

## Supplementary Information

### Iridium-catalyzed asymmetric [3 + 2] annulation of aromatic ketimines with alkynes *via* C–H activation: Unexpected inversion of the enantioselectivity induced by protic acids

Midori Nagamoto, Daisuke Yamauchi and Takahiro Nishimura\*

*Department of Chemistry, Graduate School of Science, Kyoto University*

*Sakyo, Kyoto 606-8502, Japan*

E-mail: tnishi@kuchem.kyoto-u.ac.jp

#### Contents of Supplementary Information:

|   |             |
|---|-------------|
| 1. General  | S-2         |
| 2. Materials  | S-2         |
| 3. Preparation of hemiaminals <b>1</b> and alkynes <b>2</b>           | S-2 — S-5   |
| 4. General procedure for Scheme 2                                     | S-5         |
| 5. General procedure for Table 1, Scheme 3 and Scheme 4 (Condition A) | S-5 — S-6   |
| 6. General procedure for Table 1, Scheme 3 and Scheme 4 (Condition B) | S-6         |
| 7. Characterization of the products                                   | S-6 — S-16  |
| 8. X-Ray data of (+)- <b>3br</b>                                      | S-17 — S-18 |
| 9. <sup>1</sup> H, <sup>13</sup> C NMR spectra and chiral HPLC charts | S-19 — S-82 |

## 1. General

All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen. NMR spectra were recorded on a JEOL JNM ECA-600 spectrometer (600 MHz for  $^1\text{H}$ , 150 MHz for  $^{13}\text{C}$ ). Chemical shifts are reported in  $\delta$  (ppm) referenced to the residual peaks of  $\text{CDCl}_3$  ( $\delta$  7.26) and  $\text{DMSO}-d_6$  ( $\delta$  2.49) for  $^1\text{H}$  NMR, and  $\text{CDCl}_3$  ( $\delta$  77.00) and  $\text{DMSO}$  ( $\delta$  39.50) for  $^{13}\text{C}$  NMR. The following abbreviations are used; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. High-resolution mass spectra (TOF-MS) were obtained with a Bruker micrOTOF spectrometer. Flash column chromatography was performed with Silica Gel 60 N (spherical, neutral) (Cica-Reagent). Preparative thin-layer chromatography was performed with Silica Gel 60 PF<sub>254</sub> (Merck). Alumina (activated 200) for column chromatography was purchased from Nacalai Tesque.

## 2. Materials

Toluene, dichloromethane, and THF were purified by passing through a neutral alumina column under  $\text{N}_2$ . Chlorobenzene was deaerated and dehydrated over molecular sieves (3Å). Iridium complexes  $[\text{IrCl}(\text{coe})_2]_2$ <sup>1</sup> and  $[\text{Ir}(\text{cod})_2]\text{BF}_4$ <sup>2</sup> were prepared according to the reported procedures.  $\text{NaBAR}_4^{\text{F}}$  was prepared according to the reported procedure.<sup>3</sup>

## 3. Preparation of hemiaminals **1** and alkynes **2**

Compounds **1a** (CAS: 6637-53-2), **1b** (CAS: 1629241-78-6), **1g** (CAS: 87028-38-4), **1h** (CAS: 39127-19-0), **1j** (CAS: 87028-37-3), and **1k** (CAS: 92553-10-1) were prepared according to the reported procedures.<sup>4</sup> Compounds **1c**, **1d**, **1e**, **1f**, and **1i** were prepared according to the procedure for **1b**. Diphenylacetylene (**2m**), 1-phenyl-1-hexyne (**2t**), and 4-octyne (**2u**) were purchased from commercial suppliers and used as received. Alkynes **2n** (CAS: 2789-88-0),<sup>5</sup> **2o** (CAS: 2132-62-9),<sup>5</sup> **2p** (CAS: 119757-51-6),<sup>5</sup> **2q** (CAS: 5216-31-9),<sup>6</sup> **2r** (CAS: 1820-42-4),<sup>6</sup> and **2s** (CAS: 5216-30-8)<sup>6</sup> were prepared according to the reported procedures.

---

1 R. Uson, L. A. Oro and J. A. Cabeza, *Inorg. Synth.*, 1985, **23**, 126.

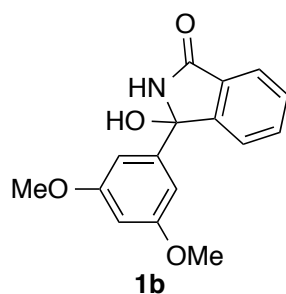
2 T. G. Schenck, J. M. Downes, C. R. C. Milne, P. B. Mackenzie, H. Boucher, J. Whelan and B. Bosnich, *Inorg. Chem.*, 1985, **24**, 2334.

3 M. Brookhart, B. Grant and A. F. Volpe, Jr., *Organometallics*, 1992, **11**, 3920.

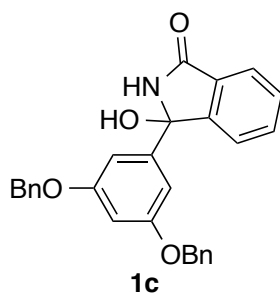
4 T. Nishimura, A. Noishiki, Y. Ebe and T. Hayashi, *Angew. Chem., Int. Ed.*, 2013, **52**, 1777.

5 T. Yamakawa and N. Yoshikai, *Org. Lett.*, 2013, **15**, 196.

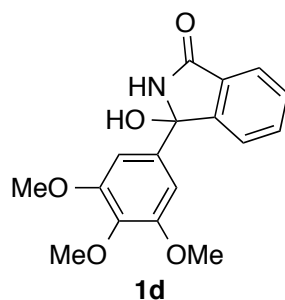
6 K. Park, G. Bae, J. Moon, J. Choe, K. H. Song and S. Lee, *J. Org. Chem.*, 2010, **75**, 6244.



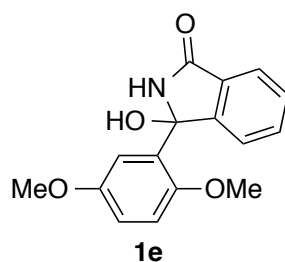
**Compound 1b.** To a solution of phthalimide (736 mg, 5.0 mmol) in  $\text{CH}_2\text{Cl}_2$  (12.5 mL) was slowly added (3,5-dimethoxyphenyl)magnesium bromide (1.0 M in THF, 15 mL, 15 mmol) at  $0^\circ\text{C}$ , and the mixture was stirred at room temperature overnight. Saturated  $\text{NH}_4\text{Cl}$  solution (12.5 mL) was added to the mixture and it was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated on a rotary evaporator. The crude mixture was recrystallized from hot  $\text{CH}_2\text{Cl}_2$  and hexane to give **1b** (999 mg, 3.5 mmol, 70% yield).



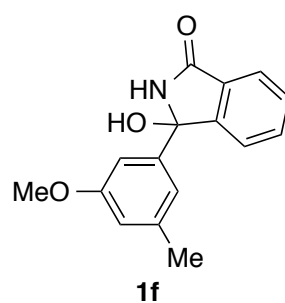
**Compound 1c.** Compound **1c** was prepared from (3,5-bis(benzyloxy)phenyl)magnesium bromide (7.5 mmol) and phthalimide (736 mg, 5.0 mmol). The crude mixture was subjected to column chromatography on silica gel with hexane/EtOAc (1:1) and recrystallized from hot  $\text{CH}_2\text{Cl}_2$  and hexane to give **1c** (513 mg, 1.2 mmol, 24% yield).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.11 (s, 1H), 5.00 (d,  $J = 12.2$  Hz, 2H), 5.01 (d,  $J = 12.2$  Hz, 2H), 6.45 (s, 1H), 6.58 (t,  $J = 2.0$  Hz, 1H), 6.81 (d,  $J = 2.0$  Hz, 2H), 7.29–7.41 (m, 11H), 7.48 (t,  $J = 7.5$  Hz, 1H), 7.51 (t,  $J = 7.5$  Hz, 1H), 7.78 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  70.1, 88.1, 102.2, 104.9, 122.8, 123.6, 127.6, 128.0, 128.6, 129.3, 129.5, 133.2, 136.6, 142.3, 149.6, 160.1, 169.7. HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{23}\text{NNaO}_4$  ( $\text{M}+\text{Na}$ ) $^+$  460.1519, found 460.1516.



**Compound 1d.** Compound **1d** was prepared from (3,4,5-trimethoxyphenyl)magnesium bromide (10.5 mmol) and phthalimide (736 mg, 5.0 mmol). The crude mixture was recrystallized from hot  $\text{CH}_2\text{Cl}_2$  and hexane to give **1d** (1.04 g, 3.3 mmol, 66% yield).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.81 (s, 10H), 6.72 (br s, 1H), 6.77 (s, 2H), 7.39 (d,  $J = 7.5$  Hz, 1H), 7.46 (t,  $J = 7.5$  Hz, 1H), 7.55 (t,  $J = 7.5$  Hz, 1H), 7.72 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  56.1, 60.8, 88.2, 102.7, 122.7, 123.6, 129.2, 129.5, 133.2, 135.6, 137.9, 149.7, 153.2, 169.9. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{17}\text{NNaO}_5$  ( $\text{M}+\text{Na}$ ) $^+$  338.0999, found 338.0996.



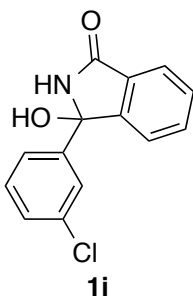
**Compound 1e.** Compound **1e** was prepared from (2,5-dimethoxyphenyl)magnesium bromide (12.0 mmol) and phthalimide (736 mg, 5.0 mmol). The crude mixture was subjected to column chromatography on silica gel with  $\text{CHCl}_3/\text{EtOAc}$  (1:1) to give **1e** (1.36 g, 4.8 mmol, 95% yield).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.68 (s, 3H), 3.92 (s, 3H), 4.95 (br s, 1H), 6.75 (d,  $J = 2.5$  Hz, 1H), 6.83 (dd,  $J = 8.9, 2.5$  Hz, 1H), 6.93 (d,  $J = 8.9$  Hz, 1H), 7.00 (br s, 1H), 7.52–7.56 (m, 1H), 7.61–7.65 (m, 2H), 7.82 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  55.7, 56.1, 87.8, 112.2, 113.4, 113.8, 123.8, 123.9, 129.2, 129.8, 131.1, 132.6, 147.0, 150.7, 153.6, 168.9. HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{15}\text{NNaO}_4$  ( $\text{M}+\text{Na}$ ) $^+$  308.0893, found 308.0888.



**Compound 1f.** Compound **1f** was prepared from (3-methoxy-5-methylphenyl)magnesium bromide (5.0 mmol) and phthalimide (368 mg, 2.5 mmol). The crude mixture was subjected to



column chromatography on silica gel with hexane/EtOAc (1:1) to give **1f** (334 mg, 1.2 mmol, 50% yield).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  2.27 (s, 3H), 3.74 (s, 3H), 4.57 (br s, 1H), 6.63 (br s, 1H), 6.88 (s, 1H), 6.95 (s, 1H), 7.02 (s, 1H), 7.35 (d,  $J = 7.5$  Hz, 1H), 7.36 (t,  $J = 7.5$  Hz, 1H), 7.48 (t,  $J = 7.5$  Hz, 1H), 7.54 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  21.6, 55.2, 88.1, 108.4, 114.9, 118.5, 122.8, 123.6, 129.35, 129.41, 133.1, 139.9, 141.2, 149.9, 159.8, 169.8. HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{15}\text{NNaO}_3$  ( $\text{M}+\text{Na}$ ) $^+$  292.0944, found 292.0937.



**Compound 1i.** Compound **1i** was prepared from (3-chlorophenyl)magnesium bromide (1.0 M in  $\text{Et}_2\text{O}$ , 15 mL, 15 mmol) and phthalimide (736 mg, 5.0 mmol). The crude product was subjected to column chromatography on silica gel with hexane/EtOAc (1:1) to give **1i** (1.09 g, 4.2 mmol, 83% yield).  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  7.08 (s, 1H), 7.34 (d,  $J = 7.5$  Hz, 1H), 7.35–7.40 (m, 3H), 7.50 (t,  $J = 7.5$  Hz, 1H), 7.51 (s, 1H), 7.56 (t,  $J = 7.5$  Hz, 1H), 7.66 (d,  $J = 7.5$  Hz, 1H), 9.30 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  86.8, 122.7, 122.8, 124.3, 125.3, 127.8, 129.2, 130.3, 130.5, 132.6, 132.9, 144.7, 150.2, 168.2. HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{10}\text{ClNNaO}_2$  ( $\text{M}+\text{Na}$ ) $^+$  282.0292, found 282.0291.

#### 4. Procedure for iridium-catalyzed asymmetric [3 + 2] annulation of hemiaminal **1b** with diphenylacetylene (**2m**) (Scheme 2)

Hemiaminal **1b** (28.5 mg, 0.10 mmol), diphenylacetylene (**2m**, 26.7 mg, 0.15 mmol),  $[\text{Ir}(\text{cod})_2]\text{BF}_4$  (2.5 mg, 0.0050 mmol, 5 mol%), (*R*)-binap (4.7 mg, 0.0075 mmol, 7.5 mol%), and carboxylic acid (0.010 mmol, 10 mol%) in some cases were placed in a Schlenk tube under nitrogen. Chlorobenzene (0.4 mL) was added and the Schlenk tube was capped with a glass stopper and heated at 80 °C for 20 h with stirring. The solvent was removed on a rotary evaporator, and the residue was subjected to preparative TLC on silica gel with  $\text{CHCl}_3/\text{EtOAc}$  (5:1) to give **3bm**.

#### 5. Procedure for iridium-catalyzed asymmetric [3 + 2] annulation of hemiaminals **1** with alkynes **2** (Table 1, Scheme 3 and Scheme 4, Condition A)

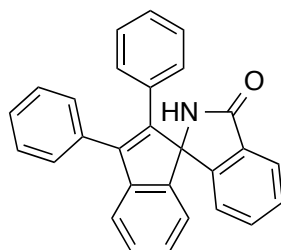
Hemiaminals **1** (0.20 mmol), alkynes **2** (0.30 mmol),  $[\text{Ir}(\text{cod})_2]\text{BF}_4$  (5.0 mg, 0.010 mmol, 5 mol%), and (*R*)-binap (9.3 mmol, 0.015 mmol, 7.5 mol%) were placed in a Schlenk tube under nitrogen. Chlorobenzene (0.8 mL) was added and the Schlenk tube was capped with a glass

stopper. The mixture was heated at 80 °C for 48 h with stirring. The solvent was removed on a rotary evaporator, and the residue was subjected to preparative TLC on silica gel to give **3**.

## 6. Procedure for iridium-catalyzed asymmetric [3 + 2] annulation of hemiaminals **1** with alkynes **2** (Table 1, Scheme 3 and Scheme 4, Condition B)

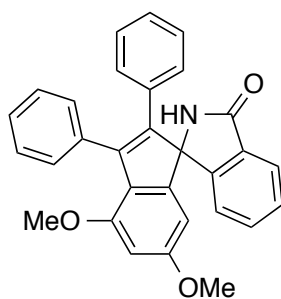
Hemiaminals **1** (0.20 mmol), alkynes **2** (0.30 mmol), [Ir(cod)<sub>2</sub>]BF<sub>4</sub> (5.0 mg, 0.010 mmol, 5 mol%), (*R*)-binap (9.3 mg, 0.015 mmol, 7.5 mol%), and benzoic acid (2.4 mg, 0.020 mmol, 10 mol%) were placed in a Schlenk tube under nitrogen. Chlorobenzene (0.8 mL) was added and the Schlenk tube was capped with a glass stopper. The mixture was heated at 80 °C for 48 h with stirring. The solvent was removed on a rotary evaporator, and the residue was subjected to preparative TLC on silica gel to give **3**.

## 7. Characterization of the products



**3am**

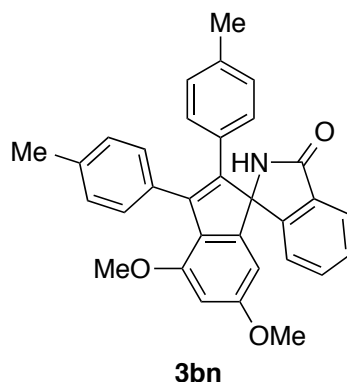
**Compound 3am** (Scheme 4, CAS: 1610474-61-7 for racemic **3am**). A solution of CHCl<sub>3</sub>/EtOAc (5:1) was used as a eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IC, hexane/chloroform/ethanol = 18:6:1, flow 0.5 mL/min, 254 nm, t<sub>1</sub> = 14.6 min (*minor*), t<sub>2</sub> = 15.8 min (*major*); [α]<sub>D</sub><sup>20</sup> +8 (c 0.25, CHCl<sub>3</sub>) for 17% ee (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 6.00 (s, 1H), 6.71 (d, *J* = 7.5 Hz, 2H), 6.99 (t, *J* = 7.5 Hz, 2H), 7.04–7.09 (m, 2H), 7.11–7.15 (m, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.31–7.42 (m, 7H), 7.46–7.51 (m, 2H), 7.86–7.91 (m, 1H).



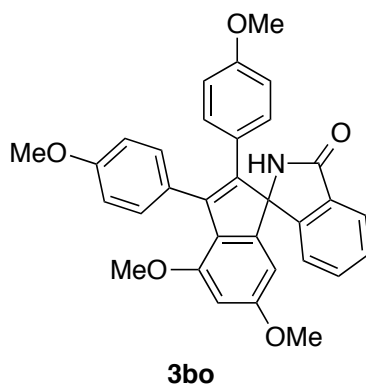
**3bm**

**Compound 3bm** (Table 1, entries 1 and 2). A solution of CHCl<sub>3</sub>/EtOAc (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm, t<sub>1</sub> = 9.1 min (*R*), t<sub>2</sub> = 12.3 min (*S*);

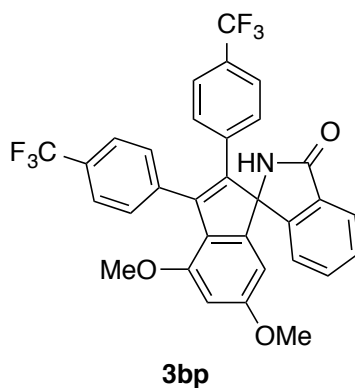
$[\alpha]_D^{20} +65$  (*c* 1.02, CHCl<sub>3</sub>) for 88% ee (*S*) (entry 1);  $[\alpha]_D^{20} -63$  (*c* 1.00, CHCl<sub>3</sub>) for 83% ee (*R*) (entry 2). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.61 (s, 3H), 3.70 (s, 3H), 6.03 (br s, 1H), 6.22 (d, *J* = 2.0 Hz, 1H), 6.40 (d, *J* = 2.0 Hz, 1H), 6.59 (d, *J* = 7.5 Hz, 2H), 6.92 (t, *J* = 7.5 Hz, 2H), 6.98 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.22–7.28 (m, 3H), 7.30–7.35 (m, 2H), 7.45–7.52 (m, 2H), 7.86 (d, *J* = 7.5 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 55.4, 55.7, 74.9, 99.9, 100.1, 121.6, 123.4, 124.1, 127.0, 127.1, 127.2, 127.8, 128.6, 128.9, 129.9, 131.6, 132.7, 133.6, 135.8, 140.4, 142.5, 147.3, 148.3, 155.3, 160.8, 171.0. HRMS (ESI) calcd for C<sub>30</sub>H<sub>23</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup> 468.1570, found 468.1560.



**Compound 3bn** (Table 1, entries 3 and 4). A solution of CHCl<sub>3</sub>/EtOAc (10:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm, *t*<sub>1</sub> = 8.7 min (*R*), *t*<sub>2</sub> = 11.3 min (*S*);  $[\alpha]_D^{20} +72$  (*c* 1.02, CHCl<sub>3</sub>) for 92% ee (*S*) (entry 3);  $[\alpha]_D^{20} -64$  (*c* 1.01, CHCl<sub>3</sub>) for 76% ee (*R*) (entry 4). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.12 (s, 3H), 2.34 (s, 3H), 3.62 (s, 3H), 3.68 (s, 3H), 6.11 (br s, 1H), 6.20 (d, *J* = 2.0 Hz, 1H), 6.39 (d, *J* = 2.0 Hz, 1H), 6.49 (d, *J* = 8.1 Hz, 2H), 6.72 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.0, 21.3, 55.4, 55.7, 74.8, 99.9, 100.1, 121.7, 123.7, 124.1, 128.0, 128.46, 128.53, 128.7, 129.8, 130.7, 131.6, 132.7, 132.8, 136.5, 136.6, 140.1, 142.0, 147.5, 148.3, 155.2, 160.6, 171.1. HRMS (ESI) calcd for C<sub>32</sub>H<sub>27</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup> 496.1883, found 496.1873.

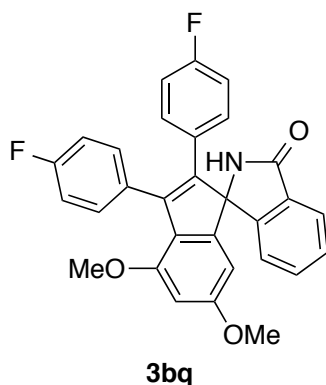


**Compound 3bo** (Table 1, entries 5 and 6). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 10.3$  min (*R*),  $t_2 = 13.0$  min (*S*);  $[\alpha]_D^{20} +79$  ( $c$  1.05,  $\text{CHCl}_3$ ) for 93% ee (*S*) (entry 5);  $[\alpha]_D^{20} -54$  ( $c$  1.00,  $\text{CHCl}_3$ ) for 59% ee (*R*) (entry 6).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  3.61 (s, 3H), 3.63 (s, 3H), 3.67 (s, 3H), 3.80 (s, 3H), 6.20 (d,  $J = 2.0$  Hz, 1H), 6.21 (br s, 1H), 6.39 (d,  $J = 2.0$  Hz, 1H), 6.46 (d,  $J = 8.1$  Hz, 2H), 6.53 (d,  $J = 8.1$  Hz, 2H), 6.79 (d,  $J = 8.1$  Hz, 2H), 7.14 (d,  $J = 7.5$  Hz, 1H), 7.25 (d,  $J = 8.1$  Hz, 2H), 7.44 (t,  $J = 7.5$  Hz, 1H), 7.46 (t,  $J = 7.5$  Hz, 1H), 7.85 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  54.9, 55.1, 55.4, 55.6, 74.8, 99.9, 100.1, 112.7, 113.3, 121.6, 123.6, 124.1, 126.1, 128.2, 128.4, 130.1, 131.2, 131.6, 132.7, 139.5, 141.2, 147.6, 148.2, 155.1, 158.2, 158.6, 160.5, 171.1. HRMS (ESI) calcd for  $\text{C}_{32}\text{H}_{27}\text{NNaO}_5$  ( $\text{M}+\text{Na}$ ) $^+$  528.1781, found 528.1782.

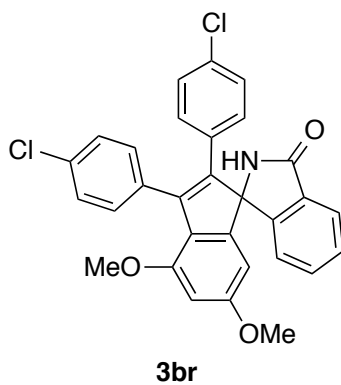


**Compound 3bp** (Table 1, entries 7 and 8). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 9.6$  min (*R*),  $t_2 = 25.8$  min (*S*);  $[\alpha]_D^{20} +48$  ( $c$  1.00,  $\text{CHCl}_3$ ) for 83% ee (*S*) (entry 7);  $[\alpha]_D^{20} -49$  ( $c$  0.97,  $\text{CHCl}_3$ ) for 87% ee (*R*) (entry 8).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  3.62 (s, 3H), 3.72 (s, 3H), 5.99 (s, 1H), 6.23 (d,  $J = 2.0$  Hz, 1H), 6.41 (d,  $J = 2.0$  Hz, 1H), 6.68 (d,  $J = 8.2$  Hz, 2H), 7.18 (d,  $J = 6.5$  Hz, 1H), 7.21 (d,  $J = 8.2$  Hz, 2H), 7.42 (d,  $J = 8.2$  Hz, 2H), 7.49–7.56 (m, 4H), 7.89 (d,  $J = 6.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  55.3, 55.7, 74.8, 99.7, 100.3, 121.5, 122.3, 123.8 (q,  $J_{\text{F-C}} = 272$  Hz), 124.1 (q,  $J_{\text{F-C}} = 272$  Hz), 124.4 (q,

$J_{\text{F-C}} = 3$  Hz), 124.5, 125.0 (q,  $J_{\text{F-C}} = 3$  Hz), 129.0, 129.1, 129.2 (q,  $J_{\text{F-C}} = 33$  Hz), 129.6 (q,  $J_{\text{F-C}} = 33$  Hz), 130.1, 131.5, 133.0, 136.9, 139.2, 140.0, 142.7, 146.5, 148.3, 155.4, 161.6, 171.0. HRMS (ESI) calcd for  $\text{C}_{32}\text{H}_{21}\text{F}_6\text{NNaO}_3$  ( $\text{M}+\text{Na}$ ) $^+$  604.1318, found 604.1329.

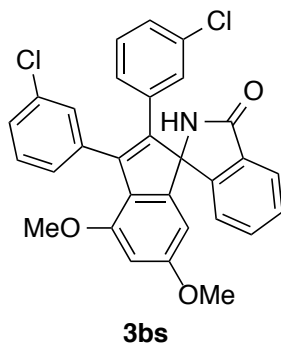


**Compound 3bq** (Table 1, entries 9 and 10). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 9.4$  min (*R*),  $t_2 = 16.5$  min (*S*);  $[\alpha]_{\text{D}}^{20} +50$  ( $c$  1.02,  $\text{CHCl}_3$ ) for 92% ee (*S*) (entry 9);  $[\alpha]_{\text{D}}^{20} -43$  ( $c$  1.01,  $\text{CHCl}_3$ ) for 79% ee (*R*) (entry 10).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.63 (s, 3H), 3.70 (s, 3H), 6.11 (br s, 1H), 6.22 (s, 1H), 6.40 (s, 1H), 6.57 (t,  $J = 8.5$  Hz, 2H), 6.64 (t,  $J = 8.5$  Hz, 2H), 6.95 (t,  $J = 8.5$  Hz, 2H), 7.15 (d,  $J = 6.8$  Hz, 1H), 7.23–7.30 (m, 2H), 7.47 (t,  $J = 6.8$  Hz, 1H), 7.50 (t,  $J = 6.8$  Hz, 1H), 7.86 (d,  $J = 6.8$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  55.3, 55.7, 74.8, 99.8, 100.2, 114.3 (d,  $J_{\text{F-C}} = 22$  Hz), 115.0 (d,  $J_{\text{F-C}} = 22$  Hz), 121.5, 122.9, 124.2, 128.7, 129.4 (d,  $J_{\text{F-C}} = 3$  Hz), 130.7 (d,  $J_{\text{F-C}} = 9$  Hz), 131.5 (d,  $J_{\text{F-C}} = 3$  Hz), 131.6 (d,  $J_{\text{F-C}} = 9$  Hz), 132.8, 139.7, 141.7, 146.9, 148.0, 155.2, 161.0, 161.7 (d,  $J_{\text{F-C}} = 247$  Hz), 162.0 (d,  $J_{\text{F-C}} = 247$  Hz), 171.1. HRMS (ESI) calcd for  $\text{C}_{30}\text{H}_{21}\text{F}_2\text{NNaO}_3$  ( $\text{M}+\text{Na}$ ) $^+$  504.1382, found 504.1378.

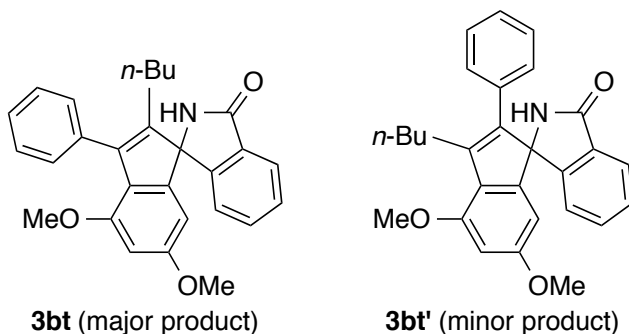


**Compound 3br** (Table 1, entries 11 and 12). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 10.8$  min (*R*),  $t_2 = 20.6$  min (*S*);

$[\alpha]_D^{20} +70$  (*c* 1.03, CHCl<sub>3</sub>) for 87% ee (*S*) (entry 11);  $[\alpha]_D^{20} -61$  (*c* 1.00, CHCl<sub>3</sub>) for 82% ee (*R*) (entry 12). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.63 (s, 3H), 3.70 (s, 3H), 6.04–6.10 (br, 1H), 6.21 (d, *J* = 2.1 Hz, 1H), 6.40 (d, *J* = 2.1 Hz, 1H), 6.52 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 5.8 Hz, 1H), 7.23 (d, *J* = 8.9 Hz, 2H), 7.24 (d, *J* = 8.9 Hz, 2H), 7.46–7.51 (m, 2H), 7.86 (d, *J* = 5.8 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 55.3, 55.7, 74.8, 99.7, 100.2, 121.5, 122.6, 124.3, 127.6, 128.2, 128.8, 130.2, 131.2, 131.6, 131.8, 132.8, 133.1, 133.2, 133.9, 139.7, 141.9, 146.7, 148.1, 155.3, 161.1, 171.1. HRMS (ESI) calcd for C<sub>30</sub>H<sub>21</sub>Cl<sub>2</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup> 536.0791, found 536.0786.



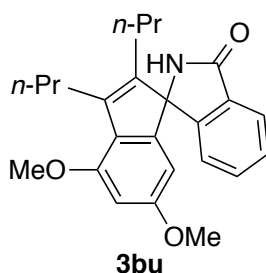
**Compound 3bs** (Table 1, entries 13 and 14). A solution of CHCl<sub>3</sub>/EtOAc (10:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm, *t*<sub>1</sub> = 9.2 min (*R*), *t*<sub>2</sub> = 12.6 min (*S*);  $[\alpha]_D^{20} +50$  (*c* 1.04, CHCl<sub>3</sub>) for 84% ee (*S*) (entry 13);  $[\alpha]_D^{20} -54$  (*c* 1.02, CHCl<sub>3</sub>) for 85% ee (*R*) (entry 14). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.65 (s, 3H), 3.70 (s, 3H), 6.05 (br s, 1H), 6.22 (d, *J* = 1.9 Hz, 1H), 6.40 (d, *J* = 1.9 Hz, 1H), 6.50 (d, *J* = 7.9 Hz, 1H), 6.54 (s, 1H), 6.89 (t, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 1H), 7.11–7.20 (m, 3H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.36 (s, 1H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.88 (d, *J* = 7.3 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 55.4, 55.7, 74.7, 99.8, 100.2, 121.6, 122.5, 124.4, 127.1, 127.5, 127.6, 127.9, 128.7, 128.9, 129.2, 129.9, 131.5, 133.0, 133.2, 133.7, 135.0, 137.1, 139.7, 142.1, 146.5, 148.1, 155.4, 161.3, 170.9. HRMS (ESI) calcd for C<sub>30</sub>H<sub>21</sub>Cl<sub>2</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup> 536.0791, found 536.0783.



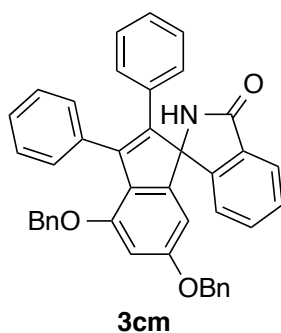
**Compound 3bt** (Table 1, entries 15 and 16). A solution of CHCl<sub>3</sub>/EtOAc (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA,

hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 8.6$  min (*R*),  $t_2 = 10.4$  min (*S*);  $[\alpha]_D^{20} -17$  ( $c$  1.00,  $\text{CHCl}_3$ ) for 73% ee (*S*) (entry 15);  $[\alpha]_D^{20} +33$  ( $c$  1.02,  $\text{CHCl}_3$ ) for 92% ee (*R*) (entry 16).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.56 (t,  $J = 7.1$  Hz, 3H), 0.81–0.90 (m, 1H), 0.93–1.08 (m, 3H), 1.74 (ddd,  $J = 14.9, 9.7, 5.3$  Hz, 1H), 2.01 (ddd,  $J = 14.9, 9.7, 5.3$  Hz, 1H), 3.54 (s, 3H), 3.66 (s, 3H), 6.03–6.24 (br, 1H), 6.18 (d,  $J = 2.0$  Hz, 1H), 6.35 (d,  $J = 2.0$  Hz, 1H), 7.03 (d,  $J = 7.2$  Hz, 1H), 7.33 (t,  $J = 6.8$  Hz, 1H), 7.35–7.41 (m, 4H), 7.45 (t,  $J = 7.2$  Hz, 1H), 7.47 (t,  $J = 7.2$  Hz, 1H), 7.91 (d,  $J = 7.2$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  13.4, 22.6, 24.8, 31.7, 55.4, 55.6, 74.7, 99.9, 100.2, 121.8, 124.0, 124.2, 127.0, 127.4, 128.5, 129.0, 131.5, 132.4, 136.4, 140.9, 142.2, 147.4, 147.5, 154.4, 160.2, 171.2. HRMS (ESI) calcd for  $\text{C}_{28}\text{H}_{27}\text{NNaO}_3$  ( $\text{M}+\text{Na}$ ) $^+$  448.1883, found 448.1878.

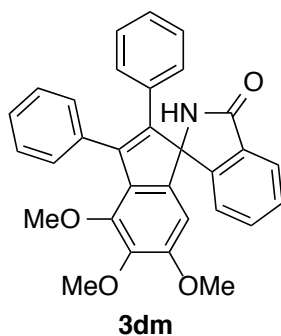
**Compound 3bt'**.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.87 (t,  $J = 7.5$  Hz, 3H), 1.29–1.40 (m, 2H), 1.53–1.68 (m, 2H), 2.55–2.64 (m, 2H), 3.68 (s, 3H), 3.89 (s, 3H), 5.91 (br s, 1H), 6.15 (d,  $J = 2.0$  Hz, 1H), 6.44 (d,  $J = 2.0$  Hz, 1H), 6.77–6.83 (m, 2H), 7.06 (d,  $J = 7.5$  Hz, 1H), 7.10–7.16 (m, 3H), 7.31–7.51 (m, 2H), 7.77 (d,  $J = 7.5$  Hz, 1H).



**Compound 3bu** (Table 1, entries 17 and 18). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 7.8$  min (*R*),  $t_2 = 9.5$  min (*S*);  $[\alpha]_D^{20} +25$  ( $c$  0.97,  $\text{CHCl}_3$ ) for 37% ee (*S*) (entry 17);  $[\alpha]_D^{20} +30$  ( $c$  0.42,  $\text{CHCl}_3$ ) for 57% ee (*S*) (entry 18).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.75 (t,  $J = 7.1$  Hz, 3H), 0.98–1.09 (m, 1H), 1.02 (t,  $J = 7.5$  Hz, 3H), 1.12–1.22 (m, 1H), 1.60–1.69 (m, 2H), 1.73 (ddd,  $J = 16.0, 9.3, 4.9$  Hz, 1H), 2.02 (ddd,  $J = 16.0, 9.3, 4.6$  Hz, 1H), 2.54–2.66 (m, 2H), 3.65 (s, 3H), 3.85 (s, 3H), 5.75 (br s, 1H), 6.09 (d,  $J = 2.0$  Hz, 1H), 6.39 (d,  $J = 2.0$  Hz, 1H), 6.88 (d,  $J = 7.5$  Hz, 1H), 7.40 (t,  $J = 7.5$  Hz, 1H), 7.44 (t,  $J = 7.5$  Hz, 1H), 7.89 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ )  $\delta$  14.3, 14.5, 22.8, 23.4, 26.9, 29.7, 55.4, 55.6, 74.7, 99.3, 99.8, 121.8, 123.9, 124.6, 128.3, 131.5, 132.3, 138.5, 141.4, 147.7, 147.8, 154.2, 159.9, 171.2. HRMS (ESI) calcd for  $\text{C}_{24}\text{H}_{27}\text{NNaO}_3$  ( $\text{M}+\text{Na}$ ) $^+$  400.1883, found 400.1873.



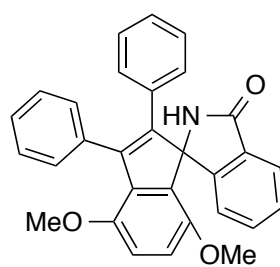
**Compound 3cm** (Scheme 3). A solution of hexane/EtOAc (1:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 9.1$  min (*R*),  $t_2 = 13.1$  min (*S*);  $[\alpha]_D^{20} +45$  ( $c$  1.02, CHCl<sub>3</sub>) for 93% ee (*S*) (Condition A);  $[\alpha]_D^{20} -20$  ( $c$  1.05, CHCl<sub>3</sub>) for 42% ee (*R*) (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.87 (d,  $J = 12.2$  Hz, 1H), 4.89 (d,  $J = 12.2$  Hz, 1H), 4.90 (d,  $J = 11.2$  Hz, 1H), 4.94 (d,  $J = 11.2$  Hz, 1H), 6.01–6.08 (br, 1H), 6.35 (d,  $J = 2.1$  Hz, 1H), 6.57 (d,  $J = 2.1$  Hz, 1H), 6.62 (d,  $J = 7.5$  Hz, 2H), 6.82 (d,  $J = 6.8$  Hz, 2H), 6.92 (t,  $J = 7.5$  Hz, 2H), 6.98 (t,  $J = 7.5$  Hz, 1H), 7.14–7.24 (m, 7H), 7.29–7.38 (m, 7H), 7.48 (t,  $J = 6.8$  Hz, 1H), 7.51 (t,  $J = 6.8$  Hz, 1H), 7.87 (d,  $J = 6.8$  Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  70.2, 70.5, 74.9, 101.6, 101.7, 121.7, 124.1, 124.2, 126.7, 126.99, 127.01, 127.4, 127.60, 127.63, 127.7, 128.08, 128.11, 128.5, 128.6, 128.9, 129.7, 131.6, 132.7, 133.5, 136.07, 136.13, 136.3, 140.6, 142.7, 147.2, 148.4, 154.3, 159.9, 171.0. HRMS (ESI) calcd for C<sub>42</sub>H<sub>31</sub>NNaO<sub>3</sub> (M+Na)<sup>+</sup> 620.2196, found 620.2196.



**Compound 3dm** (Scheme 3). A solution of CHCl<sub>3</sub>/EtOAc (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 8.8$  min (*R*),  $t_2 = 9.7$  min (*S*);  $[\alpha]_D^{20} +56$  ( $c$  0.99, CHCl<sub>3</sub>) for 86% ee (*S*) (Condition A);  $[\alpha]_D^{20} -23$  ( $c$  1.05, CHCl<sub>3</sub>) for 33% ee (*R*) (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.40 (s, 3H), 3.74 (s, 3H), 3.85 (s, 3H), 6.00 (s, 1H), 6.40 (s, 1H), 6.64 (d,  $J = 7.5$  Hz, 2H), 6.94 (t,  $J = 7.5$  Hz, 2H), 6.99 (t,  $J = 7.5$  Hz, 1H), 7.18 (d,  $J = 7.5$  Hz, 1H), 7.25–7.31 (m, 3H), 7.37 (d,  $J = 7.5$  Hz, 2H), 7.48 (t,  $J = 7.5$  Hz, 1H), 7.51 (t,  $J = 7.5$  Hz, 1H), 7.86 (d,  $J = 7.5$  Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  56.4, 61.0, 61.2, 74.9, 102.8, 121.7, 124.2, 127.2, 127.4, 127.6, 127.8, 128.3, 128.7, 128.9, 129.7, 131.6, 132.8, 133.3, 135.4, 140.7, 141.9, 142.4, 143.3, 147.1, 149.0, 153.5,

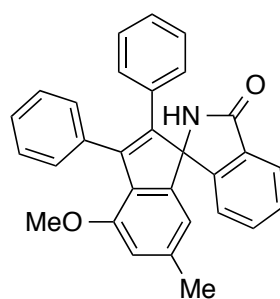


171.0. HRMS (ESI) calcd for  $C_{31}H_{25}NNaO_4$  ( $M+Na$ )<sup>+</sup> 498.1676, found 498.1672.



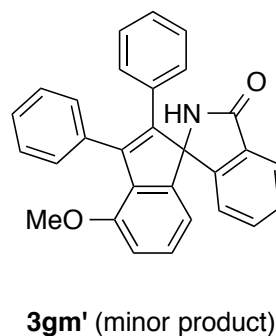
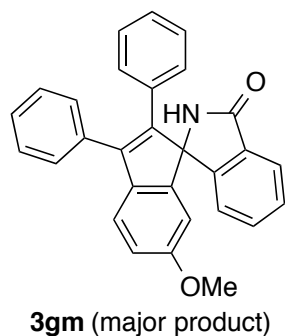
**3em**

**Compound 3em** (Scheme 3). A solution of hexane/EtOAc (1:2) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IC, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1$  = 9.8 min (*R*),  $t_2$  = 11.1 min (*S*);  $[\alpha]_D^{20}$  +59 ( $c$  0.58,  $CHCl_3$ ) for 93% ee (*S*) (Condition A);  $[\alpha]_D^{20}$  +33 ( $c$  0.79,  $CHCl_3$ ) for 59% ee (*S*) (Condition B).  $^1H$  NMR ( $CDCl_3$ )  $\delta$  3.47 (s, 3H), 3.54 (s, 3H), 5.82 (s, 1H), 6.65 (d,  $J$  = 7.5 Hz, 2H), 6.66 (d,  $J$  = 12.2 Hz, 1H), 6.84 (d,  $J$  = 12.2 Hz, 1H), 6.92 (t,  $J$  = 7.5 Hz, 2H), 6.99 (t,  $J$  = 7.5 Hz, 1H), 7.20 (d,  $J$  = 7.3 Hz, 1H), 7.23–7.28 (m, 3H), 7.30–7.34 (m, 2H), 7.44 (t,  $J$  = 7.3 Hz, 1H), 7.46 (t,  $J$  = 7.3 Hz, 1H), 7.83 (d,  $J$  = 7.3 Hz, 1H);  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  56.0, 56.4, 74.2, 111.8, 115.1, 121.1, 123.7, 127.1, 127.19, 127.23, 127.7, 128.2, 129.1, 129.9, 131.8, 132.1, 133.1, 133.3, 135.7, 142.2, 143.7, 145.5, 149.0, 150.1, 171.5. HRMS (ESI) calcd for  $C_{30}H_{23}NNaO_3$  ( $M+Na$ )<sup>+</sup> 468.1570, found 468.1566.



**3fm**

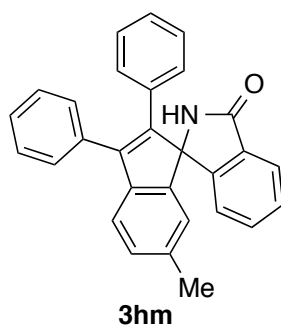
**Compound 3fm** (Scheme 3). A solution of  $CHCl_3$ /EtOAc (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1$  = 9.0 min (*R*),  $t_2$  = 12.1 min (*S*);  $[\alpha]_D^{20}$  +65 ( $c$  0.99,  $CHCl_3$ ) for 79% ee (*S*) (Condition A);  $[\alpha]_D^{20}$  +68 ( $c$  1.07,  $CHCl_3$ ) for 83% ee (*S*) (Condition B).  $^1H$  NMR ( $CDCl_3$ )  $\delta$  2.28 (s, 3H), 3.62 (s, 3H), 5.96 (br s, 1H), 6.49 (s, 1H), 6.62 (d,  $J$  = 7.5 Hz, 2H), 6.66 (s, 1H), 6.92 (t,  $J$  = 7.5 Hz, 2H), 6.99 (t,  $J$  = 7.5 Hz, 1H), 7.18 (d,  $J$  = 7.4 Hz, 1H), 7.23–7.28 (m, 3H), 7.31–7.35 (m, 2H), 7.46 (t,  $J$  = 7.4 Hz, 1H), 7.49 (t,  $J$  = 7.4 Hz, 1H), 7.86 (d,  $J$  = 7.4 Hz, 1H);  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  21.6, 55.4, 74.7, 113.5, 116.1, 121.6, 124.1, 127.09, 127.12, 127.2, 127.7, 127.8, 128.5, 129.0, 129.9, 131.7, 132.7, 133.6, 135.8, 139.0, 141.6, 142.7, 147.0, 147.2, 154.4, 171.0. HRMS (ESI) calcd for  $C_{30}H_{23}NNaO_2$  ( $M+Na$ )<sup>+</sup> 452.1621, found 452.1627.



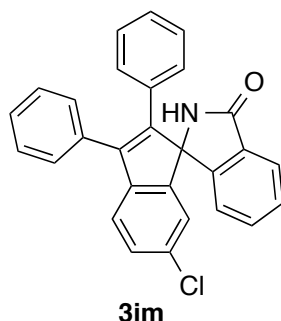
**Compound 3gm** (Scheme 4, major). A solution of CHCl<sub>3</sub>/EtOAc (5:1) was used as an eluent for preparative TLC to give a mixture of **3gm** and **3gm'**. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 13.6$  min,  $t_2 = 27.6$  min; 81% ee (*S*) (Condition A); 62% ee (*R*) (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.73 (s, 3H), 6.07 (s, 1H), 6.61 (d,  $J = 2.0$  Hz, 1H), 6.69 (d,  $J = 7.2$  Hz, 2H), 6.85 (dd,  $J = 8.2, 2.0$  Hz, 1H), 6.98 (t,  $J = 7.2$  Hz, 2H), 7.04 (t,  $J = 7.2$  Hz, 1H), 7.12–7.15 (m, 1H), 7.29 (d,  $J = 8.2$  Hz, 1H), 7.31–7.40 (m, 5H), 7.45–7.51 (m, 2H), 7.86–7.91 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 55.6, 74.7, 108.9, 114.2, 121.7, 122.0, 124.2, 127.4, 127.95, 128.03, 128.6, 128.7, 128.8, 129.3, 131.7, 132.8, 133.5, 134.2, 136.1, 141.1, 142.4, 146.7, 147.2, 159.6, 171.0. HRMS (ESI) calcd for C<sub>29</sub>H<sub>21</sub>NNaO<sub>2</sub> (M+Na)<sup>+</sup> 438.1465, found 438.1459.

**Compound 3gm'** (minor). The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 18:6:1, flow 0.5 mL/min, 254 nm,  $t_1 = 14.7$  min (*R*),  $t_2 = 43.7$  min (*S*); 16% ee (*S*) (Condition A); 18% ee (*S*) (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.64 (s, 3H), 6.05 (br s, 1H), 6.64 (d,  $J = 6.8$  Hz, 2H), 6.68 (d,  $J = 6.8$  Hz, 1H), 6.87 (d,  $J = 6.8$  Hz, 1H), 6.94 (t,  $J = 6.8$  Hz, 2H), 7.01 (t,  $J = 6.8$  Hz, 1H), 7.16 (t,  $J = 6.8$  Hz, 1H), 7.19 (d,  $J = 6.8$  Hz, 1H), 7.25–7.29 (m, 3H), 7.32–7.36 (m, 2H), 7.45–7.51 (m, 2H), 7.87 (d,  $J = 6.8$  Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 55.4, 74.8, 127.18, 127.24, 127.3, 127.8, 128.4, 128.6, 128.9, 129.9, 130.3, 131.7, 132.7, 133.4, 135.8, 142.68, 142.74, 146.9, 154.7, 171.0. HRMS (APCI) calcd for C<sub>29</sub>H<sub>22</sub>NO<sub>2</sub> (M+H)<sup>+</sup> 416.1645, found 416.1641.

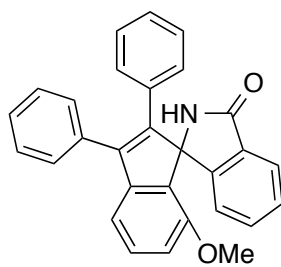
Enantiopure (*S*)-**3gm** and (*S*)-**3gm'** were obtained from a mixture of **3gm** and **3gm'** by preparative HPLC with a chiral stationary phase column (Chiralpak IA) and their specific rotations were measured. (*S*)-**3gm**:  $[\alpha]_D^{20} +66$  ( $c$  1.00, CHCl<sub>3</sub>). (*S*)-**3gm'**:  $[\alpha]_D^{20} +97$  ( $c$  0.59, CHCl<sub>3</sub>).



**Compound 3hm** (Scheme 4). A solution of hexane/EtOAc (2:1) was used as a eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 11.3$  min (*R*),  $t_2 = 20.4$  min (*S*);  $[\alpha]_D^{20} -5$  (*c* 1.01, CHCl<sub>3</sub>) for 9% ee (*S*) (Condition A);  $[\alpha]_D^{20} +11$  (*c* 1.03, CHCl<sub>3</sub>) for 17% ee (*S*) (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.28 (s, 3H), 6.16–6.32 (br, 1H), 6.72 (d, *J* = 7.6 Hz, 2H), 6.86 (s, 1H), 6.97 (t, *J* = 7.6 Hz, 2H), 7.04 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.31–7.41 (m, 5H), 7.43–7.50 (m, 2H), 7.86–7.89 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.3, 74.8, 121.1, 121.7, 123.4, 124.1, 127.4, 127.9, 128.0, 128.5, 128.8, 129.3, 129.4, 131.8, 132.7, 133.4, 134.2, 137.2, 140.8, 142.2, 142.6, 144.9, 147.1, 171.1. HRMS (ESI) calcd for C<sub>29</sub>H<sub>21</sub>NNaO<sub>1</sub> (M+Na)<sup>+</sup> 422.1515, found 422.1518.

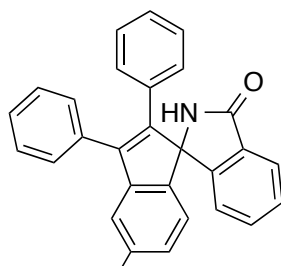


**Compound 3im** (Scheme 4). A solution of CHCl<sub>3</sub>/EtOAc (10:1) was used as a eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 18:6:1, flow 0.5 mL/min, 254 nm,  $t_1 = 13.0$  min (*R*),  $t_2 = 18.6$  min (*S*);  $[\alpha]_D^{20} -6$  (*c* 1.04, CHCl<sub>3</sub>) for 12% ee (*S*) (Condition A);  $[\alpha]_D^{20} +8$  (*c* 0.32, CHCl<sub>3</sub>) for 18% ee (*S*) (Condition B). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 6.10–6.18 (br, 1H), 6.70 (t, *J* = 6.8 Hz, 2H), 6.99 (t, *J* = 7.7 Hz, 2H), 7.02 (s, 1H), 7.07 (t, *J* = 7.7 Hz, 1H), 7.11–7.15 (m, 1H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.32–7.41 (m, 5H), 7.47–7.53 (m, 2H), 7.87–7.91 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 74.6, 121.6, 122.2, 123.2, 124.4, 127.8, 128.1, 128.2, 128.7, 128.9, 129.0, 129.2, 131.8, 132.9, 133.0, 133.5, 141.8, 141.9, 143.6, 146.1, 146.6, 170.9. HRMS (APCI) calcd for C<sub>28</sub>H<sub>19</sub>ClNO (M+H)<sup>+</sup> 420.1150, found 420.1145.



**3jm**

**Compound 3jm** (Scheme 4). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (5:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 9.9$  min (*R*),  $t_2 = 29.0$  min (*S*);  $[\alpha]_D^{20} +31$  ( $c$  1.02,  $\text{CHCl}_3$ ) for 53% ee (*S*) (Condition A);  $[\alpha]_D^{20} +9$  ( $c$  1.01,  $\text{CHCl}_3$ ) for 16% ee (*S*) (Condition B).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.54 (s, 3H), 5.83 (br s, 1H), 6.70–6.75 (m, 3H), 6.97 (t,  $J = 7.5$  Hz, 2H), 7.00 (d,  $J = 7.5$  Hz, 1H), 7.04 (t,  $J = 7.5$  Hz, 1H), 7.13–7.18 (m, 1H), 7.30–7.39 (m, 6H), 7.43–7.48 (m, 2H), 7.84–7.88 (m, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  55.5, 74.2, 110.5, 114.0, 121.2, 123.8, 127.5, 127.88, 127.92, 128.3, 128.5, 128.9, 129.4, 129.7, 130.6, 132.1, 133.1, 133.2, 134.2, 142.2, 143.9, 145.4, 145.5, 155.4, 171.5. HRMS (ESI) calcd for  $\text{C}_{29}\text{H}_{21}\text{NNaO}_2$  ( $\text{M}+\text{Na}$ ) $^+$  438.1465, found 438.1467.

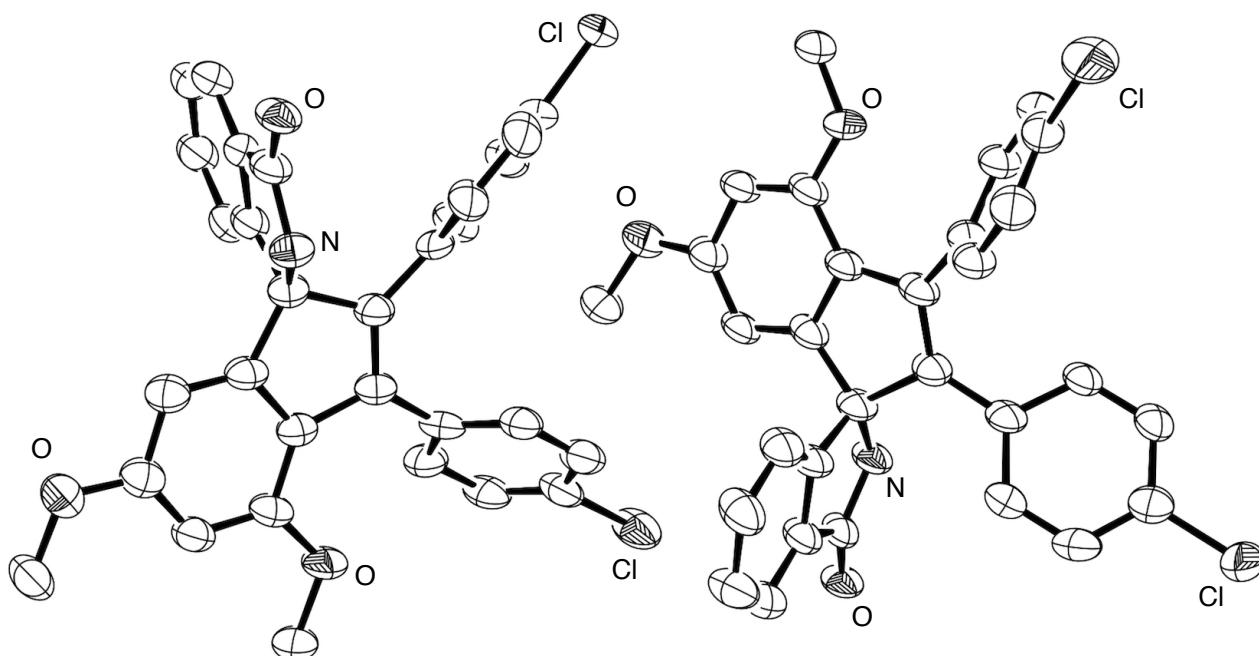


**3km**

**Compound 3km** (Scheme 4, CAS: 1610474-63-9 for racemic **3km**). A solution of  $\text{CHCl}_3/\text{EtOAc}$  (10:1) was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak IA, hexane/chloroform/ethanol = 6:2:1, flow 0.5 mL/min, 254 nm,  $t_1 = 11.1$  min (*minor*),  $t_2 = 27.5$  min (*major*);  $[\alpha]_D^{20} +13$  ( $c$  0.29,  $\text{CHCl}_3$ ) for 19% ee (Condition B).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  3.80 (s, 3H), 5.99 (br s, 1H), 6.68–6.72 (m, 3H), 6.92–6.96 (m, 2H), 6.98 (t,  $J = 7.5$  Hz, 2H), 7.05 (t,  $J = 7.5$  Hz, 1H), 7.13 (d,  $J = 5.8$  Hz, 1H), 7.31–7.39 (m, 5H), 7.46 (t,  $J = 5.8$  Hz, 1H), 7.48 (t,  $J = 5.8$  Hz, 1H), 7.86 (d,  $J = 5.8$  Hz, 1H).

## 8. X-Ray data of (+)-**3br**

A yellow crystal of (+)-**3br** suitable for X-ray crystallographic analysis was obtained by recrystallization from toluene/hexane. The ORTEP drawing of (+)-**3br** is shown in Figure S1. The crystal structure has been deposited at the Cambridge Crystallographic Centre (deposition number: CCDC 1449863). The data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif). X-Ray data were collected on a Rigaku XtaLAB P200 using a graphite monochromator with Cu- $K\alpha$  radiation ( $\lambda = 1.54187 \text{ \AA}$ ) at 93 K. The structure was solved by direct method (SHELXS-97) and refined with full-matrix least-square technique (SHELXL-97).<sup>7</sup> The absolute structure was deduced based on Flack parameter 0.078(18).<sup>8</sup> The data for (+)-**3br** is summarized in Table S1.



**Figure S1.** ORTEP illustration of (+)-**3br** with thermal ellipsoids drawn at 50% probability level (solvent molecules and hydrogen atoms are omitted for clarity).

7 G. M. Sheldrick, Program for the solution and refinement of crystal structures, University of Göttingen, Göttingen, Germany, 1997.

8 H. D. Flack, *Acta Cryst.*, 1983, **A39**, 876.

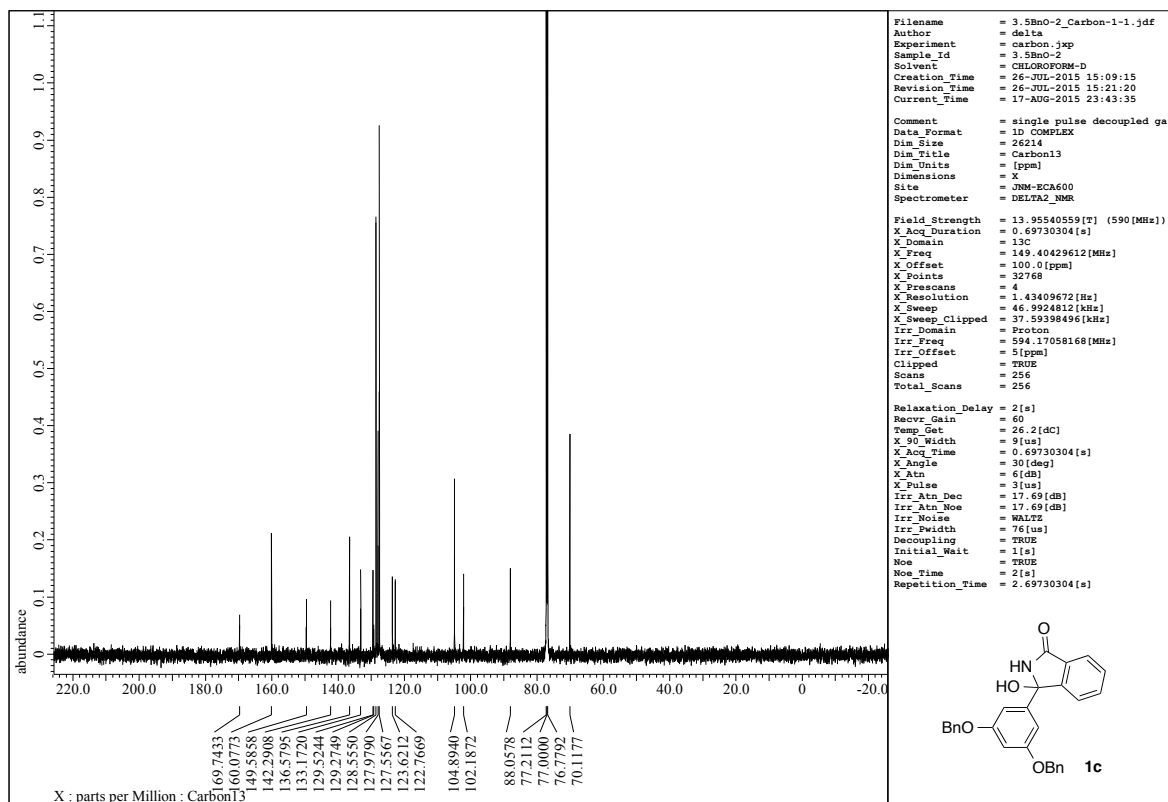
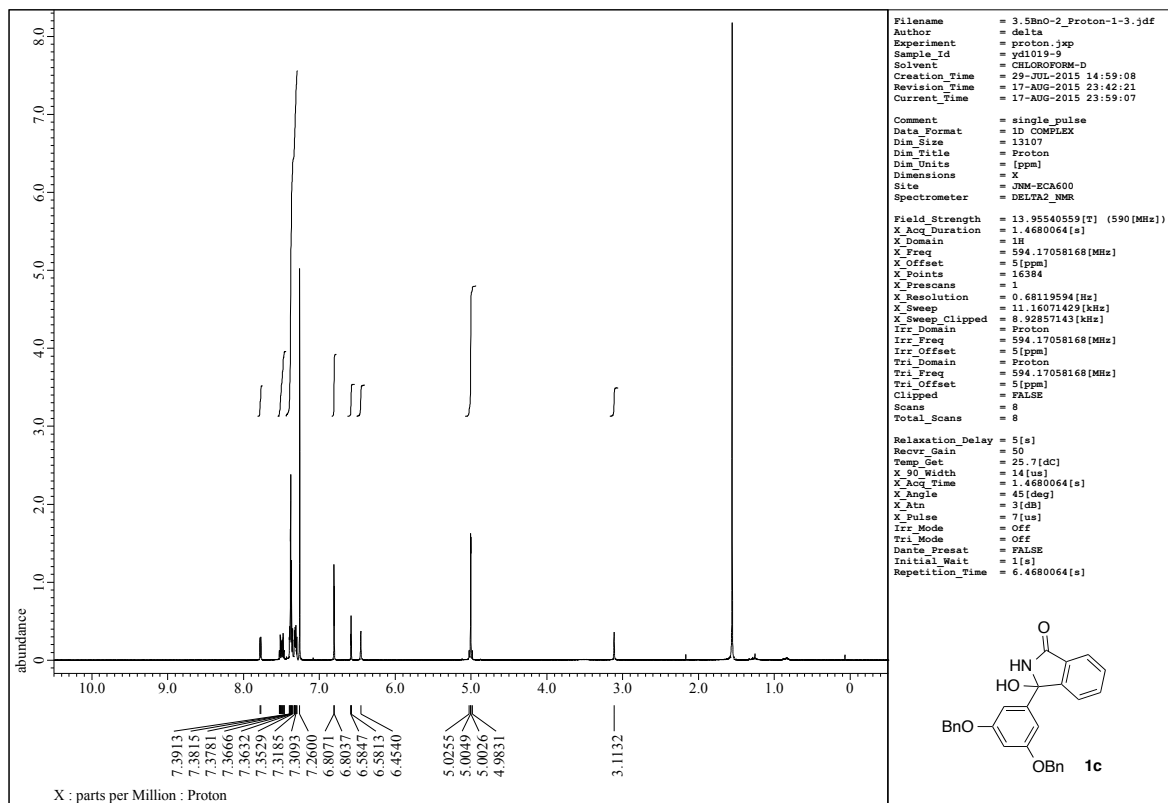
**Table 1.** Crystal data and structure refinement for (+)-**3br**.

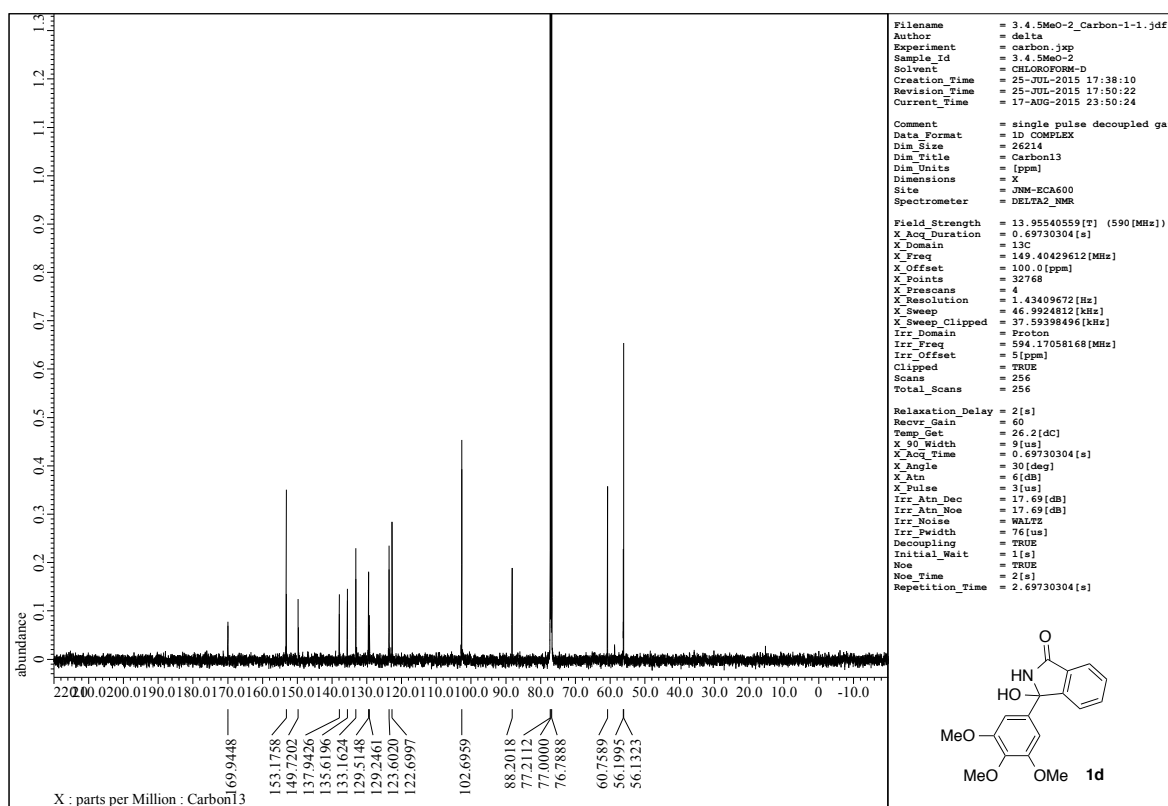
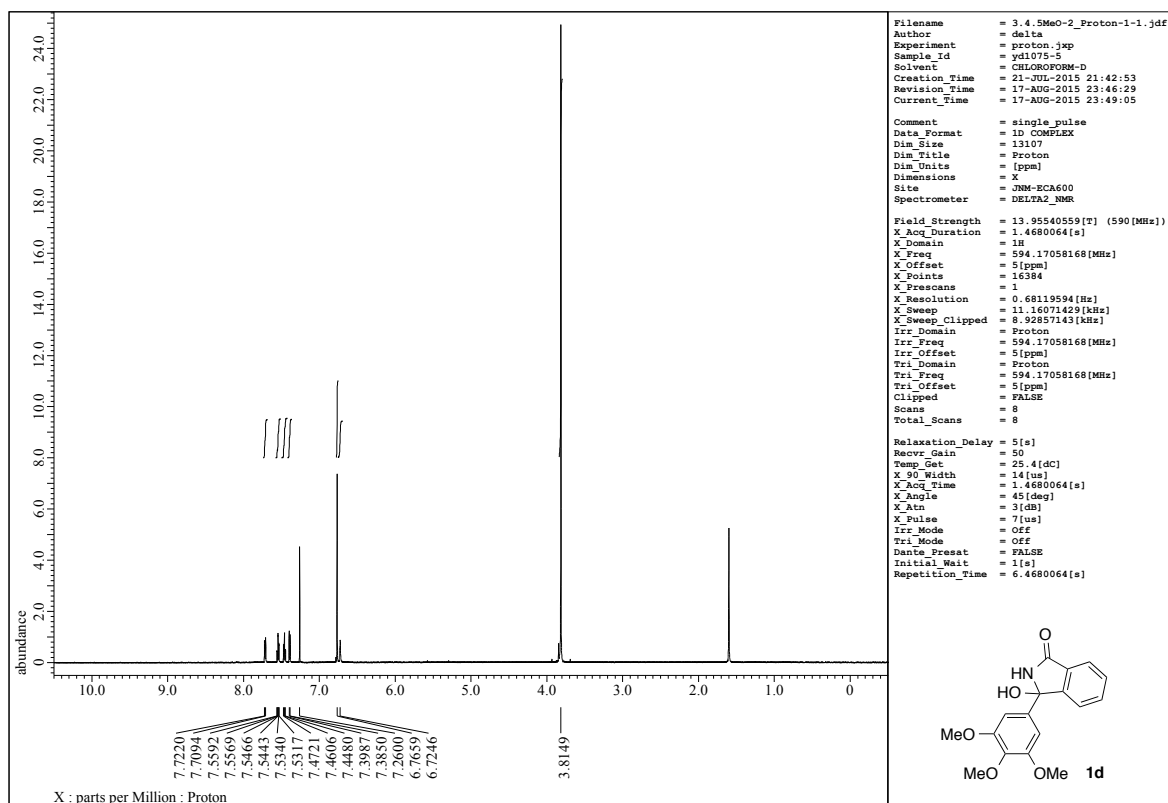
---

|  |   |
|--|---|
| Empirical formula                                | $C_{61.40}H_{43.60}Cl_4N_2O_{6.20}$                         |
| Formula weight                                   | 1050.38   |
| Temperature                                      | 93(2) K   |
| Wavelength                                       | 1.54187 Å   |
| Crystal system                                   | Trigonal  |
| Space group                                      | $P 6_3$ (#173)  |
| Unit cell dimensions                             | $a = 29.440(5)$ Å<br>$b = 29.440(5)$ Å<br>$c = 11.679(2)$ Å |
| Volume   | $8766(3)$ Å <sup>3</sup>                                    |
| <i>Z</i>   | 6   |
| Density (calculated) [Mg/m <sup>3</sup> ]        | 1.194   |
| Absorption coefficient [mm <sup>-1</sup> ]       | 2.241   |
| F(000)   | 3262  |
| Reflections collected                            | 109145  |
| Independent reflections                          | 9945 [ $R(\text{int}) = 0.0881$ ]                           |
| Completeness to $\theta$ (%)                     | 99.7  |
| Goodness-of-fit on $F^2$                         | 1.097   |
| $R_1$ [ $I > 2\sigma(I)$ ]                       | 0.0668  |
| $wR_2$ (all data)                                | 0.1890  |
| Flack parameter                                  | 0.078(18)   |
| Largest diff. peak and hole [e.Å <sup>-3</sup> ] | 0.589 and -0.410  |

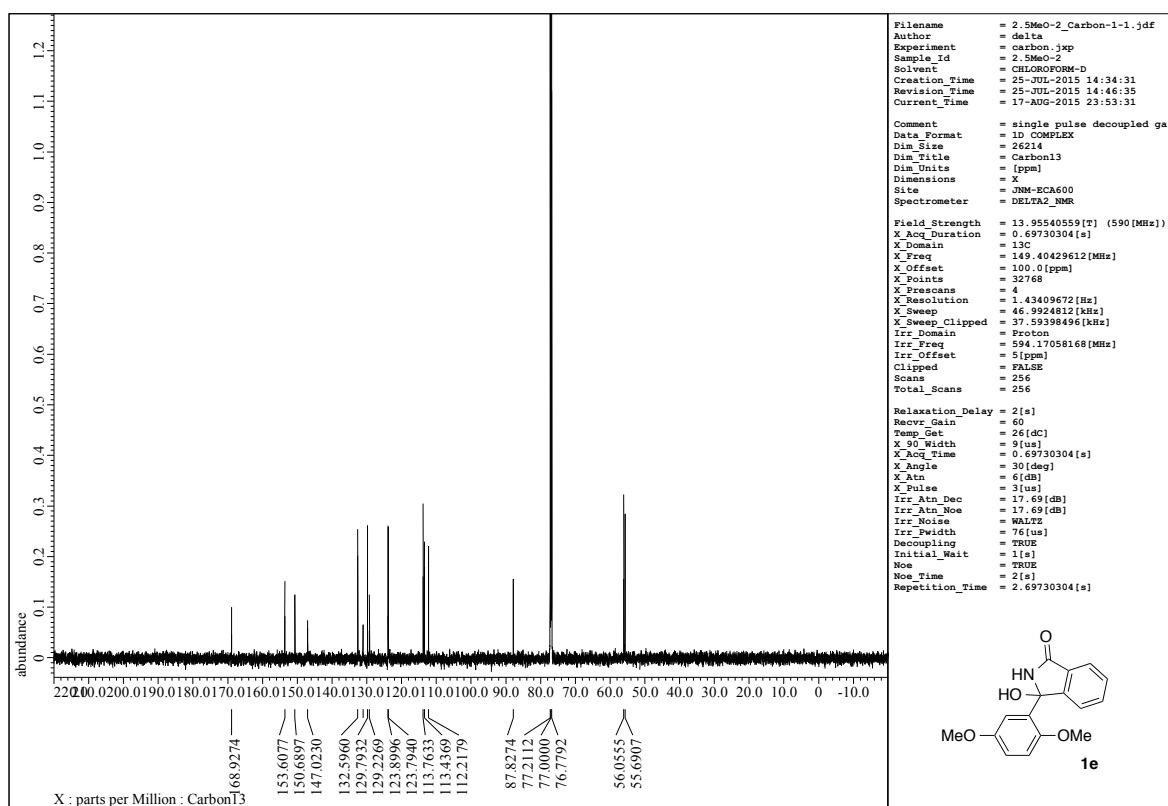
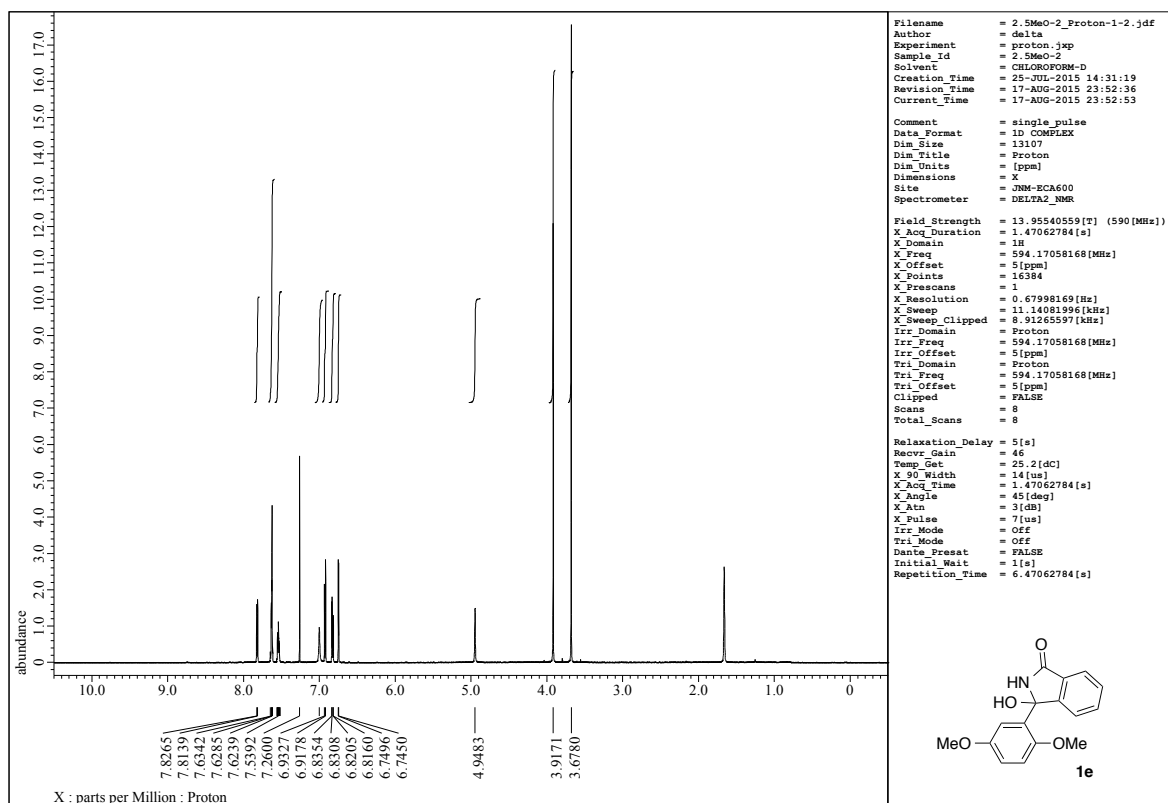
---

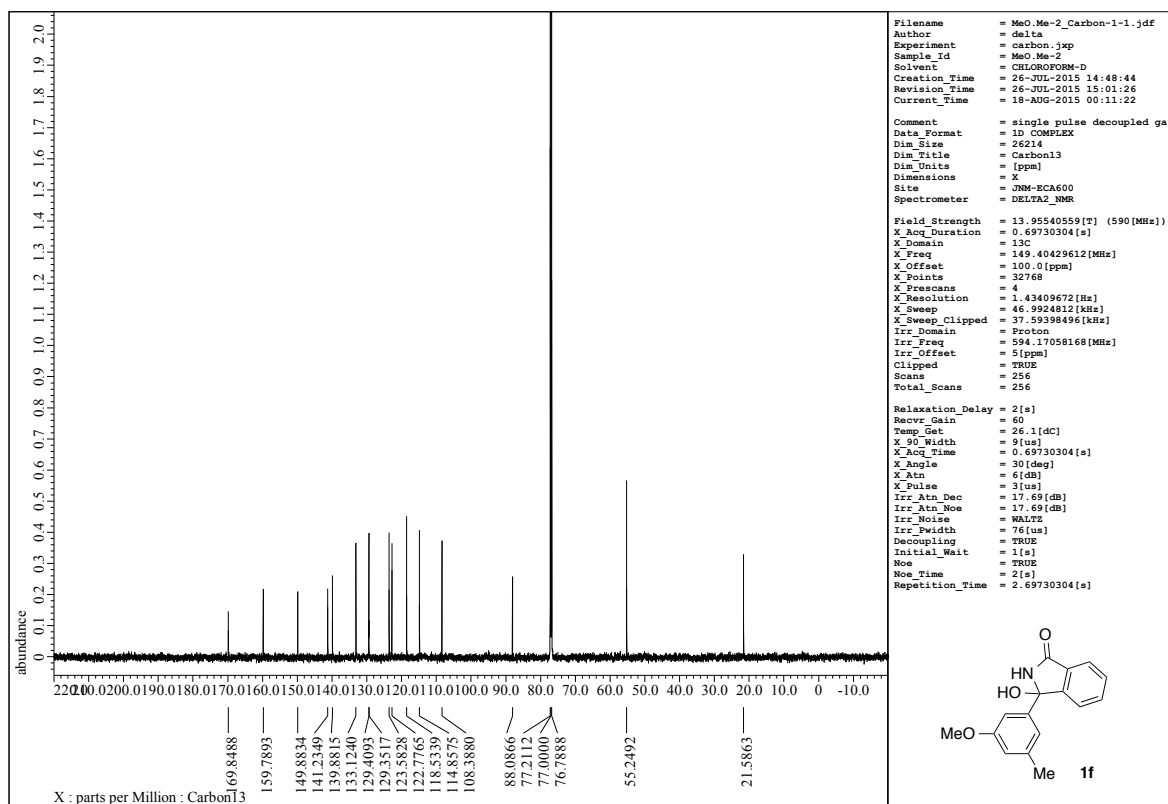
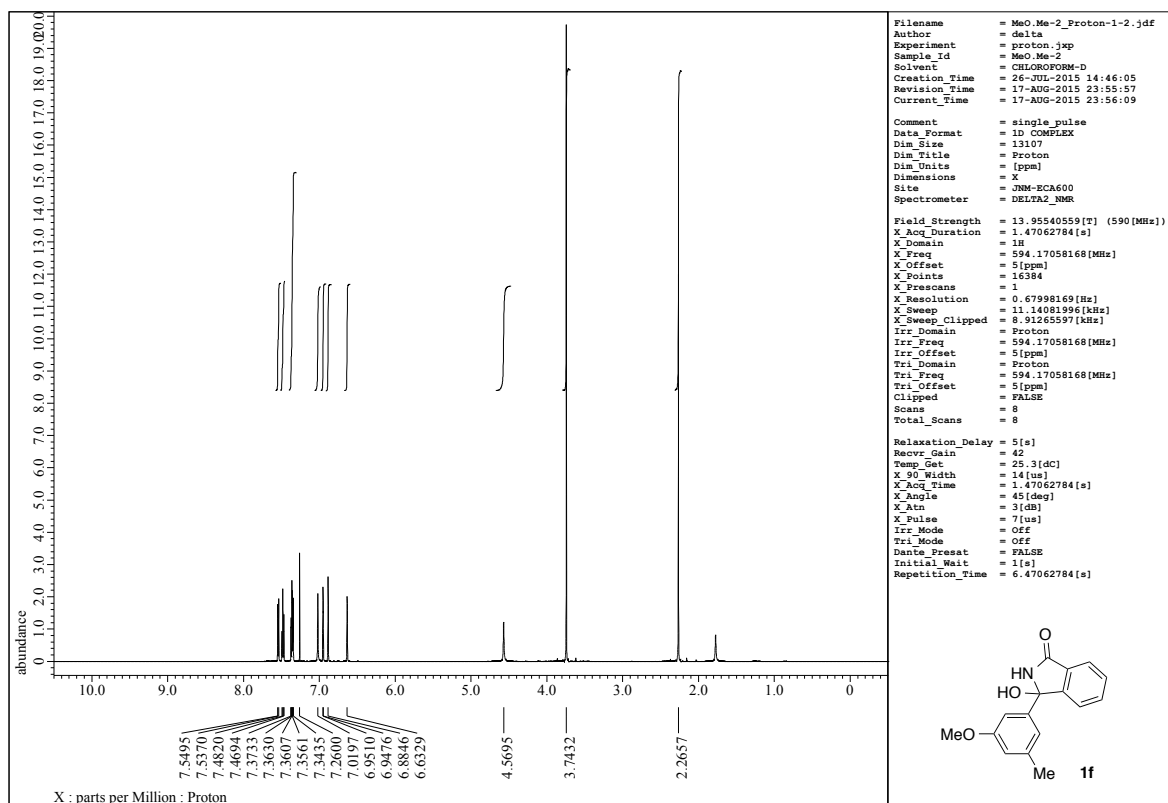
## 9. $^1\text{H}$ , $^{13}\text{C}$ NMR spectra and chiral HPLC charts

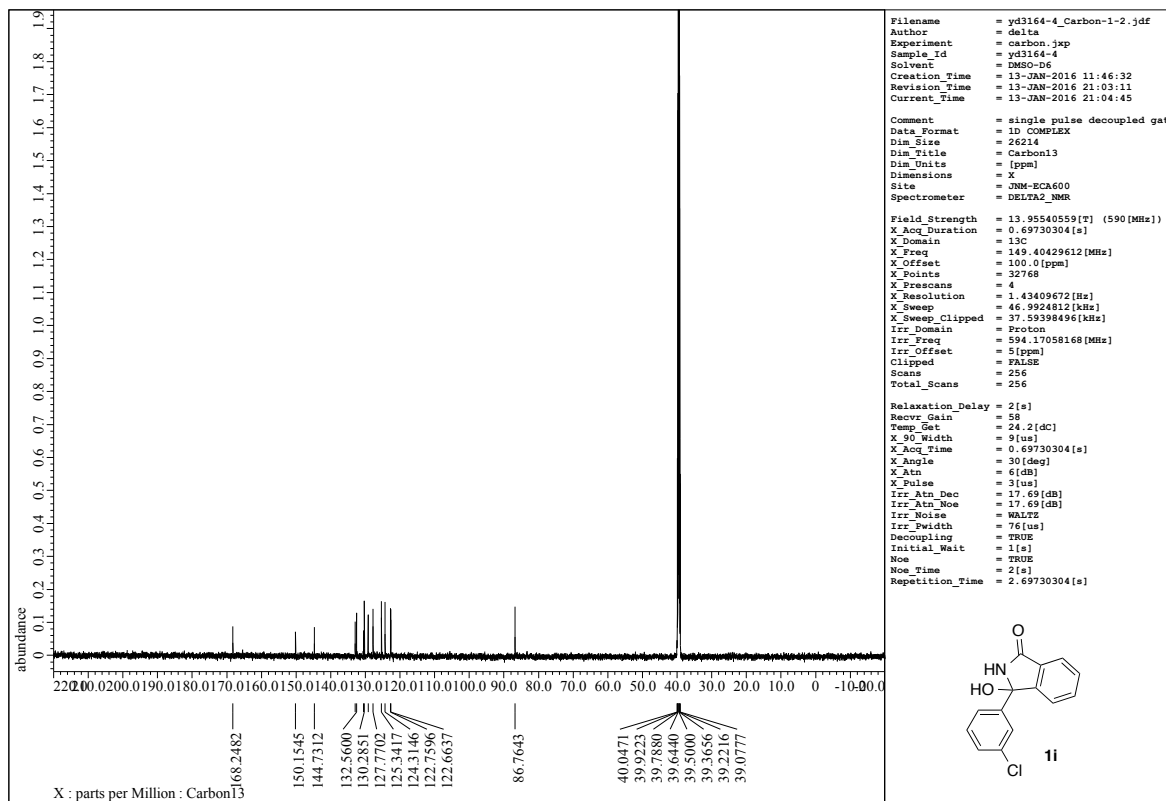
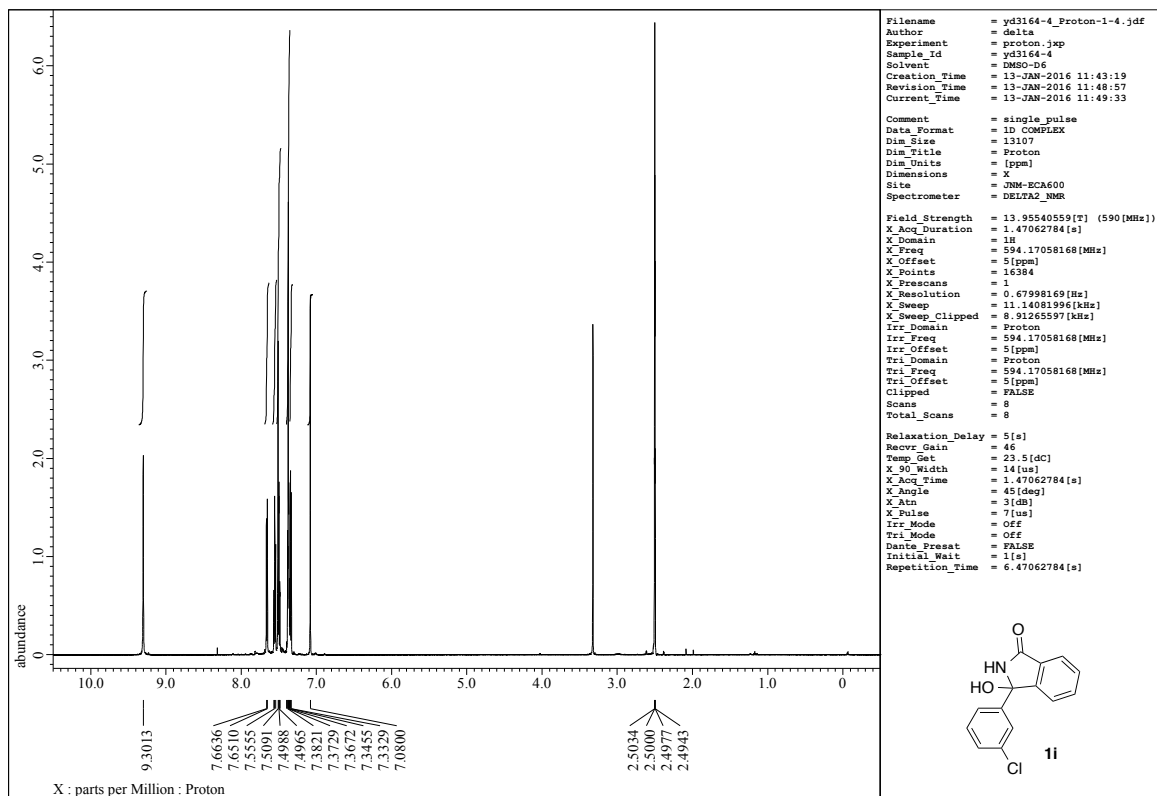


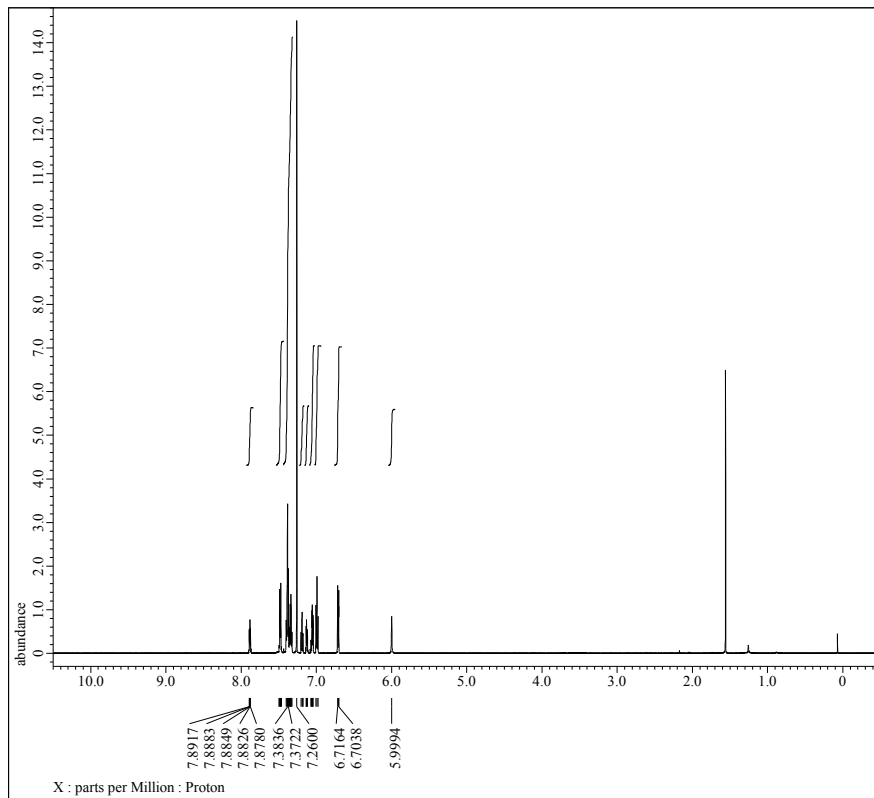












```

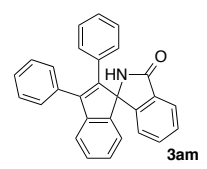
Filename      = yd3167-5 Proton-1-2.jdf
Author       = delta
Experiment   = proton.jsp
Sample_id    = yd3167-5
Solvent      = CHLOROFORM-D
Creation_Time = 4-DEC-2015 20:19:09
Revision_Time = 12-JAN-2016 22:50:42
Current_Time = 12-JAN-2016 22:51:04

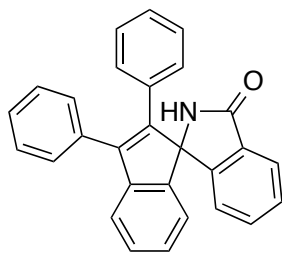
Comment      = single_pulse
Data_Format  = 1D COMPLEX
Dim_Size     = 13107
Dim_Title    = Proton
Dim_Units    = [ppm]
Dimensions   = X
Site         = JNM-ECA600
Spectrometer = DELTA2_NMR

Field_Strength = 13.95540559[T] (590[MHz])
X_Acq_Duration = 1.47062784[s]
X_Domain       = 1H
X_Freq         = 594.17058168[MHz]
X_Offset       = 5[ppm]
X_Points      = 16384
X_Fscans      = 1
X_Resolution  = 0.67998169[Hz]
X_Sweep       = 11.14081996[kHz]
X_Sweep_Clipped = 8.91265597[kHz]
Irr_Domain    = Proton
Irr_Freq      = 594.17058168[MHz]
Irr_Offset    = 5[ppm]
Tri_Domain    = Proton
Tri_Freq      = 594.17058168[MHz]
Tri_Offset    = 5[ppm]
Clipped       = FALSE
Scans         = 8
Total_scans   = 8

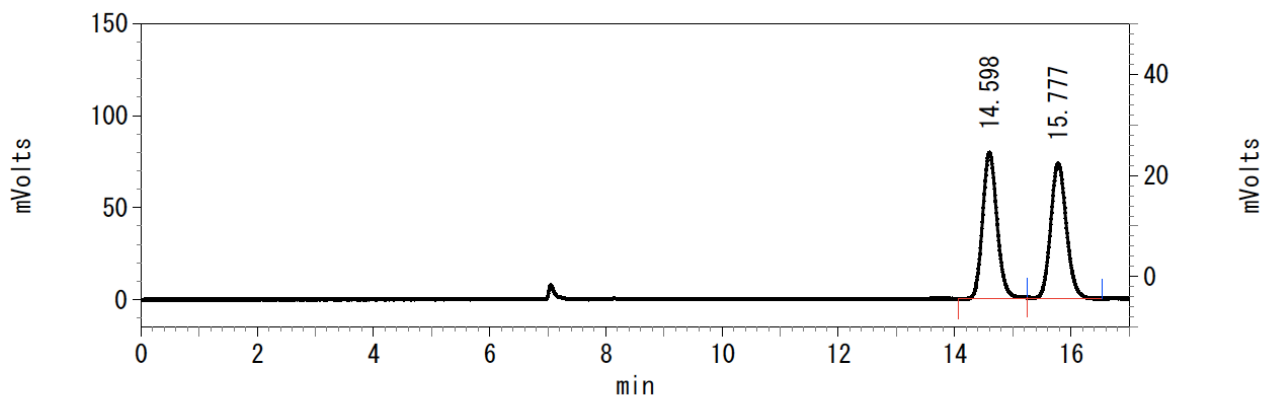
Relaxation_Delay = 5[s]
Recvr_Gain       = 52
Temp_Set         = 23.5[degC]
X_90_Width      = 14[us]
X_Acq_Time      = 1.47062784[s]
X_Angle         = 45[deg]
X_Attn          = 3[dB]
X_Pulse         = 7[us]
Irr_Mode        = OFF
Tri_Mode        = OFF
Dante_Preset    = FALSE
Initial_Wait    = 1[s]
Repetition_time = 6.47062784[s]

```



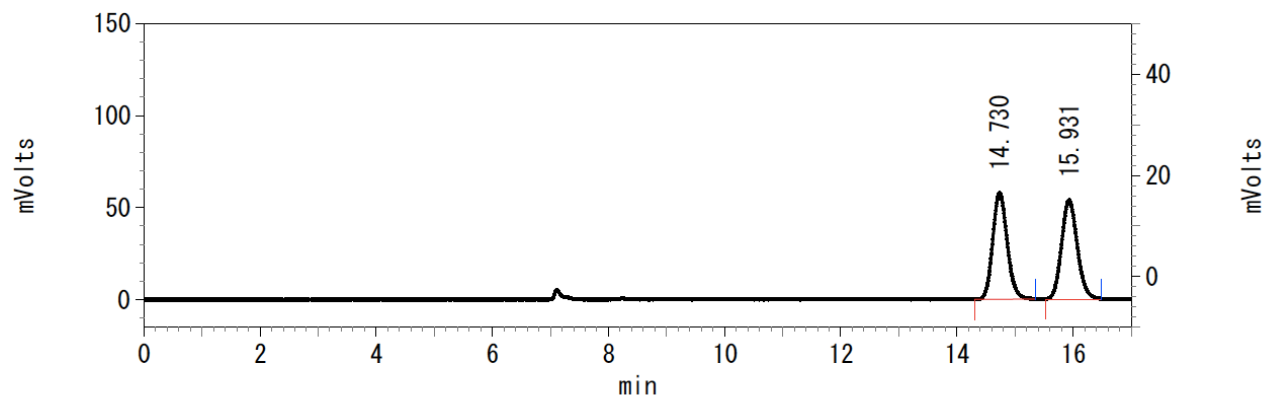


**3am** (Scheme 4, Condition A)

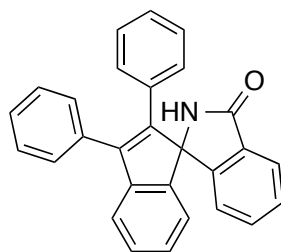


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 14.598         | 1376999 | 49.763       |
| 2    | 15.777         | 1390139 | 50.237       |

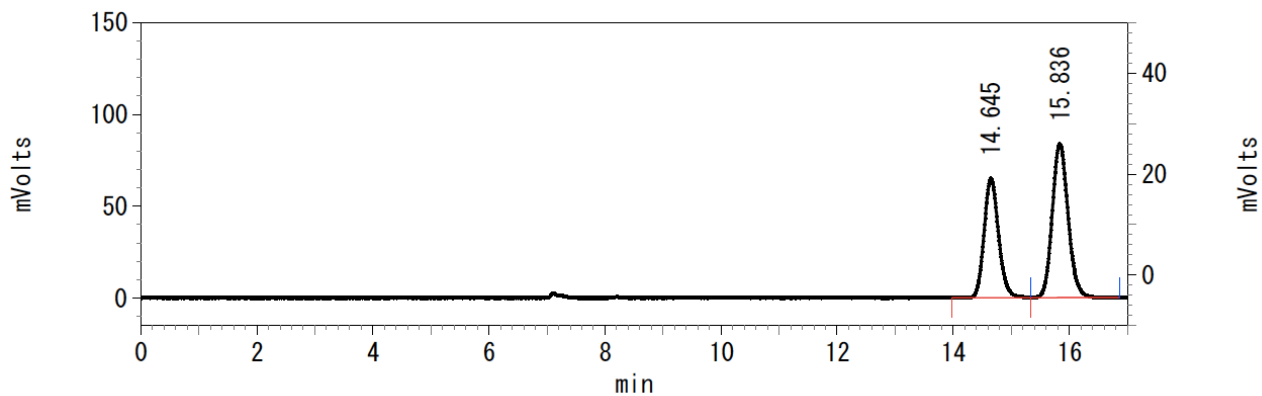
**rac-3am**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 14.730         | 1009376 | 49.916       |
| 2    | 15.931         | 1012785 | 50.084       |

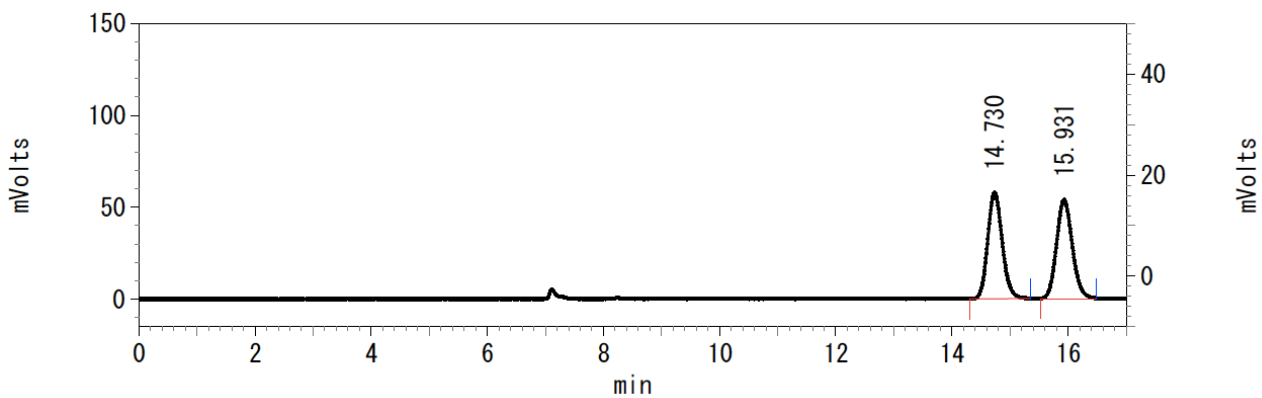


**3am** (Scheme 4, Condition B)

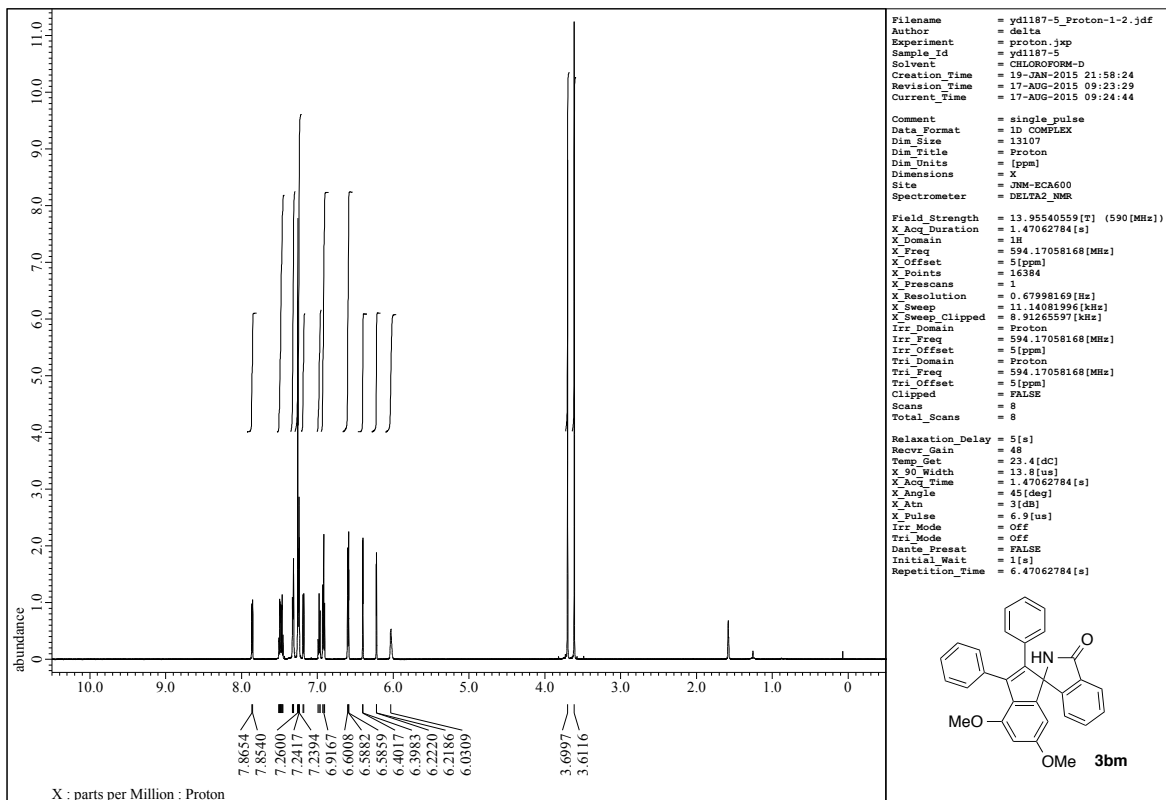


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 14.645         | 1128416 | 41.515       |
| 2    | 15.836         | 1589688 | 58.485       |

*rac*-**3am**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 14.730         | 1009376 | 49.916       |
| 2    | 15.931         | 1012785 | 50.084       |



```

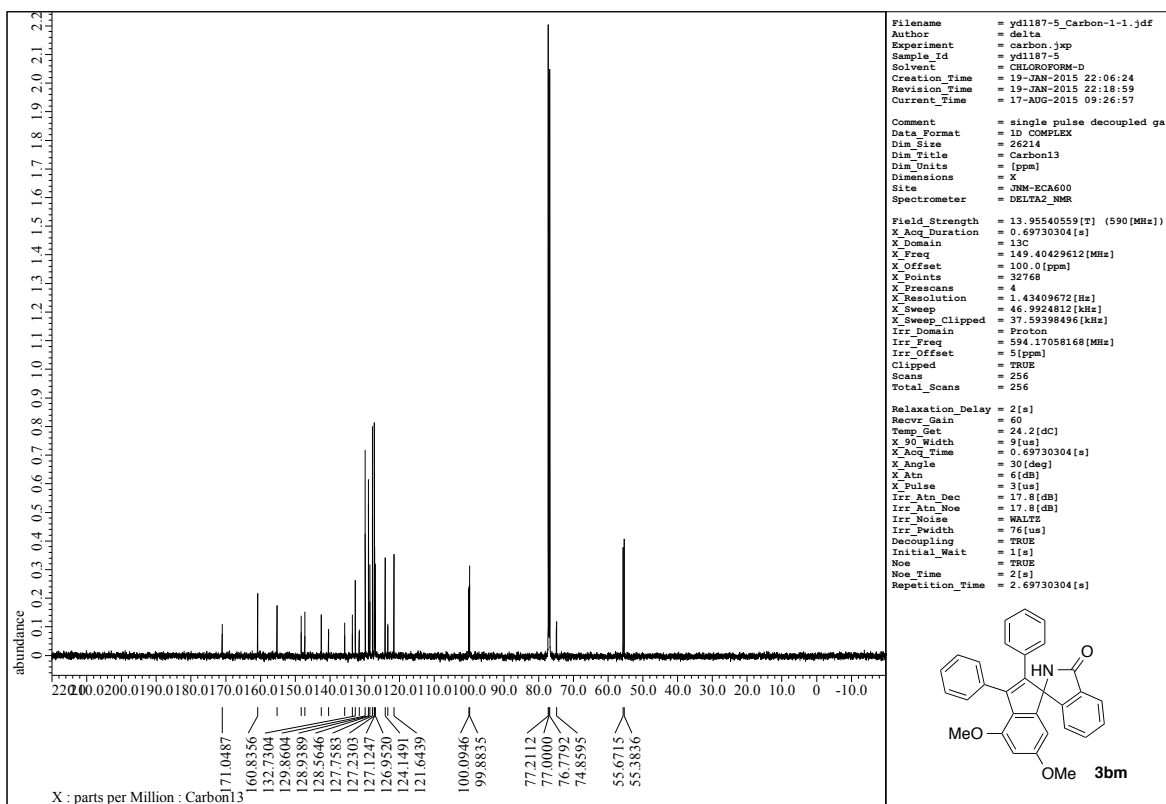
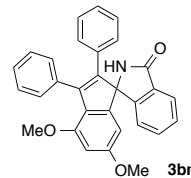
Filename      = yd1187-5_Proton-1-2.jdf
Author       = delta
Experiment   = proton.jxp
Sample_Id    = yd1187-5
Solvent      = CHLOROFORM-D
Creation_Time = 19-JAN-2015 21:58:24
Revision_Time = 17-AUG-2015 09:23:29
Current_Time = 17-AUG-2015 09:24:44

Comment      = single pulse
Data_Format  = 1D_COMPLEX
Dim_Size     = 13107
Dim_Title    = Proton
Dim_Units    = [ppm]
Dimensions   = X
Site         = JNM-ECA600
Spectrometer = DELTA2_NMR

Field_Strength = 13.9540559[T] (590[MHz])
X_Acq_Duration = 1.47062784[s]
X_Domain      = 1H
X_Freq        = 594.17058168[MHz]
X_Offset      = 5[ppm]
X_Points      = 16384
X_Prescans    = 1
X_Resolution  = 0.67998169[Hz]
X_Sweep       = 11.14081996[kHz]
X_Sweep_Clipped = 8.81245597[kHz]
Irr_Domain    = Proton
Irr_Freq      = 594.17058168[MHz]
Irr_Offset    = 5[ppm]
Irr_Domain    = Proton
Tri_Freq      = 594.17058168[MHz]
Tri_Offset    = 5[ppm]
Clipped       = FALSE
Scans         = 8
Total_Scans   = 8

Relaxation_Delay = 5[s]
Recvr_Gain       = 48
Temp_Get         = 23.4[dc]
X_90_Width      = 13.8[us]
X_Acq_Time      = 1.47062784[s]
X_Angle         = 45[deg]
X_Atn           = 3[db]
X_Pulse         = 6.9[us]
Irr_Mode        = OFF
Tri_Mode        = OFF
DanLe_Preset    = FALSE
Initial_Wait    = 1[s]
Repetition_Time = 6.47062784[s]

```



```

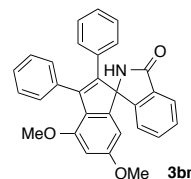
Filename      = yd1187-5_Carbon-1-1.jdf
Author       = delta
Experiment   = carbon.jxp
Sample_Id    = yd1187-5
Solvent      = CHLOROFORM-D
Creation_Time = 19-JAN-2015 22:06:24
Revision_Time = 19-JAN-2015 22:18:59
Current_Time = 17-AUG-2015 09:26:57

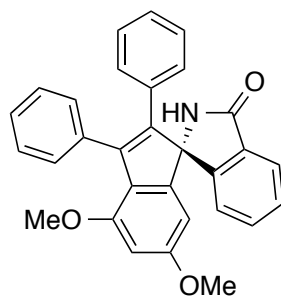
Comment      = single pulse decoupled gat
Data_Format  = 1D_COMPLEX
Dim_Size     = 26214
Dim_Title    = Carbon13
Dim_Units    = [ppm]
Dimensions   = X
Site         = JNM-ECA600
Spectrometer = DELTA2_NMR

Field_Strength = 13.9540559[T] (590[MHz])
X_Acq_Duration = 0.69730304[s]
X_Domain      = 13c
X_Freq        = 149.40429612[MHz]
X_Offset      = 100.0[ppm]
X_Points      = 32768
X_Prescans    = 4
X_Resolution  = 1.43409672[Hz]
X_Sweep       = 46.9924812[kHz]
X_Sweep_Clipped = 37.59398496[kHz]
Irr_Domain    = Proton
Irr_Freq      = 594.17058168[MHz]
Irr_Offset    = 5[ppm]
Clipped       = TRUE
Scans         = 256
Total_Scans   = 256

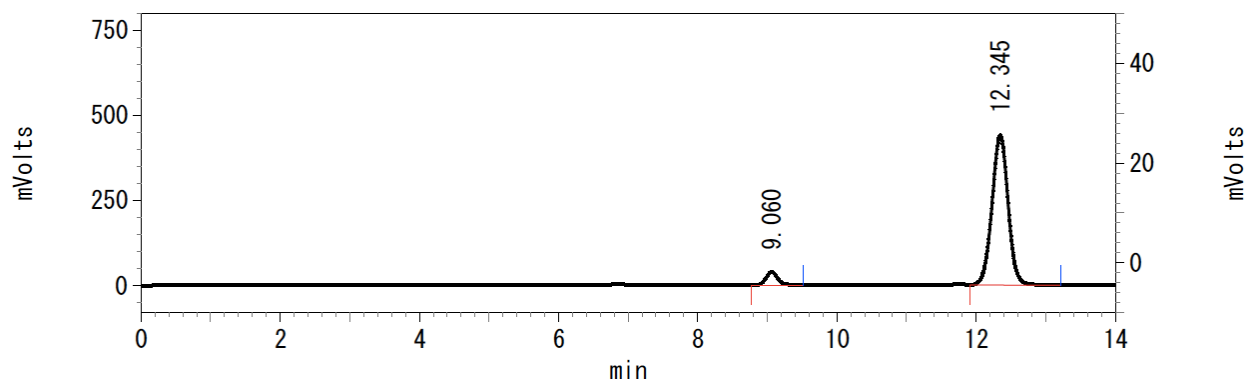
Relaxation_Delay = 2[s]
Recvr_Gain       = 60
Temp_Get         = 24.2[dc]
X_90_Width      = 9[us]
X_Acq_Time      = 0.69730304[s]
X_Angle         = 30[deg]
X_Atn           = 6[db]
X_Pulse         = 3[us]
Irr_Atn_Dec     = 17.8[db]
Irr_Atn_Noise  = 17.8[db]
Irr_Noise       = WALTZ
Irr_Pwidth      = 76[us]
Decoupling      = TRUE
Initial_Wait    = 1[s]
Noe              = TRUE
Noe_Time        = 2[s]
Repetition_Time = 2.69730304[s]

```



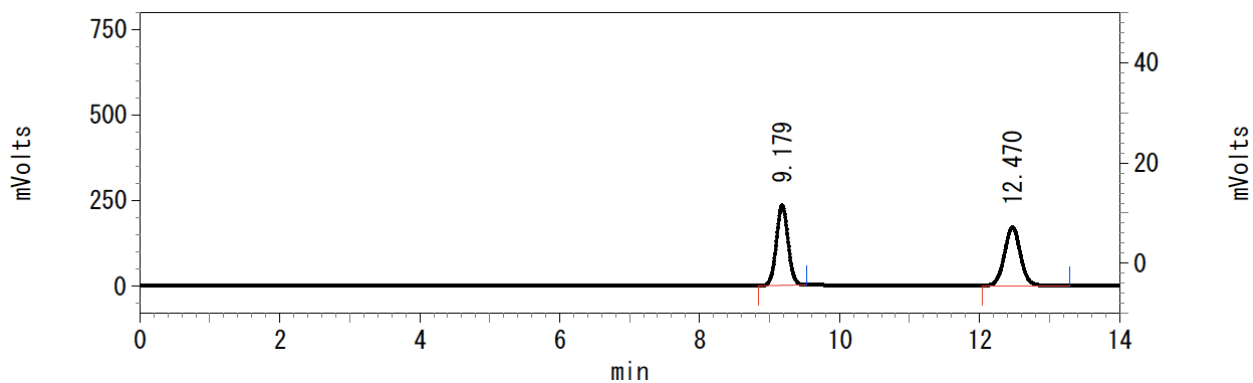


**3bm (S)** (Table 1, entry 1, Condition A)



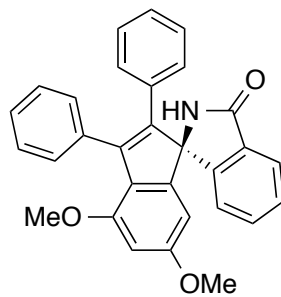
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.060          | 458242  | 6.076        |
| 2    | 12.345         | 7083350 | 93.924       |

*rac*-3bm

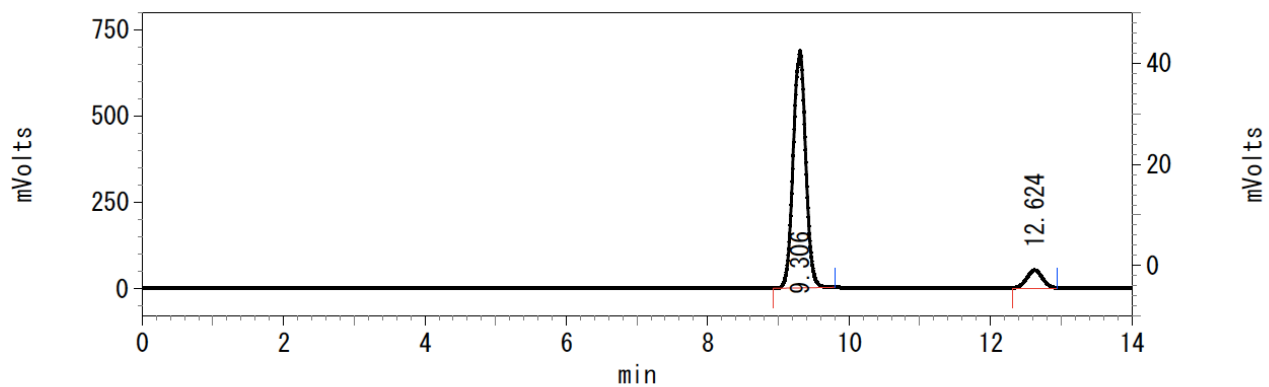


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.179          | 2725372 | 49.935       |
| 2    | 12.470         | 2732515 | 50.065       |



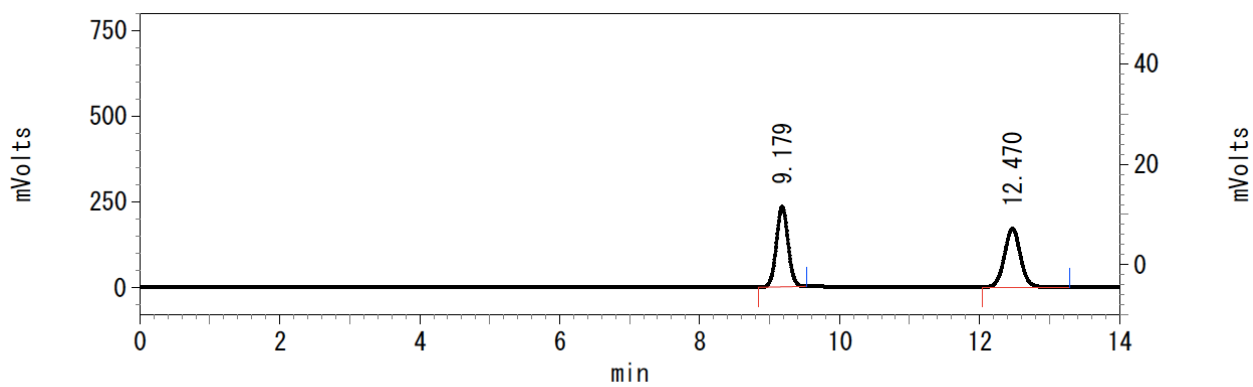


**3bm (R)** (Table 1, entry 2, Condition B)

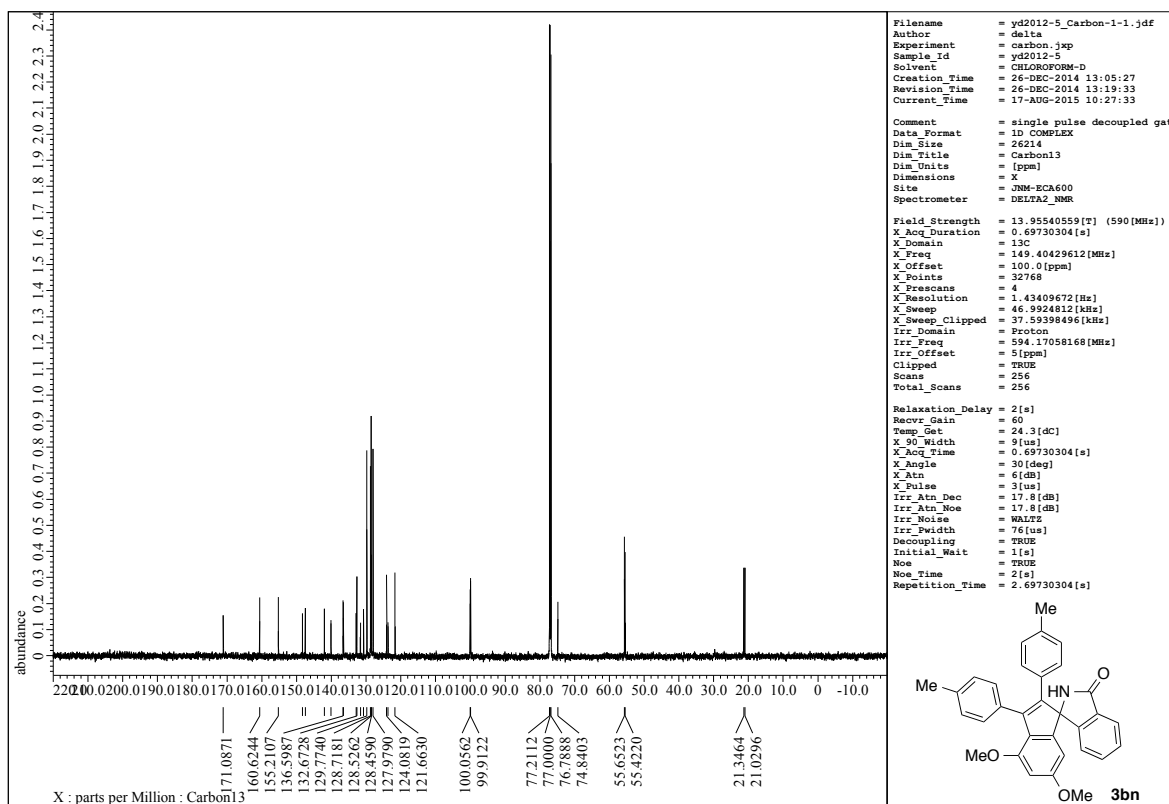
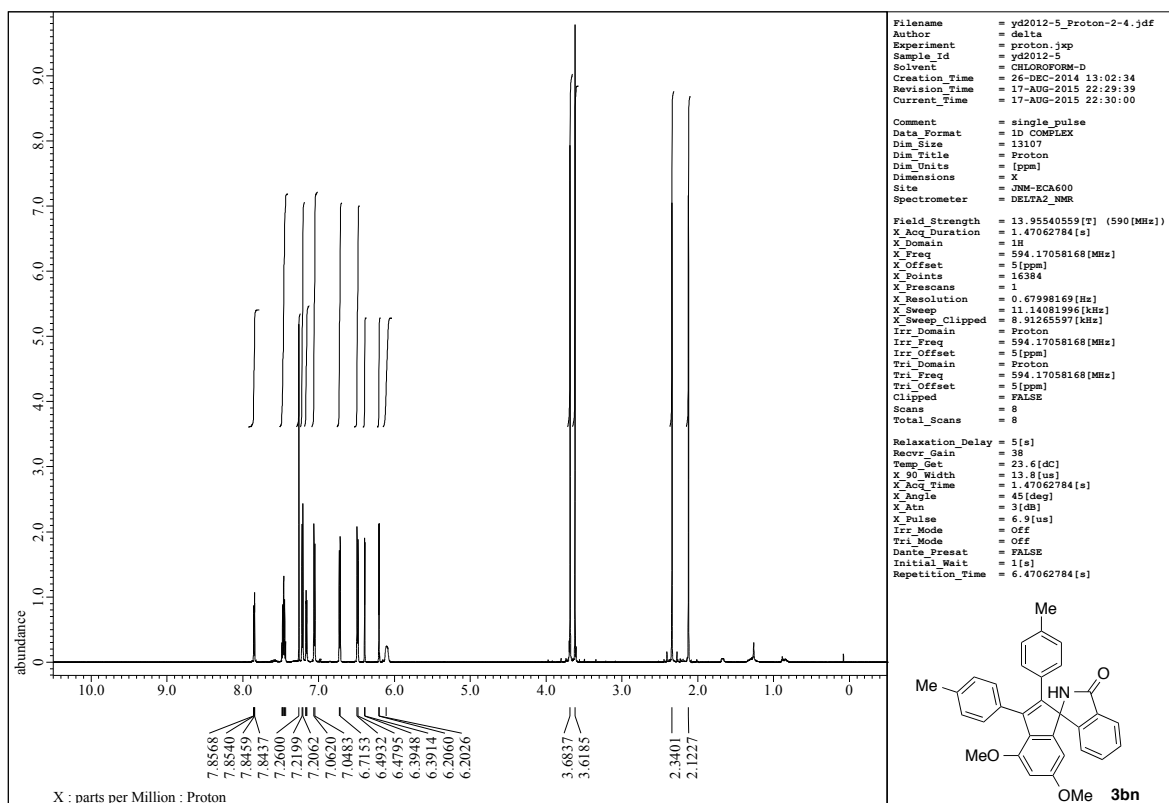


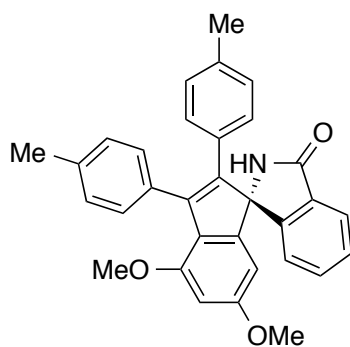
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.306          | 8480483 | 91.401       |
| 2    | 12.624         | 797856  | 8.599        |

**rac-3bm**

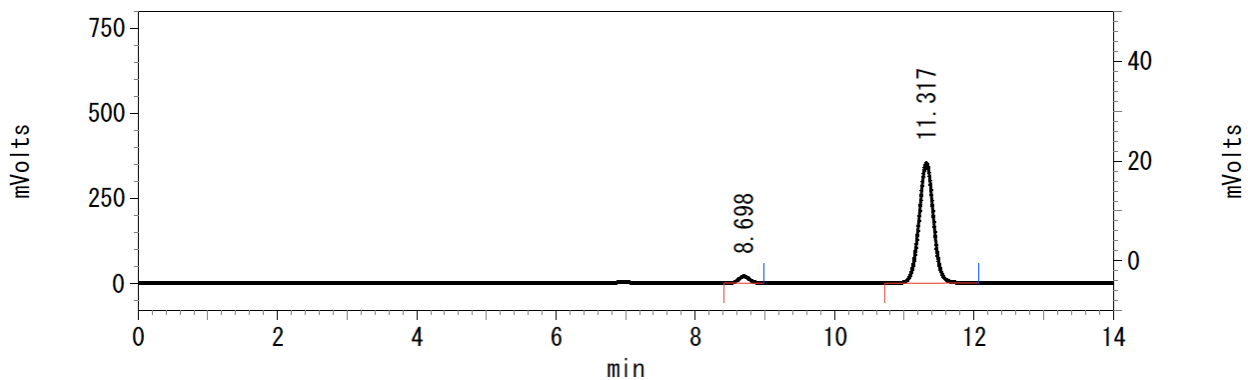


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.179          | 2725372 | 49.935       |
| 2    | 12.470         | 2732515 | 50.065       |



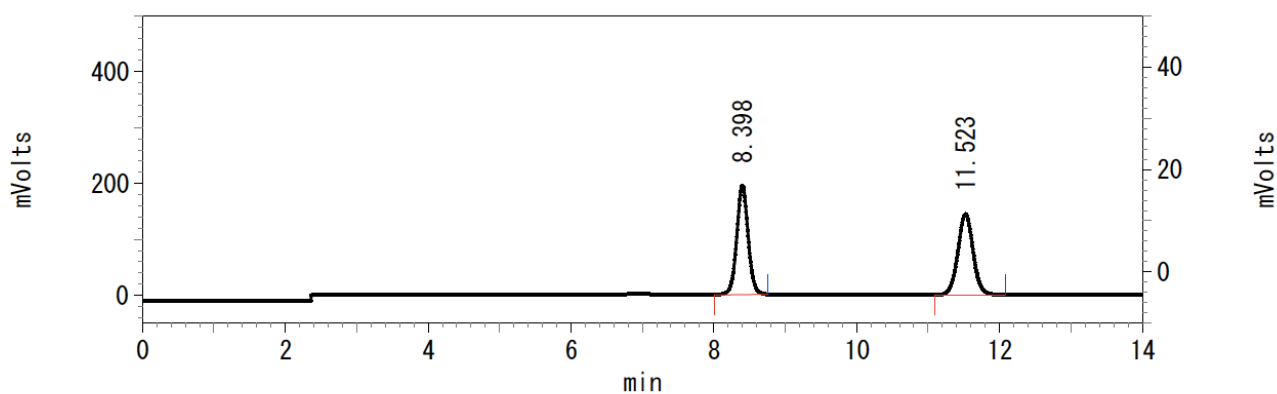


**3bn (S)** (Table 1, entry 3, Condition A)

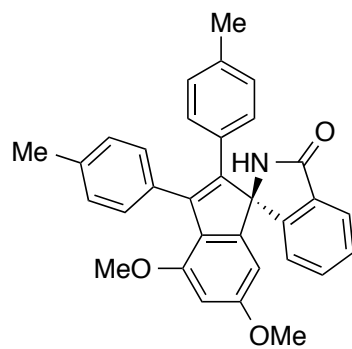


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.698          | 216309  | 4.060        |
| 2    | 11.317         | 5111392 | 95.940       |

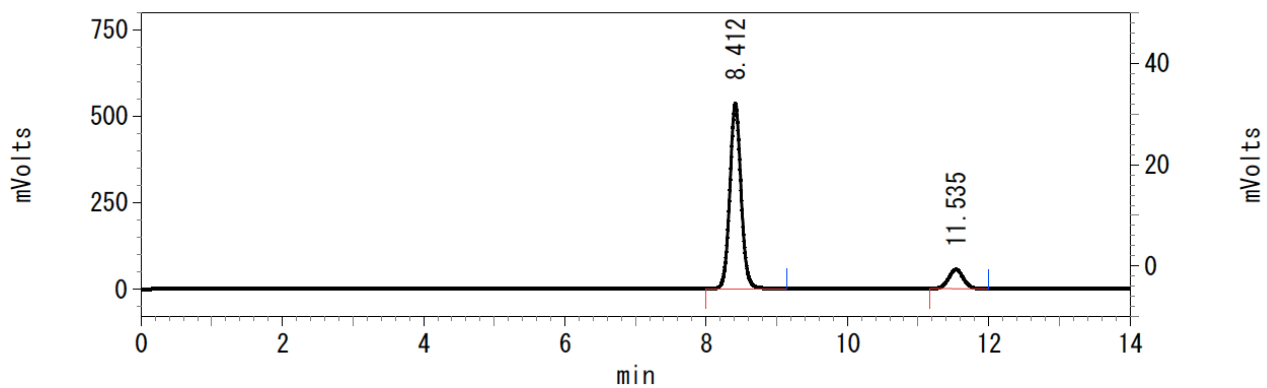
**rac-3bn**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.398          | 2169150 | 50.248       |
| 2    | 11.523         | 2147757 | 49.752       |

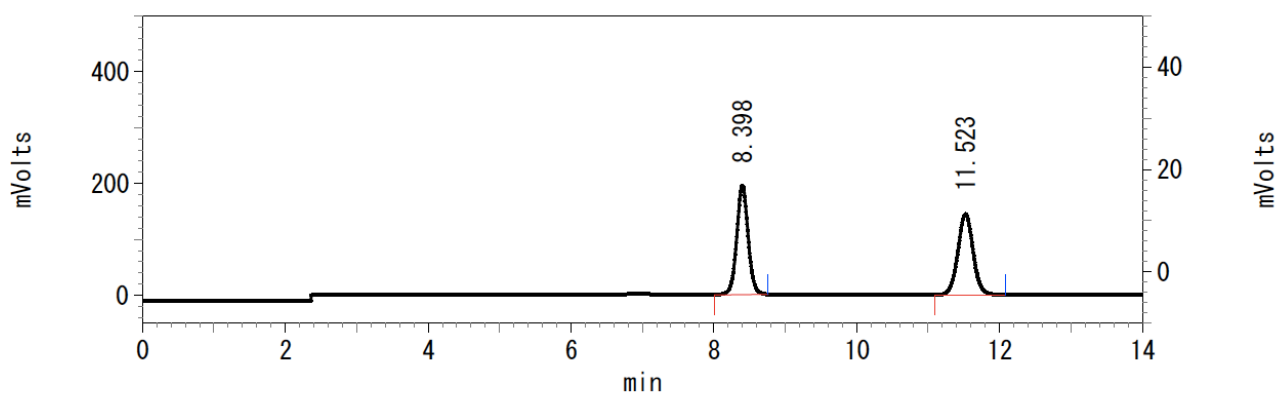


**3bn (R)** (Table 1, entry 4, Condition B)

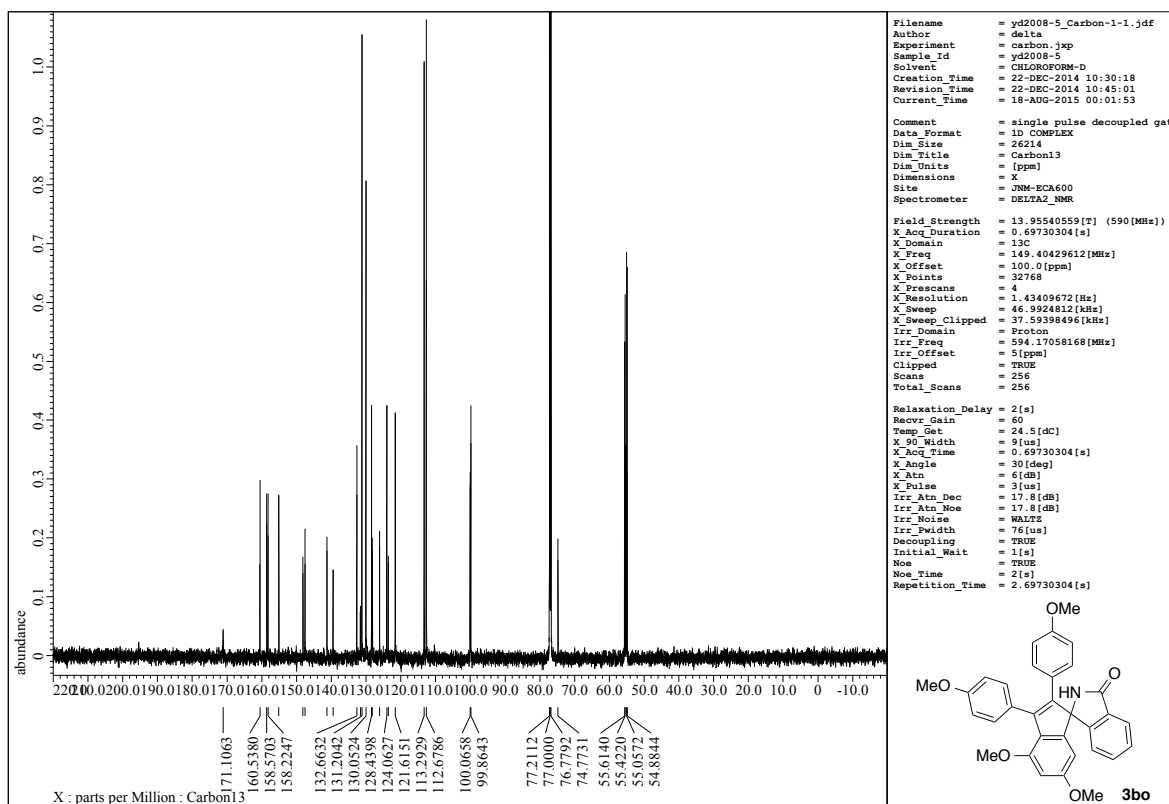
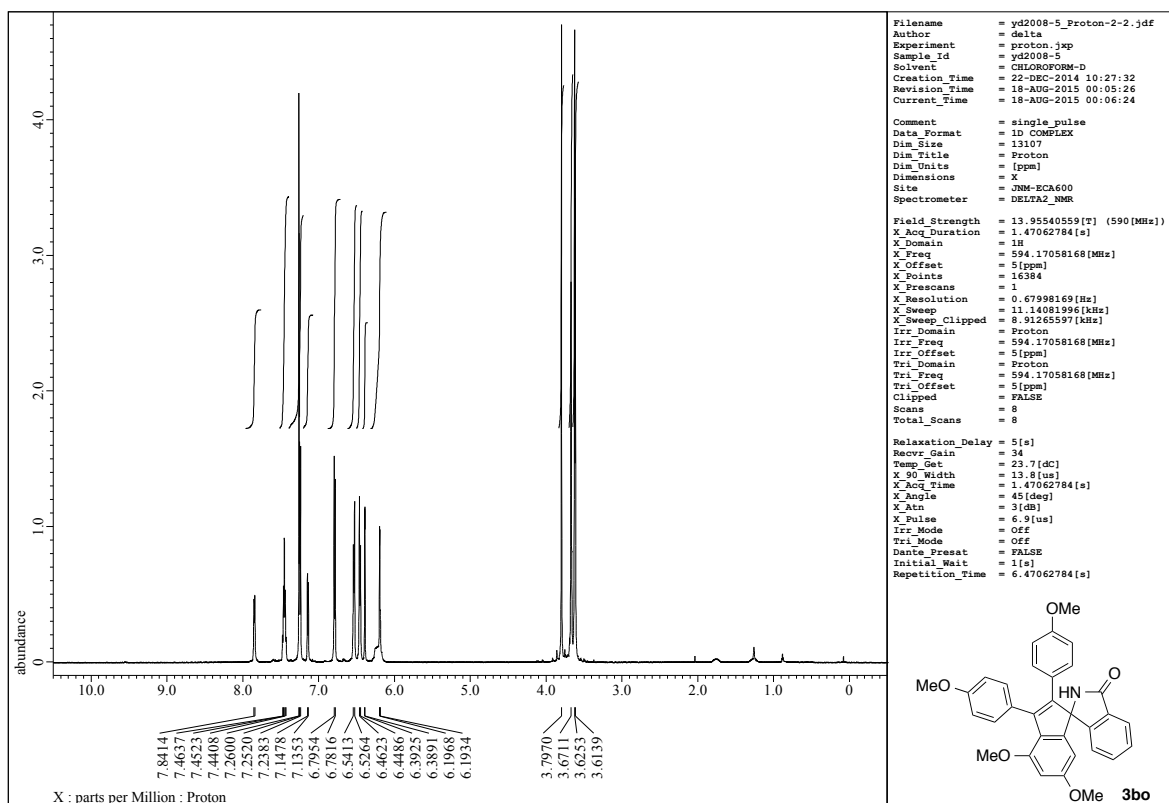


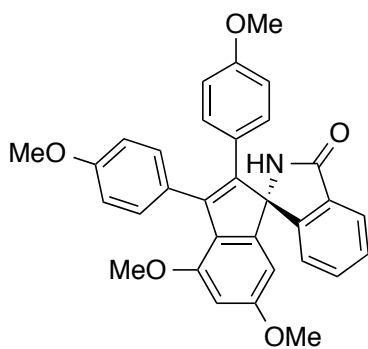
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.412          | 5939458 | 87.913       |
| 2    | 11.535         | 816582  | 12.087       |

*rac*-3bn

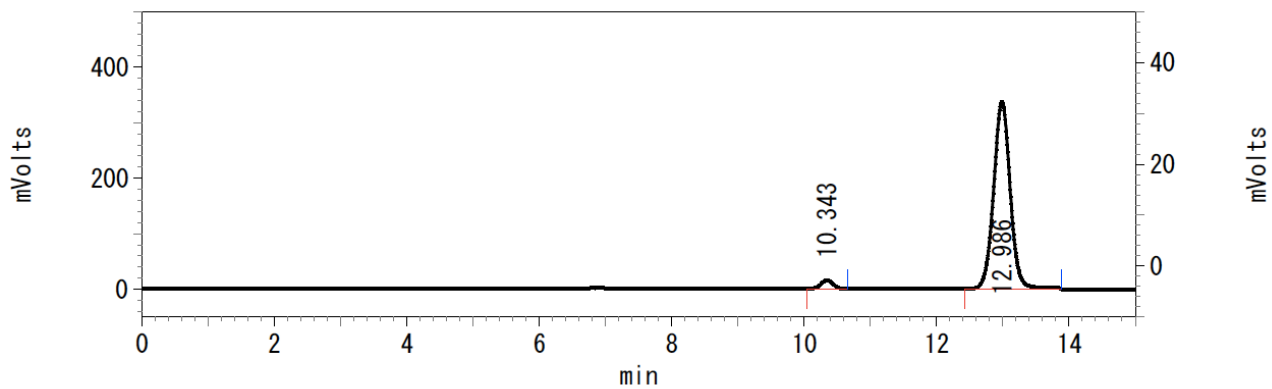


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.398          | 2169150 | 50.248       |
| 2    | 11.523         | 2147757 | 49.752       |



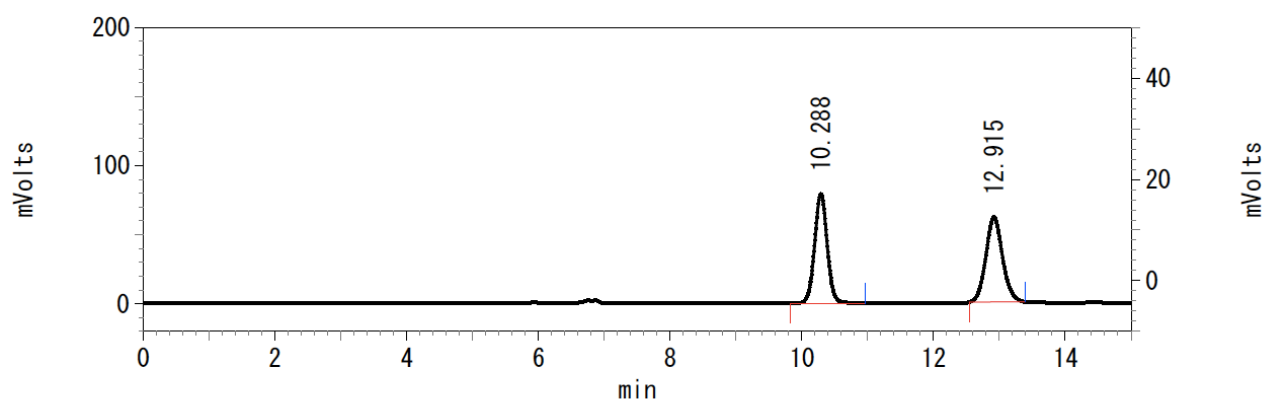


**3bo (S)** (Table 1, entry 5, Condition A)

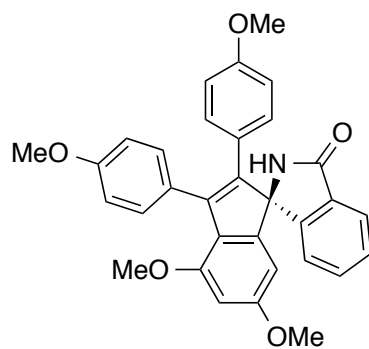


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.343         | 204409  | 3.350        |
| 2    | 12.986         | 5897229 | 96.650       |

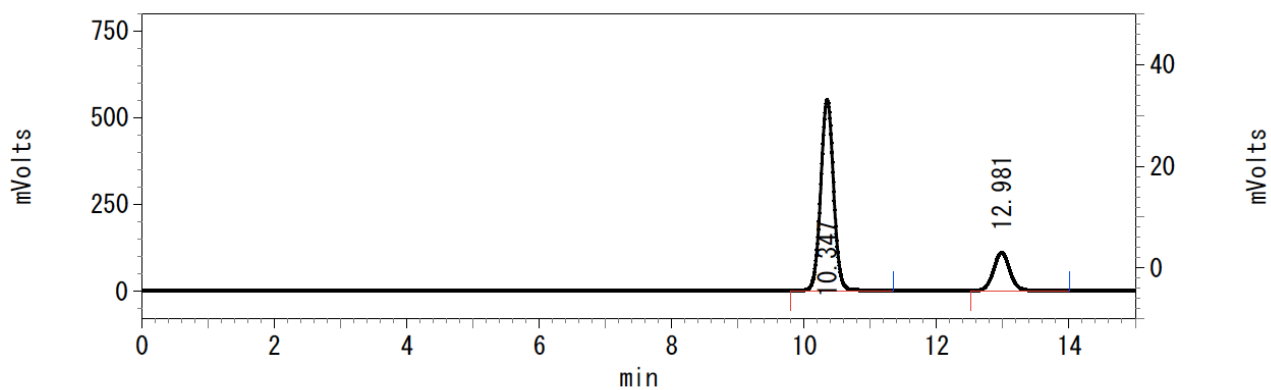
*rac*-**3bo**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.288         | 1046820 | 49.057       |
| 2    | 12.915         | 1087074 | 50.943       |

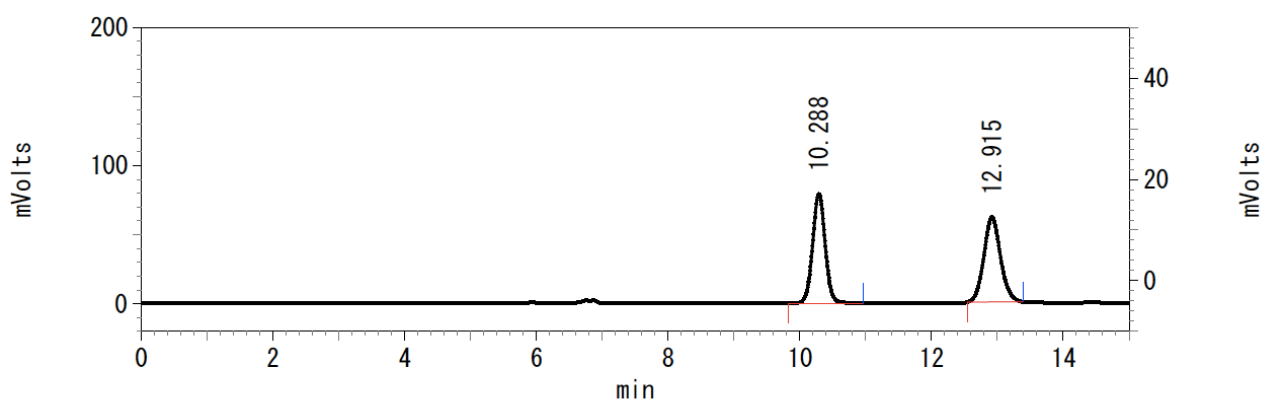


**3bo (R)** (Table 1, entry 6, Condition B)

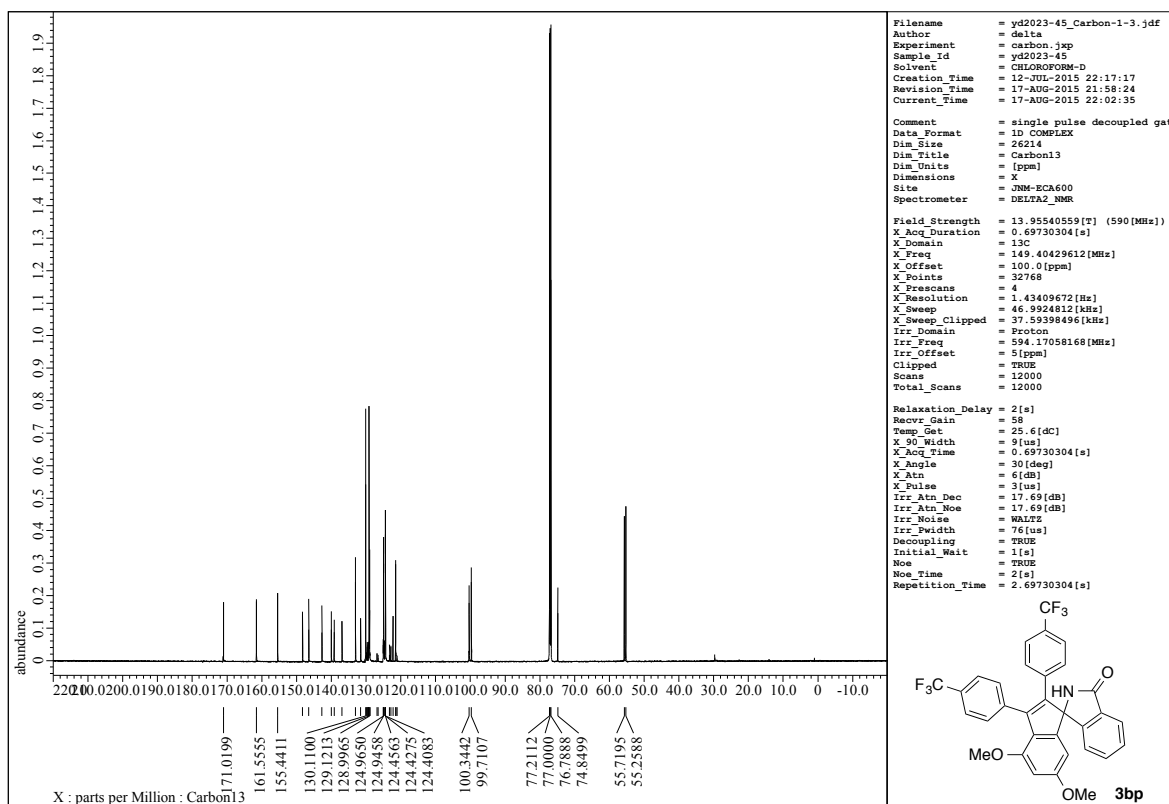
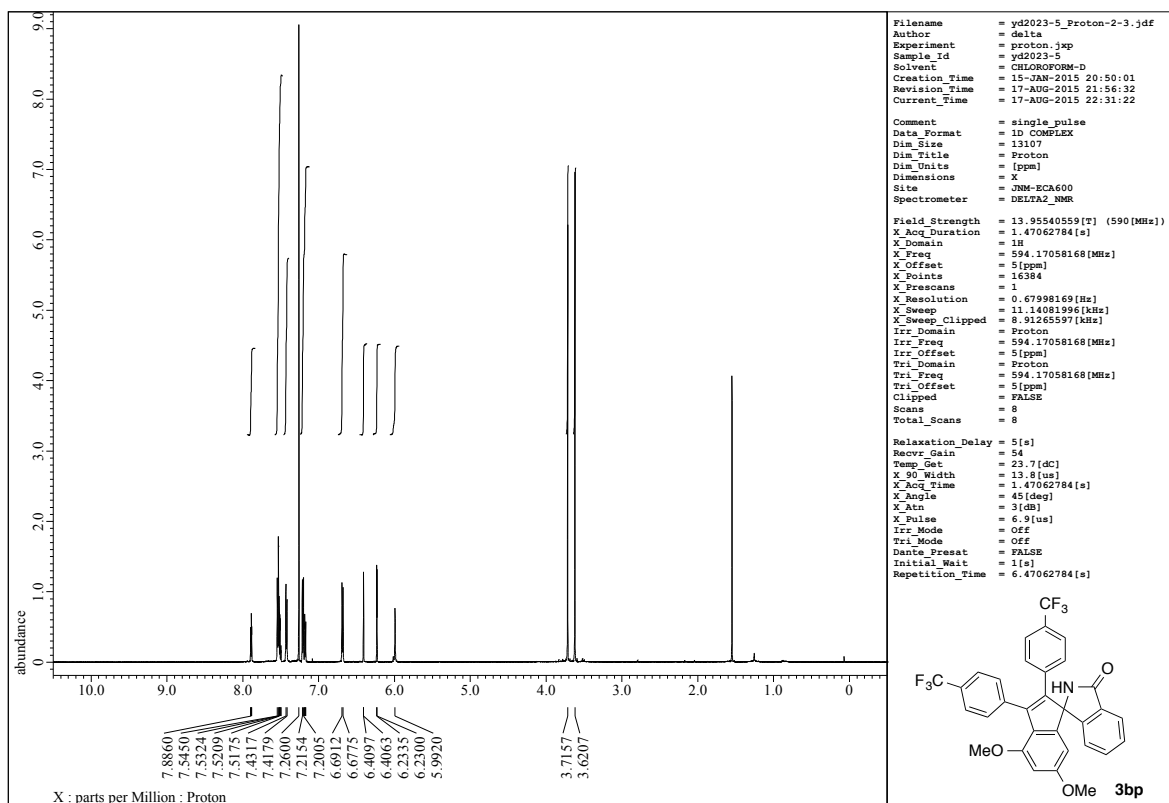


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.347         | 7474330 | 79.572       |
| 2    | 12.981         | 1918879 | 20.428       |

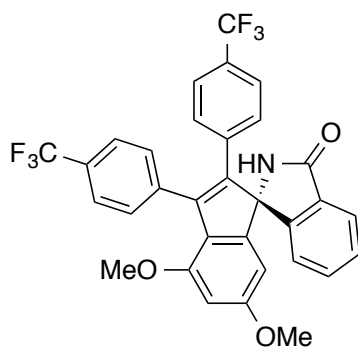
**rac-3bo**



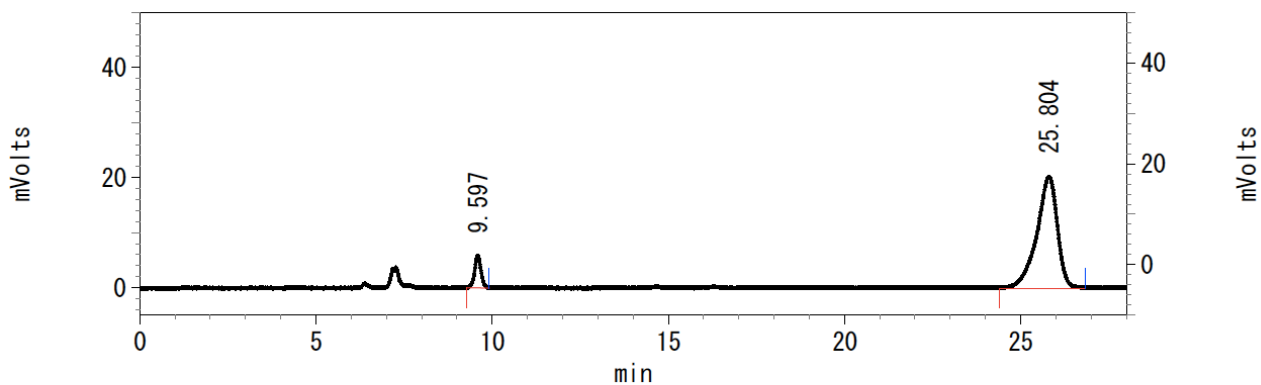
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.288         | 1046820 | 49.057       |
| 2    | 12.915         | 1087074 | 50.943       |





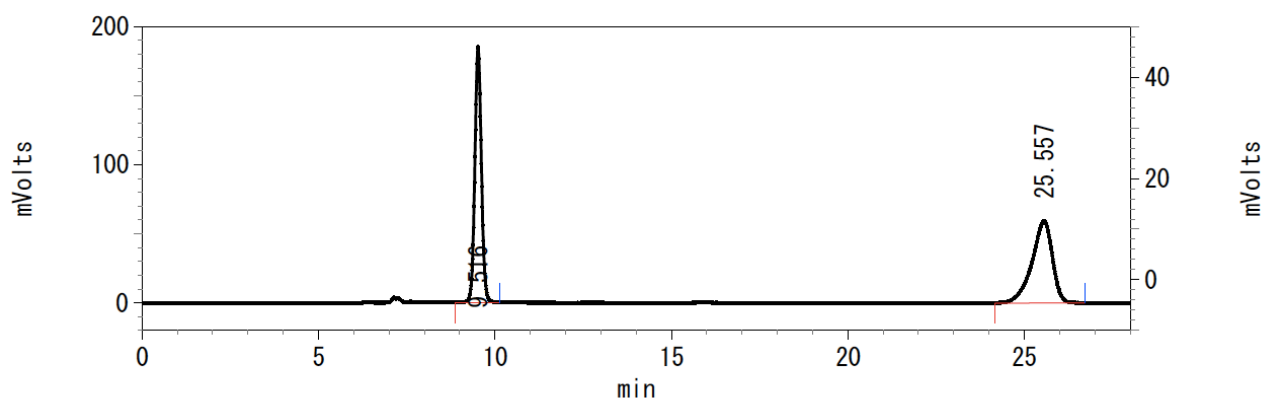


**3bp (S)** (Table 1, entry 7, Condition A)

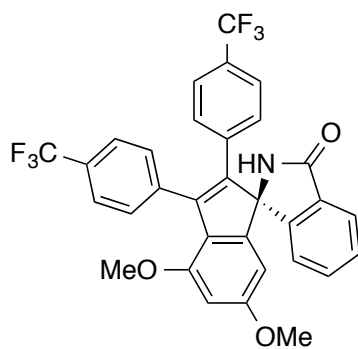


| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 9.597          | 74787  | 8.341        |
| 2    | 25.804         | 821836 | 91.659       |

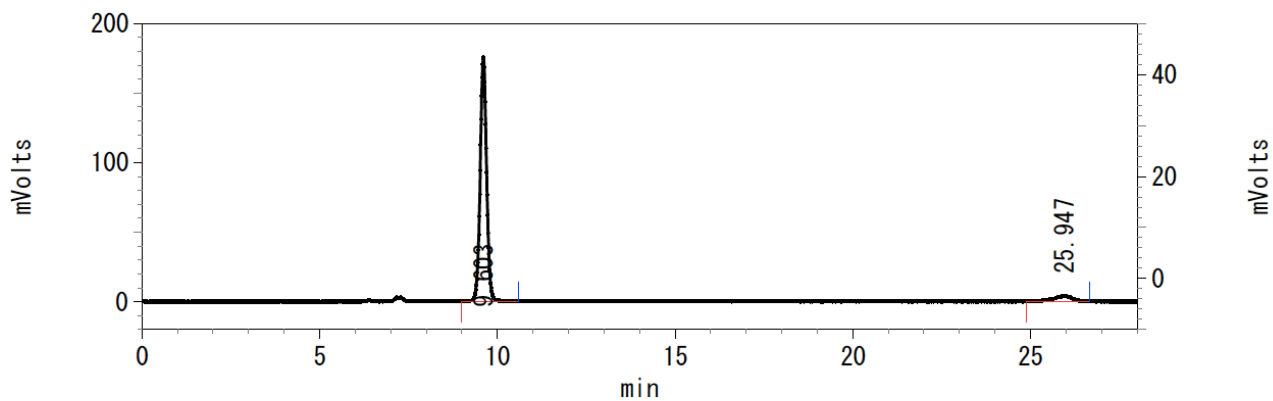
*rac*-3bp



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.516          | 2407973 | 50.080       |
| 2    | 25.557         | 2400314 | 49.920       |

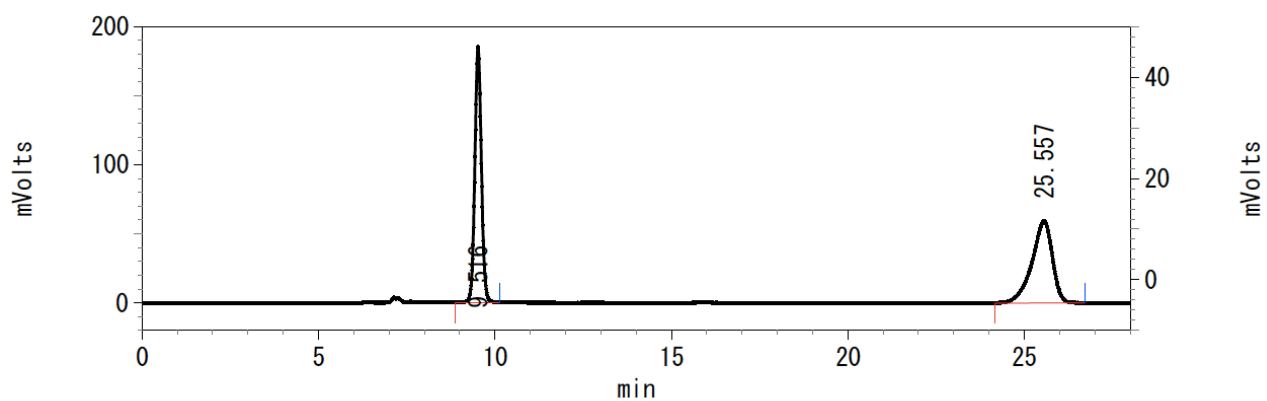


**3bp (R)** (Table 1, entry 8, Condition B)

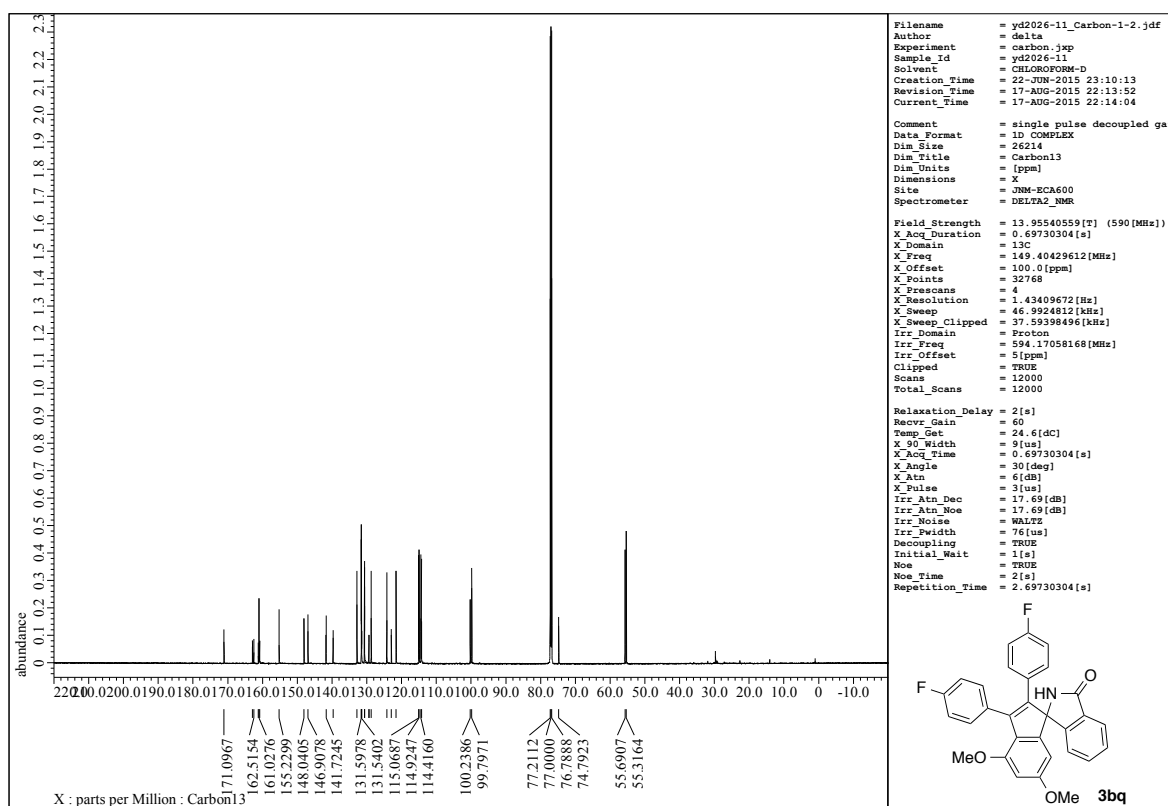
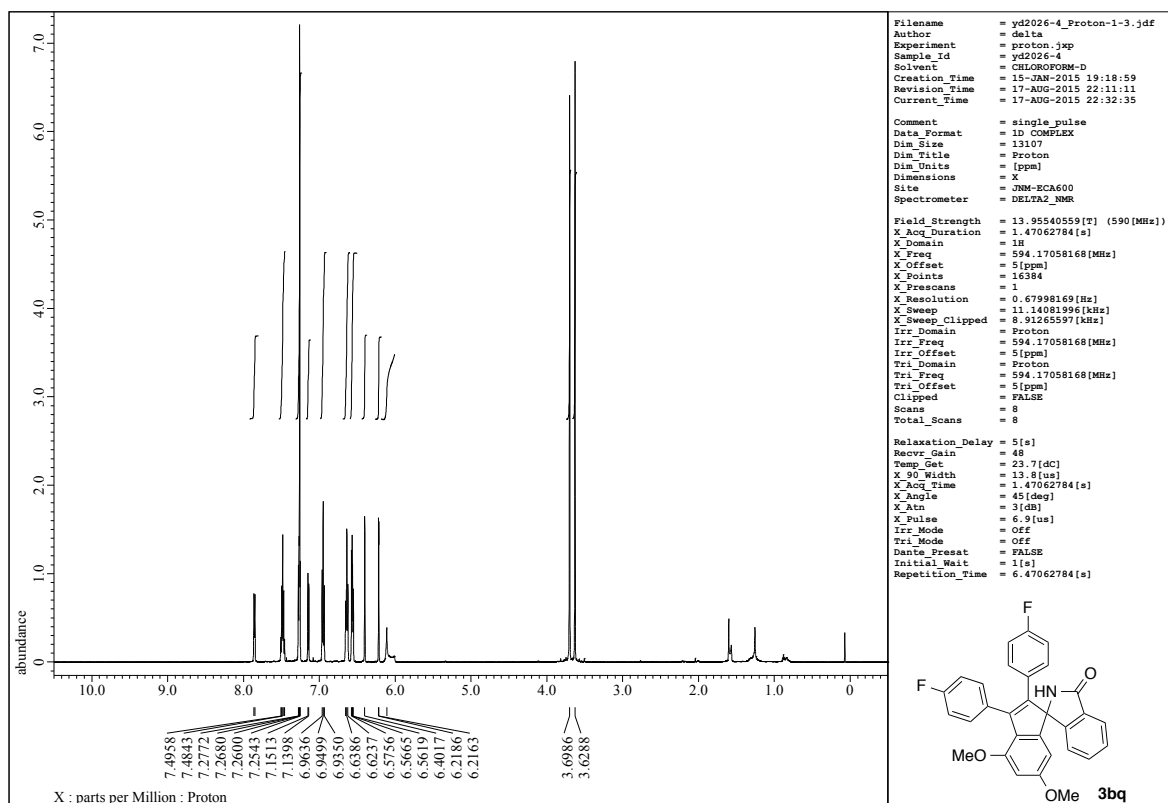


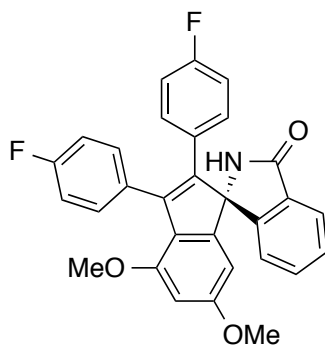
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.603          | 2229887 | 93.355       |
| 2    | 25.947         | 158732  | 6.645        |

**rac-3bp**

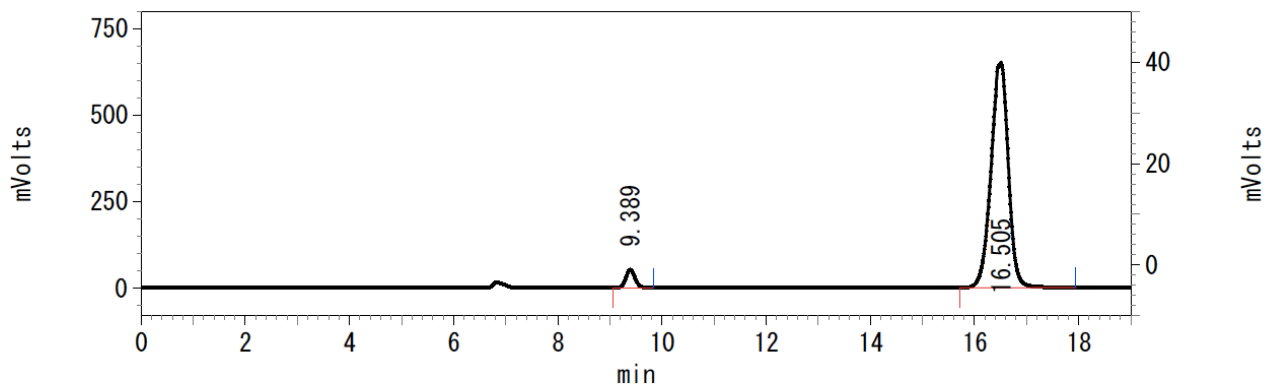


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.516          | 2407973 | 50.080       |
| 2    | 25.557         | 2400314 | 49.920       |



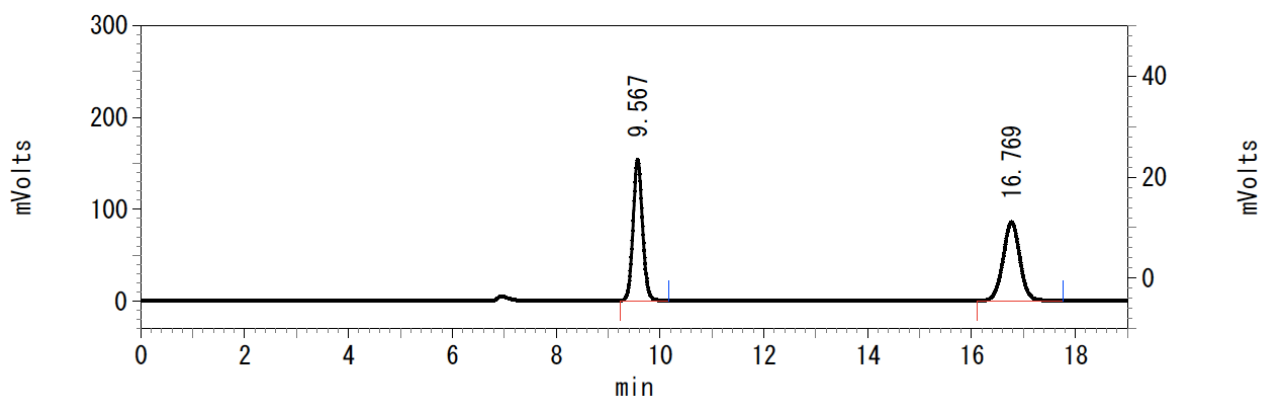


**3bq (S)** (Table 1, entry 9, Condition A)

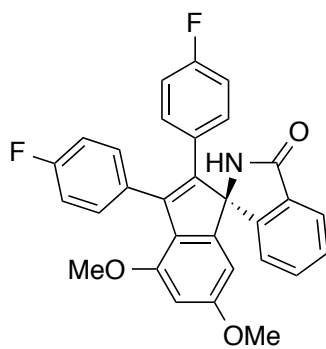


| Pk # | Retention Time | Area     | Area Percent |
|------|----------------|----------|--------------|
| 1    | 9.389          | 650079   | 4.151        |
| 2    | 16.505         | 15010762 | 95.849       |

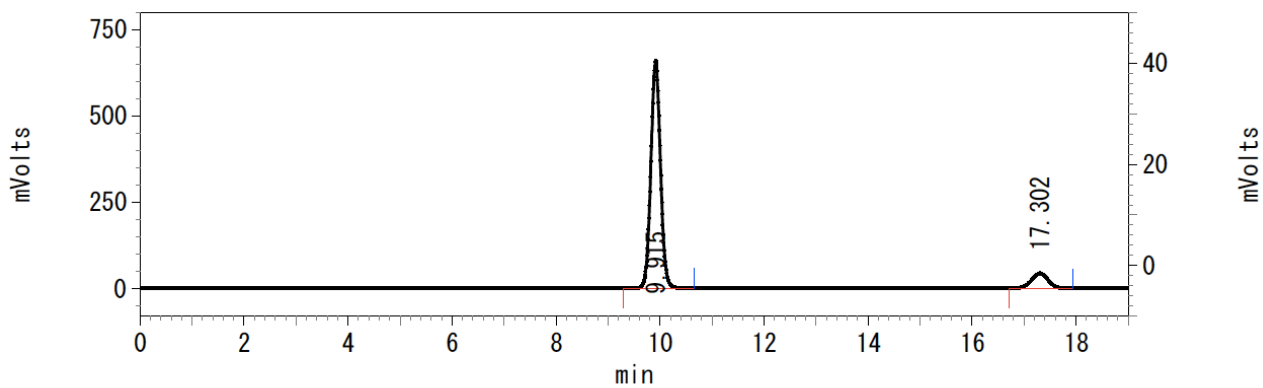
**rac-3bp**



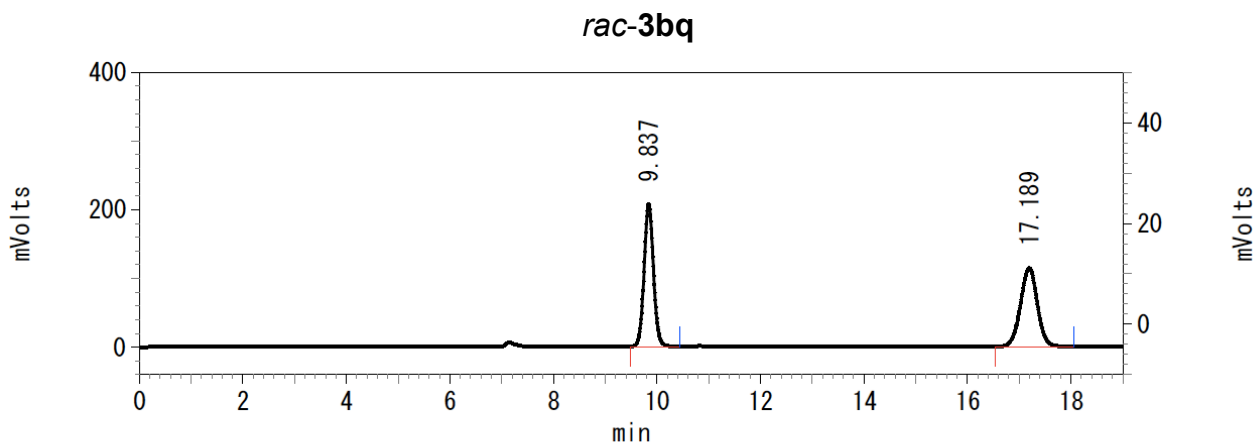
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.567          | 1935034 | 49.992       |
| 2    | 16.769         | 1935658 | 50.008       |



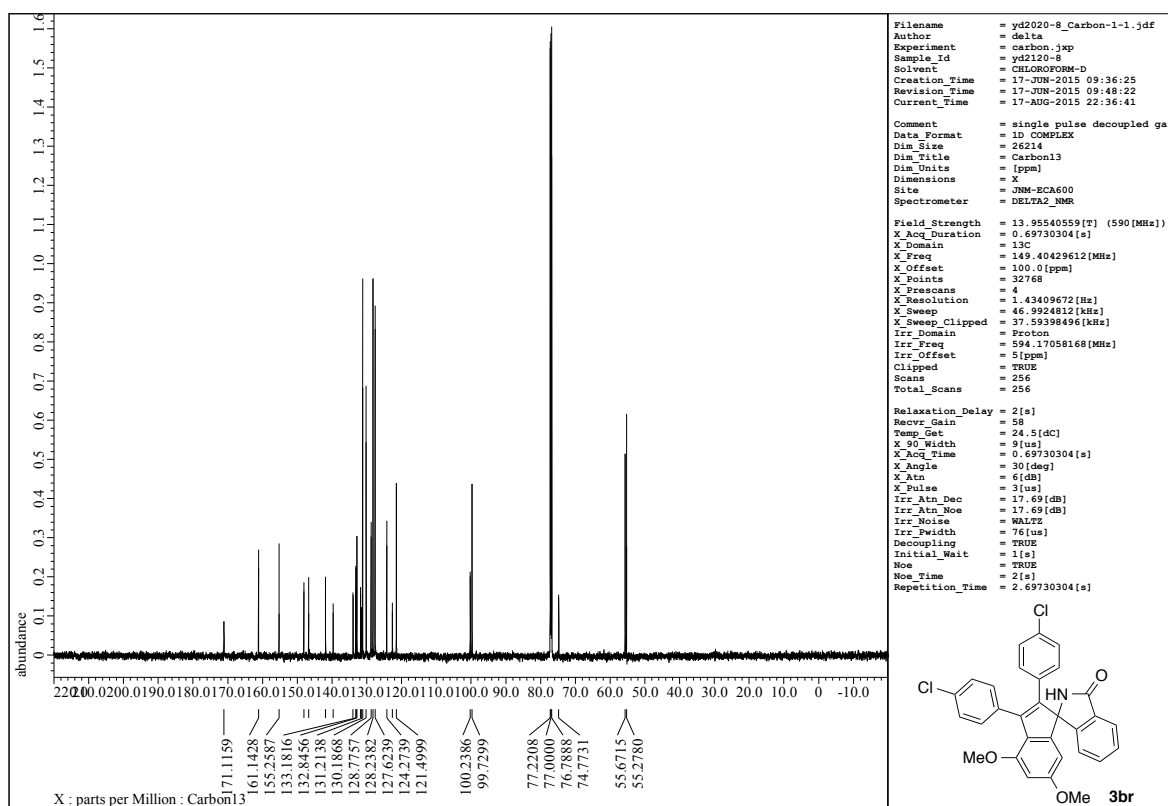
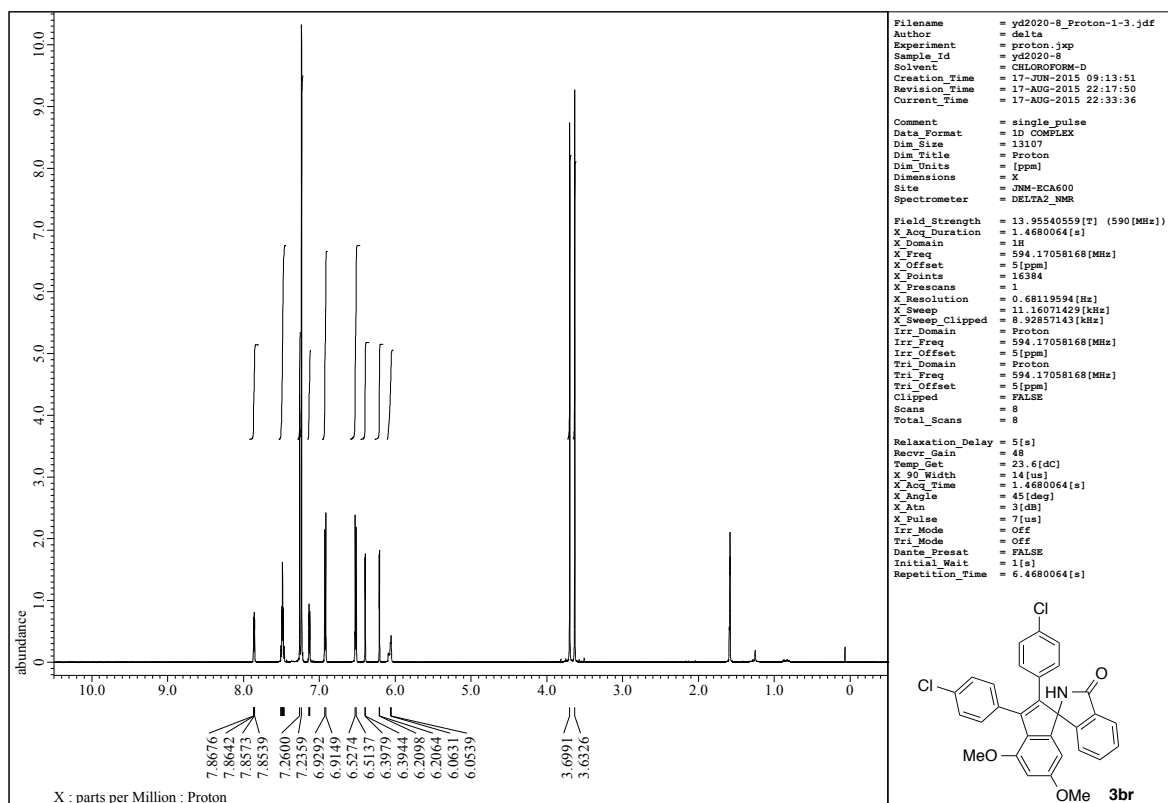
**3bq (R)** (Table 1, entry 10, Condition B)

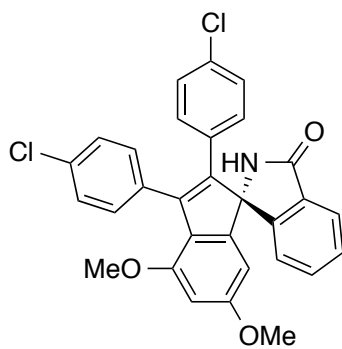


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.915          | 8483693 | 89.548       |
| 2    | 17.302         | 990162  | 10.452       |

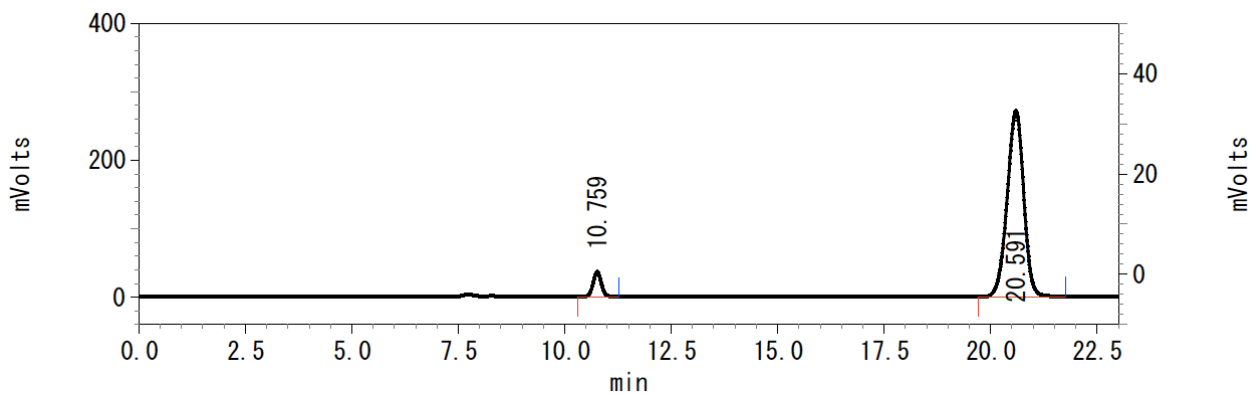


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.837          | 2616971 | 50.046       |
| 2    | 17.189         | 2612198 | 49.954       |



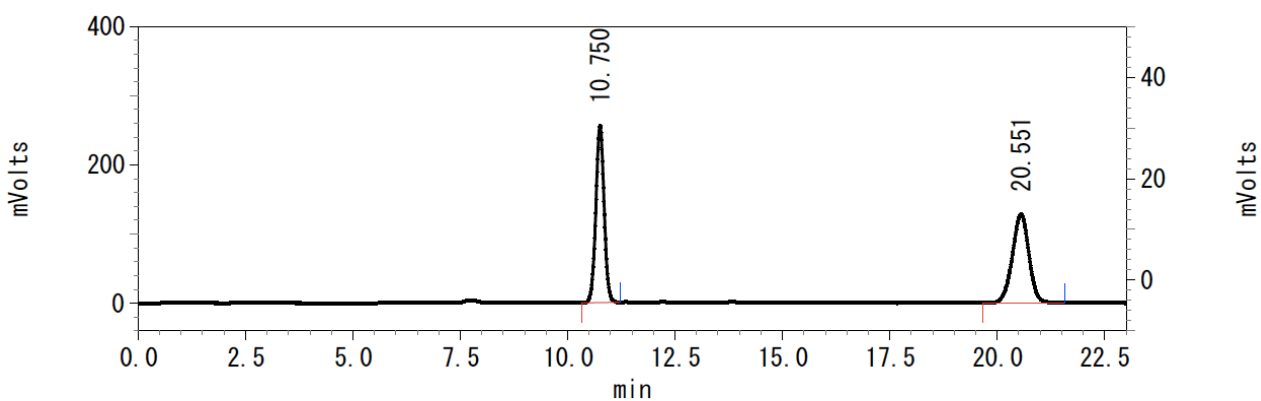


**3br (S)** (Table 1, entry 11, Condition A)

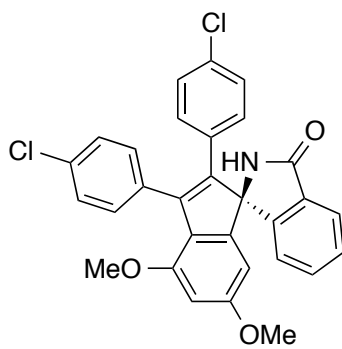


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.759         | 503487  | 6.392        |
| 2    | 20.591         | 7372735 | 93.608       |

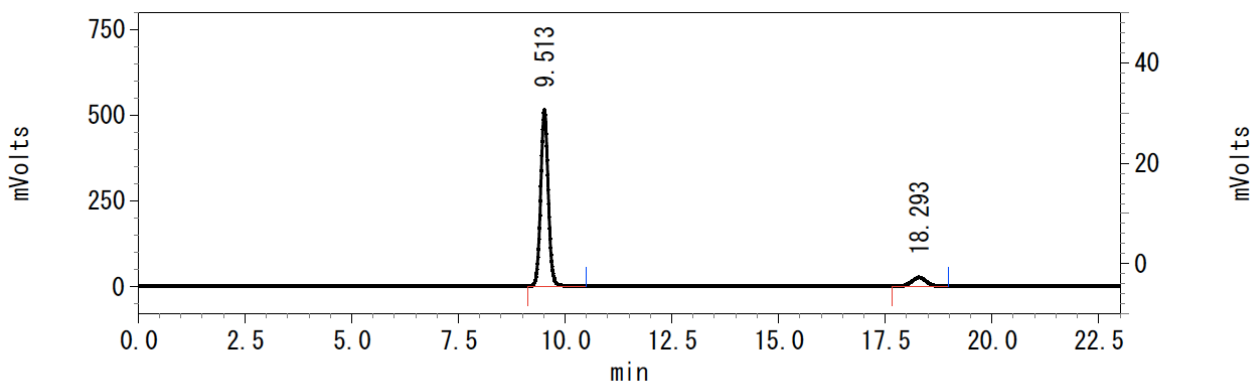
**rac-3br**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.750         | 3428194 | 49.830       |
| 2    | 20.551         | 3451635 | 50.170       |

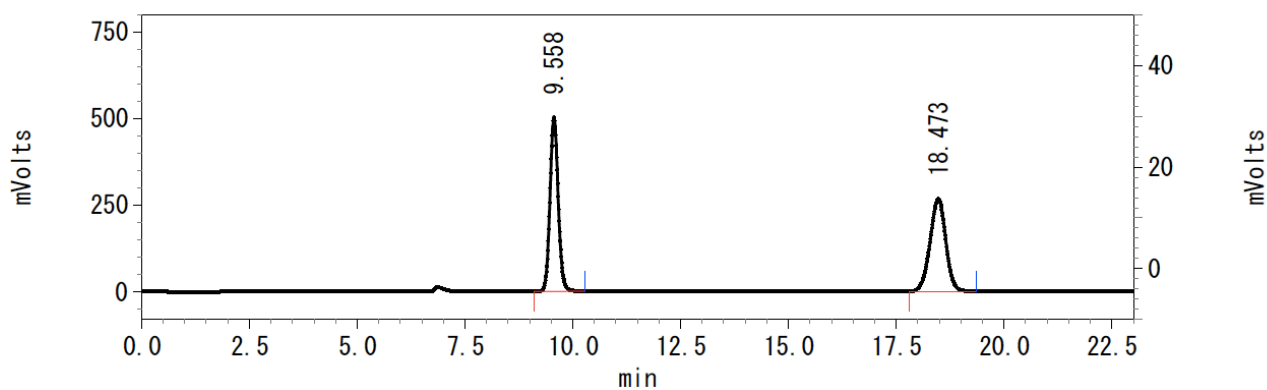


**3br (R)** (Table 1, entry 12, Condition B)



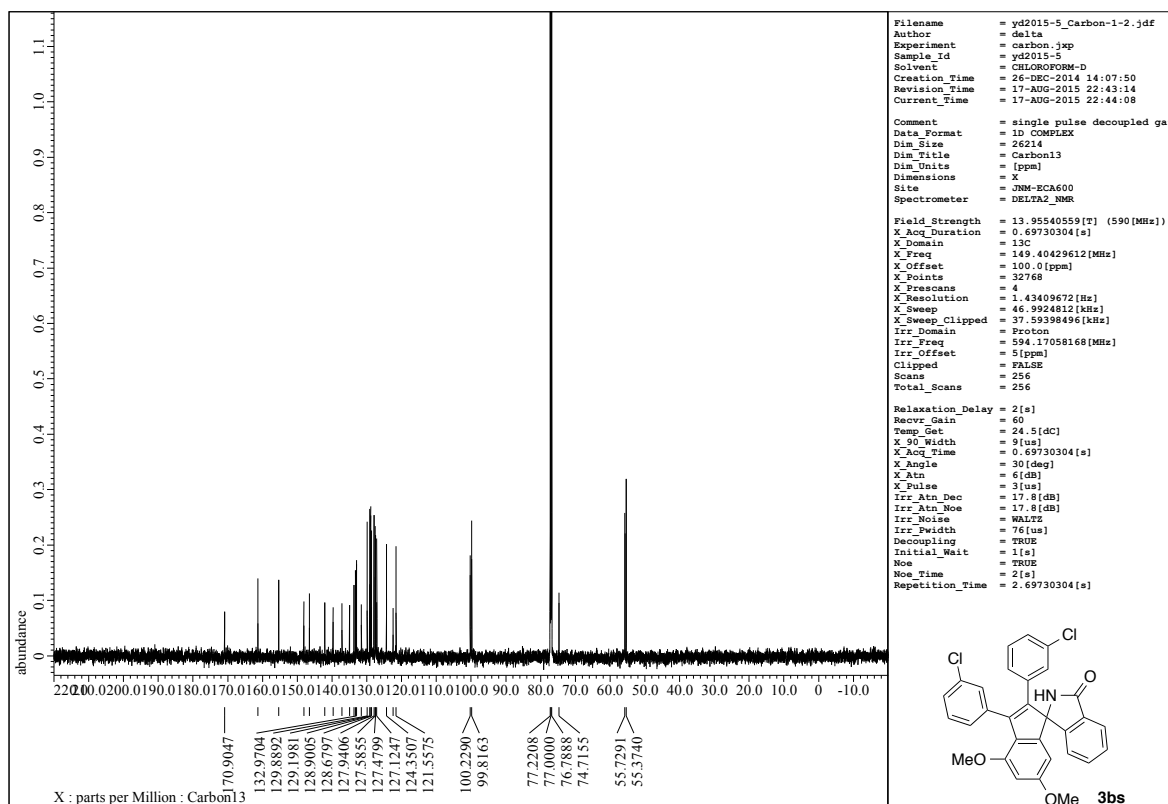
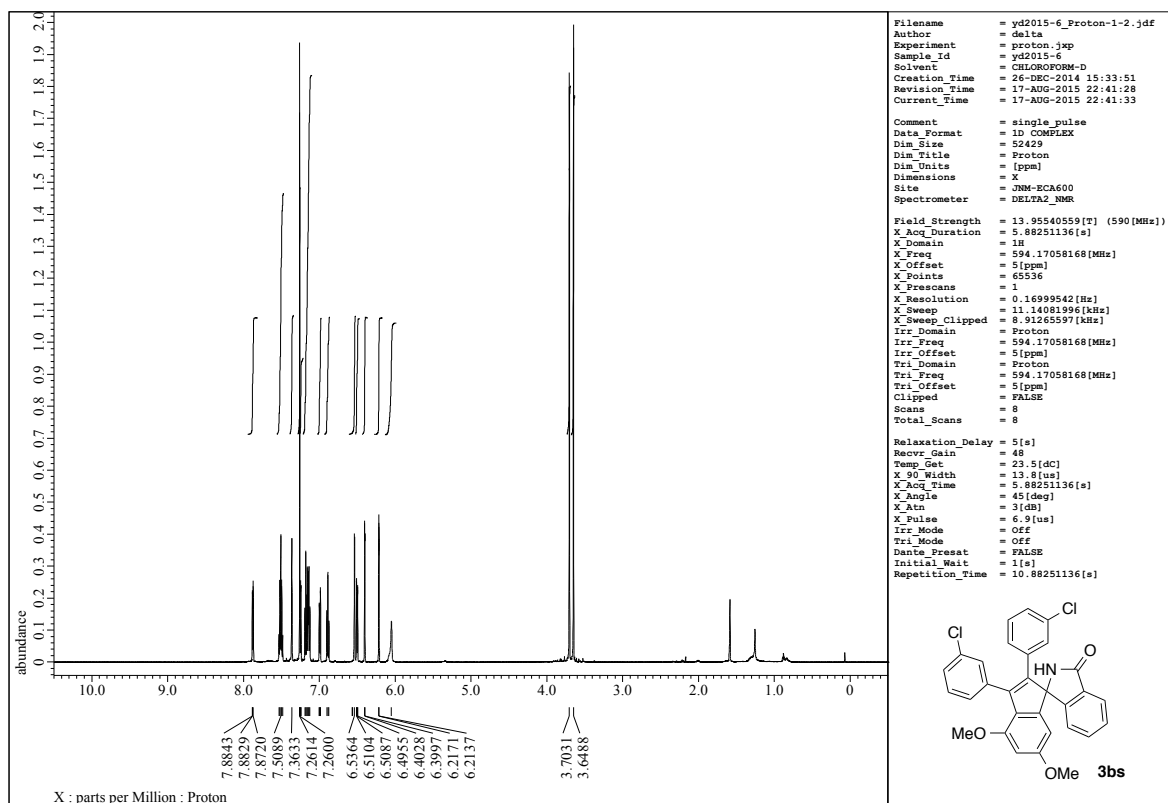
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.513          | 6356743 | 90.867       |
| 2    | 18.293         | 638930  | 9.133        |

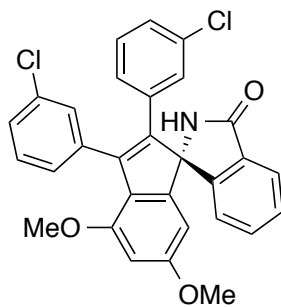
**rac-3br**



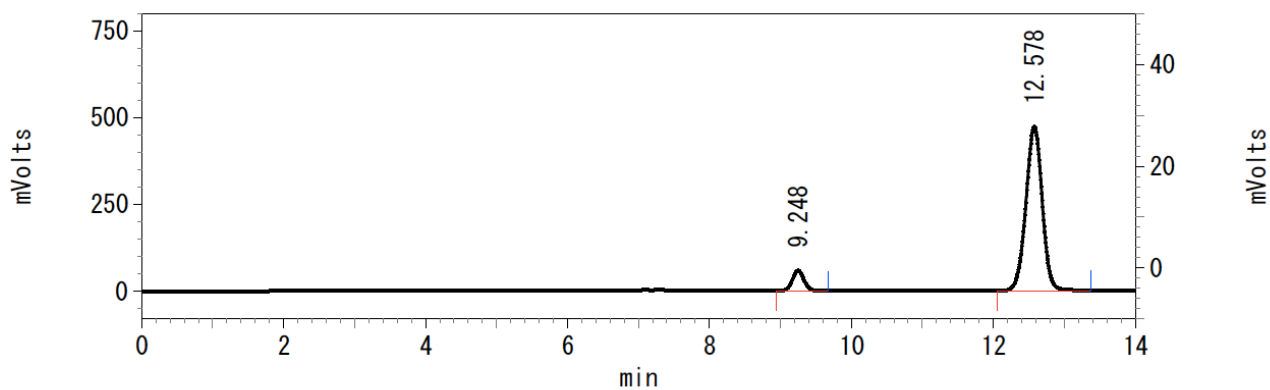
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.558          | 6702253 | 49.681       |
| 2    | 18.473         | 6788220 | 50.319       |





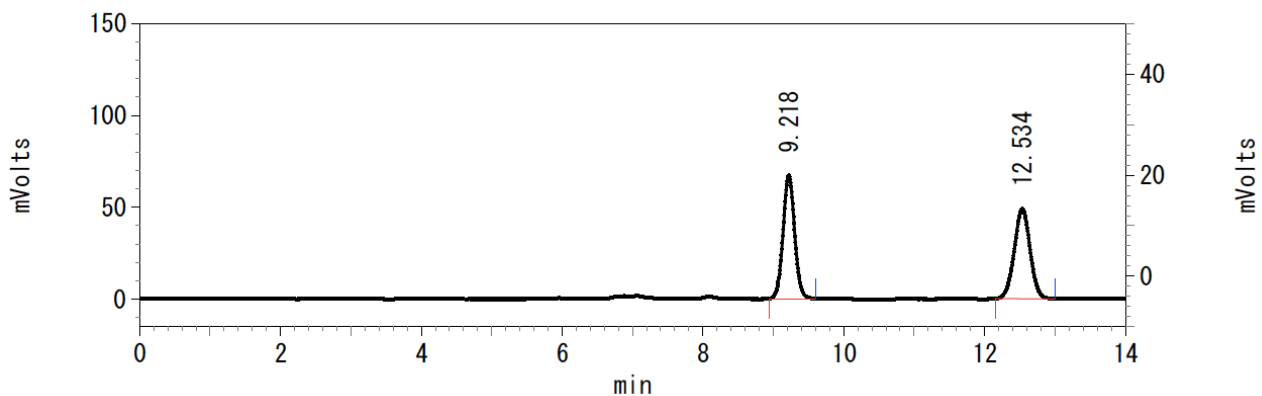


**3bs (S)** (Table 1, entry 13, Condition A)

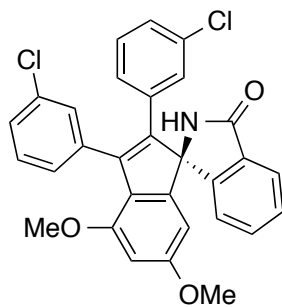


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.248          | 678841  | 8.216        |
| 2    | 12.578         | 7583645 | 91.784       |

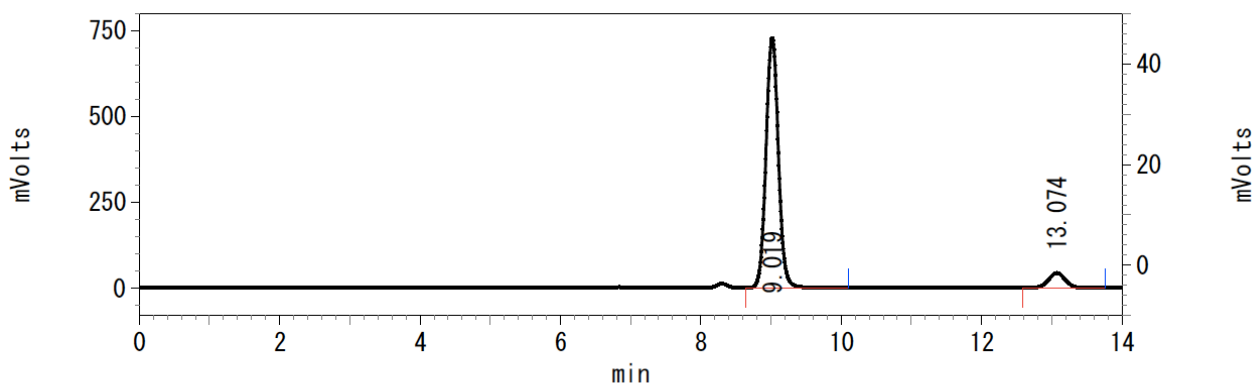
**rac-3bs**



| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 9.218          | 769411 | 50.127       |
| 2    | 12.534         | 765508 | 49.873       |

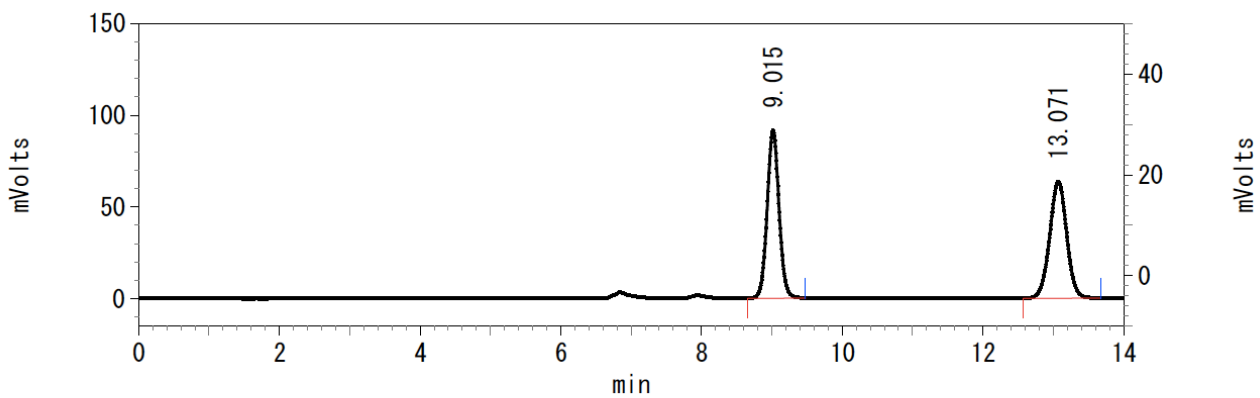


**3bs (R)** (Table 1, entry 14, Condition B)

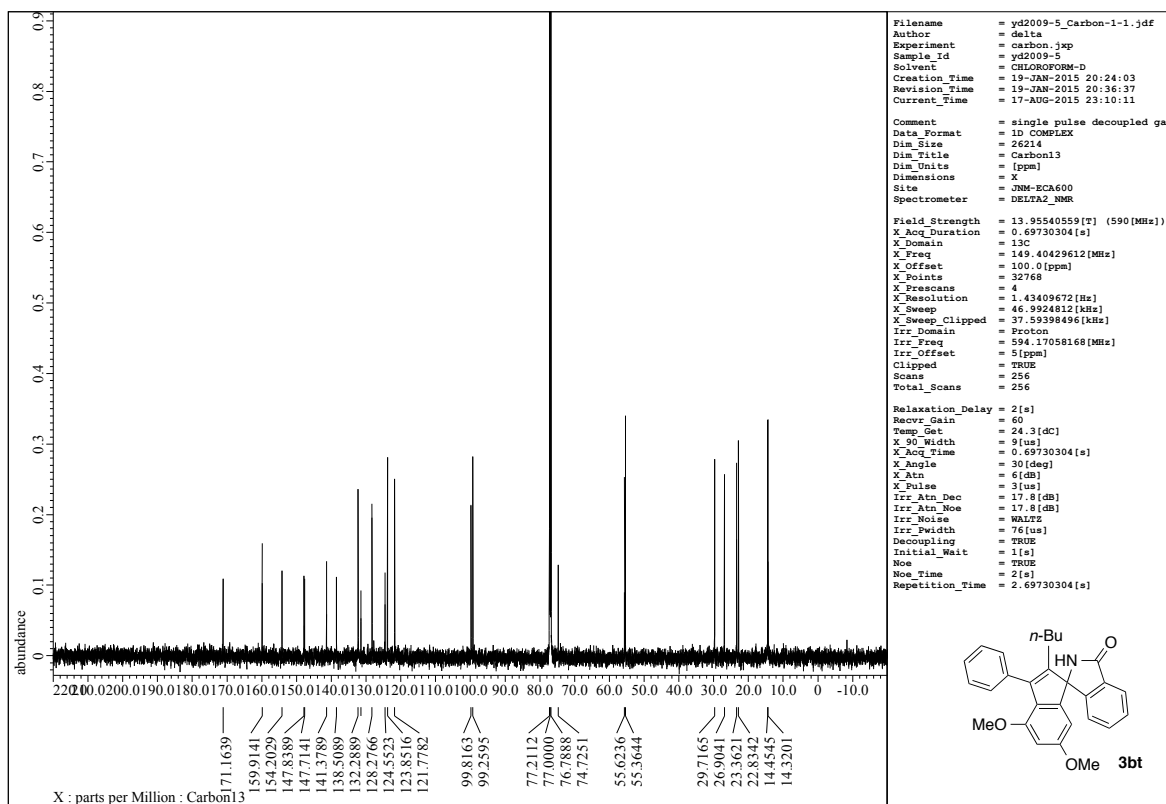
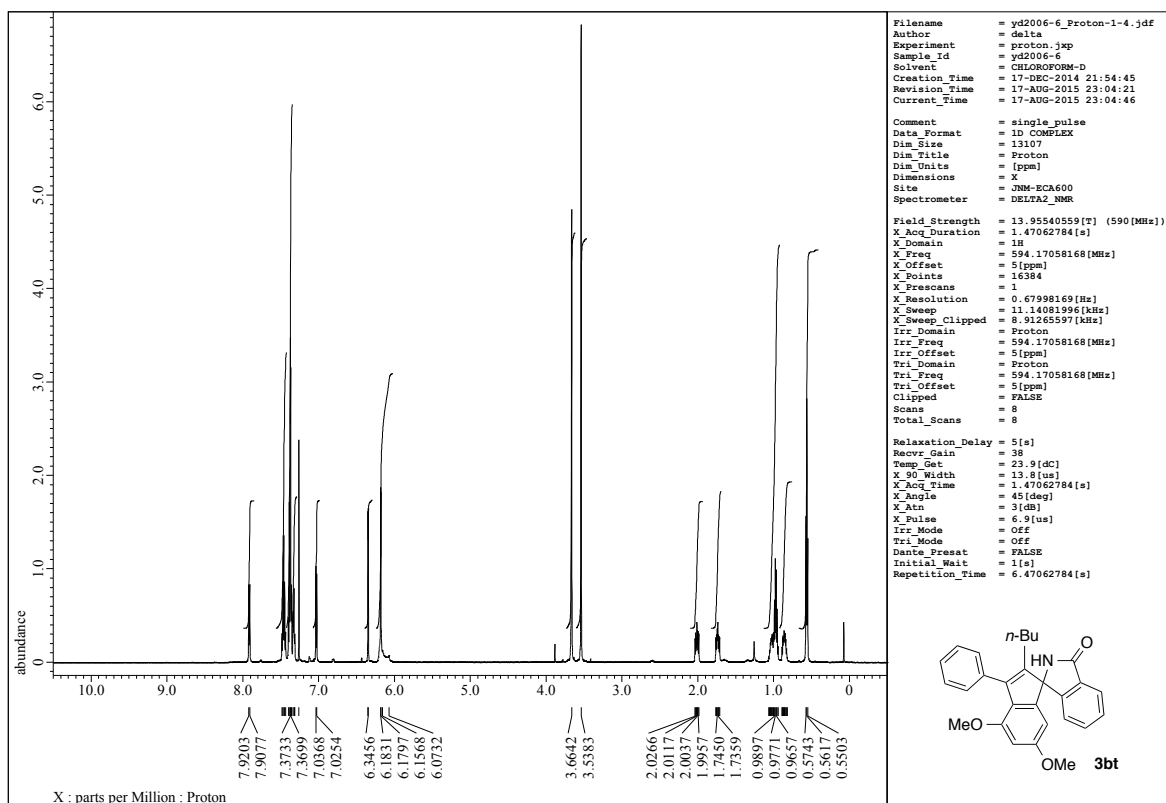


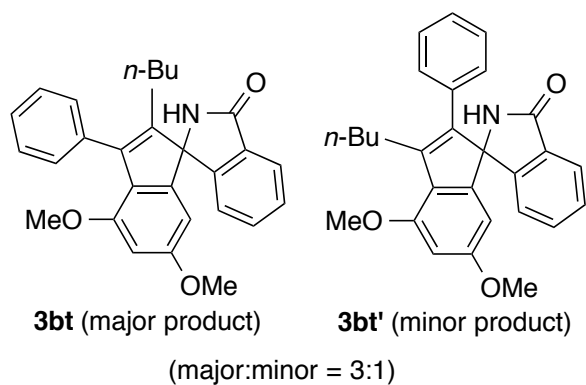
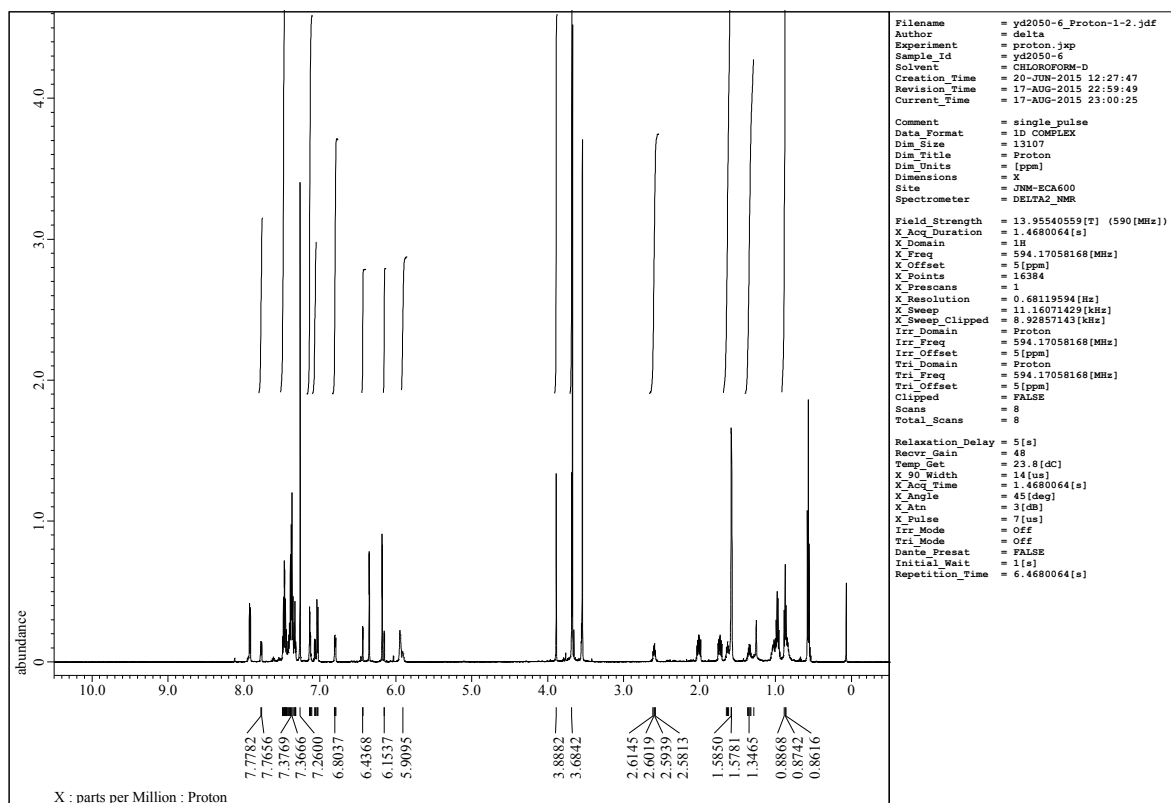
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.019          | 8964379 | 92.418       |
| 2    | 13.074         | 735443  | 7.582        |

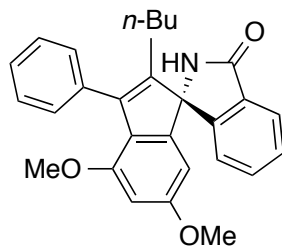
**rac-3bs**



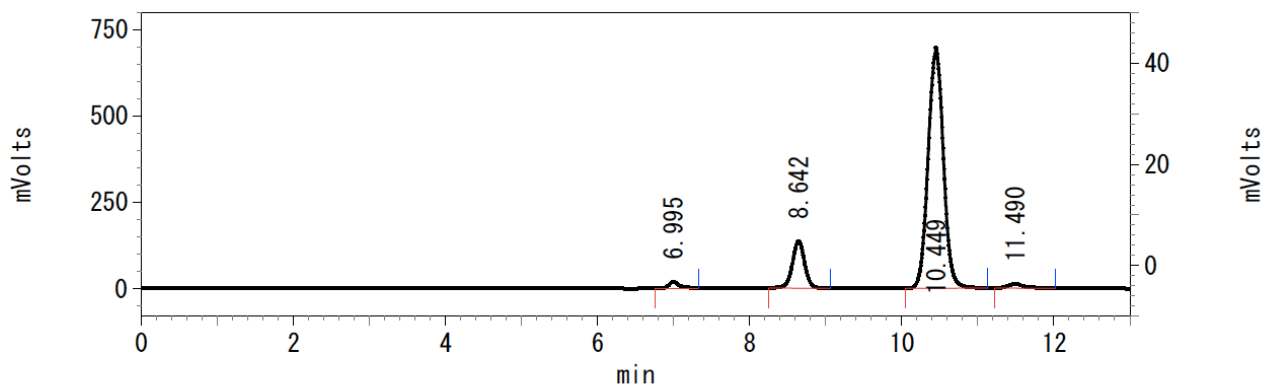
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.015          | 1071612 | 49.923       |
| 2    | 13.071         | 1074928 | 50.077       |





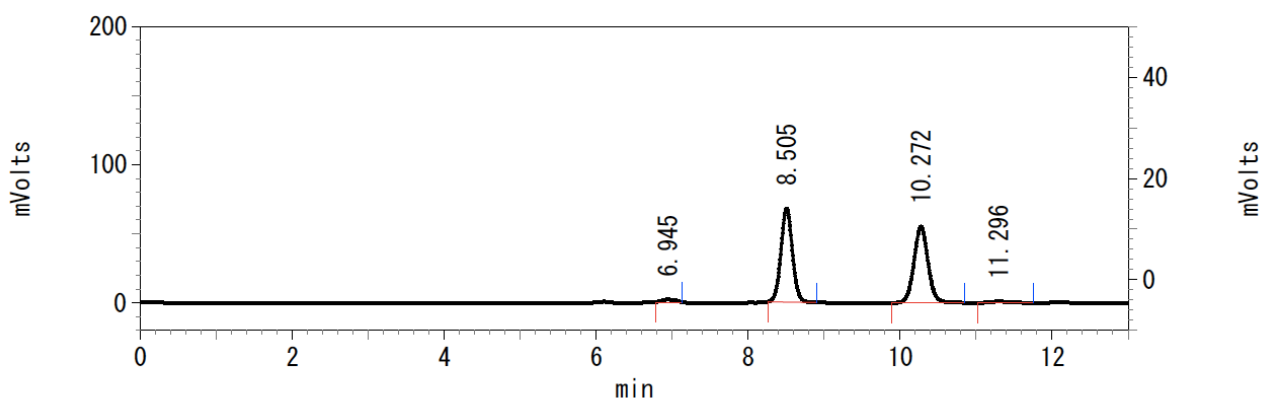


**3bt (S)** (major:minor = 97:3)  
(Table 1, entry 15, Condition A)

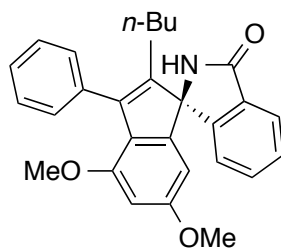


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 6.995          | 189052  | 1.627        |
| 2    | 8.642          | 1533336 | 13.192       |
| 3    | 10.449         | 9706864 | 83.514       |
| 4    | 11.490         | 193844  | 1.668        |

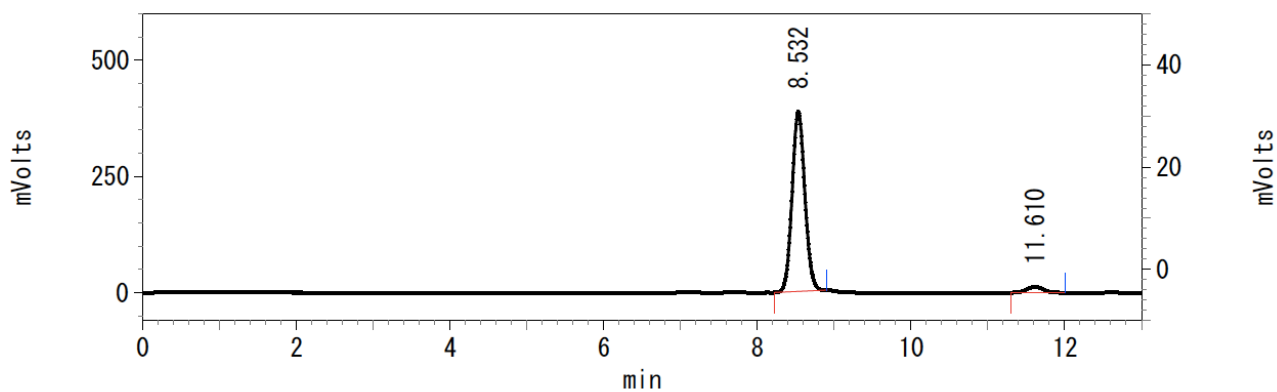
**rac-3bt**



| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 6.945          | 23027  | 1.577        |
| 2    | 8.505          | 709867 | 48.613       |
| 3    | 10.272         | 710554 | 48.660       |
| 4    | 11.296         | 16808  | 1.151        |

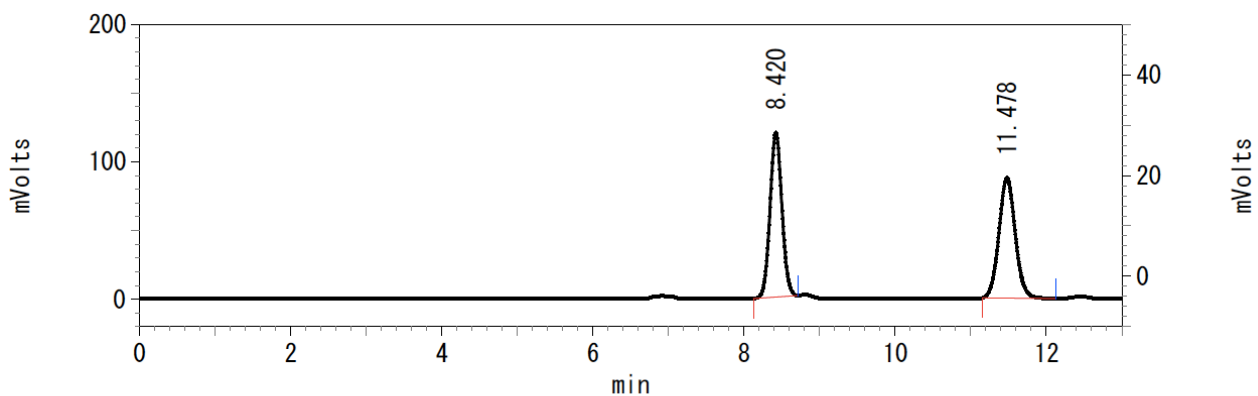


**3bt (R)** (major:minor = 99:1)  
(Table 1, entry 16, Condition B)

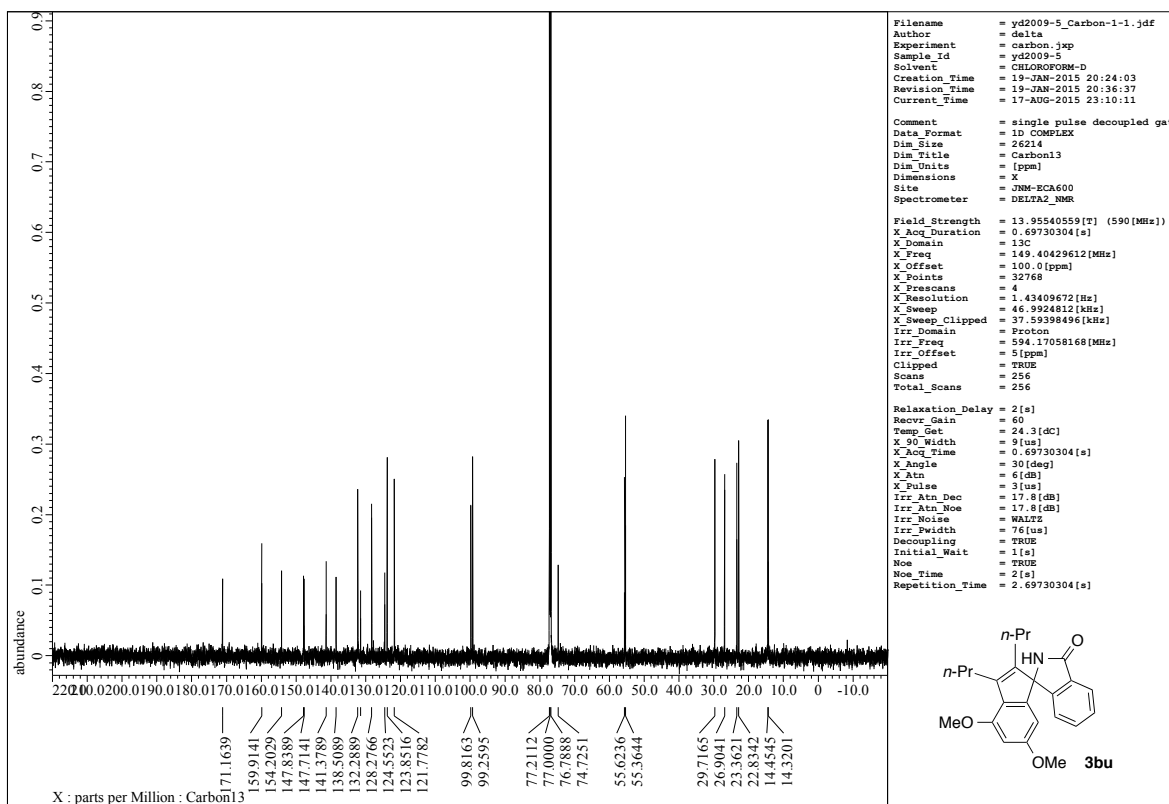
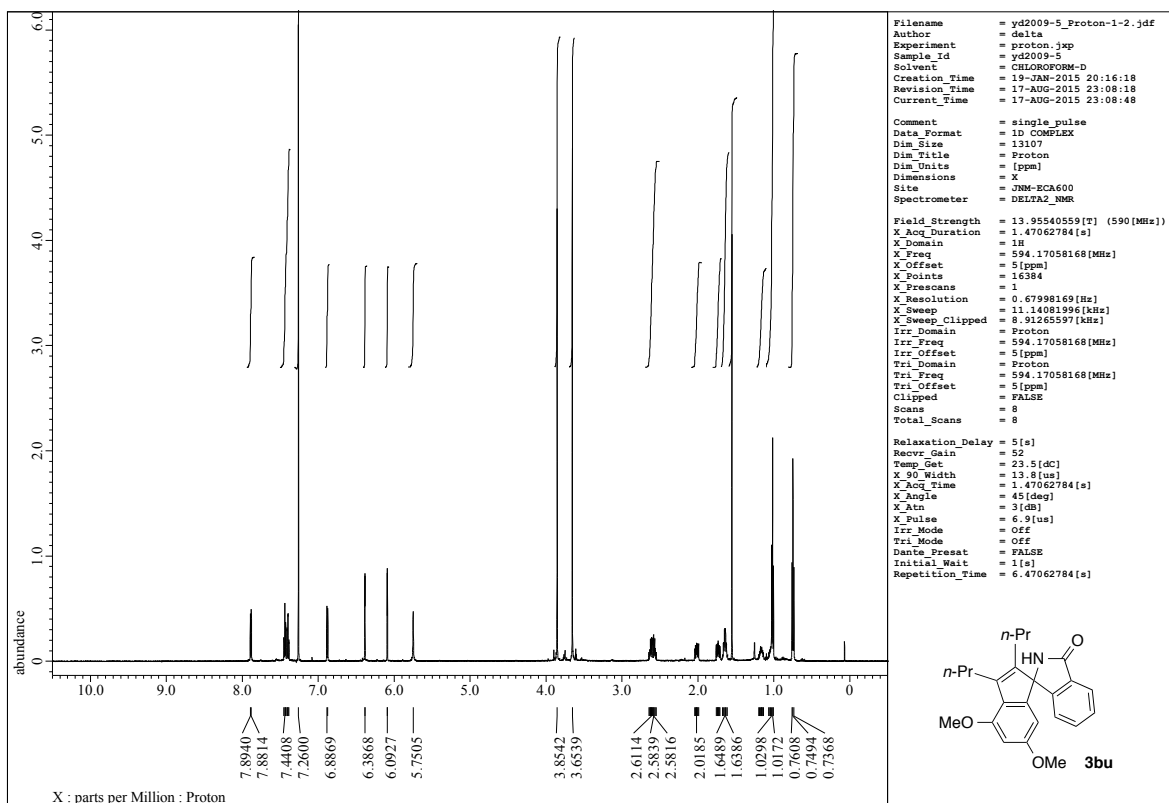


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.532          | 4477417 | 95.846       |
| 2    | 11.610         | 194061  | 4.154        |

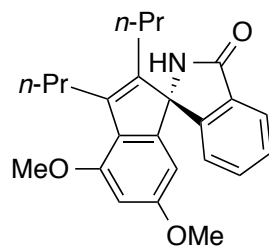
**rac-3bt**



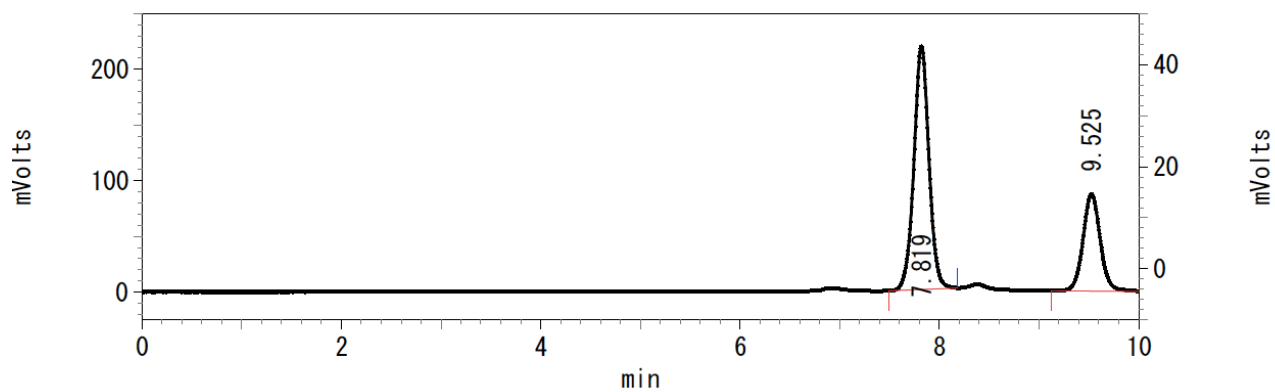
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.420          | 1306934 | 49.831       |
| 2    | 11.478         | 1315820 | 50.169       |





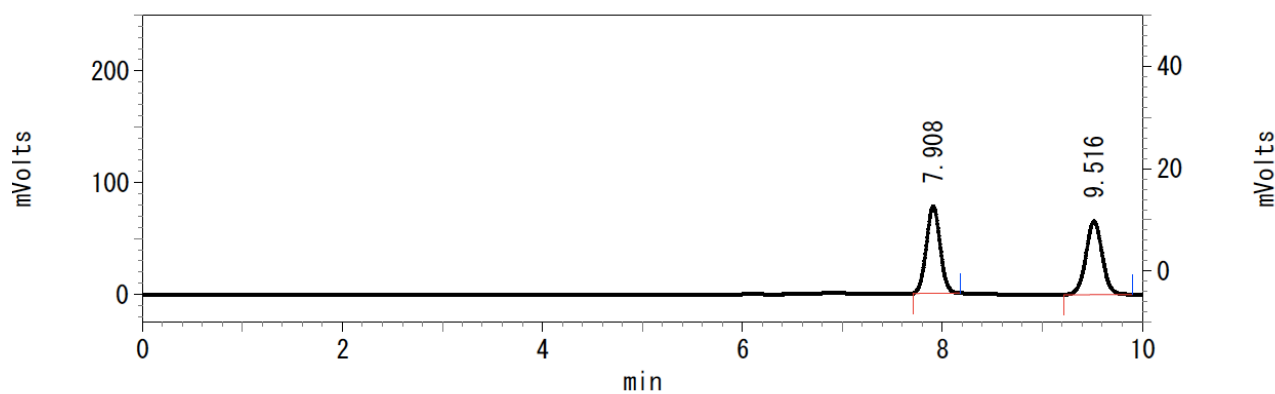


**3bu (S)** (Table 1, entry 17, Condition A)

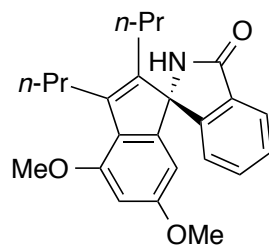


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 7.819          | 2294481 | 68.555       |
| 2    | 9.525          | 1052421 | 31.445       |

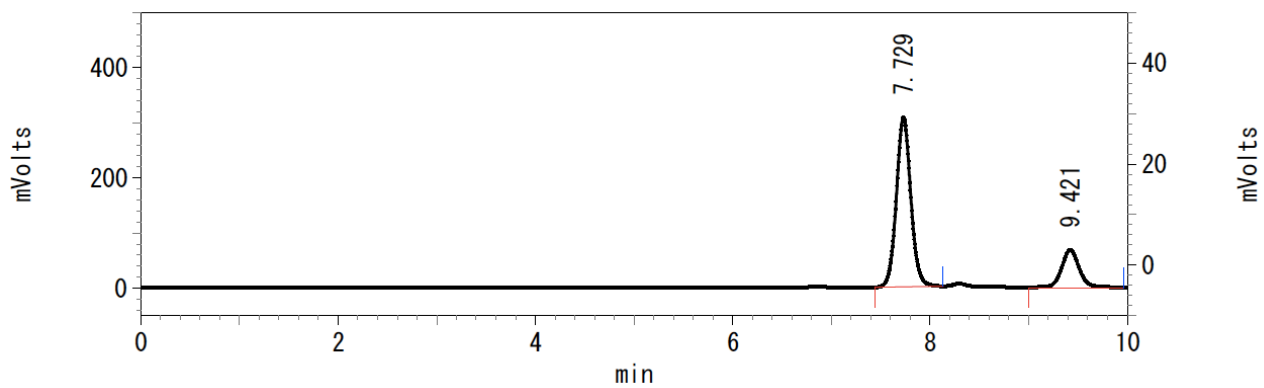
**rac-3bu**



| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 7.908          | 742980 | 50.023       |
| 2    | 9.516          | 742309 | 49.977       |

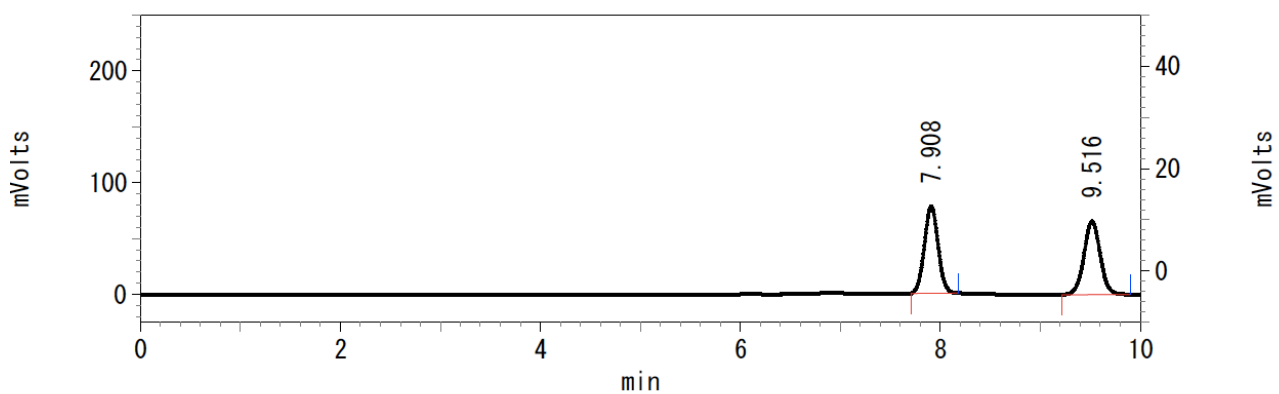


**3bu (S)** (Table 1, entry 18, Condition B)

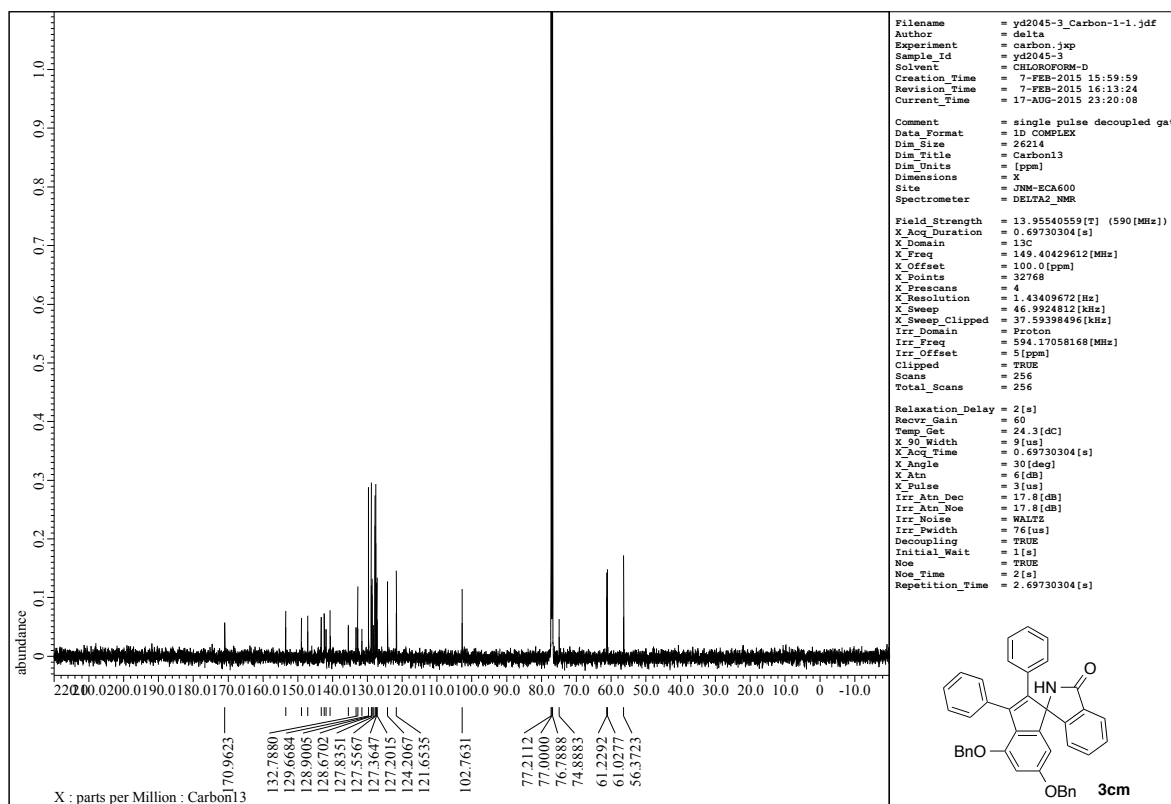
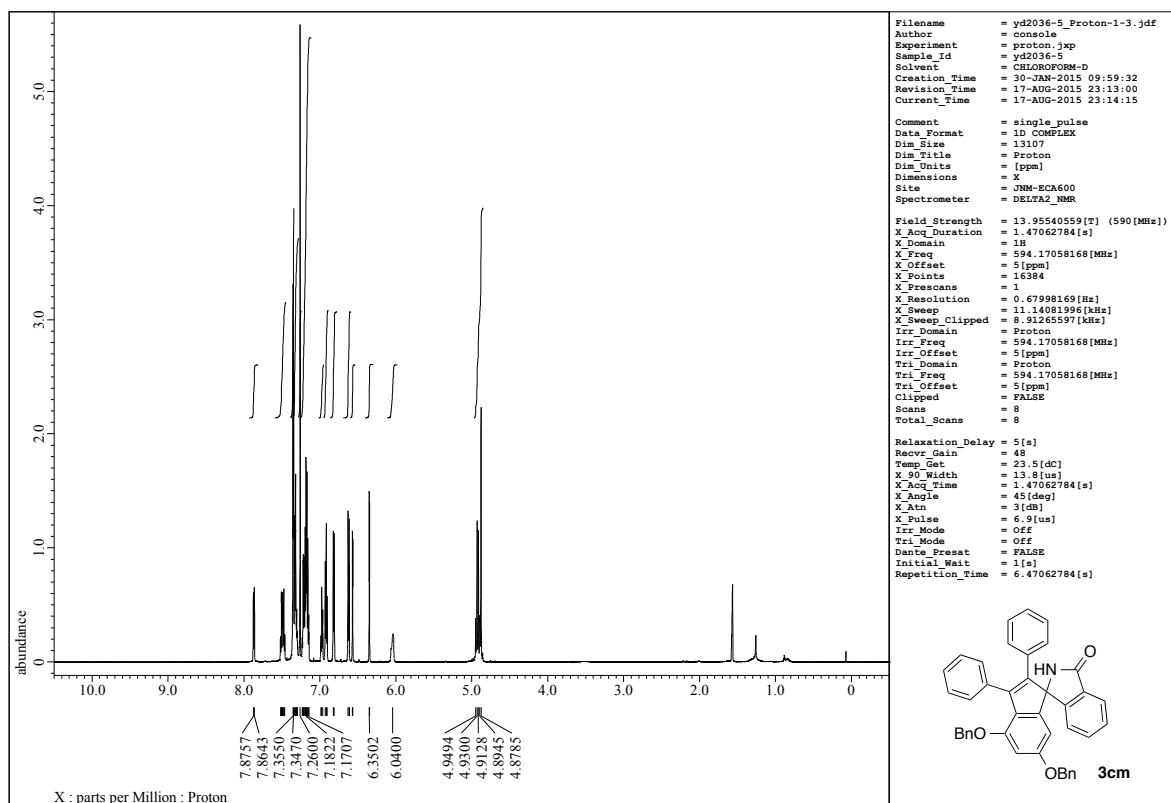


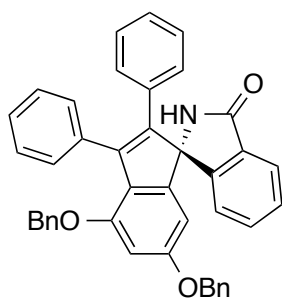
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 7.729          | 3133257 | 78.473       |
| 2    | 9.421          | 859528  | 21.527       |

**rac-3bu**

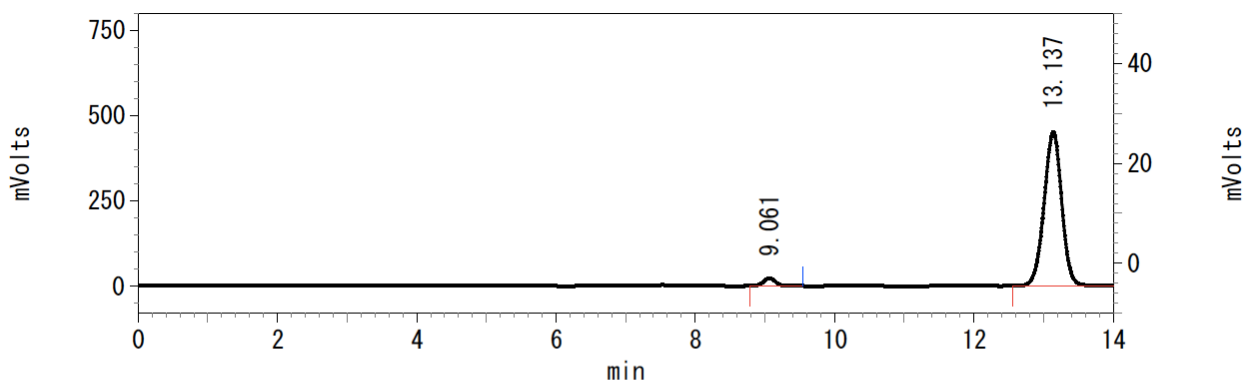


| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 7.908          | 742980 | 50.023       |
| 2    | 9.516          | 742309 | 49.977       |



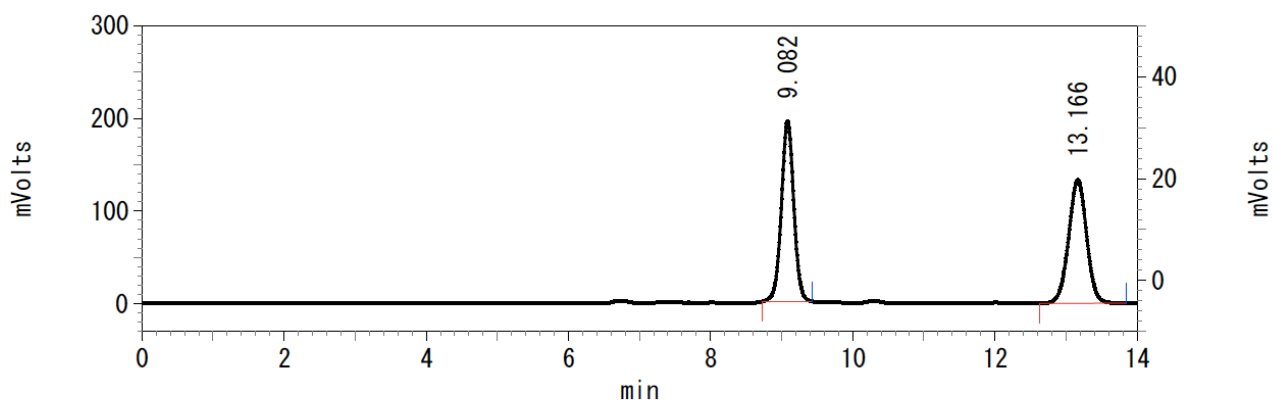


**3cm (S)** (Scheme 3, Condition A)

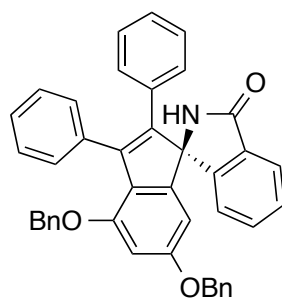


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.061          | 284171  | 3.444        |
| 2    | 13.137         | 7967580 | 96.556       |

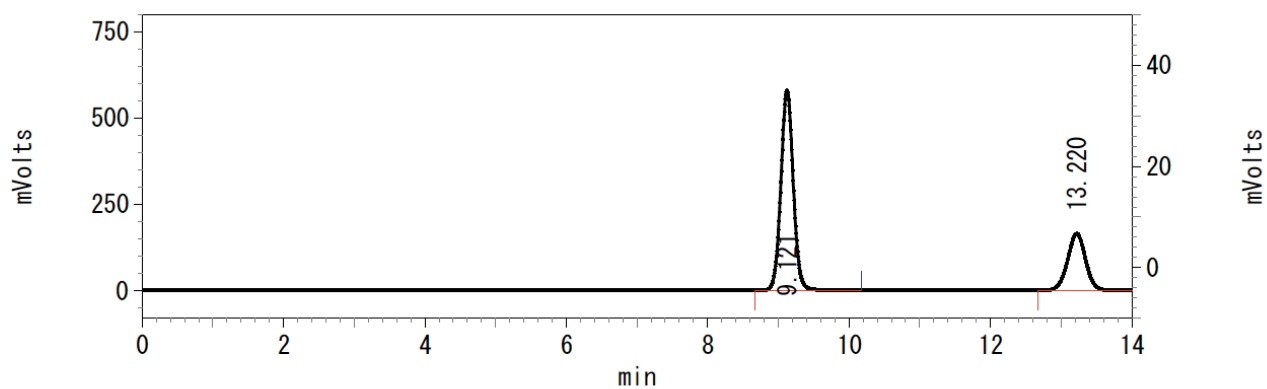
*rac*-3cm



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.082          | 2359474 | 50.106       |
| 2    | 13.166         | 2349528 | 49.894       |

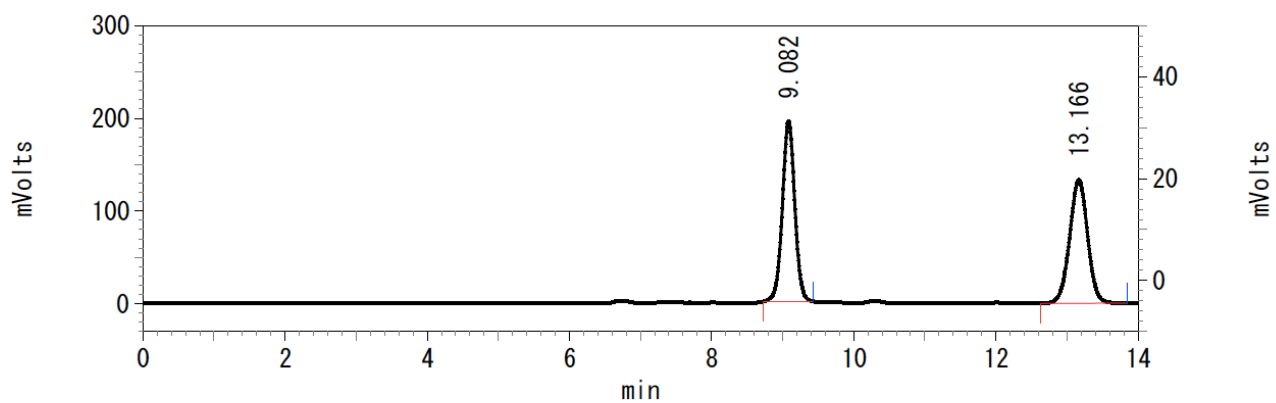


**3cm (R)** (Scheme 3, Condition B)

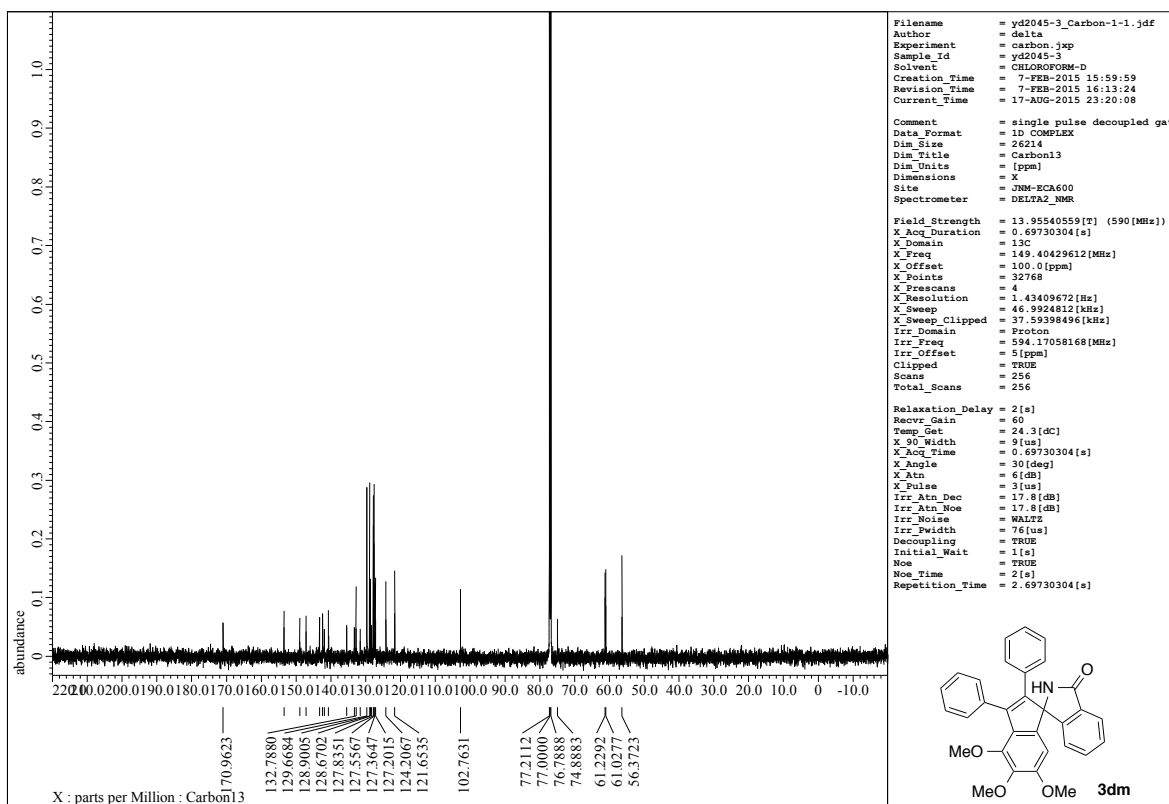
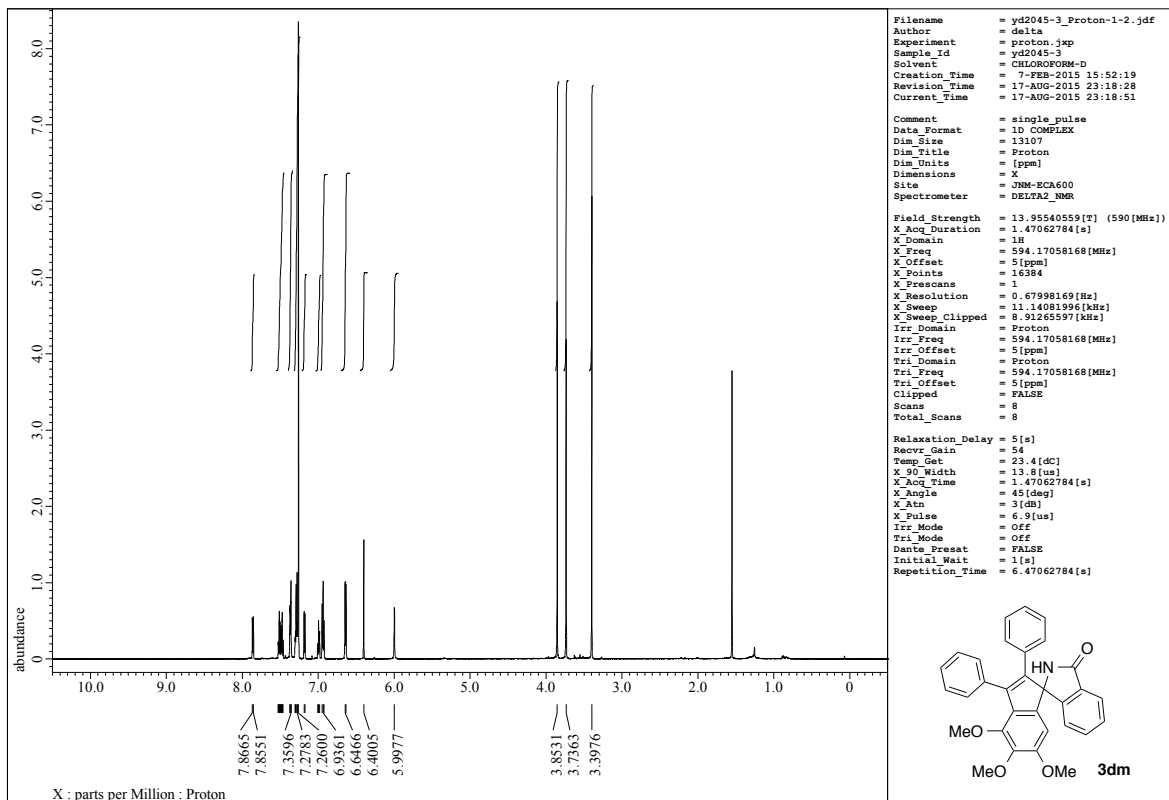


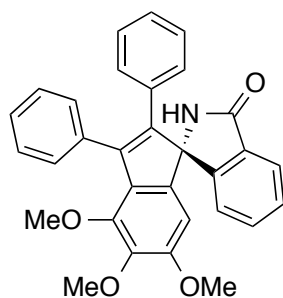
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.121          | 7105230 | 70.892       |
| 2    | 13.220         | 2917357 | 29.108       |

*rac*-3cm

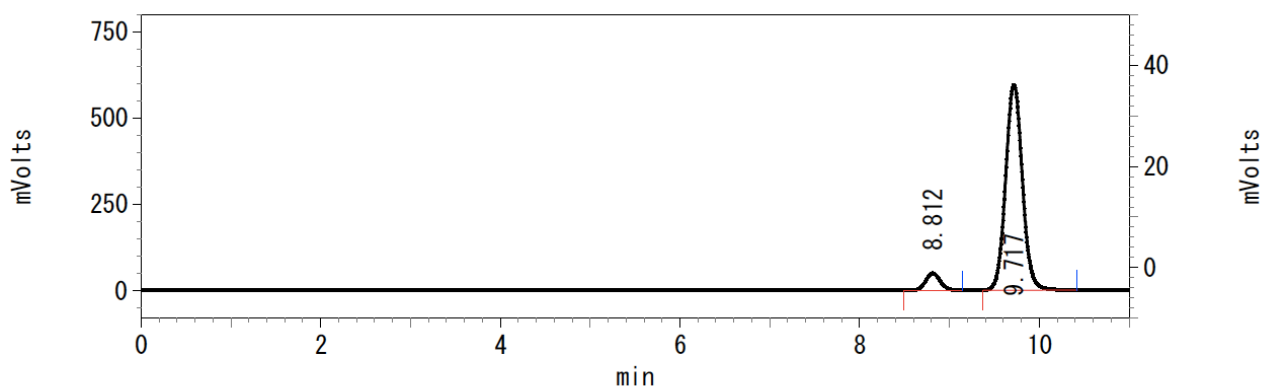


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.082          | 2359474 | 50.106       |
| 2    | 13.166         | 2349528 | 49.894       |



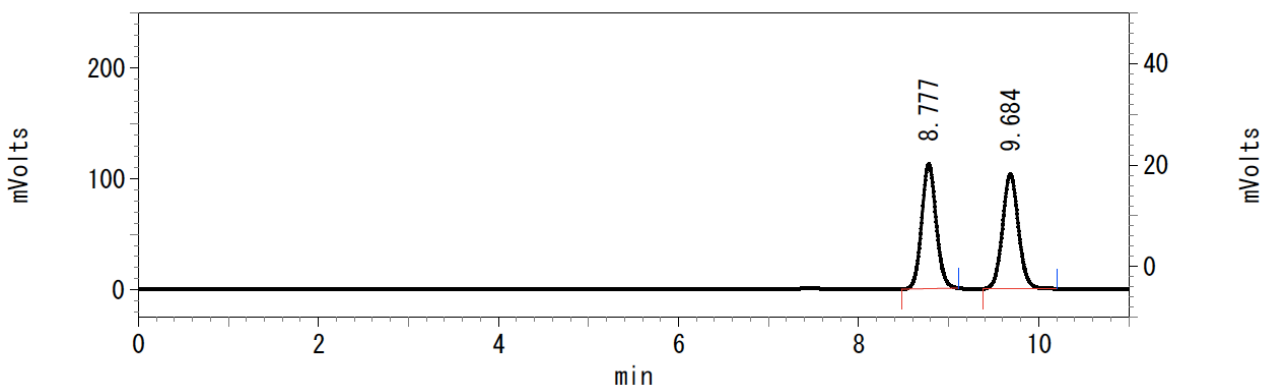


**3dm (S)** (Scheme 3, Condition A)

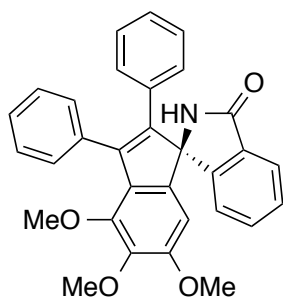


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.812          | 565126  | 6.813        |
| 2    | 9.717          | 7730086 | 93.187       |

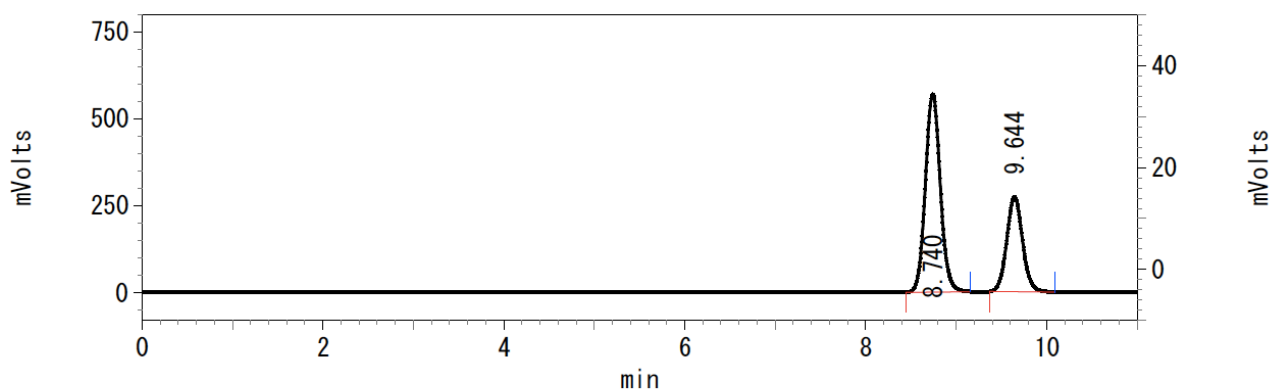
*rac*-3dm



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.777          | 1265953 | 49.784       |
| 2    | 9.684          | 1276940 | 50.216       |

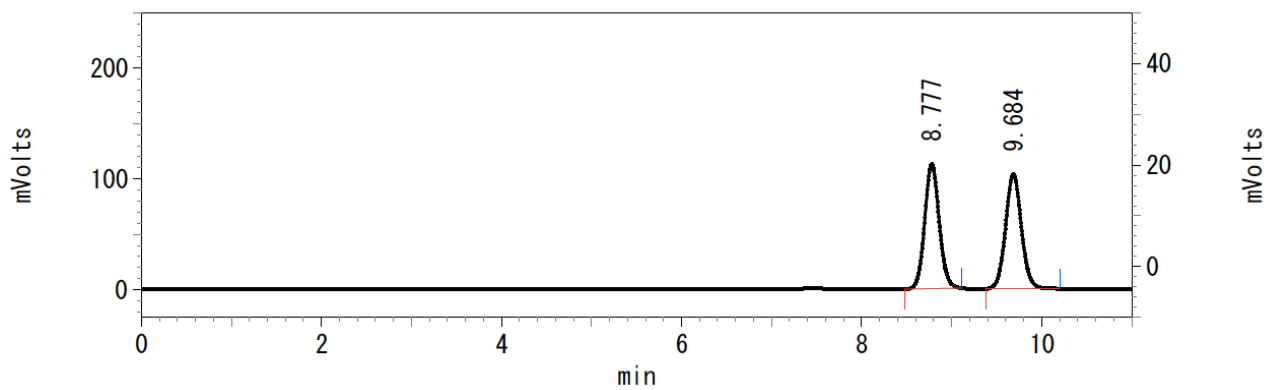


**3dm (R)** (Scheme 3, Condition B)



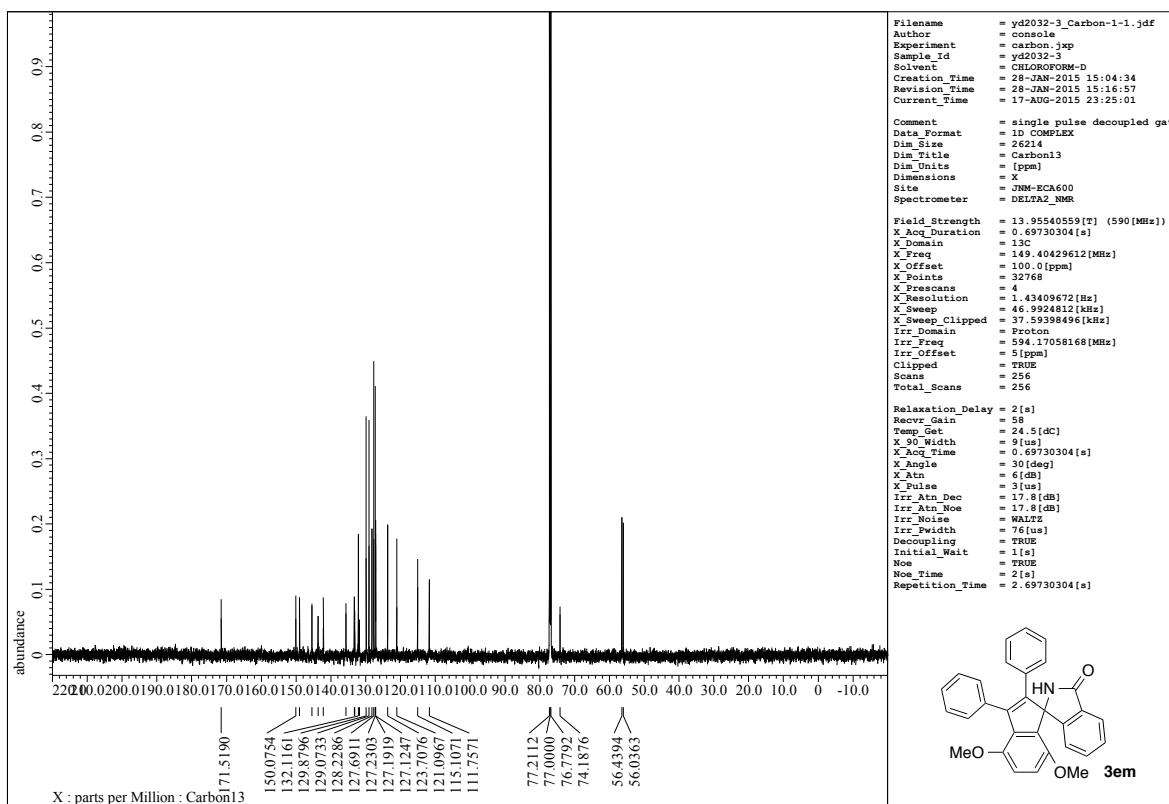
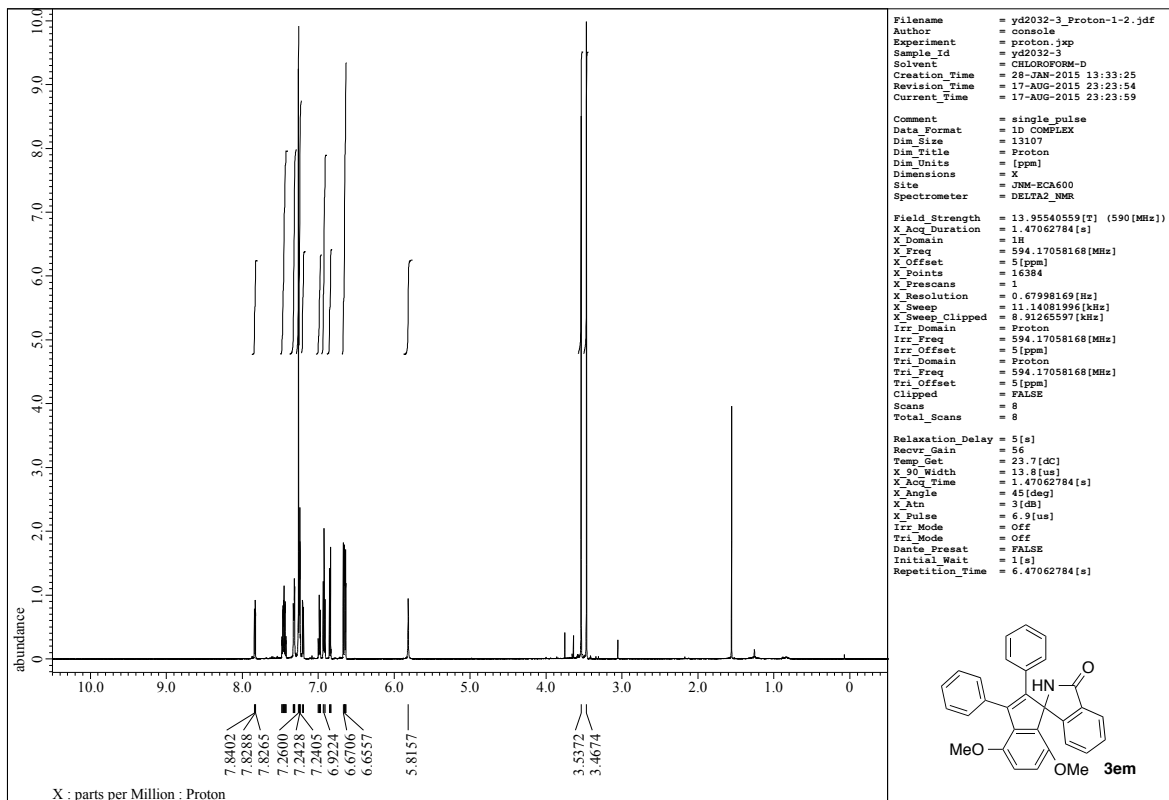
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.740          | 6546020 | 66.311       |
| 2    | 9.644          | 3325707 | 33.689       |

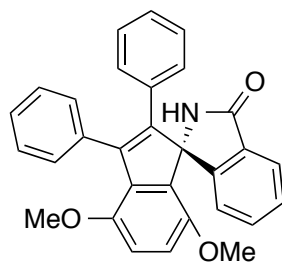
**rac-3dm**



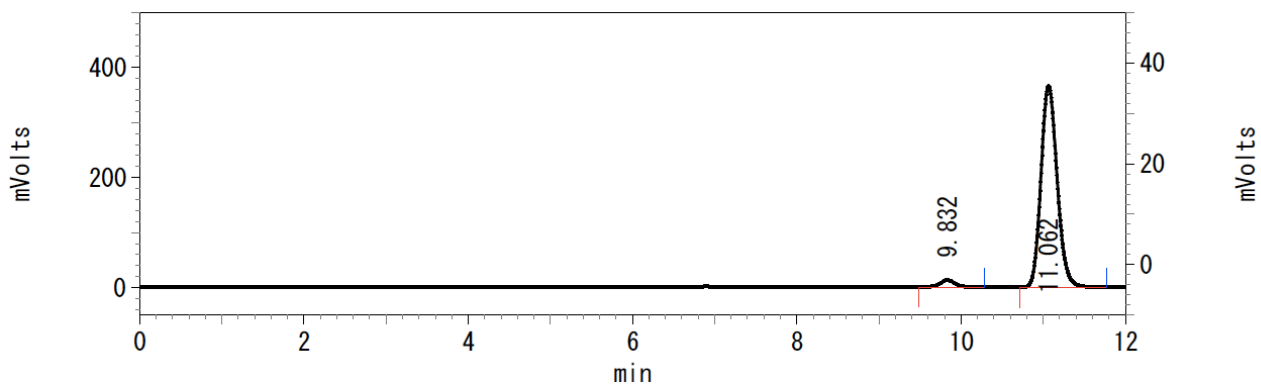
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.777          | 1265953 | 49.784       |
| 2    | 9.684          | 1276940 | 50.216       |





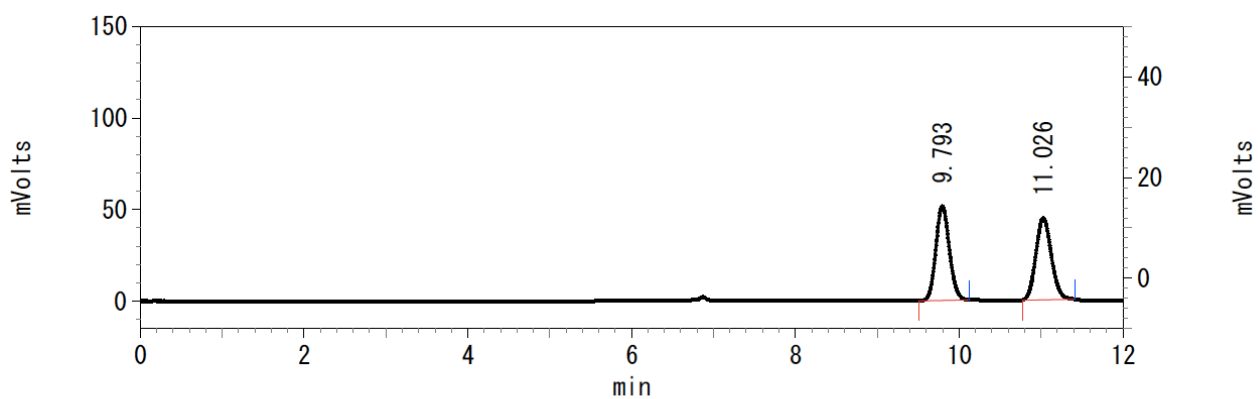


**3em (S)** (Scheme 3, Condition A)

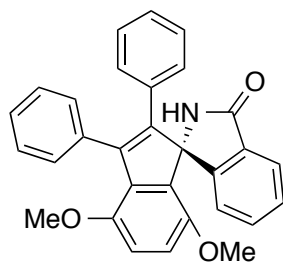


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.832          | 183919  | 3.532        |
| 2    | 11.062         | 5023120 | 96.468       |

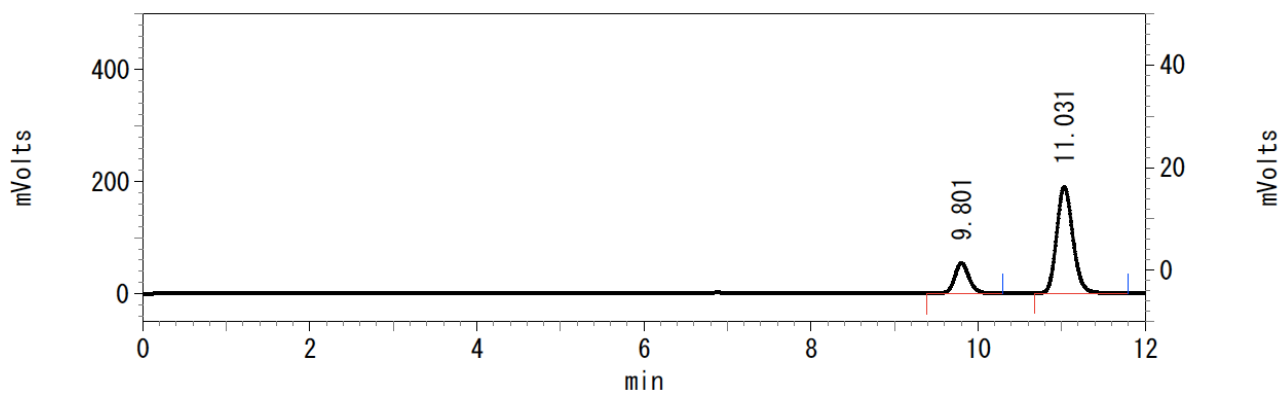
**rac-3em**



| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 9.793          | 591346 | 50.210       |
| 2    | 11.026         | 586401 | 49.790       |

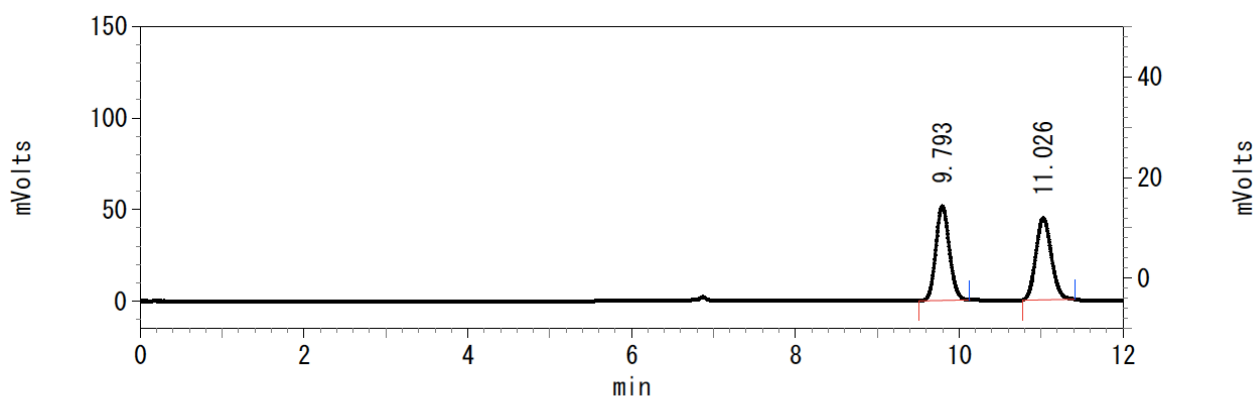


**3em (S)** (Scheme 3, Condition B)



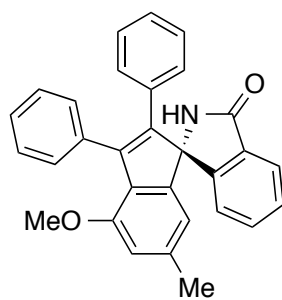
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.801          | 654318  | 20.282       |
| 2    | 11.031         | 2571809 | 79.718       |

**rac-3em**

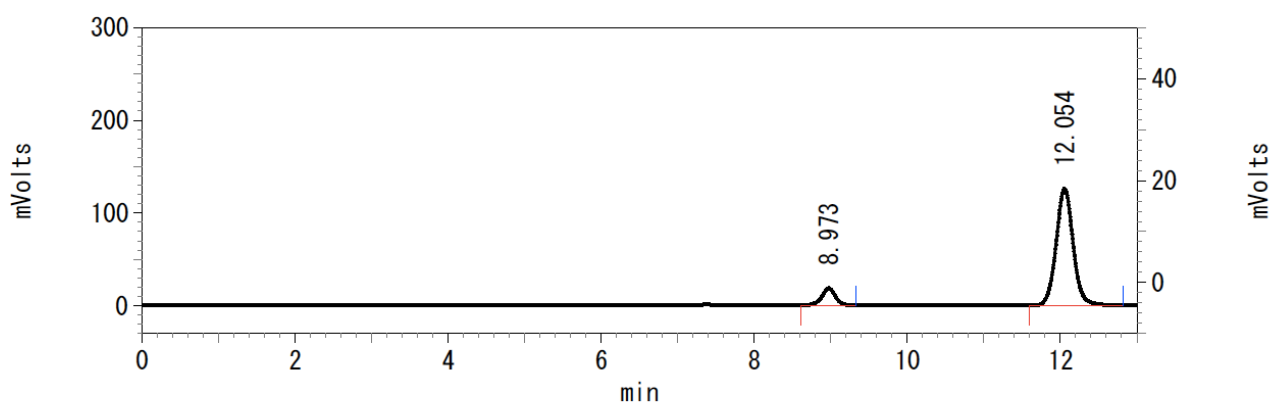


| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 9.793          | 591346 | 50.210       |
| 2    | 11.026         | 586401 | 49.790       |



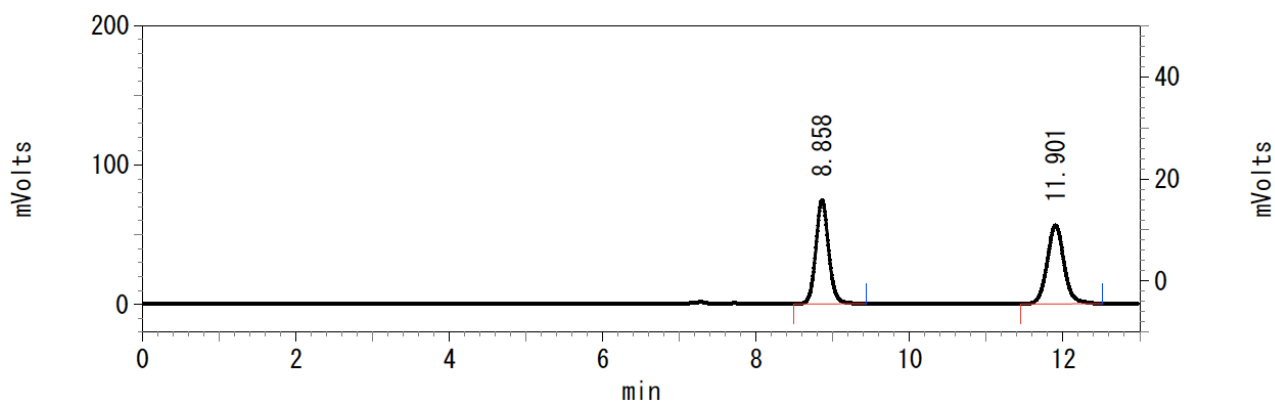


**3fm (S)** (Scheme 3, Condition A)

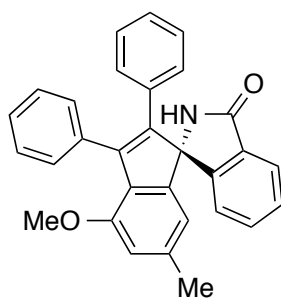


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.973          | 234379  | 10.715       |
| 2    | 12.054         | 1952983 | 89.285       |

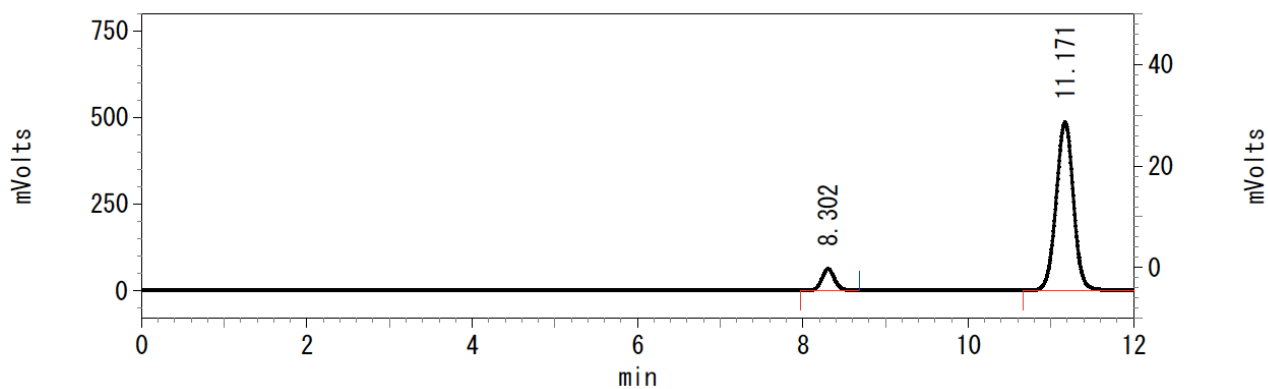
*rac*-3fm



| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 8.858          | 862770 | 49.955       |
| 2    | 11.901         | 864339 | 50.045       |

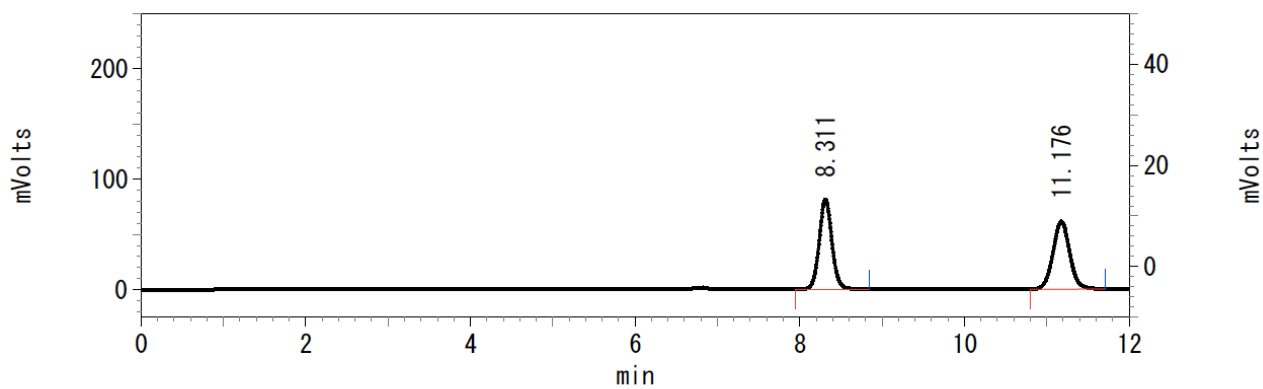


**3fm (S)** (Scheme 3, Condition B)

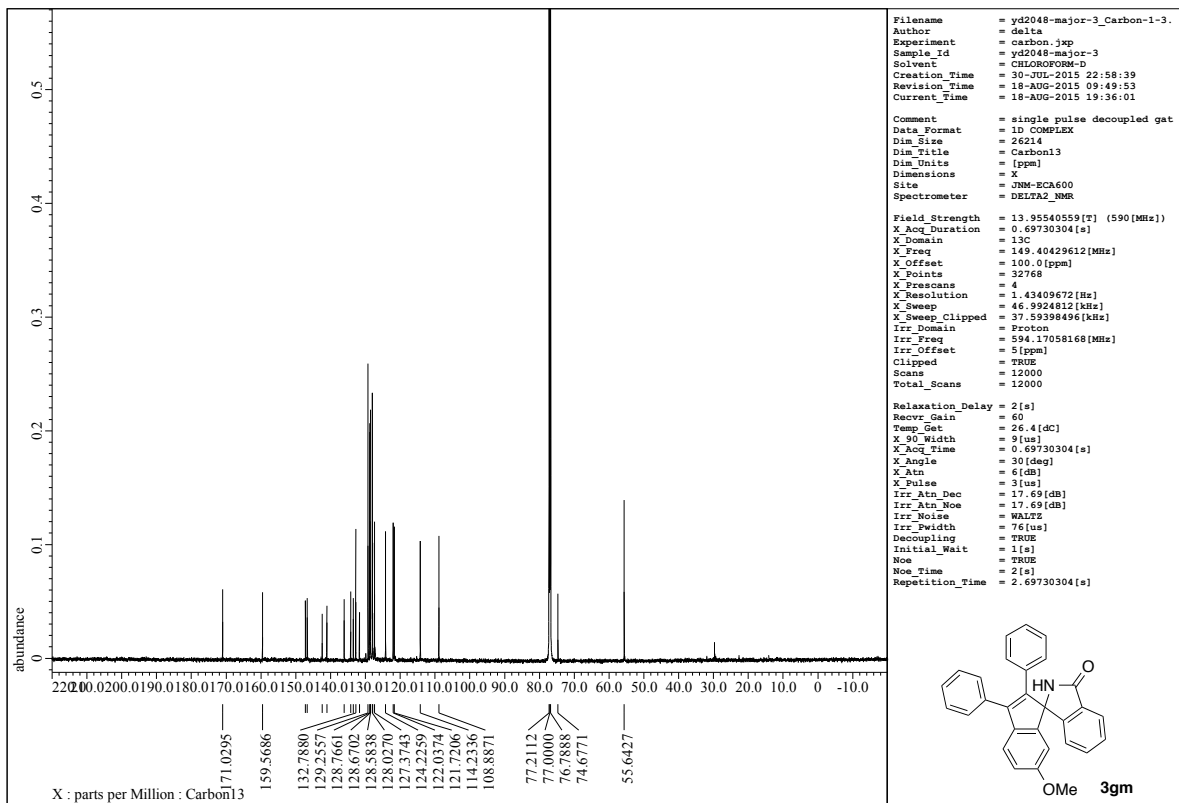
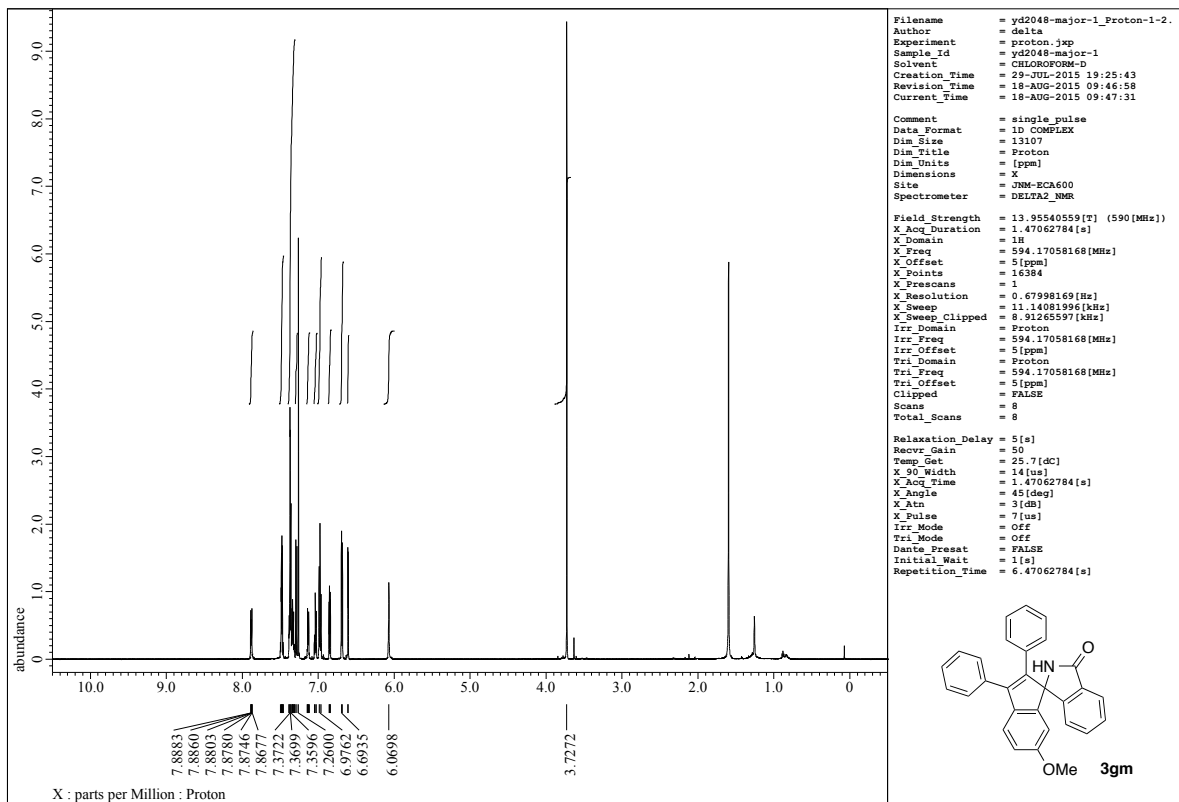


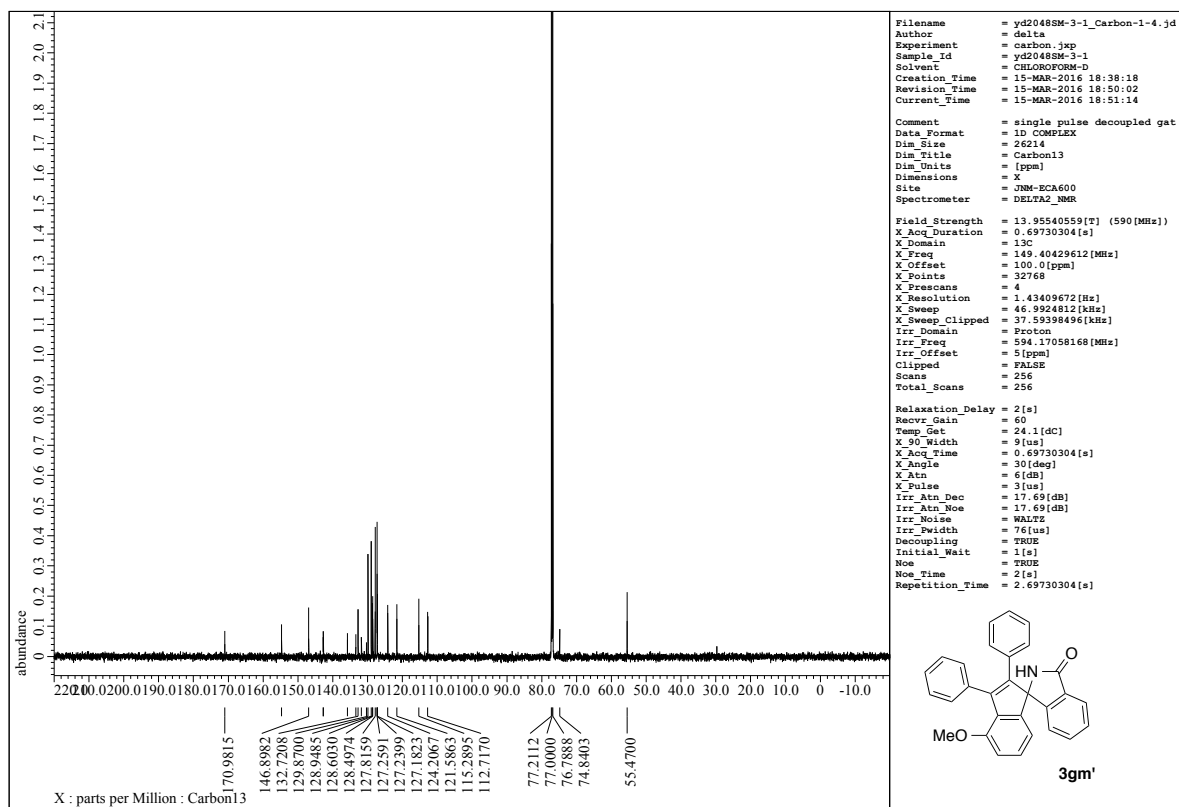
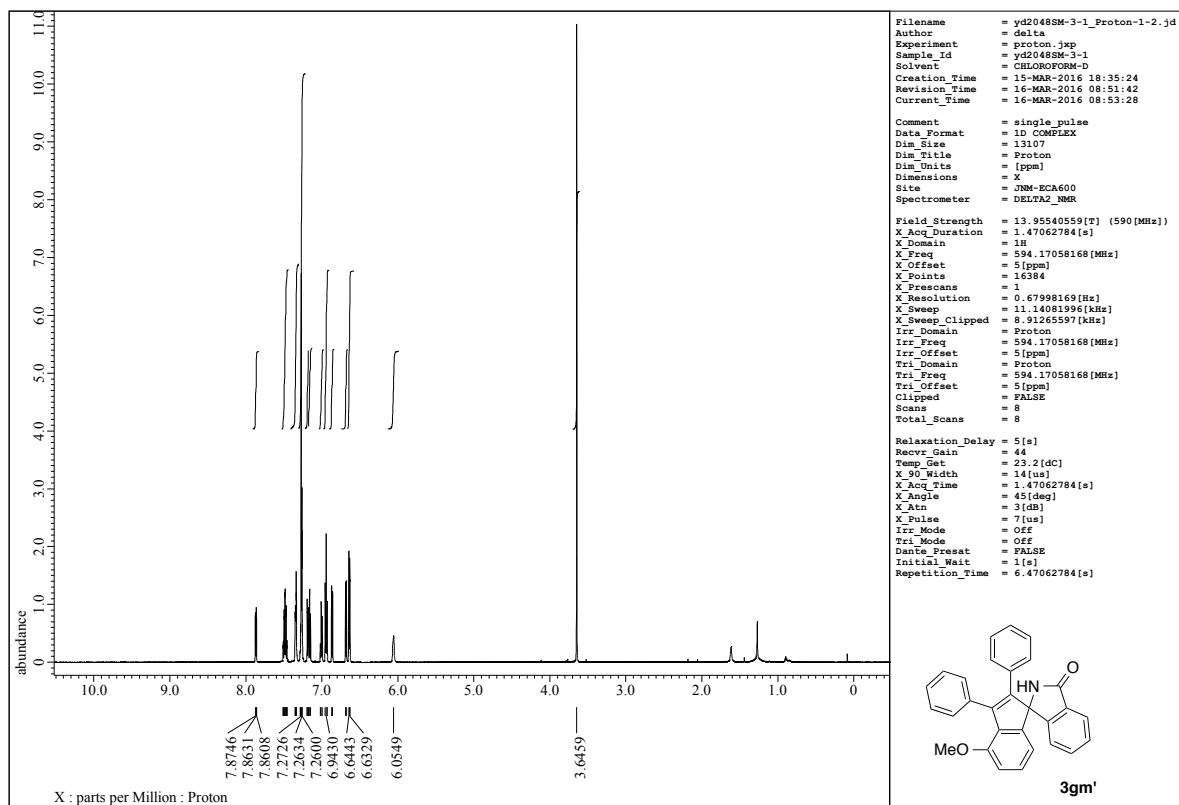
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 8.302          | 671262  | 8.657        |
| 2    | 11.171         | 7082276 | 91.343       |

*rac*-3fm

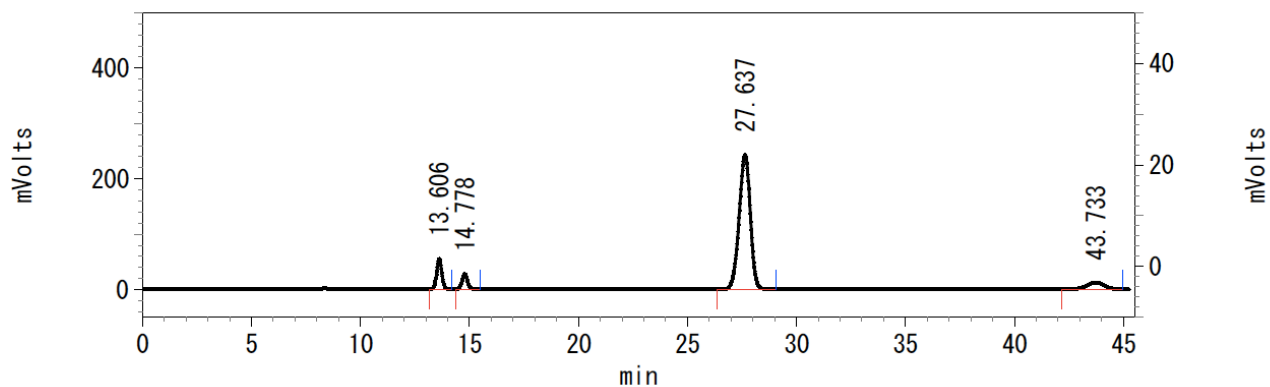
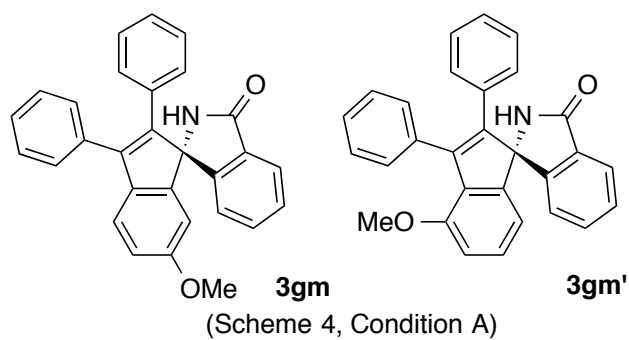


| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 8.311          | 878123 | 50.161       |
| 2    | 11.176         | 872500 | 49.839       |



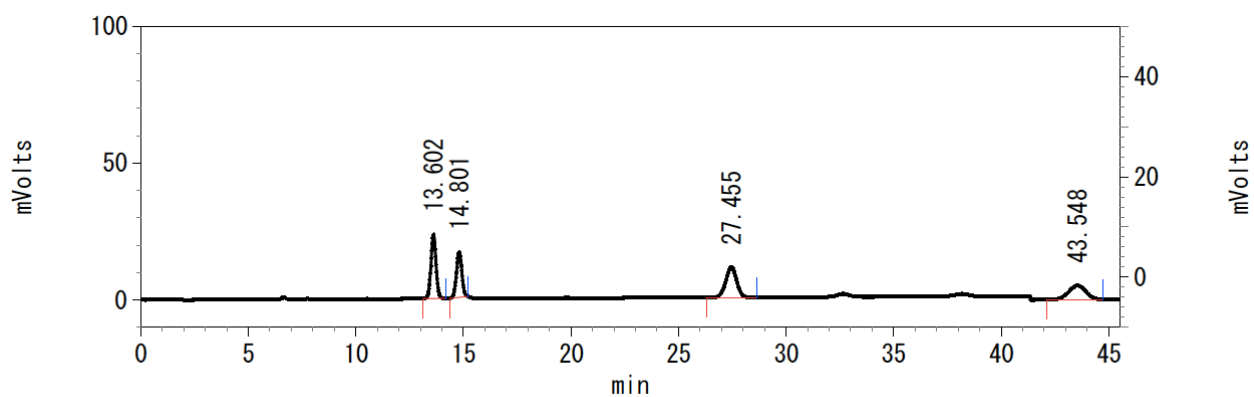




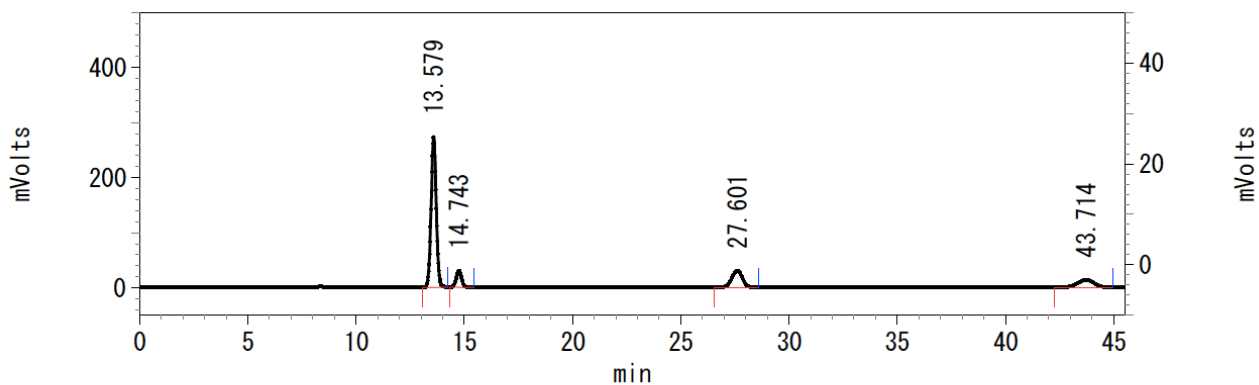
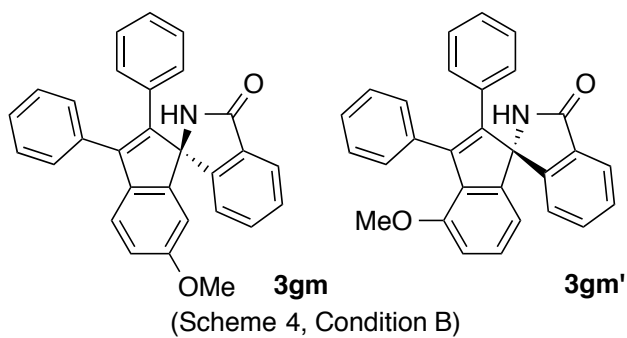


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 13.606         | 910822  | 8.461        |
| 2    | 14.778         | 500478  | 4.649        |
| 3    | 27.637         | 8663674 | 80.476       |
| 4    | 43.733         | 690523  | 6.414        |

**rac-3gm**

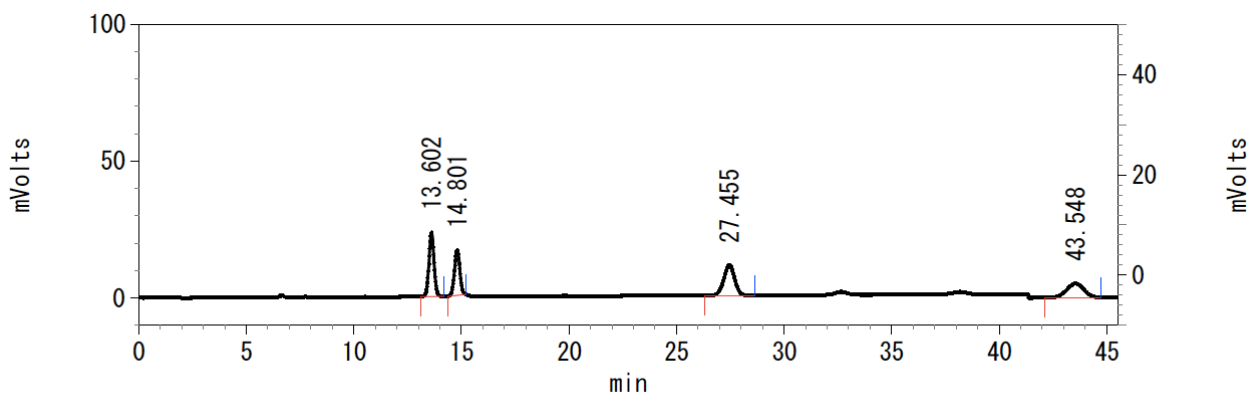


| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 13.602         | 390353 | 28.708       |
| 2    | 14.801         | 291533 | 21.440       |
| 3    | 27.455         | 387115 | 28.470       |
| 4    | 43.548         | 290742 | 21.382       |

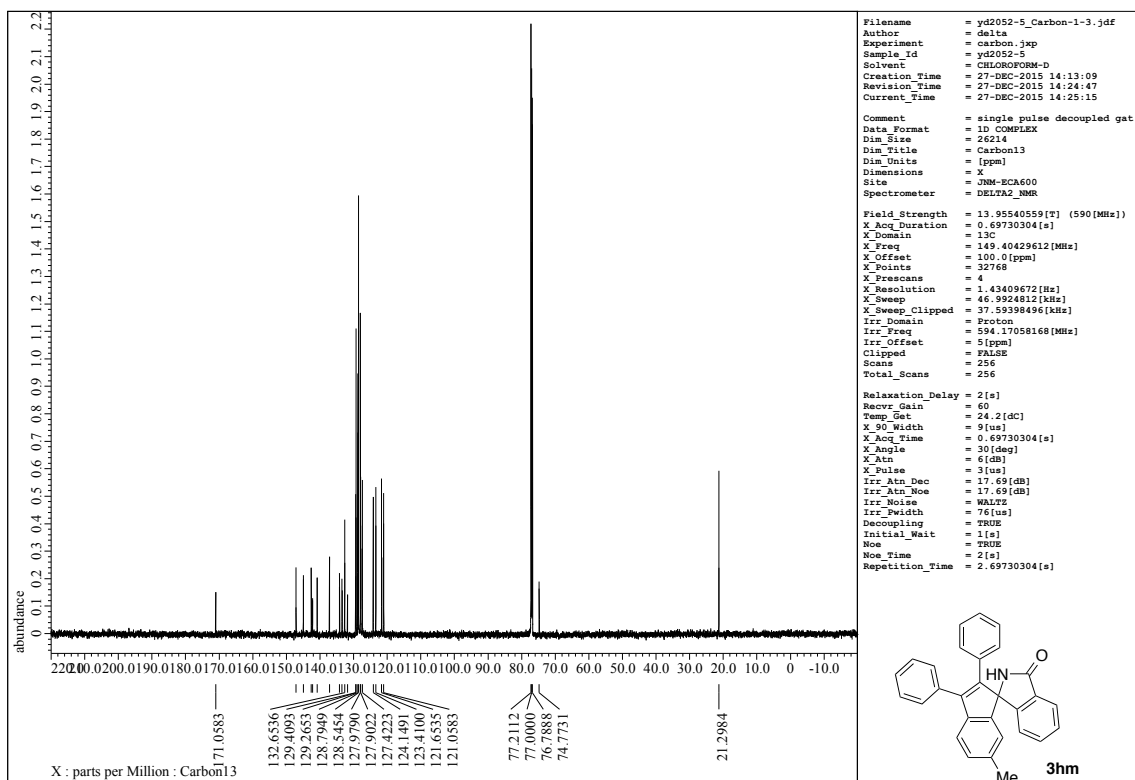
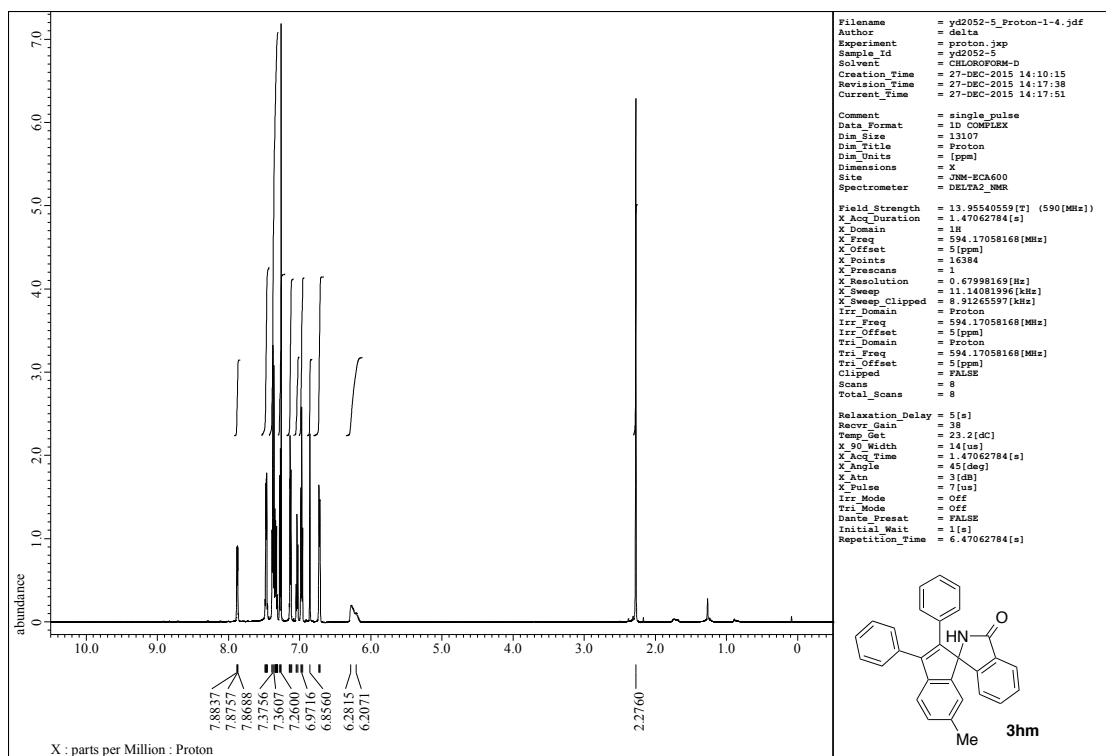


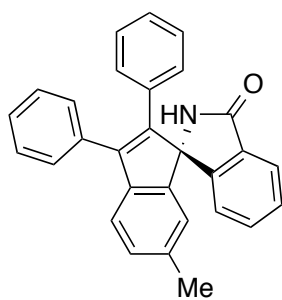
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 13.579         | 4572130 | 65.566       |
| 2    | 14.743         | 542885  | 7.785        |
| 3    | 27.601         | 1076138 | 15.432       |
| 4    | 43.714         | 782217  | 11.217       |

**rac-3gm**

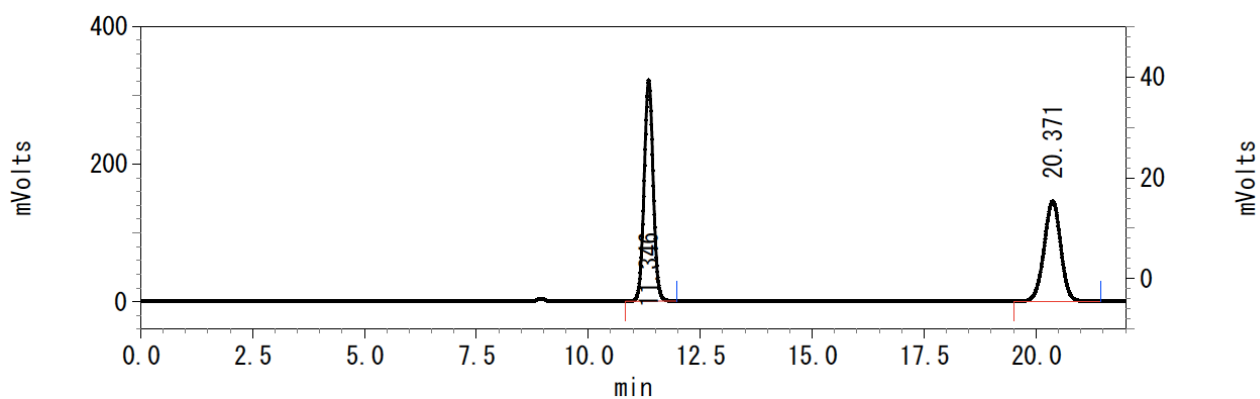


| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 13.602         | 390353 | 28.708       |
| 2    | 14.801         | 291533 | 21.440       |
| 3    | 27.455         | 387115 | 28.470       |
| 4    | 43.548         | 290742 | 21.382       |



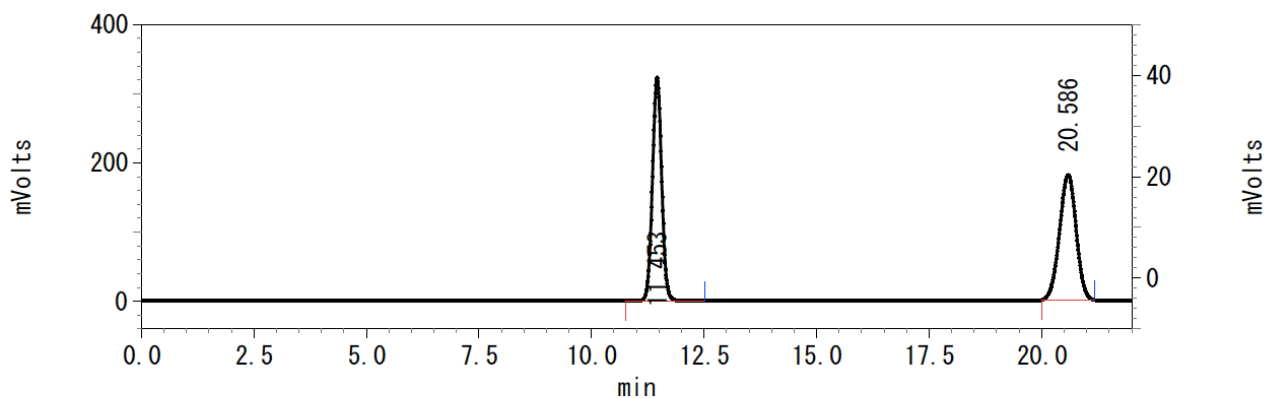


**3hm (S)** (Scheme 4, Condition A)

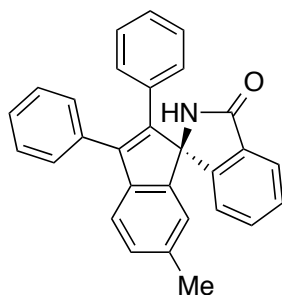


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 11.346         | 4524430 | 54.664       |
| 2    | 20.371         | 3752418 | 45.336       |

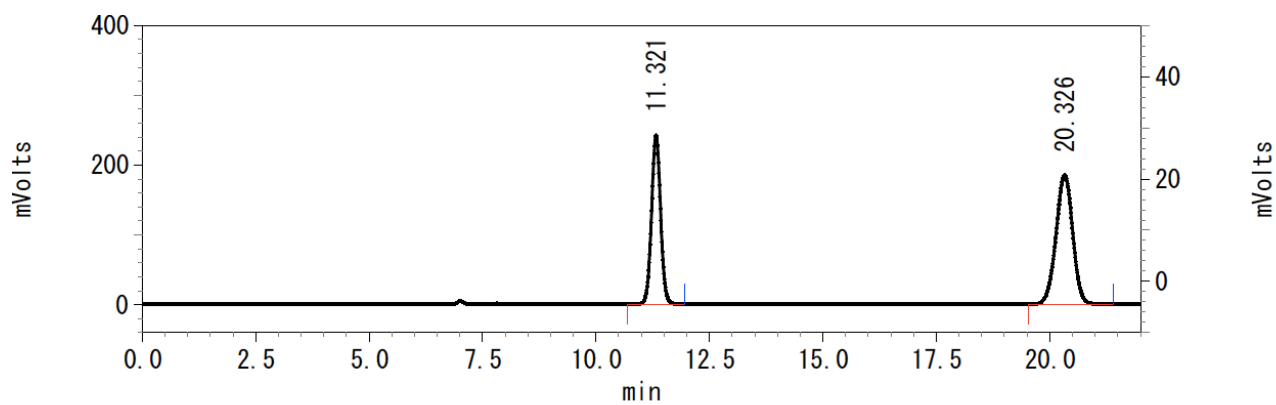
**rac-3hm**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 11.453         | 4622537 | 49.888       |
| 2    | 20.586         | 4643272 | 50.112       |

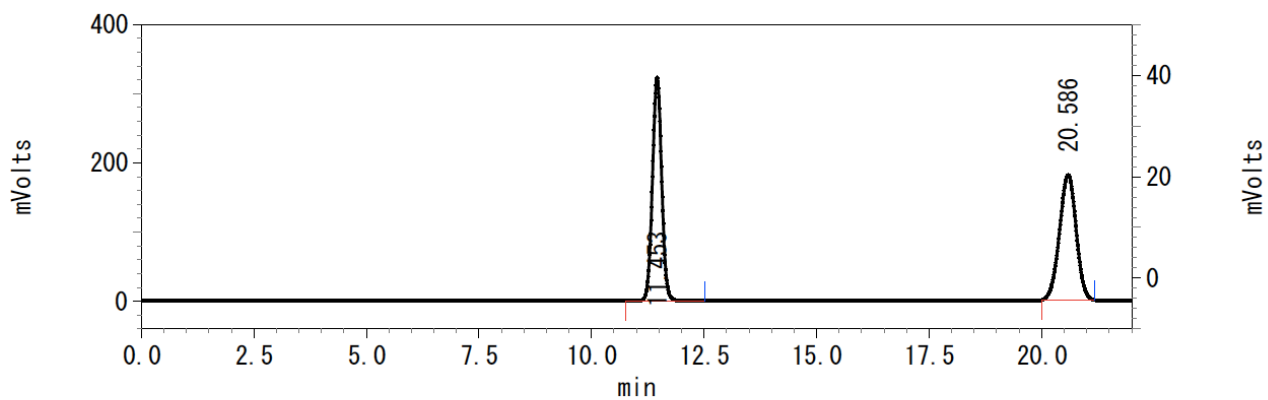


**3hm (R)** (Scheme 4, Condition B)

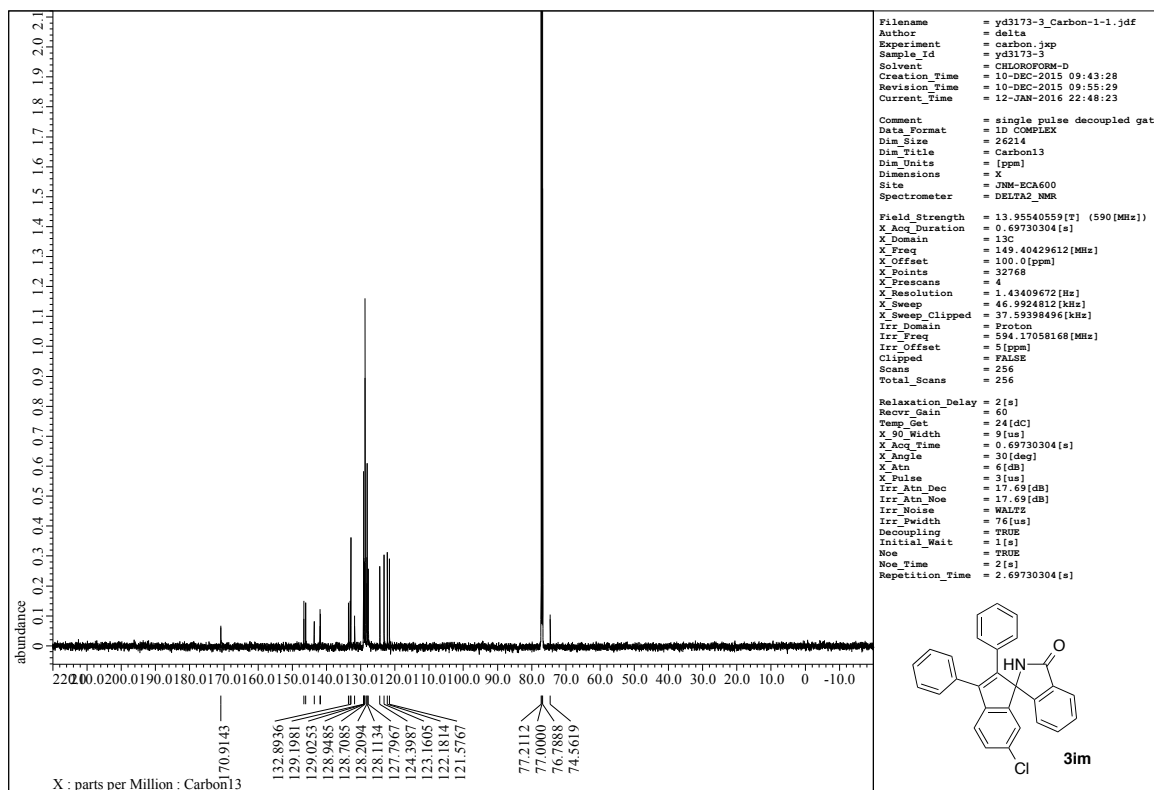
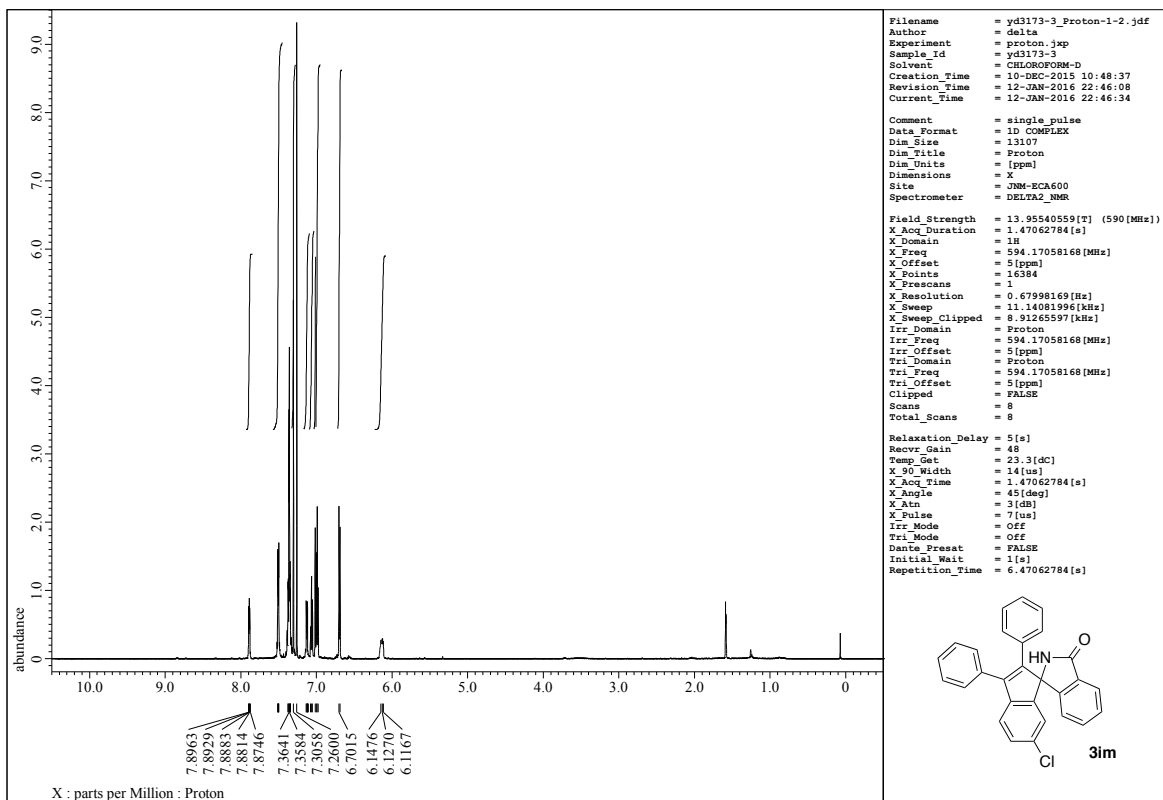


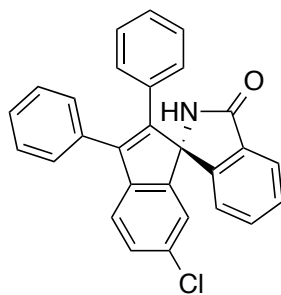
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 11.321         | 3375575 | 41.511       |
| 2    | 20.326         | 4756147 | 58.489       |

**rac-3hm**

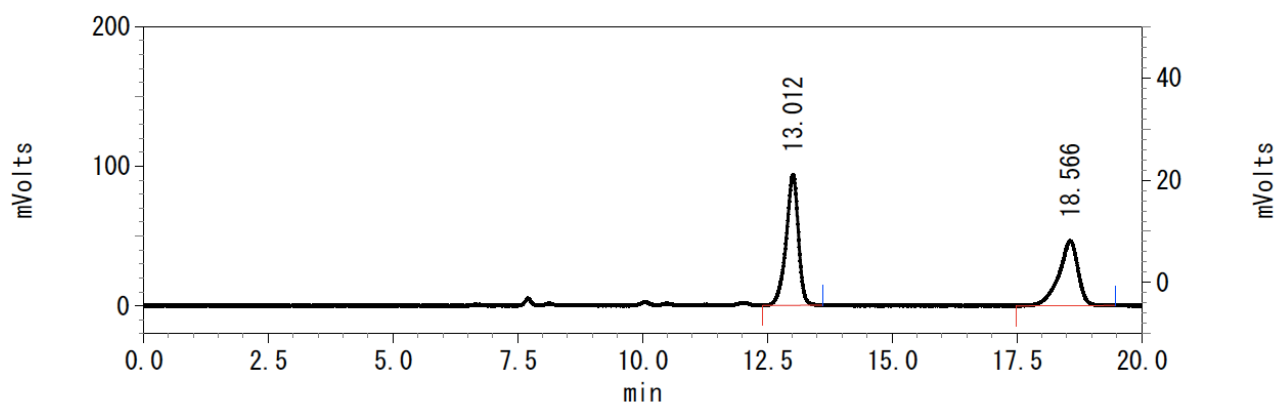


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 11.453         | 4622537 | 49.888       |
| 2    | 20.586         | 4643272 | 50.112       |



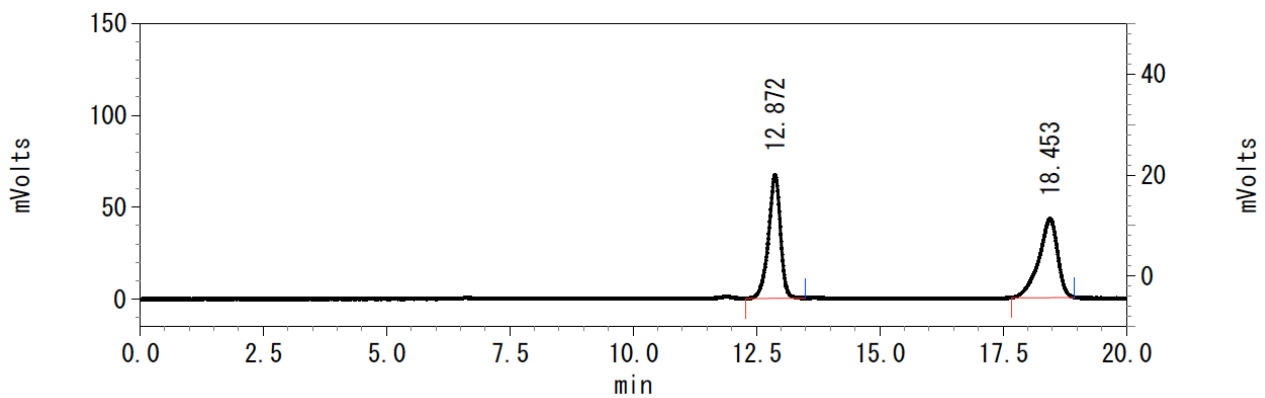


**3im (S)** (Scheme 4, Condition A)

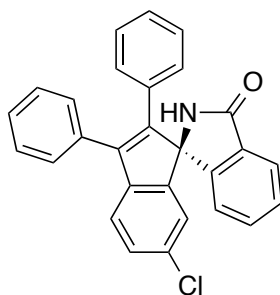


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 13.012         | 1601776 | 56.197       |
| 2    | 18.566         | 1248527 | 43.803       |

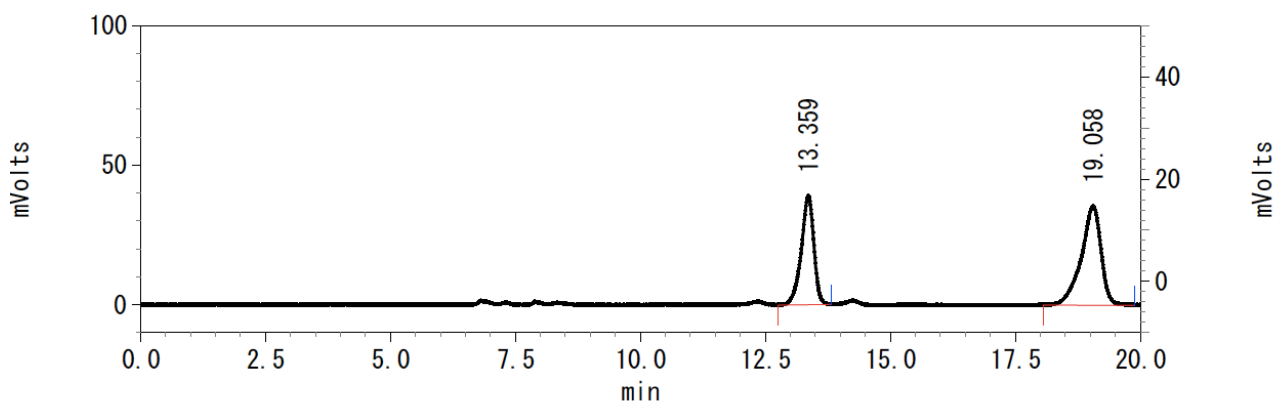
**rac-3im**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 12.872         | 1137520 | 50.054       |
| 2    | 18.453         | 1135051 | 49.946       |

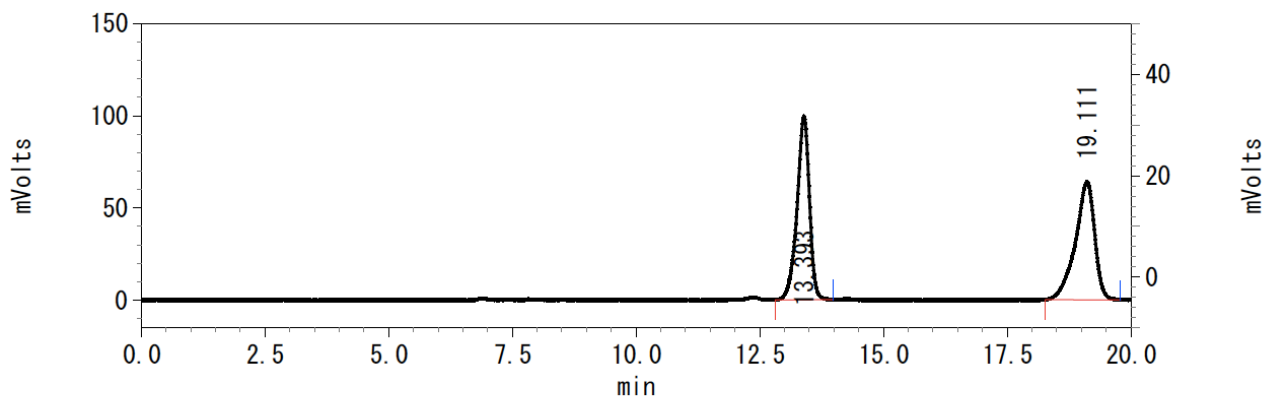


**3im (R)** (Scheme 4, Condition B)



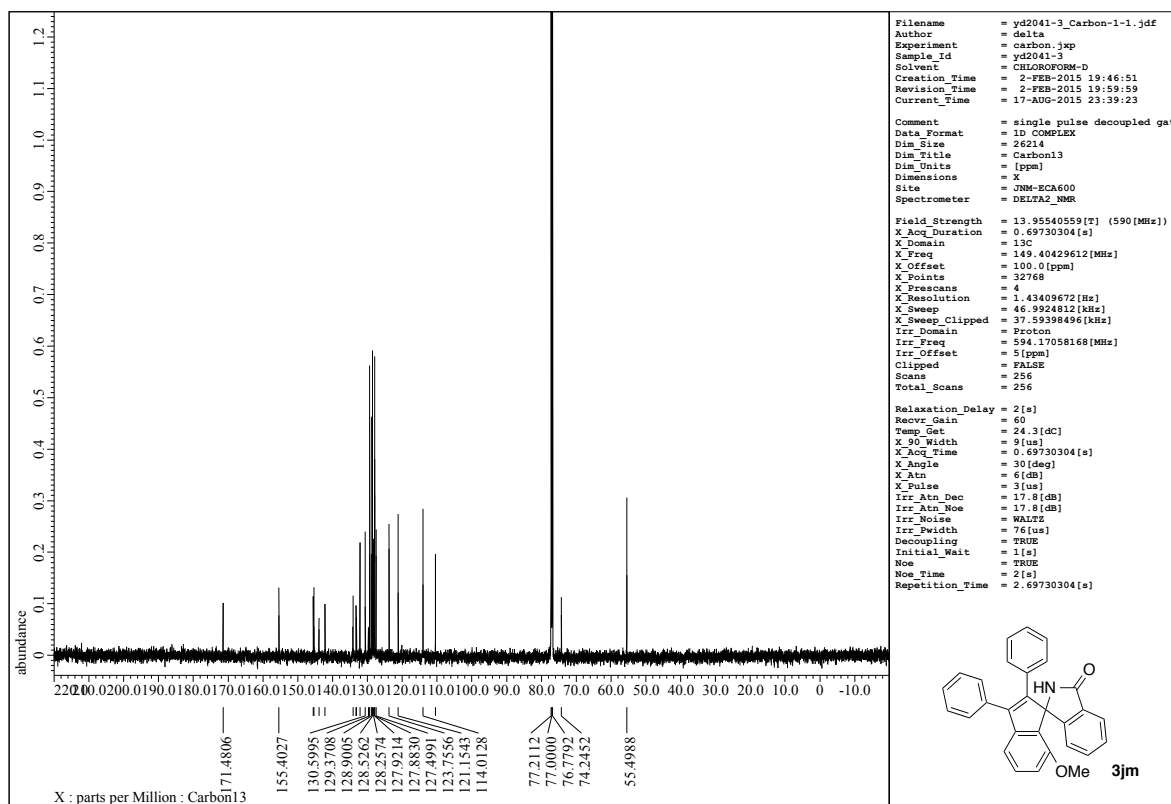
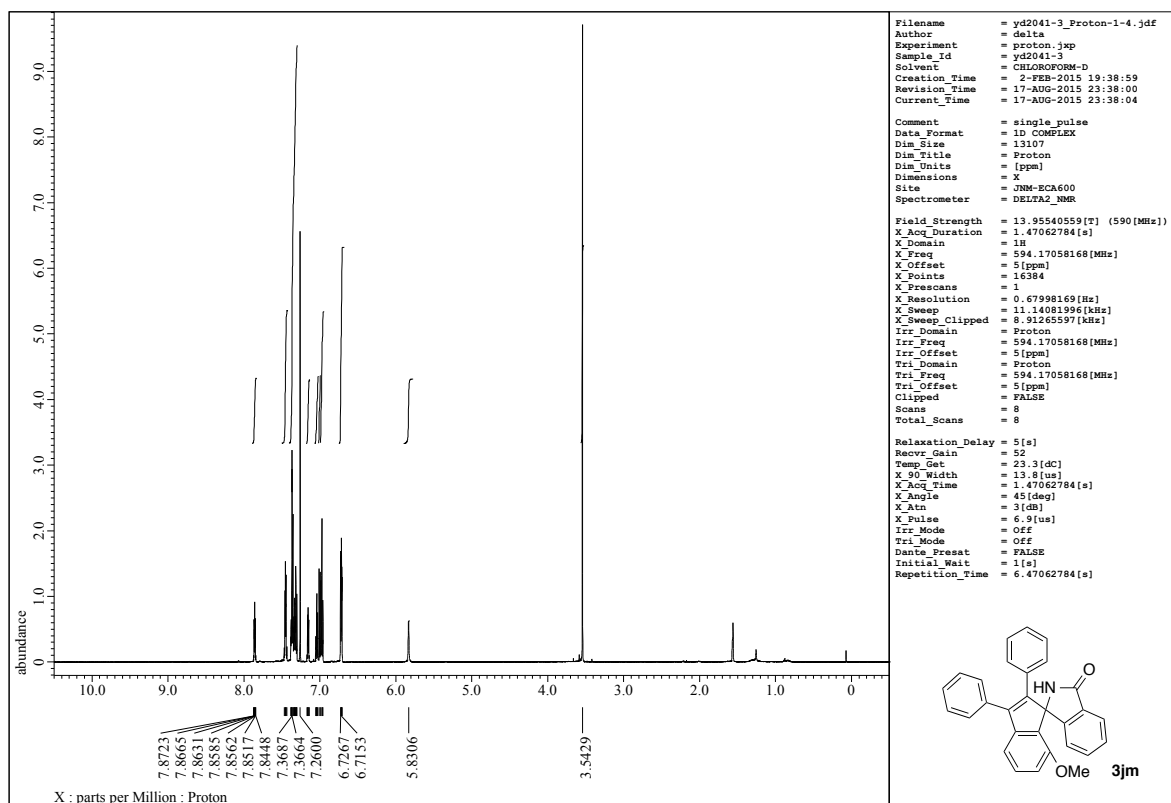
| Pk # | Retention Time | Area   | Area Percent |
|------|----------------|--------|--------------|
| 1    | 13.359         | 686872 | 41.145       |
| 2    | 19.058         | 982530 | 58.855       |

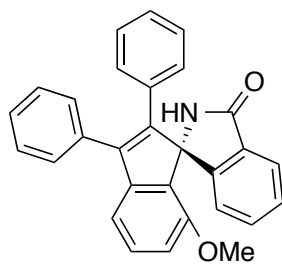
**rac-3im**



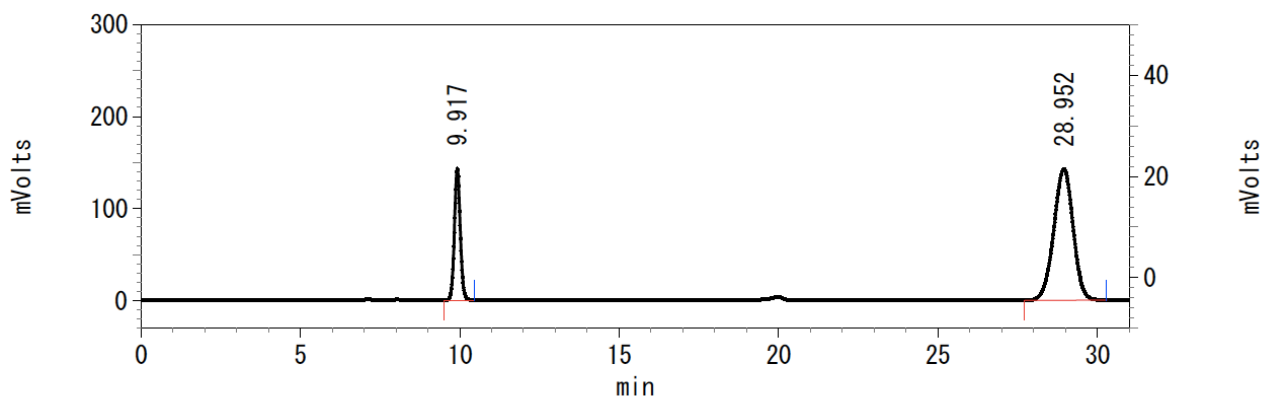
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 13.393         | 1739124 | 50.005       |
| 2    | 19.111         | 1738798 | 49.995       |





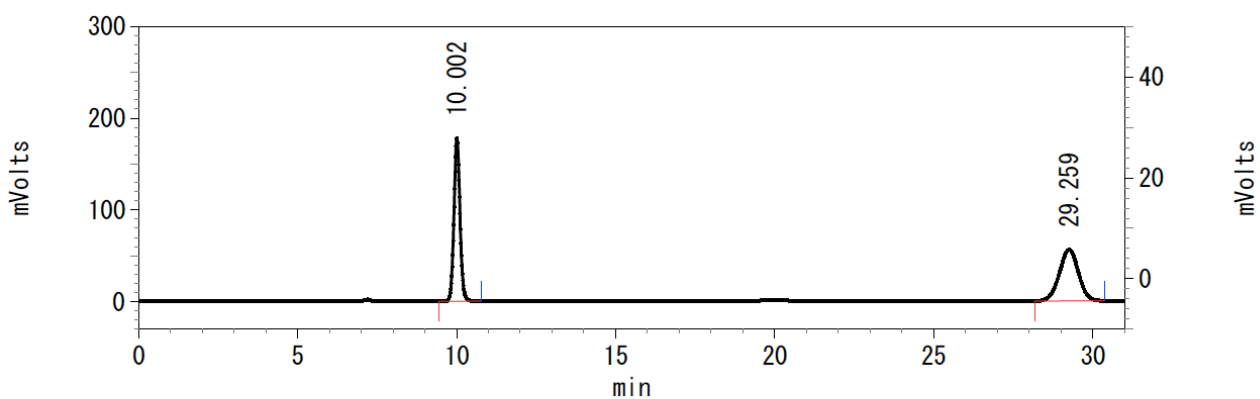


**3jm (S)** (Scheme 4, Condition A)

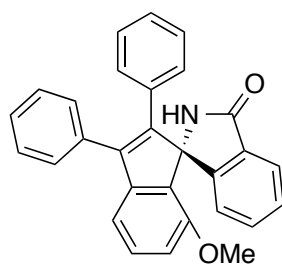


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.917          | 1844173 | 23.385       |
| 2    | 28.952         | 6041873 | 76.615       |

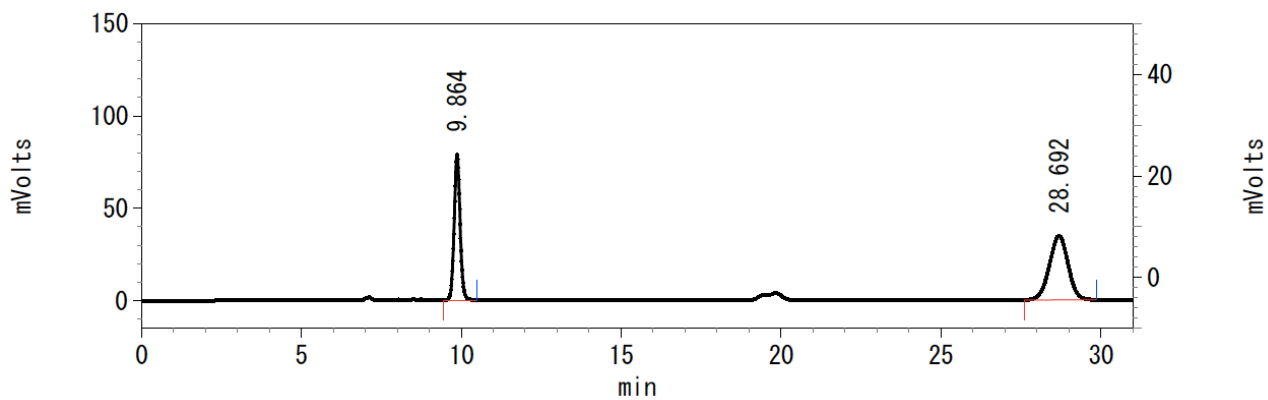
**rac-3jm**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.002         | 2347340 | 50.136       |
| 2    | 29.259         | 2334577 | 49.864       |

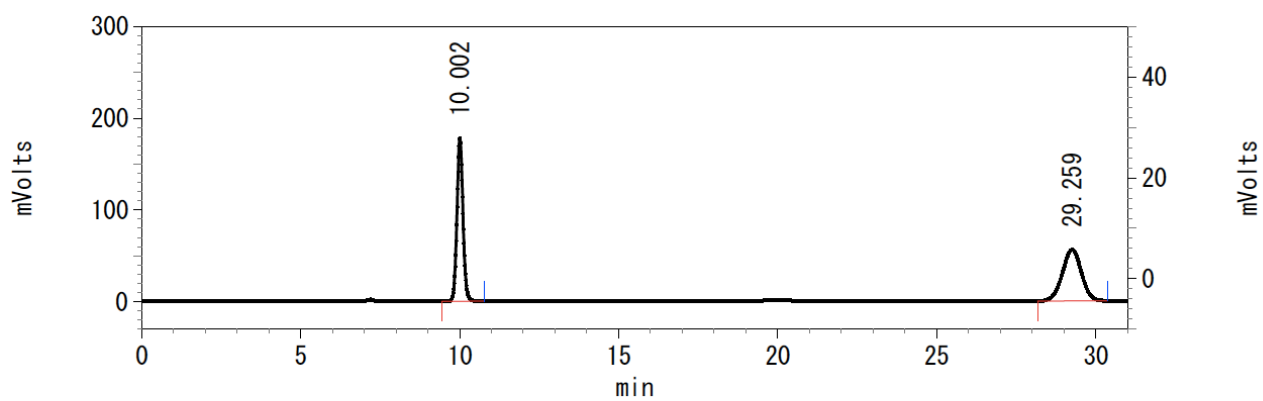


**3jm (S)** (Scheme 4, Condition B)

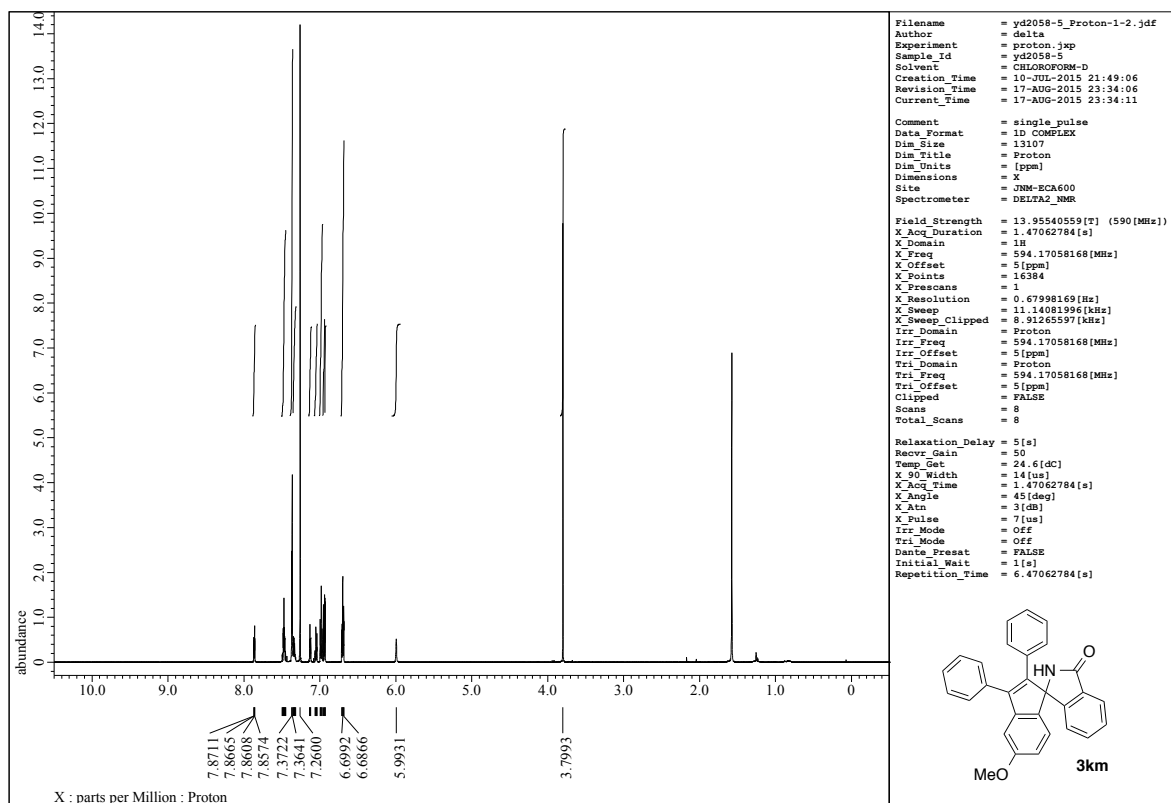


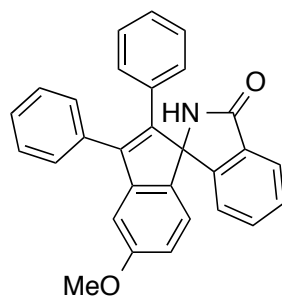
| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 9.864          | 1014708 | 41.860       |
| 2    | 28.692         | 1409323 | 58.140       |

**rac-3jm**

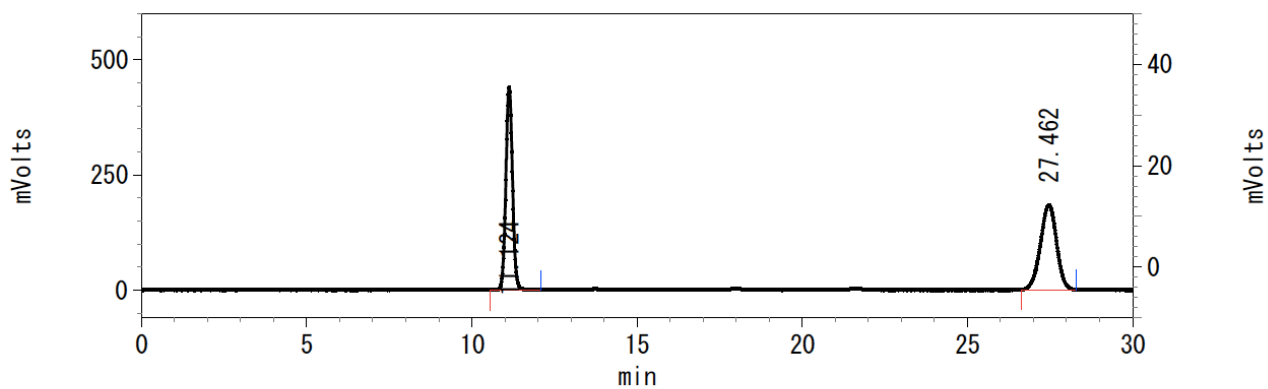


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.002         | 2347340 | 50.136       |
| 2    | 29.259         | 2334577 | 49.864       |



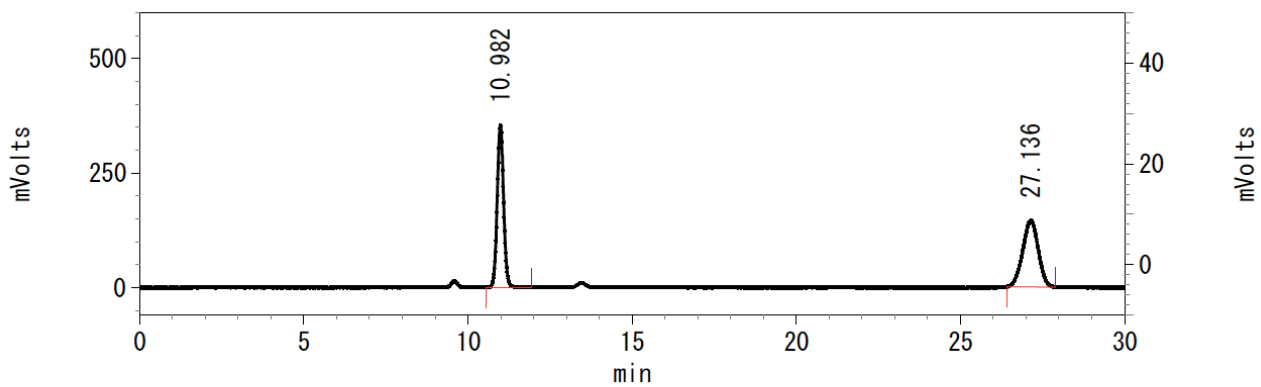


**3km** (Scheme 4, Condition A)

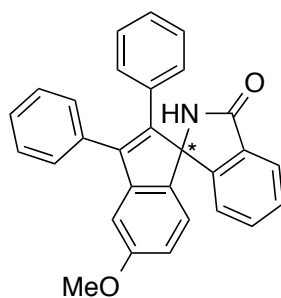


| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 11.124         | 6172499 | 49.724       |
| 2    | 27.462         | 6241011 | 50.276       |

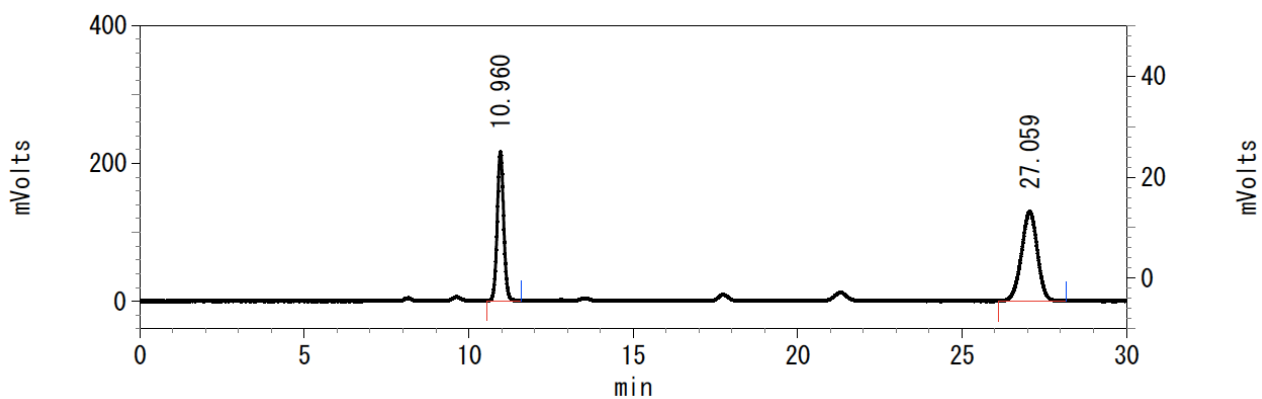
**rac-3km**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.982         | 4842303 | 50.178       |
| 2    | 27.136         | 4808009 | 49.822       |

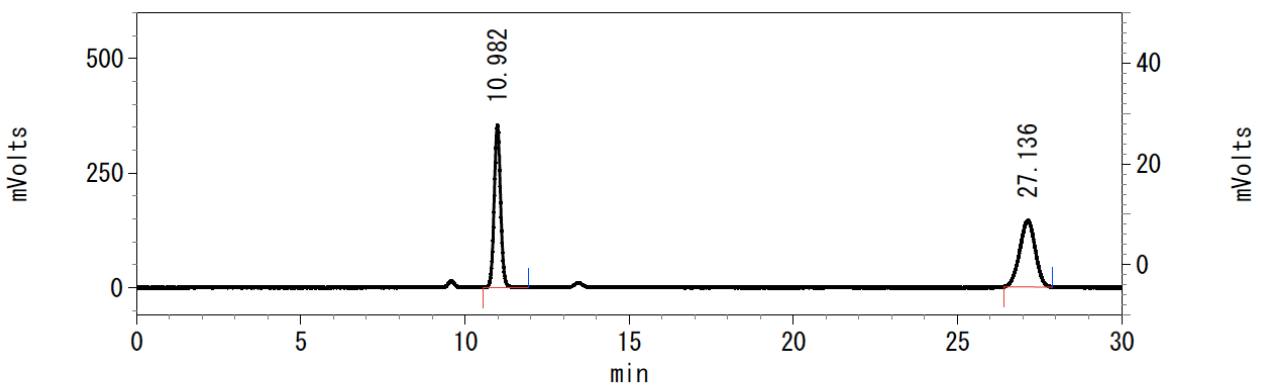


**3km** (Scheme 4, Condition B)



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.960         | 2977121 | 40.435       |
| 2    | 27.059         | 4385523 | 59.565       |

**rac-3km**



| Pk # | Retention Time | Area    | Area Percent |
|------|----------------|---------|--------------|
| 1    | 10.982         | 4842303 | 50.178       |
| 2    | 27.136         | 4808009 | 49.822       |