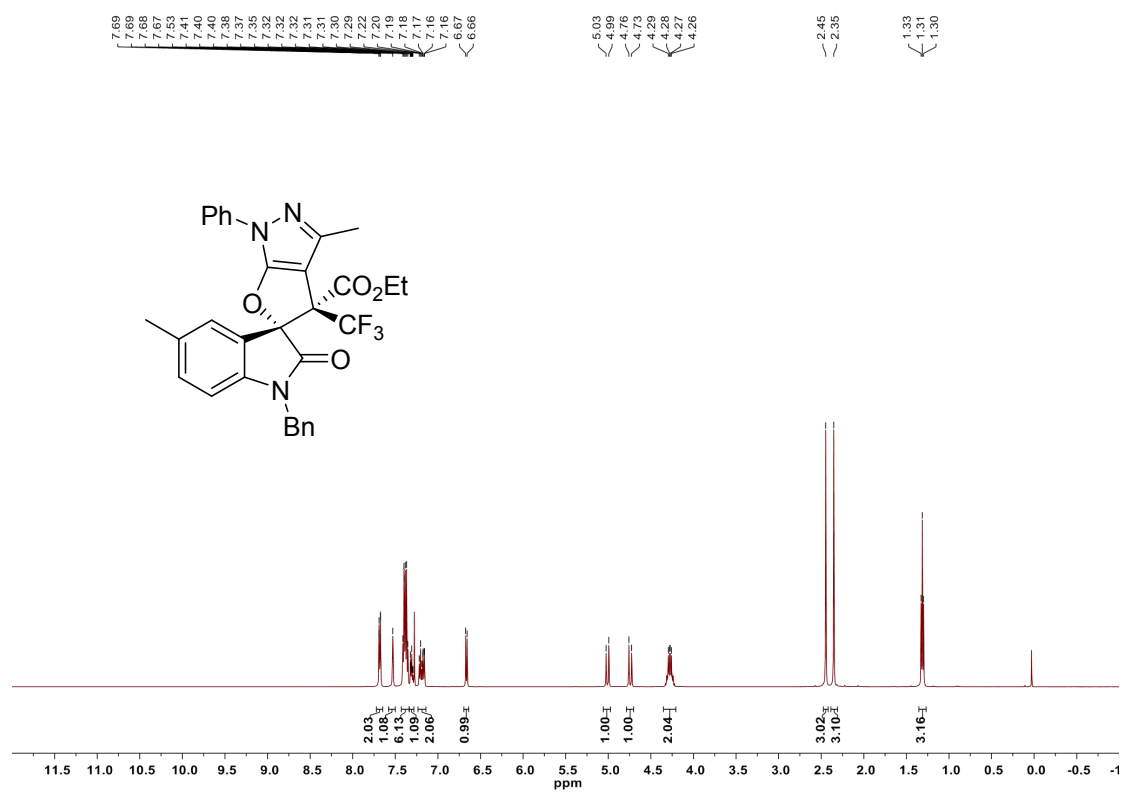
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.729	15297.7	796.2	0.3202	0.672	50.072	MM
2	16.978	15253.9	446.6	0.5693	0.875	49.928	MM

### 4h-chr

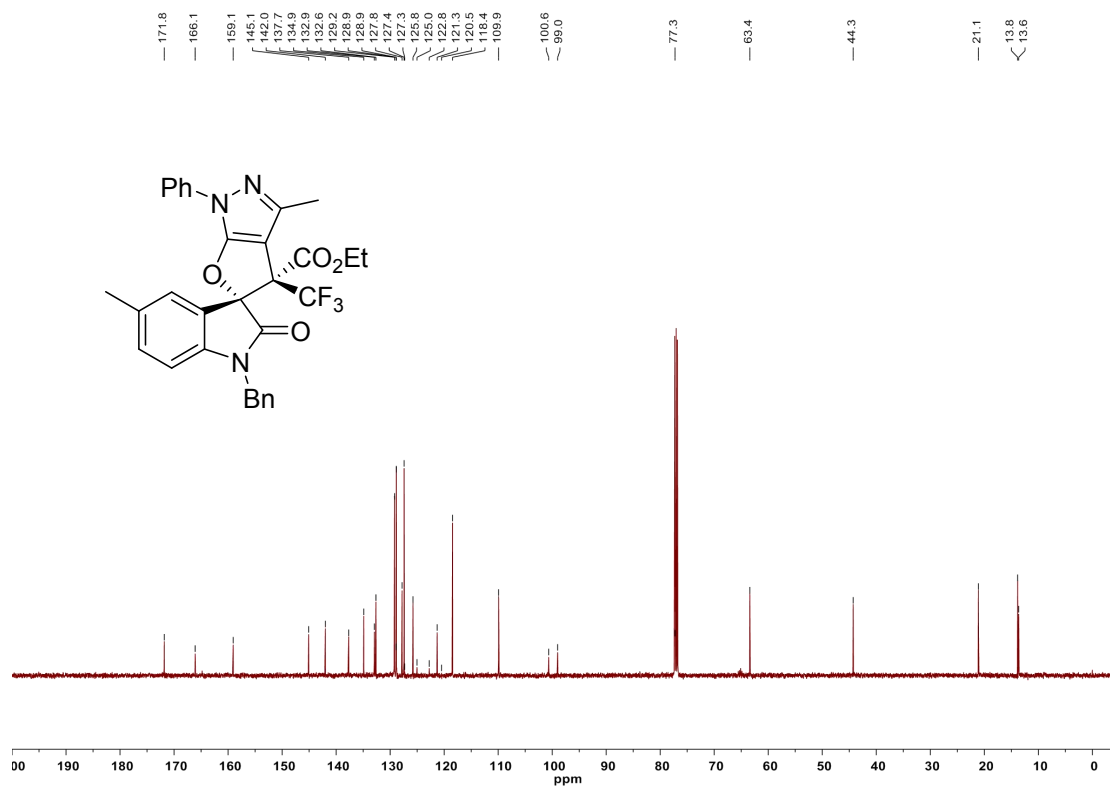


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	13.818	1234	57.3	0.3252	0.792	3.048	VB
2	17.415	39252.7	1369.9	0.4776	0.653	96.952	MM

### <sup>1</sup>H NMR spectrum of 4i (CDCl<sub>3</sub>, 500 MHz)

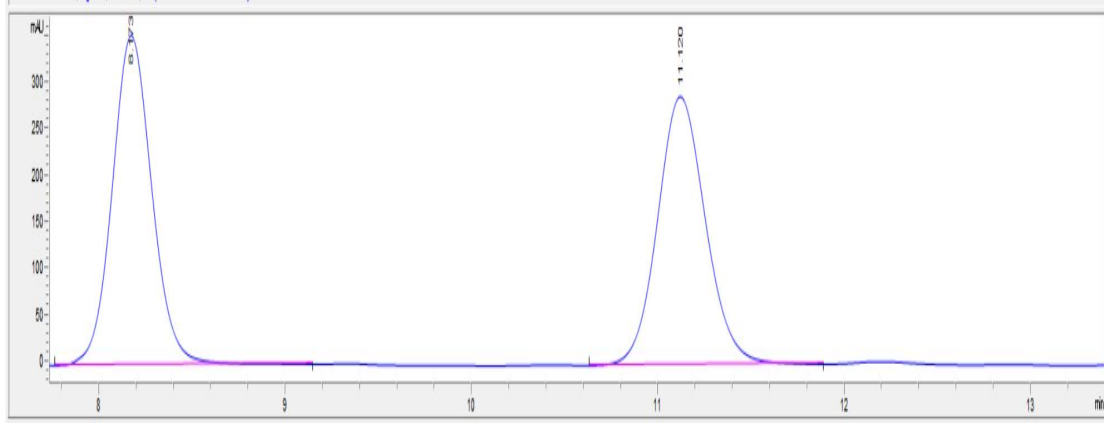


### <sup>13</sup>C NMR spectrum of 4i (CDCl<sub>3</sub>, 125 MHz)



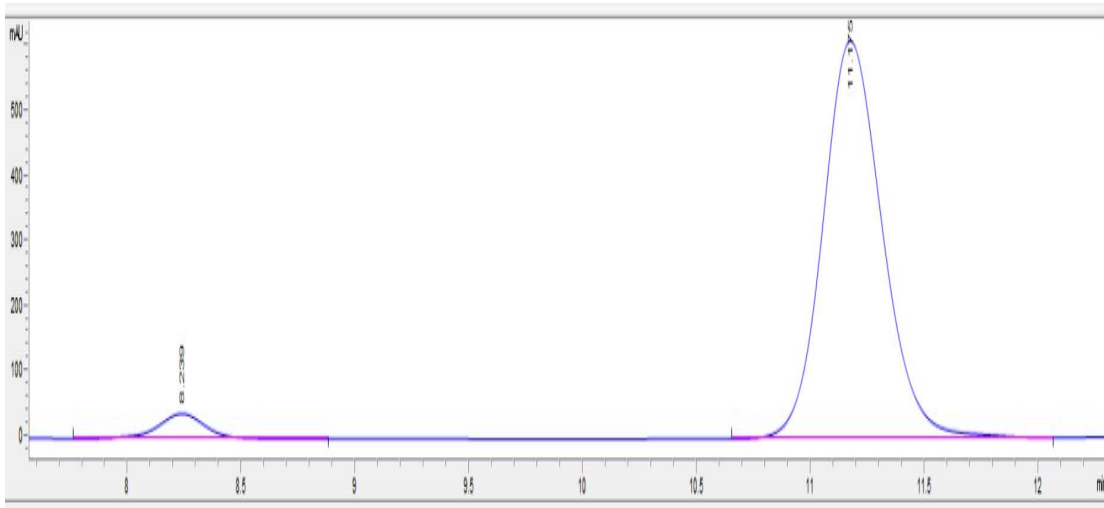
## HPLC chromatograms of 4i

### 4i-rac



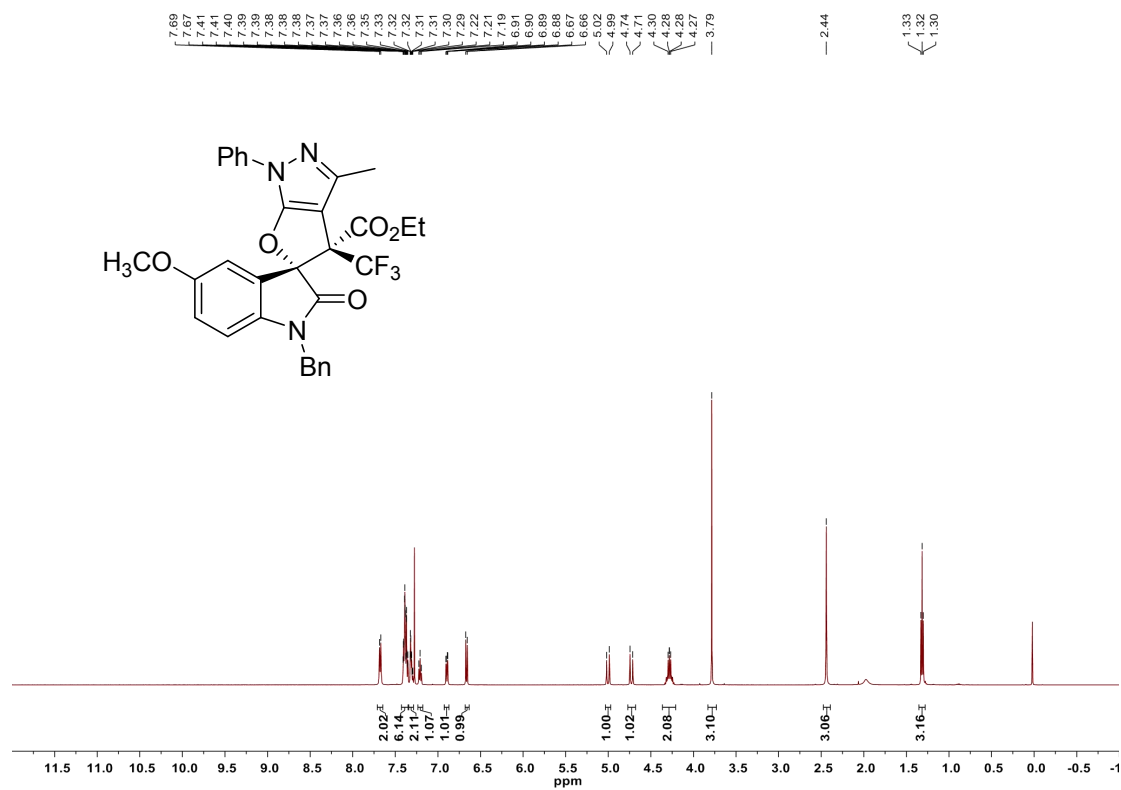
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.173	5289.6	356	0.2294	0.877	50.412	BB
2	11.12	5203.1	289.8	0.2774	0.868	49.588	BB

### 4i-chr

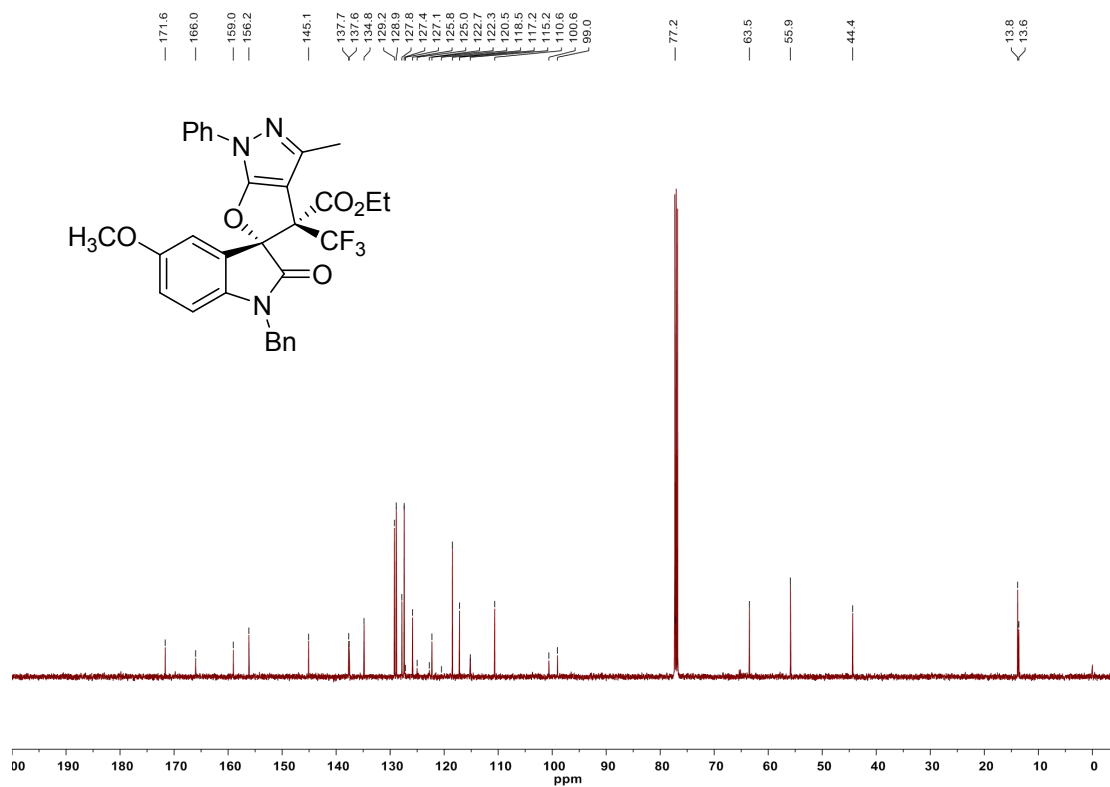


#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	8.239	560.9	38.6	0.2216	1.038	4.824	BB
2	11.175	11065.1	611	0.2793	0.825	95.176	BB

### <sup>1</sup>H NMR spectrum of 4j (CDCl<sub>3</sub>, 500 MHz)

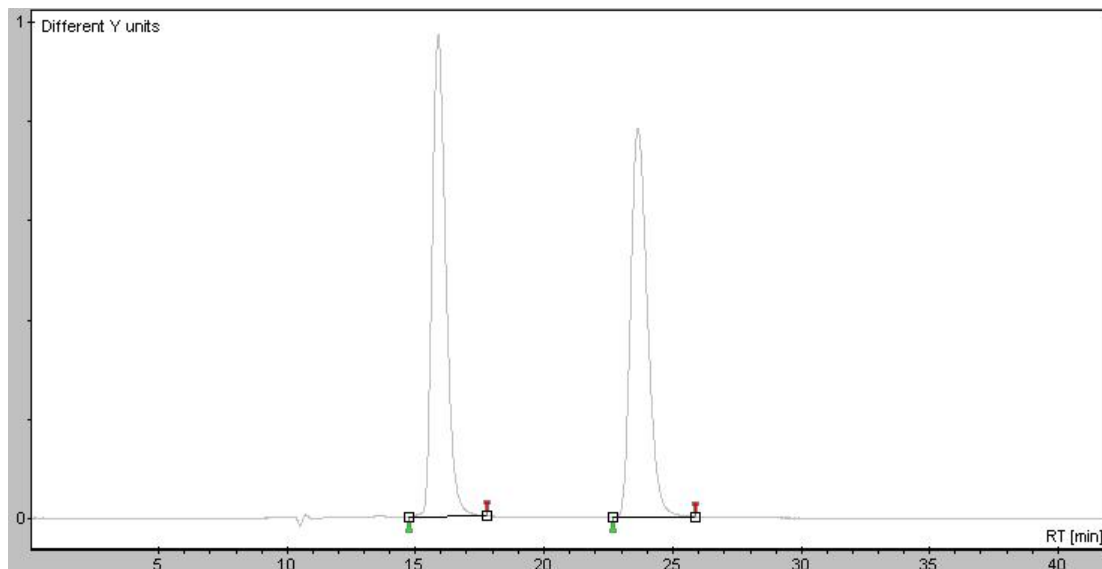


### <sup>13</sup>C NMR spectrum of 4j (CDCl<sub>3</sub>, 125 MHz)



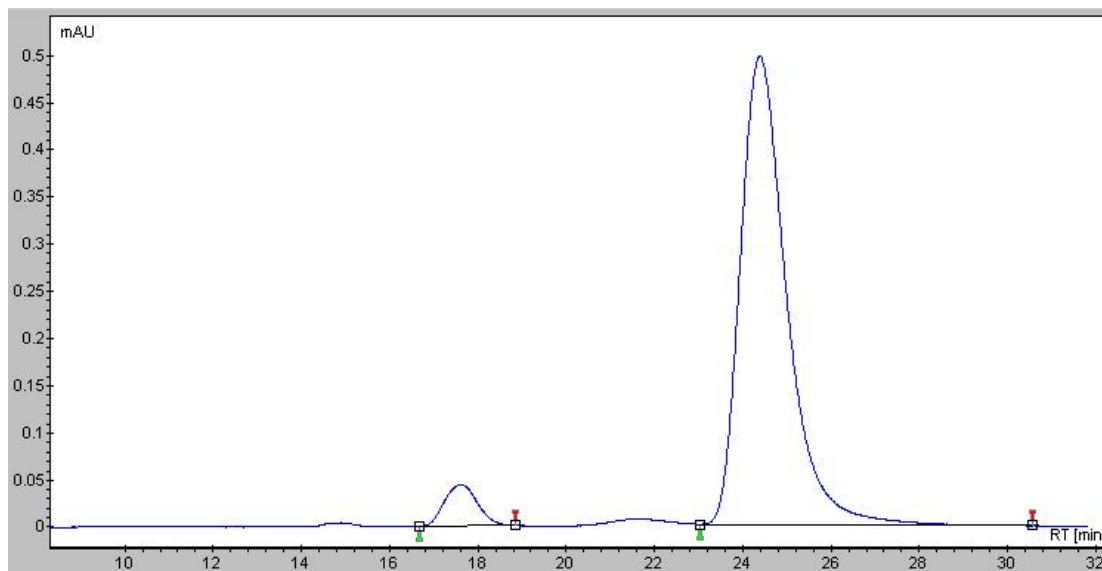
## HPLC chromatograms of 4j

### 4j-rac



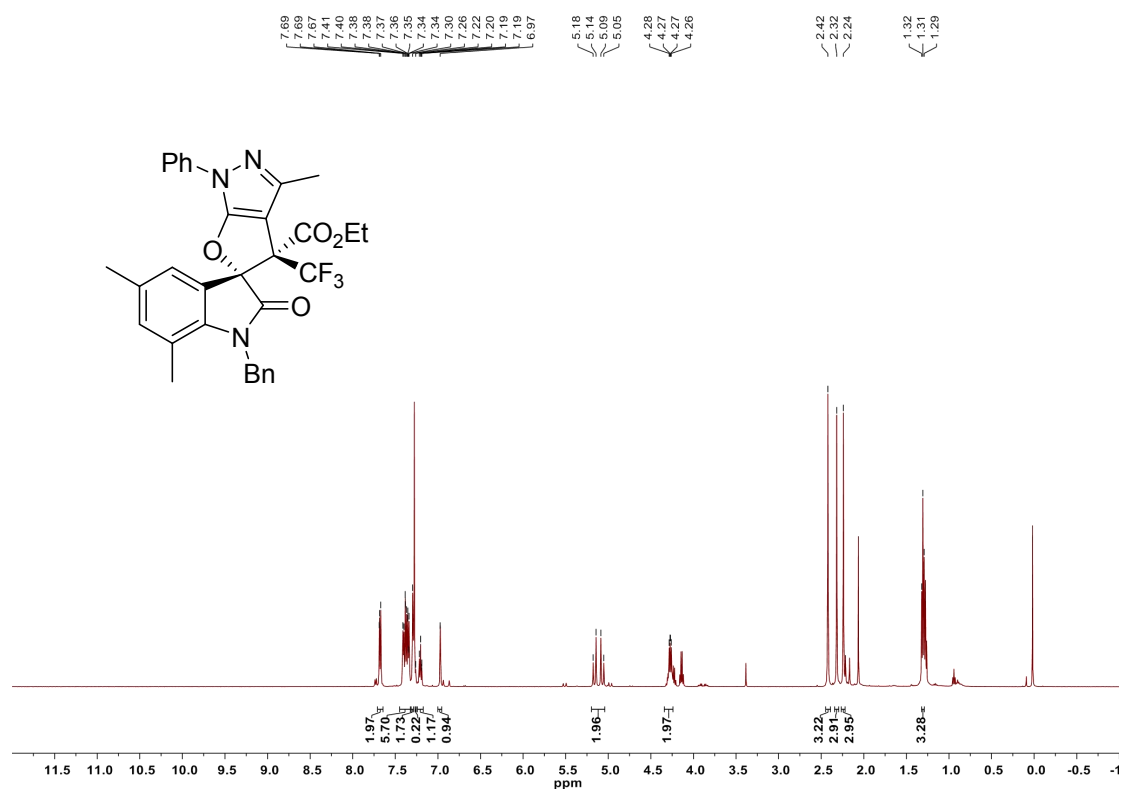
#	Start time[min]	Time[min]	End time[min]	Area%
1	14.748	15.892	17.779	50.297
2	22.675	23.638	25.881	49.703

### 4j-chr

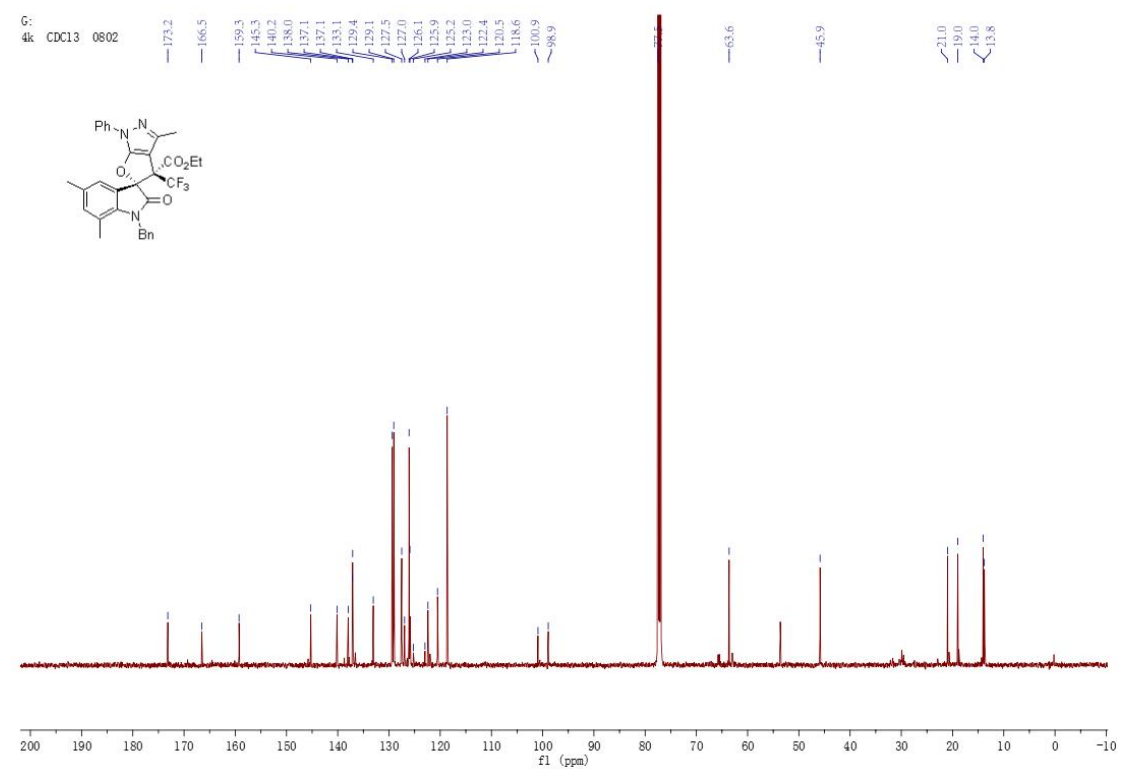


#	Start time[min]	Time[min]	End time[min]	Area%
1	16.665	17.612	18.839	5.951
2	23.050	24.385	30.574	94.049

**<sup>1</sup>H NMR spectrum of 4k (CDCl<sub>3</sub>, 500 MHz)**

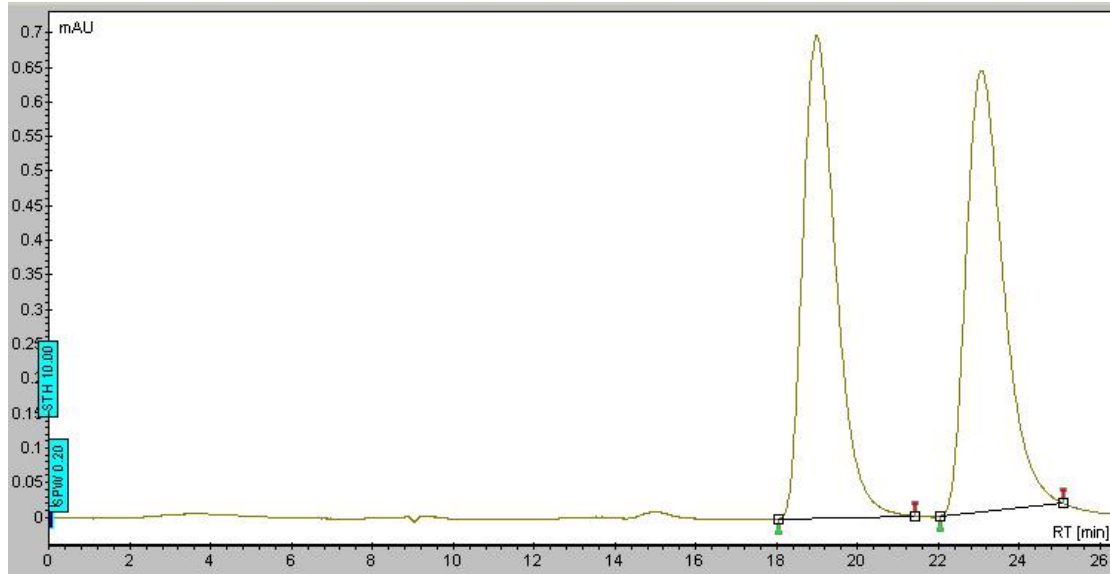


**<sup>13</sup>C NMR spectrum of 4k (CDCl<sub>3</sub>, 125 MHz)**



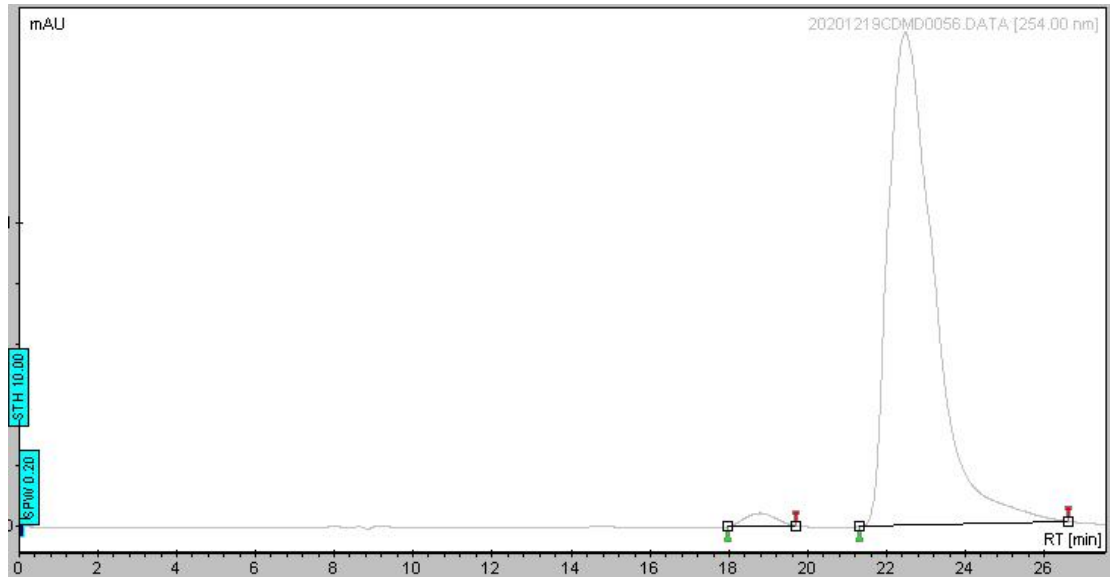
## HPLC chromatograms of 4k

### 4k-rac



#	Start time[min]	Time[min]	End time[min]	Area%
1	18.045	18.999	21.419	49.165
2	22.042	23.052	25.086	50.835

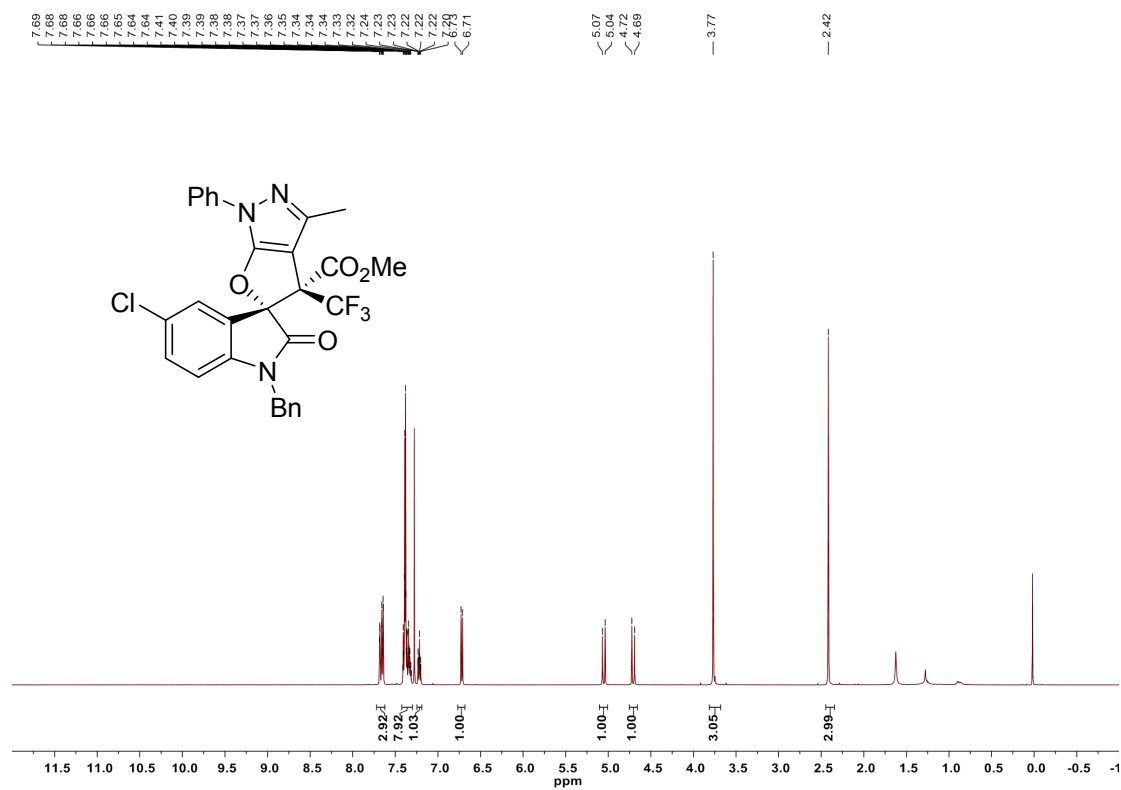
### 4k-chr



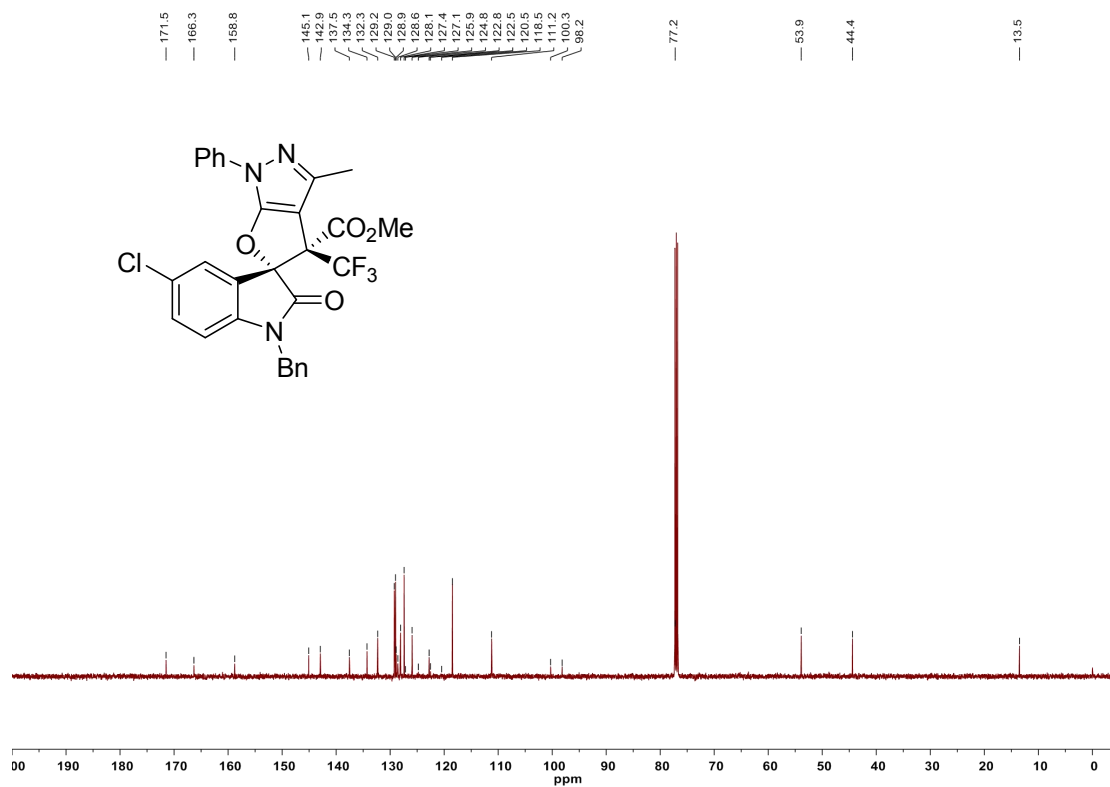
#	Start time[min]	Time[min]	End time[min]	Area%
1	17.973	18.785	19.701	1.750
2	21.314	22.465	26.613	98.250



**<sup>1</sup>H NMR spectrum of 4l (CDCl<sub>3</sub>, 500 MHz)**

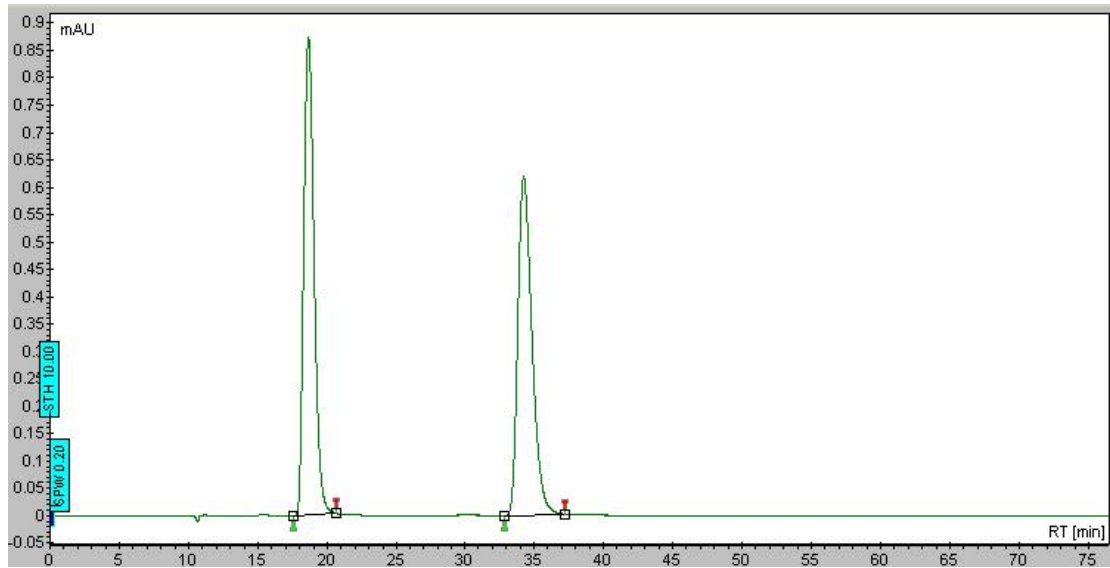


**<sup>13</sup>C NMR spectrum of 4l (CDCl<sub>3</sub>, 125 MHz)**



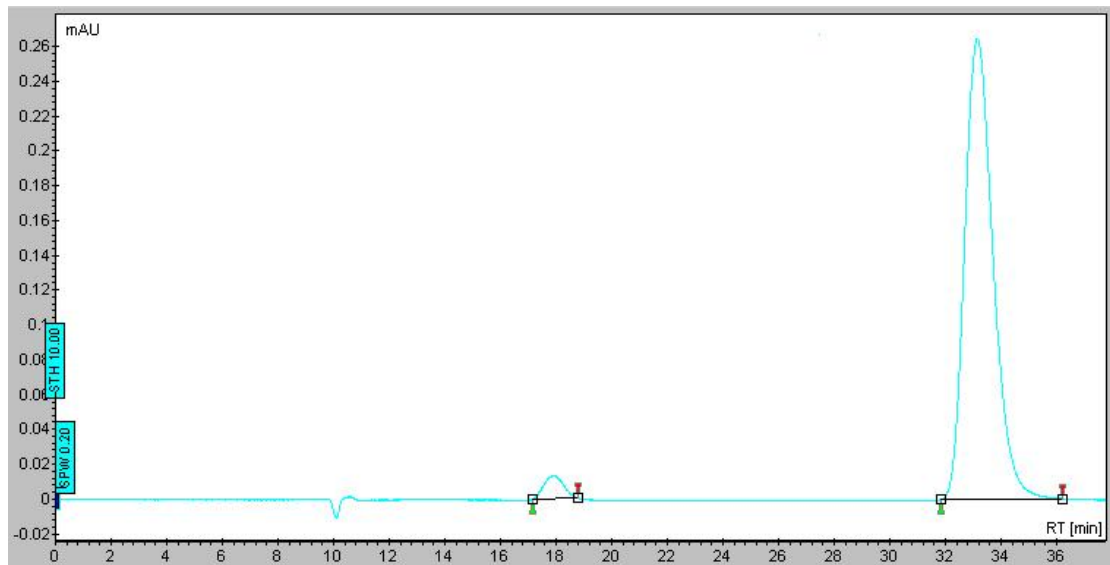
## HPLC chromatograms of 4l

### 4l-rac



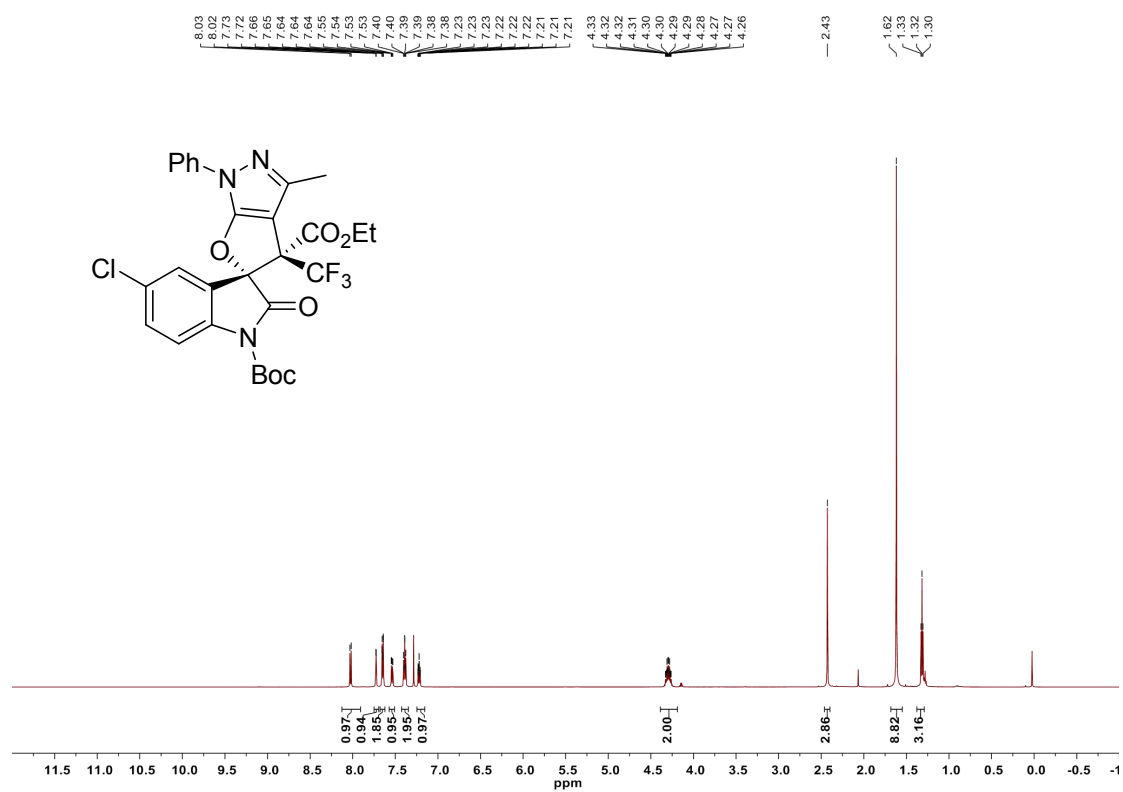
#	Start time[min]	Time[min]	End time[min]	Area%
1	17.585	18.673	20.675	50.675
2	32.825	34.214	37.194	49.325

### 4l-chr

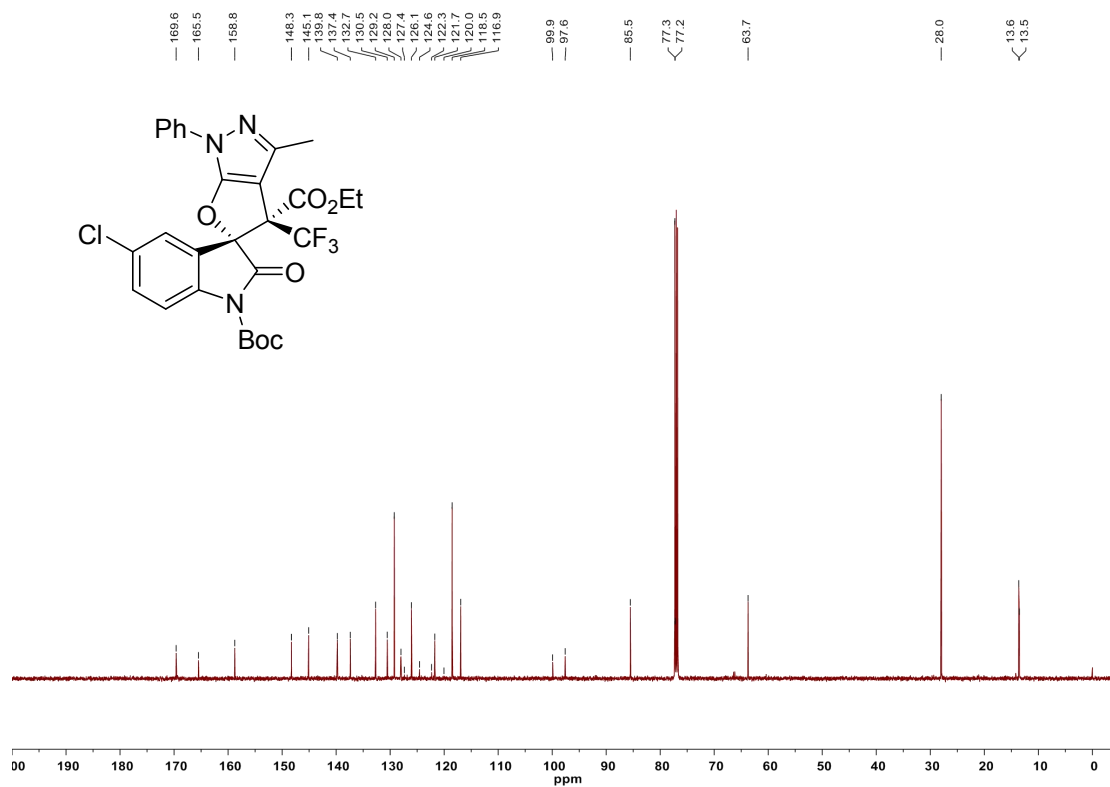


#	Start time[min]	Time[min]	End time[min]	Area%
1	17.151	17.892	18.781	3.400
2	31.829	33.118	36.195	96.600

**<sup>1</sup>H NMR spectrum of 4m (CDCl<sub>3</sub>, 500 MHz)**

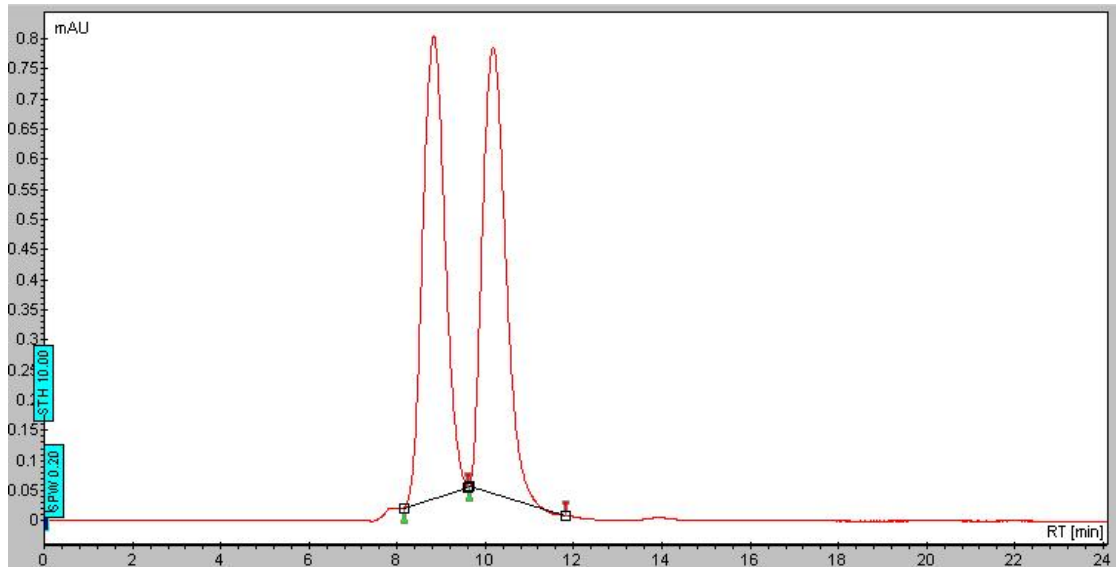


**<sup>13</sup>C NMR spectrum of 4m (CDCl<sub>3</sub>, 125 MHz)**



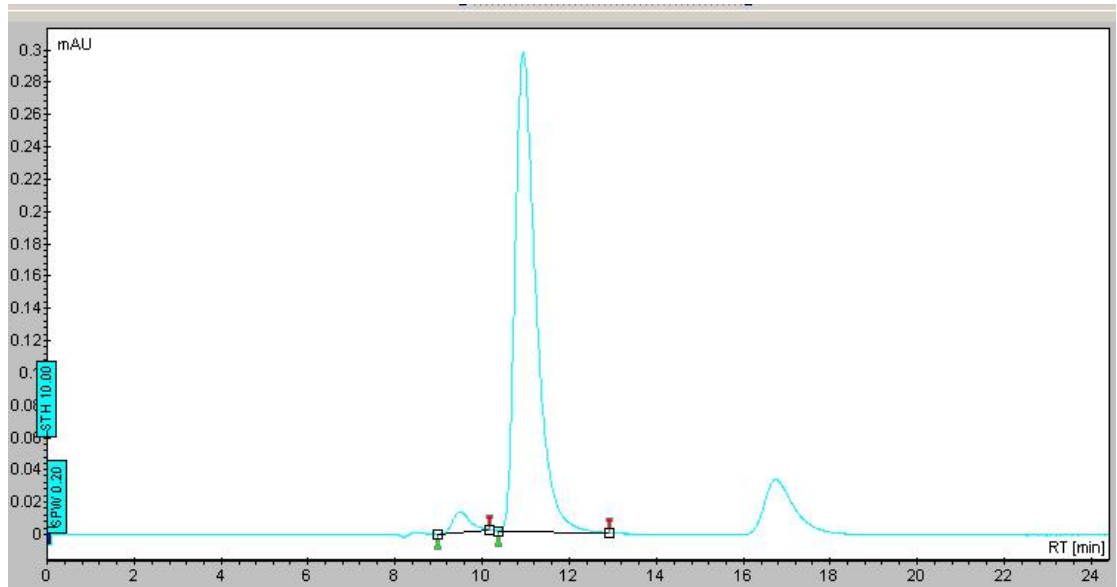
## HPLC chromatograms of 4m

### 4m-rac



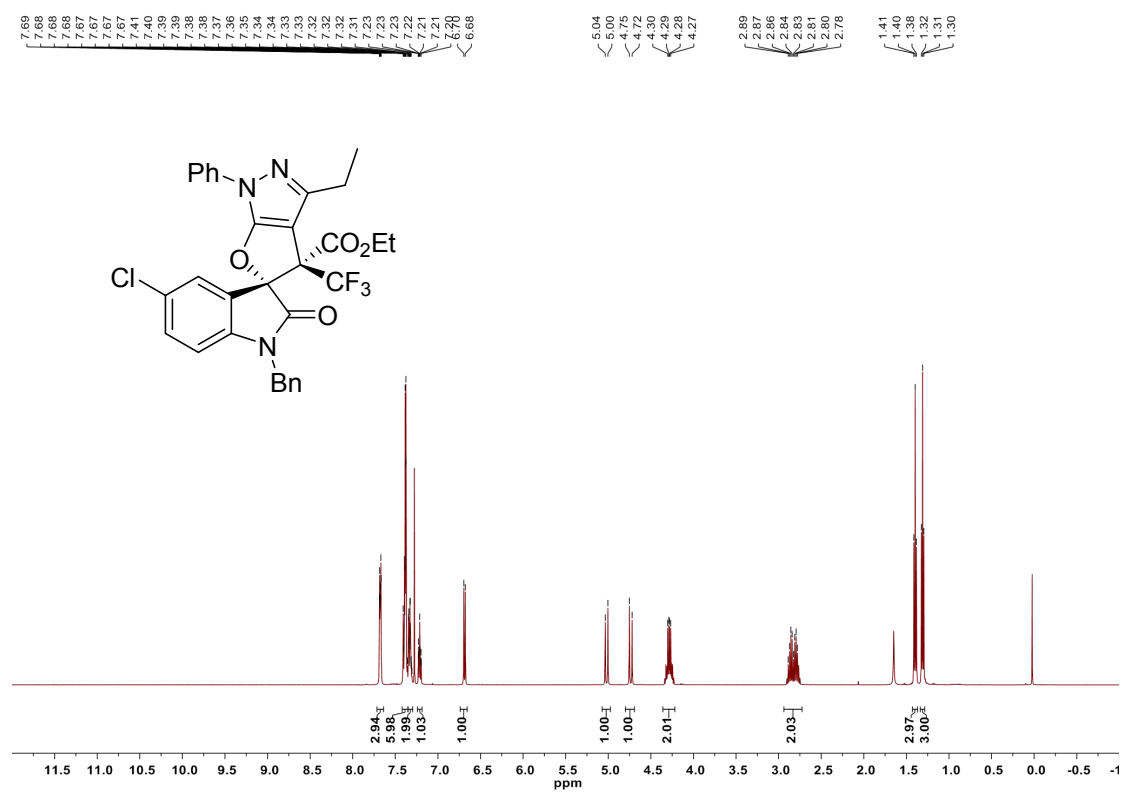
#	Start time[min]	Time[min]	End time[min]	Area%
1	8.159	8.826	9.602	50.052
2	9.636	10.173	11.818	49.948

### 4m-chr

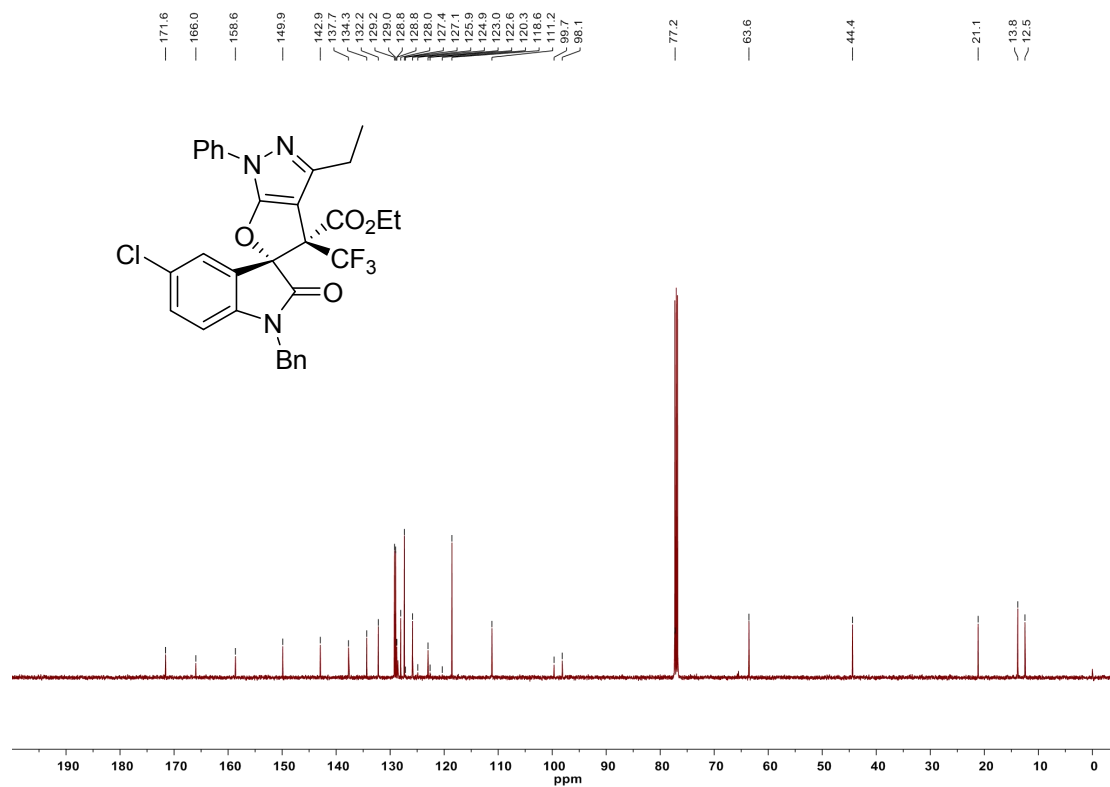


#	Start time[min]	Time[min]	End time[min]	Area%
1	8.976	9.479	10.167	3.317
2	10.371	10.946	12.921	96.683

### <sup>1</sup>H NMR spectrum of 4n (CDCl<sub>3</sub>, 500 MHz)

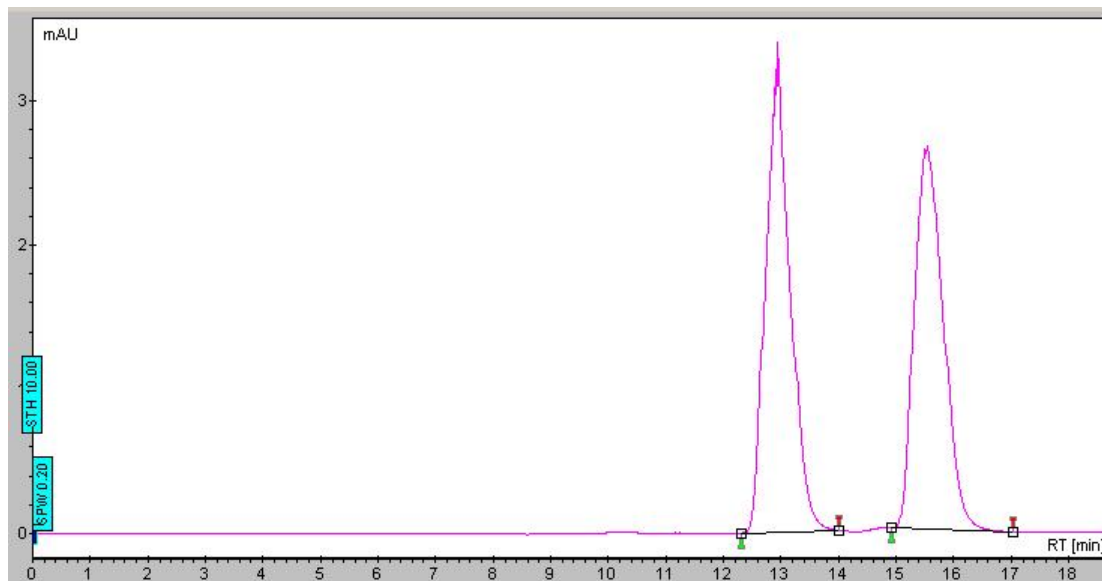


### <sup>13</sup>C NMR spectrum of 4n (CDCl<sub>3</sub>, 125 MHz)



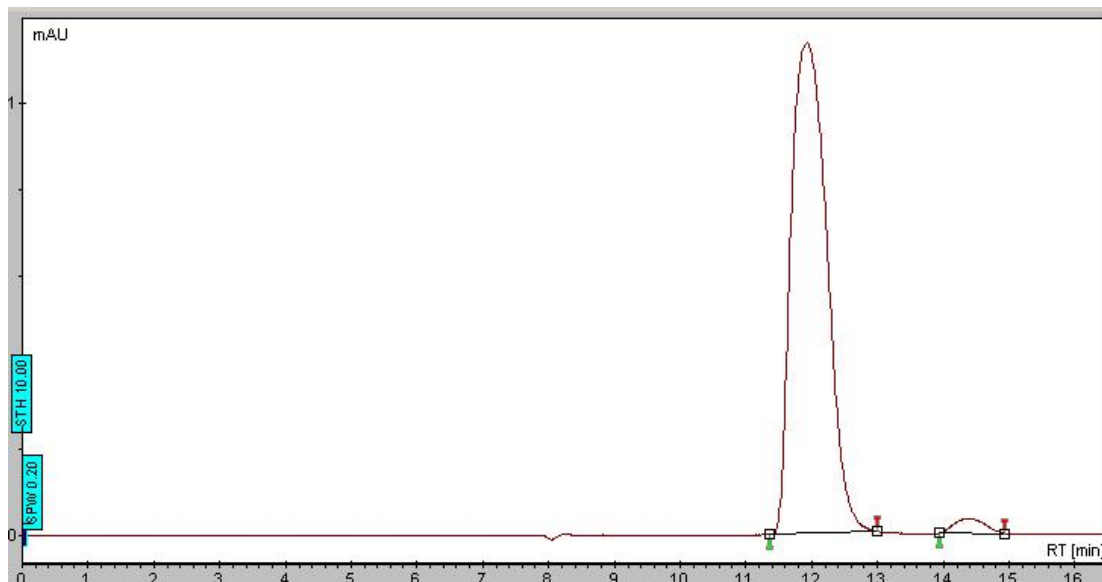
## HPLC chromatograms of 4n

### 4n-rac



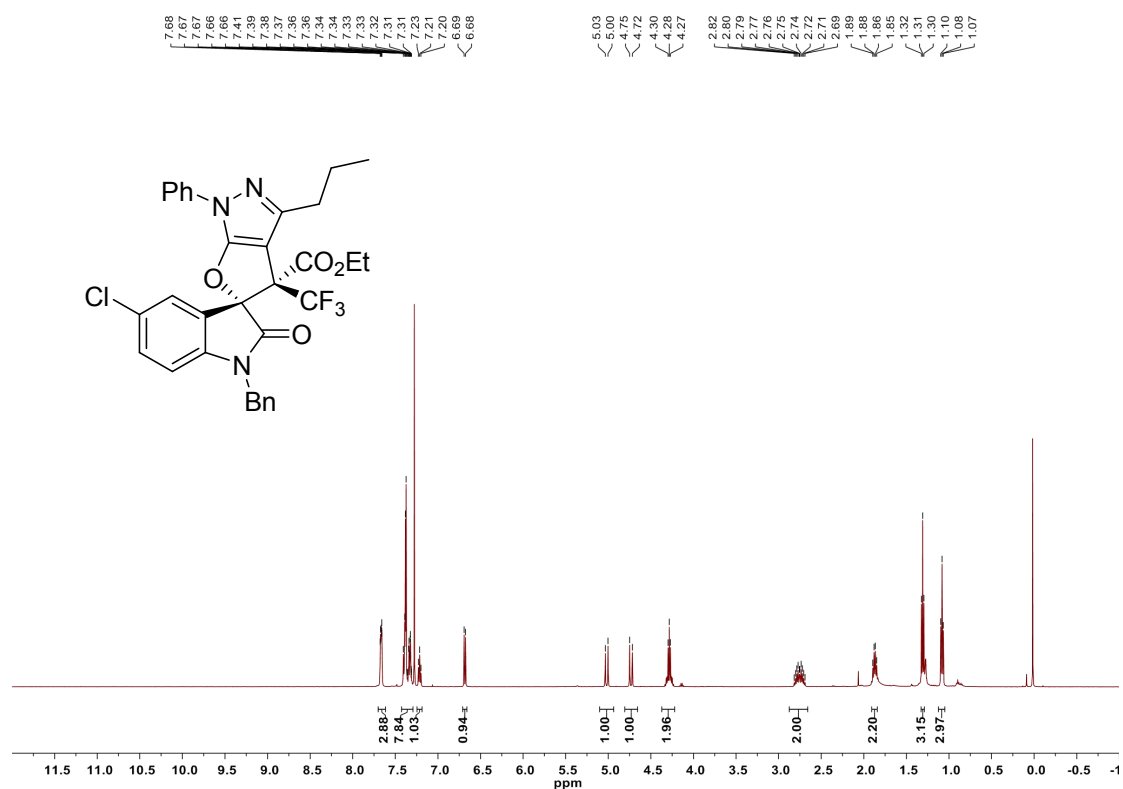
#	Start time[min]	Time[min]	End time[min]	Area%
1	12.315	12.932	14.010	50.831
2	14.924	14.546	17.037	49.169

### 4n-chr

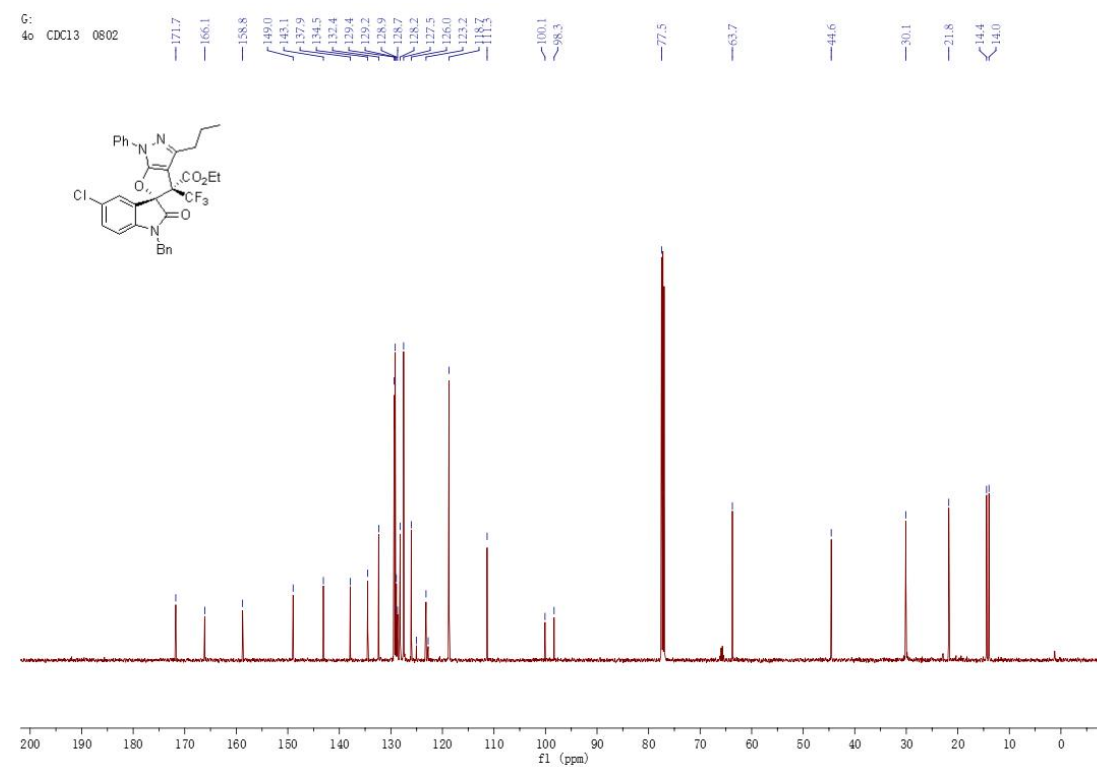


#	Start time[min]	Time[min]	End time[min]	Area%
1	11.359	11.932	12.995	97.475
2	13.939	14.386	14.930	2.525

**<sup>1</sup>H NMR spectrum of 4o (CDCl<sub>3</sub>, 500 MHz)**

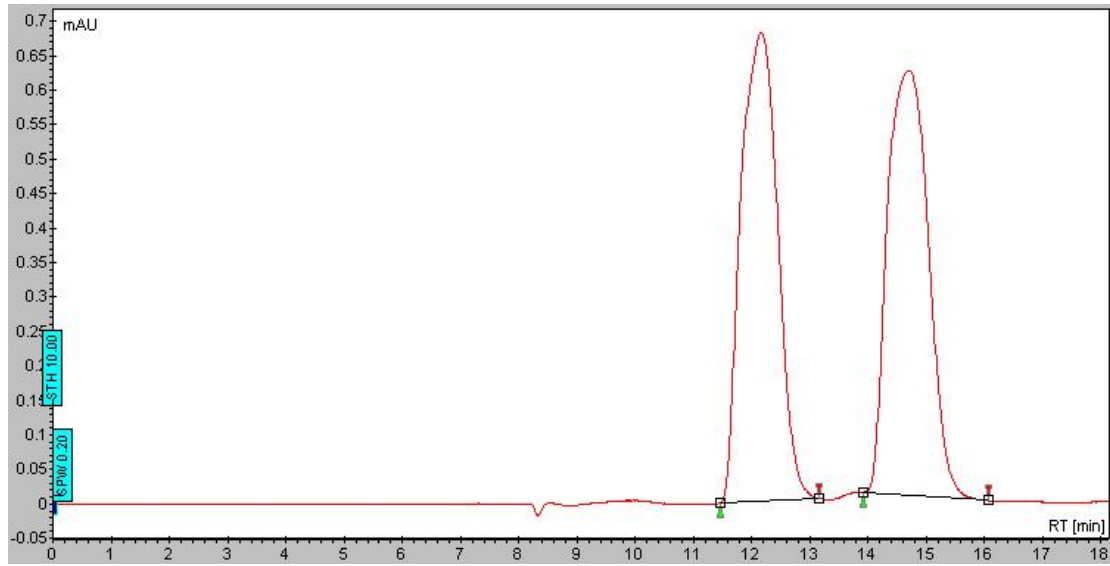


**<sup>13</sup>C NMR spectrum of 4o (CDCl<sub>3</sub>, 125 MHz)**



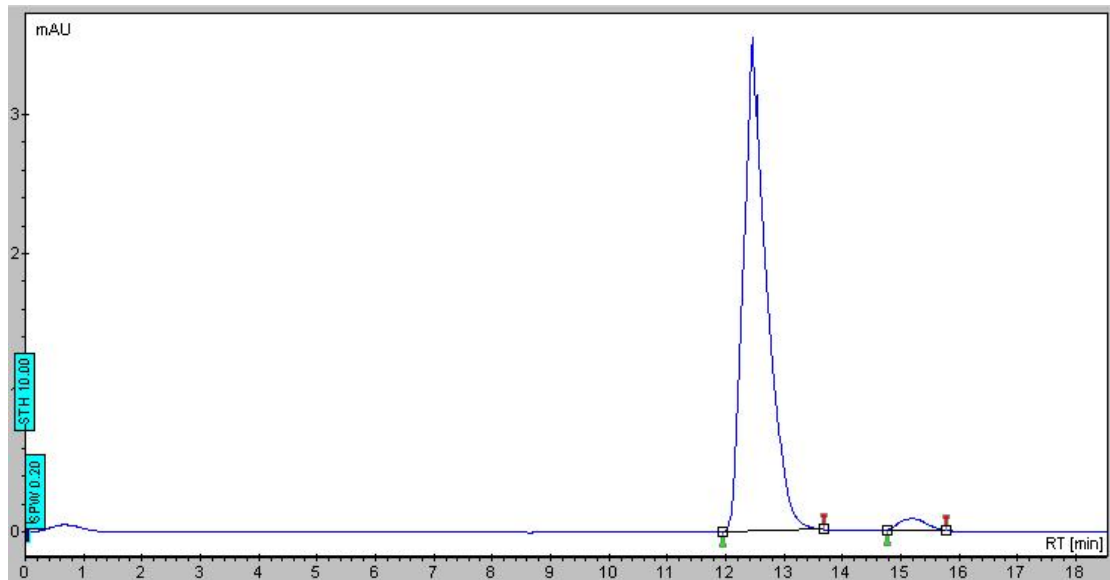
## HPLC chromatograms of 4o

### 4o-rac



#	Start time[min]	Time[min]	End time[min]	Area%
1	11.465	12.159	13.161	49.732
2	13.920	14.706	16.071	50.268

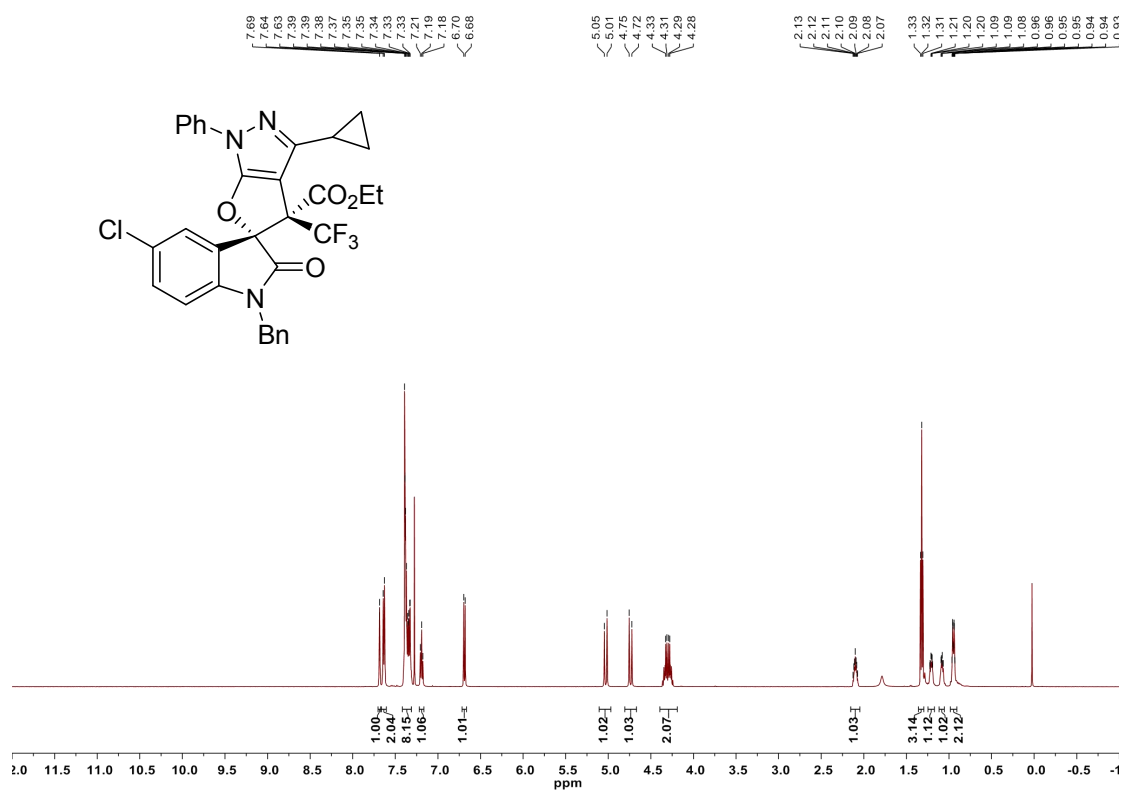
### 4o-chr



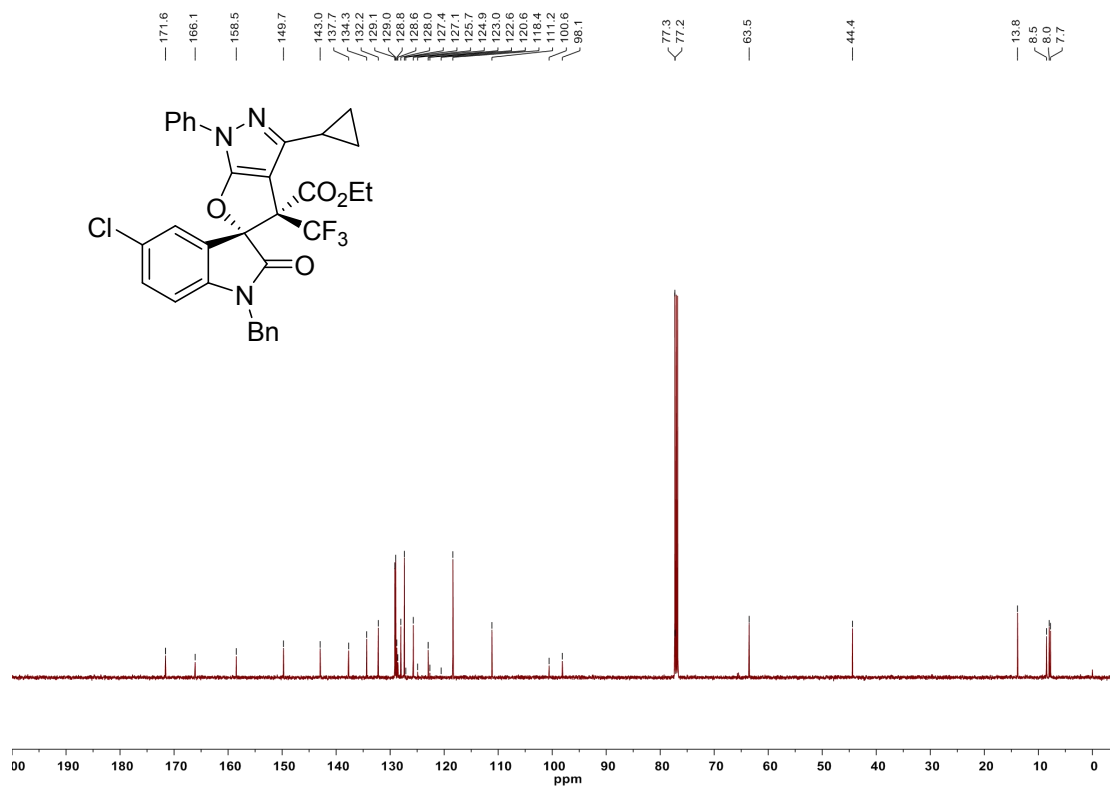
#	Start time[min]	Time[min]	End time[min]	Area%
1	11.951	12.466	13.684	97.335
2	14.770	15.186	15.779	2.665



### <sup>1</sup>H NMR spectrum of 4p (CDCl<sub>3</sub>, 500 MHz)

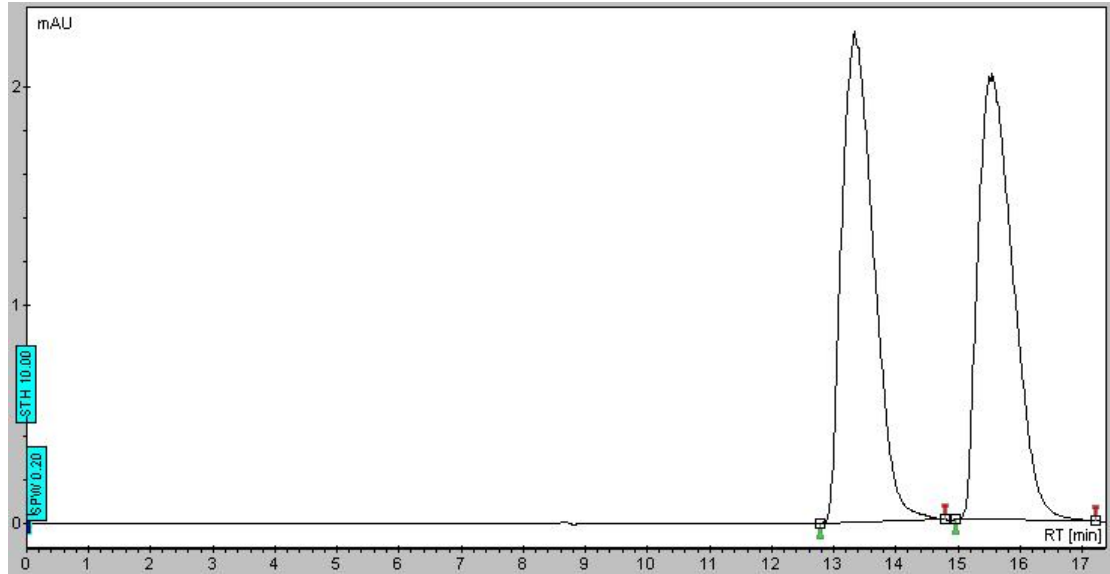


### <sup>13</sup>C NMR spectrum of 4p (CDCl<sub>3</sub>, 125 MHz)



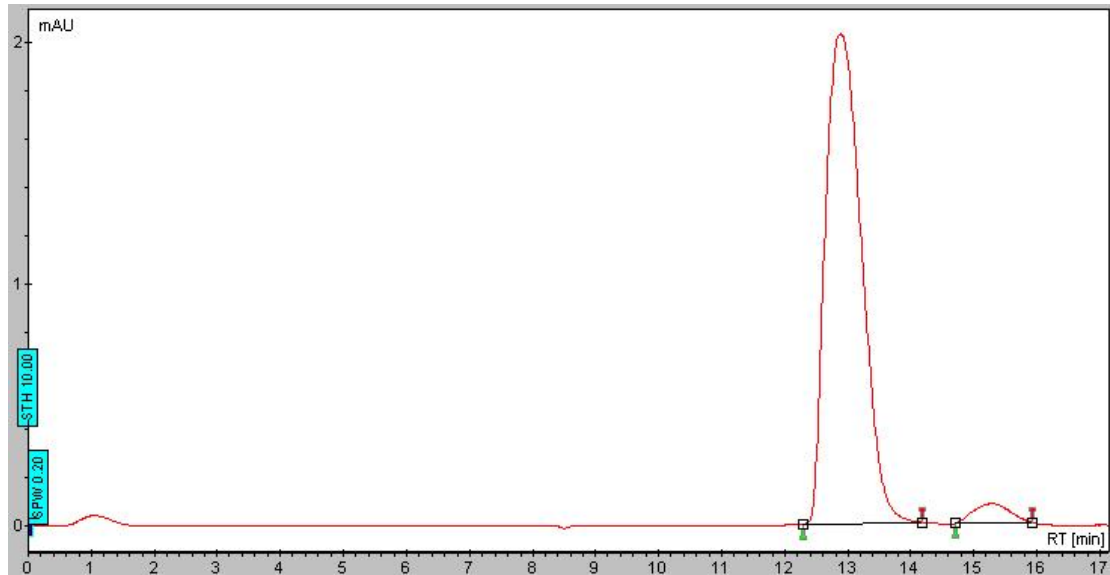
## HPLC chromatograms of 4p

### 4p-rac



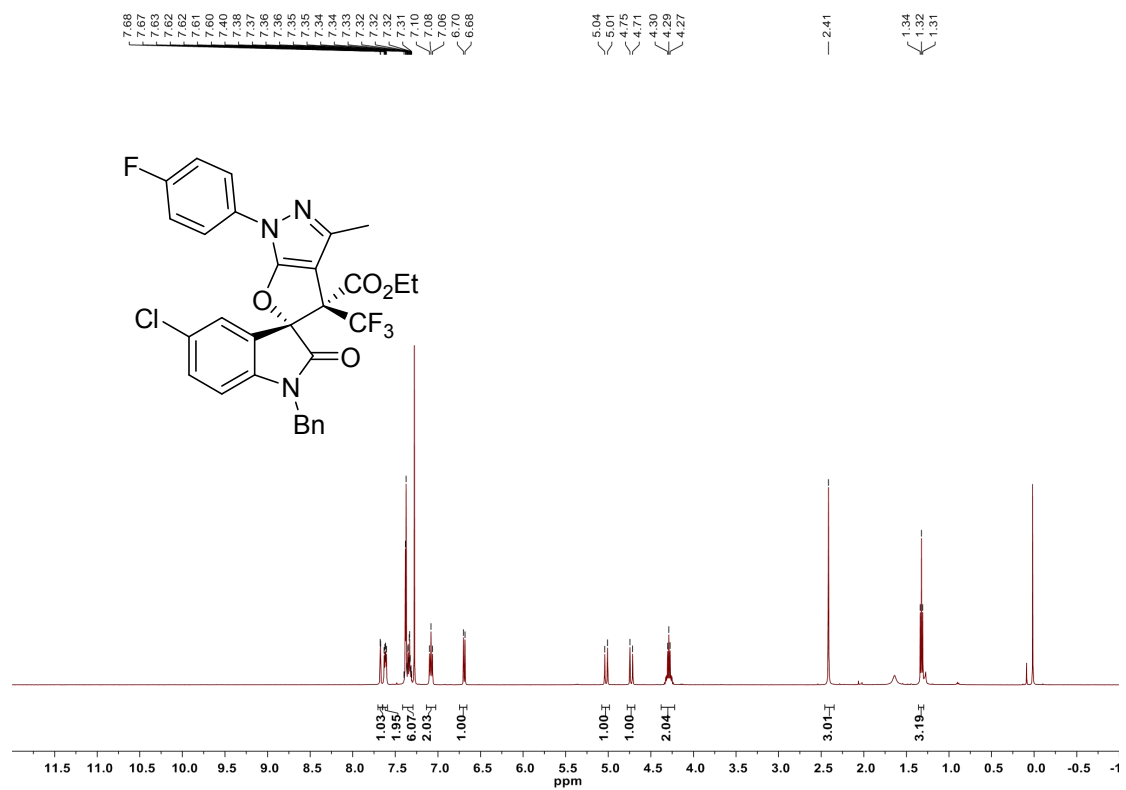
#	Start time[min]	Time[min]	End time[min]	Area%
1	12.779	13.332	14.792	50.036
2	14.962	15.532	17.217	49.964

### 4p-chr

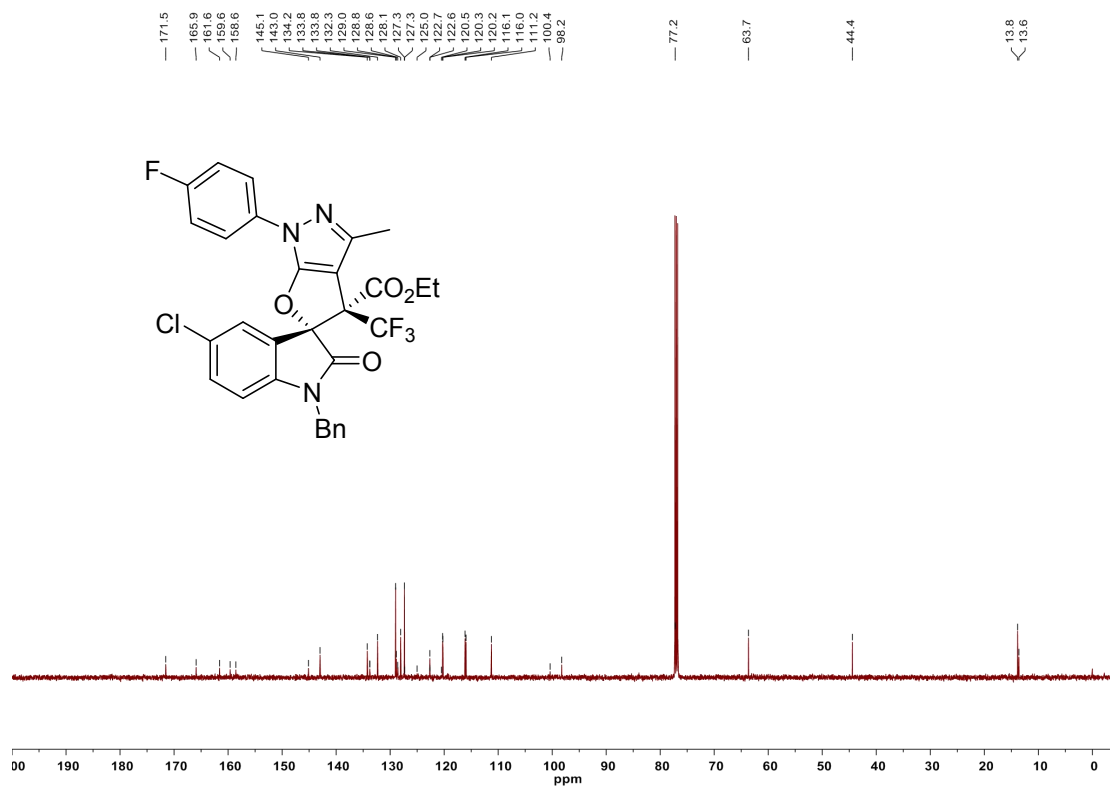


#	Start time[min]	Time[min]	End time[min]	Area%
1	12.292	12.892	14.181	96.150
2	14.707	15.292	15.927	3.850

### <sup>1</sup>H NMR spectrum of 4q (CDCl<sub>3</sub>, 500 MHz)

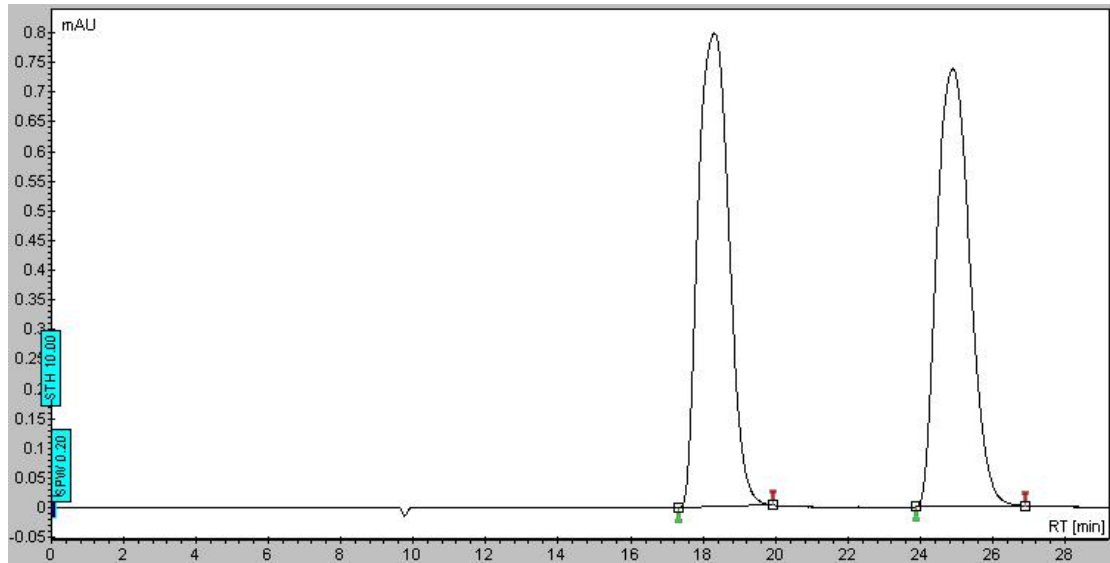


### <sup>13</sup>C NMR spectrum of 4q (CDCl<sub>3</sub>, 125 MHz)



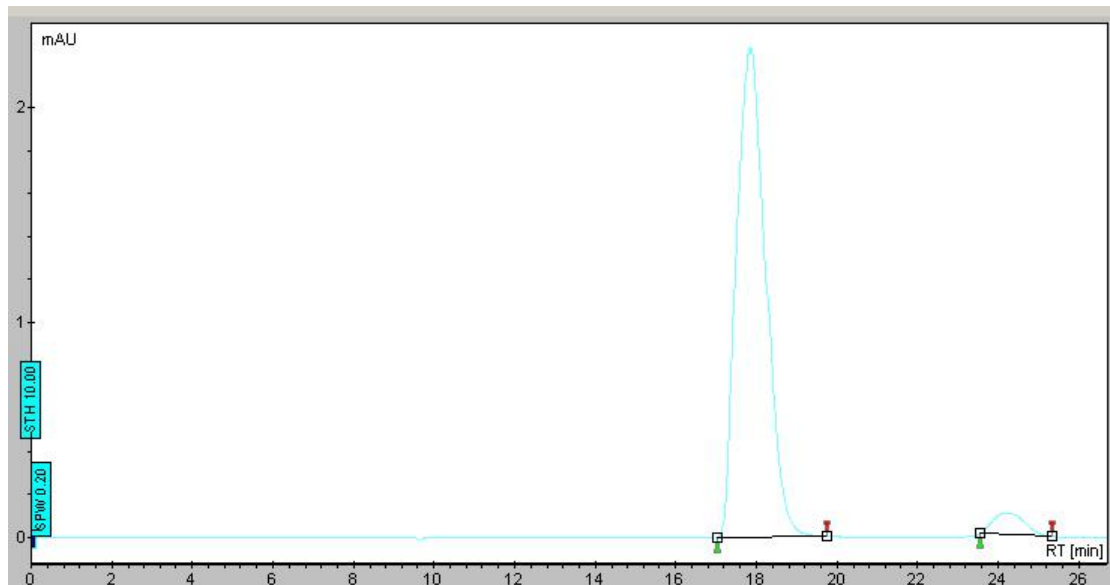
## HPLC chromatograms of 4q

### 4q-rac



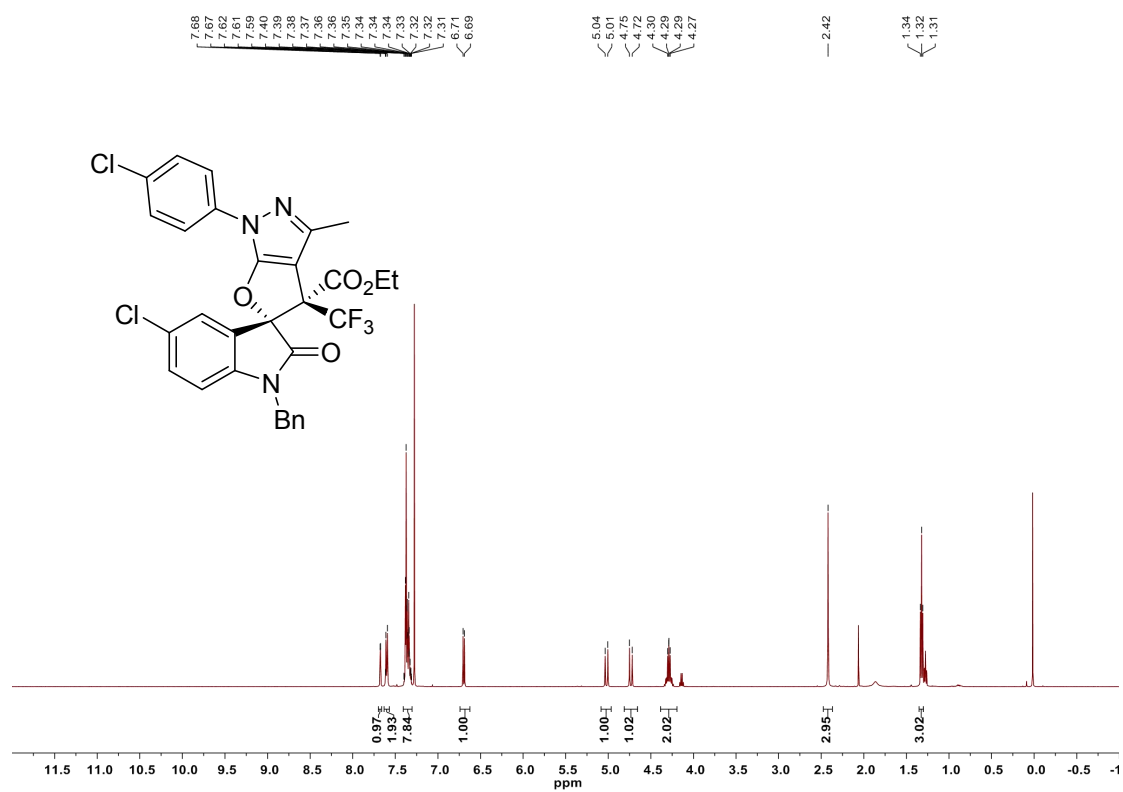
#	Start time[min]	Time[min]	End time[min]	Area%
1	17.324	18.319	19.933	50.131
2	23.887	24.905	26.903	49.869

### 4q-chr

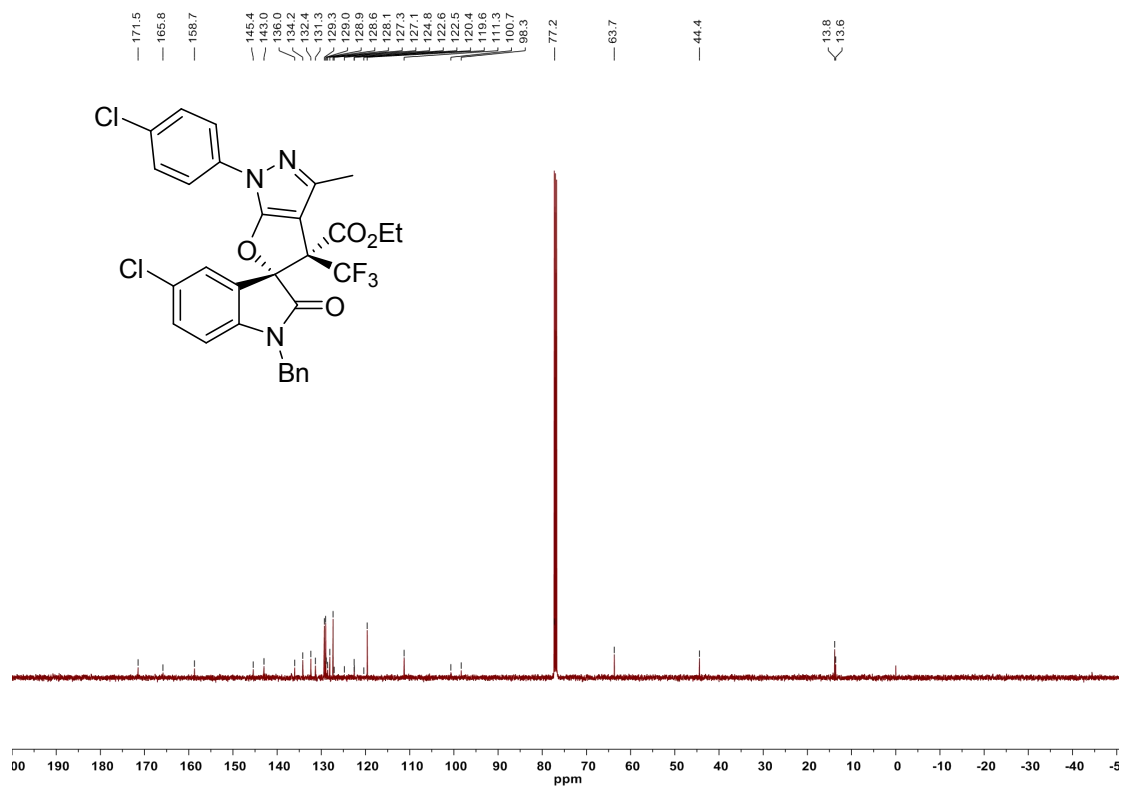


#	Start time[min]	Time[min]	End time[min]	Area%
1	17.031	17.852	19.751	95.337
2	23.552	24.252	25.341	4.663

### <sup>1</sup>H NMR spectrum of 4r (CDCl<sub>3</sub>, 500 MHz)

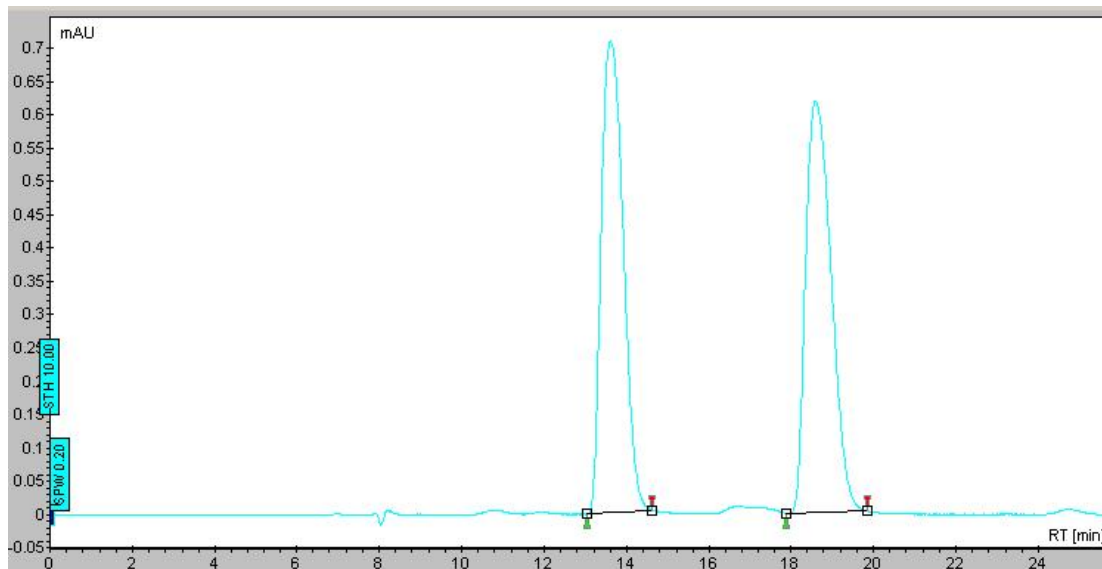


### <sup>13</sup>C NMR spectrum of 4r (CDCl<sub>3</sub>, 125 MHz)



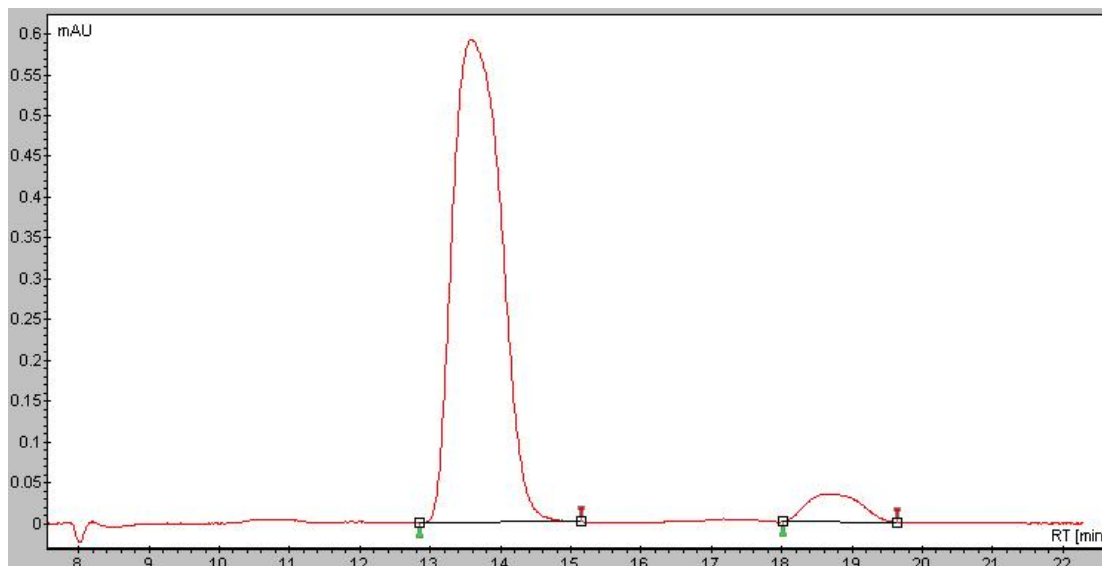
## HPLC chromatograms of 4r

### 4r-rac



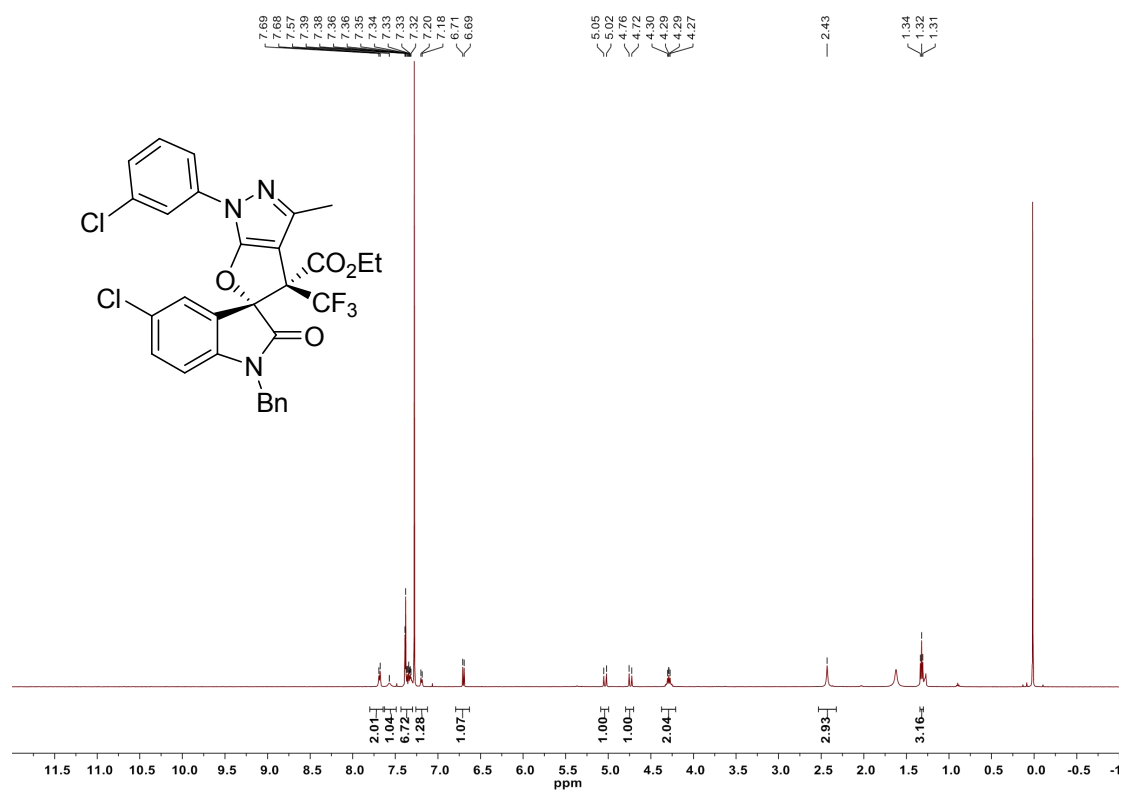
#	Start time[min]	Time[min]	End time[min]	Area%
1	13.039	13.612	14.615	49.700
2	17.875	18.585	19.845	50.300

### 4r-chr

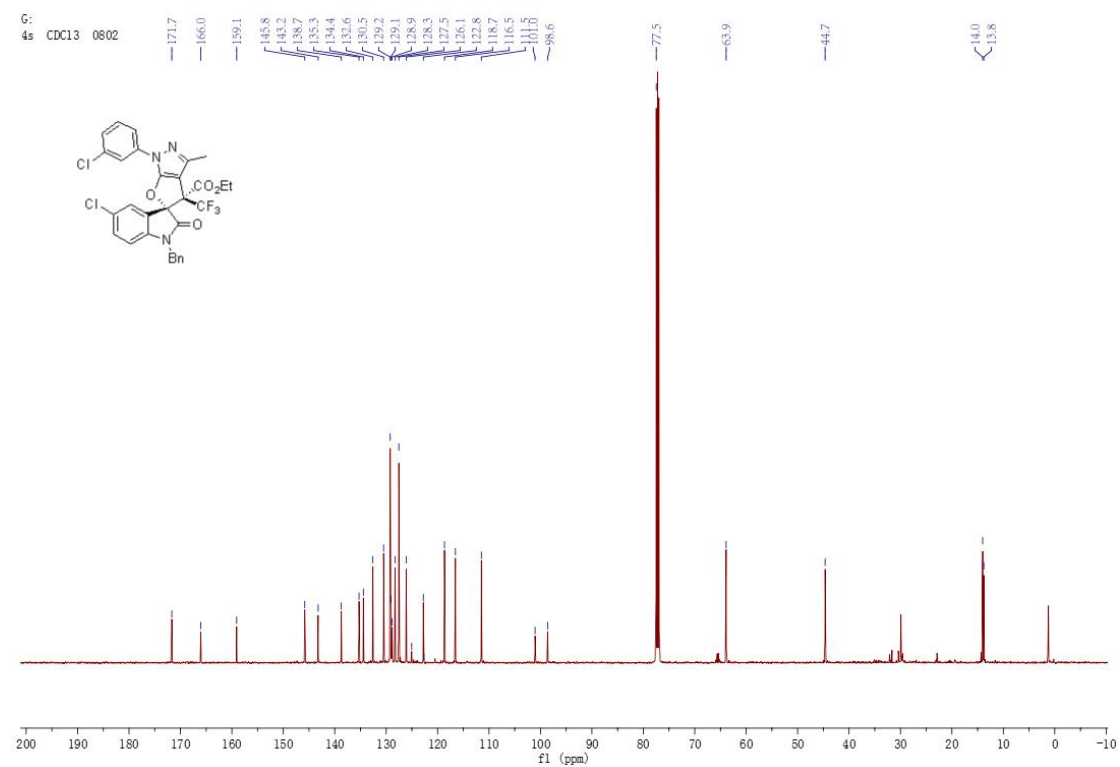


#	Start time[min]	Time[min]	End time[min]	Area%
1	12.839	13.586	15.146	93.928
2	18.025	18.639	19.636	6.072

### <sup>1</sup>H NMR spectrum of 4s (CDCl<sub>3</sub>, 500 MHz)

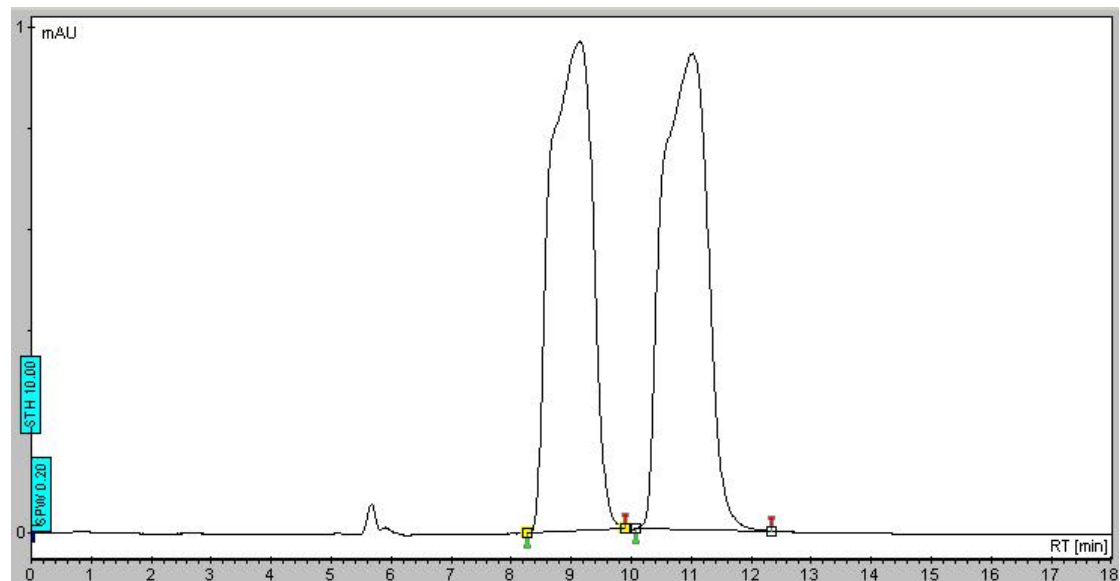


### <sup>13</sup>C NMR spectrum of 4s (CDCl<sub>3</sub>, 125 MHz)



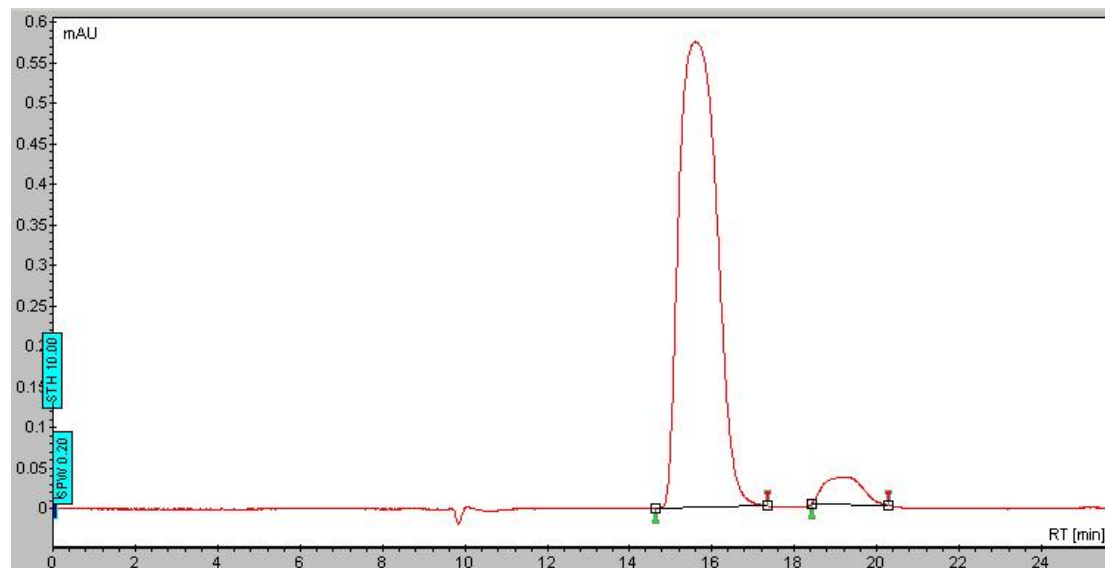
## HPLC chromatograms of 4s

### 4s-rac



#	Start time[min]	Time[min]	End time[min]	Area%
1	8.266	9.146	9.899	49.042
2	10.074	11.026	12.335	50.958

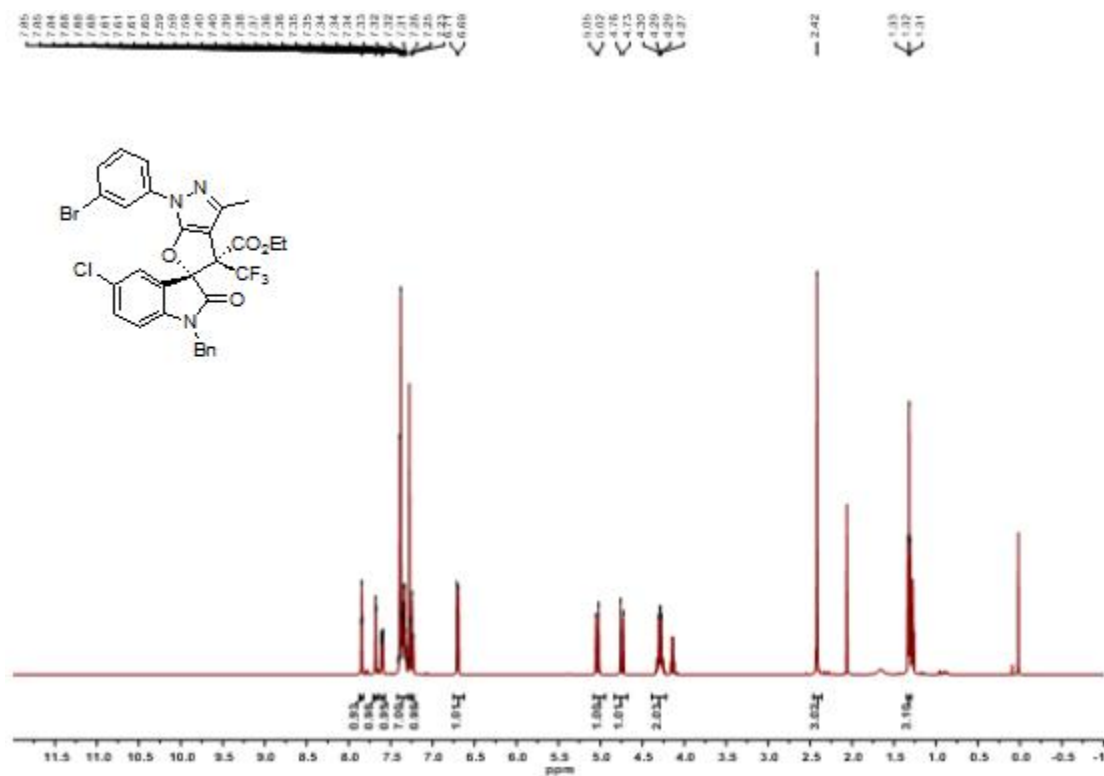
### 4s-chr



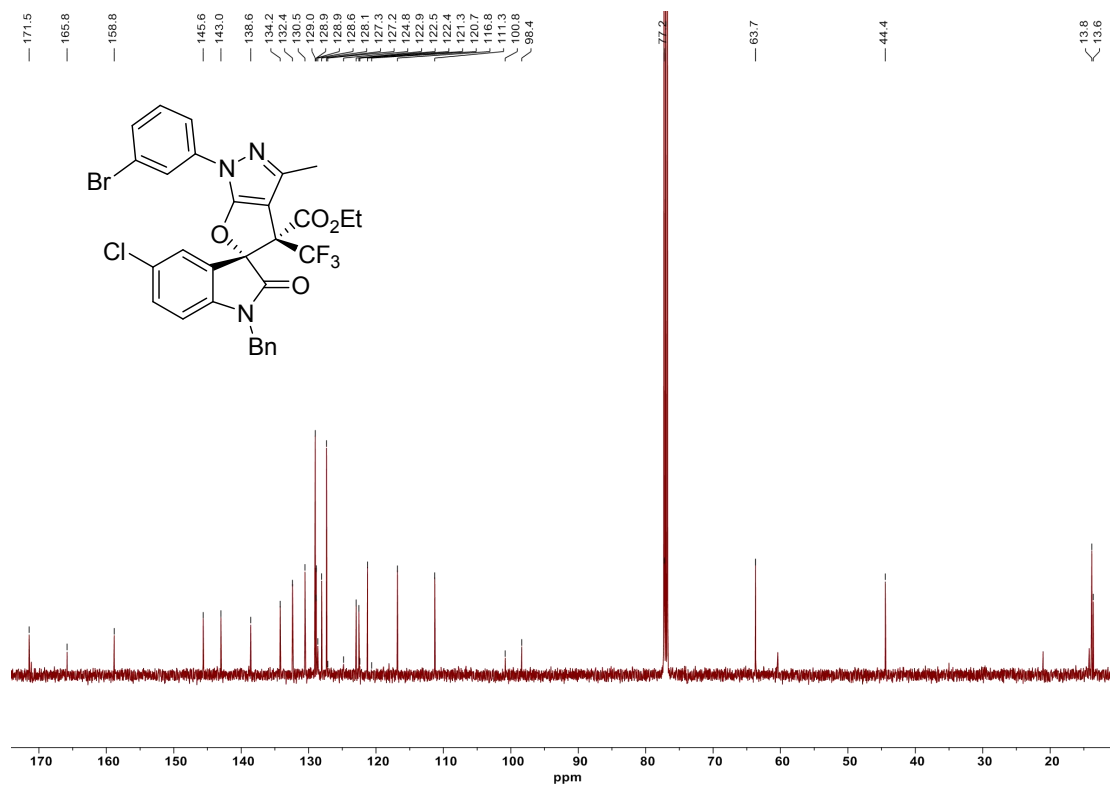
#	Start time[min]	Time[min]	End time[min]	Area%
1	14.626	15.599	17.344	94.342
2	18.416	19.279	20.276	5.658



### $^1\text{H}$ NMR spectrum of 4t ( $\text{CDCl}_3$ , 500 MHz)

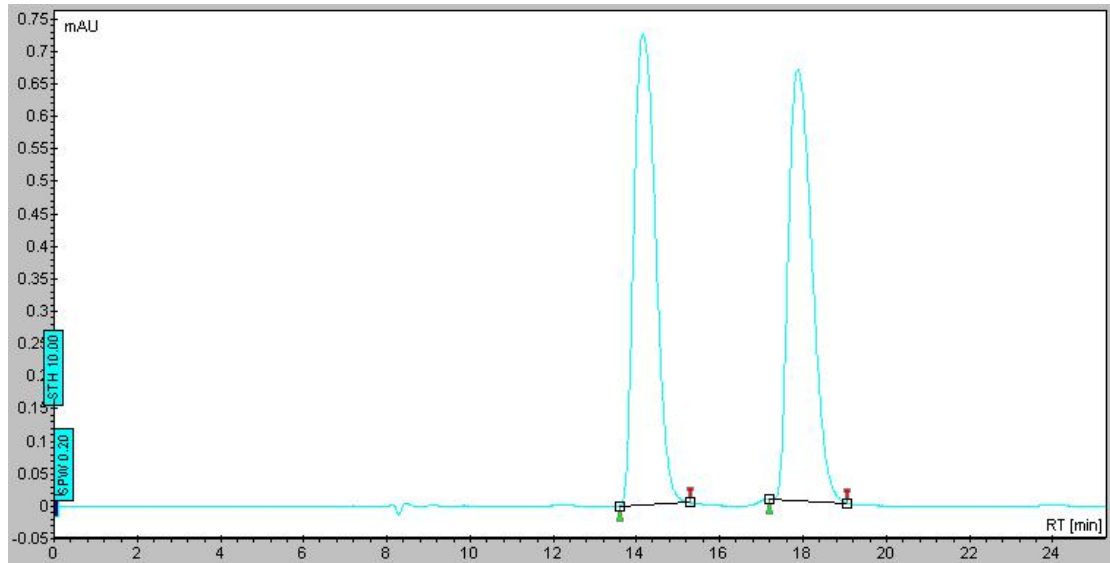


### $^{13}\text{C}$ NMR spectrum of 4t ( $\text{CDCl}_3$ , 125 MHz)



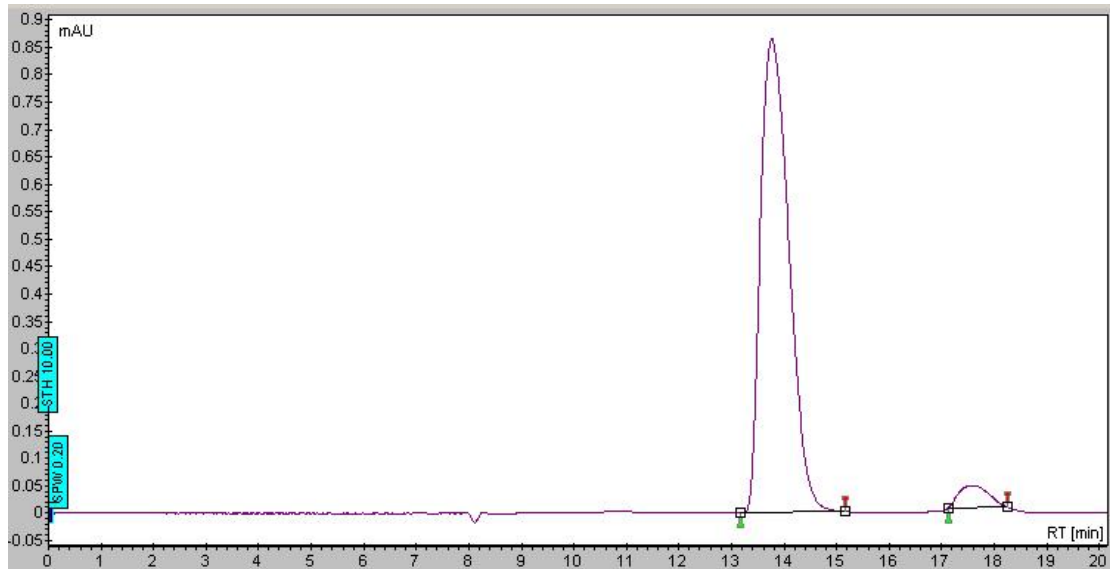
## HPLC chromatograms of 4t

### 4t-rac



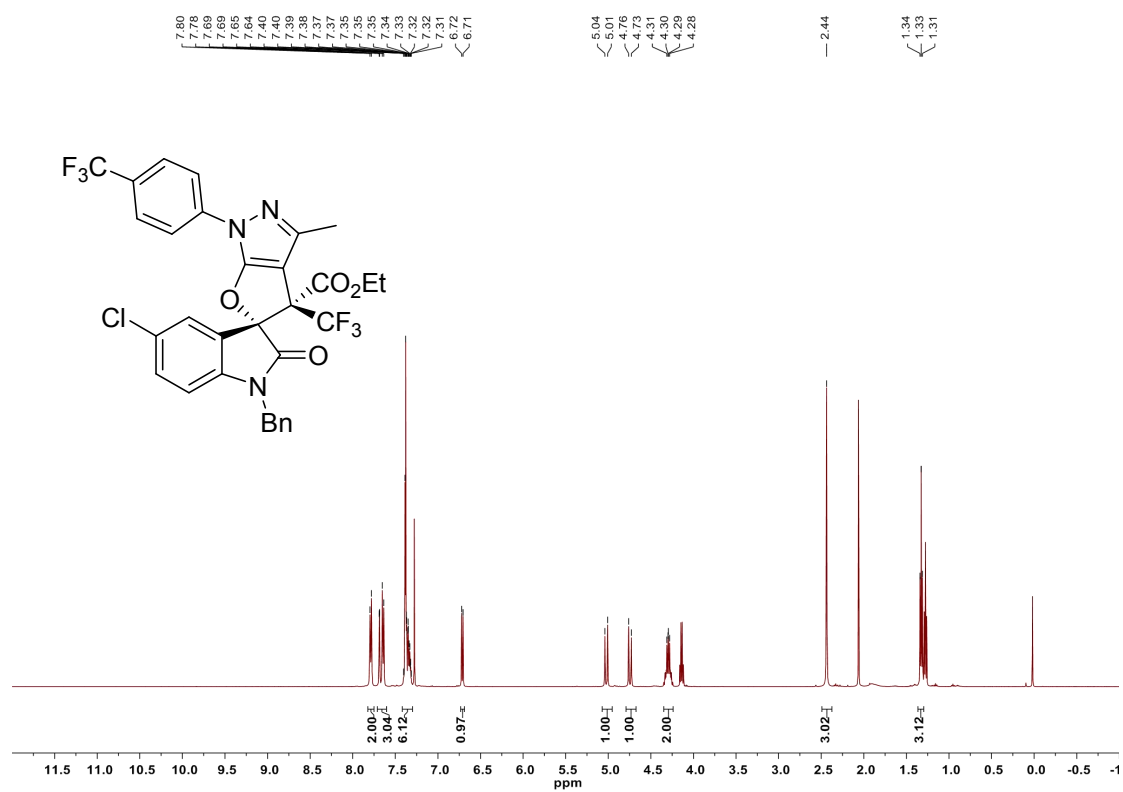
#	Start time[min]	Time[min]	End time[min]	Area%
1	13.598	14.146	15.289	50.108
2	17.191	17.892	19.058	49.892

### 4t-chr

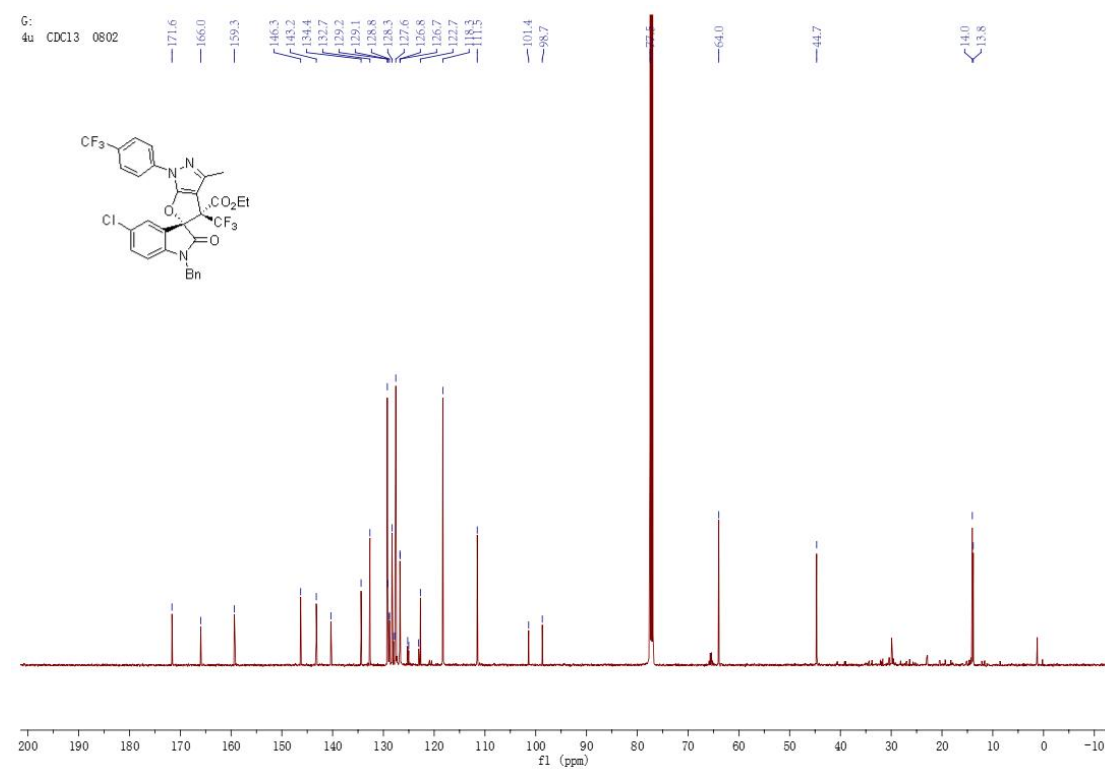


#	Start time[min]	Time[min]	End time[min]	Area%
1	13.169	13.759	15.162	95.348
2	17.128	17.559	18.251	4.652

### <sup>1</sup>H NMR spectrum of 4u (CDCl<sub>3</sub>, 500 MHz)

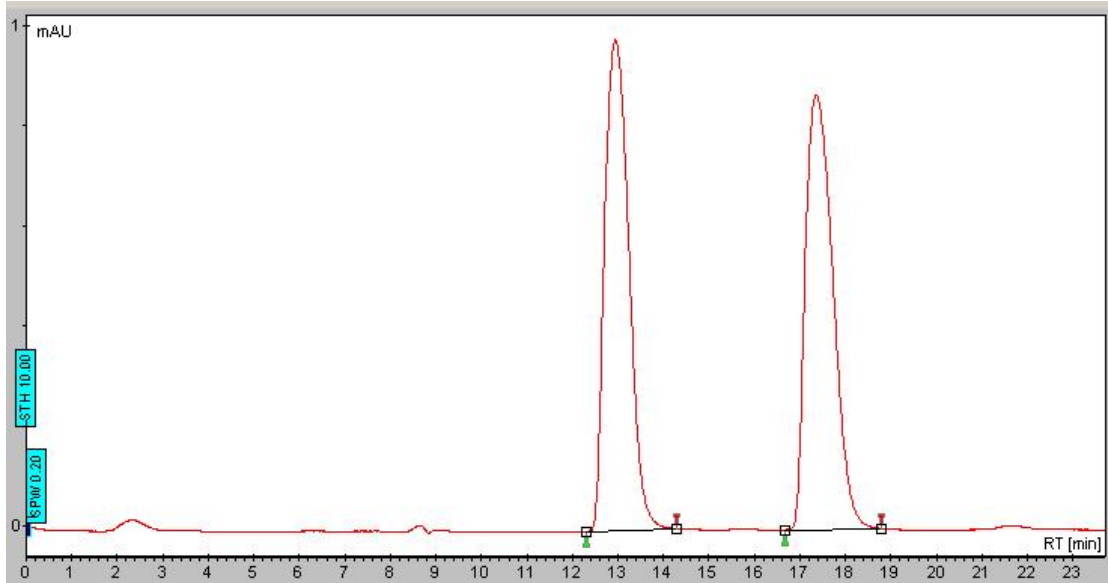


### <sup>13</sup>C NMR spectrum of 4u (CDCl<sub>3</sub>, 125 MHz)



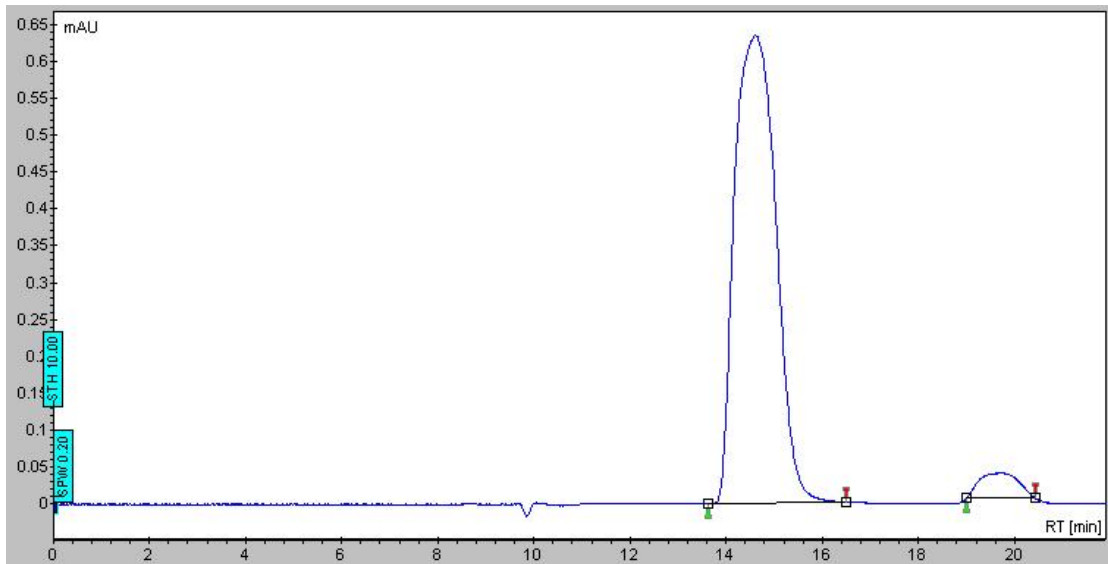
## HPLC chromatograms of 4u

### 4u-rac



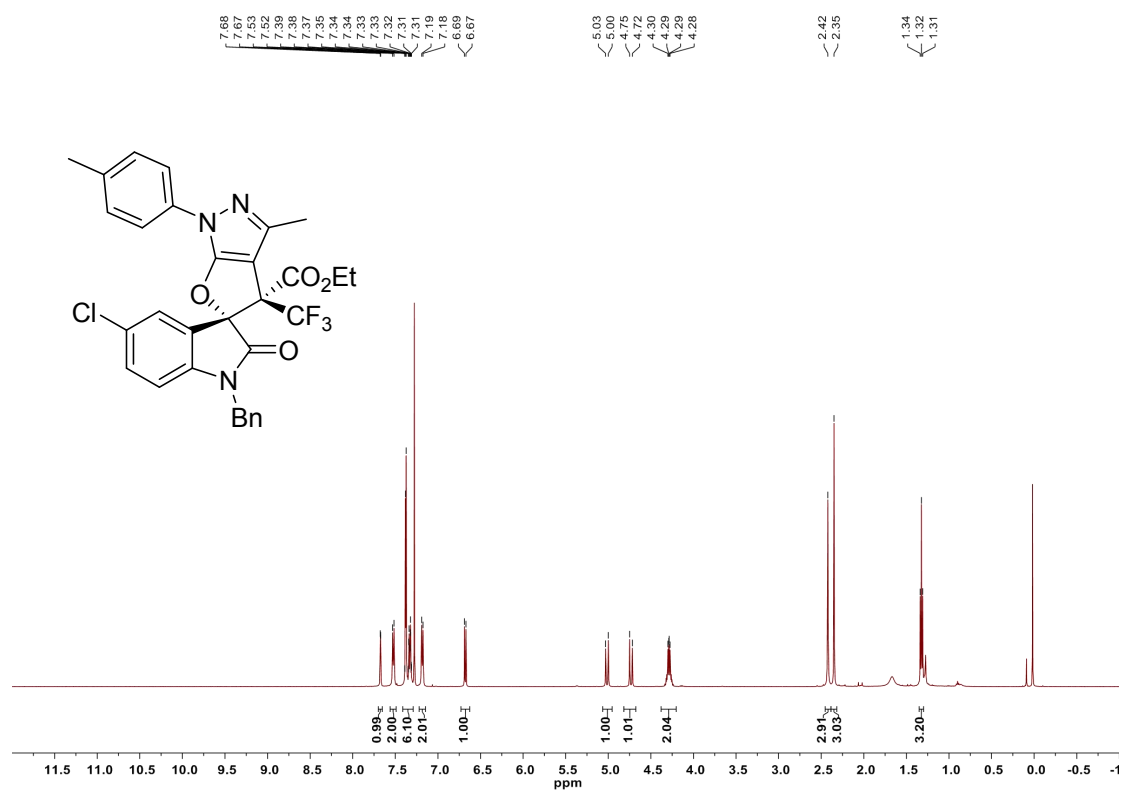
#	Start time[min]	Time[min]	End time[min]	Area%
1	12.307	12.946	14.292	49.711
2	16.673	17.345	18.791	50.289

### 4u-chr

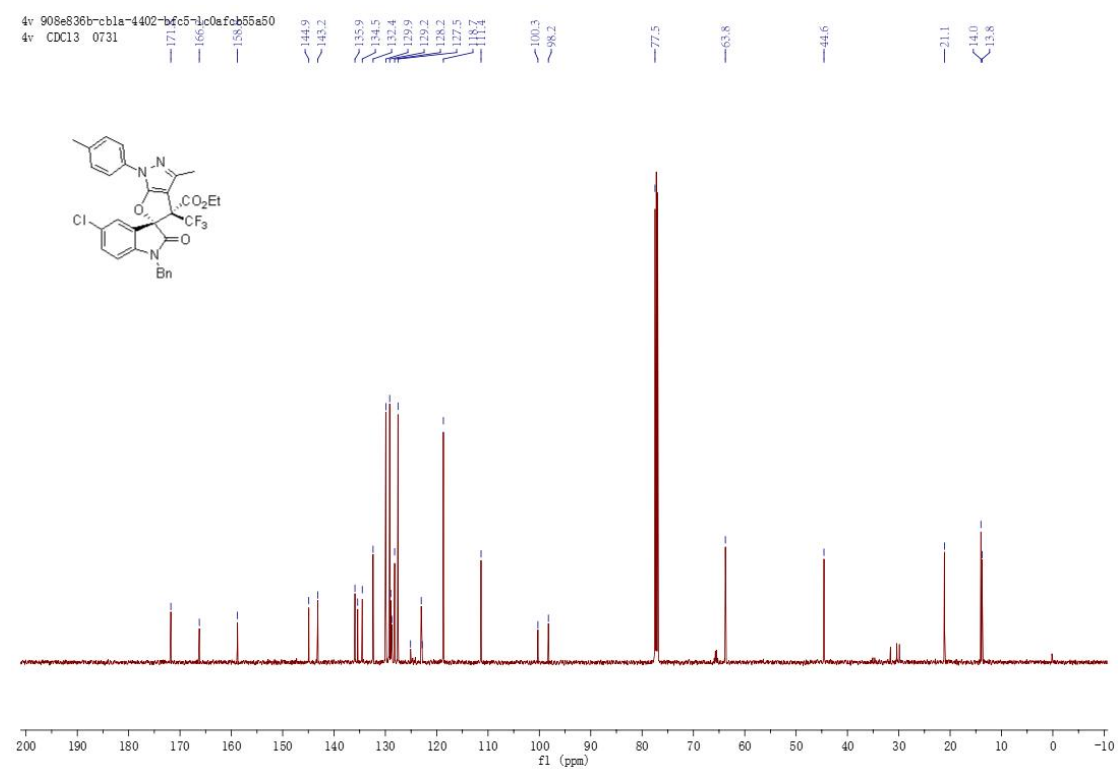


#	Start time[min]	Time[min]	End time[min]	Area%
1	13.627	14.599	16.499	95.117
2	19.004	19.732	20.440	4.883

### <sup>1</sup>H NMR spectrum of 4v (CDCl<sub>3</sub>, 500 MHz)

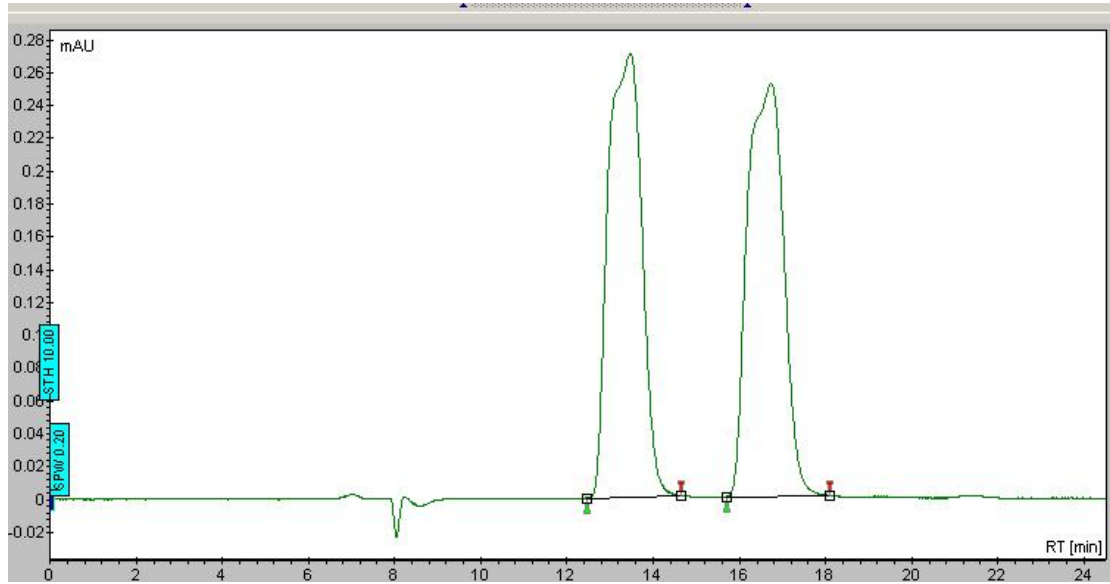


### <sup>13</sup>C NMR spectrum of 4v (CDCl<sub>3</sub>, 125 MHz)



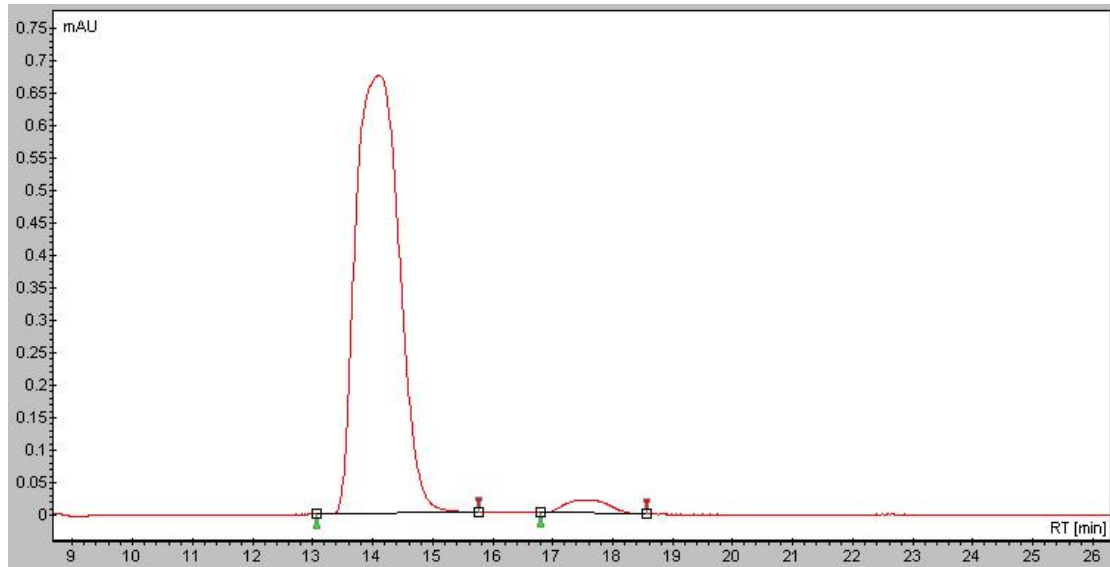
## HPLC chromatograms of 4v

### 4v-rac



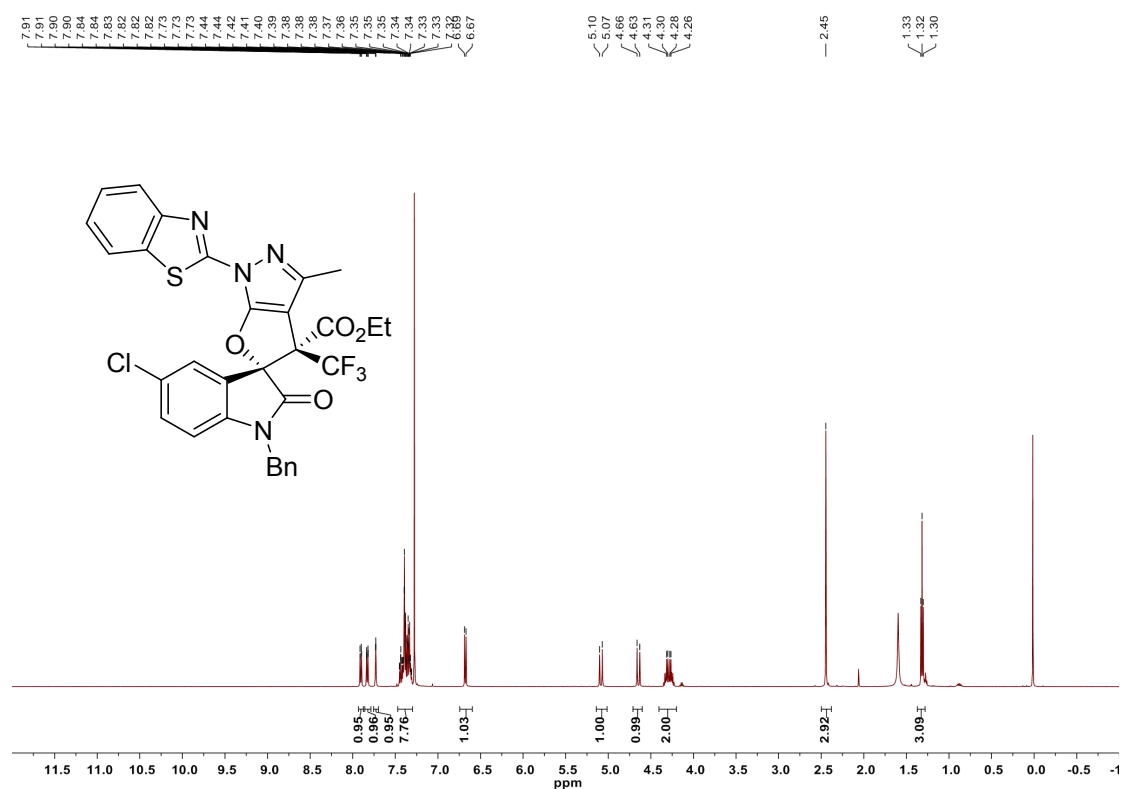
#	Start time[min]	Time[min]	End time[min]	Area%
1	12.465	13.466	14.651	50.040
2	15.709	16.732	18.100	49.960

### 4v-chr

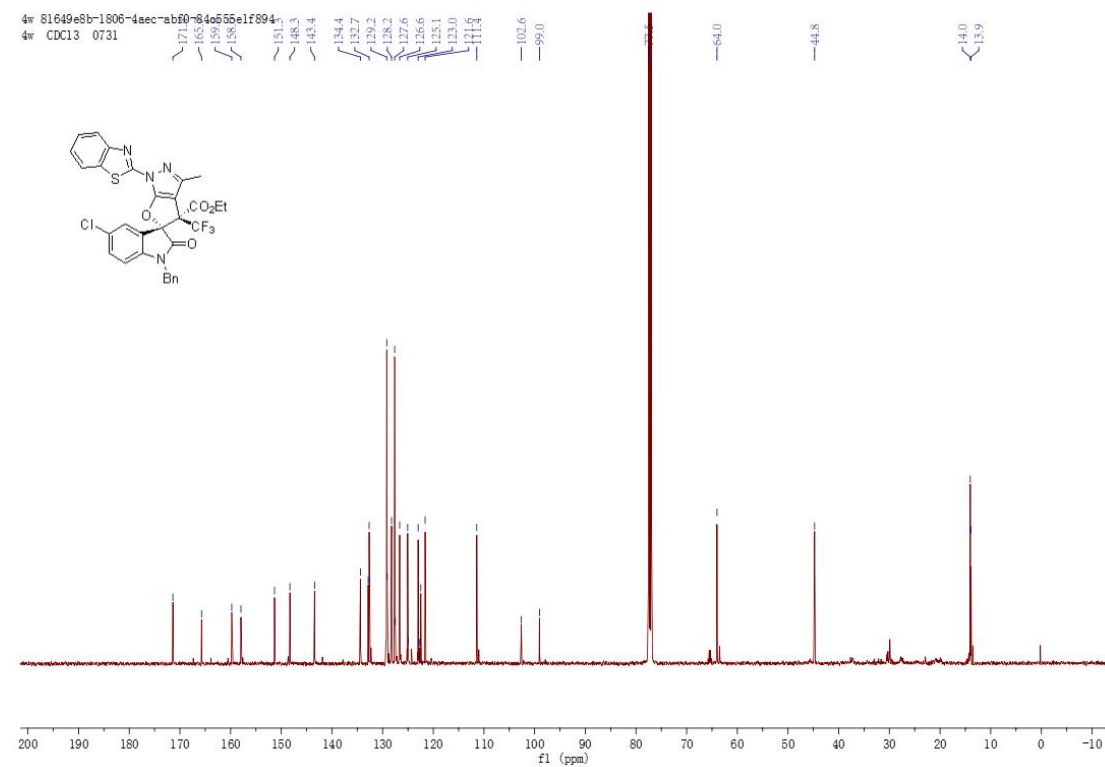


#	Start time[min]	Time[min]	End time[min]	Area%
1	13.065	14.106	15.756	96.993
2	16.802	17.625	18.563	3.007

**<sup>1</sup>H NMR spectrum of 4w (CDCl<sub>3</sub>, 500 MHz)**

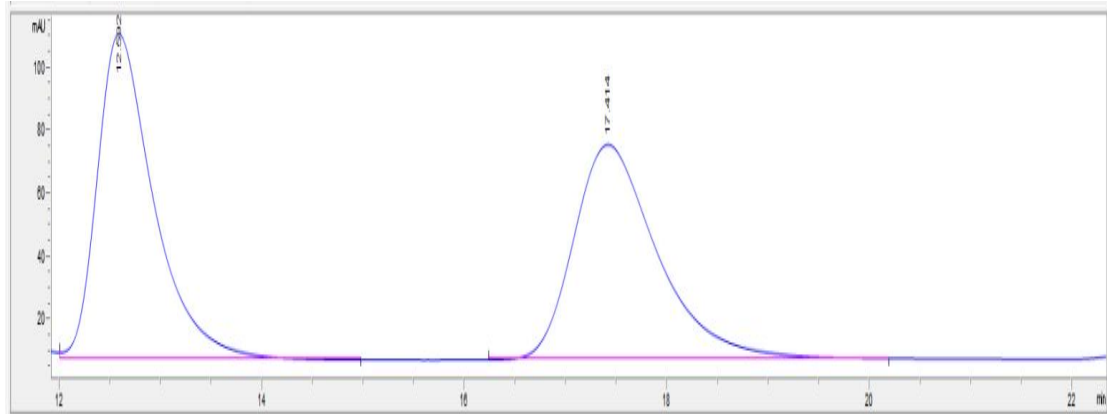


**<sup>13</sup>C NMR spectrum of 4w (CDCl<sub>3</sub>, 125 MHz)**



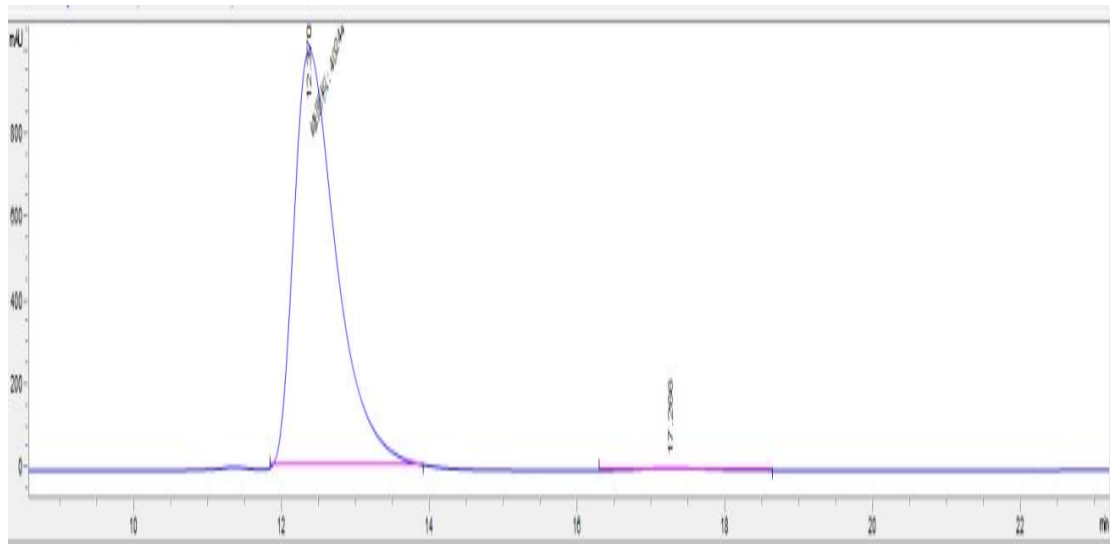
## HPLC chromatograms of 4w

### 4w-rac



#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.592	4048.7	103.8	0.5809	0.581	50.724	VB
2	17.414	3933.1	68.4	0.8687	0.652	49.276	BB

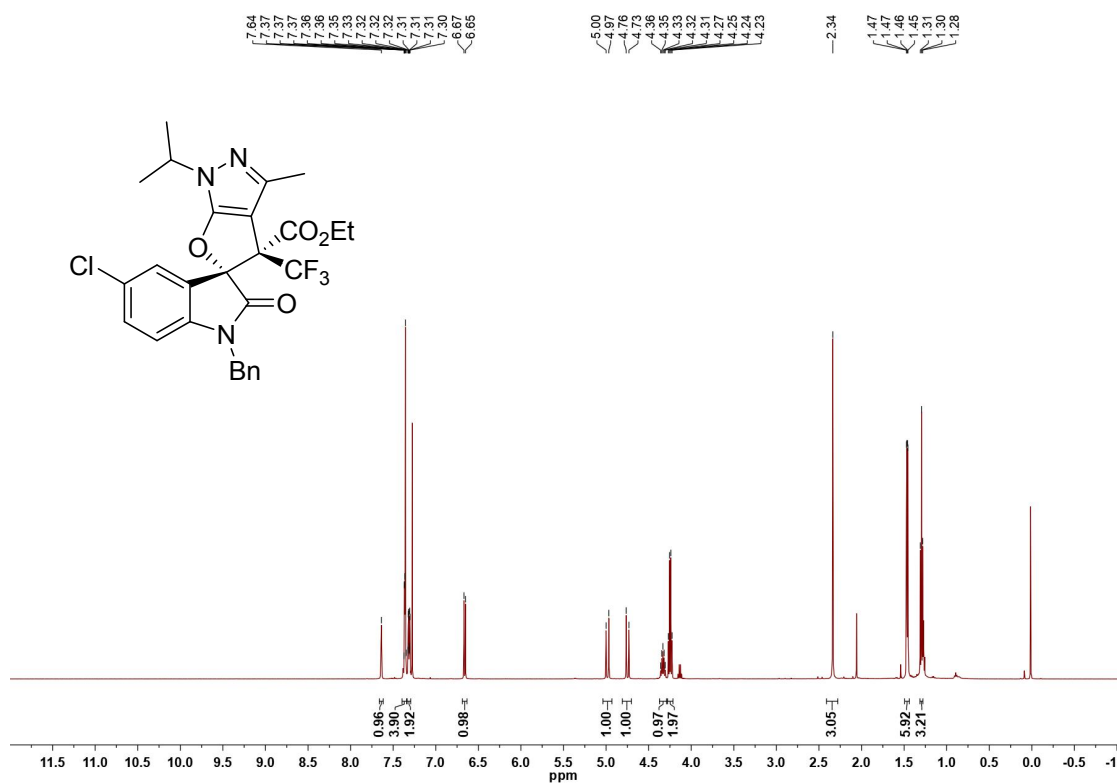
### 4w-chr



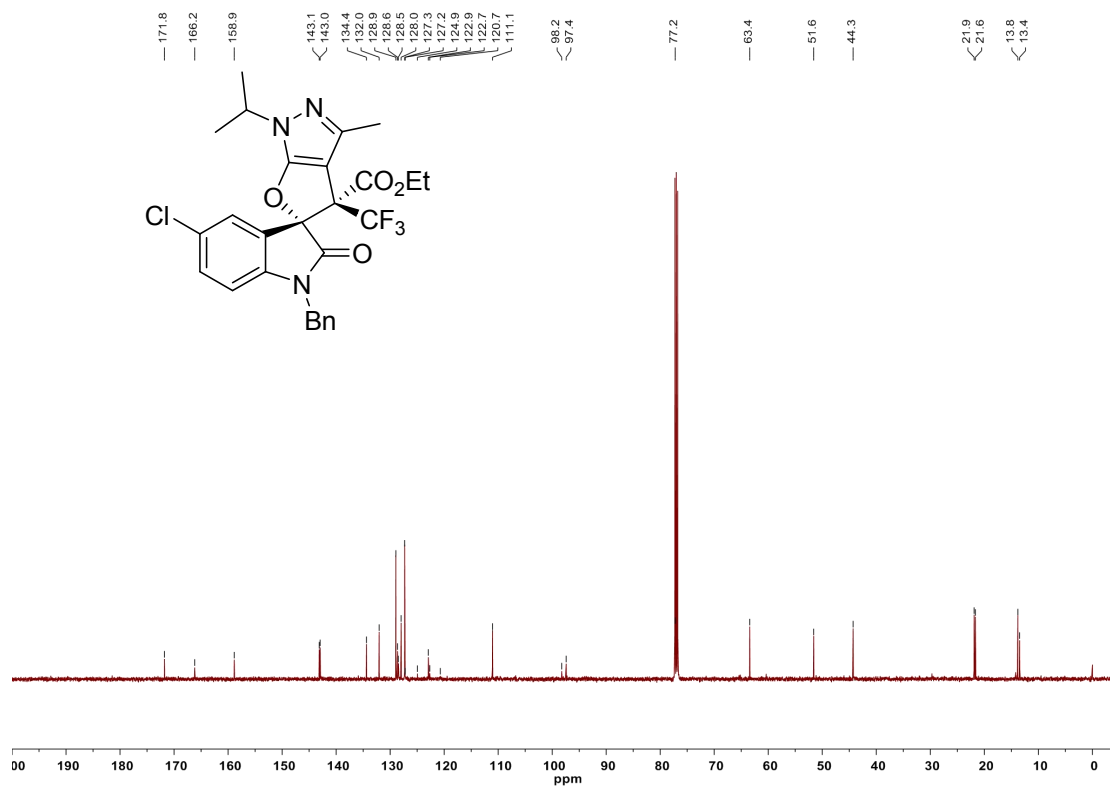
#	时间	峰面积	峰高	峰宽	对称因子	峰面积 %	类型
1	12.37	40244	1002	0.6694	0.545	99.196	MM
2	17.266	326.1	5.8	0.6617	0.808	0.804	BB



**<sup>1</sup>H NMR spectrum of 4x (CDCl<sub>3</sub>, 500 MHz)**

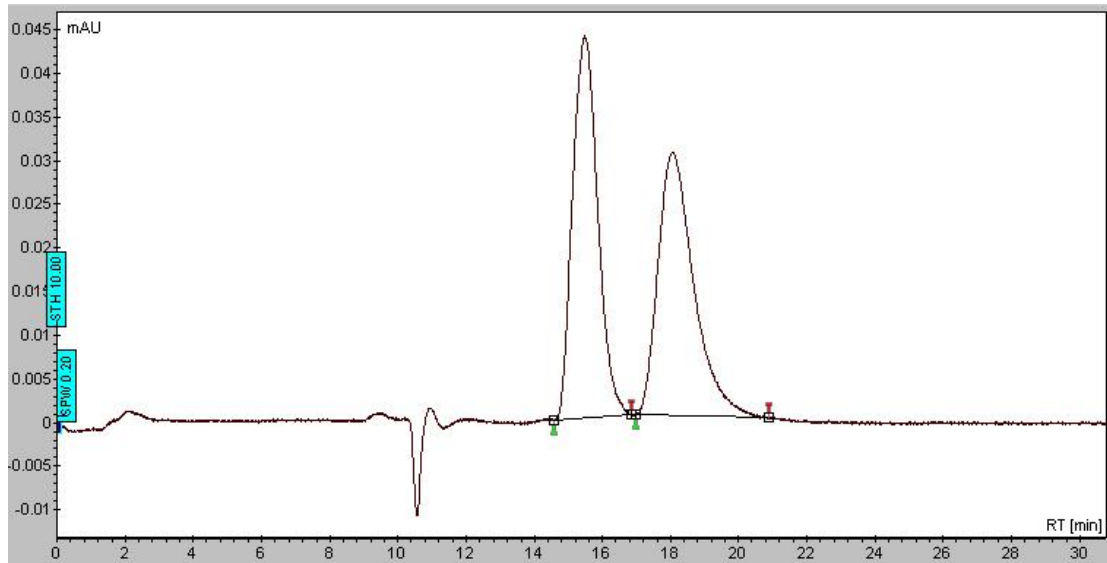


**<sup>13</sup>C NMR spectrum of 4x (CDCl<sub>3</sub>, 125 MHz)**



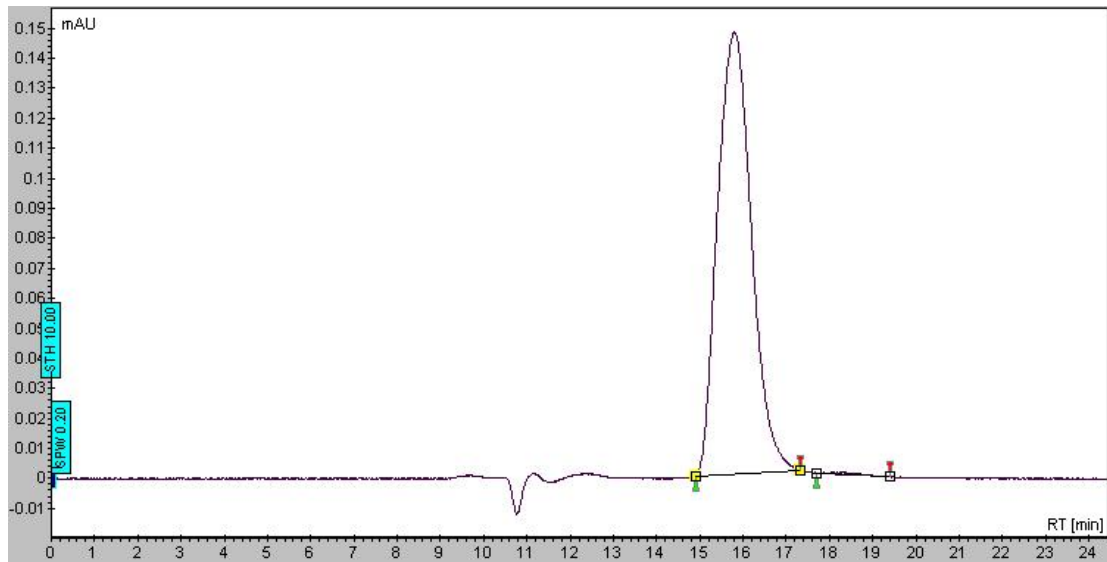
## HPLC chromatograms of 4x

### 4x-rac



#	Start time[min]	Time[min]	End time[min]	Area%
1	14.579	15.492	16.851	50.496
2	16.980	18.065	20.882	49.504

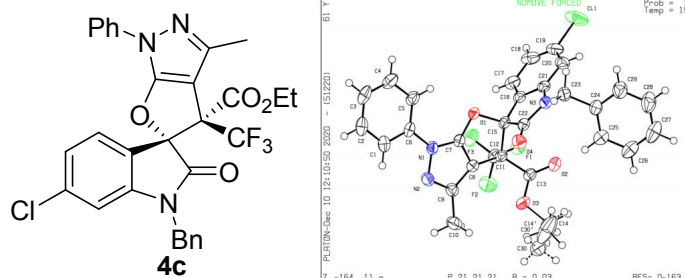
### 4x-chr



#	Start time[min]	Time[min]	End time[min]	Area%
1	14.909	15.799	17.326	99.705
2	17.700	18.359	19.402	0.295

## 6. X-ray crystal structure of the compound **4c**

Suitable crystals of enantiopure **4c** for X-ray analysis were obtained from crystallization in CH<sub>2</sub>Cl<sub>2</sub>.



The thermal ellipsoids are shown at 50% probability level

**Table S1.** Crystal data and structure refinement parameters of the compound **4c**

Parameter	Value
Formula weight	581.96
Temperature	193(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P212121
Unit cell dimensions	$a = 9.5219(5)$ Å $\alpha = 90^\circ$ $b = 11.5329(6)$ Å $\beta = 90^\circ$ $c = 24.5713(14)$ Å $\gamma = 90^\circ$
Volume	$2698.3(3)$ Å <sup>3</sup>
<i>Z</i>	4
Density (calculated)	1.433 Mg/m <sup>3</sup>
Absorption coefficient	0.205 mm <sup>-1</sup>
<i>F</i> <sub>000</sub>	1200
Crystal size	0.120 x 0.110 x 0.080 mm <sup>3</sup>
Theta range for data collection	1.951° to 27.502° $-11 \leq h \leq 12$
Index ranges	$-14 \leq k \leq 14$ $-28 \leq l \leq 31$
Reflections collected	25178
Independent reflections	6159 [R(int) = 0.0476]
Completeness to theta = 25.242°	99.2 %
Refinement method	Full-matrix least-squares on F <sup>2</sup>

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Data / restraints / parameters	6159 / 6 / 383
Goodness-of-fit on F2	1.030
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0348, \omega R_2 = 0.0824$
R indices (all data)	$R_1 = 0.0400, \omega R_2 = 0.0863$
Absolute structure parameter	0.07(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.196 and -0.239 e.Å <sup>-3</sup>

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