

Asymmetric β,γ' -Regioselective [4+3] and [4+2] Annulations of α -Vinylenals via Cascade Iminium Ion–Dienamine Catalysis

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Supplementary Information

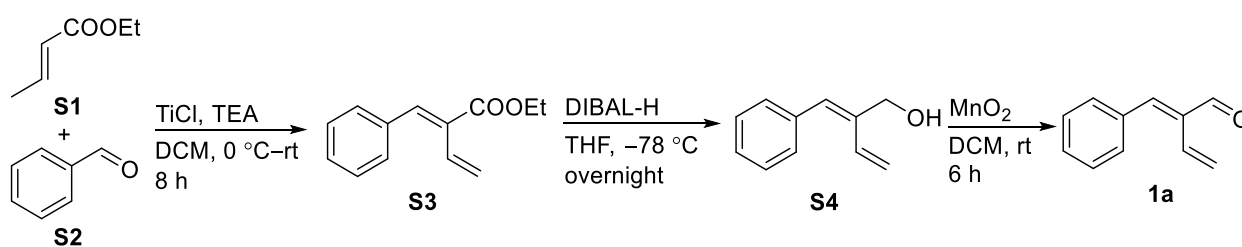
Table of Contents

1. General methods	S2
2. Typical procedure for the preparation of α -vinylenal 1a.....	S2
3. More screening conditions for asymmetric [4+3] and [4+2] annulations of α -vinylenals	S4
3.1 β,γ' -Regioselective [4+3] annulations of α -vinylenal 1a with <i>N</i> -(2,2,2-trifluoroethyl) ketimines 2 ...	S4
3.2 β,γ' -Regioselective [4+2] annulation of α -vinylenal 1a with 2-(thiochroman-4-ylidene)malononitrile 4a	S5
4. General procedure for asymmetric [4+3] and [4+2] annulations of α -vinylenals.....	S6
4.1 β,γ' -Regioselective [4+3] annulations of α -vinylenals 1 with <i>N</i> -(2,2,2-trifluoroethyl) ketimines 2....	S6
4.2 β,γ' -Regioselective [4+2] annulations of α -vinylenals 1 with α,α -dicyanoalkenes 4	S16
5. Transformation of product 3a	S22
6. More screening studies on other 1,3-dipoles, α -vinylenals and α,α -dicyanoalkenes	S23
7. Asymmetric reaction on a 1.0 mmol scale	S24
7.1 β,γ' -Regioselective [4+3] annulation of α -vinylenal 1a with <i>N</i> -(2,2,2-trifluoroethyl) ketimine 2a ..	S24
7.2 β,γ' -Regioselective [4+2] annulation of α -vinylenal 1a with 2-(thiochroman-4-ylidene)malononitrile 4a	S24
8. Crystal data and structural refinement	S24
9. Proposed catalytic cycle via cascade iminium ion-dienamine catalysis	S28
10. NMR, HRMS spectra and HPLC chromatograms.....	S29

1. General methods

Unless otherwise noted, all reactions were carried out under ambient atmosphere; when the reactions required heating, the heat source was oil bath. ^1H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR (376 MHz) spectra were recorded on Varian INOVA-400/54, Agilent DD2-600/54 or Bruker AscendTM 400 instruments (Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in CDCl_3 solution, unless otherwise noted). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, dd = double doublet, ddd = double double doublet, dt = double triplet; td = triple doublet; tt = triple triplet, m = multiplet, br = broad, and coupling constants (J) are reported in Hertz (Hz). High resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2, Agilent G1969-85000 or Shimadzu LCMS-IT-TOF using a time-of-flight mass spectrometer equipped with electrospray ionization (ESI) source. X-ray diffraction experiments were carried out on an Agilent Gemini or Xcalibur E and the data obtained were deposited at the Cambridge Crystallographic Data Centre. In each case, diastereomeric ratio was determined by ^1H NMR analysis and enantiomeric excess was determined by HPLC (Agilent Technologies: 1220 Infinity II, 1200 Series, 1260 Infinity) analysis on a chiral column in comparison with authentic racemate, using a Daicel Chiralpak AD-H Column (250 \times 4.6 mm), Chiralpak IE (250 \times 4.6 mm) or Chiralpak IA Column (250 \times 4.6 mm). UV detection was monitored at 254 nm. The specific optical rotation was obtained from Rudolph Research Analytical Autopol I automatic polarimeter in CHCl_3 solution at 25 $^\circ\text{C}$. The melting point was obtained from WRX-4 Mel-Temp apparatus. Column chromatography was performed on silica gel (200–300 mesh) eluting with ethyl acetate (EtOAc) and petroleum ether. TLC was performed on glass-backed silica plates. UV light, I_2 , and 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 (60–90 $^\circ\text{C}$) was redistilled. The secondary amine catalyst **C4**,¹ *N*-(2,2,2-trifluoroethyl) ketimines **2**,² (2*E*,3*E*)-2-benzylidene-4-phenylbut-3-enal **1i**,³ and α,α -dicyanoalkenes **4**⁴ were prepared according to the literature procedures.

2. Typical procedure for the preparation of α -vinylenal **1a**



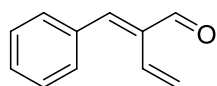
(*E*)-Ethyl 2-benzylidenebut-3-enoate **S3** was synthesized according to literature procedure.⁵

To a mixture of **S1** (1.14 g, 10.0 mmol, 1.0 equiv) and **S2** (1.06 g, 10.0 mmol, 1.0 equiv) in DCM

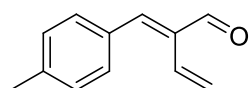
(80.0 mL) was added TEA (3.03 g, 30 mmol, 3.0 equiv). This mixture was kept in ice bath for 5 min before the slow dropwise addition of TiCl_4 (3.76 g, 20 mmol, 2.0 equiv). The mixture was stirred for further 8 h at room temperature. After completion monitored by TLC, the mixture was quenched with water (50 mL) and extracted with DCM (3 \times 30 mL). The combined organic phases were washed with brine (50 mL) and water (50 mL), dried over Na_2SO_4 , filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to afford **S3** as a yellow oil; 1.41 g, 70% yield.

To a solution of **S3** (1.41 g, 7.00 mmol, 1.0 equiv) in dry THF (15 mL) under a nitrogen atmosphere was added DIBAL-H (14.0 mL, 1.0 M solution in hexane, 14.0 mmol, 2.0 equiv) dropwise over a period of 30 min at -78°C . The mixture was then stirred overnight. After completion monitored by TLC, the reaction mixture is carefully quenched with 2 M HCl solution (10.0 mL), followed by extraction with EtOAc (3 \times 30 mL). The organic layers were combined, dried over Na_2SO_4 , filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/10) to afford **S4** as a yellow oil; 0.672 g, 60% yield.

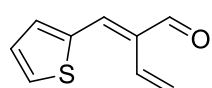
To a solution of **S4** (0.672 g, 4.20 mmol, 1.0 equiv) in DCM (10.0 mL) was added MnO_2 (1.82 g, 21.0 mmol, 5.0 equiv) in one portion and the mixture was stirred for 6 h at room temperature. After completion monitored by TLC, the mixture was filtered through a pad of celite and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to afford **1a** as a yellow oil; 531 mg, 80% yield.



(E)-2-Benzylidenebut-3-enal (1a): as a yellow oil; 531 mg, 80% yield for the last step (EtOAc/petroleum ether = 1/15); ^1H NMR (400 MHz, CDCl_3): δ (ppm) 9.67 (s, 1H), 7.51 (d, $J = 6.9$ Hz, 2H), 7.44–7.34 (m, 4H), 7.18 (s, 1H), 6.57 (dd, $J = 17.6, 11.6$ Hz, 1H), 6.15 (dd, $J = 17.9, 1.8$ Hz, 1H), 5.56 (d, $J = 12.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 193.8, 149.7, 136.5, 134.6, 130.3 (2C), 129.9, 128.6 (2C), 127.7, 122.5; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{11}\text{O}$ 159.0804; Found 159.0807.



(E)-2-(4-Methylbenzylidene)but-3-enal (1d): as a yellow oil; 420 mg, 70% yield for the last step (EtOAc/petroleum ether = 1/15); ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.66 (s, 1H), 7.44 (d, $J = 7.7$ Hz, 2H), 7.24 (d, $J = 7.8$ Hz, 2H), 7.17 (s, 1H), 6.58 (dd, $J = 17.8, 11.8$ Hz, 1H), 6.12 (d, $J = 17.6$ Hz, 1H), 5.57 (d, $J = 11.7$ Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 193.9, 150.0, 140.5, 135.9, 131.9, 130.5 (2C), 129.4 (2C), 127.9, 122.2, 21.5; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Ha}]^+$ Calcd for $\text{C}_{12}\text{H}_{12}\text{ONa}$ 195.0786; Found 195.0786.

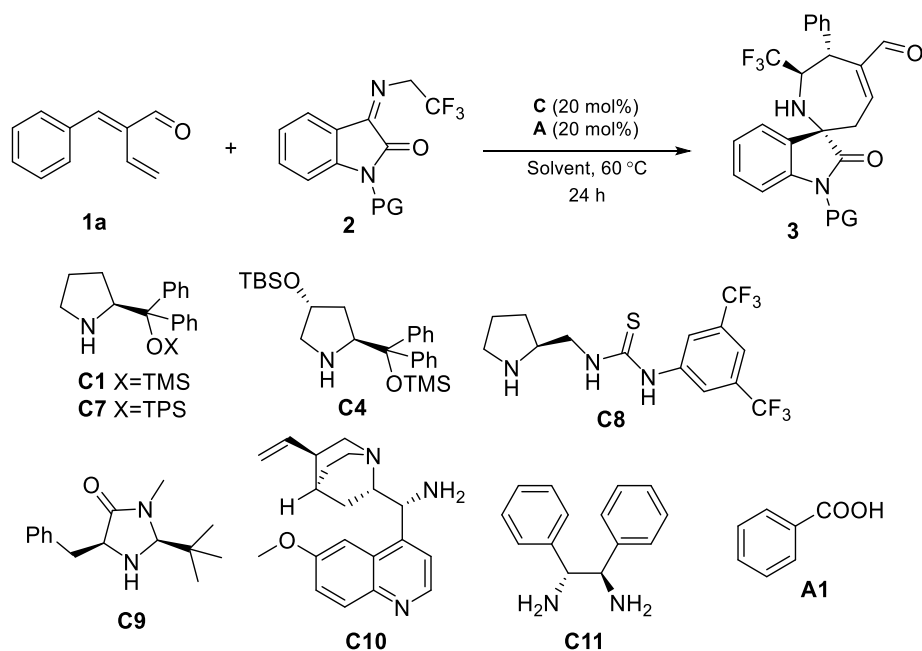


(E)-2-(Thiophen-2-ylmethylene)but-3-enal (1h): as a yellow oil; 340 mg, 72% yield for the last step (EtOAc/petroleum ether = 1/15); ^1H NMR (400 MHz, CDCl_3)

δ (ppm) 9.62 (s, 1H), 7.60 (d, $J = 5.1$ Hz, 1H), 7.41 (d, $J = 3.7$ Hz, 1H), 7.30 (s, 1H), 7.15 (t, $J = 4.3$ Hz, 1H), 6.74 (dd, $J = 17.6, 11.6$ Hz, 1H), 6.15 (d, $J = 17.0$ Hz, 1H), 5.66 (d, $J = 11.7$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 193.2, 141.5, 138.4, 134.3, 133.8, 132.4, 128.2, 127.7, 123.5; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_9\text{H}_9\text{OS}$ 165.0374; Found 165.0370.

3. More screening conditions for asymmetric [4+3] and [4+2] annulations of α -vinylenals

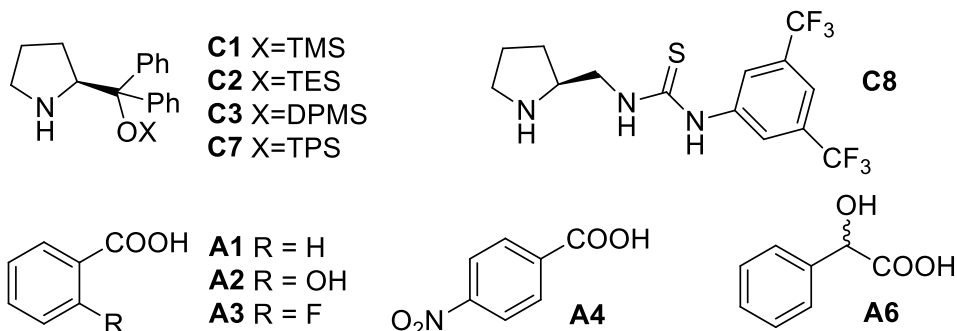
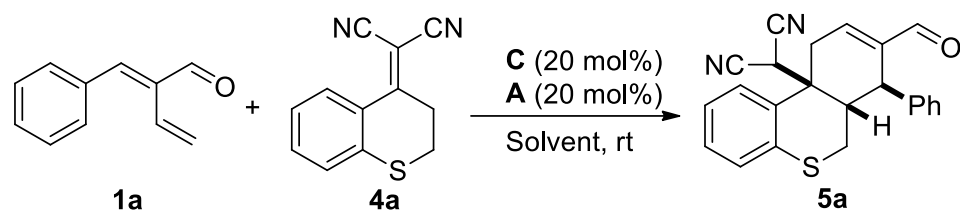
3.1 β,γ' -Regioselective [4+3] annulations of α -vinylenal **1a** with *N*-(2,2,2-trifluoroethyl) ketimines **2**^a



Entry	PG	C	A	Yield (%) ^b	ee (%) ^c
1	Boc	C1	A1	Trace	/
2	H	C1	A1	Messy	/
3	Me	C7	A1	40	82
4	Me	C8	A1	45	67
5	Me	C9	A1	NR	/
6	Me	C10	A1	NR	/
7	Me	C11	A1	NR	/
8	Me	C4	AcOH	50	80
9	Me	C4	TFA	NR	/

^a Unless noted otherwise, reactions were performed with enal **1a** (0.12 mmol, 1.2 equiv), isatin imine **2** (0.1 mmol, 1.0 equiv), amine **C** (0.02 mmol, 20 mol%) and acid **A** (0.02 mmol, 20 mol%) in solvent (0.2 mL) at 60 °C for 24 h. ^b Yield of the isolated product. ^c Determined by HPLC analysis on a chiral stationary phase; dr >19:1 by ^1H NMR analysis.

3.2 β,γ' -Regioselective [4+2] annulation of α -vinylenal **1a** with α,α -dicyanoalkene **4a**^a

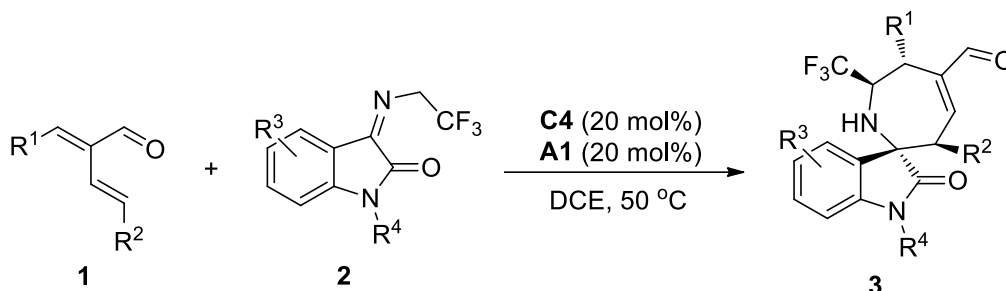


Entry	C	A	Solvent	Yield (%) ^b	ee (%) ^c
1	C1	A1	THF	69	97
2	C2	A1	THF	87	97
3	C3	A1	THF	70	98
4	C7	A1	THF	54	96
5	C8	A1	THF	90	67
6	C2	A2	THF	60	92
7	C2	A3	THF	65	96
8	C2	A4	THF	92	98
9	C2	A6	THF	86	95
10	C2	A4	Toluene	55	93
11	C2	A4	CHCl ₃	50	93
12	C2	A4	DCM	62	99
13	C2	A4	CH ₃ CN	87	92

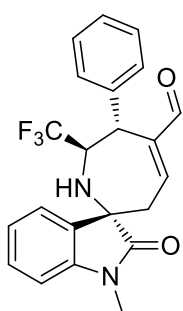
^aUnless noted otherwise, reactions were performed with enal **1a** (0.12 mmol, 1.2 equiv), α,α -dicyanoalkene **4a** (0.1 mmol, 1.0 equiv), amine **C** (0.02 mmol, 20 mol%) and acid **A** (0.02 mmol, 20 mol%) in solvent (0.2 mL) at rt for 12 h. ^bYield of the isolated product. ^cDetermined by HPLC analysis on a chiral stationary phase; dr >19:1 by ¹H NMR analysis.

4. General procedure for asymmetric [4+3] and [4+2] annulations of α -vinylenals

4.1 β,γ' -Regioselective [4+3] annulations of α -vinylenals **1** with *N*-(2,2,2-trifluoroethyl) ketimines **2**

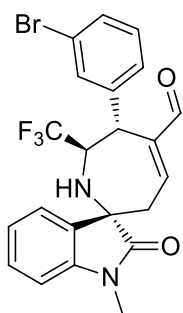


A mixture of α -vinylenal **1** (0.120 mmol, 1.2 equiv), *N*-(2,2,2-trifluoroethyl) ketimine **2** (0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12–24 h, and the reaction was monitored by TLC. After completion, the product **3** was obtained by flash chromatography on silica gel (EtOAc/petroleum ether). The racemic **3** could not be obtained by using the achiral amine catalysts, so the mixture of chiral catalyst **C1** and its enantiomer *ent*-**C1** was used for the preparation of the racemate.



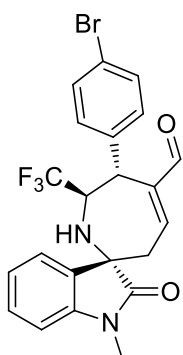
Synthesis of 3a: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 24 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3a**: 30.0 mg (0.075 mmol), as a white solid, 75% yield; mp = 230–

231 °C; $[\alpha]_D^{25} = +332.5$ ($c = 1.5$ in CHCl₃); >19:1 dr; 92% ee, determined by HPLC analysis [Chiralpak IE, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 16.22 min, t (minor) = 19.15 min]; ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.48 (s, 1H), 7.45–7.30 (m, 2H), 7.39–7.34 (m, 1H), 7.33–7.28 (m, 2H), 7.27–7.21 (m, 1H), 7.18–7.12 (m, 1H), 7.10–7.02 (m, 1H), 6.92 (dd, $J = 8.9, 6.2$ Hz, 1H), 6.89 (d, $J = 7.8$ Hz, 1H), 4.86–4.78 (m, 1H), 4.45 (d, $J = 10.8$ Hz, 1H), 3.78 (dd, $J = 14.8, 6.4$ Hz, 1H), 3.24 (s, 3H), 2.47 (dd, $J = 14.7, 8.9$ Hz, 1H), 2.07 (d, $J = 10.3$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 192.7, 177.1, 147.2, 144.6, 142.9, 139.6, 130.8, 130.0, 128.6 (2C), 128.4 (2C), 127.5, 125.9 (q, ¹ $J_{C-F} = 279.1$ Hz), 123.0, 122.3, 108.9, 61.86, 55.7 (q, ² $J_{C-F} = 27.5$ Hz), 46.2, 32.8, 26.3; ¹⁹F NMR (376 MHz, CDCl₃): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : [M + H]⁺ Calcd for C₂₂H₁₉F₃N₂O₂Na 423.1296; Found 423.1292.



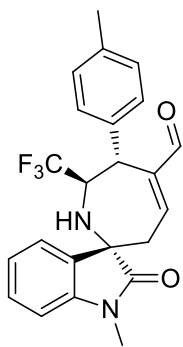
Synthesis of 3b: A mixture of (*E*)-2-(3-bromobenzylidene)but-3-enal **1b** (28.5 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 18 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3b**: 31.0 mg (0.0650 mmol), as a white solid, 65% yield; mp 134–135 °C; $[\alpha]_D^{25} = +310.4$ ($c = 1.5$ in CHCl_3); >19:1 dr; 87% ee, determined

by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 6.70 min, t (minor) = 8.14 min]; ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.47 (s, 1H), 7.51 (s, 1H), 7.40–7.30 (m, 3H), 7.20–7.12 (m, 2H), 7.06 (t, $J = 7.5$ Hz, 1H), 6.97 (dd, $J = 8.9, 6.2$ Hz, 1H), 6.89 (d, $J = 7.8$ Hz, 1H), 4.85–4.70 (m, 1H), 4.40 (d, $J = 10.8$ Hz, 1H), 3.72 (dd, $J = 14.7, 6.2$ Hz, 1H), 3.24 (s, 3H), 2.48 (dd, $J = 14.7, 8.9$ Hz, 1H), 2.07 (d, $J = 10.0$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 192.5, 177.1, 146.5, 145.2, 142.9, 141.7, 131.3, 130.7, 130.6, 130.1, 130.1, 127.4, 125.8 (q, ¹ $J_{\text{C-F}} = 279.8$ Hz), 123.1, 122.5, 122.4, 109.0, 61.8, 55.7 (q, ² $J_{\text{C-F}} = 27.5$ Hz), 45.9, 32.9, 26.3; ¹⁹F NMR (376 MHz, CDCl₃): δ (ppm) -73.8; HRMS (ESI-TOF) m/z : [M + H]⁺ Calcd for C₂₂H₁₉⁷⁹BrF₃N₂O₂ 479.0582; Found 479.0583; Calcd for C₂₂H₁₉⁸¹BrF₃N₂O₂ 481.0562; Found 481.0568.

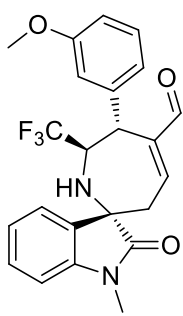


Synthesis of 3c: A mixture of (*E*)-2-(4-bromobenzylidene)but-3-enal **1c** (28.5 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 17 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3c**: 28.7 mg (0.0600 mmol), as a white solid, 60% yield; mp 233–134 °C; $[\alpha]_D^{25} = +378.7$ ($c = 1.5$ in CHCl_3); >19:1 dr; 88% ee, determined

by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 5.59 min, t (minor) = 6.34 min]; ¹H NMR (400 MHz, DMSO) δ (ppm) 8.76 (s, 1H), 6.85 (d, $J = 8.4$ Hz, 2H), 6.77–6.65 (m, 2H), 6.66 (d, $J = 8.4$ Hz, 2H), 6.46 (dd, $J = 8.9, 6.2$ Hz, 1H), 6.41 (t, $J = 7.5$ Hz, 2H), 3.93–3.78 (m, 1H), 3.65 (d, $J = 11.1$ Hz, 1H), 3.20 (d, $J = 10.2$ Hz, 1H), 2.91 (dd, $J = 14.7, 6.2$ Hz, 1H), 1.84 (s, 3H), 1.77 (dd, $J = 14.7, 9.0$ Hz, 1H); ¹³C NMR (100 MHz, DMSO) δ (ppm) 194.3, 177.3, 146.6, 146.4, 142.9, 140.5, 131.8 (2C), 131.0 (2C), 129.8, 126.8 (q, ¹ $J_{\text{C-F}} = 279.7$ Hz), 124.4, 122.6, 120.5, 109.2, 79.65, 62.4, 56.1 (q, ² $J_{\text{C-F}} = 27.7$ Hz), 45.4, 32.8, 26.4; ¹⁹F NMR (376 MHz, DMSO): δ (ppm) -66.8; HRMS (ESI-TOF) m/z : [M + Ha]⁺ Calcd for C₂₂H₁₈⁷⁹BrF₃N₂O₂Na 501.0401; Found 501.0399; Calcd for C₂₂H₁₈⁸¹BrF₃N₂O₂Na 503.0381; Found 503.0381.

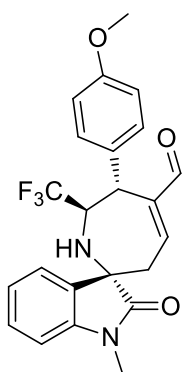


Synthesis of 3d: A mixture of (*E*)-2-(4-methylbenzylidene)but-3-enal **1d** (53.3 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3d**: 33.1 mg (0.0800 mmol), as a white solid, 80% yield; mp 297–298 °C; $[\alpha]_D^{25} = +312.2$ ($c = 1.6$ in CHCl_3); >19:1 dr; 91% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 5.22 min, t (minor) = 6.94 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.48 (s, 1H), 7.36 (t, $J = 7.7$ Hz, 1H), 7.33–7.28 (m, 2H), 7.15 (d, $J = 7.3$ Hz, 1H), 7.13–7.09 (m, 2H), 7.06 (t, $J = 7.5$ Hz, 1H), 6.90 (t, $J = 9.0$ Hz, 2H), 4.85–4.73 (m, 1H), 4.42 (d, $J = 10.8$ Hz, 1H), 3.77 (dd, $J = 14.6, 6.3$ Hz, 1H), 3.24 (s, 3H), 2.46 (dd, $J = 14.6, 8.8$ Hz, 1H), 2.31 (s, 3H), 2.07 (d, $J = 10.3$ Hz, 1H); ¹³C NMR (101 MHz, CDCl_3) δ (ppm) 192.8, 177.2, 147.3, 144.4, 142.9, 137.2, 136.6, 130.8, 130.0 (2C), 129.3 (2C), 128.3, 126.0 (q, ¹ $J_{\text{C-F}} = 279.8$ Hz), 123.0, 122.3, 108.9, 61.8, 55.6 (q, ² $J_{\text{C-F}} = 27.1$ Hz), 45.7, 32.8, 26.3, 21.1; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) -74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_2\text{Na}$ 437.1453; Found 437.1443.



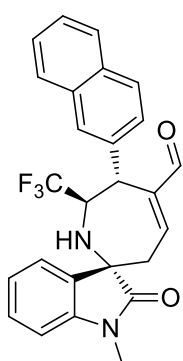
Synthesis of 3e: A mixture of (*E*)-2-(3-methoxybenzylidene)but-3-enal **1e** (22.6 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 13 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3e**: 34.4 mg (0.0800 mmol), as a white solid, 80% yield; mp 297–298 °C; $[\alpha]_D^{25} = +299.6$ ($c = 1.7$ in CHCl_3); >19:1 dr; 92% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 5.83 min, t (minor) = 6.59 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.49 (s, 1H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.24 (t, $J = 8.0$ Hz, 1H), 7.16 (d, $J = 7.6$ Hz, 1H), 7.10–7.02 (m, 2H), 6.98–6.87 (m, 3H), 6.79 (d, $J = 7.9$ Hz, 1H), 4.85–4.70 (m, 1H), 4.44 (d, $J = 10.8$ Hz, 1H), 3.81 (s, 3H), 3.77 (dd, $J = 14.6, 6.3$ Hz, 1H), 3.25 (s, 3H), 2.47 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.07 (d, $J = 10.2$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 177.1, 159.6, 147.0, 144.6, 142.9, 141.0, 130.8, 130.0, 129.6, 125.9 (q, ¹ $J_{\text{C-F}} = 276.9$ Hz), 123.0, 122.3, 108.9, 61.8, 55.6 (q, ² $J_{\text{C-F}} = 27.1$ Hz), 45.7, 32.8, 26.3, 21.1; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) -74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_3\text{Na}$ 451.1453; Found 451.1443.

(Hz), 123.0, 122.3, 120.6, 114.7, 112.5, 108.9, 61.8, 55.6 (q, $^2J_{C-F} = 27.5$ Hz), 55.2, 46.0, 32.8, 26.3. ^{19}F NMR (376 MHz, CDCl_3): δ (ppm) -74.0 ; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_3\text{Na}$ 453.1402; Found 453.1394.



Synthesis of 3f: A mixture of (*E*)-2-(4-methoxybenzylidene)but-3-enal **1f** (22.6 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 15 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3f**: 31.4 mg (0.0730 mmol), as a white solid, 73% yield; mp 235–236 °C; $[\alpha]_{\text{D}}^{25} = +315.5$ ($c = 1.5$ in CHCl_3); >19:1 dr; 86% ee, determined

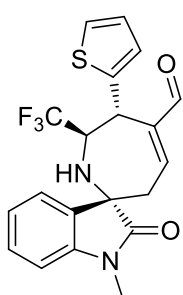
by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min^{-1} , $\lambda = 254$ nm, t (major) = 6.10 min, t (minor) = 9.28 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.48 (s, 1H), 7.36 (td, $J = 7.8, 1.3$ Hz, 1H), 7.34–7.31 (m, 2H), 7.14 (d, $J = 7.2$ Hz, 1H), 7.05 (t, $J = 7.5$ Hz, 1H), 6.92–6.87 (m, 2H), 6.83 (d, $J = 8.7$ Hz, 2H), 4.85–4.70 (m, 1H), 4.40 (d, $J = 10.8$ Hz, 1H), 3.78 (s, 3H), 3.74 (dd, $J = 14.4, 6.4$ Hz, 1H), 3.24 (s, 3H), 2.46 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.04 (d, $J = 10.1$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 192.8, 177.2, 158.8, 147.3, 144.1, 142.9, 131.7, 130.8, 130.0, 129.5 (2C), 126.0 (q, $^1J_{C-F} = 278.7$ Hz), 123.0, 122.3, 114.0 (2C), 108.9, 61.8, 55.7 (q, $^2J_{C-F} = 27.4$ Hz), 55.2, 45.3, 32.8, 26.3. ^{19}F NMR (376 MHz, CDCl_3): δ (ppm) -73.9 ; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_3\text{Na}$ 453.1402; Found 453.1392.



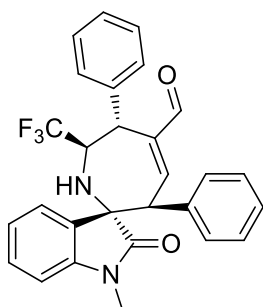
Synthesis of 3g: A mixture of (*E*)-2-(naphthalen-2-ylmethylene)but-3-enal **1g** (25.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3g**: 36.9 mg (0.0820 mmol), as a white solid, 82% yield; mp 229–230 °C; $[\alpha]_{\text{D}}^{25} = +356.7$ ($c = 1.8$ in CHCl_3); >19:1 dr; 96%

ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min^{-1} , $\lambda = 254$ nm, t (major) = 5.92 min, t (minor) = 11.05 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.47 (s, 1H),

7.86 (s, 1H), 7.84–7.75 (m, 3H), 7.53 (d, $J = 8.7$ Hz, 1H), 7.49–7.41 (m, 2H), 7.37 (t, $J = 7.7$ Hz, 1H), 7.17 (d, $J = 7.2$ Hz, 1H), 7.07 (t, $J = 7.5$ Hz, 1H), 6.98–6.92 (m, 1H), 6.89 (d, $J = 7.8$ Hz, 1H), 4.85–4.70 (m, 1H), 4.62 (d, $J = 10.8$ Hz, 1H), 3.88 (dd, $J = 14.6, 6.1$ Hz, 1H), 3.25 (s, 3H), 2.51 (dd, $J = 14.7, 8.9$ Hz, 1H), 2.12 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 177.2, 147.1, 144.6, 142.9, 137.0, 133.3, 132.7, 130.8, 130.1, 128.4, 127.9, 127.6, 127.4, 126.5, 126.2, 126.0, 125.9 (q, $^1J_{\text{C-F}} = 278.3$ Hz), 123.1, 122.4, 109.0, 61.9, 55.8 (q, $^2J_{\text{C-F}} = 27.3$ Hz), 46.4, 32.9, 26.4. ^{19}F NMR (376 MHz, CDCl_3): δ (ppm) -74.2 ; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{26}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_2\text{Na}$ 473.1453; Found 473.1456.

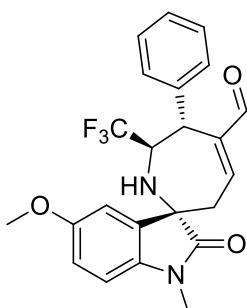


Synthesis of 3h: A mixture of (*E*)-2-(thiophen-2-ylmethylene)but-3-enal **1h** (19.7 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 20 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3h**: 32.4 mg (0.0800 mmol), as a white solid, 80% yield; mp 225–226 °C; $[\alpha]_{\text{D}}^{25} = +378.8$ ($c = 1.6$ in CHCl_3); >19:1 dr; 88% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min $^{-1}$, $\lambda = 254$ nm, t (major) = 6.70 min, t (minor) = 8.14 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.57 (s, 1H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.20–7.12 (m, 2H), 7.11–7.04 (m, 2H), 6.98–6.84 (m, 3H), 4.95–4.80 (m, 2H), 3.65 (dd, $J = 14.3, 6.7$ Hz, 1H), 3.25 (s, 3H), 2.44 (dd, $J = 14.3, 8.7$ Hz, 1H), 2.11 (d, $J = 9.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 192.1, 177.0, 146.6, 145.1, 142.9, 142.2, 130.6, 130.0, 126.9, 126.1, 125.8 (q, $^1J_{\text{C-F}} = 279.8$ Hz), 124.4, 123.0, 122.4, 109.0, 60.7, 56.2 (q, $^2J_{\text{C-F}} = 27.7$ Hz), 39.1, 33.2, 26.3. ^{19}F NMR (376 MHz, CDCl_3): δ (ppm) -74.9 ; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{17}\text{F}_3\text{NaO}_2\text{SNa}$ 429.0861; Found 429.0852.



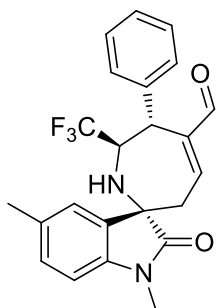
Synthesis of 3i: A mixture of (*2E,3E*)-2-benzylidene-4-phenylbut-3-enal **1i** (28.1 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (24.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash

chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3i**: 42.8 mg (0.0900 mmol), as a white solid, 90% yield; mp 226–227 °C; $[\alpha]_{\text{D}}^{25} = +298.1$ ($c = 2.0$ in CHCl_3); >19:1 dr; 92% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 4.53 min, t (major) = 4.99 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.53 (s, 1H), 7.48 (d, $J = 7.0$ Hz, 2H), 7.32 (t, $J = 7.5$ Hz, 2H), 7.28–7.22 (m, 3H), 7.14–7.04 (m, 5H), 6.98 (d, $J = 6.9$ Hz, 2H), 6.50 (d, $J = 7.7$ Hz, 1H), 5.18 (d, $J = 6.8$ Hz, 1H), 5.12–5.02 (m, 1H), 4.55 (d, $J = 10.6$ Hz, 1H), 2.84 (s, 3H), 2.29 (d, $J = 10.5$ Hz, 1H). ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 176.3, 149.8, 145.4, 143.5, 139.3, 134.6, 130.2, 128.76 (2C), 128.75 (2C), 128.4 (2C), 127.9 (2C), 127.7, 127.68, 127.65, 125.9 (q, $^1J_{\text{C-F}} = 279.1$ Hz), 122.8, 122.5, 108.5, 67.4, 55.5 (q, $^2J_{\text{C-F}} = 27.2$ Hz), 49.5, 45.6, 25.7. ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.1; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{28}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_2\text{Na}$ 499.1609; Found 499.1601.



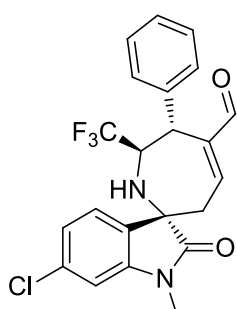
Synthesis of 3j: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-5-methoxy-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2b** (27.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 14 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3j**: 32.2 mg (0.0750 mmol), as a white solid, 75% yield; mp 220–221 °C; $[\alpha]_{\text{D}}^{25} = +335.4$ ($c = 1.6$ in

CHCl_3); >19:1 dr; 96% ee, determined by HPLC analysis [Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 9.15 min, t (minor) = 12.20 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.46 (d, $J = 1.5$ Hz, 1H), 7.41 (d, $J = 7.0$ Hz, 2H), 7.32–7.27 (m, 2H), 7.25–7.20 (m, 1H), 6.94–6.88 (m, 1H), 6.86 (dd, $J = 8.5, 2.5$ Hz, 1H), 6.79 (d, $J = 8.4$ Hz, 1H), 6.75 (d, $J = 2.5$ Hz, 1H), 4.85–4.70 (m, 1H), 4.44 (d, $J = 10.8$ Hz, 1H), 3.82–3.74 (m, 4H), 3.21 (s, 3H), 2.46 (dd, $J = 14.7, 8.9$ Hz, 1H), 2.04 (d, $J = 9.4$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 176.8, 156.2, 147.2, 144.4, 139.6, 136.2, 132.1, 128.6 (2C), 128.4 (2C), 127.5, 125.9 (q, $^1J_{\text{C-F}} = 278.4$ Hz), 113.1, 110.8, 109.2, 62.1, 55.9, 55.7 (q, $^2J_{\text{C-F}} = 27.5$ Hz), 46.1, 32.8, 26.4; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{N}_2\text{O}$ 431.1583; Found 431.1583.

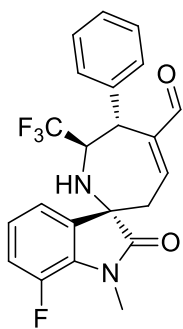


Synthesis of 3k: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1,5-dimethyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2c** (25.6 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 14 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3k**: 31.0 mg (0.0750 mmol), as a white solid, 75% yield; mp 225–226 °C; $[\alpha]_{\text{D}}^{25} = +295.5$ ($c = 1.5$ in CHCl_3); >19:1

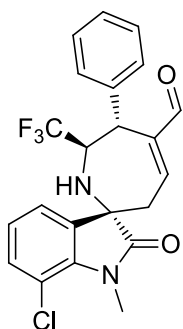
dr; 96% ee, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 4.70 min, t (minor) = 5.43 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.50 (s, 1H), 7.45–7.40 (m, 2H), 7.30 (t, $J = 7.3$ Hz, 2H), 7.23 (t, $J = 7.3$ Hz, 1H), 7.16 (d, $J = 7.8$ Hz, 1H), 6.98–6.89 (m, 2H), 6.78 (d, $J = 8.0$ Hz, 1H), 4.85–4.70 (m, 1H), 4.46 (d, $J = 10.8$ Hz, 1H), 3.77 (dd, $J = 14.6, 6.2$ Hz, 1H), 3.22 (s, 3H), 2.46 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.33 (s, 3H), 2.04 (d, $J = 10.0$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.8, 177.1, 147.1, 144.8, 140.4, 139.6, 132.7, 130.9, 130.2, 128.6 (2C), 128.4 (2C), 127.5, 125.9 (q, ¹ $J_{\text{C-F}} = 280.0$ Hz), 123.1, 108.7, 61.9, 55.7 (q, ² $J_{\text{C-F}} = 27.2$ Hz), 46.1, 32.8, 26.4, 21.1; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_2$ 415.1633; Found 415.1639.



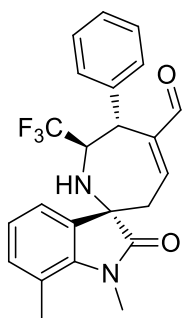
Synthesis of 3l: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-6-chloro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2d** (27.7 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 24 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3l**: 29.5 mg (0.0680 mmol), as a white solid, 68% yield; mp 223–224 °C; $[\alpha]_{\text{D}}^{25} = +348.7$ ($c = 1.4$ in CHCl_3); >19:1 dr; 94% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 8.28 min, t (minor) = 9.19 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.46 (s, 1H), 7.45–7.35 (m, 2H), 7.34–7.26 (m, 2H), 7.24 (t, $J = 7.3$ Hz, 1H), 7.08 (d, $J = 7.9$ Hz, 1H), 7.03 (dd, $J = 7.9, 1.8$ Hz, 1H), 6.93–6.85 (m, 2H), 4.84–4.67 (m, 1H), 4.44 (d, $J = 10.8$ Hz, 1H), 3.76 (dd, $J = 14.6, 6.1$ Hz, 1H), 3.22 (s, 3H), 2.45 (dd, $J = 14.7, 8.9$ Hz, 1H), 2.04 (d, $J = 9.9$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.6, 177.1, 147.4, 144.2, 143.9, 139.4, 136.0, 129.1, 128.7 (2C), 128.4 (2C), 127.6, 125.9 (q, ¹ $J_{\text{C-F}} = 279.8$ Hz), 123.4, 122.8, 109.7, 61.6, 55.8 (q, ² $J_{\text{C-F}} = 27.4$ Hz), 46.2, 32.7, 26.5; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –73.9; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{19}^{35}\text{ClF}_3\text{N}_2\text{O}_2$ 435.1087; Found 435.1089; Calcd for $\text{C}_{22}\text{H}_{19}^{37}\text{ClF}_3\text{N}_2\text{O}_2$ 437.1058; Found 437.1079.



Synthesis of 3m: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-7-fluoro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2e** (26.0 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3m**: 25.0 mg (0.0600 mmol), as a white solid, 60% yield; mp 220–221 °C; $[\alpha]_{\text{D}}^{25} = +315.8$ ($c = 1.2$ in CHCl_3); >19:1 dr; 94% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 6.91 min, t (minor) = 9.37 min]; ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.47 (s, 1H), 7.43–7.38 (m, 2H), 7.33–7.28 (m, 2H), 7.26–7.21 (m, 1H), 7.13–7.06 (m, 1H), 7.03–6.97 (m, 1H), 6.94 (dd, $J = 7.4, 1.3$ Hz, 1H), 6.89 (dd, $J = 8.9, 6.2$ Hz, 1H), 4.85–4.70 (m, 1H), 4.45 (d, $J = 10.8$ Hz, 1H), 3.77 (dd, $J = 14.7, 6.1$ Hz, 1H), 3.46 (d, $J = 2.8$ Hz, 3H), 2.48 (dd, $J = 14.7, 8.9$ Hz, 1H), 2.05 (d, $J = 10.1$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 192.6, 176.7, 148.0 (d, $^1J_{\text{C-F}} = 243.6$ Hz), 147.3, 144.0, 139.4, 133.6 (d, $^4J_{\text{C-F}} = 3.1$ Hz), 129.6 (d, $^3J_{\text{C-F}} = 8.5$ Hz), 128.7 (2C), 128.4 (2C), 127.6, 125.8 (q, $^1J_{\text{C-F}} = 279.6$ Hz), 123.8 (d, $^3J_{\text{C-F}} = 6.3$ Hz), 118.2, 118.1 (d, $^2J_{\text{C-F}} = 23.6$ Hz), 61.9, 55.6 (q, $^2J_{\text{C-F}} = 27.5$ Hz), 46.1, 32.8, 28.8; ¹⁹F NMR (376 MHz, CDCl₃): δ (ppm) –74.0, –135.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for C₂₂H₁₉F₄N₂O₂ 419.1383; Found 419.1384.

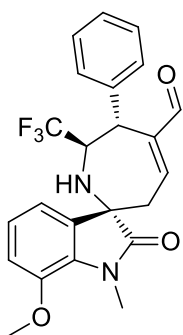


Synthesis of 3n: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-7-chloro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2f** (27.7 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 17 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3n**: 26.0 mg (0.0600 mmol), as a white solid, 60% yield; mp 233–234 °C; $[\alpha]_{\text{D}}^{25} = +348.2$ ($c = 1.2$ in CHCl_3); >19:1 dr; 94% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 7.17 min, t (minor) = 10.67 min]; ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.47 (s, 1H), 7.42–7.38 (m, 2H), 7.33–7.22 (m, 4H), 7.05 (d, $J = 7.0$ Hz, 1H), 6.96 (t, $J = 7.8$ Hz, 1H), 6.91–6.85 (m, 1H), 4.90–4.75 (m, 1H), 4.44 (d, $J = 10.8$ Hz, 1H), 3.76 (dd, $J = 14.5, 6.1$ Hz, 1H), 3.61 (s, 3H), 2.45 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.02 (d, $J = 10.2$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 192.6, 177.4, 147.3, 144.0, 139.4, 138.9, 133.5, 132.3, 128.7 (2C), 128.4 (2C), 127.6, 125.9 (q, $^1J_{\text{C-F}} = 279.8$ Hz), 123.8, 120.9, 116.5, 61.4, 55.7 (q, $^2J_{\text{C-F}} = 27.4$ Hz), 46.1, 32.9, 29.8; ¹⁹F NMR (376 MHz, CDCl₃): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for C₂₂H₁₈³⁵ClF₃N₂O₂Na 457.0907; Found 457.0892; Calcd for C₂₂H₁₈³⁷ClF₃N₂O₂Na 459.0877; Found 459.0868.



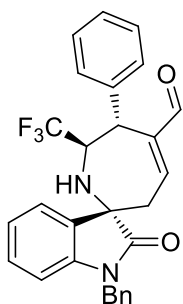
Synthesis of 3o: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1,7-dimethyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2g** (25.6 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3o**: 31.1 mg (0.0750 mmol), as a white solid, 75% yield; mp 219–220 °C; $[\alpha]_D^{25} = +307.6$ ($c = 1.5$ in CHCl_3); >19:1 dr; 80% ee, determined

by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 7.03 min, t (minor) = 8.89 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.47 (s, 1H), 7.44–7.39 (m, 2H), 7.33–7.27 (m, 2H), 7.23 (t, $J = 7.3$ Hz, 1H), 7.08 (d, $J = 7.4$ Hz, 1H), 6.98 (d, $J = 6.3$ Hz, 1H), 6.95–6.89 (m, 2H), 4.89–4.74 (m, 1H), 4.44 (d, $J = 10.8$ Hz, 1H), 3.76 (dd, $J = 14.6, 6.2$ Hz, 1H), 3.52 (s, 3H), 2.59 (s, 3H), 2.45 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.02 (d, $J = 10.2$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 177.8, 147.0, 144.8, 140.5, 139.6, 133.7, 131.6, 128.6 (2C), 128.4 (2C), 127.4, 125.9 (q, $^1J_{\text{C-F}} = 279.9$ Hz), 123.0, 120.7, 120.2, 61.1, 55.7 (q, $^2J_{\text{C-F}} = 27.47$ Hz), 46.1, 33.0, 29.7, 19.0; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_2$ 415.1633; Found 415.1635.



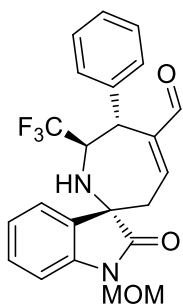
Synthesis of 3p: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-7-methoxy-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2h** (27.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 14 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3p**: 33.5 mg (0.0780 mmol), as a white solid, 78% yield;

mp 227–228 °C; $[\alpha]_D^{25} = +346.3$ ($c = 1.6$ in CHCl_3); >19:1 dr; 94% ee, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 7.69 min, t (minor) = 9.50 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.46 (s, 1H), 7.46–7.38 (m, 2H), 7.34–7.26 (m, 2H), 7.26–7.20 (m, 1H), 7.00 (t, $J = 7.9$ Hz, 1H), 6.95–6.85 (m, 2H), 6.76 (d, $J = 7.3$ Hz, 1H), 4.85–4.70 (m, 1H), 4.44 (d, $J = 10.8$ Hz, 1H), 3.86 (s, 3H), 3.75 (dd, $J = 14.7, 6.2$ Hz, 1H), 3.50 (s, 3H), 2.46 (dd, $J = 14.7, 8.8$ Hz, 1H), 2.04 (d, $J = 10.0$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 177.3, 147.0, 145.9, 144.9, 139.6, 132.3, 130.7, 128.6 (2C), 128.4 (2C), 127.4, 125.9 (q, $^1J_{\text{C-F}} = 279.4$ Hz), 123.8, 114.8, 113.8, 61.7, 56.1, 55.6 (q, $^2J_{\text{C-F}} = 27.2$ Hz), 46.0, 33.0, 29.7; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_3\text{Na}$ 453.1402; Found 453.1403.



Synthesis of 3q: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-benzyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2i** (31.8 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3q**: 37.1 mg (0.0780 mmol), as a white solid, 78% yield; mp 223–

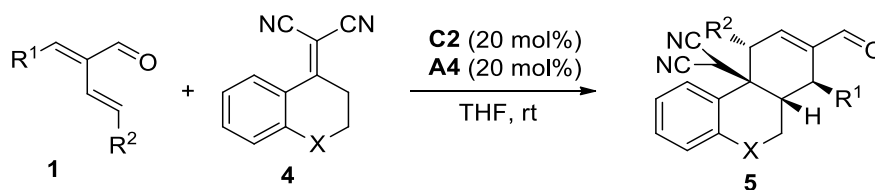
224 °C; $[\alpha]_D^{25} = +298.4$ ($c = 1.8$ in CHCl_3); >19:1 dr; 93% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 9.24 min, t (minor) = 11.90 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.48 (s, 1H), 7.46–7.40 (m, 2H), 7.35–7.27 (m, 6H), 7.26–7.20 (m, 3H), 7.15 (d, $J = 7.3$ Hz, 1H), 7.01 (t, $J = 7.5$ Hz, 1H), 6.97–6.91 (m, 1H), 6.77 (d, $J = 7.7$ Hz, 1H), 5.00–4.88 (m, 3H), 4.47 (d, $J = 10.7$ Hz, 1H), 3.86 (dd, $J = 14.7, 6.2$ Hz, 1H), 2.54 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.09 (d, $J = 9.6$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 177.2, 147.2, 144.5, 142.0, 139.6, 135.3, 130.9, 129.9, 128.9 (2C), 128.7 (2C), 128.4 (2C), 127.8, 127.5, 127.2 (2C), 126.7 (q, $^1J_{\text{C-F}} = 279.3$ Hz), 123.1, 122.4, 109.9, 61.8, 55.7 (q, $^2J_{\text{C-F}} = 27.8$ Hz), 46.1, 43.7, 32.6; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{28}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_2\text{Na}$ 499.1609; Found 499.1612.



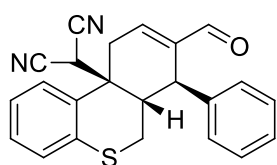
Synthesis of 3r: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), (*Z*)-1-(methoxymethyl)-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2j** (27.2 mg, 0.100 mmol, 1.0 equiv), **C4** (9.1 mg, 0.020 mmol, 0.2 equiv) and **A1** (2.4 mg, 0.020 mmol, 0.2 equiv) in DCE (0.2 mL) was stirred at 50 °C for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave product **3r**: 34.4 mg (0.0800 mmol), as a white semisolid, 80%

yield; $[\alpha]_D^{25} = +326.7$ ($c = 1.7$ in CHCl_3); >19:1 dr; 94% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (major) = 6.98 min, t (minor) = 8.75 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.49 (s, 1H), 7.45–7.40 (m, 2H), 7.38 (t, $J = 7.9$ Hz, 1H), 7.34–7.28 (m, 2H), 7.27–7.23 (m, 1H), 7.22–7.17 (m, 1H), 7.13–7.08 (m, 2H), 6.96 (dd, $J = 8.9, 6.1$ Hz, 1H), 5.17 (s, 2H), 4.85–4.70 (m, 1H), 4.46 (d, $J = 10.8$ Hz, 1H), 3.83 (dd, $J = 14.6, 6.2$ Hz, 1H), 3.37 (s, 3H), 2.55 (dd, $J = 14.6, 8.9$ Hz, 1H), 2.12 (br, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 192.7, 177.7, 147.2, 144.3, 141.1, 139.5, 130.4, 130.2, 128.7 (2C), 128.4 (2C), 127.5, 125.9 (q, $^1J_{\text{C-F}} = 279.0$ Hz), 123.6, 122.5, 110.4, 71.3, 62.1, 56.3, 55.7 (q, $^2J_{\text{C-F}} = 27.1$ Hz), 46.2, 32.6; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.1; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_3$ 431.1580; Found 431.1588.

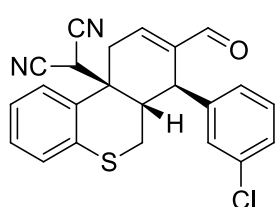
4.2 β,γ' -Regioselective [4+2] annulations of α -vinylenals **1** with 2-(thiochroman-4-ylidene)malononitriles **4**



A mixture of α -vinylenal **1** (0.120 mmol, 1.2 equiv), α,α -dicyanoalkene **4** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at rt for 12 h, and the reaction was monitored by TLC. After completion, the product **5** was obtained by flash chromatography on silica gel (EtOAc/petroleum ether). The racemic **5** was obtained under the catalysis of racemic amine **C1**.

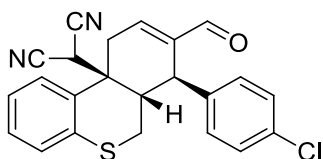


Synthesis of 5a: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5a**: 34.0 mg (0.0920 mmol), as a yellow solid, 92% yield; mp = 121–122 °C; $[\alpha]_D^{25} = +112.3$ ($c = 1.7$ in CHCl_3); >19:1 dr; 98% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 14.28 min, t (major) = 21.55 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.18 (s, 1H), 7.34–7.22 (m, 6H), 7.20–7.15 (m, 2H), 7.14–7.09 (m, 1H), 6.96 (d, $J = 4.2$ Hz, 1H), 4.36 (s, 1H), 3.65 (dd, $J = 18.7, 6.5$ Hz, 1H), 3.35 (d, $J = 9.9$ Hz, 1H), 3.12 (d, $J = 18.7$ Hz, 1H), 3.00–2.90 (m, 2H), 2.72–2.64 (m, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 191.2, 143.5, 143.3, 139.9, 132.4, 129.5, 128.9 (2C), 128.3 (2C), 127.69, 127.63, 127.5, 127.2, 125.3, 110.7, 110.5, 43.3, 42.2, 41.8, 31.5, 31.1, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{OSNa}$ 393.1038; Found 393.1033.



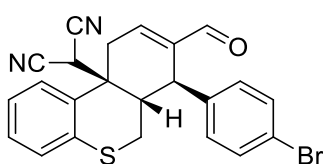
Synthesis of 5b: A mixture of (*E*)-2-(3-chlorobenzylidene)but-3-enal **1j** (23.1 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5b**: 30.3 mg (0.0750 mmol), as a yellow solid, 75% yield; mp = 128–129 °C; $[\alpha]_D^{25} = +100.4$ ($c = 1.5$ in CHCl_3); >19:1 dr; 94% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor)

= 8.64 min, t (major) = 12.10 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) δ 9.20 (s, 1H), 7.30–7.20 (m, 5H), 7.17–7.11 (m, 2H), 7.10–7.07 (m, 1H), 7.00 (d, $J = 5.8$ Hz, 1H), 4.35 (s, 1H), 3.67 (dd, $J = 18.8, 6.5$ Hz, 1H), 3.33 (d, $J = 10.8$ Hz, 1H), 3.13 (d, $J = 19.1$ Hz, 1H), 3.00 (dd, $J = 13.7, 5.3$ Hz, 1H), 2.90 (d, $J = 13.7$ Hz, 1H), 2.64 (dd, $J = 9.9, 4.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 191.0, 144.2, 143.0, 142.1, 134.8, 132.2, 130.1, 129.6, 128.1, 127.8, 127.7, 127.5, 127.0, 126.7, 125.4, 110.6, 110.4, 43.3, 41.9, 41.6, 31.5, 31.1, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{18}^{35}\text{ClN}_2\text{OS}$ 403.0672; Found 403.0677; Calcd for $\text{C}_{23}\text{H}_{18}^{37}\text{ClN}_2\text{OS}$ 405.0642; Found 405.0652.



Synthesis of 5c: A mixture of (*E*)-2-(4-chlorobenzylidene)but-3-enal **1k** (23.1 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene) malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2

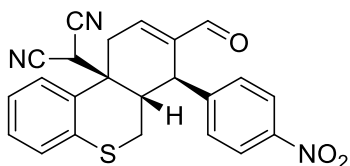
mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5c**: 37.1 mg (0.0920 mmol), as a yellow solid, 92% yield; mp = 123–124 °C; $[\alpha]_{\text{D}}^{25} = +102.3$ ($c = 1.8$ in CHCl_3); >19:1 dr; 98% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min^{-1} , $\lambda = 254$ nm, t (minor) = 9.09 min, t (major) = 13.12 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.19 (s, 1H), 7.32–7.22 (m, 5H), 7.15–7.10 (m, 3H), 6.98 (d, $J = 6.5$ Hz, 1H), 4.35 (s, 1H), 3.66 (dd, $J = 18.8, 6.5$ Hz, 1H), 3.34 (d, $J = 10.2$ Hz, 1H), 3.11 (d, $J = 18.7$ Hz, 1H), 2.98 (dd, $J = 13.7, 5.4$ Hz, 1H), 2.88 (d, $J = 12.7$ Hz, 1H), 2.63 (dd, $J = 9.9, 4.3$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 191.1, 144.1, 143.2, 138.5, 133.3, 132.2, 129.6, 129.5 (2C), 129.14, 129.12, 127.7, 127.5, 127.0, 125.4, 110.6, 110.4, 43.3, 41.7, 41.6, 31.5, 31.1, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} - \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{16}^{35}\text{ClN}_2\text{OS}$ 403.0672; Found 403.0674; Calcd for $\text{C}_{23}\text{H}_{16}^{37}\text{ClN}_2\text{OS}$ 405.0642; Found 405.0640.



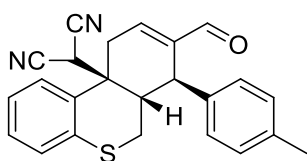
Synthesis of 5d: A mixture of (*E*)-2-(4-bromobenzylidene)but-3-enal **1c** (28.3 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene) malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2

mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5d**: 38.5 mg (0.0860 mmol), as a yellow solid, 86% yield; mp = 127–128 °C; $[\alpha]_{\text{D}}^{25} = +107.2$ ($c = 1.9$ in CHCl_3); >19:1 dr; 96% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min^{-1} , $\lambda = 254$ nm, t (minor) = 9.59 min, t (major) = 14.44 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.19 (s, 1H), 7.44 (d, $J = 8.0$ Hz, 2H), 7.30–7.22 (m, 3H), 7.16–7.10 (m, 1H), 7.07 (d, $J = 8.1$ Hz, 2H), 6.98 (d, $J = 6.6$ Hz, 1H), 4.34 (s, 1H), 3.66 (dd, $J = 18.8, 6.5$ Hz, 1H), 3.33 (d, $J = 10.3$ Hz, 1H), 3.11 (d, $J = 18.7$ Hz,

1H), 2.98 (dd, $J = 13.7, 5.3$ Hz, 1H), 2.88 (d, $J = 13.6$ Hz, 1H), 2.62 (dd, $J = 10.3, 4.3$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 191.1, 144.1, 143.1, 139.0, 132.2, 132.0 (2C), 129.9 (2C), 129.6, 127.7, 127.5, 127.0, 125.4, 121.4, 110.6, 110.4, 43.2, 41.7, 41.6, 31.5, 31.1, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{17}^{79}\text{BrN}_2\text{OSNa}$ 471.0143; Found 471.0141; Calcd for $\text{C}_{23}\text{H}_{17}^{81}\text{BrN}_2\text{OSNa}$ 473.0122; Found 473.0118.

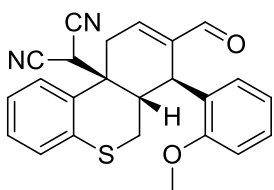


Synthesis of 5e: A mixture of (*E*)-2-(4-nitrobenzylidene)but-3-enal **11** (24.4 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene) malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5e**: 26.9 mg (0.0650 mmol), as a yellow solid, 65% yield; mp = 136–137 °C; $[\alpha]_{\text{D}}^{25} = +104.5$ ($c = 1.5$ in CHCl_3); >19:1 dr; 92% ee, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 16.51 min, t (major) = 21.01 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.22 (s, 1H), 8.20 (d, $J = 8.3$ Hz, 2H), 7.39 (d, $J = 8.3$ Hz, 2H), 7.34–7.25 (m, 3H), 7.19–7.13 (m, 1H), 7.09 (d, $J = 6.5$ Hz, 1H), 4.35 (s, 1H), 3.73 (dd, $J = 19.0, 6.5$ Hz, 1H), 3.50 (d, $J = 10.4$ Hz, 1H), 3.17 (d, $J = 18.7$ Hz, 1H), 3.02 (dd, $J = 13.9, 5.3$ Hz, 1H), 2.79 (d, $J = 13.8$ Hz, 1H), 2.67 (dd, $J = 10.3, 4.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 191.0, 147.9, 147.3, 145.5, 142.6, 132.0, 129.8, 129.1 (2C), 127.7, 127.6, 126.8, 125.6, 124.1 (2C), 110.5, 110.3, 43.2, 42.0, 41.3, 31.6, 31.2, 22.7. HRMS (ESI-TOF) m/z : $[\text{M} - \text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{16}\text{N}_3\text{O}_3\text{S}$ 414.0912; Found 414.0916.



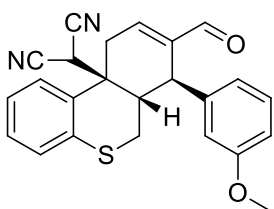
Synthesis of 5f: A mixture of (*E*)-2-(4-methylbenzylidene)but-3-enal **1d** (20.6 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5f**: 34.1 mg (0.0890 mmol), as a yellow solid, 89% yield; mp = 130–131 °C; $[\alpha]_{\text{D}}^{25} = +89.2$ ($c = 1.7$ in CHCl_3); >19:1 dr; 99% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 8.83 min, t (major) = 10.13 min]; ^1H NMR (400 MHz, CDCl_3) δ (ppm) 9.17 (s, 1H), 7.30–7.22 (m, 3H), 7.15–7.09 (m, 3H), 7.08–7.04 (m, 2H), 6.94 (d, $J = 6.5$ Hz, 1H), 4.36 (s, 1H), 3.65 (dd, $J = 18.5, 6.3$ Hz, 1H), 3.32 (d, $J = 10.0$ Hz, 1H), 3.12 (d, $J = 19.3$ Hz, 1H), 2.96 (d, $J = 3.7$ Hz, 2H), 2.66 (dt, $J = 10.6, 3.7$ Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 191.4, 143.6, 143.1, 137.2, 136.8, 132.4, 129.6 (2C), 129.4, 128.1 (2C), 127.68, 127.62, 127.3, 125.2, 110.8, 110.6, 43.3, 41.9

(2C), 31.5, 31.0, 22.9, 21.1. HRMS (ESI-TOF) m/z : $[M + Na]^+$ Calcd for $C_{24}H_{20}N_2OSNa$ 407.1194; Found 407.1190.



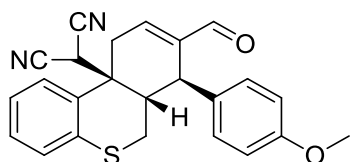
Synthesis of 5g: A mixture of (*E*)-2-(2-methoxybenzylidene)but-3-enal **1m** (22.5 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography

on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5g**: 28.0 mg (0.0700 mmol), as a yellow solid, 70% yield; mp = 127–128 °C; $[\alpha]_D^{25} = +78.0$ ($c = 1.4$ in $CHCl_3$); >19:1 dr; 98% ee, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 17.20 min, t (major) = 24.69 min]; ¹H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.17 (s, 1H), 7.34–7.18 (m, 5H), 7.18–7.05 (m, 1H), 6.99–6.77 (m, 3H), 4.45 (br, 1H), 4.10–3.75 (m, 4H), 3.63 (dd, $J = 18.4, 6.6$ Hz, 1H), 3.30 (br, 1H), 3.14–3.04 (m, 1H), 3.01–2.86 (m, 2H), 3.30 (br, 1H); ¹³C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.4, 142.7, 132.7, 129.3, 128.7, 127.7, 127.6, 127.4, 125.1, 121.0, 111.3, 110.9, 110.7, 55.5, 43.5, 31.4, 23.4. HRMS (ESI-TOF) m/z : $[M + Na]^+$ Calcd for $C_{24}H_{20}N_2O_2SNa$ 423.1143; Found 423.1137.

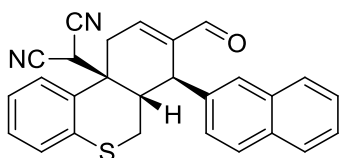


Synthesis of 5h: A mixture of (*E*)-2-(3-methoxybenzylidene)but-3-enal **1e** (22.6 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography

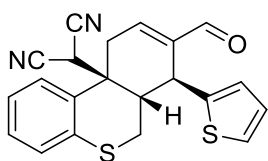
on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5h**: 36.0 mg (0.0900 mmol), as a yellow solid, 90% yield; mp = 124–125 °C; $[\alpha]_D^{25} = +108.7$ ($c = 1.8$ in $CHCl_3$); >19:1 dr; 97% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 11.14 min, t (major) = 16.20 min]; ¹H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.19 (s, 1H), 7.30–7.20 (m, 4H), 7.15–7.05 (m, 1H), 6.96 (d, $J = 6.6$ Hz, 1H), 6.81–6.75 (m, 2H), 6.71 (s, 1H), 4.35 (s, 1H), 3.79 (s, 3H), 3.64 (dd, $J = 18.8, 6.5$ Hz, 1H), 3.31 (d, $J = 11.5$ Hz, 1H), 3.10 (d, $J = 18.6$ Hz, 1H), 2.71–2.62 (m, 2H), 2.68 (dt, $J = 10.7, 3.6$ Hz, 1H); ¹³C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.2, 159.9, 143.4, 143.1, 141.5, 132.4, 129.9, 129.5, 127.7, 127.6, 127.2, 125.3, 120.7, 114.5, 112.2, 110.7, 110.5, 55.2, 43.3, 42.2, 41.7, 31.5, 31.1, 22.9. HRMS (ESI-TOF) m/z : $[M + Na]^+$ Calcd for $C_{24}H_{20}N_2O_2SNa$ 423.1143; Found 423.1136.



Synthesis of 5i: A mixture of (*E*)-2-(4-methoxybenzylidene)but-3-enal **1f** (22.6 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene) malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5i**: 36.0 mg (0.0900 mmol), as a yellow solid, 90% yield; mp = 118–119 °C; $[\alpha]_{\text{D}}^{25} = +121.4$ ($c = 1.8$ in CHCl_3); >19:1 dr; 96% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 13.16 min, t (major) = 16.70 min]; ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.17 (s, 1H), 7.29–7.22 (m, 3H), 7.14–7.06 (m, 3H), 6.93 (d, $J = 6.7$ Hz, 1H), 6.84 (d, $J = 8.4$ Hz, 2H), 4.36 (s, 1H), 3.78 (s, 3H), 3.64 (dd, $J = 18.7, 6.5$ Hz, 1H), 3.30 (d, $J = 10.3$ Hz, 1H), 3.10 (d, $J = 18.0$ Hz, 1H), 2.96 (d, $J = 3.8$ Hz, 2H), 2.65 (dt, $J = 10.6, 3.7$ Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 191.4, 158.8, 143.6, 142.9, 132.4, 131.7, 129.4, 129.3 (2C), 127.6, 127.6, 127.3, 125.3, 114.3 (2C), 110.8, 110.6, 55.2, 43.3, 42.0, 41.5, 31.5, 31.1, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for C₂₄H₂₀N₂O₂SNa 423.1143; Found 423.1142.

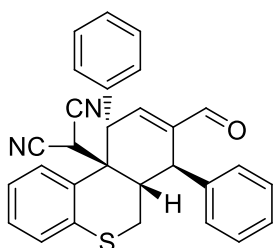


Synthesis of 5j: A mixture of (*E*)-2-(naphthalen-2-ylmethylene)but-3-enal **1g** (25.0 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5j**: 31.9 mg (0.0760 mmol), as a yellow solid, 76% yield; mp = 129–130 °C; $[\alpha]_{\text{D}}^{25} = +112.9$ ($c = 1.6$ in CHCl_3); >19:1 dr; 98% ee, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 9.43 min, t (major) = 14.68 min]; ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.19 (s, 1H), 7.83–7.77 (m, 3H), 7.67 (s, 1H), 7.51–7.42 (m, 2H), 7.32–7.25 (m, 4H), 7.16–7.10 (m, 1H), 7.00 (d, $J = 6.3$ Hz, 1H), 4.37 (s, 1H), 3.68 (dd, $J = 18.8, 6.5$ Hz, 1H), 3.52 (d, $J = 9.0$ Hz, 1H), 3.17 (d, $J = 18.5$ Hz, 1H), 3.00–2.90 (m, 2H), 2.81–2.75 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 191.2, 143.4, 137.2, 133.4, 132.7, 132.4, 129.5, 128.8, 127.78 (2C), 127.74 (2C), 127.6, 127.4, 127.3, 126.4, 126.0, 125.8, 125.3, 110.7, 110.6, 43.4, 42.4, 41.7, 31.6, 31.1, 22.9. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for C₂₇H₂₀N₂OSNa 443.1194; Found 443.1185.



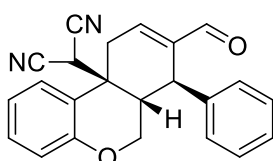
Synthesis of 5k: A mixture of (*E*)-2-(thiophen-2-ylmethylene)but-3-enal **1h** (19.7 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room

temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5k**: 35.7 mg (0.0950 mmol), as a yellow solid, 95% yield; mp = 122–123 °C; $[\alpha]_D^{25} = +93.4$ ($c = 1.7$ in CHCl_3); >19:1 dr; 99% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 9.50 min, t (major) = 11.51 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.22 (s, 1H), 7.28–7.22 (m, 3H), 7.20 (d, $J = 4.9$ Hz, 1H), 7.15–7.08 (m, 1H), 7.00–6.97 (m, 1H), 6.96–6.93 (m, 1H), 6.91 (d, $J = 6.4$ Hz, 1H), 4.38 (s, 1H), 3.71 (d, $J = 8.9$ Hz, 1H), 3.63 (dd, $J = 18.8, 6.5$ Hz, 1H), 3.15–3.00 (m, 3H), 2.28–2.72 (m, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 190.9, 142.8, 142.4, 142.3, 132.3, 129.6, 127.7, 127.6, 127.15, 127.10, 126.9, 125.3, 124.8, 110.6, 110.4, 43.4, 42.6, 37.6, 31.4, 31.1, 23.1. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{OS}_2\text{Na}$ 399.0602; Found 399.0600.



Synthesis of 5l: A mixture of (*2E,3E*)-2-benzylidene-4-phenylbut-3-enal **1i** (28.1 mg, 0.120 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34 mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5l**: 31.2 mg

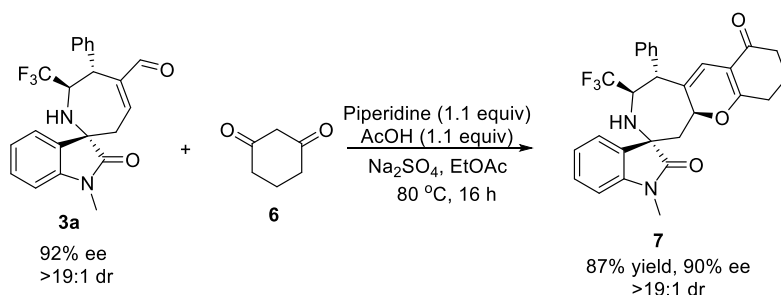
(0.0700 mmol), as a yellow solid, 70% yield; mp = 128–129 °C; $[\alpha]_D^{25} = +98.2$ ($c = 1.5$ in CHCl_3); >19:1 dr; 55% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 9.47 min, t (major) = 21.67 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.27 (s, 1H), 7.82 (br, 2H), 7.64–7.54 (m, 4H), 7.44–7.32 (m, 5H), 7.30–7.28 (m, 2H), 7.23–7.17 (m, 1H), 6.97 (d, $J = 3.7$ Hz, 1H), 5.09 (d, $J = 5.9$ Hz, 1H), 4.41 (s, 1H), 3.37 (d, $J = 10.9$ Hz, 1H), 3.07 (dd, $J = 11.0, 4.0$ Hz, 1H), 2.98 (d, $J = 13.7$ Hz, 1H), 2.84 (dd, $J = 13.7, 5.4$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 191.5, 146.2, 142.4, 139.5, 134.2, 132.6, 131.8 (2C), 130.2, 129.7 (2C), 129.2, 129.1 (2C), 128.3 (2C), 127.9, 127.7, 127.1, 125.4, 111.4, 108.6, 46.8, 45.3, 42.4, 35.3, 28.6, 22.8. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{29}\text{H}_{22}\text{N}_2\text{OSNa}$ 469.1351; Found 469.1331.



Synthesis of 5m: A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (19.0 mg, 0.120 mmol, 1.2 equiv), 2-(chroman-4-ylidene)malononitrile **4b** (21.2 mg, 0.100 mmol, 1.0 equiv), **C2** (4.72 mg, 0.020 mmol, 0.2 equiv) and **A4** (3.34

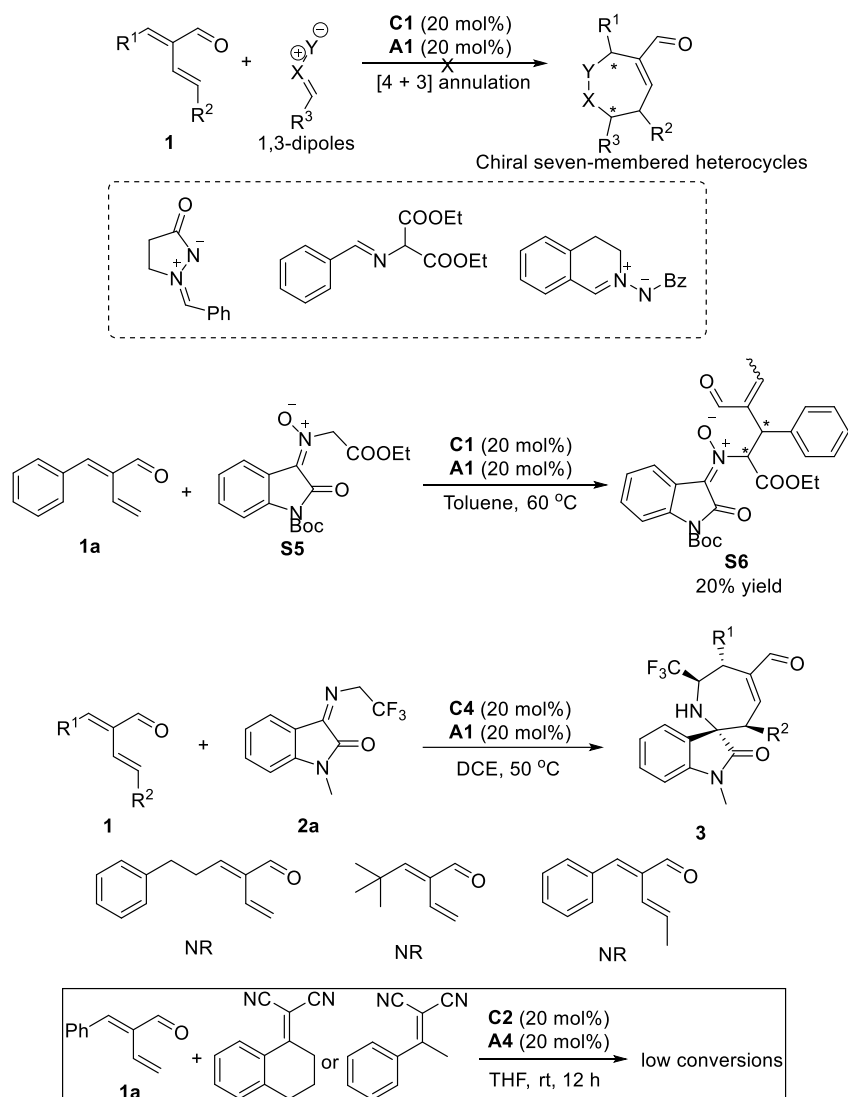
mg, 0.020 mmol, 0.2 equiv) in THF (0.2 mL) was stirred at room temperature for 12 h. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5m**: 17.0 mg (0.0480 mmol), as a yellow solid, 48% yield; mp = 119–120 °C; $[\alpha]_D^{25} = +100.3$ ($c = 0.8$ in CHCl_3); >19:1 dr; 93% ee, determined by HPLC analysis [Chiralpak IA, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 9.16 min, t (major) = 9.91 min]; ¹H NMR (400 MHz, CDCl_3) δ (ppm) 9.21 (s, 1H), 7.37–7.33 (m, 2H), 7.32–7.29 (m, 2H), 7.28–7.25 (m, 2H), 7.22 (d, $J = 7.2$ Hz, 2H), 6.99–6.93 (m, 2H), 6.91 (d, $J = 5.4$ Hz, 1H), 4.31 (d, $J = 12.6$ Hz, 1H), 4.24–4.13 (m, 2H), 3.65–3.55 (m, 2H), 3.14 (d, $J = 18.7$ Hz, 1H), 2.49 (d, $J = 9.5$ Hz, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 191.3, 153.2, 143.0, 142.7, 140.6, 131.0, 128.9 (2C), 128.4 (2C), 127.3, 126.2, 121.4, 118.1, 117.7, 110.6, 110.4, 61.9, 41.4, 40.6, 40.4, 35.2, 30.4. HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}$ 377.1266; Found 377.1268.

5. Transformation of product **3a**



Synthesis of 7: To a solution of **3a** (40.0 mg, 0.100 mmol, 1.0 equiv) in EtOAc (1.0 mL) was added cyclohexane-1,3-dione **6** (16.8 mg, 0.150 mmol, 1.5 equiv), piperidine (9.36 mg, 0.110 mmol, 1.1 equiv), AcOH (6.60 mg, 0.110 mmol, 1.1 equiv) and Na_2SO_4 (4.26 mg, 0.030 mmol, 0.3 equiv). The mixture was stirred at 80 °C for 16 h. After completion, it was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **7**: 42.9 mg (0.0870 mmol), as a white semisolid, 87% yield; $[\alpha]_D^{25} = +288.2$ ($c = 2.0$ in CHCl_3); >19:1 dr; 90% ee, determined by HPLC analysis [Chiralpak AD-H, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL min⁻¹, $\lambda = 254$ nm, t (minor) = 6.15 min, t (major) = 8.07 min]; ¹H NMR (400 MHz, CHCl_3) δ (ppm) 7.55–7.49 (m, 2H), 7.40–7.30 (m, 3H), 7.29–7.21 (m, 2H), 7.10 (t, $J = 7.5$ Hz, 1H), 6.88 (d, $J = 7.7$ Hz, 1H), 6.60 (s, 1H), 5.90 (dd, $J = 10.8, 3.2$ Hz, 1H), 5.35–5.20 (m, 1H), 3.96 (d, $J = 10.3$ Hz, 1H), 3.26 (s, 3H), 2.51 (dd, $J = 13.3, 10.8$ Hz, 1H), 2.38 (t, $J = 6.4$ Hz, 2H), 2.28 (t, $J = 5.7$ Hz, 2H), 2.05 (dd, $J = 13.3, 3.2$ Hz, 1H), 1.98–1.80 (m, 3H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 194.9, 176.3, 170.1, 142.2, 140.7, 132.0, 131.1, 129.4, 129.1 (2C), 127.1, 126.8 (2C), 125.9 (q, $^1J_{\text{C-F}} = 280.0$ Hz), 123.3, 122.6, 115.7, 111.9, 108.7, 71.8, 59.4, 53.8 (q, $^2J_{\text{C-F}} = 26.9$ Hz), 51.9, 43.0, 36.3, 27.9, 26.1, 20.5; ¹⁹F NMR (376 MHz, CDCl_3): δ (ppm) –74.2; HRMS (ESI-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{26}\text{F}_3\text{N}_2\text{O}_3$ 495.1896; Found 495.1892.

6. More screening studies on other 1,3-dipoles, α -vinylenals and α,α -dicyanoalkenes



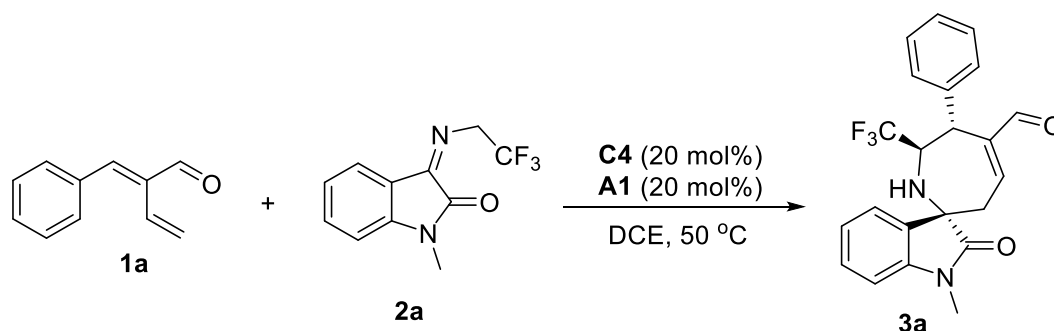
To further expand the utility of this strategy, more 1,3-dipoles were explored in the reactions with α -vinylenals **1** under similar catalytic conditions. Unfortunately, the 1,3-dipoles outlined in the above scheme did not react with α -vinylenal **1a** and failed to give the desired [4+3] cycloadducts. Isatin-derived nitron **S5** could react with α -vinylenal **1a** to give Michael addition product **S6** in a low yield under similar catalytic conditions.

On the other hand, the desired annulation products were not formed by using α -vinylenals **1** having a γ '-alkyl or β -alkyl group.

In addition, the α,α -dicyanoalkenes from other ketones, as outlined in the above scheme, also showed low reactivity with enal **1a**.

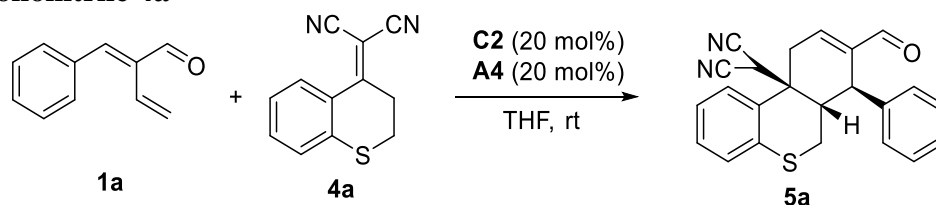
7. Asymmetric reaction on a 1.0 mmol scale

7.1 β,γ' -Regioselective [4+3] annulation of α -vinylenal **1a** with *N*-(2,2,2-trifluoroethyl) ketimine **2a**



A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (189.6 mg, 1.20 mmol, 1.2 equiv), (*Z*)-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one **2a** (242 mg, 1.00 mmol, 1.0 equiv), **C4** (91 mg, 0.200 mmol, 0.2 equiv) and **A1** (24 mg, 0.200 mmol, 0.2 equiv) in DCE (2 mL) was stirred at 50 °C for 12 h, and the reaction was monitored by TLC. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **3a**: 280.0 mg (0.700 mmol), as a white solid, 70% yield; >19:1 dr; 90% ee.

7.2 β,γ' -Regioselective [4+2] annulation of α -vinylenal **1a** with 2-(thiochroman-4-ylidene)malononitrile **4a**



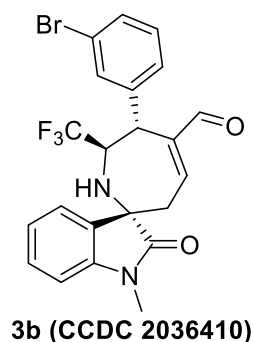
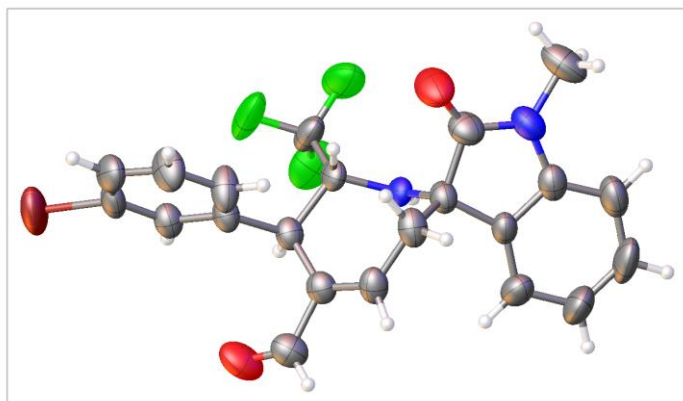
A mixture of (*E*)-2-benzylidenebut-3-enal **1a** (189.6 mg, 1.20 mmol, 1.2 equiv), 2-(thiochroman-4-ylidene)malononitrile **4a** (212 mg, 1.00 mmol, 1.0 equiv), **C2** (47.2 mg, 0.200 mmol, 0.2 equiv) and **A4** (33.4 mg, 0.200 mmol, 0.2 equiv) in THF (2 mL) was stirred at room temperature for 12 h, and the reaction was monitored by TLC. After completion, purification by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) gave the product **5a**: 321.9 mg (0.870 mmol), as a yellow solid, 87% yield; >19:1 dr; 97% ee.

8. Crystal data and structural refinement

8.1 Crystal data and structural refinement for enantiopure **3b**

Preparation of the single crystals of enantiopure **3b**: 30.0 mg of compound **3b** (87% ee) was dissolved in CHCl_3 (1.0 mL) in a 10 mL tube, and *n*-hexane (3.0 mL) was added. The tube was sealed by a piece of weighing paper with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After 4 days, several small particles could be observed at the bottom of the tube.

The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the absolute configuration of **3b**. The data were collected by an Agilent Gemini equipped with a Cu radiation source ($K\alpha = 1.54184 \text{ \AA}$) at 293.9(3) K. CCDC 2036410 (**3b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.



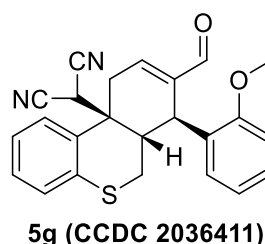
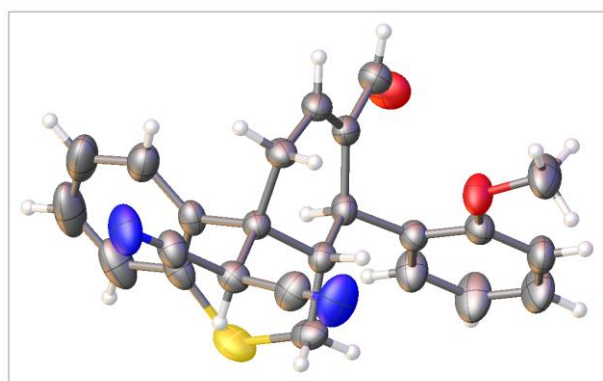
(ellipsoid contour probability 50%)

Identification code	3b
Empirical formula	$C_{22}H_{18}BrF_3N_2O_2$
Formula weight	479.29
Temperature/K	293.9(3)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
$a/\text{\AA}$	6.2936(3)
$b/\text{\AA}$	14.1248(7)
$c/\text{\AA}$	23.2960(9)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/ \AA^3	2070.91(17)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.537
μ/mm^{-1}	3.136
F(000)	968.0
Crystal size/ mm^3	$0.5 \times 0.3 \times 0.3$
Radiation	$\text{CuK}\alpha$ ($\lambda = 1.54184$)
2θ range for data collection/ $^\circ$	7.32 to 142.742
Index ranges	$-7 \leq h \leq 3, -15 \leq k \leq 17, -22 \leq l \leq 28$
Reflections collected	9369
Independent reflections	3888 [$R_{\text{int}} = 0.0434, R_{\text{sigma}} = 0.0437$]
Data/restraints/parameters	3888/0/272
Goodness-of-fit on F^2	1.056

Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0634$, $wR_2 = 0.1675$
Final R indexes [all data]	$R_1 = 0.0674$, $wR_2 = 0.1749$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.58/-0.52
Flack parameter	0.001(18)

8.2 Crystal data and structural refinement for enantiopure **5g**

Preparation of the single crystals of enantiopure **5g**: 30.0 mg of compound **5g** (93% ee) was dissolved in THF (1.0 mL) in a 10 mL tube and *n*-hexane (3.0 mL) was added. The tube was sealed by a piece of weighing paper with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After 24 h, several small particles could be observed at the bottom of the tube. The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the absolute configuration of **5g**. The data were collected by an Agilent Gemini equipped with a Cu radiation source ($K\alpha = 1.54184 \text{ \AA}$) at 295.1(4) K. CCDC 2036411 (**5g**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

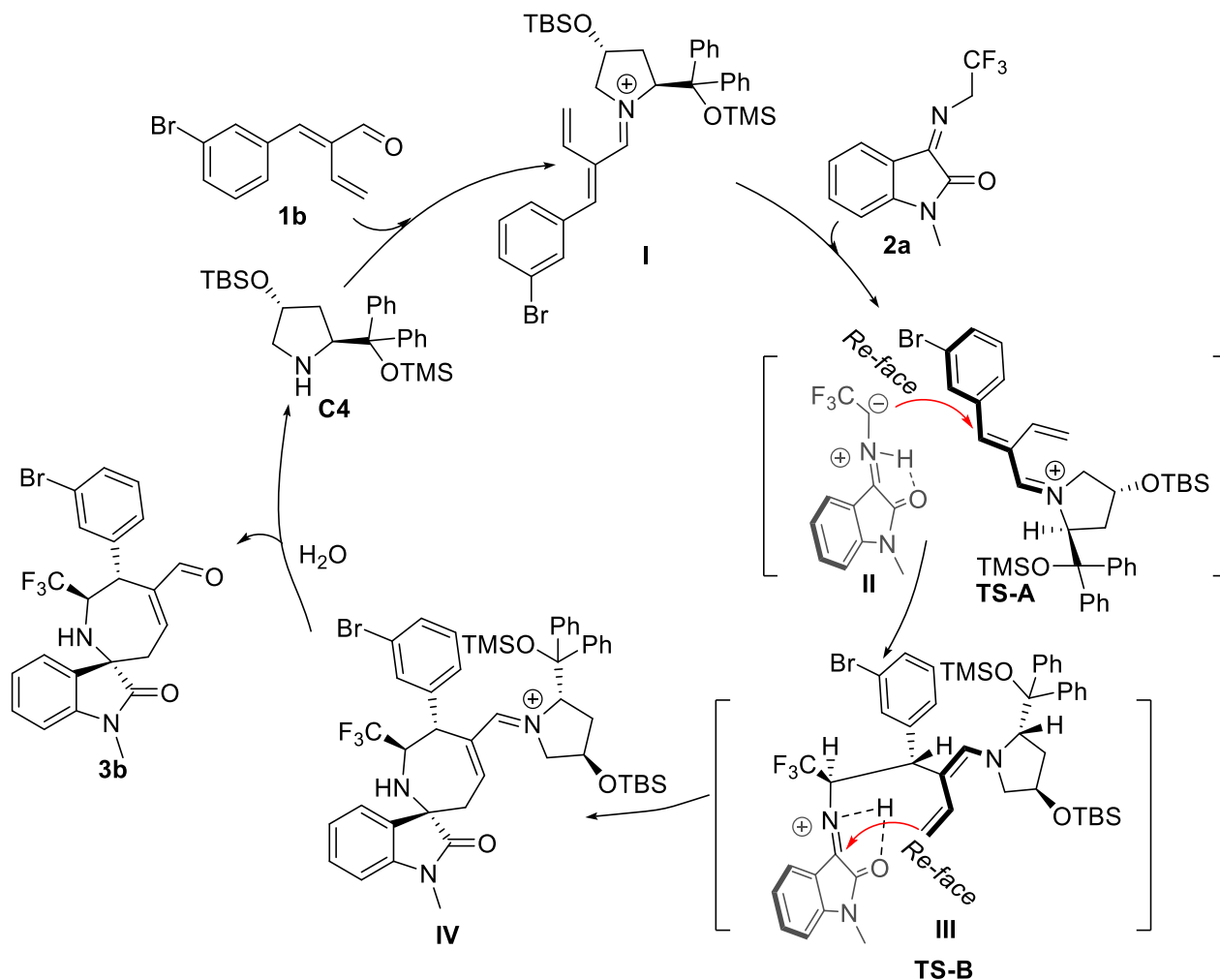


(ellipsoid contour probability 50%)

Identification code	5g
Empirical formula	$C_{24}H_{20}N_2O_2S$
Formula weight	400.48
Temperature/K	295.1(4)
Crystal system	monoclinic
Space group	$P2_1$
$a/\text{\AA}$	8.1897(3)
$b/\text{\AA}$	12.2546(5)
$c/\text{\AA}$	10.5538(4)
$\alpha/^\circ$	90
$\beta/^\circ$	90.193(3)
$\gamma/^\circ$	90
Volume/ \AA^3	1059.19(7)
Z	2
$\rho_{\text{calc}}/\text{cm}^3$	1.256

μ/mm^{-1}	1.528
F(000)	420.0
Crystal size/ mm^3	$0.4 \times 0.2 \times 0.1$
Radiation	$\text{CuK}\alpha$ ($\lambda = 1.54184$)
2Θ range for data collection/ $^\circ$	8.378 to 142.924
Index ranges	$-10 \leq h \leq 10, -11 \leq k \leq 15, -12 \leq l \leq 12$
Reflections collected	11399
Independent reflections	3390 [$R_{\text{int}} = 0.0484, R_{\text{sigma}} = 0.0376$]
Data/restraints/parameters	3390/1/263
Goodness-of-fit on F^2	1.033
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0492, wR_2 = 0.1245$
Final R indexes [all data]	$R_1 = 0.0531, wR_2 = 0.1319$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.23/-0.47
Flack parameter	-0.010(14)

9. Proposed catalytic cycle via cascade iminium ion-dienamine catalysis

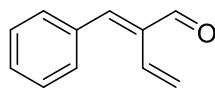


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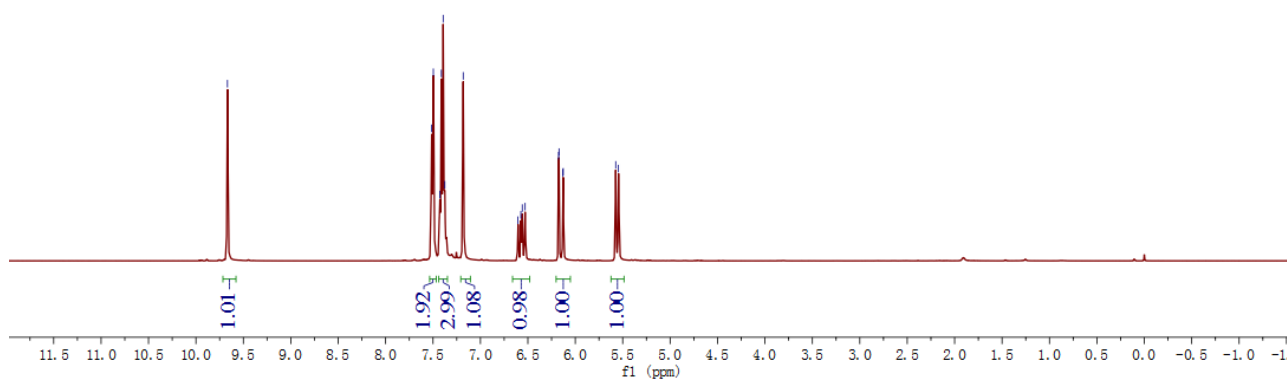
10. NMR, HRMS spectra and HPLC chromatograms

7.514
7.497
7.427
7.395
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7.182
6.605
6.559
6.529
6.176
6.132
6.127
5.574
5.565

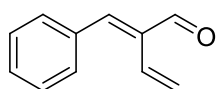


1a

¹H-NMR (400MHz, CDCl₃)

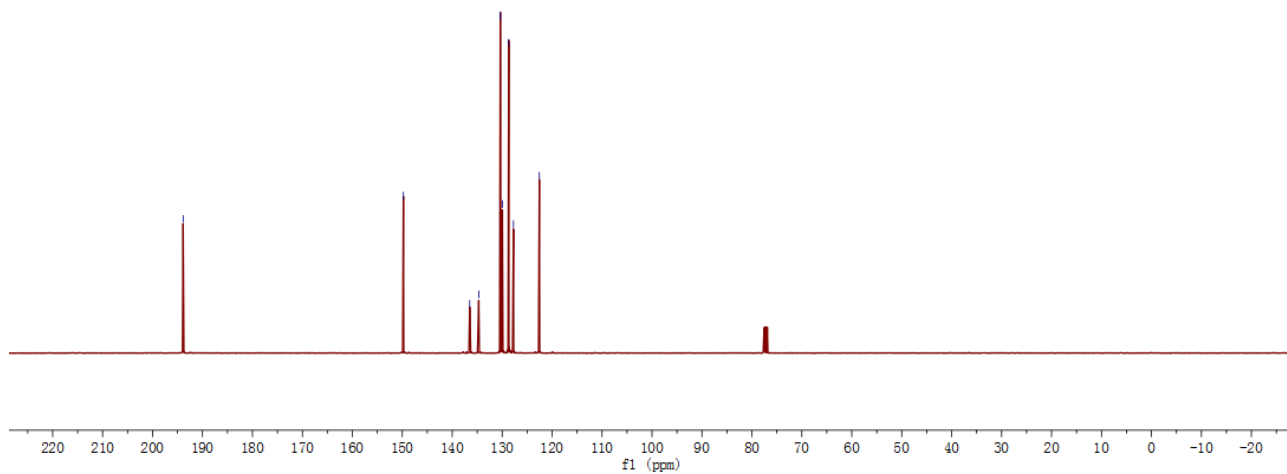


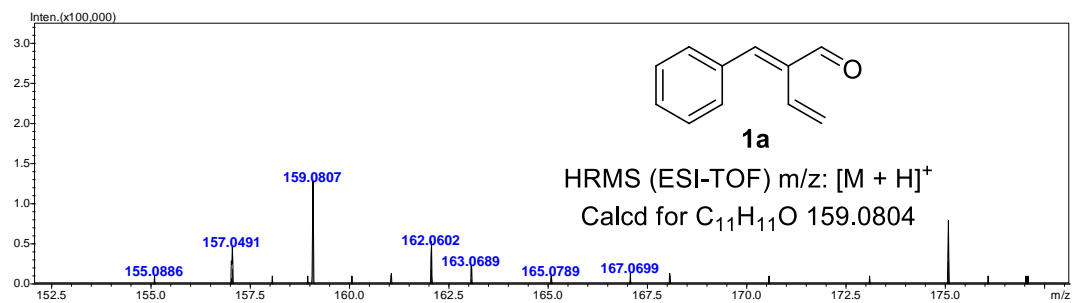
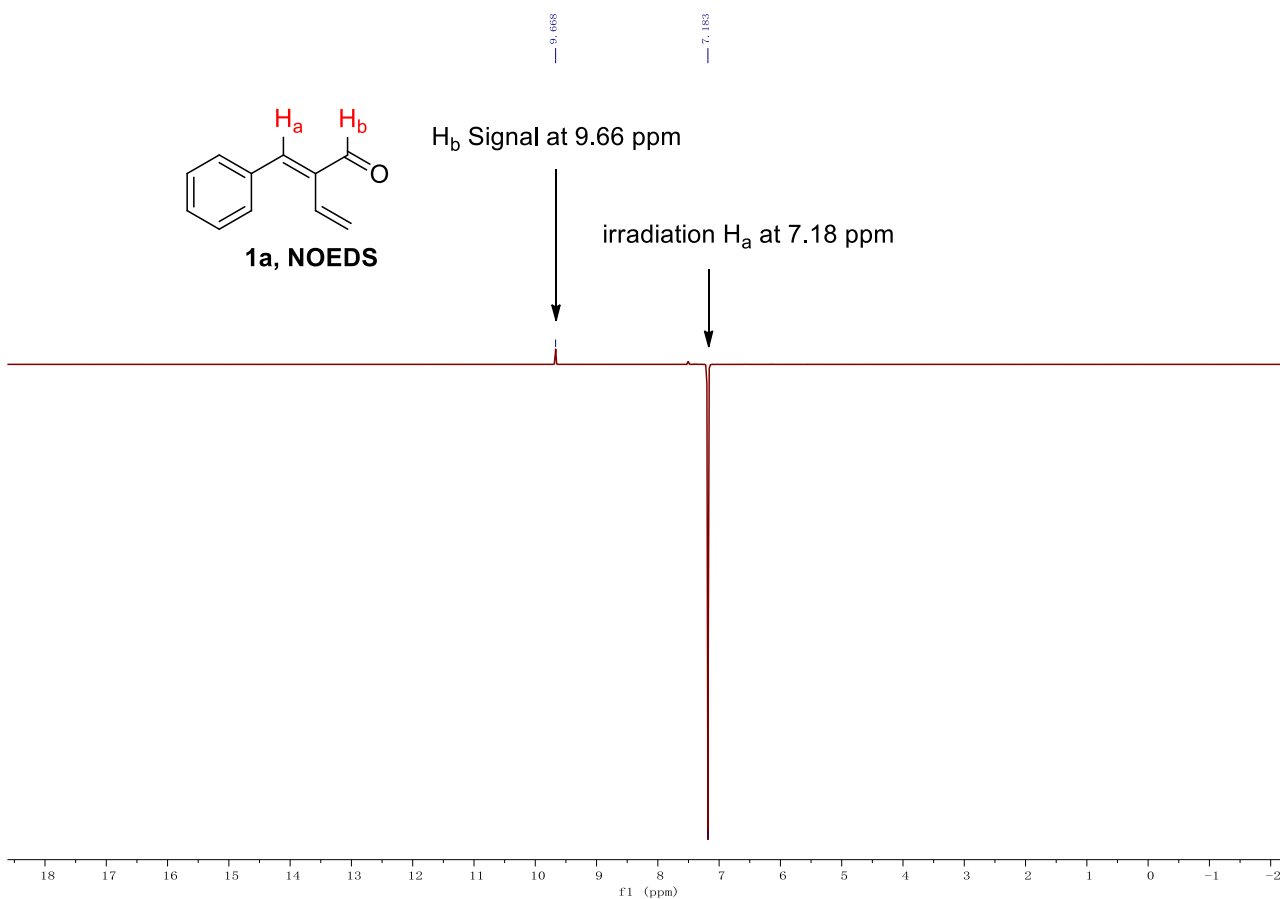
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122.560

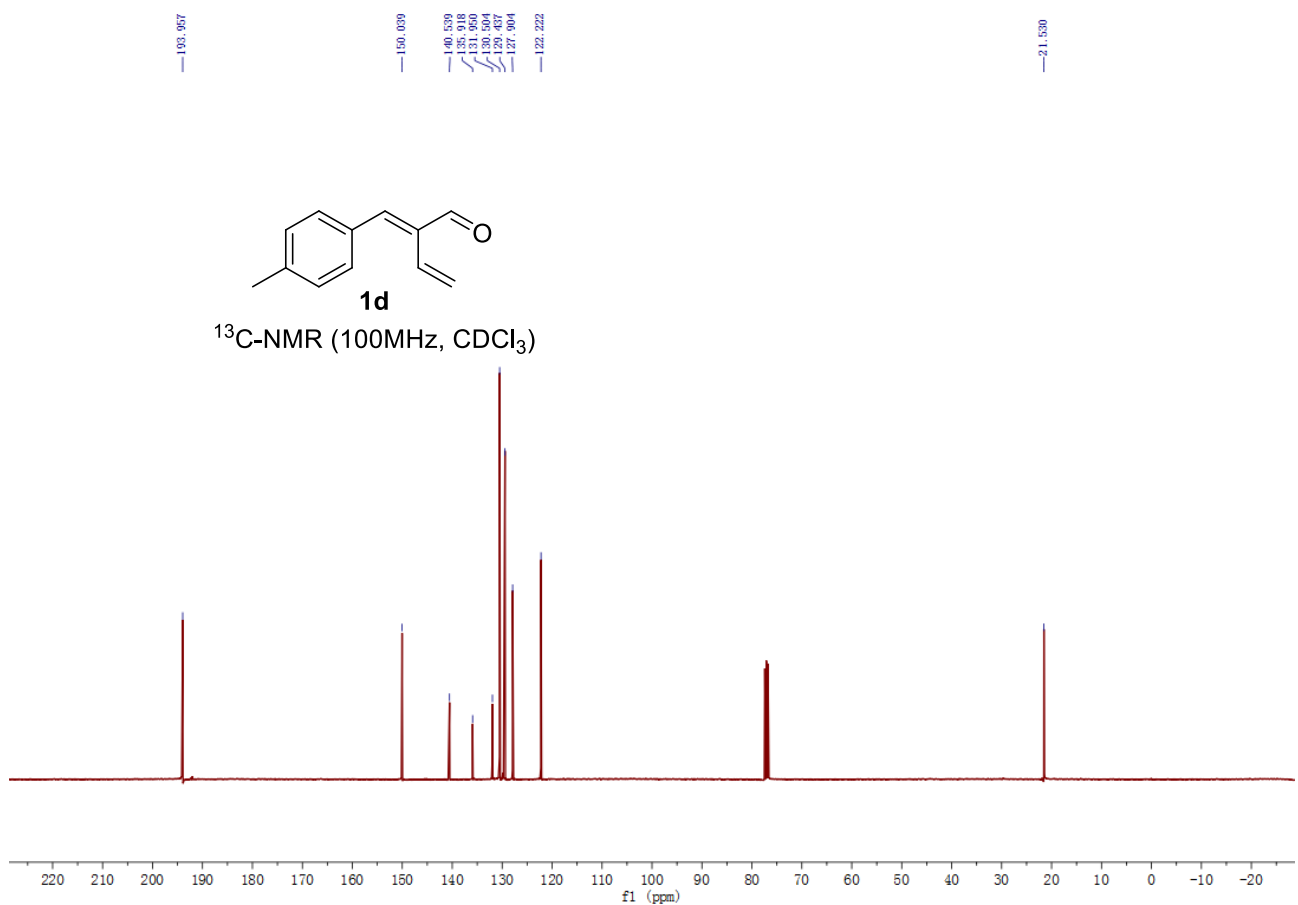
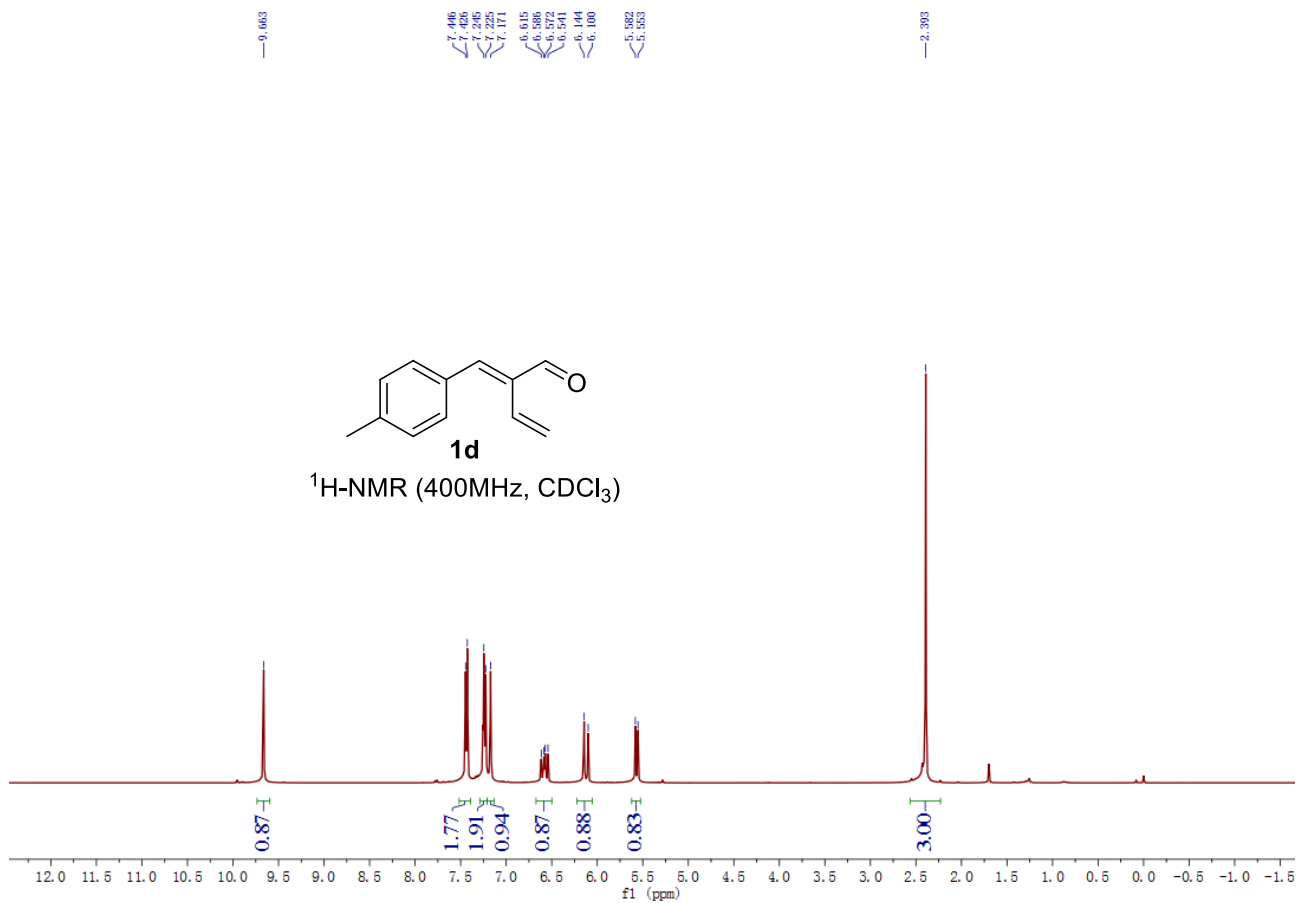


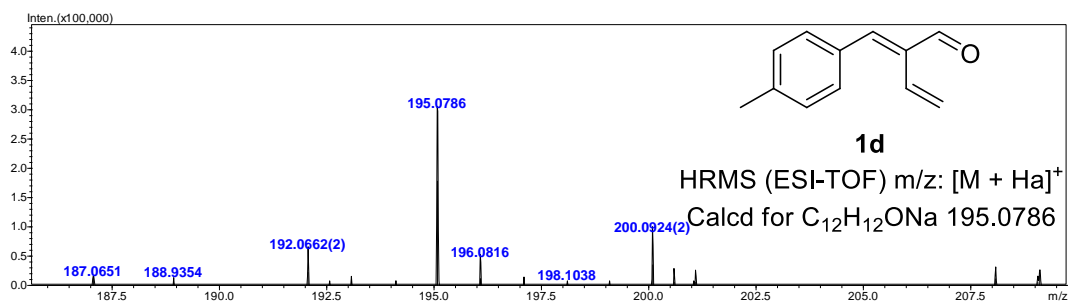
1a

¹³C-NMR (100MHz, CDCl₃)

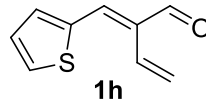




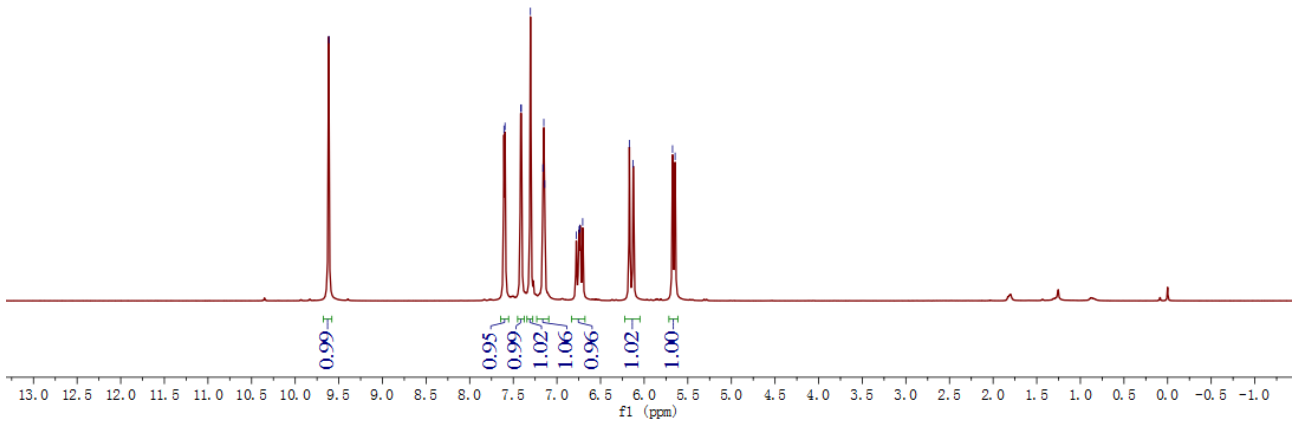




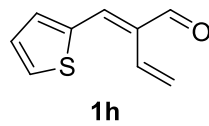
9.614
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6.788
6.746
6.737
6.700
6.126
5.854
5.846



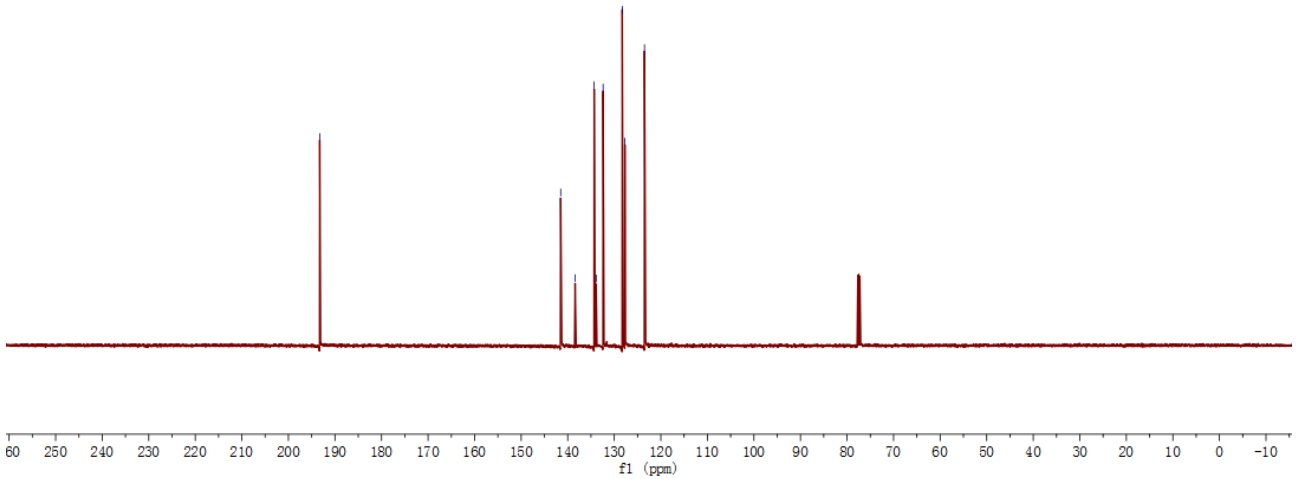
¹H-NMR (400MHz, CDCl₃)



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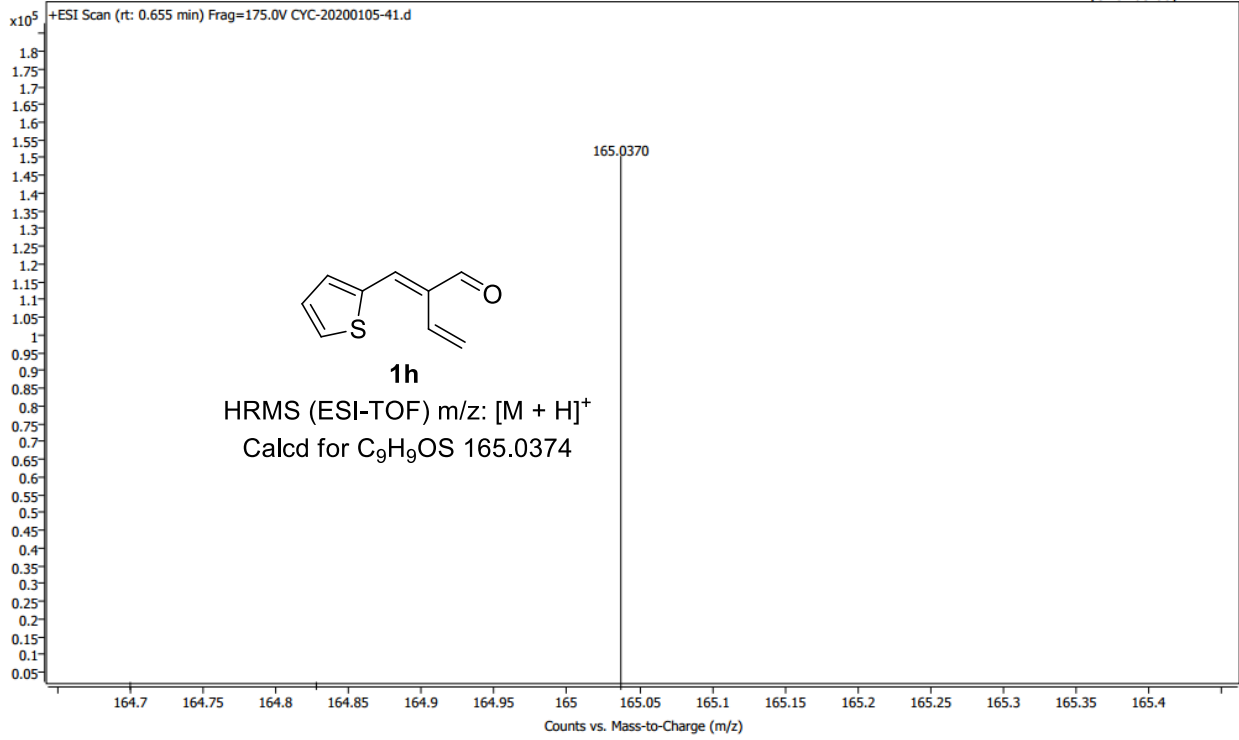


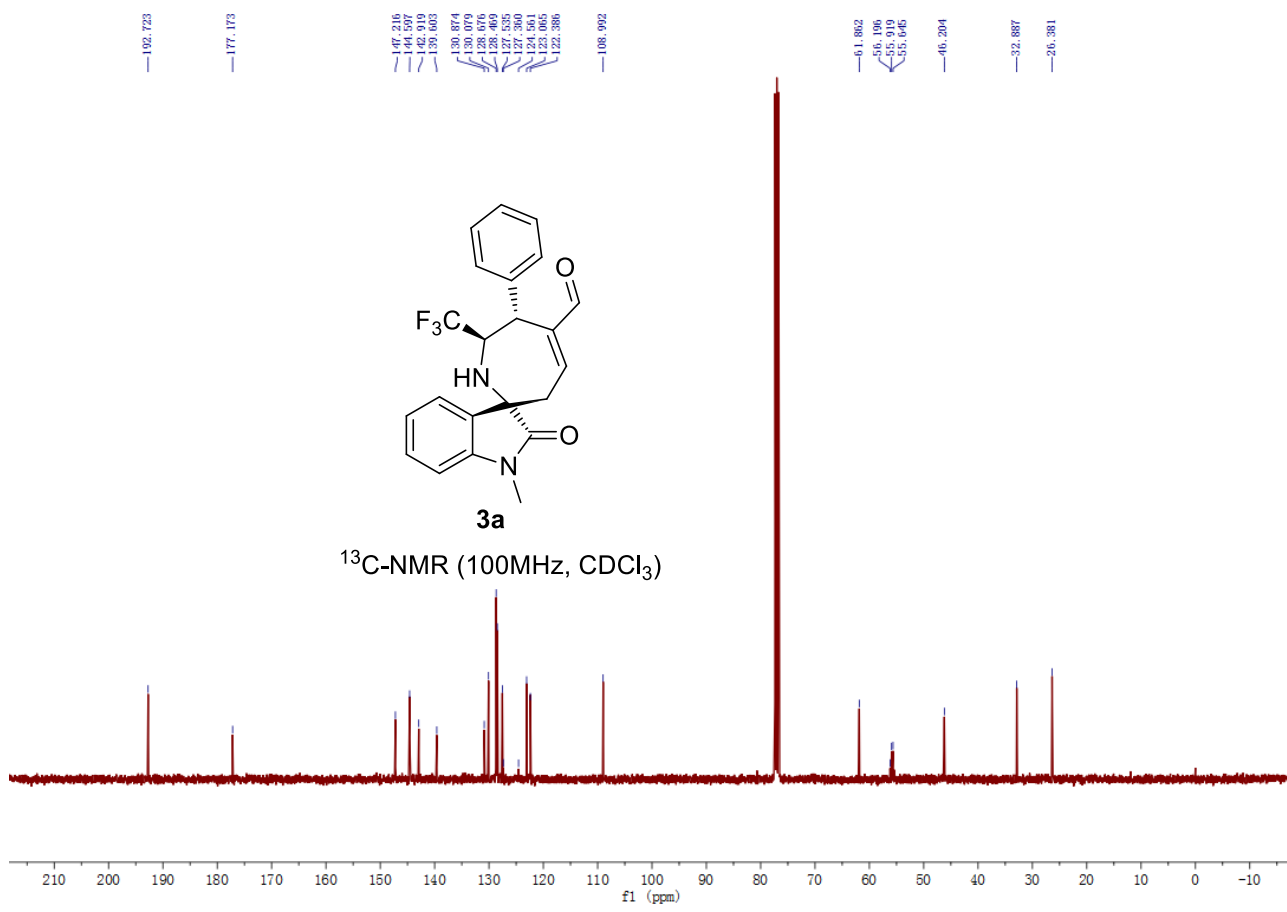
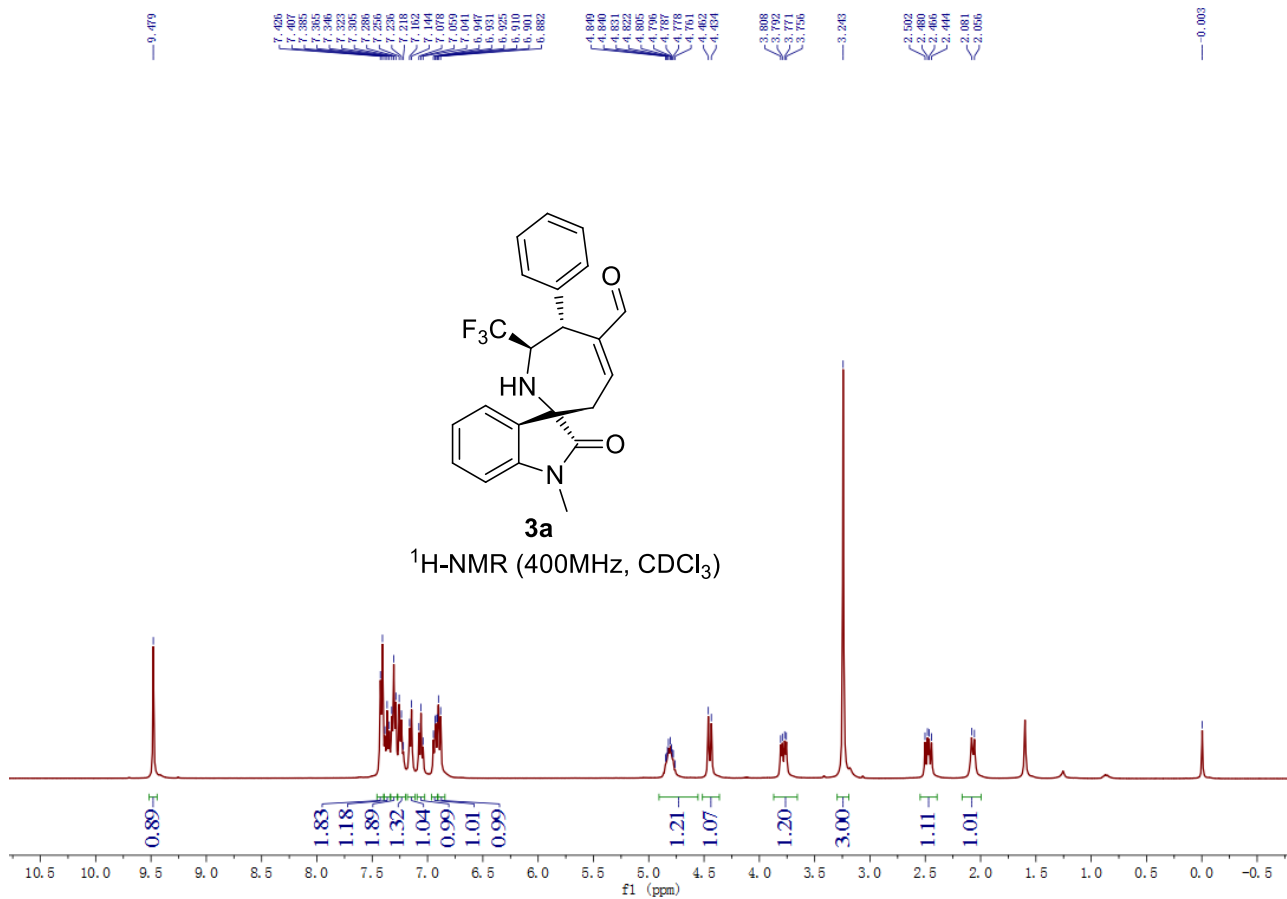
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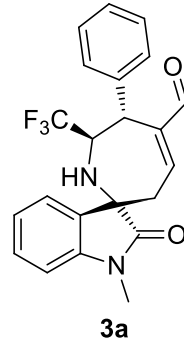
Spectrum Plot Report

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Inj. Vol. (ul)	10	Plate Pos.		IRM Status	Success		
Data File	CYC-20200105-41.d	Method (Acq)	TOF.m	Comment		Acq. Time (Local)	1/10/2020 8:39:47 PM (UTC+08:00)

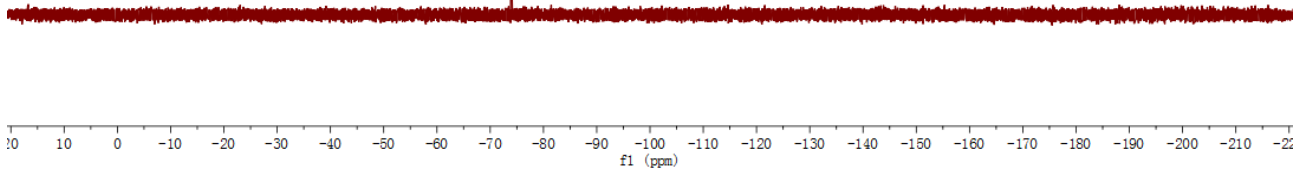




-74.026

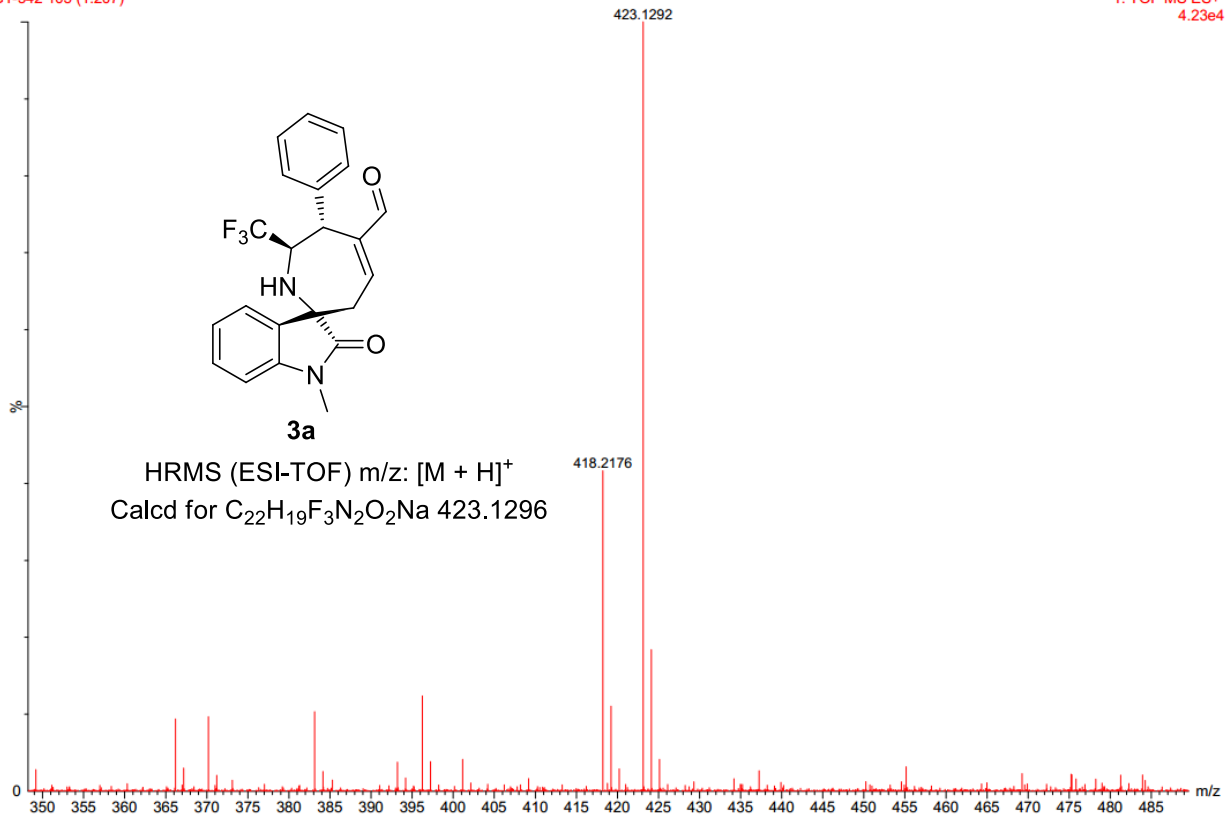


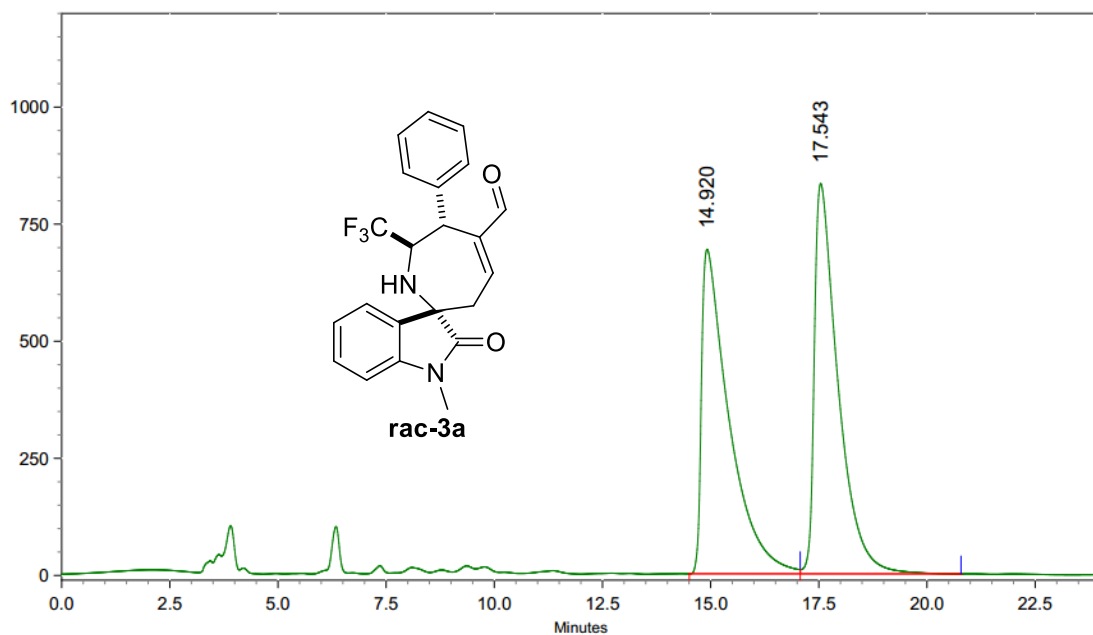
^{19}F -NMR (376MHz, CDCl_3)



GY-542 105 (1.207)

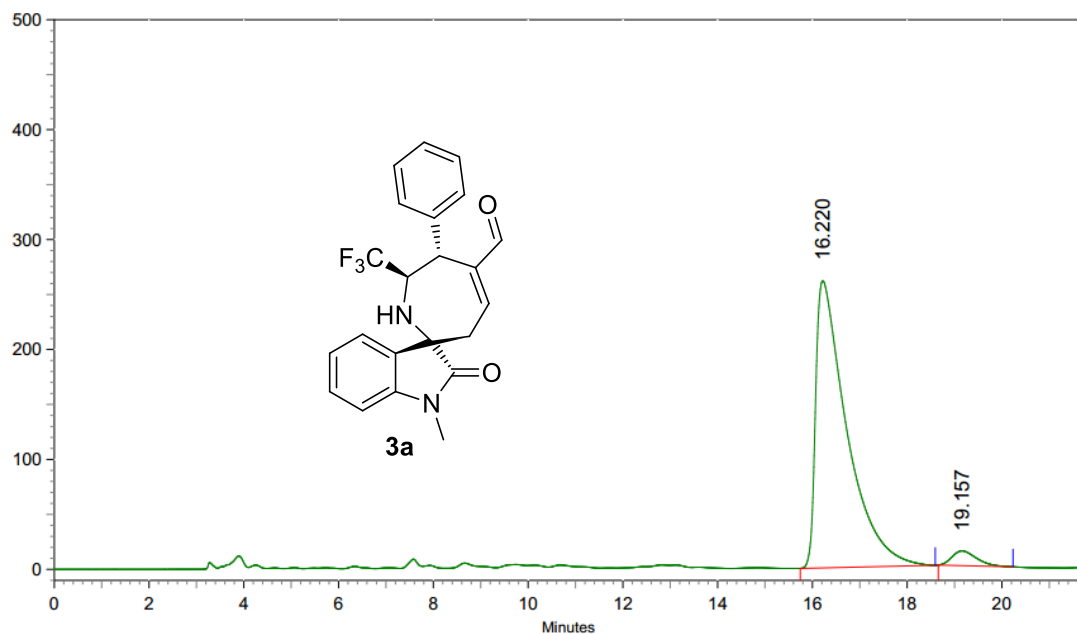
1: TOF MS ES+
4.23e4





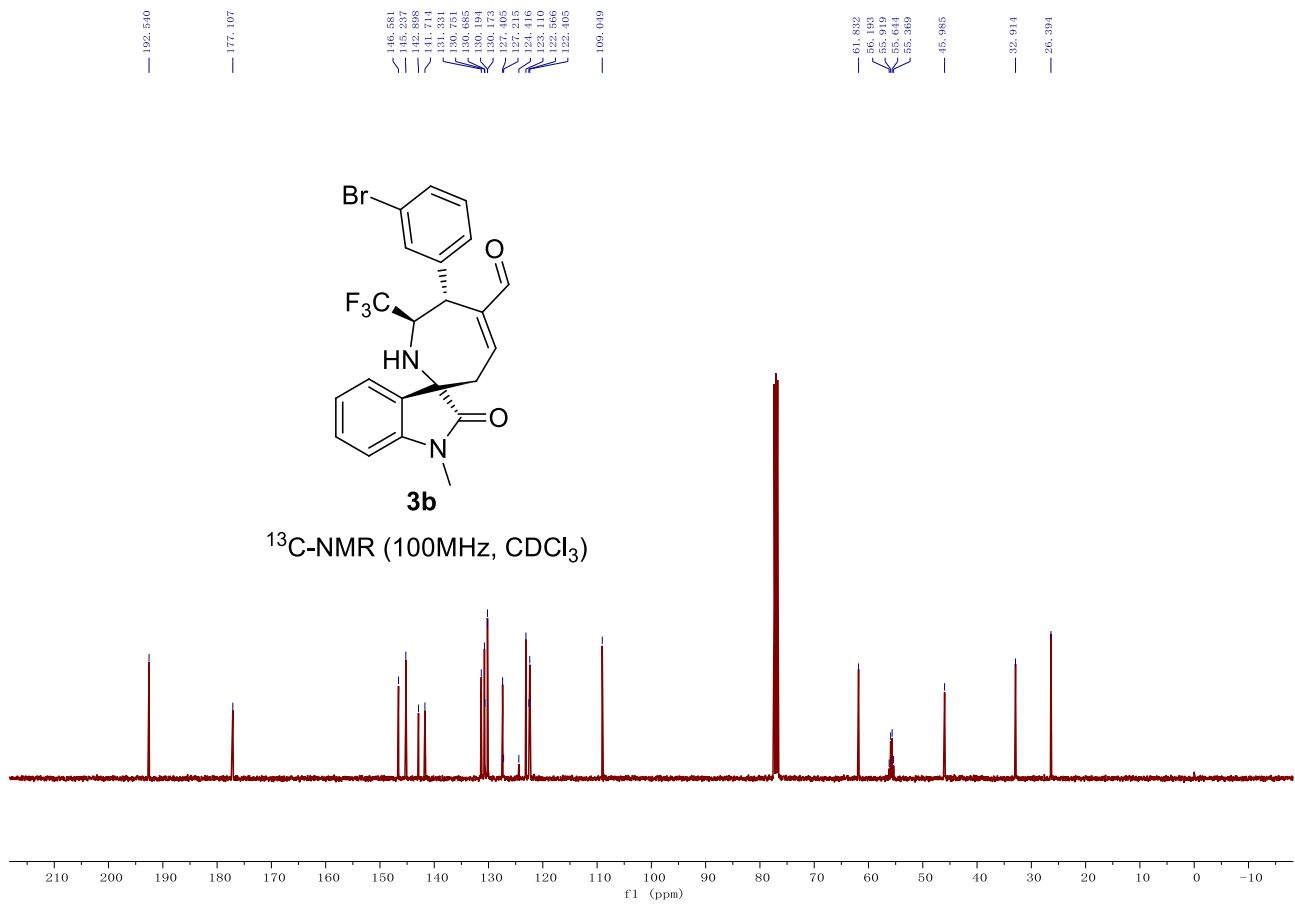
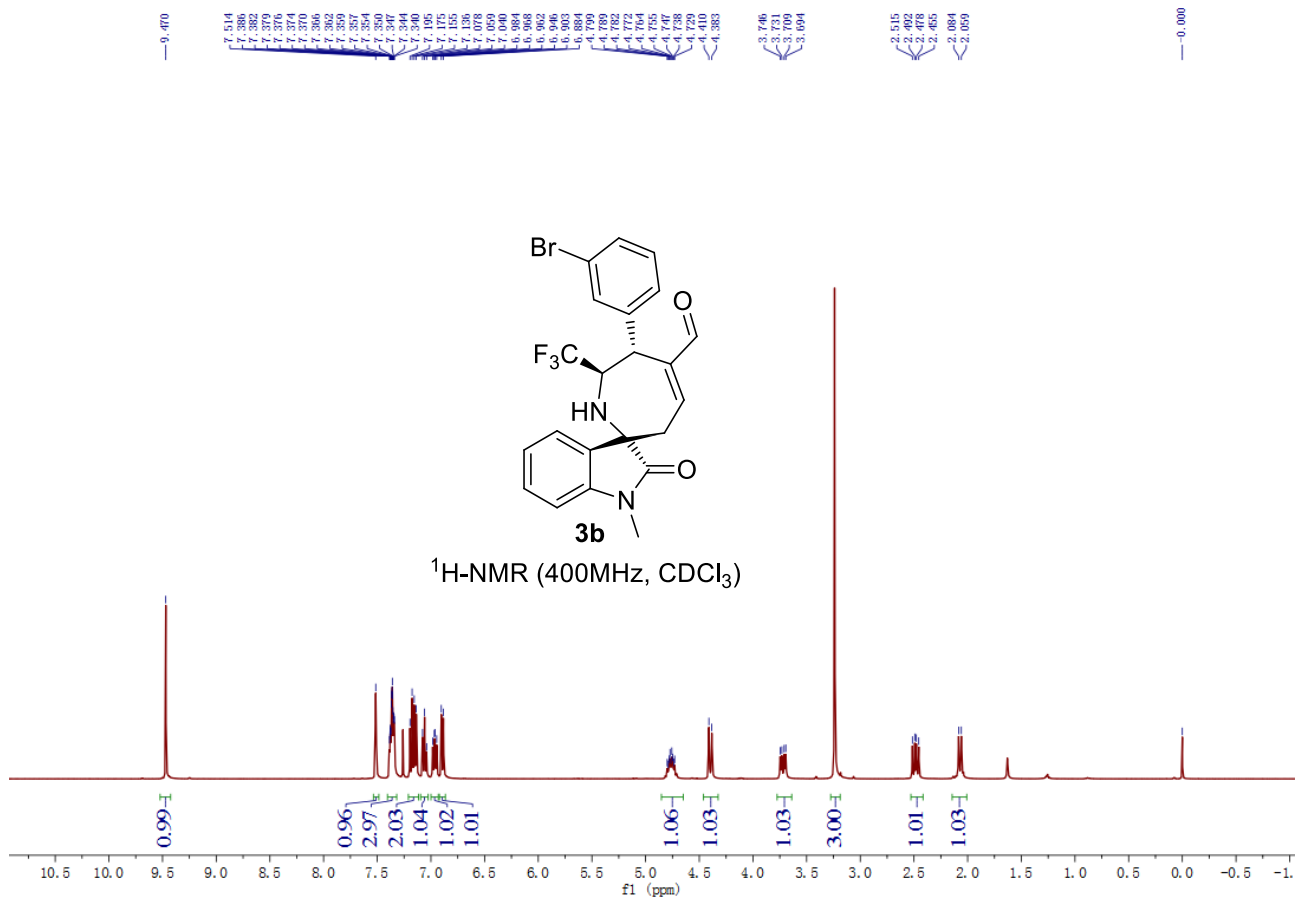
AREA PERCENT REPORT

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1	14.920	2.563	11622156	514131367	49.1405
2	17.543	3.717	13978743	532115617	50.8595

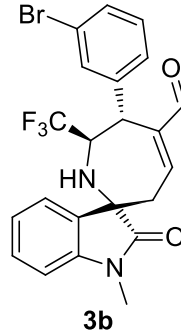


AREA PERCENT REPORT

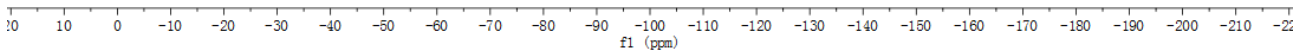
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	16.220	2.850	4383154	199090561	96.1076
2	19.157	1.577	224393	8063292	3.8924



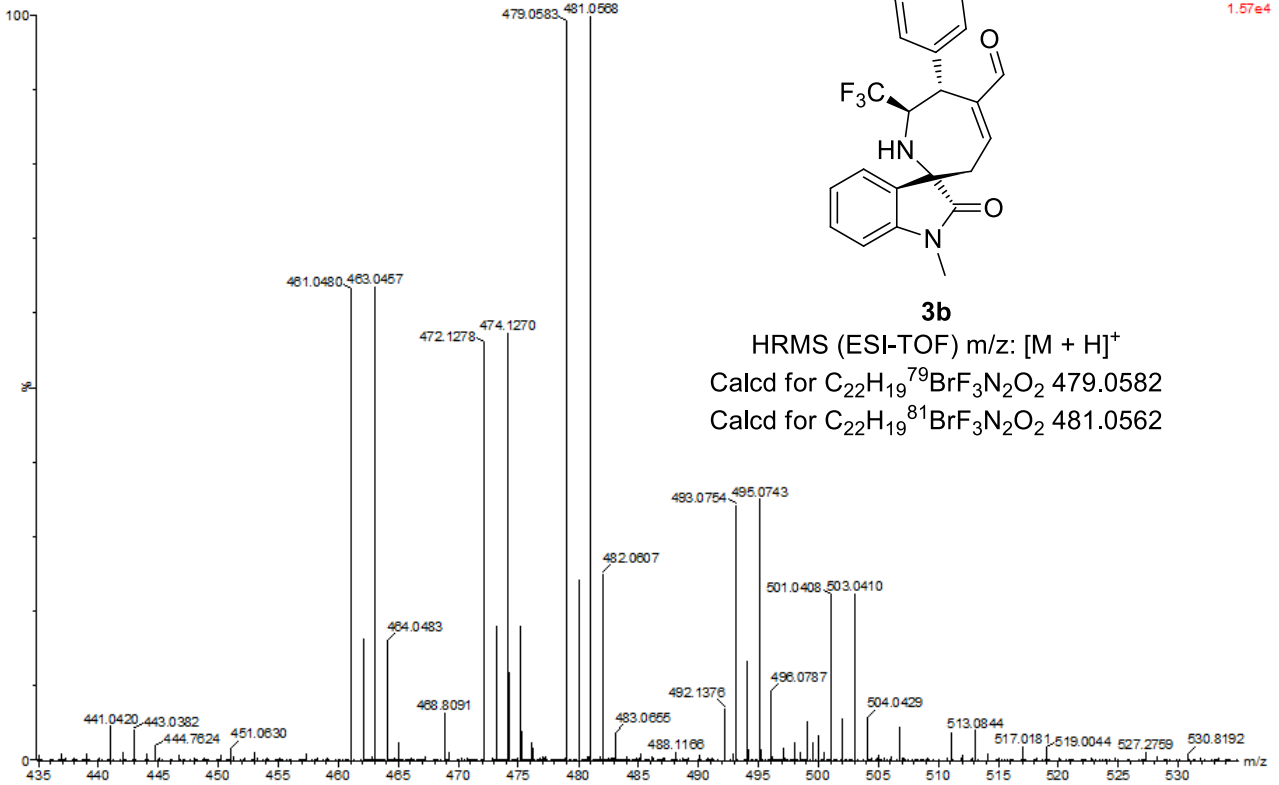
-73.852

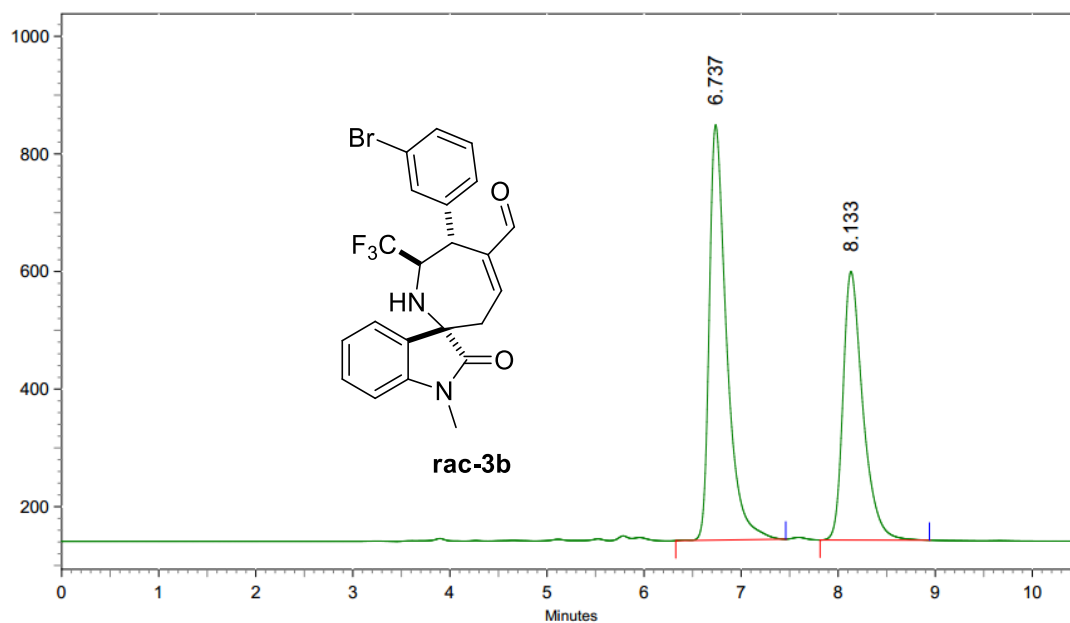


3b
 ^{19}F -NMR (376MHz, CDCl_3)



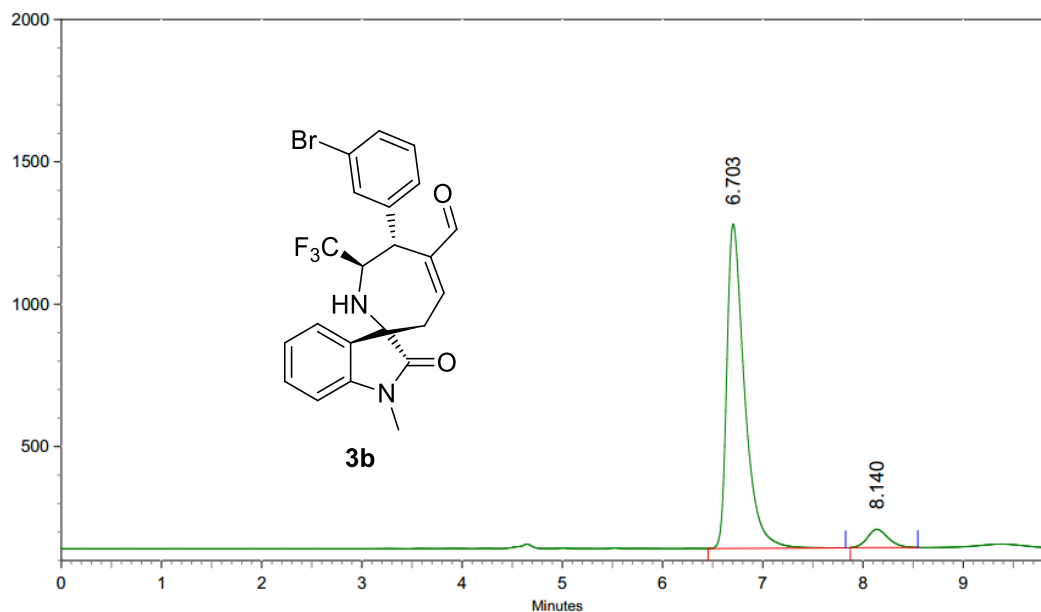
200117_GY_SS_25 14 (0.239) Cm (3.24)





AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.737	1.133	11848156	147141819	57.4872
2	8.133	1.127	7659915	108814018	42.5128



AREA PERCENT REPORT

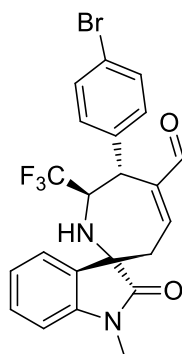
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.703	1.373	19103979	234131608	93.7380
2	8.140	0.673	1079181	15640819	6.2620

8.755

6.860
6.839
6.729
6.720
6.694
6.678
6.670
6.649
6.464
6.457
6.441
6.428
6.388

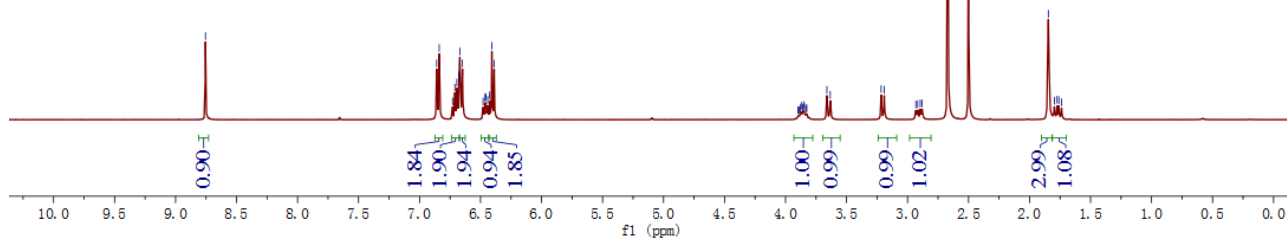
3.898
3.890
3.880
3.871
3.858
3.852
3.845
3.833
3.826
3.661
3.633
3.491
2.932
2.917
2.895
2.886

1.846
1.797
1.774
1.759
1.737



3c

¹H-NMR (400MHz, DMSO)



194.297

177.393

146.687
146.466
142.919
140.500
131.833
131.094
129.863
128.203
127.863
124.403
122.687
120.564

109.225

79.650

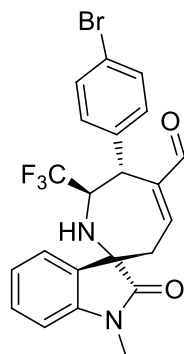
62.446

56.319
56.051

45.494

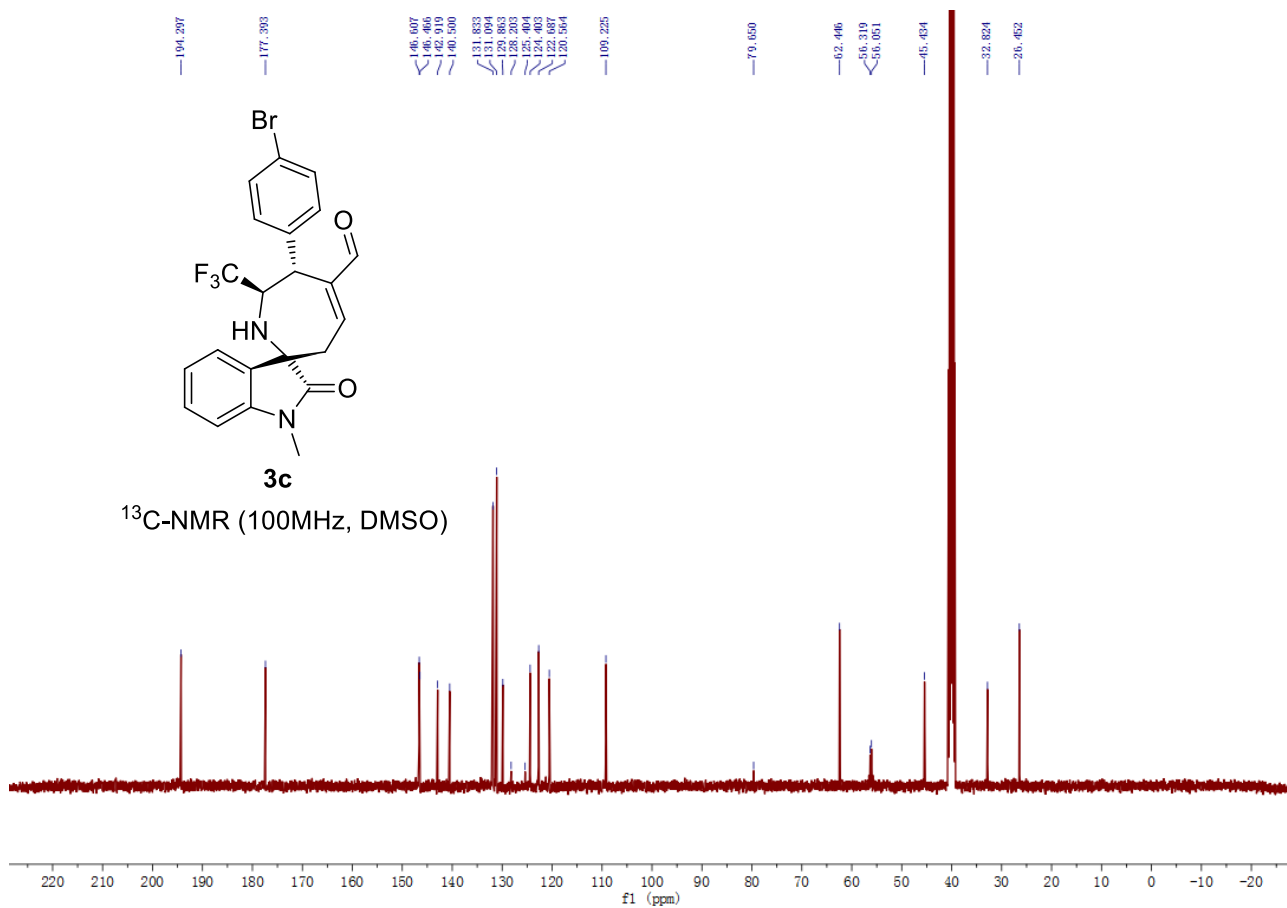
32.824

26.462

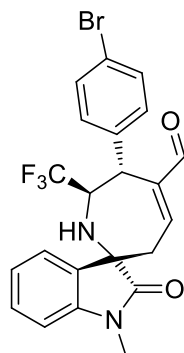


3c

¹³C-NMR (100MHz, DMSO)

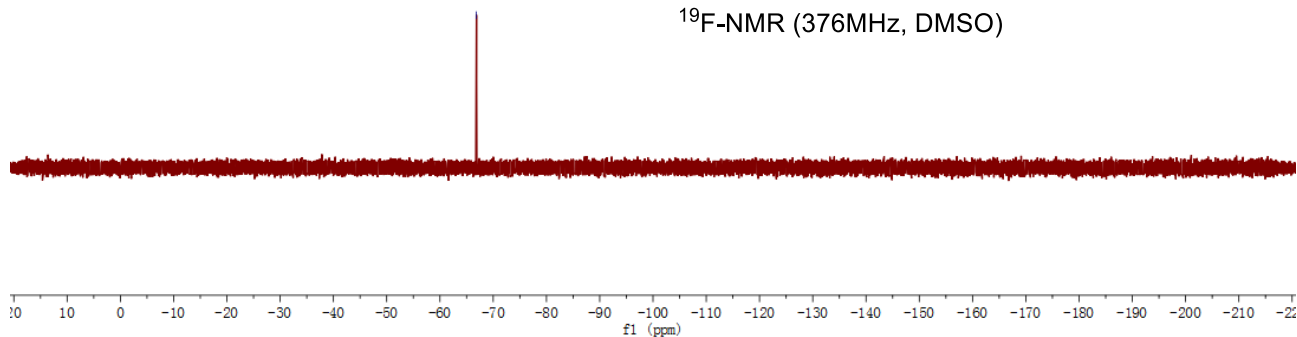


016.8488



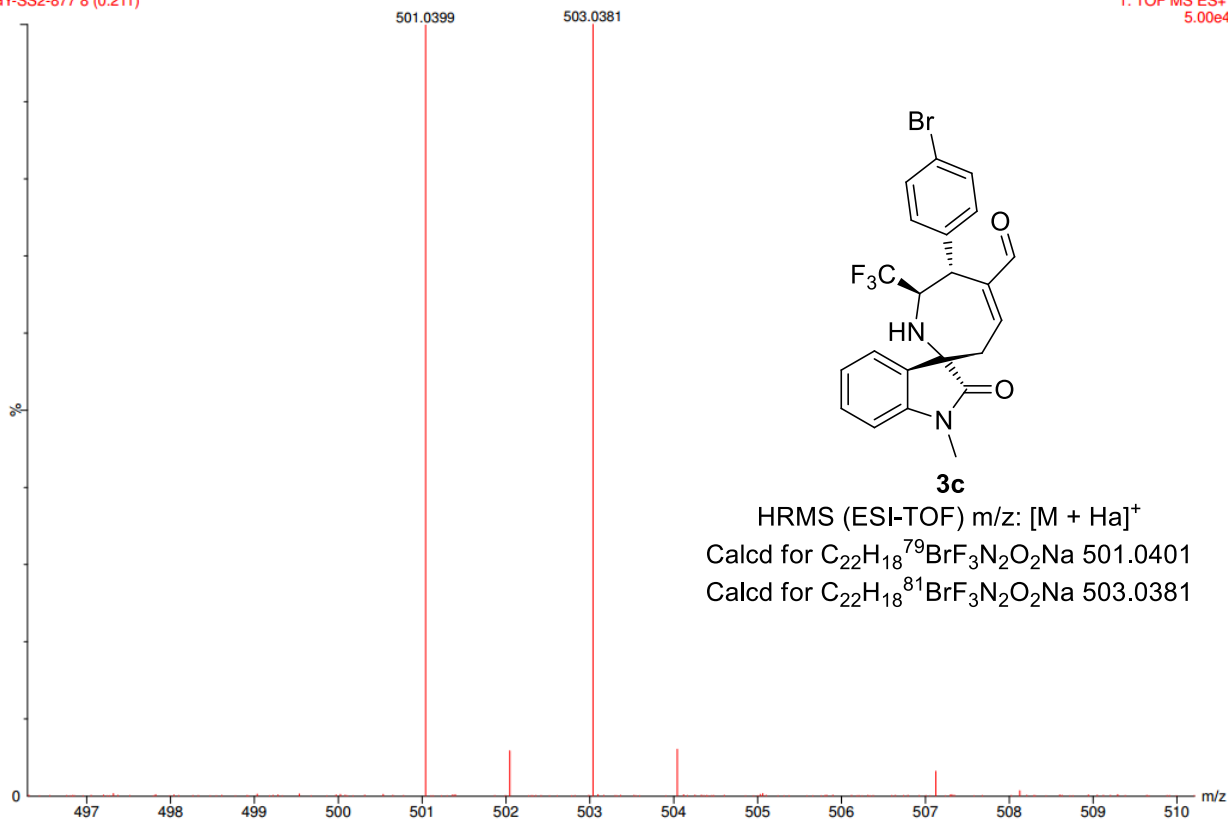
3c

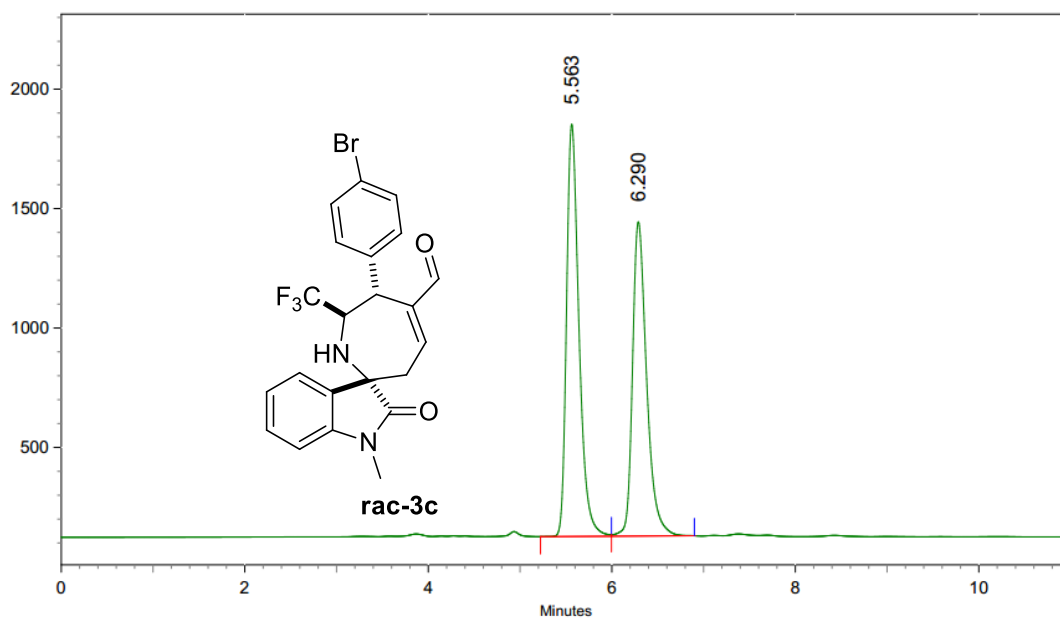
¹⁹F-NMR (376MHz, DMSO)



GY-SS2-877 8 (0.211)

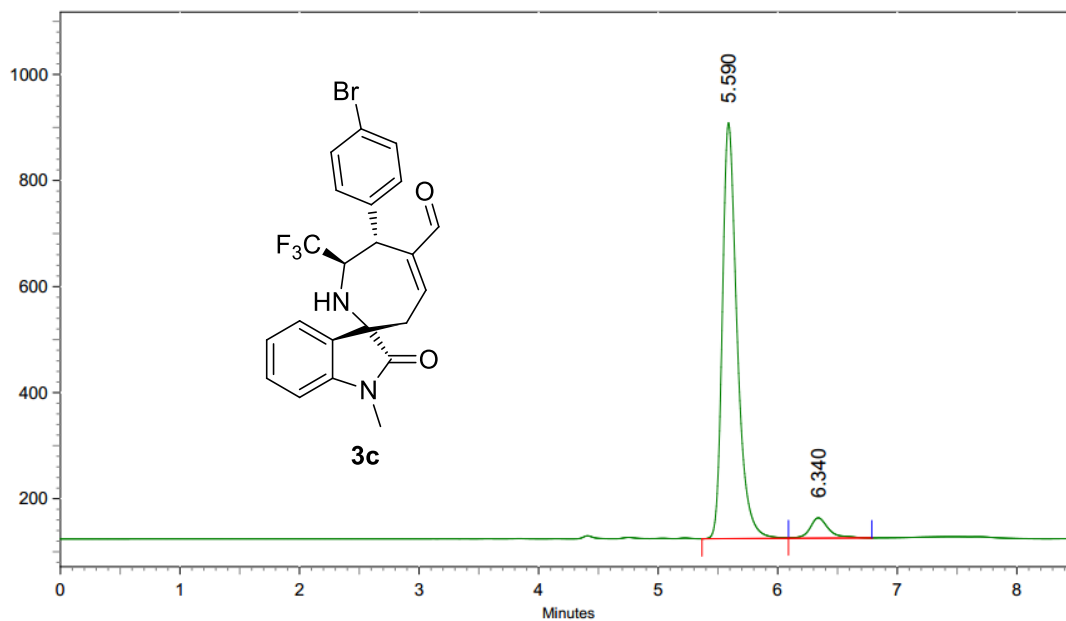
1: TOF MS ES+
5.00e4





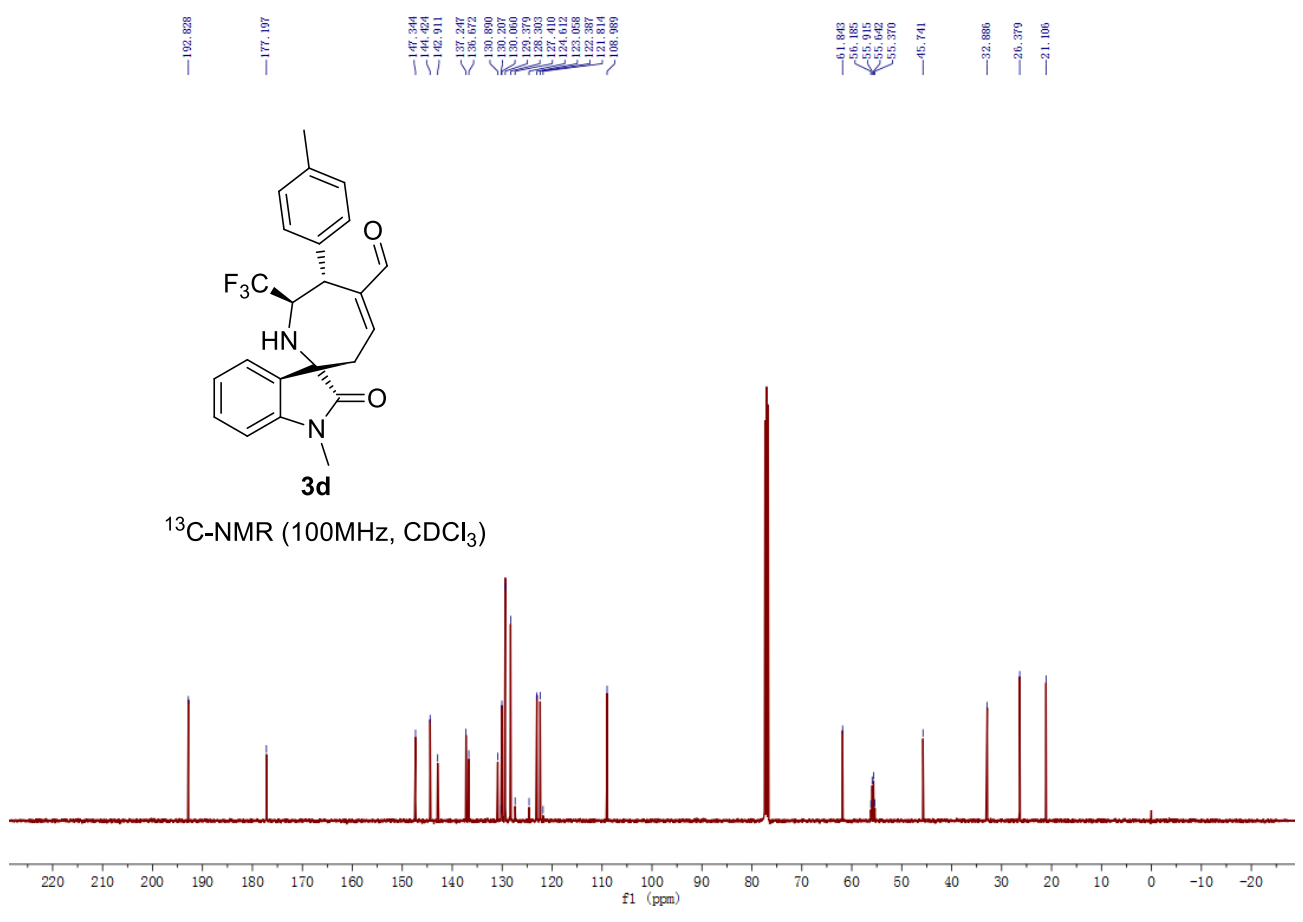
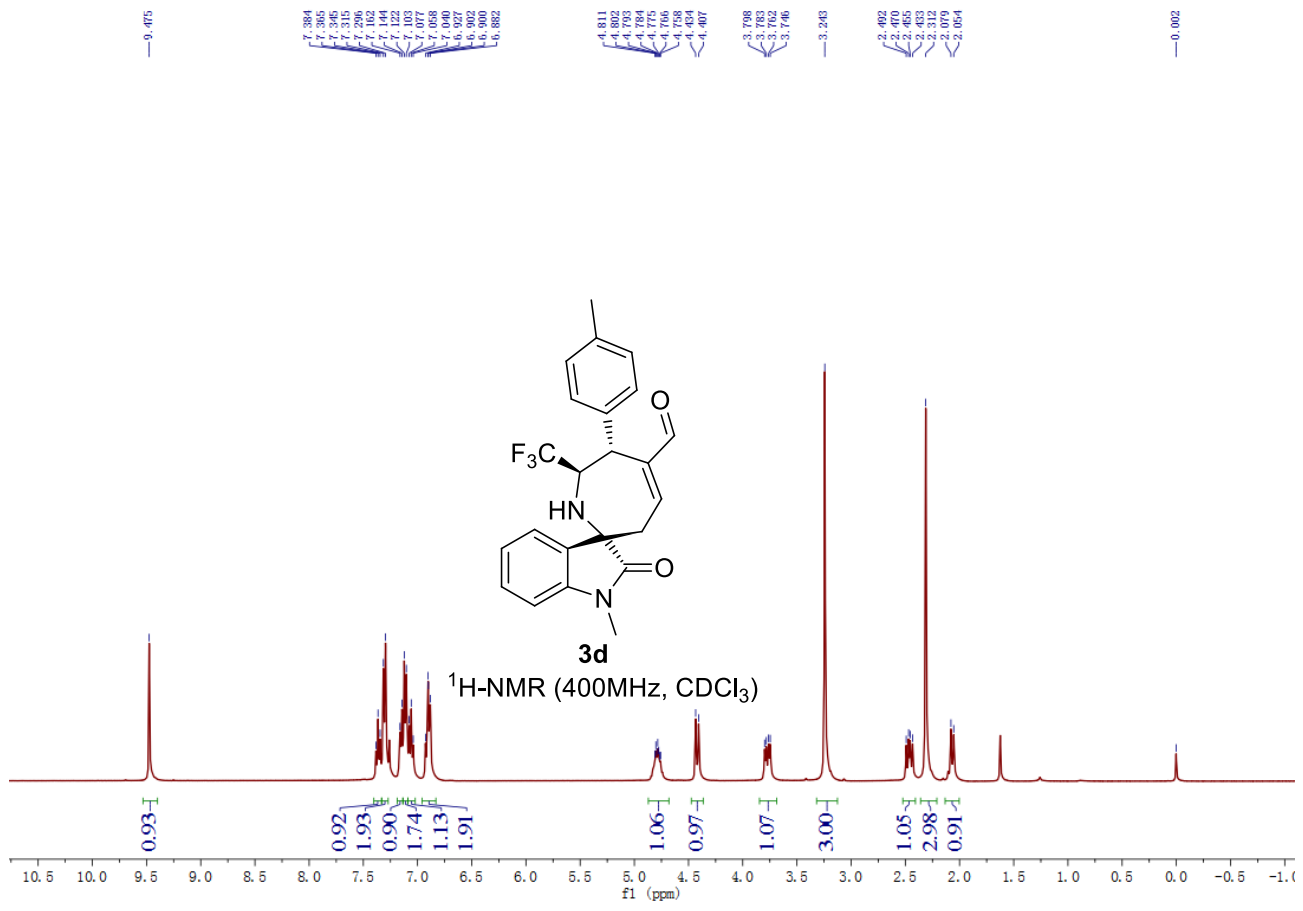
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.563	0.773	28955456	272437985	53.5868
2	6.290	0.903	22071340	235967286	46.4132

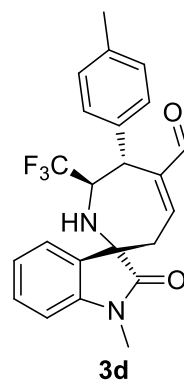


AREA PERCENT REPORT

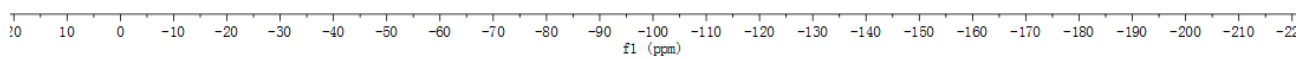
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.590	0.723	13149877	112710668	94.1583
2	6.340	0.697	642660	6992692	5.8417



-71.035



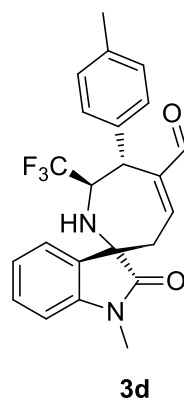
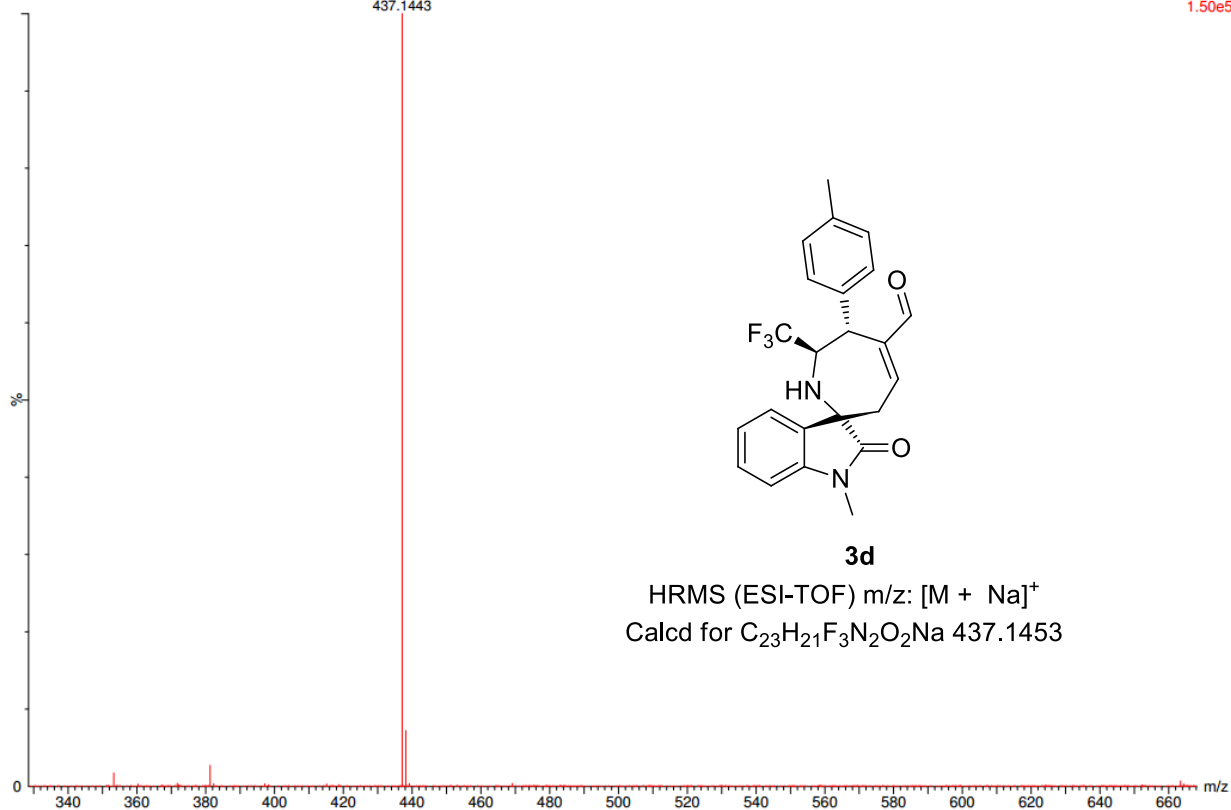
3d
¹⁹F-NMR (376MHz, CDCl₃)



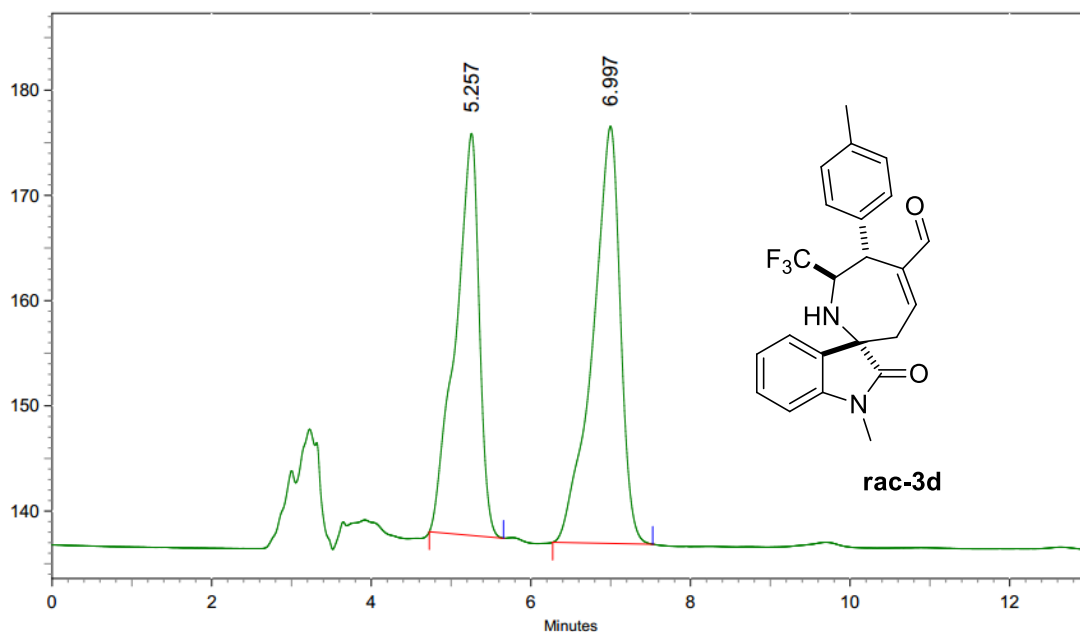
GY-SS3-862 12 (0.299)

437.1443

1: TOF MS ES+
1.50e5

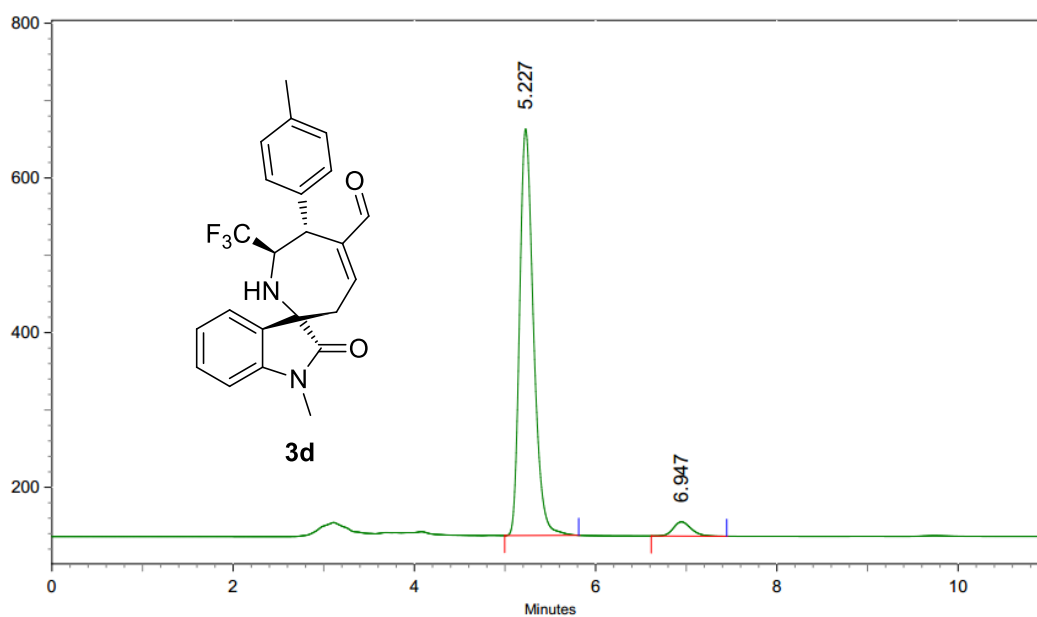


3d
HRMS (ESI-TOF) m/z: [M + Na]⁺
Calcd for C₂₃H₂₁F₃N₂O₂Na 437.1453



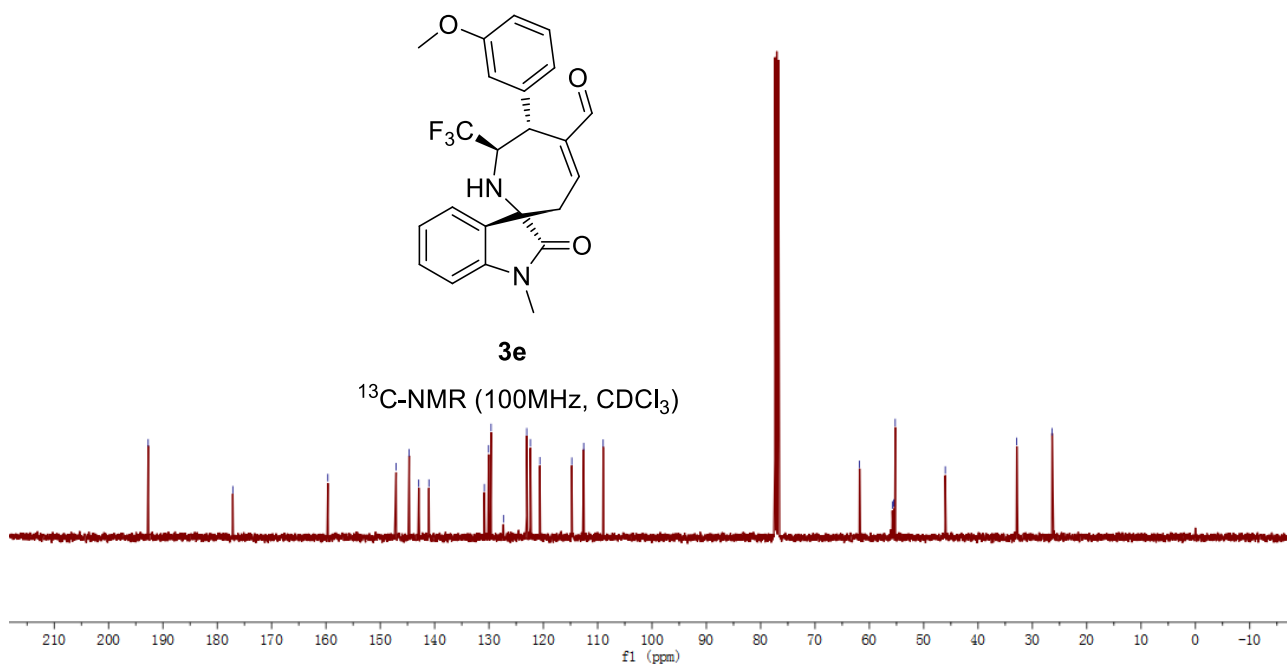
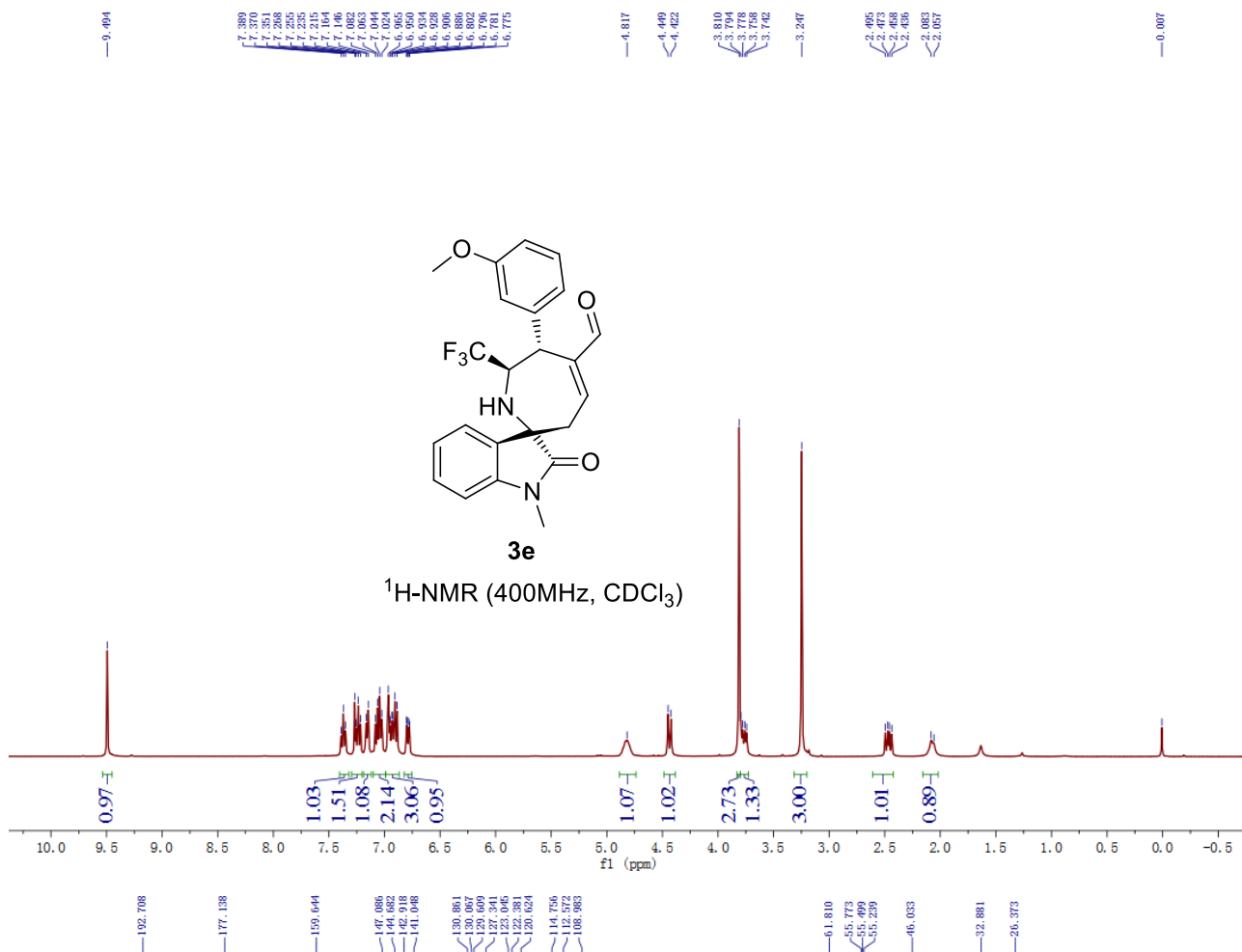
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.257	0.930	640914	13166767	45.0624
2	6.997	1.253	665000	16052198	54.9376

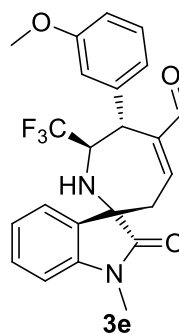


AREA PERCENT REPORT

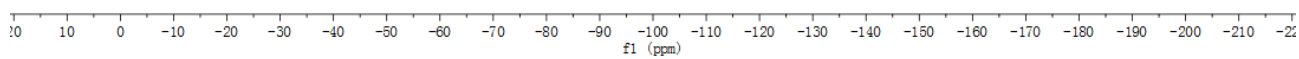
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.227	0.817	8818510	93455631	95.6570
2	6.947	0.833	309458	4243078	4.3430



-71.077



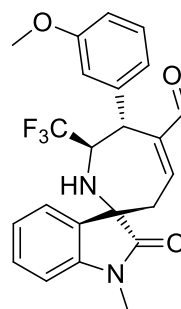
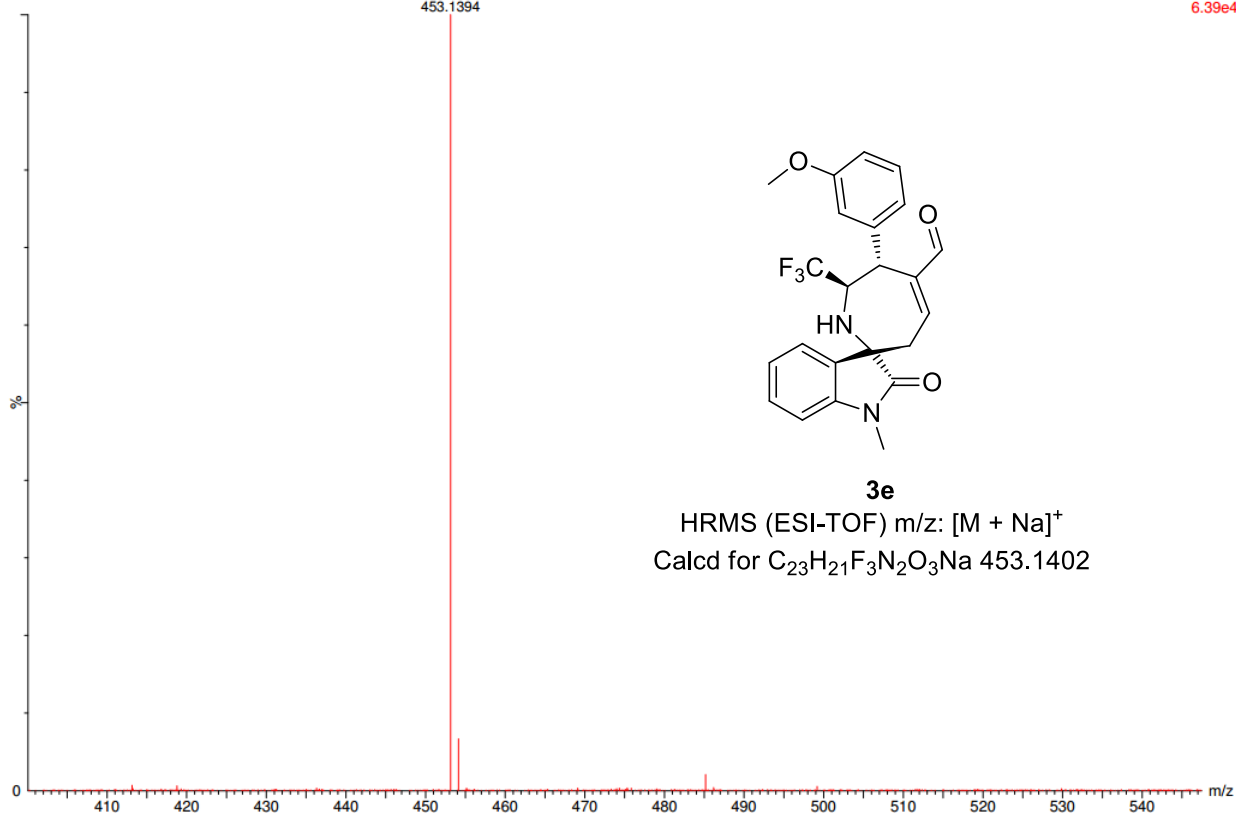
¹⁹F-NMR (376MHz, CDCl₃)



GY-SS6-862 18 (0.440)

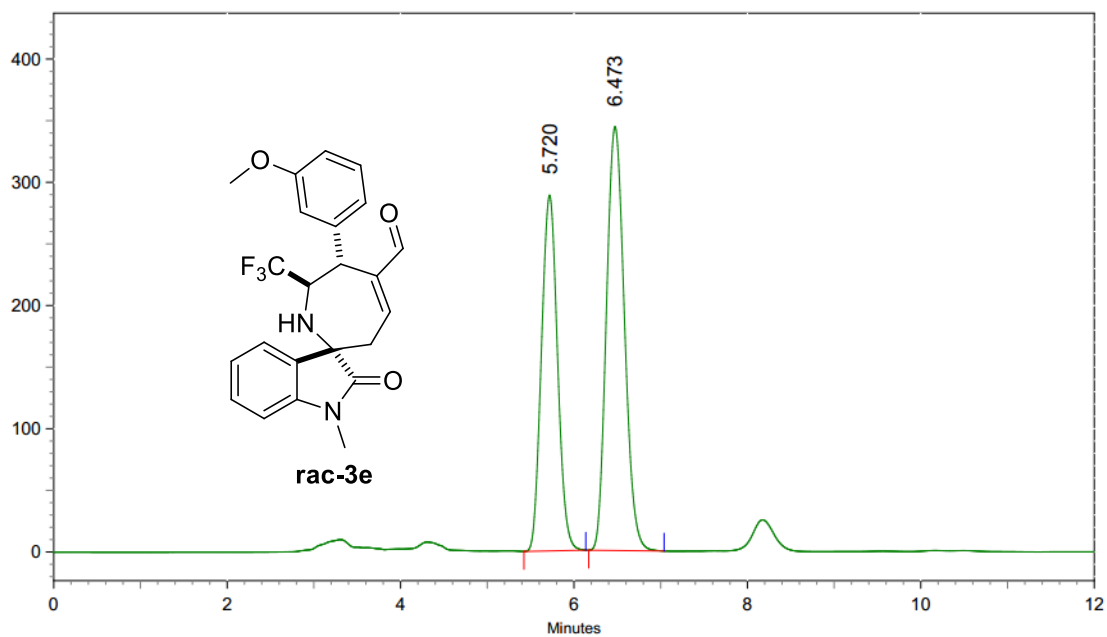
453.1394

1: TOF MS ES+
6.39e4



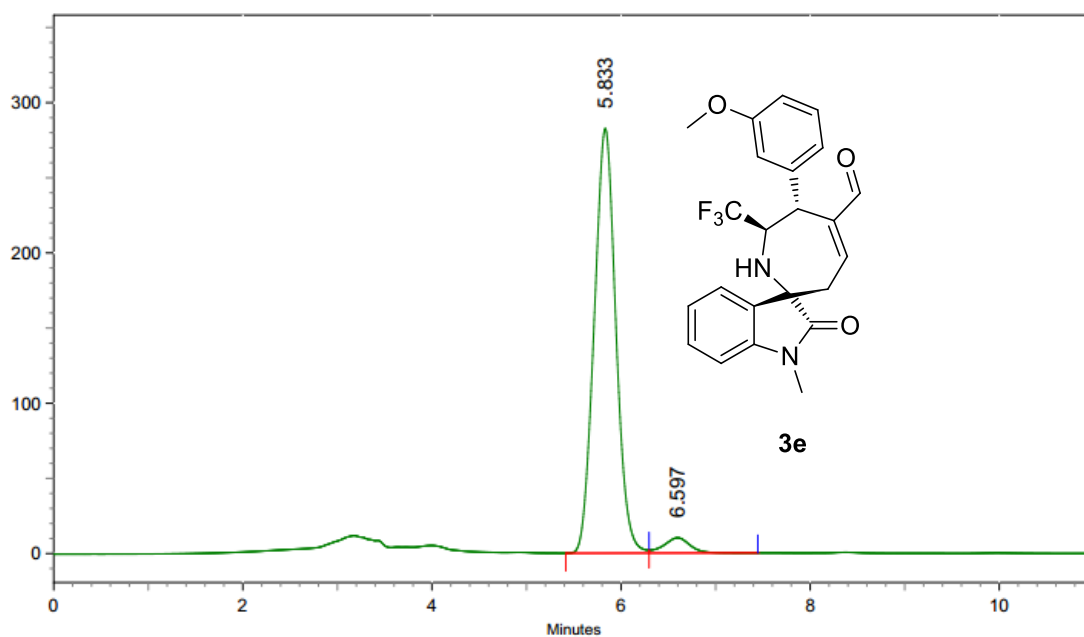
3e

HRMS (ESI-TOF) m/z: [M + Na]⁺
Calcd for C₂₃H₂₁F₃N₂O₃Na 453.1402



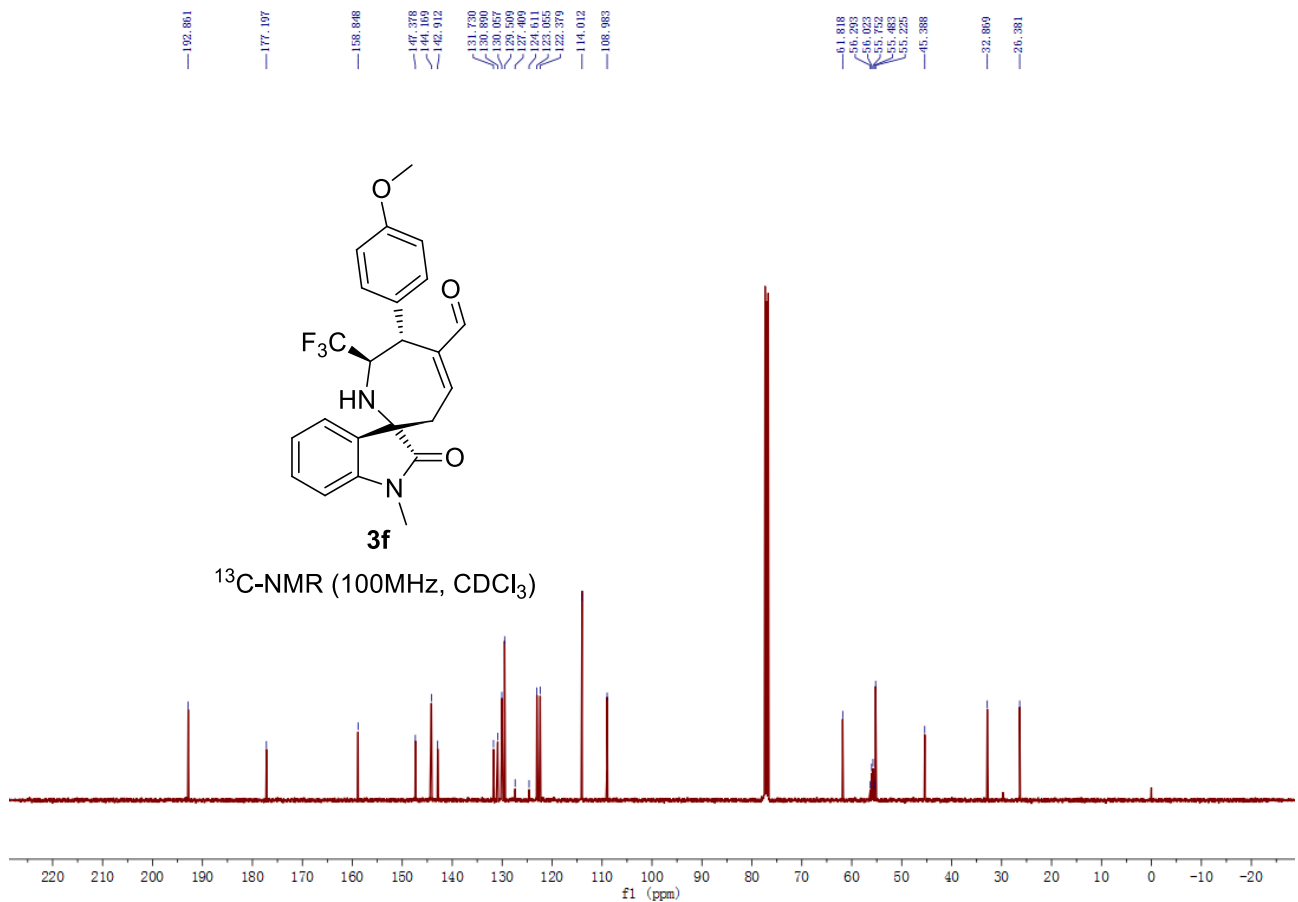
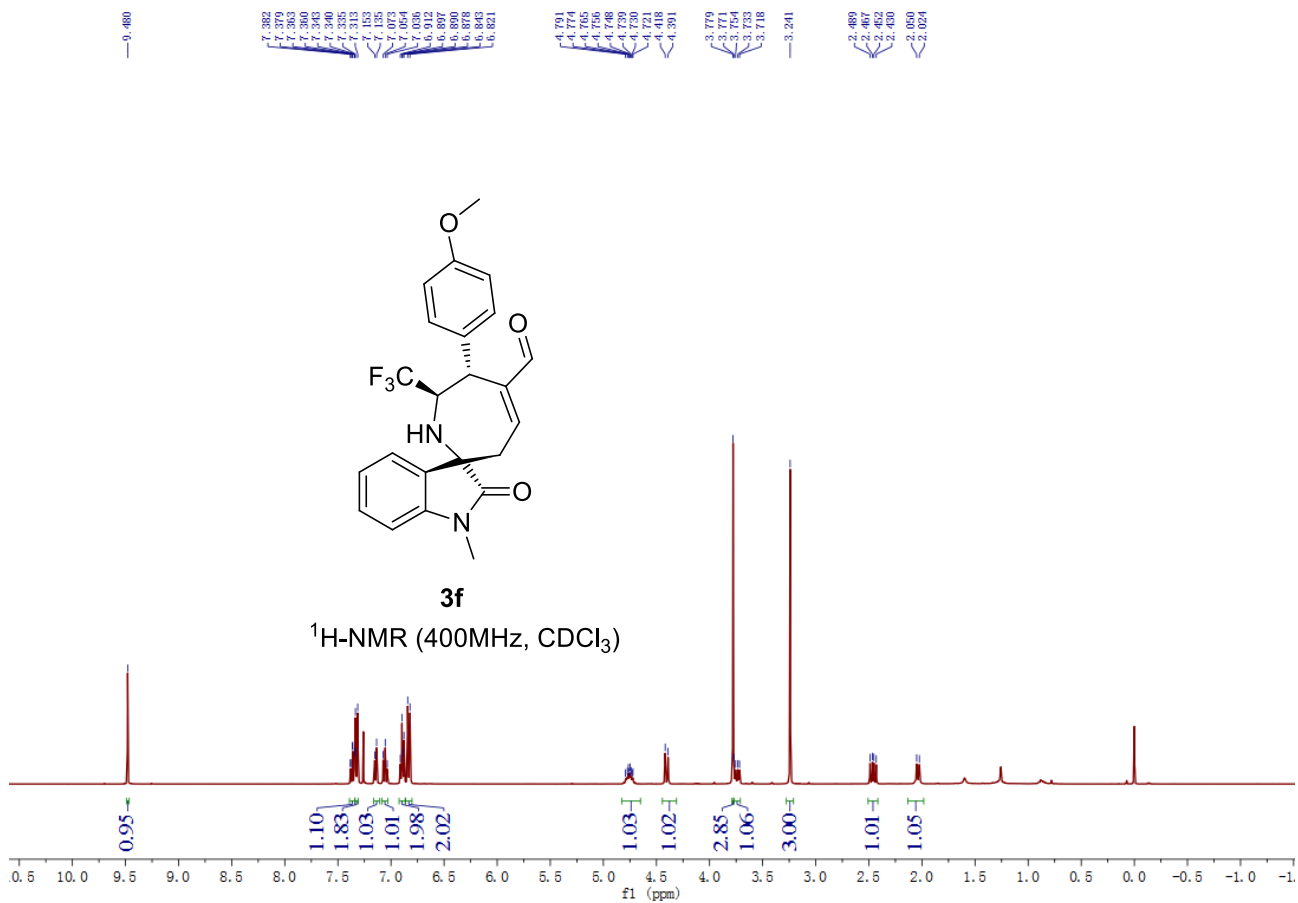
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.720	0.713	4843244	62270743	42.8676
2	6.473	0.870	5771079	82992359	57.1324

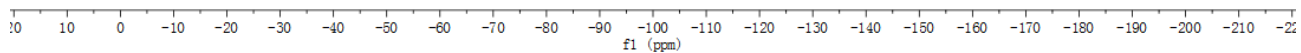
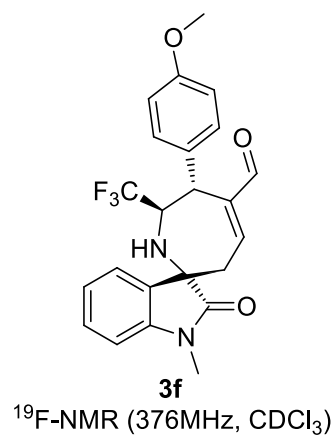


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.833	0.880	4740436	75314050	95.8647
2	6.597	1.150	170545	3248789	4.1353

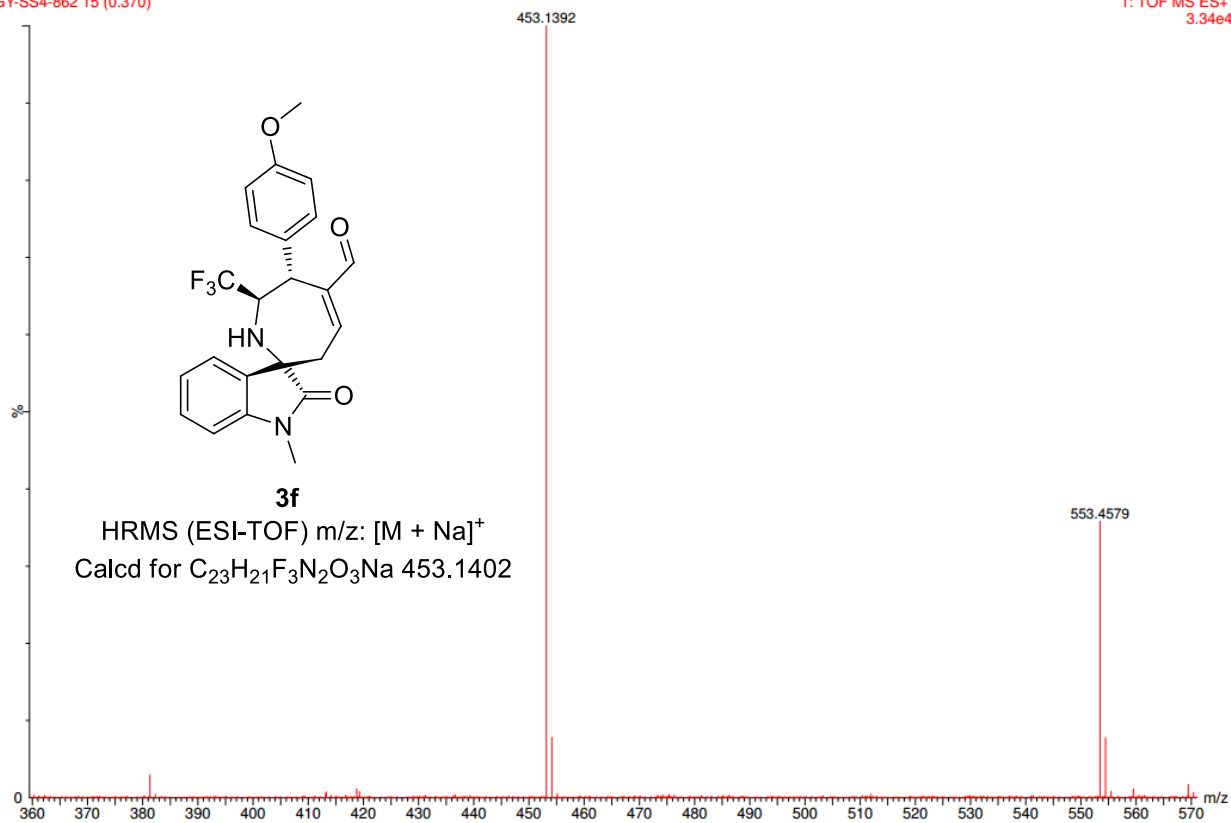


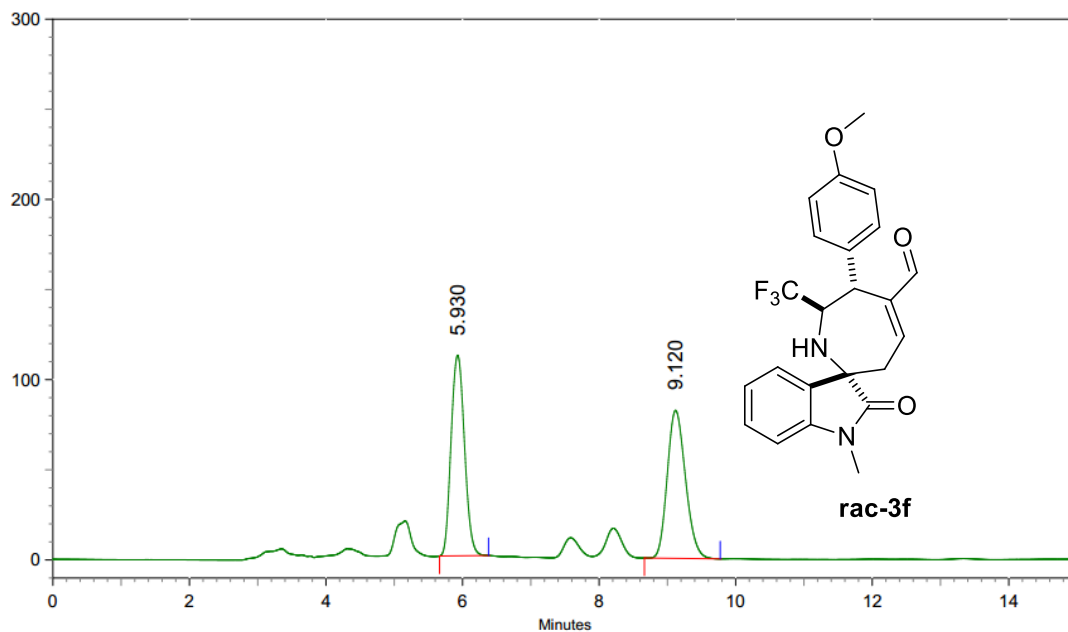
73.996



GY-SS4-862 15 (0.370)

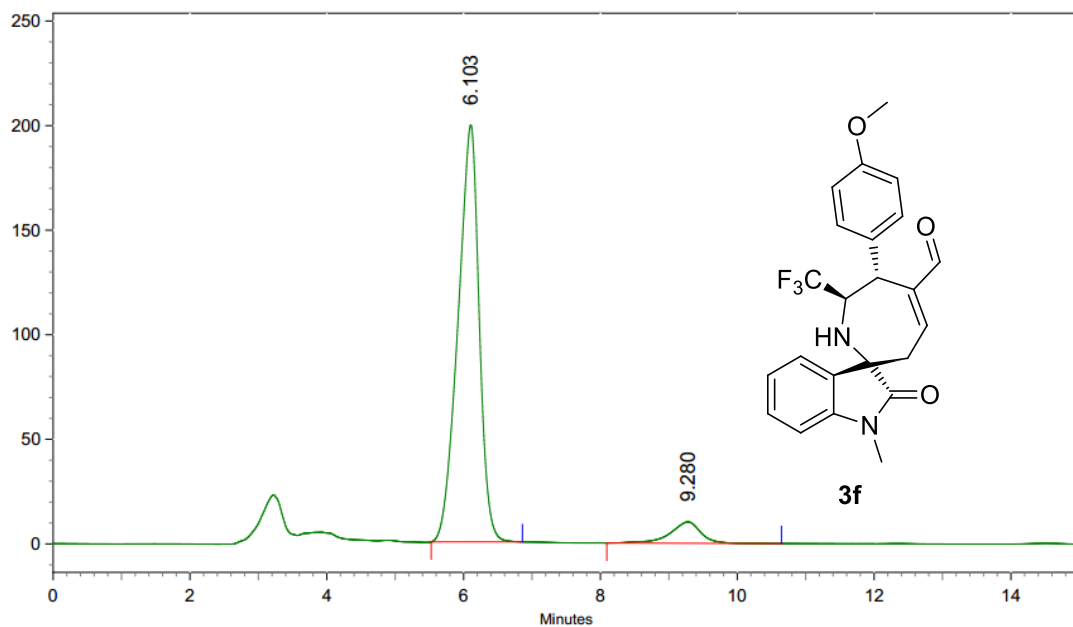
1: TOF MS ES+
3.34e4





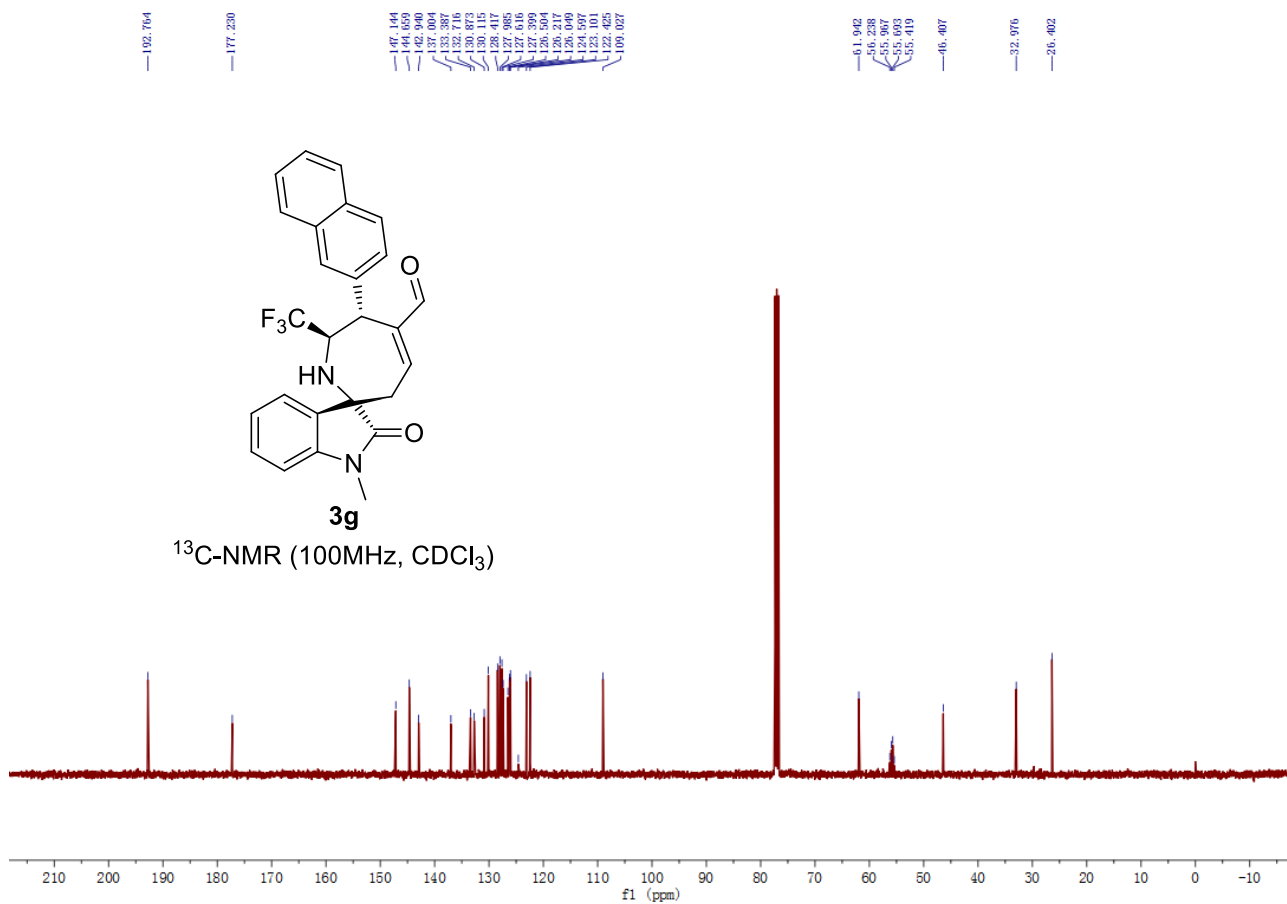
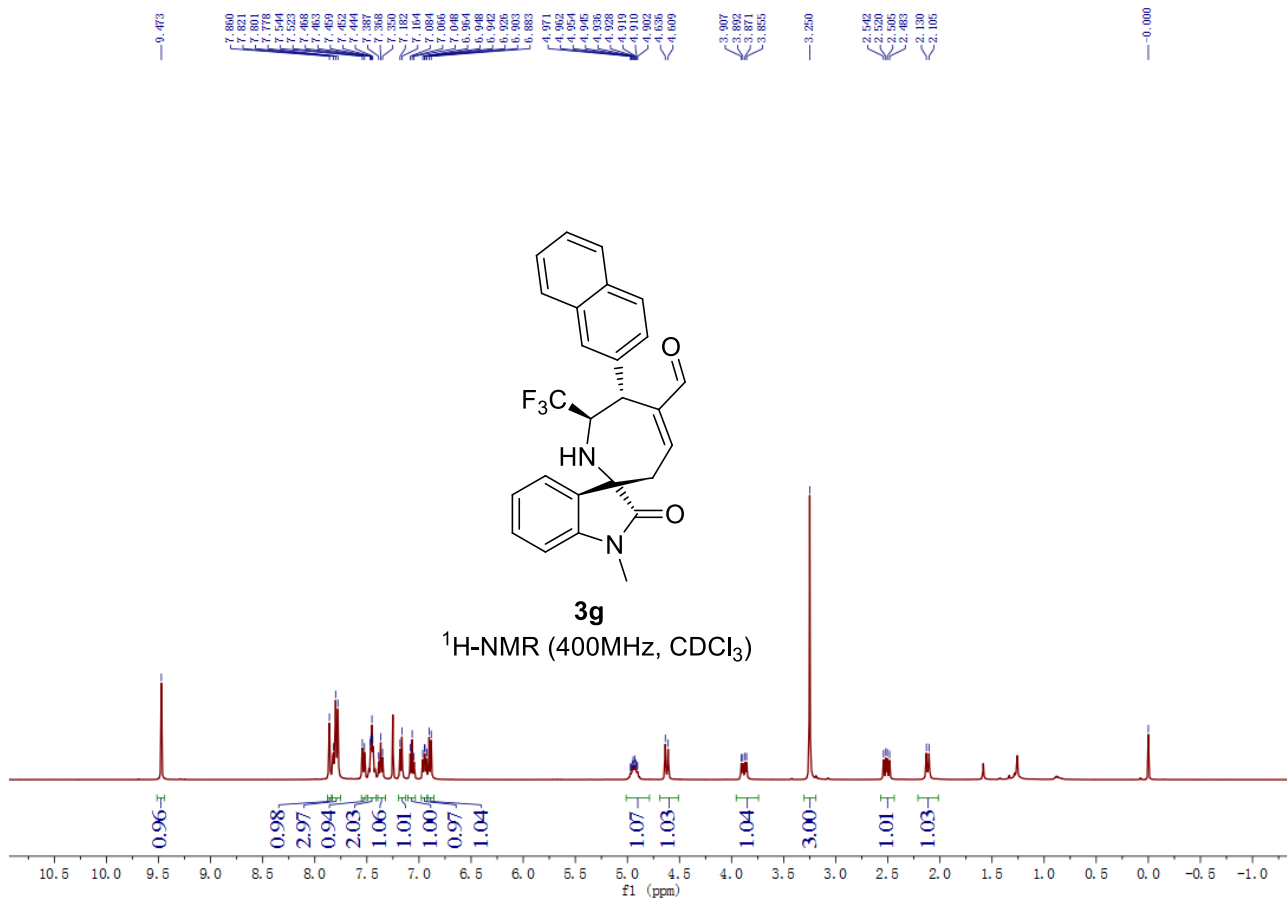
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.930	0.717	1867296	25496602	49.9390
2	9.120	1.110	1376944	25558919	50.0610

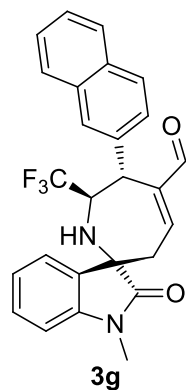


AREA PERCENT REPORT

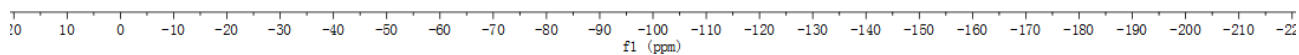
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.103	1.333	3343993	71825240	93.0758
2	9.280	2.553	170982	5343271	6.9242



71.265



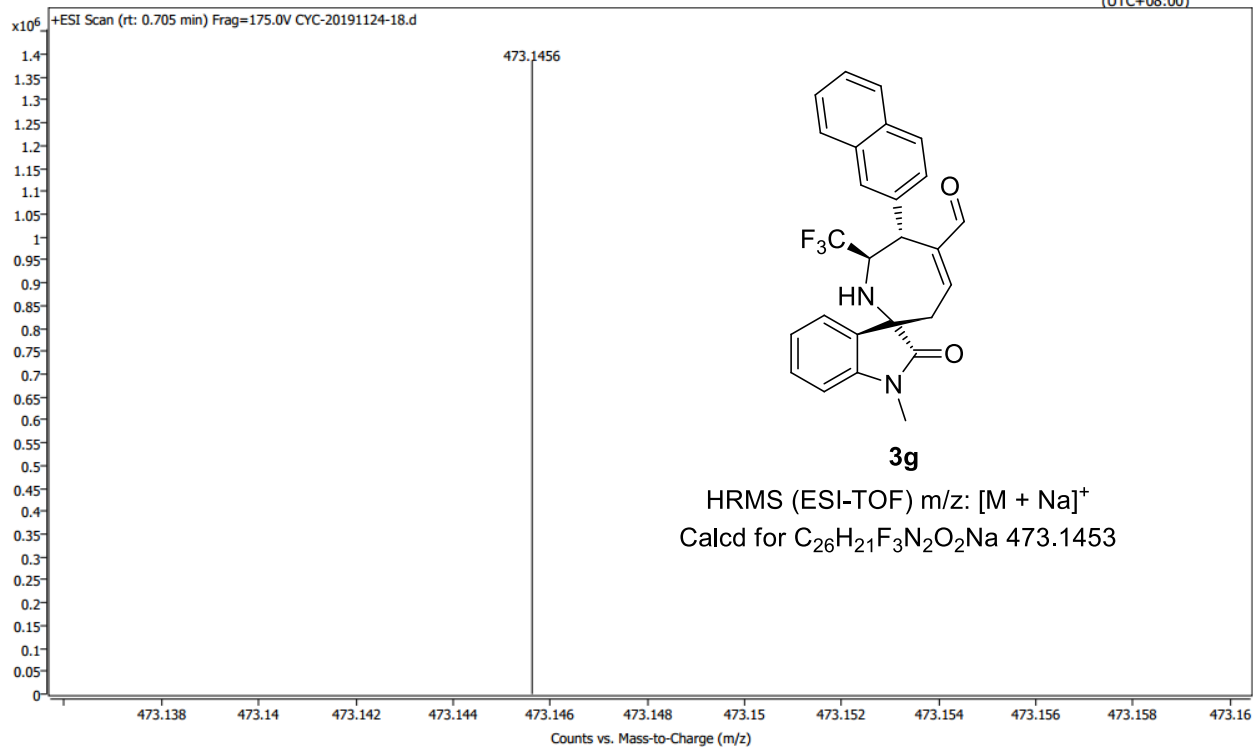
¹⁹F-NMR (376MHz, CDCl₃)

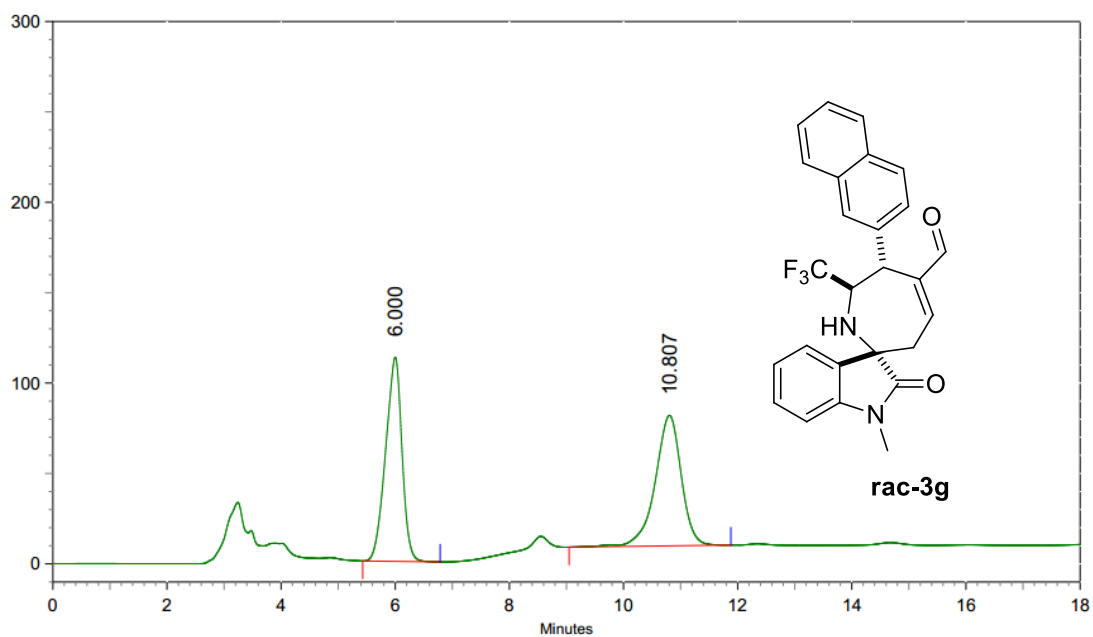


Spectrum Plot Report

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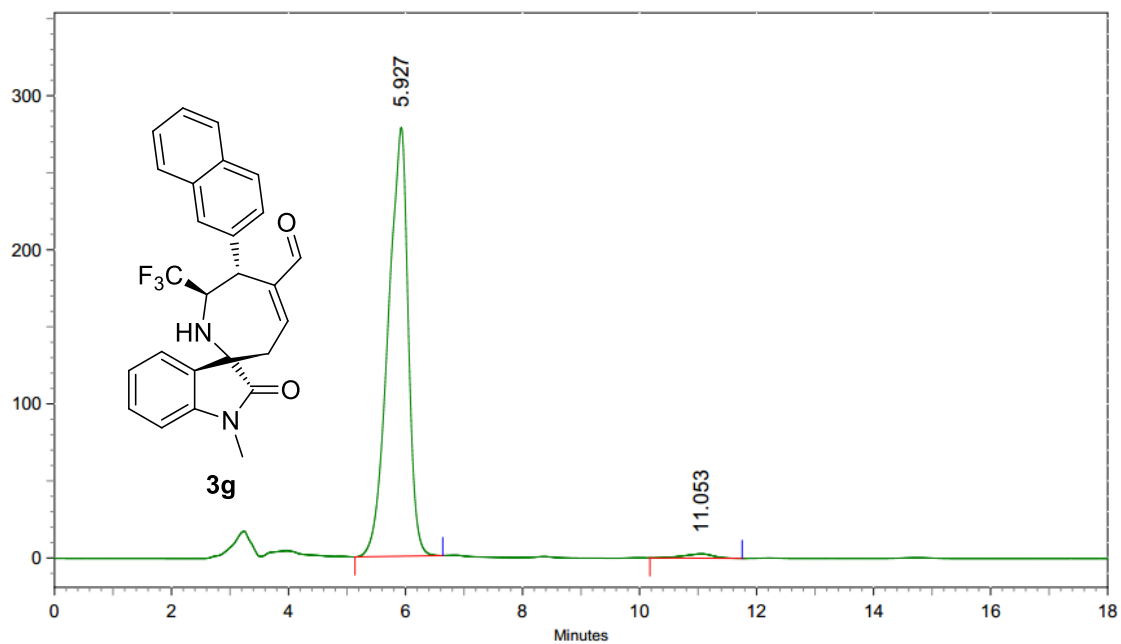
Name	CYC-20191124-18	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-18.d	Method (Acq)	TOF.m		Acq. Time (Local)
					12/5/2019 5:24:28 PM (UTC+08:00)





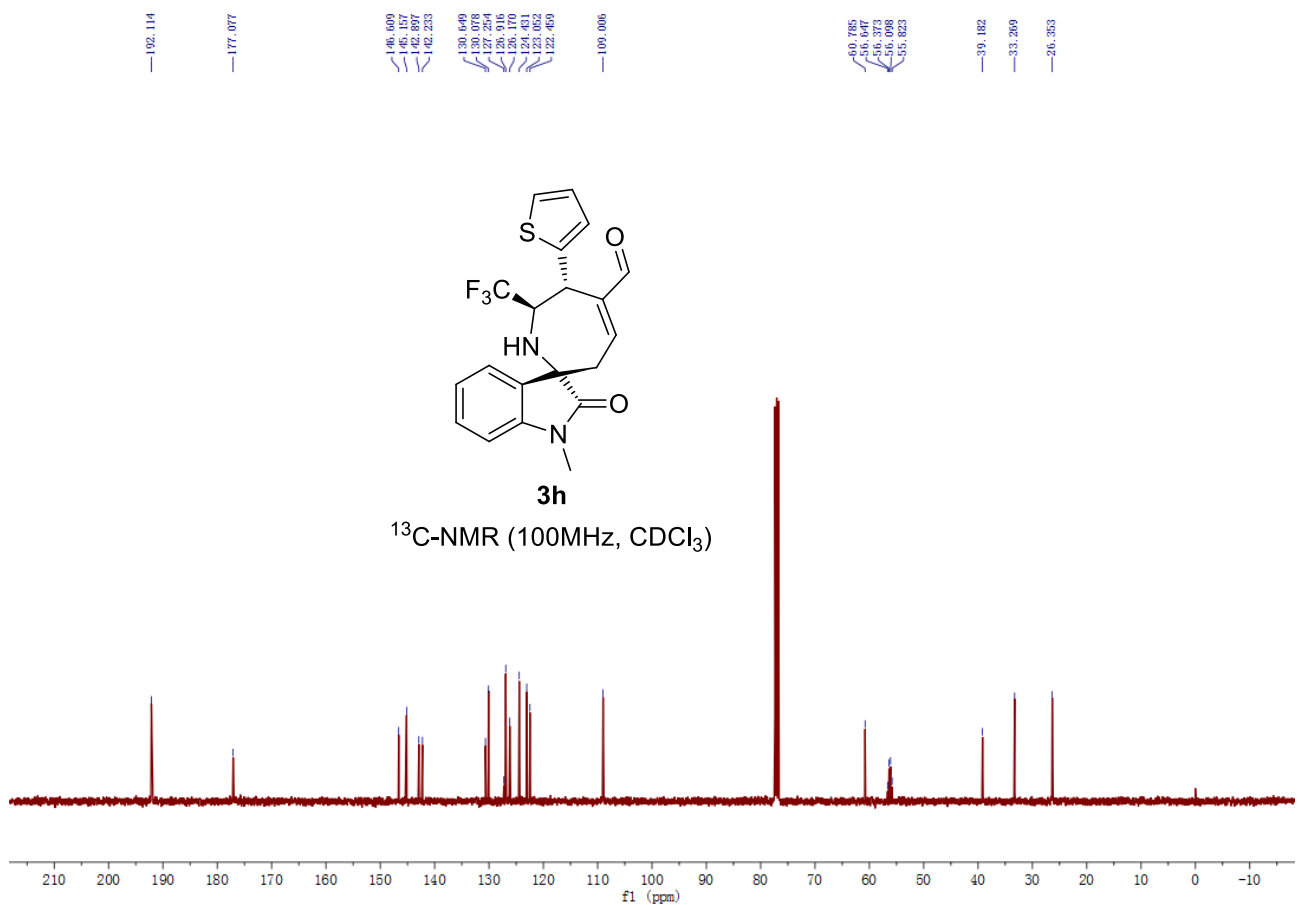
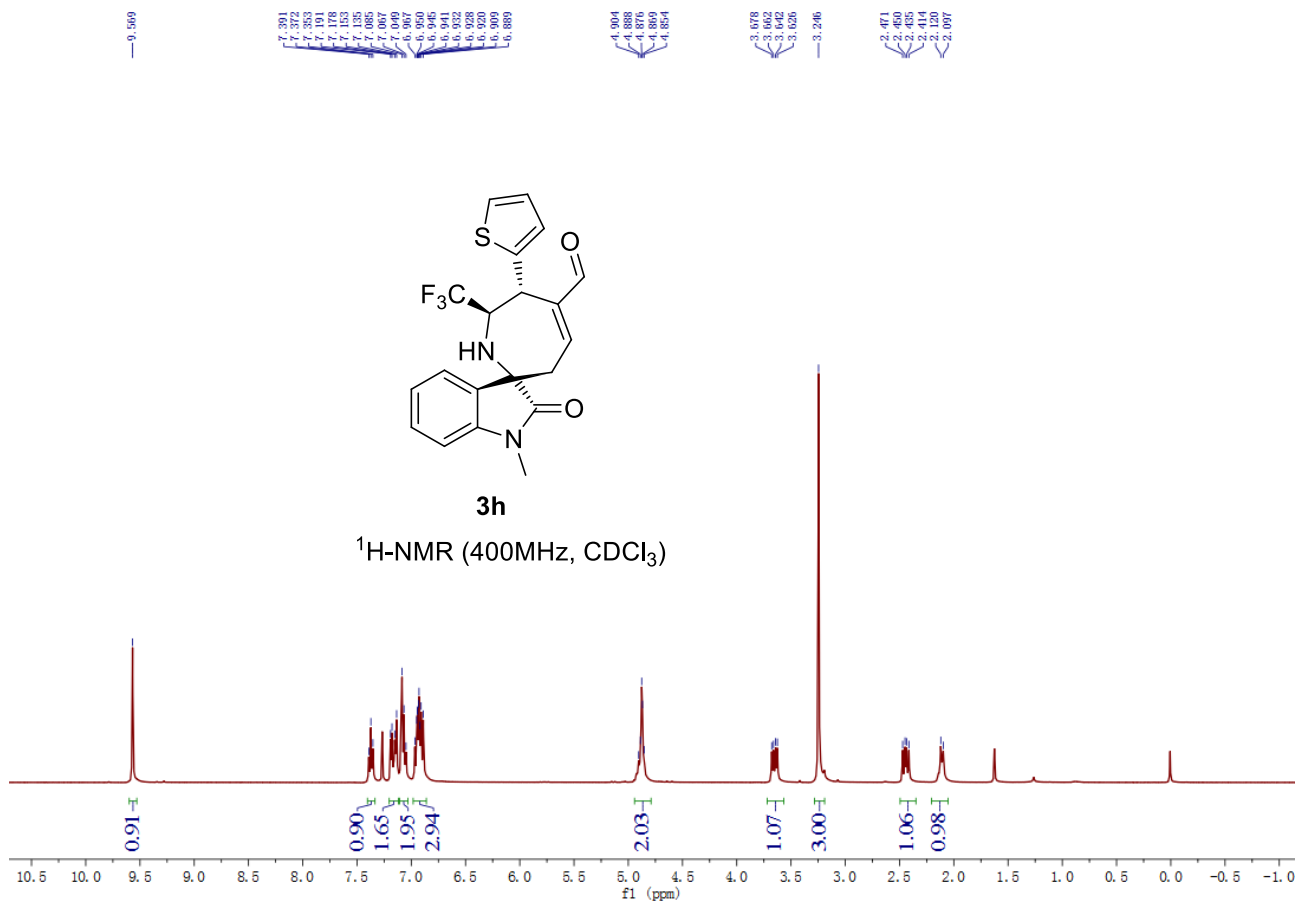
AREA PERCENT REPORT

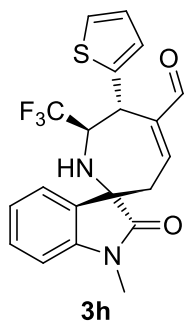
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.000	1.357	1895198	37807900	49.5270
2	10.807	2.833	1210333	38530011	50.4730



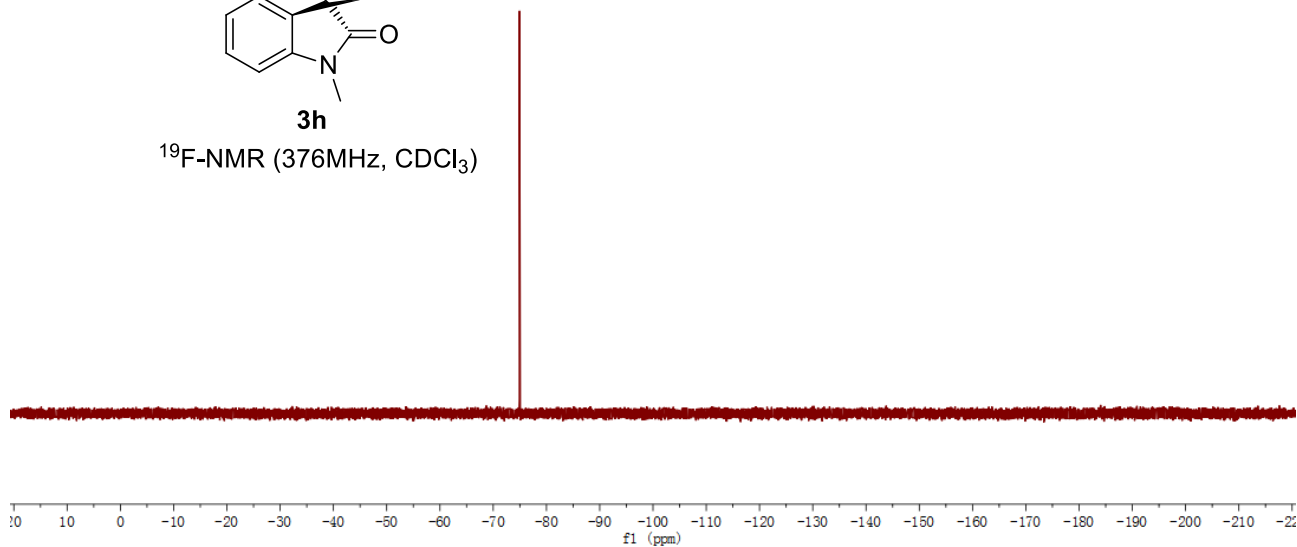
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	5.927	1.500	4665881	110335939	98.5397
2	11.053	1.577	46737	1635156	1.4603





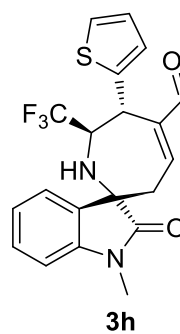
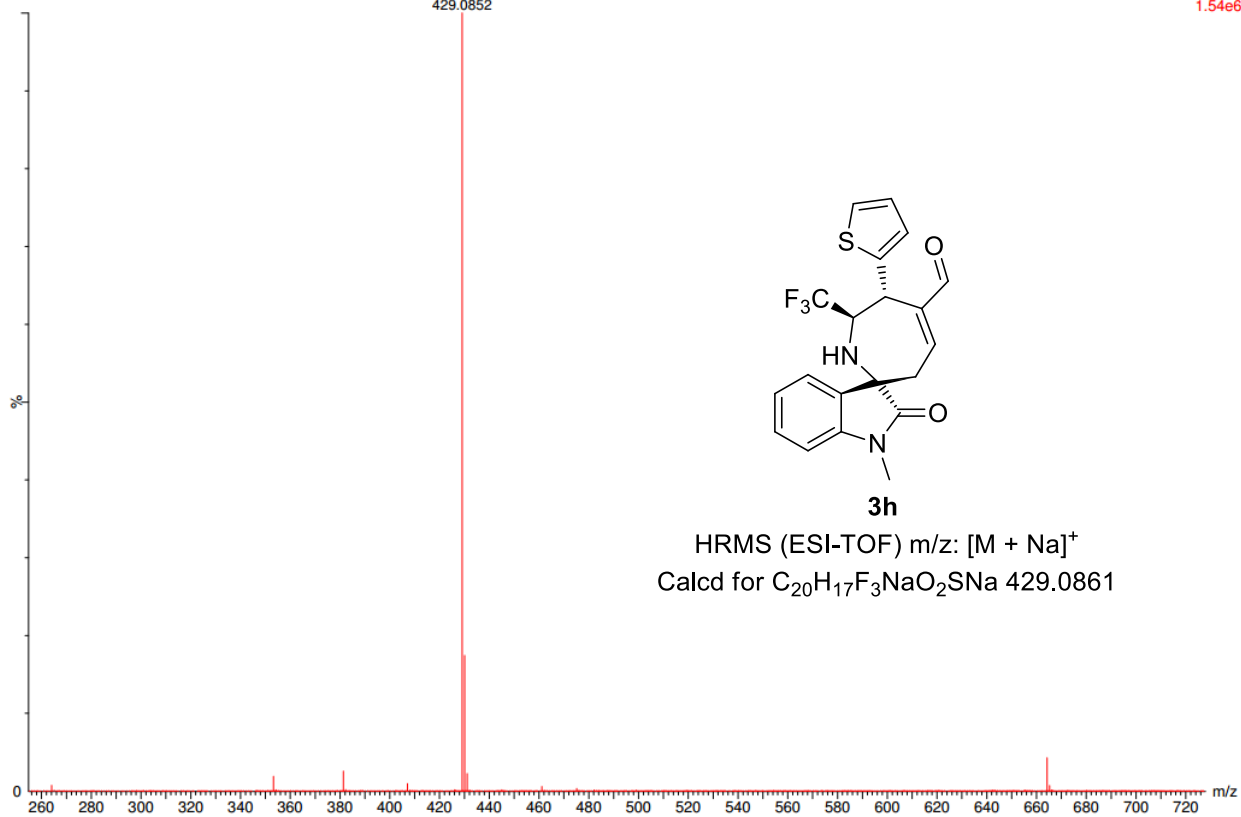
^{19}F -NMR (376MHz, CDCl_3)



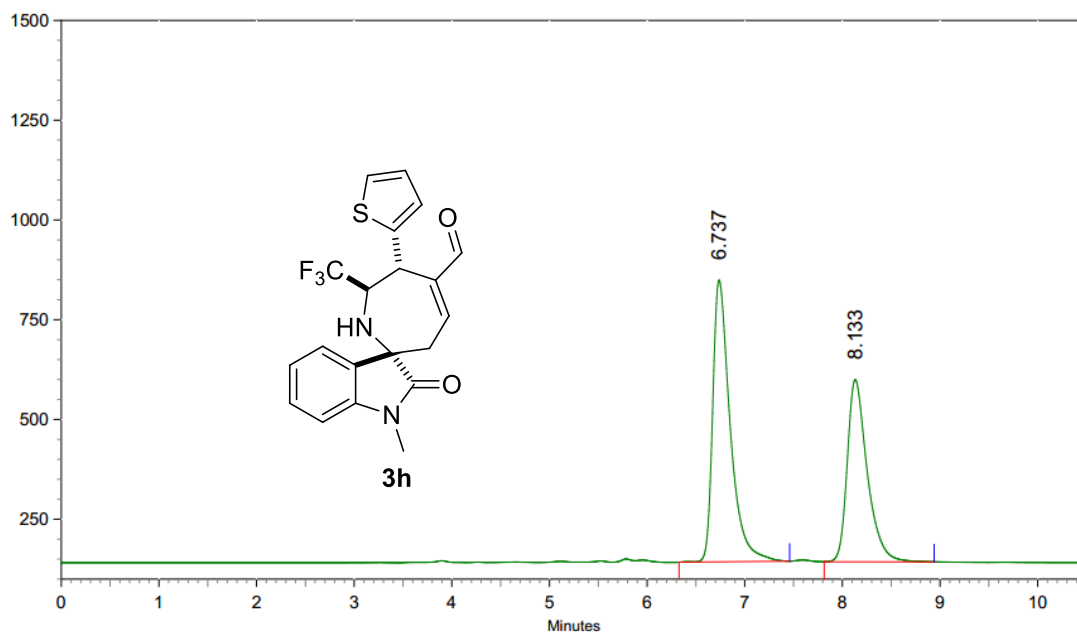
GY-SS8-862 9 (0.228)

429.0852

1: TOF MS ES+
1.54e6

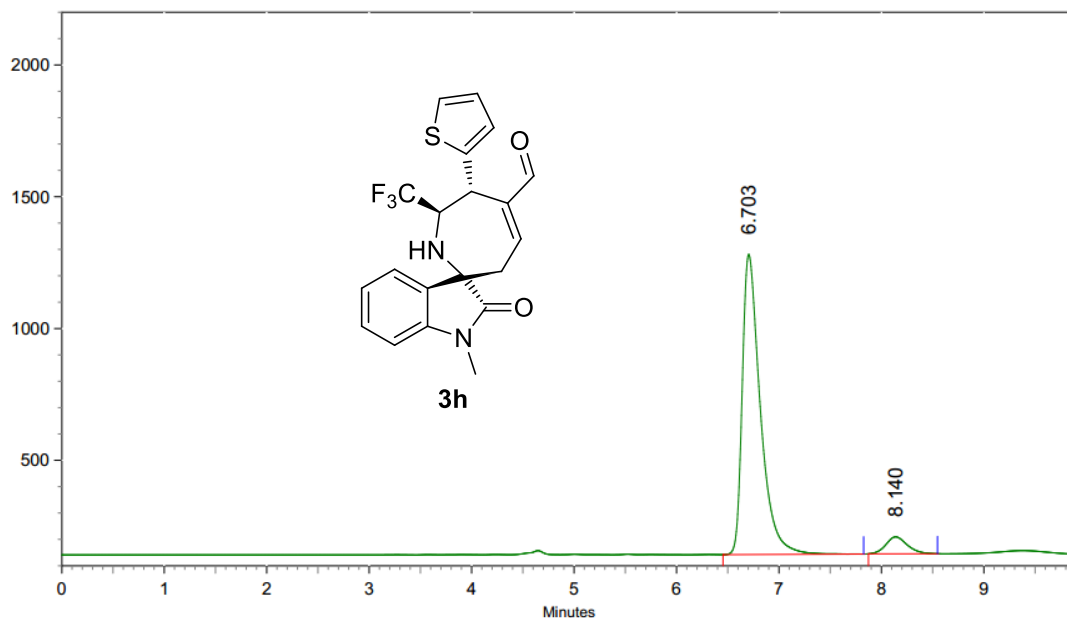


HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$
Calcd for $\text{C}_{20}\text{H}_{17}\text{F}_3\text{NaO}_2\text{SNa}$ 429.0861



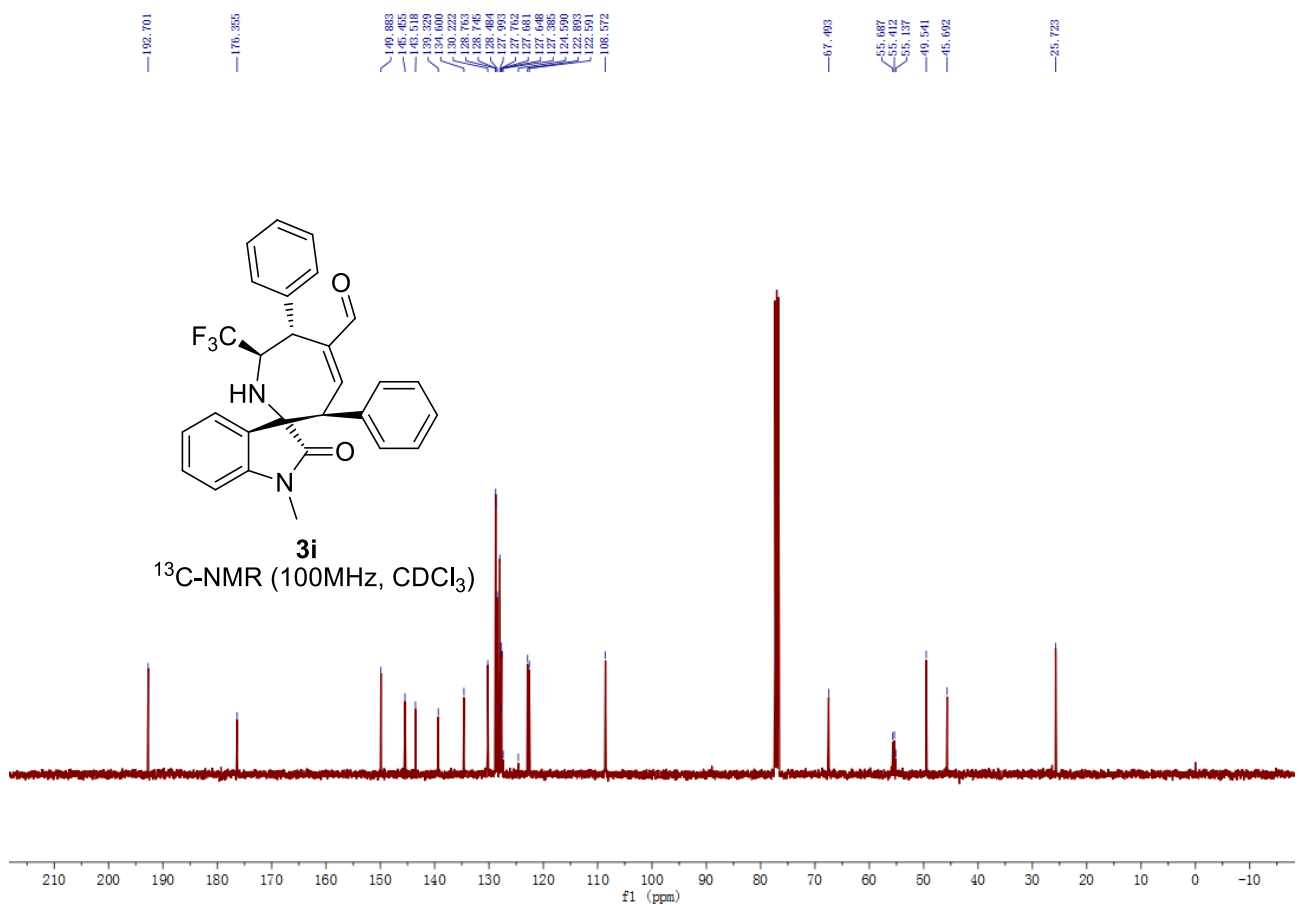
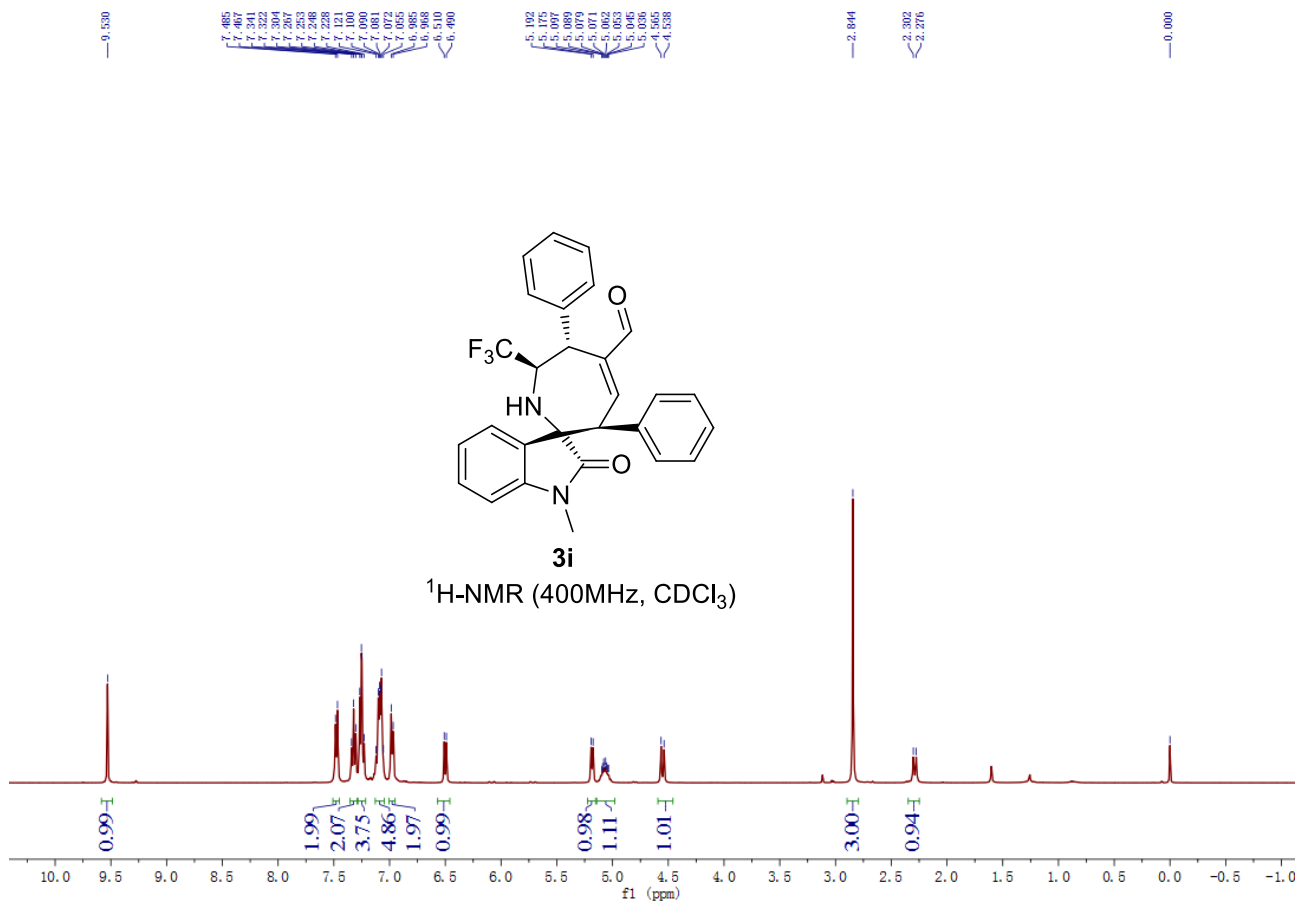
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.737	1.133	11848156	147141819	57.4872
2	8.133	1.127	7659915	108814018	42.5128

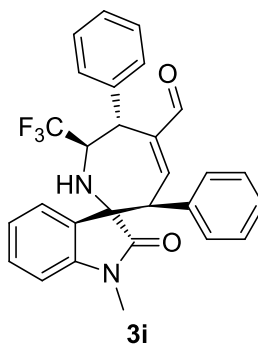


AREA PERCENT REPORT

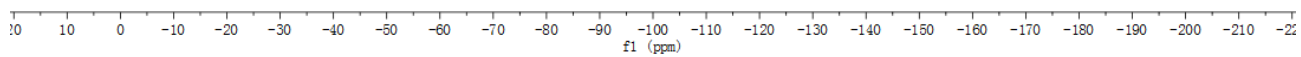
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.703	1.373	19103979	234131608	93.7380
2	8.140	0.673	1079181	15640819	6.2620



-71.195



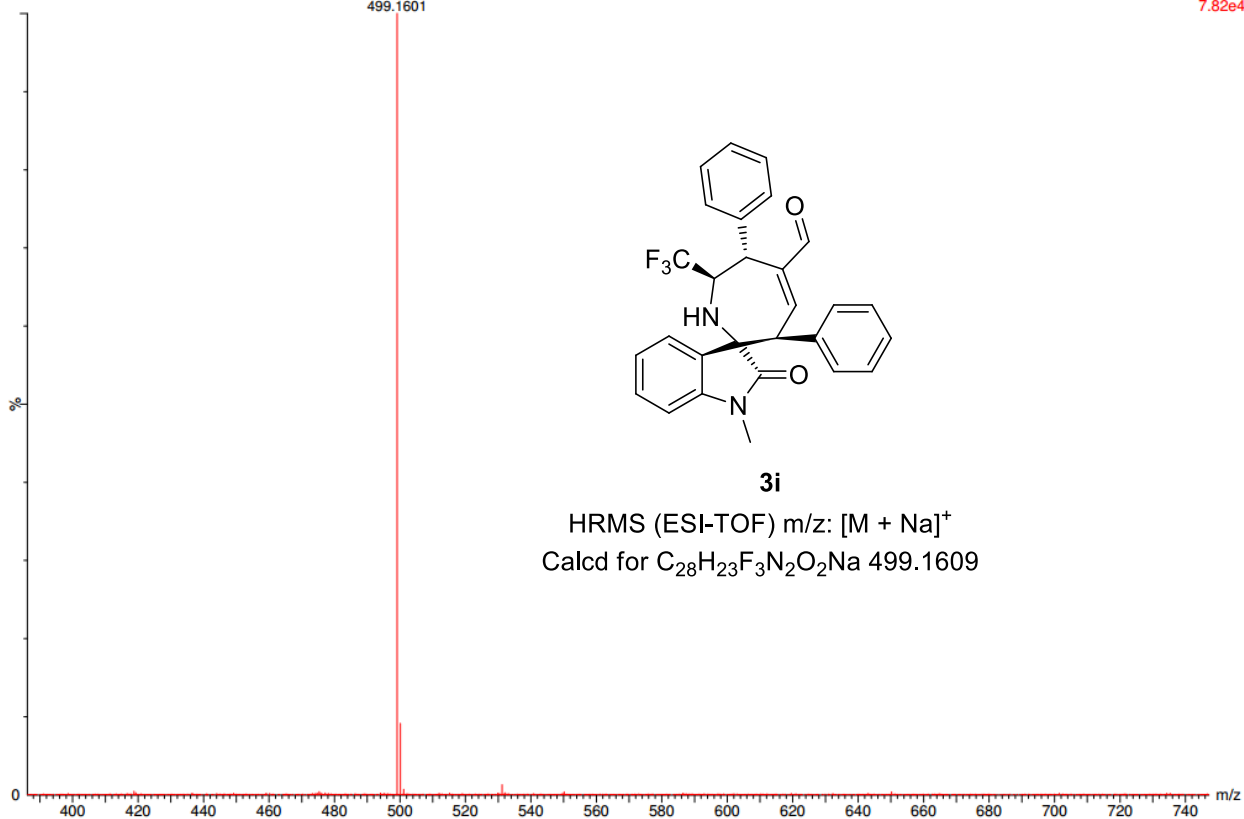
3i
¹⁹F-NMR (376MHz, CDCl₃)

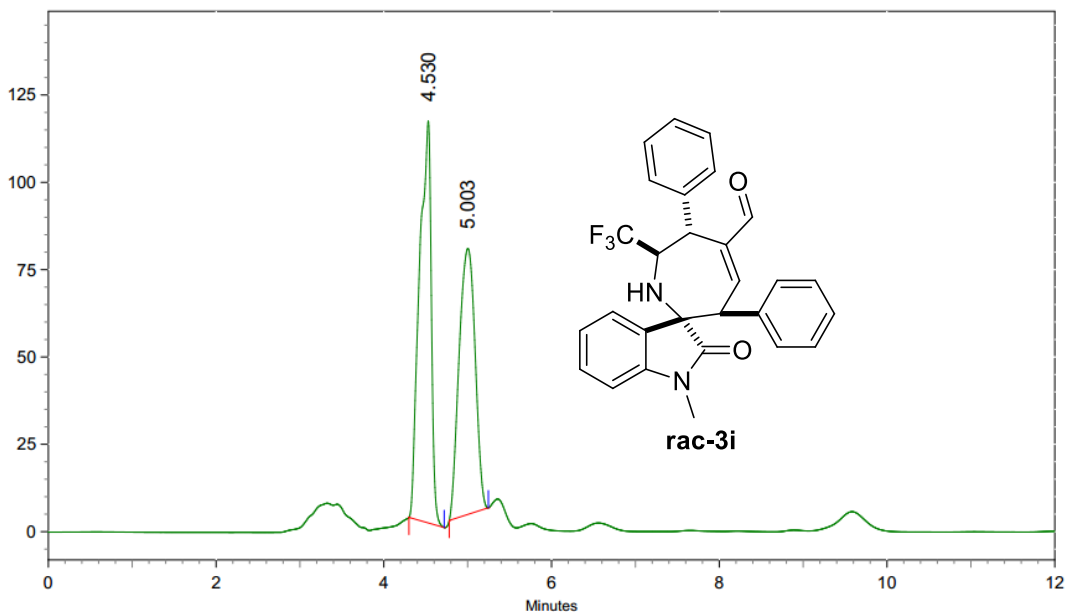


GY-SS9-862 22 (0.548)

499.1601

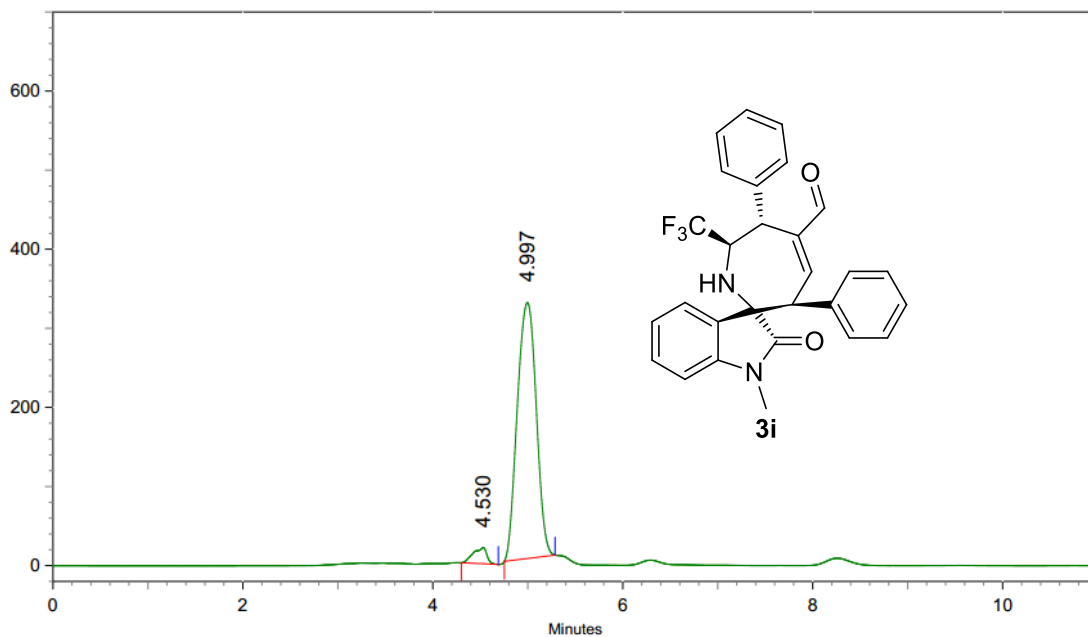
1: TOF MS ES+
7.82e4





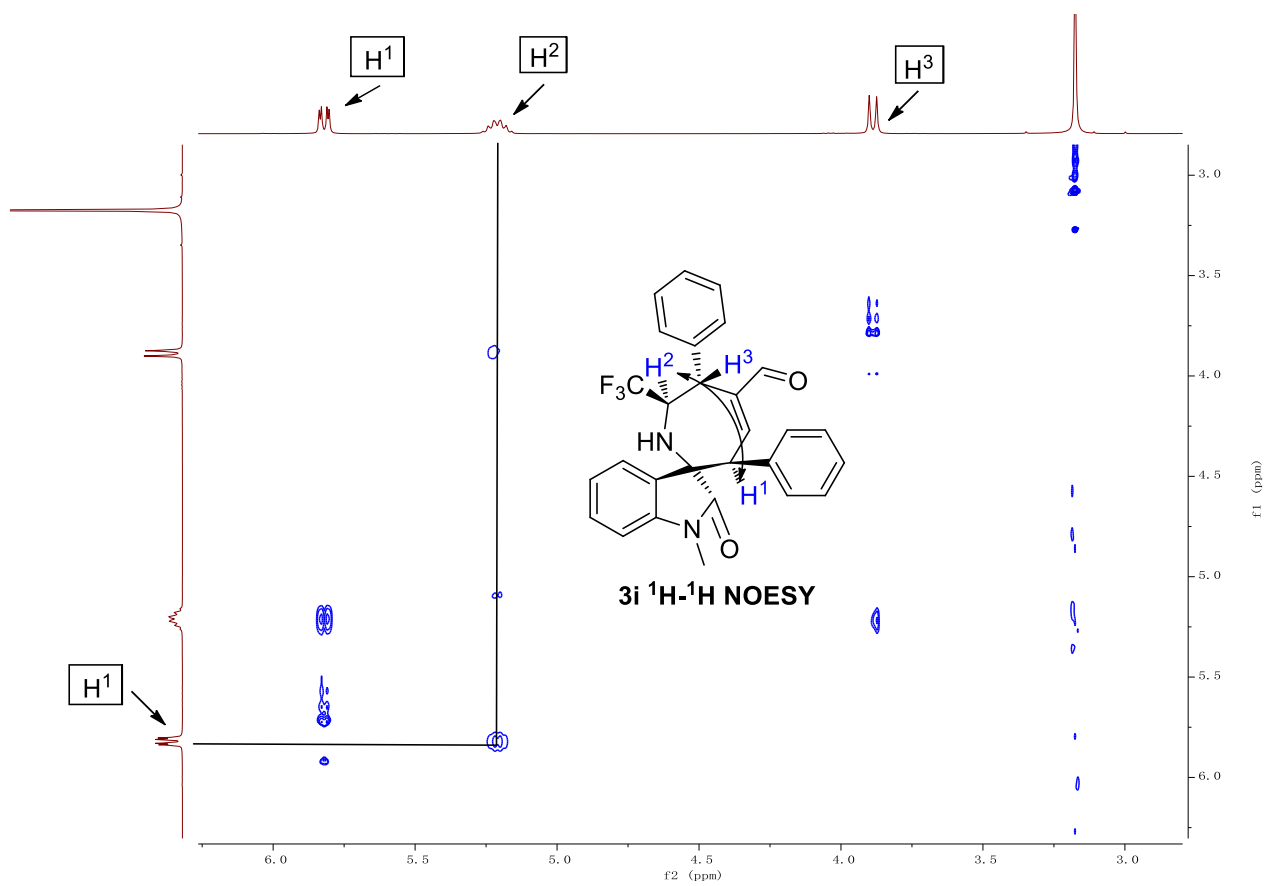
AREA PERCENT REPORT

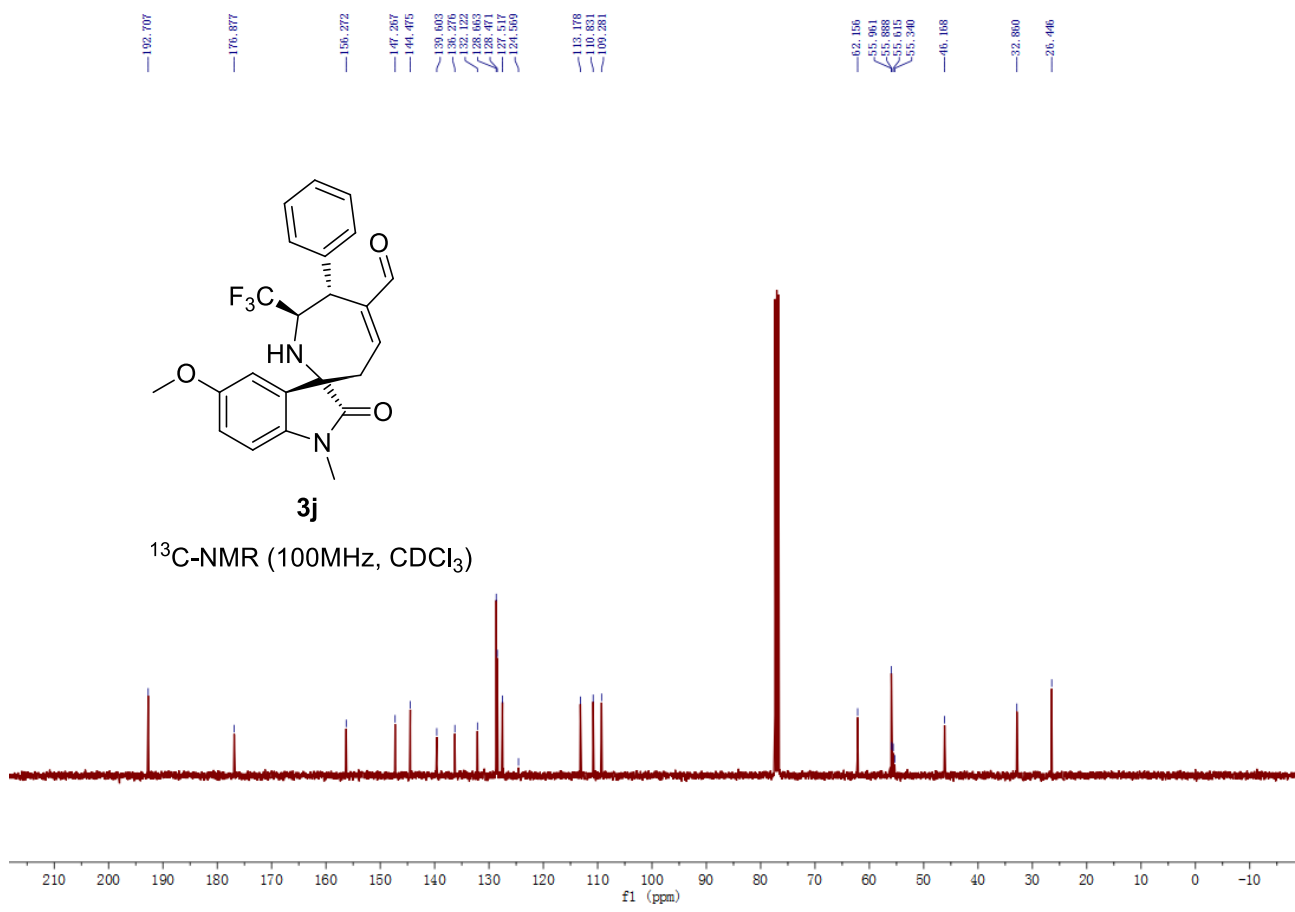
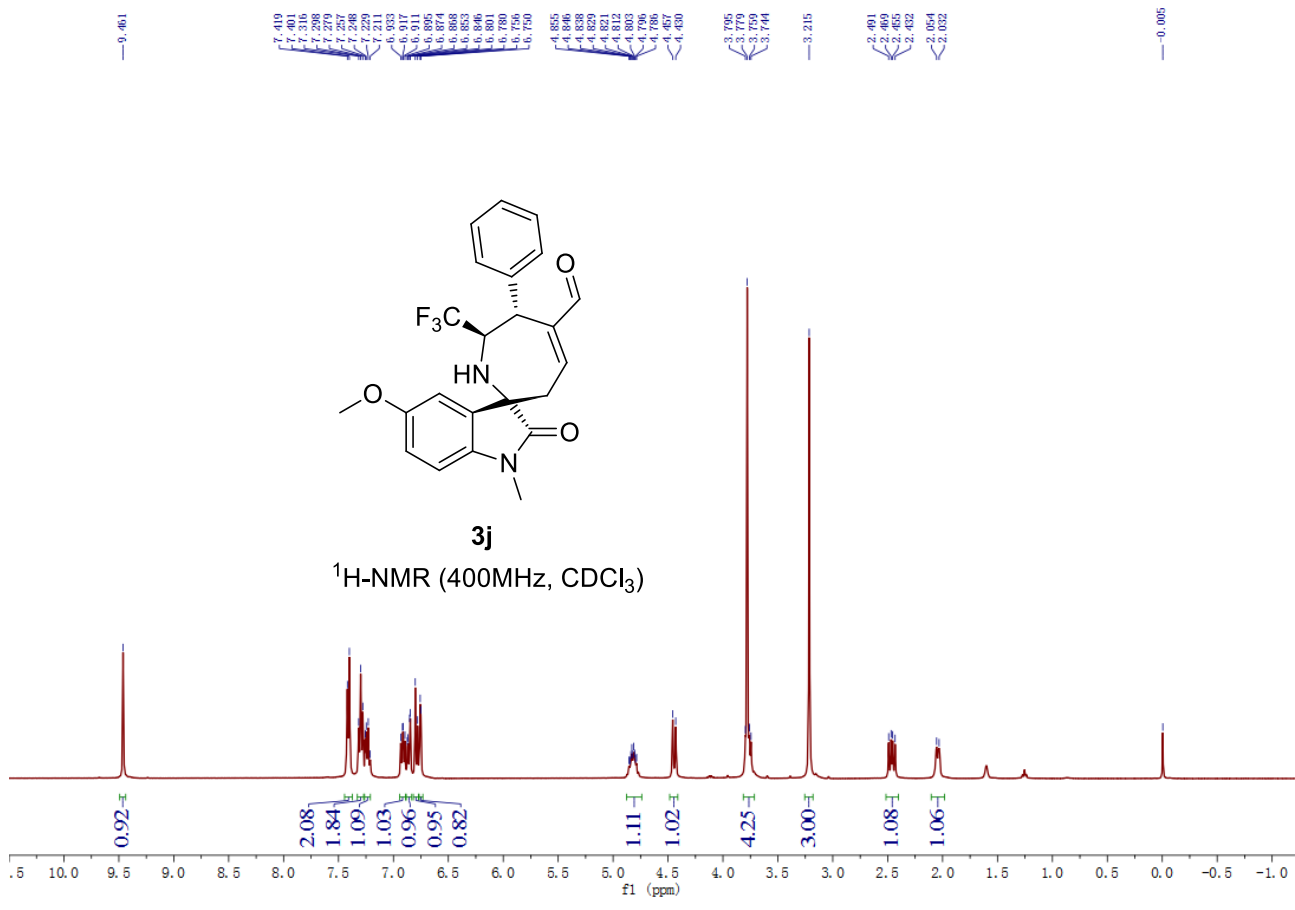
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	4.530	0.420	1930576	18780875	52.5026
2	5.003	0.467	1276887	16990450	47.4974



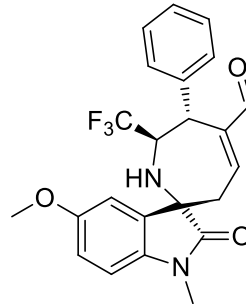
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	4.530	0.390	342402	3382765	4.2997
2	4.997	0.533	5428105	75292217	95.7003

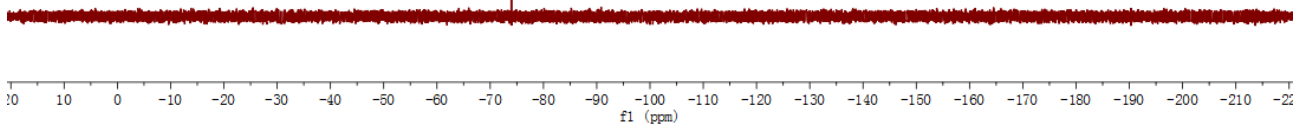




74.021



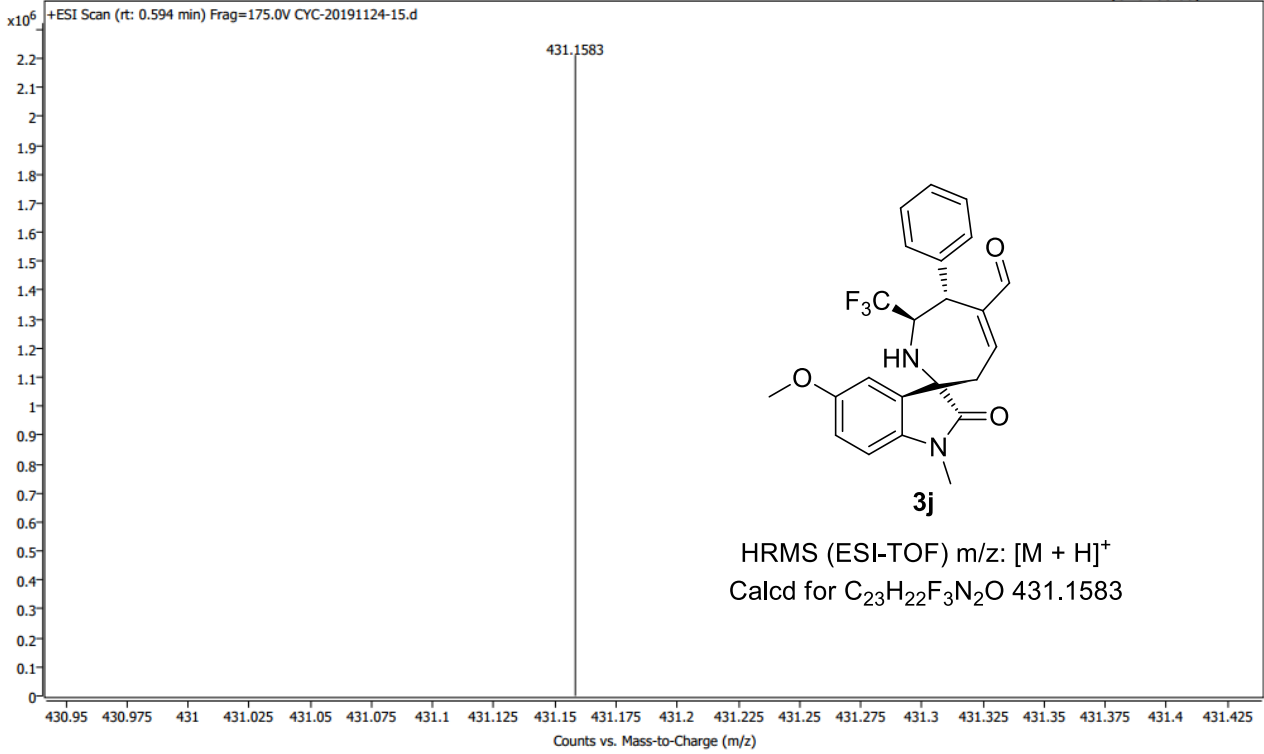
¹⁹F-NMR (376MHz, CDCl₃)

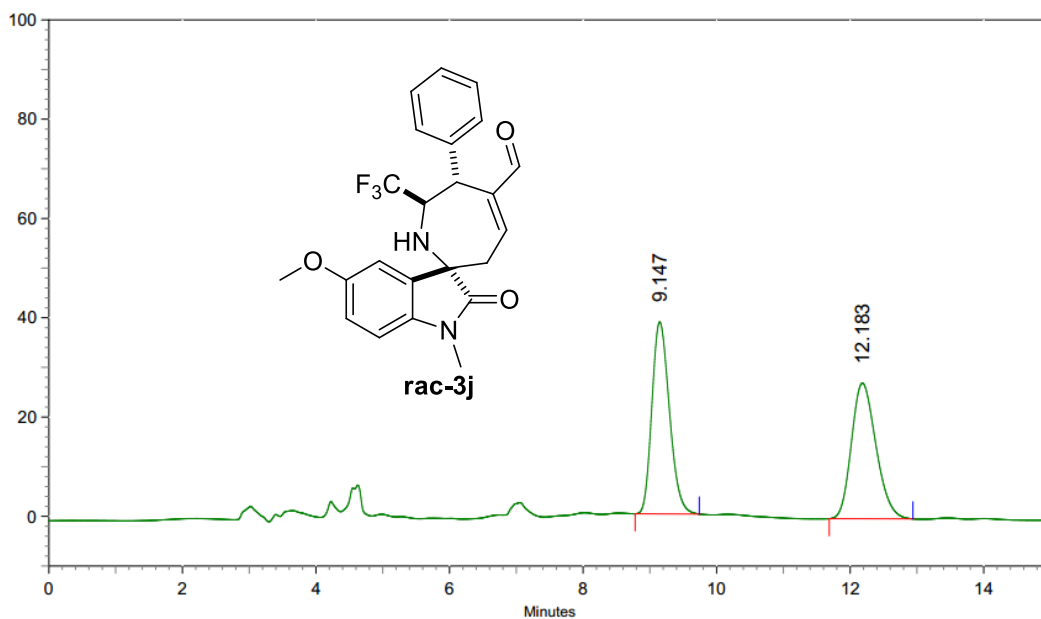


Spectrum Plot Report

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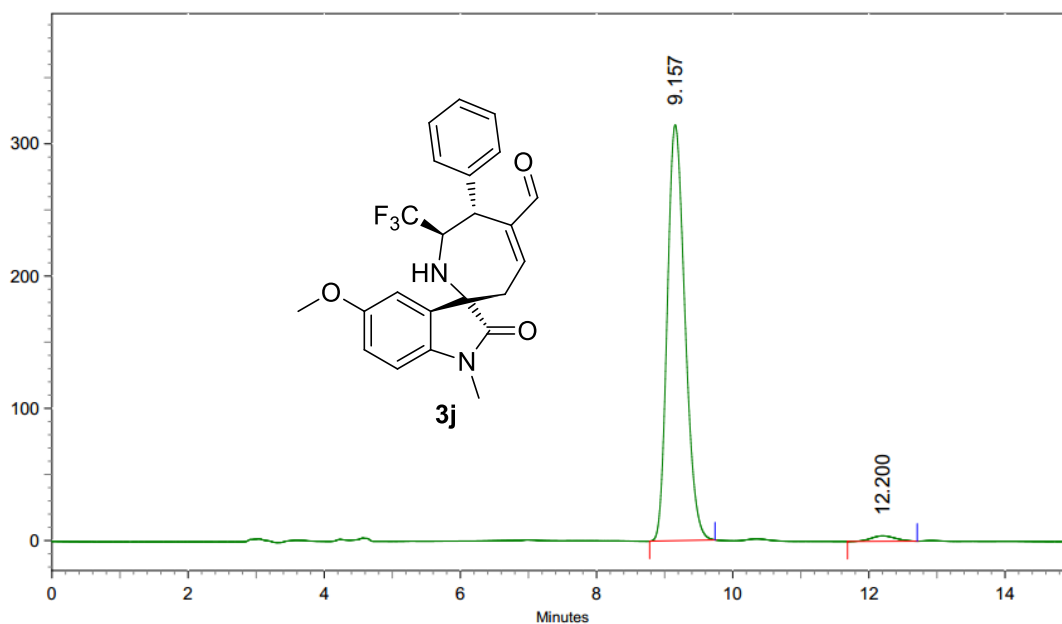
Name	CYC-20191124-15	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-15.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					12/5/2019 5:15:28 PM (UTC+08:00)





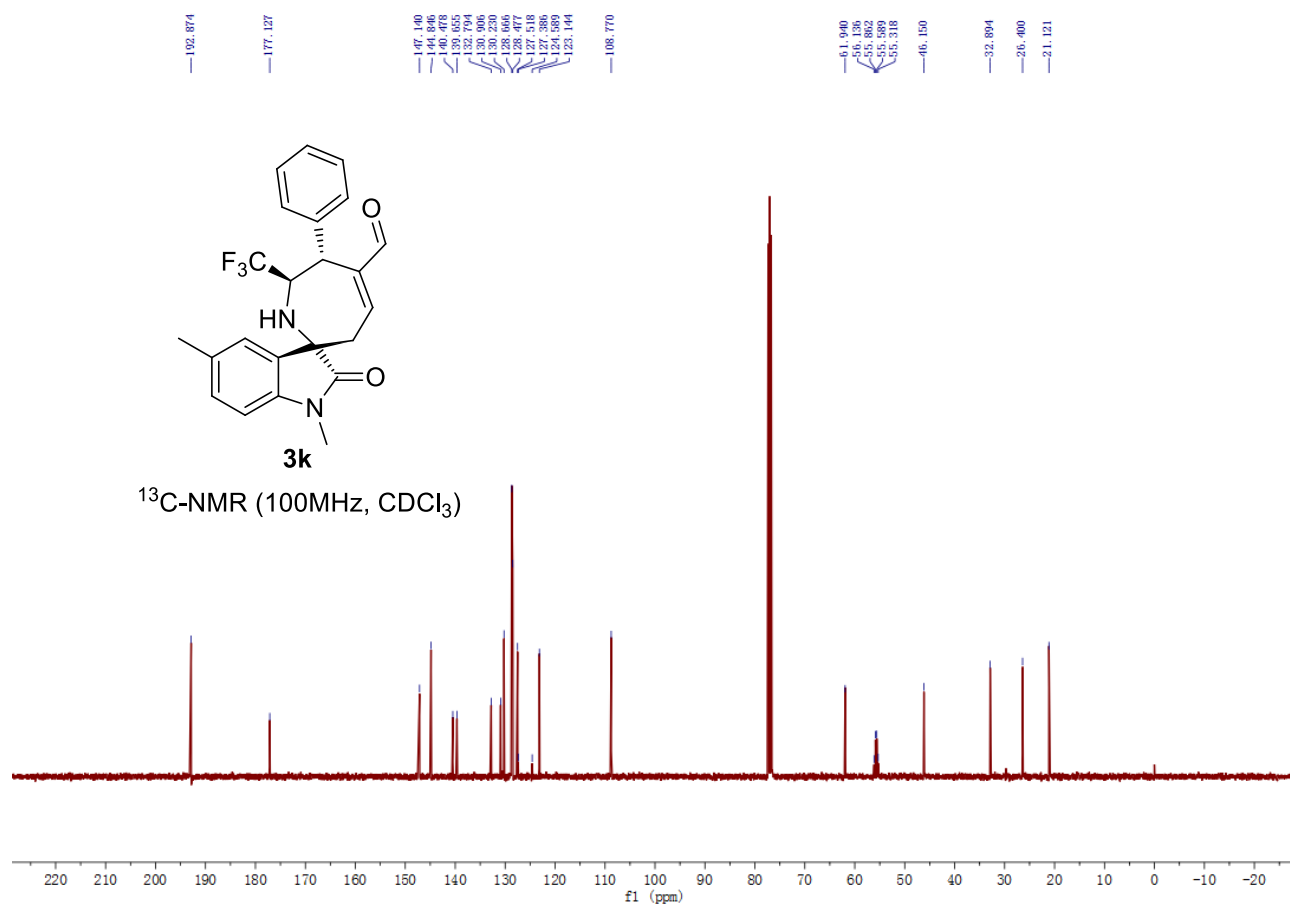
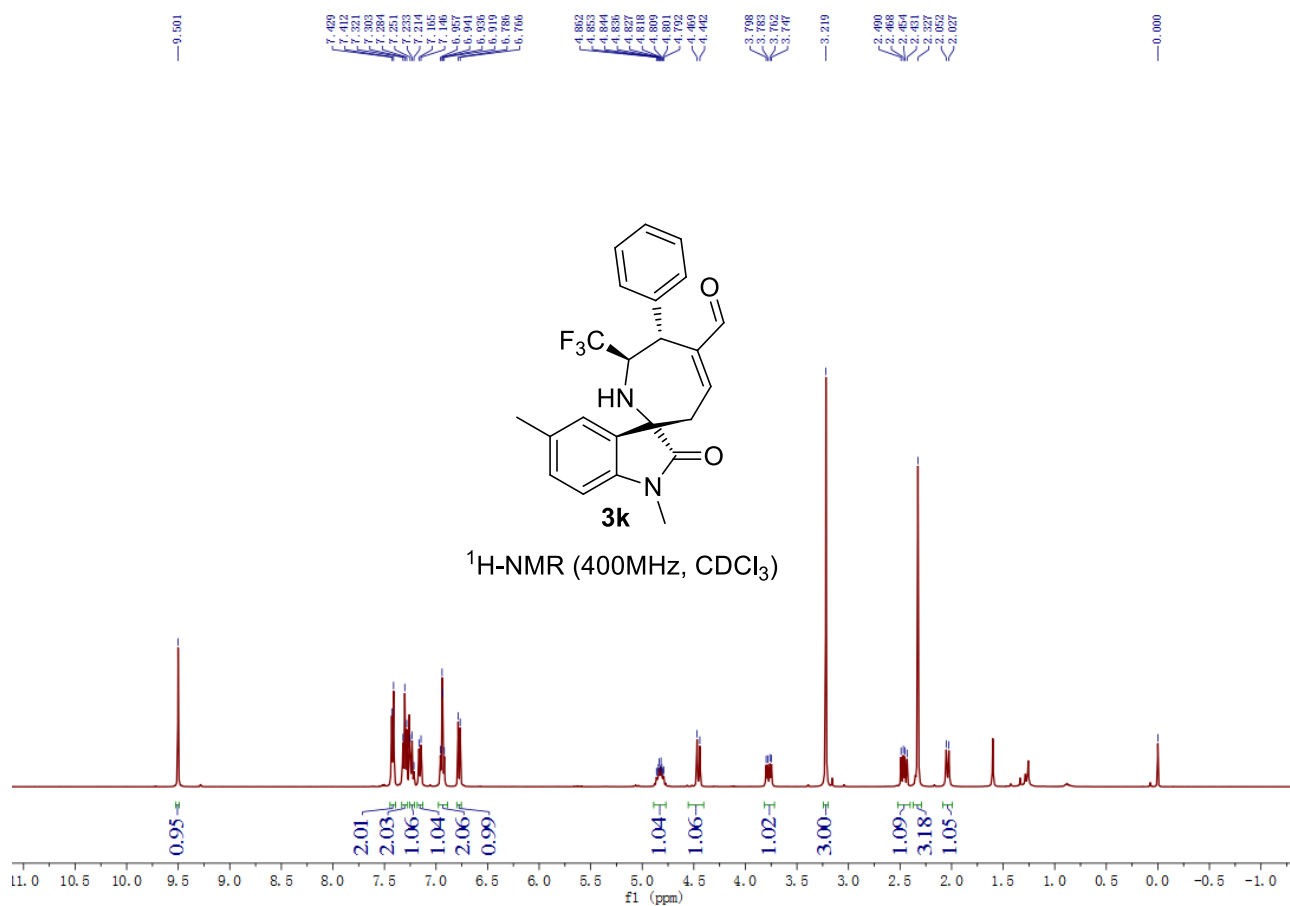
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.147	0.960	648668	11841980	50.2999
2	12.183	1.253	458651	11700755	49.7001

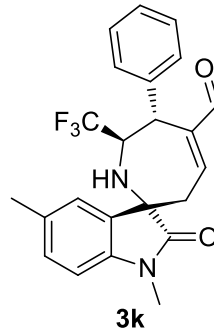


AREA PERCENT REPORT

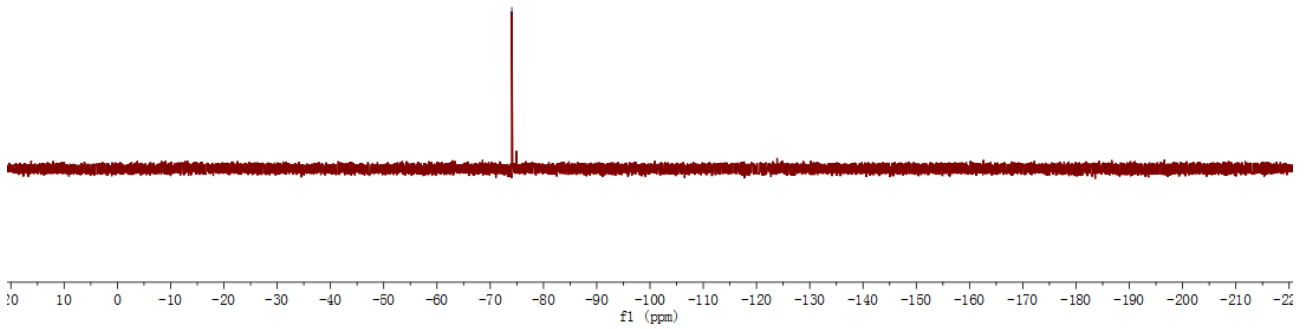
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.157	0.960	5274313	94870112	98.2319
2	12.200	1.023	69022	1707616	1.7681



-71.088



^{19}F -NMR (376MHz, CDCl_3)

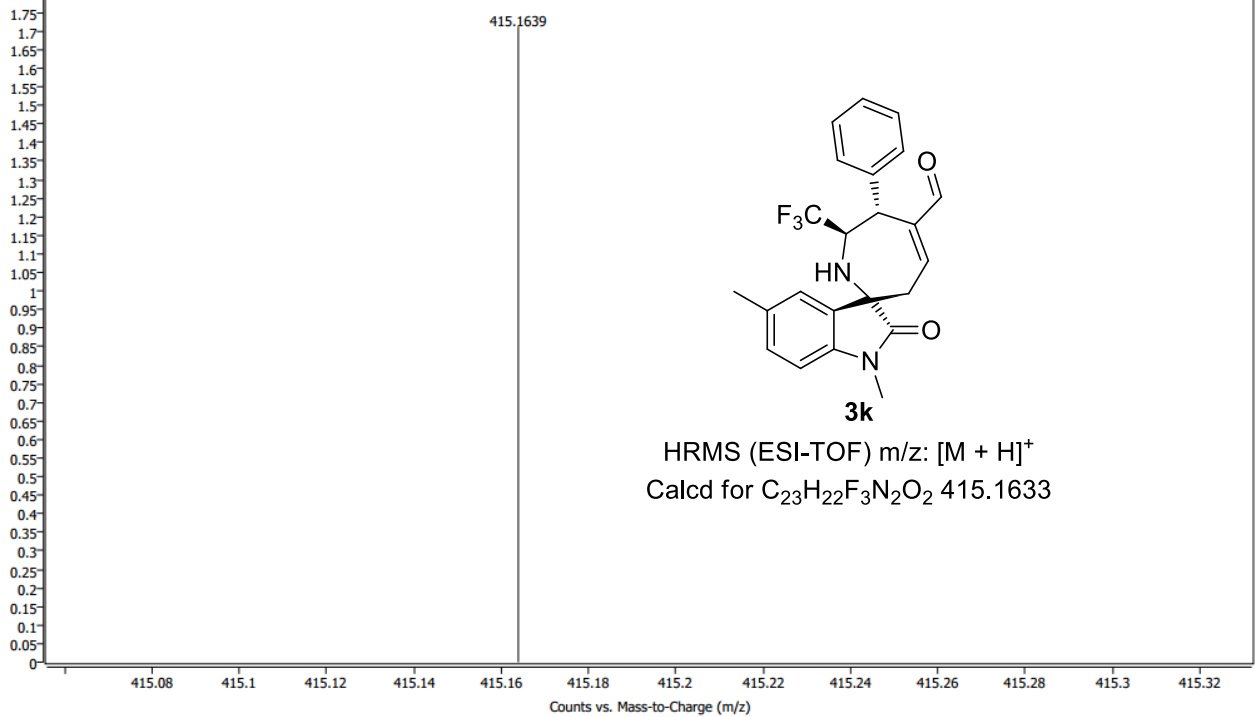


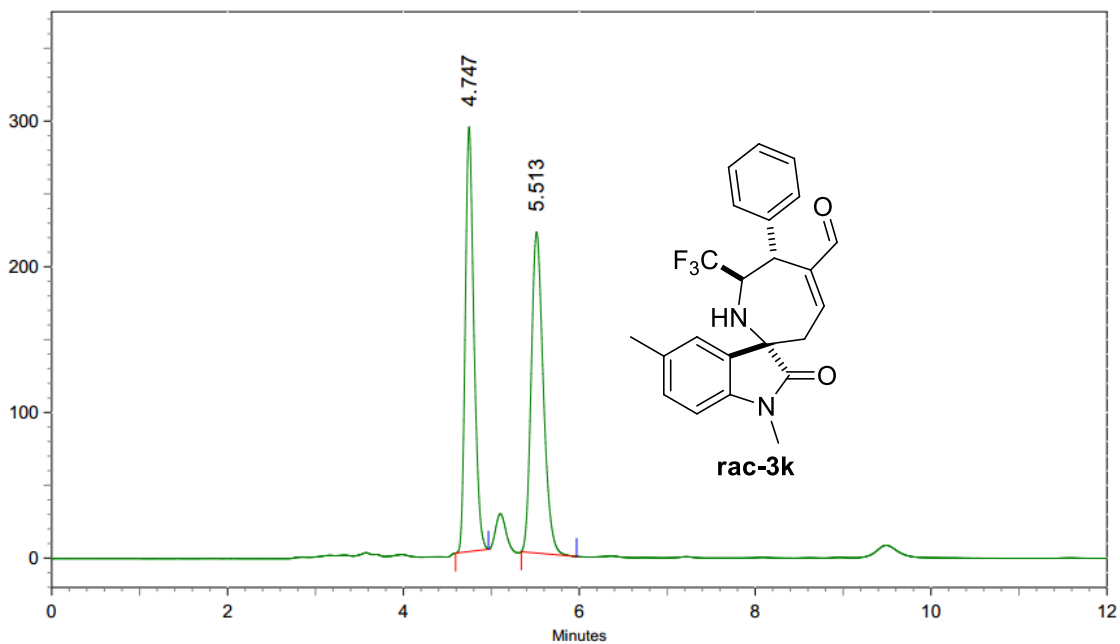
Spectrum Plot Report

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Name	CYC-20191124-14	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-14.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					12/5/2019 5:12:27 PM (UTC+08:00)

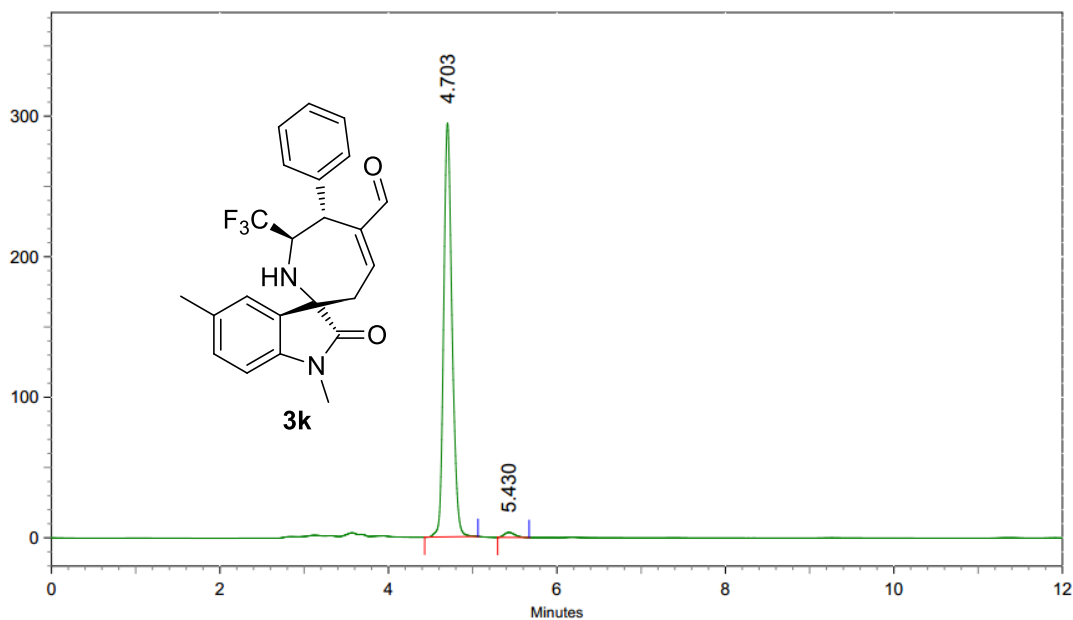
+ESI Scan (rt: 0.682 min) Frag=175.0V CYC-20191124-14.d





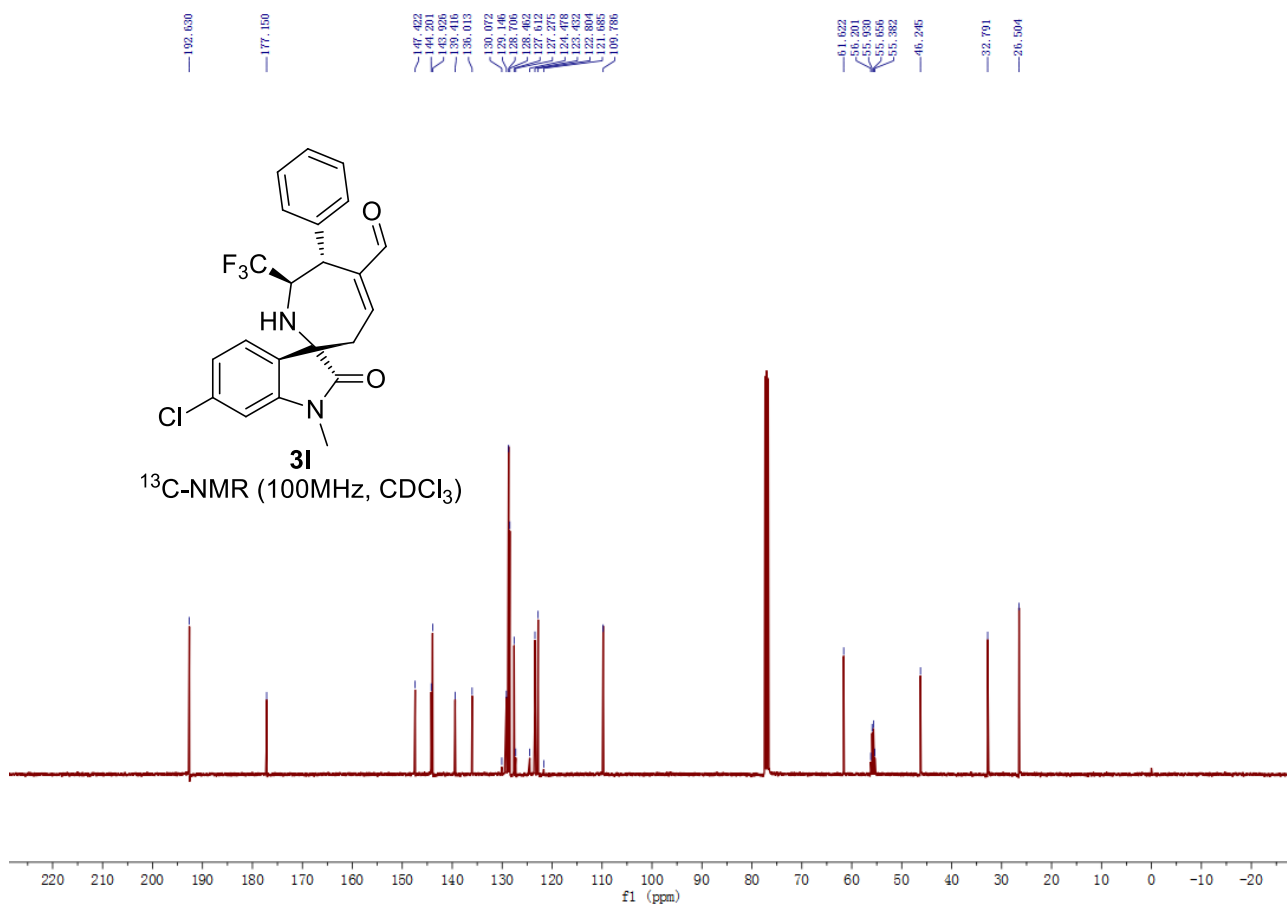
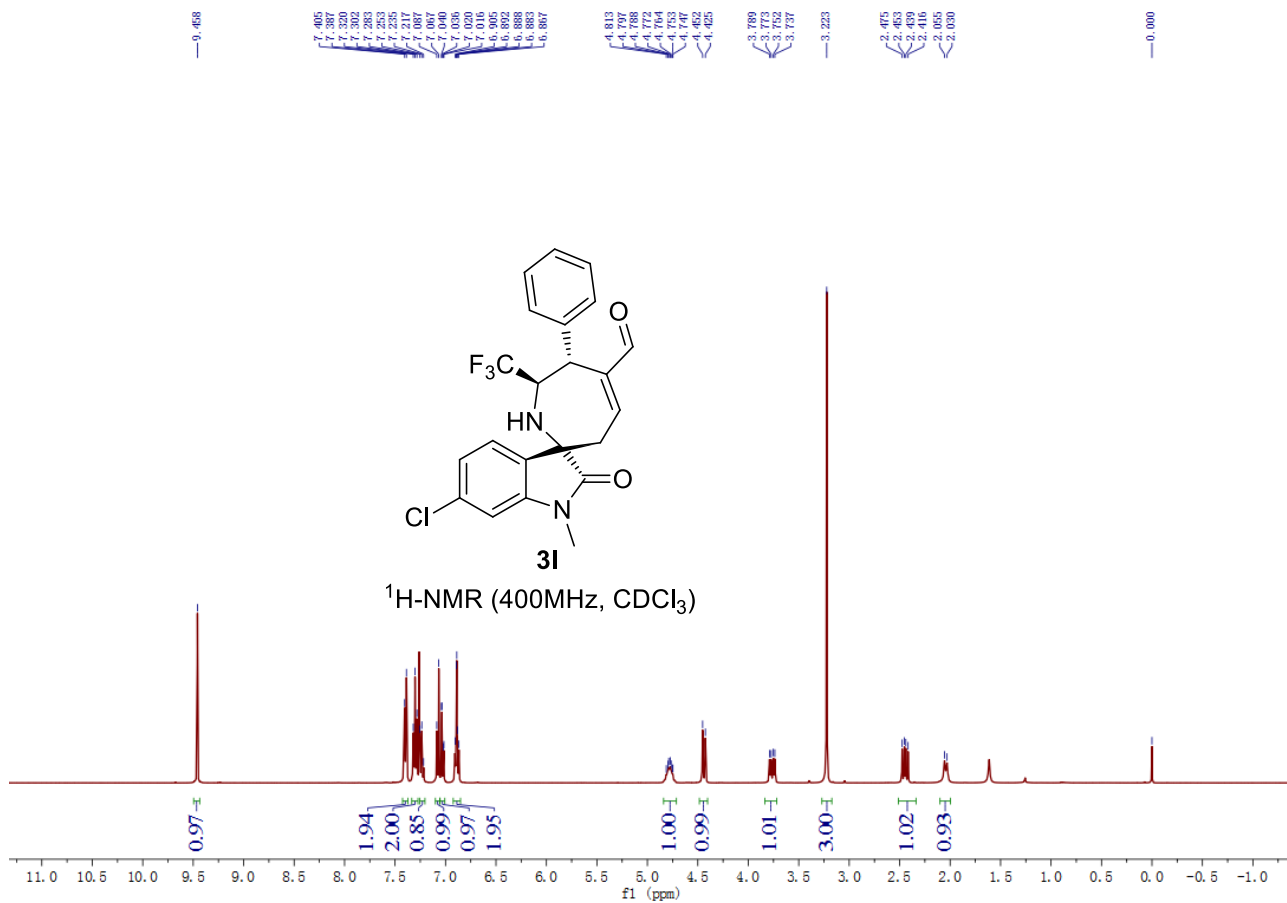
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	4.747	0.373	4891148	33331364	48.5124
2	5.513	0.630	3697894	35375590	51.4876

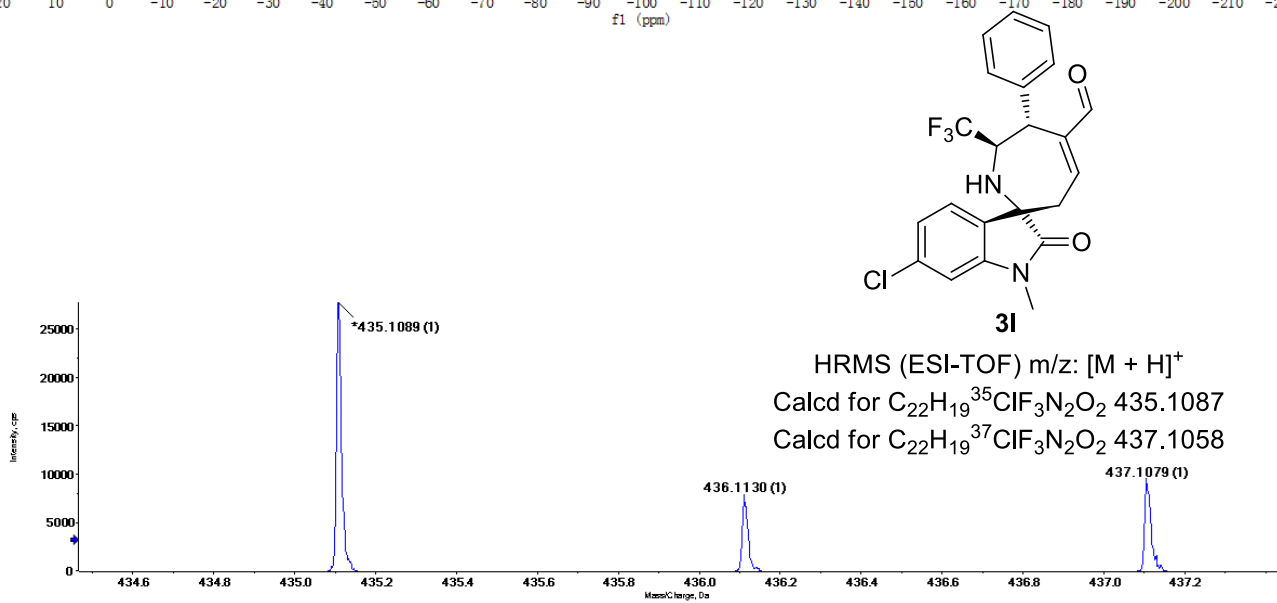
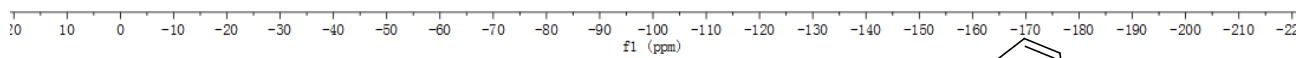
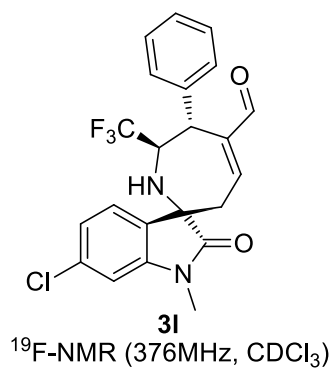


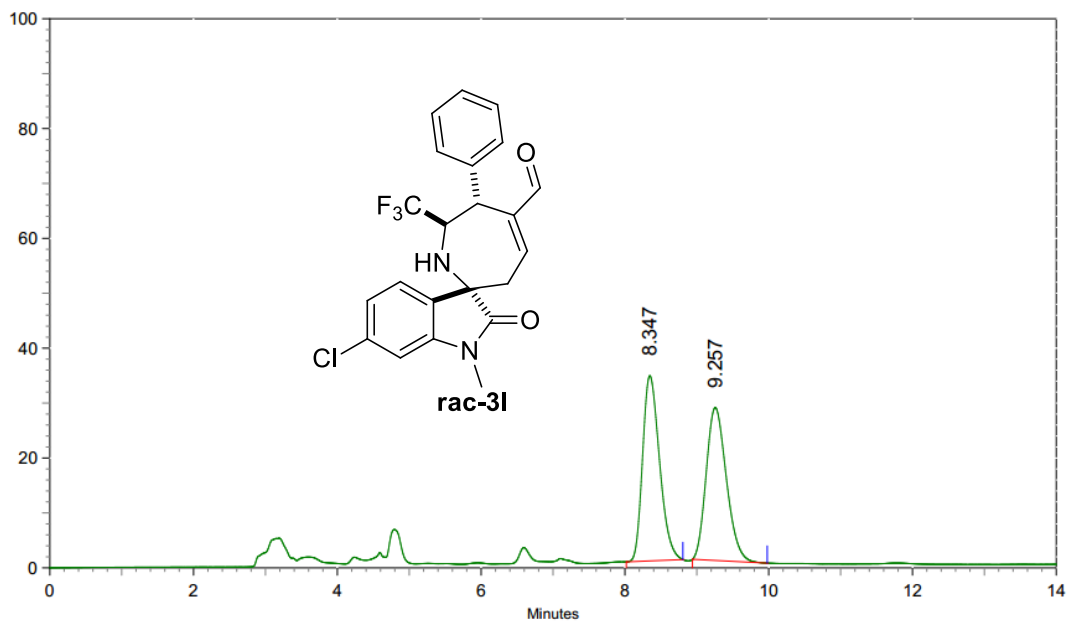
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	4.703	0.633	4938617	34028702	98.4496
2	5.430	0.373	60399	535901	1.5504



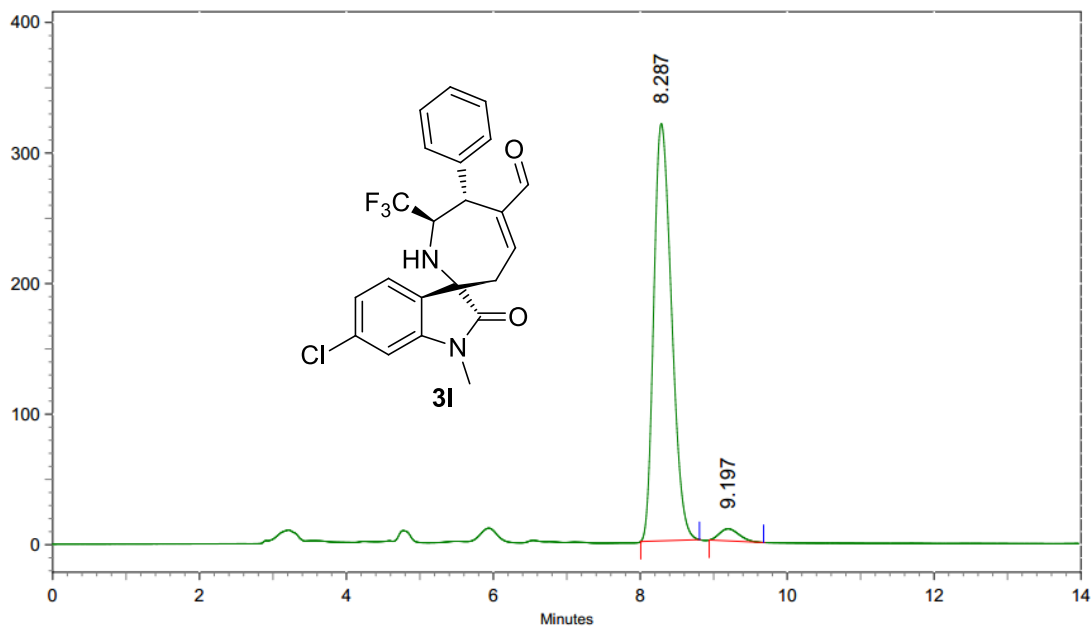
-73.977





AREA PERCENT REPORT

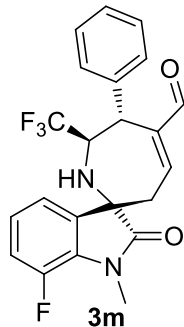
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.347	0.787	565885	9260058	50.3627
2	9.257	1.040	467158	9126689	49.6373



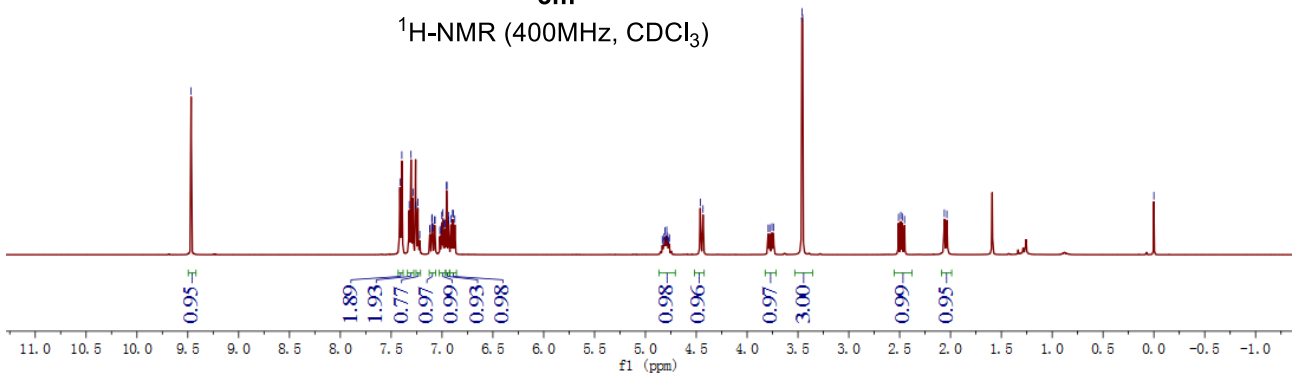
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.287	0.800	5361022	90034511	96.8980
2	9.197	0.740	155581	2882304	3.1020

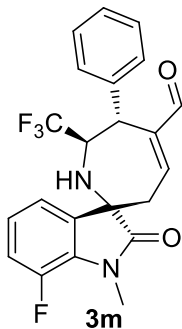
9.467
7.913
7.322
7.305
7.286
7.277
7.219
7.121
7.118
7.083
7.097
7.093
7.089
7.072
7.072
7.010
6.992
6.982
6.971
6.955
6.952
6.934
6.934
6.912
6.889
6.889
6.834
4.825
4.817
4.805
4.799
4.790
4.782
4.773
4.661
4.434
3.793
3.778
3.756
3.741
3.461
3.464
2.511
2.489
2.474
2.462
2.051
2.035
-0.000



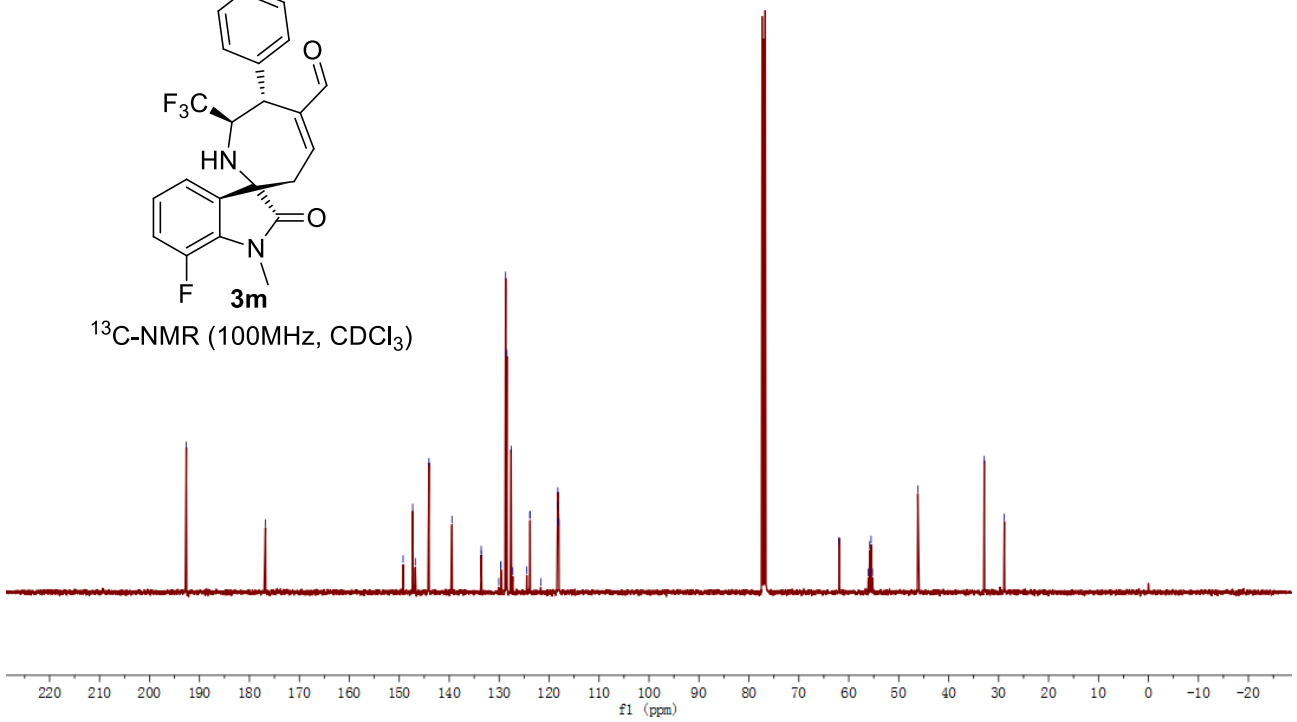
¹H-NMR (400MHz, CDCl₃)

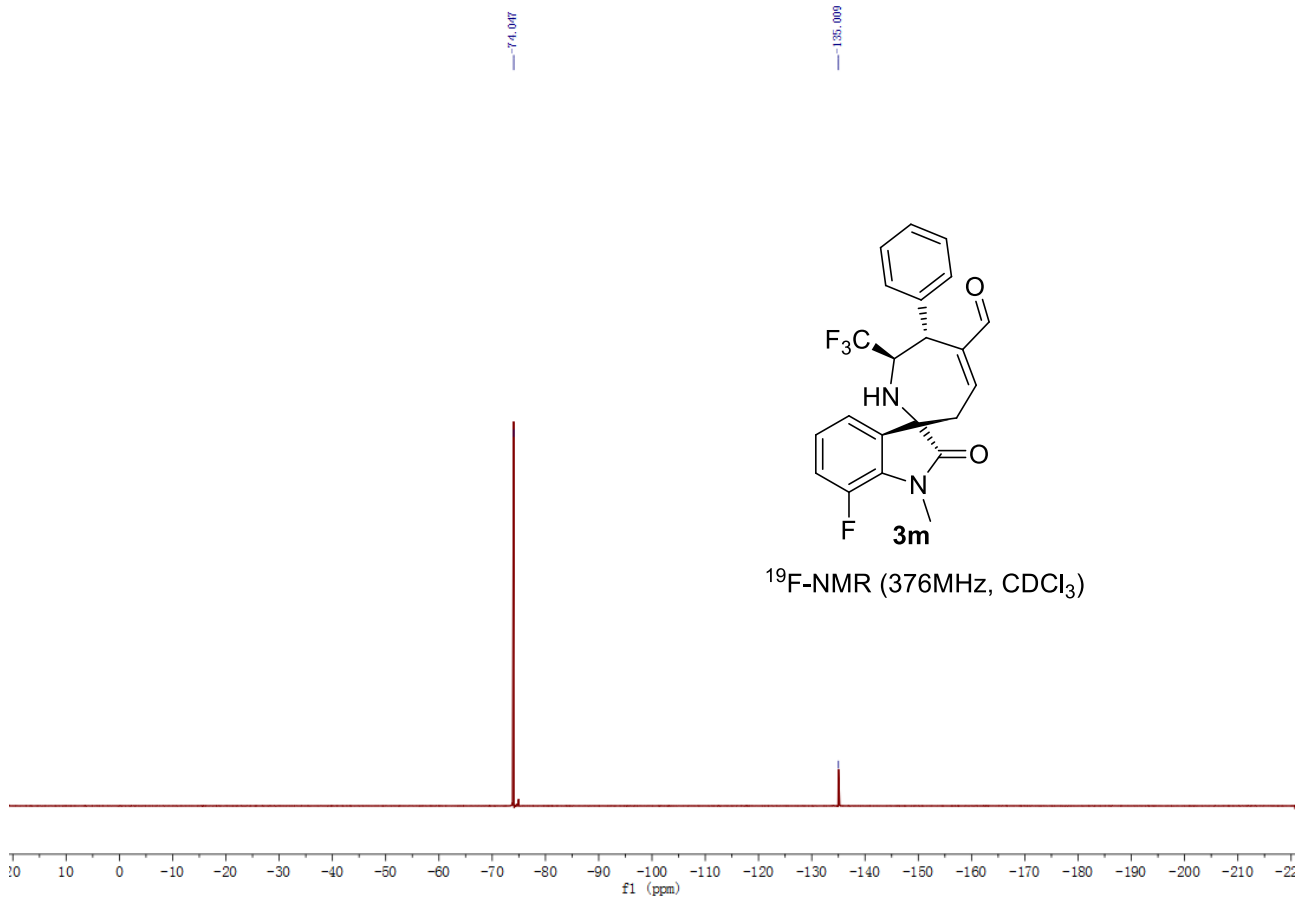


192.638
176.788
148.230
146.375
146.375
146.061
139.447
133.000
133.000
130.079
129.719
129.654
128.795
128.795
127.598
127.275
124.478
123.873
121.675
118.285
118.247
118.090
61.906
55.080
55.532
55.286
46.174
32.876
28.853



¹³C-NMR (100MHz, CDCl₃)

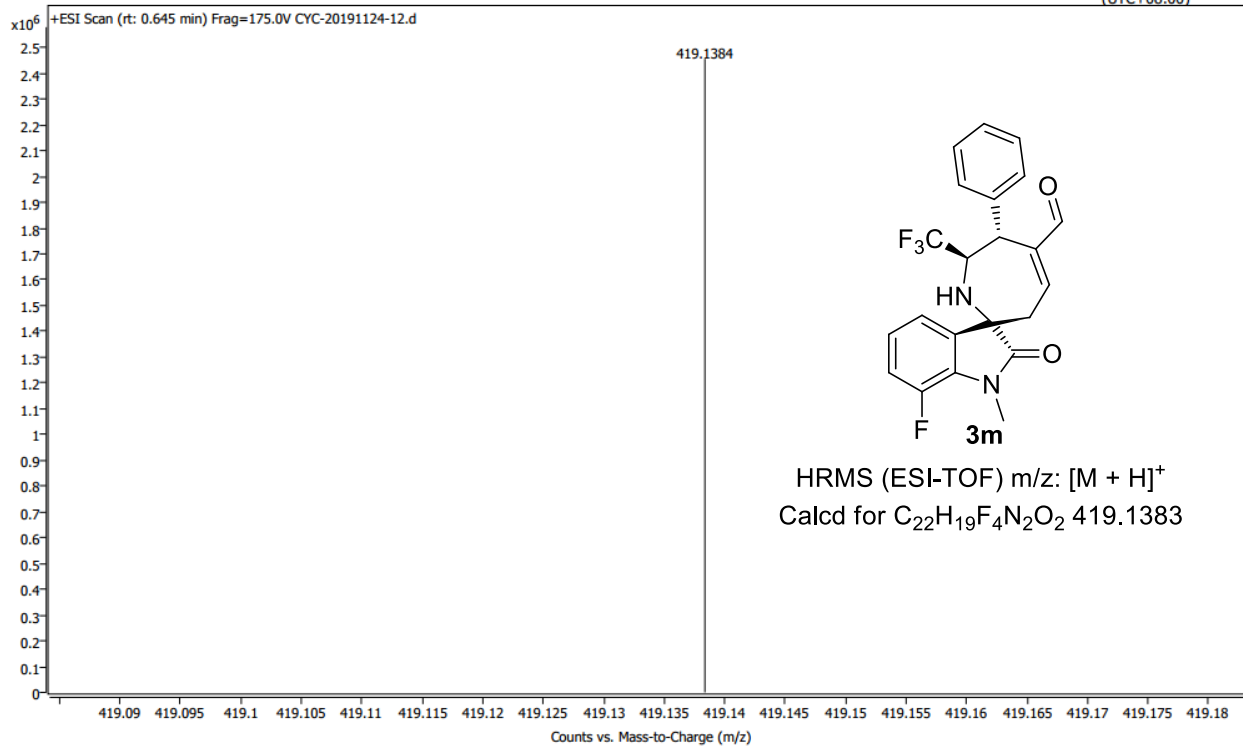


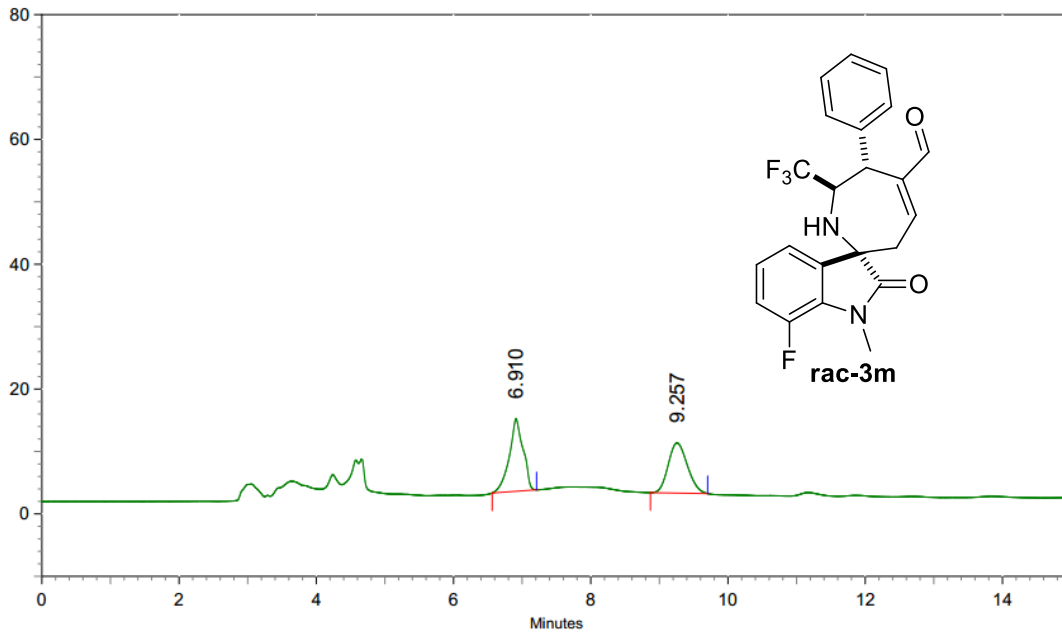


Spectrum Plot Report

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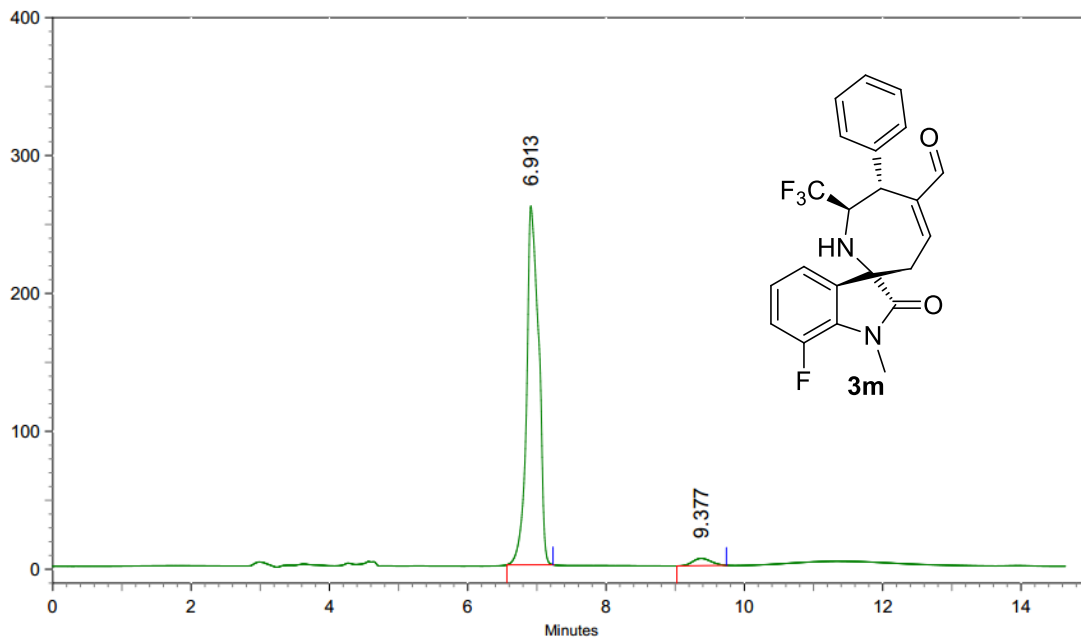
Name	CYC-20191124-12	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-12.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					12/5/2019 5:06:25 PM (UTC+08:00)





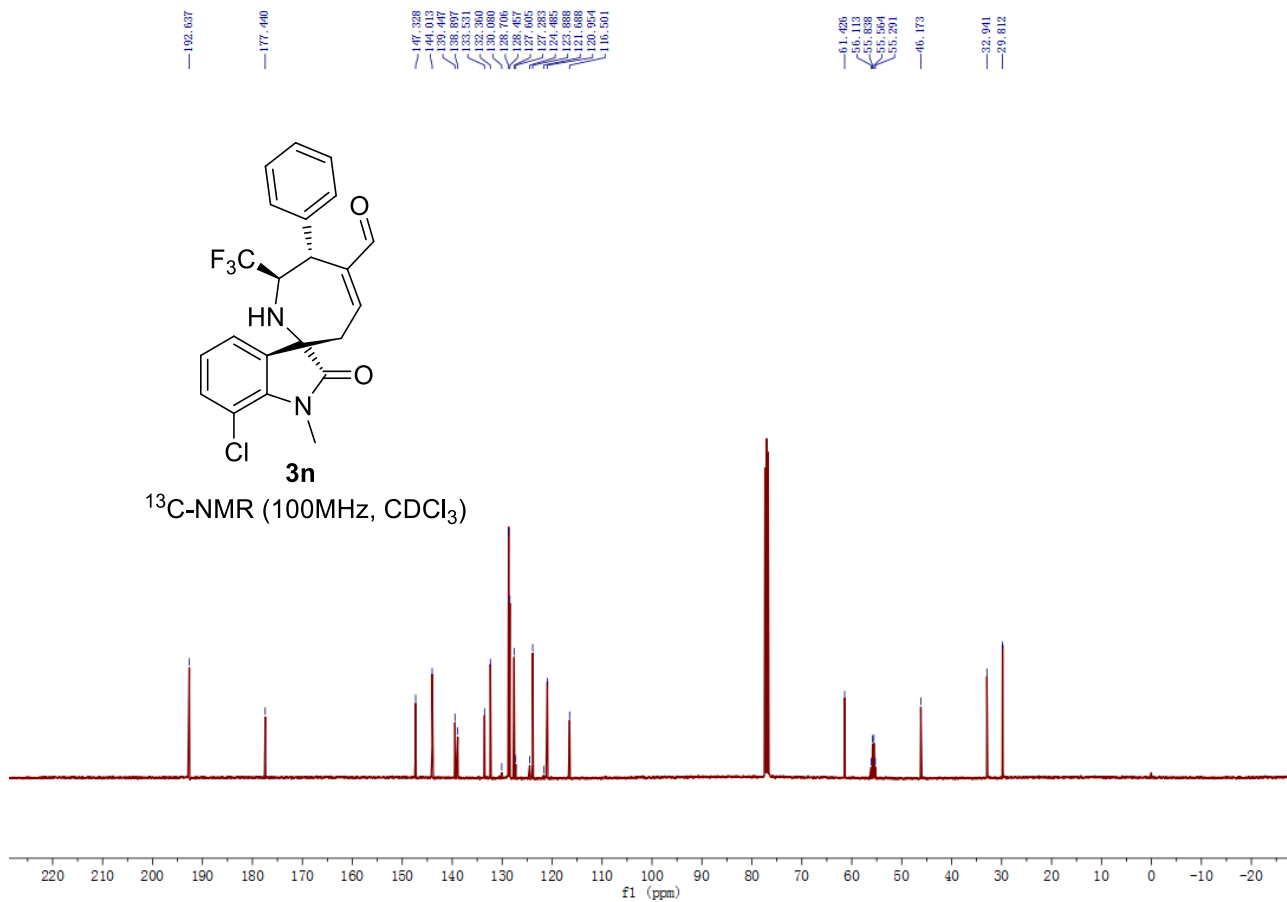
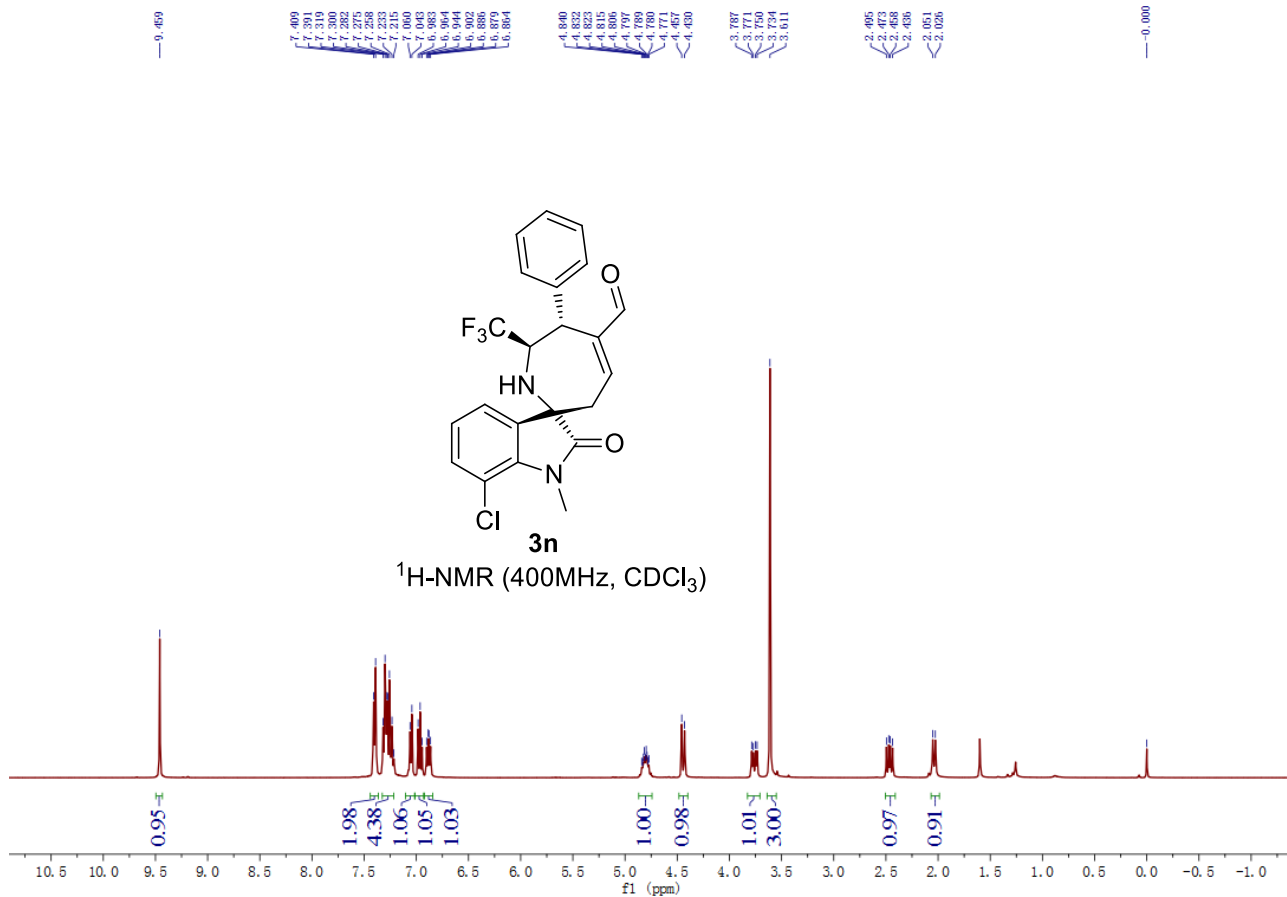
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.910	0.647	194790	2717854	50.9807
2	9.257	0.833	134753	2613284	49.0193

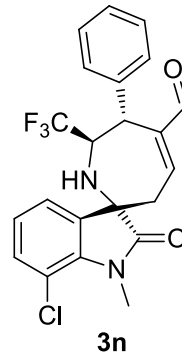


AREA PERCENT REPORT

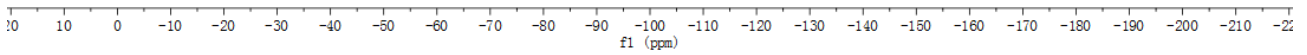
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.913	0.667	4363296	52819314	97.0171
2	9.377	0.717	88622	1623985	2.9829



-71.080



^{19}F -NMR (376MHz, CDCl_3)

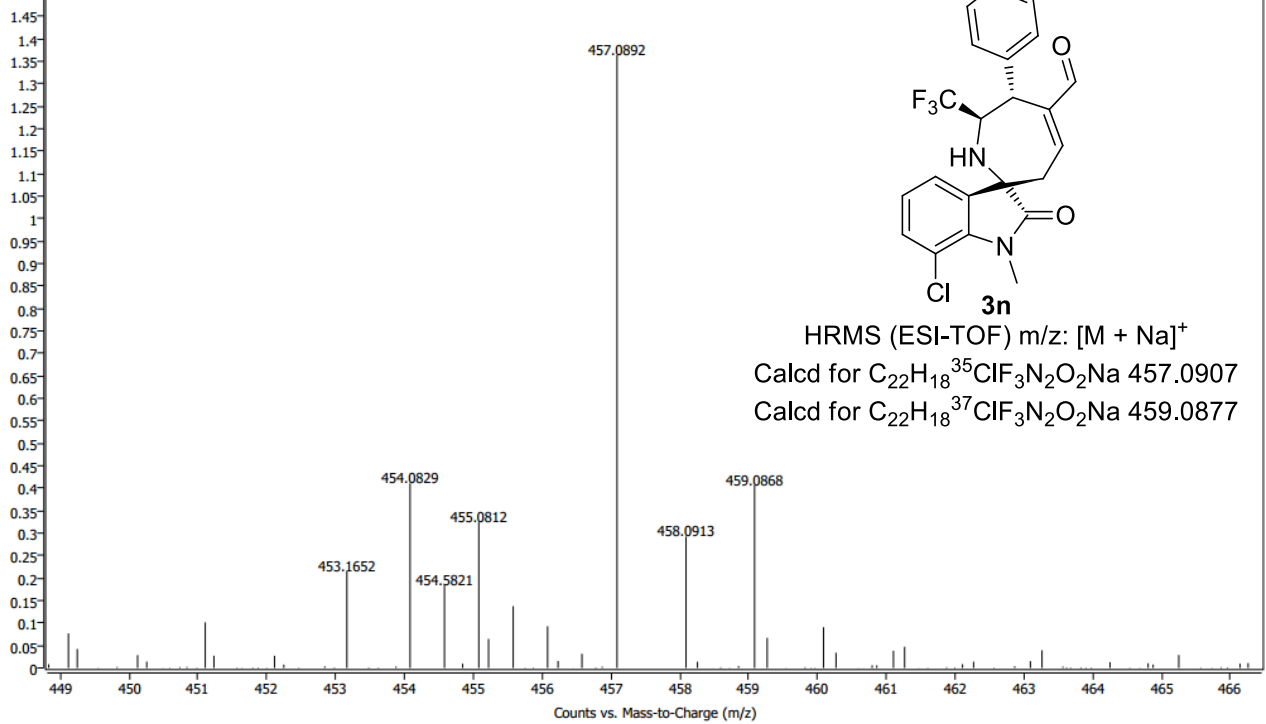


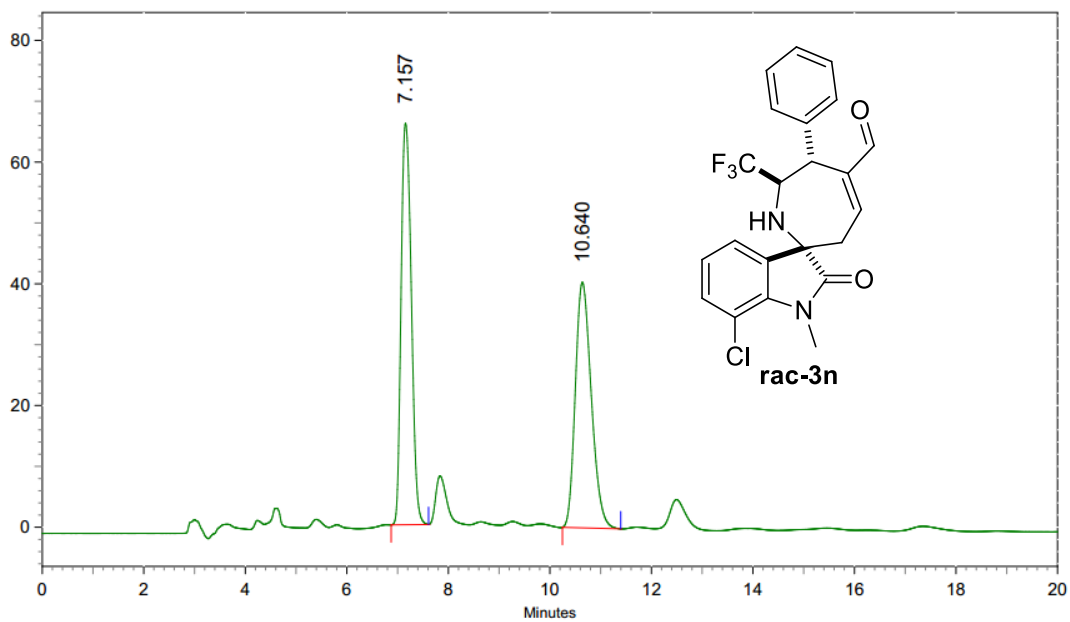
Spectrum Plot Report



Name	CYC-20200105-47	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20200105-47.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					1/10/2020 8:57:53 PM (UTC+08:00)

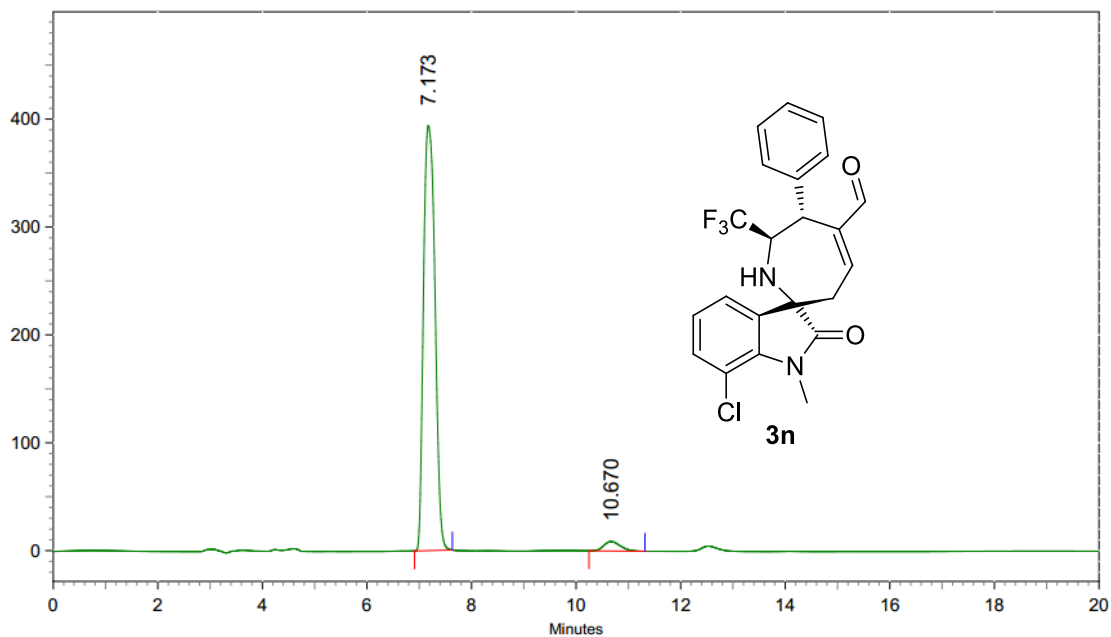
+ESI Scan (rt: 0.735 min) Frag=175.0V CYC-20200105-47.d





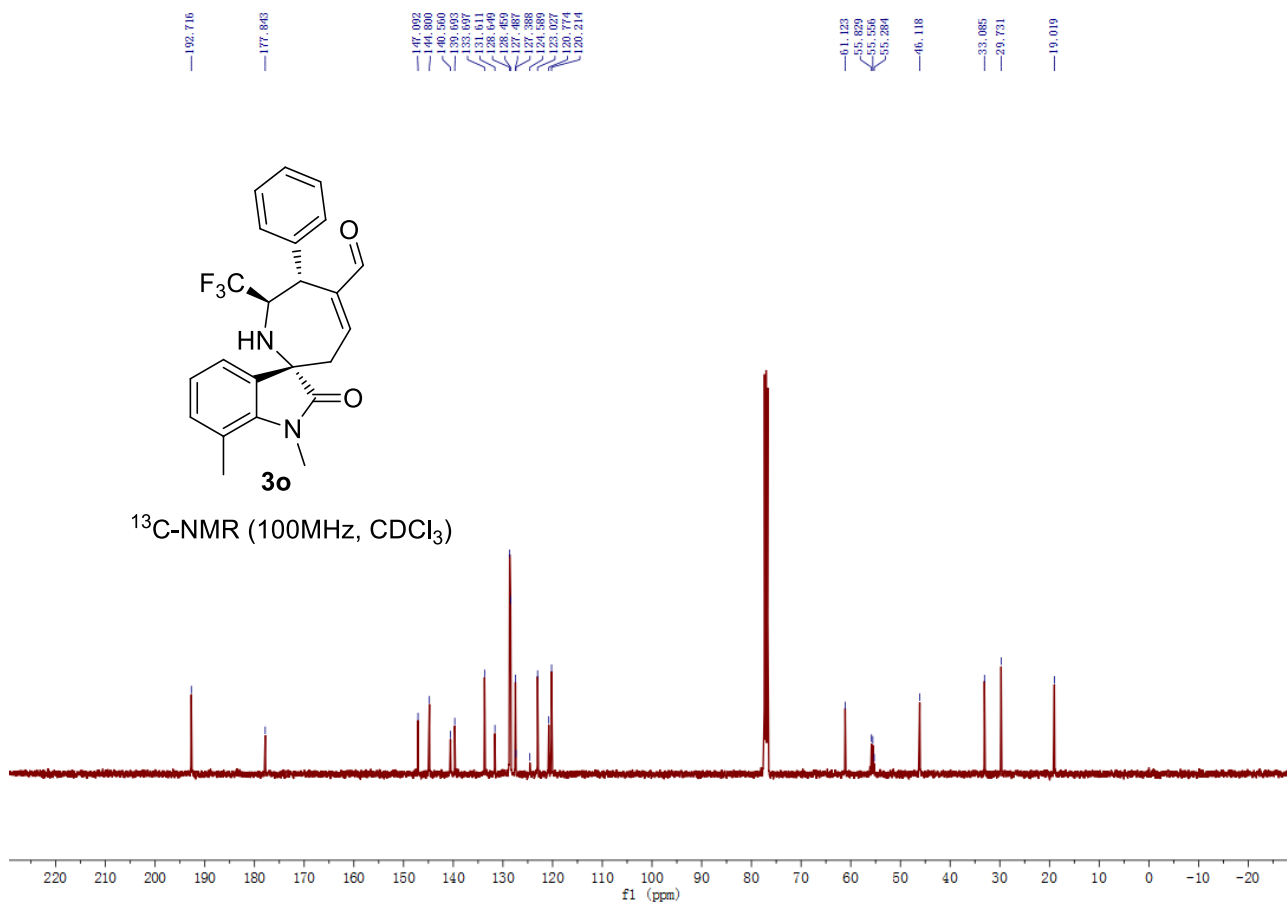
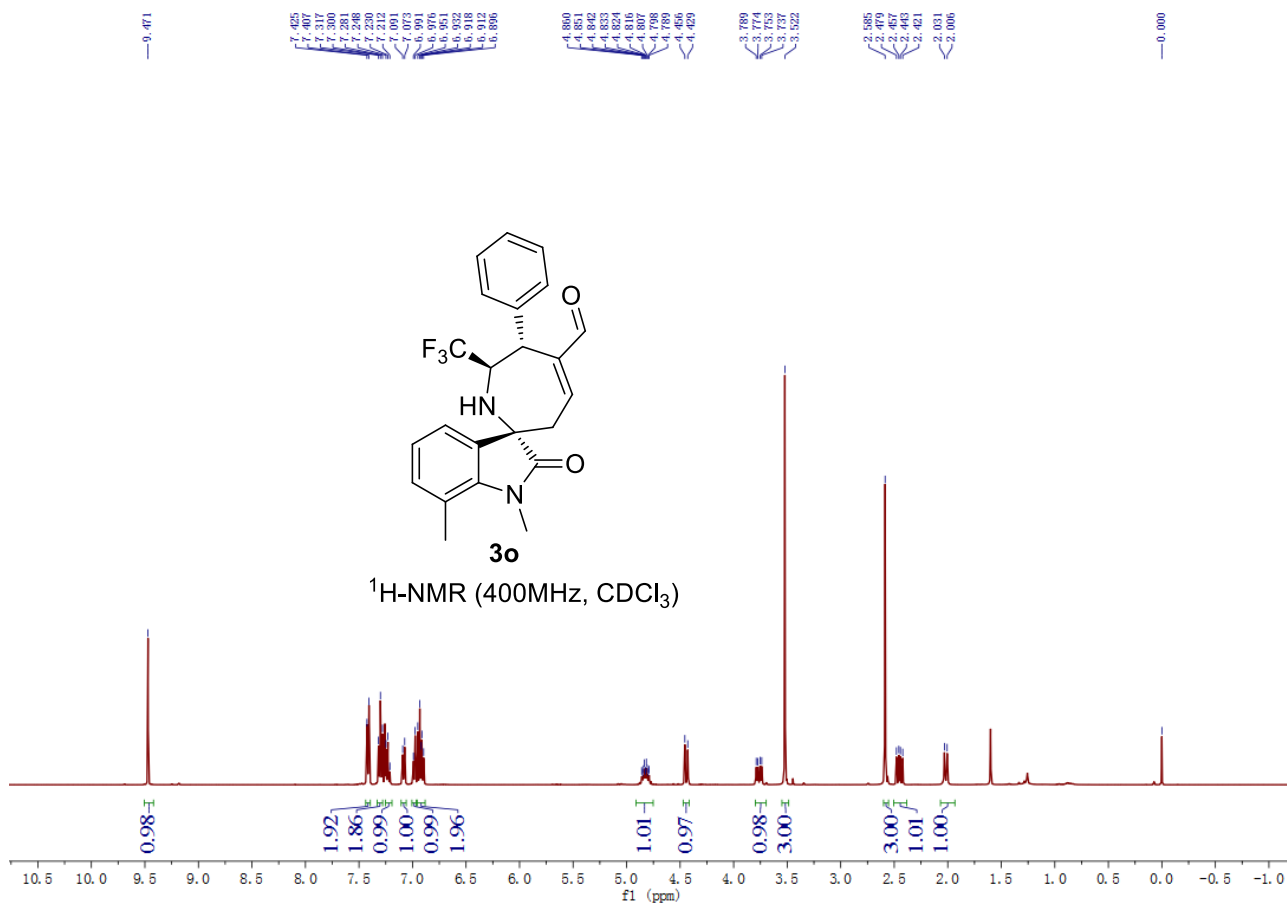
AREA PERCENT REPORT

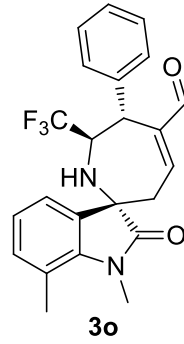
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.157	0.737	1106715	15458011	51.0955
2	10.640	1.150	676884	14795167	48.9045



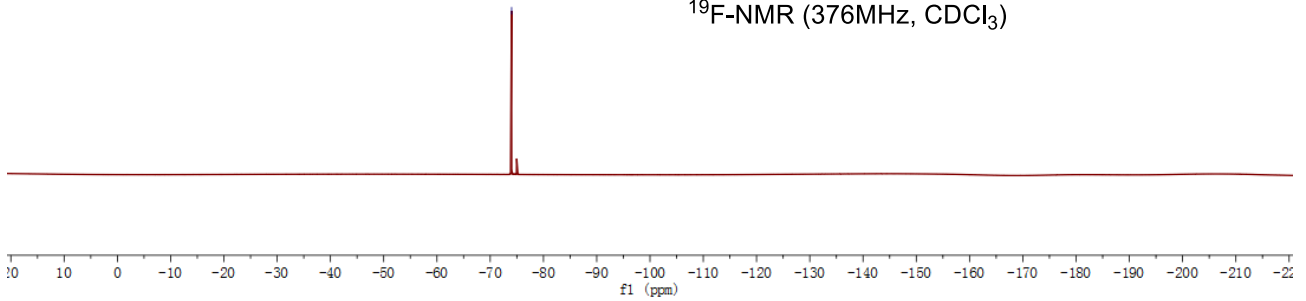
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.173	0.723	6607631	100701015	96.8848
2	10.670	1.070	147864	3237940	3.1152





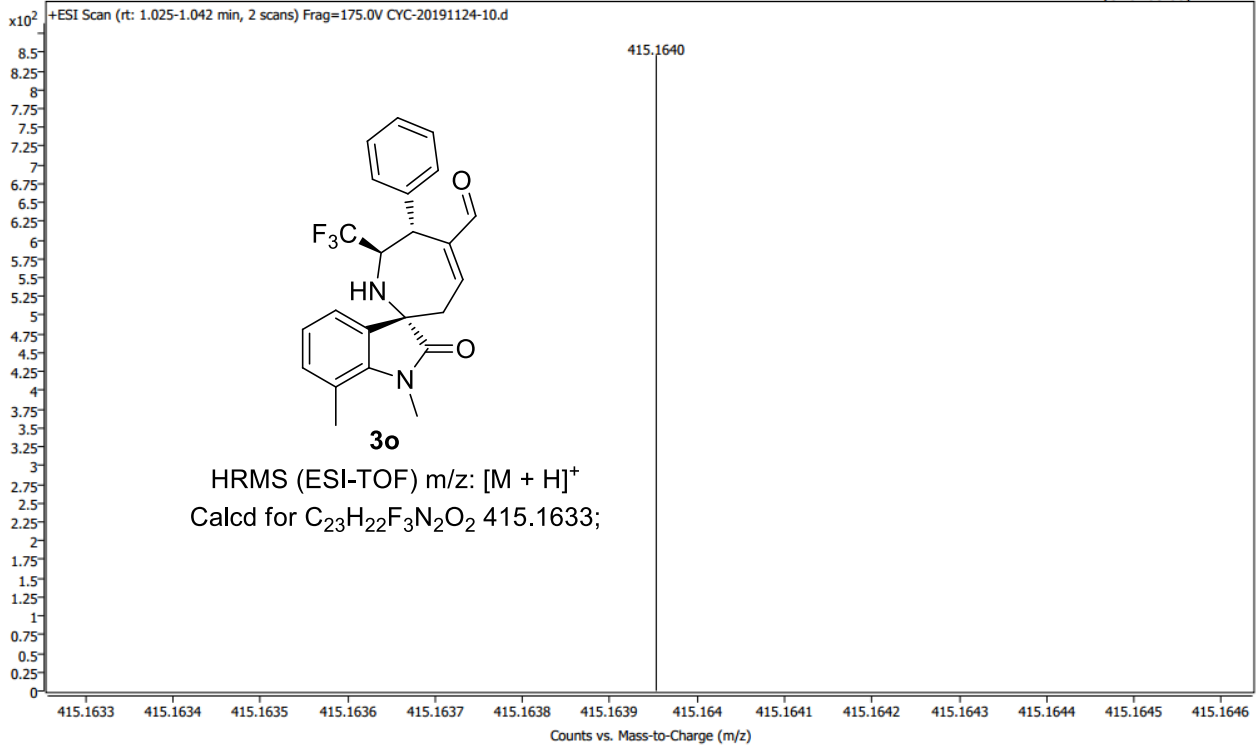
¹⁹F-NMR (376MHz, CDCl₃)

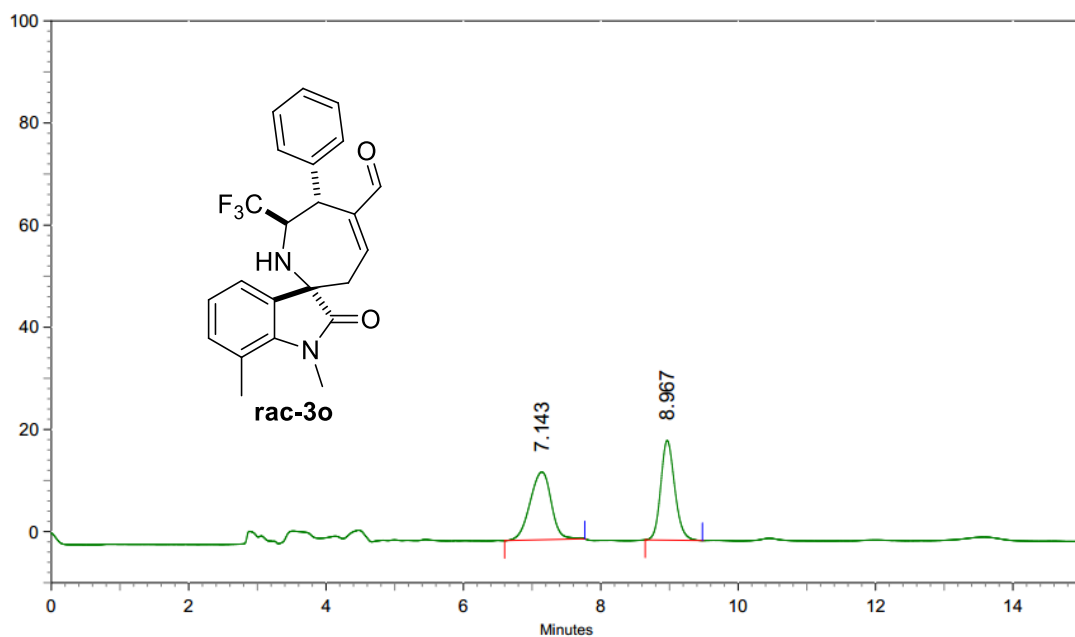


Spectrum Plot Report



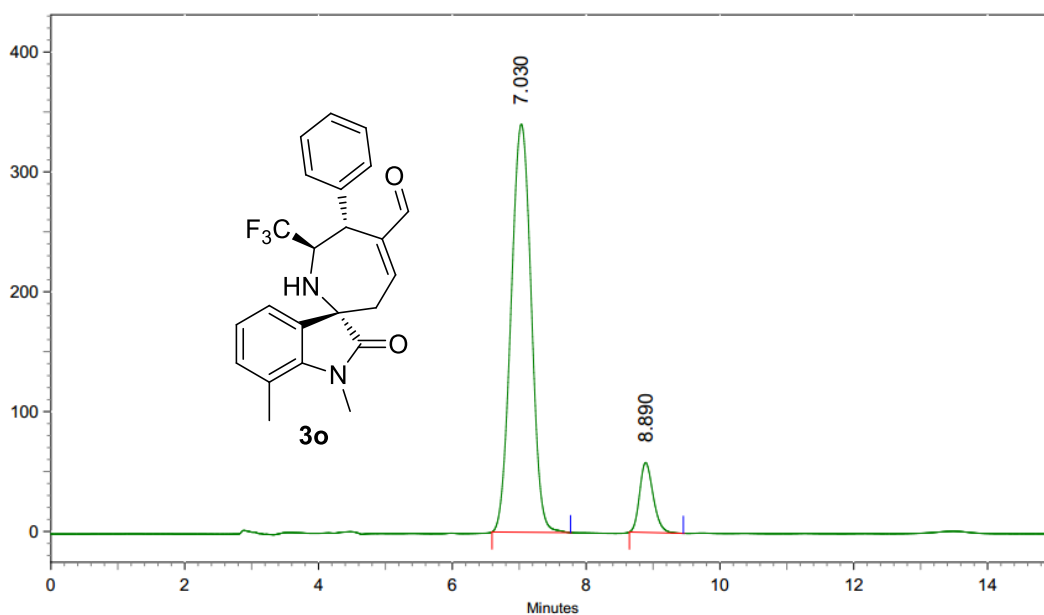
Name	CYC-20191124-10	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-10.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local) 12/5/2019 5:00:23 PM (UTC+08:00)





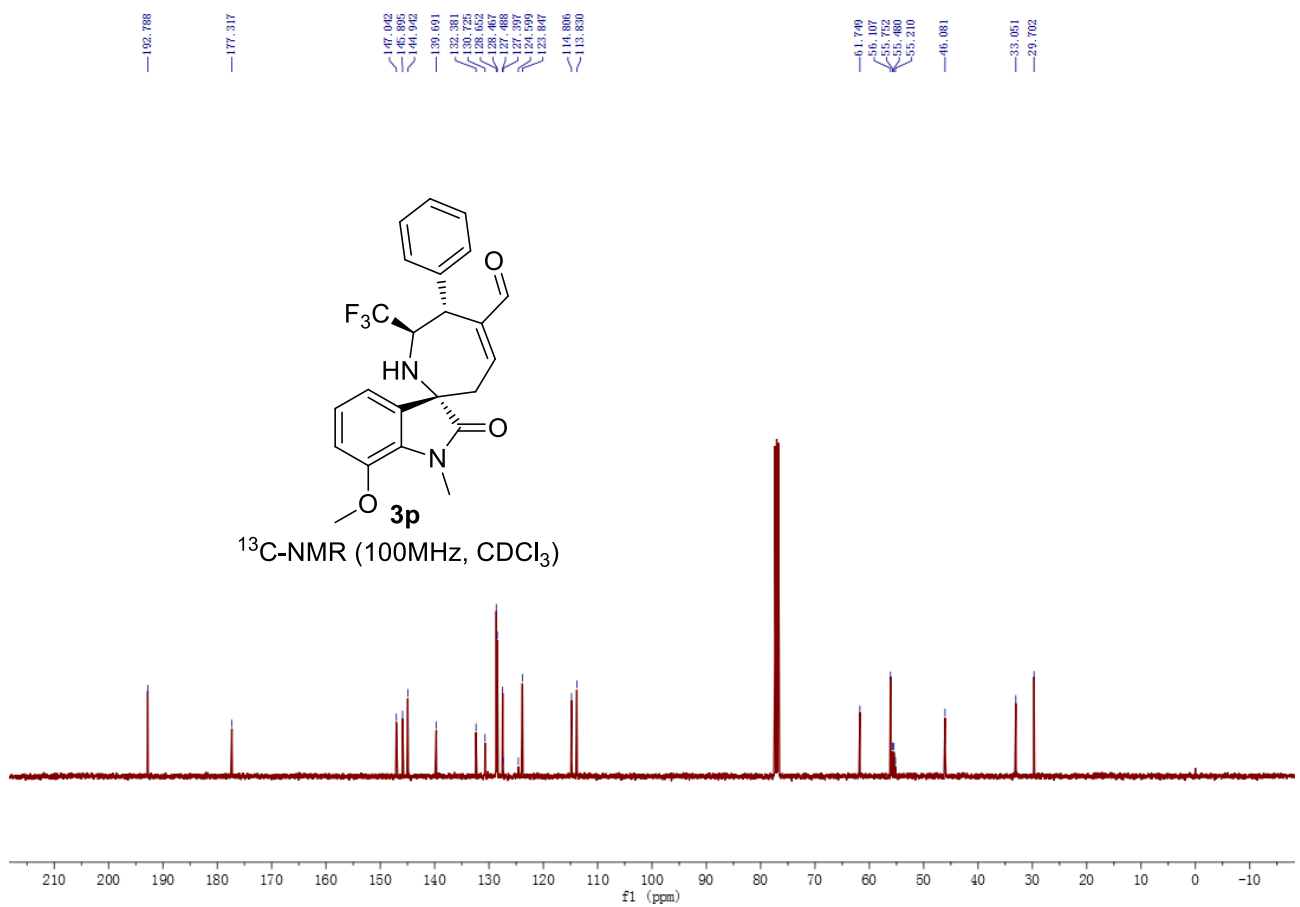
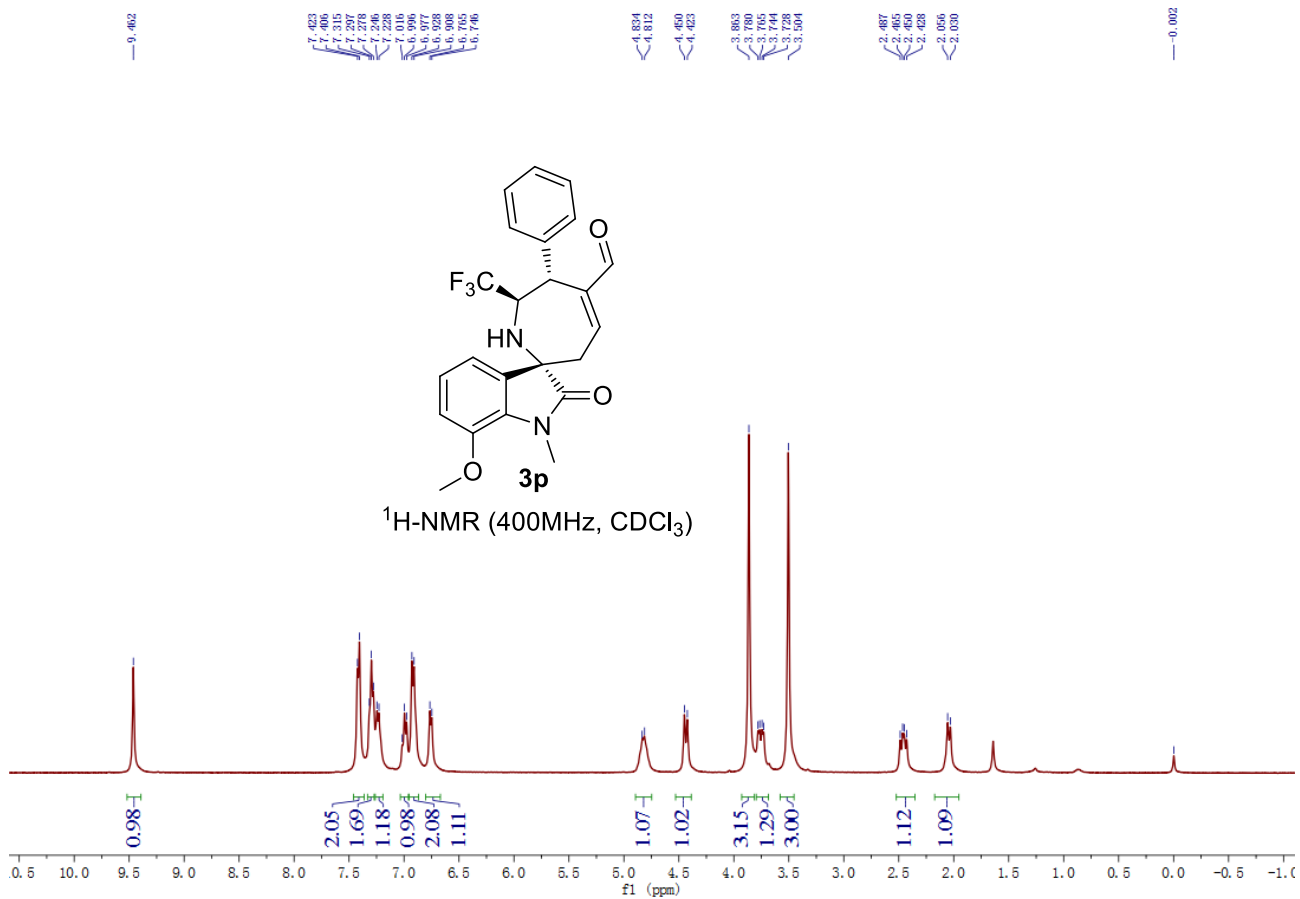
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.143	1.167	222635	4793233	50.7573
2	8.967	0.833	327218	4650212	49.2427

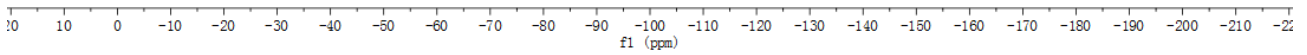
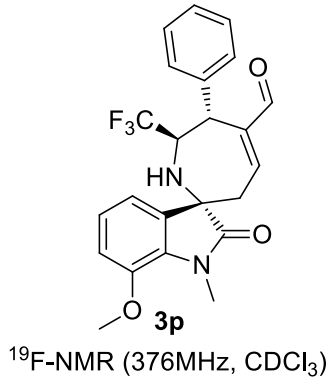


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.030	1.173	5710888	119099835	89.6330
2	8.890	0.807	978082	13775193	10.3670



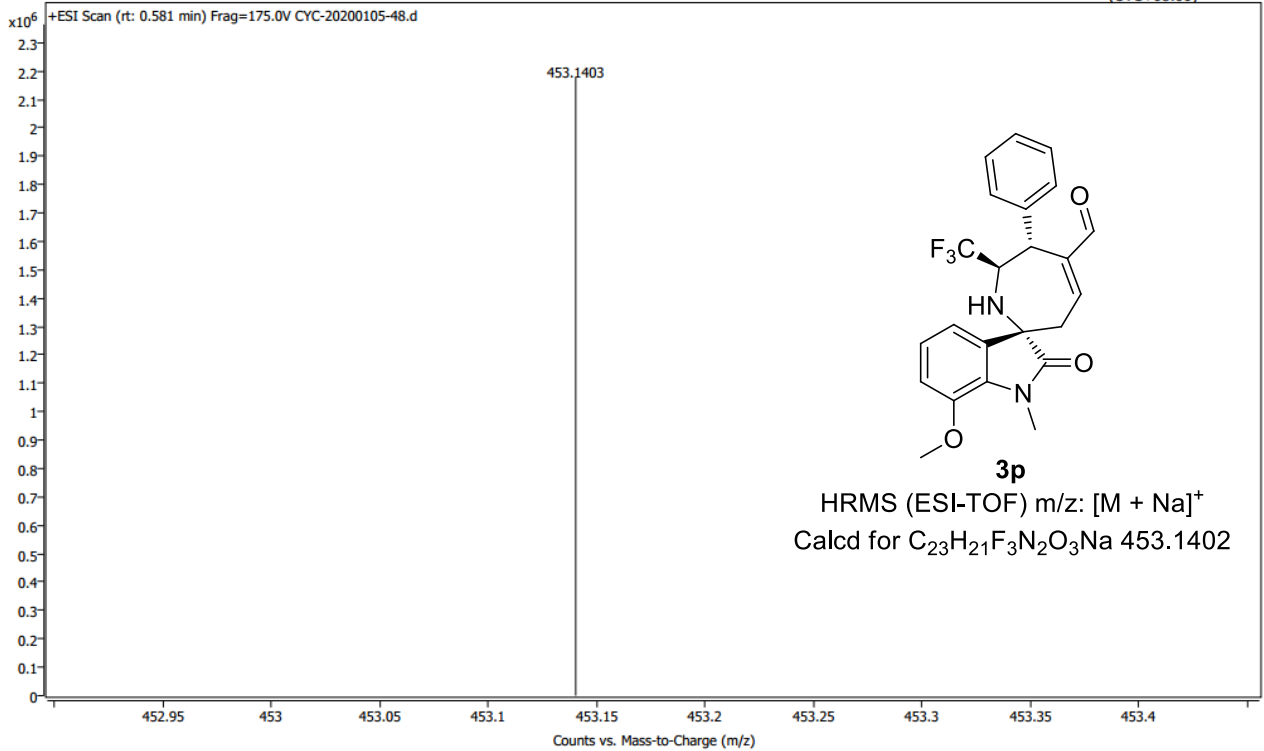
-71.009

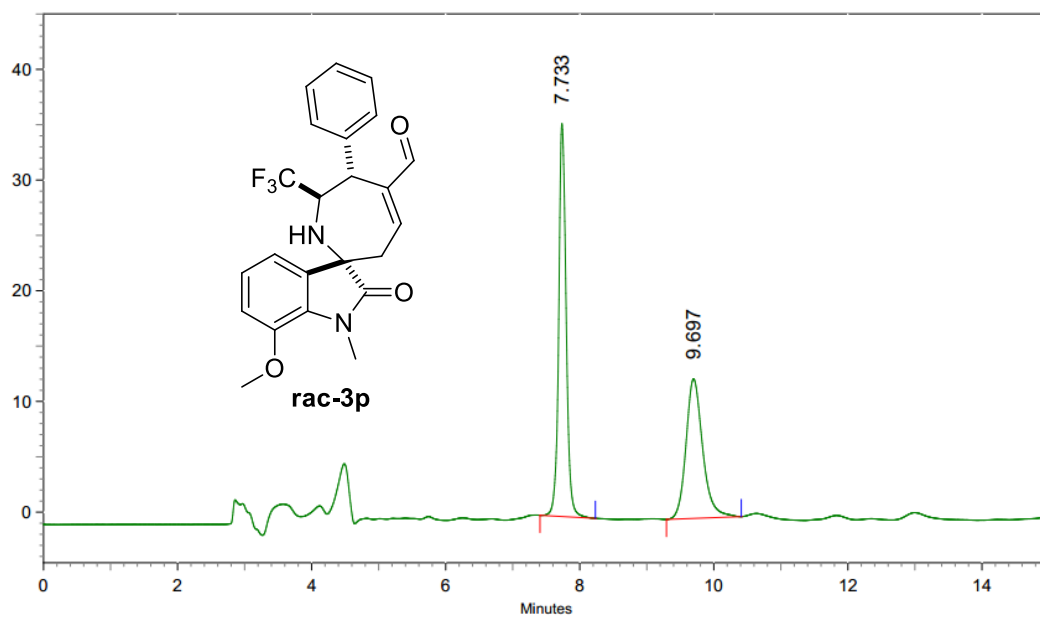


Spectrum Plot Report

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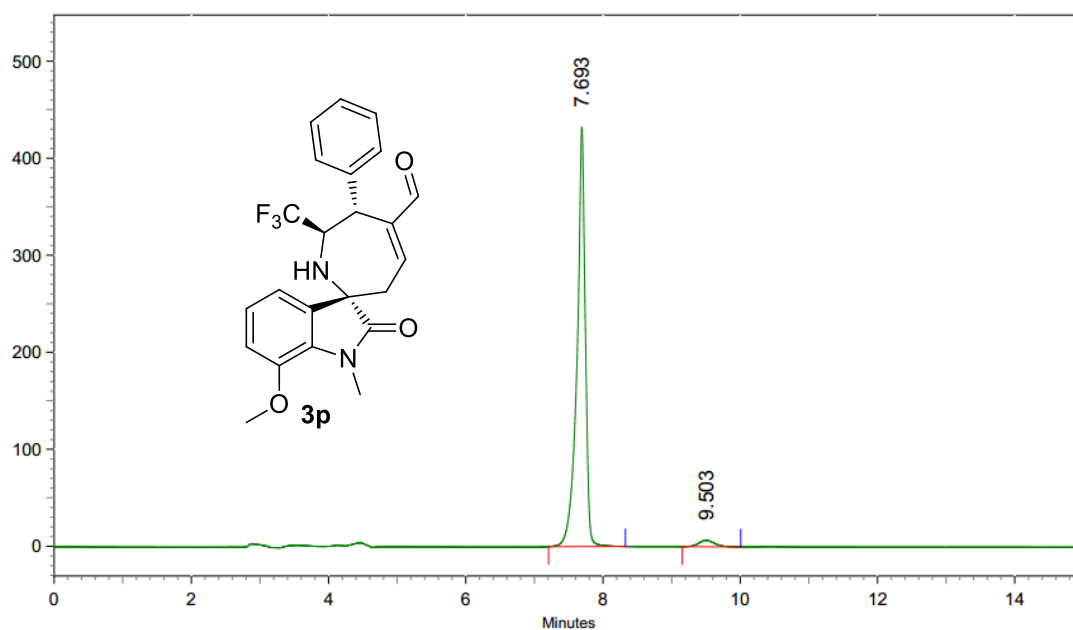
Name	CYC-20200105-48	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20200105-48.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					1/10/2020 9:00:52 PM (UTC+08:00)





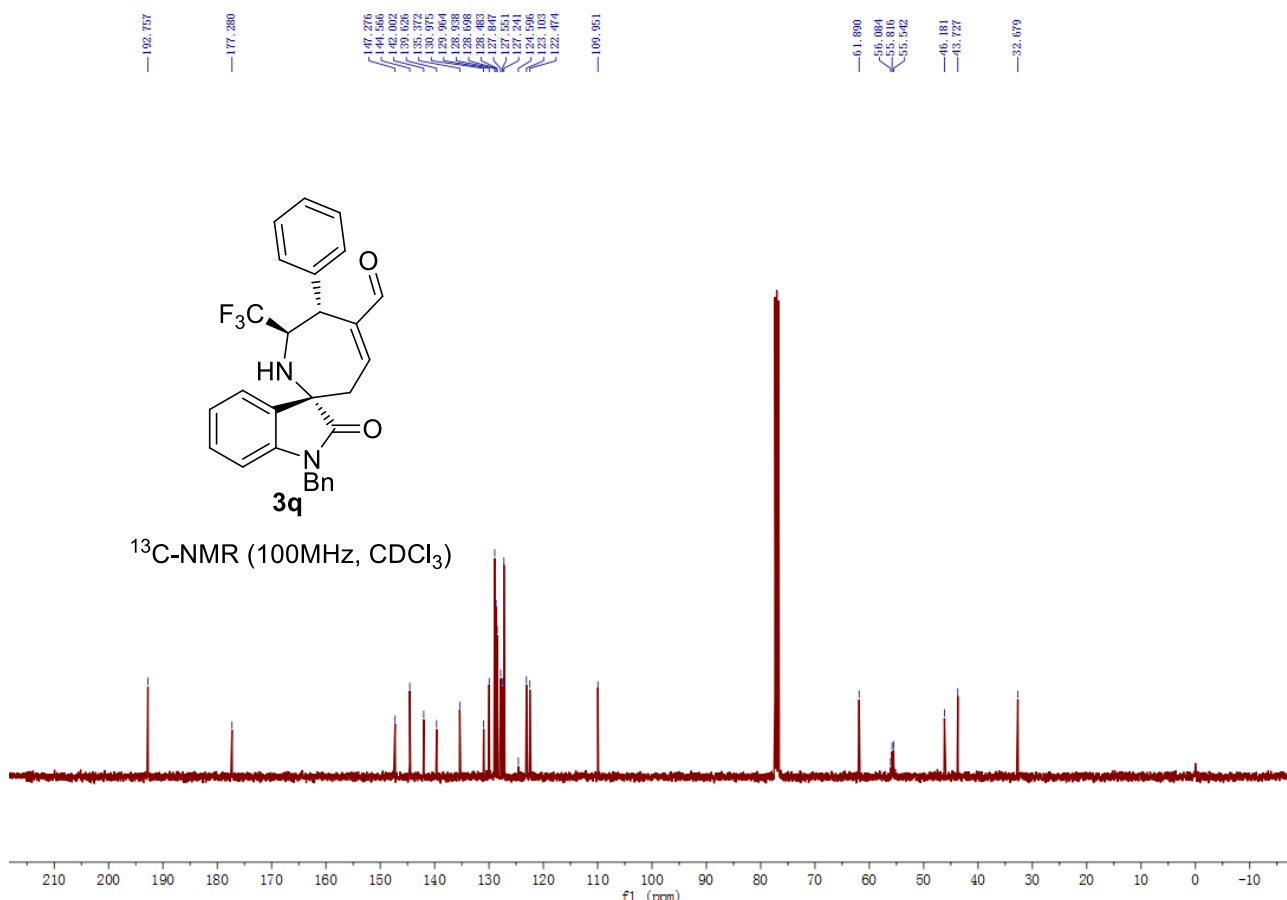
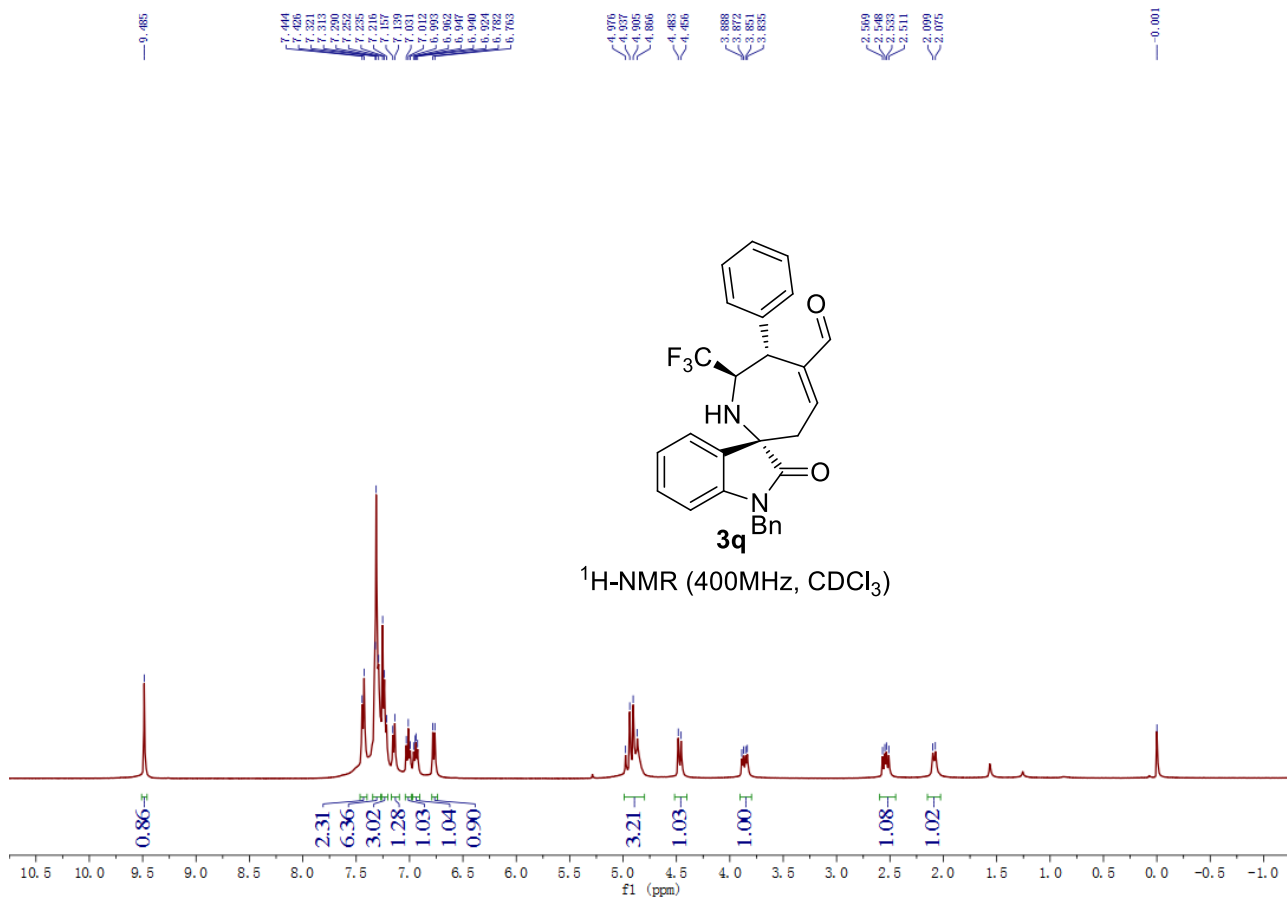
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.733	0.827	595570	4593409	55.6611
2	9.697	1.117	211508	3659042	44.3389

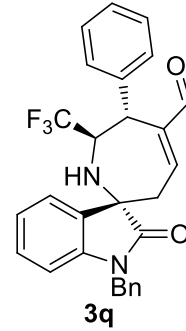


AREA PERCENT REPORT

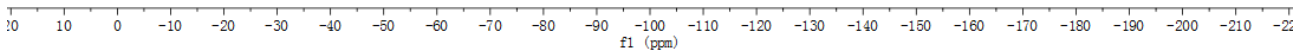
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.693	1.120	7252583	60924393	97.0955
2	9.503	0.853	112154	1822483	2.9045



-71.088



¹⁹F-NMR (376MHz, CDCl₃)

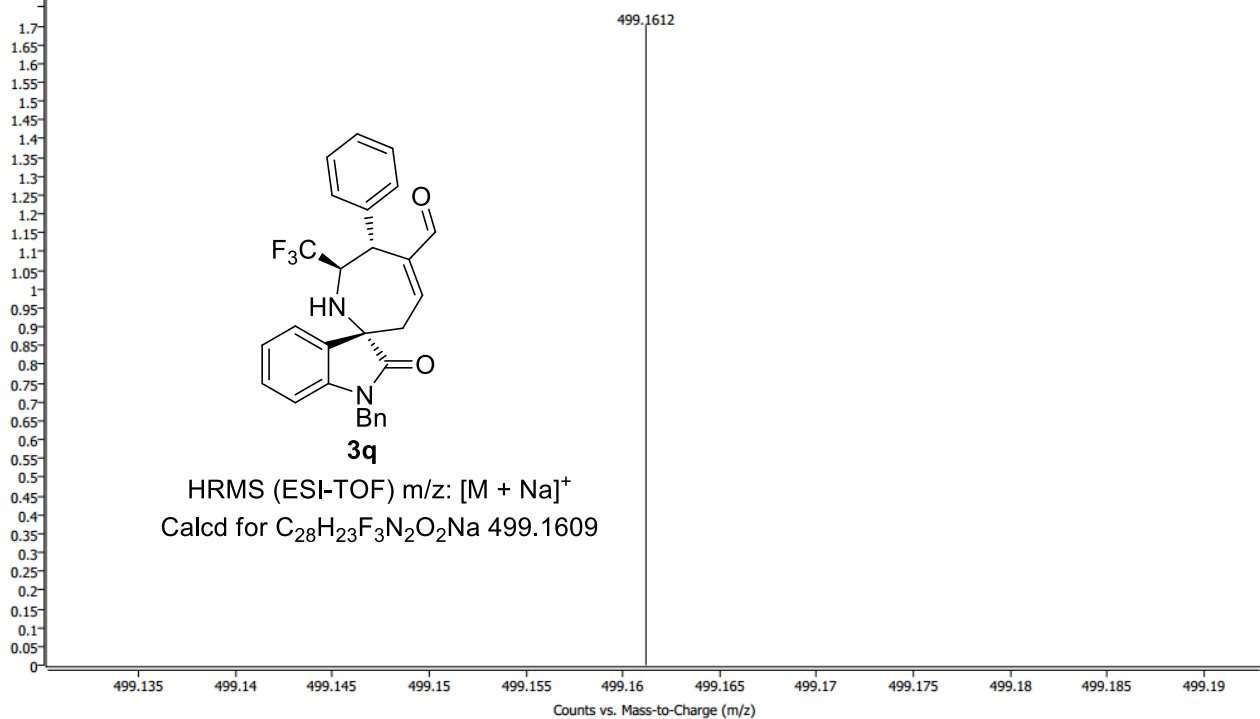


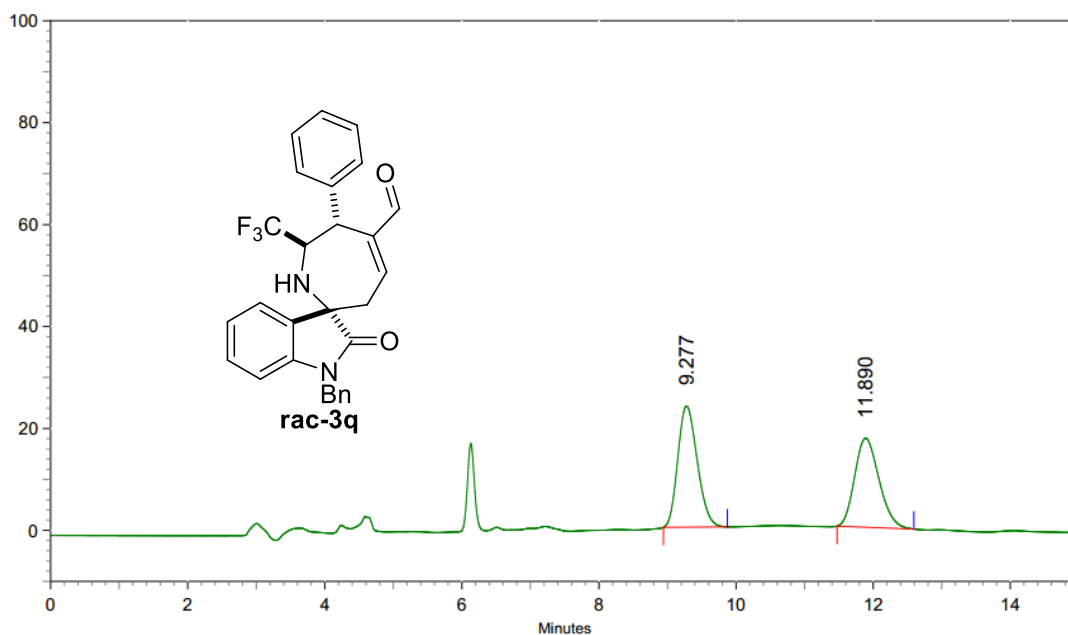
Spectrum Plot Report



Name	CYC-20191124-17	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-17.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					12/5/2019 5:21:28 PM (UTC+08:00)

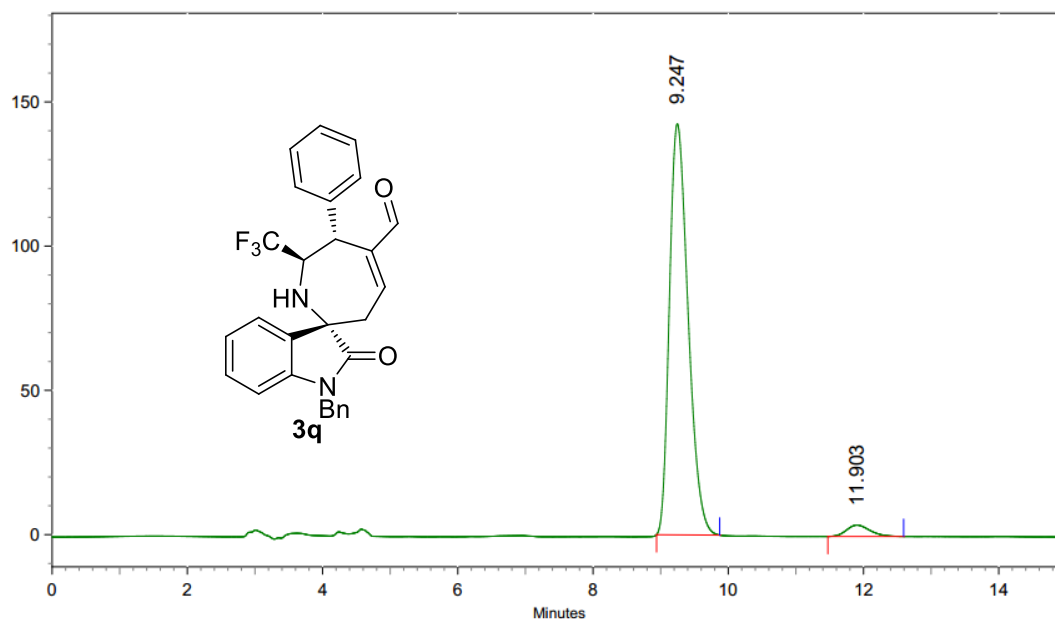
+ESI Scan (rt: 0.835 min) Frag=175.0V CYC-20191124-17.d





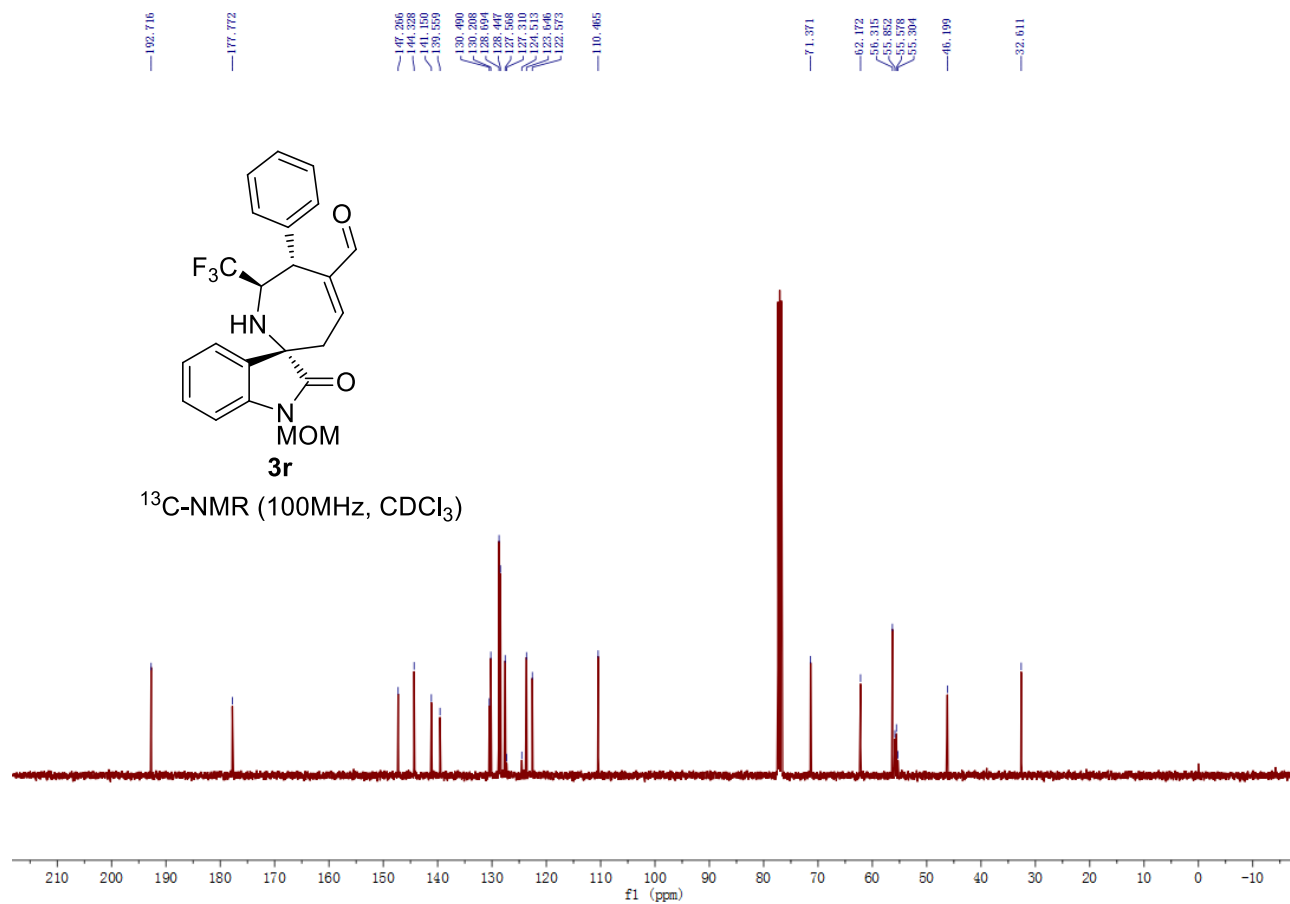
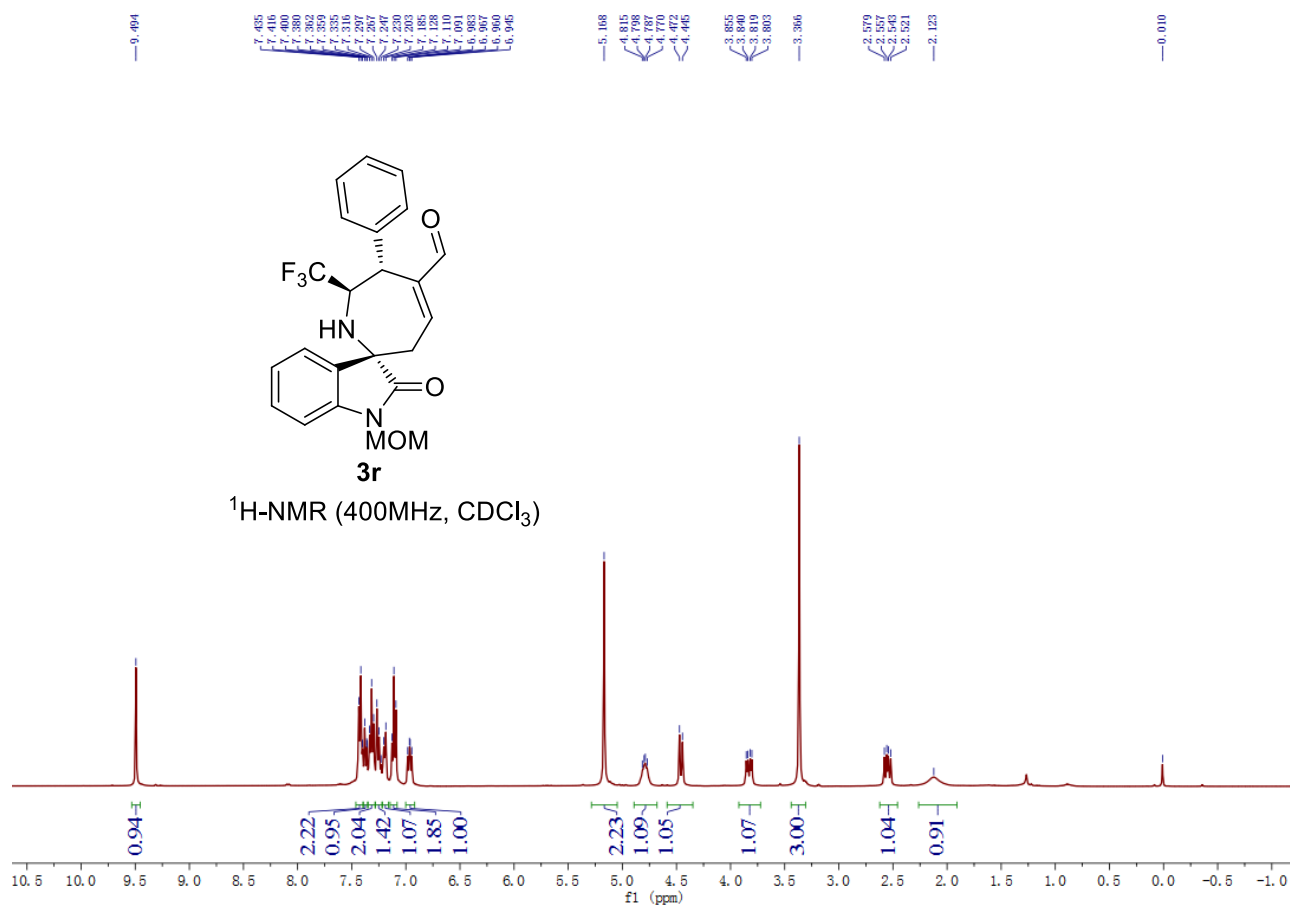
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.277	0.933	399017	7866308	52.0840
2	11.890	1.120	293113	7236798	47.9160

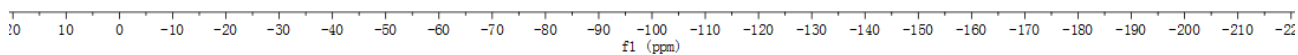
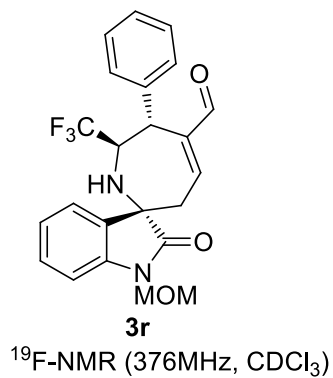


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.247	0.933	2389861	45812612	96.6662
2	11.903	1.120	65822	1579989	3.3338



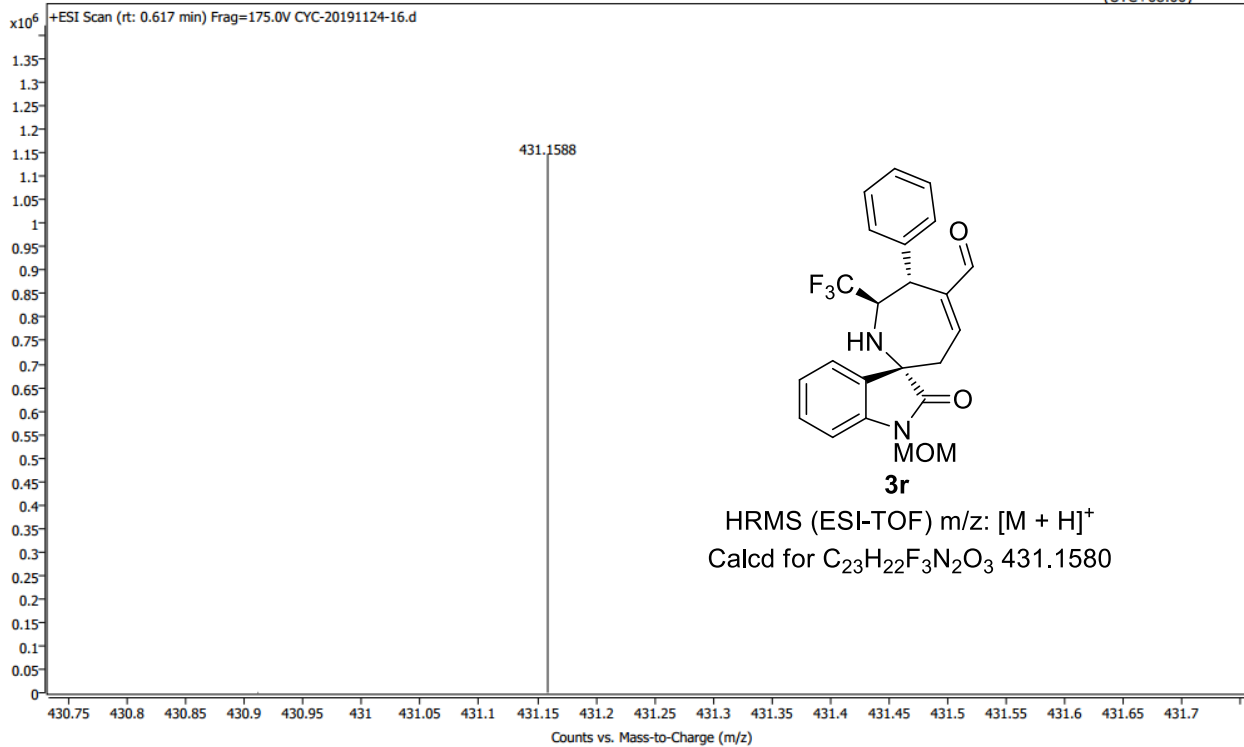
71.154

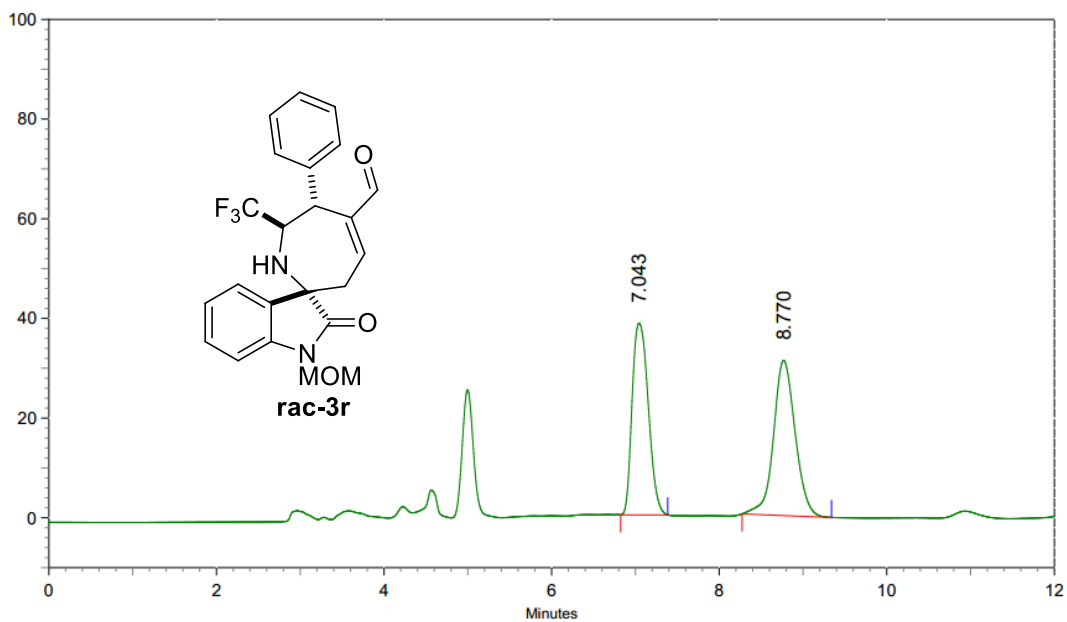


Spectrum Plot Report

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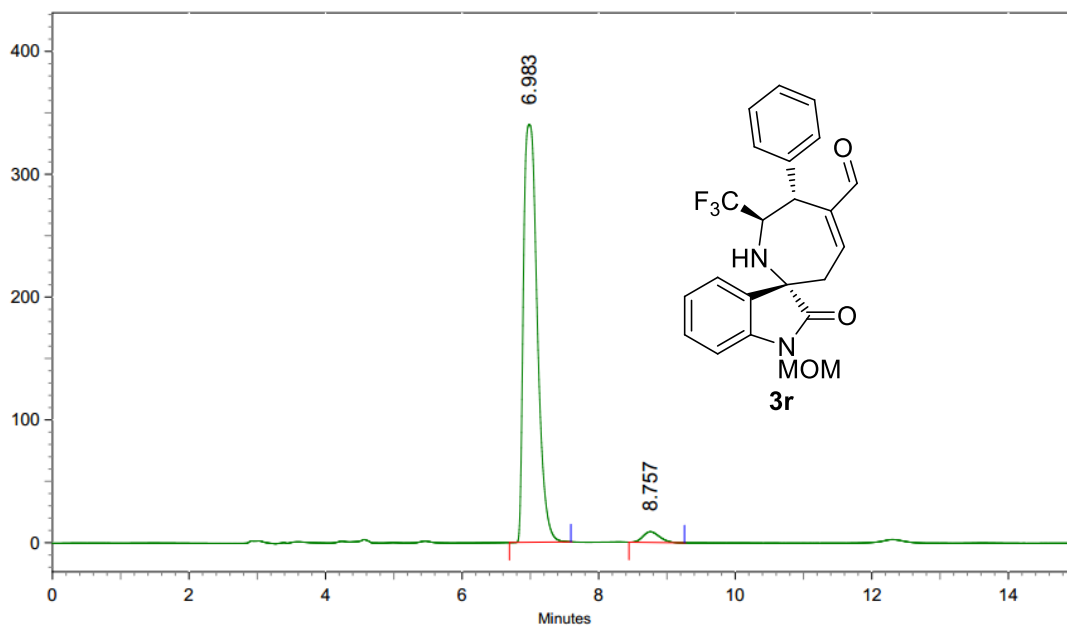
Name	CYC-20191124-16	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-16.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local) 12/5/2019 5:18:27 PM (UTC+08:00)





AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	7.043	0.563	645526	8648263	47.9638
2	8.770	1.067	522614	9382550	52.0362



AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	6.983	0.900	5706553	79816728	97.0092
2	8.757	0.813	146107	2460725	2.9908

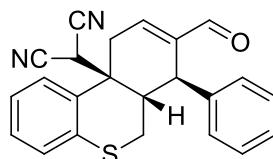
—0.181

7.332
7.316
7.296
7.283
7.263
7.243
7.193
7.172
7.138
7.127
7.117
7.096
4.975
4.959

—4.360

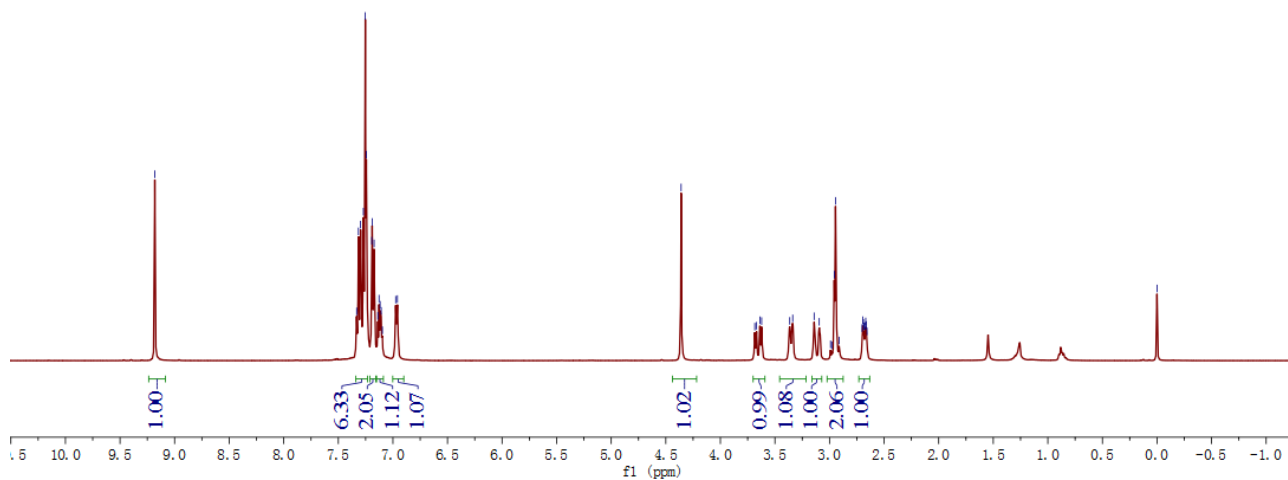
3.685
3.669
3.638
3.622
3.606
3.337
3.141
3.094
2.970
2.954
2.936
2.913
2.892
2.875
2.690
2.683
2.675
2.668
2.653
2.637

—0.000



5a

¹H-NMR (400MHz, CDCl₃)



—101.268

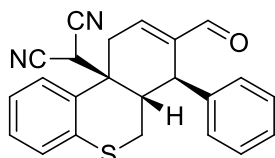
143.561
143.303
139.987
136.447
135.222
128.950
128.308
127.689
127.629
127.277
126.327

110.782
110.595

43.395
42.293
41.894

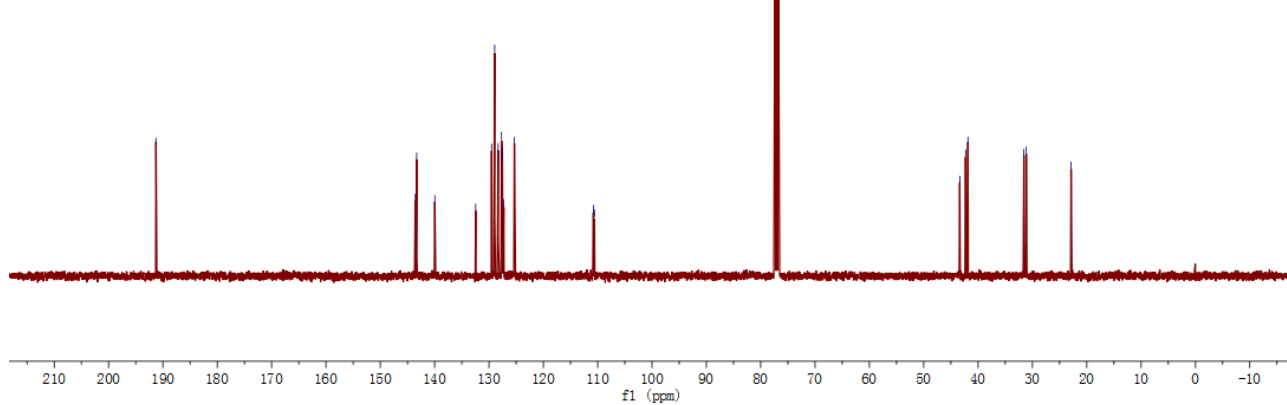
31.574
31.131

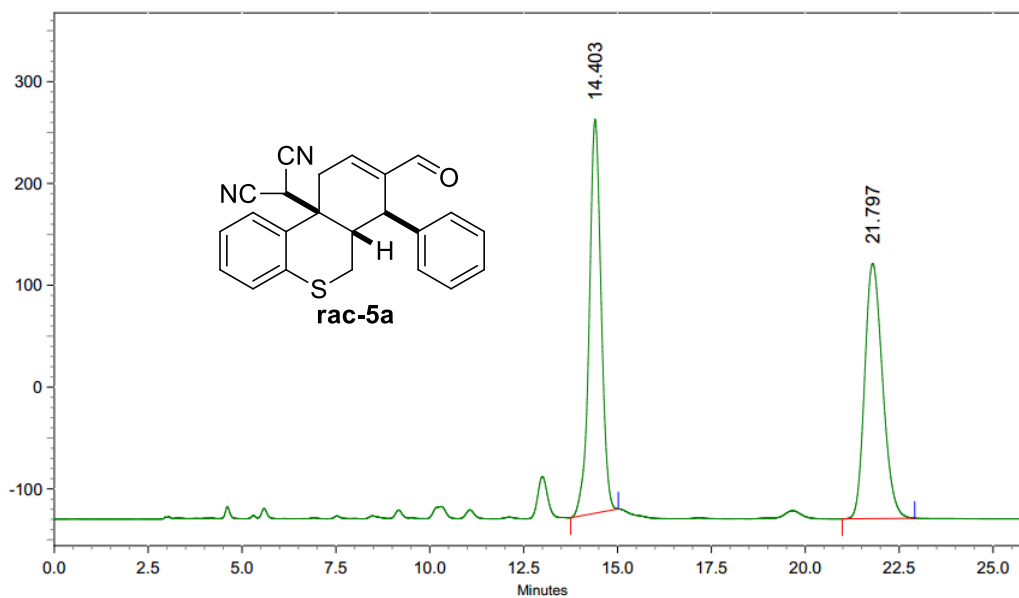
—22.887



5a

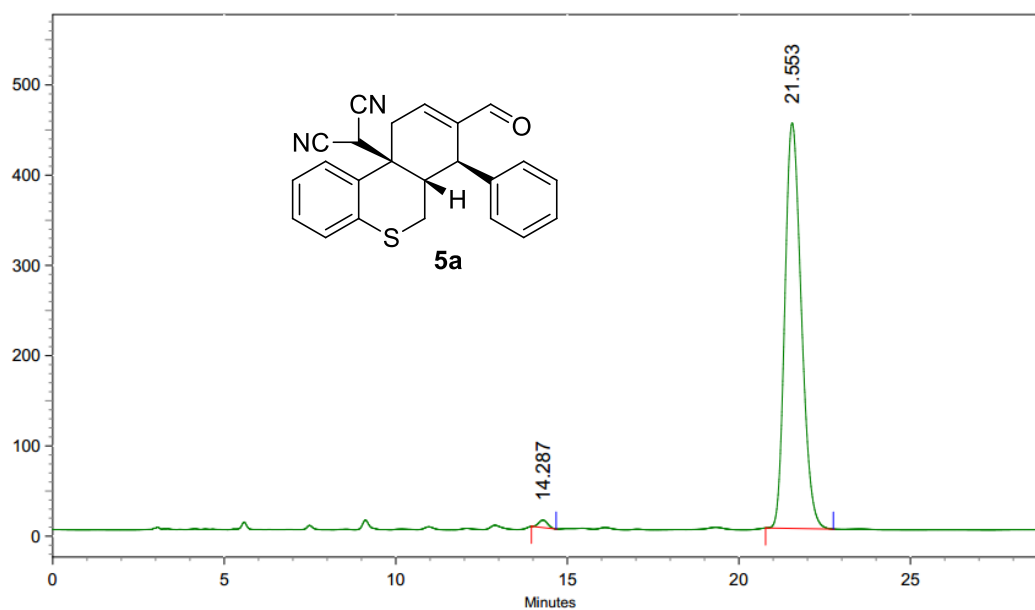
¹³C-NMR (100MHz, CDCl₃)





AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	14.403	1.270	6488628	142653584	50.6021
2	21.797	1.930	4206350	139259011	49.3979



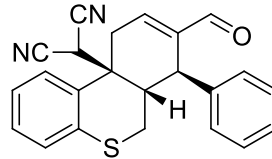
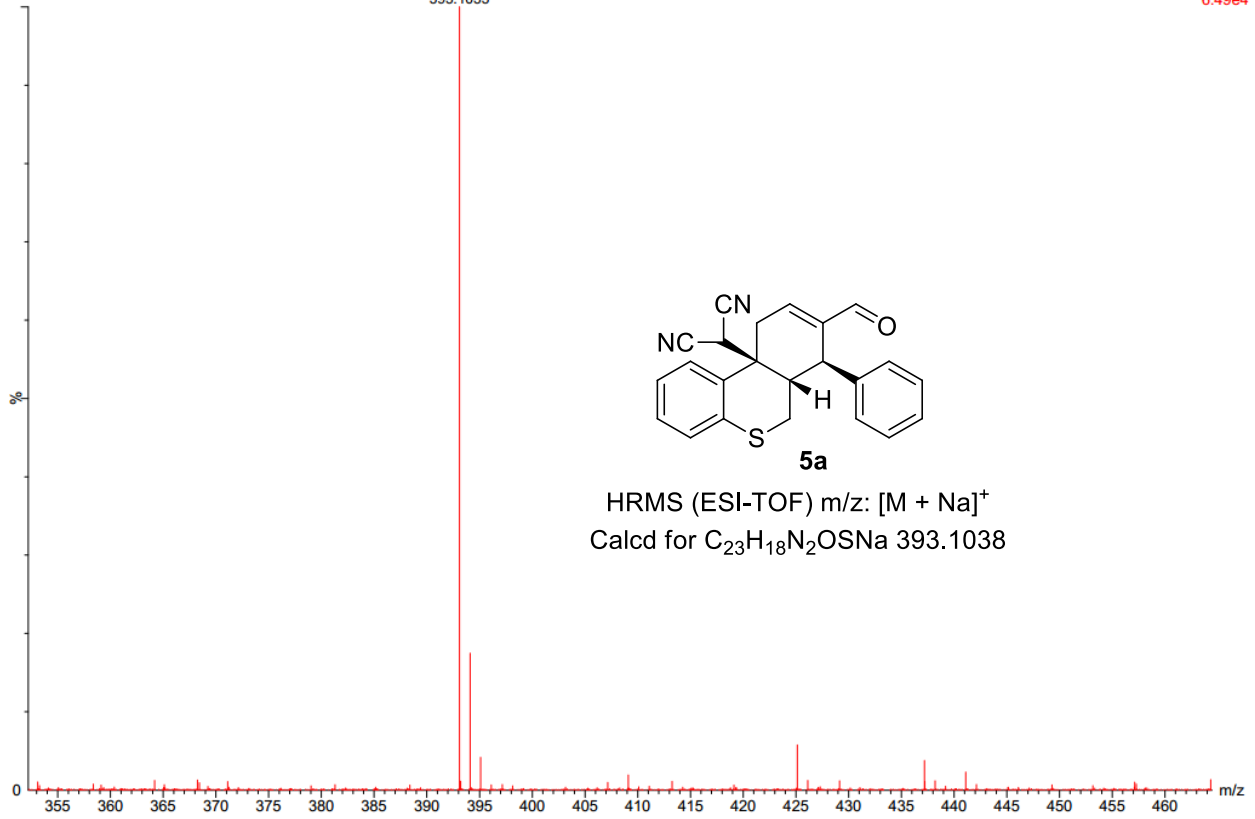
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	14.287	0.720	139183	2529988	0.9993
2	21.553	1.973	7537649	250646561	99.0007

GY-471 18 (0.232)

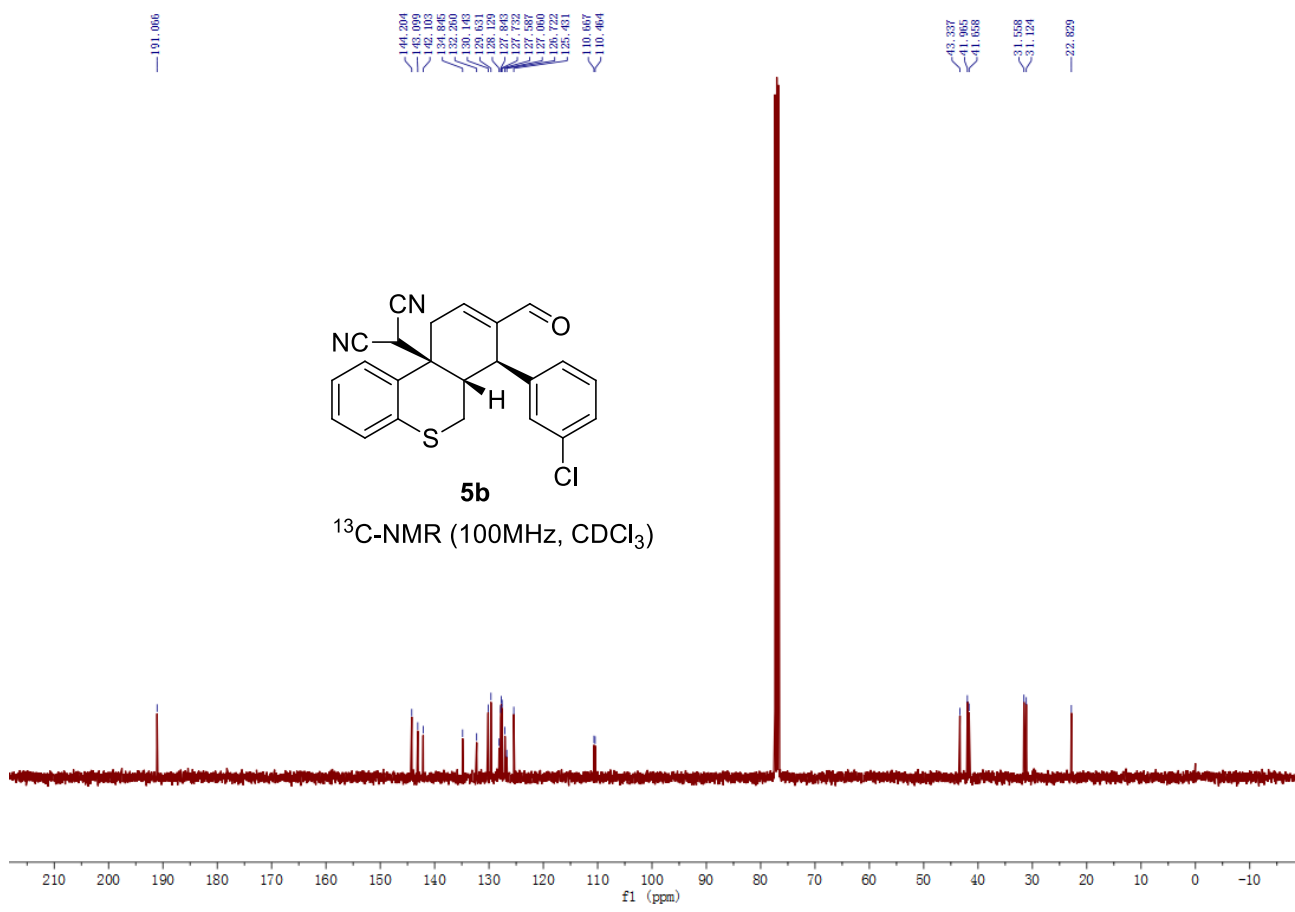
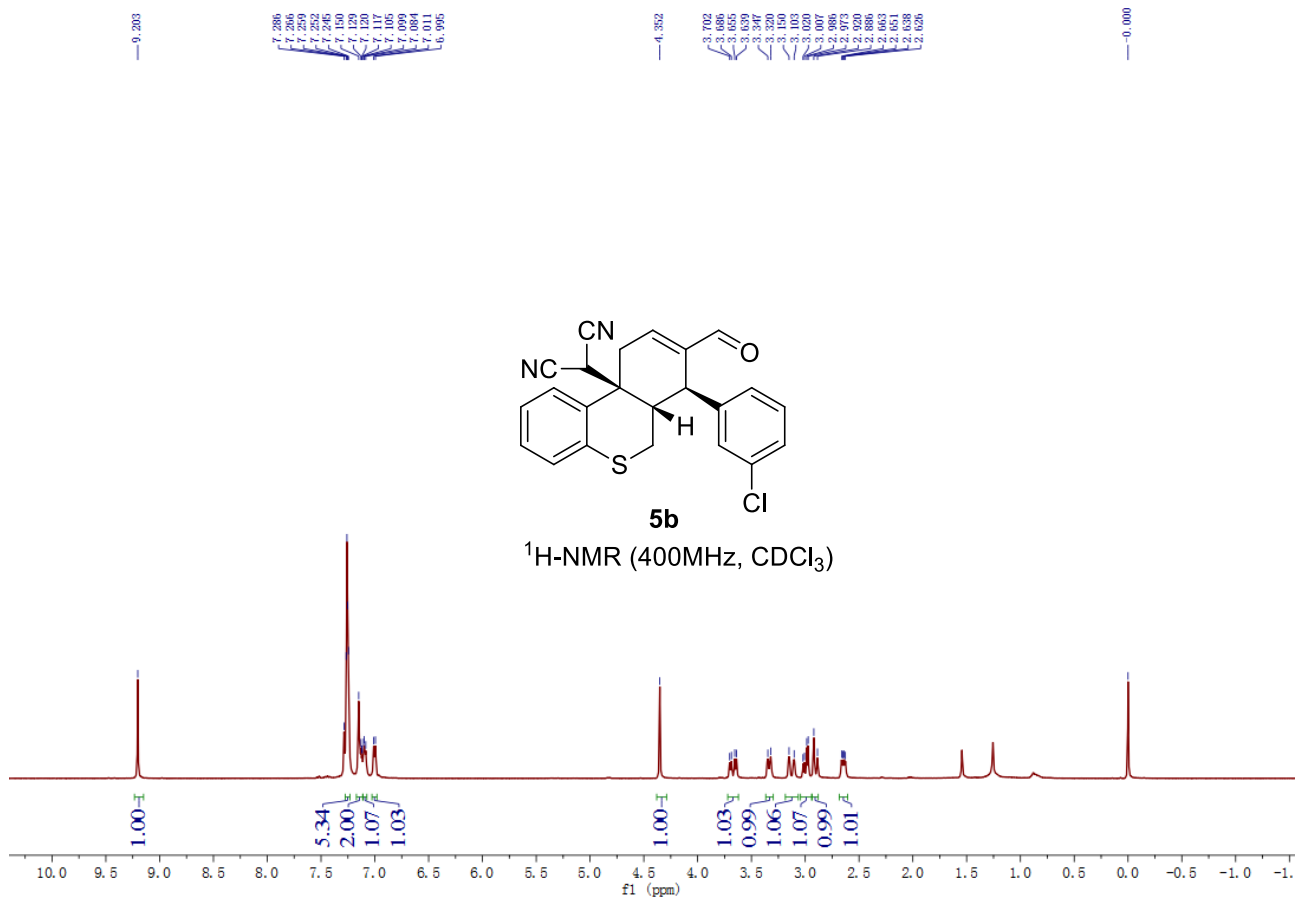
1: TOF MS ES+
6.49e4

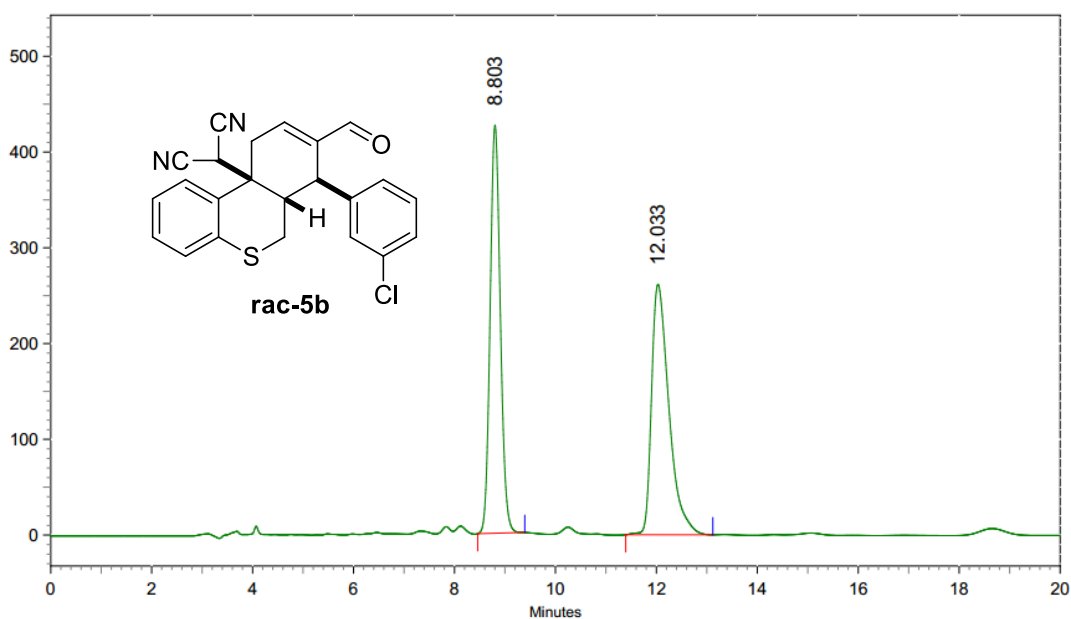
393.1033



5a

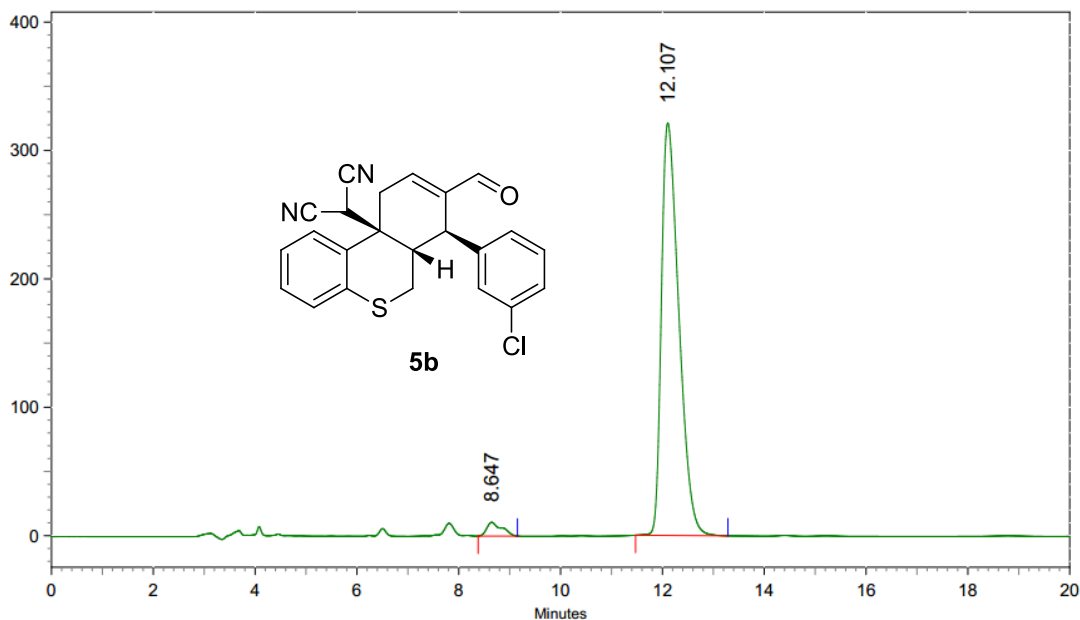
HRMS (ESI-TOF) m/z: [M + Na]⁺
Calcd for C₂₃H₁₈N₂OSNa 393.1038





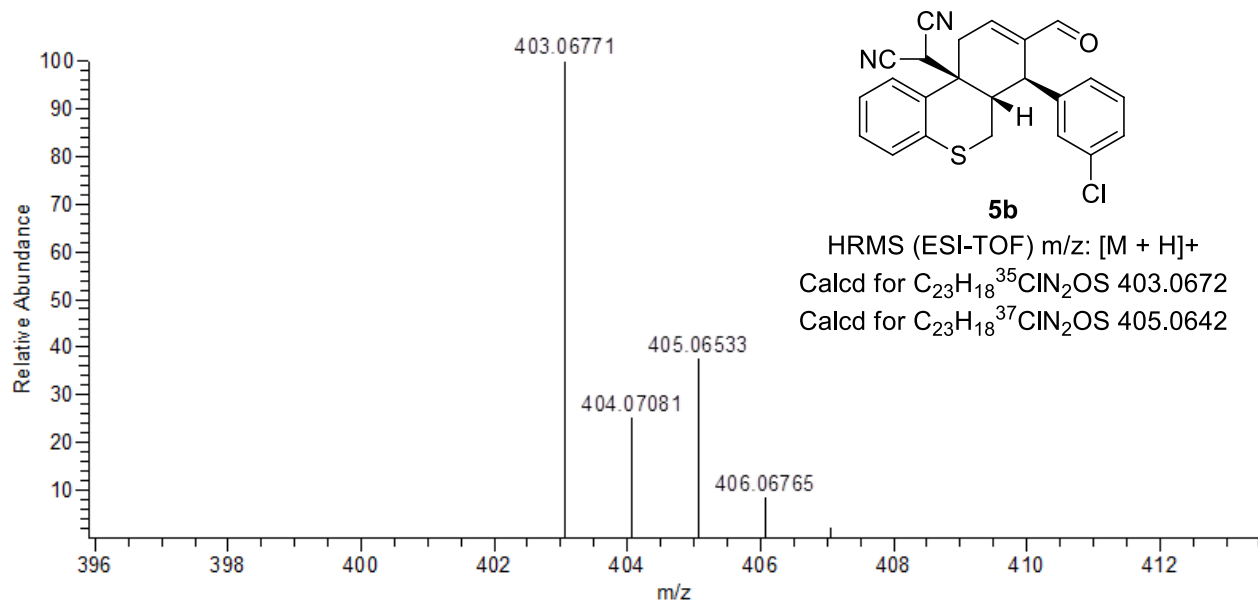
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.803	0.933	7148432	100455553	48.8676
2	12.033	1.727	4386462	105111288	51.1324



AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.647	0.773	179830	3709411	2.8119
2	12.107	1.813	5388844	128209110	97.1881



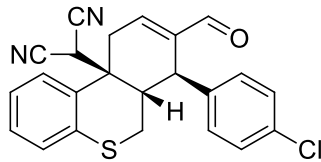
— 9.191

7.303
7.297
7.292
7.287
7.281
7.277
7.271
7.136
7.116
6.991
6.974

— 4.345

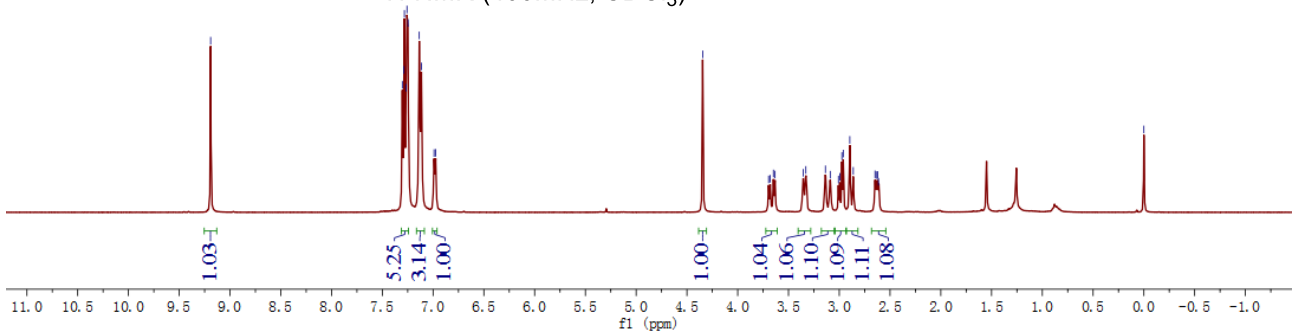
3.696
3.680
3.640
3.633
3.555
3.529
3.522
3.136
3.089
3.008
2.974
2.971
2.896
2.862
2.836
2.622
2.614

— 0.000



5c

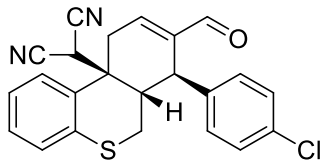
¹H-NMR (400MHz, CDCl₃)



— 191.176

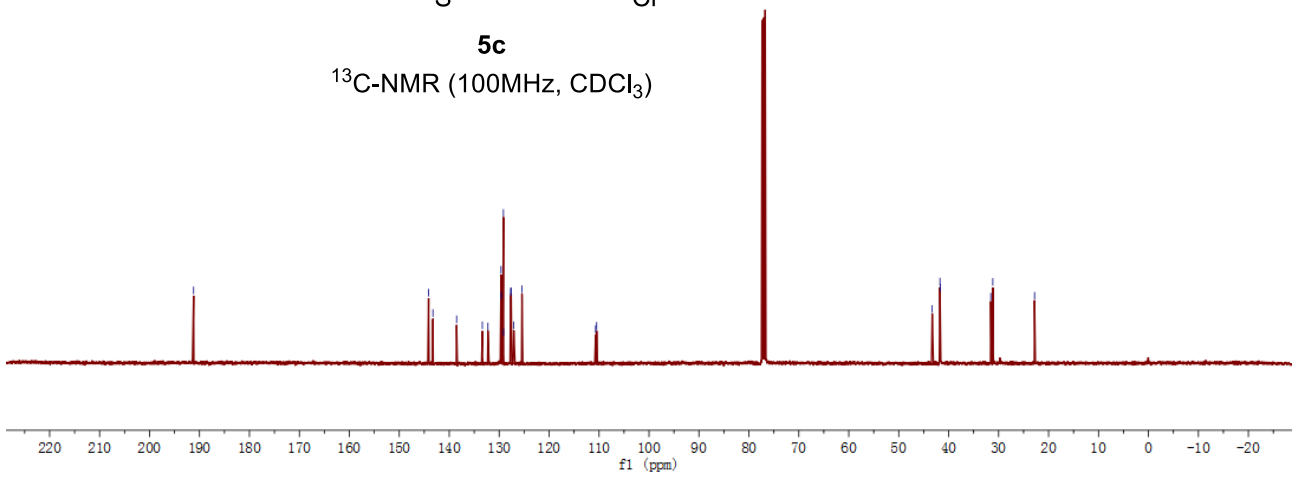
144.189
143.239
138.523
133.374
132.290
128.625
128.496
129.145
129.126
127.716
127.591
126.436
110.690
110.482

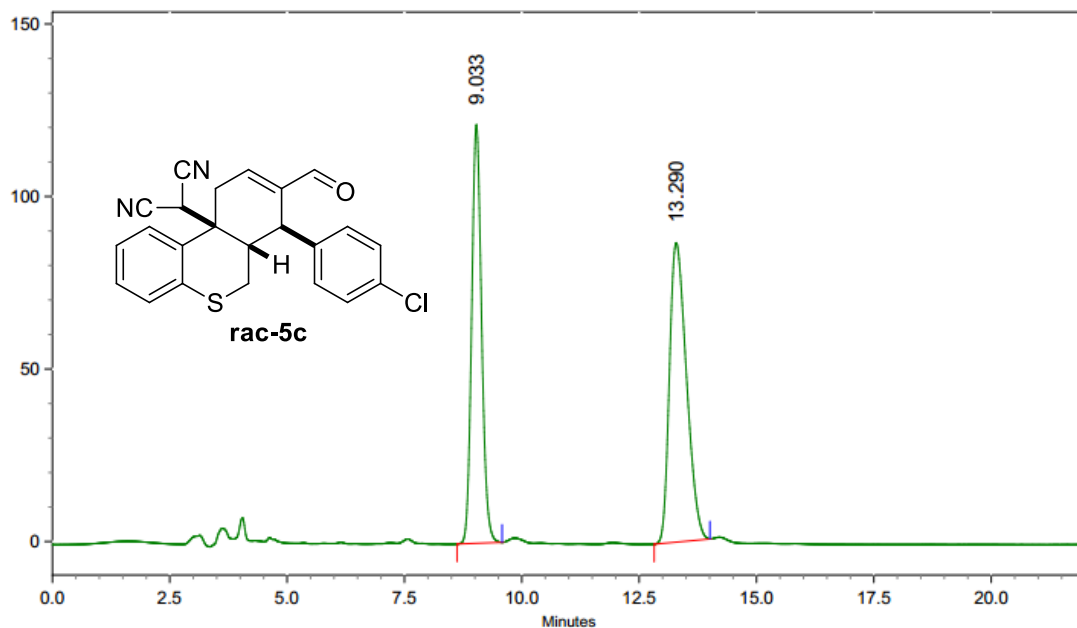
43.296
41.050
31.556
31.194
22.894



5c

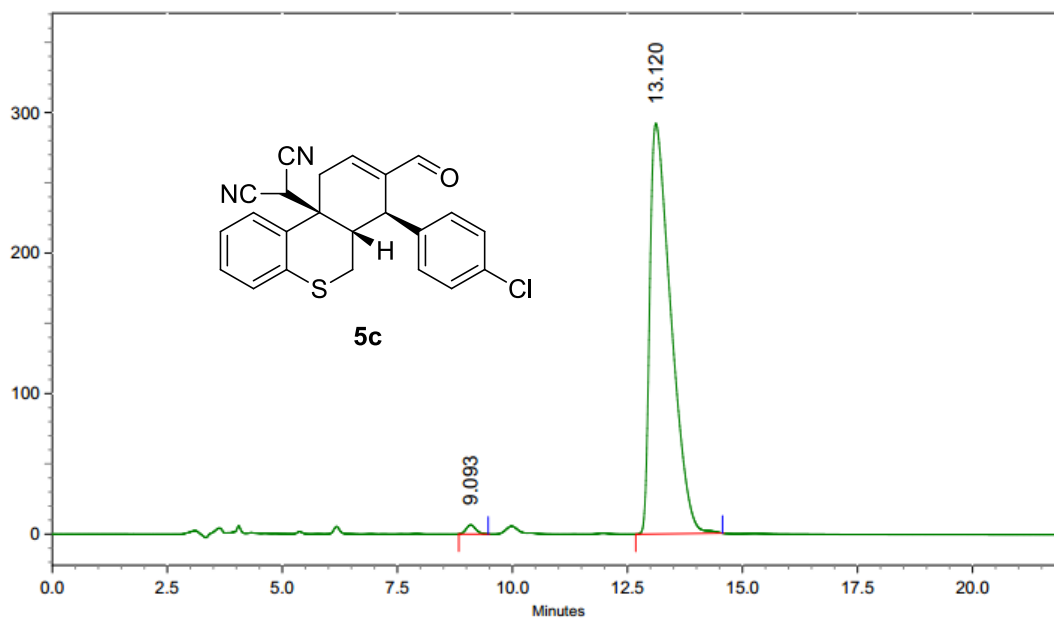
¹³C-NMR (100MHz, CDCl₃)





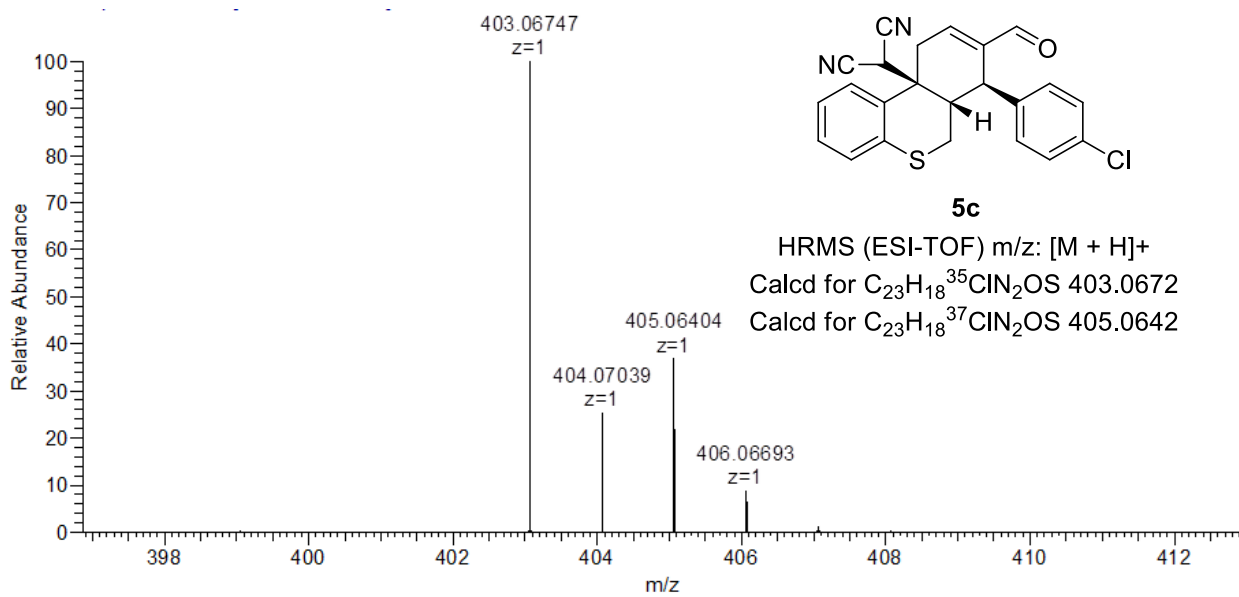
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.033	0.960	2035773	29889218	44.9493
2	13.290	1.187	1455614	36606223	55.0507



AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.093	0.640	108901	1592998	1.0108
2	13.120	1.887	4900547	156009519	98.9892



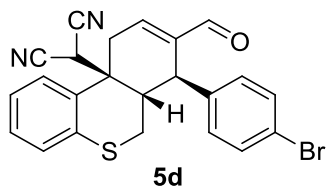
9.189

7.465
7.454
7.452
7.257
7.246
7.146
7.138
7.124
7.118
7.111
7.095
6.991
6.974

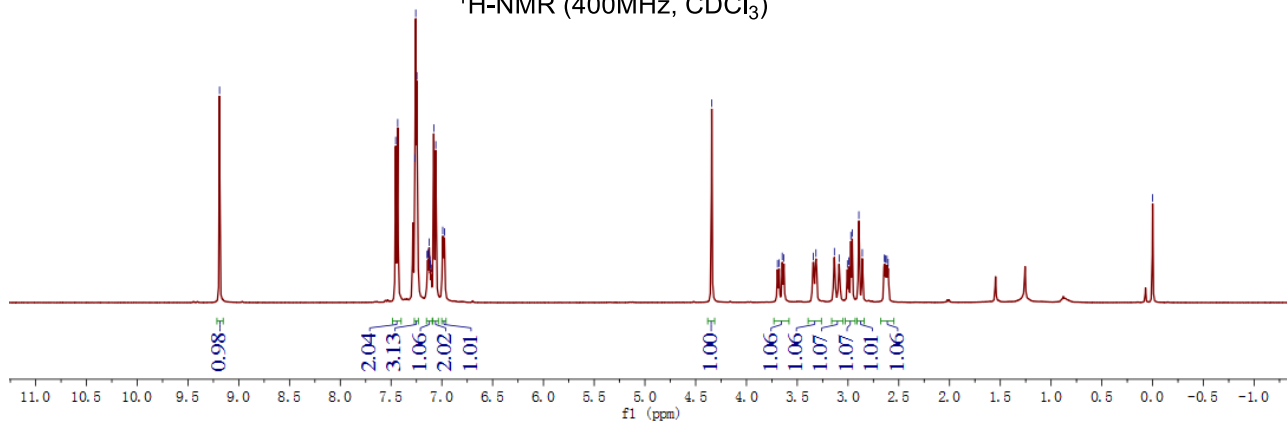
4.342

3.695
3.679
3.669
3.632
3.341
3.316
3.287
3.095
2.993
2.972
2.965
2.893
2.859
2.641
2.631
2.605

0.000



¹H-NMR (400MHz, CDCl₃)



191.132

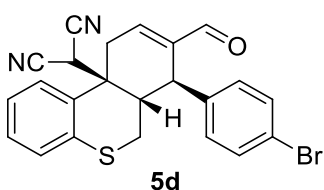
144.139
143.194
139.071
132.248
132.087
129.625
127.719
127.593
127.022
125.465
121.869

110.681
110.472

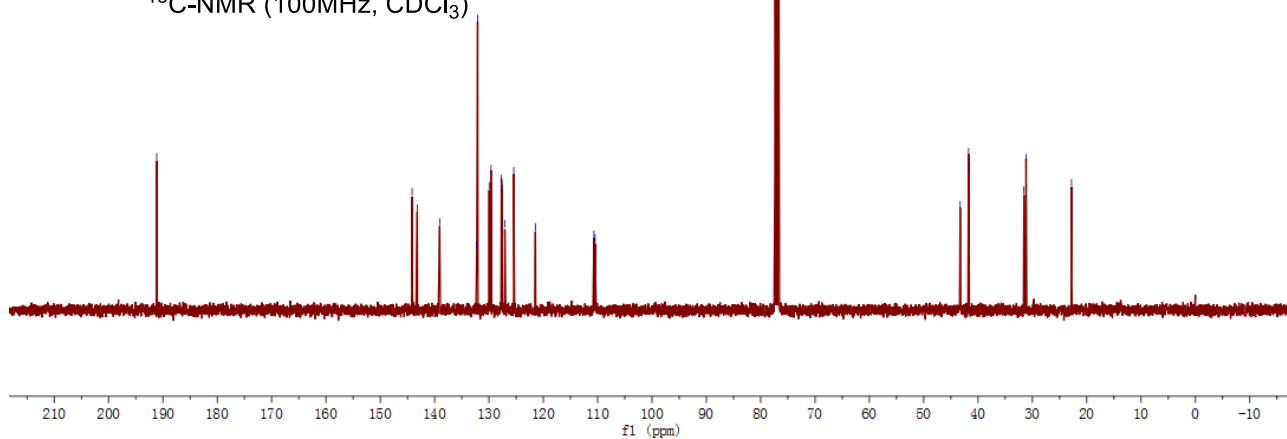
43.293
41.748

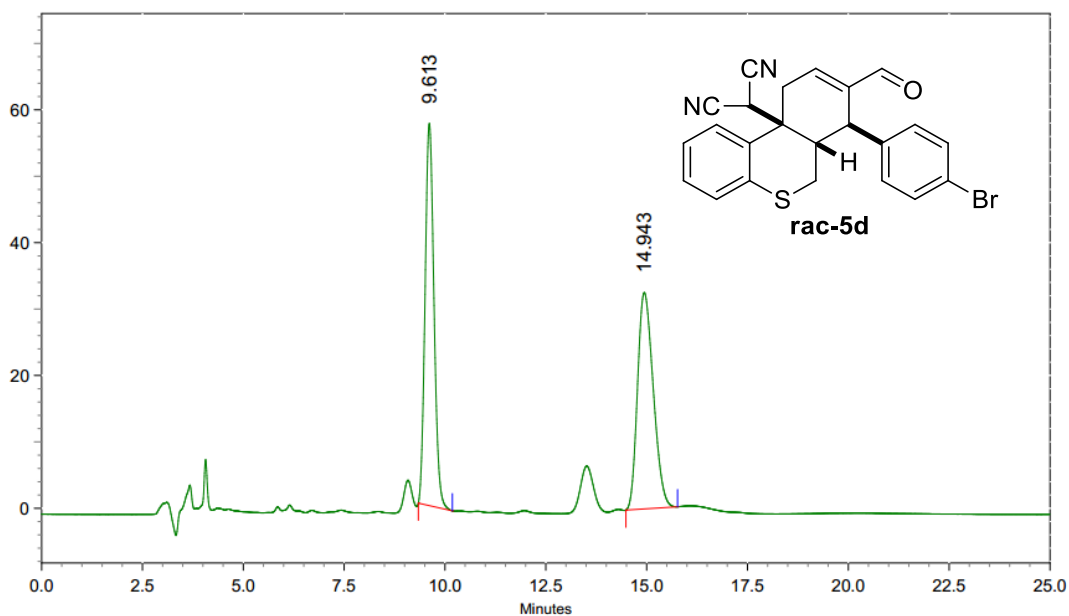
31.569
31.168

22.813



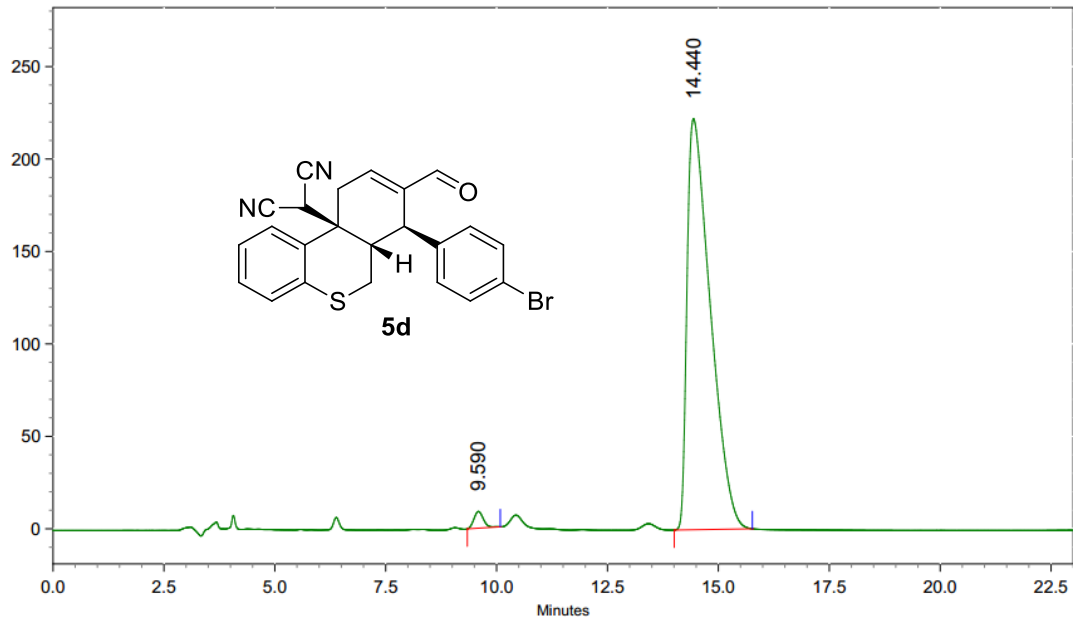
¹³C-NMR (100MHz, CDCl₃)





AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.613	0.843	965619	14726867	49.8767
2	14.943	1.280	546357	14799707	50.1233

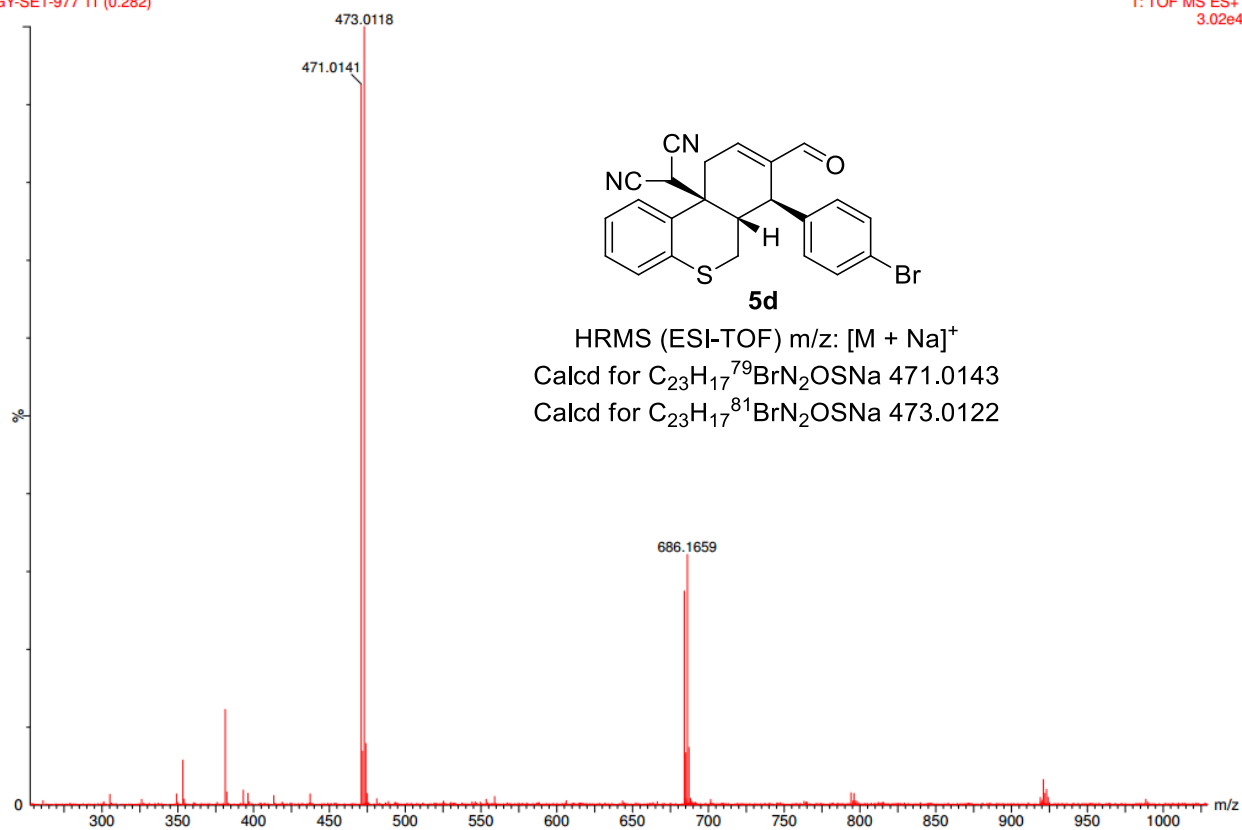


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.590	0.743	151395	2243914	1.6256
2	14.440	1.760	3728994	135795686	98.3744

GY-SE1-977 11 (0.282)

1: TOF MS ES+
3.02e4



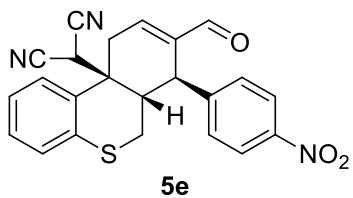
— 9.224

8.207
8.186
7.396
7.376
7.356
7.297
7.279
7.179
7.172
7.157
7.152
7.143
7.100
7.084

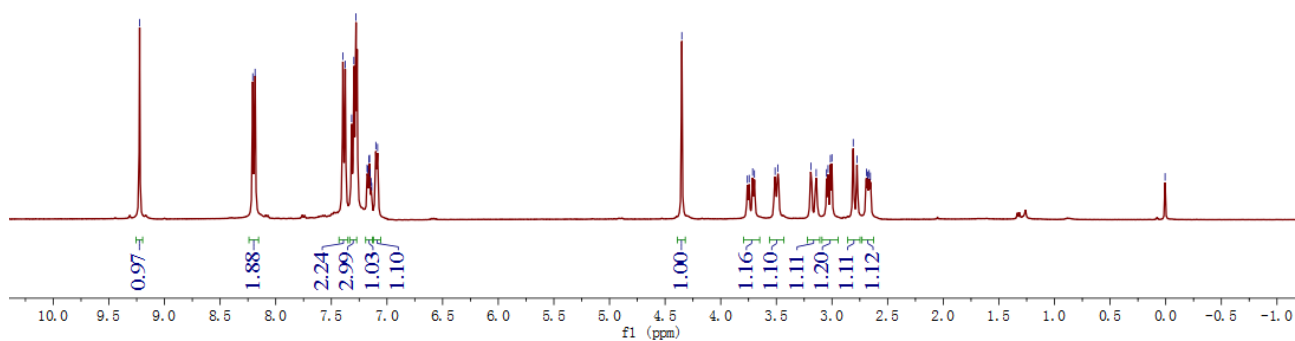
— 4.350

3.761
3.745
3.637
3.512
3.486
3.100
3.040
3.035
3.014
3.001
3.000
2.775
2.691
2.678
2.656
2.635

— 0.006



¹H-NMR (400MHz, CDCl₃)

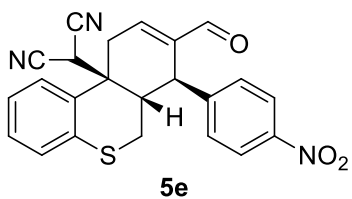


— 191.043

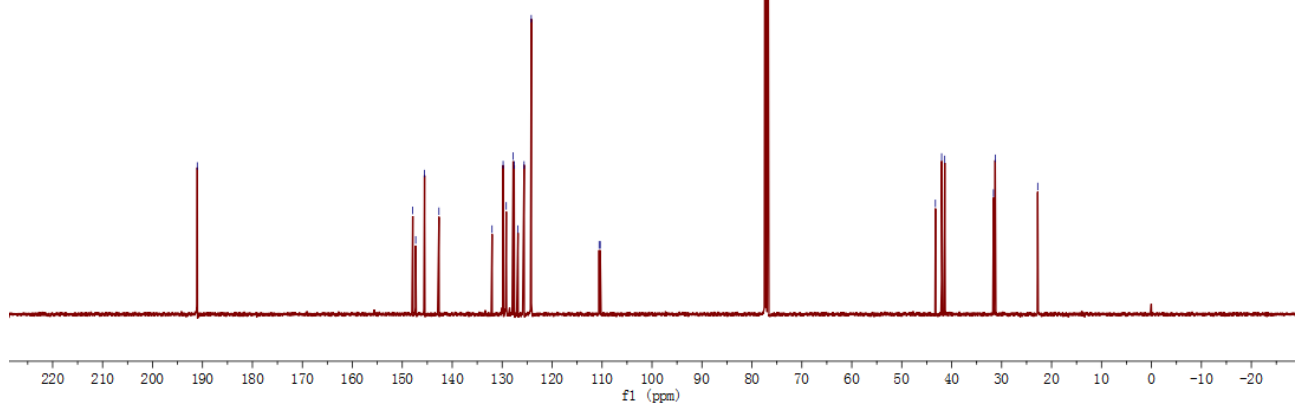
147.902
147.305
146.653
132.021
130.699
129.894
127.786
127.598
126.836
124.171

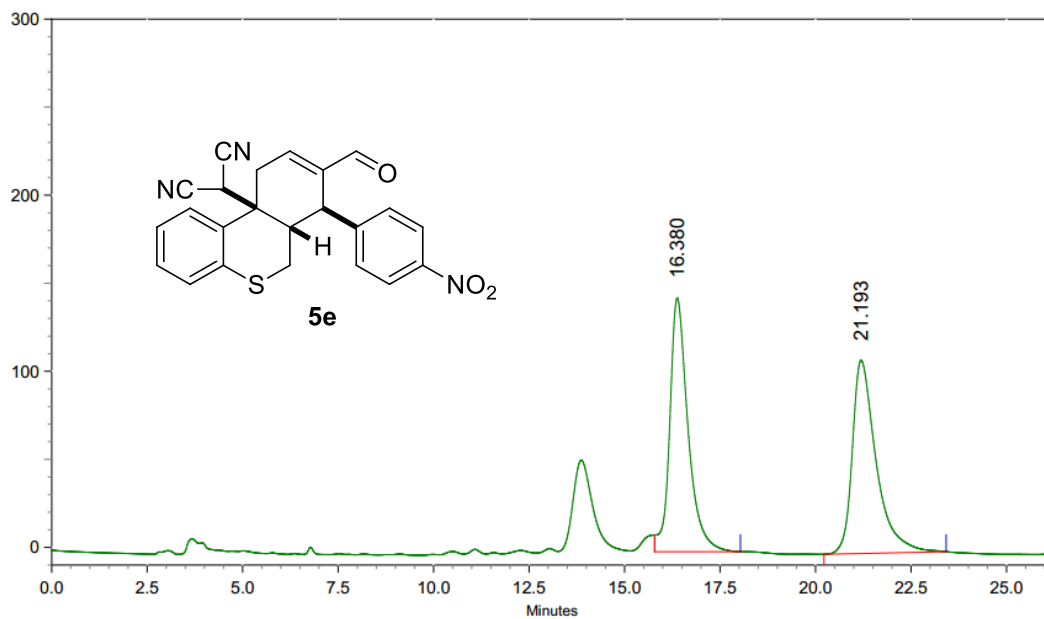
— 110.584
— 110.384

43.256
41.387
31.629
31.281
22.772



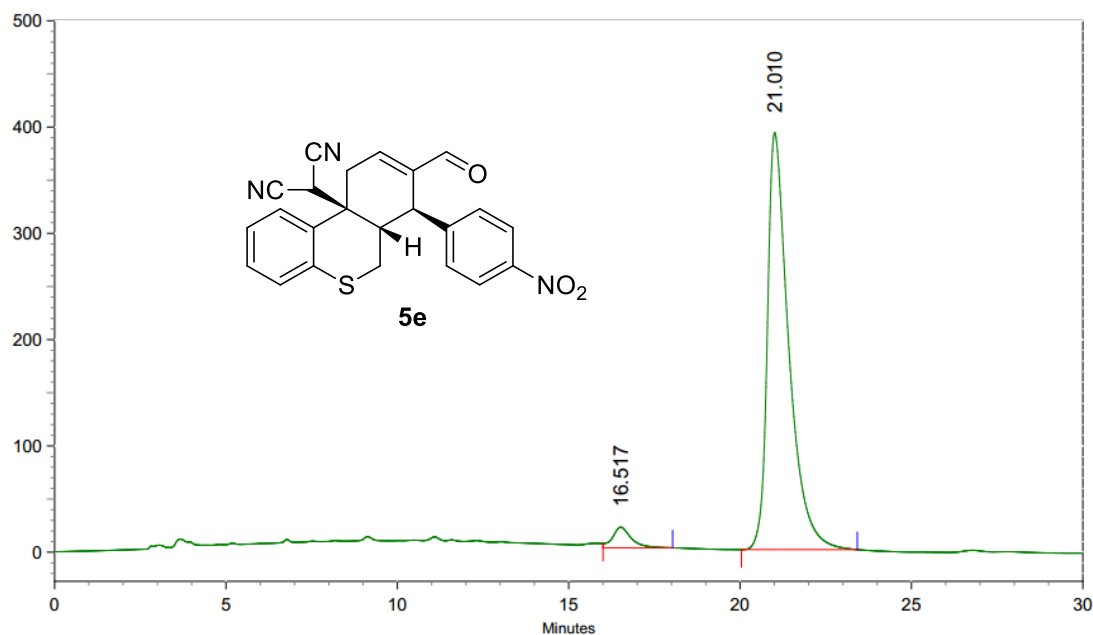
¹³C-NMR (100MHz, CDCl₃)





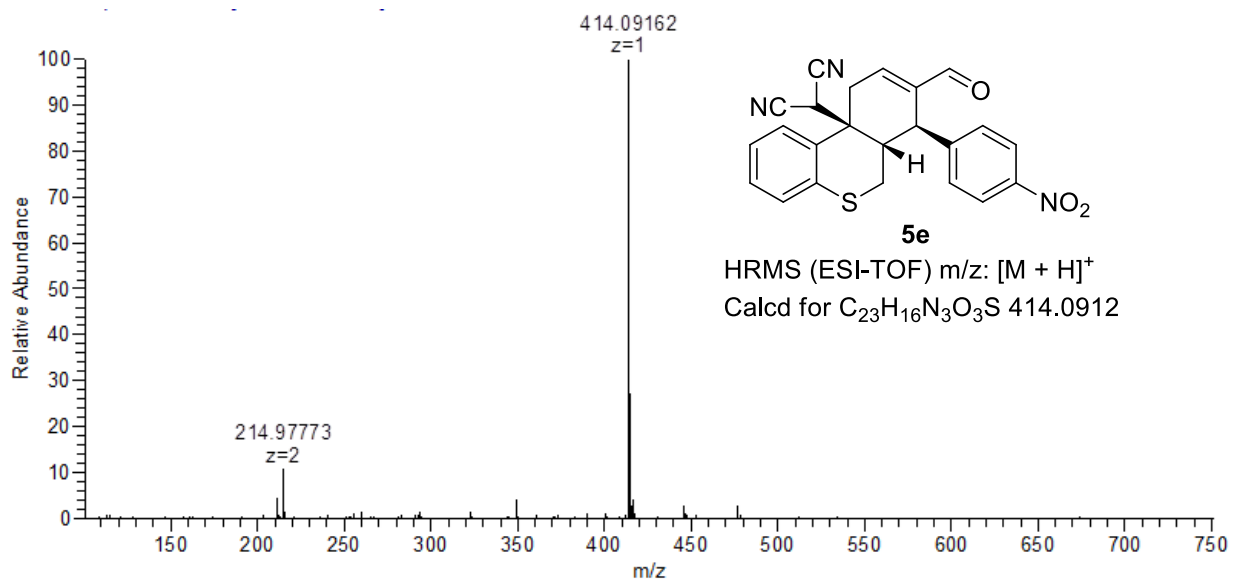
AREA PERCENT REPORT

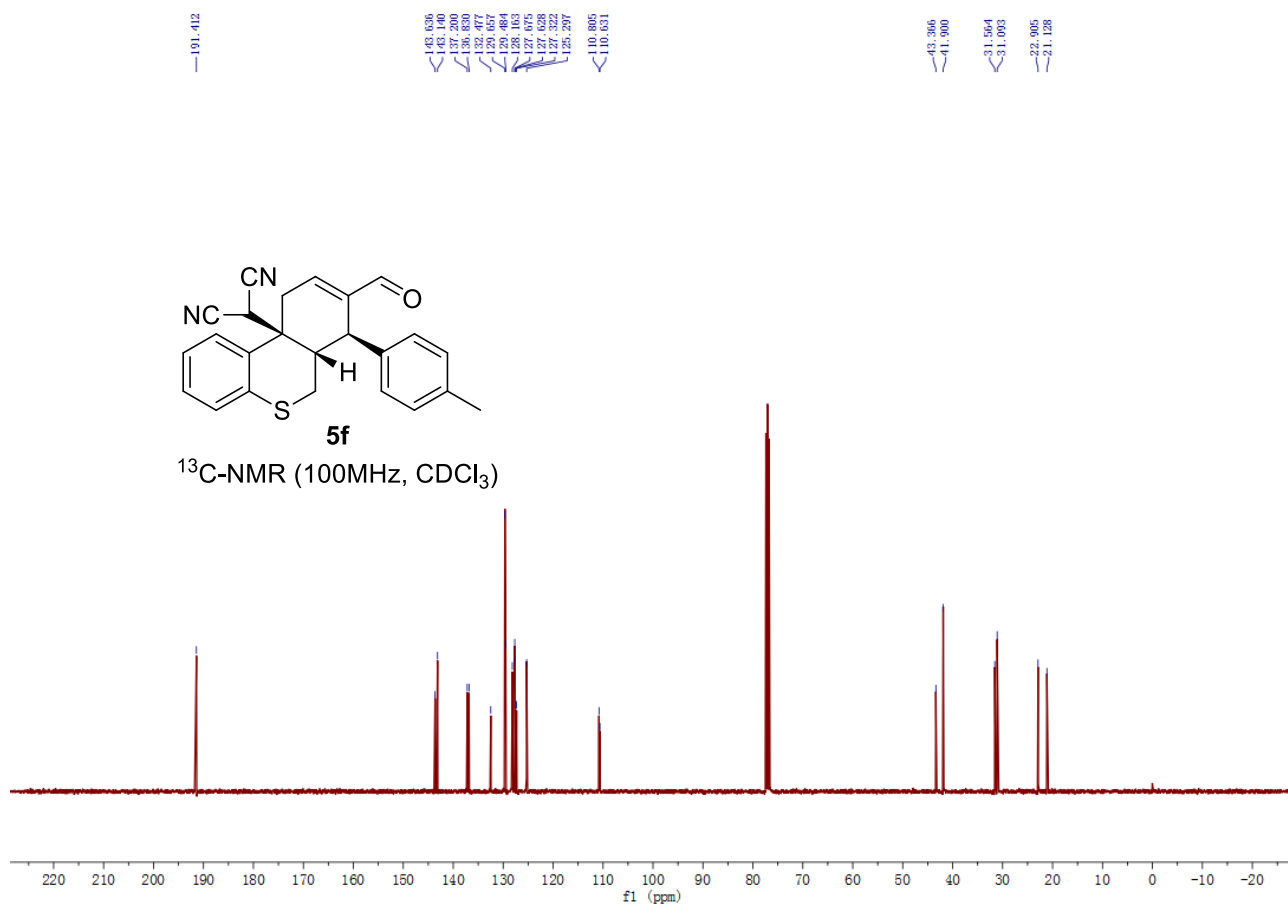
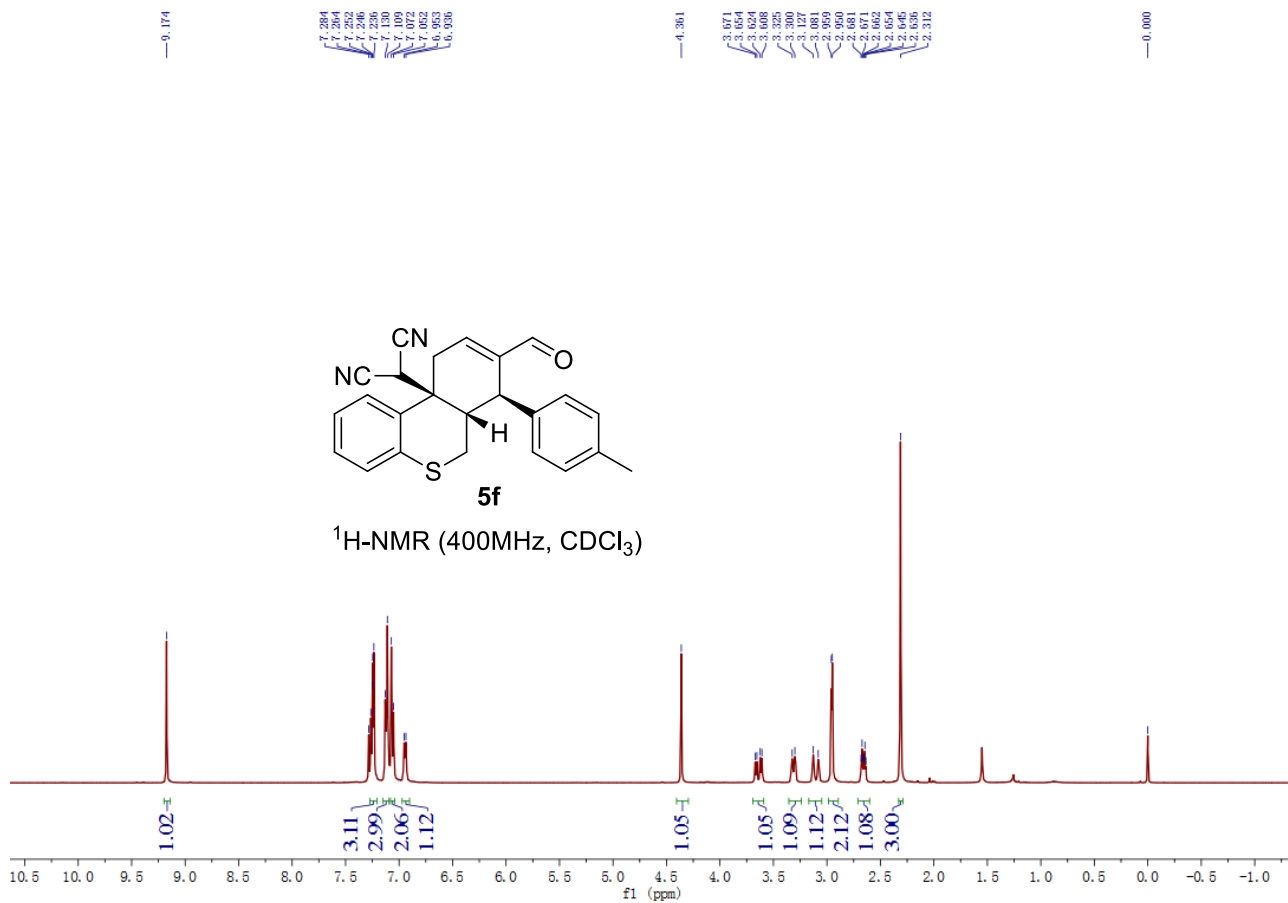
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	16.380	2.247	2418504	80615197	50.1971
2	21.193	3.200	1840778	79982262	49.8029

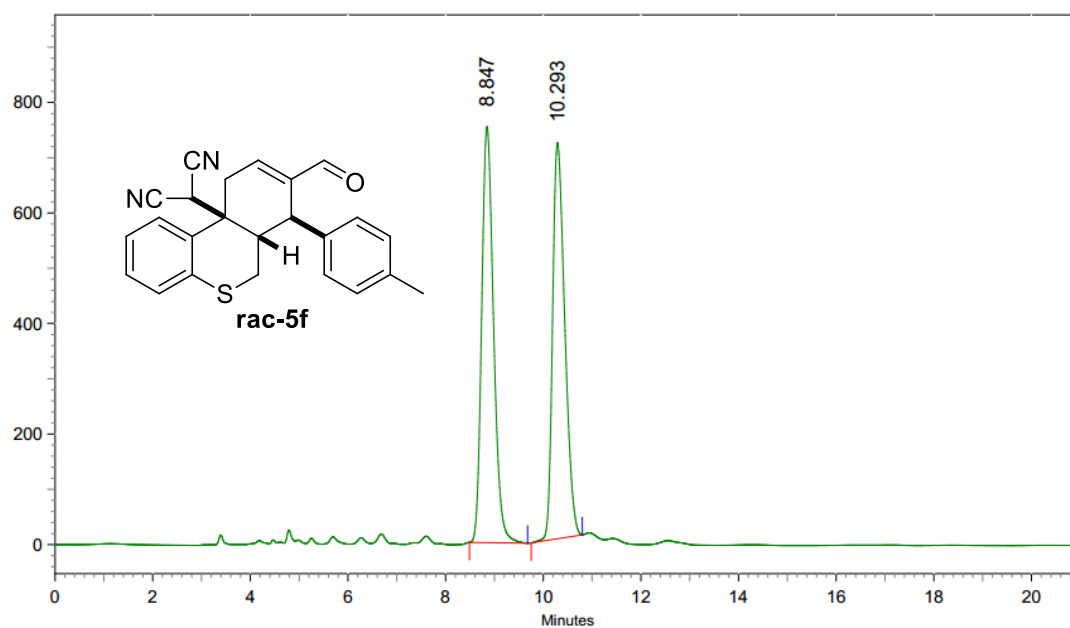


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	16.517	2.033	325781	12414739	4.1728
2	21.010	3.380	6579863	285098273	95.8272

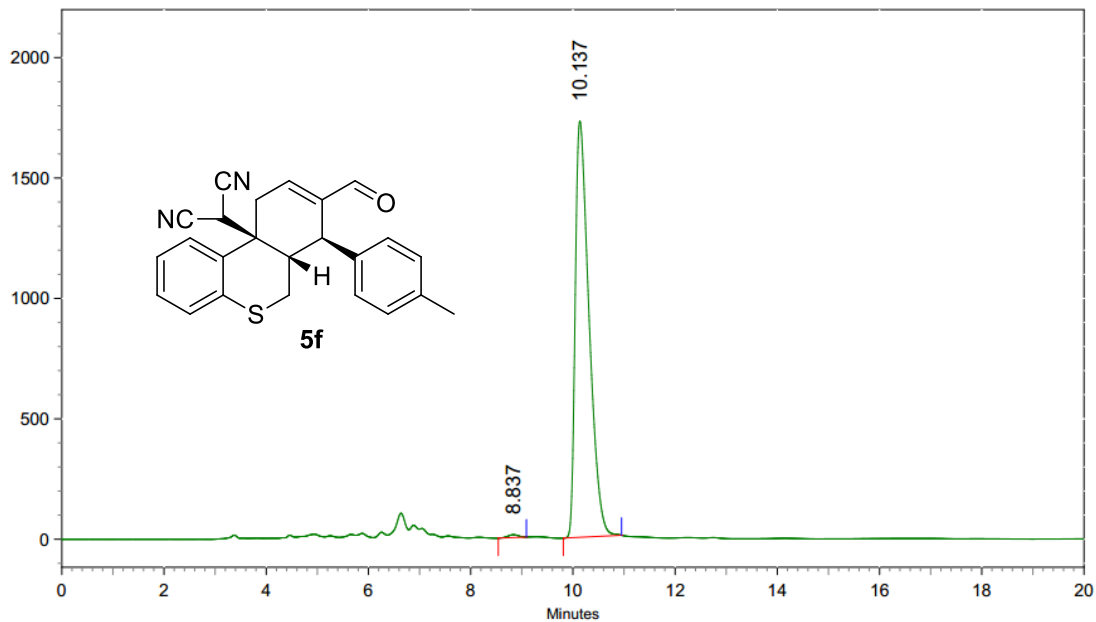






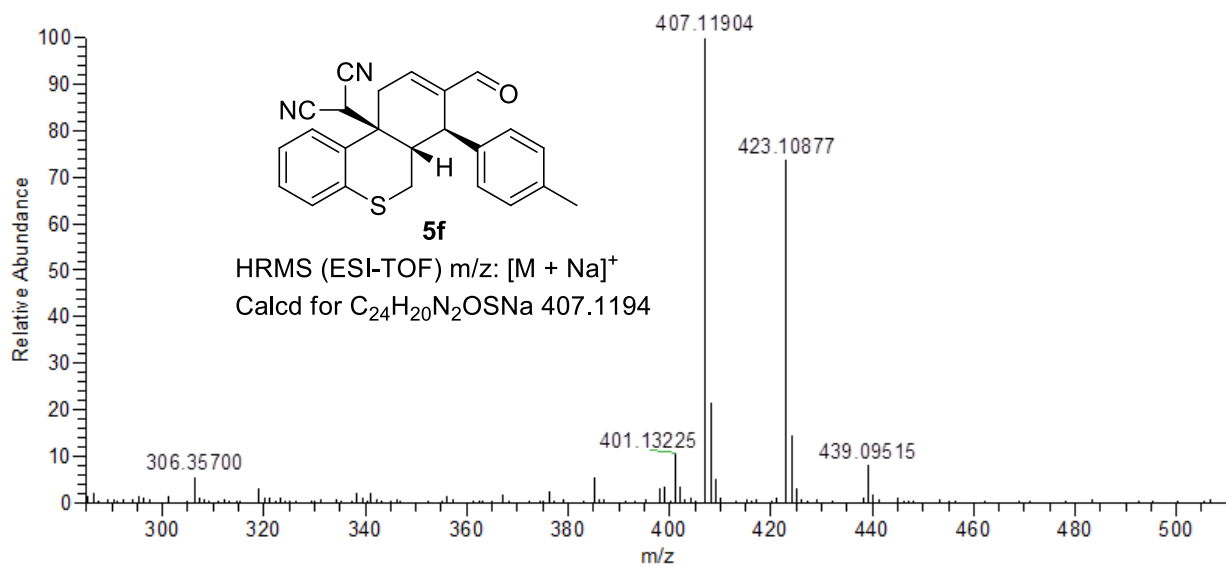
AREA PERCENT REPORT

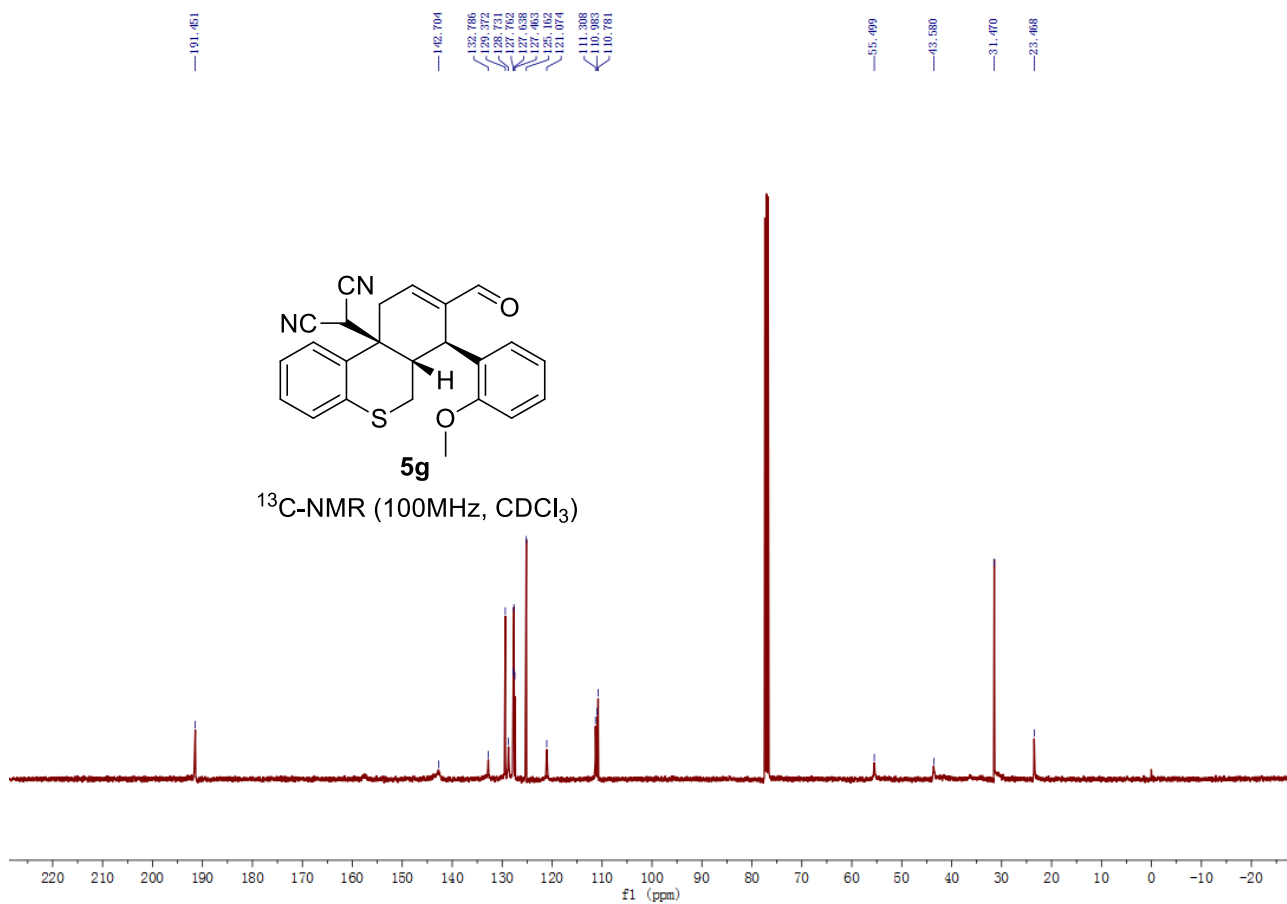
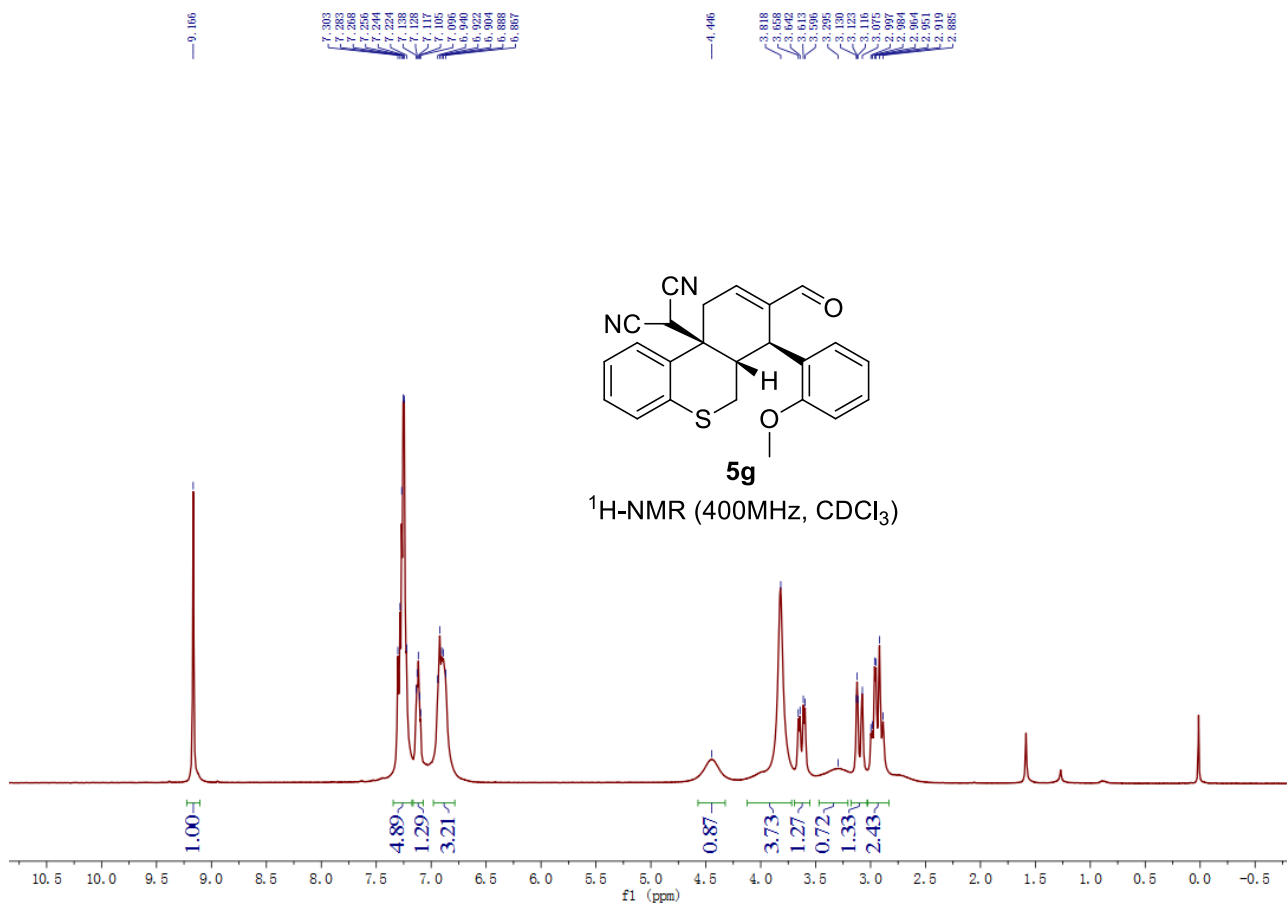
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.847	1.193	12627300	212568655	50.5630
2	10.293	1.047	12027011	207835062	49.4370

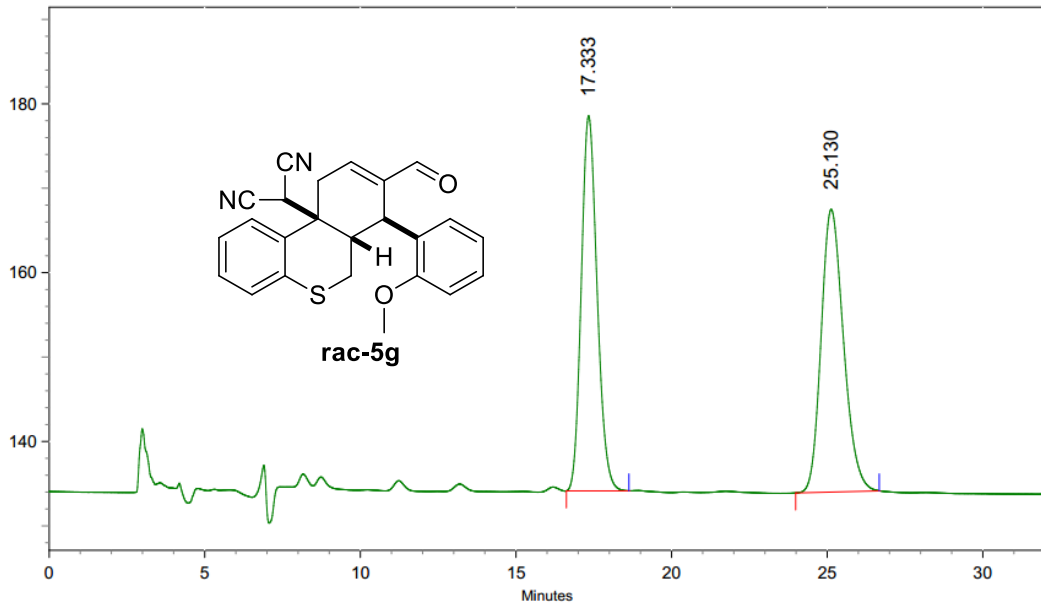


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	8.837	0.550	193193	2738285	0.5017
2	10.137	1.140	28996731	543057023	99.4983

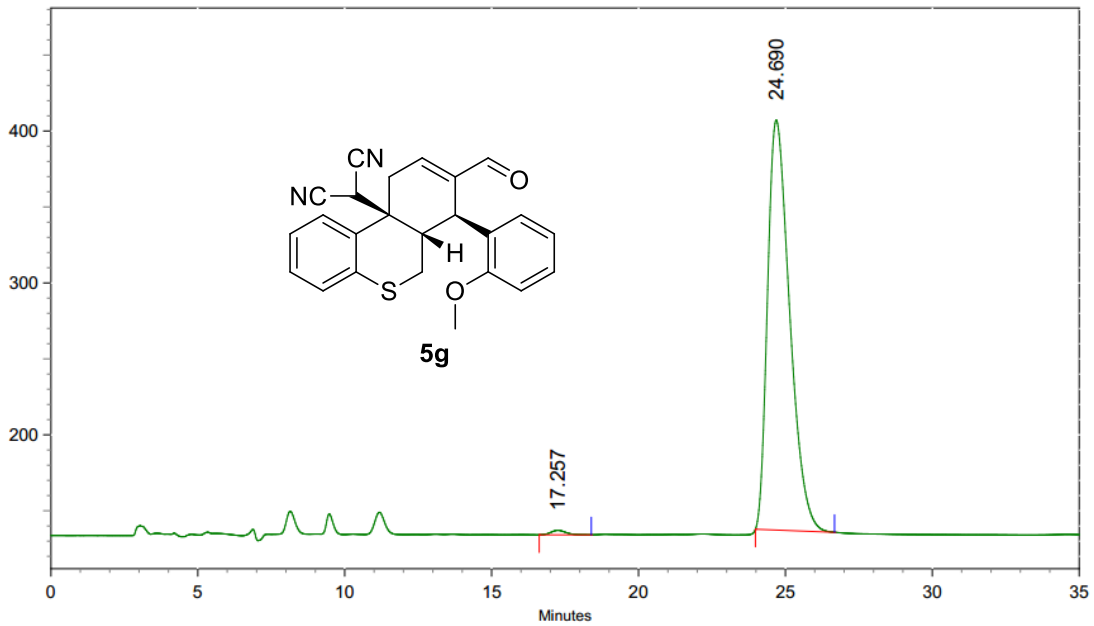






AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	17.333	2.010	745531	26338573	48.3732
2	25.130	2.687	561890	28110145	51.6268

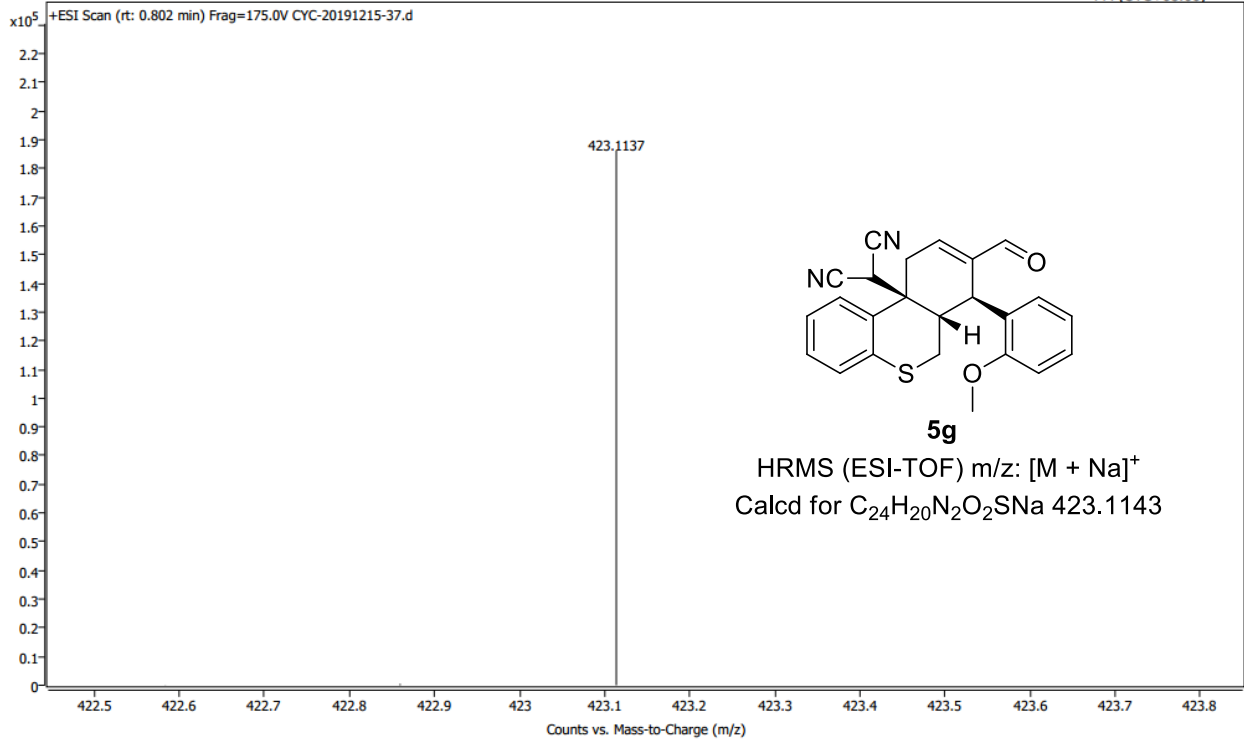


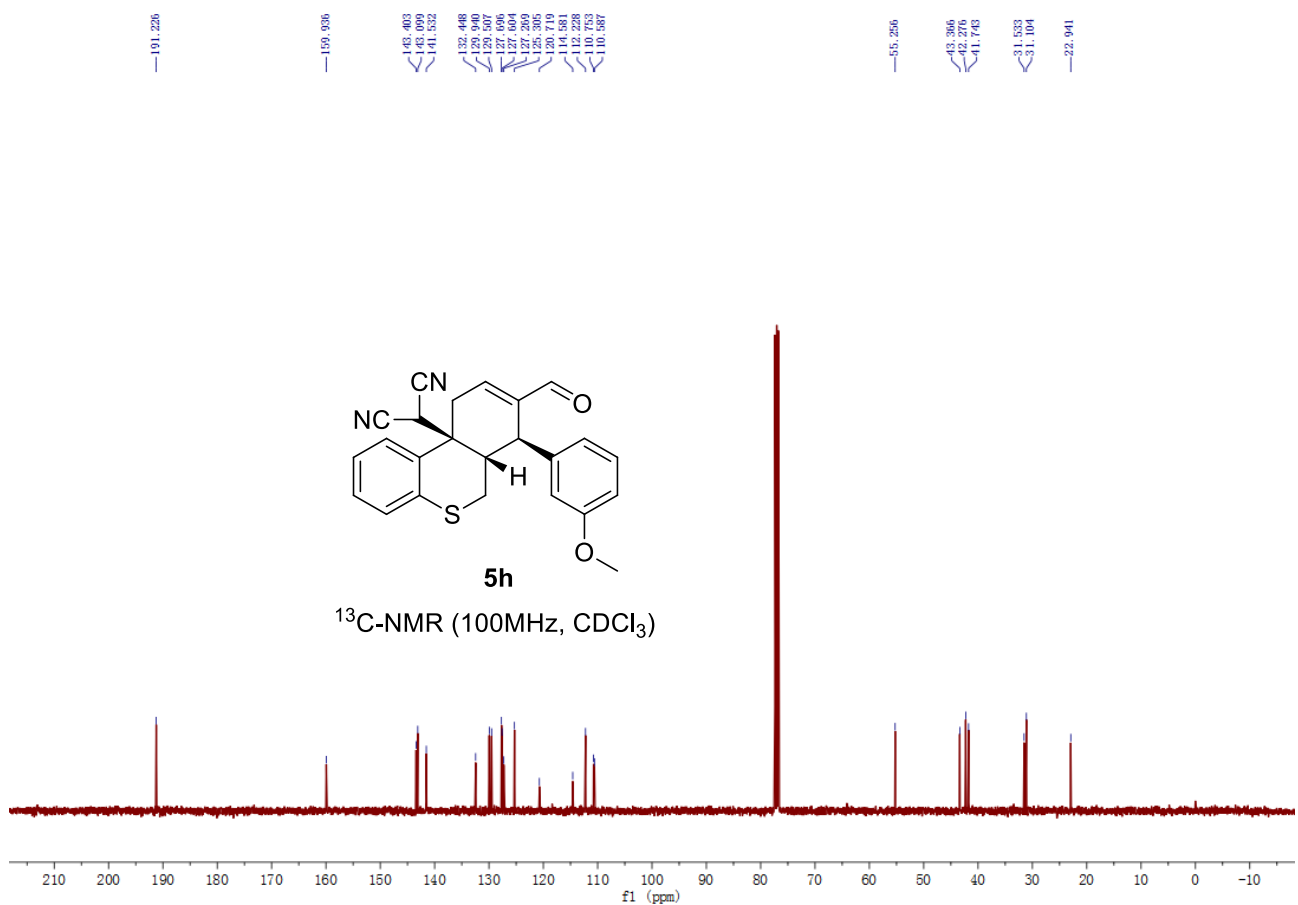
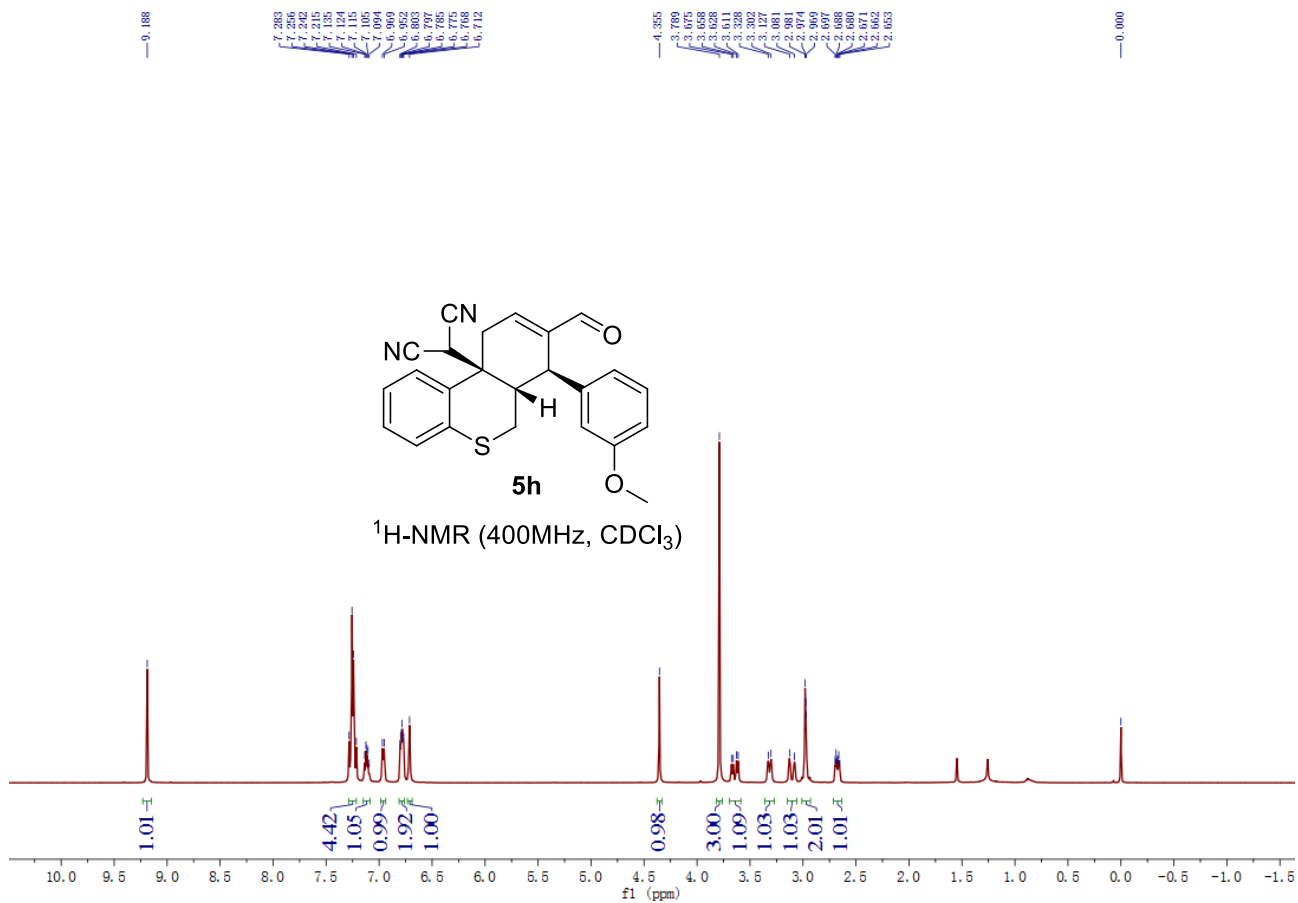
AREA PERCENT REPORT

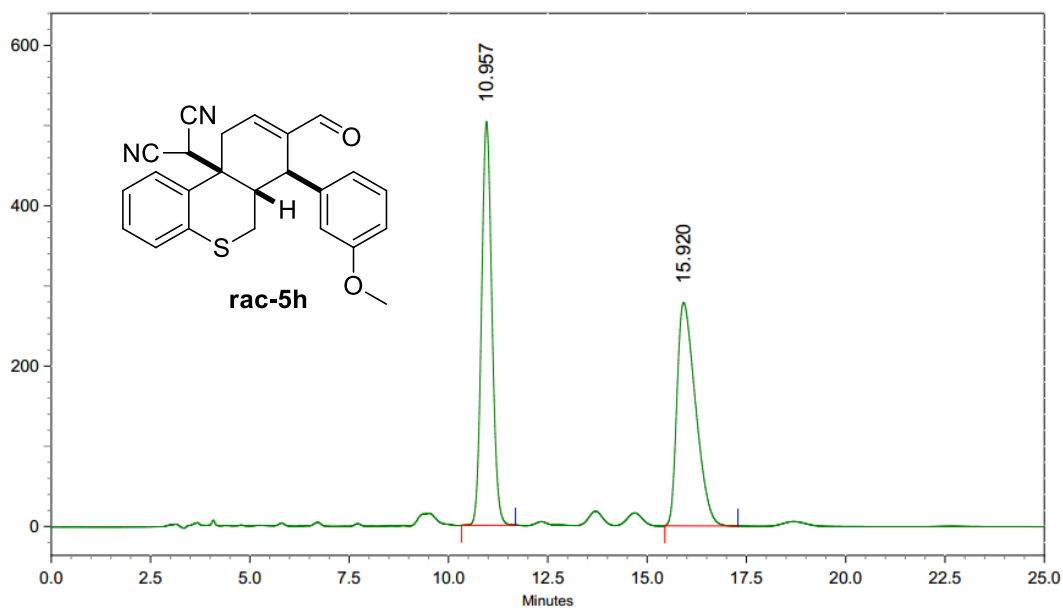
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	17.257	1.773	50013	1763779	0.7402
2	24.690	2.693	4528479	236509529	99.2598

Spectrum Plot Report

Name	CYC-20191215-37	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	10	Plate Pos.		IRM Status	Success	Acq. Time (Local)	12/20/2019 3:53:20 PM (UTC+08:00)
Data File	CYC-20191215-37.d	Method (Acq)	TOF.m	Comment			

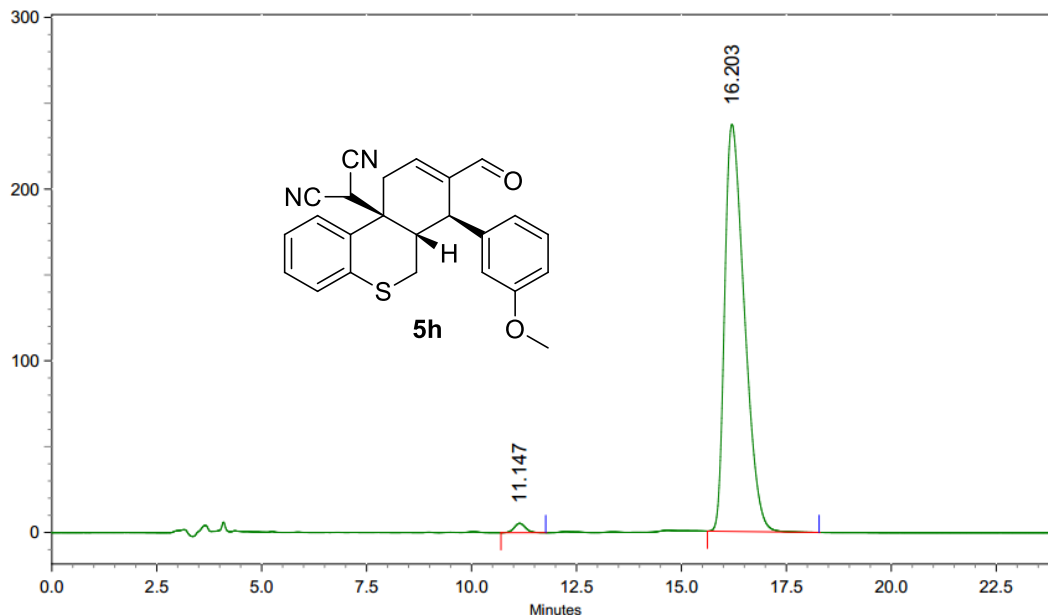






AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	10.957	1.360	8444780	153227894	50.2324
2	15.920	1.840	4674183	151810219	49.7676

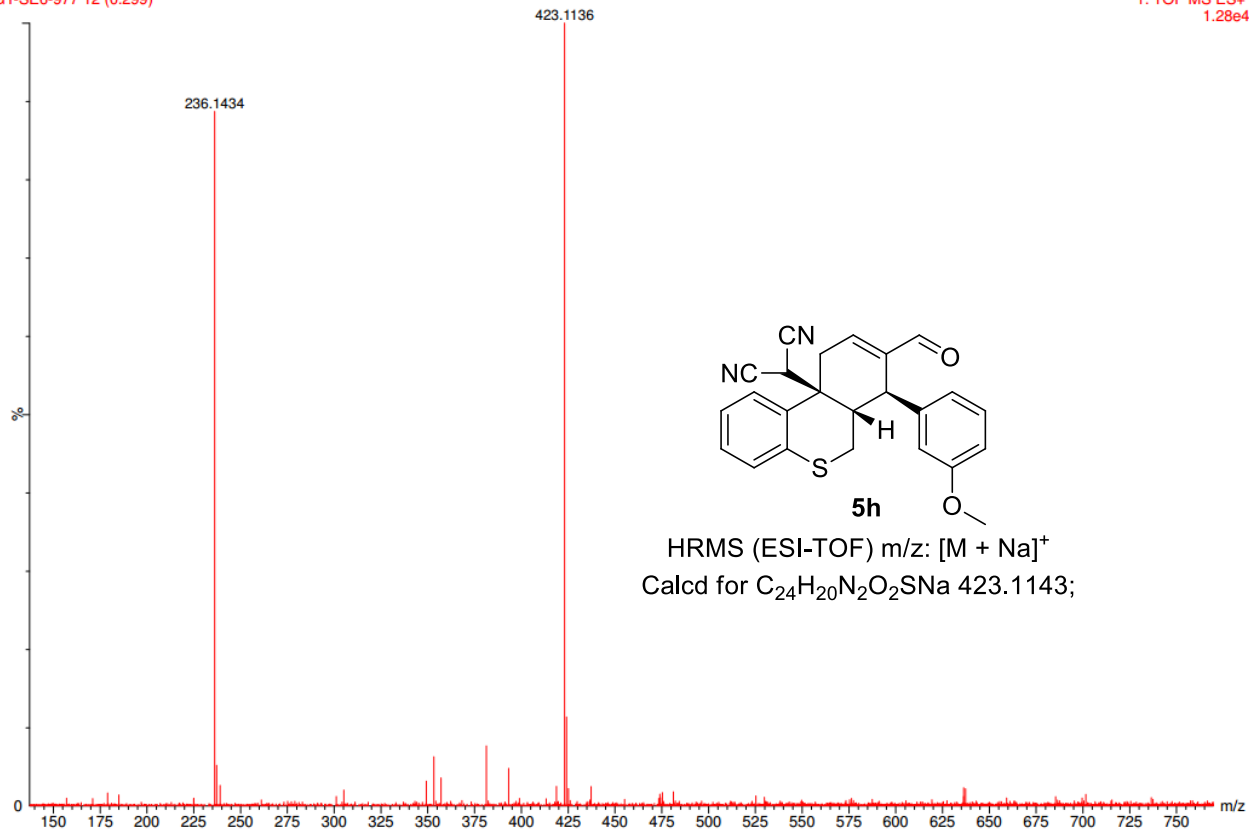


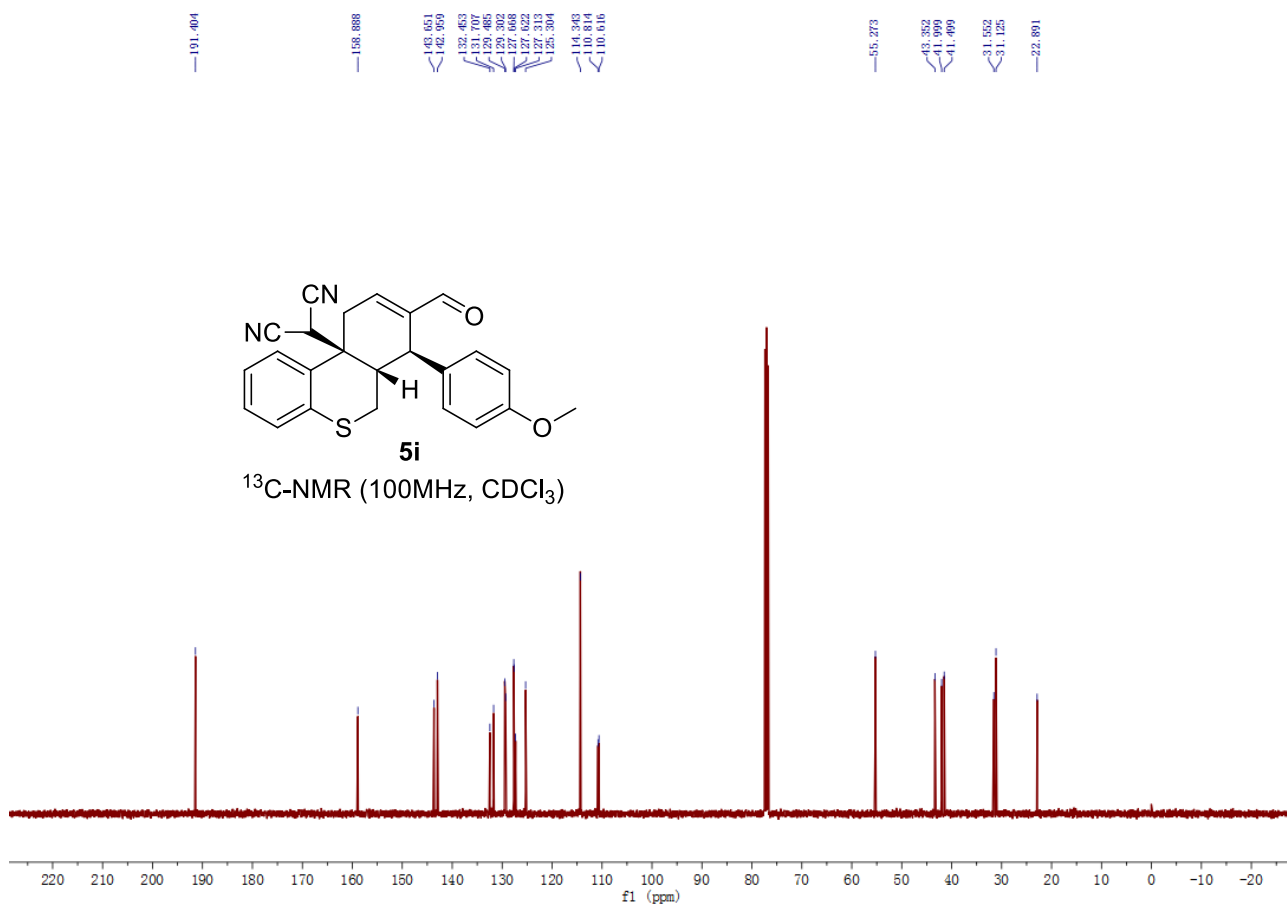
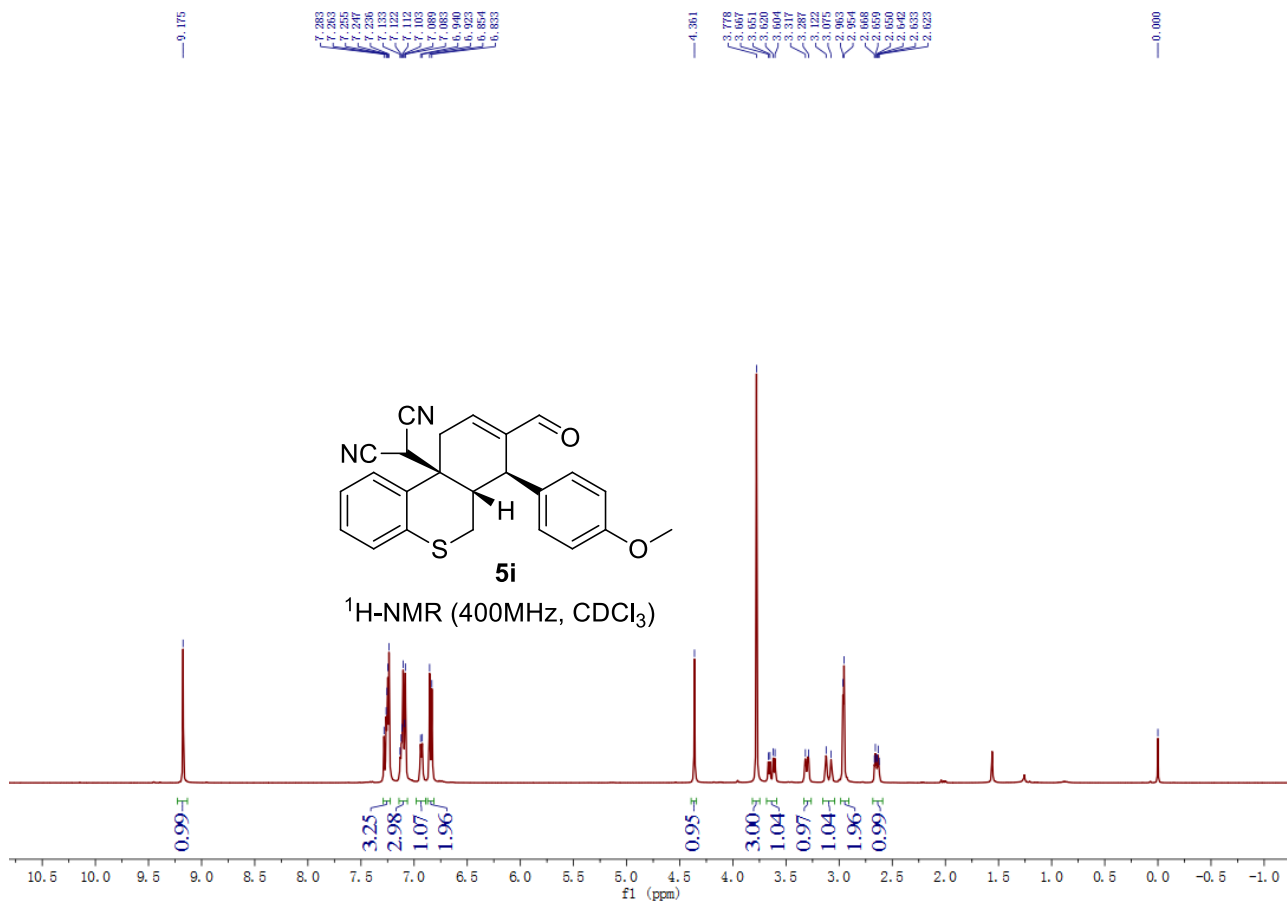
AREA PERCENT REPORT

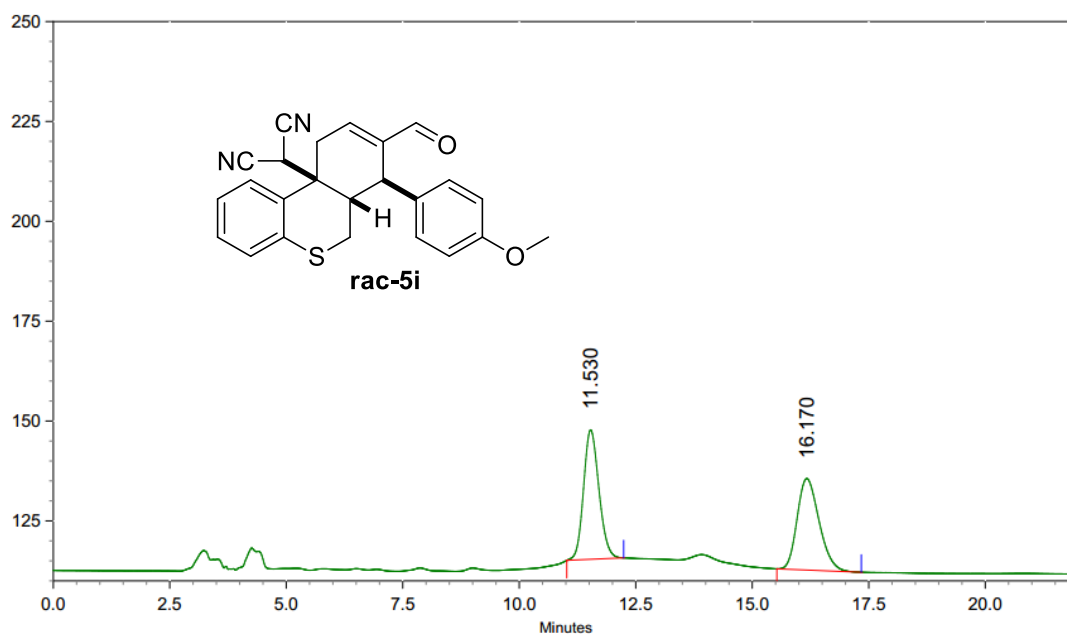
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	11.147	1.067	90838	1691916	1.2888
2	16.203	2.660	3977075	129587048	98.7112

GY-SE6-977 12 (0.299)

1: TOF MS ES+
1.28e4

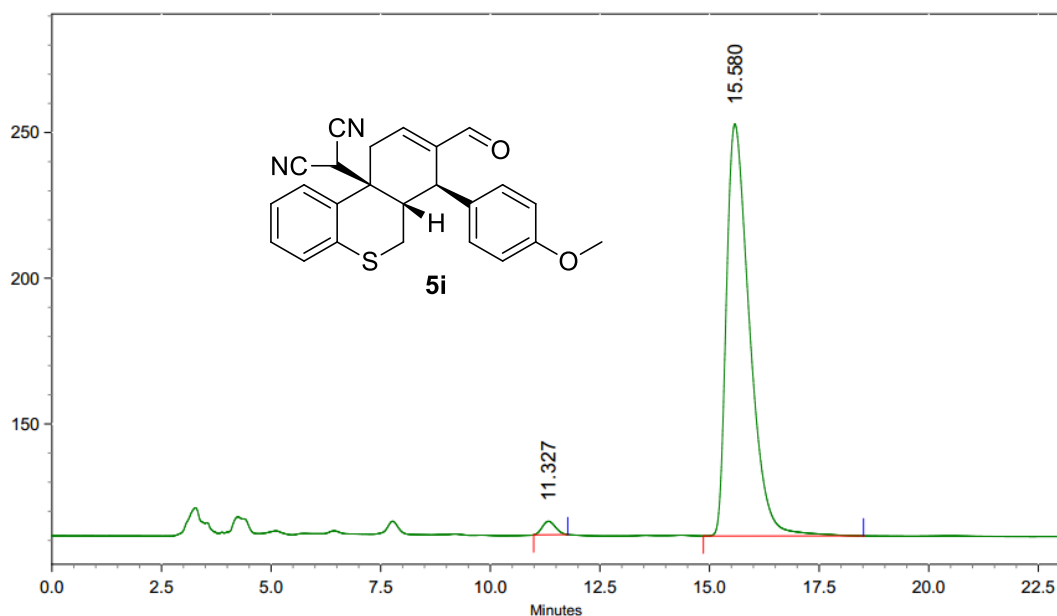






AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	11.530	1.220	543649	12495122	49.8220
2	16.170	1.813	384107	12584423	50.1780

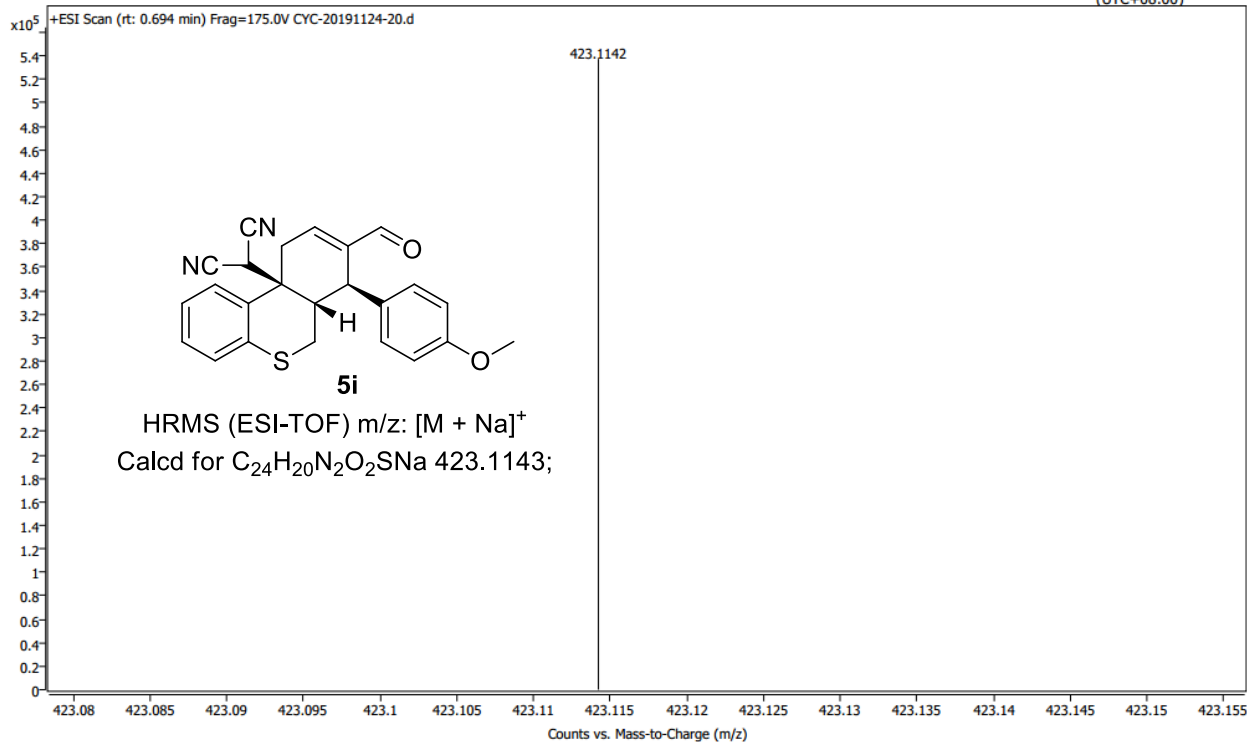


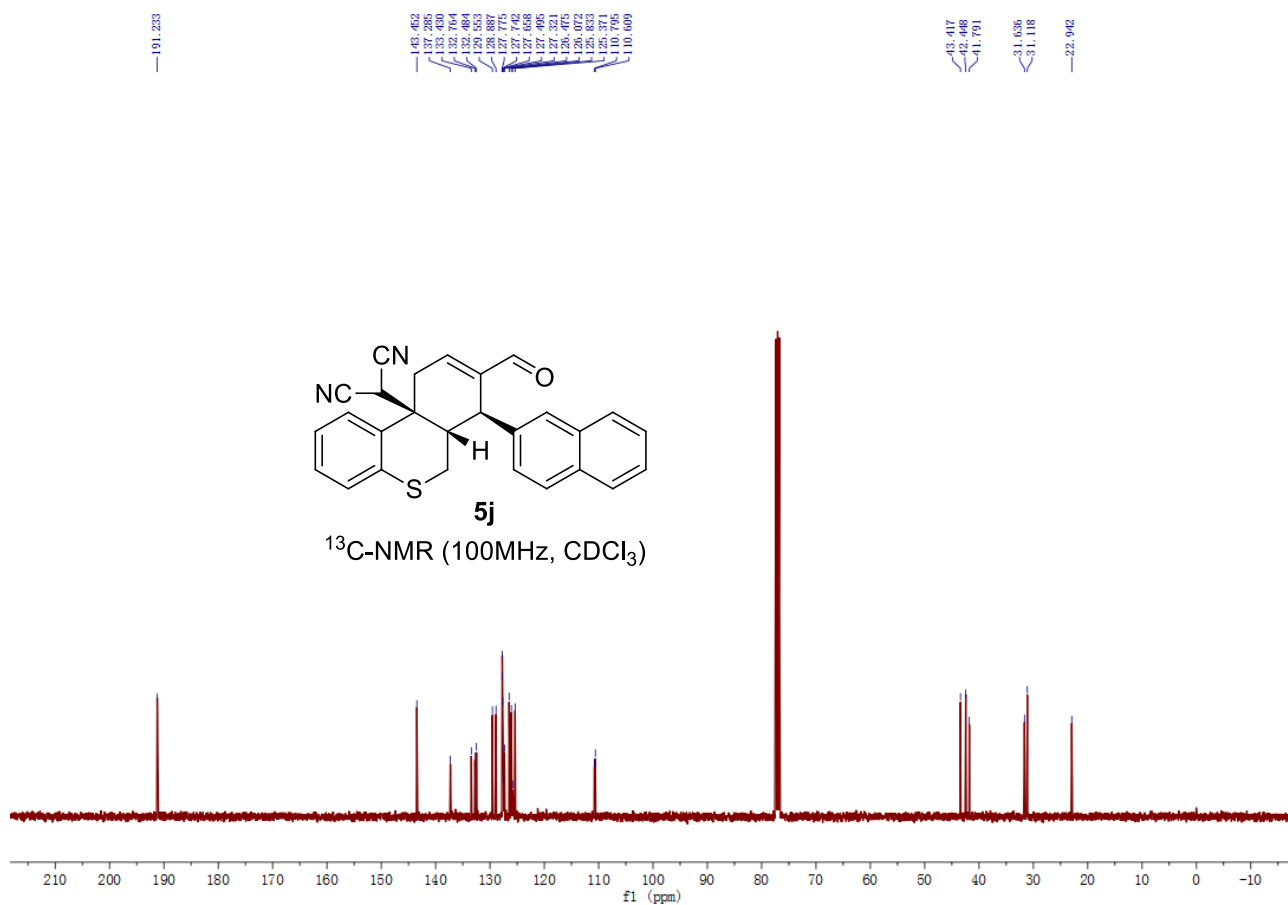
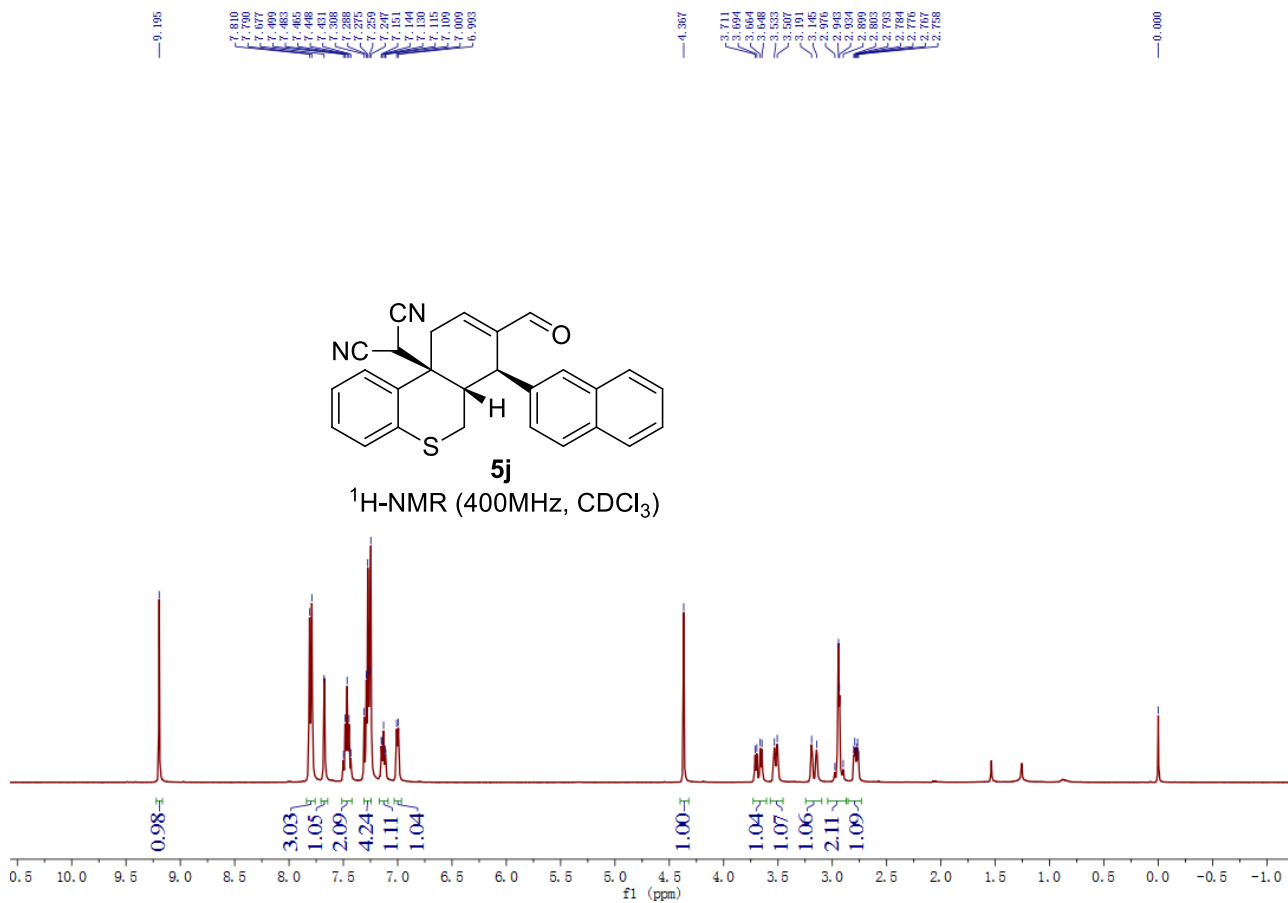
AREA PERCENT REPORT

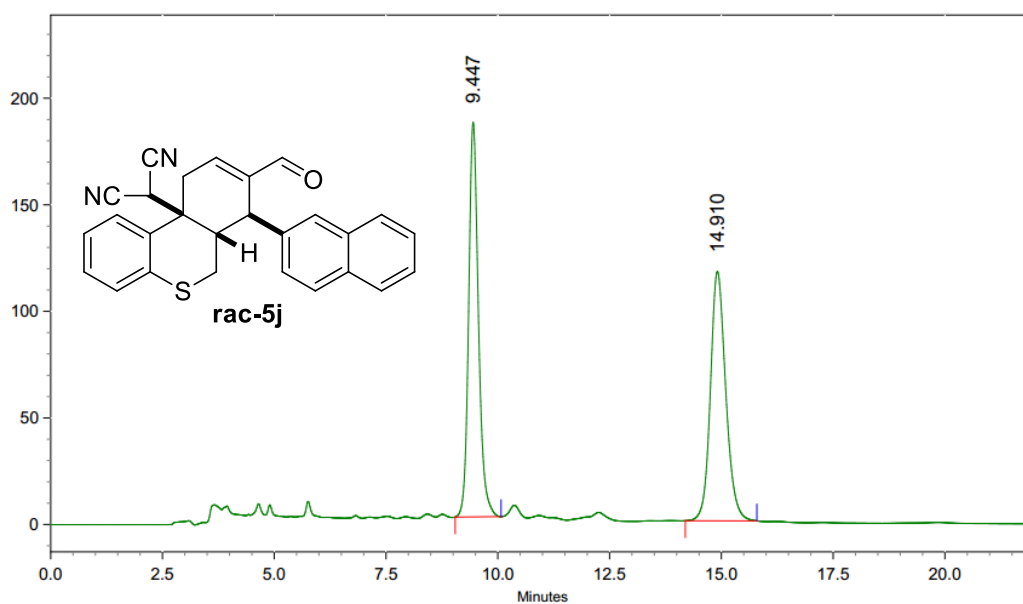
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	11.327	0.777	77795	1628720	1.8429
2	15.580	3.653	2372209	86749209	98.1571

Spectrum Plot Report

Name	CYC-20191124-20	Rack Pos.		Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.		IRM Status	Success	
Data File	CYC-20191124-20.d	Method (Acq)	TOF.m	Comment		Acq. Time (Local)
						12/5/2019 6:24:56 PM (UTC+08:00)

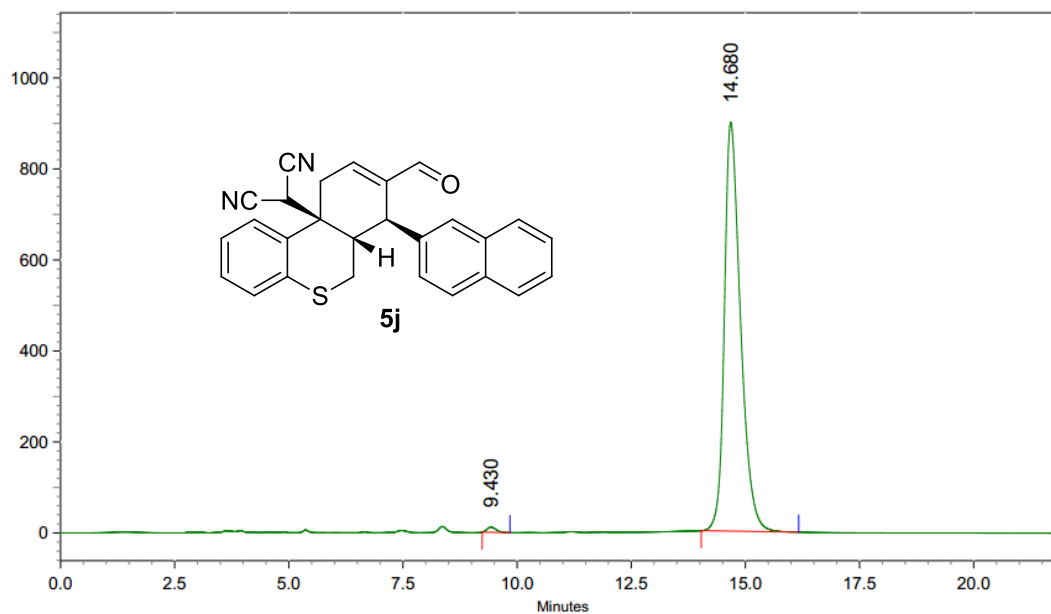






AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.447	1.027	3105805	47249504	50.1853
2	14.910	1.600	1962717	46900547	49.8147

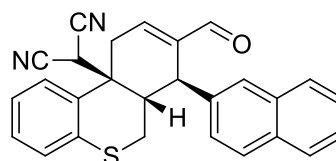
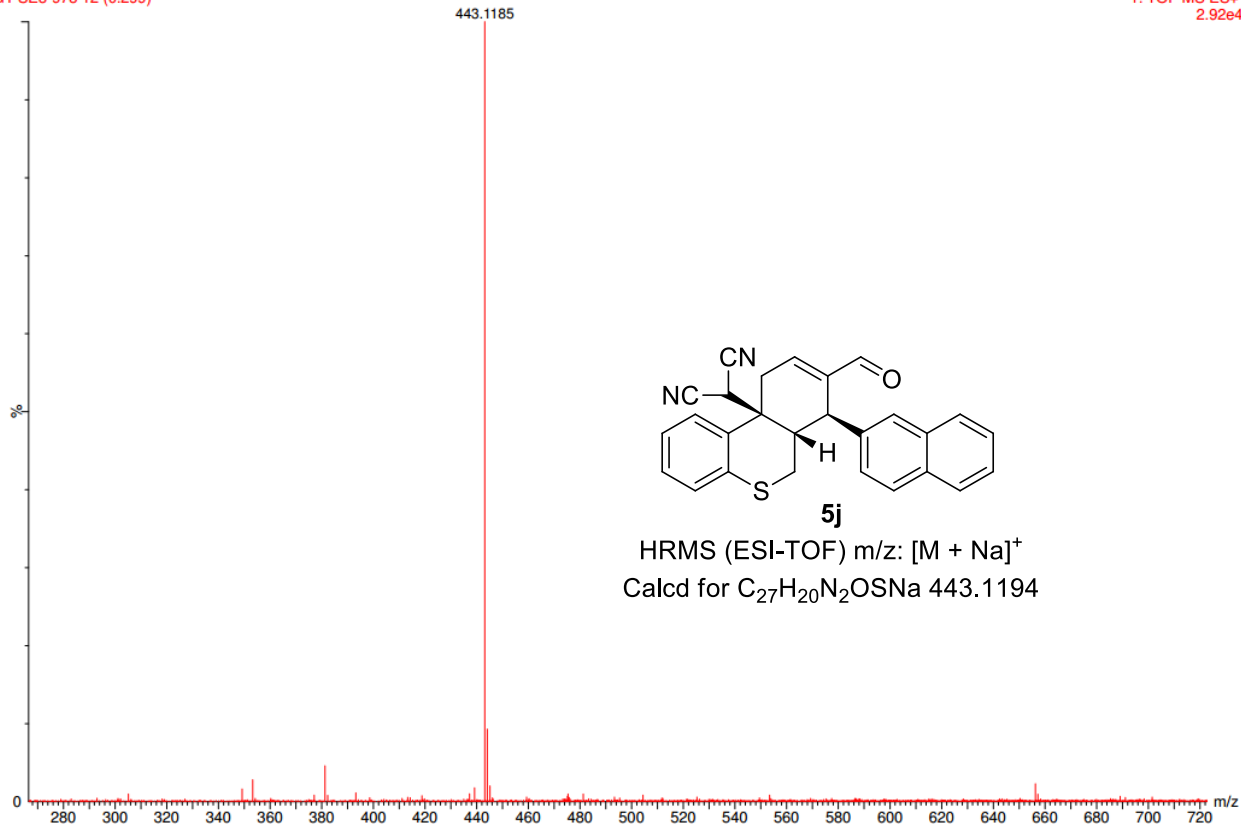


AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.430	0.610	191829	2625011	0.7032
2	14.680	2.133	15072484	370676964	99.2968

GY-SE8-978 12 (0.299)

1: TOF MS ES+
2.92e4



5j

HRMS (ESI-TOF) m/z: [M + Na]⁺
Calcd for C₂₇H₂₀N₂OSNa 443.1194

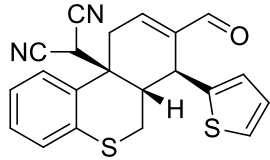
-0.219

7.271
7.257
7.249
7.243
7.201
7.191
7.138
7.130
7.117
7.110
7.104
7.096
6.978
6.957
6.948
6.945
6.921
6.905

-4.384

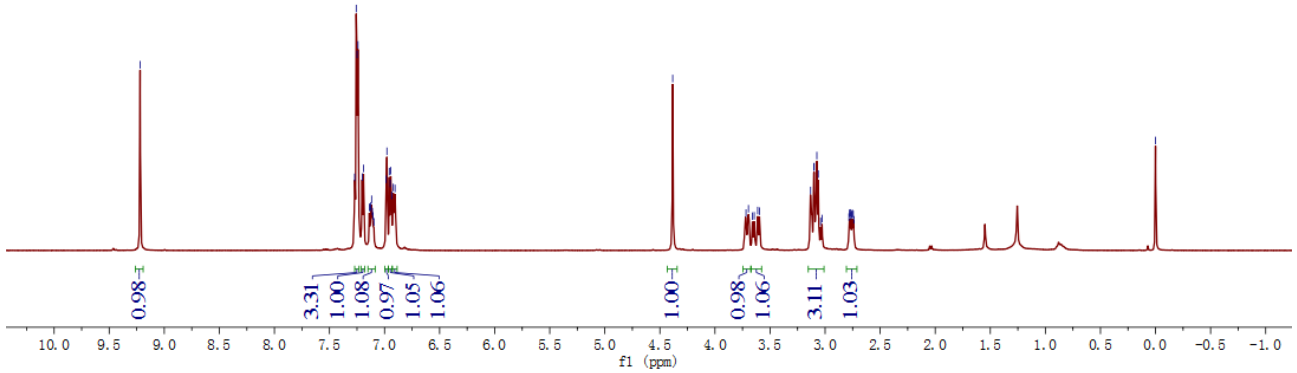
3.718
3.698
3.660
3.643
3.612
3.595
3.102
3.099
3.075
3.052
3.041
2.784
2.779
2.765
2.757
2.752
2.739

-0.000



5k

¹H-NMR (400MHz, CDCl₃)



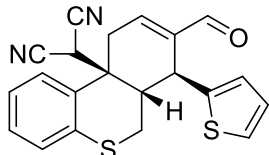
-100.901

142.839
142.499
142.345
142.345
129.016
127.788
127.631
127.095
126.906
125.387
124.859

110.881
110.479

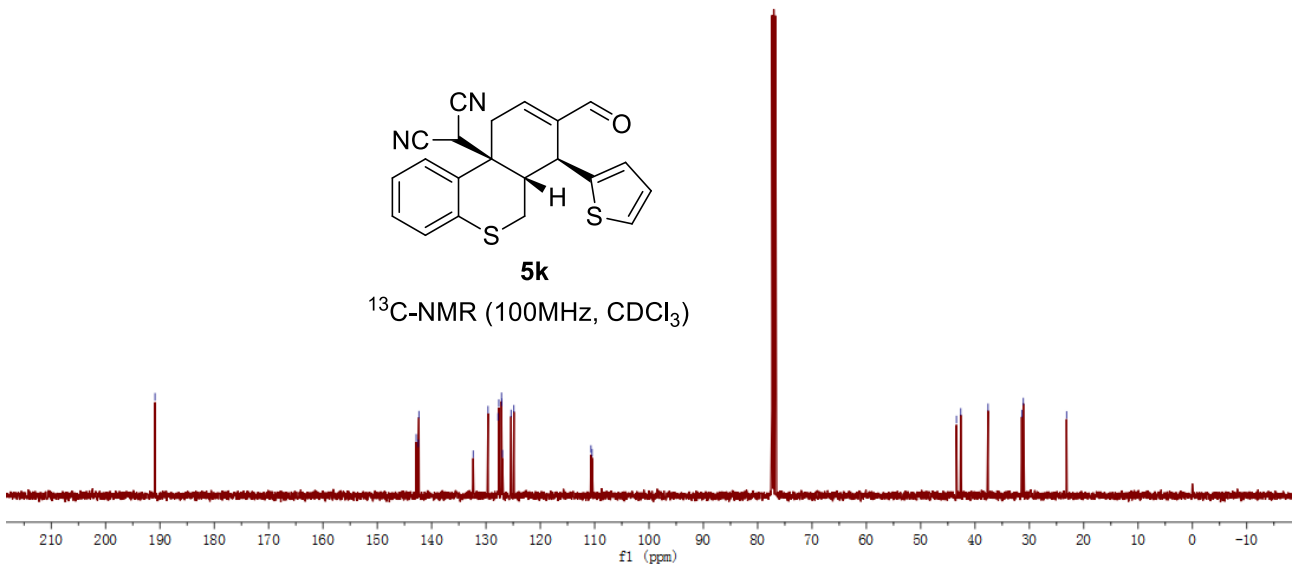
42.451
42.620
37.610
31.413
31.110

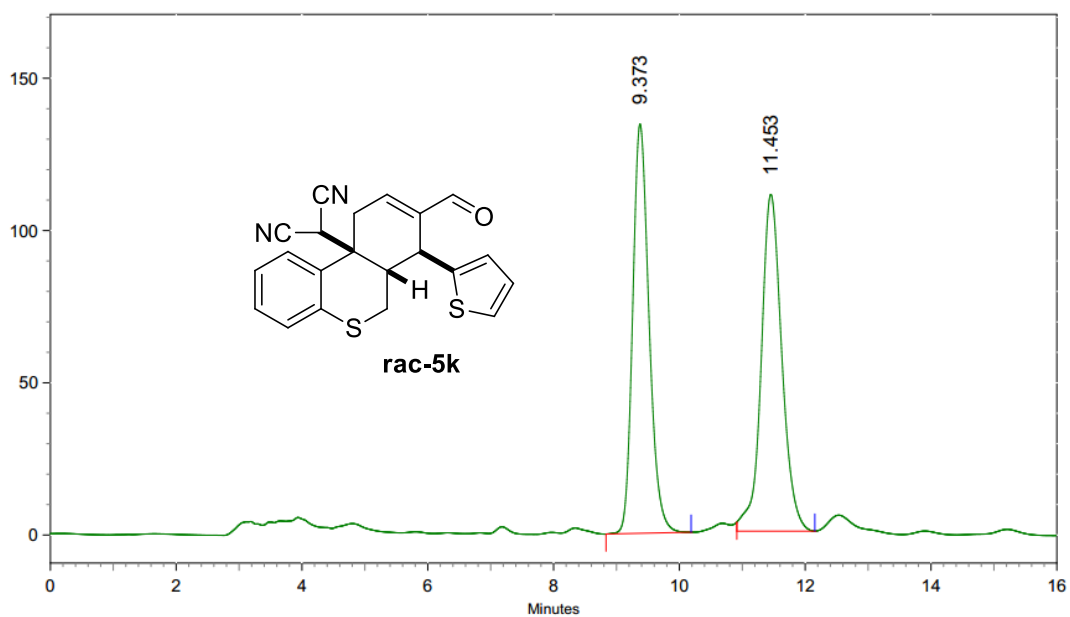
23.106



5k

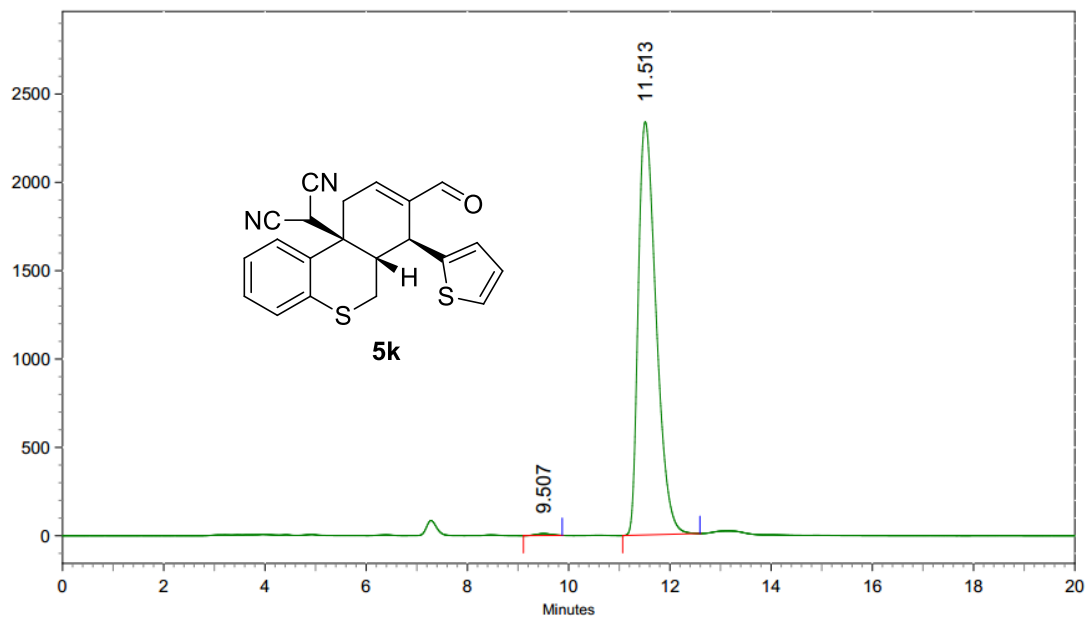
¹³C-NMR (100MHz, CDCl₃)





AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.373	1.353	2254551	40665370	49.0060
2	11.453	1.240	1855338	42315011	50.9940

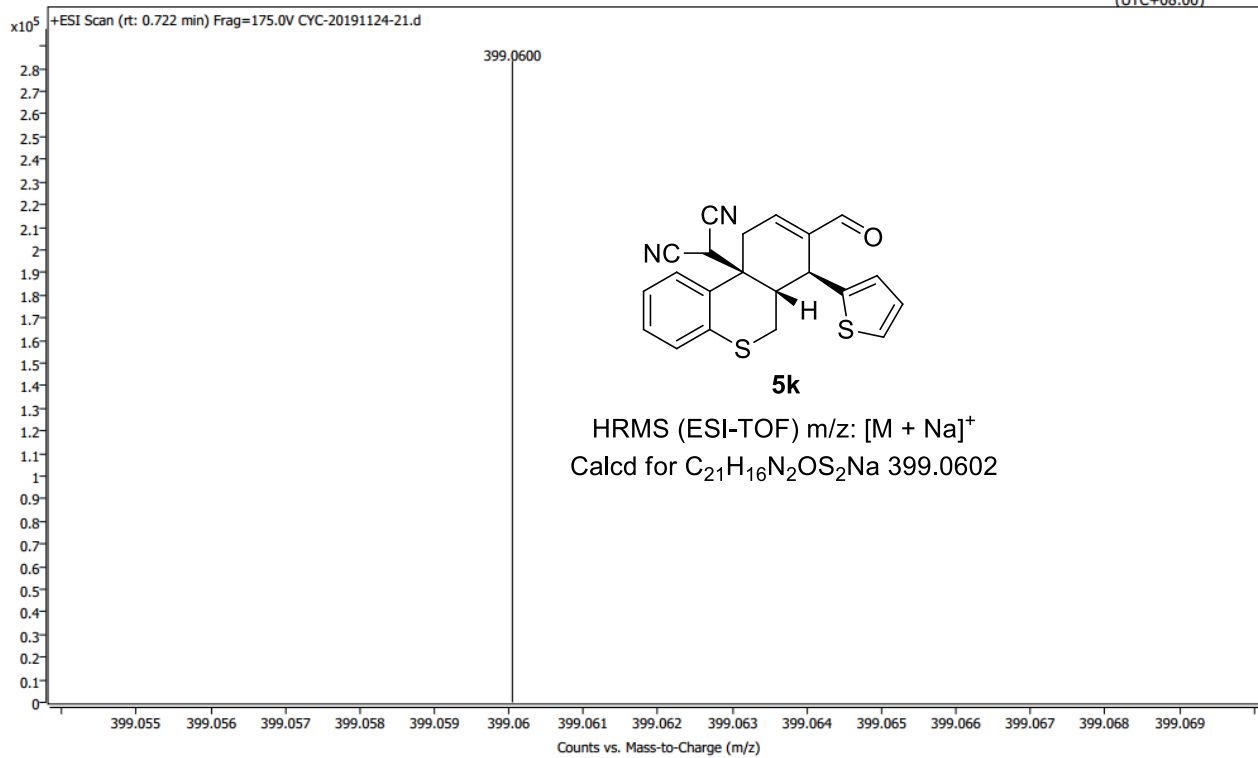


AREA PERCENT REPORT

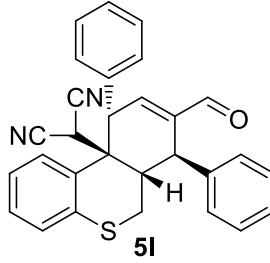
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.507	0.767	180212	3686255	0.3822
2	11.513	1.527	39232253	960719689	99.6178

Spectrum Plot Report

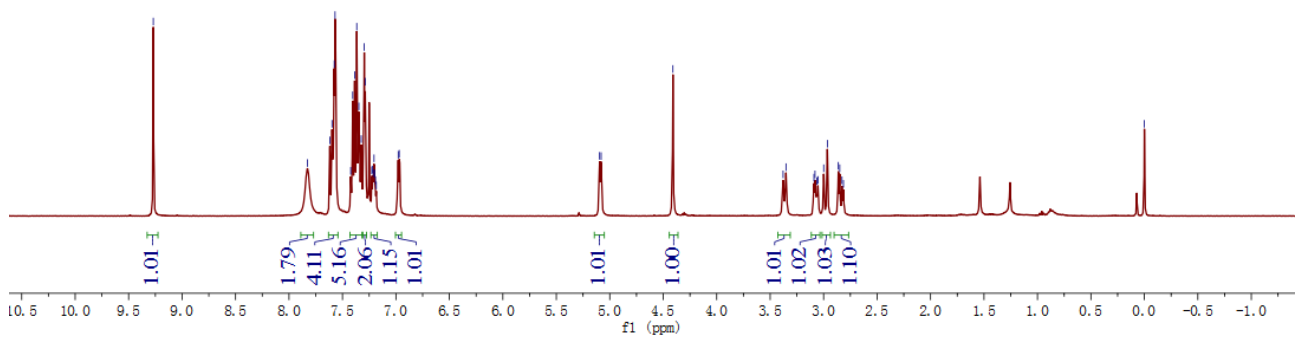
Name	CYC-20191124-21	Rack Pos.	Instrument	Instrument 1	Operator
Inj. Vol. (ul)	10	Plate Pos.	IRM Status	Success	
Data File	CYC-20191124-21.d	Method (Acq)	TOF.m	Comment	Acq. Time (Local)
					12/5/2019 6:28:08 PM (UTC+08:00)



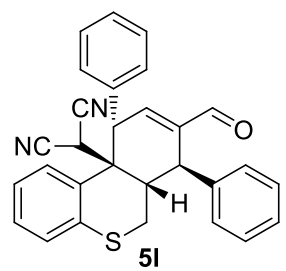
9.260
 7.827
 7.618
 7.598
 7.577
 7.557
 7.423
 7.404
 7.386
 7.360
 7.324
 7.296
 7.288
 7.272
 7.217
 7.212
 7.205
 7.198
 7.184
 7.181
 6.978
 6.969
 5.095
 4.409
 3.379
 3.352
 3.091
 3.081
 3.053
 2.999
 2.965
 2.952
 2.896
 2.828
 2.815
 -0.000



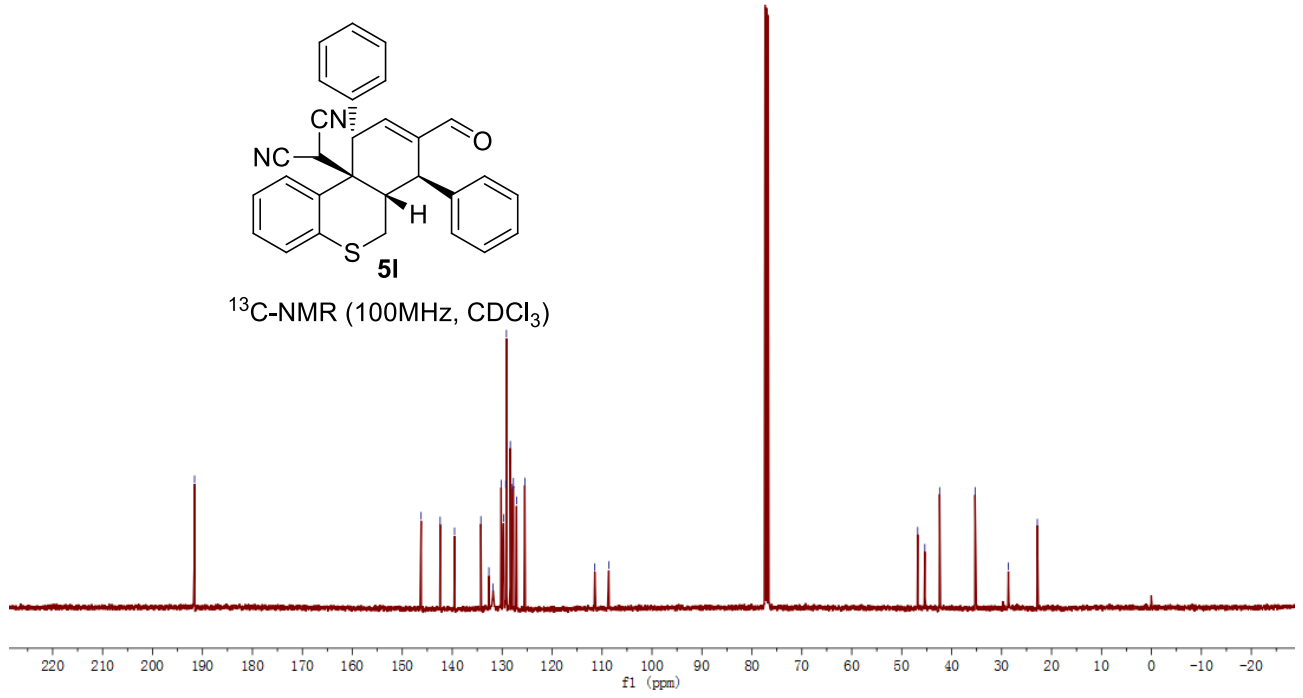
¹H-NMR (400MHz, CDCl₃)

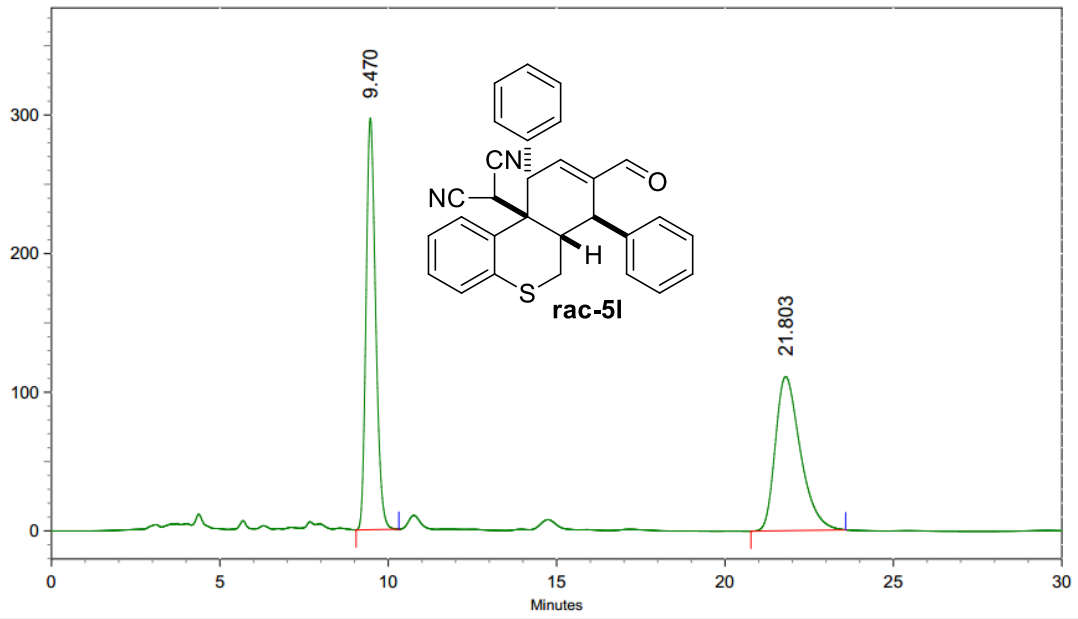


191.564
 146.228
 142.410
 139.529
 138.030
 132.653
 131.814
 130.197
 129.739
 129.135
 129.145
 128.368
 127.981
 127.126
 125.467
 111.468
 108.652
 46.800
 45.376
 42.415
 35.312
 28.641
 22.899



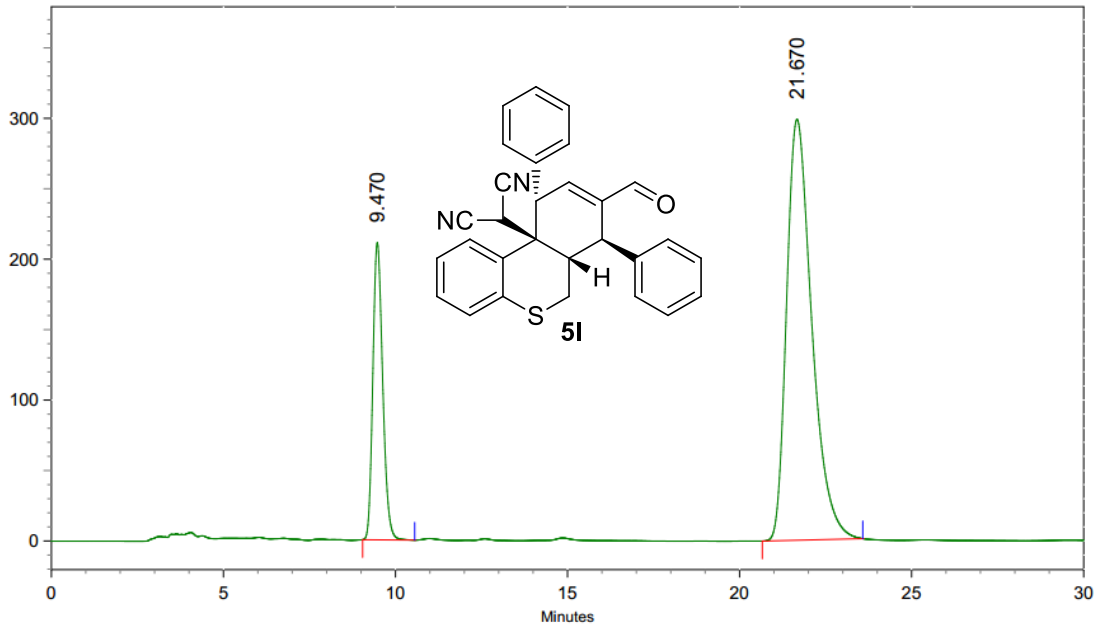
¹³C-NMR (100MHz, CDCl₃)





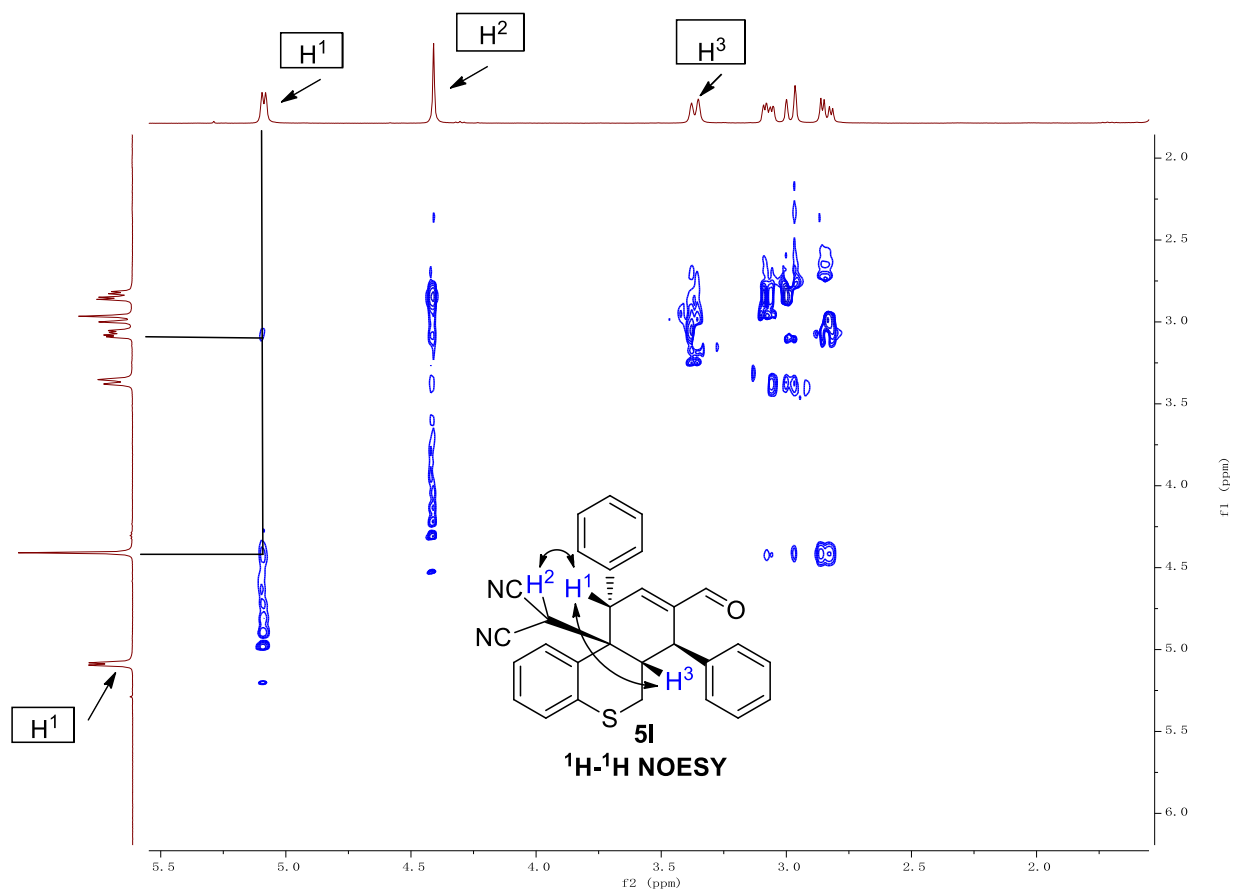
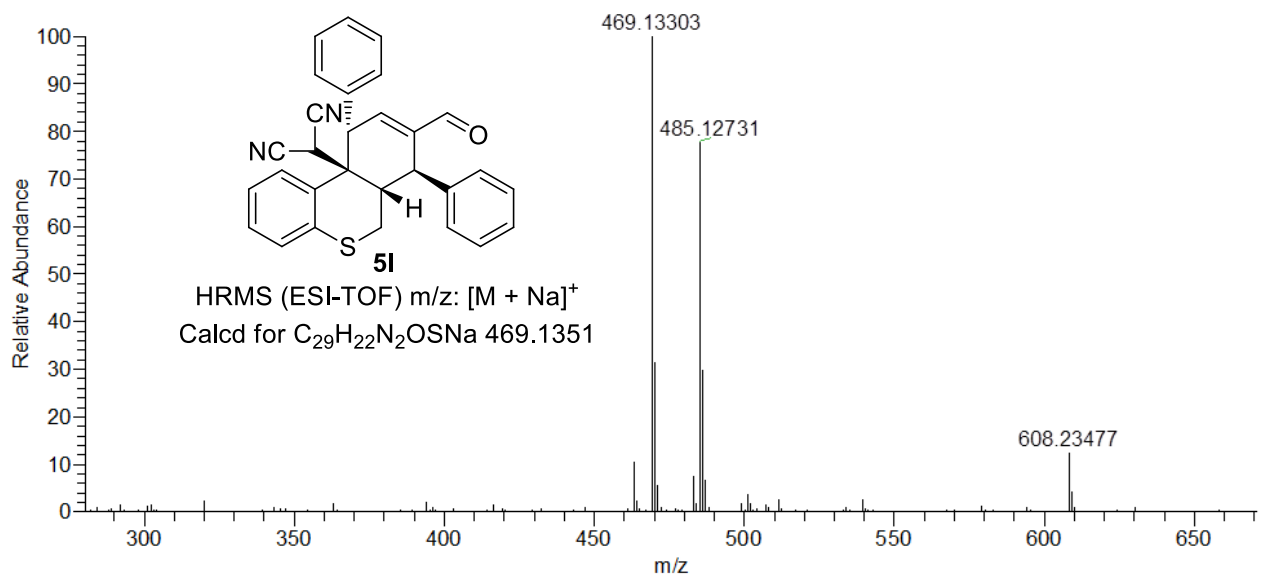
AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.470	1.270	4981769	98357123	50.5030
2	21.803	2.810	1866011	96398073	49.4970



AREA PERCENT REPORT

Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.470	1.513	3538913	70390617	21.6262
2	21.670	2.920	5012651	255096578	78.3738



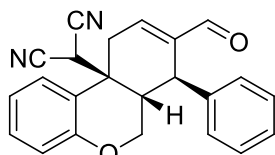
-9.211

7.360
7.355
7.335
7.330
7.308
7.298
7.296
7.274
7.228
7.216
6.964
6.950
6.937
6.914
6.904

4.322
4.170
4.156
3.627
3.616
3.604
3.594
3.159
3.127

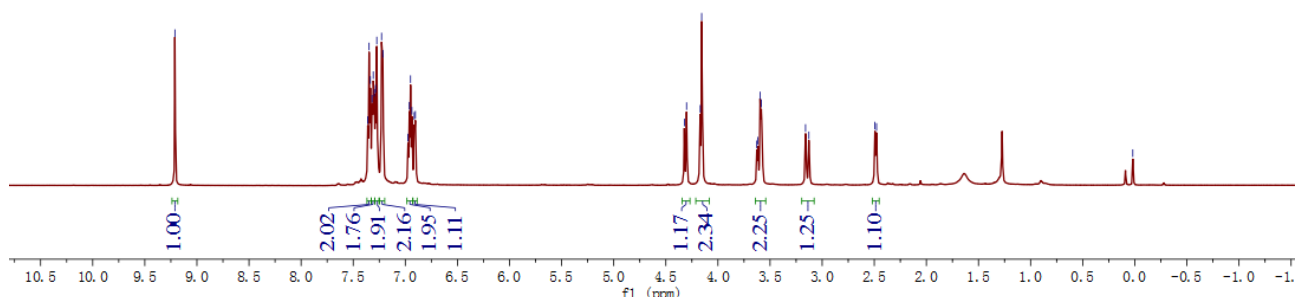
2.494
2.478

-0.019

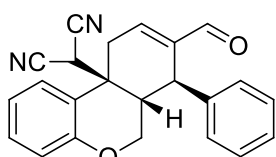


5m

¹H-NMR (400MHz, CDCl₃)

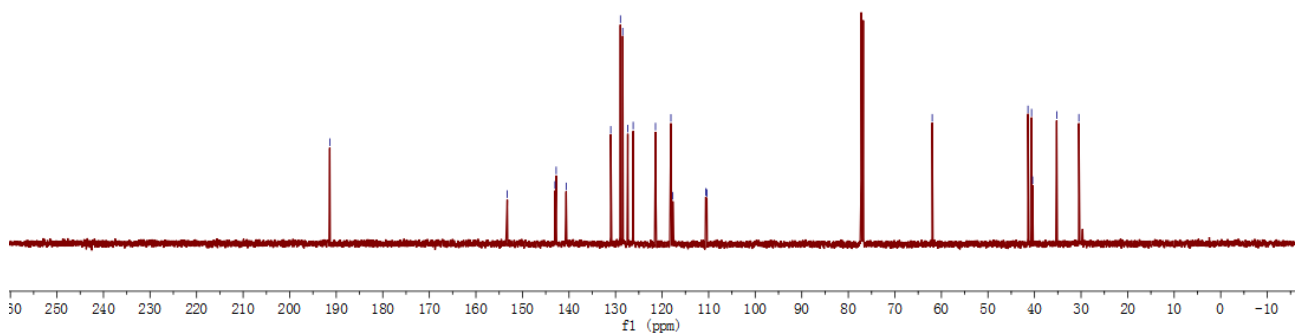


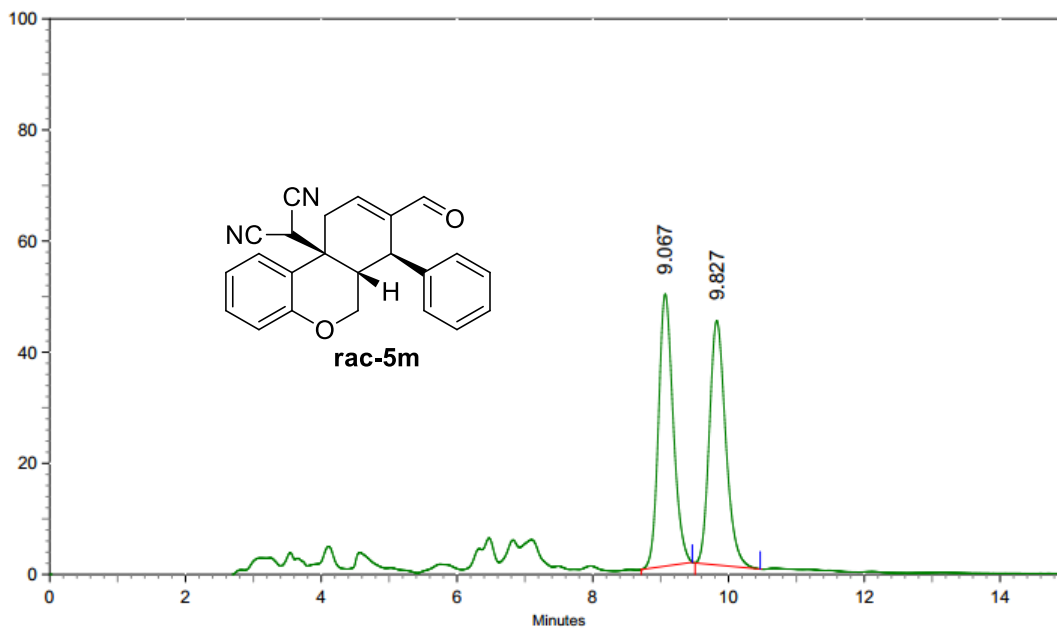
101.387
153.264
143.017
142.796
140.610
131.020
128.966
127.973
126.214
121.417
119.112
110.644
110.396
61.969
41.403
40.635
40.208
30.475



5m

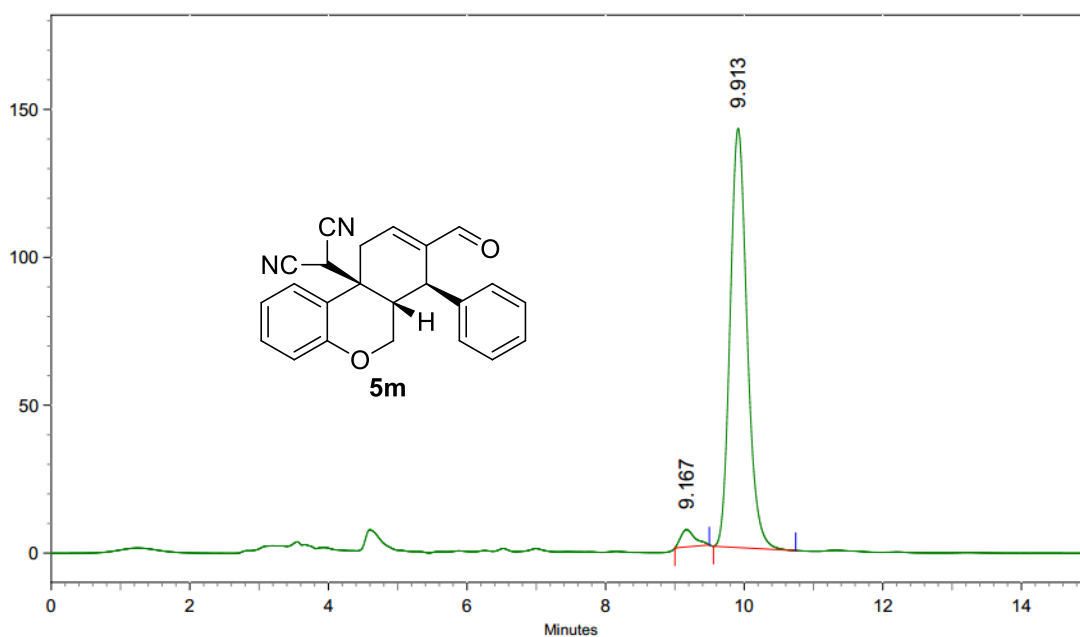
¹³C-NMR (100MHz, CDCl₃)





AREA PERCENT REPORT

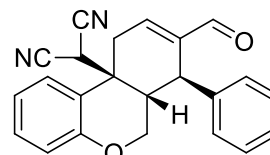
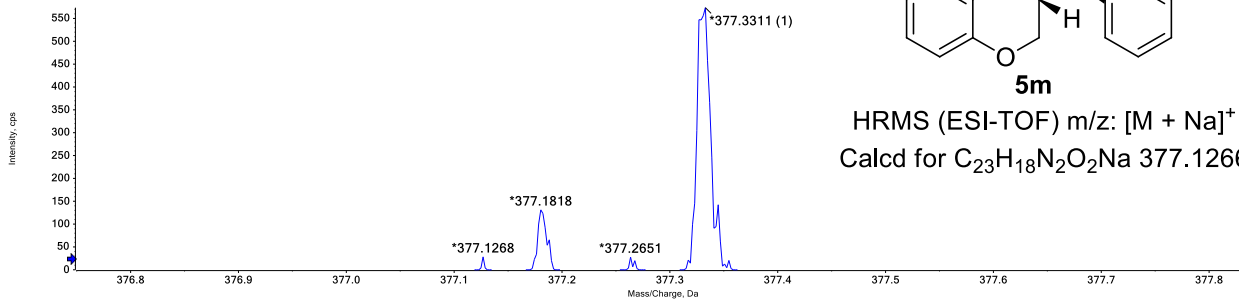
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.067	0.753	821111	12351248	50.0465
2	9.827	0.960	737535	12328273	49.9535



AREA PERCENT REPORT

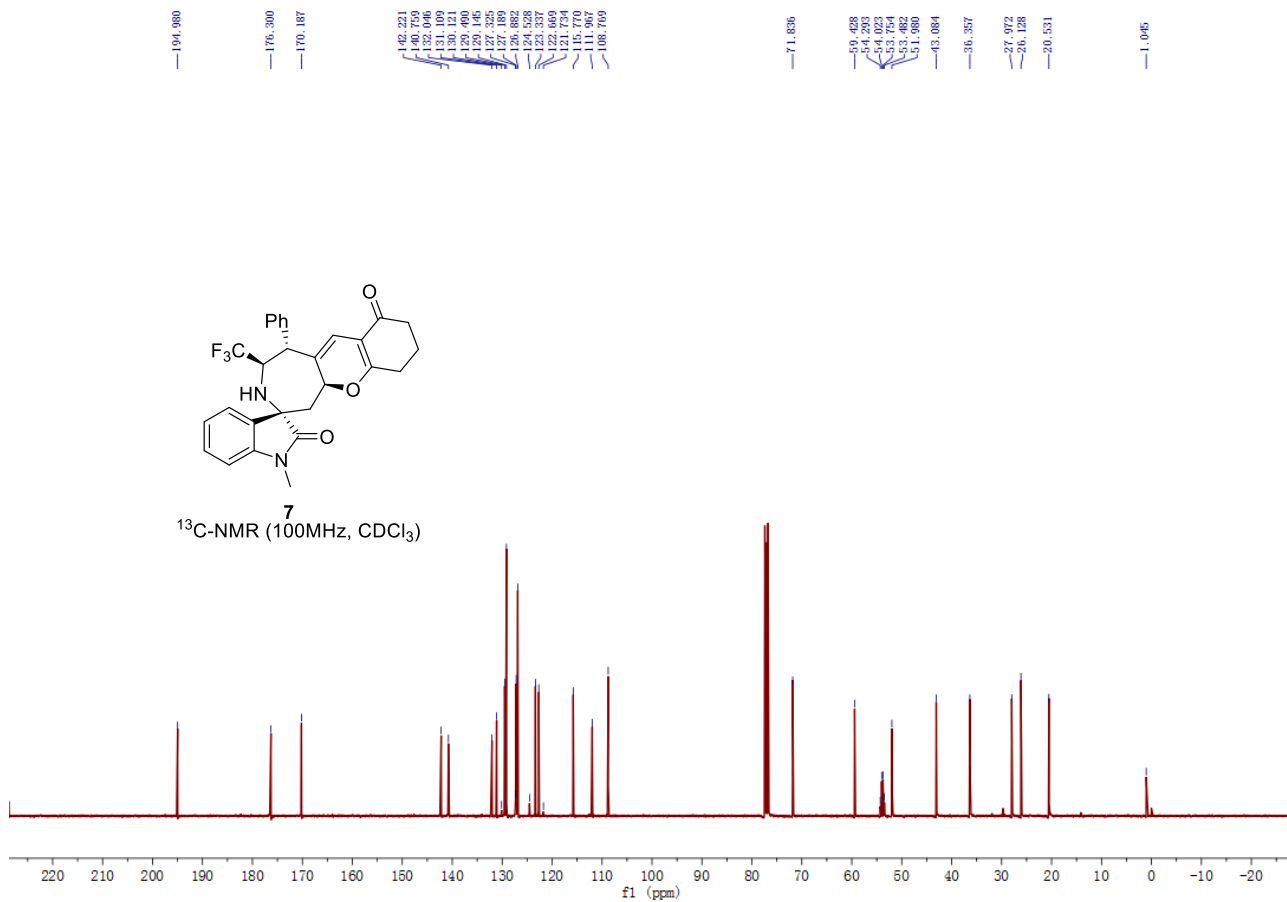
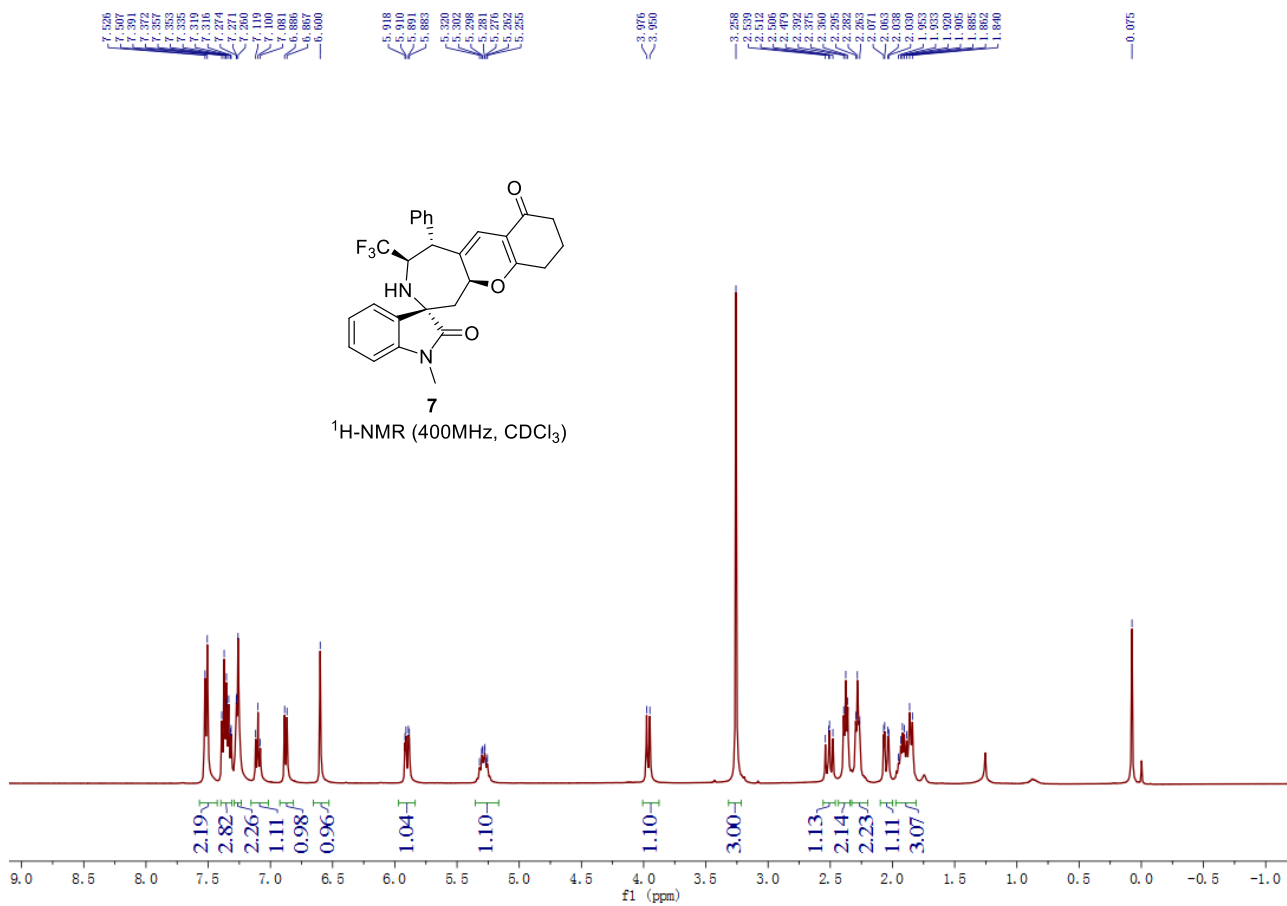
Peak No.	Ret Time	Width	Height	Area	Area [%]
1	9.167	0.497	97672	1389840	3.3247
2	9.913	1.187	2377380	40413871	96.6753

Spectrum from 20201003.wiff2 (sample 10) - GY-E02, +TOF MS (300 - 450) from 0.132 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)

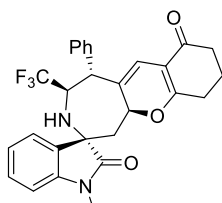


5m

HRMS (ESI-TOF) m/z: [M + Na]⁺
Calcd for C₂₃H₁₈N₂O₂Na 377.1266

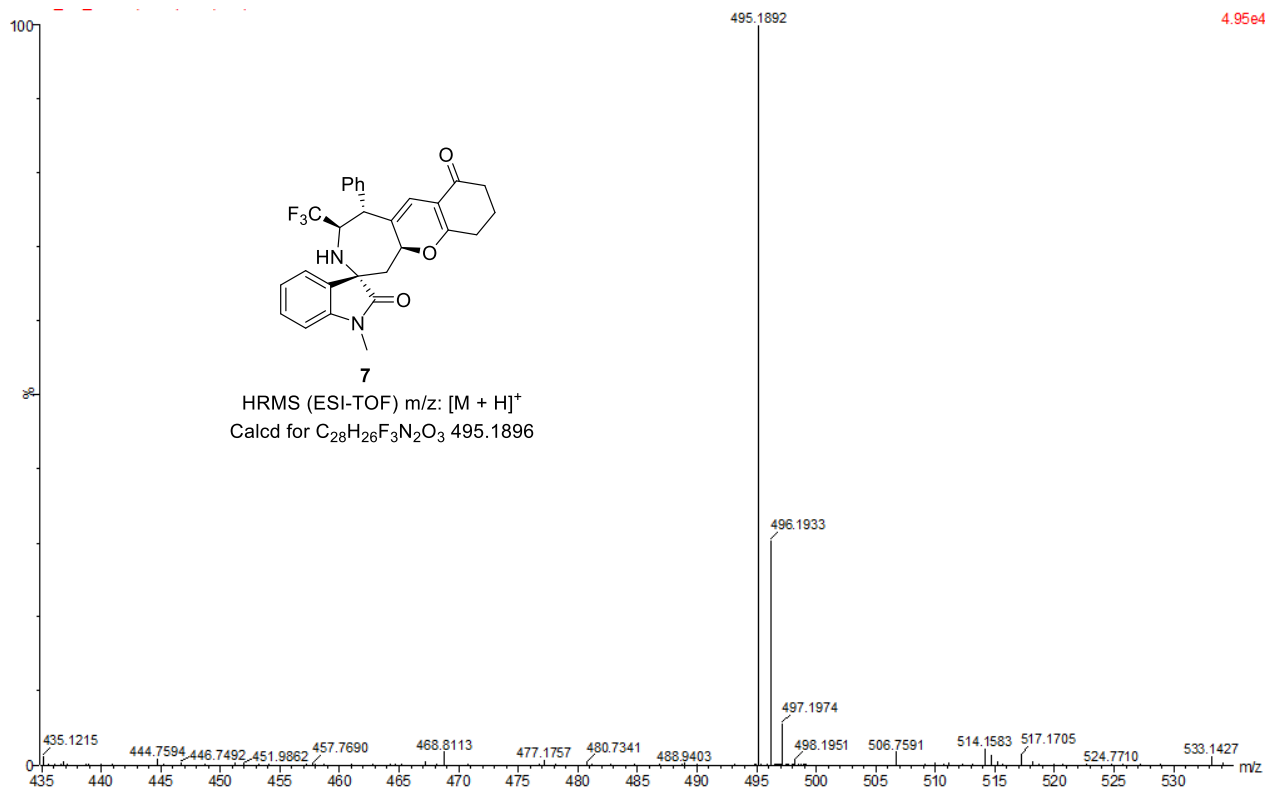
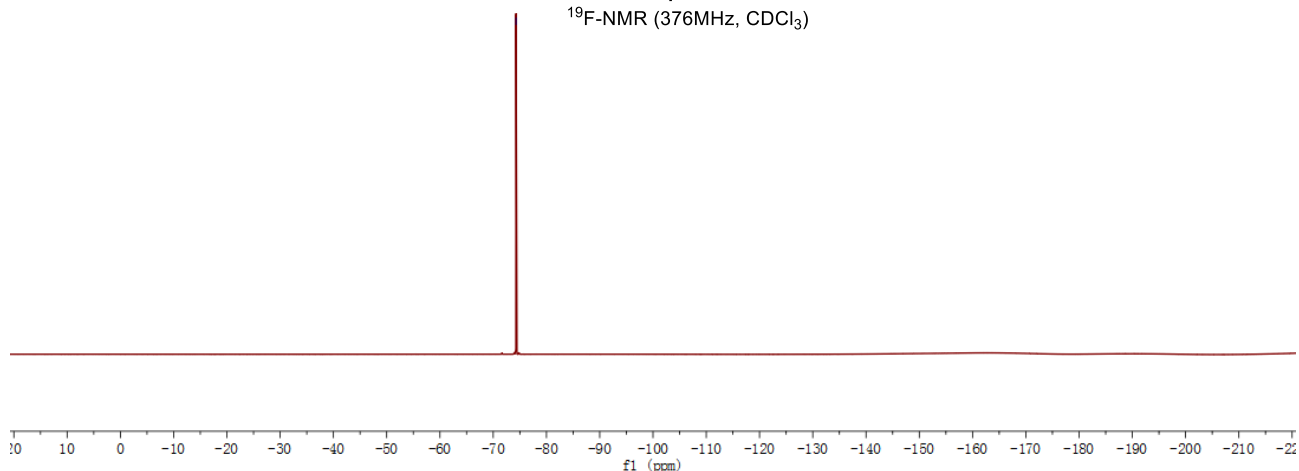


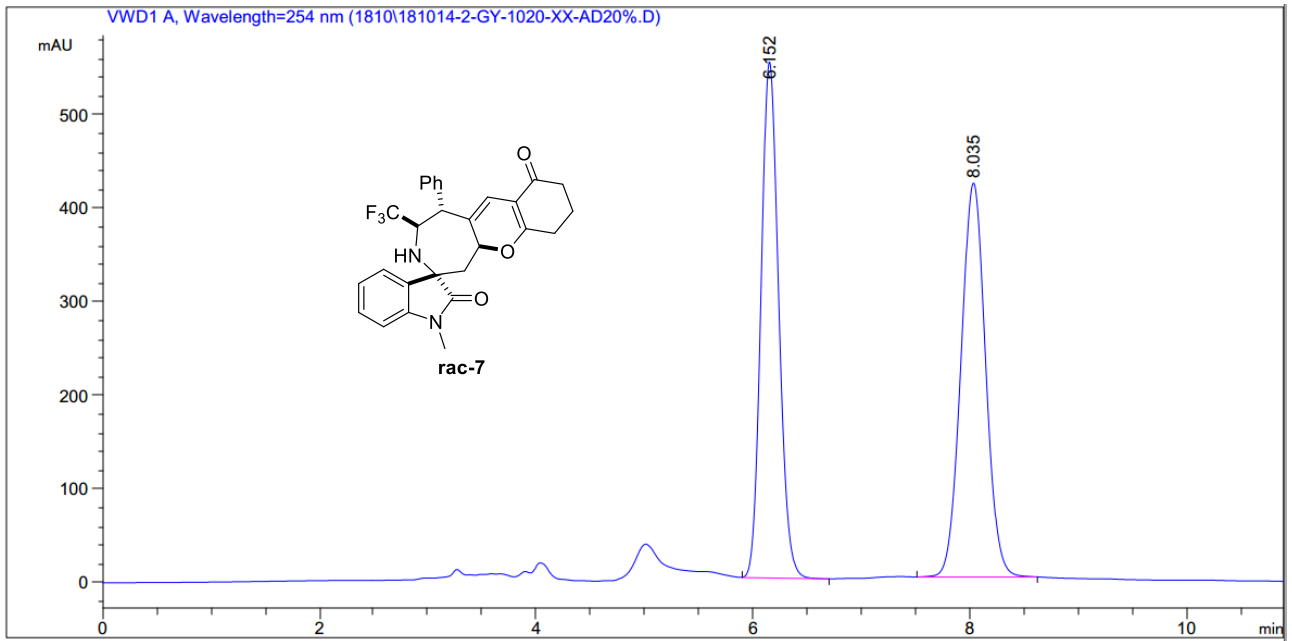
-71.283



7

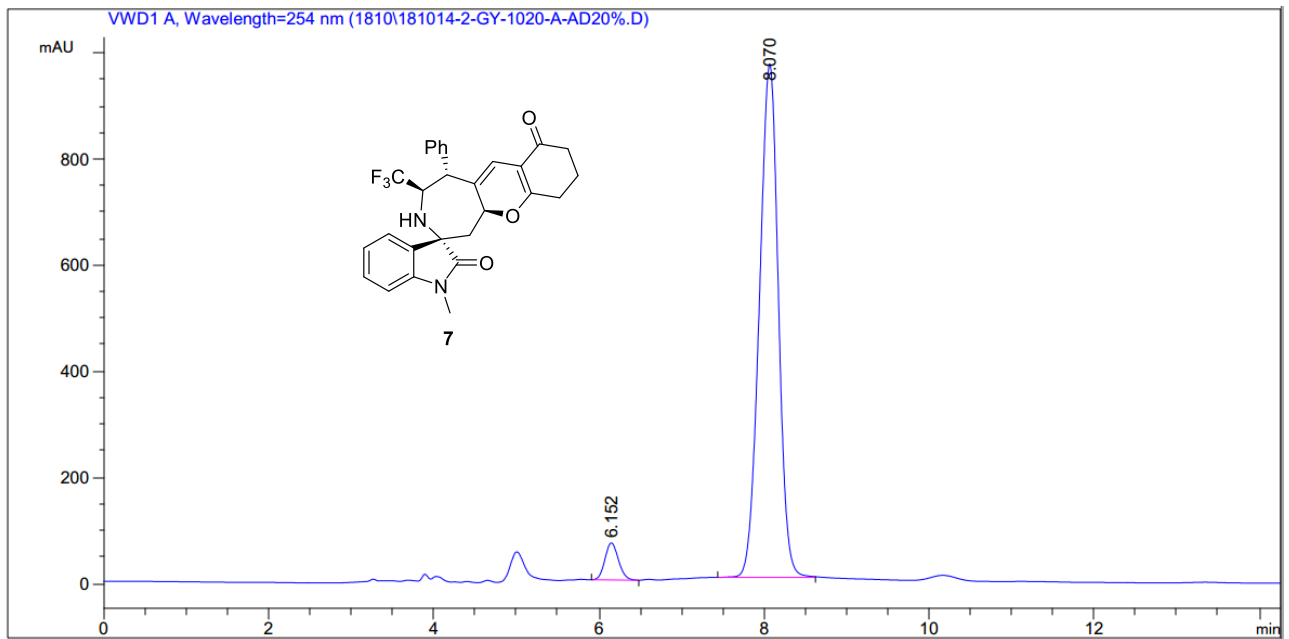
^{19}F -NMR (376MHz, CDCl_3)





Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.152	BV	0.1754	6227.13428	551.47760	48.3744
2	8.035	BBA	0.2467	6645.65039	421.08829	51.6256

Totals : 1.28728e4 972.56589



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.152	BV	0.1768	796.09375	69.79441	4.9089
2	8.070	BBA	0.2469	1.54212e4	968.48712	95.0911

Totals : 1.62173e4 1038.28153

