

Phosphine-Catalysed Asymmetric Dearomative Formal [4 + 2] Cycloadditions of 3-Benzofuranyl Vinyl Ketones

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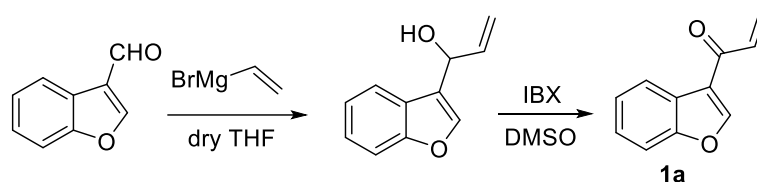
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1. General methods

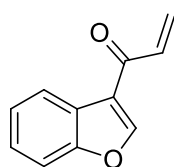
NMR data were obtained for ^1H at 400 MHz or 600 MHz, and for ^{13}C at 100 MHz or 150 MHz. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in CDCl_3 solution. ESI-HRMS was recorded on a Waters SYNAPT G2. In each case, diastereomeric ratio was determined by ^1H NMR and enantiomeric ratio was determined by HPLC analysis on a chiral column in comparison with authentic racemate, using a Daicel Chiralpak AD-H Column (250×4.6 mm), Chiralpak ID Column (250×4.6 mm), Chiralpak IE Column (250×4.6 mm). UV detection was monitored at 254 nm. Optical rotation was measured in CHCl_3 solution at 25 °C. Column chromatography was performed on silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. UV light, I_2 , solution of potassium permanganate were used to visualize products or starting materials. All chemicals were used without purification as commercially available unless otherwise noted. Petroleum ether and ethyl acetate (EtOAc) were distilled.

2. General procedure for synthesis of substrates 1

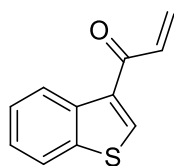


A suspension of benzofuran-3-carbaldehyde (0.73 g, 5.0 mmol) in anhydrous THF (15 mL) was stirred and cooled to 0 °C, and vinylmagnesium bromide (6 mL, 1.0 M in hexane, 6.0 mmol) was slowly added under argon atmosphere. The resulting yellow suspension was warmed to room temperature and stirred for 6 h. After complete conversion (monitored by TLC), the reaction was quenched with aqueous NH_4Cl and extracted with EtOAc. The combined organic phases were dried (Na_2SO_4), filtered and evaporated. The crude residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1:10) to give the alcohol as a yellow oil, in 80% yield (0.7 g).

The alcohol (0.7 g, 4.0 mmol) was dissolved in DMSO (10 mL), and IBX (1.68 g, 6.0 mmol) was added at room temperature. After complete conversion (monitored by TLC), the mixture was extracted with EtOAc. The combined organic phases were dried over Na_2SO_4 . The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1:20) to give **1a** as a white solid in 97% yield (0.68 g).

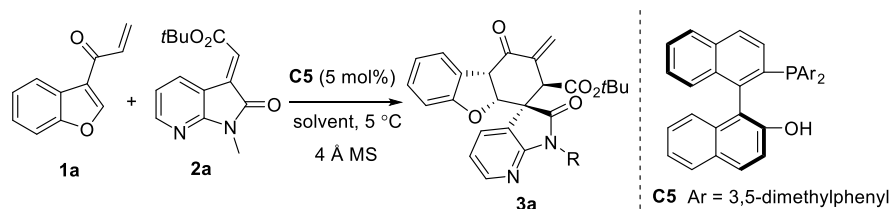


1-(Benzofuran-3-yl)prop-2-en-1-one (1a): white solid; mp 86–88 °C; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.31–8.28 (m, 2H), 7.55–7.53 (m, 1H), 7.40–7.38 (m, 2H), 6.94 (dd, *J* = 17.2, 10.4 Hz, 1H), 6.50 (d, *J* = 17.2 Hz, 1H), 5.88 (d, *J* = 10.4 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃): δ (ppm) 185.2, 155.7, 151.0, 133.3, 128.6, 125.9, 124.6, 124.5, 123.1, 122.3, 111.5.



1-(Benzo[*b*]thiophen-3-yl)prop-2-en-1-one (4d): white solid; mp 64–66 °C; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.76 (d, *J* = 8.0 Hz, 1H), 8.30 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.15 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.48 (d, *J* = 17.2 Hz, 1H), 5.92 (d, *J* = 10.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 185.4, 139.9, 137.2, 136.9, 135.3, 133.6, 129.1, 125.8, 125.7, 125.6, 122.3.

3. More screening conditions for formal [4 + 2] cycloaddition of **1a** and **2a**^a

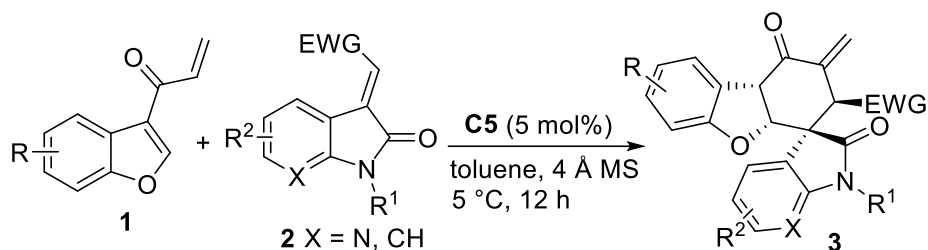


Entry	Solvent	<i>t</i> (h)	Yield (%) ^b	dr ^c	ee (%) ^d
1	toluene	12	66	>19:1	99
2 ^e	toluene	12	54	/	/
3	Et ₂ O	12	63	>19:1	97
4	DCM	12	60	4:1	/
5	CF ₃ Ph	12	25	>19:1	99
6	mesitylene	12	60	>19:1	/
7	THF	48	30	/	/
9 ^f	toluene	12	69	>19:1	99
10 ^{f,g}	toluene	5	68	>19:1	99

^a Unless noted otherwise, the reactions were carried out with **1a** (0.05 mmol), **2a** (0.075 mmol), catalyst **C5** (5 mol%), and 4 Å MS (20 mg) in solvent (0.5 mL) at 5 °C. Substrate **1a** was added in two portions. ^b Yield of isolated product. ^c Determined by ¹H NMR analysis. ^d Determined by HPLC analysis on a chiral stationary phase.

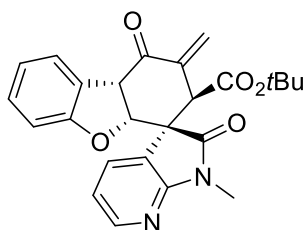
^e Without 4 Å MS. ^f Solvent (1 mL). ^g Catalyst **C5** (10 mol%).

4 General procedure for phosphine-catalysed asymmetric dearomative [4 + 2] cycloadditions of 3-benzofuranyl vinyl ketones **1** and 3-olefinic (7-aza)oxindoles **2**

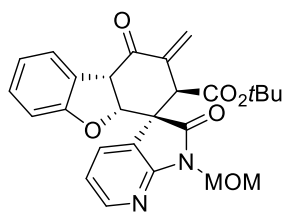


A mixture of 3-benzofuranyl vinyl ketone **1** (0.1 mmol, 1.0 equiv), 3-olefinic (7-aza)oxindole **2** (0.15 mmol, 1.5 equiv), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h or 3 h under Ar. Substrate **1** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/4–1/10) gave the product **3**.

The racemates could not be obtained by using the achiral phosphine catalysts, so the mixture of chiral catalyst **C5** and its enantiomer *ent*-**C5** was used for the preparation of the racemates.

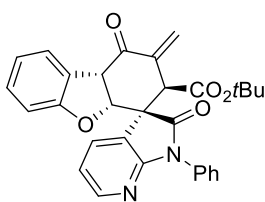


Synthesis of 3a: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2a** (39.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) gave the product **3a**: white solid, 38.0 mg, 88% yield; mp 135–137 °C; $[\alpha]_{\text{D}}^{25} = +20.3$ ($c = 1.25$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, *i*PrOH/*n*Hexane = 20/80, flow rate: 1.0 mL/min, 254 nm, *t* (major) = 16.06 min, *t* (minor) = 22.87 min]; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 8.29 (d, $J = 5.2$ Hz, 1H), 7.80 (d, $J = 6.8$ Hz, 1H), 7.35 (d, $J = 7.6$ Hz, 1H), 7.22 (t, $J = 7.6$ Hz, 1H), 7.05 (dd, $J = 7.2, 5.6$ Hz, 1H), 6.93 (t, $J = 7.2$ Hz, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 6.44 (d, $J = 2.8$ Hz, 1H), 5.32 (d, $J = 2.8$ Hz, 1H), 4.94 (d, $J = 9.6$ Hz, 1H), 4.53 (d, $J = 9.6$ Hz, 1H), 4.33 (s, 1H), 3.33 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 190.2, 174.6, 167.3, 158.9, 157.2, 148.0, 136.5, 133.5, 129.9, 125.8, 124.0, 123.9, 122.6, 122.0, 118.3, 109.7, 82.8, 82.5, 51.8, 50.6, 49.7, 27.3, 25.5; ESI-HRMS: calcd. for $\text{C}_{25}\text{H}_{24}\text{N}_2\text{O}_5 + \text{Na}^+$ 455.1577, found 455.1577.



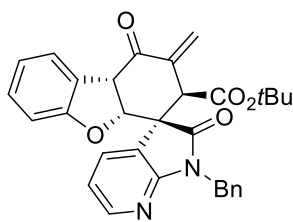
Synthesis of 3b: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2b** (43.5 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel

(EtOAc/petroleum ether = 1/6) gave the product **3b**: white solid, 43.0 mg, 93% yield; mp 81–83 °C; $[\alpha]_D^{25} = +15.4$ ($c = 1.35$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 19.93 min, t (minor) = 30.40 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.32 (d, $J = 4.8$ Hz, 1H), 7.81 (d, $J = 6.8$ Hz, 1H), 7.35 (d, $J = 7.2$ Hz, 1H), 7.21 (t, $J = 7.6$ Hz, 1H), 7.08 (t, $J = 6.4$ Hz, 1H), 6.93 (t, $J = 7.2$ Hz, 1H), 6.86 (d, $J = 4.0$ Hz, 1H), 6.44 (d, $J = 2.8$ Hz, 1H), 5.34 (d, $J = 2.4$ Hz, 1H), 5.25 (s, 2H), 5.01 (d, $J = 9.6$ Hz, 1H), 4.54 (d, $J = 9.6$ Hz, 1H), 4.32 (s, 1H), 3.46 (s, 3H), 1.12 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.4, 175.2, 167.5, 158.8, 156.2, 148.4, 136.4, 133.9, 129.9, 125.8, 124.5, 124.0, 122.0, 122.0, 118.8, 109.7, 82.9, 82.7, 70.2, 57.6, 51.8, 50.8, 49.8, 27.3. ESI-HRMS: calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_6 + \text{Na}^+$ 485.1683, found 485.1684.



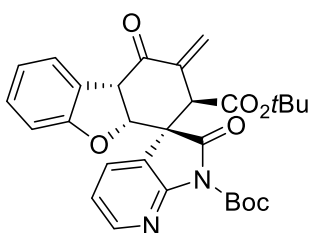
Synthesis of 3c: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2c** (48.3 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval.

After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) gave the product **3c**: white solid, 38.5 mg, 78% yield; mp 133–135 °C; $[\alpha]_D^{25} = -14.3$ ($c = 1.0$, in CHCl_3); 98% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 14.57 min, t (minor) = 18.60 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.30–8.29 (m, 1H), 7.92 (d, $J = 8.8$ Hz, 1H), 7.65 (d, $J = 8.0$ Hz, 2H), 7.53–7.49 (m, 2H), 7.40–7.36 (m, 2H), 7.26–7.22 (m, 1H), 7.13 (dd, $J = 7.2, 5.6$ Hz, 1H), 6.97–6.90 (m, 2H), 6.47 (d, $J = 2.8$ Hz, 1H), 5.38 (d, $J = 2.4$ Hz, 1H), 5.10 (d, $J = 9.2$ Hz, 1H), 4.53 (d, $J = 9.2$ Hz, 1H), 4.43–4.42 (m, 1H), 1.14 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.2, 173.9, 167.8, 158.8, 156.9, 148.2, 136.4, 134.1, 132.7, 129.9, 129.0, 128.0, 126.1, 125.9, 124.5, 124.1, 122.3, 122.0, 118.9, 109.7, 82.9, 82.8, 51.7, 50.5, 50.0, 27.5; ESI-HRMS: calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_2\text{O}_5 + \text{Na}^+$ 517.1734, found 517.1736.



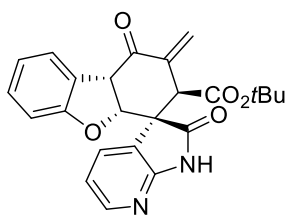
Synthesis of 3d: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2d** (50.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography

on silica gel (EtOAc/petroleum ether = 1/10) gave the product **3d**: white solid, 34.4 mg, 68% yield; mp 102–104 °C; $[\alpha]^{25}_D = +5.2$ ($c = 0.7$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak AD-H column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 10.12 min, t (major) = 12.77 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.28 (d, $J = 4.8$ Hz, 1H), 7.76 (d, $J = 7.2$ Hz, 1H), 7.48–7.47 (m, 2H), 7.38–7.15 (m, 5H), 7.02 (dd, $J = 6.8, 5.6$ Hz, 1H), 6.92 (t, $J = 7.2$ Hz, 1H), 6.84 (d, $J = 8.0$ Hz, 1H), 6.45 (d, $J = 2.8$ Hz, 1H), 5.34 (d, $J = 2.8$ Hz, 1H), 5.05–4.97 (m, 2H), 4.89 (d, $J = 9.6$ Hz, 1H), 4.52 (d, $J = 9.6$ Hz, 1H), 4.31 (s, 1H), 1.11 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.5, 174.5, 167.4, 158.9, 156.7, 148.1, 136.5, 136.2, 133.6, 129.9, 128.6, 128.4, 127.7, 125.7, 124.2, 124.0, 122.4, 121.9, 118.3, 109.7, 82.73, 82.67, 51.8, 50.6, 49.7, 42.9, 27.3. ESI-HRMS: calcd. for $\text{C}_{31}\text{H}_{28}\text{N}_2\text{O}_5 + \text{Na}^+$ 531.1896, found 531.1886.



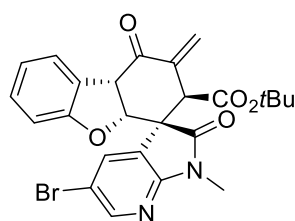
Synthesis of 3e: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2e** (52.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography

on silica gel (EtOAc/petroleum ether = 1/8) gave the product **3e**: white solid, 36.8 mg, 71 % yield; mp 101–103 °C; $[\alpha]^{25}_D = +35.3$ ($c = 1.4$, in CHCl_3); >99% ee, determined by HPLC analysis [Chiralpak AD-H column, $i\text{PrOH}/n\text{Hexane} = 10/90$, flow rate: 1.0 mL/min, 254 nm, t (major) = 8.63 min, t (minor) = 29.74 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.47 (d, $J = 4.8$ Hz, 1H), 7.88 (d, $J = 7.6$ Hz, 1H), 7.34 (d, $J = 7.2$ Hz, 1H), 7.26–7.16 (m, 2H), 6.93 (t, $J = 7.2$ Hz, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 6.44 (d, $J = 2.8$ Hz, 1H), 5.35 (d, $J = 2.0$ Hz, 1H), 5.02 (d, $J = 9.6$ Hz, 1H), 4.52 (d, $J = 9.6$ Hz, 1H), 4.32 (s, 1H), 1.61 (s, 9H), 1.11 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.2, 171.7, 166.8, 158.7, 154.2, 148.8, 147.1, 135.9, 134.3, 130.0, 125.8, 124.6, 123.8, 122.1, 121.6, 120.0, 109.7, 85.4, 83.3, 82.5, 51.6, 50.4, 50.3, 27.9, 27.1; ESI-HRMS: calcd. for $\text{C}_{29}\text{H}_{30}\text{N}_2\text{O}_7 + \text{Na}^+$ 541.1945, found 541.1948.



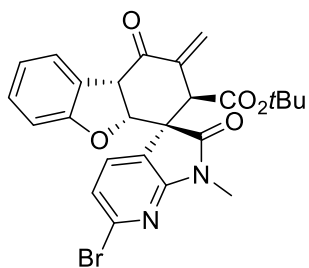
Synthesis of 3f: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2f** (37.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel

(EtOAc/petroleum ether = 1/8) gave the product **3f**: semisolid, 31.0 mg, 74 % yield; $[\alpha]_D^{25} = +55.0$ ($c = 1.2$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak AD-H column, $i\text{PrOH}/n\text{Hexane} = 10/90$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 19.72 min, t (major) = 21.90 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 11.24 (s, 1H), 8.22 (dd, $J = 5.2, 1.6$ Hz, 1H), 7.82 (d, $J = 7.2$ Hz, 1H), 7.36 (d, $J = 7.6$ Hz, 1H), 7.24-7.20 (m, 1H), 7.04 (dd, $J = 7.2, 5.6$ Hz, 1H), 6.93 (t, $J = 8.0$, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 6.44 (d, $J = 2.8$ Hz, 1H), 5.35 (d, $J = 2.8$ Hz, 1H), 5.06 (d, $J = 9.2$ Hz, 1H), 4.55 (d, $J = 9.2$ Hz, 1H), 4.32 (t, $J = 2.8$ Hz, 1H), 1.13 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.4, 175.8, 167.4, 158.8, 156.9, 147.0, 136.4, 134.6, 129.9, 125.8, 124.2, 124.1, 123.5, 122.0, 118.2, 109.7, 82.9, 82.6, 51.7, 51.2, 49.7, 27.2; ESI-HRMS: calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_5 + \text{Na}^+$ 441.1421, found 441.1424.



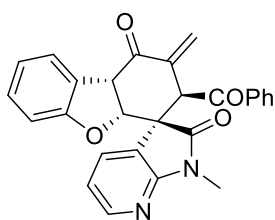
Synthesis of 3g: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2g** (50.7 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on

silica gel (EtOAc/petroleum ether = 1/9) gave the product **3g**: faint yellow semisolid, 41.6 mg, 82% yield; $[\alpha]_D^{25} = -23.0$ ($c = 1.0$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 12.27 min, t (minor) = 14.71 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.35 (d, $J = 2.4$ Hz, 1H), 7.89 (d, $J = 2.0$ Hz, 1H), 7.34 (d, $J = 7.6$ Hz, 1H), 7.25-7.21 (m, 1H), 6.96-6.90 (m, 2H), 6.43 (d, $J = 2.8$ Hz, 1H), 5.32 (d, $J = 2.8$ Hz, 1H), 4.92 (d, $J = 9.4$ Hz, 1H), 4.50 (d, $J = 9.4$ Hz, 1H), 4.29 (t, $J = 2.8$ Hz, 1H), 3.29 (s, 3H), 1.13 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.0, 174.1, 167.2, 158.7, 155.9, 148.7, 136.1, 136.1, 130.0, 125.8, 124.3, 124.2, 123.8, 122.2, 113.7, 109.8, 82.8, 82.4, 51.7, 50.8, 49.6, 27.4, 25.6; ESI-HRMS: calcd. for $\text{C}_{25}\text{H}_{23}\text{BrN}_2\text{O}_5 + \text{Na}^+$ 533.0688 (^{79}Br), 535.0668 (^{81}Br), found 533.0682 (^{79}Br), 535.0670 (^{81}Br).



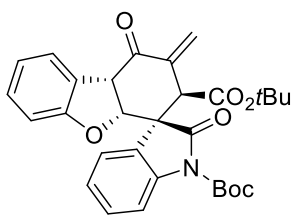
Synthesis of 3h: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaaxindole **2h** (50.7 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/9) gave the product **3h**: white

solid, 40.6 mg, 80% yield; mp 187–189 °C; $[\alpha]_D^{25} = +16.7$ ($c = 1.0$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 15.74 min, t (minor) = 19.94 min]; $^1\text{H NMR}$ (600 MHz, CDCl_3): δ (ppm) 7.63 (d, $J = 7.2$ Hz, 1H), 7.34 (d, $J = 7.2$ Hz, 1H), 7.24–7.21 (m, 2H), 6.93 (t, $J = 7.8$ Hz, 1H), 6.86 (d, $J = 7.8$ Hz, 1H), 6.44 (d, $J = 2.4$ Hz, 1H), 5.34 (d, $J = 2.4$ Hz, 1H), 4.92 (d, $J = 9.0$ Hz, 1H), 4.52 (d, $J = 9.0$ Hz, 1H), 4.29 (s, 1H), 3.31 (s, 3H), 1.15 (s, 9H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ (ppm) 190.1, 174.4, 167.2, 158.7, 157.5, 140.8, 136.2, 135.2, 123.0, 125.8, 124.3, 123.9, 122.1, 121.5, 121.2, 109.7, 82.9, 82.5, 51.7, 50.6, 49.6, 27.4, 25.8; ESI-HRMS: calcd. for $\text{C}_{25}\text{H}_{23}\text{BrN}_2\text{O}_5 + \text{Na}^+$ 533.0688 (^{79}Br), 535.0668 (^{81}Br), found 533.0681 (^{79}Br), 535.0667 (^{81}Br).



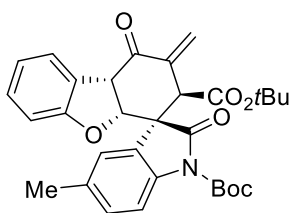
Synthesis of 3i: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic 7-azaaxindole **2i** (39.6 mg, 0.15 mmol), and catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica

gel (EtOAc/petroleum ether = 1/6) gave the product **3i**: faint yellow solid, 25.0 mg, 57% yield; mp 129–130 °C; $[\alpha]_D^{25} = +56.7$ ($c = 0.55$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak AD-H column, $i\text{PrOH}/n\text{Hexane} = 10/90$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 41.75 min, t (major) = 44.36 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.20 (d, $J = 4.8$ Hz, 1H), 7.71 (d, $J = 7.6$ Hz, 2H), 7.57–7.54 (m, 2H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.43–7.39 (m, 2H), 7.28–7.24 (m, 1H), 7.00 (t, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 8.0$ Hz, 1H), 6.82 (dd, $J = 7.2, 5.6$ Hz, 1H), 6.42 (d, $J = 2.8$ Hz, 1H), 5.48 (s, 1H), 5.07 (d, $J = 2.4$ Hz, 1H), 4.99 (d, $J = 9.2$ Hz, 1H), 4.57 (d, $J = 9.2$ Hz, 1H), 3.42 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 196.9, 190.9, 175.2, 158.8, 157.3, 147.9, 138.3, 137.0, 134.2, 132.6, 129.9, 129.1, 128.4, 126.1, 125.8, 124.6, 122.8, 122.1, 117.9, 109.7, 83.1, 51.5, 50.8, 48.8, 25.7; ESI-HRMS: calcd. for $\text{C}_{27}\text{H}_{20}\text{N}_2\text{O}_4 + \text{Na}^+$ 459.1315, found 459.1313.



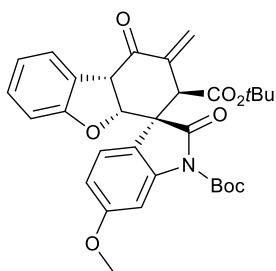
Synthesis of 3j: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic oxindole **2j** (52.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 3 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel

(EtOAc/petroleum ether = 1/10) gave the product **3j**: white semisolid, 32.5 mg, 63% yield; $[\alpha]_D^{25} = +34.7$ ($c = 1.1$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 7.36 min, t (major) = 9.79 min]; $^1\text{H NMR}$ (600 MHz, CDCl_3): δ (ppm) 7.94 (d, $J = 8.4$ Hz, 1H), 7.61 (d, $J = 7.8$ Hz, 1H), 7.41 (t, $J = 7.8$ Hz, 1H), 7.35 (d, $J = 7.8$ Hz, 1H), 7.26-7.20 (m, 2H), 6.94-6.88 (m, 2H), 6.42 (d, $J = 3.0$ Hz, 1H), 5.35 (d, $J = 2.4$ Hz, 1H), 5.00 (d, $J = 9.0$ Hz, 1H), 4.52 (d, $J = 9.0$ Hz, 1H), 4.37 (s, 1H), 1.62 (s, 9H), 1.06 (s, 9H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ (ppm) 190.5, 173.3, 167.0, 158.9, 148.9, 140.1, 136.4, 129.9, 129.5, 126.7, 126.0, 125.8, 124.6, 124.2, 124.1, 121.9, 114.9, 109.8, 84.9, 83.0, 82.6, 51.7, 50.8, 50.6, 28.0, 27.0; ESI-HRMS: calcd. for $\text{C}_{30}\text{H}_{31}\text{NO}_7 + \text{Na}^+$ 540.1993, found 540.1993.



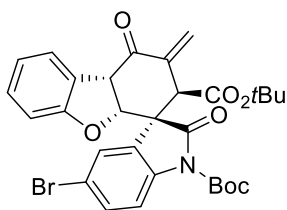
Synthesis of 3k: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic oxindole **2k** (54.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 3 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel

(EtOAc/petroleum ether = 1/10) gave the product **3k**: white solid, 44.0 mg, 83% yield; mp 81–82 °C; $[\alpha]_D^{25} = +21.2$ ($c = 1.15$, in CHCl_3); 98% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 6.72 min, t (major) = 9.88 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 7.80 (d, $J = 8.0$ Hz, 1H), 7.40 (s, 1H), 7.35 (d, $J = 8.0$ Hz, 1H), 7.23-7.10 (m, 2H), 6.93-6.90 (m, 2H), 6.41 (d, $J = 3.2$ Hz, 1H), 5.34 (d, $J = 2.8$ Hz, 1H), 4.98 (d, $J = 9.2$ Hz, 1H), 4.50 (d, $J = 9.2$ Hz, 1H), 4.35-4.34 (m, 1H), 2.41 (s, 3H), 1.61 (s, 9H), 1.06 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.5, 173.4, 167.1, 158.9, 149.0, 137.7, 136.5, 134.3, 129.9, 129.8, 126.6, 126.4, 125.8, 124.1, 124.1, 121.9, 114.7, 109.8, 84.7, 83.1, 82.5, 51.7, 50.8, 50.6, 28.0, 27.0, 21.2; ESI-HRMS: calcd. for $\text{C}_{31}\text{H}_{33}\text{NO}_7 + \text{Na}^+$ 554.2149, found 554.2149.



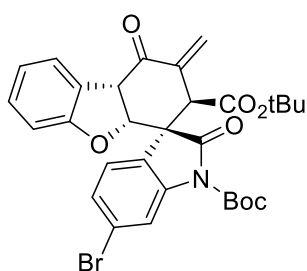
Synthesis of 3l: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic oxindole **2l** (56.3 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 3 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) gave the product **3l**: white semisolid, 31.0

mg, 57% yield; $[\alpha]_D^{25} = +19.9$ ($c = 1.5$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 9.45 min, t (major) = 11.40 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 7.58 (d, $J = 2.0$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 1H), 7.33 (d, $J = 7.6$ Hz, 1H), 7.21 (t, $J = 7.6$ Hz, 1H), 6.93-6.87 (m, 2H), 6.78 (dd, $J = 8.4, 2.0$ Hz, 1H), 6.41 (d, $J = 2.8$ Hz, 1H), 5.33 (d, $J = 2.8$ Hz, 1H), 4.96 (d, $J = 9.2$ Hz, 1H), 4.50 (d, $J = 9.2$ Hz, 1H), 4.33-4.31 (m, 1H), 3.86 (s, 3H), 1.62 (s, 9H), 1.10 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.6, 173.7, 167.2, 160.8, 158.9, 148.9, 141.1, 136.6, 129.9, 126.6, 125.8, 124.2, 124.2, 121.9, 118.5, 109.8, 109.76, 101.9, 84.9, 83.4, 82.5, 55.7, 51.7, 50.8, 50.4, 28.1, 27.1; ESI-HRMS: calcd. for $\text{C}_{31}\text{H}_{33}\text{NO}_8 + \text{Na}^+$ 570.2098, found 570.2098.

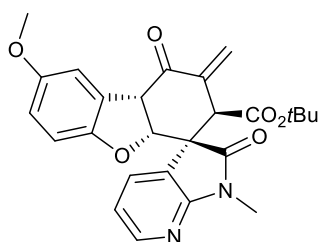


Synthesis of 3m: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic oxindole **2m** (63.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 3 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel

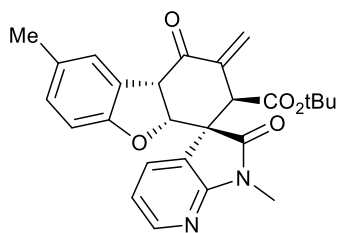
(EtOAc/petroleum ether = 1/10) gave the product **3m**: white solid, 46.0 mg, 77% yield; mp 95–97 °C; $[\alpha]_D^{25} = +12.3$ ($c = 0.8$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 6.13 min, t (major) = 7.89 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 7.85 (d, $J = 8.8$ Hz, 1H), 7.72 (d, $J = 2.0$ Hz, 1H), 7.54 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.35 (d, $J = 8.0$ Hz, 1H), 7.23 (t, $J = 8.0$ Hz, 1H), 6.96-6.92 (m, 2H), 6.43 (d, $J = 3.2$ Hz, 1H), 5.36 (d, $J = 2.8$ Hz, 1H), 4.97 (d, $J = 9.2$ Hz, 1H), 4.50 (d, $J = 9.2$ Hz, 1H), 4.32 (t, $J = 3.2$ Hz, 1H), 1.61 (s, 9H), 1.10 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.2, 172.4, 166.9, 158.7, 148.8, 139.2, 136.1, 132.4, 130.0, 128.9, 128.8, 125.8, 124.6, 123.9, 122.1, 117.5, 116.5, 109.9, 85.3, 82.9, 82.7, 51.6, 50.8, 50.5, 28.0, 27.1. ESI-HRMS: calcd. for $\text{C}_{30}\text{H}_{30}\text{BrNO}_7 + \text{Na}^+$ 618.1103 (^{79}Br), 620.1083 (^{81}Br), found 618.1102 (^{79}Br), 620.1088 (^{81}Br).



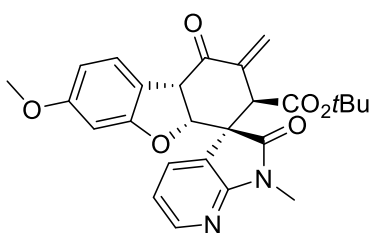
Synthesis of 3n: A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic oxindole **2n** (63.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 3 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) gave the product **3n**: white solid, 48.0 mg, 81% yield; mp 131–132 °C; $[\alpha]^{25}_D = +16.2$ ($c = 1.2$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 7.23 min, t (major) = 8.74 min]; **^1H NMR** (400 MHz, CDCl_3): δ (ppm) 8.19 (d, $J = 2.0$ Hz, 1H), 7.47 (d, $J = 8.0$ Hz, 1H), 7.40 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.34 (d, $J = 7.6$ Hz, 1H), 7.21 (t, $J = 7.6$ Hz, 1H), 6.95–6.87 (m, 2H), 6.43 (d, $J = 2.8$ Hz, 1H), 5.35 (d, $J = 2.4$ Hz, 1H), 4.97 (d, $J = 9.2$ Hz, 1H), 4.50 (d, $J = 9.2$ Hz, 1H), 4.33–4.32 (m, 1H), 1.62 (s, 9H), 1.11 (s, 9H); **^{13}C NMR** (100 MHz, CDCl_3): δ (ppm) 190.3, 172.6, 166.9, 158.7, 148.7, 141.1, 136.1, 130.0, 127.5, 127.1, 125.8, 125.6, 124.5, 123.9, 123.3, 122.0, 118.3, 109.8, 85.4, 82.9, 82.7, 51.6, 50.7, 50.5, 28.0, 27.1; ESI-HRMS: calcd. for $\text{C}_{30}\text{H}_{30}\text{BrNO}_7 + \text{Na}^+$ 618.1103 (^{79}Br), 620.1083 (^{81}Br), found 618.1102 (^{79}Br), 620.1082 (^{81}Br).



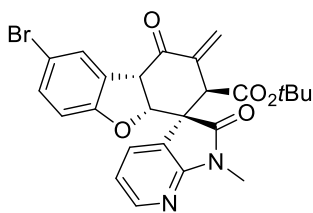
Synthesis of 3o: A mixture of 3-benzofuranyl vinyl ketone **1b** (20.2 mg, 0.1 mmol), 3-olefinic 7-azaioxindole **2a** (39.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1b** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) gave the product **3o**: white solid, 37.5 mg, 81% yield; mp 90–92 °C; $[\alpha]^{25}_D = +12.2$ ($c = 1.0$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 24.61 min, t (minor) = 33.91 min]; **^1H NMR** (400 MHz, CDCl_3): δ (ppm) 8.27 (dd, $J = 5.2, 1.6$ Hz, 1H), 7.79 (dd, $J = 7.2, 1.2$ Hz, 1H), 7.03 (dd, $J = 7.2, 5.2$ Hz, 1H), 6.89 (d, $J = 1.2$ Hz, 1H), 6.75 (s, 2H), 6.43 (d, $J = 3.2$ Hz, 1H), 5.32 (d, $J = 2.8$ Hz, 1H), 4.91 (d, $J = 9.2$ Hz, 1H), 4.48 (d, $J = 9.2$ Hz, 1H), 4.35 (t, $J = 2.8$ Hz, 1H), 3.74 (s, 3H), 3.31 (s, 3H), 1.08 (s, 9H); **^{13}C NMR** (101 MHz, CDCl_3): δ (ppm) 190.32, 174.72, 167.35, 157.18, 155.08, 152.93, 148.00, 136.54, 133.48, 124.65, 124.01, 122.69, 118.27, 116.23, 110.34, 109.94, 82.9, 82.5, 56.0, 52.3, 50.6, 49.7, 27.3, 25.5; ESI-HRMS: calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_6 + \text{Na}^+$ 485.1683, found 485.1683.



Synthesis of 3p: A mixture of 3-benzofuranyl vinyl ketone **1c** (18.6 mg, 0.1 mmol), 3-olefinic 7-azaioxindole **2a** (39.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1c** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) gave the product **3p**: white solid, 37.0 mg, 83% yield; mp 160–162 °C; $[\alpha]^{25}_D = +6.6$ ($c = 1.0$, in CHCl_3); >99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 14.99 min, t (minor) = 22.90 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.28 (dd, $J = 5.2, 1.6$ Hz, 1H), 7.80 (dd, $J = 7.2, 1.6$ Hz, 1H), 7.15 (s, 1H), 7.05–6.99 (m, 2H), 6.74 (d, $J = 8.0$ Hz, 1H), 6.43 (d, $J = 3.2$ Hz, 1H), 5.31 (d, $J = 3.2$ Hz, 1H), 4.90 (d, $J = 9.2$ Hz, 1H), 4.47 (d, $J = 9.2$ Hz, 1H), 4.33 (t, $J = 3.2$ Hz, 1H), 3.32 (s, 3H), 2.26 (s, 3H), 1.08 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.3, 174.7, 167.4, 157.2, 155.1, 152.9, 148.0, 136.5, 133.5, 124.7, 124.0, 122.7, 118.3, 116.2, 110.3, 109.9, 82.9, 82.5, 56.0, 52.3, 50.6, 49.7, 27.3, 25.5; ESI-HRMS: calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_5 + \text{Na}^+$ 469.1734, found 469.1740.

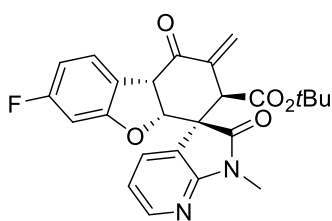


Synthesis of 3q: A mixture of 3-benzofuranyl vinyl ketone **1d** (20.2 mg, 0.1 mmol), 3-olefinic 7-azaioxindole **2a** (39.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1d** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) gave the product **3q**: faint yellow solid, 88% yield; mp 156–158 °C; $[\alpha]^{25}_D = +22.0$ ($c = 0.6$, in CHCl_3); 96% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 40/60$, flow rate: 1.0 mL/min, 254 nm, t (major) = 13.61min, t (minor) = 18.10min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.27 (d, $J = 5.2$ Hz, 1H), 7.78 (d, $J = 7.2$ Hz, 1H), 7.18 (d, $J = 8.4$ Hz, 1H), 7.03 (t, $J = 6.4$ Hz, 1H), 6.48–6.42 (m, 3H), 5.30 (s, 1H), 4.94 (d, $J = 9.6$ Hz, 1H), 4.44 (d, $J = 9.6$ Hz, 1H), 4.30 (s, 1H), 3.77 (s, 3H), 3.31 (s, 3H), 1.08 (s, 9H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ (ppm) 190.3, 174.6, 167.3, 161.7, 160.2, 157.2, 148.0, 136.5, 133.5, 125.9, 123.8, 122.6, 118.2, 115.8, 107.7, 96.3, 83.6, 82.5, 55.6, 51.2, 50.6, 49.7, 27.3, 25.5; ESI-HRMS: calcd. for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_6 + \text{Na}^+$ 485.1689, found 485.1684.



Synthesis of 3r: A mixture of 3-benzofuran-2-yl vinyl ketone **1e** (24.9 mg, 0.1 mmol), 3-olefinic 7-azaoxindole (39.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1e** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica

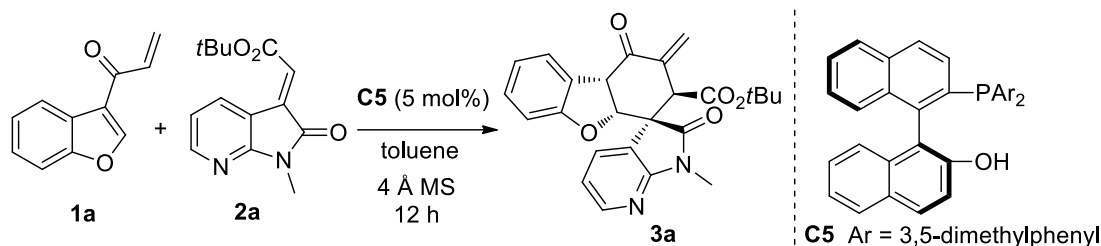
gel (EtOAc/petroleum ether = 1/6) gave the product **3r**: faint yellow solid, 33.0 mg, 65% yield; mp 172–173 °C; $[\alpha]_D^{25} = -41.4$ ($c = 1.0$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak AD-H column, $i\text{PrOH}/n\text{Hexane} = 40/60$, flow rate: 1.0 mL/min, 254 nm, t (major) = 8.66 min, t (minor) = 20.74 min]; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) 8.28 (dd, $J = 5.2, 1.6$ Hz, 1H), 7.74 (d, $J = 6.8$ Hz, 1H), 7.48 (s, 1H), 7.30 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.03 (dd, $J = 7.2, 5.2$ Hz, 1H), 6.73 (d, $J = 8.8$ Hz, 1H), 6.45 (d, $J = 2.8$ Hz, 1H), 5.35 (d, $J = 2.8$ Hz, 1H), 4.97 (d, $J = 9.6$ Hz, 1H), 4.48 (d, $J = 9.6$ Hz, 1H), 4.28 (t, $J = 2.8$ Hz, 1H), 3.32 (s, 3H), 1.10 (s, 9H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3): δ (ppm) 189.9, 174.5, 167.2, 158.0, 157.2, 148.2, 136.2, 133.4, 132.8, 128.7, 126.5, 124.6, 122.4, 118.3, 113.9, 111.3, 83.4, 82.7, 51.5, 50.4, 49.7, 27.3, 25.6; ESI-HRMS: calcd. for $\text{C}_{25}\text{H}_{23}\text{BrN}_2\text{O}_5 + \text{Na}^+$ 533.0688 (^{79}Br), 535.0668 (^{81}Br), found 533.0685 (^{79}Br), 535.0665 (^{81}Br).



Synthesis of 3s: A mixture of 3-benzofuran-2-yl vinyl ketone **1f** (19.0 mg, 0.1 mmol), 3-olefinic 7-azaoxindole **2a** (39.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1f** was added in two portions at 1 h interval. After completion, purification by flash chromatography

on silica gel (EtOAc/petroleum ether = 1/6) gave the product **3s**: white solid, 33.0 mg, 73% yield; mp 189–191 °C; $[\alpha]_D^{25} = +17.5$ ($c = 1.0$, in CHCl_3); 99% ee, determined by HPLC analysis [Chiralpak ID column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (major) = 13.78 min, t (minor) = 21.64 min]; $^1\text{H NMR}$ (600 MHz, CDCl_3): δ (ppm) 8.29 (d, $J = 4.8$ Hz, 1H), 7.75 (d, $J = 7.2$ Hz, 1H), 7.28–7.25 (m, 1H), 7.04 (dd, $J = 7.2, 5.6$ Hz, 1H), 6.66–6.58 (m, 2H), 6.44 (d, $J = 2.8$ Hz, 1H), 5.34 (d, $J = 2.8$ Hz, 1H), 5.00 (d, $J = 9.4$ Hz, 1H), 4.45 (d, $J = 9.2$ Hz, 1H), 4.29 (s, 1H), 3.32 (s, 3H), 1.10 (s, 9H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ (ppm) 190.2, 174.5, 167.2, 164.1 (d, $J = 245.2$ Hz), 159.8 (d, $J = 13.0$ Hz), 157.2, 148.2, 136.3, 133.4, 126.3 (d, $J = 10.5$ Hz), 124.4, 122.4, 119.7 (d, $J = 2.6$ Hz), 118.3, 108.9 (d, $J = 22.9$ Hz), 98.3 (d, $J = 26.9$ Hz), 84.1, 82.7, 50.9, 50.5, 49.7, 27.3, 25.5; ESI-HRMS: calcd. for $\text{C}_{25}\text{H}_{23}\text{FN}_2\text{O}_5 + \text{Na}^+$ 473.1483, found 473.1480.

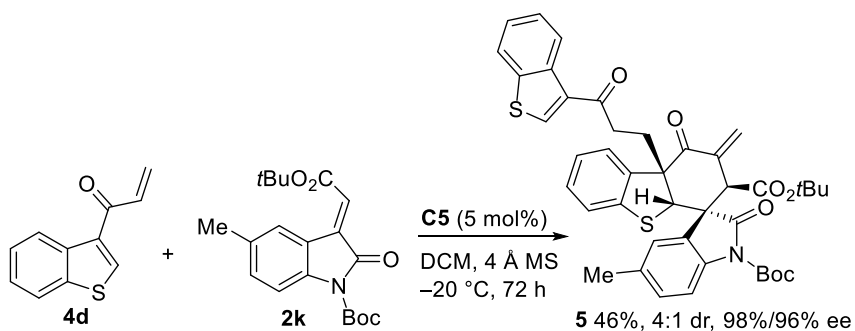
5. Asymmetric reaction at 1.0 mmol and gram scales



A 1.0 mmol scale: A mixture of 3-benzofuranyl vinyl ketone **1a** (172 mg, 1.0 mmol), 3-olefinic 7-azaoxindole **2a** (390 mg, 1.5 mmol), catalyst **C5** (26.0 mg, 5 mol%) and 4 Å MS (400 mg) in toluene (20.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) gave the product **3a**: 367 mg, white solid, 85% yield, 99% ee, >19:1 dr.

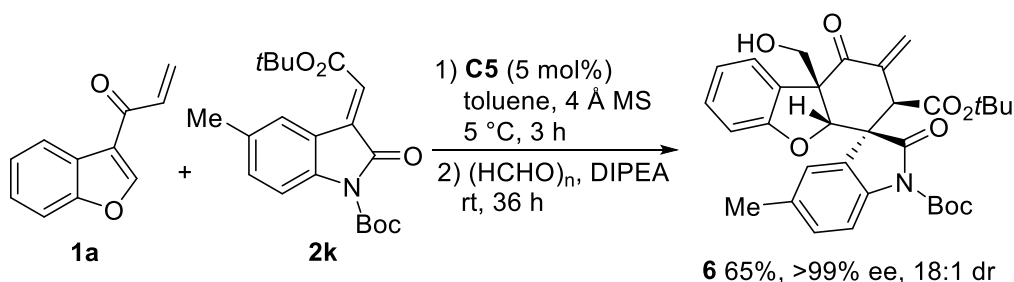
A gram scale: A mixture of 3-benzofuranyl vinyl ketone **1a** (1000 mg, 5.81 mmol), 3-olefinic 7-azaoxindole **2a** (2267 mg, 8.7 mmol), catalyst **C5** (148 mg, 0.29 mmol) and 4 Å MS (2300 mg) in toluene (116.0 mL) was stirred at 5 °C for 12 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **3a**: 2160 mg, white solid, 86% yield, 99% ee, >19:1 dr.

6. General procedure for the synthesis of compounds 5, 6, 7 and 8

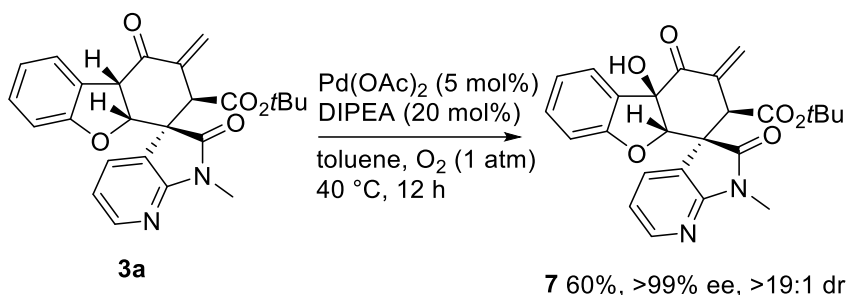


A mixture of 3-benzothiophenyl vinyl ketone **4d** (41.4 mg, 0.22 mmol), 3-olefinic oxindole **2k** (39.0 mg, 0.1 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in DCM (2.0 mL) was stirred at -20 °C for 72 h under Ar. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) gave the product **5**: white solid, 33.5 mg, 46% yield; mp 118–120 °C; $[\alpha]^{25}_D = -29.3$ ($c = 0.9$, in CHCl_3); 4:1 dr, determined by ^1H NMR analysis; 98% ee (major)/96% ee (minor), determined by HPLC analysis [Chiralpak IE column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, **major**: t (major) = 18.49 min, t (minor) = 20.52 min; **minor**: t (major) = 31.69 min, t (minor) = 36.52 min]; ^1H NMR (400 MHz, CDCl_3): δ (major, ppm) 8.71 (d,

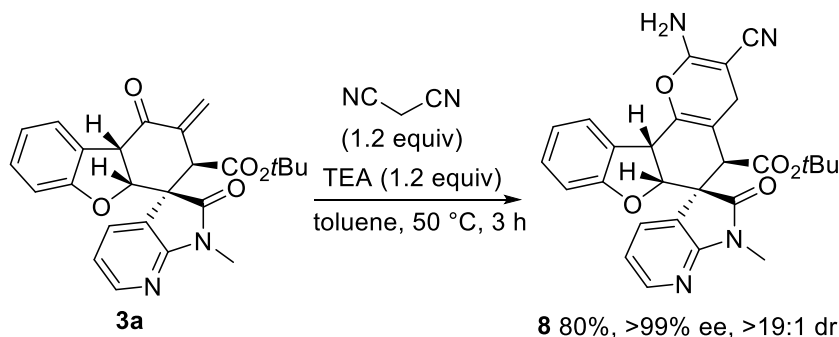
$J = 8.4$ Hz, 1H), 8.27 (s, 1H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 1H), 7.59–7.57 (m, 1H), 7.47–7.37 (m, 2H), 7.21 (d, $J = 8.4$ Hz, 1H), 7.16 (s, 1H), 7.09–7.07 (m, 1H), 6.99–6.97 (m, 1H), 6.49 (s, 1H), 5.53 (s, 1H), 3.63 (s, 1H), 3.36–3.29 (m, 1H), 3.22–3.14 (m, 1H), 2.63–2.49 (m, 2H), 2.35 (s, 3H), 1.44 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ (major, ppm) 195.8, 194.9, 172.5, 170.2, 148.9, 141.6, 139.7, 138.3, 137.7, 137.3, 136.7, 136.6, 135.0, 134.1, 130.1, 127.9, 127.8, 127.7, 125.8, 125.7, 125.2, 125.0, 124.7, 124.5, 122.1, 121.4, 114.7, 84.1, 83.0, 62.7, 55.4, 52.9, 52.4, 36.2, 35.2, 27.9, 27.9, 21.1; ESI-HRMS: calcd. for $\text{C}_{42}\text{H}_{41}\text{NO}_7\text{S}_2 + \text{Na}^+$ 758.2217, found 758.2214.



A mixture of 3-benzofuranyl vinyl ketone **1a** (17.2 mg, 0.1 mmol), 3-olefinic oxindole **2k** (54.0 mg, 0.15 mmol), catalyst **C5** (2.6 mg, 5 mol%) and 4 Å MS (40 mg) in toluene (2.0 mL) was stirred at 5 °C for 3 h under Ar. Substrate **1a** was added in two portions at 1 h interval. After completion, paraformaldehyde (18.0 mg, 0.6 mmol) and DIPEA (21.0 μL , 0.12 mmol) were added, and the mixture was stirred for 36 h. Purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) gave the product **6**: white solid, 36.5 mg, 65% yield; mp 84–86 °C; $[\alpha]_D^{25} = -7.0$ ($c = 0.95$, in CHCl_3); 18:1 dr, determined by ^1H NMR analysis; >99% ee, determined by HPLC analysis [Chiralpak AD-H column, $i\text{PrOH}/n\text{Hexane} = 20/80$, flow rate: 1.0 mL/min, 254 nm, t (minor) = 4.36 min, t (major) = 5.01 min]; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.79 (d, $J = 8.0$ Hz, 1H), 7.34 (s, 1H), 7.27–7.25 (m, 1H), 7.20 (dd, $J = 8.0, 1.2$ Hz, 1H), 7.09 (dd, $J = 8.0, 1.2$ Hz, 1H), 6.97 (d, $J = 8.0$ Hz, 1H), 6.91 (d, $J = 7.2$ Hz, 1H), 6.39 (d, $J = 3.2$ Hz, 1H), 5.32 (d, $J = 2.8$ Hz, 1H), 4.99 (s, 1H), 4.31 (dd, $J = 11.2, 5.2$ Hz, 1H), 4.16 (t, $J = 3.2$ Hz, 1H), 3.78 (dd, $J = 11.2, 8.4$ Hz, 1H), 2.40 (s, 3H), 2.23–2.20 (m, 1H), 1.59 (s, 9H), 1.03 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 191.4, 173.5, 166.9, 159.6, 148.8, 137.6, 137.2, 134.2, 130.7, 129.9, 126.6, 126.3, 124.9, 124.9, 123.6, 121.9, 114.5, 109.9, 85.7, 84.7, 82.6, 66.6, 60.7, 51.2, 50.0, 28.0, 26.9, 21.2; ESI-HRMS: calcd. for $\text{C}_{32}\text{H}_{35}\text{N}_1\text{O}_5 + \text{Na}^+$ 584.2260, found 584.2259.



A mixture of **3a** (43.2 mg, 0.1 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and DIPEA (3.5 μ L, 0.02 mmol) in toluene (1.0 mL) was stirred at 40 °C for 12 h under O₂ (1 atm). After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) gave the product **7**: white semisolid, 27.0 mg, 60% yield; $[\alpha]^{25}_{\text{D}} = +11.6$ ($c = 0.9$, in CHCl₃); >99% ee, determined by HPLC analysis [Chiralpak ID column, *i*PrOH/*n*Hexane = 40/60, flow rate: 1.0 mL/min, 254 nm, t (major) = 17.64 min, t (minor) = 23.95 min]; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.30 (d, $J = 4.8$ Hz, 1H), 7.79 (d, $J = 7.2$ Hz, 1H), 7.34 (t, $J = 8.0$ Hz, 1H), 7.15 (d, $J = 7.6$ Hz, 1H), 7.06 (dd, $J = 6.8, 5.6$ Hz, 1H), 7.00–6.96 (m, 2H), 6.49 (d, $J = 2.8$ Hz, 1H), 5.39 (d, $J = 2.8$ Hz, 1H), 4.80 (s, 1H), 4.73 (s, 1H), 4.08 (t, $J = 2.8$ Hz, 1H), 3.31 (s, 3H), 1.05 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 191.6, 174.3, 166.8, 160.2, 157.2, 148.2, 135.9, 133.7, 132.0, 126.2, 124.9, 124.8, 122.4, 121.9, 118.4, 110.4, 89.1, 82.8, 82.2, 49.9, 49.3, 27.2, 25.5; ESI-HRMS: calcd. for C₂₅H₂₄N₂O₆ + Na⁺ 471.1532, found 471.1528.

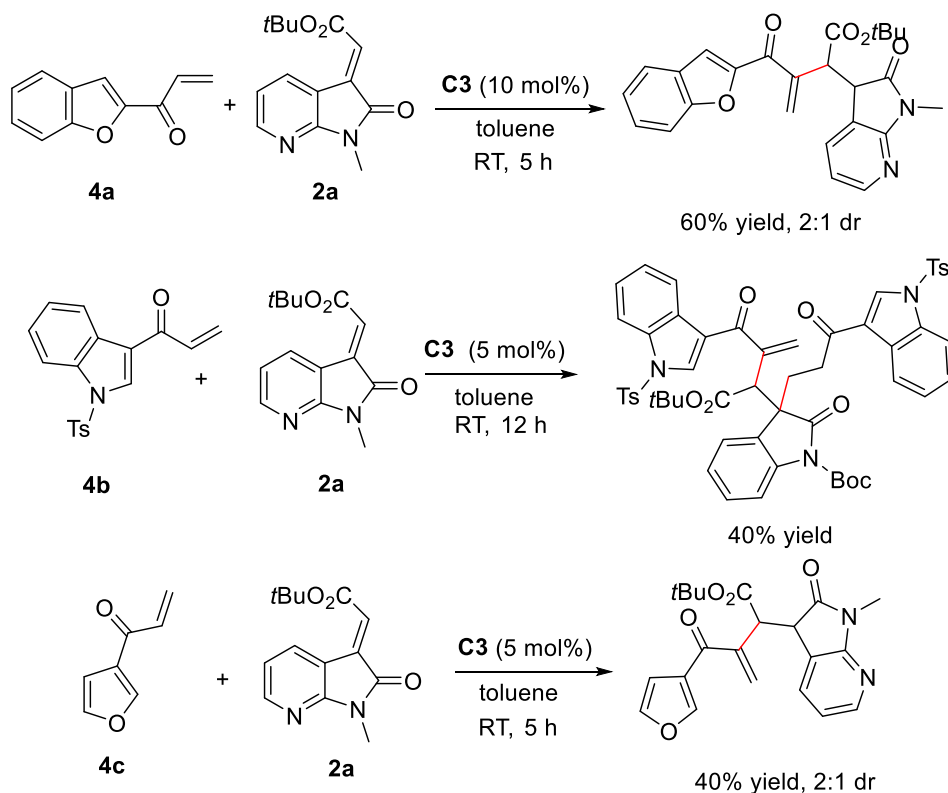


3a (43.2 mg, 0.1 mmol) and malononitrile (8.0 mg, 0.12 mmol) was dissolved in toluene (1.0 mL), and TEA (16.0 μ L, 0.12 mmol) was added at room temperature. The mixture was stirred at 50 °C for 3 h. After complete conversion (monitored by TLC), purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) gave the product **8**: faint yellow semisolid, 33.0 mg, 80% yield; $[\alpha]^{25}_{\text{D}} = -34.5$ ($c = 0.7$, in CHCl₃); >99% ee, determined by HPLC analysis [Chiralpak ID column, *i*PrOH/*n*Hexane = 40/60, flow rate: 1.0 mL/min, 254 nm, t (major) = 6.53 min, t (minor) = 13.37 min]; ¹H NMR (600 MHz, CDCl₃): δ (ppm) 8.19 (d, $J = 4.6$ Hz, 1H), 7.56 (brs, 1H), 7.38 (d, $J = 7.2$ Hz, 1H), 7.13 (t, $J = 7.8$ Hz, 1H), 6.90–6.87 (m, 2H), 6.68 (brs, 1H), 5.05 (brs, 1H), 4.55 (s, 2H), 4.30 (brs, 1H), 3.63 (brs, 1H), 3.33 (s, 3H), 2.81 (dd, $J = 17.4, 1.8$ Hz, 1H), 2.70 (d, $J = 17.4$, 1H), 1.23 (s, 9H); ¹³C NMR (150 MHz, CDCl₃): δ (ppm) 174.3, 168.1, 159.5, 159.5, 158.5,

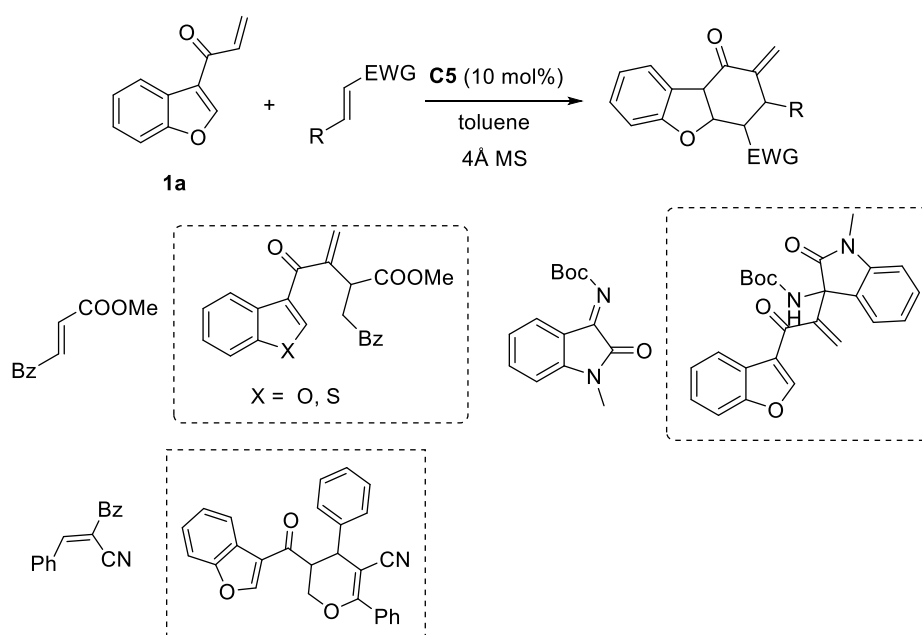
156.9, 147.9, 143.2, 133.1, 129.4, 126.1, 125.4, 122.5, 121.4, 119.8, 117.8, 110.1, 82.9, 82.4, 53.9, 51.2, 49.6, 41.8, 27.6, 25.6, 23.4; ESI-HRMS: calcd. for $\text{C}_{28}\text{H}_{26}\text{N}_4\text{O}_5 + \text{Na}^+$ 521.1801, found 521.1791.

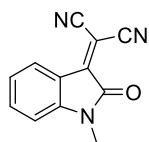
7. More screening studies on diverse heteroaromatic substrates and activated alkenes

To further expand the substrate scope of this catalytic dearomative protocol, heteroaromatic substrates **4a–4c** were investigated. Unfortunately, only the cross-RC adducts were obtained in the reactions with alkene **2a**.

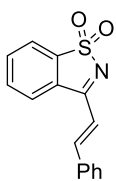


Meanwhile, a few activated alkenes were investigated under the standard conditions. However, but only the cross-RC products or even no reaction occurred.

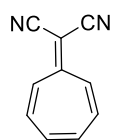




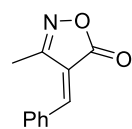
NR



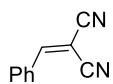
NR



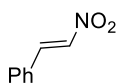
NR



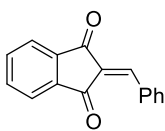
40-60 °C trace



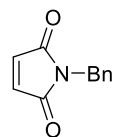
40-60 °C trace



40-60 °C trace

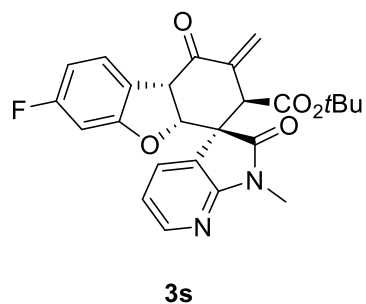
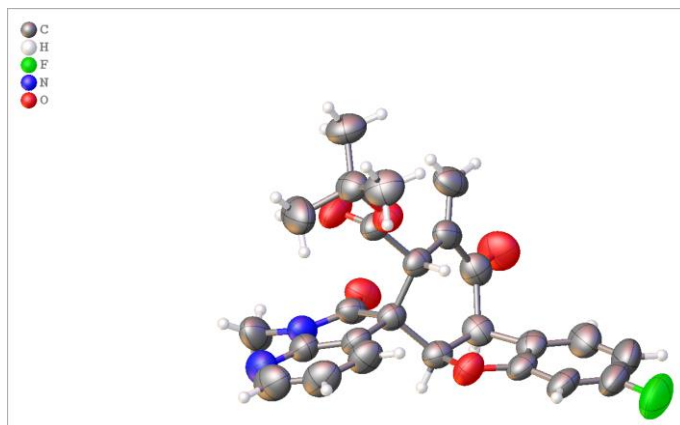


40-60 °C trace



40-60 °C trace

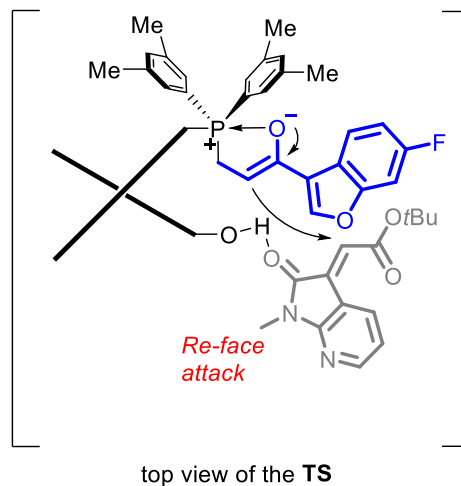
8. Crystal data and structure refinement for enantiopure 3s and the proposed transition state



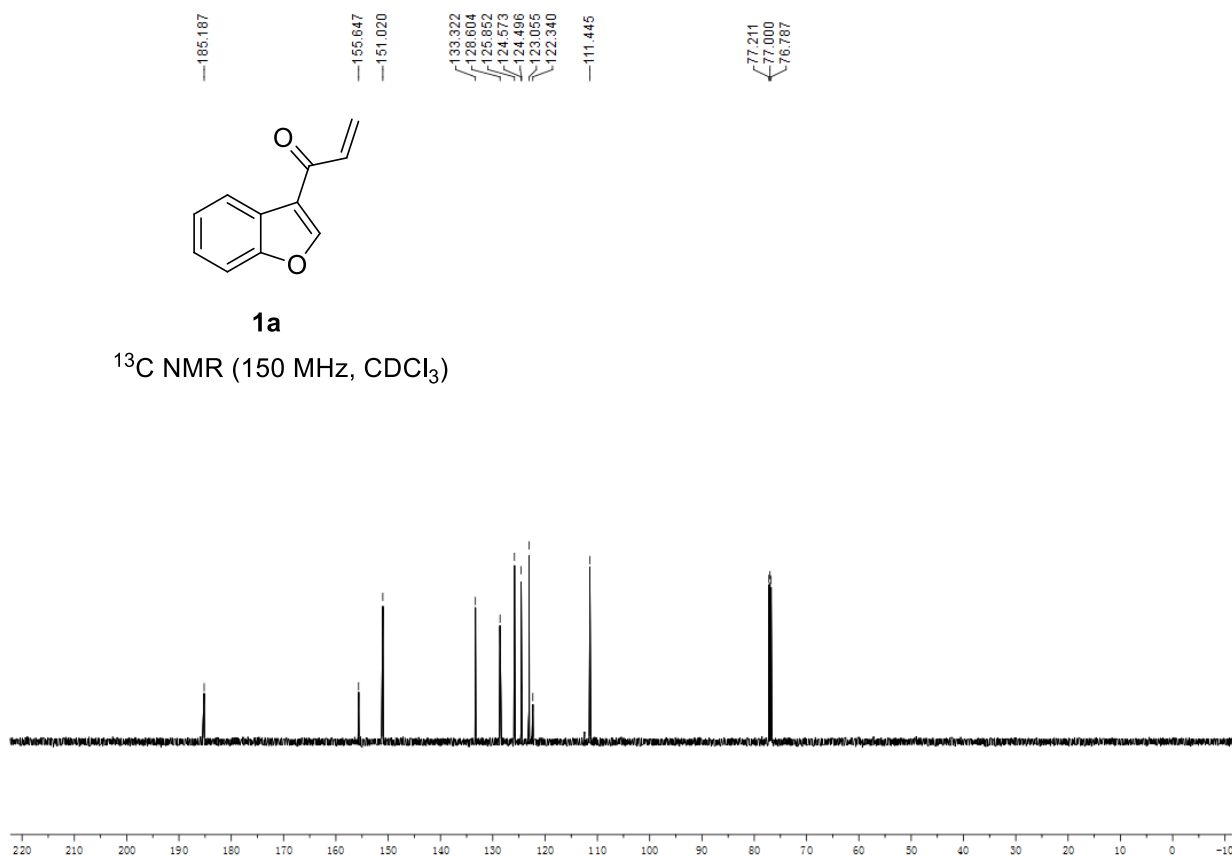
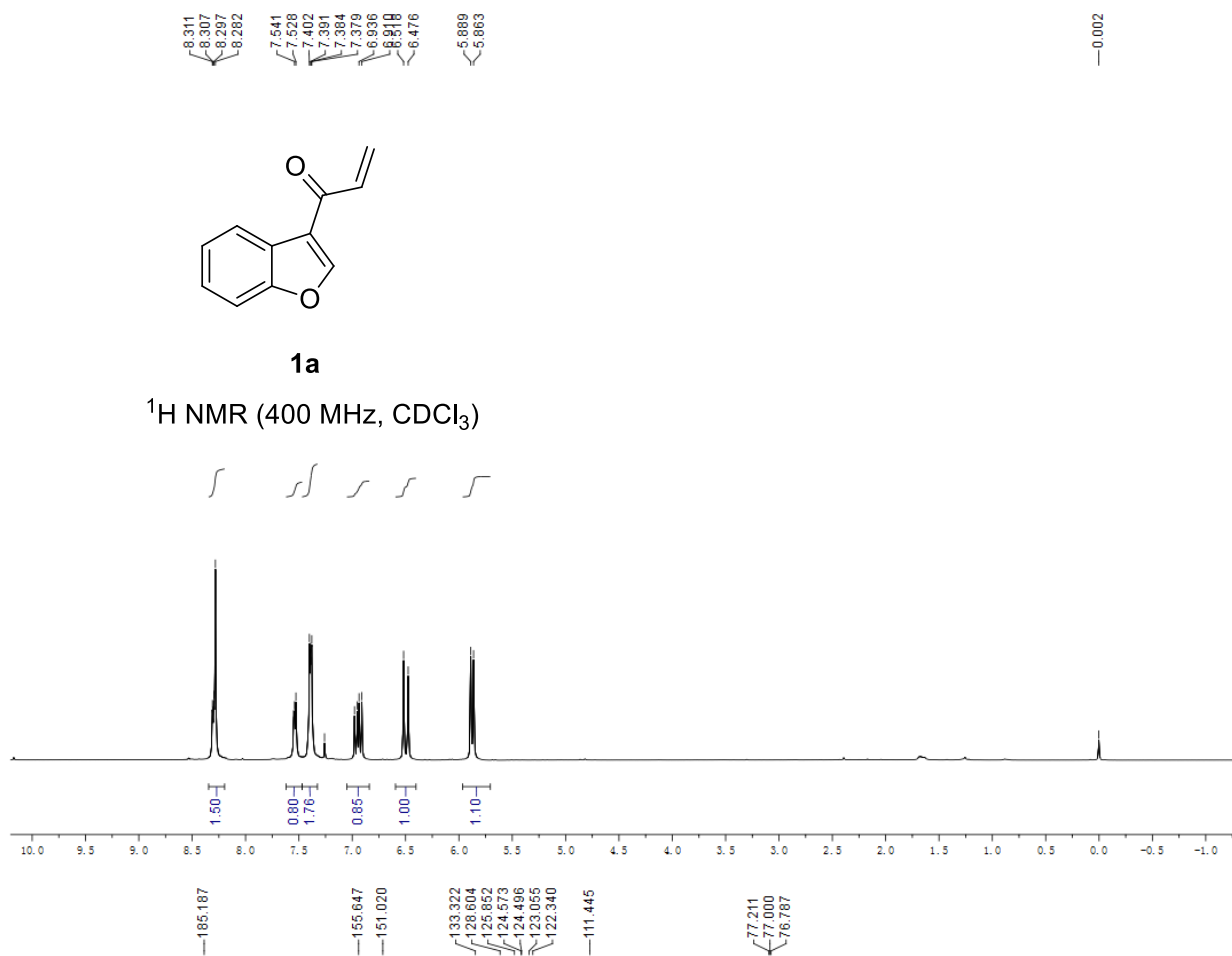
Identification code	3s
Empirical formula	C ₂₅ H ₂₃ FN ₂ O ₅
Formula weight	450.45
Temperature/K	295.4(8)
Crystal system	tetragonal
Space group	P4 ₁ 2 ₁ 2
a/Å	18.2786(4)
b/Å	18.2786(4)
c/Å	13.4615(4)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	4497.6(2)
Z	8
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.330
μ/mm^{-1}	0.823
F(000)	1888.0

Crystal size/mm ³	0.7 × 0.3 × 0.3
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/	6.838 to 146.14
Index ranges	-22 ≤ h ≤ 19, -22 ≤ k ≤ 21, -13 ≤ l ≤ 16
Reflections collected	21241
Independent reflections	4402 [R _{int} = 0.0329, R _{sigma} = 0.0200]
Data/restraints/parameters	4402/0/310
Goodness-of-fit on F ²	1.050
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0515, wR ₂ = 0.1396
Final R indexes [all data]	R ₁ = 0.0562, wR ₂ = 0.1457
Largest diff. peak/hole / e Å ⁻³	0.17/-0.20
Flack parameter	0.04(9)

Based on the absolute configuration of **3s**, a plausible catalytic transition state was proposed, as outlined in the following scheme.



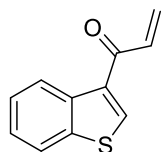
9. NMR spectra and HPLC chromatograms



δ 8.771
 δ 8.751
 δ 8.303
 δ 7.894
 δ 7.874
 δ 7.514
 δ 7.496
 δ 7.462
 δ 7.443
 δ 7.260
 δ 7.140
 δ 6.116
 δ 6.456
 δ 5.935
 δ 5.908

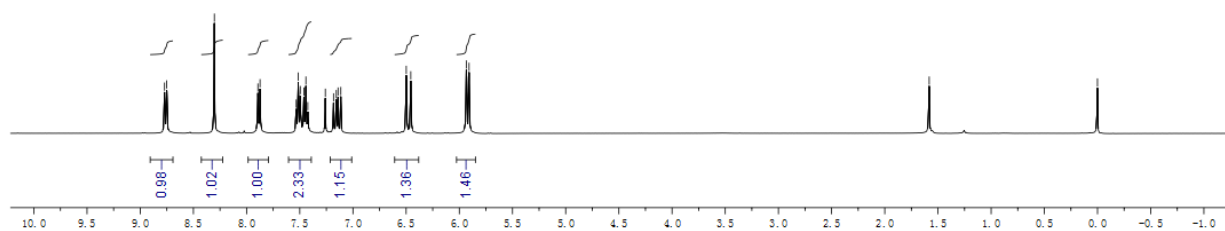
δ 1.562

δ 0.000



4d

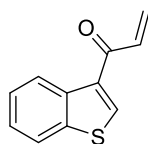
^1H NMR (400 MHz, CDCl_3)



δ 185.409

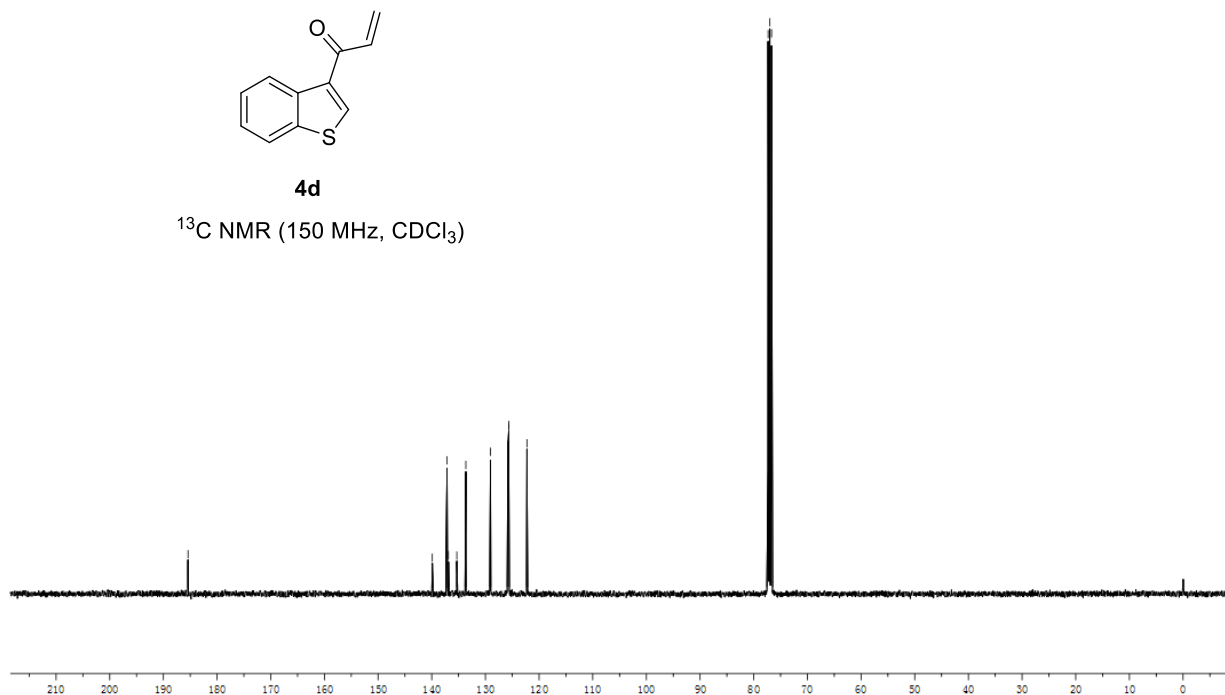
δ 139.892
 δ 137.148
 δ 136.892
 δ 135.326
 δ 133.643
 δ 129.053
 δ 125.824
 δ 125.661
 δ 125.640
 δ 122.261

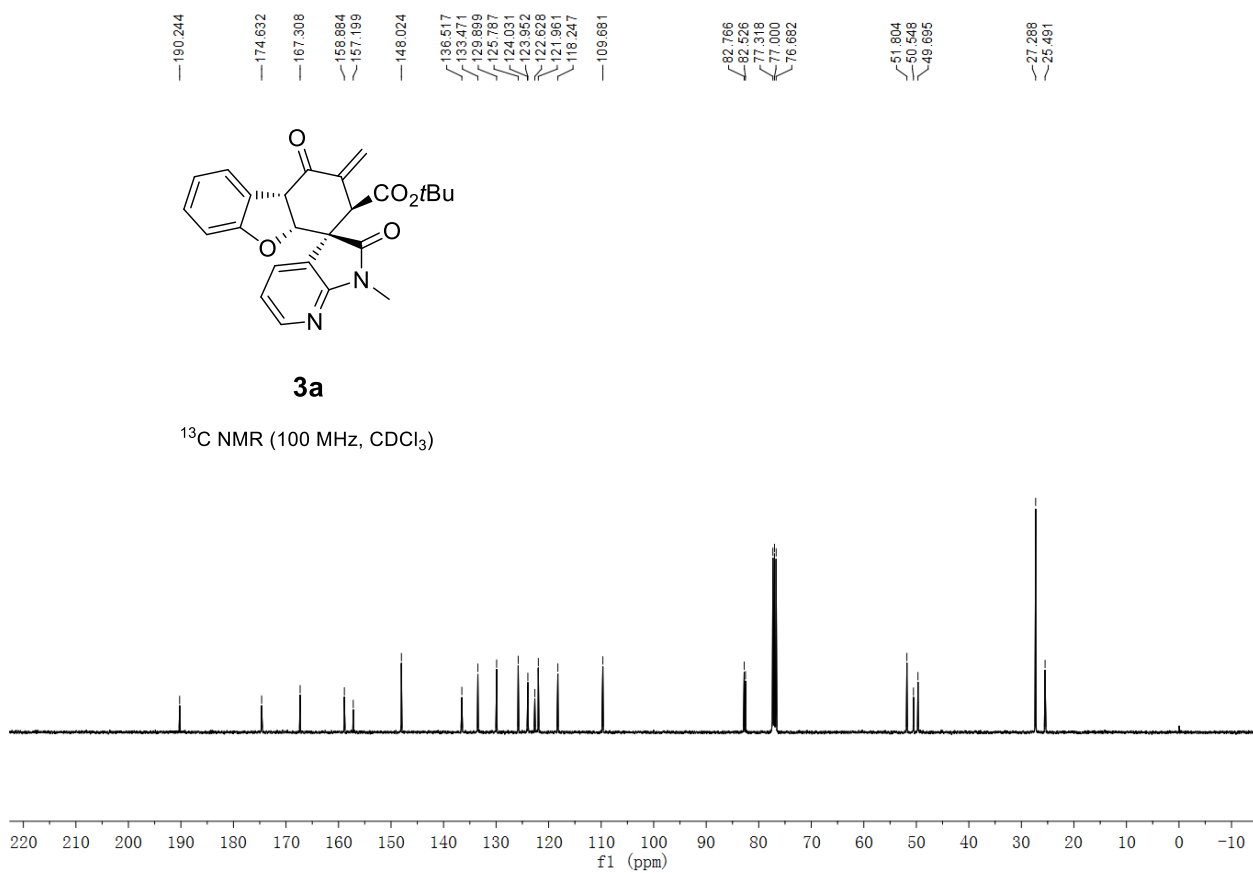
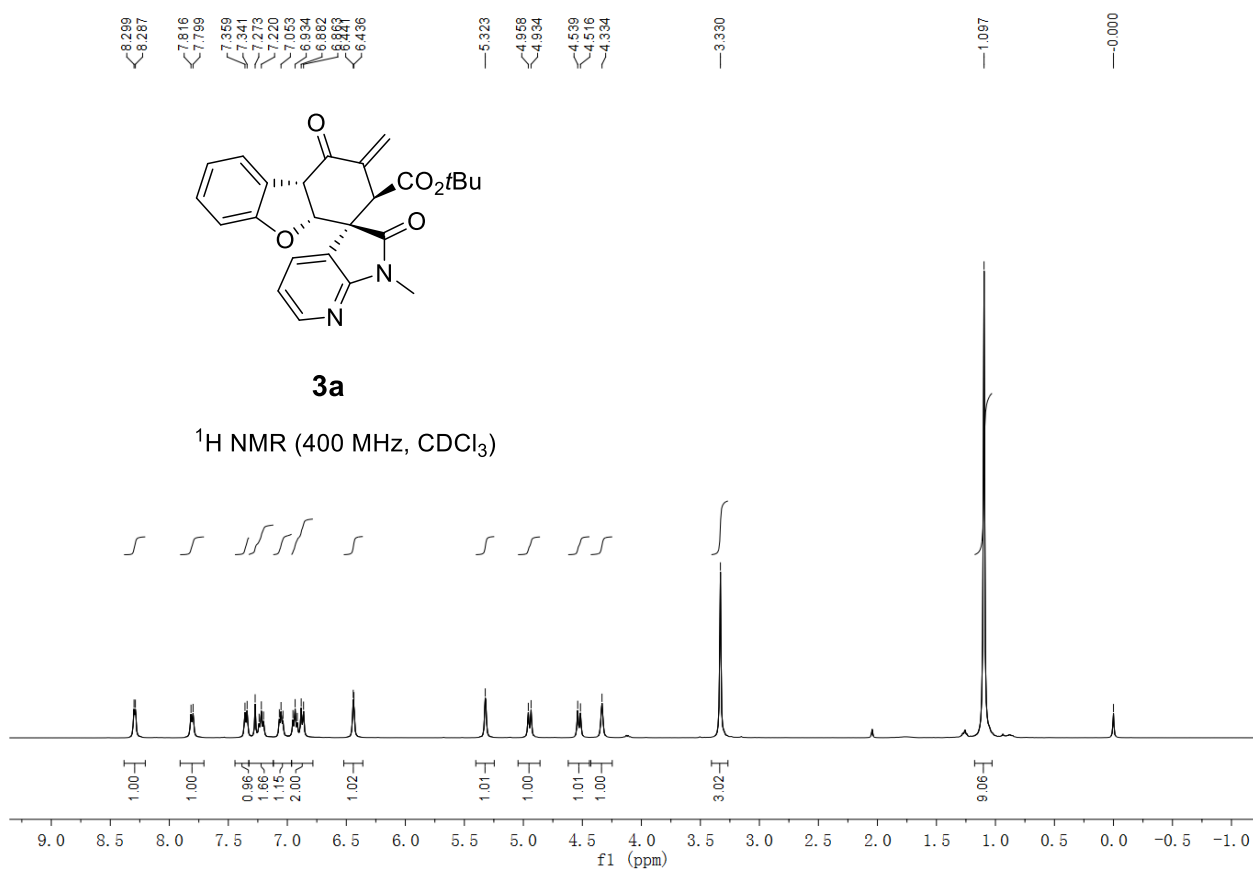
δ 77.318
 δ 77.000
 δ 76.683

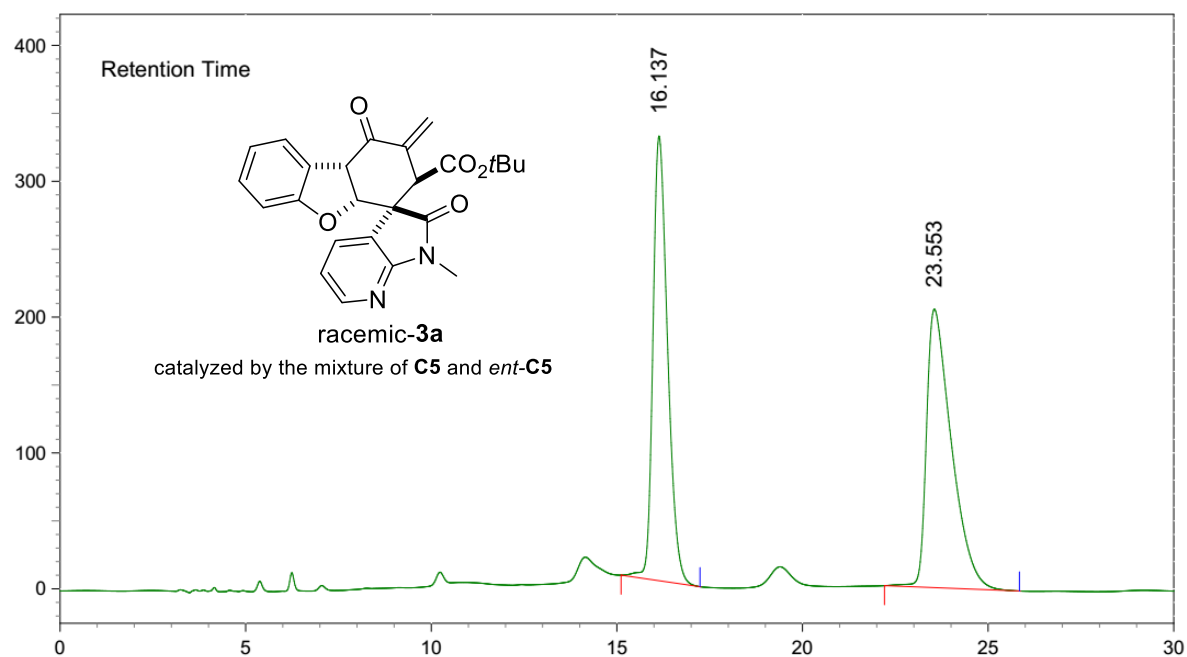


4d

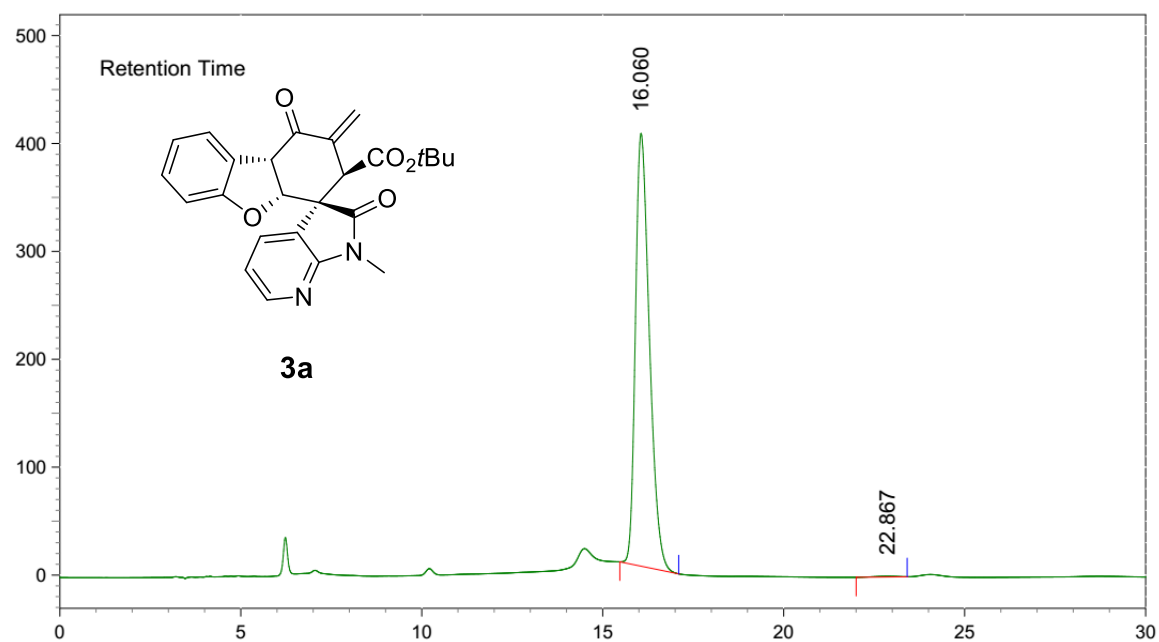
^{13}C NMR (150 MHz, CDCl_3)



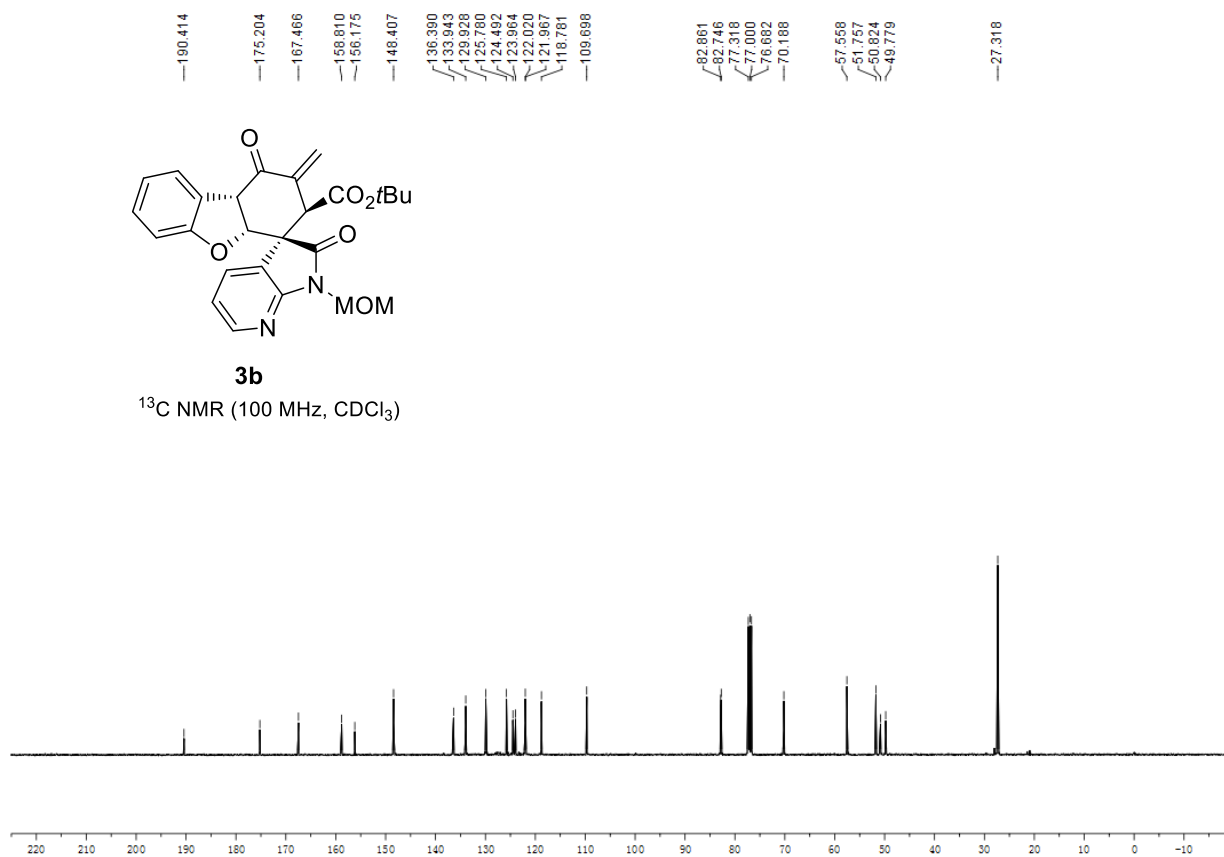
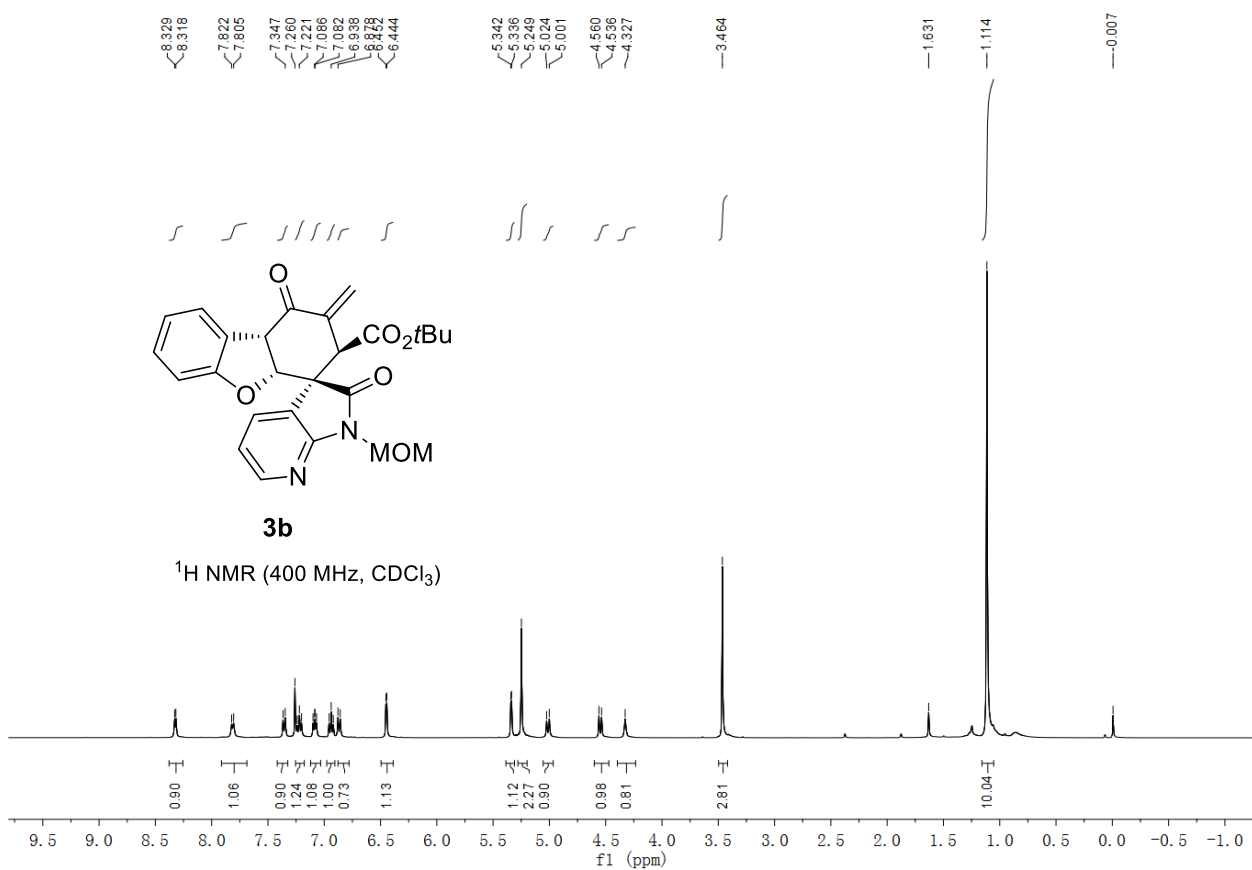


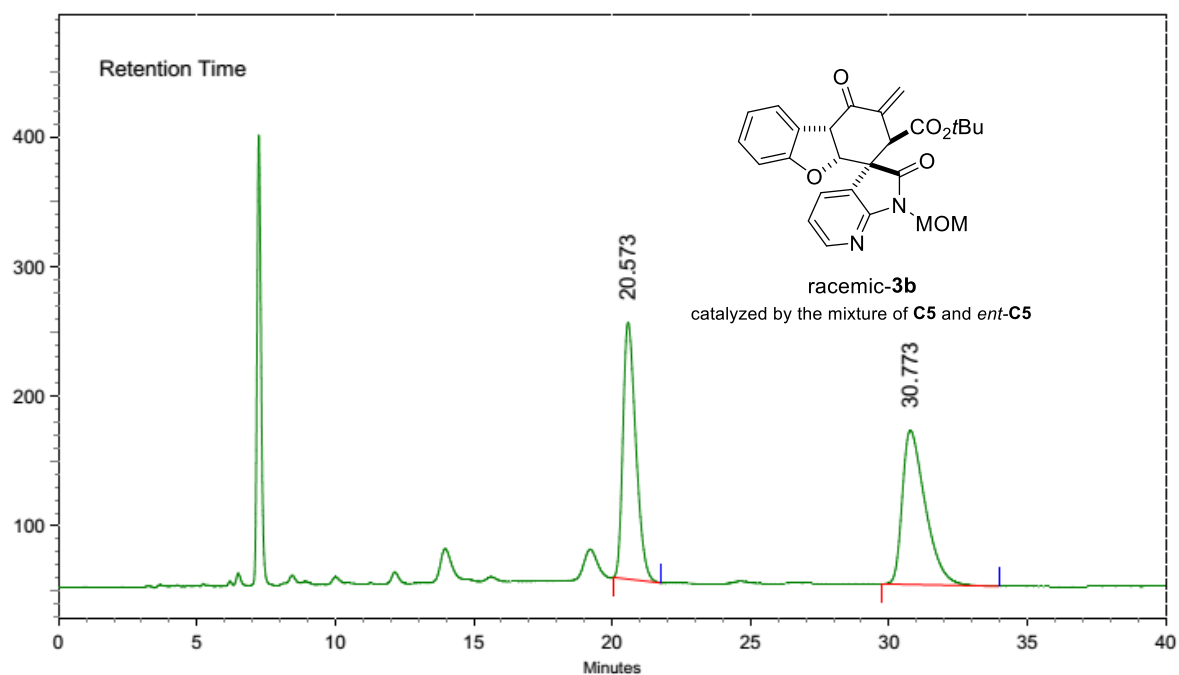


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	16.137	2.127	5491997	150769058	48.4158
2	23.553	3.637	3439401	160635514	51.5842

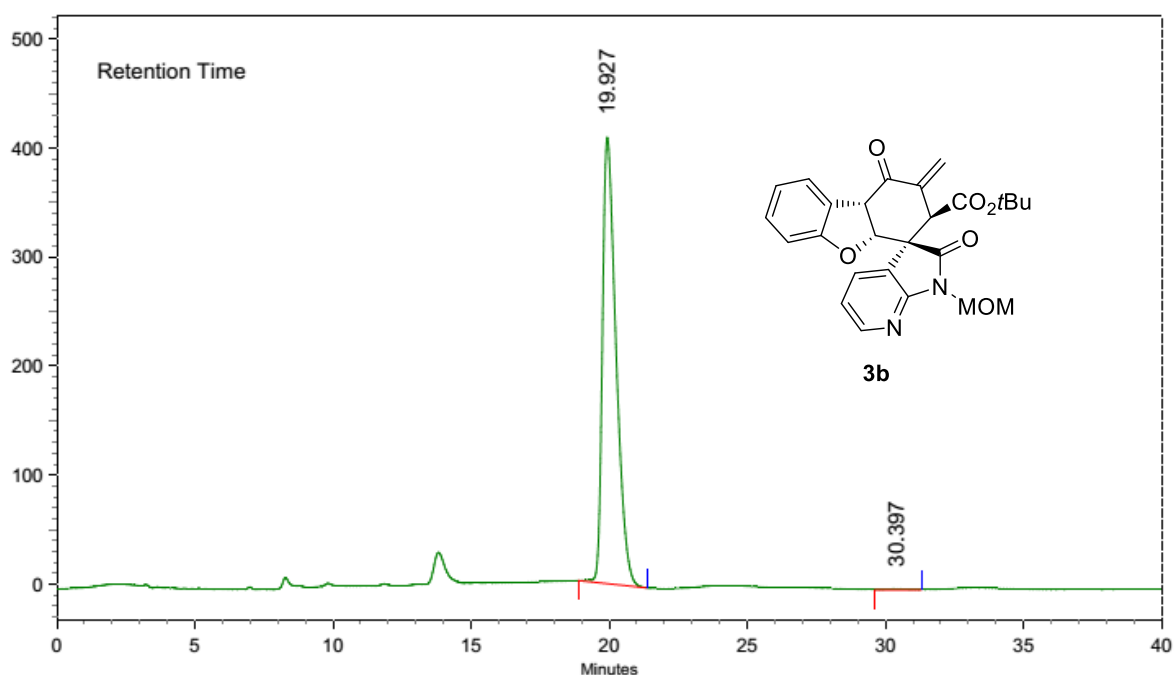


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	16.060	1.627	6729760	180707664	99.7627
2	22.867	1.407	9551	429761	0.2373

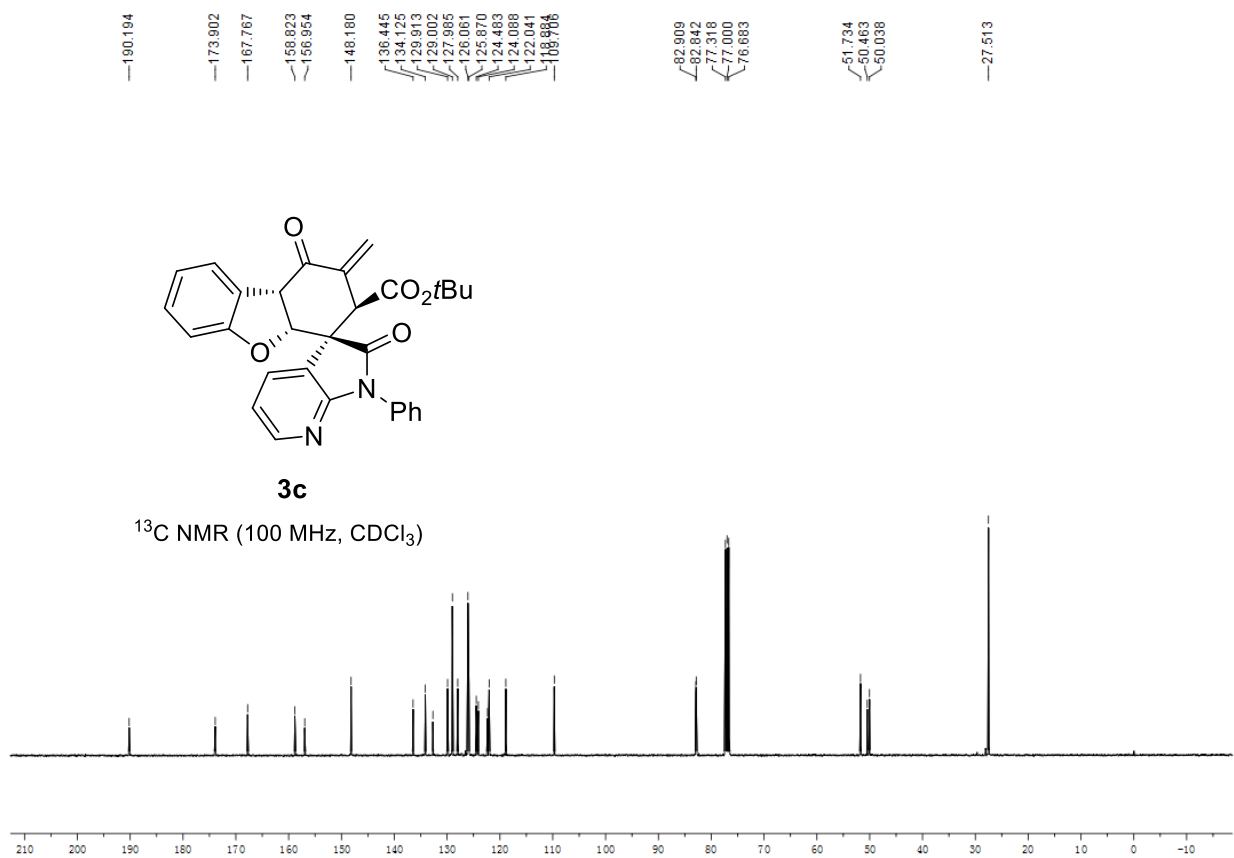
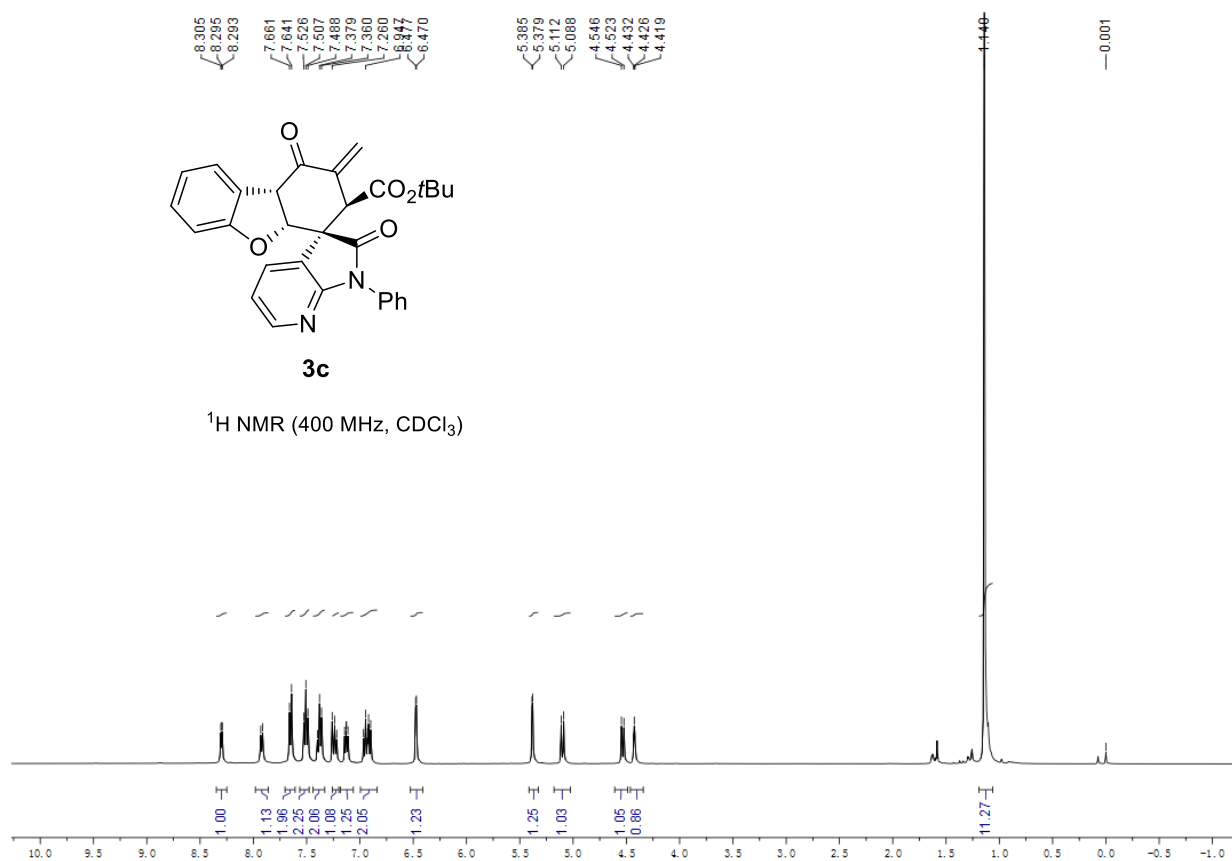


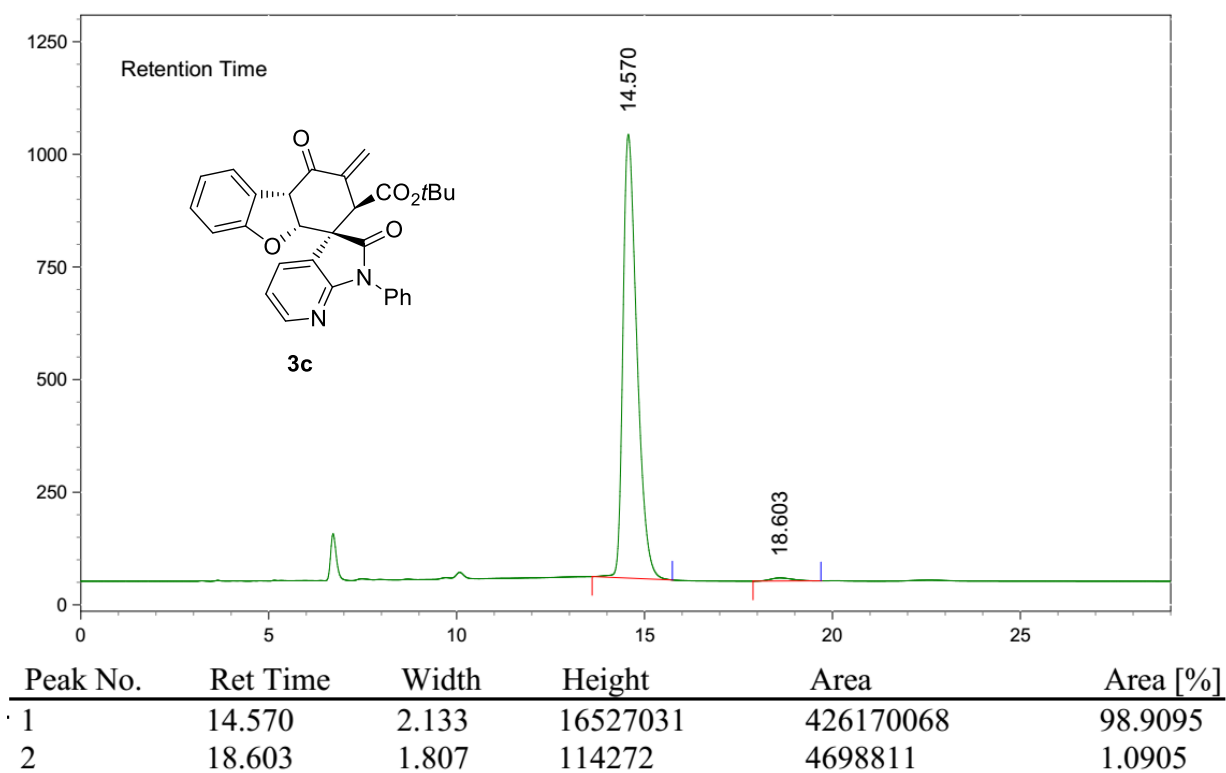
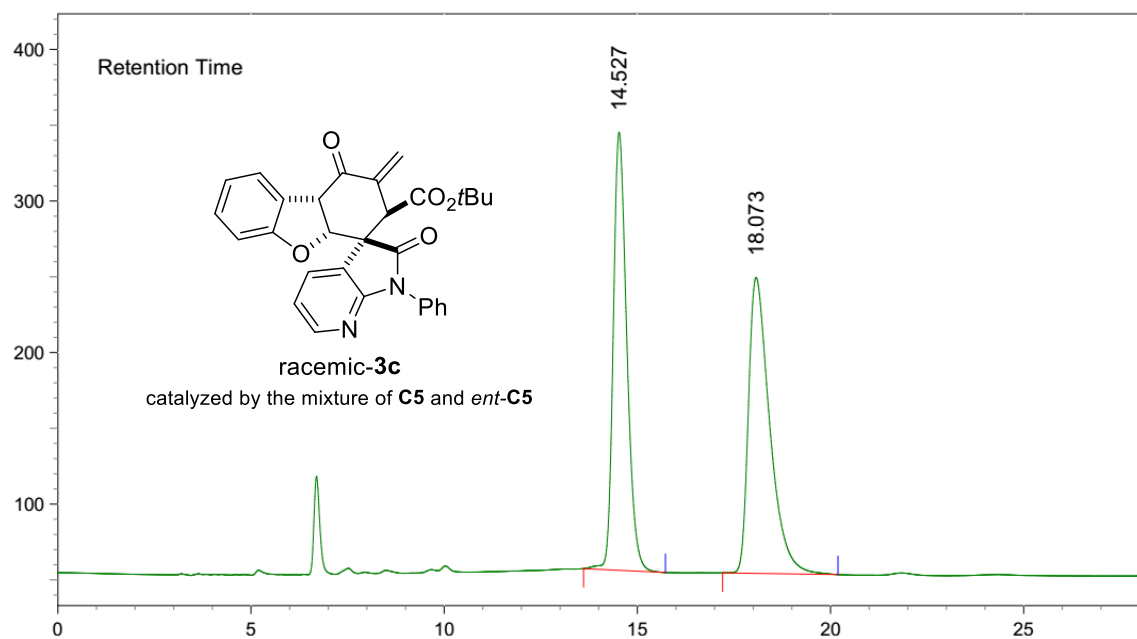


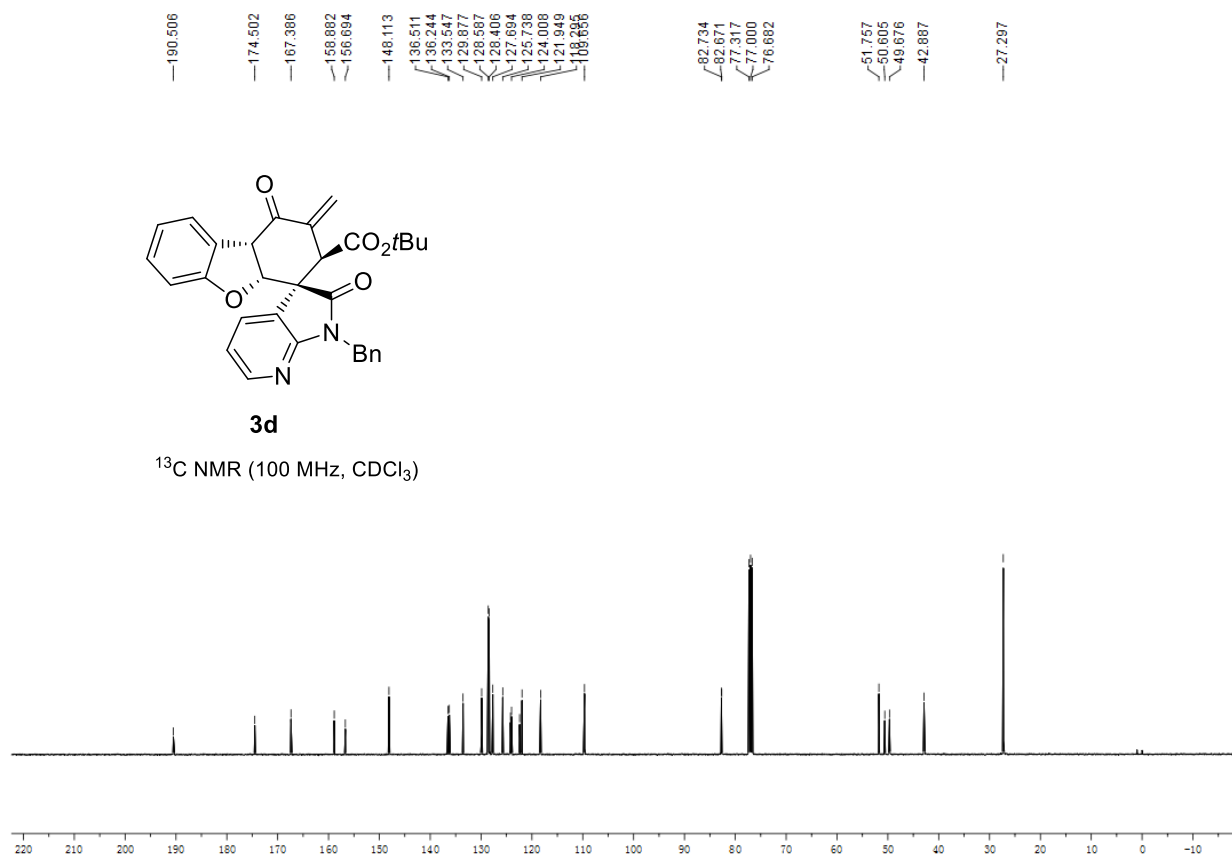
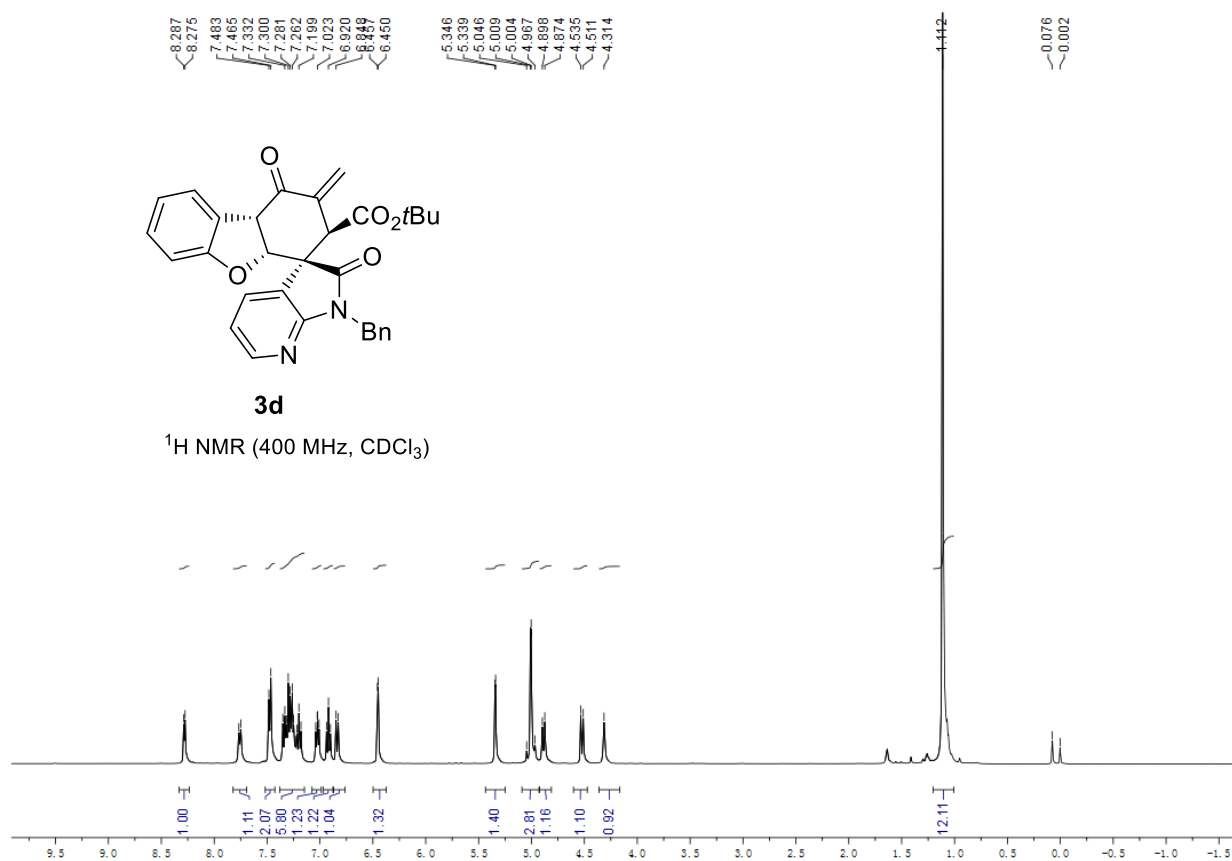
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	20.573	1.733	3321189	107507126	48.2490
2	30.773	4.257	1994639	115310098	51.7510

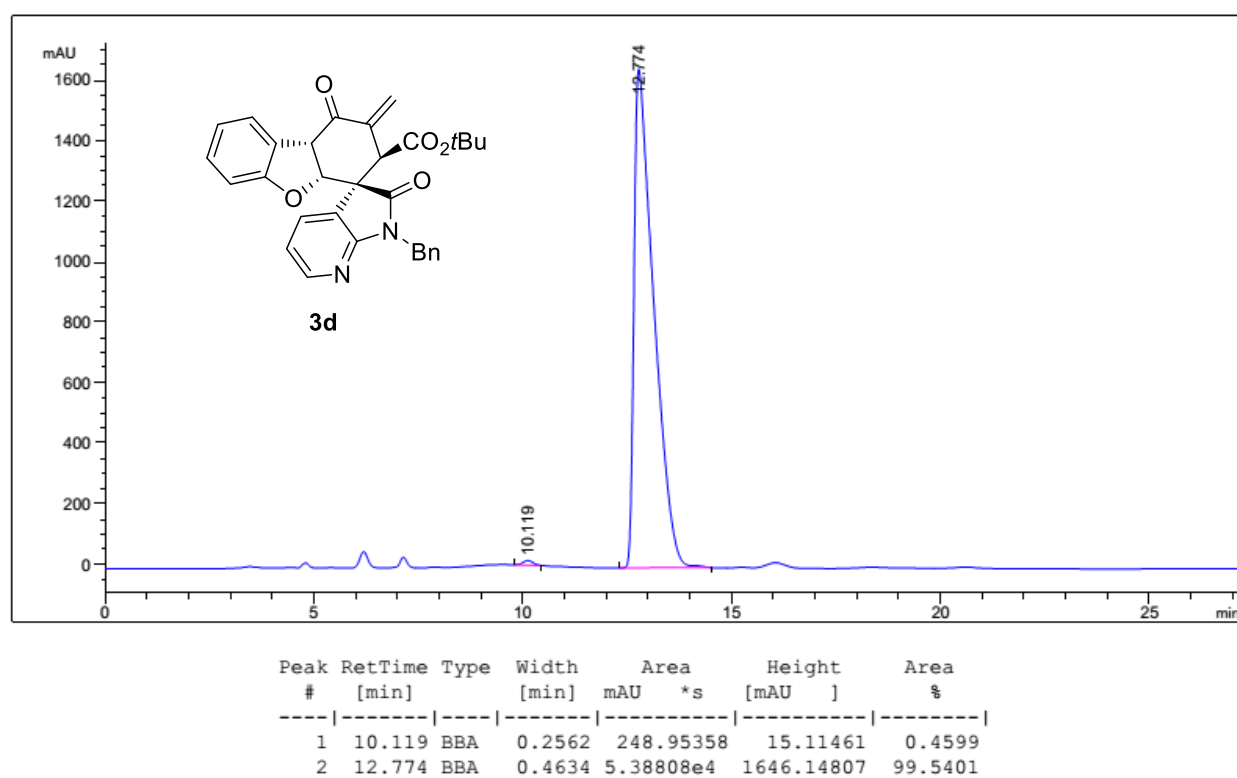
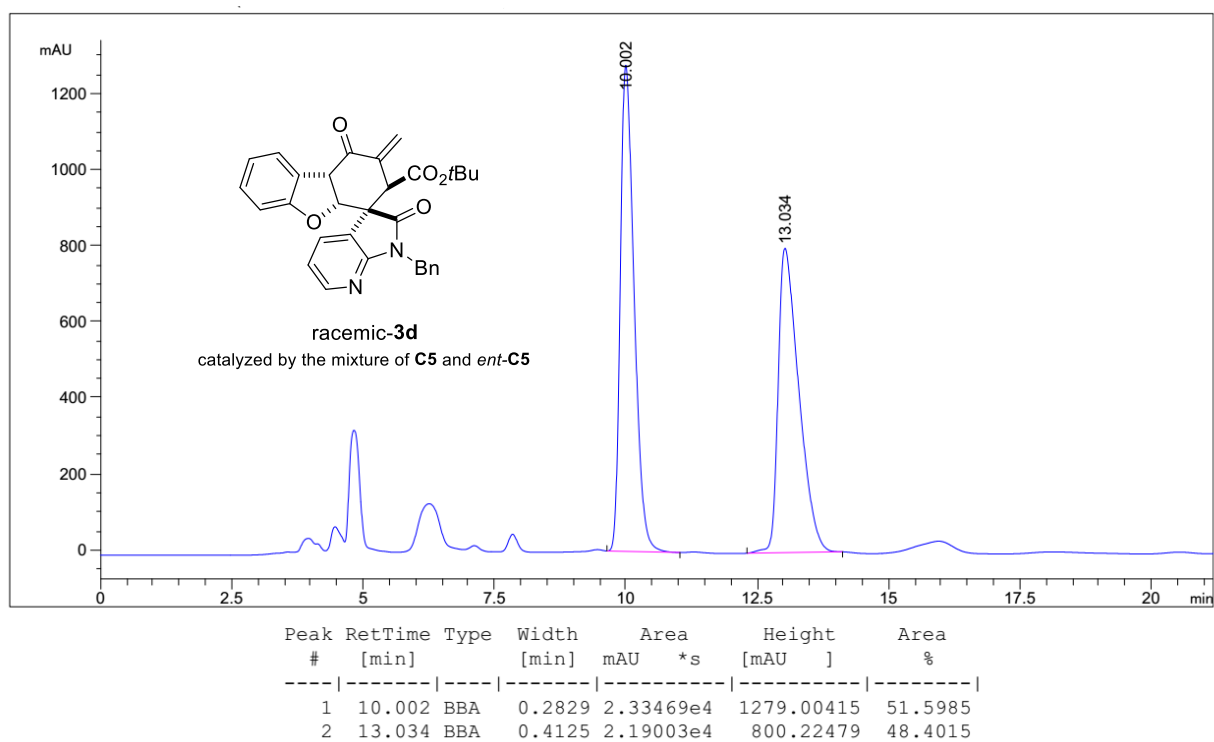


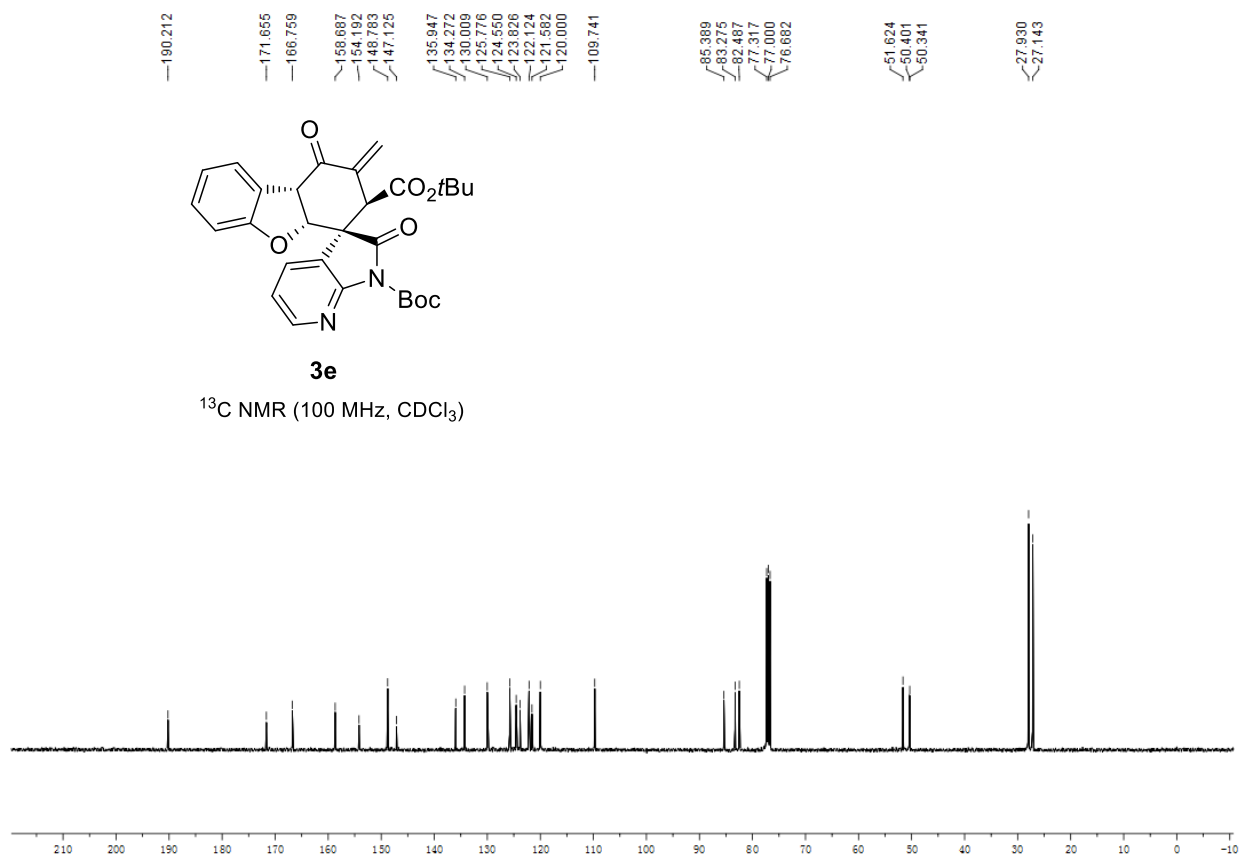
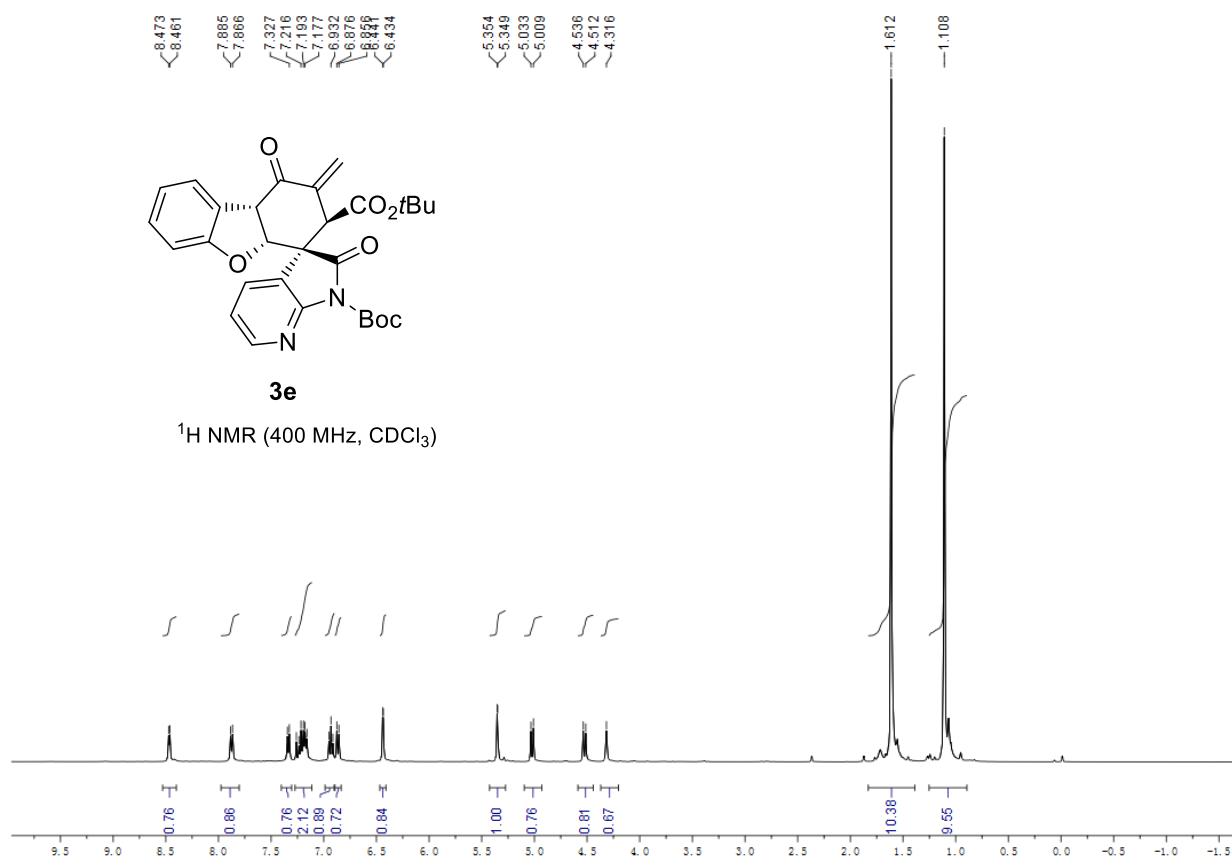
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	19.927	2.493	6868783	234108885	99.7261
2	30.397	1.680	14080	642917	0.2739

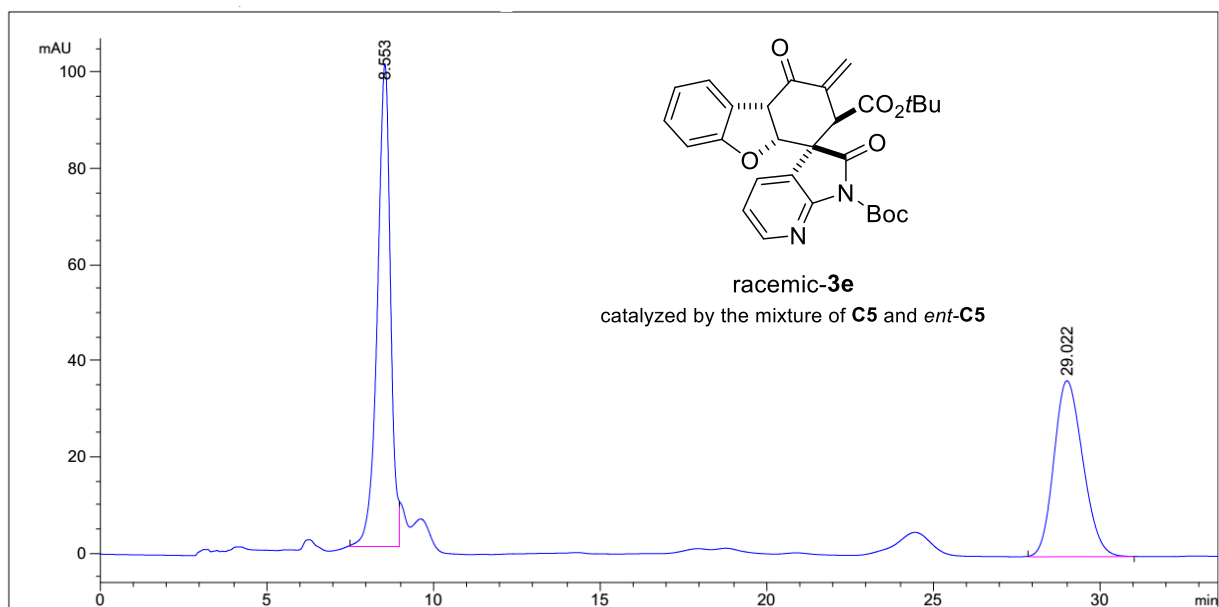




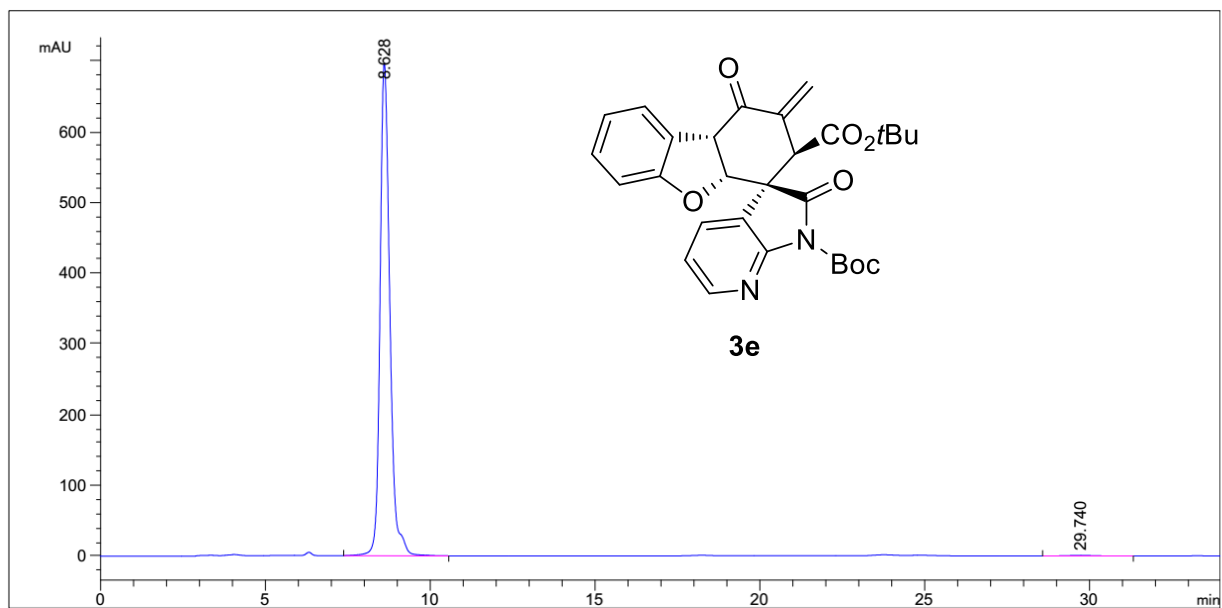




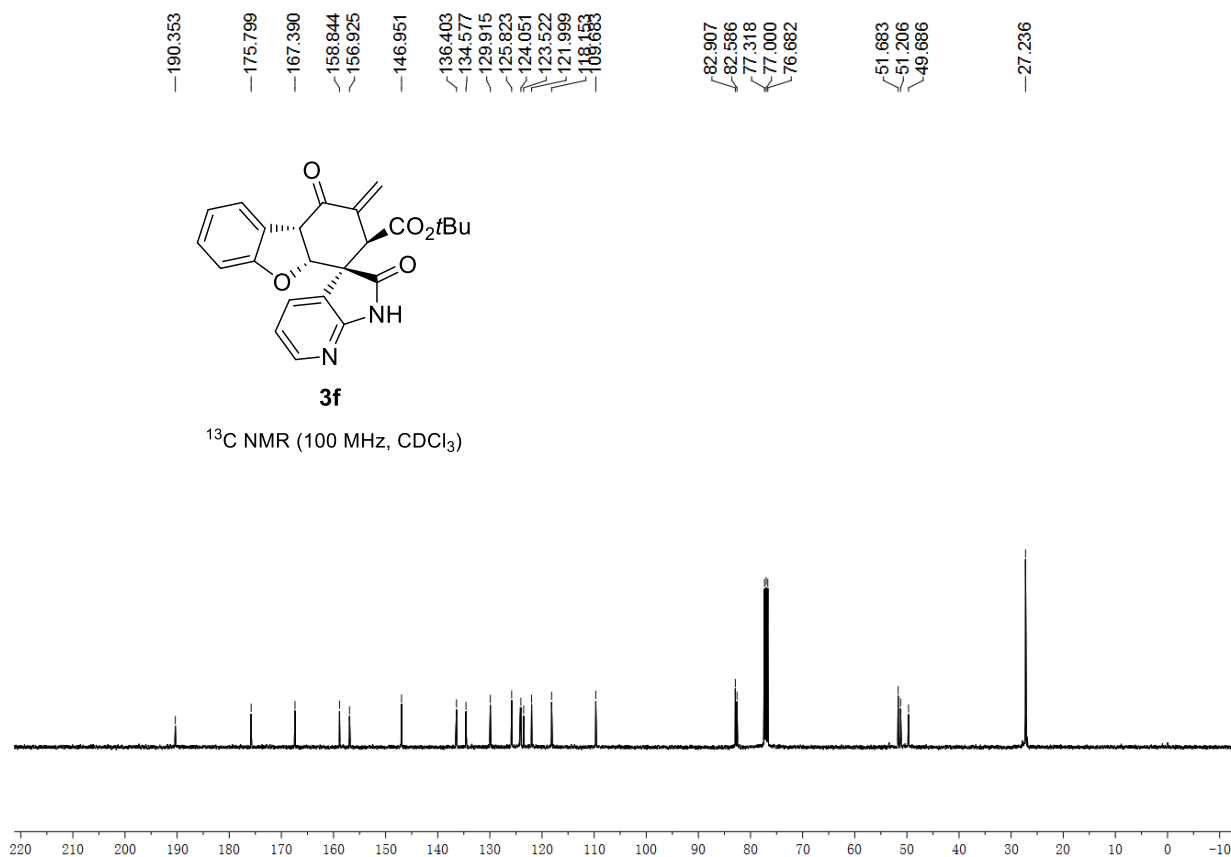
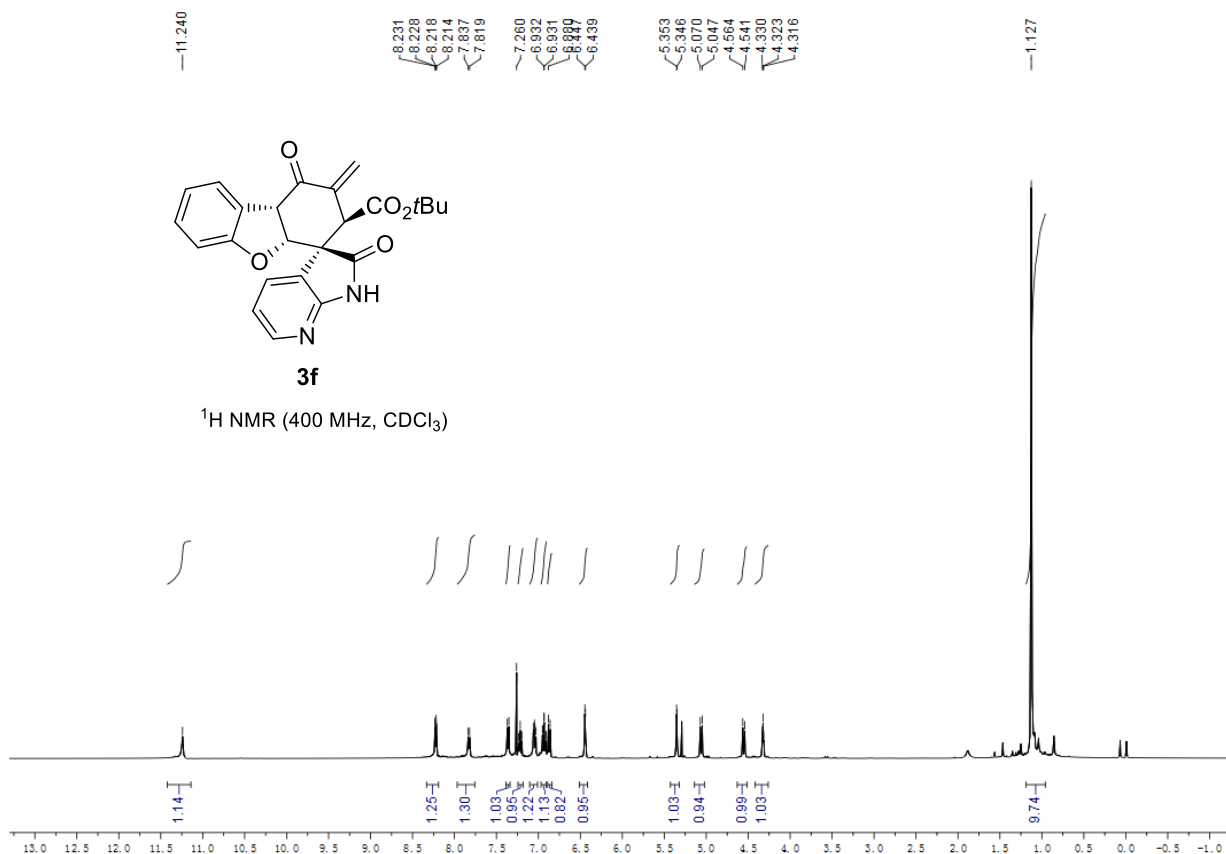


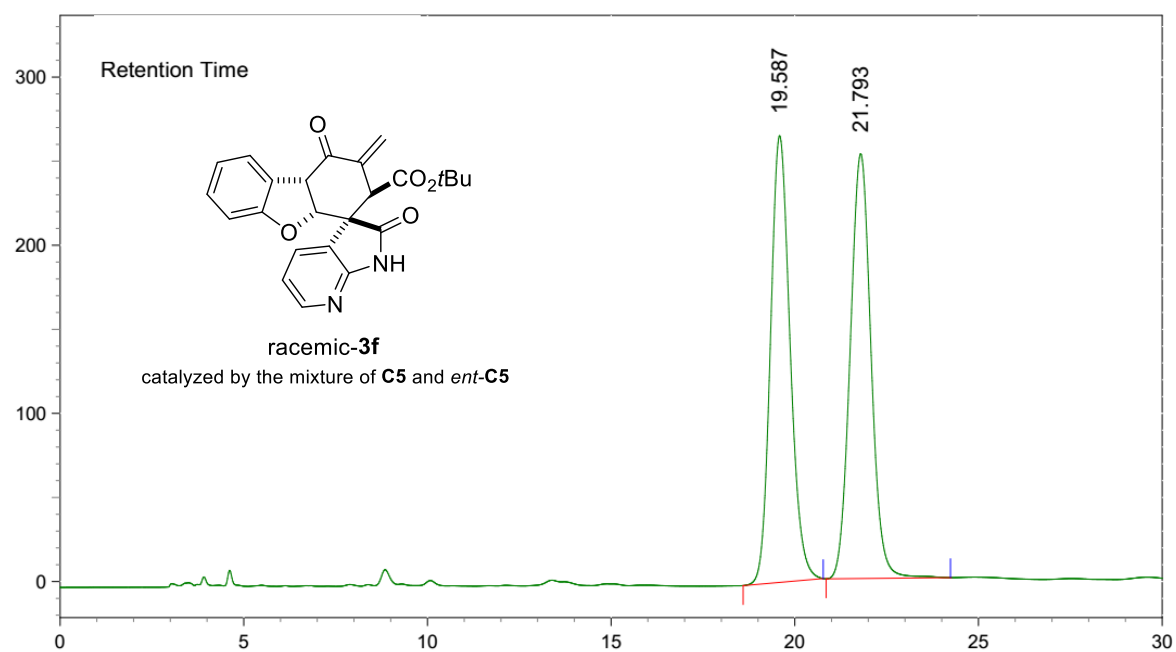


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.553	BBA	0.4117	2734.59302	100.17559	55.2888
2	29.022	BB	0.9383	2211.41943	36.57603	44.7112

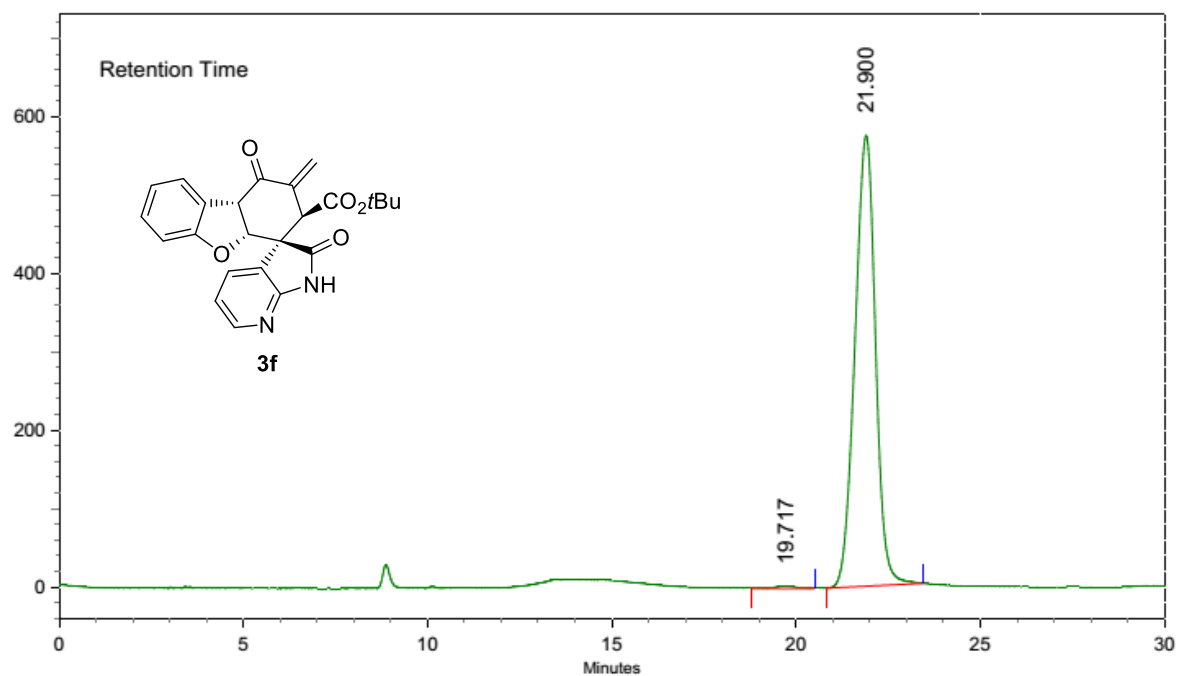


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.628	BB	0.3242	1.44110e4	692.82611	99.6692
2	29.740	BB	0.9464	47.83330	7.95184e-1	0.3308

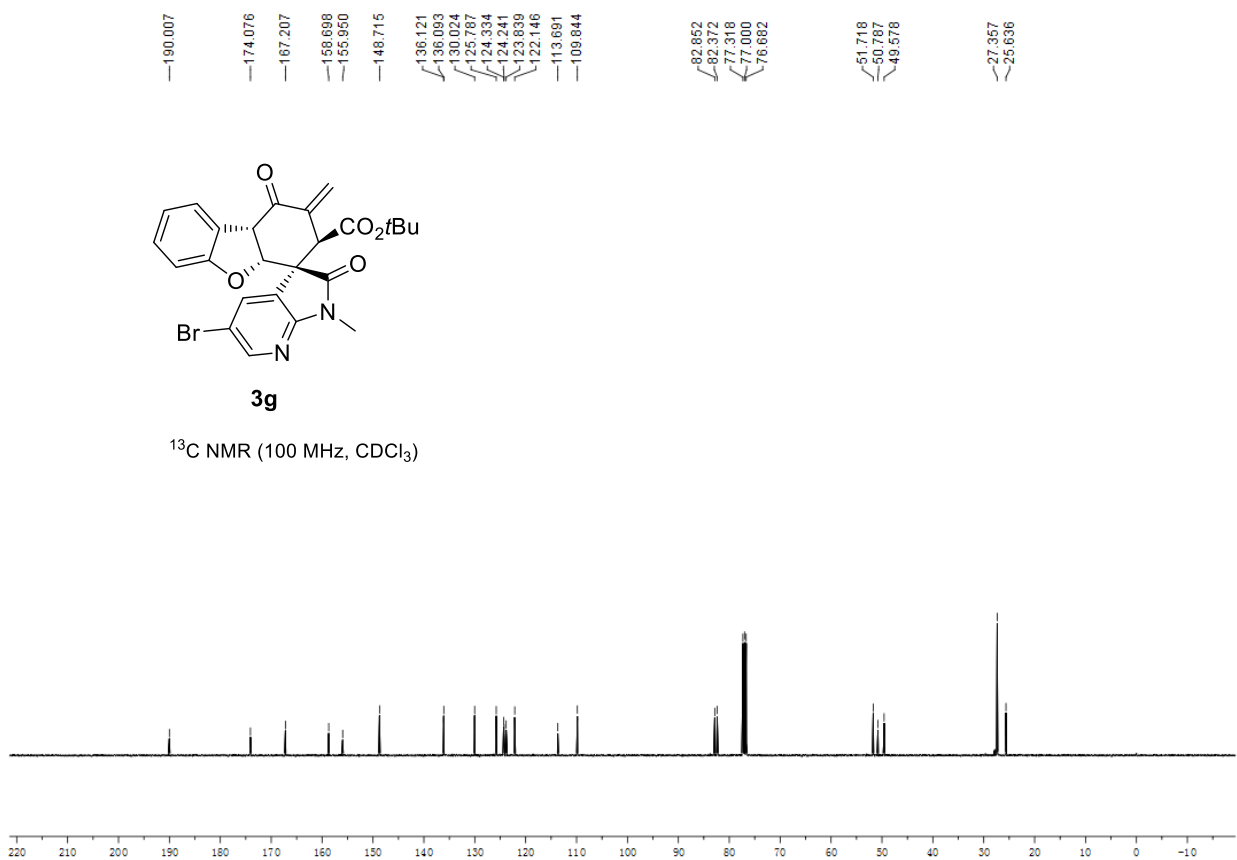
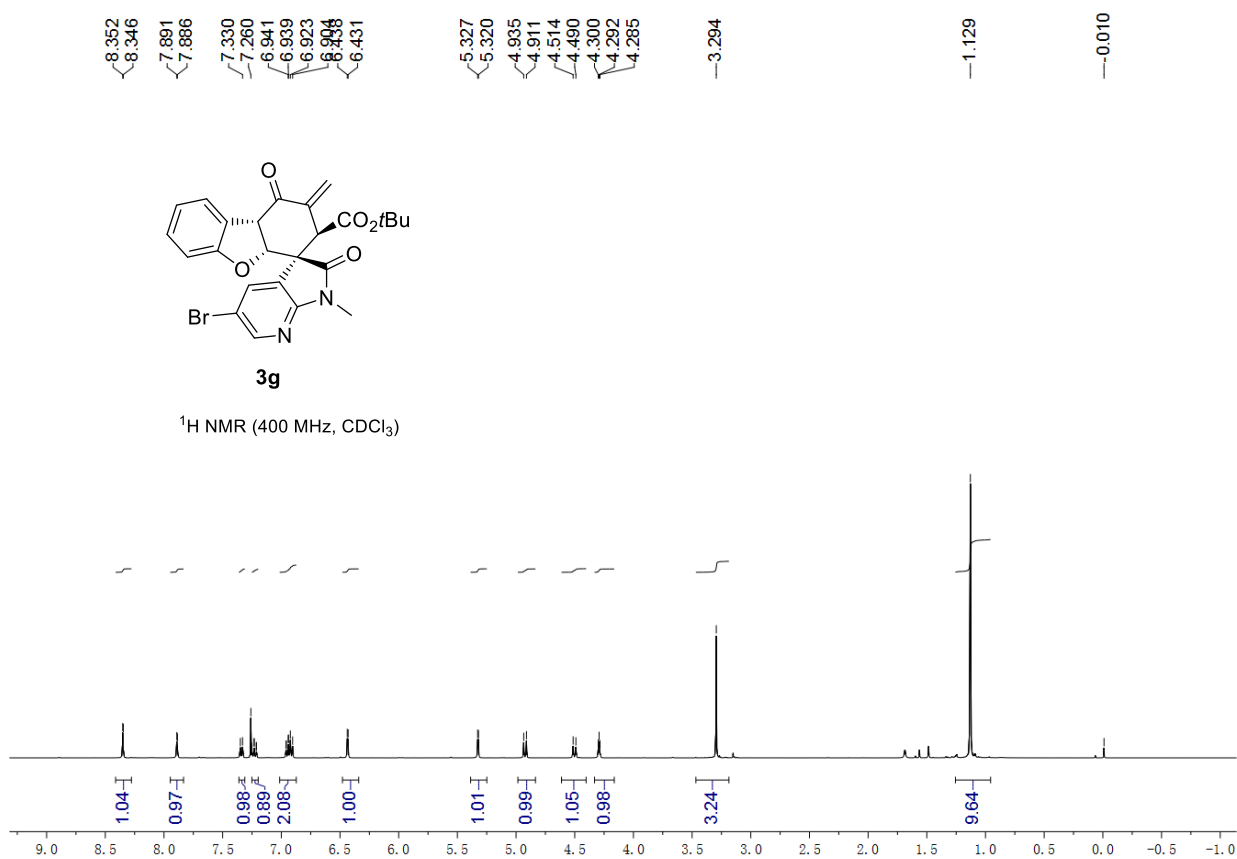


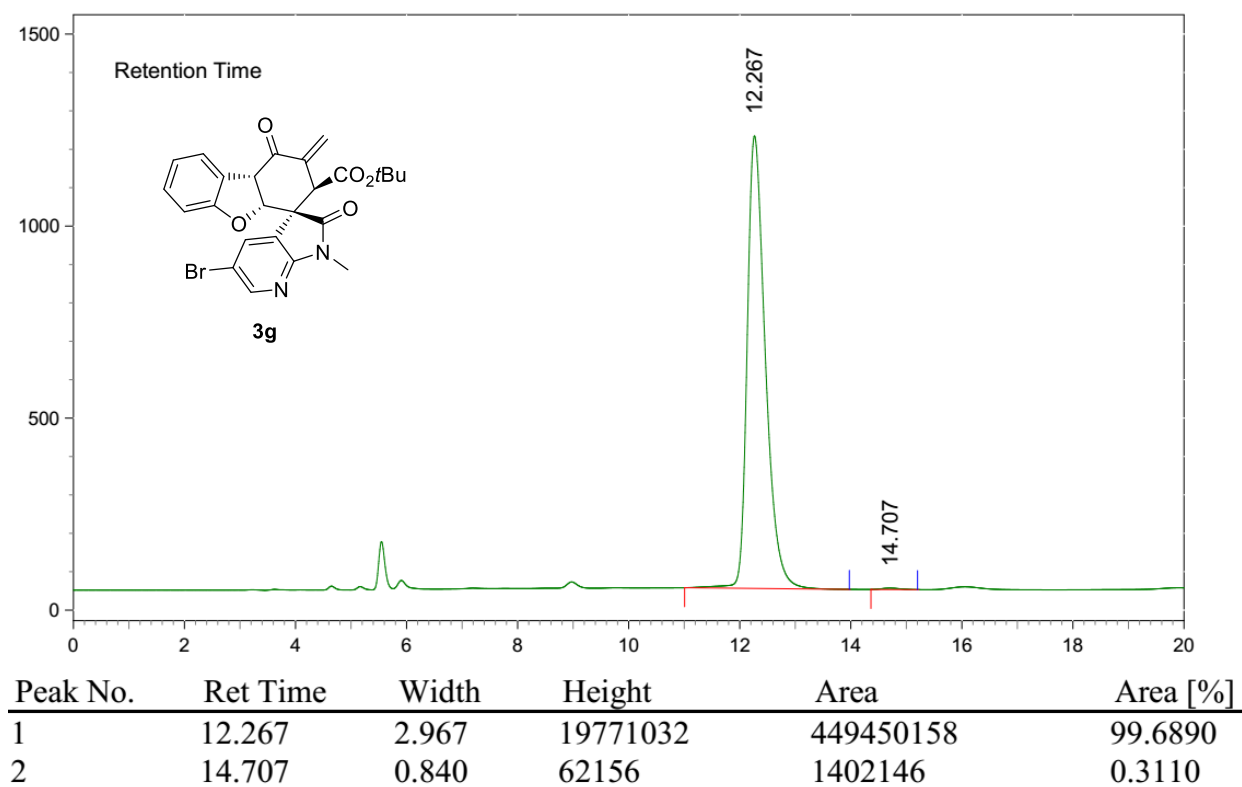
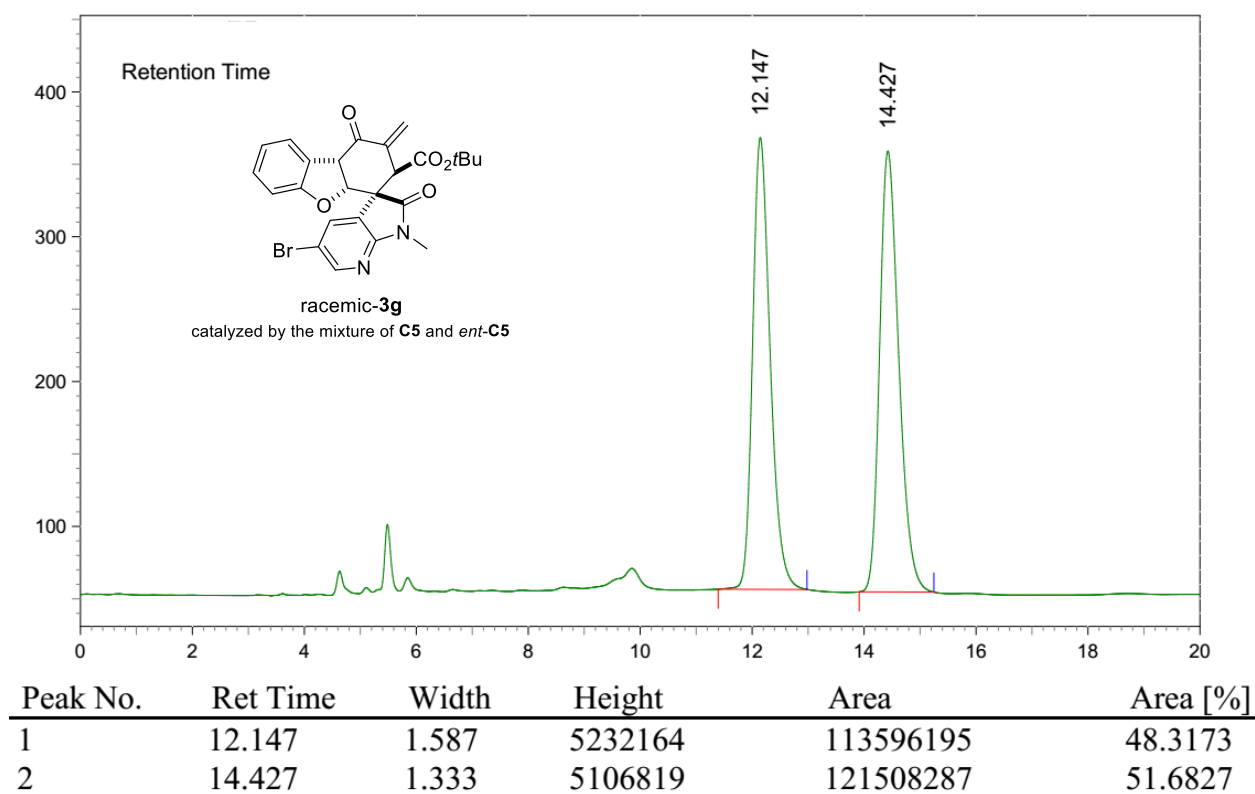


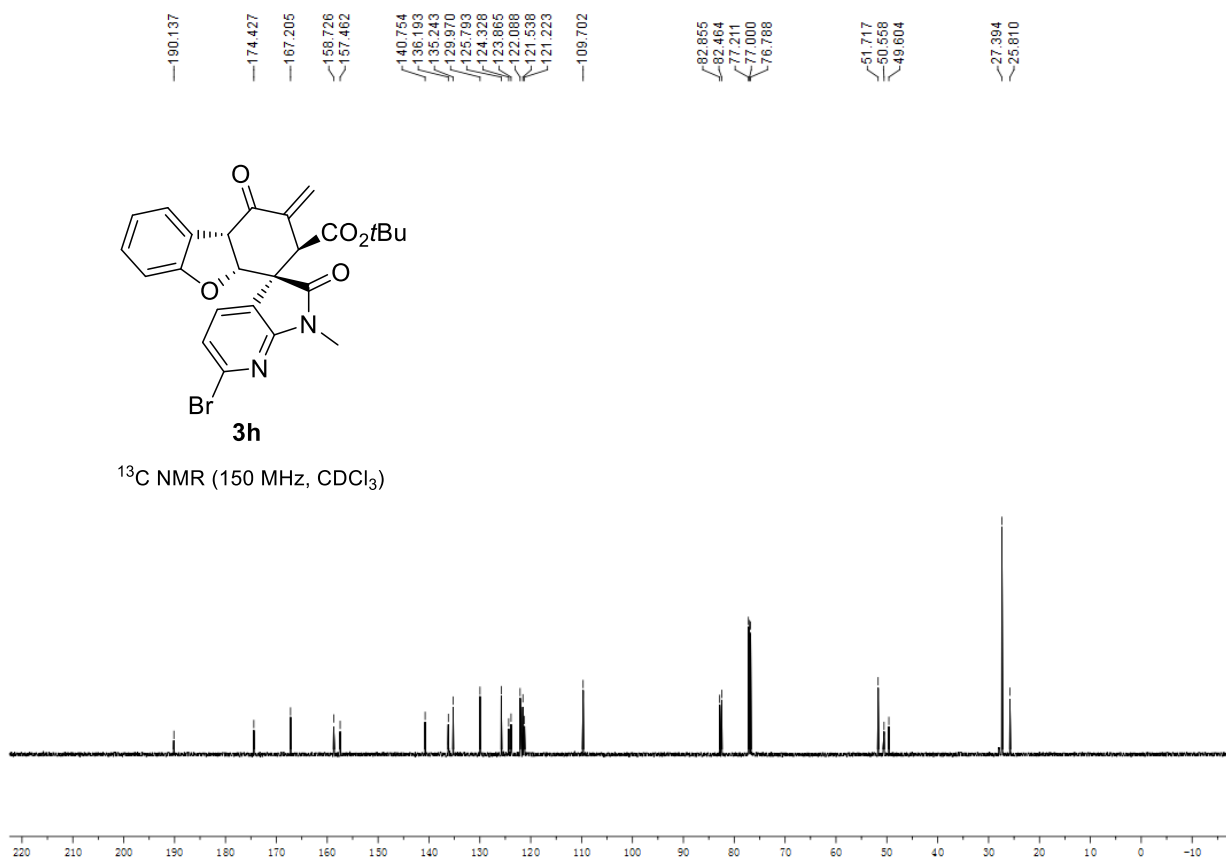
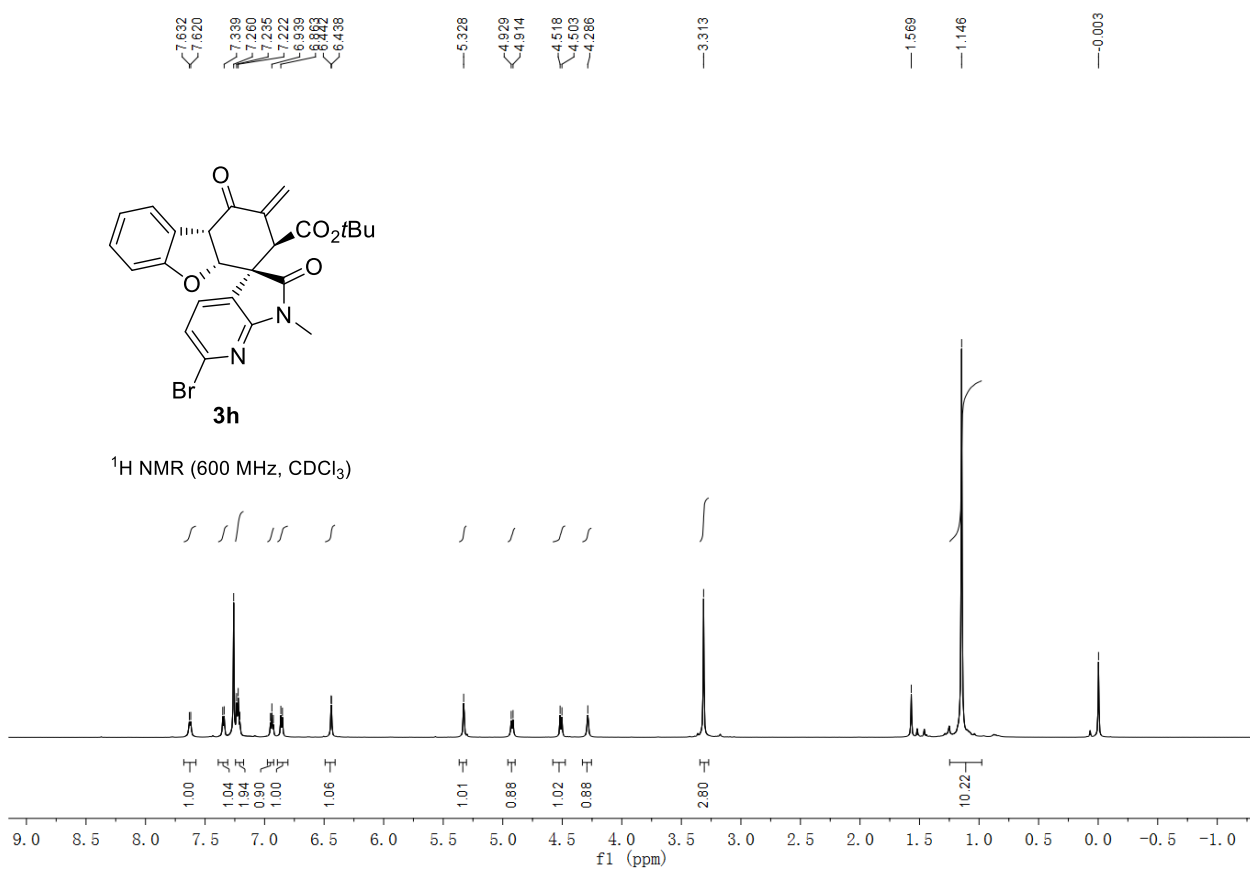
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	19.587	2.180	4456594	164768083	49.7135
2	21.793	3.383	4238102	166667052	50.2865

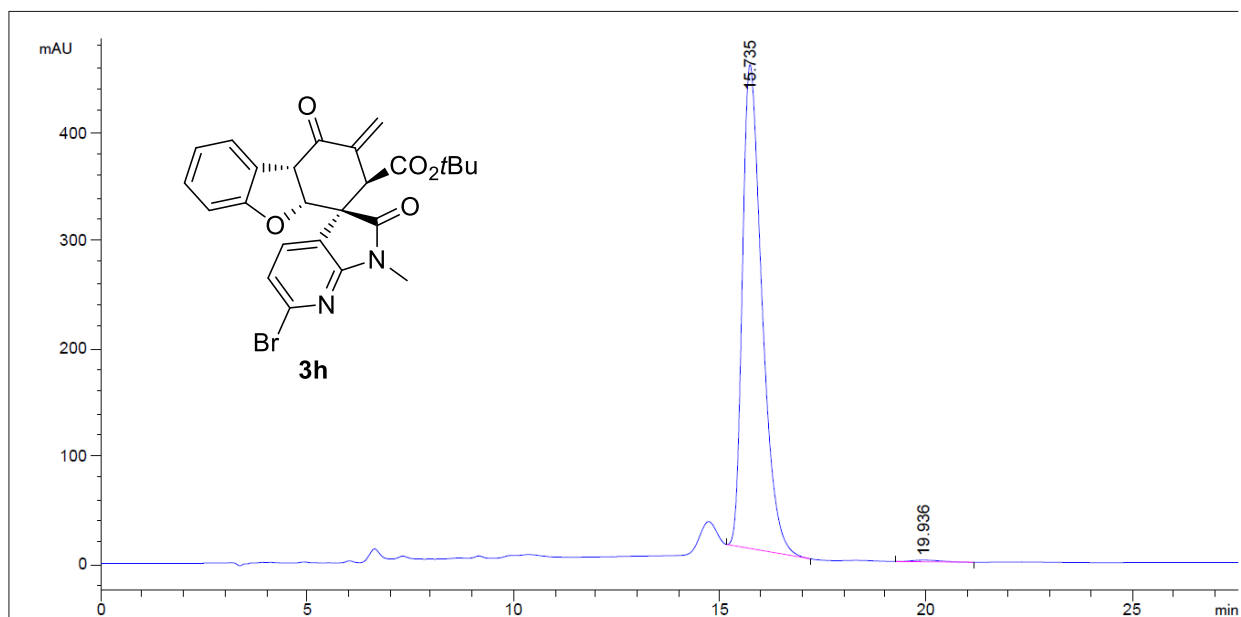
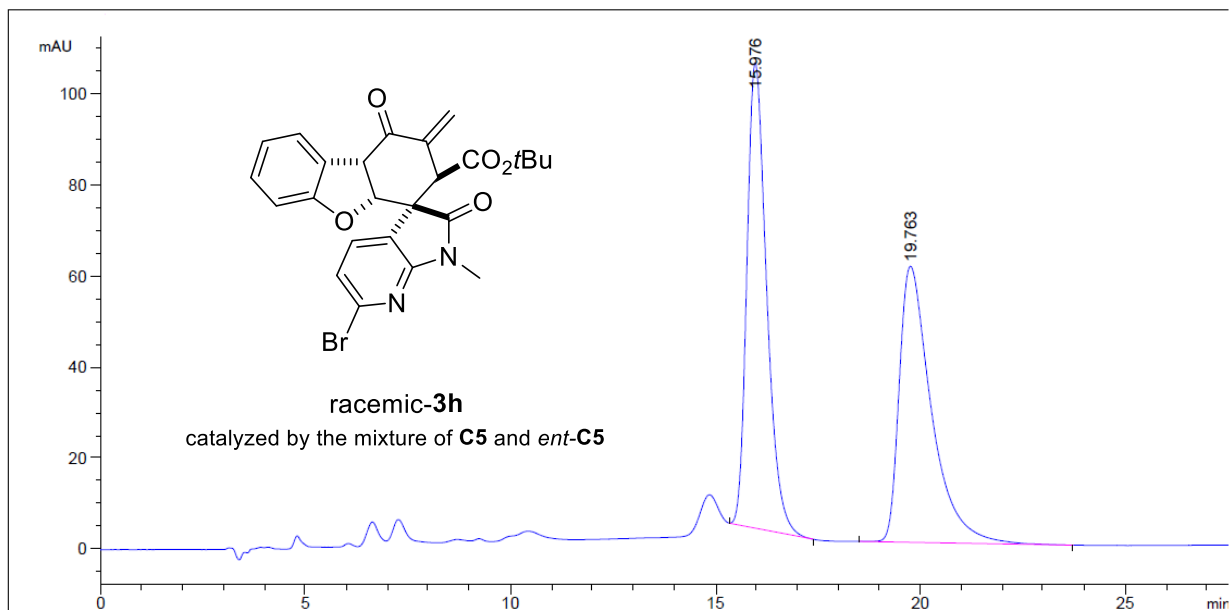


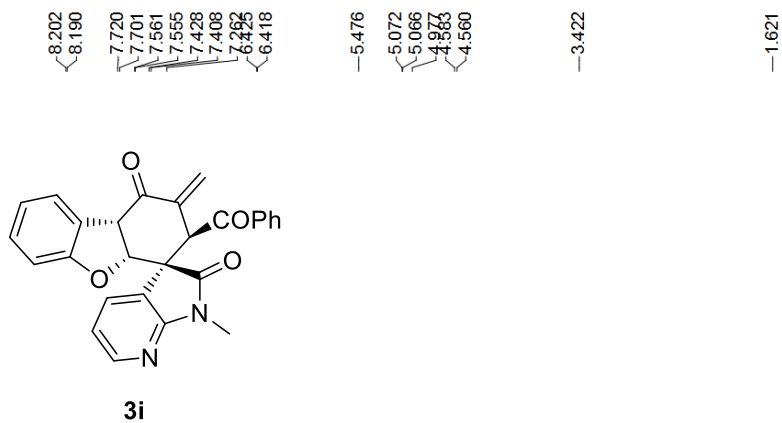
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	19.717	1.723	52223	1916363	0.5114
2	21.900	2.633	9646880	372845655	99.4886



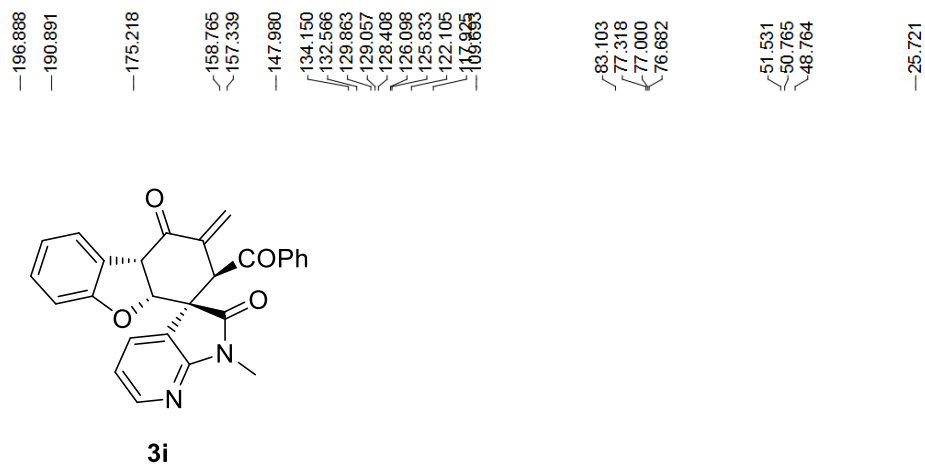
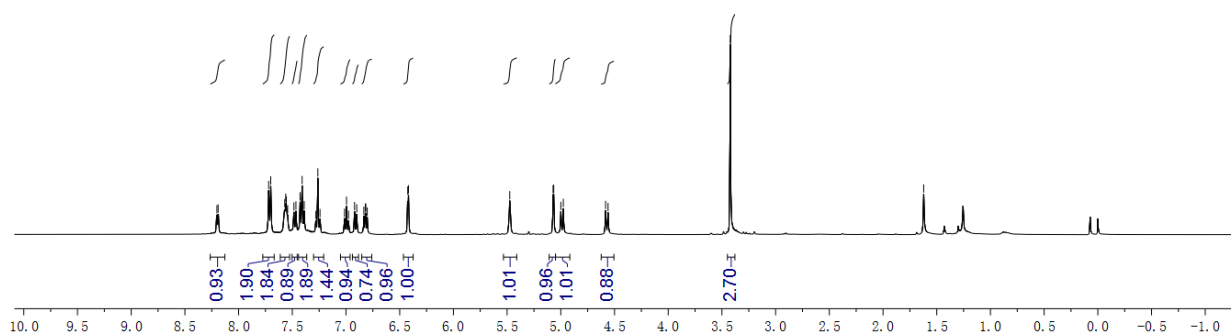




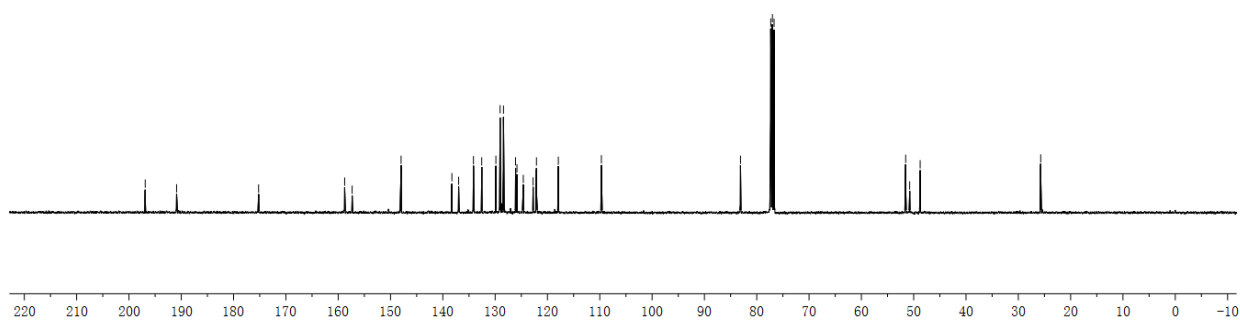


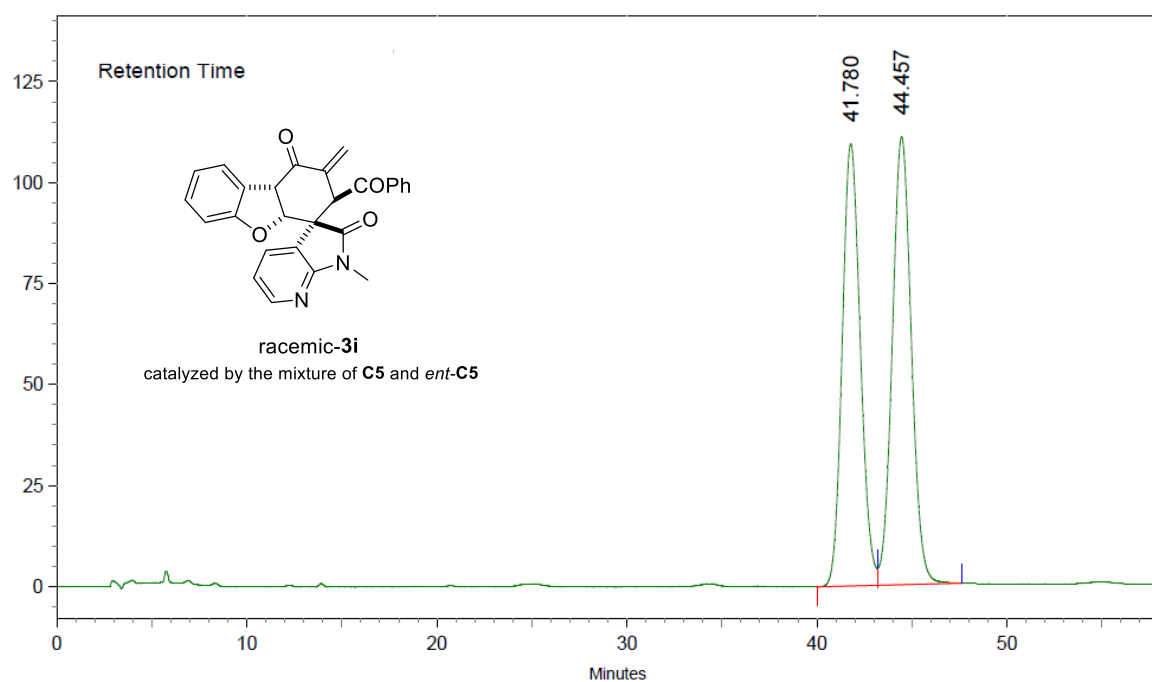


^1H NMR (400 MHz, CDCl_3)

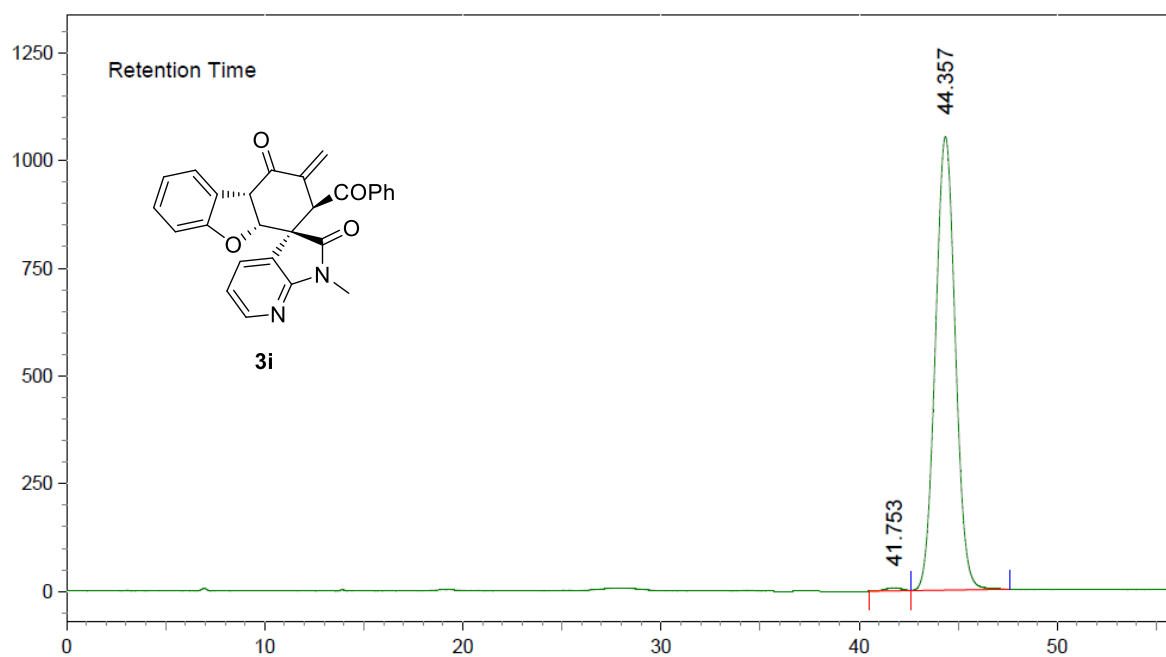


^{13}C NMR (100 MHz, CDCl_3)

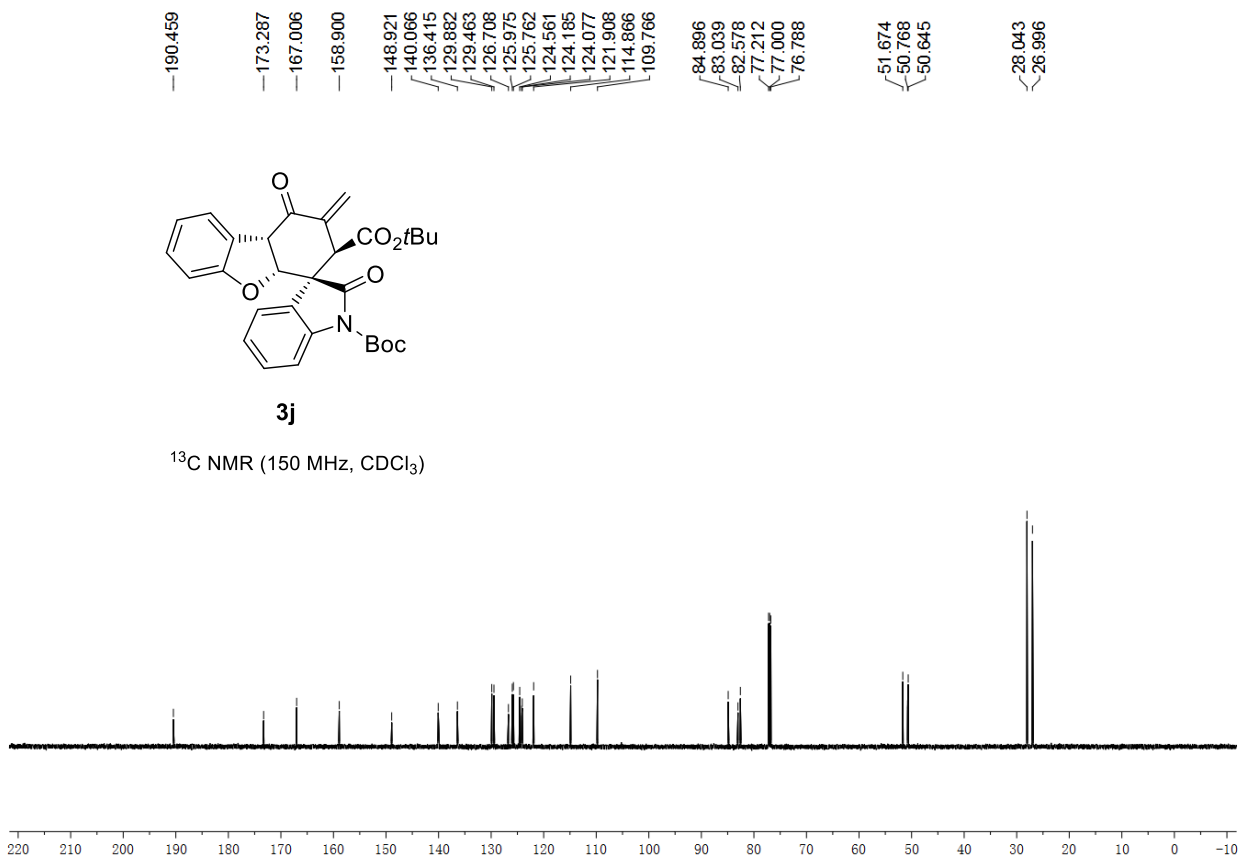
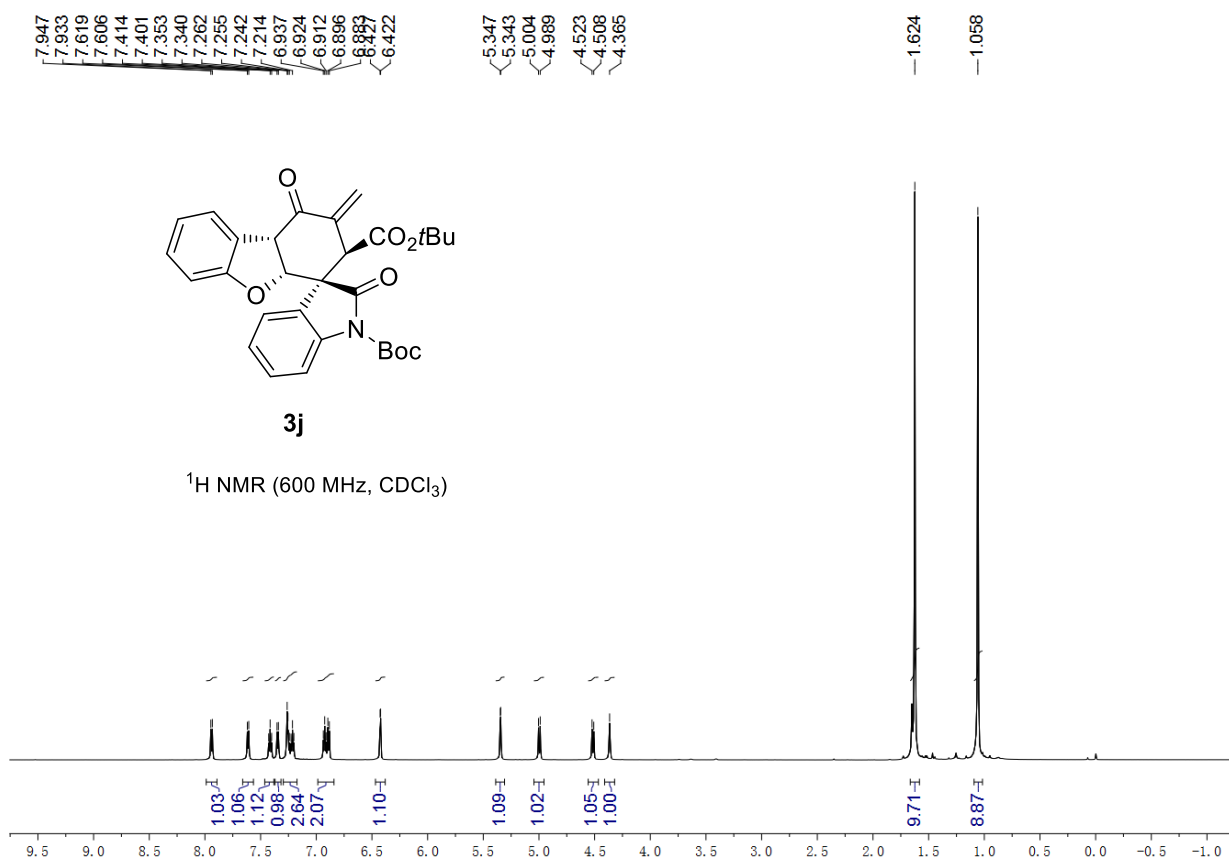


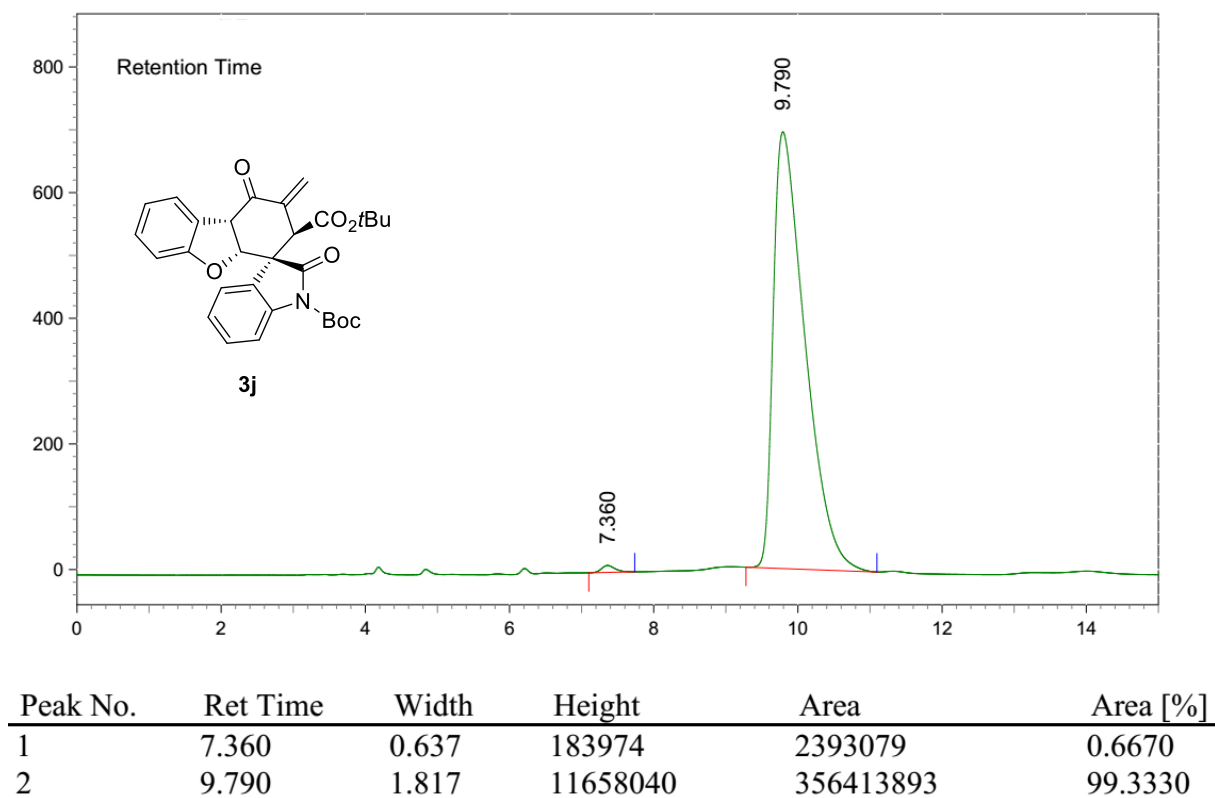
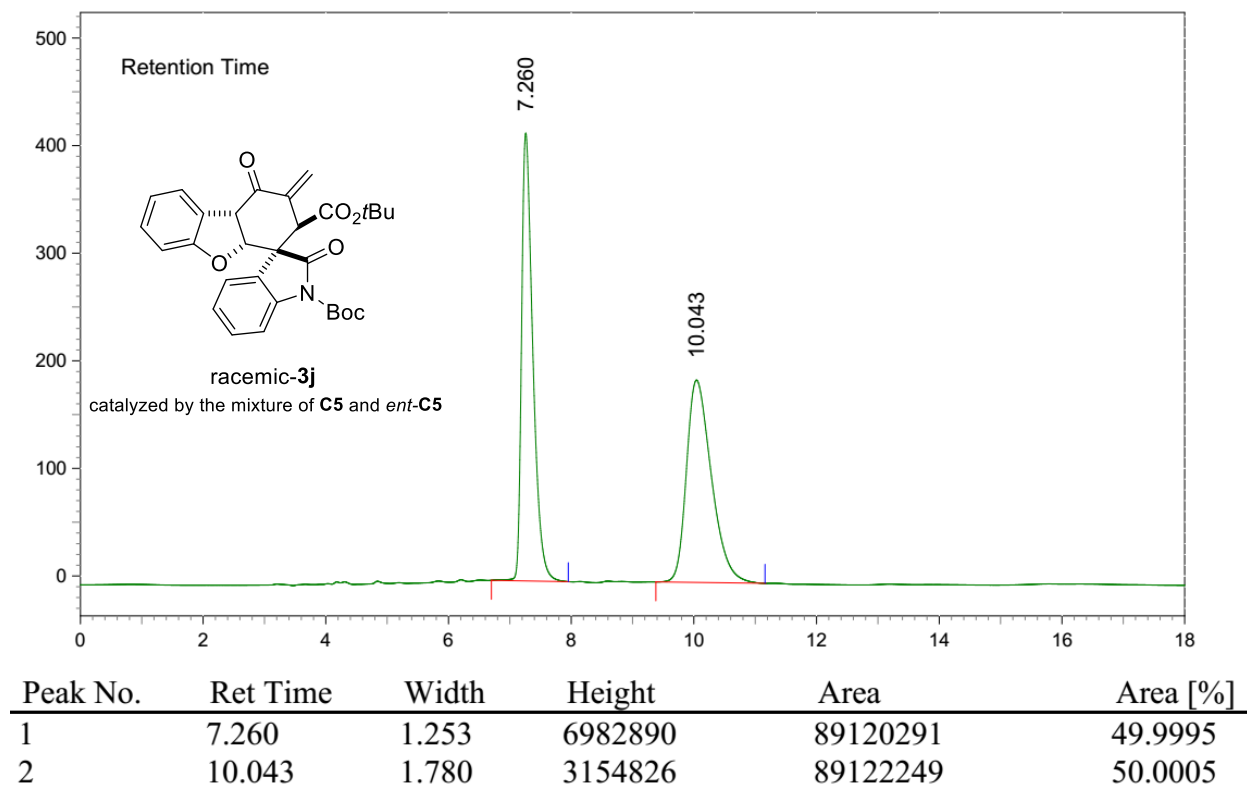


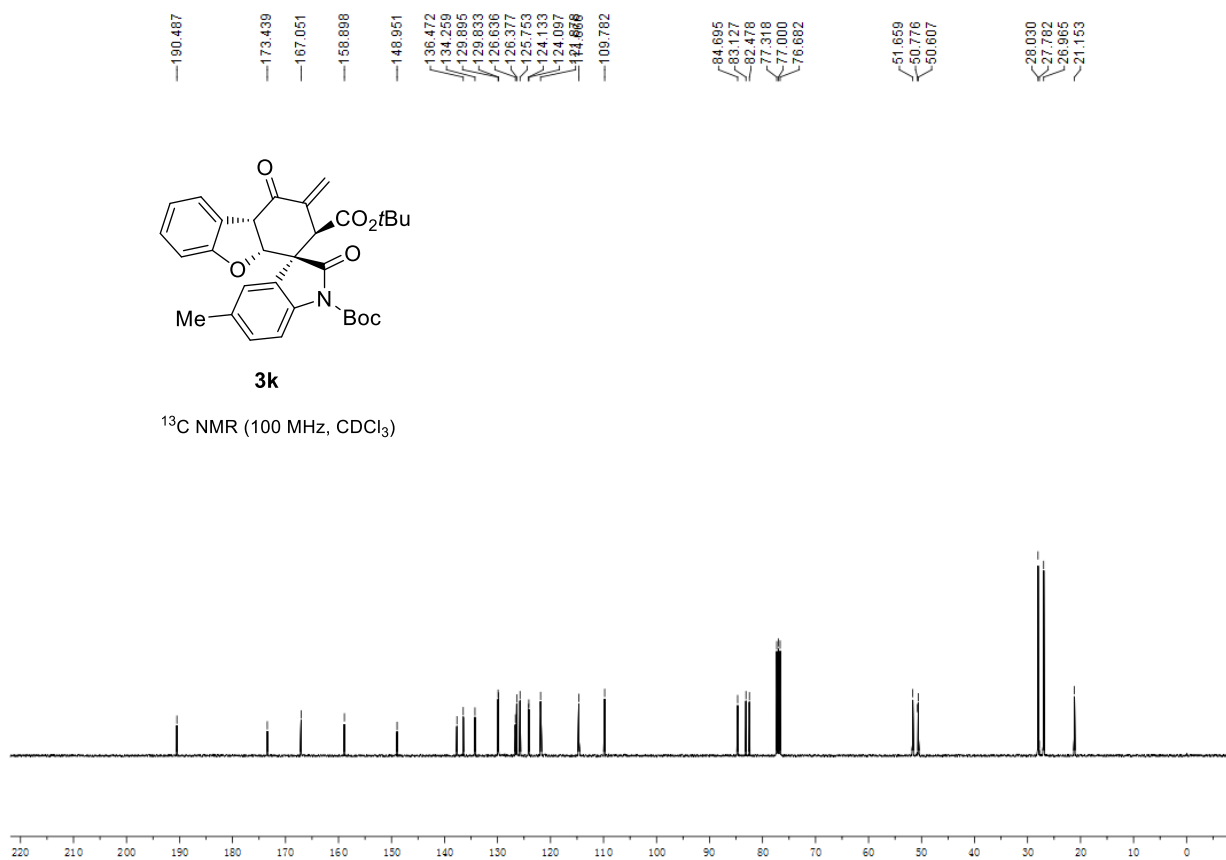
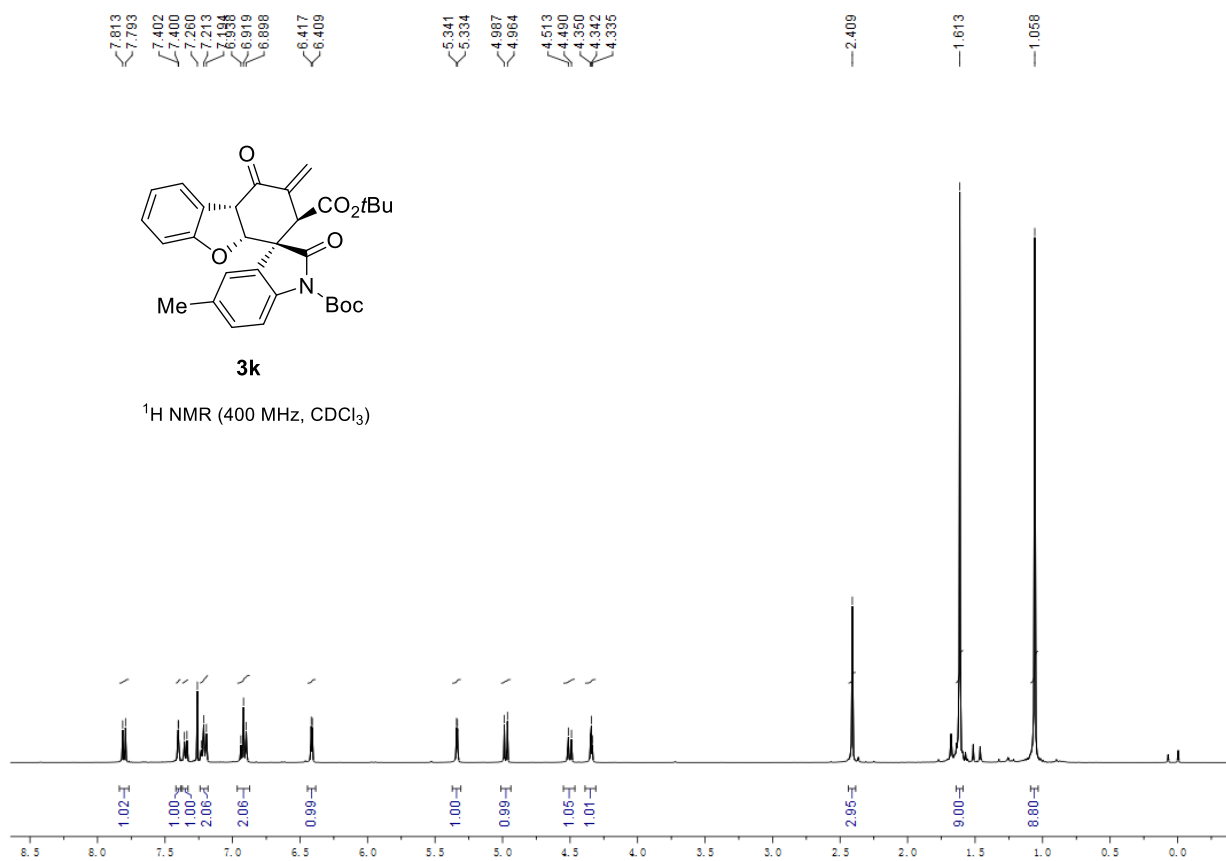
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	41.780	3.157	1837605	121352069	48.2999
2	44.457	4.423	1860899	129894889	51.7001

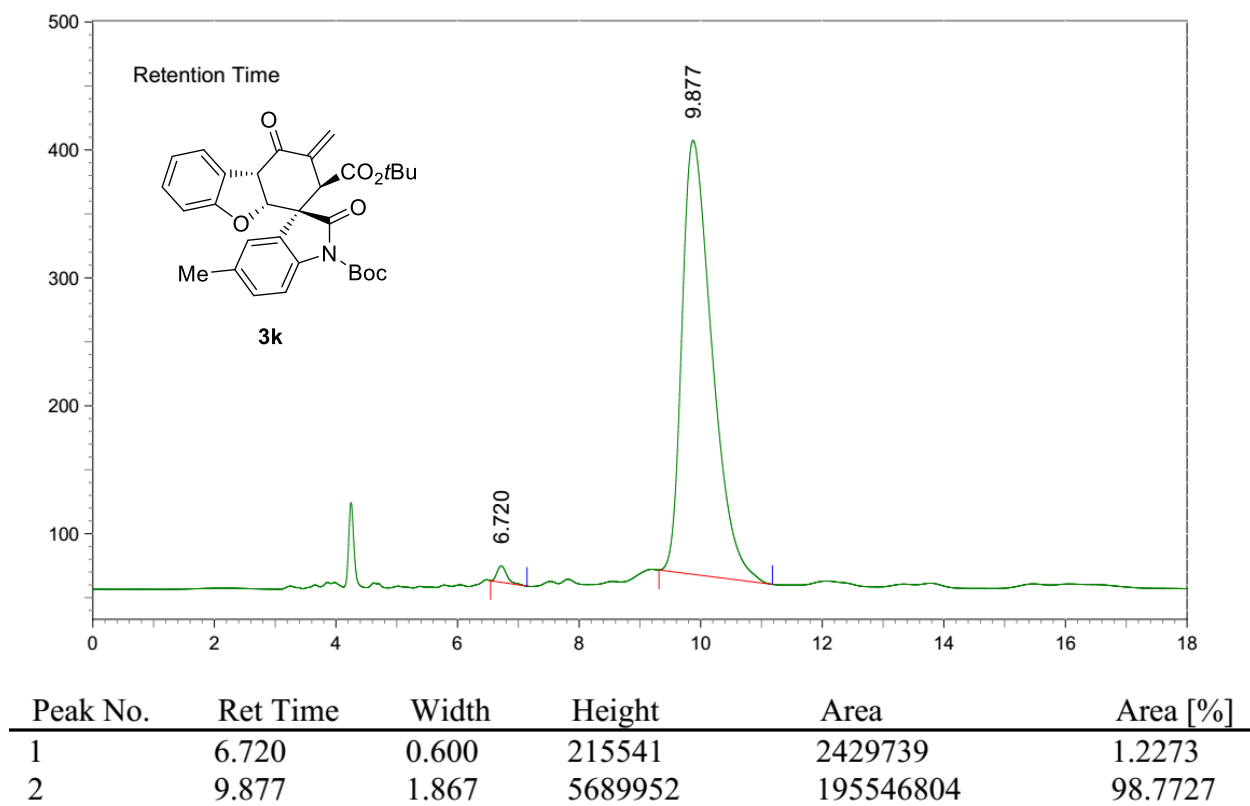
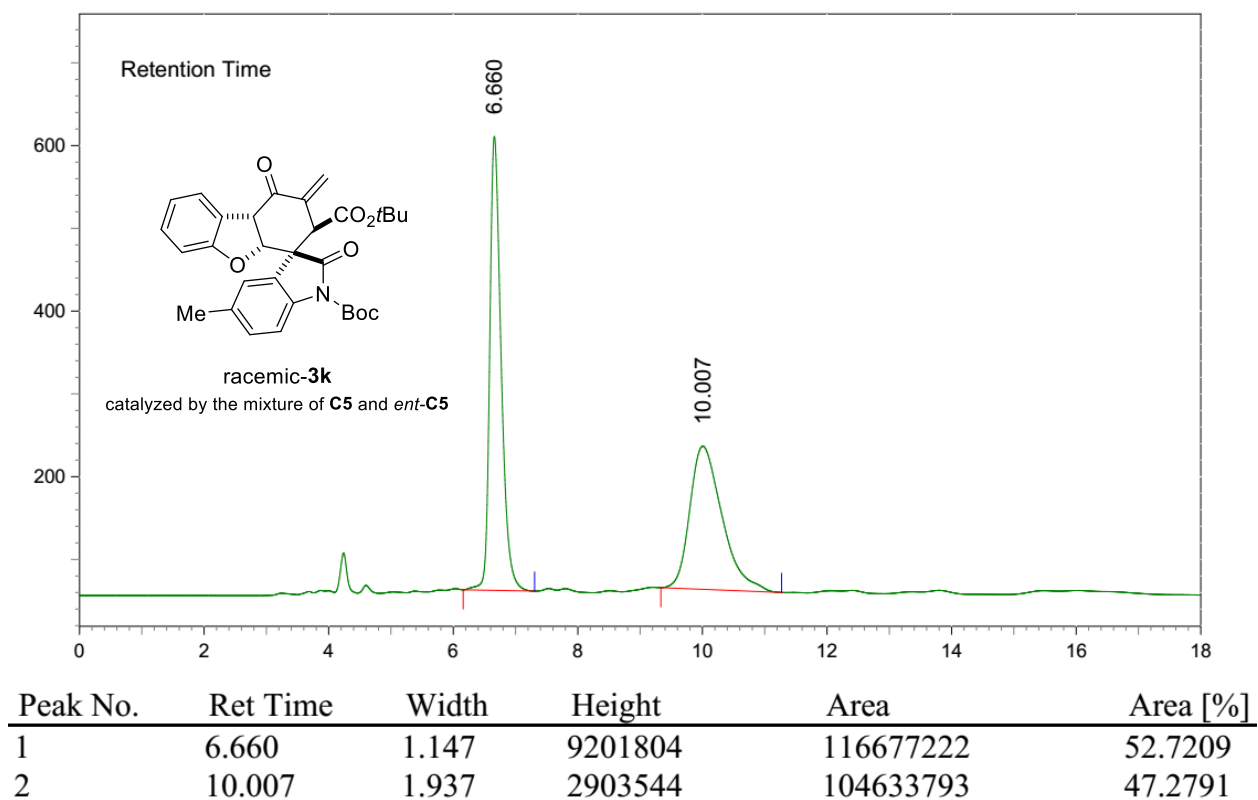


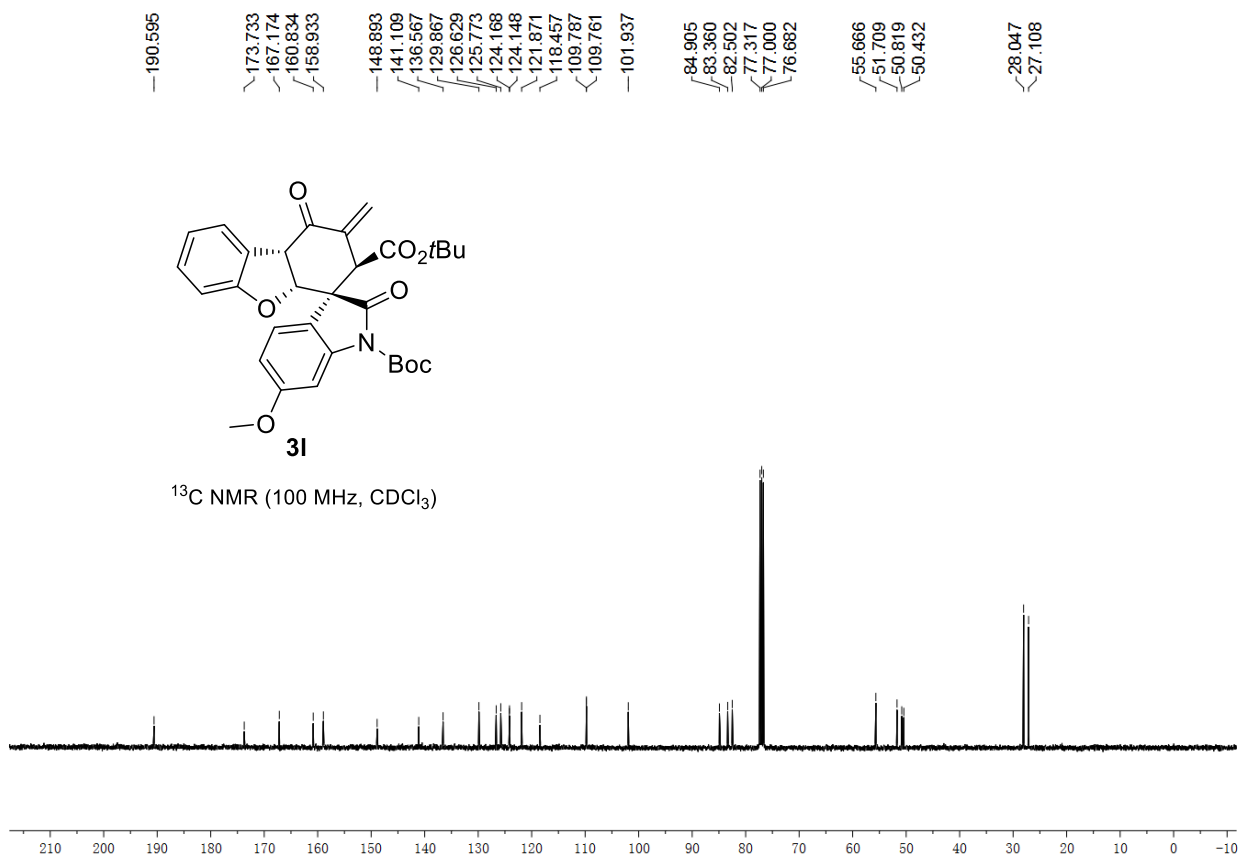
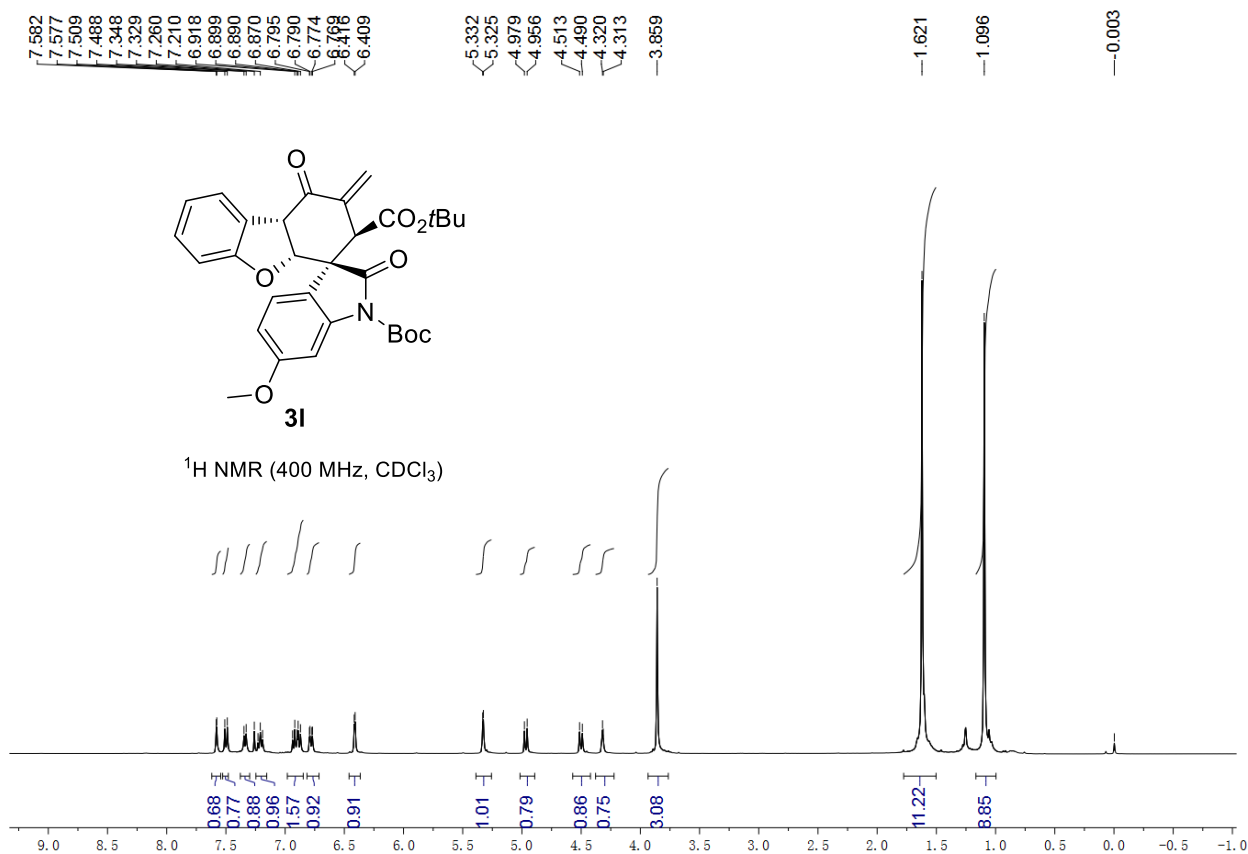
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	41.753	2.103	118320	6823847	0.5494
2	44.357	4.980	17663442	1235264380	99.4506

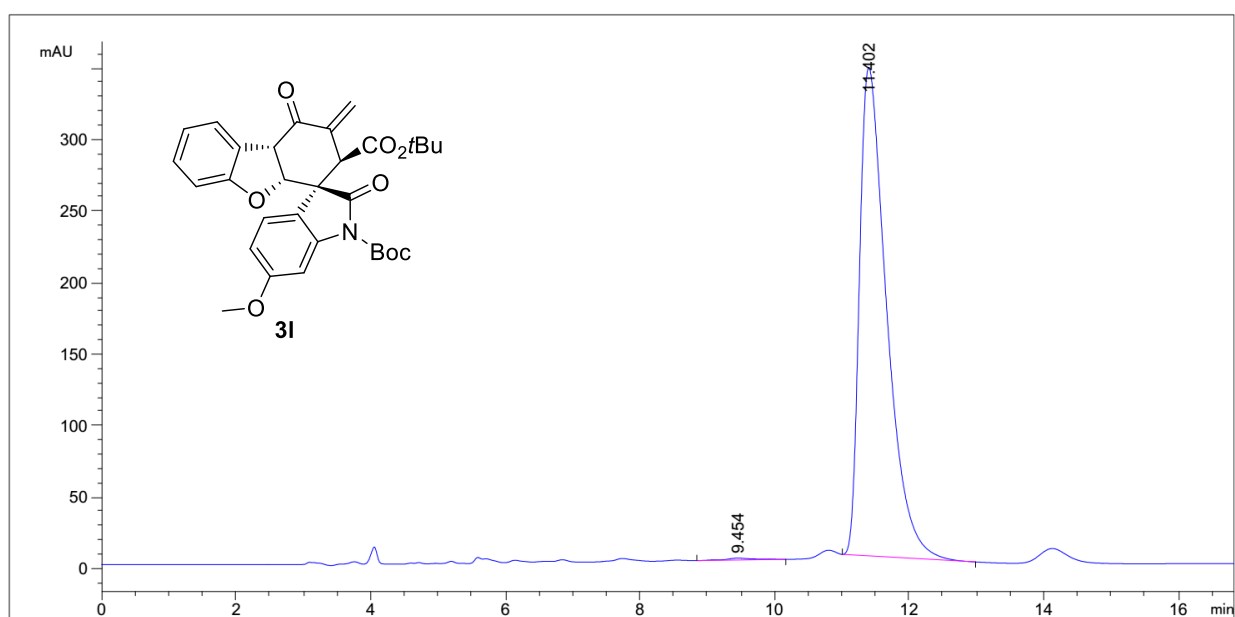
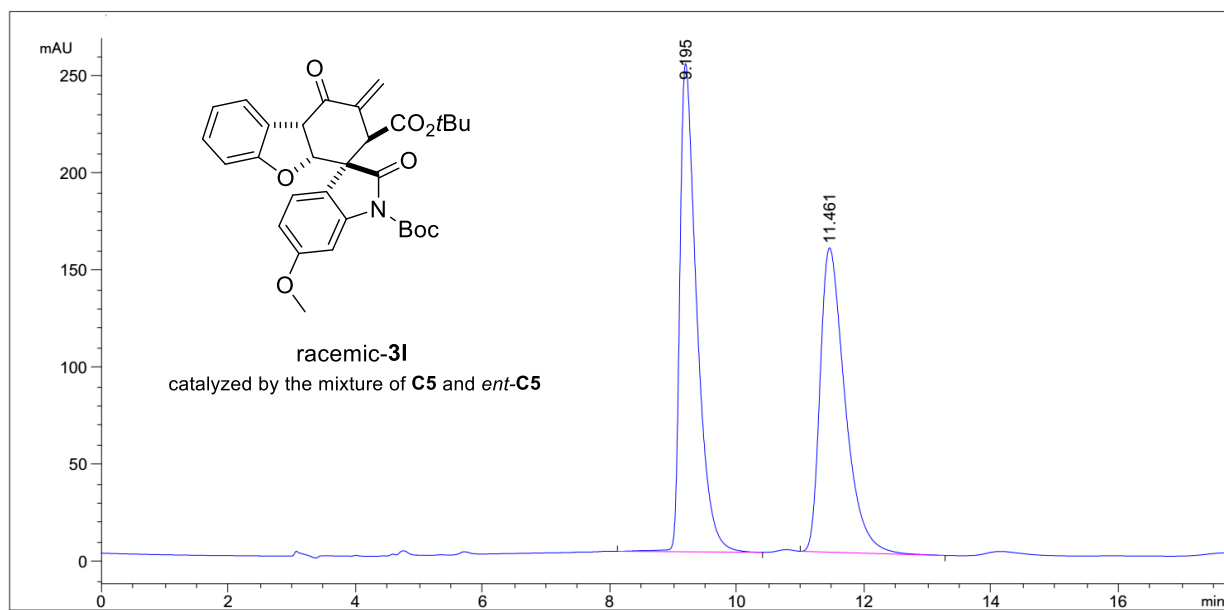


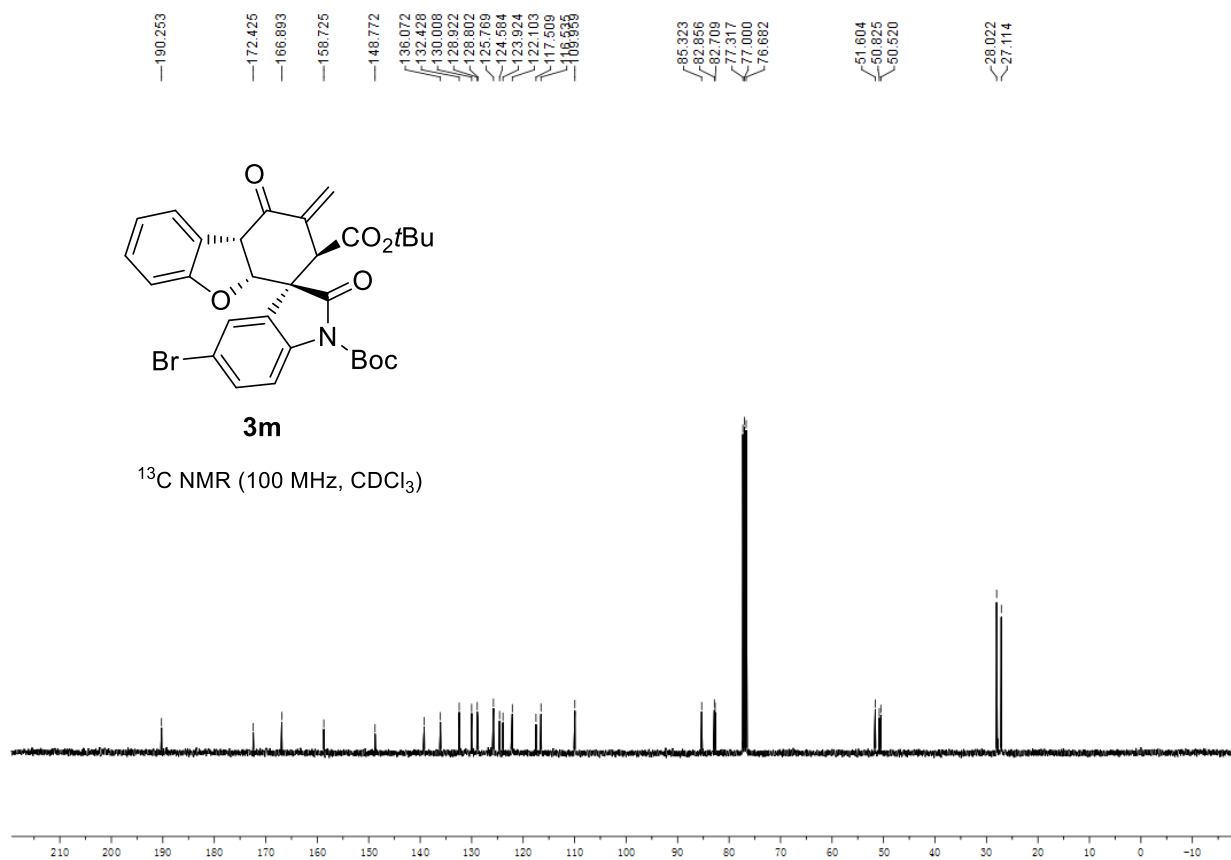
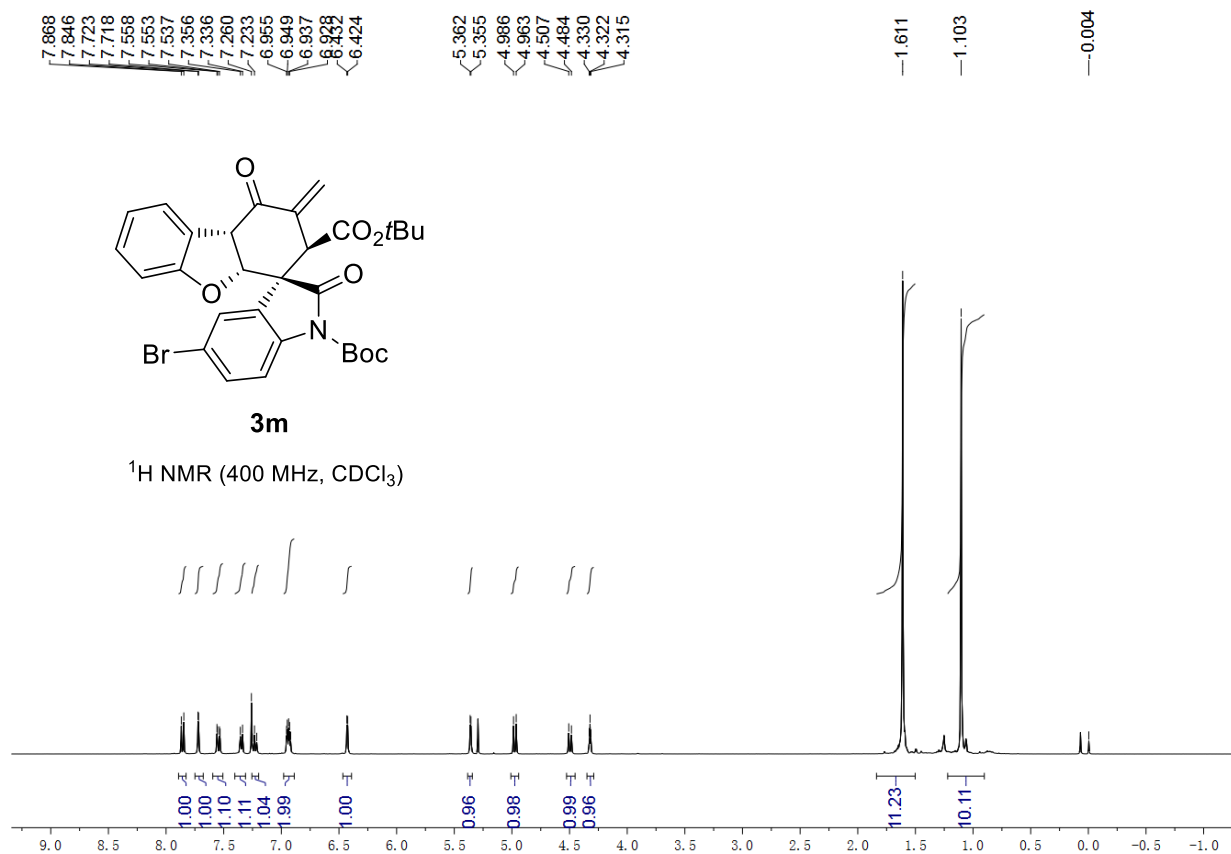


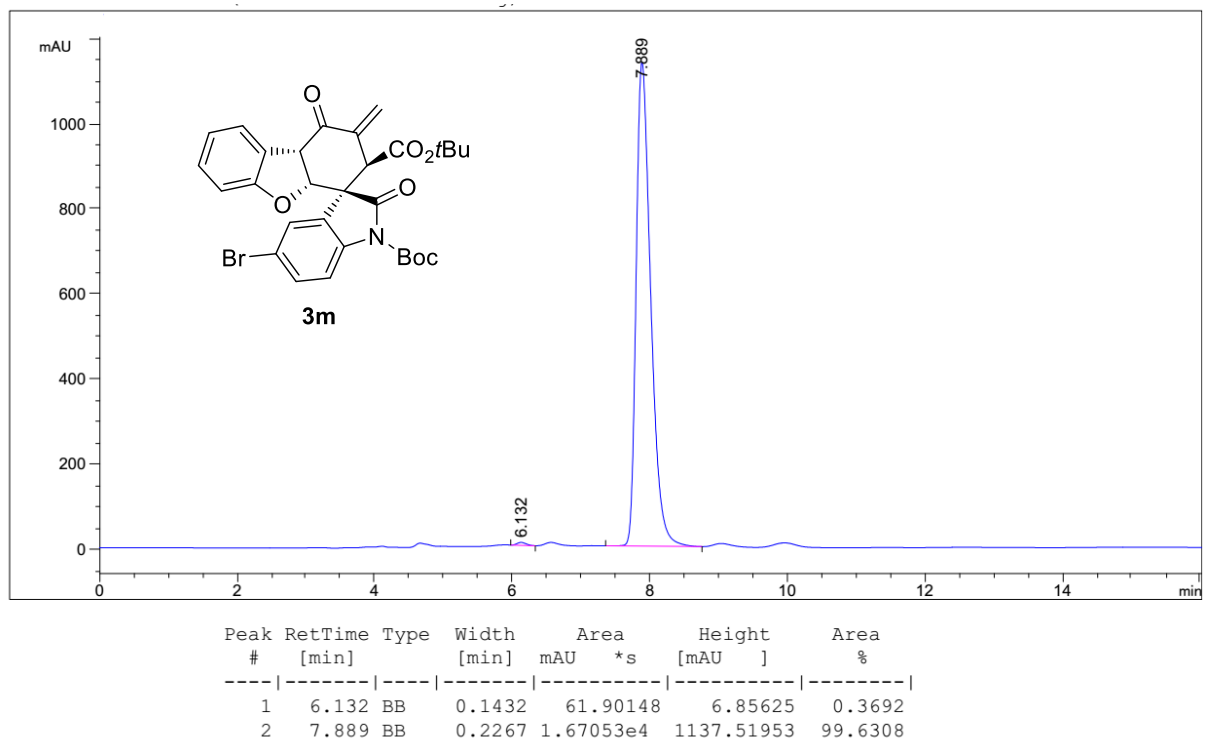
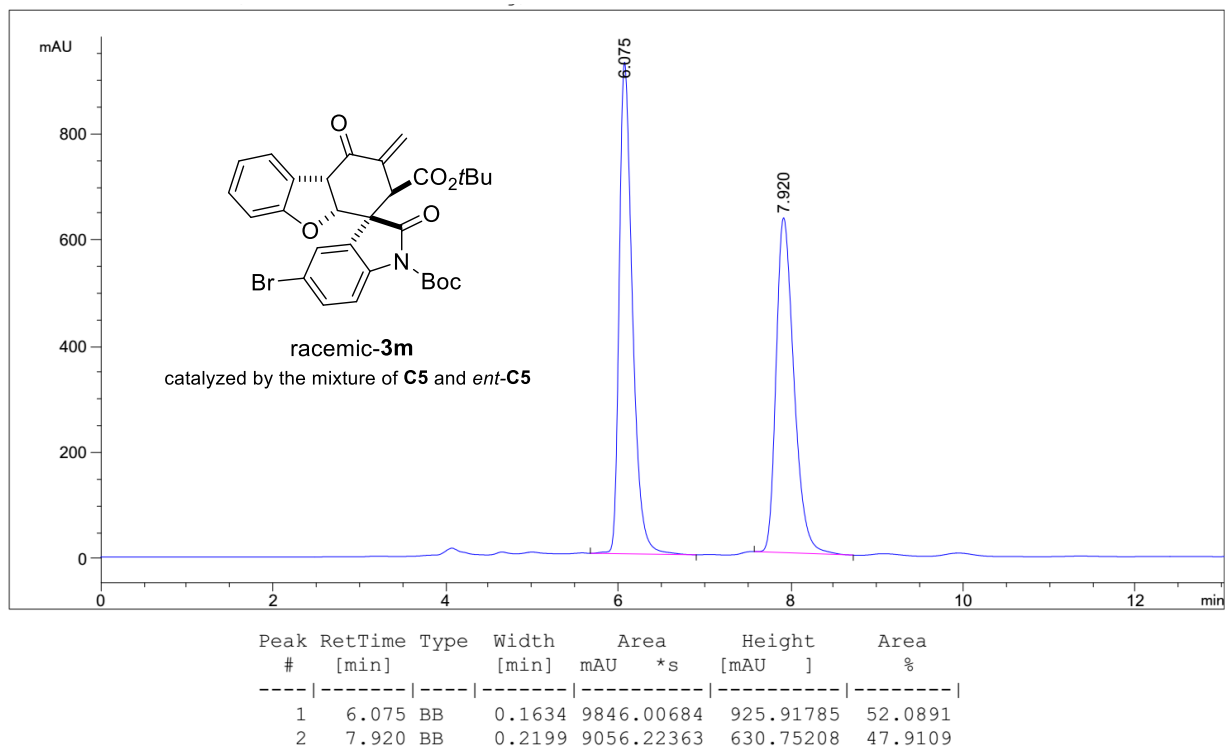


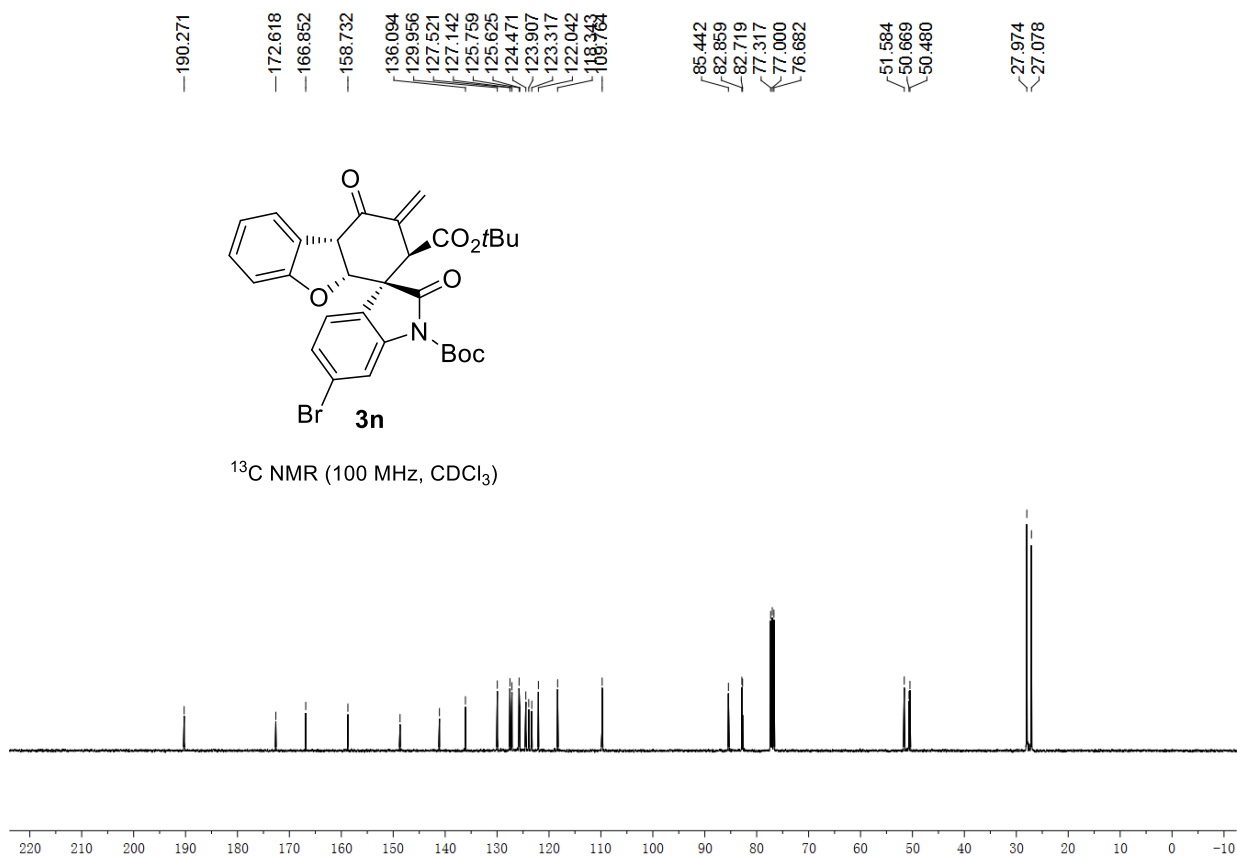
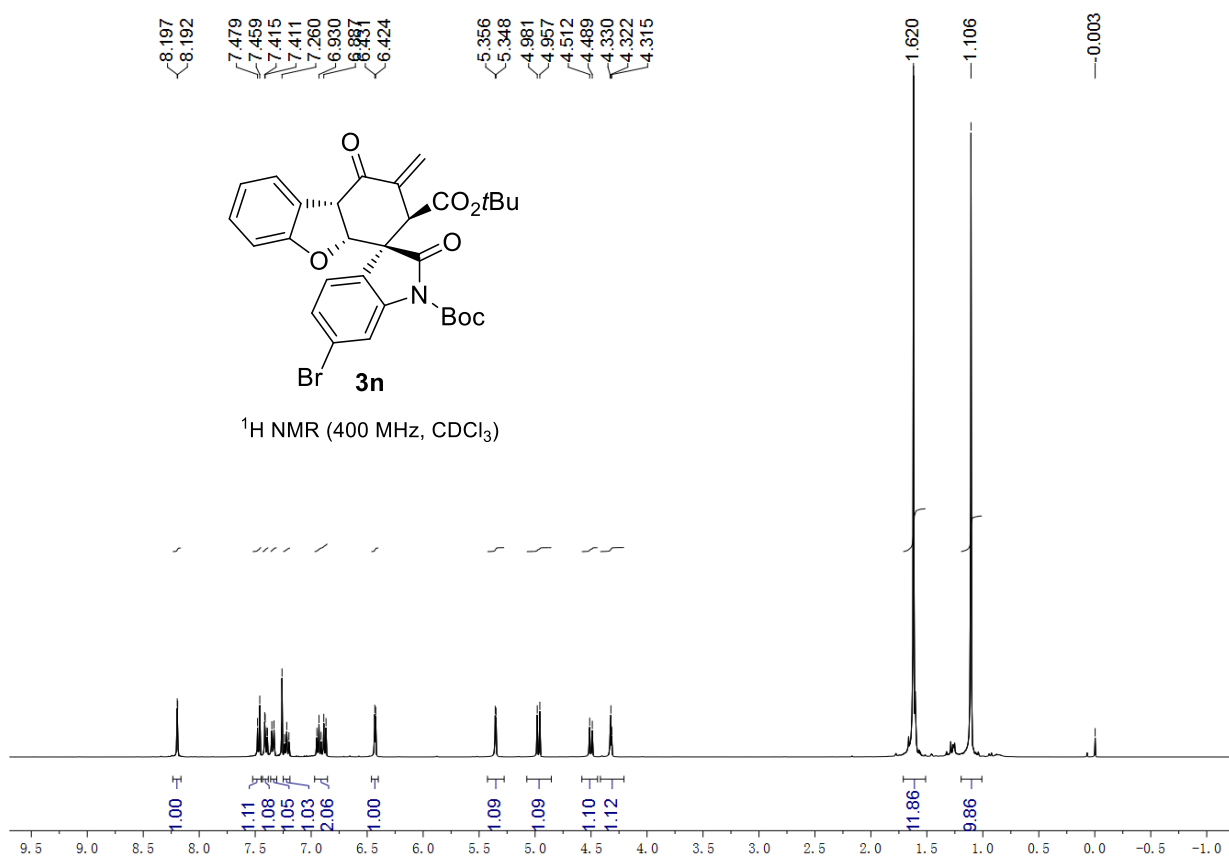


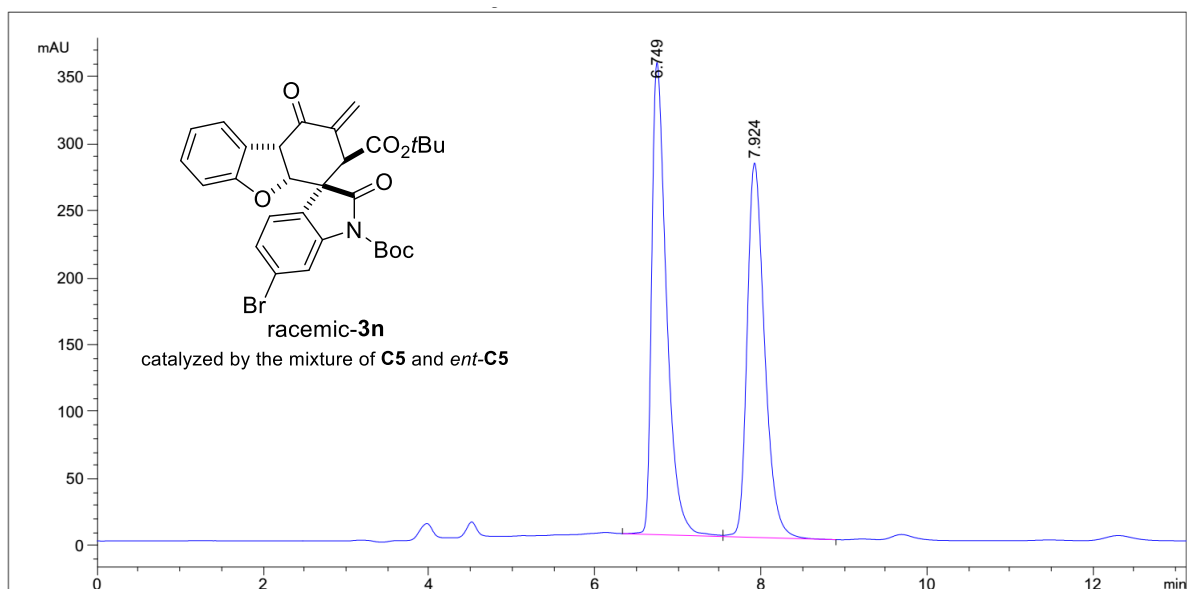




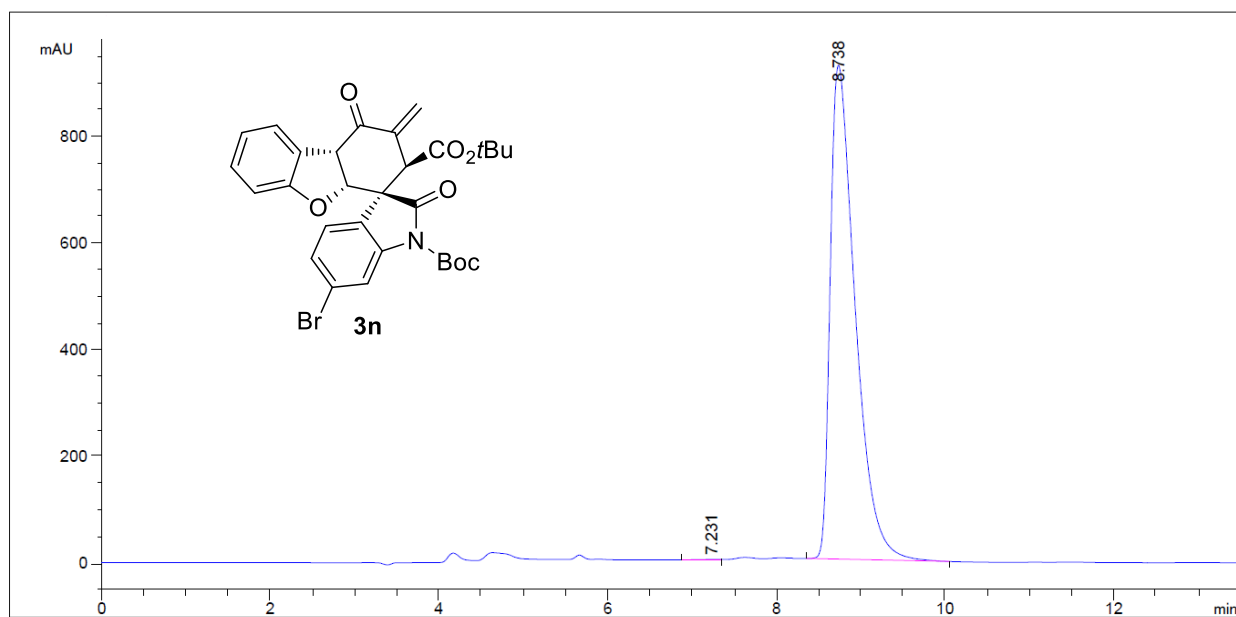




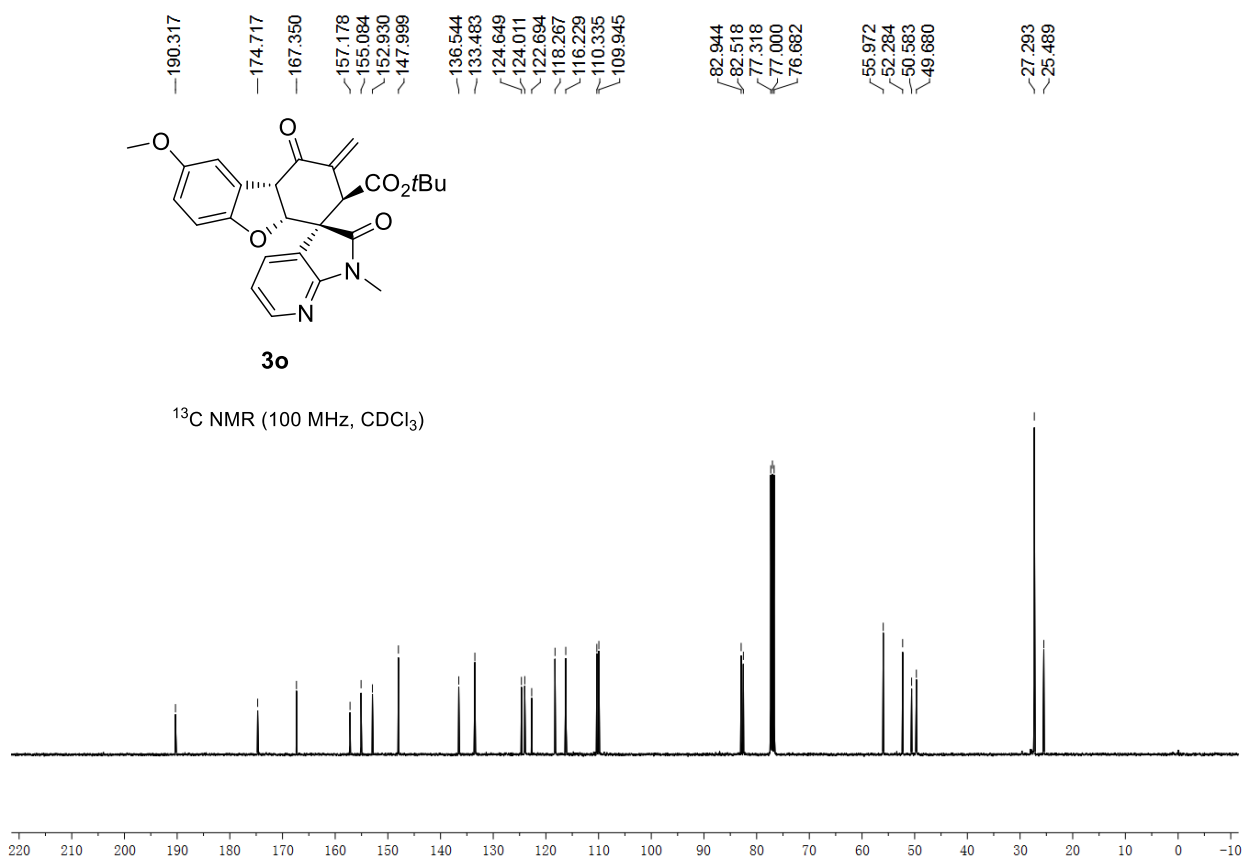
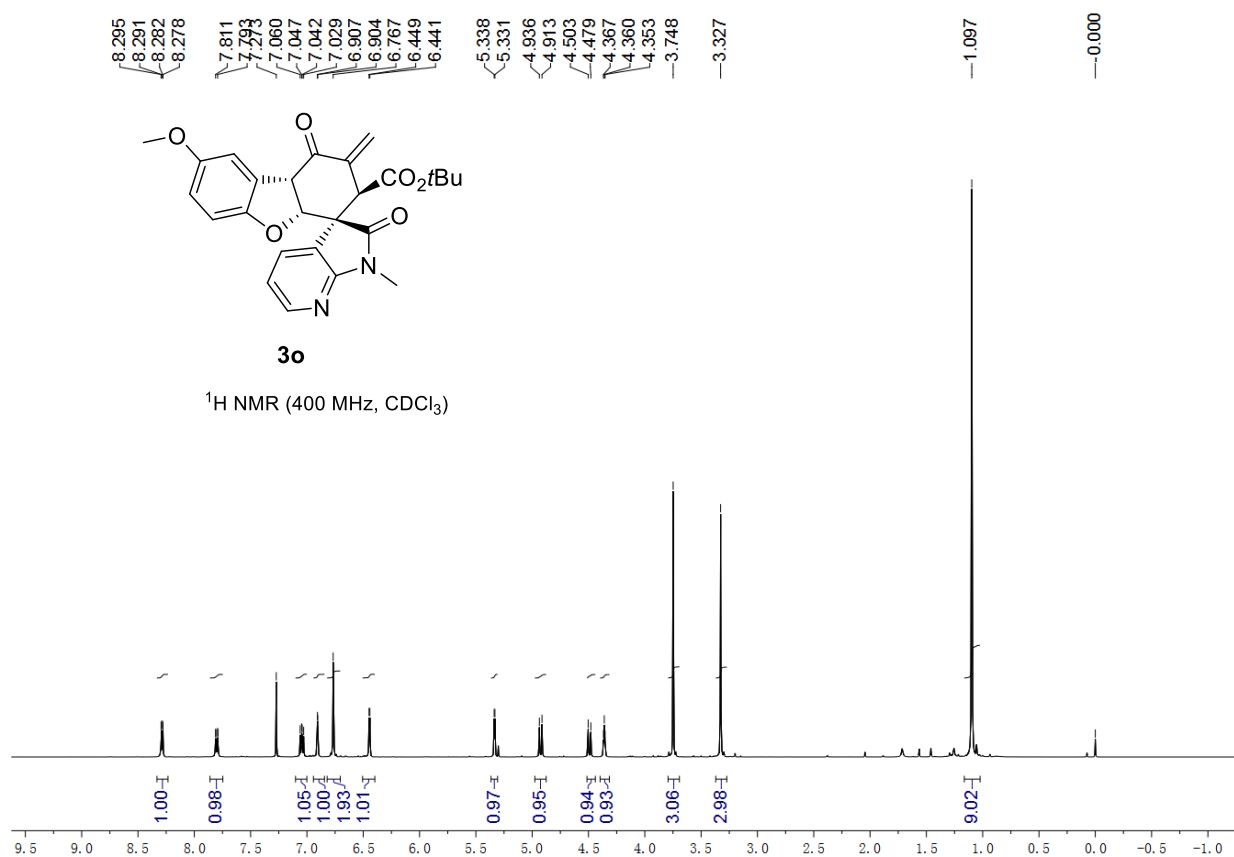


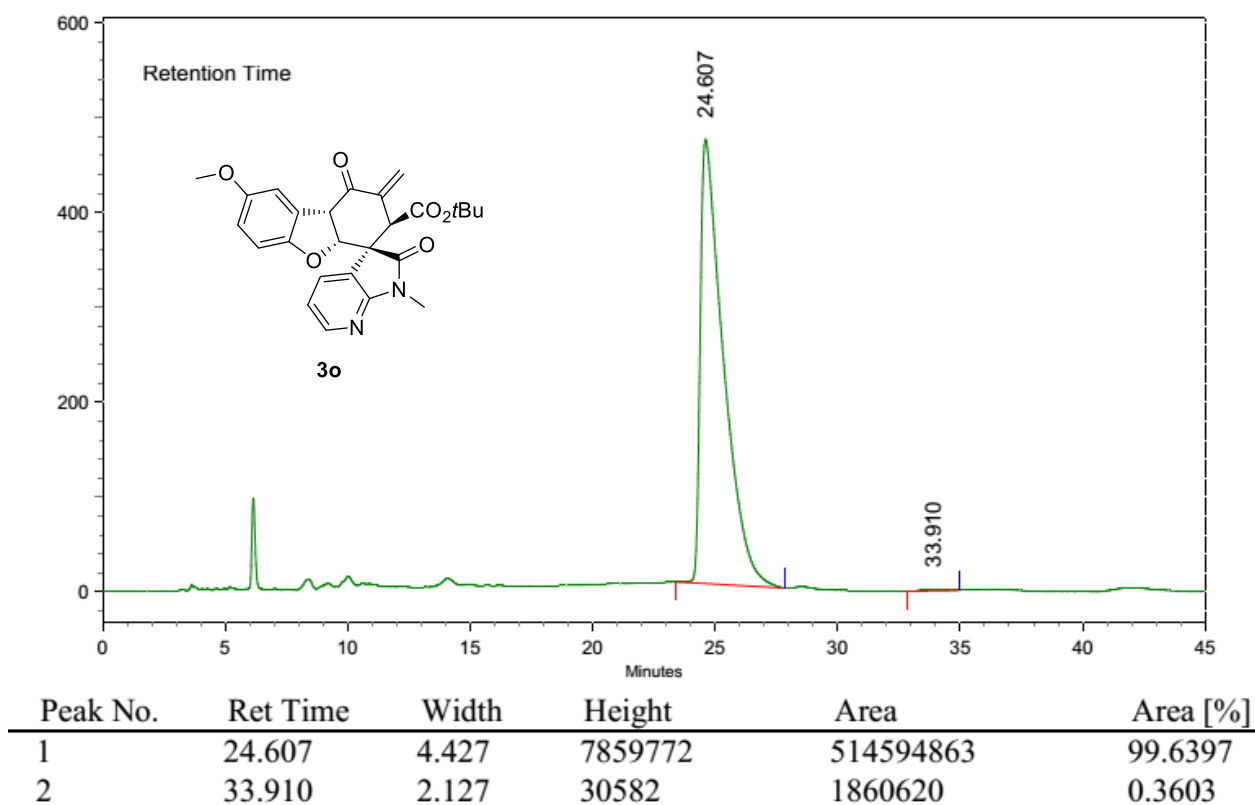
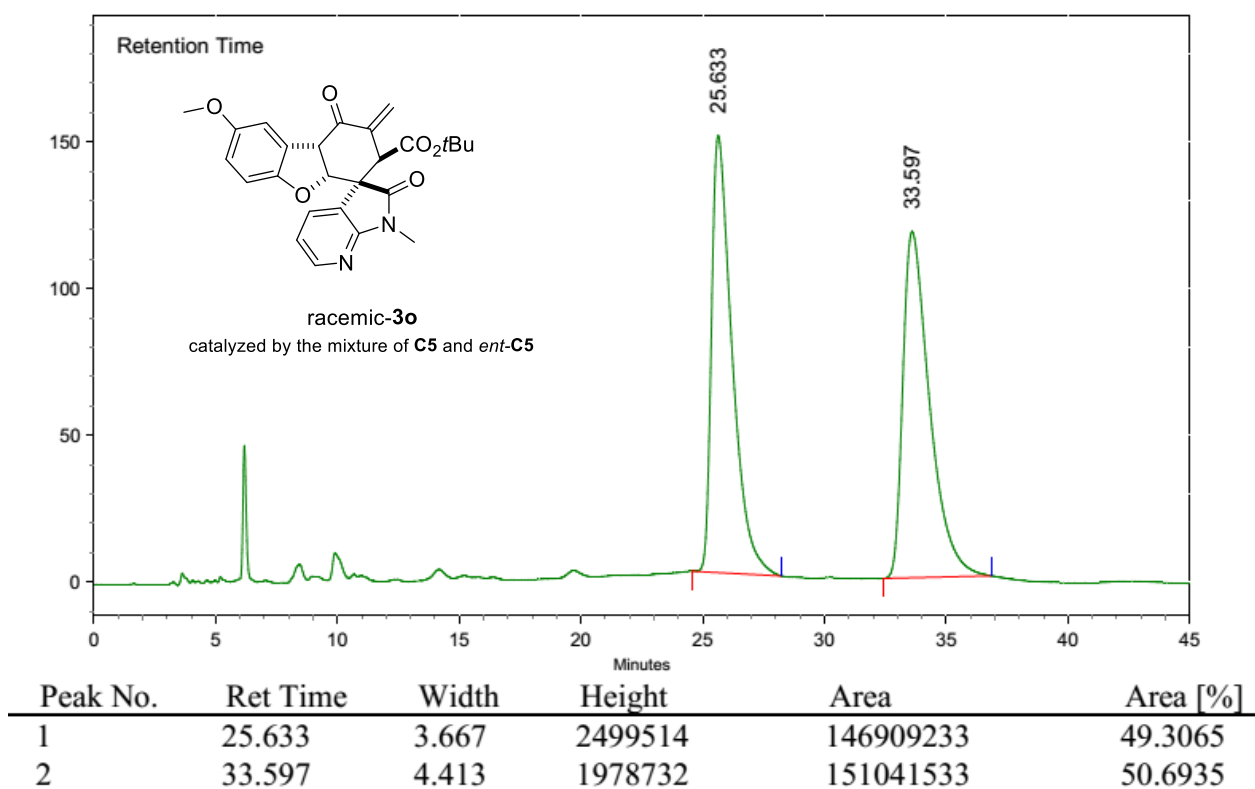


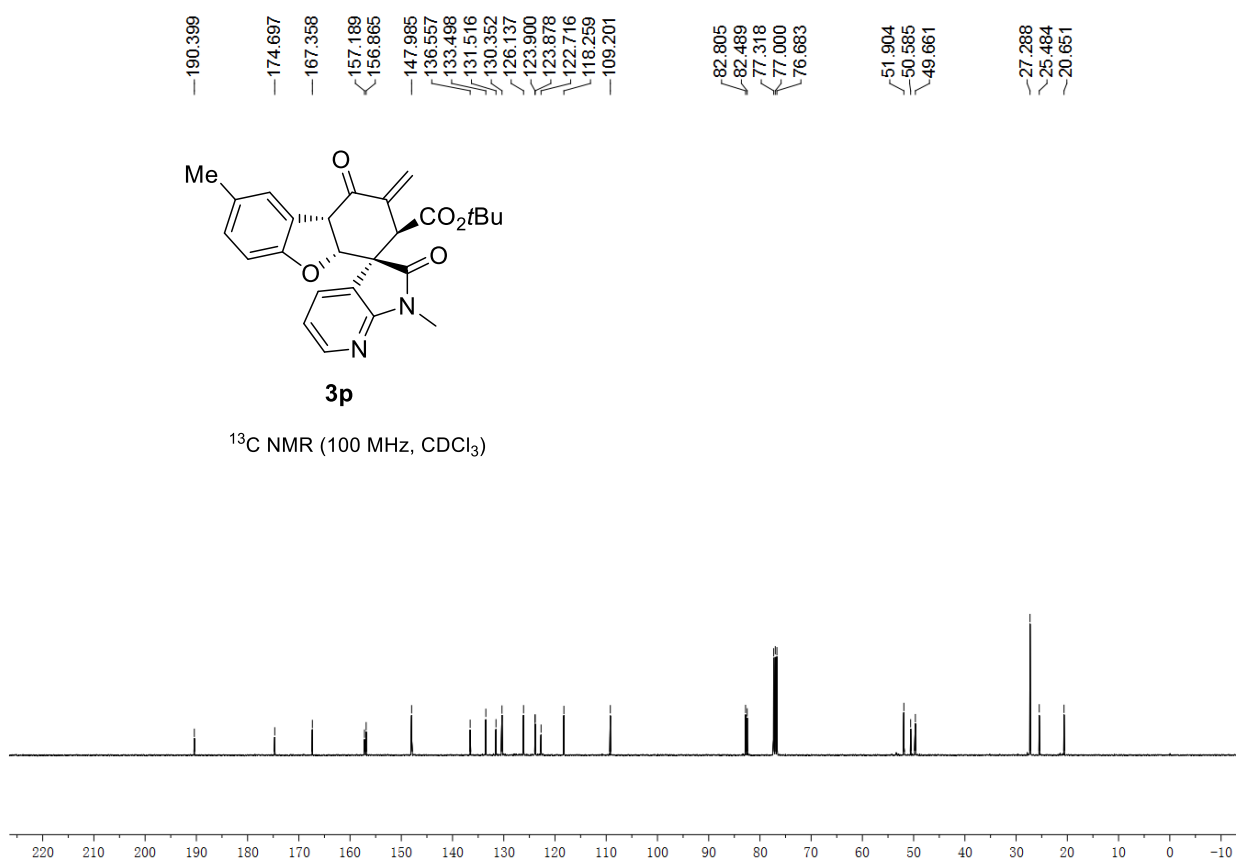
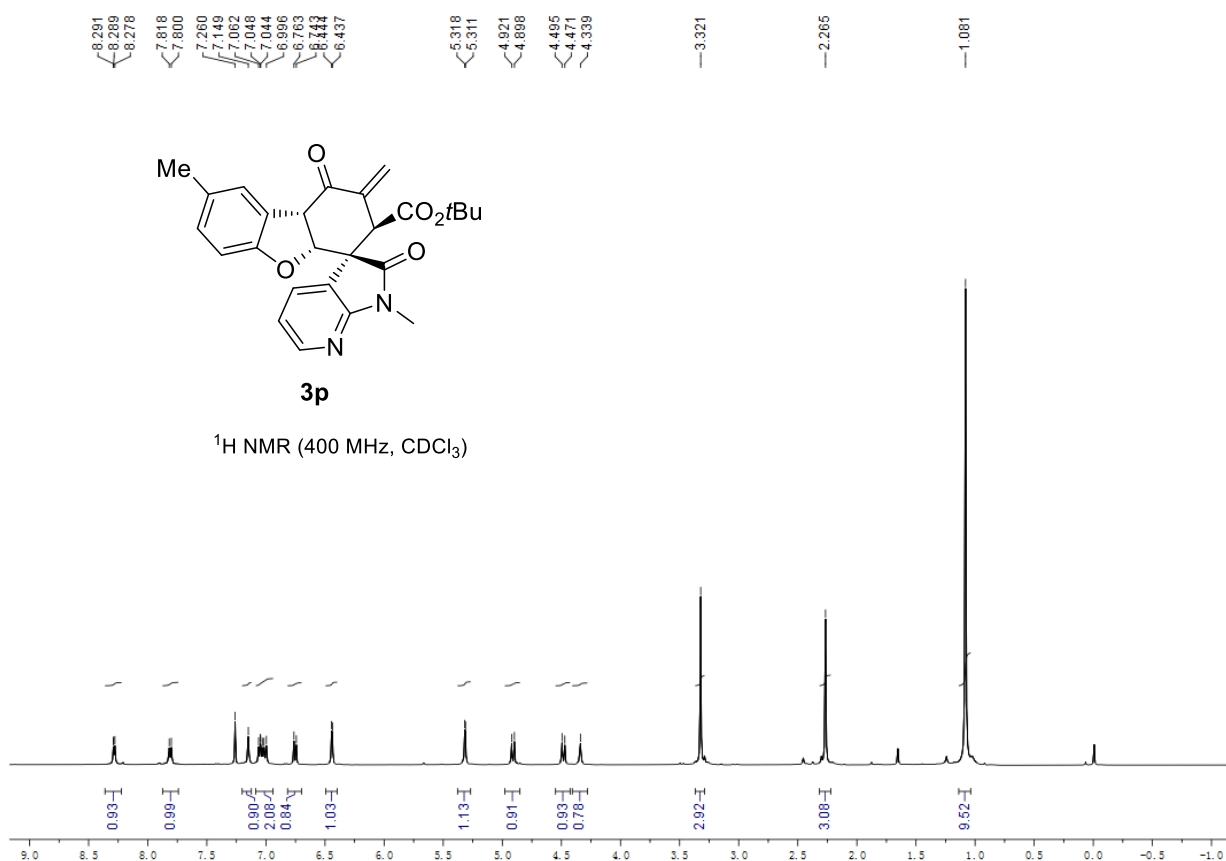
Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	6.749	BV	0.1868	4366.49805		352.34720	51.7347
2	7.924	VB	0.2240	4073.67871		279.39337	48.2653

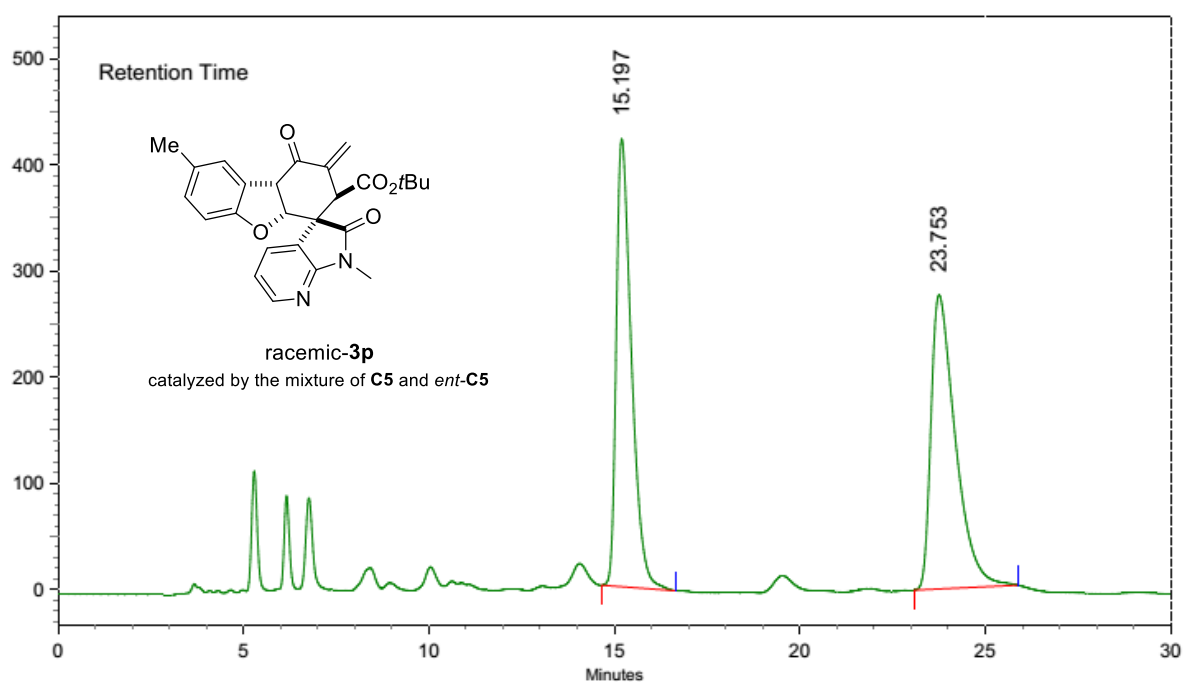


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	7.231	BV	0.2265	9.35004		6.01416e-1	0.0491
2	8.738	BBA	0.3126	1.90243e4		925.60120	99.9509

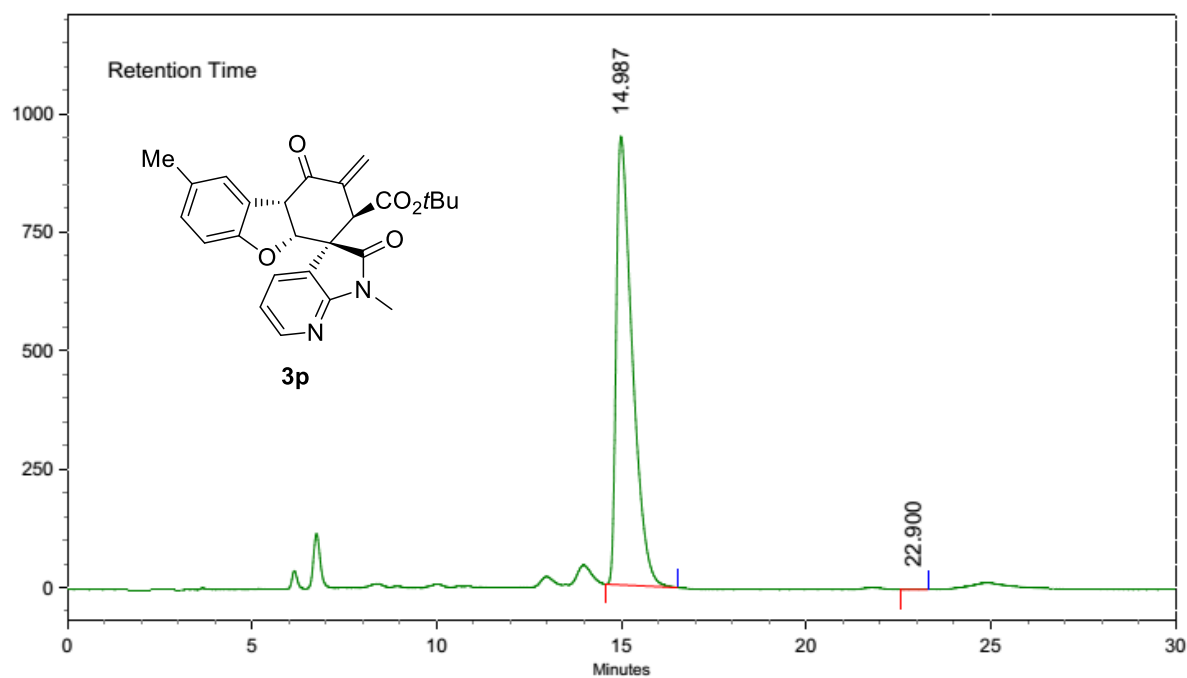




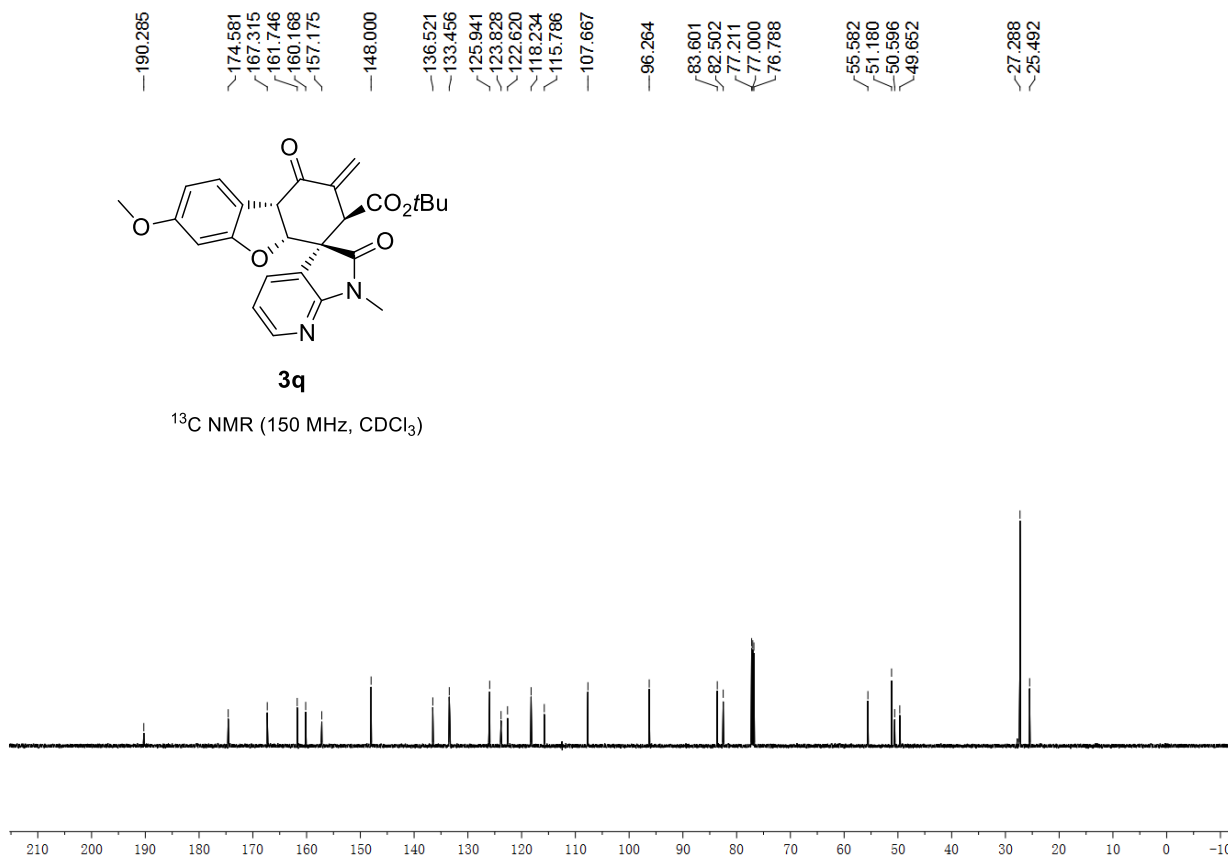
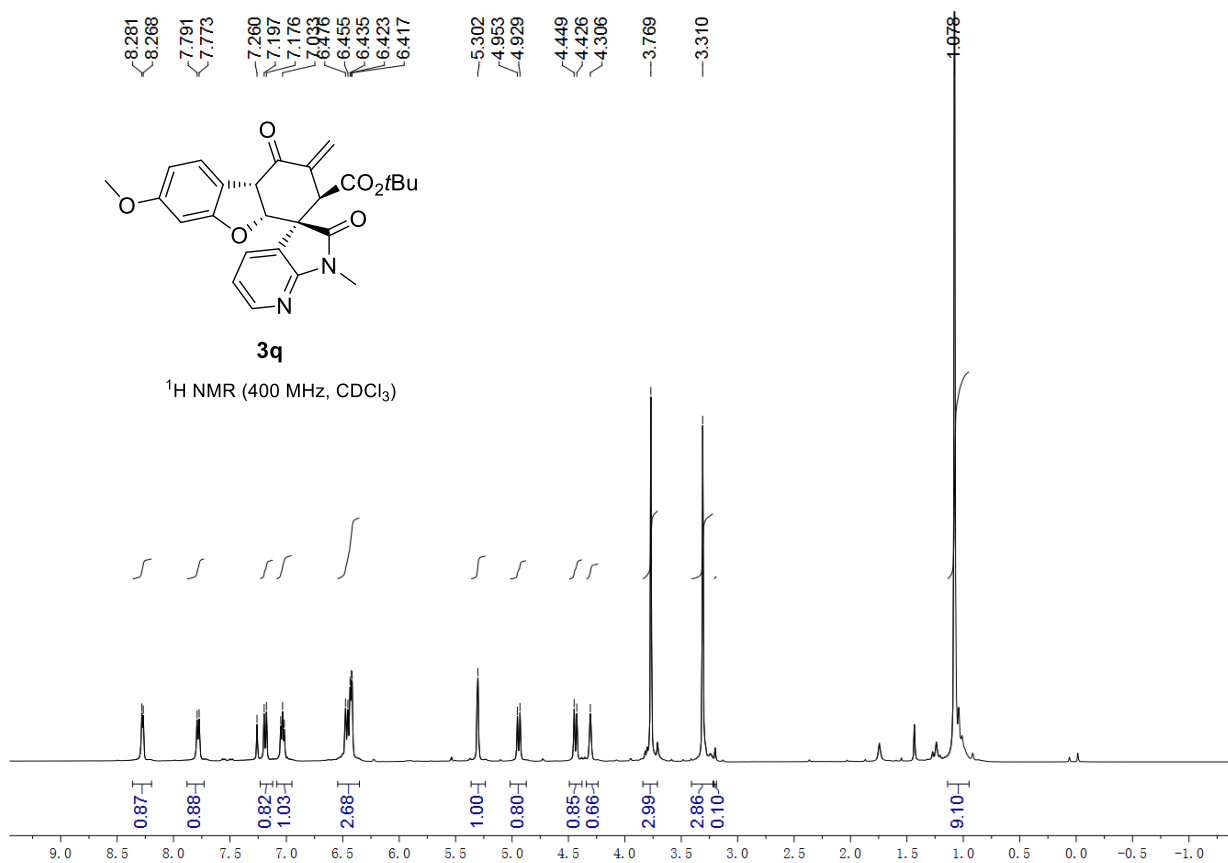


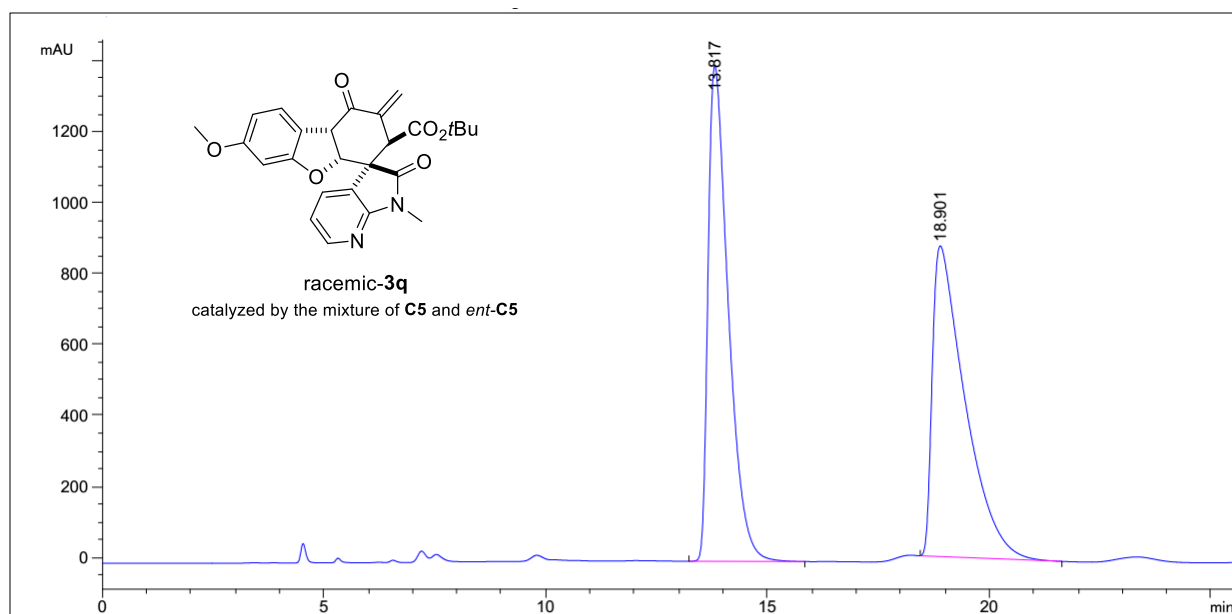


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	15.197	2.000	7076670	201610357	48.6253
2	23.753	2.813	4646401	213009541	51.3747

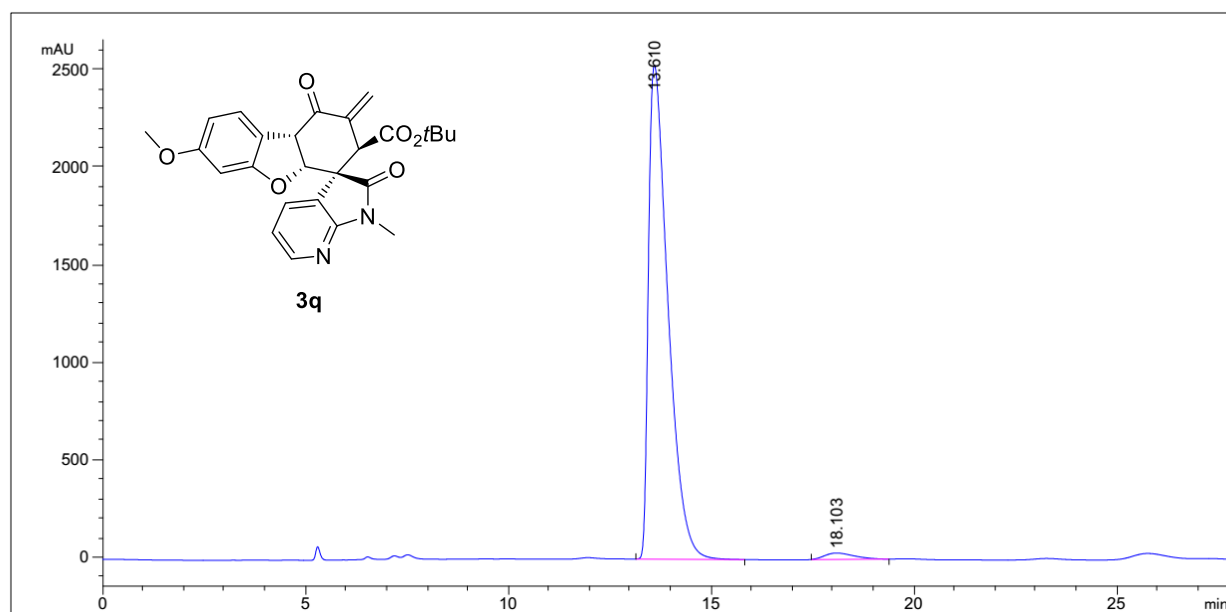


Peak No.	Ret Time	Width	Height	Area	Area [%]
1	14.987	1.920	15879390	479264236	99.9818
2	22.900	0.737	3866	87041	0.0182

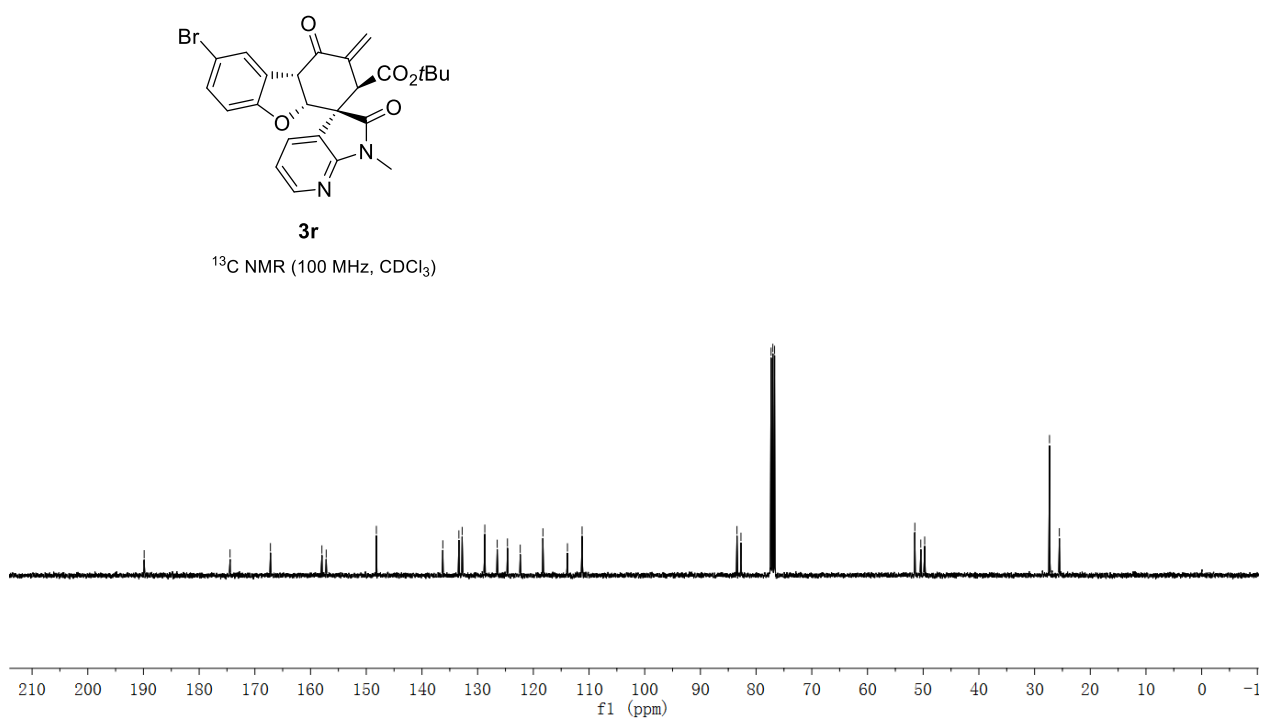
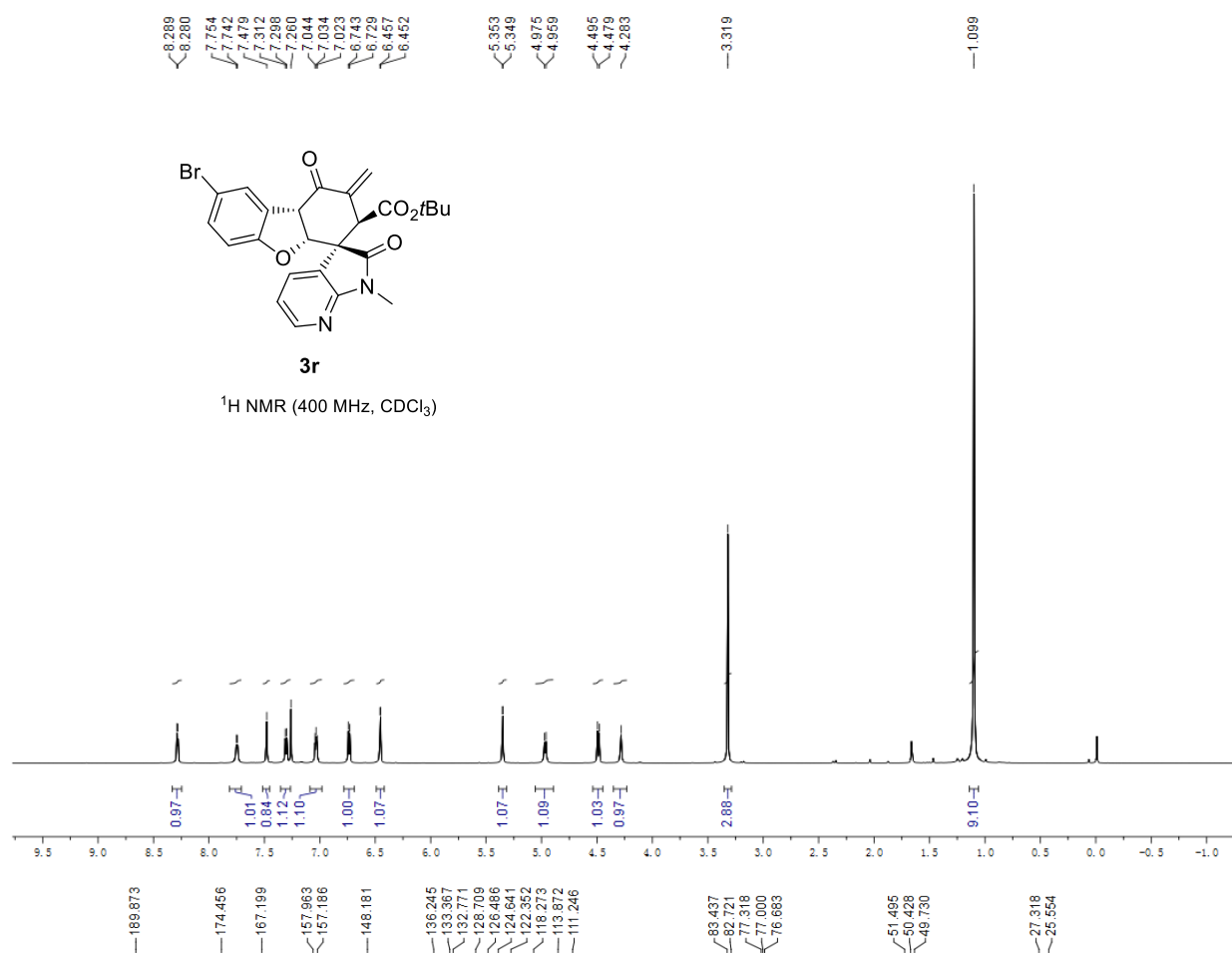


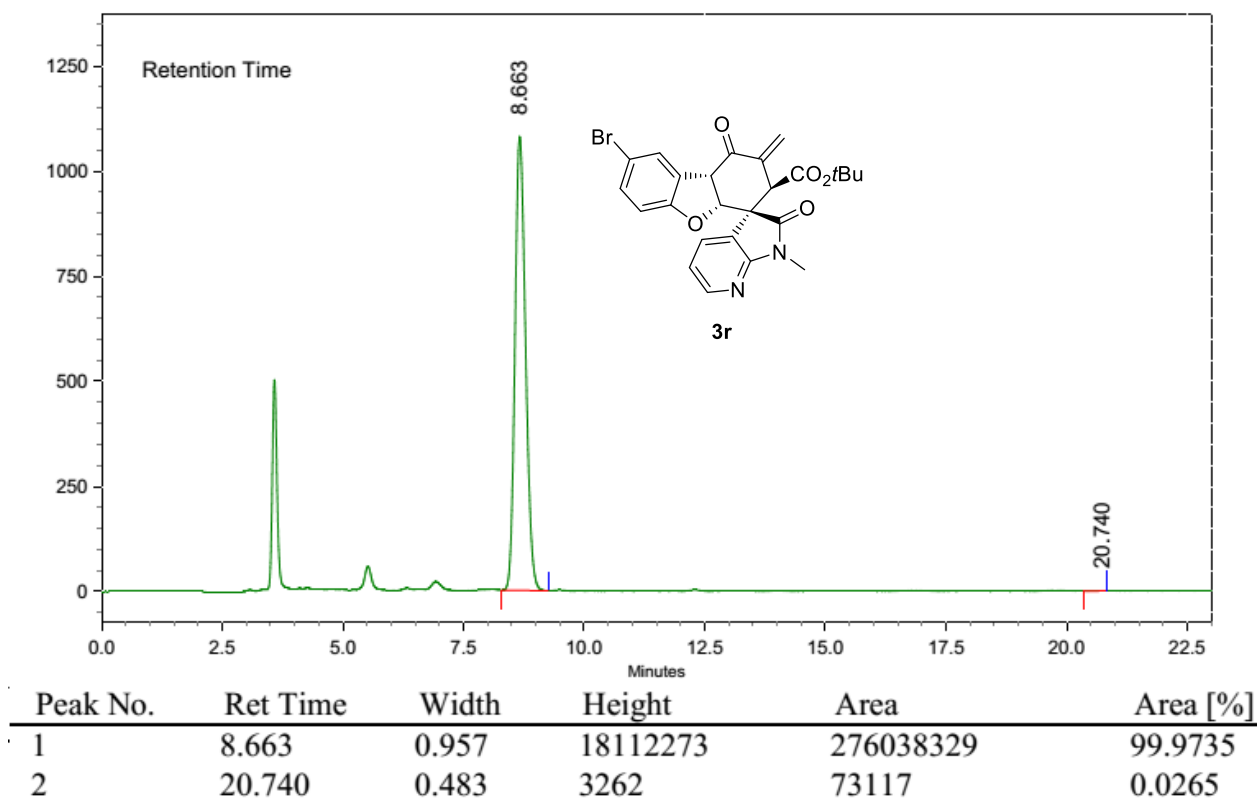
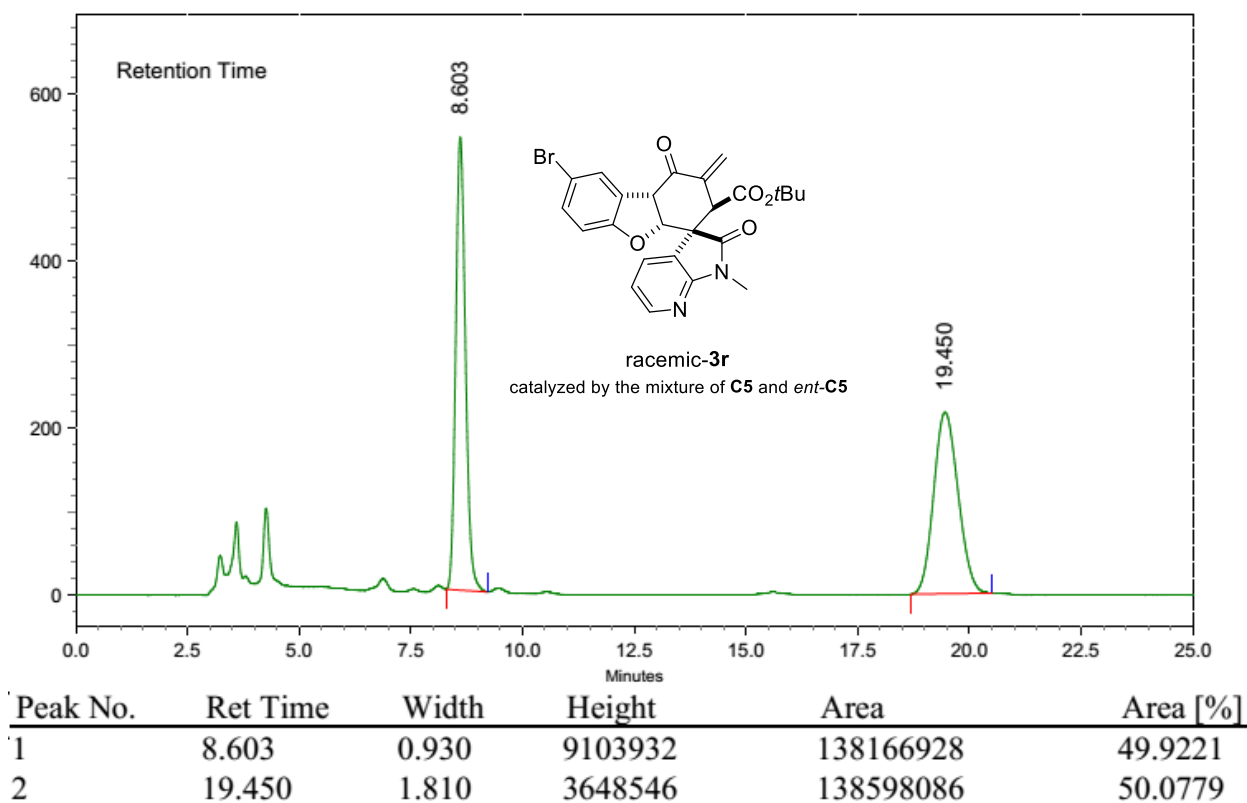


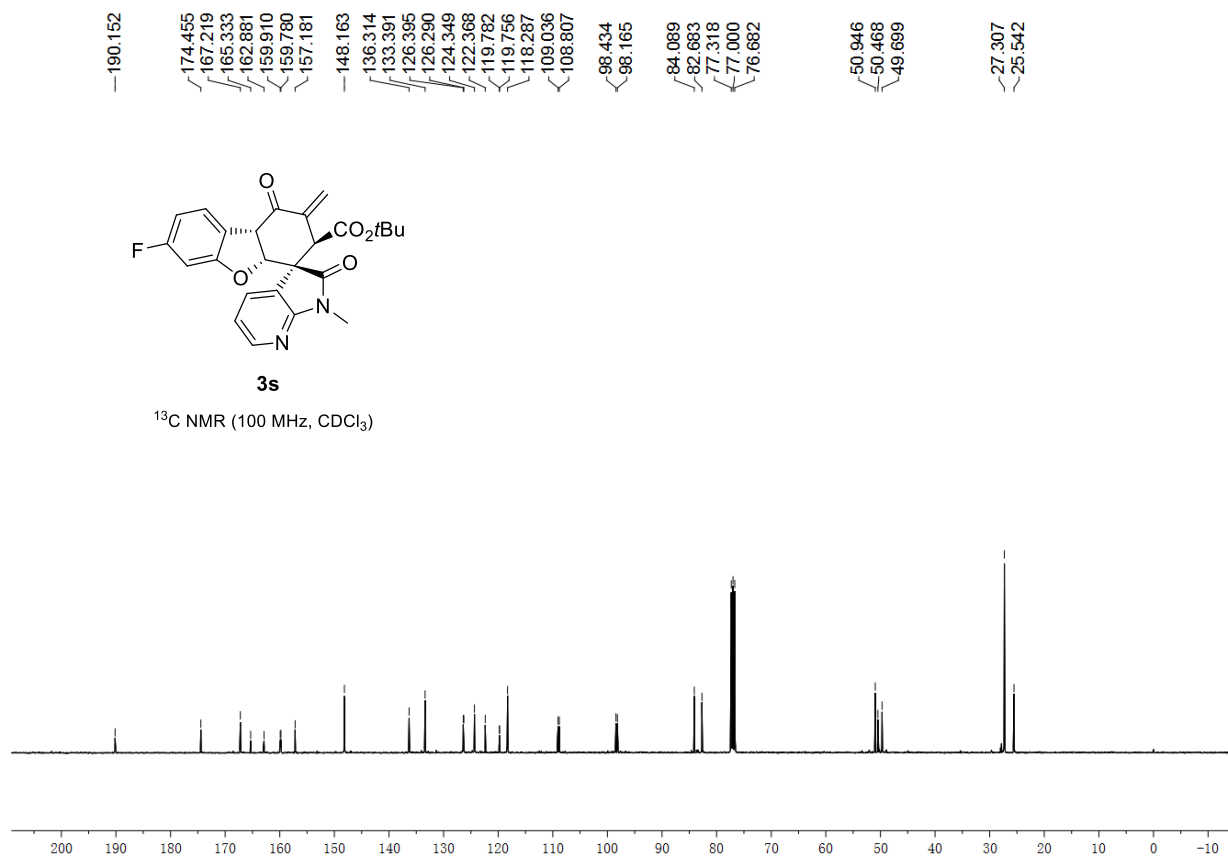
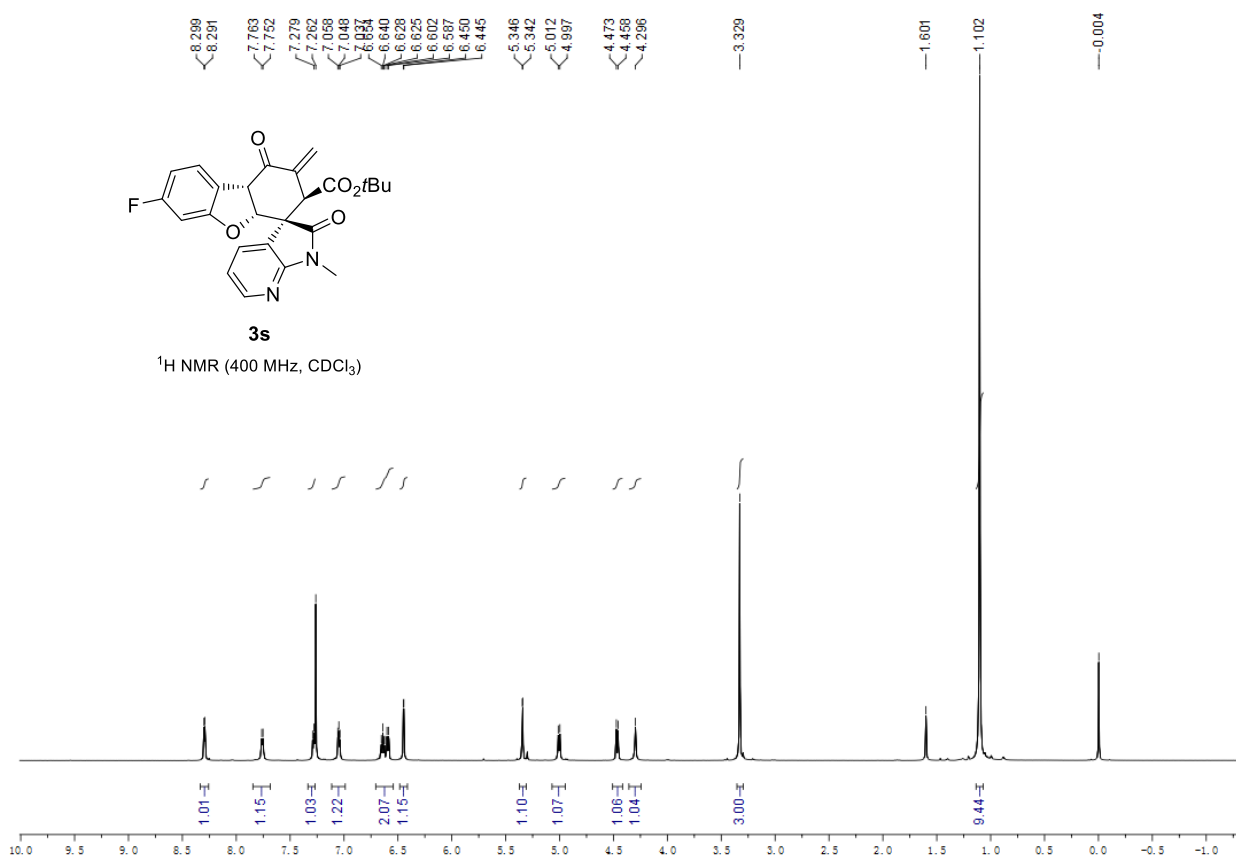
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.817	BBA	0.4834	4.42926e4	1397.26831	49.7165
2	18.901	BBA	0.7396	4.47978e4	875.59393	50.2835

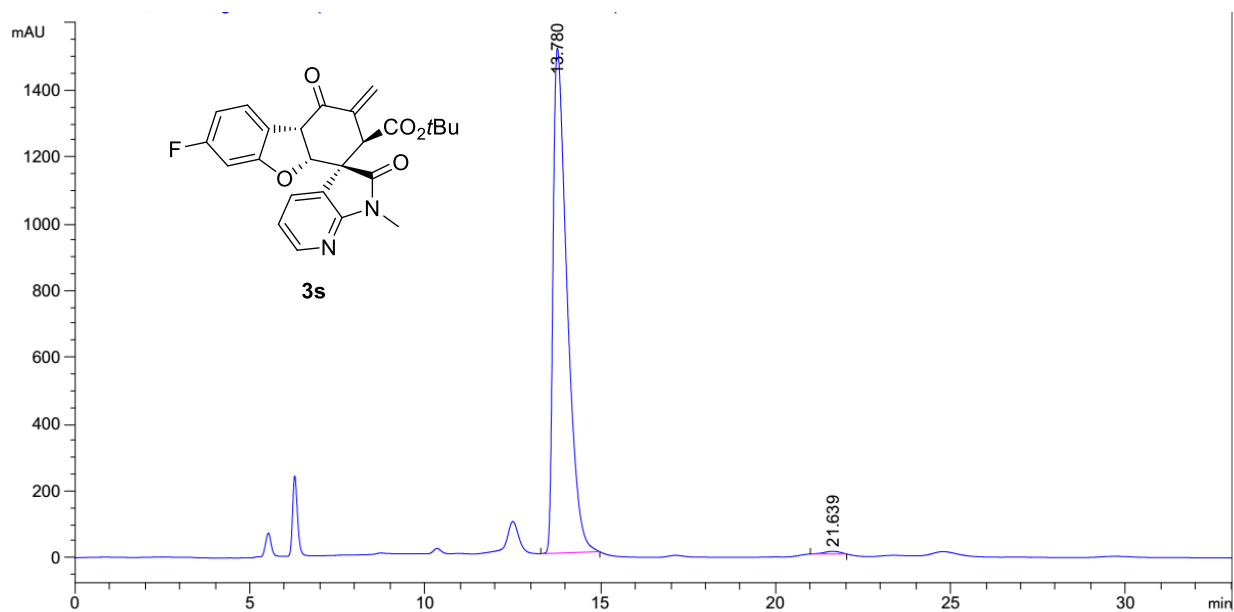
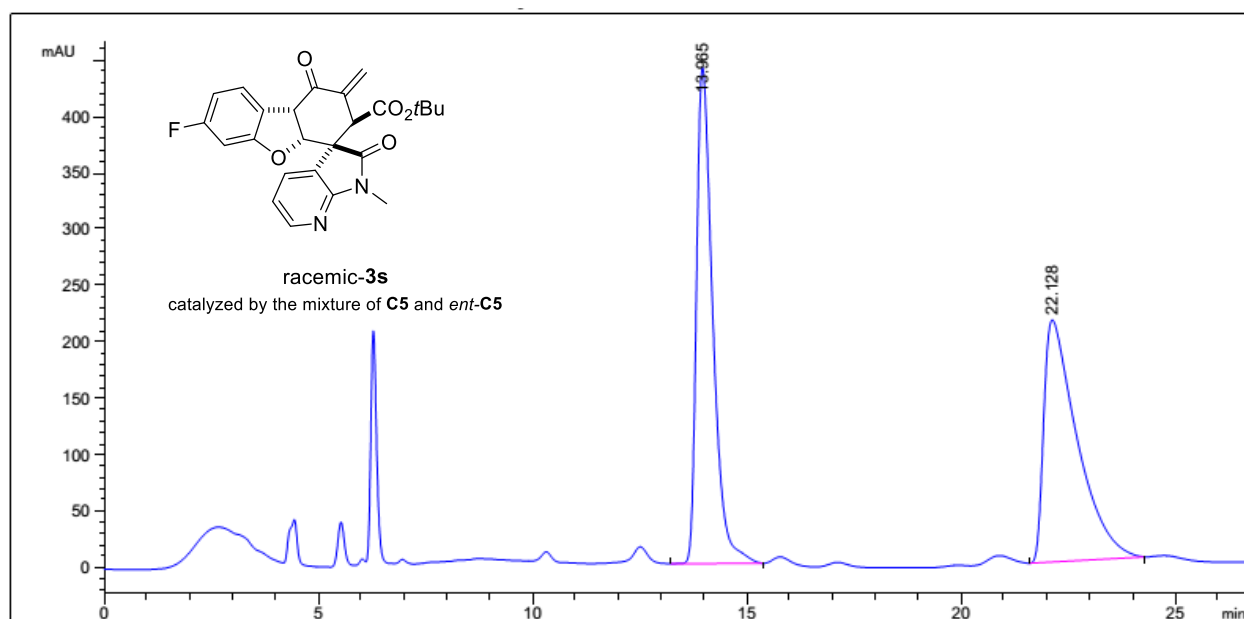


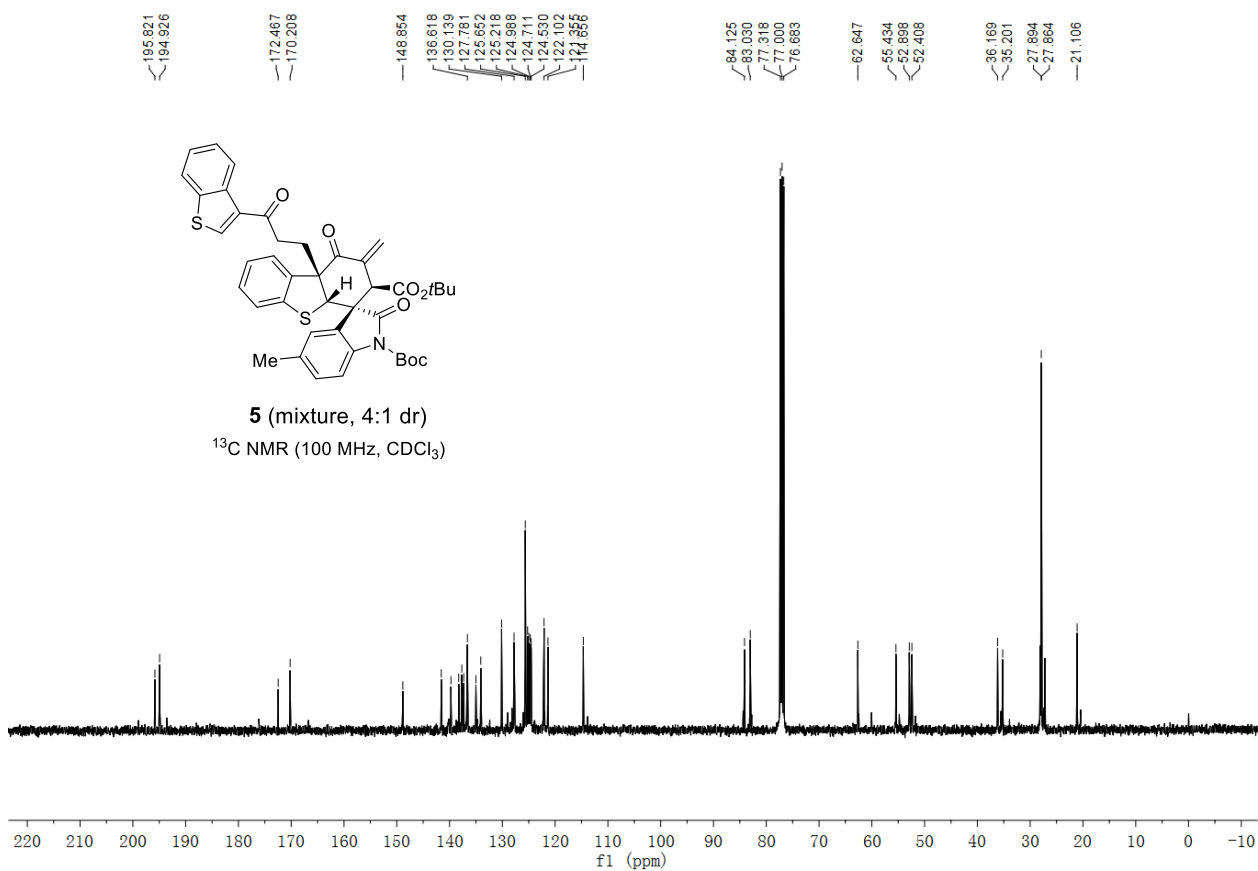
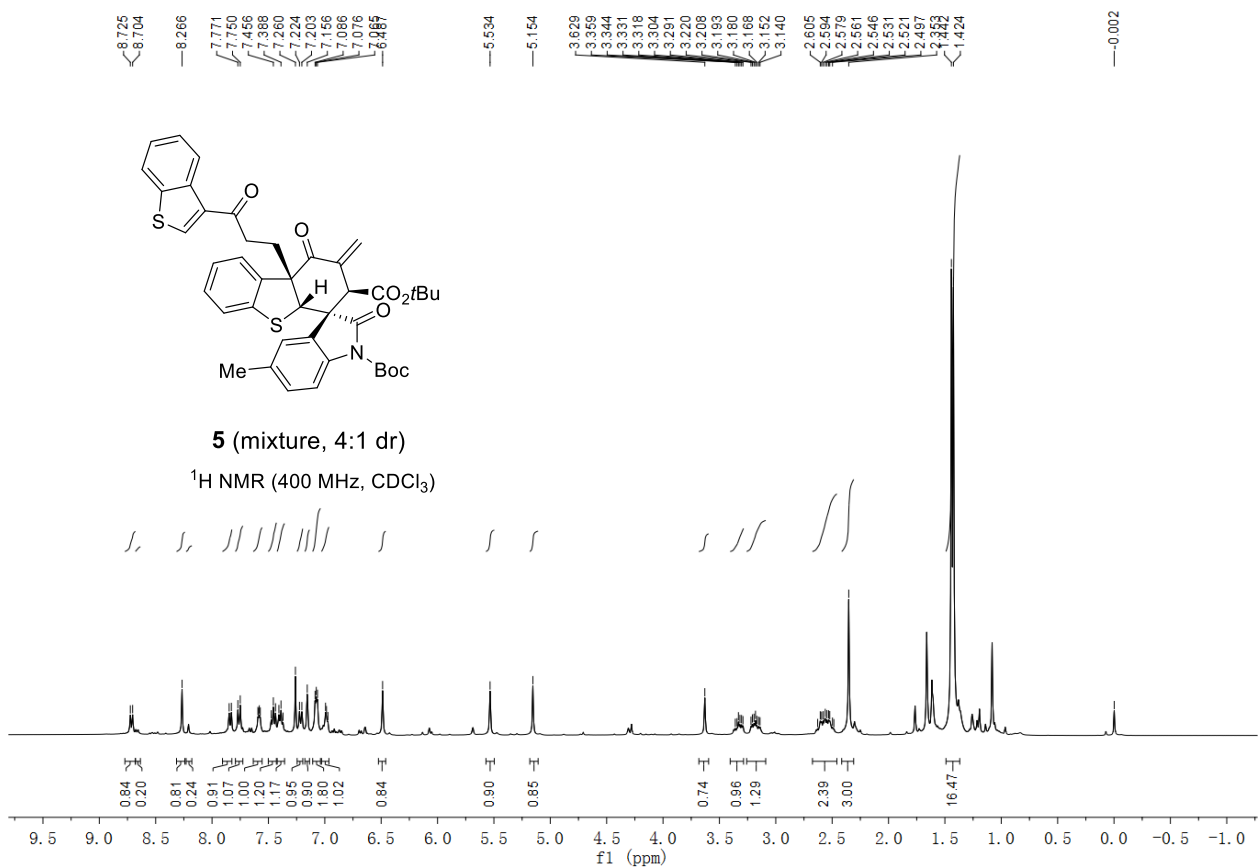
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.610	BBA	0.5057	8.44397e4	2531.21631	98.0960
2	18.103	BBA	0.7861	1638.90247	32.51322	1.9040

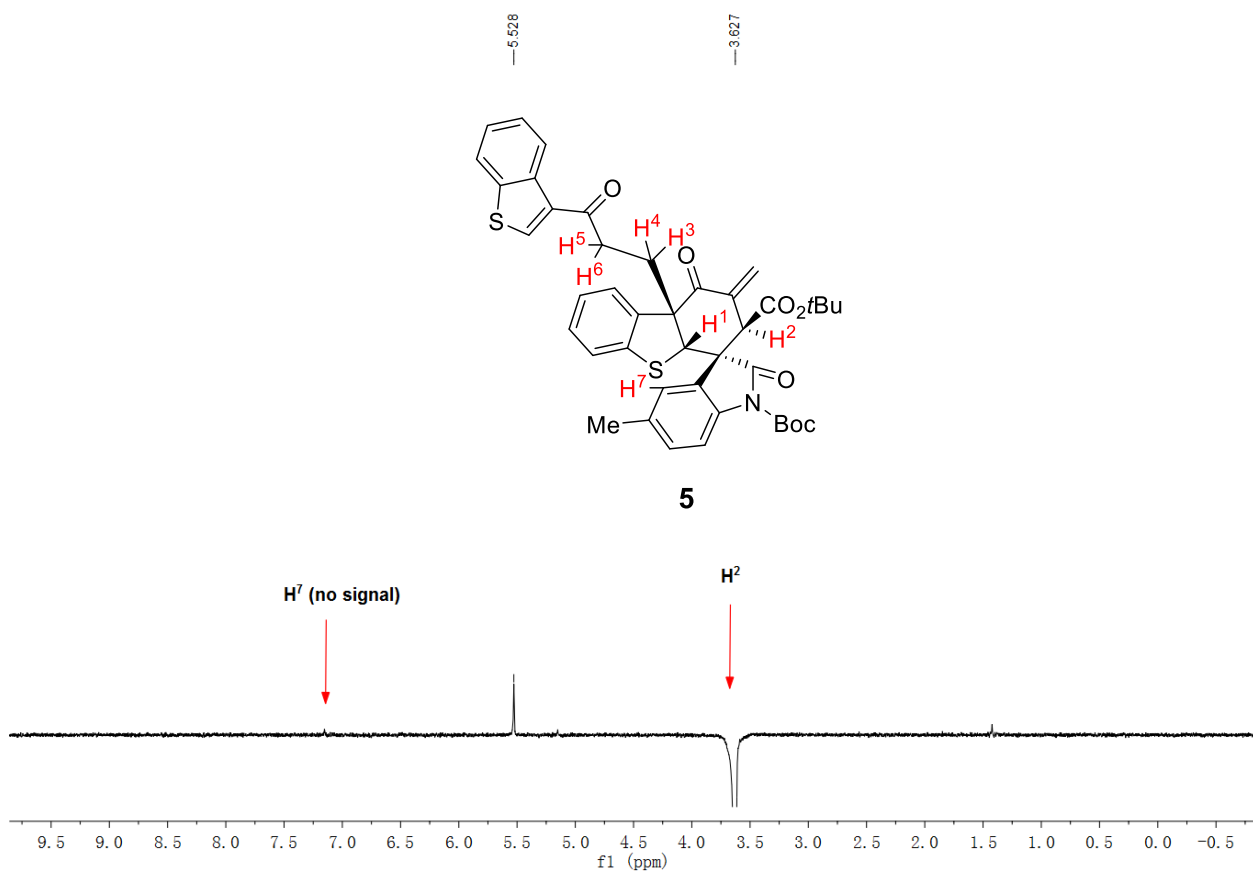
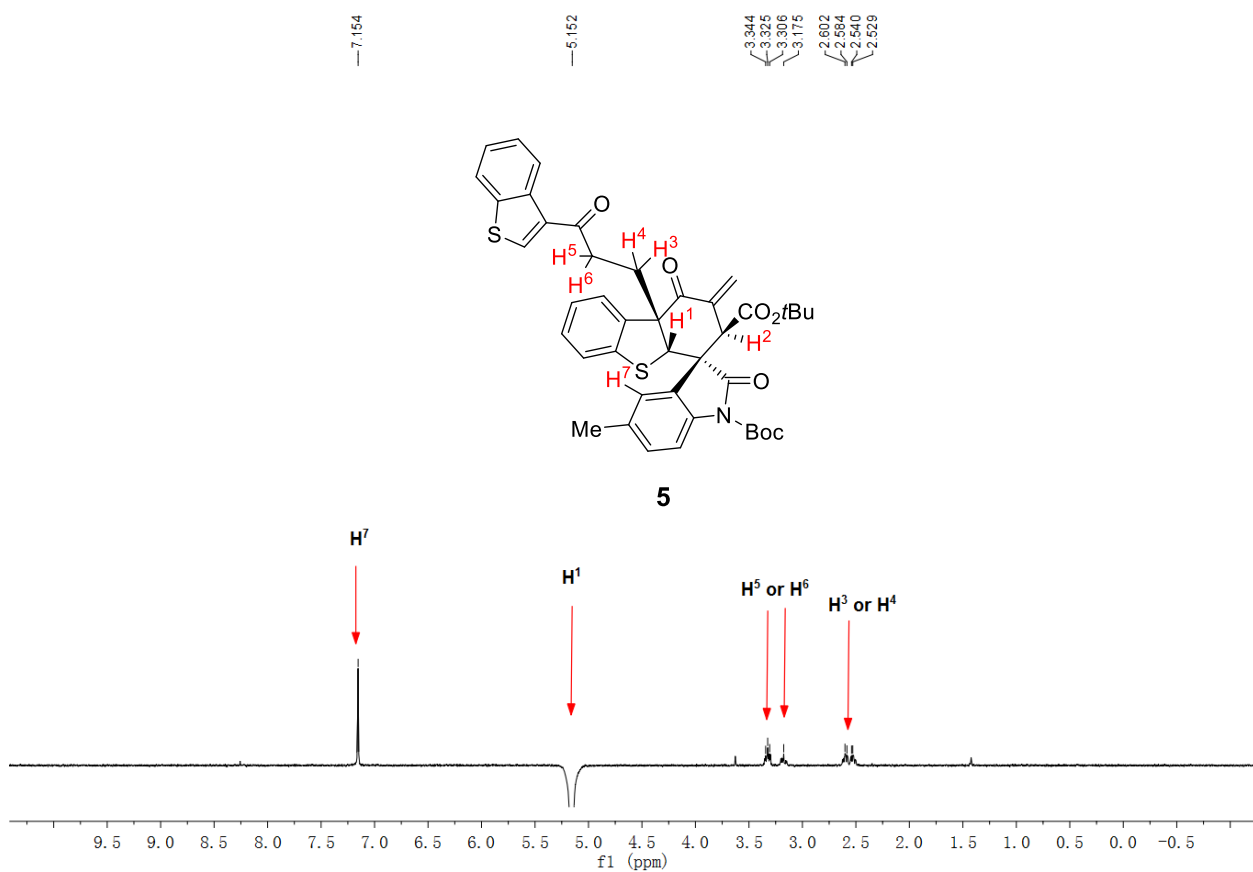


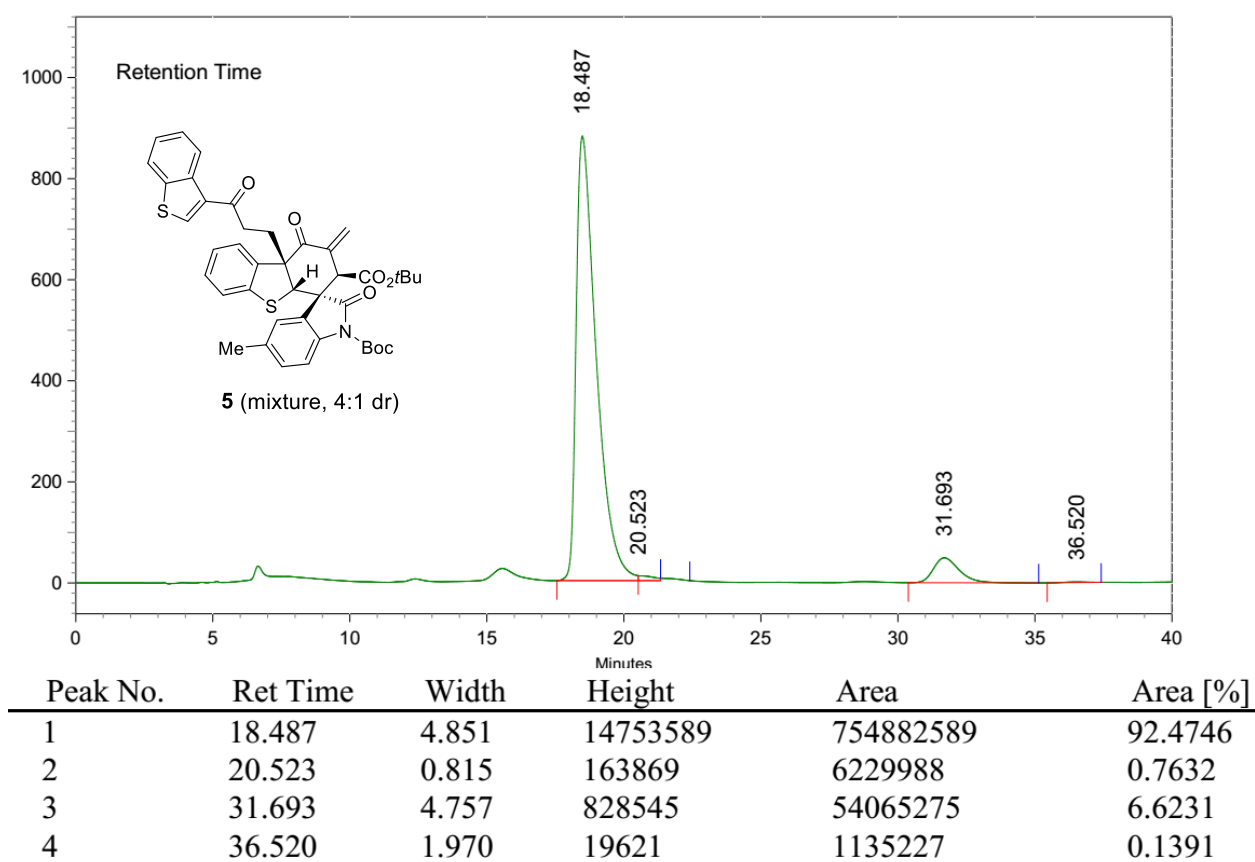
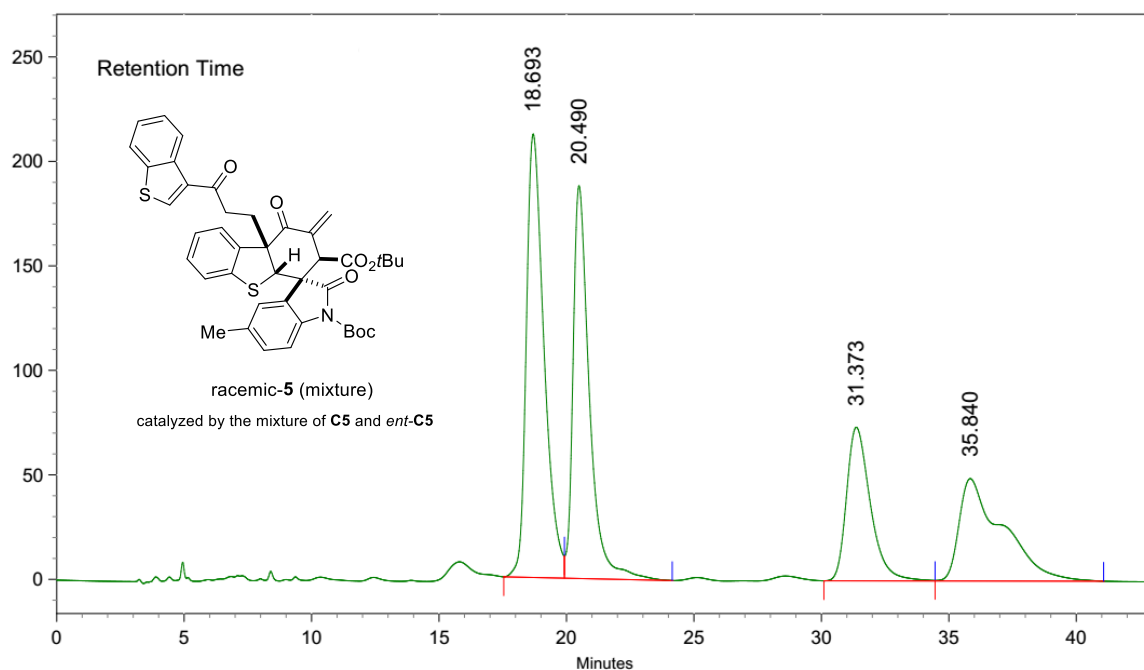


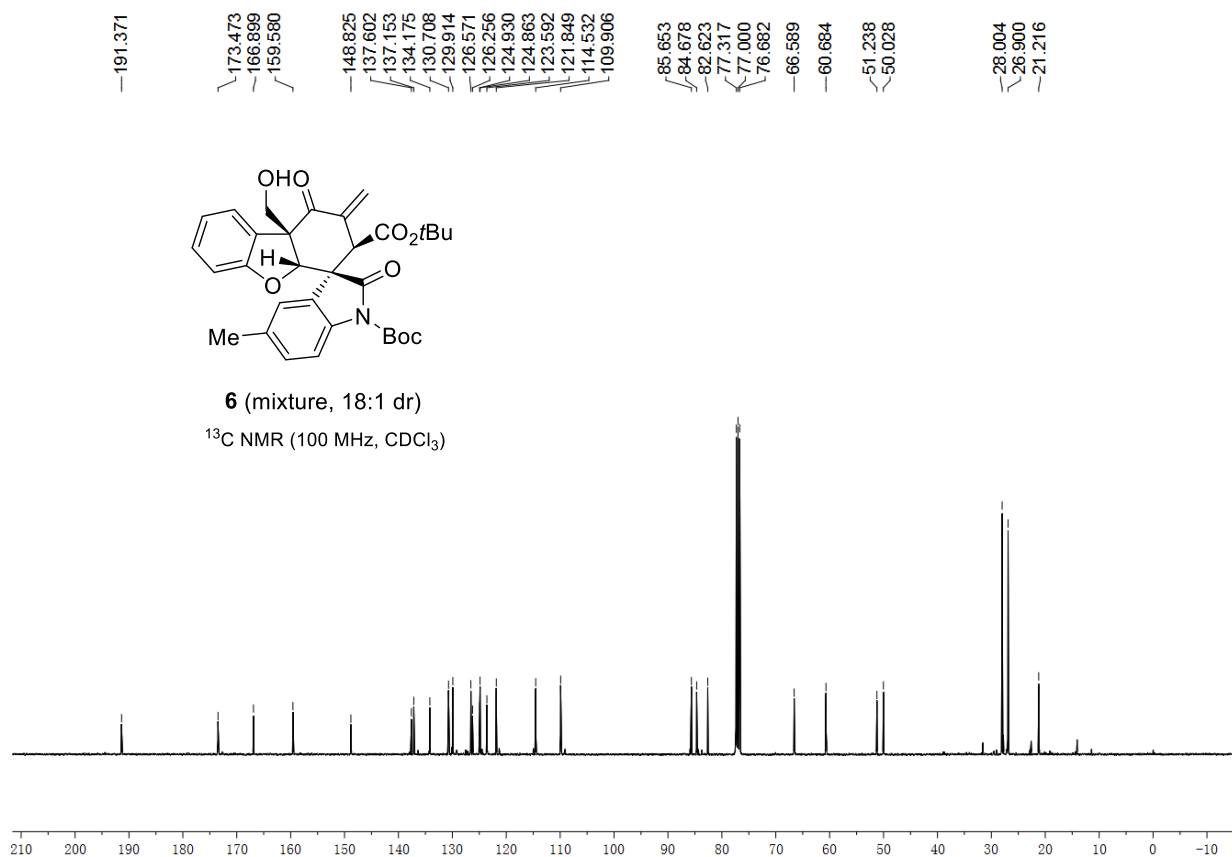
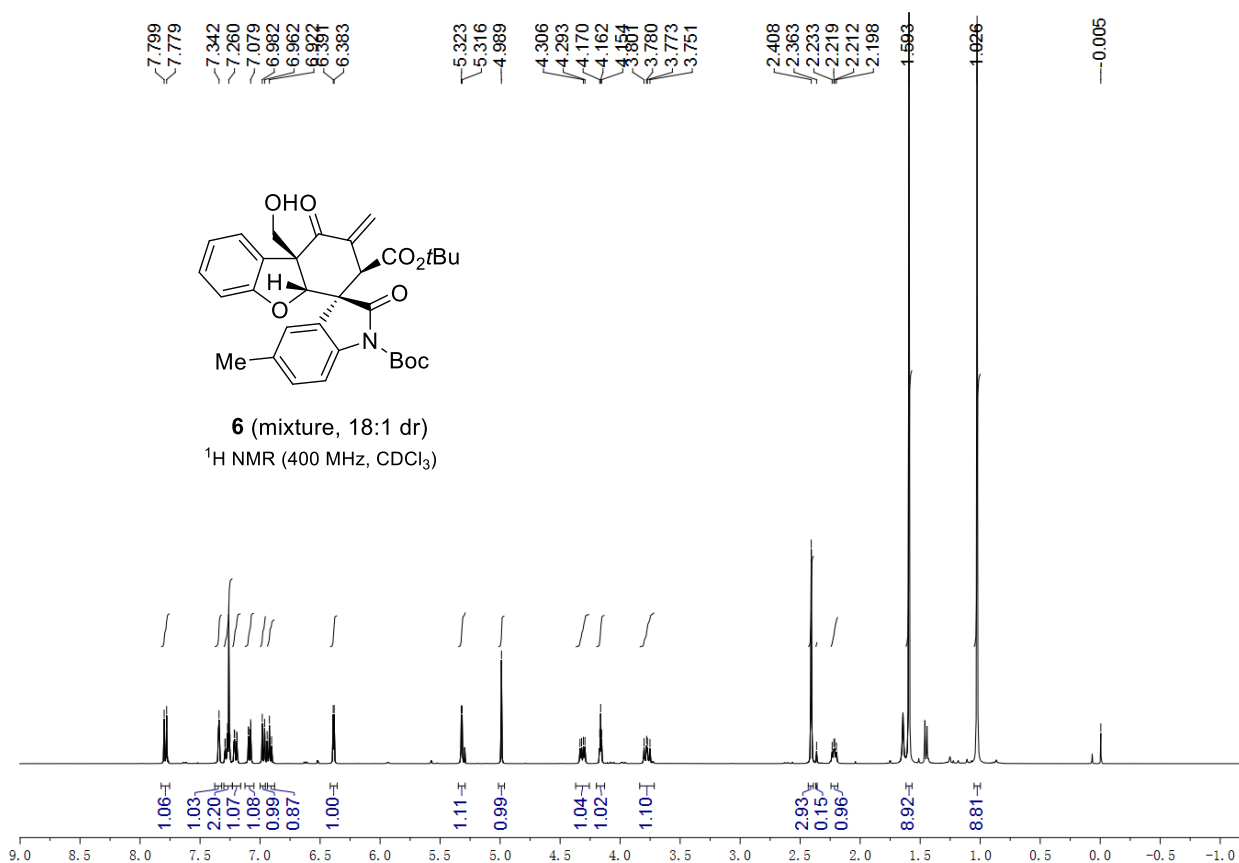




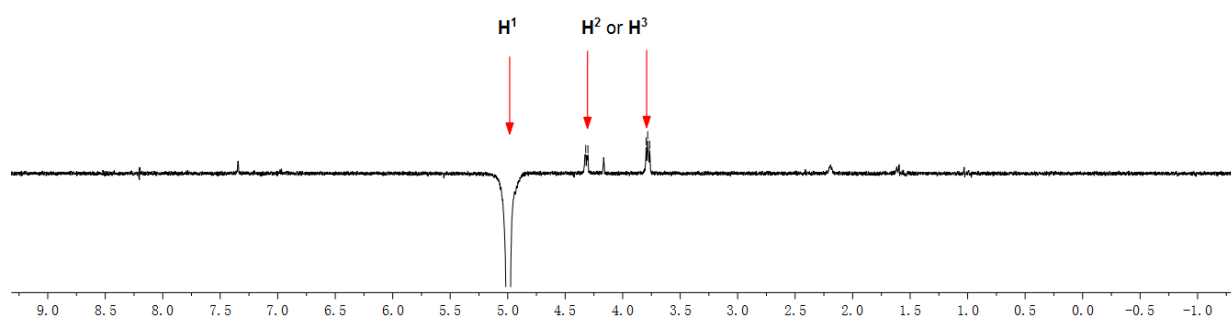
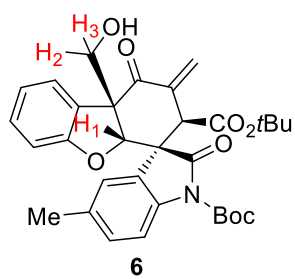


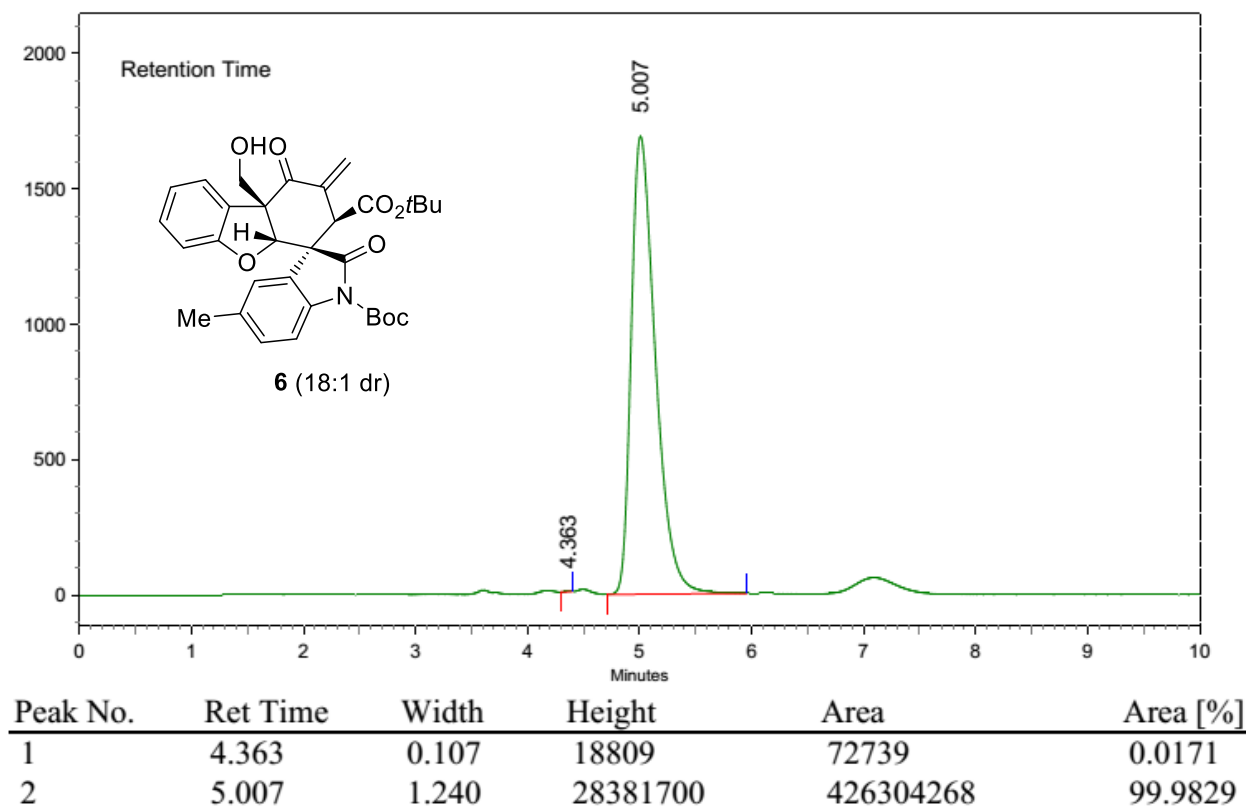
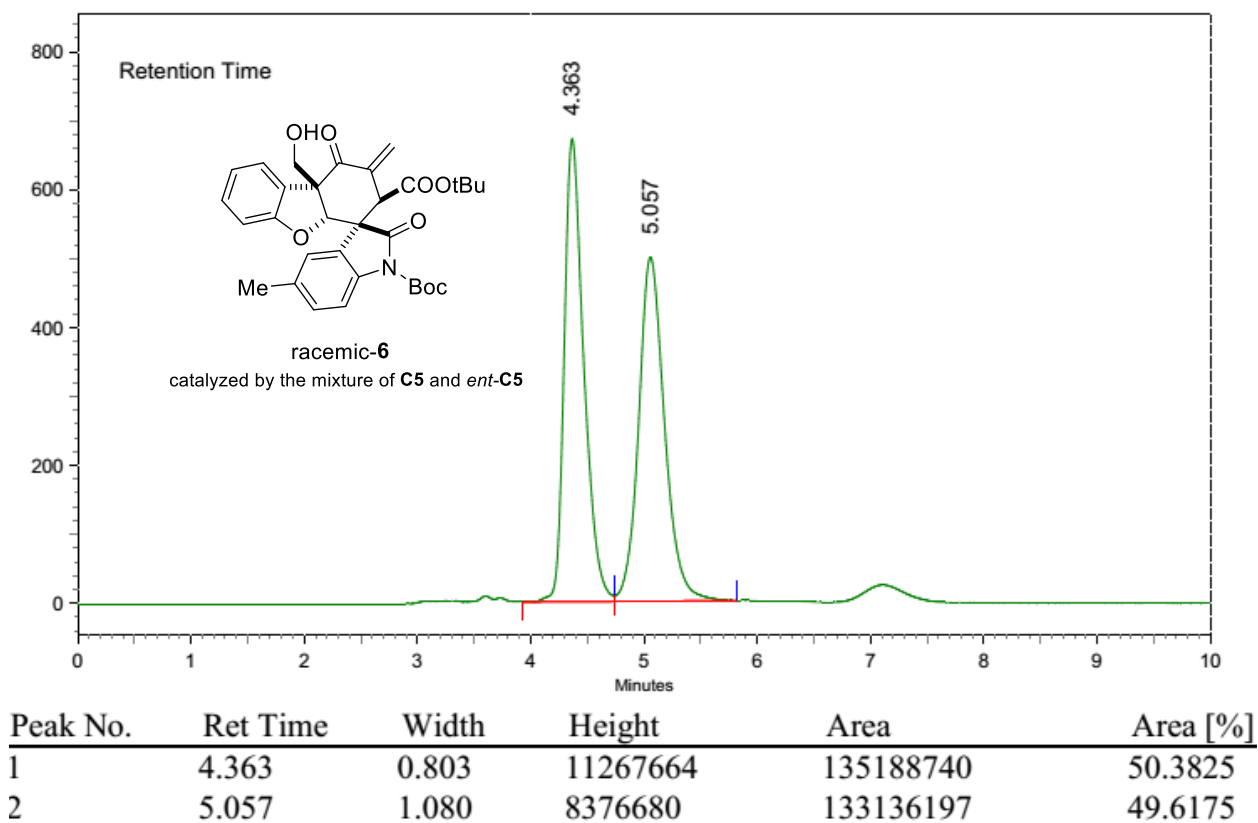


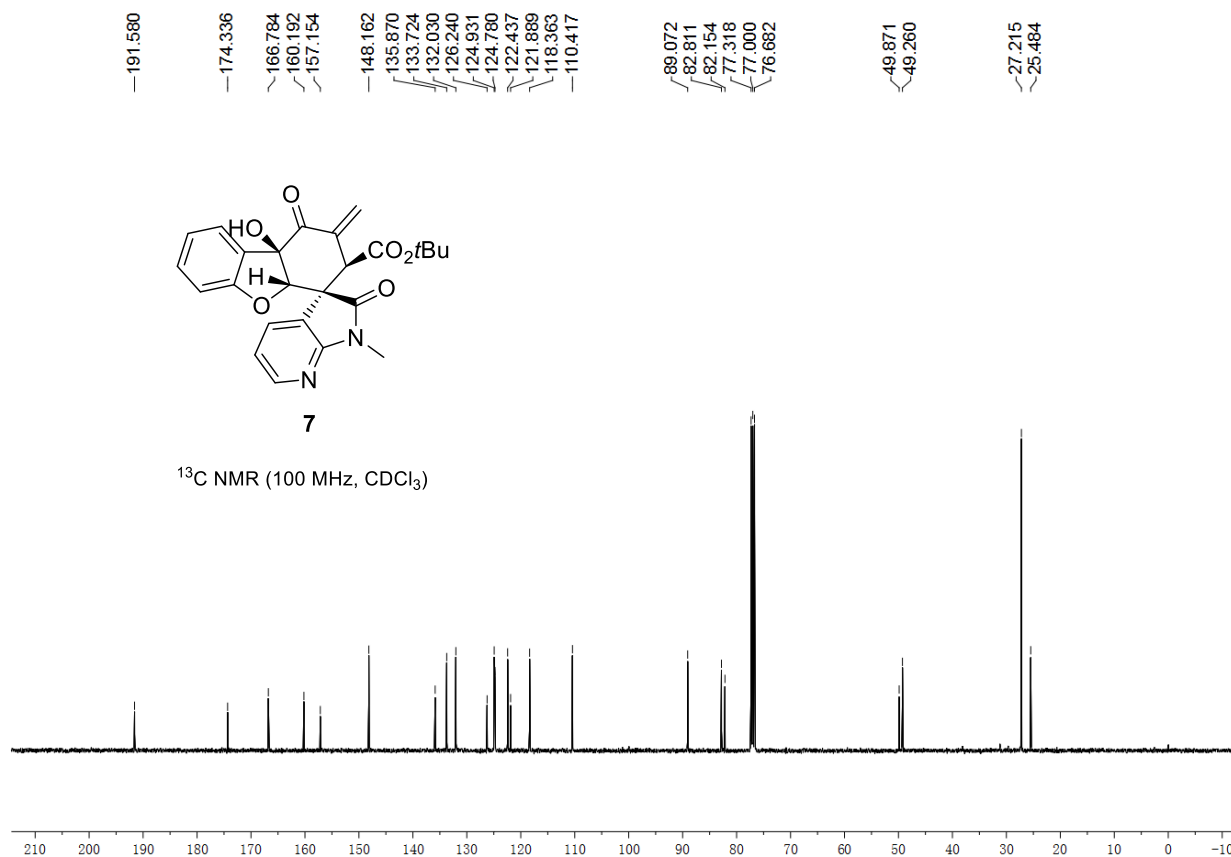
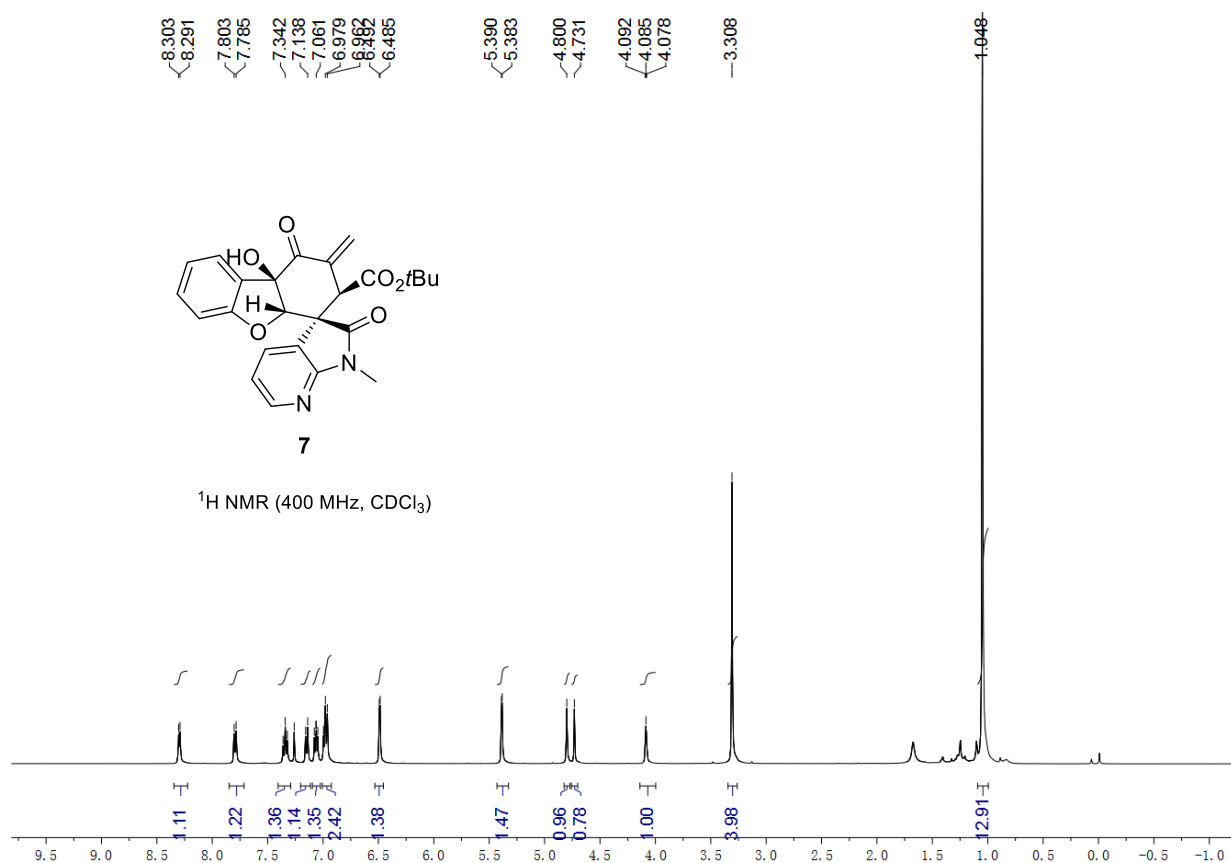


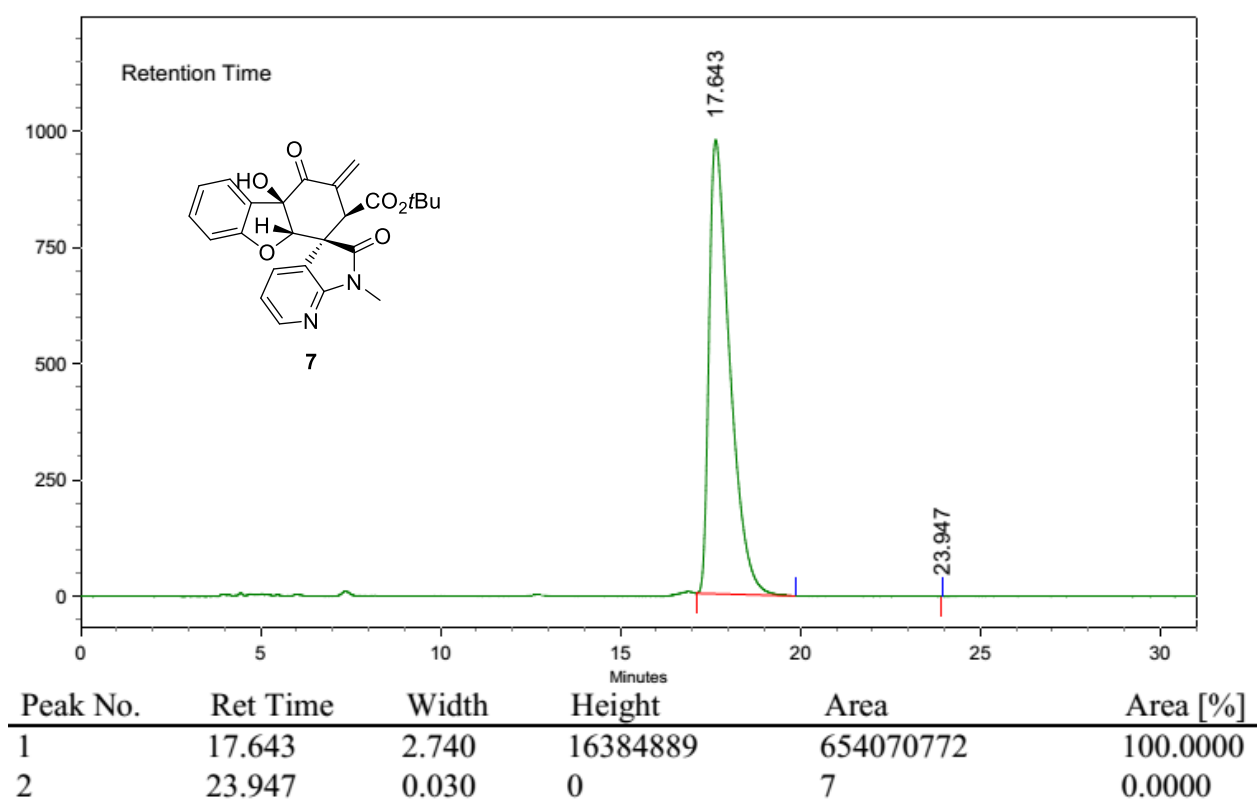
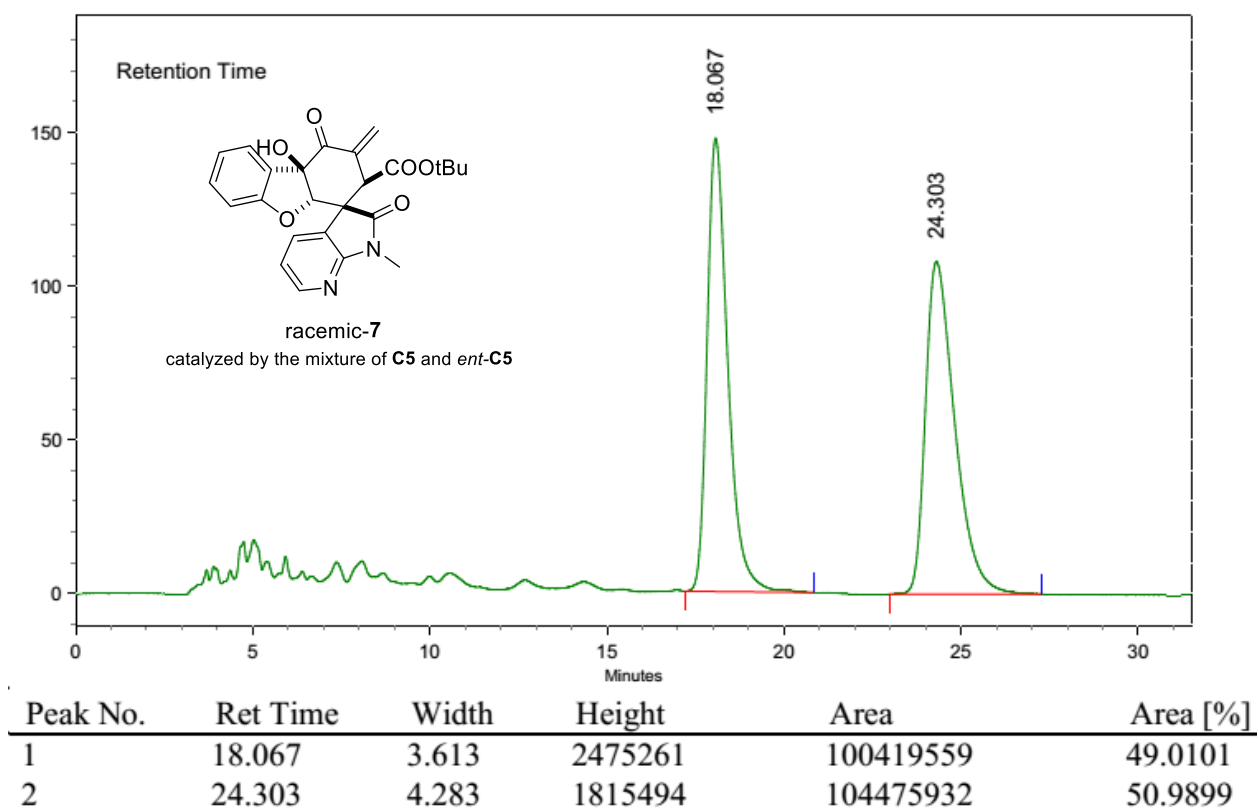


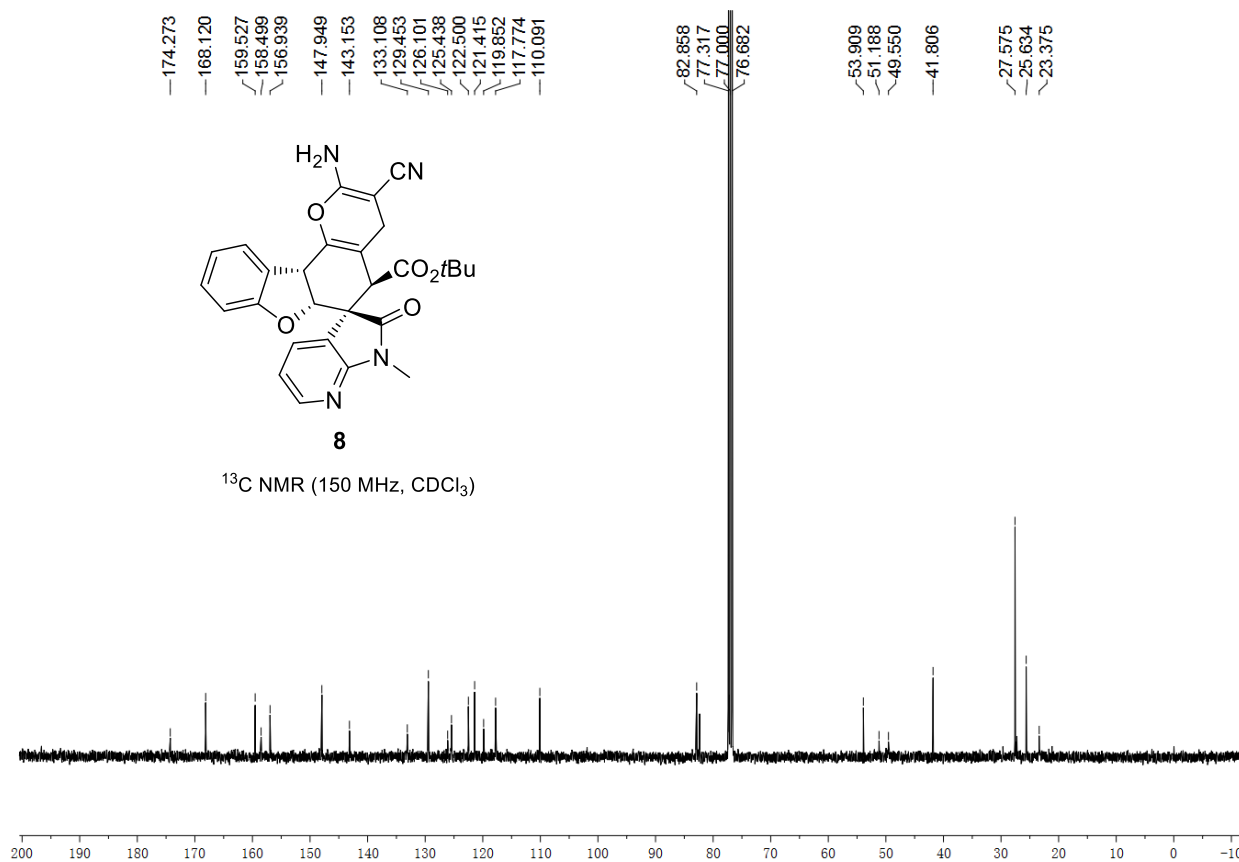
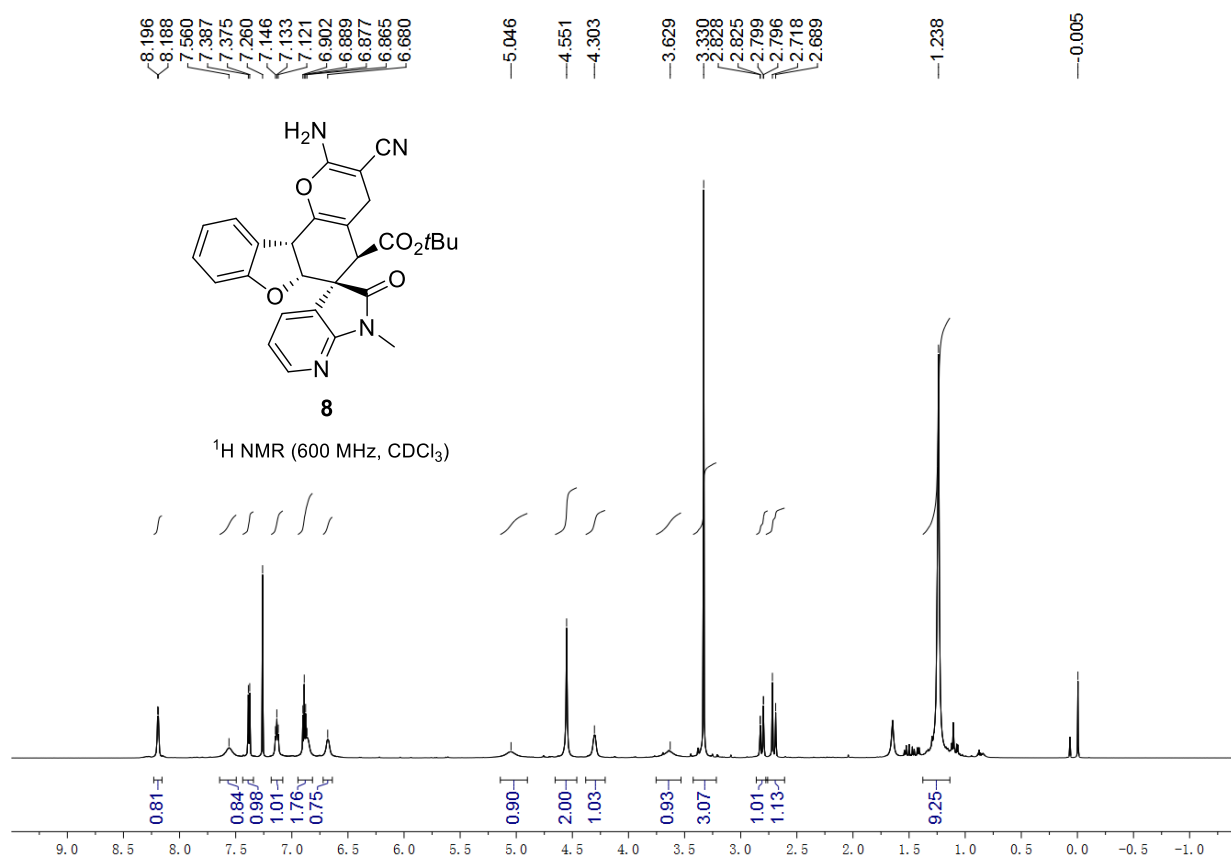
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3.764

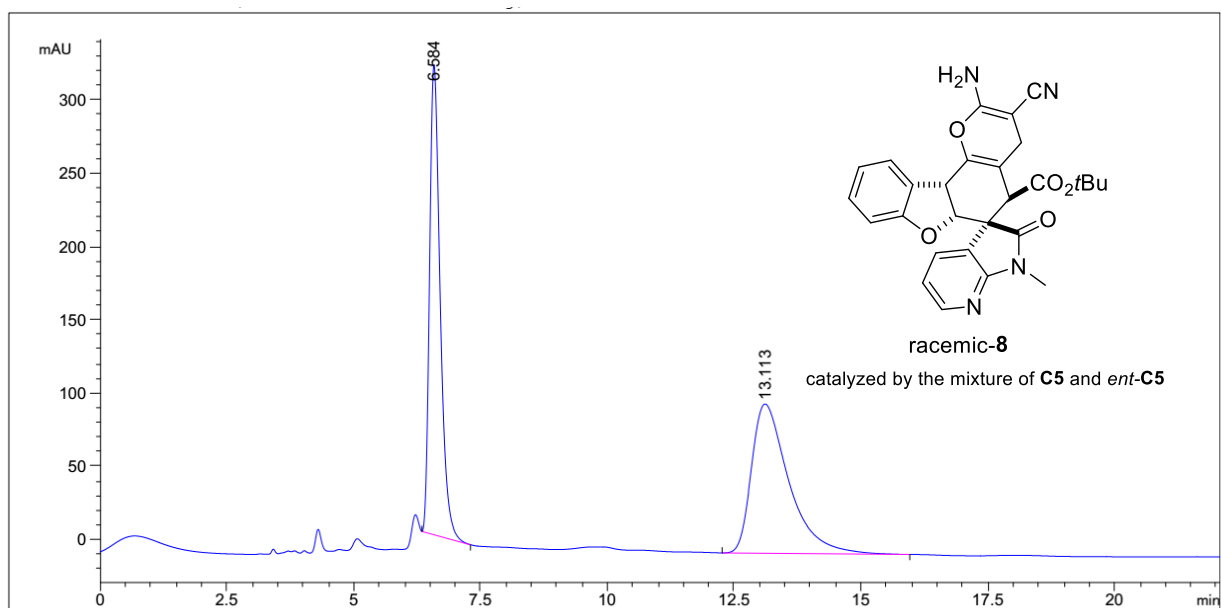




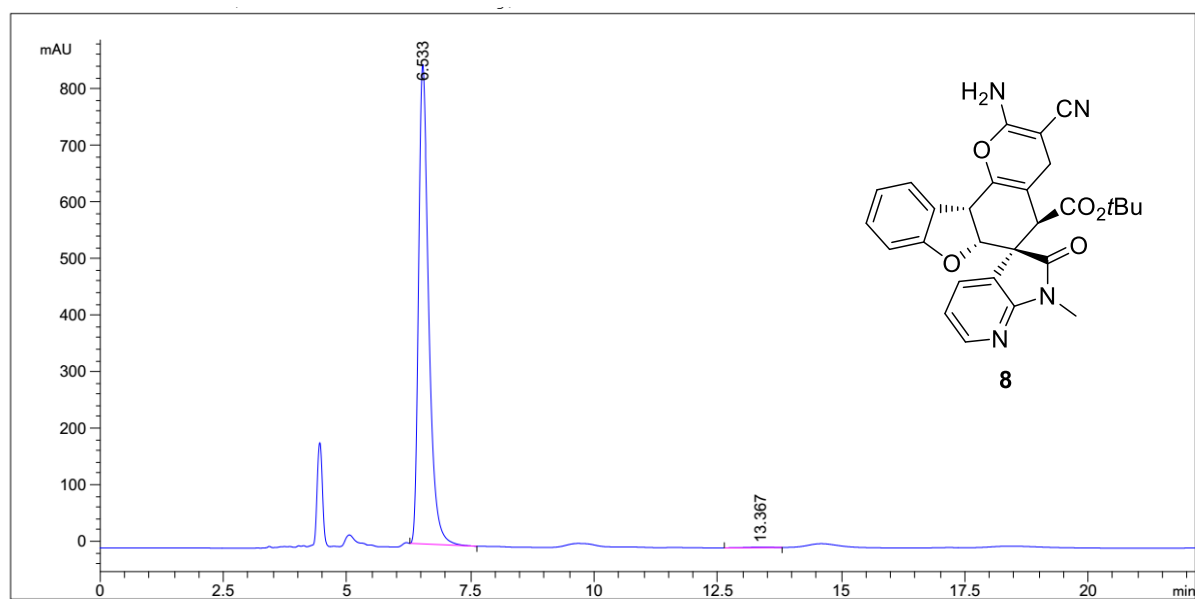








Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	6.584	BBA	0.2207	4626.56055		320.79388	47.0136
2	13.113	BBA	0.7691	5214.34424		101.84964	52.9864



Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	6.533	BBA	0.2182	1.21527e4		847.97198	99.8083
2	13.367	BB	0.4252	23.34227		7.79223e-1	0.1917