Palladium-catalysed asymmetric cascade transformations of 4-alken-2-ynyl carbonates to construct complex frameworks

Ze-Liang He,[a] Li Li,[a] Zhi-Chao Chen,*[a] Wei Du,[a] and Ying-Chun Chen*[ab]

[a] Key Laboratory of Drug-Targeting and Drug Delivery System of the Ministry of Education and Sichuan Research Center for Drug Precision Industrial Technology, West China School of Pharmacy, Sichuan University, Chengdu 610041, China

[b] College of Pharmacy, Third Military Medical University, Shapingba, Chongqing 400038, China

Email: chenzhichao@scu.edu.cn; ycchen@scu.edu.cn

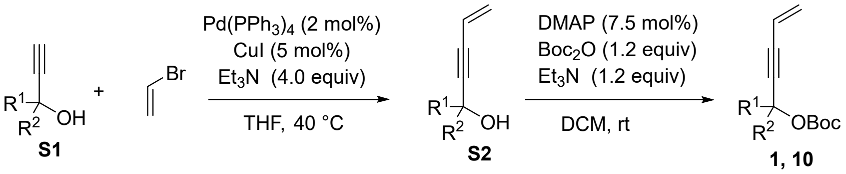
Supplementary Information

1. General methods

Unless otherwise noted, the reactions were carried out under ambient atmosphere; when the reactions required heating, the heat source was oil bath. ^{1}H NMR (400 or 600 MHz), ^{13}C NMR (100 or 150 MHz) and ^{19}F NMR (375 MHz) spectra were recorded on Varian INOVA-400/54, Agilent DD2-600/54 or Bruker Ascend^{TM} 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, q = quartet, dd = double doublet, m = multiplet and coupling constants (*J*) are reported in Hertz (Hz). High resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2 or Agilent G1969-85000 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 Burker D8 Venture and the data obtained were deposited at the Cambridge Crystallographic Data Centre (CCDC 2381131–2381135). In each case, diastereomeric ratio was determined by ^{1}H 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 × 4.6 mm), Chiralpak IA Column (250 × 4.6 mm), Chiralpak IB Column (250 × 4.6mm), IBN-5 Column (250 × 4.6 mm), Chiralpak ID Column (250 × 4.6 mm), Chiralpak IE Column(250 × 4.6 mm), Chiralpak IF Column (250 × 4.6 mm). UV detection was monitored at 220 nm or 254 nm. Optical rotation was measured in $CHCl_3$ solution at 25 °C. Column chromatography was performed on silica gel (200–300 mesh) eluting with 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 and EtOAc were re-distilled. Experiments involving moisture and/or air sensitive components were performed under a positive pressure of argon in oven-dried glassware equipped with a rubber septum inlet. Toluene was freshly distilled from CaH_2 under an atmosphere of dry argon. Dried solvents reagents were transferred by oven-dried syringe.

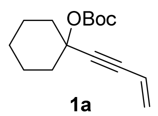
2. Preparation and characterization of substrates

2.1 General procedure for the preparation of 4-alken-2-ynyl carbonates[1]



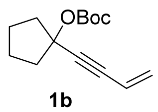
To an oven-dried flask were added CuI (57 mg, 0.3 mmol) and Pd(PPh$_3$)$_4$ (346 mg, 0.3 mmol). The flask was capped, purged and back-filled with argon for five times. Dry THF (20 mL), propargylic alcohol **S1** (10 mmol), vinyl bromide (1.0 M in THF, 15 mL, 15 mmol) and triethylamine (5 mL, 40 mmol) were added sequentially via syringe. The mixture was stirred at 40 °C until complete consumption of **S1**. The mixture was cooled to room temperature and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography to give **S2**.

To a solution of **S2** (10 mmol) in DCM (30 mL) were added triethylamine (1.7 mL, 12 mmol) and Boc$_2$O (2.6 g, 12 mmol) followed by DMAP (92 mg, 0.75 mmol). The mixture was stirred at room temperature overnight and then poured into water. The phases were separated and the aqueous phase was extracted three times with DCM. The combined organic phases were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and the filtrate was concentrated and the residue was purified by flash column chromatography to give substrate **1** or **10**.



1a

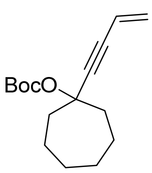
1-(But-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate (1a): eluent (petroleum ether/ethyl acetate = 75/1); colourless oil; 71% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.86 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.64 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.48 (dd, *J* = 11.2, 2.0 Hz, 1H), 2.24–2.14 (m, 2H), 1.89–1.78 (m, 2H), 1.73–1.55 (m, 5H), 1.49 (s, 9H), 1.34–1.25 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 151.3, 127.1, 116.8, 89.4, 85.1, 81.9, 37.1, 27.8, 25.2, 22.8; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{15}H_{22}O_3Na^+$ 273.1461; Found 273.1459.



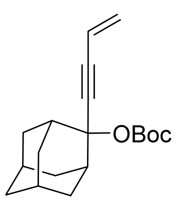
1b

1-(But-3-en-1-yn-1-yl)cyclopentyl *tert*-butyl carbonate (1b): eluent (petroleum ether/ethyl acetate = 75/1); colorless oil; 72% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.89–5.77 (m, 1H), 5.61 (dd, *J* = 17.6, 2.0 Hz, 1H), 5.46 (dd, *J* = 11.2, 2.4 Hz, 1H), 2.32–2.25 (m, 2H), 2.17–2.09 (m, 2H), 1.81–1.72 (m, 4H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 151.8, 127.1, 116.8, 90.0, 83.4, 82.5, 82.1, 40.5, 27.8, 23.4; HRMS (ESI-TOF) *m/z*:

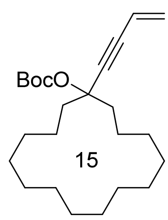
$[M + Na]^+$ Calcd for $C_{14}H_{20}O_3Na^+$ 259.1305; Found 259.1304.


1d

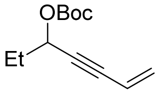
1-(But-3-en-1-yn-1-yl)cycloheptyl *tert*-butyl carbonate (1d): eluent (petroleum ether/ethyl acetate = 70/1); colourless oil; 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.85 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.63 (dd, *J* = 17.6, 2.0 Hz, 1H), 5.47 (dd, *J* = 11.2, 2.0 Hz, 1H), 2.31–2.24 (m, 2H), 2.15–2.06 (m, 2H), 1.66–1.55 (m, 8H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 151.4, 127.1, 116.9, 90.6, 84.2, 81.9, 80.7, 40.1, 28.2, 27.9, 22.2; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{24}O_3Na^+$ 287.1618; Found 287.1624.


1f

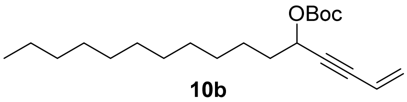
2-(But-3-en-1-yn-1-yl)adamantan-2-yl *tert*-butyl carbonate (1f): eluent (petroleum ether/ethyl acetate = 75/1); colourless oil; 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.86 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.62 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.46 (dd, *J* = 11.2, 2.4 Hz, 1H), 2.50 (s, 2H), 2.17 (d, *J* = 12.4 Hz, 2H), 2.06 (d, *J* = 12.0 Hz, 2H), 1.83–1.70 (m, 6H), 1.63–1.57 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 151.4, 126.9, 116.9, 90.0, 85.6, 81.7, 81.6, 37.5, 36.1, 35.0, 31.9, 27.9, 26.8, 26.3; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{26}O_3Na^+$ 325.1774; Found 325.1771.


1g

1-(But-3-en-1-yn-1-yl)cyclopentadecyl *tert*-butyl carbonate (1g): eluent (petroleum ether/ethyl acetate = 70/1); colourless oil; 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.84 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.62 (dd, *J* = 17.6, 2.0 Hz, 1H), 5.46 (dd, *J* = 11.2, 2.0 Hz, 1H), 2.12–2.02 (m, 2H), 1.95–1.81 (m, 2H), 1.49 (s, 9H), 1.45–1.21 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 150.3, 126.1, 115.8, 89.0, 83.3, 80.8, 78.8, 35.5, 26.8, 26.2, 25.9, 25.6, 25.4, 20.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{24}H_{40}O_3Na^+$ 399.2870; Found 399.2870.

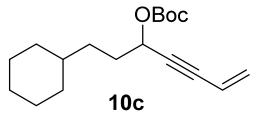

10a

***tert*-Butyl hept-6-en-4-yn-3-yl carbonate (10a):** eluent (petroleum ether/ethyl acetate = 75/1); colourless oil; 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.87–5.74 (m, 1H), 5.66 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.50 (dd, *J* = 11.2, 2.4 Hz, 1H), 5.25 (t, *J* = 6.4 Hz, 1H), 1.88–1.80 (m, 2H), 1.50 (s, 9H), 1.03 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 152.7, 127.8, 116.5, 86.6, 84.4, 82.6, 68.5, 28.2, 27.7, 9.4; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{18}O_3Na^+$ 233.1148; Found 233.1141.



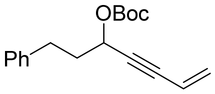
10b

***tert*-Butyl hexadec-1-en-3-yn-5-yl carbonate (10b):** eluent (petroleum ether/ethyl acetate = 80/1); colourless oil; 64% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.87–5.75 (m, 1H), 5.65 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.49 (dd, *J* = 11.2, 2.4 Hz, 1H), 5.34–5.23 (m, 1H), 1.86–1.75 (m, 2H), 1.50 (s, 9H), 1.47–1.41 (m, 2H), 1.30–1.21 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, CDCl$_3$): δ (ppm) 152.7, 127.8, 116.5, 87.0, 84.3, 82.6, 67.5, 34.9, 31.9, 29.6, 29.52, 29.51, 29.45, 29.3, 29.1, 27.8, 25.0, 22.7, 14.1; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{21}H_{36}O_3Na^+$ 359.2557; Found 359.2563.



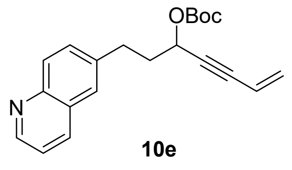
10c

***tert*-Butyl (1-cyclohexylhept-6-en-4-yn-3-yl) carbonate (10c):** eluent (petroleum ether/ethyl acetate = 75/1); colourless oil; 76% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.86–5.76 (m, 1H), 5.65 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.50 (dd, *J* = 11.6, 2.4 Hz, 1H), 5.26 (t, *J* = 6.8 Hz, 1H), 1.85–1.77 (m, 2H), 1.74–1.64 (m, 5H), 1.50 (s, 9H), 1.37–1.30 (m, 2H), 1.27–1.11 (m, 4H), 0.95–0.84 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 152.7, 127.8, 116.5, 87.0, 84.4, 82.6, 67.8, 37.3, 33.3, 33.2, 32.5, 32.4, 27.8, 26.6, 26.3; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{18}H_{28}O_3Na^+$ 315.1931; Found 315.1936.



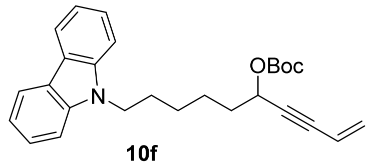
10d

***tert*-Butyl (1-phenylhept-6-en-4-yn-3-yl) carbonate (10d):** eluent (petroleum ether/ethyl acetate = 70/1); colourless oil; 73% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.31–7.26 (m, 2H), 7.22–7.17 (m, 3H), 5.89–5.77 (m, 1H), 5.67 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.52 (dd, *J* = 11.2, 2.4 Hz, 1H), 5.31–5.26 (m, 1H), 2.80 (t, *J* = 8.0 Hz, 2H), 2.20–2.08 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 152.6, 140.7, 128.5, 128.4, 128.0, 126.1, 116.4, 86.5, 84.8, 82.7, 66.8, 36.4, 31.2, 27.8; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{18}H_{22}O_3Na^+$ 309.1461; Found 309.1467.

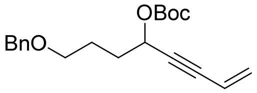


10e

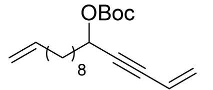
***tert*-Butyl (1-(quinolin-6-yl)hept-6-en-4-yn-3-yl) carbonate (10e):** eluent (petroleum ether/ethyl acetate = 12/1); colourless oil; 62% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.91–8.82 (m, 1H), 8.11–8.01 (m, 2H), 7.63–7.56 (m, 2H), 7.40–7.34 (m, 1H), 5.90–5.77 (m, 1H), 5.72–5.64 (m, 1H), 5.56–5.49 (m, 1H), 5.37–5.31 (m, 1H), 3.00 (t, *J* = 7.6 Hz, 2H), 2.30–2.19 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 152.6, 149.9, 147.2, 139.2, 135.6, 130.8, 129.6, 128.3, 128.2, 126.3, 121.2, 116.4, 86.4, 85.0, 82.8, 66.7, 36.1, 31.2, 27.8; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{24}NO_3^+$ 338.1751; Found 338.1747.


10f

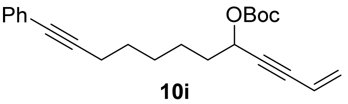
10-(9*H*-carbazol-9-yl)dec-1-en-3-yn-5-yl *tert*-butyl carbonate (10f): eluent (petroleum ether/ethyl acetate = 15/1); colourless oil; 68% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.10 (d, *J* = 7.6 Hz, 2H), 7.48–7.44 (m, 2H), 7.41–7.37 (m, 2H), 7.24–7.20 (m, 2H), 5.84–5.73 (m, 1H), 5.64 (dd, *J* = 17.6, 2.0 Hz, 1H), 5.49 (dd, *J* = 10.8, 2.4 Hz, 1H), 5.27 (t, *J* = 6.4 Hz, 1H), 4.30 (t, *J* = 7.2 Hz, 2H), 1.93–1.85 (m, 2H), 1.82–1.73 (m, 2H), 1.55–1.50 (m, 2H), 1.48 (s, 9H), 1.46–1.40 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 152.7, 140.4, 128.0, 125.6, 122.8, 120.4, 118.8, 116.4, 108.6, 86.7, 84.6, 82.7, 67.2, 42.9, 34.7, 28.8, 27.8, 26.8, 24.7; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{27}H_{31}NO_3Na^+$ 440.2196; Found 440.2198.


10g

1-(Benzyloxy)oct-7-en-5-yn-4-yl *tert*-butyl carbonate (10g): eluent (petroleum ether/ethyl acetate = 70/1); colourless oil; 75% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.37–7.26 (m, 5H), 5.85–5.72 (m, 1H), 5.65 (dd, *J* = 17.6, 2.0 Hz, 1H), 5.49 (dd, *J* = 11.2, 2.4 Hz, 1H), 5.36–5.31 (m, 1H), 4.50 (s, 2H), 3.52 (t, *J* = 6.4 Hz, 2H), 1.96–1.89 (m, 2H), 1.83–1.76 (m, 2H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 152.7, 138.5, 128.4, 127.9, 127.6, 127.6, 116.5, 86.7, 84.6, 82.7, 72.9, 69.6, 67.2, 31.8, 27.8, 25.3; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{20}H_{26}O_4Na^+$ 353.1723; Found 353.1719.

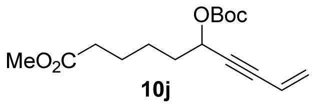

10h

***tert*-Butyl pentadeca-1,14-dien-3-yn-5-yl carbonate (10h):** eluent (petroleum ether/ethyl acetate = 80/1); colourless oil; 67% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.92–5.74 (m, 2H), 5.72–5.60 (m, 1H), 5.55–5.45 (m, 1H), 5.28 (t, *J* = 6.4 Hz, 1H), 5.06–4.86 (m, 2H), 2.10–1.98 (m, 2H), 1.87–1.74 (m, 2H), 1.50 (s, 9H), 1.46–1.25 (m, 12H); ^{13}C NMR (100 MHz, CDCl$_3$) δ (ppm) 152.7, 139.2, 127.8, 116.5, 114.1, 87.0, 84.3, 82.6, 67.5, 34.9, 33.8, 29.4, 29.3, 29.1, 28.9, 27.8, 25.0; HRMS (ESI-TOF): *m/z*: [M + Na]$^+$ Calcd for $C_{20}H_{32}O_3Na^+$ 343.2244; Found 343.2250.


10i

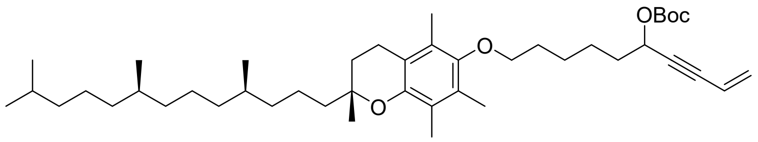
***tert*-Butyl (12-phenyldodeca-1-en-3,11-diyn-5-yl) carbonate (10i):** eluent (petroleum ether/ethyl acetate = 75/1); colourless oil; 69% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.42–7.36 (m, 2H), 7.31–

7.26 (m, 3H), 5.86–5.75 (m, 1H), 5.66 (dd, J = 17.6, 2.4 Hz, 1H), 5.50 (dd, J = 11.2, 2.4 Hz, 1H), 5.31 (t, J = 6.4 Hz, 1H), 2.41 (t, J = 6.8 Hz, 2H), 1.89–1.81 (m, 2H), 1.66–1.61 (m, 2H), 1.56–1.51 (m, 4H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 152.7, 131.6, 128.2, 127.9, 127.5, 124.0, 116.5, 90.1, 86.8, 84.5, 82.6, 80.8, 67.4, 34.8, 28.6, 28.4, 27.8, 24.6, 19.3; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{27}H_{28}O_3Na^+$ 375.1931; Found 375.1937.



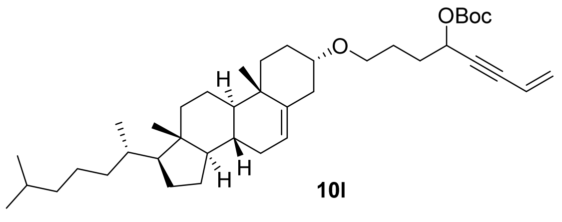
10j

Methyl 6-((*tert*-butoxycarbonyl)oxy)dec-9-en-7-ynoate (10j): eluent (petroleum ether/ethyl acetate = 30/1); colourless oil; 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.89–5.74 (m, 1H), 5.66 (dd, J = 17.6, 2.4 Hz, 1H), 5.51 (dd, J = 10.8, 2.4 Hz, 1H), 5.29 (t, J = 6.4 Hz, 1H), 3.67 (s, 3H), 2.33 (t, J = 7.2 Hz, 2H), 1.88–1.78 (m, 2H), 1.72–1.63 (m, 2H), 1.55–1.50 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 173.9, 152.6, 128.0, 116.4, 86.6, 84.5, 82.7, 67.1, 51.6, 34.5, 33.9, 27.8, 24.6, 24.5; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{16}H_{24}O_5Na^+$ 319.1516; Found 319.1518.



10k

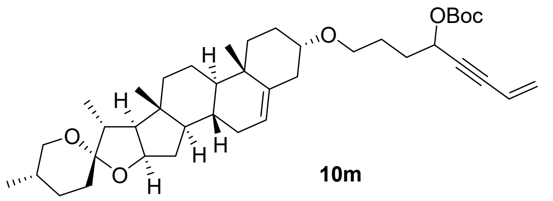
***tert*-Butyl (10-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)dec-1-en-3-yn-5-yl) carbonate (10k):** eluent (petroleum ether/ethyl acetate = 20/1); colourless oil; 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.87–5.74 (m, 1H), 5.66 (dd, J = 17.6, 2.2 Hz, 1H), 5.50 (dd, J = 11.0, 2.2 Hz, 1H), 5.34–5.28 (m, 1H), 3.63 (t, J = 6.5 Hz, 2H), 2.56 (t, J = 6.7 Hz, 2H), 2.15 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 1.88–1.71 (m, 6H), 1.58–1.52 (m, 6H), 1.50 (s, 9H), 1.45–1.23 (m, 11H), 1.22 (s, 3H), 1.18–0.97 (m, 7H), 0.94–0.74 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 152.7, 148.3, 147.7, 127.9, 127.8, 125.8, 122.8, 117.5, 116.5, 86.9, 84.4, 82.6, 74.7, 72.8, 67.4, 40.11, 40.07, 39.4, 37.4, 37.3, 34.9, 32.80, 32.78, 32.70, 32.68, 31.30, 31.25, 30.2, 28.0, 27.8, 25.8, 24.9, 24.8, 24.4, 23.9, 22.7, 22.6, 21.1, 21.0, 20.7, 19.8, 19.7, 19.6, 12.7, 11.9, 11.8; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{44}H_{72}O_5Na^+$ 703.5272; Found 703.5270.



10l

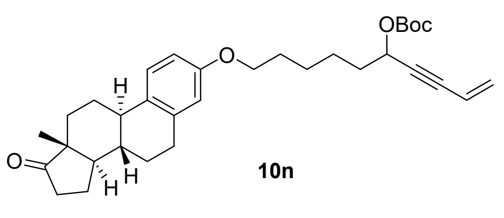
***tert*-Butyl (1-(((3*S*,8*R*,9*R*,10*S*,13*S*,14*R*,17*S*)-10,13-dimethyl-17-((*S*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)oct-7-en-5-yn-4-yl)**

carbonate (10l): eluent (petroleum ether/ethyl acetate = 20/1); colourless oil; 51% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.87–5.74 (m, 1H), 5.65 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.49 (dd, *J* = 11.2, 2.4 Hz, 1H), 5.36–5.30 (m, 2H), 3.50 (t, *J* = 6.4 Hz, 2H), 3.17–3.08 (m, 1H), 2.38–2.32 (m, 1H), 2.18 (t, *J* = 11.8 Hz, 1H), 2.04–1.94 (m, 2H), 1.92–1.69 (m, 7H), 1.60–1.51 (m, 3H), 1.49 (s, 9H), 1.49–1.00 (m, 17H), 1.00 (s, 3H), 1.00–0.90 (m, 4H), 0.88–0.84 (m, 6H), 0.68 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 152.6, 141.0, 127.9, 121.5, 116.5, 86.7, 84.5, 82.6, 79.0, 67.22, 67.19, 56.8, 56.1, 50.2, 42.3, 39.8, 39.5, 39.1, 37.3, 36.9, 36.2, 35.8, 31.94, 31.88, 31.82, 28.4, 28.2, 28.0, 27.8, 25.7, 24.3, 23.8, 22.8, 22.6, 21.1, 19.4, 18.7, 11.8; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{40}H_{64}O_4Na^+$ 631.4697; Found 631.4703.



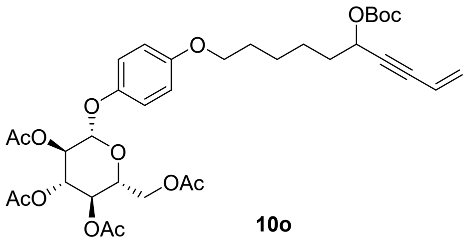
10m

***tert*-Butyl (1-(((4*S*,5'*S*,6a*S*,6b*R*,8a*R*,8b*S*,9*R*,10*S*,11a*R*,12a*R*,12b*R*)-5',6a,8a,9-tetramethyl-1,3,3',4,4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12b-icosahydrospiro[naphtho[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran]-4-yl)oxy)oct-7-en-5-yn-4-yl) carbonate (10m)**: eluent (petroleum ether/ethyl acetate = 25/1); colourless oil; 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.89–5.74 (m, 1H), 5.65 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.50 (dd, *J* = 10.8, 2.0 Hz, 1H), 5.36–5.29 (m, 2H), 4.41 (q, *J* = 7.2 Hz, 1H), 3.53–3.44 (m, 3H), 3.37 (t, *J* = 10.8 Hz, 1H), 3.17–3.07 (m, 1H), 2.40–2.32 (m, 1H), 2.22–2.13 (m, 1H), 2.03–1.95 (m, 2H), 1.92–1.82 (m, 5H), 1.80–1.52 (m, 12H), 1.49 (s, 9H), 1.47–1.08 (m, 6H), 1.01 (s, 3H), 0.99–0.93 (m, 4H), 0.81–0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 152.7, 141.1, 127.9, 121.2, 116.5, 109.3, 86.7, 84.5, 82.6, 80.8, 79.0, 67.2, 66.9, 62.1, 56.5, 50.1, 41.6, 40.3, 39.8, 39.1, 37.2, 37.0, 32.1, 31.9, 31.8, 31.5, 31.4, 30.3, 28.8, 28.4, 27.8, 25.8, 20.9, 19.4, 17.1, 16.3, 14.5; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{40}H_{60}O_6Na^+$ 659.4282; Found 659.4283.



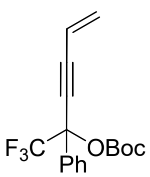
10n

***tert*-Butyl (10-(((8*S*,9*R*,13*R*,14*R*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)dec-1-en-3-yn-5-yl) carbonate (10n)**: eluent (petroleum ether/ethyl acetate = 20/1); colourless oil; 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.19 (d, *J* = 8.4 Hz, 1H), 6.73–6.67 (m, 1H), 6.66–6.60 (m, 1H), 5.80 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.65 (d, *J* = 17.6 Hz, 1H), 5.50 (d, *J* = 11.2 Hz, 1H), 5.30 (t, *J* = 6.4 Hz, 1H), 3.93 (t, *J* = 6.4 Hz, 2H), 2.94–2.84 (m, 2H), 2.54–2.46 (m, 1H), 2.44–2.36 (m, 1H), 2.29–2.21 (m, 1H), 2.17–1.93 (m, 4H), 1.87–1.75 (m, 4H), 1.64–1.51 (m, 8H), 1.50 (s, 9H), 1.47–1.39 (m, 2H), 0.91 (s, 3H); ^{13}C NMR (150 MHz, CDCl$_3$): δ (ppm) 221.0, 157.1, 152.7, 137.7, 131.9, 127.9, 126.3, 116.5, 114.5, 112.1, 86.8, 84.5, 82.6, 67.6, 67.3, 50.4, 48.0, 44.0, 38.4, 35.9, 34.8, 31.6, 29.6, 29.1, 27.8, 26.6, 25.9, 25.7, 24.8, 21.6, 13.8; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{33}H_{44}O_5Na^+$ 543.3081; Found 543.3077.



10o

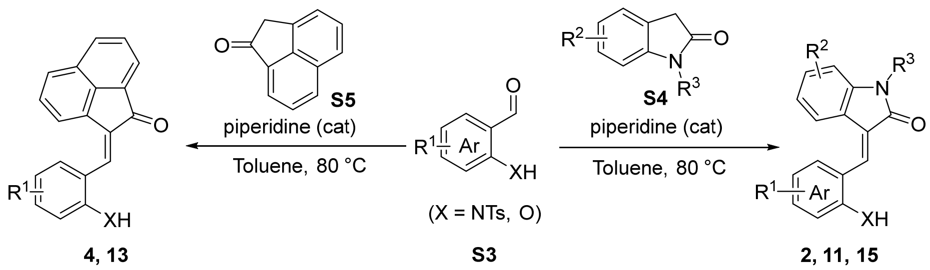
(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-(4-((6-((*tert*-butoxycarbonyl)oxy)dec-9-en-7-yn-1-yl)oxy)phenoxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (10o): eluent (petroleum ether/ethyl acetate = 20/1); colourless oil; 57% yield; ^{1}H NMR (600 MHz, CDCl$_3$): δ (ppm) 6.92–6.90 (m, 2H), 6.79–6.77 (m, 2H), 5.84–5.75 (m, 1H), 5.63 (dd, *J* = 17.6, 2.4 Hz, 1H), 5.48 (dd, *J* = 10.8, 2.0 Hz, 1H), 5.29–5.20 (m, 3H), 5.16–5.12 (m, 1H), 4.93 (d, *J* = 7.8 Hz, 1H), 4.29–4.25 (m, 1H), 4.16–4.13 (m, 1H), 3.89 (t, *J* = 6.6 Hz, 2H), 3.80–3.77 (m, 1H), 2.06 (d, *J* = 6.0 Hz, 6H), 2.02 (d, *J* = 6.0 Hz, 6H), 1.85–1.81 (m, 2H), 1.78–1.74 (m, 2H), 1.54–1.49 (m, 4H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 170.6, 170.3, 169.4, 169.3, 155.3, 152.7, 150.8, 128.0, 118.7, 116.4, 115.2, 100.3, 86.7, 84.5, 82.7, 72.7, 71.9, 71.2, 68.3, 68.2, 67.3, 61.9, 34.8, 29.1, 27.8, 25.6, 24.8, 20.8, 20.69, 20.65, 20.6; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{35}H_{46}O_{14}Na^+$ 713.2780; Found 713.2783.



10y

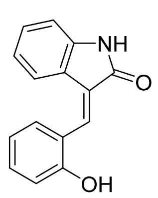
***tert*-Butyl (1,1,1-trifluoro-2-phenylhex-5-en-3-yn-2-yl) carbonate (10y)**: eluent (petroleum ether/ethyl acetate = 70/1); colourless oil; 68% yield; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.69–7.64 (m, 2H), 7.44–7.40 (m, 3H), 6.02–5.91 (m, 1H), 5.91–5.85 (m, 1H), 5.71 (dd, *J* = 10.8, 2.8 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 149.3, 133.3, 130.4, 129.7, 128.4, 122.1 (q, $^1J_{FC}$ = 282.7 Hz), 115.6, 88.4, 84.2, 81.1, 78.8 (q, $^2J_{FC}$ = 32.2 Hz), 27.6; ^{19}F NMR (375 MHz, CDCl$_3$): δ (ppm) –78.4; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{17}H_{17}F_3O_3Na^+$ 349.1022; Found 349.1026.

2.2 Procedure for preparation of *ortho*-functionalised aryl enones[2]



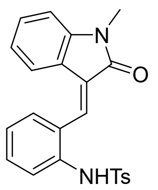
To a solution of **S3** (2.0 mmol) in toluene (10 mL) were added **S4** or **S5** (2.2 mmol) and piperidine (2−3 drops). The mixture was heated at 80 °C for 3–8 h, and monitored by TLC (petroleumether/EtOAc = 5/1). After completion, the mixture was cooled to room temperature and the solid was collected by filtration and then dried in vacuum to give *ortho*-functionalised aryl enones **2**, **11** and **15**.

Characterisation for selected *ortho*-functionalised aryl enones:



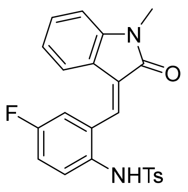
2m

Yellow solid, 71% yield; mp 233−235 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.57 (s, 1H), 10.19 (s, 1H), 7.72 (s, 1H), 7.64 (d, *J* = 6.8 Hz, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.37–7.29 (m, 1H), 7.26–7.18 (m, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.96–6.91 (m, 1H), 6.91–6.80 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 169.3, 157.0, 143.1, 133.0, 132.1, 130.2, 130.0, 127.0, 122.8, 121.82, 121.79, 121.5, 119.3, 116.5, 110.4; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{15}H_{11}NO_2Na^+$ 260.0682; Found 260.0682.



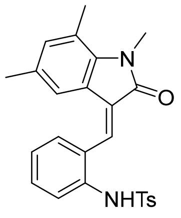
11a

Yellow solid, 75% yield; mp 247−249 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.01 (s, 1H), 7.65 (s, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.48–7.43 (m, 1H), 7.42–7.37 (m, 2H), 7.37–7.27 (m, 3H), 7.05 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.86–6.79 (m, 1H), 3.20 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 167.2, 144.4, 143.3, 137.4, 135.7, 133.9, 131.8, 131.0, 130.4, 130.2, 129.8, 128.5, 128.1, 127.0, 126.9, 122.6, 121.9, 120.6, 109.1, 26.3, 21.2; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{23}H_{20}N_2O_3SNa^+$ 427.1087; Found 427.1089.



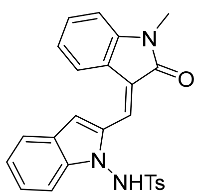
11c

Yellow solid, 77% yield; mp 272–274 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 9.97 (s, 1H), 7.53 (s, 1H), 7.42–7.25 (m, 6H), 7.01 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.89–6.81 (m, 1H), 3.20 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 167.0, 160.5 (d, $^{1}J_{\mathrm{FC}}$ = 243.8 Hz), 144.5, 143.3, 137.1, 134.4 (d, $^{3}J_{\mathrm{FC}}$ = 8.7 Hz), 132.2, 131.9 (d, $^{4}J_{\mathrm{FC}}$ = 2.8 Hz), 131.5 (d, $^{3}J_{\mathrm{FC}}$ = 9.0 Hz), 130.7, 129.8, 128.9, 126.9, 122.7, 122.0, 120.2, 117.7 (d, $^{1}2_{\mathrm{FC}}$ = 22.3 Hz), 116.5 (d, $^{2}J_{\mathrm{FC}}$ = 23.2 Hz), 109.2, 26.4, 21.2; ^{19}F NMR (375 MHz, DMSO-d_6): δ (ppm) –114.6; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{23}H_{19}FN_2O_3SNa^+$ 445.0993; Found 445.0996.



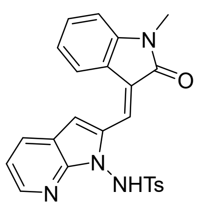
11d

Yellow solid, 74% yield; mp 248–250 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 9.99 (s, 1H), 7.59 (s, 1H), 7.51–7.46 (m, 1H), 7.46–7.37 (m, 3H), 7.35–7.26 (m, 2H), 6.99 (d, J = 7.6 Hz, 2H), 6.84 (s, 1H), 6.65 (s, 1H), 3.45 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 168.0, 143.3, 140.0, 137.5, 135.6, 134.5, 133.4, 131.8, 130.8, 130.3, 130.1, 129.8, 128.2, 127.9, 127.0, 126.7, 121.32, 121.28, 119.9, 29.5, 21.2, 20.9, 18.9; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{25}H_{24}N_2O_3SNa^+$ 455.1400; Found 455.1401.



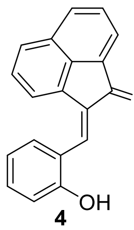
15a

Yellow solid, 62% yield; mp 286–288 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 11.70 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.47–7.32 (m, 4H), 7.32–7.25 (m, 1H), 7.22–7.11 (m, 3H), 7.10–6.99 (m, 2H), 6.88 (d, J = 8.0 Hz, 2H), 3.21 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 167.4, 144.5, 144.2, 138.1, 134.6, 133.2, 130.5, 128.0, 125.5, 125.4, 125.1, 122.9, 122.7, 122.2, 121.90, 121.86, 120.6, 111.1, 109.0, 106.5, 26.4, 21.0; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{25}H_{21}N_3O_3SNa^+$ 466.1196; Found 466.1195.



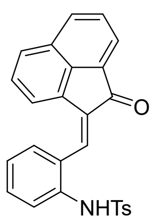
15b

Yellow solid, 67% yield; mp 297–299 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 11.72 (s, 1H), 8.45 (s, 1H), 8.29–8.22 (m, 1H), 8.16–8.09 (m, 1H), 7.59–7.48 (m, 2H), 7.39–7.31 (m, 2H), 7.25–7.12 (m, 4H), 7.11–7.05 (m, 1H), 7.03 (d, J = 8.0 Hz, 1H), 3.24 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 165.4, 147.9, 146.8, 144.7, 142.4, 136.0, 133.3, 130.9, 130.3, 129.9, 128.0, 125.5, 123.3, 122.1, 120.5, 119.8, 118.7, 118.3, 109.0, 108.5, 26.4, 21.3; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{24}H_{20}N_4O_3SNa^+$ 467.1148; Found 467.1152.



4

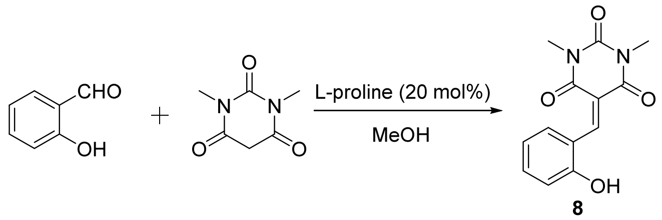
Yellow solid, 82% yield; mp 196–198 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.27 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 6.8 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 1H), 7.89–7.82 (m, 2H), 7.79 (d, *J* = 6.8 Hz, 1H), 7.68–7.60 (m, 1H), 7.44–7.34 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 7.04–6.97 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 192.2, 157.3, 139.9, 132.7, 132.4, 132.2, 131.6, 130.8, 130.3, 128.9, 128.7, 126.4, 121.9, 121.8, 120.3, 119.3, 116.5; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{19}H_{13}O_2^+$ 273.0910; Found 273.0911.



13

Yellow solid, 65% yield; mp 218–220 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.04 (s, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.10–7.97 (m, 2H), 7.91–7.83 (m, 1H), 7.74 (s, 1H), 7.71–7.65 (m, 1H), 7.59–7.49 (m, 2H), 7.45–7.38 (m, 2H), 7.38–7.23 (m, 3H), 6.68 (d, *J* = 7.6 Hz, 2H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 191.6, 142.9, 140.1, 137.3, 135.8, 134.6, 132.2, 131.99, 131.97, 131.90, 131.0, 130.8, 130.4, 129.6, 129.1, 128.8, 127.1, 126.9, 126.5, 121.8, 120.5, 20.4; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{26}H_{20}NO_3S^+$ 426.1158; Found 426.1157.

2.3 Procedure for the preparation of substrate 8



To a solution of salicylaldehyde (1.22 g, 10.0 mmol) in MeOH (30 mL) were added 1,3-dimethylbarbituric acid (1.72 g, 11.0 mmol) and L-proline (0.23 g, 2.0 mmol). The mixture was stirred at room temperature for 5 h, and monitored by TLC (petroleumether/EtOAc = 5/1). After completion, the solid was collected by filtration and then dried in vacuo to give product **8**: 1.85 g (7.11 mmol), as a yellow solid, 71% yield; mp 204–206 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.59 (s, 1H), 8.67 (s, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 7.41–7.34 (m, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.86–6.80 (m, 1H), 3.23 (s, 3H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 162.9, 160.9, 159.4, 151.8, 151.7, 135.1, 133.1, 120.5, 118.6, 117.4, 115.9, 29.0, 28.4; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{13}H_{13}N_2O_4^+$ 261.0807; Found 261.0814.

Other substrates, including **2a**–**2l**, **6** and **10x** are known compounds, and the spectra of these compounds were consistent with the reports.[1,3]

References

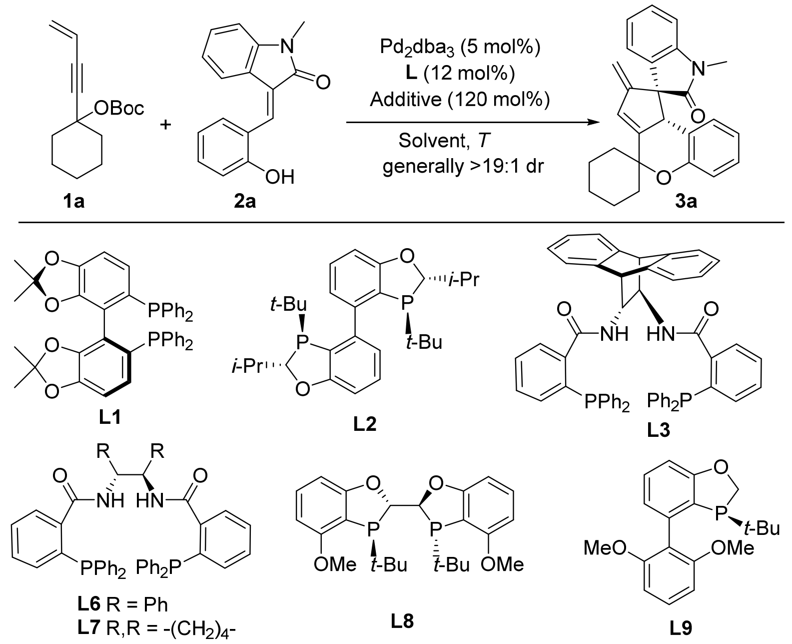
1. (*a*) C. Li, Z. Zhou, Y. Li, Y. Guo and S. Ma, *Chem. Commun.* 2023, **59**, 3727–3730; (*b*) Z.-L. Wang and R. Zhu, *J. Am. Chem. Soc.* 2024, **146**, 19377–19385.

2. S. Sambhaji Vagh, B.-J. Hou, A. Edukondalu, P.-C. Wang, Y.-R. Chen and W. Lin, *Adv. Synth. Catal.* 2021, **363**, 5429–5435.

3. J. Sun, X. Liu, Q. Sun, Y. Han and C.-G. Yan, *J. Org. Chem.* 2023, **88**, 11562–11580.

3. Detailed condition optimisations

3.1 Detailed condition optimisations for asymmetric synthesis of 3a[a]

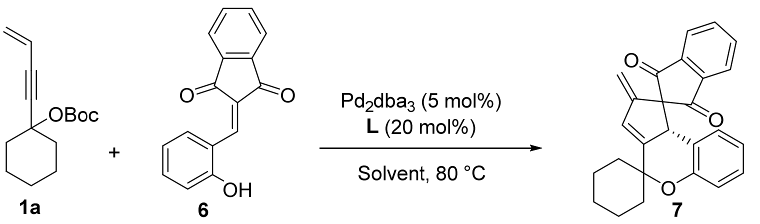


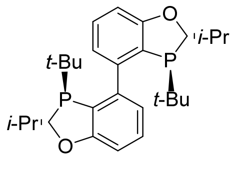
Entry	Ligand	Solvent	*T* (° C)	*t* (h)	Additive	Yield (%)[b]	ee (%)[c]
1	**L1**	MeCN	80	24	/	56	29
2	**L2**	MeCN	80	24	/	33	58
3	**L3**	MeCN	80	24	/	63	74
4	**L6**	MeCN	80	24	/	trace	/
5	**L7**	MeCN	80	24	/	trace	/
6	**L8**	MeCN	80	24	/	40	9
7[d]	**L9**	MeCN	80	24	/	48	8
8	**L3**	MeCN	50	48	/	63	85
9	**L3**	DCE	50	48	/	32	78
10	**L3**	NMP	50	48	/	58	87
11	**L3**	DMF	50	48	/	62	85

12	**L3**	DMA	50	48	/	57	88
13[e]	**L3**	DMA	50	48	/	60	88
14[e]	**L3**	DMA	50	48	KHCO$_3$	73	89
15[e]	**L3**	DMA	45	60	KHCO$_3$	64	91
16[e]	**L3**	DMA	45	60	K$_2$CO$_3$	62	91
17[e]	**L3**	DMA	45	60	K$_3$PO$_4$	61	91
18[e]	**L3**	DMA	45	60	Et$_3$N	trace	/
19[e]	**L3**	DMA	45	60	BzOH	trace	/
20[e,f]	**L3**	DMA	45	60	KHCO$_3$	72	91
21[e,f,g]	**L3**	DMA	45	60	KHCO$_3$	48	91

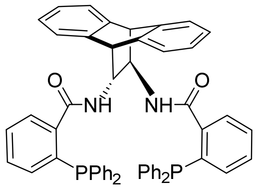
[a] Unless noted otherwise, reactions were performed with 3-vinyl propargylic carbonate **1a** (0.1 mmol), (*E*)-3-(2-hydroxybenzylidene)oxindole **2a** (0.120 mmol), Pd$_2$dba$_3$ (5 mol%), ligand **L** (12 mol%) in degassed solvent (1.0 mL) under Ar atmosphere. [b] Yield of the isolated product. [c] Determined by HPLC analysis on a chiral stationary phase, and >19:1 dr was determined by ^{1}H NMR analysis of crude product. [d] With **L9** (20 mol%). [e] With DMA (2.0 mL). [f] With **1a** (0.15 mmol) and **2a** (0.1 mmol). [g] With Pd$_2$dba$_3$ (2.5 mol%), **L3** (6 mol%). NMP = *N*-methylpyrrolidin-2-one; DMF = Dimethylformamide; DMA = Dimethylacetamide.

3.2 Detailed condition optimisations for asymmetric synthesis of 7[a]

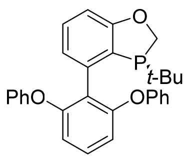




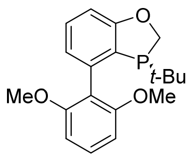
L2



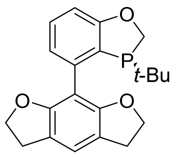
L3



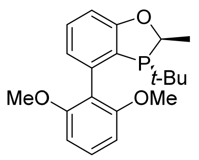
L4



L9



L10



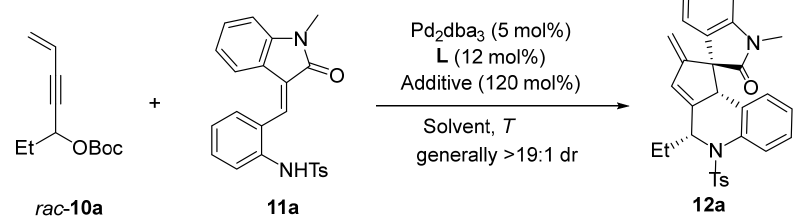
L11

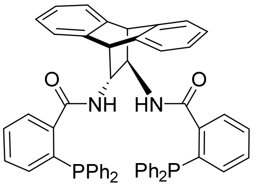
Entry	Ligand	Solvent	*T* (° C)	*t* (h)	Yield (%)[b]	ee (%)[c]
1[d]	**L2**	MeCN	80	24	trace	/
2[d]	**L3**	MeCN	80	24	trace	/
3	**L3**	toluene	80	24	trace	/
4	**L4**	MeCN	80	24	trace	/
5	**L4**	toluene	80	24	57	51

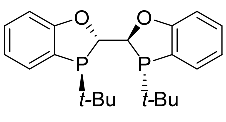
6	**L9**	toluene	80	24	65	3
7	**L10**	toluene	80	24	64	42
8	**L11**	toluene	80	24	63	10
9	**L4**	THF	80	24	53	48
10	**L4**	DMA	80	24	trace	/
11	**L4**	DCE	80	24	46	49
12	**L4**	toluene	60	36	35	52

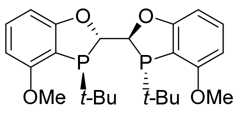
[a] Unless noted otherwise, reactions were performed with 3-vinyl propargylic carbonate **1a** (0.15 mmol), 2-(2-hydroxybenzylidene)-1*H*-indene-1,3(2*H*)-dione **6** (0.1 mmol), Pd_2dba_3 (5 mol%) and ligand **L** (20 mol%) in degassed solvent (1.0 mL) under Ar atmosphere. [b] Yield of the isolated product. [c] Determined by HPLC analysis on a chiral stationary phase, and >19:1 dr was determined by ^{1}H NMR analysis of crude product. [d] With ligand **L** (12 mol%).

3.3 Detailed condition optimisations for asymmetric synthesis of 12a[a]







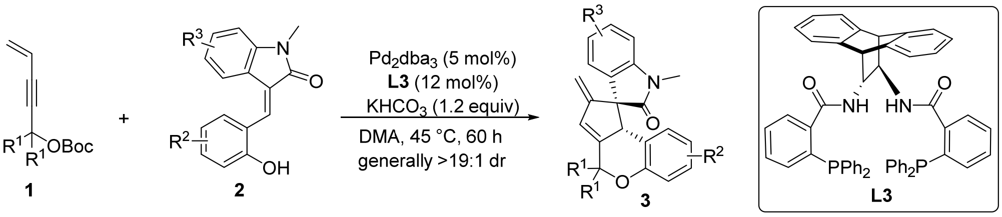


Entry	Ligand	Solvent	*T* (° C)	*t* (h)	Additive	Yield (%)[b]	ee (%)[c]
1	**L3**	MeCN	60	36	$KHCO_3$	54	36
2	**L5**	MeCN	60	36	$KHCO_3$	72	83
3	**L8**	MeCN	60	36	$KHCO_3$	52	85
4	**L5**	MeCN	50	48	$KHCO_3$	71	85
5	**L5**	MeCN	45	72	$KHCO_3$	70	93
6	**L5**	MeCN	40	72	$KHCO_3$	low conv.	/
7	**L5**	MeCN	45	72	/	low conv.	/
8[d]	**L5**	MeCN	45	72	$KHCO_3$	35	92
9[e]	**L5**	MeCN	45	72	$KHCO_3$	71	85
10	**L5**	MeCN	45	72	K_2CO_3	low conv	/
11	**L5**	toluene	45	72	$KHCO_3$	38	74
12	**L5**	THF	45	72	$KHCO_3$	71	75
13	**L5**	DMA	45	72	$KHCO_3$	low conv.	/

[a] Unless noted otherwise, reactions were performed with *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (0.2 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (0.1 mmol), Pd_2dba_3 (5 mol%), ligand **L** (12 mol%) in degassed solvent (1.0 mL) under Ar atmosphere. [b] Yield of the isolated product. [c] Determined by HPLC analysis on a chiral stationary phase, and >19:1 dr was determined by ^1H NMR analysis of crude product. [d] With MeCN (0.5 mL). [e] With MeCN (2.0 mL).

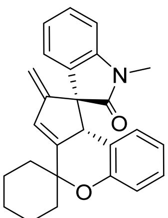
4. General procedure for the reactions of achiral 4-alken-2-ynyl carbonates

4.1 General procedure for synthesis of 3 and 5



General procedure: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 4-alken-2-ynyl carbonate **1** (0.15 mmol, 1.5 equiv), activated alkene **2** (0.1 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give the product.

*Note: racemic **3** was prepared from **1** and **2** through the same procedure under the catalysis of* $Pd(PPh_3)_4$ *(5 mol%).*



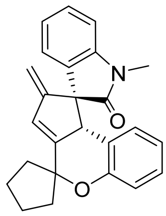
3a

Synthesis of 3a: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3a**: 27.6 mg (0.0720 mmol), as a white solid, 72% yield; mp 157−159 °C; >19:1 dr, determind by ^1H

NMR analysis of crude product; $[\alpha_D^{25}]$ = −58.3 (*c* = 3.46 in $CHCl_3$); 91% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.10 min (minor), t_R = 7.36 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.12–7.05 (m, 1H), 6.95–6.87 (m, 1H), 6.84–6.76 (m, 2H), 6.70–6.61 (m, 2H), 6.48–6.41 (m, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 6.17 (d, *J* = 7.6 Hz, 1H), 4.96 (s, 1H), 4.76 (s, 1H), 4.55 (s, 1H), 3.40 (s, 3H), 2.15–2.05 (m, 1H), 2.04–1.93 (m, 3H), 1.81–1.67 (m, 2H), 1.59–1.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.7, 155.8, 152.9, 152.5, 142.6, 132.5, 127.74, 127.68, 127.6, 124.5, 122.9, 122.7, 121.8, 120.4, 117.5, 108.0, 105.3, 76.1, 62.9, 49.9, 34.4, 32.5, 26.8, 25.6, 21.7, 21.3; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{26}H_{25}NO_2Na^+$ 406.1778; Found 406.1777.

Asymmetric synthesis of 3a on a 1.0 mmol scale

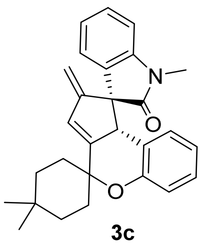
To an oven-dried 50 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (375.5 mg, 1.500 mmol), (*E*)-3-(2-hydroxy benzylidene) -1-methylindolin-2-one **2a** (251.3 mg, 1.000 mmol) , Pd_2dba_3 (45.8 mg, 0.0500 mmol, 5 mol%), **L3** (97.5 mg, 0.120 mmol, 12 mol%) and $KHCO_3$ (120.2 mg, 1.201 mmol). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (20 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3a**: 268.5 mg (0.7001 mmol), as a white solid, 70% yield, >19:1 dr, 91% ee.



3b

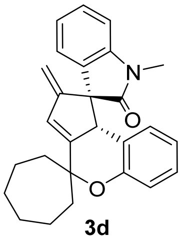
Synthesis of 3b: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclopentyl *tert*-butyl carbonate **1b** (35.5 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3b**: 28.1 mg (0.0761 mmol), as a white solid, 76% yield; mp 146–148 °C; >19:1 dr, determind by ^{1}H

NMR analysis of crude product; $[\alpha_D^{25}]$ = −77.6 (*c* = 5.28 in $CHCl_3$); 95% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t_R = 7.61 min (minor), t_R = 9.69 min (major); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13–7.05 (m, 1H), 6.93–6.86 (m, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.75–6.70 (m, 1H), 6.70–6.62 (m, 2H), 6.48–6.41 (m, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 6.16 (d, *J* = 8.0 Hz, 1H), 4.96 (s, 1H), 4.77 (s, 1H), 4.55 (s, 1H), 3.40 (s, 3H), 2.29–2.14 (m, 2H), 2.11–1.99 (m, 2H), 1.91–1.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.7, 155.7, 153.5, 150.5, 142.6, 132.4, 127.8, 127.6, 123.6, 123.0, 122.7, 121.8, 120.4, 117.6, 108.0, 105.5, 86.3, 63.1, 50.7, 36.4, 36.0, 26.8, 23.8, 23.6; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{25}H_{23}NO_2Na^+$ 392.1621; Found 392.1623.



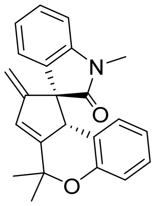
3c

Synthesis of 3c: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)-4,4-dimethylcyclohexyl *tert*-butyl carbonate **1c** (41.7 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **3c**: 24.7 mg (0.0600 mmol), as a white solid, 60% yield; mp 197−198 °C; >19:1 dr, determind by ^1H NMR analysis of crude product; $[\alpha_D^{25}]$ = −31.5 (*c* = 6.32 in $CHCl_3$); 56% ee, determined by HPLC analysis (Daicel Chiralpak IBN-5, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.87 min (minor), t_R = 8.54 min (major); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.12–7.02 (m, 1H), 6.95–6.87 (m, 1H), 6.84–6.73 (m, 2H), 6.70–6.57 (m, 2H), 6.48–6.41 (m, 1H), 6.25 (d, *J* = 2.8 Hz, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 4.96 (s, 1H), 4.76 (s, 1H), 4.55 (s, 1H), 3.39 (s, 3H), 2.18–2.08 (m, 1H), 2.06–1.99 (m, 1H), 1.96–1.80 (m, 2H), 1.68–1.58 (m, 1H), 1.55–1.40 (m, 2H), 1.20–1.13 (m, 1H), 1.01 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.7, 155.8, 152.9, 152.3, 142.6, 132.4, 127.8, 127.7, 127.6, 124.4, 122.9, 122.7, 121.8, 120.4, 117.5, 108.0, 105.4, 75.9, 62.9, 50.0, 34.3, 34.0, 31.2, 30.5, 29.7, 28.6, 26.8, 25.2; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{30}NO_2^+$ 412.2271; Found 412.2274.



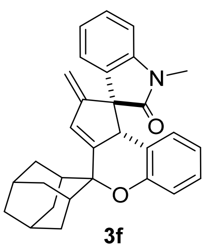
3d

Synthesis of 3d: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cycloheptyl *tert*-butyl carbonate **1d** (39.7 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **3d**: 25.1 mg (0.0631 mmol), as a white solid, 63% yield; mp 174–176 °C; >19:1 dr, determind by ^1H NMR analysis of crude product; $[\alpha_D^{25}] = -55.6$ (c = 4.32 in $CHCl_3$); 81% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.26 min (minor), t_R = 7.18 min (major); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13–7.04 (m, 1H), 6.94–6.85 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.78–6.71 (m, 1H), 6.70–6.57 (m, 2H), 6.48–6.39 (m, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 6.15 (d, *J* = 7.6 Hz, 1H), 4.96 (s, 1H), 4.74 (s, 1H), 4.55 (s, 1H), 3.40 (s, 3H), 2.36–2.26 (m, 1H), 2.19–2.05 (m, 2H), 2.02–1.91 (m, 1H), 1.84–1.61 (m, 6H), 1.56–1.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.7, 155.7, 153.2, 153.0, 142.6, 132.5, 127.74, 127.67, 127.5, 124.4, 122.9, 122.7, 121.6, 120.2, 117.6, 108.0, 105.3, 80.7, 62.9, 49.8, 38.4, 35.3, 30.0, 29.8, 26.8, 22.4, 21.6; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{28}NO_2^+$ 398.2115; Found 398.2111.

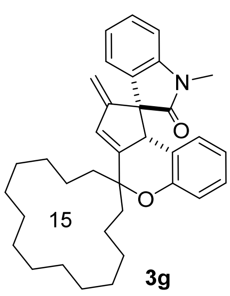


3e

Synthesis of 3e: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (2-methylhex-5-en-3-yn-2-yl) carbonate **1e** (31.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3e**: 23.1 mg (0.0672 mmol), as a white solid, 67% yield; mp 135−137 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −96.5 (c = 7.23 in $CHCl_3$); 92% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.07 min (minor), t_R = 6.70 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13–7.06 (m, 1H), 6.95–6.86 (m, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.76–6.70 (m, 1H), 6.70–6.64 (m, 1H), 6.64–6.56 (m, 1H), 6.47–6.40 (m, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 4.97 (s, 1H), 4.78 (s, 1H), 4.56 (s, 1H), 3.40 (s, 3H), 1.74 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.6, 155.6, 153.2, 152.2, 142.6, 132.4, 127.8, 127.73, 127.70, 124.2, 122.9, 122.7, 121.0, 120.3, 117.4, 108.0, 105.5, 75.3, 63.0, 49.8, 26.8, 26.2, 24.9; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{22}NO_2^+$ 344.1645; Found 344.1644.

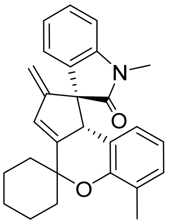

3f

Synthesis of 3f: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 2-(but-3-en-1-yn-1-yl)adamantan-2-yl *tert*-butyl carbonate **1f** (45.4 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methyl indolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (5.8 mg, 0.0050 mmol, 5 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 60 °C for 24 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **3f**: 25.7 mg (0.0590 mmol), as a white solid, 59% yield; mp 188–190 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.11–7.02 (m, 1H), 6.95–6.87 (m, 1H), 6.85–6.74 (m, 2H), 6.69–6.61 (m, 1H), 6.59–6.53 (m, 1H), 6.48–6.39 (m, 2H), 6.15 (d, *J* = 8.0 Hz, 1H), 4.96 (s, 1H), 4.70 (s, 1H), 4.50 (s, 1H), 3.38 (s, 3H), 2.66–2.57 (m, 1H), 2.46–2.40 (m, 1H), 2.35–2.27 (m, 1H), 2.25–2.17 (m, 1H), 2.10–2.00 (m, 1H), 2.00–1.88 (m, 3H), 1.85–1.69 (m, 5H), 1.50–1.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.9, 156.0, 152.7, 151.4, 142.6, 132.8, 127.74, 127.68, 127.63, 126.7, 123.4, 123.3, 122.6, 120.5, 117.6, 107.8, 105.3, 80.9, 62.5, 51.0, 37.5, 35.4, 34.8, 33.8, 32.6, 31.8, 31.6, 27.3, 27.1, 26.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{30}H_{29}NO_2Na^+$ 458.2091; Found 458.2101.



3g

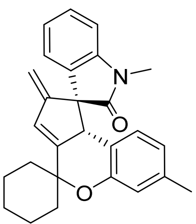
Synthesis of 3g: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclopentadecyl *tert*-butyl carbonate **1g** (55.2 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methyl indolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), Pd(PPh$_3$)$_4$ (5.8 mg, 0.0050 mmol, 5 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 60 °C for 24 h, and monitored by TLC (EtOAc/petroleum ether = 1/9). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/9) to give the product **3g**: 33.7 mg (0.0661 mmol), as a white solid, 66% yield; mp 115–117 °C; dr = 10:1, determind by ^{1}H NMR analysis of crude product; ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.10–7.05 (m, 1H), 6.92–6.87 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.68–6.61 (m, 2H), 6.45–6.39 (m, 1H), 6.26 (d, *J* = 2.8 Hz, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 4.96 (s, 1H), 4.69 (s, 1H), 4.55 (s, 1H), 3.39 (s, 3H), 2.06–1.72 (m, 4H), 1.52–1.25 (m, 24H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 178.6, 155.6, 153.1, 151.7, 142.6, 132.4, 127.7, 127.7, 127.5, 125.7, 122.9, 122.7, 121.4, 120.2, 117.3, 108.0, 105.2, 80.1, 62.9, 49.8, 35.2, 32.4, 27.8, 27.5, 27.0, 26.9, 26.8, 26.7, 26.6, 26.4, 26.3, 21.8, 21.0; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{35}H_{44}NO_2^+$ 510.3367; Found 510.3368.



3h

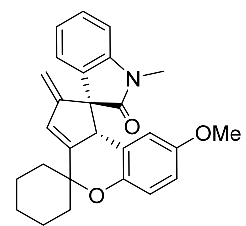
Synthesis of 3h: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxy-3-methylbenzylidene)-1-methylindolin-2-one **2b** (26.5 mg, 0.0999 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3h**: 23.9 mg (0.0601 mmol), as a white solid, 60% yield; mp 151–153 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = +96.5 (*c* = 5.22 in CHCl$_3$); 90% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0

mL/min, l = 254 nm) t_R = 5.09 min (minor), t_R = 6.26 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) δ 7.14–7.03 (m, 1H), 6.84–6.73 (m, 2H), 6.71–6.57 (m, 2H), 6.34 (t, *J* = 7.2 Hz, 1H), 6.20 (d, *J* = 2.8 Hz, 1H), 6.01 (d, *J* = 7.6 Hz, 1H), 4.94 (s, 1H), 4.76 (s, 1H), 4.53 (s, 1H), 3.39 (s, 3H), 2.21 (s, 3H), 2.19–2.12 (m, 1H), 2.05–1.91 (m, 3H), 1.85–1.68 (m, 2H), 1.60–1.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.8, 155.9, 153.0, 151.0, 142.6, 132.6, 128.9, 127.7, 126.5, 125.1, 123.8, 122.9, 122.6, 121.1, 119.7, 108.0, 105.1, 75.9, 63.0, 50.0, 34.5, 32.5, 26.8, 25.7, 21.6, 16.3; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{28}NO_2^+$ 398.2115; Found 398.2114.



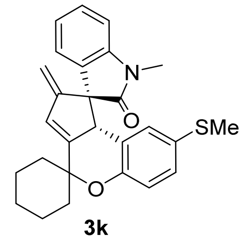
3i

Synthesis of 3i: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxy-4-methylbenzylidene)-1-methylindolin-2-one **2c** (26.5 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3h**: 29.9 mg (0.0752 mmol), as a white solid, 75% yield; mp 155−157 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = +84.3 (*c* = 5.87 in $CHCl_3$); 90% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.33 min (minor), t_R = 8.62 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) δ 7.14–7.05 (m, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.72–6.58 (m, 3H), 6.31–6.23 (m, 1H), 6.21 (d, *J* = 2.8 Hz, 1H), 6.04 (d, *J* = 8.0 Hz, 1H), 4.94 (s, 1H), 4.72 (s, 1H), 4.53 (s, 1H), 3.39 (s, 3H), 2.12 (s, 3H), 2.11–1.83 (m, 4H), 1.80–1.67 (m, 2H), 1.62–1.24 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.8, 155.9, 152.8, 152.7, 142.6, 137.6, 132.5, 127.7, 127.3, 124.3, 123.0, 122.7, 121.4, 118.7, 117.9, 107.9, 105.2, 76.0, 62.9, 49.7, 34.4, 32.6, 26.7, 25.6, 21.7, 21.3, 21.1; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{28}NO_2^+$ 398.2115; Found 398.2111.



3j

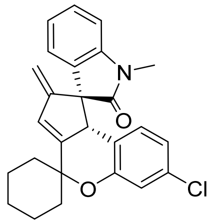
Synthesis of 3j: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxy-5-methoxy benzylidene) -1-methylindolin-2-one **2d** (28.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3j**: 29.8 mg (0.0721 mmol), as a white solid, 72% yield; mp 167−169 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = +142.2 (*c* = 6.34 in $CHCl_3$); 90% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 8.19 min (minor), t_R = 12.70 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.1–7.07 (m, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.74–6.65 (m, 3H), 6.52–6.47 (m, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 5.71 (d, *J* = 3.4 Hz, 1H), 4.97 (s, 1H), 4.71 (s, 1H), 4.56 (s, 1H), 3.39 (s, 3H), 3.36 (s, 3H), 2.15–1.89 (m, 4H), 1.79–1.64 (m, 2H), 1.57–1.33 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.7, 155.6, 153.2, 152.6, 147.0, 142.6, 132.4, 127.9, 124.5, 123.0, 122.9, 122.3, 118.2, 114.8, 111.4, 107.9, 105.4, 75.9, 62.9, 55.4, 50.4, 34.4, 32.3, 26.8, 25.6, 21.7, 21.3; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{28}NO_3^+$ 414.2064; Found 414.2069.



3k

Synthesis of 3k: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxy-5-(methyl thio)benzylidene)-1-methylindolin-2-one **2e** (29.7 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3k**: 34.0 mg (0.0791 mmol), as a white solid, 79%

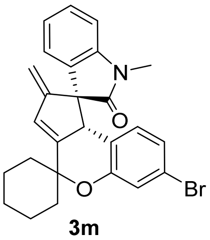
yield; mp 211–213 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −131.7 (*c* = 5.81 in CHCl$_3$); 89% ee, determined by HPLC analysis (Daicel Chiralpak IB, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t$_R$ = 6.27 min (minor), t$_R$ = 7.28 min (major); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.14–7.05 (m, 1H), 6.94–6.88 (m, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.73–6.65 (m, 2H), 6.63–6.58 (m, 1H), 6.25 (d, *J* = 2.8 Hz, 1H), 6.19–6.10 (m, 1H), 4.98 (s, 1H), 4.72 (s, 1H), 4.56 (s, 1H), 3.40 (s, 3H), 2.15–2.00 (m, 2H), 1.99 (s, 3H), 1.98–1.89 (m, 2H), 1.81–1.67 (m, 2H), 1.59–1.27 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 178.6, 155.4, 151.9, 151.7, 142.6, 132.3, 129.3, 128.6, 128.2, 127.9, 124.9, 123.1, 122.9, 122.6, 118.0, 108.0, 105.8, 76.4, 62.7, 50.0, 34.3, 32.6, 26.8, 25.6, 21.6, 21.3, 18.1; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{27}H_{27}NO_2SNa^+$ 452.1655; Found 452.1648.



3l

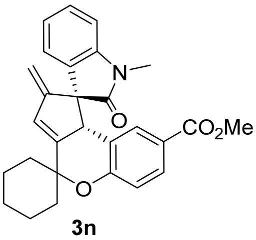
Synthesis of 3l: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(4-chloro-2-hydroxybenzylidene)-1-methylindolin-2-one **2f** (28.6 mg, 0.100 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3l**: 30.6 mg (0.0732 mmol), as a white solid, 73% yield; mp 176–178 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −73.4 (*c* = 6.72 in CHCl$_3$); 88% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t$_R$ = 5.75 min (minor), t$_R$ = 6.88 min (major); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.15–7.04 (m, 1H), 6.90–6.76 (m, 2H), 6.74–6.66 (m, 1H), 6.64–6.58 (m, 1H), 6.48–6.37 (m, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 6.07 (d, *J* = 8.4 Hz, 1H), 4.97 (s, 1H), 4.70 (s, 1H), 4.55 (s, 1H), 3.39 (s, 3H), 2.18–2.05 (m, 1H), 2.04–1.90 (m, 3H), 1.81–1.67 (m, 2H), 1.58–1.29 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 178.5, 155.5, 153.7, 151.5, 142.5, 132.7, 132.1, 128.5, 128.0, 124.9, 122.93, 122.91, 120.6, 120.4, 117.8, 108.1, 105.8, 62.7, 49.4, 34.3, 32.6, 26.8, 25.5, 21.6, 21.3; HRMS (ESI-TOF) *m/z*: $C_{26}H_{24}{}^{35}ClNO_2Na^+$ 440.1388; Found 440.1398; [M + Na]$^+$ Calcd for $C_{26}H_{24}{}^{37}ClNO_2Na^+$

442.1358; Found 442.1350.



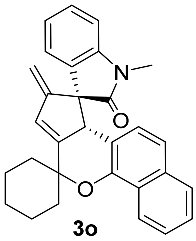
3m

Synthesis of 3m: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(4-bromo-2-hydroxybenzylidene)-1-methylindolin-2-one **2g** (33.0 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3m**: 33.9 mg (0.0733 mmol), as a white solid, 73% yield; mp 144–146 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −174.8 (*c* = 8.32 in $CHCl_3$); 85% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.19 min (minor), t_R = 8.25 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.16–7.08 (m, 1H), 6.98 (d, *J* = 2.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.74–6.68 (m, 1H), 6.63–6.59 (m, 1H), 6.59–6.54 (m, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 6.01 (d, *J* = 8.4 Hz, 1H), 4.97 (s, 1H), 4.68 (s, 1H), 4.55 (s, 1H), 3.39 (s, 3H), 2.13–2.06 (m, 1H), 2.03–1.90 (m, 3H), 1.78–1.68 (m, 2H), 1.61–1.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.5, 155.5, 153.8, 151.4, 142.5, 132.1, 128.8, 128.0, 124.9, 123.5, 123.0, 122.9, 120.9, 120.7, 120.5, 108.1, 105.8, 62.6, 49.4, 34.3, 32.7, 26.8, 25.5, 21.4, 21.3; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{25}{}^{79}BrNO_2{}^+$ 462.1063; Found 462.1060; Calcd for $C_{26}H_{25}{}^{81}BrNO_2{}^+$ 464.1043; Found 464.1046.



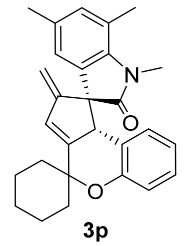
3n

Synthesis of 3n: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), methyl (*E*)-4-hydroxy -3-((1-methyl-2-oxoindolin-3-ylidene)methyl)benzoate **2h** (30.9 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **3n**: 23.5 mg (0.0532 mmol), as a white solid, 53% yield; mp 211–213 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = +82.6 (*c* = 4.25 in $CHCl_3$); 91% ee, determined by HPLC analysis (Daicel Chiralpak IB, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.85 min (minor), t_R = 8.02 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58 (d, *J* = 8.4 Hz, 1H), 7.07–7.03 (m, 1H), 6.93 (s, 1H), 6.85–6.76 (m, 2H), 6.67–6.55 (m, 2H), 6.29 (d, *J* = 2.0 Hz, 1H), 5.02 (s, 1H), 4.75 (s, 1H), 4.62 (s, 1H), 3.71 (s, 3H), 3.43 (s, 3H), 2.16–2.07 (m, 1H), 2.07–1.93 (m, 3H), 1.80–1.69 (m, 2H), 1.60–1.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.3, 166.3, 157.0, 154.9, 150.9, 142.7, 132.0, 130.0, 129.4, 128.1, 125.4, 122.7, 122.5, 122.0, 121.4, 117.3, 108.2, 106.3, 63.0, 51.6, 50.0, 34.2, 32.9, 26.8, 25.5, 21.6, 21.3; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{28}H_{27}NO_4Na^+$ 464.1832; Found 464.1836.



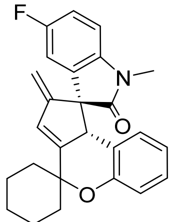
3o

Synthesis of 3o: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-((1-hydroxynaphthalen-2-yl)methylene)-1-methyl indolin-2-one **2i** (30.1 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **3o**: 26.5 mg (0.0611 mmol), as a white solid, 61% yield; mp 193−195 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −212.6 (*c* = 7.32 in $CHCl_3$); 97% ee, determined by HPLC analysis (Daicel Chiralpak IF, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 9.75 min (minor), t_R = 13.43 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.49–7.44 (m, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.19–7.11 (m, 1H), 7.11–7.05 (m, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 6.81–6.70 (m, 1H), 6.56–6.45 (m, 1H), 6.44–6.36 (m, 2H), 6.34 (d, *J* = 2.8 Hz, 1H), 5.17 (s, 1H), 4.96 (s, 1H), 4.56 (s, 1H), 3.27 (s, 3H), 2.26–2.14 (m, 1H), 2.14–1.96 (m, 3H), 1.86–1.65 (m, 2H), 1.62–1.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.7, 156.0, 153.4, 151.8, 142.2, 132.9, 131.9, 128.9, 128.6, 128.0, 127.3, 125.1, 125.0, 122.9, 122.8, 122.0, 121.9, 119.2, 114.9, 107.6, 105.2, 63.7, 48.6, 34.4, 30.7, 26.9, 25.7, 22.0, 21.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{30}H_{28}NO_2^+$ 434.2115; Found 434.2113.



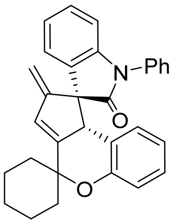
3p

Synthesis of 3p: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1,5,7-trimethyl indolin-2-one **2j** (27.9 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **3p**: 29.4 mg (0.0714 mmol), as a white solid, 71% yield; mp 167−168 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -132.5$ (*c* = 5.43 in $CHCl_3$); 82% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.01 min (minor), t_R = 6.70 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) δ 6.95–6.86 (m, 1H), 6.82–6.75 (m, 1H), 6.60 (s, 1H), 6.52–6.42 (m, 1H), 6.24 (s, 1H), 6.21 (d, *J* = 2.8 Hz, 1H), 6.18 (d, *J* = 7.6 Hz, 1H), 4.95 (s, 1H), 4.73 (s, 1H), 4.54 (s, 1H), 3.64 (s, 3H), 2.52 (s, 3H), 2.16–2.06 (m, 1H), 2.05–1.94 (m, 3H), 1.93 (s, 3H), 1.83–1.67 (m, 2H), 1.63–1.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.5, 156.5, 153.0, 152.5, 138.0, 133.1, 131.99, 131.96, 127.8, 127.5, 124.4, 121.9, 121.6, 120.3, 119.0, 117.3, 105.2, 76.1, 62.3, 50.2, 34.4, 32.6, 30.1, 25.7, 21.7, 21.4, 20.6, 19.0; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{30}NO_2^+$ 412.2271; Found 412.2270.



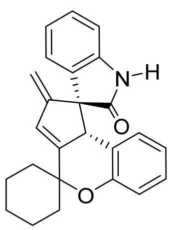
3q

Synthesis of 3q: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-5-fluoro-3-(2-hydroxybenzylidene)-1-methyl indolin-2-one **2k** (26.9 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3q**: 29.4 mg (0.0732 mmol), as a white solid, 73% yield; mp 133−135 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −89.5 (*c* = 8.32 in $CHCl_3$); 92% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.90 min (minor), t_R = 6.77 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.97–6.90 (m, 1H), 6.83–6.75 (m, 2H), 6.74–6.69 (m, 1H), 6.51–6.44 (m, 1H), 6.43–6.35 (m, 1H), 6.22 (d, *J* = 3.2 Hz, 1H), 6.18 (d, *J* = 7.6 Hz, 1H), 4.97 (s, 1H), 4.76 (s, 1H), 4.55 (s, 1H), 3.38 (s, 3H), 2.19–2.04 (m, 1H), 2.04–1.90 (m, 3H), 1.79–1.68 (m, 2H), 1.60–1.24 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.3, 159.1 (d, $^1J_{FC}$ = 239.5 Hz), 155.2, 153.0, 152.6, 138.6 (d, *J* = 1.9 Hz), 134.0 (d, $^3J_{FC}$ = 8.6 Hz), 128.0, 127.3, 124.3, 121.4, 120.5, 117.7, 114.1 (d, $^2J_{FC}$ = 23.6 Hz), 111.0 (d, $^1J_{FC}$ = 24.9 Hz), 108.4 (d, *J* = 8.2 Hz), 105.7, 76.1, 63.2, 49.8, 34.4, 32.5, 26.9, 25.6, 21.6, 21.3; ^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) −120.2; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{26}H_{25}FNO_2^+$ 402.1864; Found 402.1865.



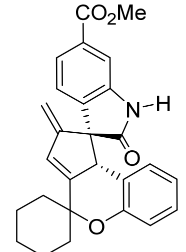
3r

Synthesis of 3r: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-phenylindolin-2-one **2l** (31.4 mg, 0.0100 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3r**: 27.7 mg (0.0622 mmol), as a white solid, 62% yield; mp 189−191 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −132.4 (*c* = 6.43 in $CHCl_3$); 91% ee, determined by HPLC analysis (Daicel Chiralpak IB, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 7.09 min (minor), t_R = 8.68 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.69–7.50 (m, 4H), 7.50–7.41 (m, 1H), 7.03–6.97 (m, 1H), 6.97–6.91 (m, 1H), 6.86–6.80 (m, 1H), 6.80–6.75 (m, 1H), 6.74–6.61 (m, 2H), 6.57–6.48 (m, 1H), 6.46–6.36 (m, 1H), 6.27 (d, *J* = 2.8 Hz, 1H), 5.04 (s, 1H), 4.86 (s, 1H), 4.75 (s, 1H), 2.20–2.09 (m, 1H), 2.08–1.92 (m, 3H), 1.84–1.67 (m, 2H), 1.58–1.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 178.0, 156.0, 153.1, 152.5, 142.5, 134.7, 132.2, 129.8, 128.2, 127.8, 127.63, 127.62, 126.5, 124.4, 123.2, 123.1, 121.8, 120.5, 117.6, 109.4, 105.6, 76.2, 63.1, 50.3, 34.4, 32.5, 25.6, 21.7, 21.3; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{31}H_{28}NO_2^+$ 446.2115; Found 446.2112.



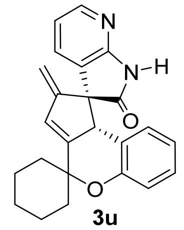
3s

Synthesis of 3s: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)indolin-2-one **2m** (23.7 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/8). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/8) to give the product **3s**: 26.3 mg (0.0712 mmol), as a white solid, 71% yield; mp 151−153 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = –231.5 (*c* = 4.34 in $CHCl_3$); 88% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.08 min (minor), t_R = 9.23 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.40–8.81 (m, 1H), 7.04–6.98 (m, 1H), 6.96–6.85 (m, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.68–6.57 (m, 2H), 6.52–6.44 (m, 1H), 6.38 (d, *J* = 7.6 Hz, 1H), 6.26 (d, *J* = 2.8 Hz, 1H), 5.02 (s, 1H), 4.80 (s, 1H), 4.73 (s, 1H), 2.19–2.08 (m, 1H), 2.06–1.93 (m, 3H), 1.77–1.39 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 155.7, 153.0, 152.6, 139.8, 133.0, 127.79, 127.77, 124.4, 123.3, 122.6, 121.7, 120.5, 117.5, 110.0, 105.6, 76.1, 63.4, 49.9, 34.4, 32.6, 25.6, 21.7, 21.4; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{25}H_{24}NO_2^+$ 370.1802; Found 370.1804.



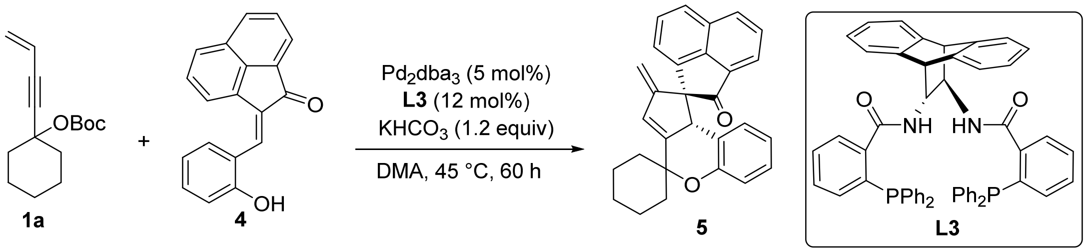
3t

Synthesis of 3t: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), methyl (*E*)-3-(2-hydroxybenzylidene)-2-oxo indoline-6-carboxylate **2n** (29.5 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3t**: 27.0 mg (0.0632 mmol), as a white solid, 63% yield; mp 175−177 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -176.2$ (*c* = 6.22 in $CHCl_3$); 96% ee, determined by HPLC analysis (Daicel Chiralpak IB, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t_R = 15.80 min (major), t_R = 20.27 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.62 (s, 1H), 7.55 (s, 1H), 7.42–7.32 (m, 1H), 6.96–6.89 (m, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.51–6.43 (m, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 6.25 (d, *J* = 2.4 Hz, 1H), 5.02 (s, 1H), 4.83 (s, 1H), 4.71 (s, 1H), 3.84 (s, 3H), 2.16–1.94 (m, 4H), 1.79–1.67 (m, 2H), 1.61–1.27 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 180.6, 166.5, 155.0, 152.9, 152.6, 139.8, 138.0, 129.8, 128.0, 127.5, 124.5, 124.2, 123.2, 121.3, 120.7, 117.6, 110.6, 106.0, 76.2, 63.3, 52.1, 49.9, 34.4, 32.5, 25.6, 21.6, 21.3; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{27}H_{26}NO_4^+$ 428.1856; Found 428.1853.



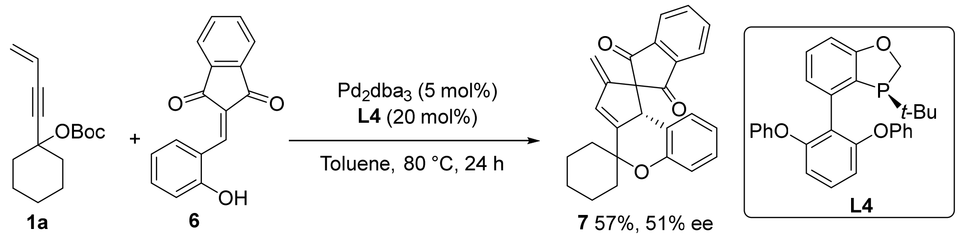
3u

Synthesis of 3u: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1,3-dihydro-2*H*-pyrrolo[2,3-*b*]pyridin-2-one **2o** (23.8 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **3u**: 24.5 mg (0.0661 mmol), as a white solid, 66% yield; mp 193−195 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -95.3$ (*c* = 6.12 in $CHCl_3$); 93% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.63 min (minor), t_R = 9.88 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.31 (s, 1H), 8.04 (d, *J* = 5.2 Hz, 1H), 6.99–6.94 (m, 1H), 6.89–6.85 (m, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.62–6.58 (m, 1H), 6.57–6.53 (m, 1H), 6.44 (d, *J* = 7.6 Hz, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 5.03 (s, 1H), 4.83 (s, 1H), 4.79 (s, 1H), 2.11–1.94 (m, 4H), 1.73–1.35 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.4, 155.5, 154.8, 152.9, 152.4, 146.2, 131.1, 128.1, 127.64, 127.60, 124.2, 121.3, 120.8, 118.2, 117.7, 106.1, 76.2, 63.2, 49.5, 34.3, 32.3, 25.6, 21.7, 21.3; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{24}H_{23}N_2O_2^+$ 371.1754; Found 371.1756.

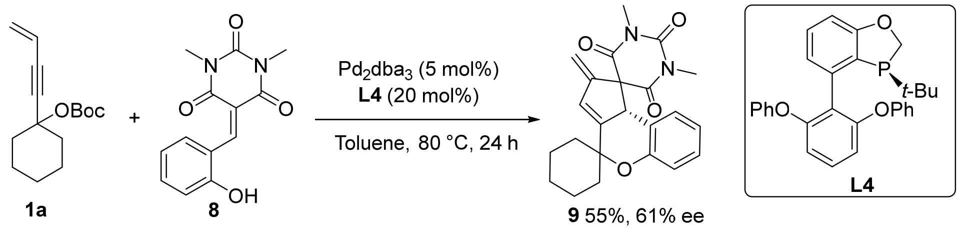


To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-2-(2-hydroxy benzylidene)acenaphthylen-1(2*H*)-one **4** (27.2 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L3** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry DMA (2.0 mL) was added via syringe. The mixture was stirred at 45 °C for 60 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **5**: 30.4 mg (0.0751 mmol), as a white solid, 75% yield; mp 163–165 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = +154.2 (*c* = 9.43 in $CHCl_3$); 83% ee, determined by HPLC analysis (Daicel Chiralpak IE, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t_R = 8.08 min (minor), t_R = 8.62 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) δ 8.19–8.05 (m, 2H), 7.77 (t, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.25–7.21 (m, 1H), 6.90–6.75 (m, 3H), 6.25 (d, *J* = 2.4 Hz, 1H), 6.21–6.12 (m, 1H), 5.79 (d, *J* = 7.6 Hz, 1H), 4.90 (s, 2H), 4.33 (s, 1H), 2.24–2.12 (m, 1H), 2.11–1.96 (m, 3H), 1.86–1.62 (m, 3H), 1.60–1.53 (m, 1H), 1.53–1.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 206.2, 157.9, 152.8, 152.6, 141.9, 141.6, 133.6, 132.0, 130.8, 128.8, 128.0, 127.8, 127.5, 124.4, 123.7, 122.2, 122.1, 120.1, 119.7, 117.5, 105.6, 76.2, 68.1, 49.7, 34.5, 32.6, 25.7, 21.8, 21.4; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{25}O_2^+$ 405.1849; Found 405.1851.

4.2 Procedure for asmmytric synthesis of 7 and 9



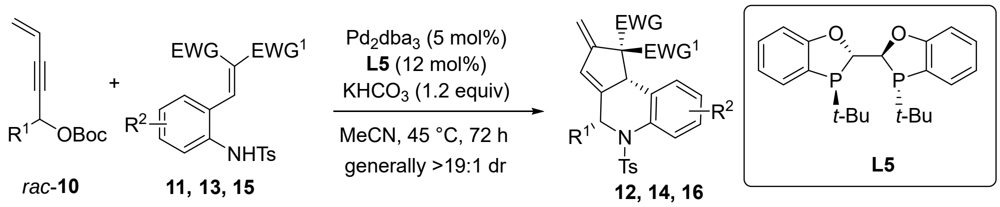
To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), 2-(2-hydroxy benzylidene)-1*H*-indene-1,3(2*H*)-dione **6** (25.0 mg, 0.0999 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%) and **L4** (9.1 mg, 0.020 mmol, 20 mol%). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry Tol (1.0 mL) was added via syringe. The mixture was stirred at 80 °C for 24 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **7**: 21.9 mg (0.0573 mmol), as a white solid, 57% yield; mp 234–236 °C; $[\alpha_D^{25}] = +175.3$ ($c = 4.23$ in CHCl$_3$); 51% ee, determined by HPLC analysis (Daicel Chiralpak IB, *n*-hexane/*i*-PrOH = 90/10, flow rate =1.0 mL/min, l = 254 nm) t$_R$ = 7.75 min (major), t$_R$ = 8.49 min (minor); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.20–8.13 (m, 1H), 7.94–7.84 (m, 3H), 7.07–6.98 (m, 1H), 6.94–6.85 (m, 1H), 6.58–6.50 (m, 1H), 6.21 (d, *J* = 7.6 Hz, 1H), 6.10 (d, *J* = 2.8 Hz, 1H), 4.97 (s, 1H), 4.86 (s, 1H), 4.28 (s, 1H), 2.17–2.10 (m, 1H), 2.03–1.88 (m, 3H), 1.78–1.68 (m, 2H), 1.60–1.23 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 201.3, 195.1, 154.4, 153.1, 153.0, 143.6, 142.7, 136.1, 135.6, 128.1, 126.6, 124.7, 123.71, 123.68, 121.9, 120.5, 118.1, 106.2, 76.0, 68.6, 47.2, 34.2, 32.8, 25.6, 21.6, 21.4; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{26}H_{22}NO_3Na^+$ 405.1461; Found 405.1459.



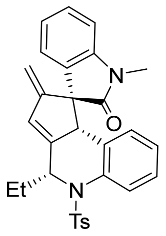
To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), 5-(2-hydroxy benzylidene)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione **8** (26.0 mg, 0.0999 mmol, 1.0 equiv),

Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%) and **L4** (9.1 mg, 0.020 mmol, 20 mol%). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry toluene (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 24 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **9**: 21.6 mg (0.0550 mmol), as a white solid, 55% yield; mp 148–150 °C; $[\alpha_D^{25}]$ = +98.3 (*c* = 5.32 in $CHCl_3$); 61% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.22 min (minor), t_R = 6.21 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.14–7.07 (m, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.82–6.75 (m, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 6.01 (d, *J* = 2.8 Hz, 1H), 5.13 (s, 1H), 5.07 (s, 1H), 4.76 (s, 1H), 3.52 (s, 3H), 3.08 (s, 3H), 2.15–2.06 (m, 1H), 2.02–1.85 (m, 3H), 1.77–1.60 (m, 3H), 1.52–1.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.0, 165.7, 154.5, 153.7, 153.2, 151.2, 128.2, 125.3, 122.3, 121.6, 120.9, 118.2, 105.7, 76.1, 65.6, 50.4, 34.2, 32.7, 29.4, 28.8, 25.5, 21.5, 21.2; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{24}N_2O_4Na^+$ 415.1628; Found 415.1628.

5 General procedure for reactions of racemic 1-alkyl-substituted 4-aken-2-ynyl carbonates 10



General procedure: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-alkyl-substituted 4-aken-2-ynyl carbonate **10** (0.2 mmol, 2.0 equiv), activated alkene **11**, **13** or **15** (0.1 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (9.8 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give the product.

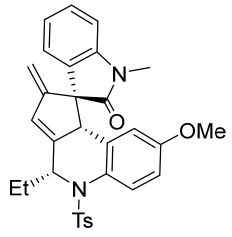


12a

Synthesis of 12a: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)-phenyl) benzene sulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12a**: 34.8 mg (0.0701 mmol), as a white solid, 70% yield; mp 134–136 °C; >19:1 dr, determind by ^1H NMR analysis of crude product; $[\alpha_D^{25}]$ = −135.7 (*c* = 12.3 in $CHCl_3$); 93% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 4.92 min (minor), t_R = 7.77 min (major); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (d, *J* = 8.0 Hz, 1H), 7.34–7.27 (m, 2H), 7.21–7.14 (m, 3H), 7.14–7.08 (m, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.79–6.68 (m, 2H), 6.58 (d, *J* = 6.8 Hz, 1H), 6.05 (s, 1H), 5.74 (d, *J* = 7.6 Hz, 1H), 5.33–5.20 (m, 1H), 4.71 (s, 1H), 4.38 (s, 1H), 3.31 (s, 3H), 3.02 (s, 1H), 2.45 (s, 3H), 1.73–1.52 (m, 2H), 1.17 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.3, 144.8, 142.5, 135.8, 134.3, 132.3, 131.6, 129.8, 129.5, 128.1, 126.7, 126.6, 126.5, 126.2, 124.4, 122.6, 122.4, 108.5, 103.3, 61.6, 58.1, 50.1, 31.5, 26.7, 21.7, 10.8; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{30}H_{28}N_2O_3SNa^+$ 519.1713; Found 519.1720.

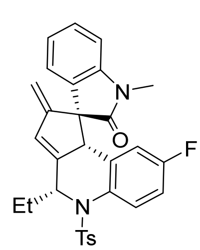
Recovered *S*-**10a**: 43% yield; $[\alpha_D^{25}]$ = −75.5 (*c* = 2.2 in $CHCl_3$); 68% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 99/1, flow rate =0.4 mL/min, l = 254 nm) t_R = 11.24 min (minor), t_R = 13.06 min (major).

Asymmetric synthesis of 12a on a 1.0 mmol scale: To an oven-dried 50 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (420.6 mg, 2.000 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl) benzenesulfon amide **11a** (404.5 mg, 1.000 mmol), $Pd_2(dba)_3$ (45.8 mg, 0.0500 mmol, 5 mol%), **L5** (46.4 mg, 0.120 mmol, 12 mol%) and $KHCO_3$ (120.2 mg, 1.201 mmol). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (10 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12a**: 322.9 mg (0.6502 mmol), as a white solid, 65% yield, >19:1 *dr*, 93% ee.



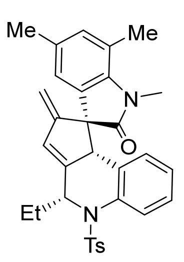
12b

Synthesis of 12b: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butylhept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-*N*-(4-methoxy-2-((1-methyl-2-oxoindolin-3-ylidene) methyl)phenyl)-4-methylbenzenesulfonamide **11b** (43.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12b**: 34.9 mg (0.0663 mmol), as a white solid, 66% yield; mp 154–156 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −114.7 (*c* = 0.30 in $CHCl_3$); 93% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.17 min (minor), t_R = 8.29 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51 (d, *J* = 8.8 Hz, 1H), 7.33–7.29 (m, 2H), 7.23–7.16 (m, 3H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.70–6.63 (m, 1H), 6.61 (d, *J* = 7.2 Hz, 1H), 6.04 (s, 1H), 5.29–5.16 (m, 2H), 4.72 (s, 1H), 4.37 (s, 1H), 3.31 (s, 3H), 3.28 (s, 3H), 2.93 (s, 1H), 2.47 (s, 3H), 1.70–1.62 (m, 1H), 1.59–1.49 (m, 1H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 157.7, 154.9, 153.2, 144.8, 142.5, 135.8, 133.4, 131.8, 130.6, 129.8, 128.2, 126.9, 126.6, 124.5, 122.9, 122.8, 112.9, 111.2, 108.3, 103.4, 61.5, 58.0, 55.0, 50.5, 31.4, 26.7, 21.7, 10.8; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{31}H_{30}N_2O_4SNa^+$ 549.1818; Found 549.1816.



12c

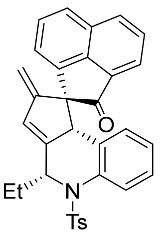
Synthesis of 12c: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-*N*-(4-fluoro-2-((1-methyl-2-oxoindolin-3-ylidene) methyl)phenyl)-4-methylbenzenesulfonamide **11c** (42.2 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12c**: 36.6 mg (0.0711 mmol), as a white solid, 71% yield; mp 132–134 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -85.8$ (c = 0.86 in CHCl$_3$); 90% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t$_R$ = 5.20 min (minor), t$_R$ = 8.58 min (major); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.60 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.34–7.28 (m, 2H), 7.25–7.15 (m, 3H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.86–6.80 (m, 1H), 6.80–6.74 (m, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.06 (s, 1H), 5.47–5.39 (m, 1H), 5.28–5.22 (m, 1H), 4.74 (s, 1H), 4.38 (s, 1H), 3.32 (s, 3H), 2.92 (s, 1H), 2.48 (s, 3H), 1.71–1.62 (m, 1H), 1.58–1.50 (m, 1H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 176.4, 160.7 (d, $^1J_{FC}$ = 245.1 Hz), 154.7, 152.4, 145.1, 142.5, 135.6, 134.7 (d, $^3J_{FC}$ = 8.3 Hz), 131.2, 131.14, 131.10, 130.2 (d, *J* = 2.9 Hz), 129.9, 128.5, 126.6, 124.8, 122.8, 122.5, 113.7 (d, $^2J_{FC}$ = 22.3 Hz), 113.3 (d, $^2J_{FC}$ = 24.3 Hz), 108.7, 103.8, 61.4, 58.0, 50.2, 31.4, 26.7, 21.7, 10.7; ^{19}F NMR (375 MHz, CDCl$_3$): δ (ppm) –113.6; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{30}H_{27}FN_2O_3SNa^+$ 537.1619; Found 537.1617.



12d

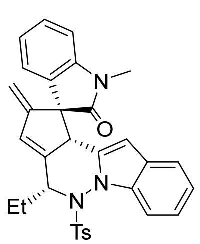
Synthesis of 12d: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1,5,7-trimethyl-2-oxoindolin-3-ylidene) methyl)phenyl)benzenesulfonamide **11d** (43.2 mg, 0.0999 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12d**: 36.8 mg (0.0701 mmol), as a white solid, 70% yield; mp 160–161 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -65.8$ (c = 8.23 in CHCl$_3$); 94% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH =

90/10, flow rate =1.0 mL/min, l = 254 nm) t_R = 8.90 min (minor), t_R = 12.76 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (d, *J* = 8.0 Hz, 1H), 7.33–7.27 (m, 2H), 7.20–7.08 (m, 3H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.71 (s, 1H), 6.22 (s, 1H), 6.02 (s, 1H), 5.80 (d, *J* = 8.0 Hz, 1H), 5.31–5.20 (m, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.55 (s, 3H), 3.02 (s, 1H), 2.56 (s, 3H), 2.45 (s, 3H), 1.98 (s, 3H), 1.75–1.64 (m, 1H), 1.61–1.52 (m, 1H), 1.17 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 177.6, 155.7, 153.4, 144.8, 137.8, 135.9, 134.3, 132.4, 132.39, 132.35, 131.8, 129.8, 129.4, 126.6, 126.5, 126.4, 124.4, 121.2, 119.6, 103.2, 61.1, 58.1, 50.5, 31.4, 30.0, 21.7, 20.7, 19.1, 10.8; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{32}H_{33}N_2O_3S^+$ 525.2206; Found 525.2210.



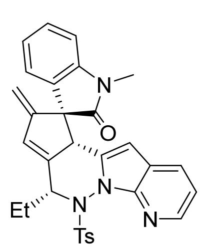
14

Synthesis of 14: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((2-oxoacenaphthylen-1(2*H*)-ylidene)methyl) phenyl)benzenesulfonamide **13** (42.5 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **14**: 31.6 mg (0.0610 mmol), as a white solid, 61% yield; mp 126–128 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −75.3 (*c* = 0.56 in $CHCl_3$); 90% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 4.77 min (minor), t_R = 6.70 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.14 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 6.8 Hz, 1H), 7.81–7.77 (m, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.65–7.61 (m, 1H), 7.35–7.29 (m, 3H), 7.23–7.19 (m, 2H), 7.07 (t, *J* = 6.8 Hz, 1H), 6.81 (d, *J* = 6.8 Hz, 1H), 6.53 (t, *J* = 7.6 Hz, 1H), 6.04 (s, 1H), 5.39 – 5.30 (m, 2H), 4.65 (s, 1H), 4.12 (s, 1H), 3.09 (s, 1H), 2.56 (s, 3H), 1.79–1.63 (m, 2H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 203.9, 157.3, 153.5, 144.9, 141.2, 141.1, 135.8, 134.3, 133.1, 132.9, 132.0, 131.2, 129.8, 129.7, 128.7, 128.3, 126.61, 126.59, 126.4, 126.3, 124.3, 124.1, 122.1, 119.3, 103.8, 66.8, 58.2, 49.7, 31.7, 21.8, 10.8; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{33}H_{28}NO_3S^+$ 518.1784; Found 518.1793.



16a

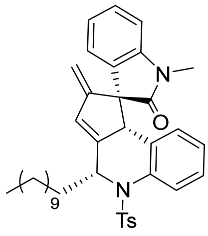
Synthesis of 16a: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)-1*H*-indol-1-yl)benzenesulfonamide **15a** (44.3 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **16a**: 39.2 mg (0.0732 mmol), as a white solid, 73% yield; mp 114–116 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = –37.6 (*c* = 0.73 in $CHCl_3$); 85% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 95/5, flow rate =1.0 mL/min, l = 254 nm) t_R = 10.67 min (minor), t_R = 13.42 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55 (d, *J* = 8.4 Hz, 1H), 7.50–7.42 (m, 2H), 7.27–7.25 (m, 2H), 7.25–7.22 (m, 1H), 7.22–7.18 (m, 1H), 7.18–7.12 (m, 1H), 7.06–6.98 (m, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.76–6.72 (m, 1H), 6.57 (d, *J* = 7.6 Hz, 1H), 6.15–6.08 (m, 1H), 5.37–5.28 (m, 1H), 4.84 (s, 1H), 4.72 (s, 1H), 4.43 (s, 1H), 3.29 (s, 3H), 3.10 (s, 1H), 2.54 (s, 3H), 1.58–1.49 (m, 1H), 1.39–1.26 (m, 1H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.4, 154.5, 148.1, 146.9, 142.8, 136.8, 132.8, 132.0, 131.2, 130.3, 128.5, 128.3, 126.4, 125.3, 123.8, 122.4, 122.3, 120.8, 120.1, 110.8, 108.2, 105.6, 98.1, 61.0, 60.8, 48.7, 30.0, 26.7, 21.9, 11.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{32}H_{29}N_3O_3SNa^+$ 558.1822; Found 558.1819.



16b

Synthesis of 16b: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hept-6-en-4-yn-3-yl carbonate **10a** (42.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene) methyl)-1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)benzenesulfonamide **15b** (44.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/3).

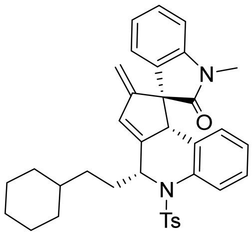
After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) to give the product **16b**: 23.2 mg (0.0432 mmol), as a white solid, 43% yield; mp 176–178 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −74.8 (*c* = 0.57 in CHCl$_3$); 96% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t$_R$ = 8.32 min (minor), t$_R$ = 10.30 min (major); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.22 (d, *J* = 3.6 Hz, 1H), 7.82–7.70 (m, 2H), 7.68–7.58 (m, 1H), 7.41–7.37 (m, 1H), 7.26 (s, 2H), 7.14–7.10 (m, 1H), 7.05–6.91 (m, 3H), 6.25 (s, 1H), 5.52 (s, 1H), 5.29–5.18 (m, 1H), 4.87 (s, 1H), 4.25 (s, 1H), 3.91 (s, 1H), 3.23 (s, 3H), 2.50 (s, 3H), 1.64–1.55 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 174.9, 152.7, 147.4, 147.3, 145.2, 144.2, 143.6, 134.5, 134.1, 129.8, 129.3, 129.2, 128.5, 126.5, 124.0, 122.9, 118.5, 117.1, 108.2, 105.7, 93.9, 61.7, 60.3, 49.6, 29.5, 26.4, 21.8, 10.5; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{31}H_{28}N_4O_3SNa^+$ 559.1774; Found 559.1780.



12e

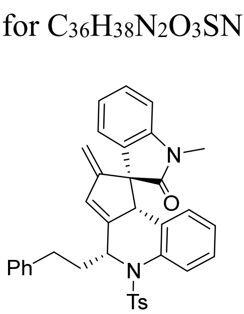
Synthesis of 12e: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl hexadec-1-en-3-yn-5-yl carbonate **10b** (67.3 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol %) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12e**: 38.1 mg (0.0612 mmol), as a white solid, 61% yield; mp 112–114 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −32.0 (*c* = 0.15 in CHCl$_3$); 95% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t$_R$ = 3.85 min (minor), t$_R$ = 7.33 min (major); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.65–7.59 (m, 1H), 7.33–7.27 (m, 2H), 7.22–7.10 (m, 4H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.79–6.72 (m, 2H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.06–6.00 (m, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.34 (t, *J* = 7.2 Hz, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.32 (s, 3H), 2.99 (s, 1H), 2.46 (s, 3H), 1.64–1.59 (m, 2H), 1.36–1.17 (m, 18H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$):

δ (ppm) 176.7, 155.1, 153.6, 144.8, 142.5, 135.8, 134.3, 132.4, 131.7, 129.8, 129.6, 128.1, 126.7, 126.58, 126.56, 126.1, 124.3, 122.7, 122.5, 108.5, 103.2, 61.6, 56.7, 50.1, 38.4, 32.0, 29.68, 29.66, 29.63, 29.57, 29.4, 29.1, 26.7, 26.0, 22.7, 21.7, 14.2; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{39}H_{46}N_2O_3SNa^+$ 645.3121; Found 645.3130.



12f

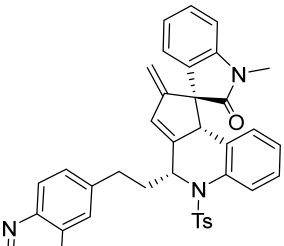
Synthesis of 12f: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (1-cyclohexylhept-6-en-4-yn-3-yl) carbonate **10c** (58.5 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **12f**: 40.7 mg (0.0703 mmol), as a white solid, 70% yield; mp 116–118 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = +78.5 (*c* = 0.43 in $CHCl_3$); 94% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 4.05 min (minor), t_R = 5.87 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 8.0 Hz, 1H), 7.32–7.27 (m, 2H), 7.23–7.10 (m, 4H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.80– 6.72 (m, 2H), 6.58 (d, *J* = 7.2 Hz, 1H), 6.03 (s, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.37 – 5.24 (m, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.32 (s, 3H), 2.97 (s, 1H), 2.46 (s, 3H), 1.80–1.64 (m, 5H), 1.61–1.44 (m, 4H), 1.32–1.11 (m, 4H), 1.00–0.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.1, 153.6, 144.9, 142.5, 135.8, 134.3, 132.4, 131.7, 129.8, 129.6, 128.1, 126.8, 126.60, 126.57, 126.1, 124.3, 122.7, 122.5, 108.5, 103.3, 61.6, 57.0, 50.1, 37.2, 35.8, 33.6, 33.5, 33.3, 26.7, 26.6, 26.40, 26.37, 21.7; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{36}H_{38}N_2O_3SNa^+$ 601.2495; Found 601.2498.



12g

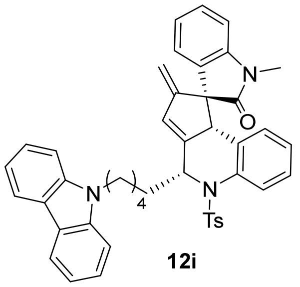
Synthesis of 12g: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (1-phenylhept-6-en-4-yn-3-yl) carbonate **10d** (57.3 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0

equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **12g**: 41.3 mg (0.0721 mmol), as a white solid, 72% yield; mp 147−149 °C; >19:1 dr, determind by ^1H NMR analysis of crude product; $[\alpha_D^{25}]$ = +132.8 (*c* = 0.45 in $CHCl_3$); 93% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.01 min (minor), t_R = 10.28 min (major); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66 (d, *J* = 8.0 Hz, 1H), 7.34–7.27 (m, 4H), 7.27–7.25 (m, 1H), 7.25–7.12 (m, 6H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 6.71 (t, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.07–6.02 (m, 1H), 5.73 (d, *J* = 8.0 Hz, 1H), 5.47–5.39 (m, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.31 (s, 3H), 3.07–2.90 (m, 3H), 2.47 (s, 3H), 1.95–1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.1, 145.0, 142.5, 141.4, 135.7, 134.2, 132.5, 131.6, 129.9, 129.7, 128.7, 128.5, 128.1, 126.9, 126.7, 126.6, 126.3, 126.1, 124.7, 122.7, 122.5, 108.5, 103.6, 61.6, 56.7, 50.1, 40.3, 32.6, 26.7, 21.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{36}H_{32}N_2O_3SNa^+$ 595.2026; Found 595.2033.



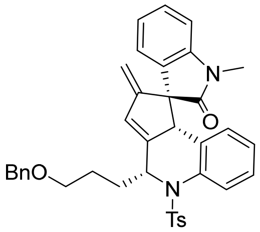
12h

Synthesis of 12h: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (1-(quinolin-6-yl)hept-6-en-4-yn-3-yl) carbonate **10e** (67.5 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/4). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/4) to give the product **12h**: 33.8 mg (0.0542 mmol), as a white solid, 54% yield; mp 154–156 °C; >19:1 dr, determind by ^1H NMR analysis of crude product; $[\alpha_D^{25}]$ = +76.8 (*c* = 0.68 in $CHCl_3$); 97% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.59 min (minor), t_R = 12.87 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.95–8.83 (m, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.74 (s, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.65–7.56 (m, 1H), 7.43–7.36 (m, 1H), 7.33–7.27 (m, 2H), 7.25–7.10 (m, 4H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.80 (t, *J* = 7.2 Hz, 1H), 6.70 (t, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 7.2 Hz, 1H), 6.05 (s, 1H), 5.75 (d, *J* = 7.6 Hz, 1H), 5.53–5.41 (m, 1H), 4.71 (s, 1H), 4.38 (s, 1H), 3.31 (s, 3H), 3.26–3.12 (m, 2H), 2.96 (s, 1H), 2.47 (s, 3H), 2.02–1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.6, 154.9, 153.0, 149.9, 147.2, 145.1, 142.5, 139.7, 135.8, 135.5, 134.1, 132.5, 131.6, 131.0, 129.9, 129.7, 129.5, 128.4, 128.2, 127.0, 126.9, 126.8, 126.6, 126.4, 124.8, 122.7, 122.5, 121.2, 108.5, 103.7, 61.6, 56.5, 50.0, 40.2, 32.6, 26.7, 21.7; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{39}H_{34}N_3O_3S^+$ 624.2315; Found 624.2323.



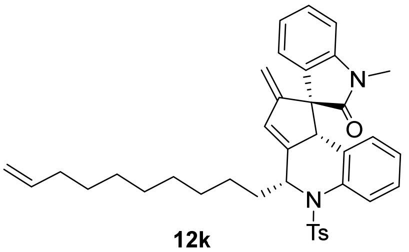
12i

Synthesis of 12i: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 10-(9*H*-carbazol-9-yl)dec-1-en-3-yn-5-yl *tert*-butyl carbonate **10f** (83.5 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/4). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/4) to give the product **12i**: 47.3 mg (0.0672 mmol), as a white solid, 67% yield; mp 95–97 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −56.8 (*c* = 3.68 in $CHCl_3$); 93% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.75 min (minor), t_R = 8.94 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.10 (d, *J* = 8.0 Hz, 2H), 7.66–7.57 (m, 1H), 7.46–7.38 (m, 4H), 7.29–7.25 (m, 2H), 7.24–7.19 (m, 2H), 7.19–7.13 (m, 3H), 7.13–7.06 (m, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.67 (t, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 7.2 Hz, 1H), 5.98–5.90 (m, 1H), 5.71 (d, *J* = 7.6 Hz, 1H), 5.31 (t, *J* = 7.6 Hz, 1H), 4.68 (s, 1H), 4.40–4.29 (m, 3H), 3.30 (s, 3H), 2.96 (s, 1H), 2.45 (s, 3H), 2.01–1.89 (m, 2H), 1.76–1.64 (m, 2H), 1.57–1.33 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.3, 144.9, 142.5, 140.5, 135.7, 134.2, 132.4, 131.7, 129.8, 129.6, 128.1, 126.9, 126.7, 126.6, 126.3, 125.7, 124.5, 122.8, 122.7, 122.5, 120.3, 118.8, 108.7, 108.5, 103.4, 61.6, 56.6, 50.1, 42.9, 38.2, 28.9, 26.7, 26.5, 25.8, 21.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{45}H_{41}N_3O_3SNa^+$ 726.2761; Found 726.2757.



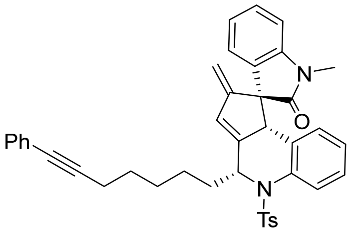
12j

Synthesis of 12j: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(benzyloxy)oct-7-en-5-yn-4-yl *tert*-butyl carbonate **10g** (66.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **12j**: 47.6 mg (0.0772 mmol), as a white solid, 77% yield; mp 167–169 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = −88.4 (*c* = 12.5 in $CHCl_3$); 95% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.18 min (minor), t_R = 9.08 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.60 (d, *J* = 7.6 Hz, 1H), 7.38–7.33 (m, 3H), 7.32–7.28 (m, 2H), 7.28–7.25 (m, 2H), 7.22–7.15 (m, 3H), 7.14–7.09 (m, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.80–6.68 (m, 2H), 6.58 (d, *J* = 7.2 Hz, 1H), 6.04 (s, 1H), 5.73 (d, *J* = 8.0 Hz, 1H), 5.38–5.31 (m, 1H), 4.71 (s, 1H), 4.53 (s, 2H), 4.37 (s, 1H), 3.71–3.63 (m, 1H), 3.59–3.52 (m, 1H), 3.31 (s, 3H), 2.97 (s, 1H), 2.46 (s, 3H), 2.01–1.91 (m, 2H), 1.83–1.74 (m, 1H), 1.60–1.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.2, 144.9, 142.5, 138.6, 135.7, 134.2, 132.4, 131.7, 129.8, 129.7, 128.4, 128.1, 127.7, 127.6, 126.8, 126.64, 126.59, 126.2, 124.6, 122.7, 122.5, 108.5, 103.4, 72.8, 69.2, 61.6, 56.4, 50.1, 34.9, 26.7, 26.1, 21.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{38}H_{36}N_2O_4SNa^+$ 639.2288; Found 639.2295.



12k

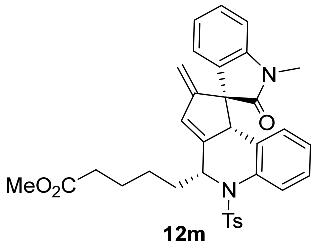
Synthesis of 12k: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl pentadeca-1,14-dien-3-yn-5-yl carbonate **10h** (64.1 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl) phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **12k**: 46.3 mg (0.0763 mmol), as a white solid, 76% yield; mp 105−107 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; [α_D^{25}] = −65.8 (*c* = 7.67 in CHCl$_3$); 94% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 4.18 min (minor), t_R = 8.45 min (major); ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.61 (d, *J* = 7.6 Hz, 1H), 7.35–7.27 (m, 2H), 7.24–7.08 (m, 4H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.81–6.68 (m, 2H), 6.58 (d, *J* = 7.2 Hz, 1H), 6.03 (s, 1H), 5.88–5.77 (m, 1H), 5.73 (d, *J* = 8.0 Hz, 1H), 5.34 (t, *J* = 7.6 Hz, 1H), 5.06–4.96 (m, 1H), 4.94 (d, *J* = 10.8 Hz, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.31 (s, 3H), 2.98 (s, 1H), 2.46 (s, 3H), 2.09–1.99 (m, 2H), 1.63–1.52 (m, 4H), 1.47–1.26 (m, 10H); ^{13}C NMR (150 MHz, CDCl$_3$): δ (ppm) 176.7, 155.1, 153.6, 144.8, 142.5, 139.2, 135.8, 134.3, 132.4, 131.7, 129.8, 129.6, 128.1, 126.7, 126.6, 126.5, 126.1, 124.3, 122.6, 122.4, 114.1, 108.4, 103.2, 61.6, 56.7, 50.1, 38.4, 33.8, 29.5, 29.4, 29.1, 29.0, 28.9, 26.6, 25.9, 21.6; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for C$_{38}$H$_{43}$N$_2$O$_3$S$^+$ 607.2989; Found 607.2994.



12l

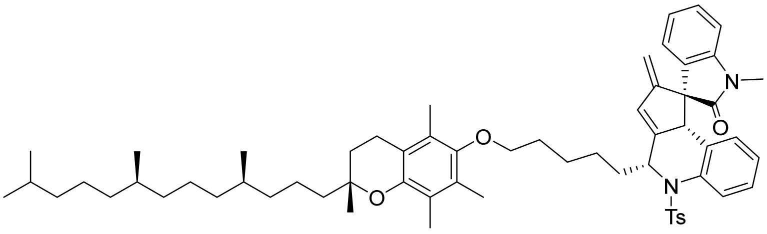
Synthesis of 12l: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (12-phenyldodeca 1-en-3,11-diyn-5-yl) carbonate **10i** (70.5 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl) phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd$_2$dba$_3$ (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and KHCO$_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/7) to give the product **12l**: 47.4 mg (0.0742 mmol), as a white solid, 74%

yield; mp 124–126 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = –125.8 (*c* = 8.56 in $CHCl_3$); 94% ee, determined by HPLC analysis (Daicel Chiralpak ID, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 9.01 min (minor), t_R = 12.36 min (major); ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.62 (d, *J* = 7.8 Hz, 1H), 7.44–7.36 (m, 2H), 7.35–7.26 (m, 5H), 7.21–7.15 (m, 3H), 7.14–7.10 (m, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.79–6.71 (m, 2H), 6.57 (d, *J* = 7.2 Hz, 1H), 6.03 (s, 1H), 5.73 (d, *J* = 7.8 Hz, 1H), 5.39–5.33 (m, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.31 (s, 3H), 2.98 (s, 1H), 2.46 (s, 3H), 1.75–1.63 (m, 5H), 1.63–1.58 (m, 3H), 1.57–1.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.4, 144.9, 142.5, 135.8, 134.3, 132.4, 131.7, 131.6, 129.8, 129.7, 128.2, 128.1, 127.5, 126.8, 126.61, 126.58, 126.2, 124.4, 124.1, 122.7, 122.5, 108.5, 103.3, 90.7, 80.8, 61.6, 56.6, 50.1, 38.3, 28.7, 28.3, 26.7, 25.6, 21.7, 19.4; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{41}H_{38}N_2O_3SNa^+$ 661.2495; Found 661.2496.



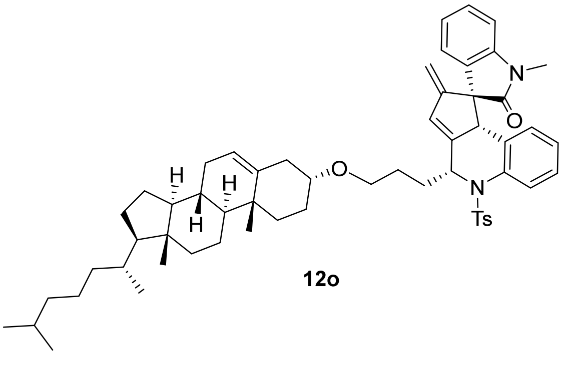
12m

Synthesis of 12m: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added methyl 6-((*tert*-butoxycarbonyl)oxy)dec-9-en-7-ynoate **10j** (59.3 mg, 0.200 mmol, 2.0 equiv), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **12m**: 29.9 mg (0.0513 mmol), as a white solid, 51% yield; mp 97–99 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = –67.9 (*c* = 6.95 in $CHCl_3$); 95% ee, determined by HPLC analysis (Daicel Chiralpak IA, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.71 min (minor), t_R = 11.76 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 8.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.22–7.10 (m, 4H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.82–6.70 (m, 2H), 6.56 (d, *J* = 6.8 Hz, 1H), 6.07–6.00 (m, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.41–5.28 (m, 1H), 4.72 (s, 1H), 4.38 (s, 1H), 3.68 (s, 3H), 3.32 (s, 3H), 2.97 (s, 1H), 2.46 (s, 3H), 2.43–2.33 (m, 2H), 1.84–1.74 (m, 1H), 1.74–1.64 (m, 3H), 1.61–1.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 174.1, 155.0, 153.2, 144.9, 142.5, 135.7, 134.1, 132.3, 131.7, 129.8, 129.6, 128.2, 126.8, 126.7, 126.6, 126.2, 124.5, 122.7, 122.5, 108.5, 103.4, 61.6, 56.4, 51.6, 50.0, 38.0, 34.0, 26.7, 25.5, 24.3, 21.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{34}H_{34}N_2O_5SNa^+$ 605.2081; Found 605.2086.



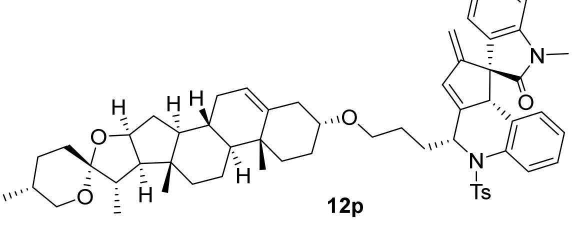
12n

Synthesis of 12n: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (10-(((*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl) chroman-6-yl)oxy)dec-1-en-3-yn-5-yl) carbonate **10k** (136.2 mg, 0.2000 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **12n**: 59.1 mg (0.0611 mmol), as a white solid, 61% yield; mp 81–83 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -35.5$ (*c* = 6.87 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 (d, *J* = 8.0 Hz, 1H), 7.33–7.27 (m, 2H), 7.23–7.15 (m, 3H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.79–6.72 (m, 2H), 6.58 (d, *J* = 6.8 Hz, 1H), 6.07–6.02 (m, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.37 (t, *J* = 7.2 Hz, 1H), 4.72 (s, 1H), 4.38 (s, 1H), 3.66 (t, *J* = 6.4 Hz, 2H), 3.32 (s, 3H), 2.99 (s, 1H), 2.57 (t, *J* = 6.4 Hz, 2H), 2.46 (s, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 1.85–1.62 (m, 8H), 1.58–1.20 (m, 20H), 1.15–1.01 (m, 6H), 0.88–0.83 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.1, 153.5, 148.4, 147.7, 144.9, 142.5, 135.8, 134.3, 132.4, 131.7, 129.8, 129.7, 128.1, 127.8, 126.8, 126.6, 126.2, 125.8, 124.4, 122.8, 122.7, 122.5, 117.5, 108.5, 103.3, 74.8, 72.9, 61.6, 56.7, 50.1, 40.1, 39.4, 38.4, 37.6, 37.5, 37.4, 37.3, 32.8, 32.7, 31.3, 30.3, 28.0, 26.7, 26.1, 25.8, 24.84, 24.82, 24.5, 23.9, 22.8, 22.7, 21.7, 21.1, 20.7, 19.8, 19.7, 19.7, 19.6, 12.8, 12.0, 11.8; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{62}H_{82}N_2O_5SNa^+$ 989.5837; Found 989.5841.



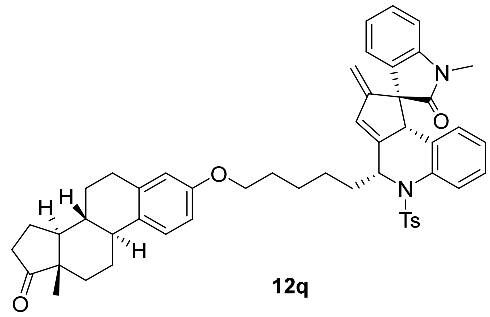
12o

Synthesis of 12o: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl carbonate **10l** (121.8 mg, 0.2000 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene) methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12o**: 60.9 mg (0.0680 mmol), as a white solid, 68% yield; mp 110–112 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}]$ = –27.9 (*c* = 8.17 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 8.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.22–7.16 (m, 3H), 7.15–7.10 (m, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.80–6.70 (m, 2H), 6.59 (d, *J* = 7.2 Hz, 1H), 6.06 (s, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.40–5.32 (m, 2H), 4.72 (s, 1H), 4.37 (s, 1H), 3.69–3.60 (m, 1H), 3.59–3.52 (m, 1H), 3.31 (s, 3H), 3.21–3.13 (m, 1H), 2.97 (s, 1H), 2.46 (s, 3H), 2.42–2.32 (m, 1H), 2.25–2.16 (m, 1H), 2.03–1.75 (m, 8H), 1.60–1.02 (m, 21H), 1.01 (s, 3H), 0.98–0.95 (m, 1H), 0.93–0.91 (m, 3H),, 0.87 (dd, *J* = 6.4, 1.6 Hz, 6H), 0.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.3, 144.9, 142.5, 141.0, 135.7, 134.2, 132.4, 131.7, 129.8, 129.7, 128.1, 126.8, 126.62, 126.59, 126.2, 124.6, 122.7, 122.6, 121.6, 121.5, 108.5, 103.4, 78.9, 66.8, 61.6, 56.8, 56.3, 56.2, 50.2, 50.1, 42.3, 39.8, 39.5, 39.2, 37.3, 36.9, 36.2, 35.8, 34.9, 32.0, 31.9, 28.55, 28.51, 28.3, 28.0, 26.7, 26.5, 24.3, 23.8, 22.8, 22.6, 21.7, 21.1, 19.4, 18.7, 11.9; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{58}H_{74}N_2O_4SNa^+$ 917.5262; Found 917.5263.



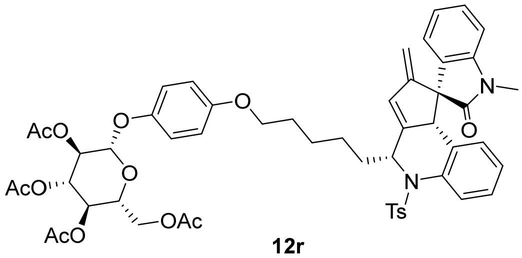
12p

Synthesis of 12p: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (1-(((4*S*,5'*S*,6a*S*,6b*R*,8a*R*,8b*S*, 9*R*, 10*S*,11a*R*,12a*R*,12b*R*)-5',6a,8a,9-tetramethyl-1,3,3',4,4',5,5',6,6a,6b,6',7,8,8a,8b,9,11a,12,12a,12bicosahydrospiro[naphtho[2',1':4,5]indeno[2,1-*b*]furan-10,2'-pyran]-4-yl)oxy)oct-7-en-5-yn-4-yl) carbonate **10m** (127.4 mg, 0.2000 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene) methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12p**: 66.6 mg (0.0721 mmol), as a white solid, 72% yield; mp 107−109 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -76.9$ (c = 5.84 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 8.0 Hz, 1H), 7.30–7.27 (m, 2H), 7.20–7.15 (m, 3H), 7.15–7.10 (m, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.79–6.71 (m, 2H), 6.59 (d, *J* = 7.2 Hz, 1H), 6.06 (s, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.40–5.32 (m, 2H), 4.72 (s, 1H), 4.44–4.39 (m, 1H), 4.37 (s, 1H), 3.68–3.60 (m, 1H), 3.59–3.51 (m, 1H), 3.50–3.45 (m, 1H), 3.38 (t, *J* = 10.9 Hz, 1H), 3.32 (s, 3H), 3.21–3.13 (m, 1H), 2.97 (s, 1H), 2.46 (s, 3H), 2.42–2.33 (m, 1H), 2.24–2.15 (m, 1H), 2.06–1.66 (m, 12H), 1.61–1.40 (m, 8H), 1.34–1.05 (m, 5H), 1.03 (s, 3H), 1.00–0.94 (m, 4H), 0.81–0.76 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 155.0, 153.3, 144.9, 142.5, 141.1, 135.7, 134.2, 132.4, 131.7, 129.8, 129.7, 128.1, 126.8, 126.62, 126.58, 126.2, 124.6, 122.7, 122.5, 121.30, 121.26, 109.3, 108.5, 103.4, 80.9, 78.9, 78.8, 66.9, 62.1, 61.6, 56.5, 56.3, 50.12, 50.06, 41.6, 40.3, 39.8, 39.2, 37.3, 37.1, 34.9, 32.1, 31.9, 31.5, 31.4, 30.3, 28.8, 28.52, 28.48, 26.7, 26.5, 21.7, 20.9, 19.5, 17.2, 16.3, 14.5; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{58}H_{71}N_2O_6S^+$ 923.5027; Found 923.5032.



12q

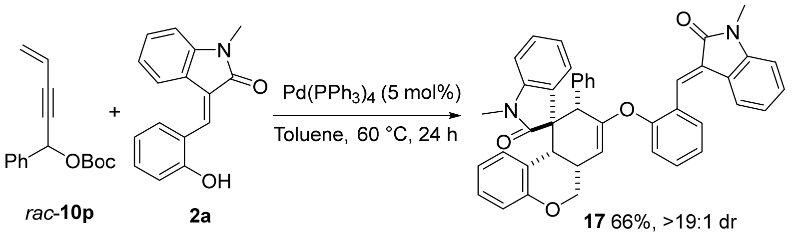
Synthesis of 12q: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (10-(((8*S*,9*R*,13*R*,14*R*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3-yl)oxy)dec-1-en-3-yn-5-yl) carbonate **10n** (104.2 mg, 0.2001 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12q**: 56.6 mg (0.0701 mmol), as a white solid, 70% yield; mp 133−134 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; [α_D^{25}] = −88.5 (*c* = 7.54 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 8.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.23–7.09 (m, 5H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.80–6.69 (m, 3H), 6.69–6.64 (m, 1H), 6.57 (d, *J* = 7.6 Hz, 1H), 6.03 (s, 1H), 5.73 (d, *J* = 7.6 Hz, 1H), 5.36 (t, *J* = 7.6 Hz, 1H), 4.71 (s, 1H), 4.37 (s, 1H), 3.97 (t, *J* = 6.0 Hz, 2H), 3.32 (s, 3H), 2.97 (s, 1H), 2.95–2.85 (m, 2H), 2.46 (s, 3H), 2.41–2.35 (m, 1H), 2.28–1.94 (m, 5H), 1.89–1.77 (m, 2H), 1.77–1.44 (m, 13H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 221.0, 176.7, 157.1, 155.0, 153.4, 144.9, 142.5, 137.7, 135.8, 134.2, 132.4, 131.9, 131.7, 129.8, 129.6, 128.1, 126.8, 126.63, 126.58, 126.3, 126.2, 124.4, 122.7, 122.5, 114.6, 112.2, 108.5, 103.4, 67.8, 61.6, 56.6, 50.4, 50.1, 48.1, 44.0, 38.4, 38.3, 35.9, 31.6, 29.7, 29.3, 26.7, 26.6, 26.0, 25.8, 25.6, 21.7, 21.6, 13.9; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{51}H_{54}N_2O_5SNa^+$ 829.3646; Found 829.3645.



12r

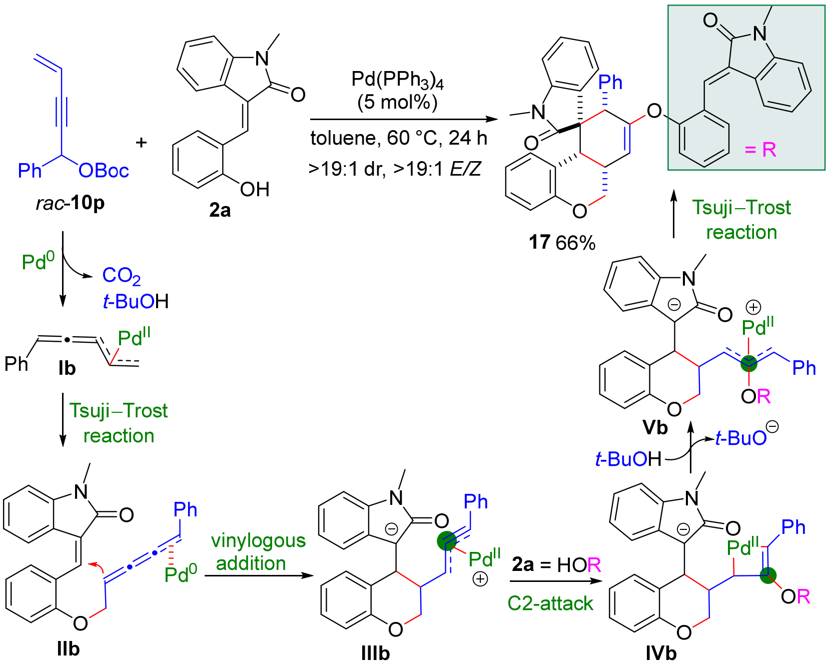
Synthesis of 12r: To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added (2*R*,3*R*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-(4-((6-((*tert*-butoxycarbonyl)oxy)dec-9-en-7-yn-1-yl)oxy)phenoxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate **10o** (138.2 mg, 0.2000 mmol), (*E*)-4-methyl-*N*-(2-((1-methyl-2-oxoindolin-3-ylidene)methyl)phenyl)benzenesulfonamide **11a** (40.4 mg, 0.0999 mmol, 1.0 equiv), Pd_2dba_3 (4.6 mg, 0.0050 mmol, 5 mol%), **L5** (4.6 mg, 0.012 mmol, 12 mol%) and $KHCO_3$ (12.0 mg, 0.120 mmol, 1.2 equiv). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (1.0 mL) was added via syringe. The mixture was stirred at 45 °C for 72 h, and monitored by TLC (EtOAc/petroleum ether = 1/5). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/5) to give the product **12r**: 65.6 mg (0.0671 mmol), as a white solid, 67% yield; mp 126–128 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -54.6$ (c = 8.65 in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, J = 8.0 Hz, 1H), 7.31–7.28 (m, 1H), 7.22–7.16 (m, 3H), 7.15–7.10 (m, 1H), 6.96–6.79 (m, 6H), 6.78–6.71 (m, 2H), 6.56 (d, J = 7.6 Hz, 1H), 6.03 (s, 1H), 5.73 (d, J = 7.6 Hz, 1H), 5.37 (t, J = 7.2 Hz, 1H), 5.31–5.24 (m, 2H), 5.17 (t, J = 9.6 Hz, 1H), 4.96 (d, J = 7.2 Hz, 1H), 4.71 (s, 1H), 4.38 (s, 1H), 4.32–4.28 (m, 1H), 4.19–4.14 (m, 1H), 3.95 (t, J = 6.4 Hz, 2H), 3.84–3.79 (m, 1H), 3.32 (s, 3H), 2.96 (s, 1H), 2.46 (s, 3H), 2.09 (d, J = 2.0 Hz, 6H), 2.04 (d, J = 3.6 Hz, 6H), 1.87–1.79 (m, 2H), 1.75–1.53 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.7, 170.7, 170.3, 169.5, 169.4, 155.3, 155.0, 153.4, 150.8, 145.0, 142.5, 135.7, 134.2, 132.4, 131.6, 129.8, 129.6, 128.2, 126.8, 126.7, 126.5, 126.2, 124.4, 122.7, 122.4, 118.7, 115.2, 108.6, 103.4, 100.3, 72.8, 71.9, 71.2, 68.32, 68.29, 61.9, 61.6, 56.5, 50.0, 38.3, 29.2, 26.7, 25.7, 25.5, 21.7, 20.8, 20.73, 20.68, 20.65; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{53}H_{56}N_2O_{14}SNa^+$ 999.3344; Found 999.3341.

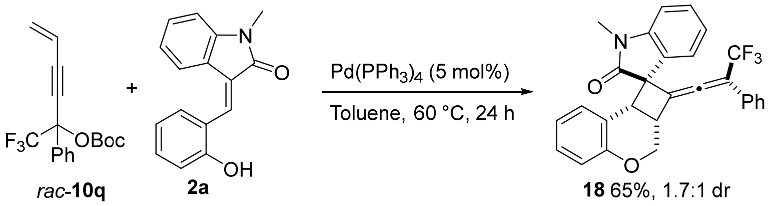
6. Transformations of 1-aryl-4-alken-2-ynyl carbonates



To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (1-phenylpent-4-en-2-yn-1-yl) carbonate **10p** (51.7 mg, 0.200 mmol, 2.0 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv) and $Pd(PPh_3)_4$ (5.8 mg, 0.0050 mmol). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry toluene (1.0 mL) was added via syringe. The mixture was stirred at 60 °C for 24 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product **17**: 42.5 mg (0.0661 mmol), as a white solid, 66% yield; mp 184−186 °C; >19:1 dr, determind by ^1H NMR analysis of crude product;^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.76 (s, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.45–7.40 (m, 1H), 7.29–7.26 (m, 1H), 7.25–7.23 (m, 1H), 7.21–7.13 (m, 3H), 6.97–6.78 (m, 10H), 6.67–6.62 (m, 1H), 6.57–6.53 (m, 1H), 6.23 (d, J = 7.6 Hz, 1H), 5.15–5.08 (m, 1H), 4.71 (t, J = 2.8 Hz, 1H), 4.25 (t, J = 11.4 Hz, 1H), 3.95 (d, J = 7.3 Hz, 1H), 3.80–3.70 (m, 1H), 3.33 (s, 3H), 3.15–3.07 (m, 1H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) 178.7, 167.9, 154.8, 154.4, 153.3, 144.2, 144.0, 133.6, 133.2, 131.1, 130.9, 130.0, 129.9, 129.7, 128.5, 128.2, 128.1, 127.7, 127.3, 126.8, 126.6, 124.0, 122.8, 121.8, 121.2, 121.0, 120.4, 120.0, 116.9, 108.2, 107.7, 104.1, 64.9, 59.5, 50.8, 39.4, 33.7, 26.2, 26.0; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{43}H_{34}N_2O_4Na^+$ 665.2411; Found 665.2419.

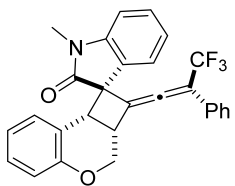
A possible mechanism for the formation of **17** was proposed. Activation of 1-phenyl-substituted propargylic carbonate *rac*-**10p** by Pd(0) led to the formation of thermally more stable allenyl-π-allyl species **Ib**, which underwent Tsuji–Trost reaction of with **2a** with distinct terminal regioselectivity. The resultant 1,2,3-butatriene intermediate **IIb** could be further HOMO-activated by Pd(0) via similar π-Lewis base catalysis, thus facilitated intramolecular vinylogous addition to generate η^3-propargylpalladium **IIIb**. Interestingly, **IIIb** was attacked by another **2a**, and subseqent protonation of **IVb** and intramolecular allylation of **Vb** provided complex **17** in a good yield with outstanding diastereo- and *E*/*Z*-selectivity.





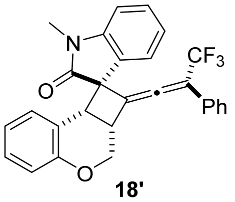
To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added *tert*-butyl (1,1,1-trifluoro-2-phenylhex-5-en-3-yn-2-yl) carbonate **10q** (65.3 mg, 0.200 mmol, 2.0 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv) and

$Pd(PPh_3)_4$ (5.8 mg, 0.0050 mmol). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry toluene (1.0 mL) was added via syringe. The mixture was stirred at 60 °C for 24 h, and monitored by TLC (EtOAc/petroleum ether = 1/7). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel EtOAc/petroleum ether = 1/7 to 1/5) to give the products **18** and **18′** as seperable isomers.



18

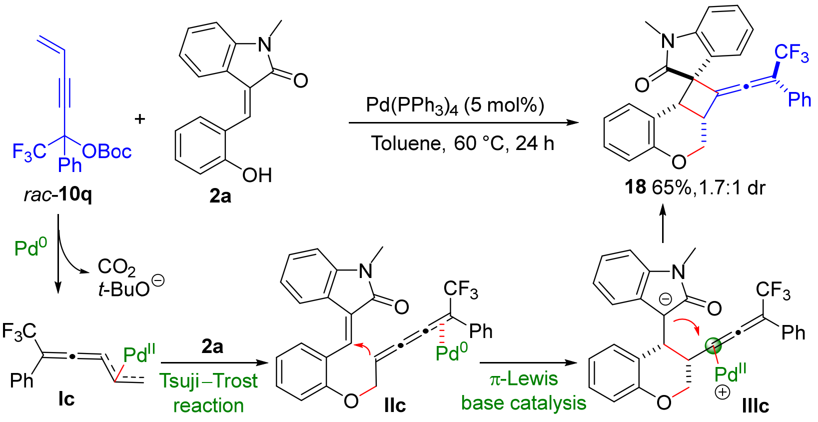
18: 18.9 mg (0.0411 mmol), as a white solid, 41% yield; mp 154–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.48–7.41 (m, 2H), 7.34–7.26 (m, 3H), 7.24–7.19 (m, 1H), 7.13–7.05 (m, 2H), 6.79–6.71 (m, 2H), 6.56–6.49 (m, 2H), 5.88 (d, *J* = 7.6 Hz, 1H), 4.56 (d, *J* = 9.2 Hz, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.03–3.97 (m, 2H), 3.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 195.5, 176.3, 155.9, 143.9, 132.1, 129.1, 128.9, 128.7, 128.6, 128.4, 127.1, 125.8, 125.2, 123.7, 122.2, 121.9, 121.6, 120.7, 117.7, 111.6, 107.8, 64.8, 59.7, 41.7, 41.5, 26.6; ^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) −60.1; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{21}F_3NO_2^+$ 460.1519; Found 460.1523.



18'

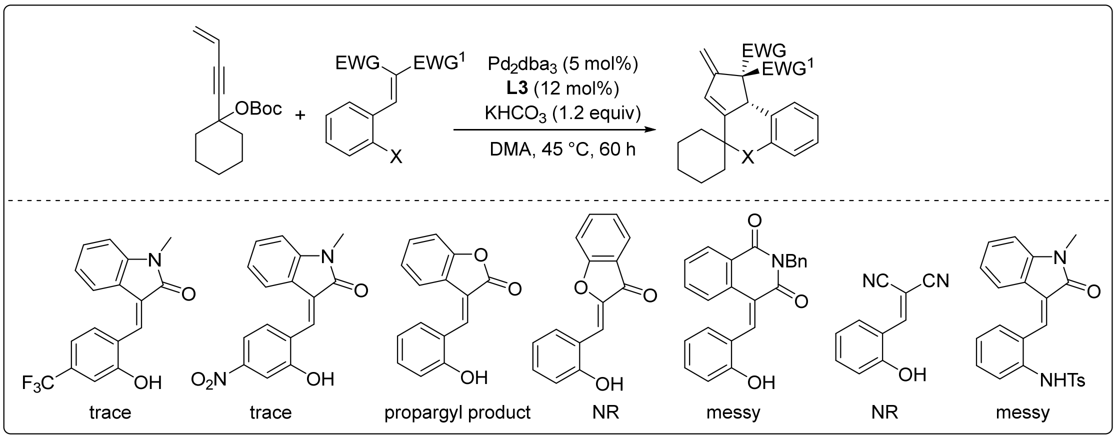
18′: 11.1 mg (0.0241 mmol), as a white solid, 24% yield; mp 152–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39–7.26 (m, 5H), 7.21–7.12 (m, 2H), 7.11–7.06 (m, 1H), 6.77–6.66 (m, 3H), 6.51 (d, *J* = 7.6 Hz, 1H), 6.13 (d, *J* = 7.5 Hz, 1H), 4.56–4.48 (m, 1H), 4.41 (d, *J* = 12.0 Hz, 1H), 4.06–3.94 (m, 2H), 3.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 195.3, 176.8, 156.2, 143.6, 131.7, 129.2, 128.9, 128.8, 128.6, 128.5, 127.1, 125.8, 125.6, 123.8, 122.5, 122.0, 121.4, 120.4, 117.9, 111.6, 107.7, 64.8, 59.3, 41.8, 41.5, 26.6; ^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) −59.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{28}H_{20}F_3NO_2Na^+$ 482.1338; Found 482.1346.

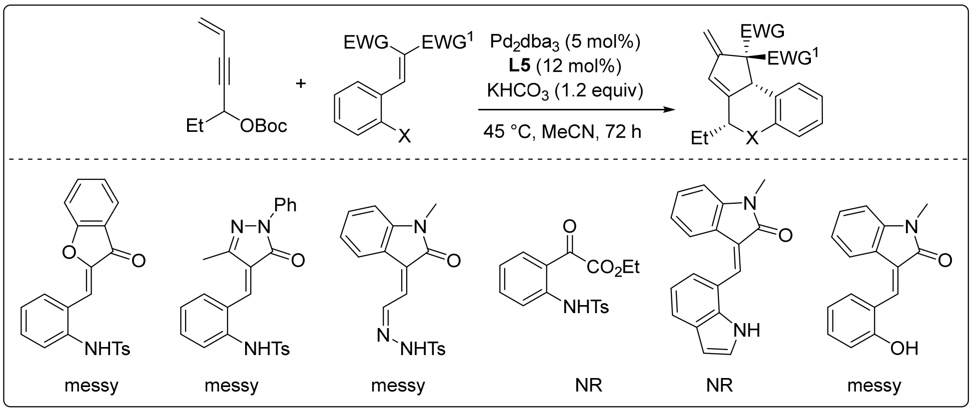
The possible mechanism for the formation of **18** was proposed. (*E*)-3-(2-hydroxy benzylidene) oxindole **2a** underwent similar Tsuji–Trost reaction/vinylogous addition with **2a** efficiently through intermediates **Ic** and **IIc**, respectively, whereas the formed η^1-allenylpalladium moiety of **IIIc** was intramolecularly captured by enolate to provide intriguing cyclobutane-fused chromanone **18** having a tetrasubstituted exocyclic allene motif in a moderate yield with fair diastereoselectivity

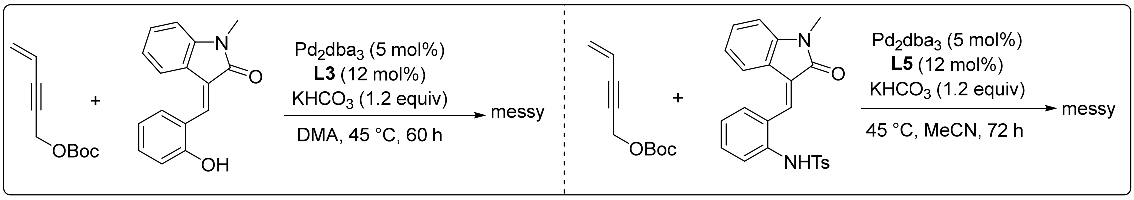


7. Unsuccessful substrates exploration

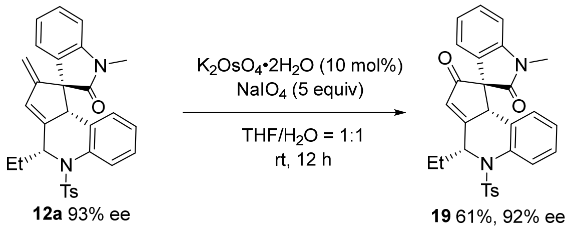
To further expand substrate scope, more *ortho*-functionalised activated alkenes derived from different backbones and primary carbonates were tested. Unfortunately, messy reaction profiles or no apparent conversions were generally observed, as summarised below.



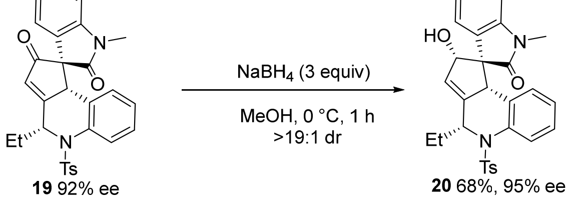




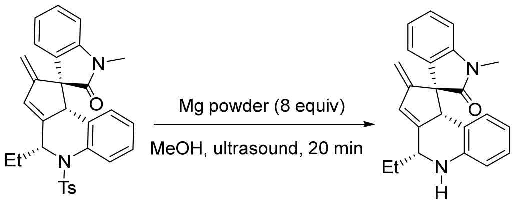
8. Transformations of product 12a



To a solution of **12a** (49.7 mg, 0.100 mmol) in THF/H_2O (0.5 mL/ 0.5 mL) was added $K_2OsO_4{\cdot}2H_2O$ (3.1 mg, 0.010 mmol) and $NaIO_4$ (108.0 mg, 0.5002 mmol). The mixture was stirred at room temperature for 10 h, and monitored by TLC (petroleumether/EtOAc = 5/1). After complete consumption of **12a**, the mixture was quenched with saturated aqueous Na_2SO_3, and extracted with ethyl acetate (3.0 mL × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (petroleumether/EtOAc = 5/1) to afford product **19**: 30.5 mg (0.0612 mmol), as a white solid, 61% yield; mp 235–237 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; $[\alpha_D^{25}] = -158.4$ (*c* = 6.88 in $CHCl_3$); 92% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.85 min (minor), t_R = 11.40 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.68 (d, *J* = 8.0 Hz, 1H), 7.35–7.29 (m, 2H), 7.26–7.14 (m, 4H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.84 (t, *J* = 7.6 Hz, 1H), 6.76 (t, *J* = 7.6 Hz, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 6.01 (s, 1H), 5.78 (d, *J* = 7.6 Hz, 1H), 5.52–5.42 (m, 1H), 3.30 (s, 3H), 3.08 (s, 1H), 2.47 (s, 3H), 1.82–1.72 (m, 1H), 1.67–1.62 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.7, 183.2, 172.7, 145.6, 144.3, 135.6, 134.4, 130.2, 129.74, 129.67, 129.0, 127.6, 127.1, 126.7, 126.4, 125.1, 123.6, 122.9, 122.4, 109.1, 66.5, 59.0, 46.6, 31.2, 26.8, 21.7, 10.9; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{29}H_{26}N_2O_4SNa^+$ 521.1505; Found 521.1509.



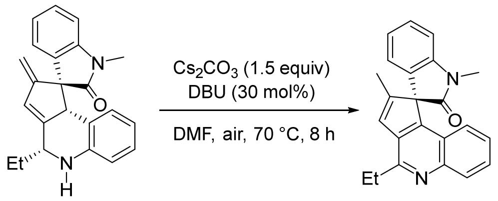
To a solution of **19** (30.5 mg, 0.0612 mmol) in MeOH (0.5 mL) was added $NaBH_4$ (7.0 mg, 0.185 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h, and monitored by TLC (petroleumether/EtOAc = 3/1). After complete consumption of **19**, the mixture was quenched with water, and extracted with ethyl acetate (3.0 mL × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo, The residue was purified by flash chromatography on silica gel (petroleumether/EtOAc = 3/1) to afford product **20**: 23.3 mg (0.0416 mmol), as a white solid, 68% yield; mp 178–180 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; [α_D^{25}] = –190.5 (*c* = 3.54 in $CHCl_3$); 95% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 60/40, flow rate =1.0 mL/min, l = 254 nm) t_R = 4.68 min (minor), t_R = 12.62 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.56 (d, *J* = 7.6 Hz, 1H), 7.36–7.30 (m, 2H), 7.26–7.18 (m, 3H), 7.15–7.08 (m, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.83–6.74 (m, 3H), 5.79 (d, *J* = 8.0 Hz, 1H), 5.52 (s, 1H), 5.12–5.05 (m, 1H), 4.93 (d, *J* = 11.2 Hz, 1H), 3.28 (s, 3H), 2.62 (s, 1H), 2.52 (s, 3H), 1.60–1.45 (m, 2H), 1.40–1.33 (m, 1H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 176.8, 147.5, 145.0, 144.7, 136.0, 134.1, 133.1, 129.9, 129.8, 129.2, 127.0, 126.8, 126.7, 125.1, 124.8, 124.5, 123.9, 122.3, 108.7, 83.7, 65.6, 57.4, 47.6, 30.8, 26.7, 21.7, 10.8; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{29}H_{28}N_2O_4SNa^+$ 523.1662; Found 523.1672.



12a 93% ee

21 86%, 91% ee

To a solution of **12a** (49.7 mg, 0.100 mmol) in MeOH (1.0 mL) was added Mg powder (19.5 mg, 0.802 mmol), and the resultant mixture was sonicated for 20 minutes. After complete consumption of **12a**, the mixture was quenched with water, and extracted with ethyl acetate (3.0 mL × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo, The residue was purified by flash chromatography on silica gel (petroleumether/EtOAc = 5/1) to afford product **21**: 29.5 mg (0.0861 mmol), as a white solid, 86% yield; mp 132–134 °C; >19:1 dr, determind by ^{1}H NMR analysis of crude product; [α_D^{25}] = –232.5 (*c* = 4.67 in $CHCl_3$); 91% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 6.84 min (minor), t_R = 8.78 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13–7.04 (m, 1H), 6.83–6.74 (m, 2H), 6.72–6.64 (m, 2H), 6.49 (d, *J* = 7.6 Hz, 1H), 6.29–6.23 (m, 1H), 6.17 (s, 1H), 6.08 (d, *J* = 7.6 Hz, 1H), 4.93 (s, 1H), 4.80 (s, 1H), 4.51 (s, 1H), 3.97–3.80 (m, 2H), 3.38 (s, 3H), 2.10–1.98 (m, 1H), 1.82–1.72 (m, 1H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 179.0, 156.3, 150.8, 145.0, 142.7, 132.6, 128.0, 127.6, 127.0, 123.6, 123.0, 122.7, 120.6, 118.2, 114.9, 108.0, 104.6, 63.2, 53.9, 53.3, 26.8, 26.1, 10.4; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{23}N_2O^+$ 343.1805; Found 343.1809.

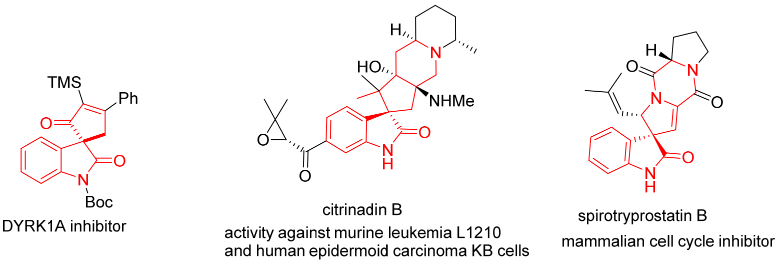


21 91% ee

22 89%, 90% ee

To a solution of **21** (29.5 mg, 0.0861 mmol) in DMF (0.8 mL) was added Cs_2CO_3 (42.1 mg, 0.129 mmol) and DBU (4.0 mg, 0.026 mmol). The mixture was stirred at 70 °C for 8 h and monitored by TLC (petroleumether/EtOAc = 6/1). After complete consumption of **21**, the mixture was quenched with water, and extracted with ethyl acetate (3.0 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (petroleumether/EtOAc = 6/1) to afford product **22**: 26.1 mg (0.0767 mmol), as a white solid, 89% yield; mp 105–107 °C; $[\alpha_D^{25}] = -57.3$ (*c* = 4.89 in $CHCl_3$); 90% ee, determined by HPLC analysis (Daicel Chiralpak AD, *n*-hexane/*i*-PrOH = 80/20, flow rate =1.0 mL/min, l = 254 nm) t_R = 5.98 min (minor), t_R = 13.51 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.02 (d, *J* = 8.8 Hz, 1H), 7.50–7.43 (m, 1H), 7.42–7.37 (m, 1H), 7.20–7.15 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.00–6.94 (m, 1H), 6.91–6.88 (m, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 3.46 (s, 3H), 3.16 (q, *J* = 7.6,7.6 Hz, 2H), 1.79 (s, 3H), 1.47 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 173.7, 157.3, 148.9, 148.4, 146.7, 144.7, 138.3, 129.8, 129.2, 127.8, 127.8, 127.4, 126.4, 123.6, 123.5, 123.1, 121.4, 108.9, 68.4, 29.9, 27.2, 13.7, 12.9; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{21}N_2O^+$ 341.1648; Found 341.1652.

It should be noted that the oxindole-fused polycyclic products and their derivatives are core structural subunits of many bioactive natural products and drug candidates, as briefly exemplified below.



DYRK1A inhibitor

citrinadin B
activity against murine leukemia L1210
and human epidermoid carcinoma KB cells

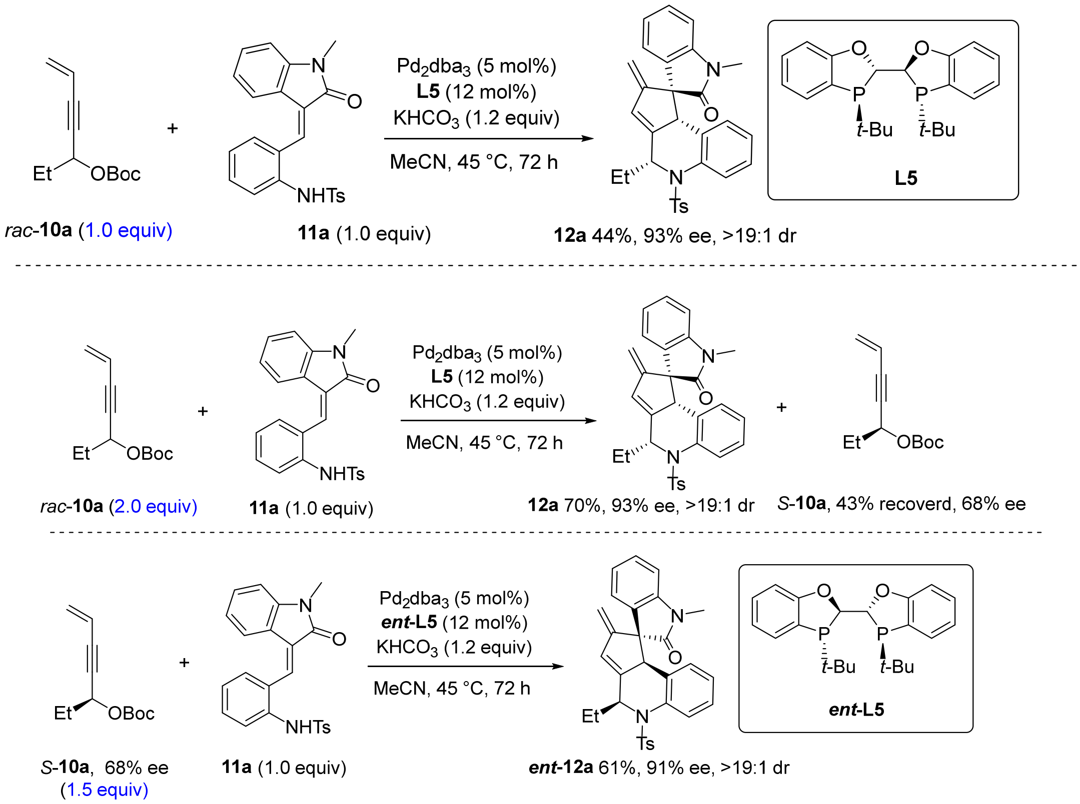
spirotryprostatin B
mammalian cell cycle inhibitor

(*a*) M. Banerjee, H. Liu, O. Wiest, J. Zartman, and B. L. Ashfeld, *ChemMedChem* 2022, **17**, e202100512;
(*b*) T. Mugishima, M. Tsuda, Y. Kasai, H. Ishiyama, E. Fukushi, J. Kawabata, M. Watanabe, K. Akao, and J. Kobayashi, *J. Org. Chem.* 2005, **70**, 9430–9435;
(*c*) C.-B. Cui, H. Kakeya, and H. Osada, *J. Antibiot.* 1996, **49**, 832–835.

FigureS1. Selected bioactive spirooxindoles

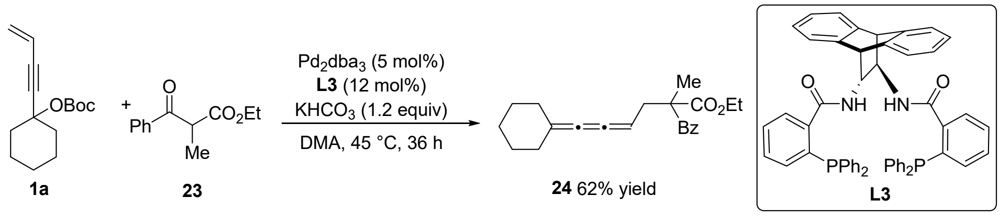
9. Preliminary mechanism investigation

9.1 Kinetic studies of the reaction between 10a and 11a



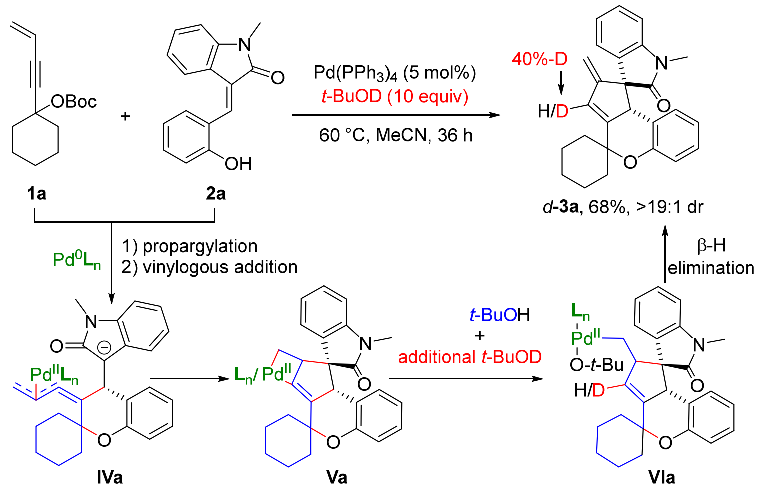
The reaction of *rac*-**10a** (1.0 equiv) with (2-aminobenzylidene)oxindole **11a** delivered product **12a** in 44% yield under standard conditions, while a significantly improved yiled was attained by increasing the amounts of *rac*-**10a** (2.0 equiv). Meanwhile, *S*-**10a** was recovered in 43% yield with 68% ee. In addition, the reaction of optically active (*S*)-**10a** under the standard conditions with *ent*-**L5** as ligand afforded product *ent*-**12a** in 61% yield with 91% ee. These results indicated that a kinetic resolution process of *rac*-**10a** was involved in current tandem transformations.

9.2 Elucidation of the origin of regioselectivity



To shed some light on the origin of the unusual regioselectivity and the complicated reaction process, some control experiments were conducted. As depicted above, the assembly of 4-alken-2-ynyl carbonate **1a** with carbon-centered nucleophile β-ketoesters **23** delivered 1,2,3-butatriene product **24** under the standard conditions, which indicated that the regioselectivity for substitution was governed by the nucleophiles.

9.3 Elucidation of the reaction pathway



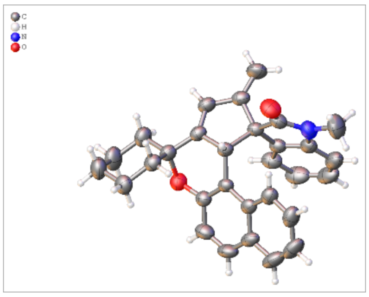
Moreover, adding *t*-BuOD to the reaction mixture led to product ***d*-3a** with 40% deuterium incorporated into *endo*-cyclic double bond, as outlined above. As nucleophilic attack on the central carbon of π-allylpalladium had been documented (*JACS* **2007**, *129*, 14866; *JACS* **2010**, *132*, 7508; *Org. Lett.* **2024**, *26*, 5782), this result further indicated that the key palladacyclobutane **Va** indeed be involved in the reaction process.

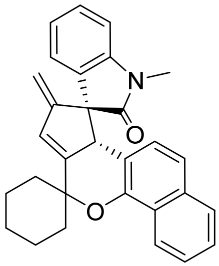
Procedure for deuterium labeling experiments

To an oven-dried 10 mL Schlenk tube equipped with a magnetic stirring bar were added 1-(but-3-en-1-yn-1-yl)cyclohexyl *tert*-butyl carbonate **1a** (37.6 mg, 0.150 mmol, 1.5 equiv), (*E*)-3-(2-hydroxybenzylidene)-1-methylindolin-2-one **2a** (25.1 mg, 0.0999 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (5.8 mg, 0.0050 mmol) and *t*-BuOD (75.1 mg, 1.00 mmol). The tube was capped, evacuated and back-filled with argon for five times. Then degassed dry MeCN (2.0 mL) was added via syringe. The mixture was stirred at 60 °C for 36 h, and monitored by TLC (EtOAc/petroleum ether = 1/6). After completion, the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give the product ***d*-3a**: 26.1 mg (0.0681 mmol), as a white solid, 68% yield; 40%-D; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.12–7.05 (m, 1H), 6.94–6.88 (m, 1H), 6.84–6.75 (m, 2H), 6.69–6.60 (m, 2H), 6.48–6.41 (m, 1H), 6.24 (d, *J* = 2.8 Hz, 0.6H), 6.17 (d, *J* = 7.6 Hz, 1H), 4.96 (s, 1H), 4.76 (s, 1H), 4.55 (s, 1H), 3.40 (s, 3H), 2.13–2.05 (m, 1H), 2.05–1.93 (m, 3H), 1.81–1.68 (m, 2H), 1.59–1.31 (m, 4H).

10. Crystal data and structural refinement

Procedure for the recrystallization of 3o: To a 10 mL tube containing enantiopure **3o** (32 mg) were added *n*-hexane (0.3 mL) and EtOAc (1.4 mL). The mixture was heated until a clear solution was formed, which was kept aside at room temperature to obtain crystals. The crystals were subjected for single crystal XRD to determine the absolute configuration of **3o**. The data were collected by an Bruker D8 Venture equipped with a Cu radiation source (Kα = 1.54178 Å) at 273.0 K. CCDC 2381131 (**3o**) 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.



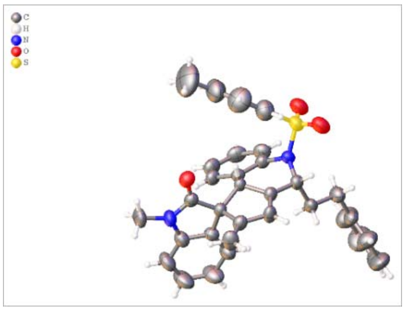


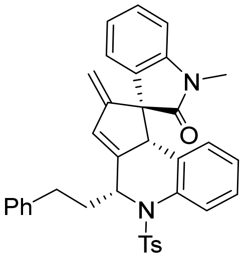
3o

Identification code	**3o**
Empirical formula	$C_{30}H_{27}NO_2$
Formula weight	433.52
Temperature/K	273.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.6278(4)
b/Å	12.3083(6)
c/Å	10.9519(5)
α/°	90
β/°	95.711(3)
γ/°	90
Volume/Å^3	1157.25(9)
Z	2
ρ_{calc}g/cm^3	1.244
μ/mm^{-1}	0.604
F(000)	460.0
Crystal size/mm^3	0.38 × 0.25 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.112 to 140.378

Index ranges	$-10 \leqslant h \leqslant 10, -15 \leqslant k \leqslant 14, -13 \leqslant l \leqslant 12$
Reflections collected	7672
Independent reflections	3988 [R_{int} = 0.0402, R_{sigma} = 0.0528]
Data/restraints/parameters	3988/1/300
Goodness-of-fit on F^2	1.077
Final R indexes [I>=2σ (I)]	R_1 = 0.0380, wR_2 = 0.0971
Final R indexes [all data]	R_1 = 0.0437, wR_2 = 0.1013
Largest diff. peak/hole / e $Å^{-3}$	0.16/-0.12
Flack parameter	-0.01(18)

Procedure for the recrystallization of 12g: To a 10 mL tube containing enantiopure **12g** (45 mg) were added *n*-hexane (0.5 mL) and EtOAc (1.5 mL). The mixture was heated until a clear solution was formed, which was kept aside at room temperature to obtain crystals. The crystals were subjected for single crystal XRD to determine the absoulte configuration of **12g**. The data were collected by an Bruker D8 Venture equipped with a Mo radiation source (Kα = 0.71073 Å) at 303.0 K. CCDC 2381132 (**12g**) 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.



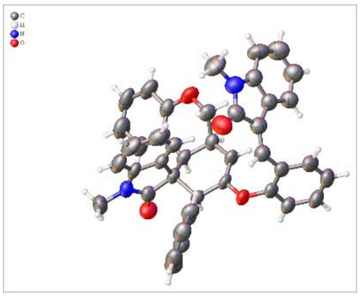


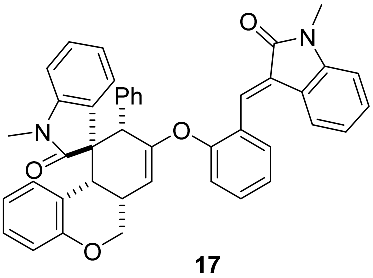
12g

Identification code	**12g**
Empirical formula	$C_{36}H_{32}N_2O_3S$
Formula weight	572.69
Temperature/K	303.0
Crystal system	tetragonal
Space group	$P4_32_12$
a/Å	12.4257(6)
b/Å	12.4257(6)
c/Å	42.988(4)
α/°	90
β/°	90

γ/°	90
Volume/Å^3	6637.3(9)
Z	8
ρ_{calc}g/cm^3	1.146
μ/mm^{-1}	0.133
F(000)	2416.0
Crystal size/mm^3	0.48 × 0.42 × 0.26
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.786 to 54.894
Index ranges	$-12 \leqslant h \leqslant 15, -16 \leqslant k \leqslant 11, -55 \leqslant l \leqslant 41$
Reflections collected	22897
Independent reflections	7524 [R_{int} = 0.0566, R_{sigma} = 0.0770]
Data/restraints/parameters	7524/7/381
Goodness-of-fit on F^2	0.985
Final R indexes [I>=2σ (I)]	R_1 = 0.0542, wR_2 = 0.1043
Final R indexes [all data]	R_1 = 0.1202, wR_2 = 0.1296
Largest diff. peak/hole / e Å^{-3}	0.14/-0.21
Flack parameter	0.00(6)

Procedure for the recrystallization of 17: To a 10 mL tube containing racemic **17** (48 mg) were added *n*-hexane (0.5 mL) and EtOAc (1.5 mL). The mixture was heated until a clear solution was formed, which was kept aside at room temperature to obtain crystals. The crystals were subjected for single crystal XRD to determine the relative configuration of **17**. The data were collected by an Bruker D8 Venture equipped with a Mo radiation source (Kα = 0.71073 Å) at 304.0 K. CCDC 2381133 (**17**) 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.





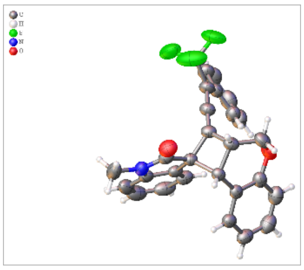
17

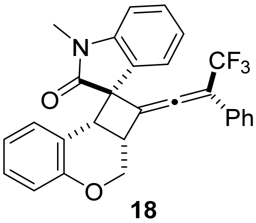
17

Identification code	
Empirical formula	$C_{43}H_{34}N_2O_4$
Formula weight	642.72
Temperature/K	304.0
Crystal system	monoclinic
Space group	C2/c
a/Å	21.731(4)
b/Å	9.1510(15)
c/Å	34.748(7)
α/°	90
β/°	107.204(9)
γ/°	90
Volume/Å^3	6601(2)
Z	8
ρ_{calc}g/cm^3	1.293
μ/mm^{-1}	0.083
F(000)	2704.0
Crystal size/mm^3	0.12 × 0.07 × 0.05
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.924 to 49.98
Index ranges	$-25 \leqslant h \leqslant 25, -10 \leqslant k \leqslant 10, -41 \leqslant l \leqslant 41$
Reflections collected	34640
Independent reflections	5737 [R_{int} = 0.1452, R_{sigma} = 0.1134]
Data/restraints/parameters	5737/0/445
Goodness-of-fit on F^2	1.025
Final R indexes [I>=2σ (I)]	R_1 = 0.0831, wR_2 = 0.1892
Final R indexes [all data]	R_1 = 0.1959, wR_2 = 0.2470
Largest diff. peak/hole / e Å^{-3}	0.24/-0.25

Procedure for the recrystallization of 18: To a 10 mL tube containing racemic **18** (42 mg) were added *n*-hexane (0.5 mL) and EtOAc (1.4 mL). The mixture was heated until a clear solution was formed, which was kept aside at room temperature to obtain crystals. The crystals were subjected for single crystal XRD to determine the relative configuration of **18**. The data were collected by an Bruker

D8 Venture equipped with a Mo radiation source (Kα = 0.71073 Å) at 227.0 K. CCDC 2381134 (**18**) 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.



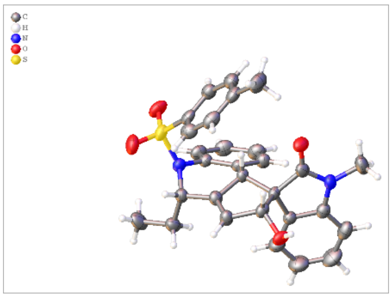


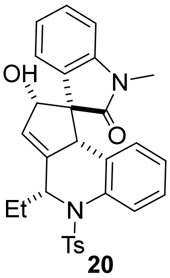
18

Identification code	**18**
Empirical formula	$C_{28}H_{20}F_3NO_2$
Formula weight	459.45
Temperature/K	227.0
Crystal system	triclinic
Space group	P-1
a/Å	9.9196(10)
b/Å	9.9973(9)
c/Å	11.8824(11)
α/°	91.791(4)
β/°	104.104(4)
γ/°	102.384(3)
Volume/Å^3	1111.91(18)
Z	2
ρ_{calc}g/cm^3	1.372
μ/mm^{-1}	0.103
F(000)	476.0
Crystal size/mm^3	0.45 × 0.37 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.858 to 55.012
Index ranges	$-12 \leqslant h \leqslant 12, -11 \leqslant k \leqslant 12, -15 \leqslant l \leqslant 15$
Reflections collected	18358
Independent reflections	5062 [R_{int} = 0.0935, R_{sigma} = 0.0893]
Data/restraints/parameters	5062/0/308

Goodness-of-fit on F^2	1.055
Final R indexes [I>=2σ (I)]	$R_1 = 0.0703$, $wR_2 = 0.1888$
Final R indexes [all data]	$R_1 = 0.1065$, $wR_2 = 0.2161$
Largest diff. peak/hole / e Å^{-3}	0.25/-0.28

Procedure for the recrystallization of 20: To a 10 mL tube containing racemic **20** (37 mg) were added *n*-hexane (0.4 mL) and EtOAc (1.4 mL). The mixture was heated until a clear solution was formed, which was kept aside at room temperature to obtain crystals. The crystals were subjected for single crystal XRD to determine the relative configuration of **20**. The data were collected by an Bruker D8 Venture equipped with a Mo radiation source (Kα = 0.71073 Å) at 150.0 K. CCDC 2381135 (**20**) 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.



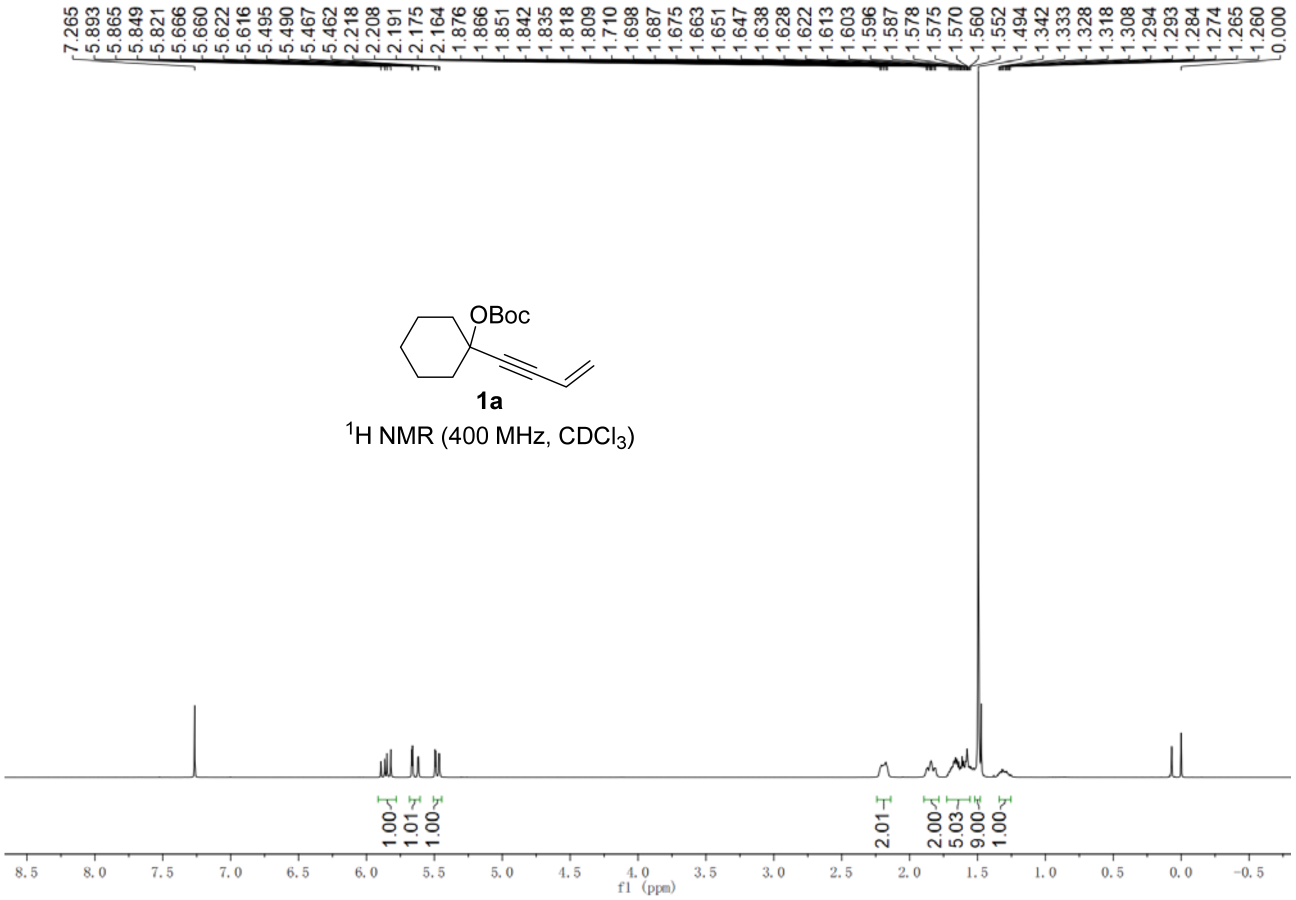


20

Identification code	**20**
Empirical formula	$C_{29}H_{28}N_2O_4S$
Formula weight	500.59
Temperature/K	150.0
Crystal system	triclinic
Space group	P-1
a/Å	7.4687(15)
b/Å	12.636(2)
c/Å	14.057(3)
α/°	86.841(7)
β/°	76.742(7)
γ/°	75.308(7)
Volume/Å^3	1249.1(4)
Z	2
ρ_{calc}g/cm^3	1.331
μ/mm^{-1}	0.168
F(000)	528.0

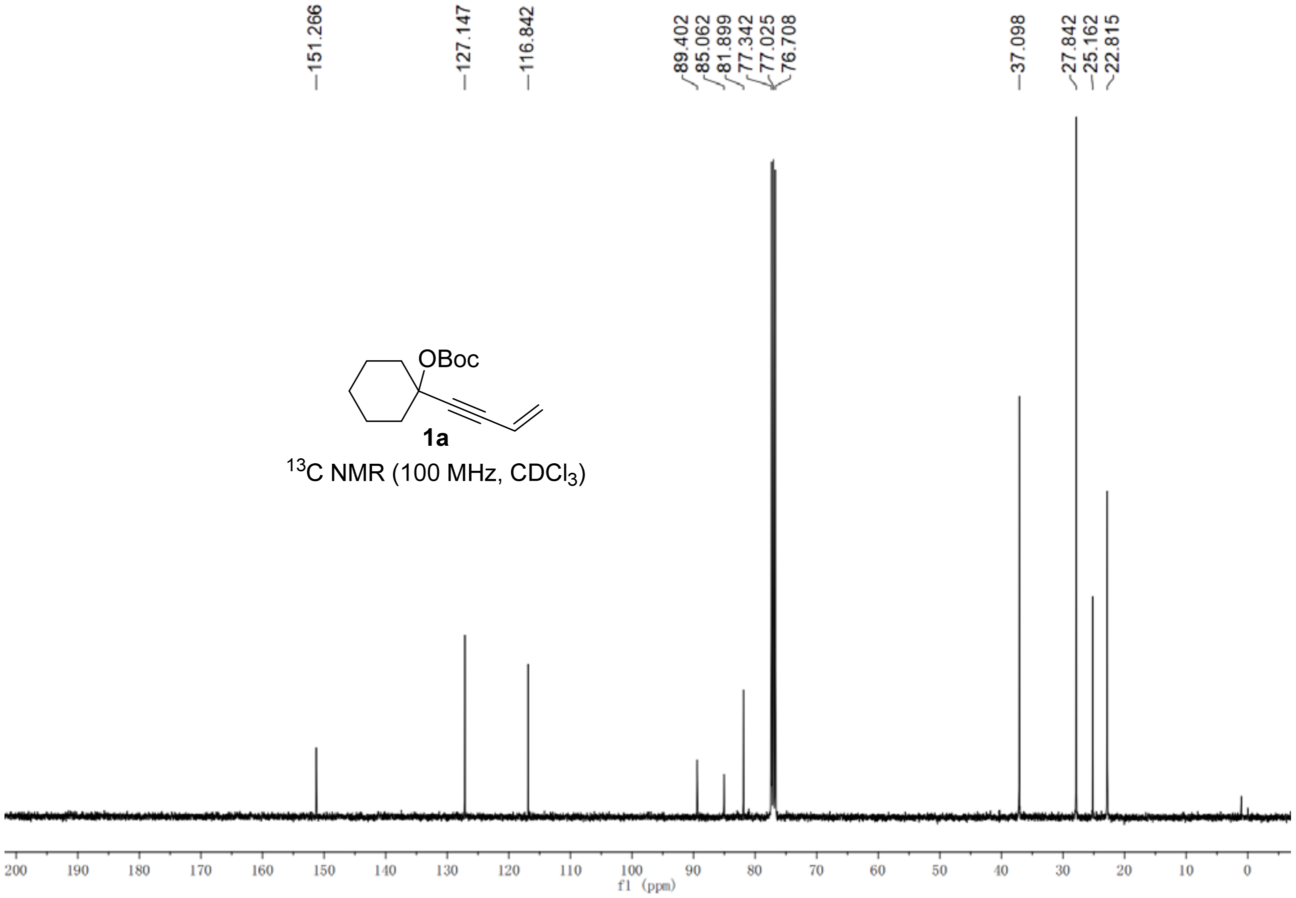
Crystal size/mm^3	0.24 × 0.15 × 0.1
Radiation	MoKα ($\lambda = 0.71073$)
2Θ range for data collection/°	4.462 to 49.992
Index ranges	$-8 \leqslant h \leqslant 8$, $-15 \leqslant k \leqslant 15$, $-16 \leqslant l \leqslant 16$
Reflections collected	17419
Independent reflections	4281 [$R_{int} = 0.0923$, $R_{sigma} = 0.0765$]
Data/restraints/parameters	4281/0/330
Goodness-of-fit on F^2	1.113
Final R indexes [I>=2σ (I)]	$R_1 = 0.0965$, $wR_2 = 0.2626$
Final R indexes [all data]	$R_1 = 0.1265$, $wR_2 = 0.2881$
Largest diff. peak/hole / e Å^{-3}	0.90/-0.44

11. NMR, HRMS spectra and HPLC chromatograms



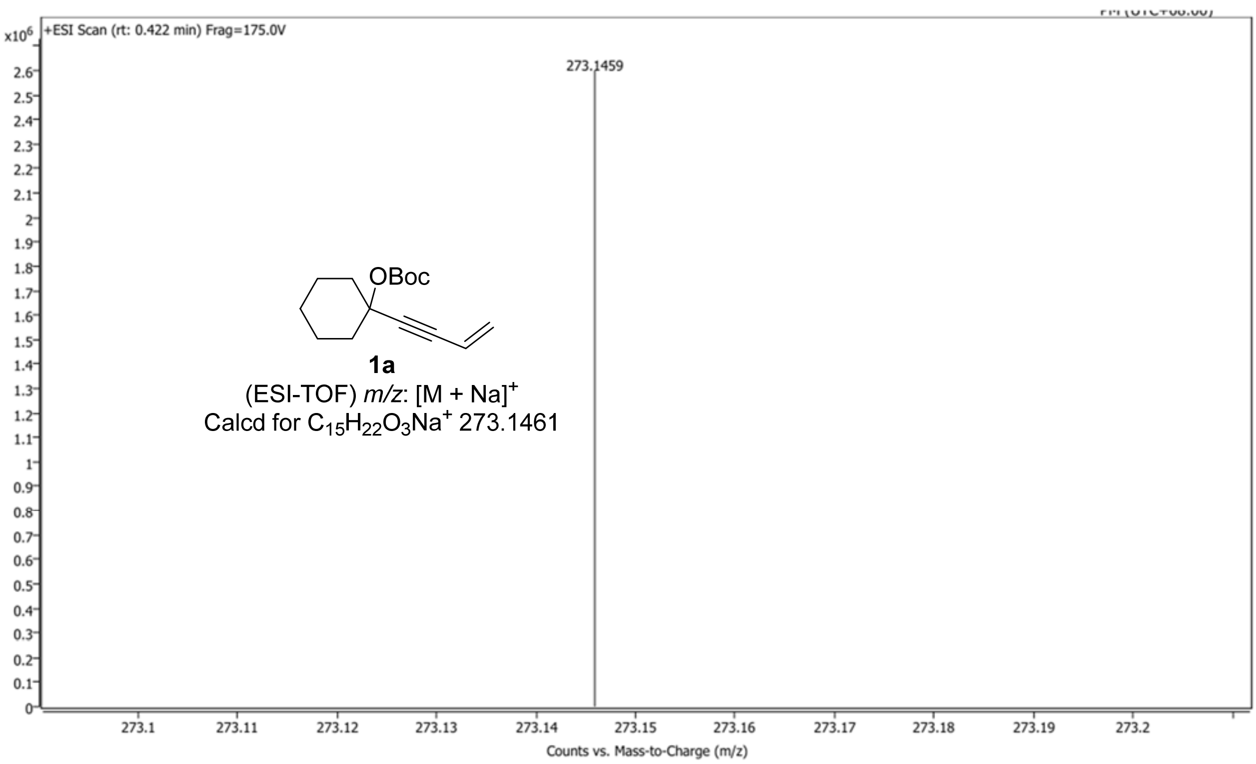
1a

^{1}H NMR (400 MHz, $CDCl_3$)



1a

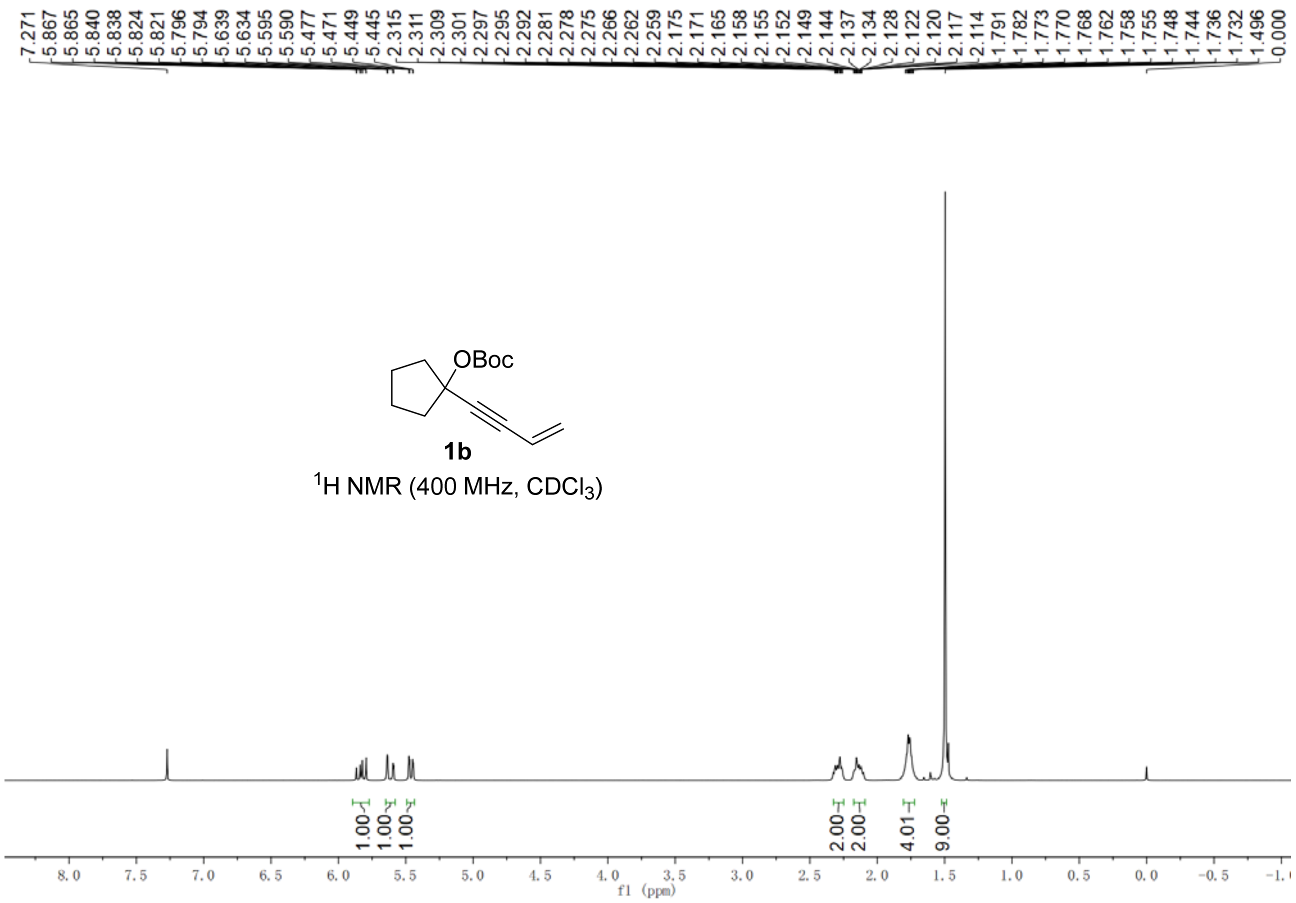
^{13}C NMR (100 MHz, $CDCl_3$)



1a

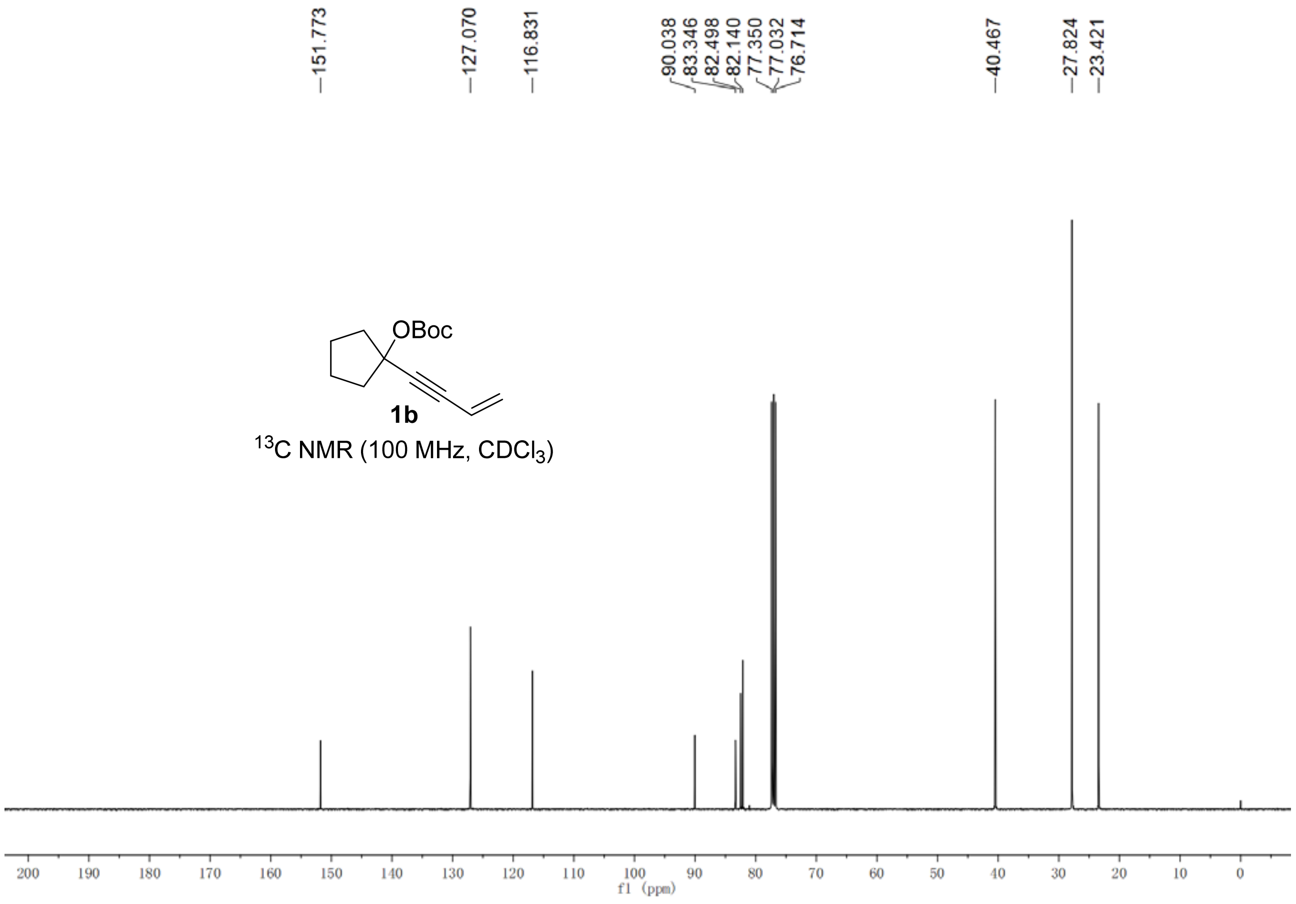
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{15}H_{22}O_3Na^+$ 273.1461



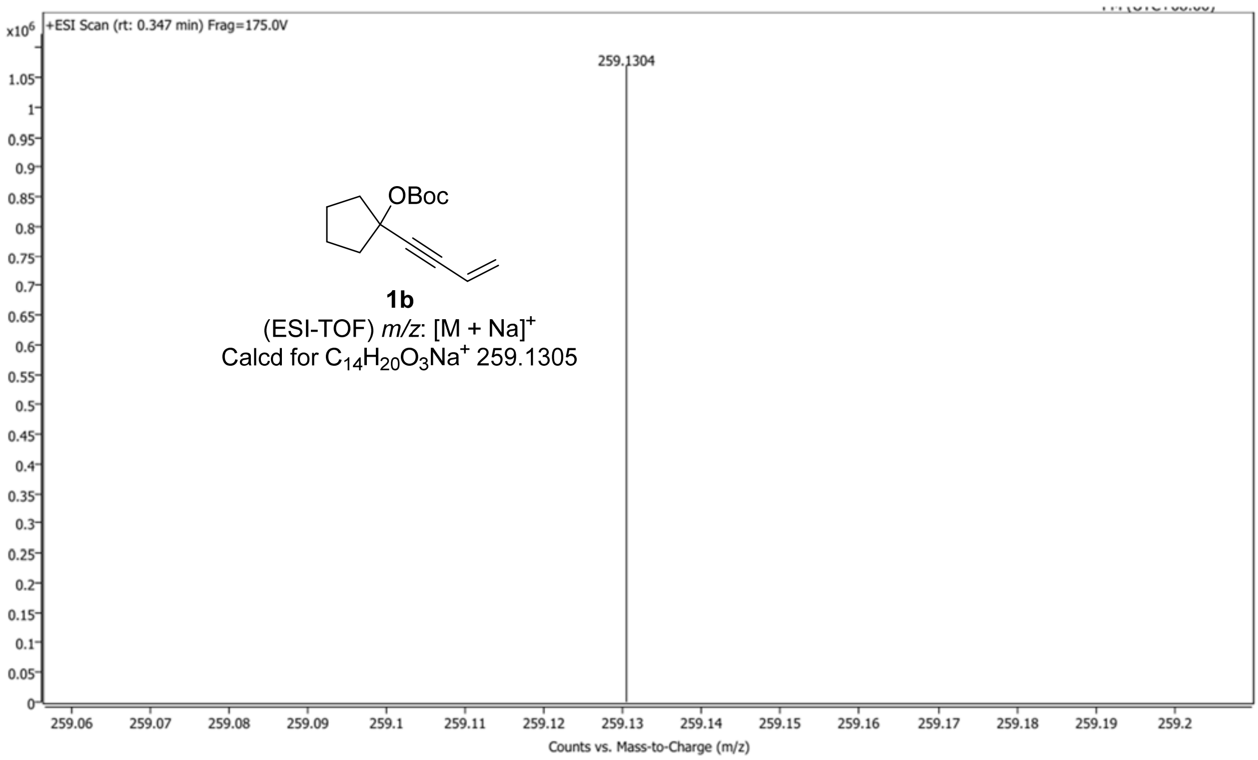
1b

^{1}H NMR (400 MHz, $CDCl_3$)



1b

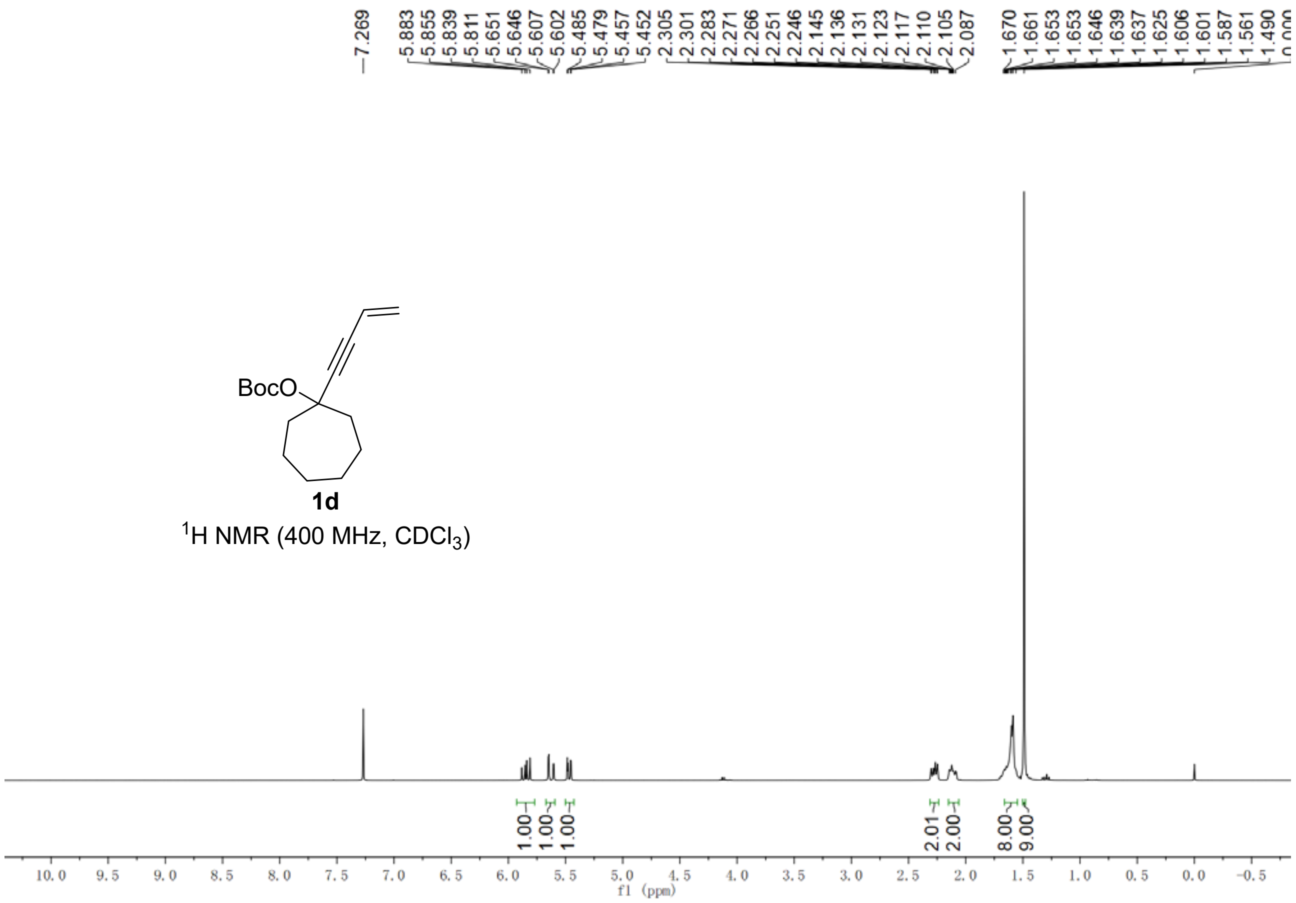
^{13}C NMR (100 MHz, $CDCl_3$)



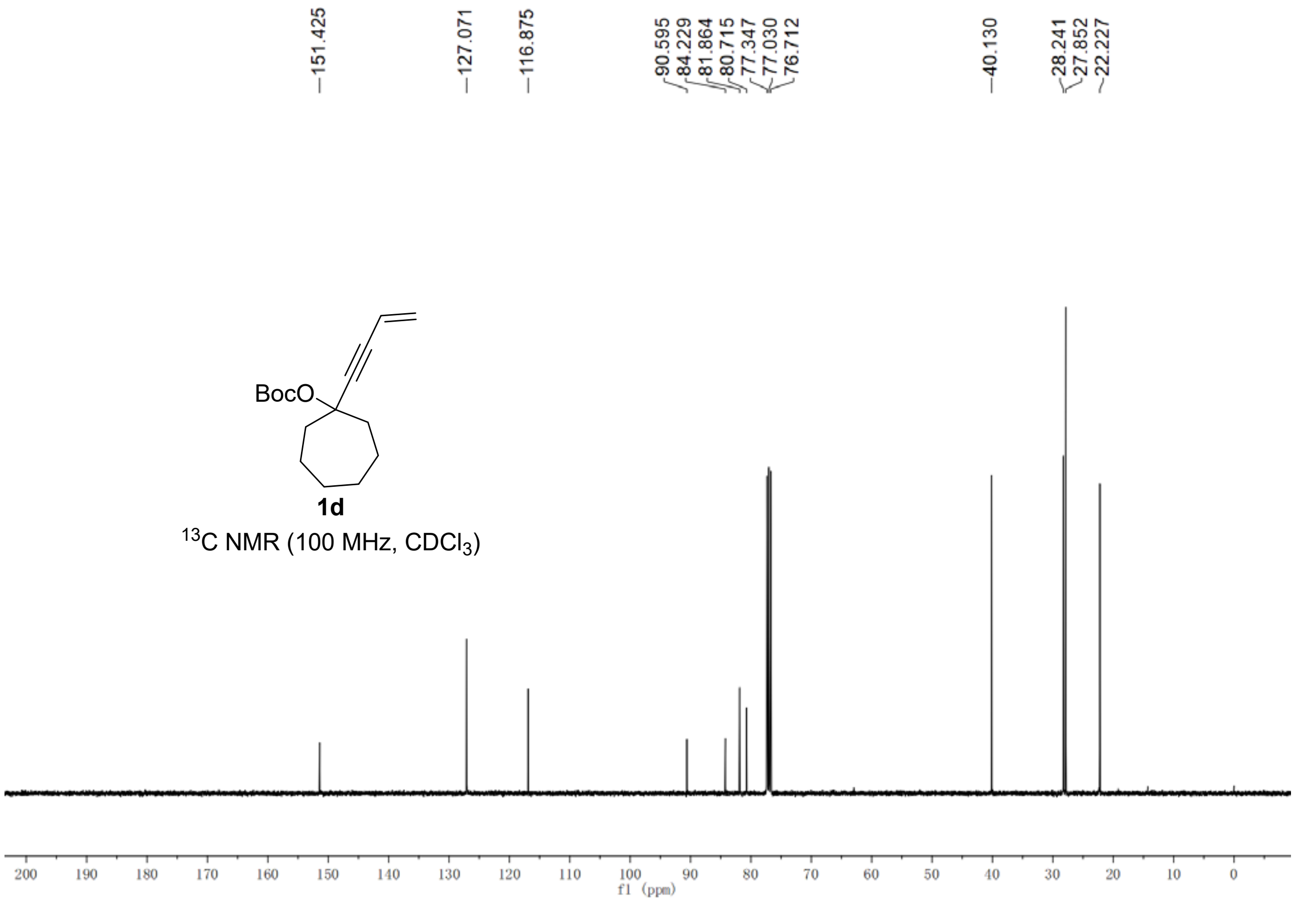
1b

(ESI-TOF) *m/z*: $[M + Na]^+$

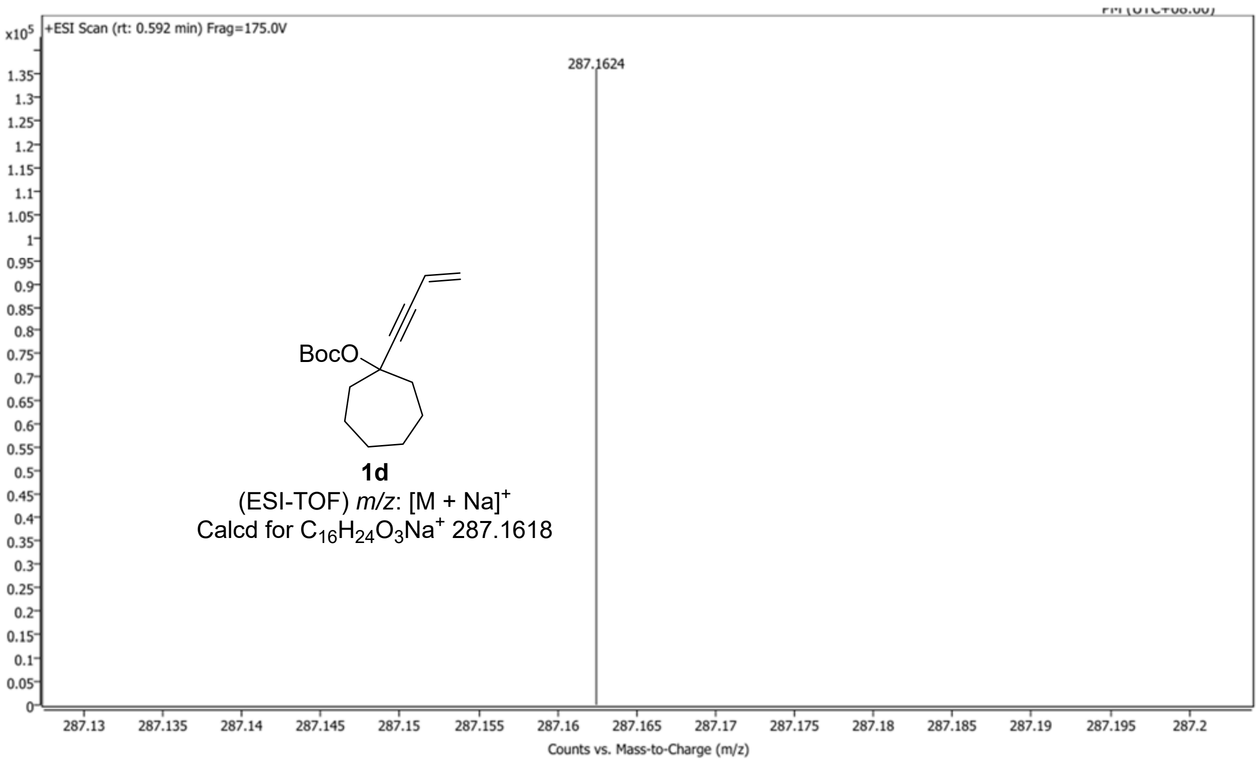
Calcd for $C_{14}H_{20}O_3Na^+$ 259.1305



7.269
5.883
5.855
5.839
5.811
5.651
5.646
5.607
5.602
5.485
5.479
5.457
5.452
2.305
2.301
2.283
2.271
2.266
2.251
2.246
2.145
2.136
2.131
2.123
2.117
2.110
2.105
2.087
1.670
1.661
1.653
1.653
1.646
1.639
1.637
1.625
1.606
1.601
1.587
1.561
1.490
0.000
BocO
1d
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.00
1.00
2.01
2.00
8.00
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



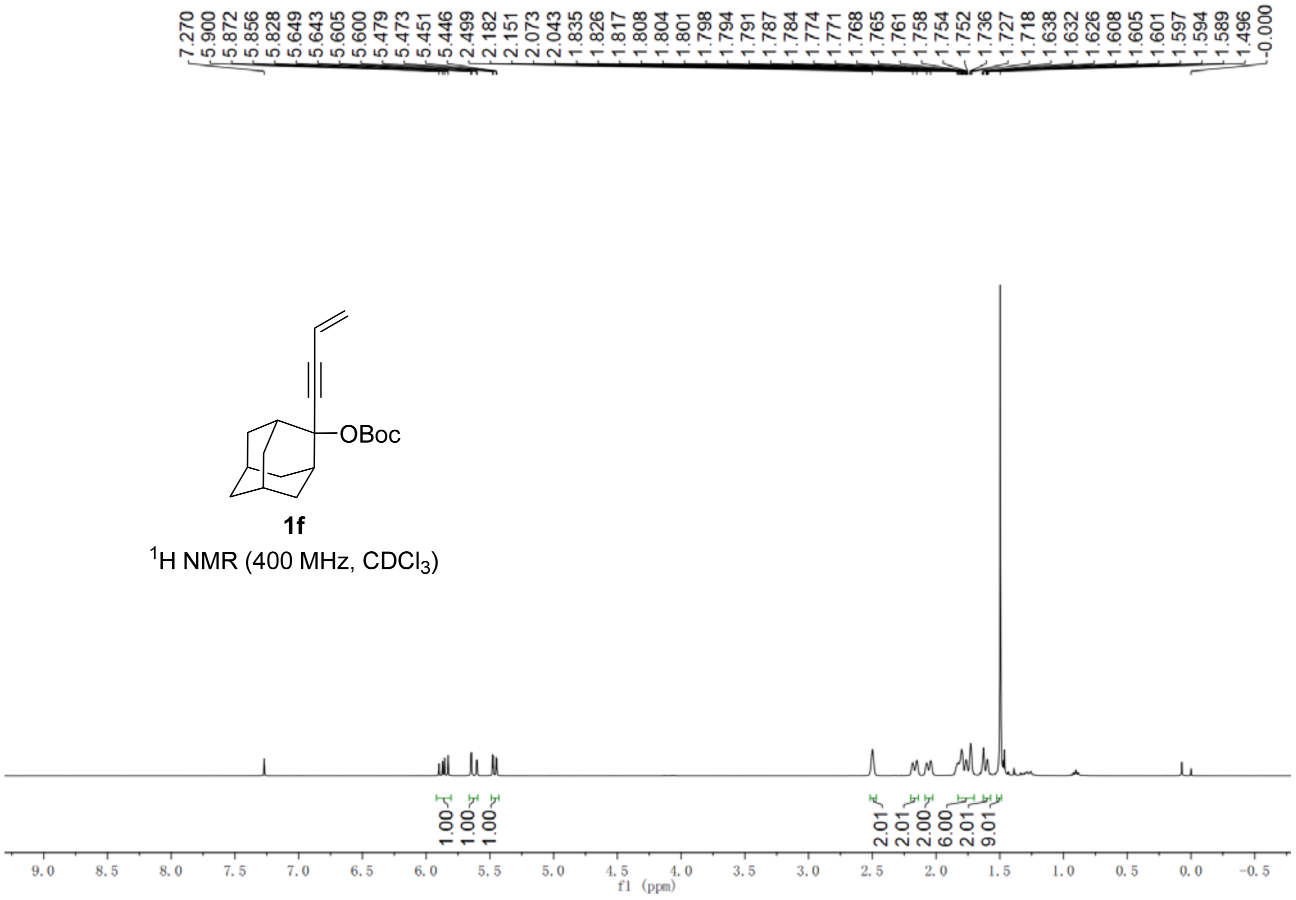
151.425
127.071
116.875
90.595
84.229
81.864
80.715
77.347
77.030
76.712
40.130
28.241
27.852
22.227
BocO
1d
^{13}C NMR (100 MHz, CDCl$_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



1d

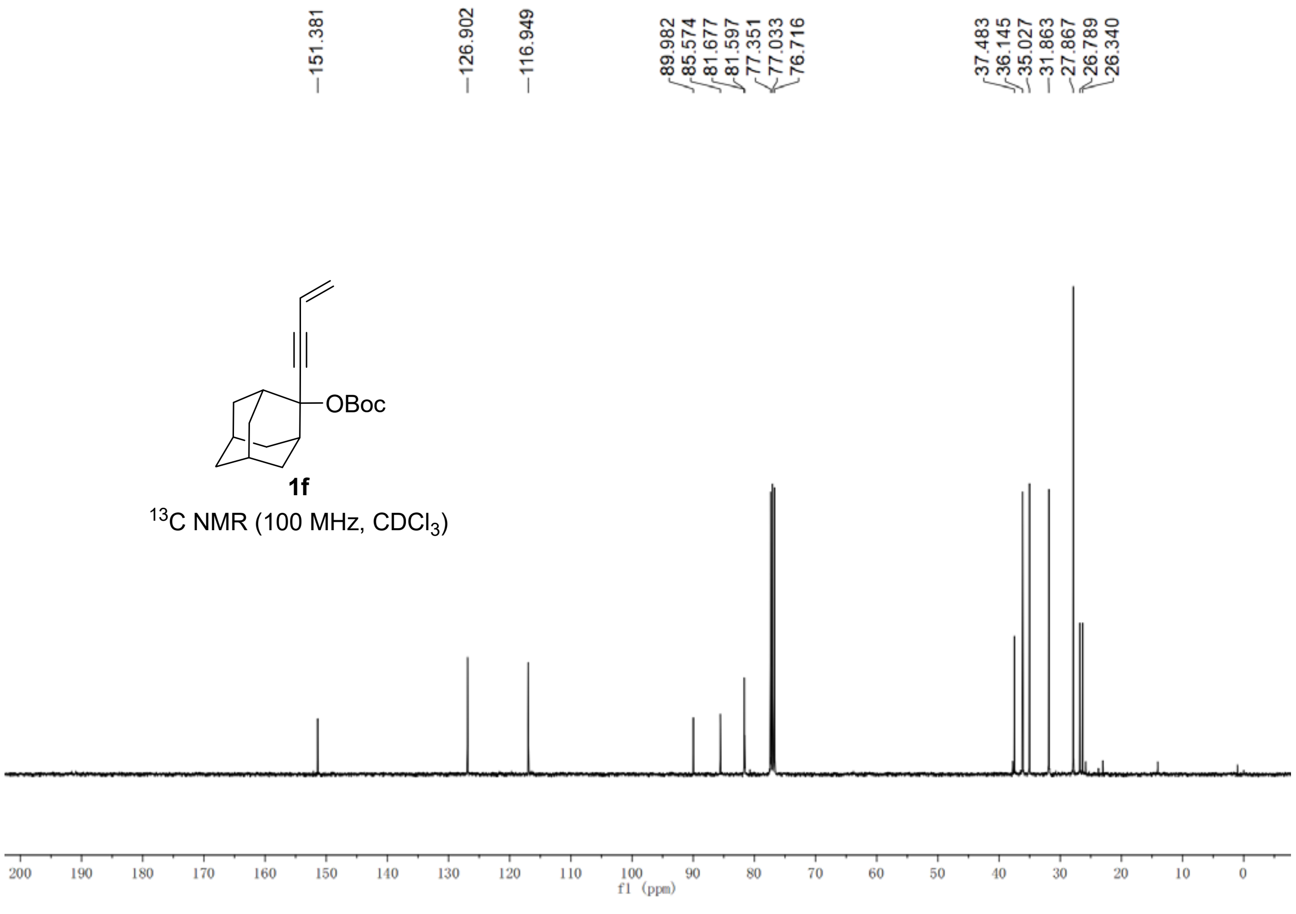
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{16}H_{24}O_3Na^+$ 287.1618



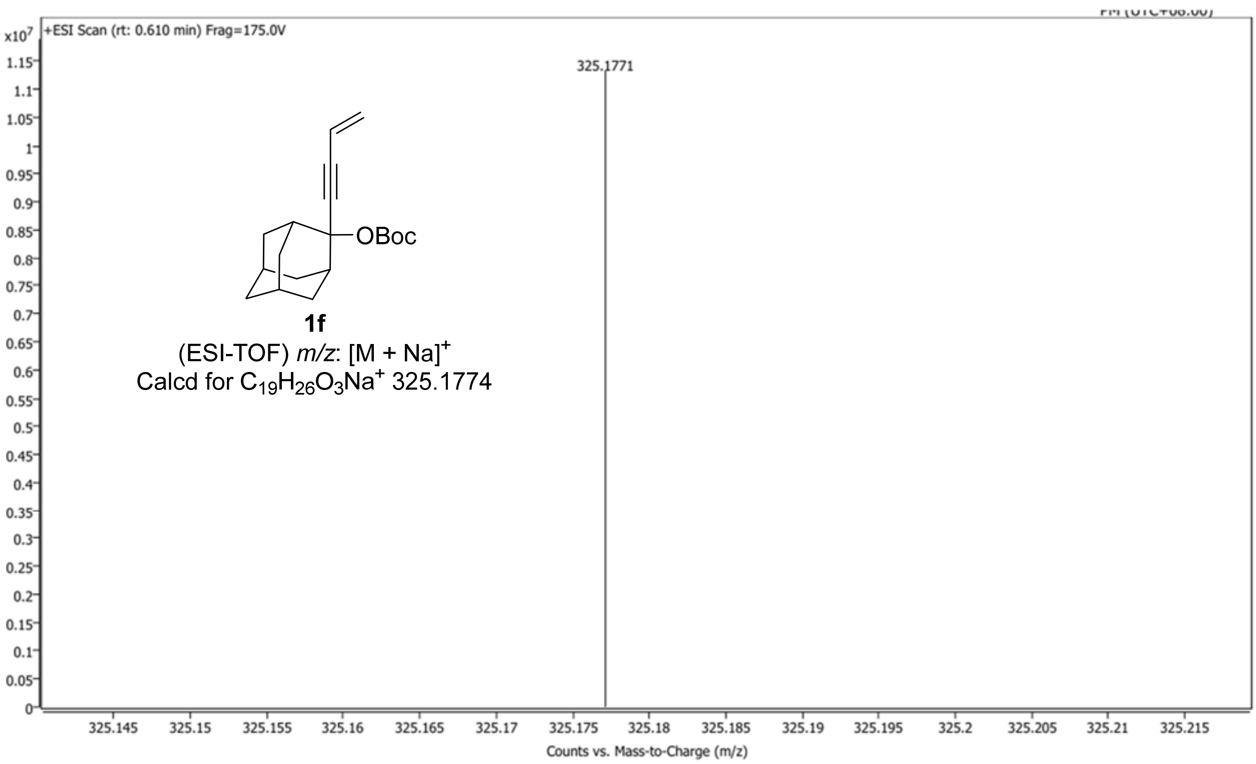
1f

^{1}H NMR (400 MHz, CDCl$_3$)



1f

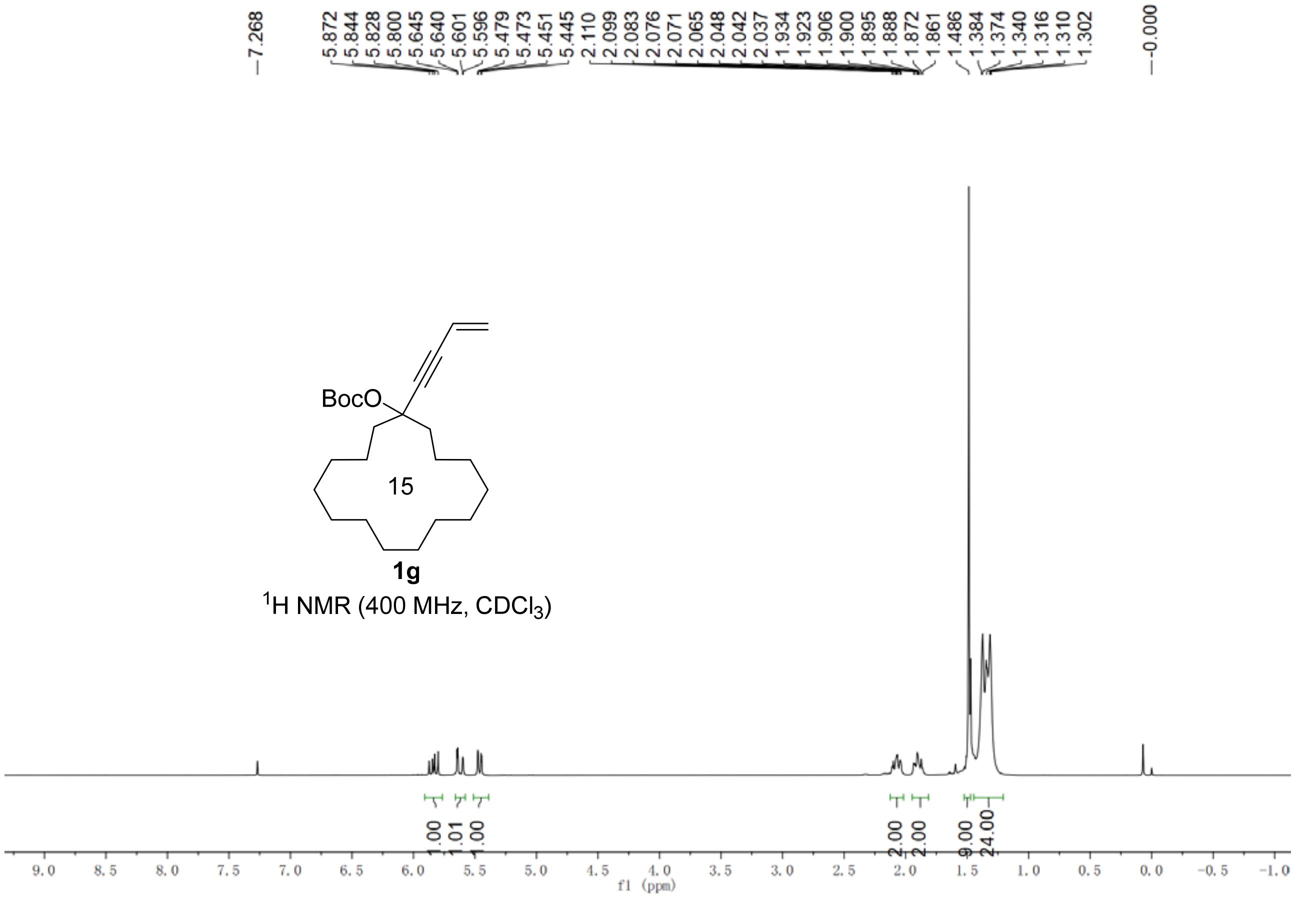
^{13}C NMR (100 MHz, CDCl$_3$)



1f

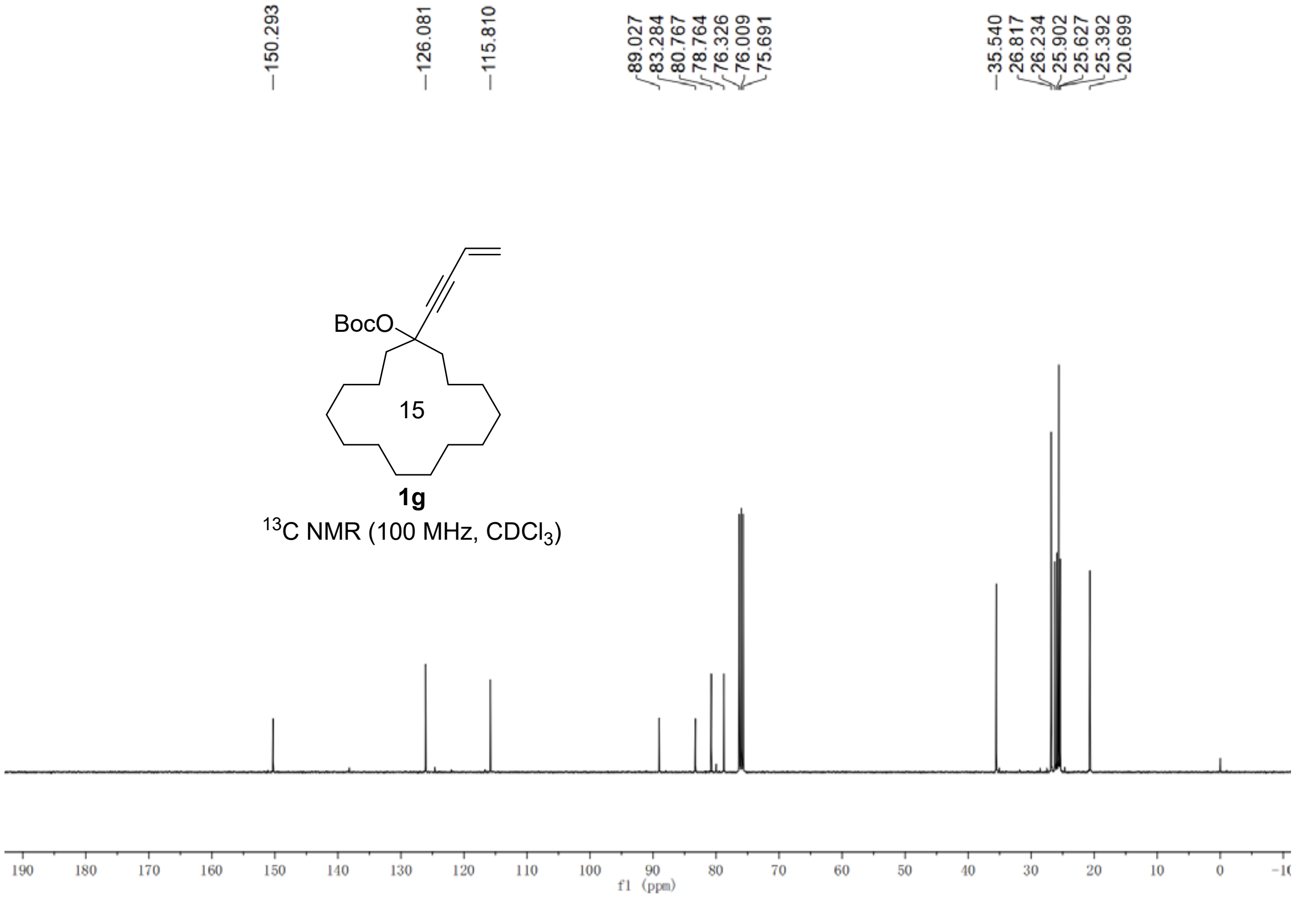
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{19}H_{26}O_3Na^+$ 325.1774



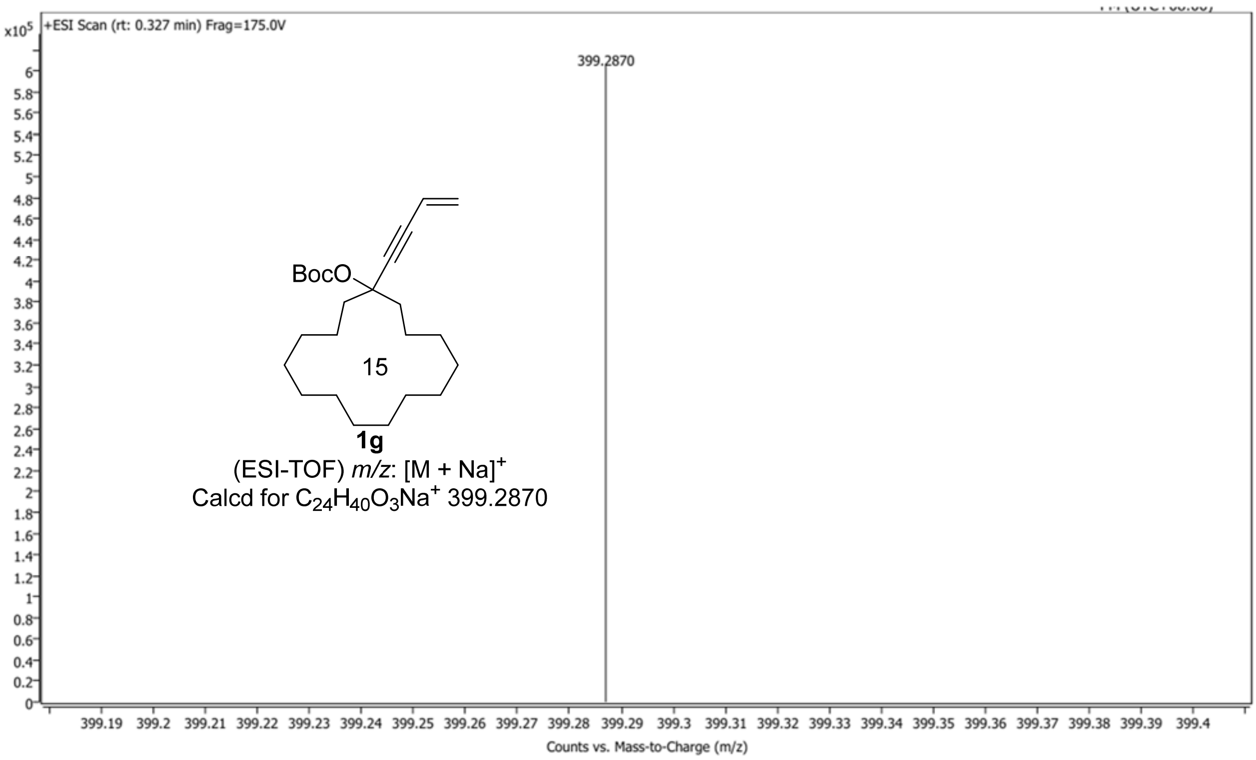
1g

^{1}H NMR (400 MHz, CDCl$_3$)



1g

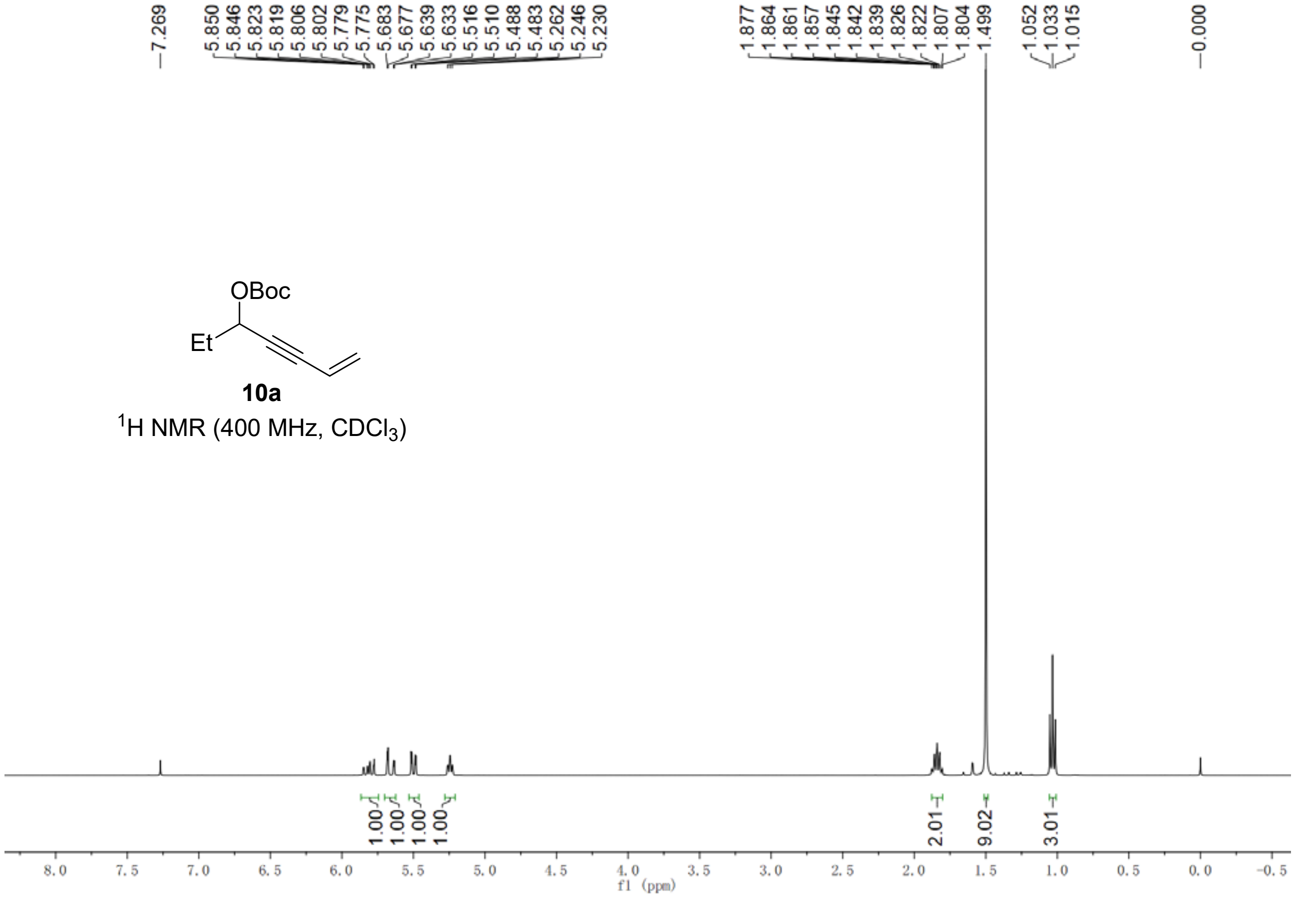
^{13}C NMR (100 MHz, CDCl$_3$)



1g

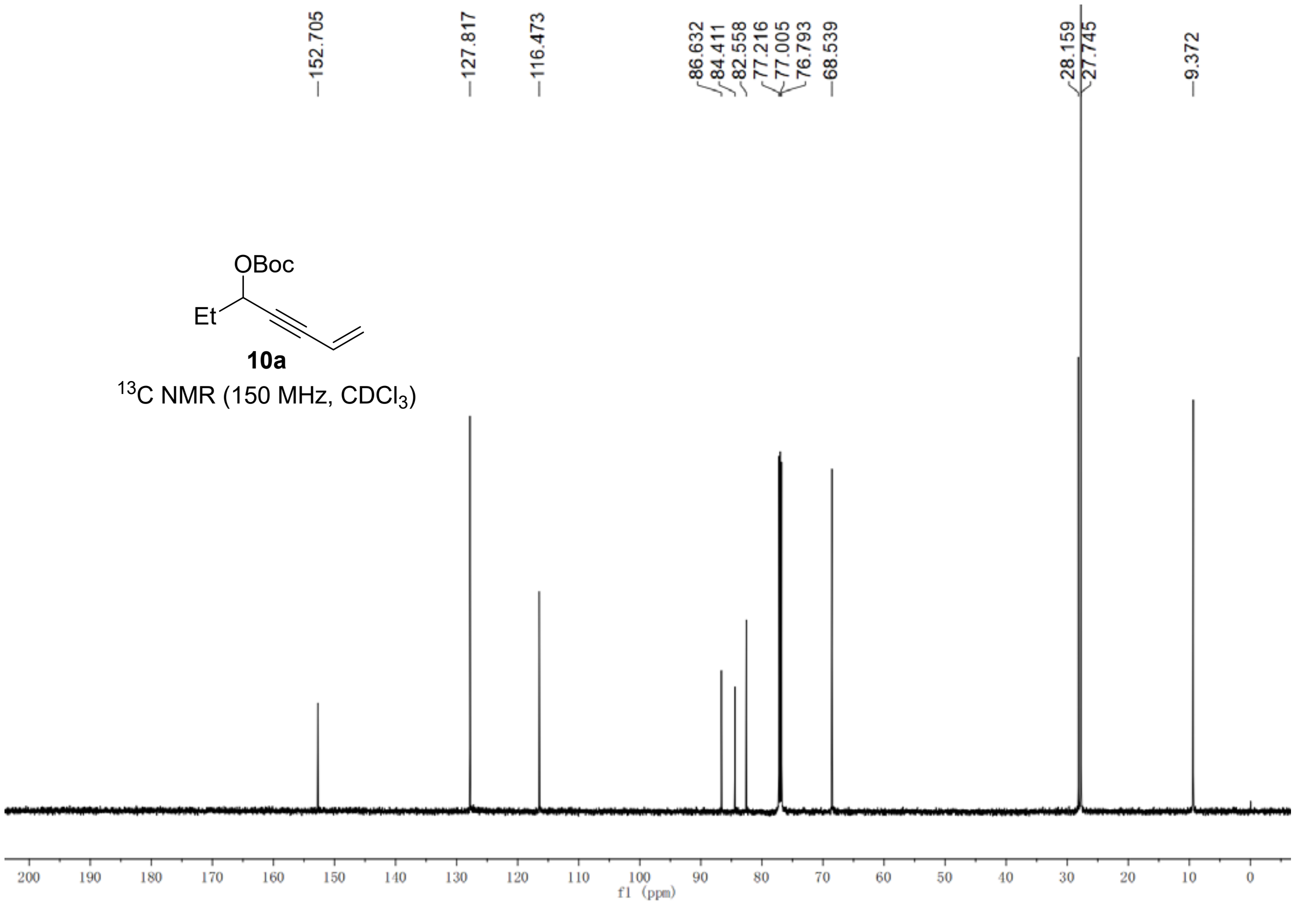
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{24}H_{40}O_3Na^+$ 399.2870



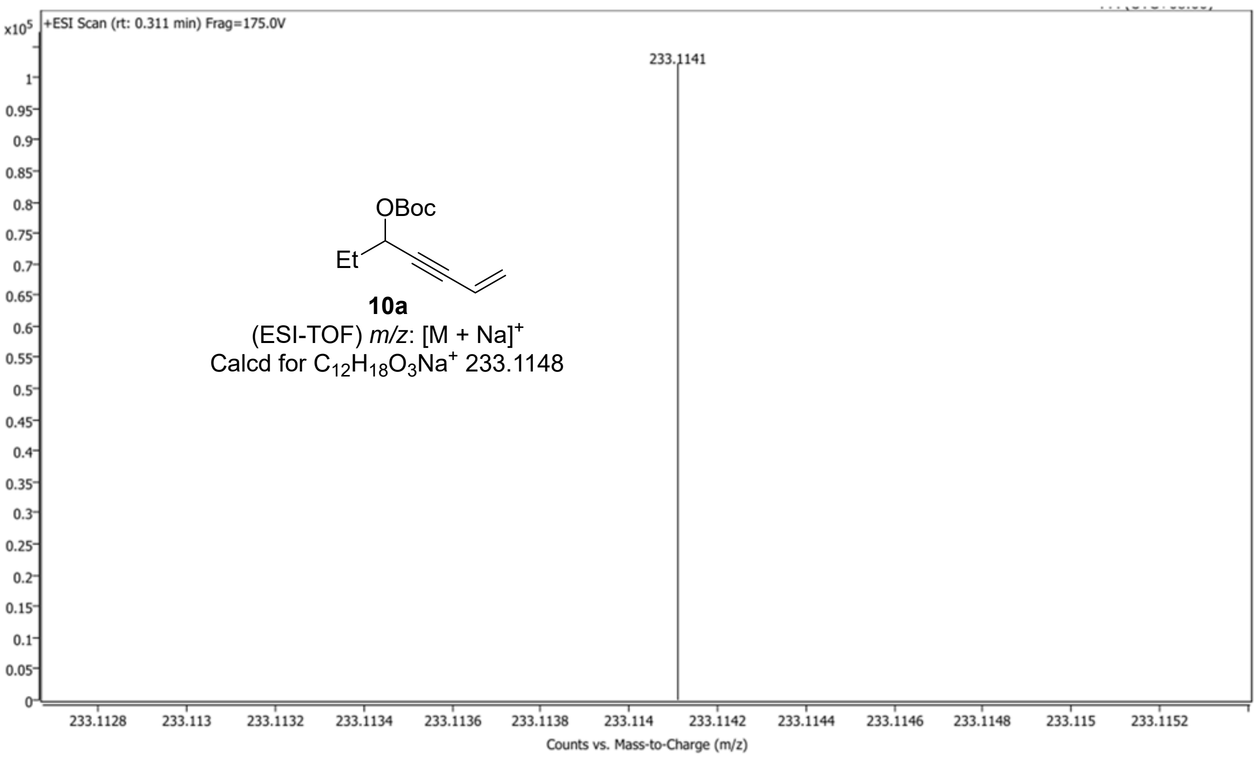
10a

^{1}H NMR (400 MHz, CDCl$_3$)



10a

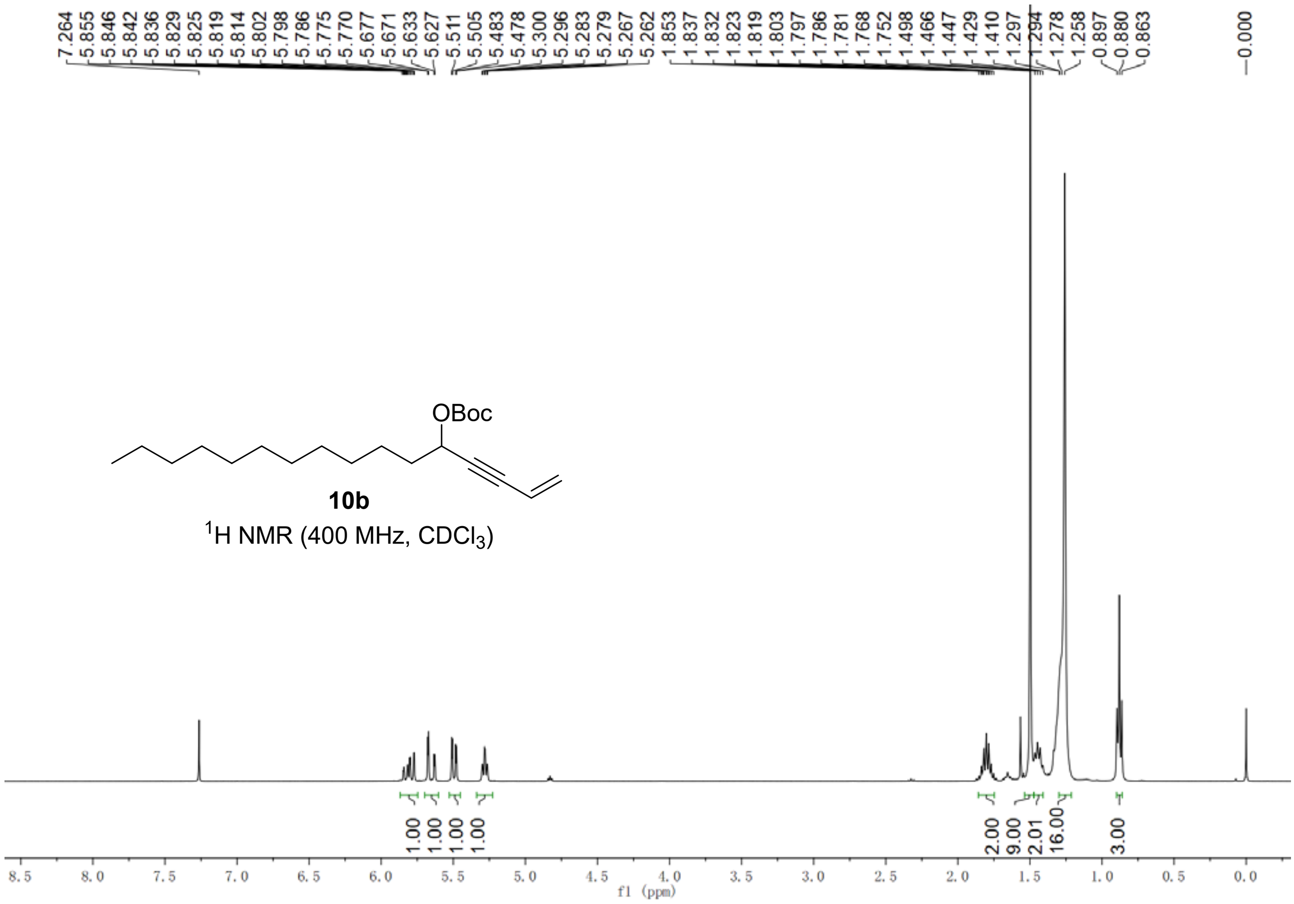
^{13}C NMR (150 MHz, CDCl$_3$)

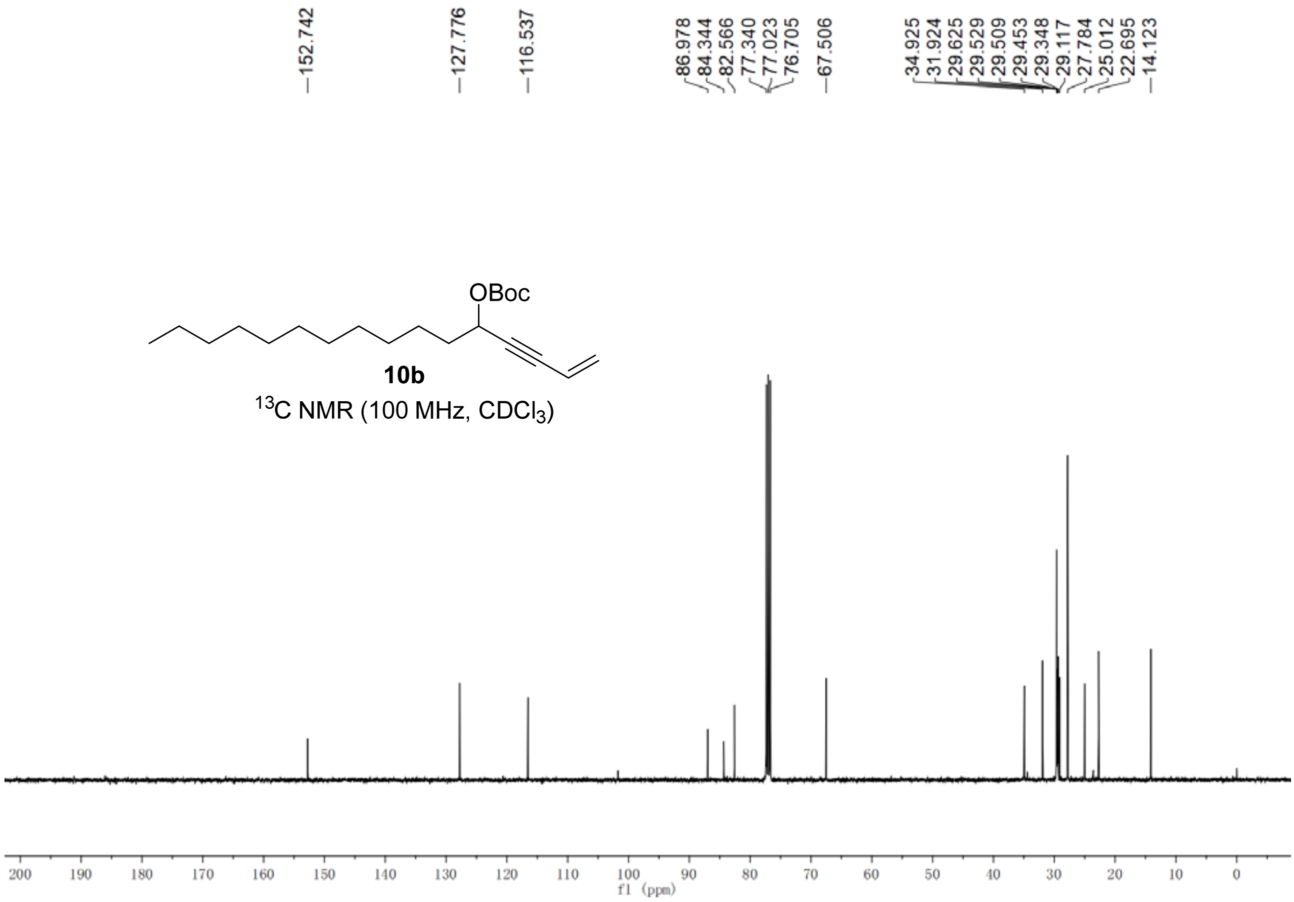


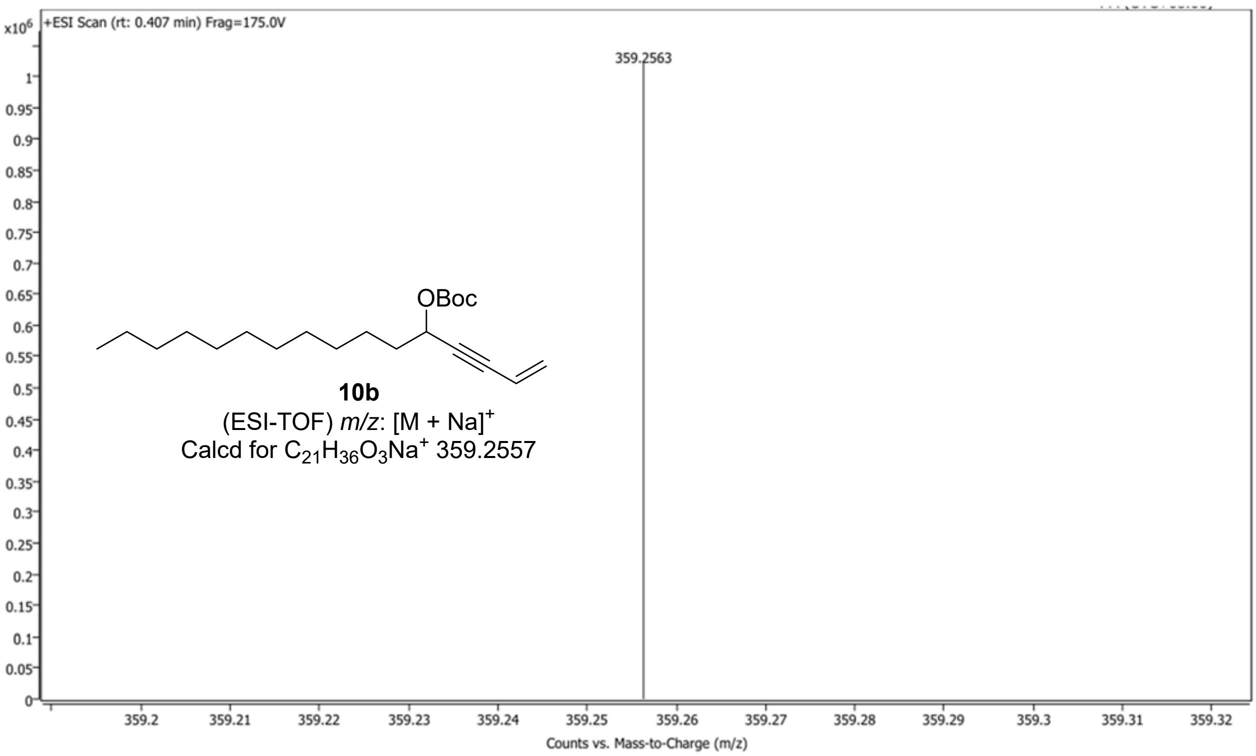
10a

(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{12}H_{18}O_3Na^+$ 233.1148


7.264
5.855
5.846
5.842
5.836
5.829
5.825
5.819
5.814
5.802
5.798
5.786
5.775
5.770
5.677
5.671
5.633
5.627
5.511
5.505
5.483
5.478
5.300
5.296
5.283
5.279
5.267
5.262
1.853
1.837
1.832
1.823
1.819
1.803
1.797
1.786
1.781
1.768
1.752
1.498
1.466
1.447
1.429
1.410
1.297
1.294
1.278
1.258
0.897
0.880
0.863
0.000
OBoc
10b
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.00
1.00
1.00
2.00
9.00
2.01
16.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

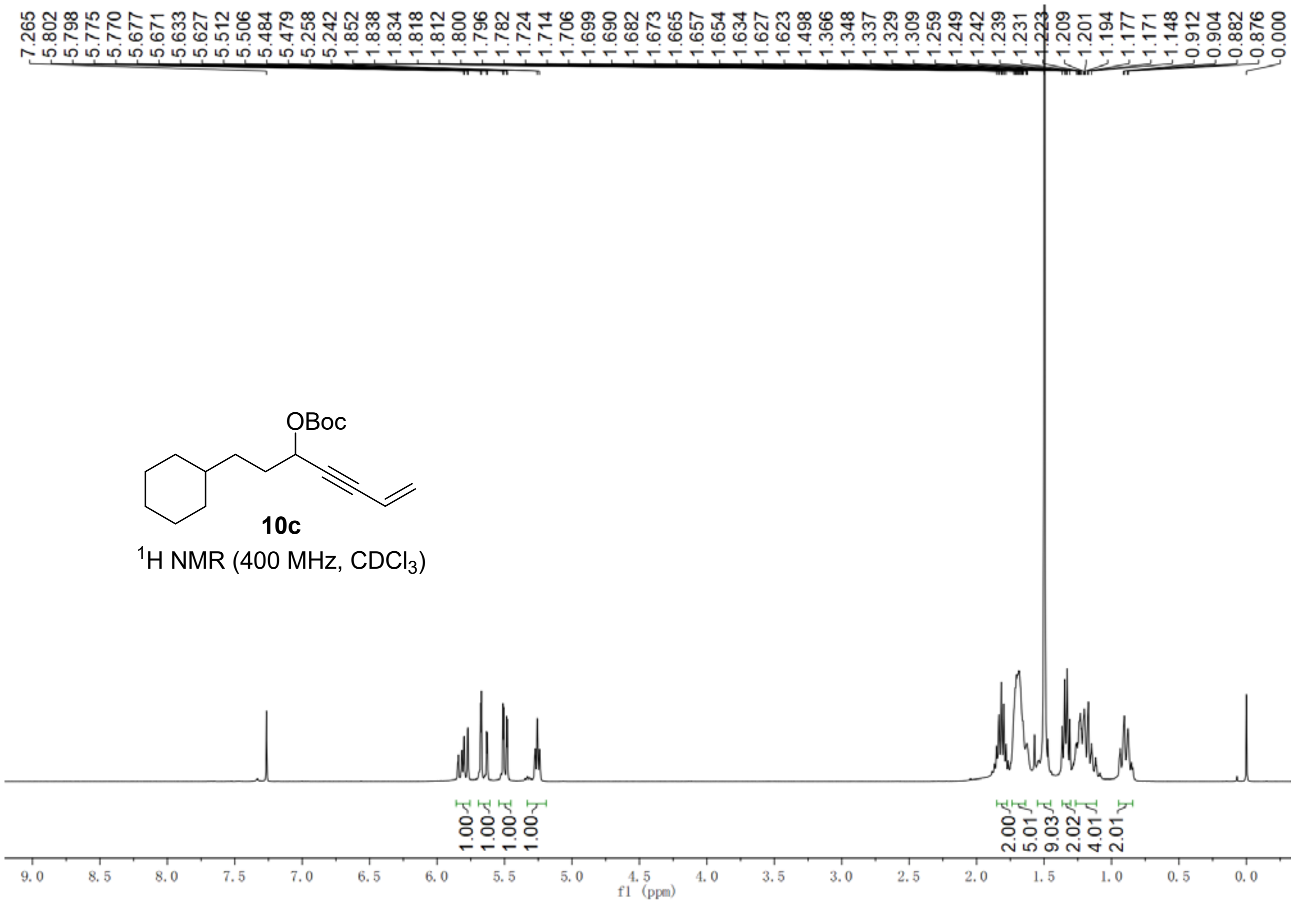

152.742
127.776
116.537
86.978
84.344
82.566
77.340
77.023
76.705
67.506
34.925
31.924
29.625
29.529
29.509
29.453
29.348
29.117
27.784
25.012
22.695
14.123
OBoc
10b
^{13}C NMR (100 MHz, CDCl$_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



10b

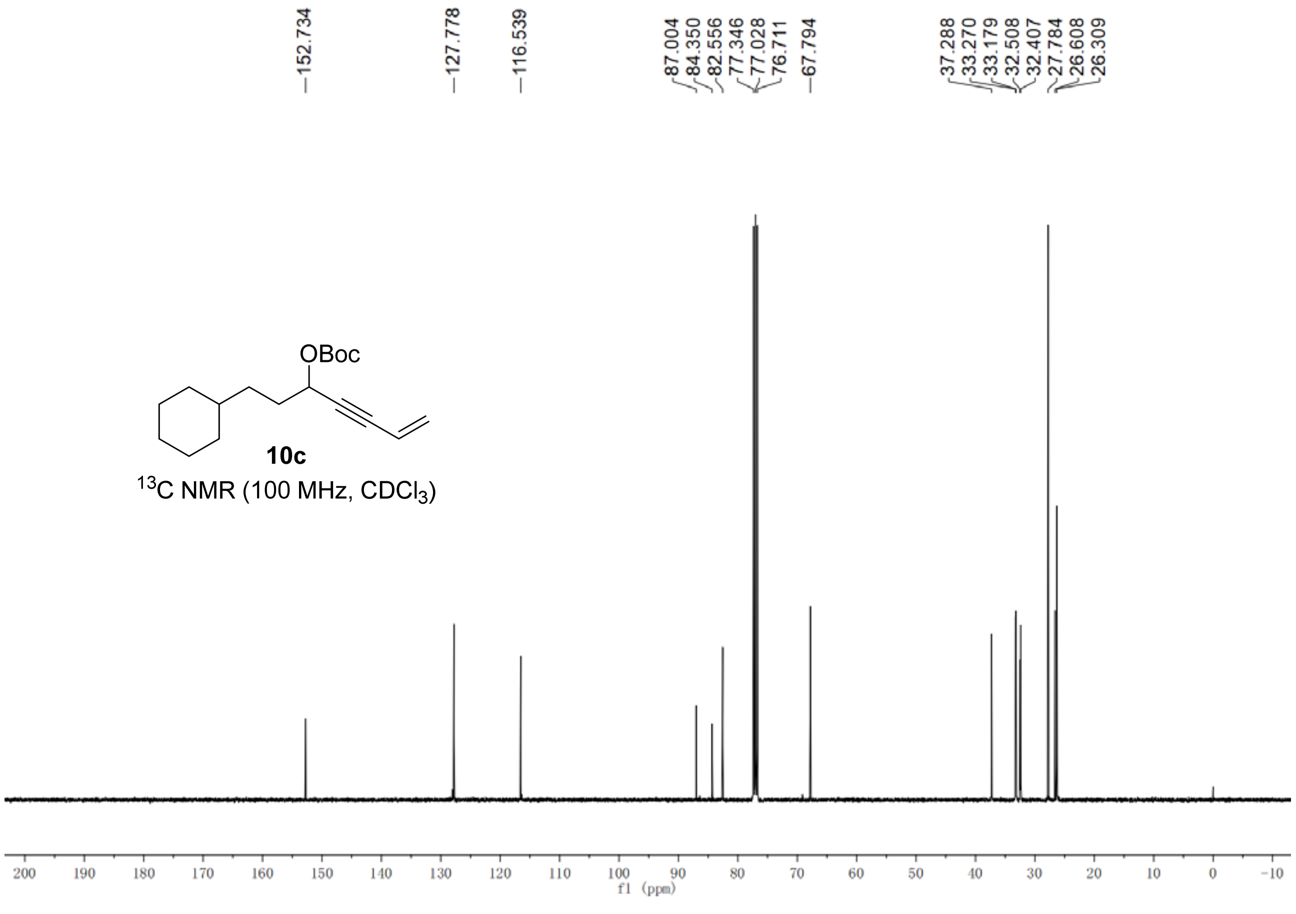
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{21}H_{36}O_3Na^+$ 359.2557



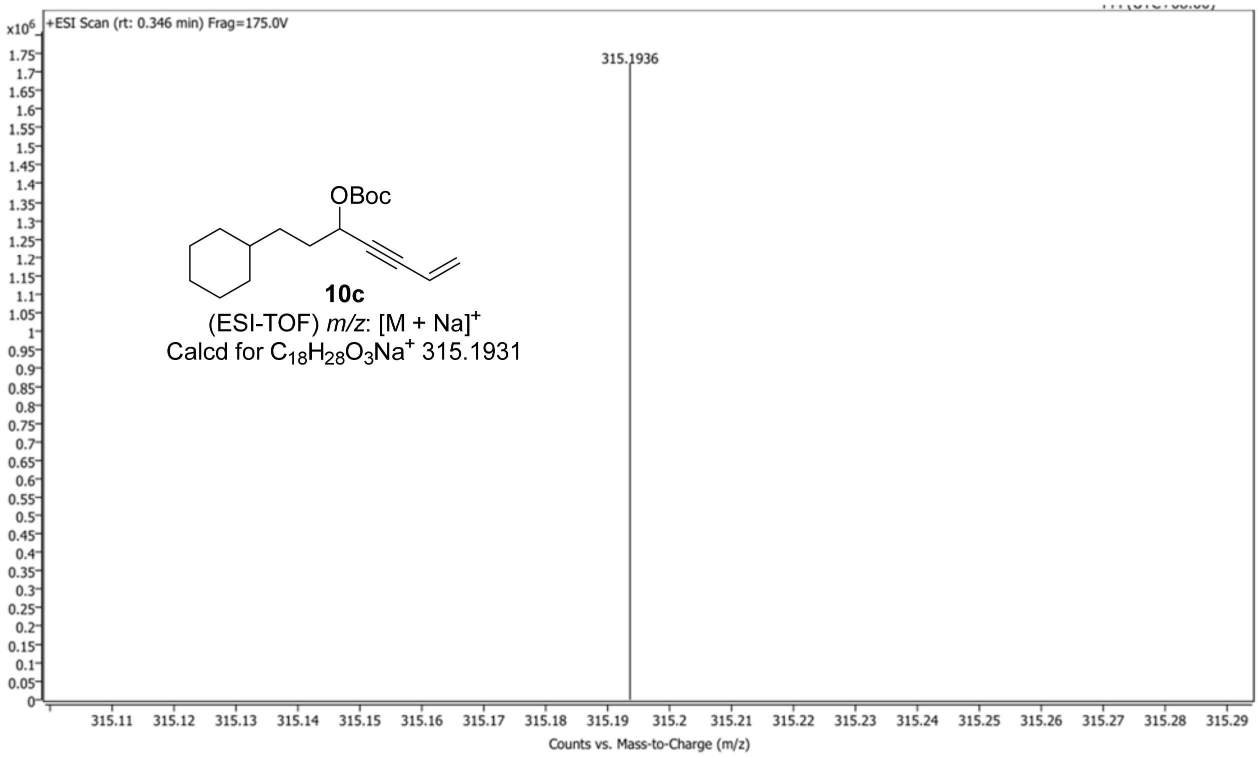
10c

^{1}H NMR (400 MHz, CDCl$_3$)



10c

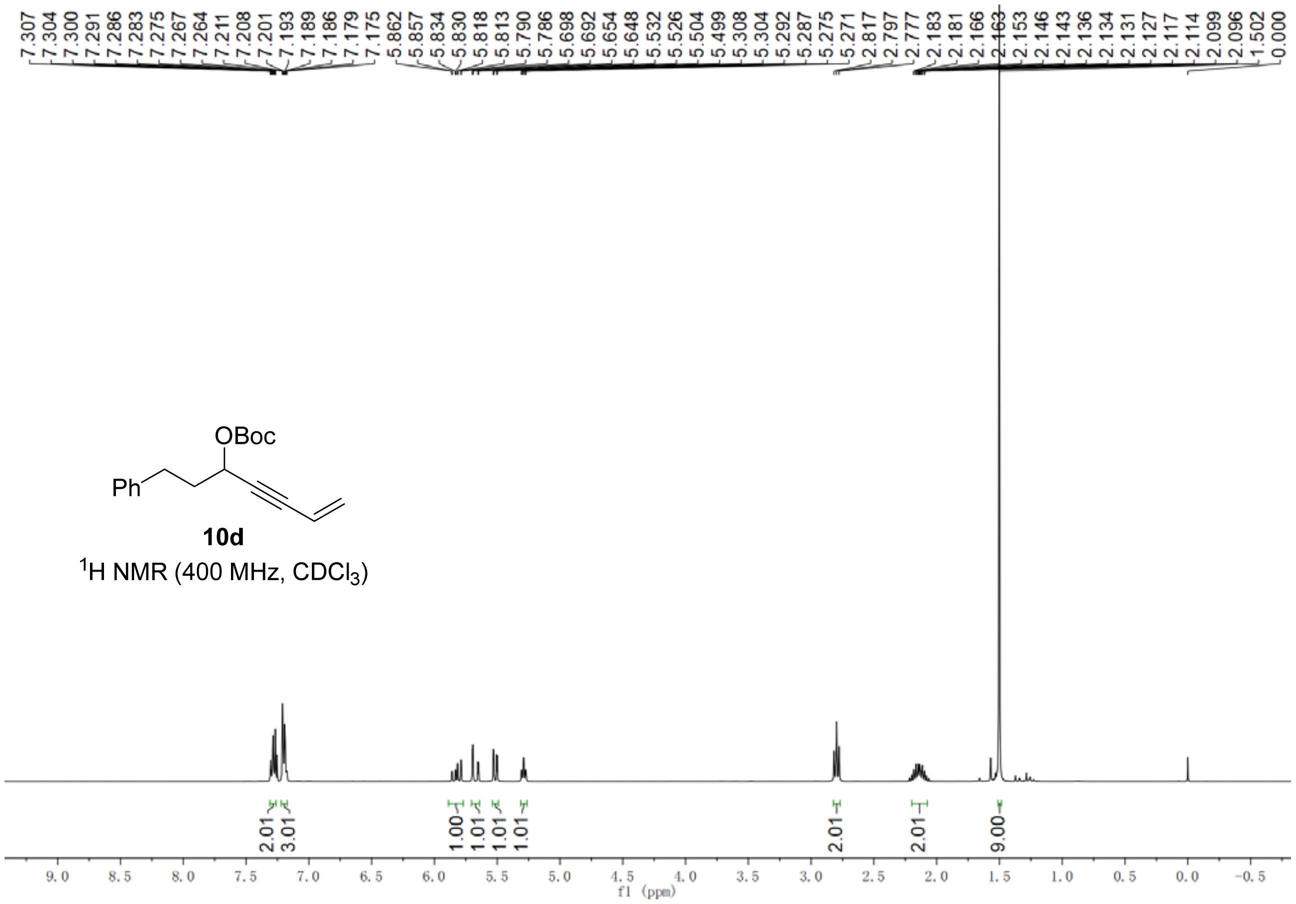
^{13}C NMR (100 MHz, CDCl$_3$)



10c

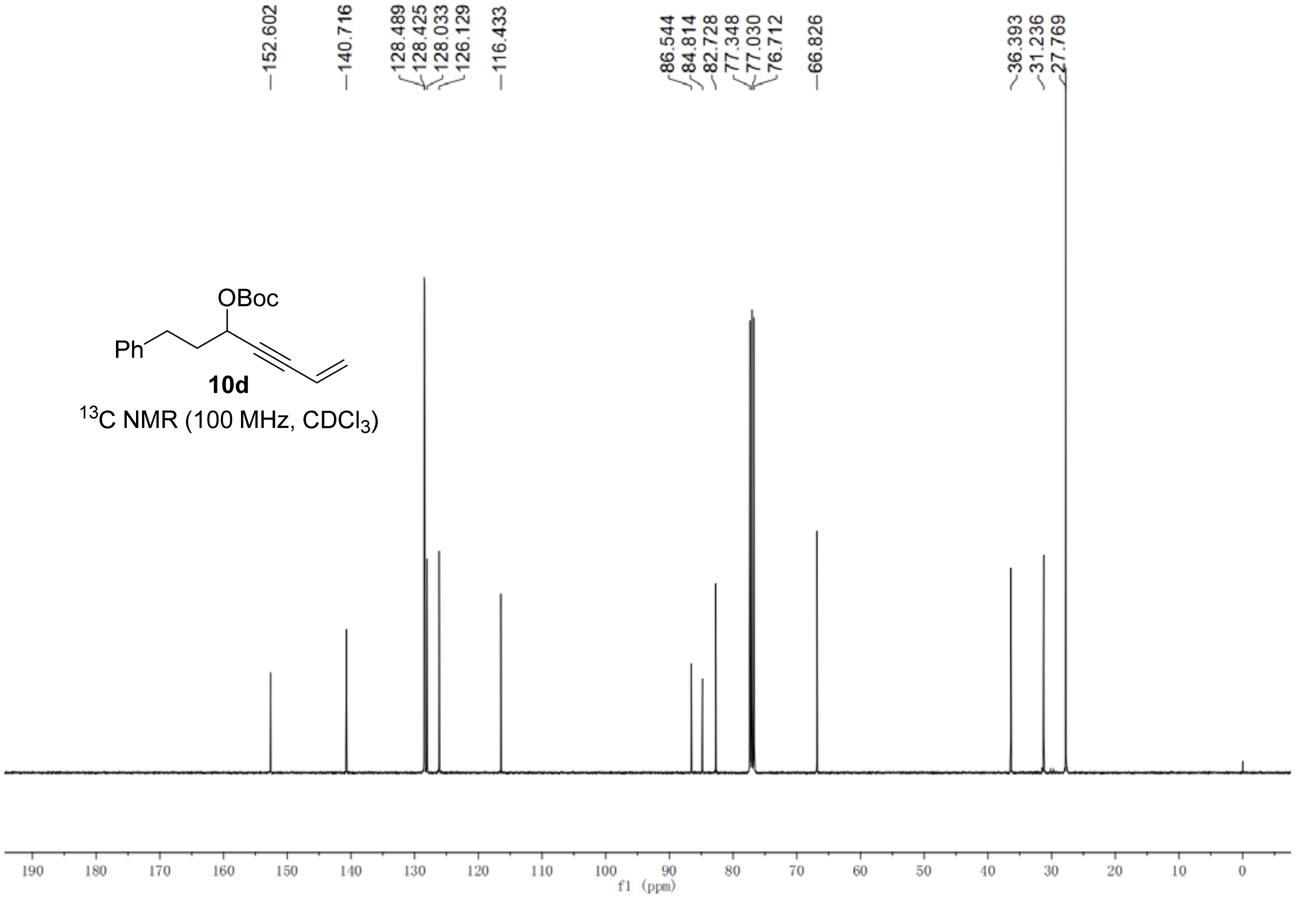
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{18}H_{28}O_3Na^+$ 315.1931



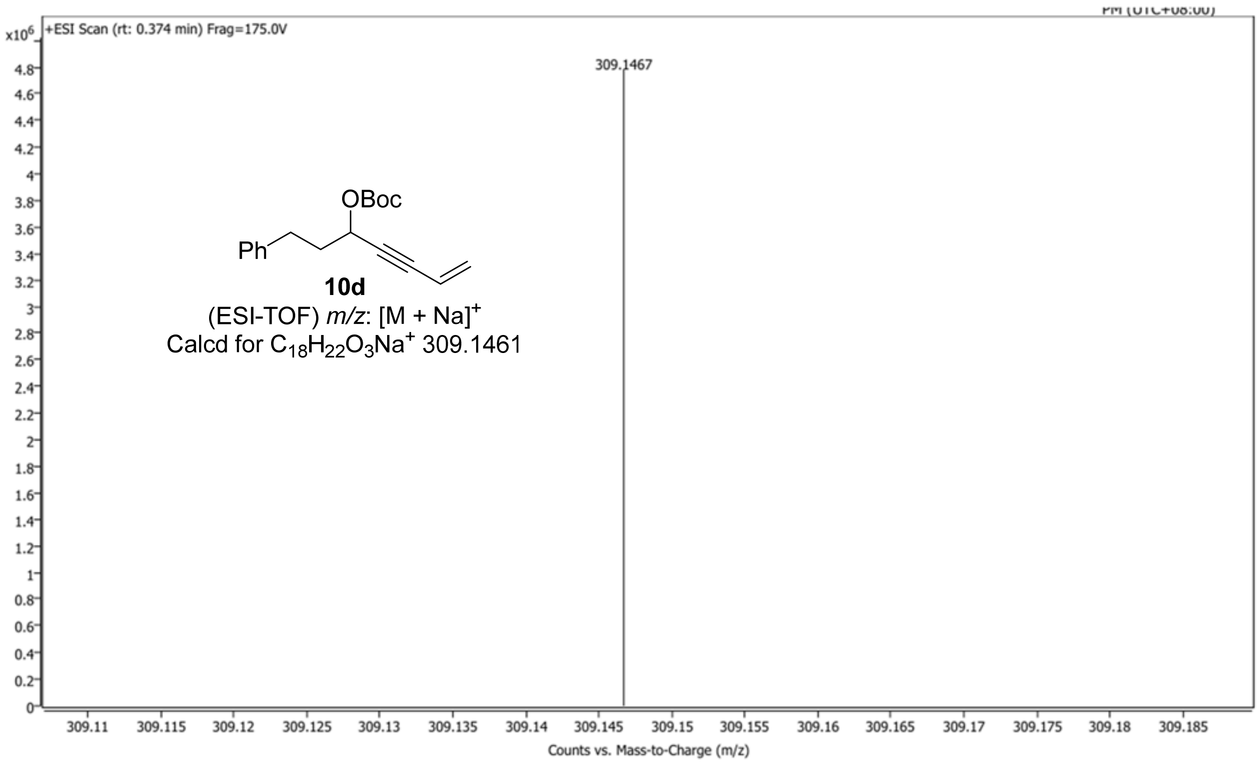
10d

^{1}H NMR (400 MHz, $CDCl_3$)



10d

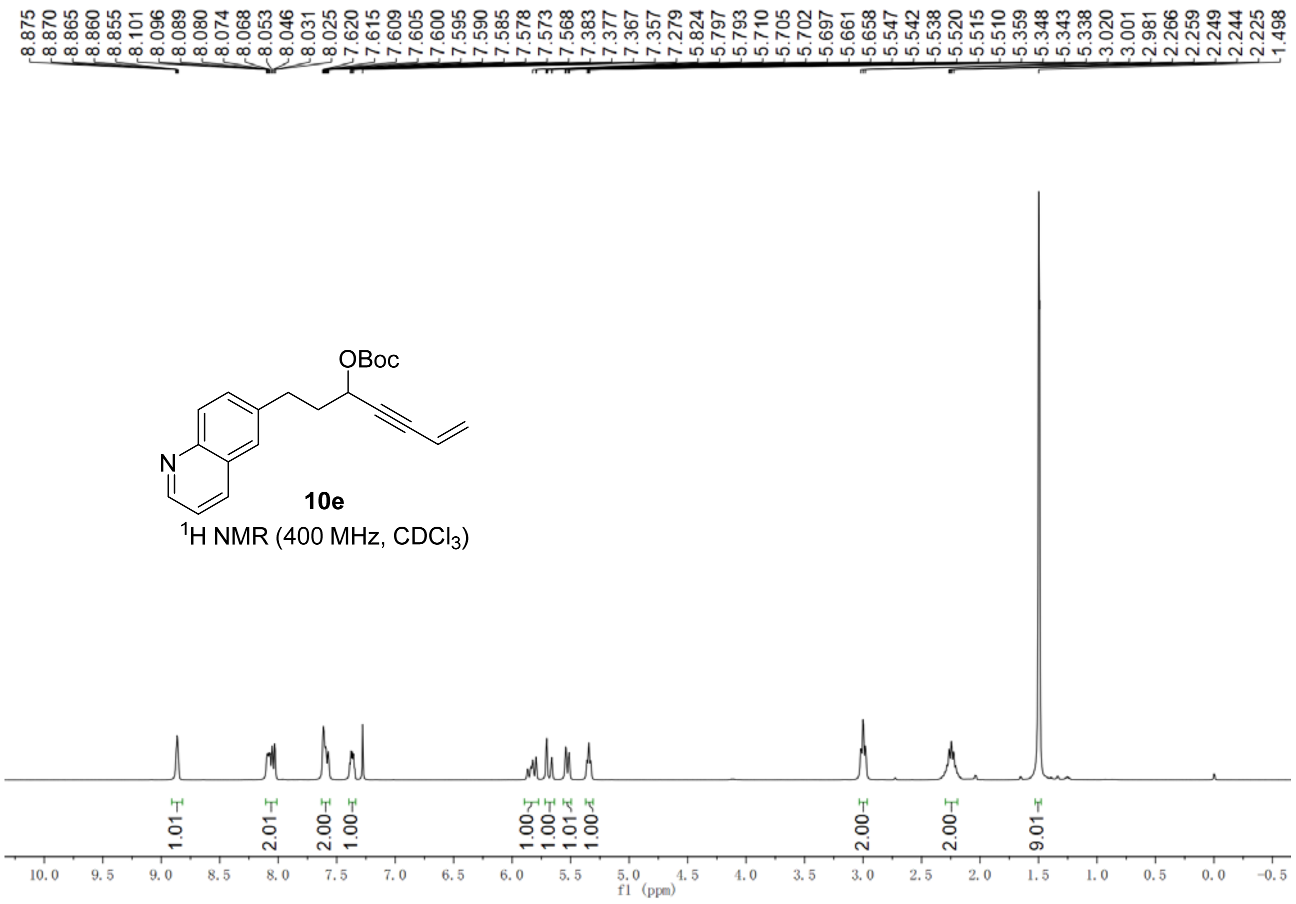
^{13}C NMR (100 MHz, $CDCl_3$)



10d

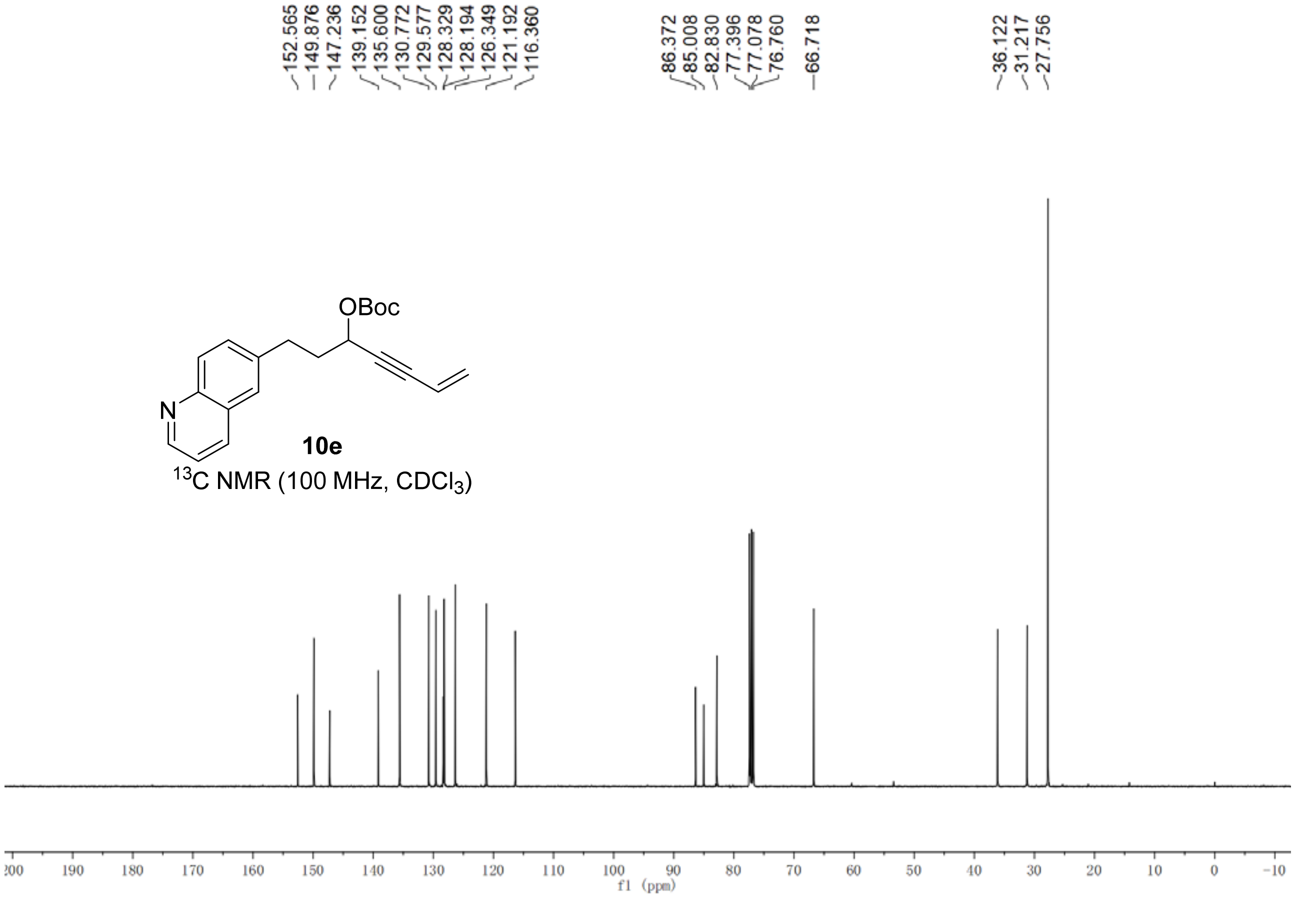
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{18}H_{22}O_3Na^+$ 309.1461



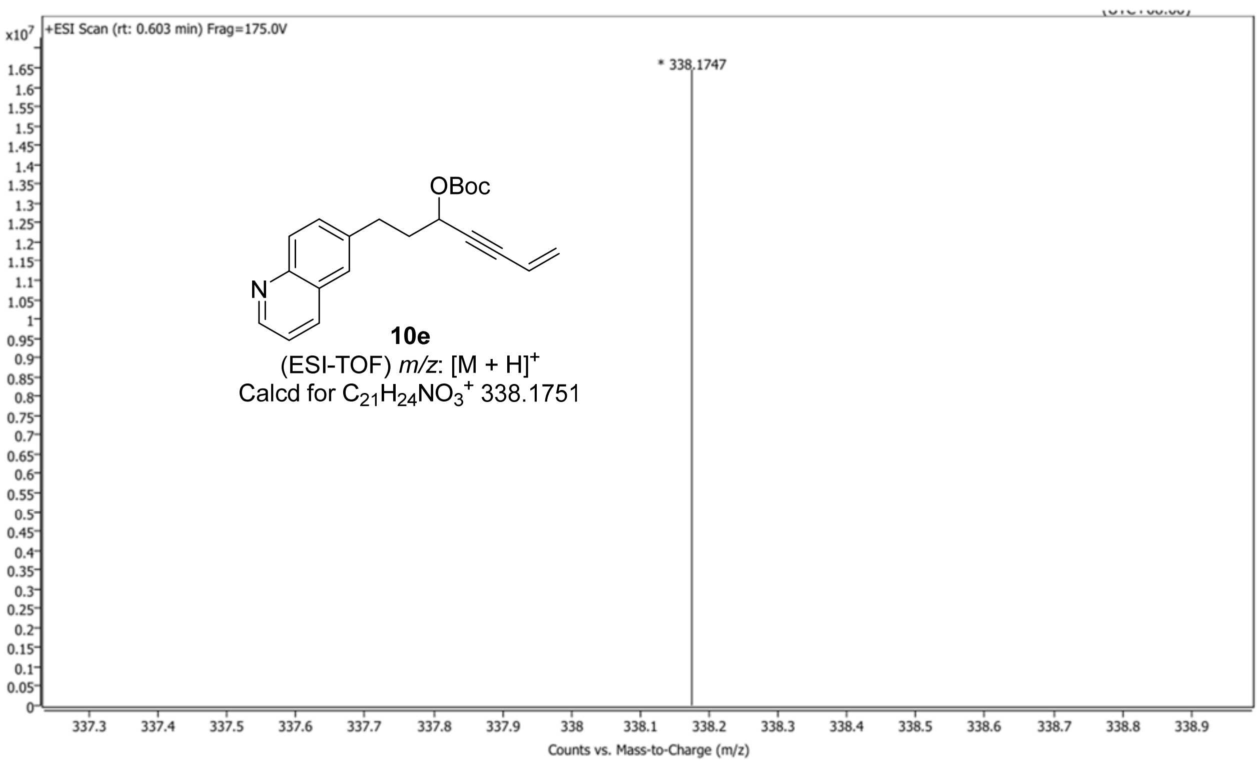
10e

^{1}H NMR (400 MHz, CDCl$_3$)



10e

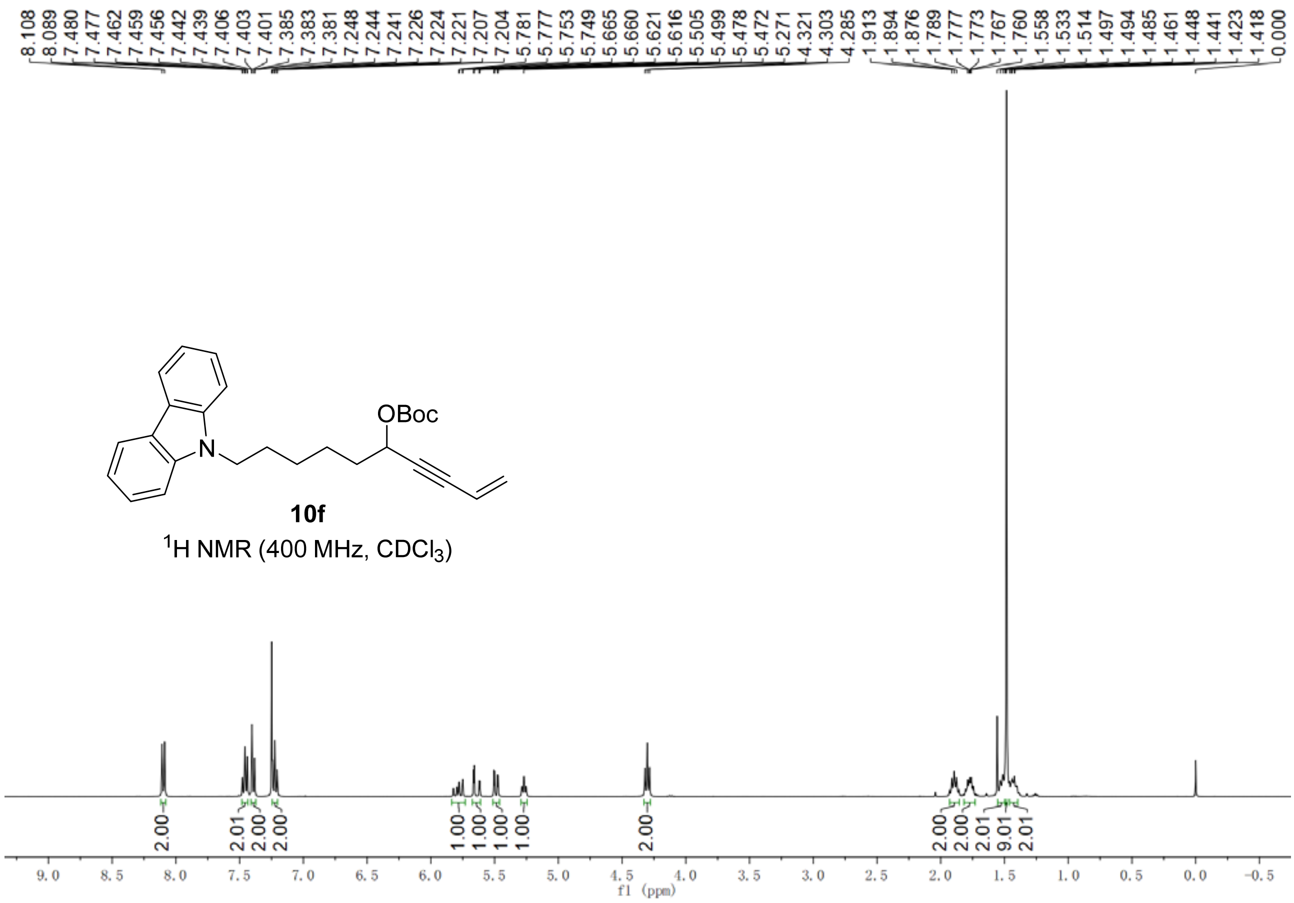
^{13}C NMR (100 MHz, CDCl$_3$)



10e

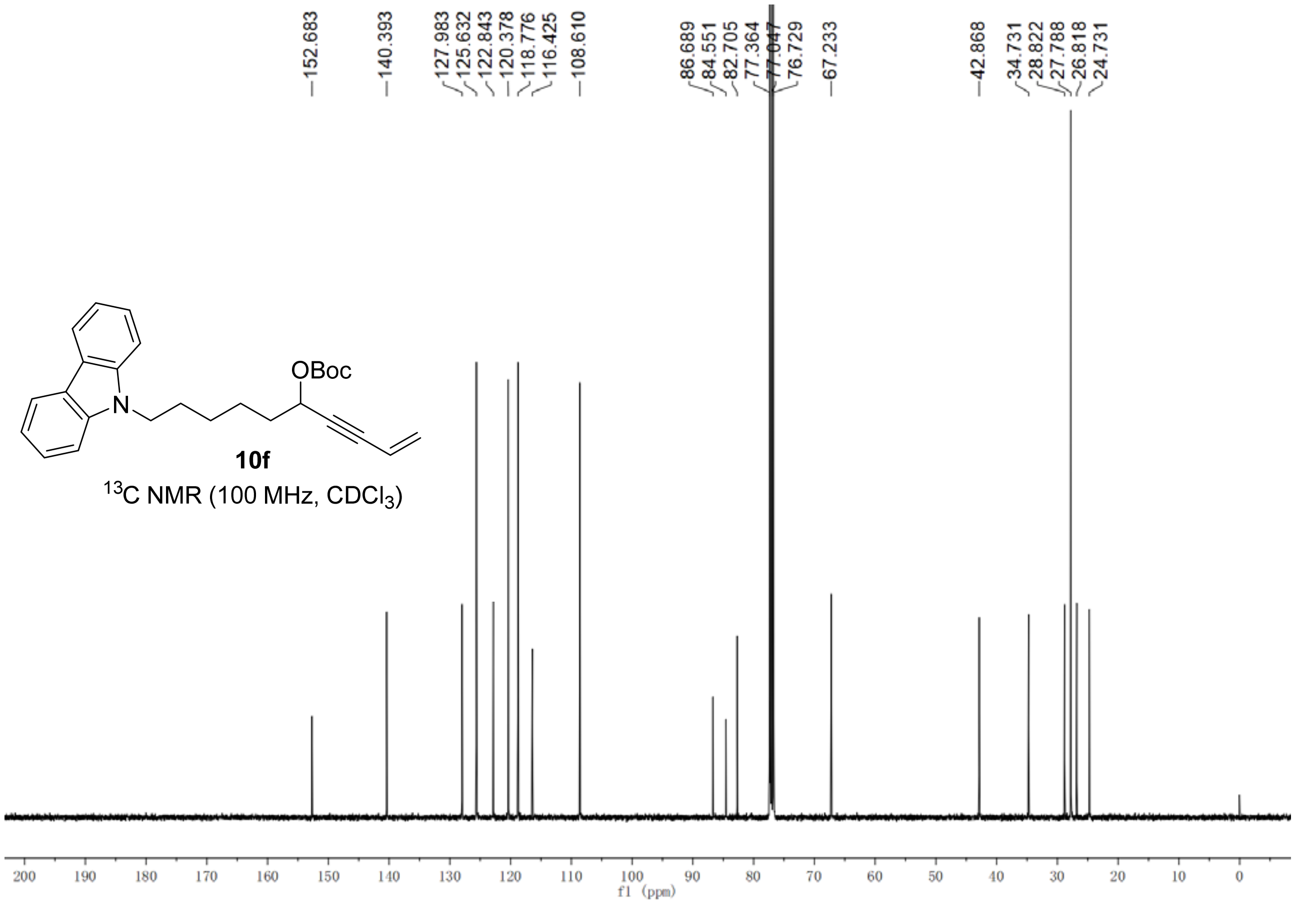
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{21}H_{24}NO_3^+$ 338.1751



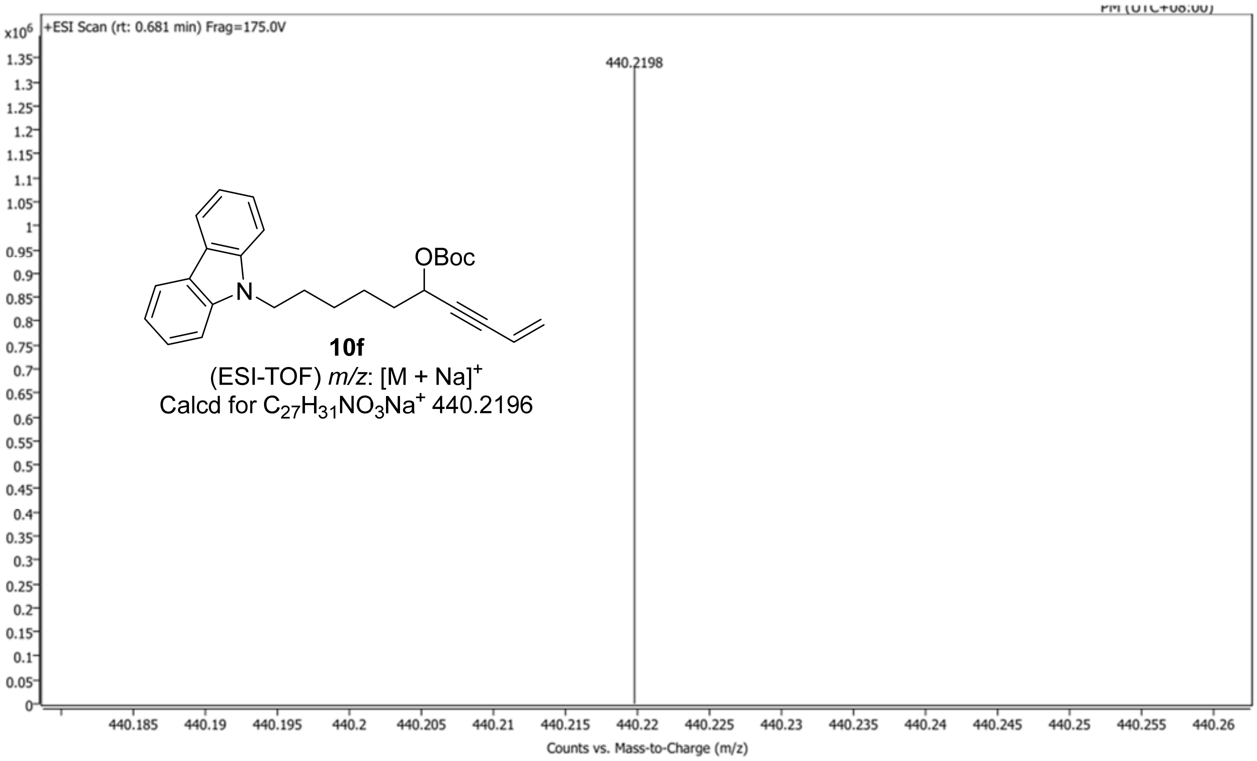
10f

^{1}H NMR (400 MHz, CDCl$_3$)



10f

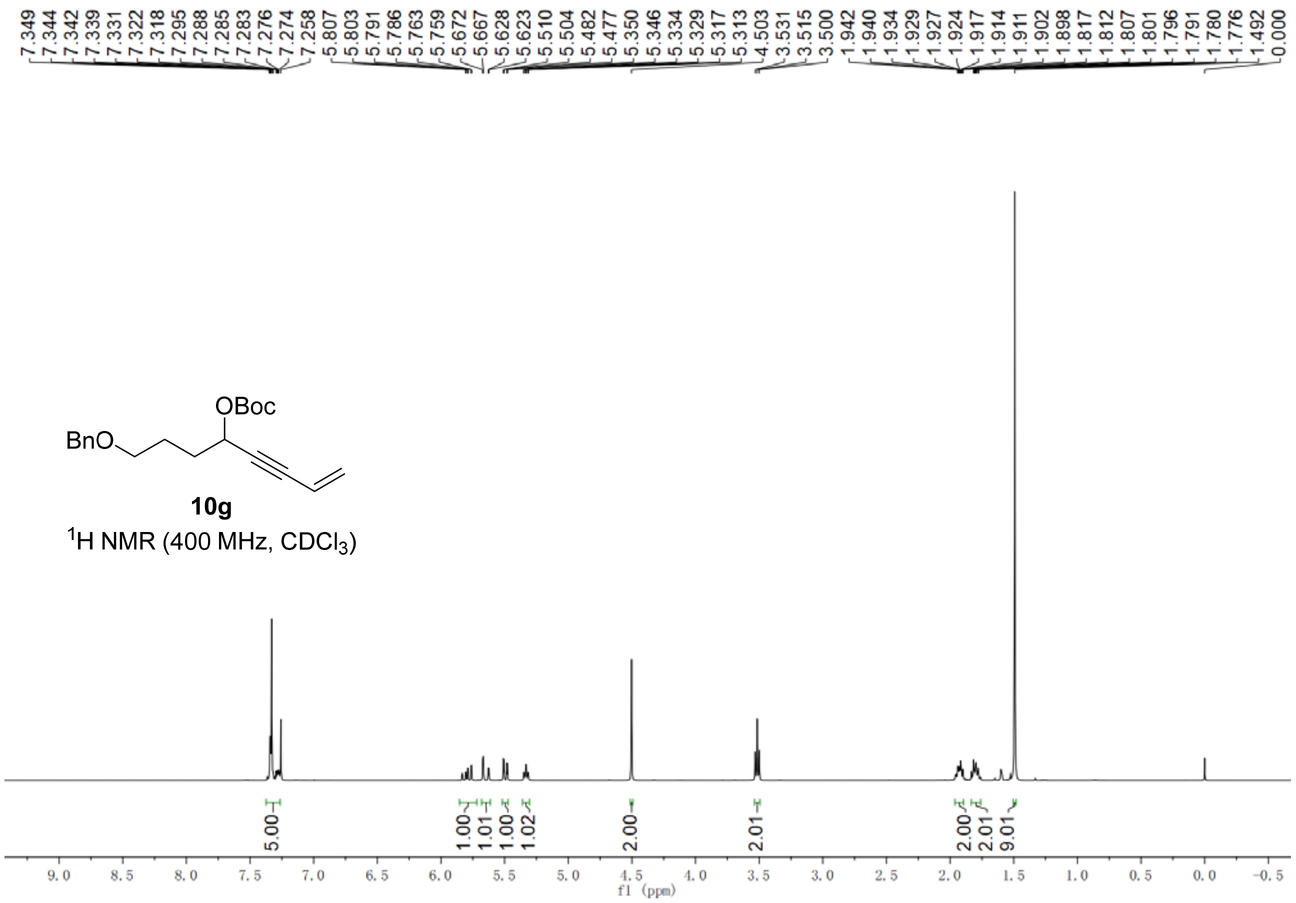
^{13}C NMR (100 MHz, CDCl$_3$)

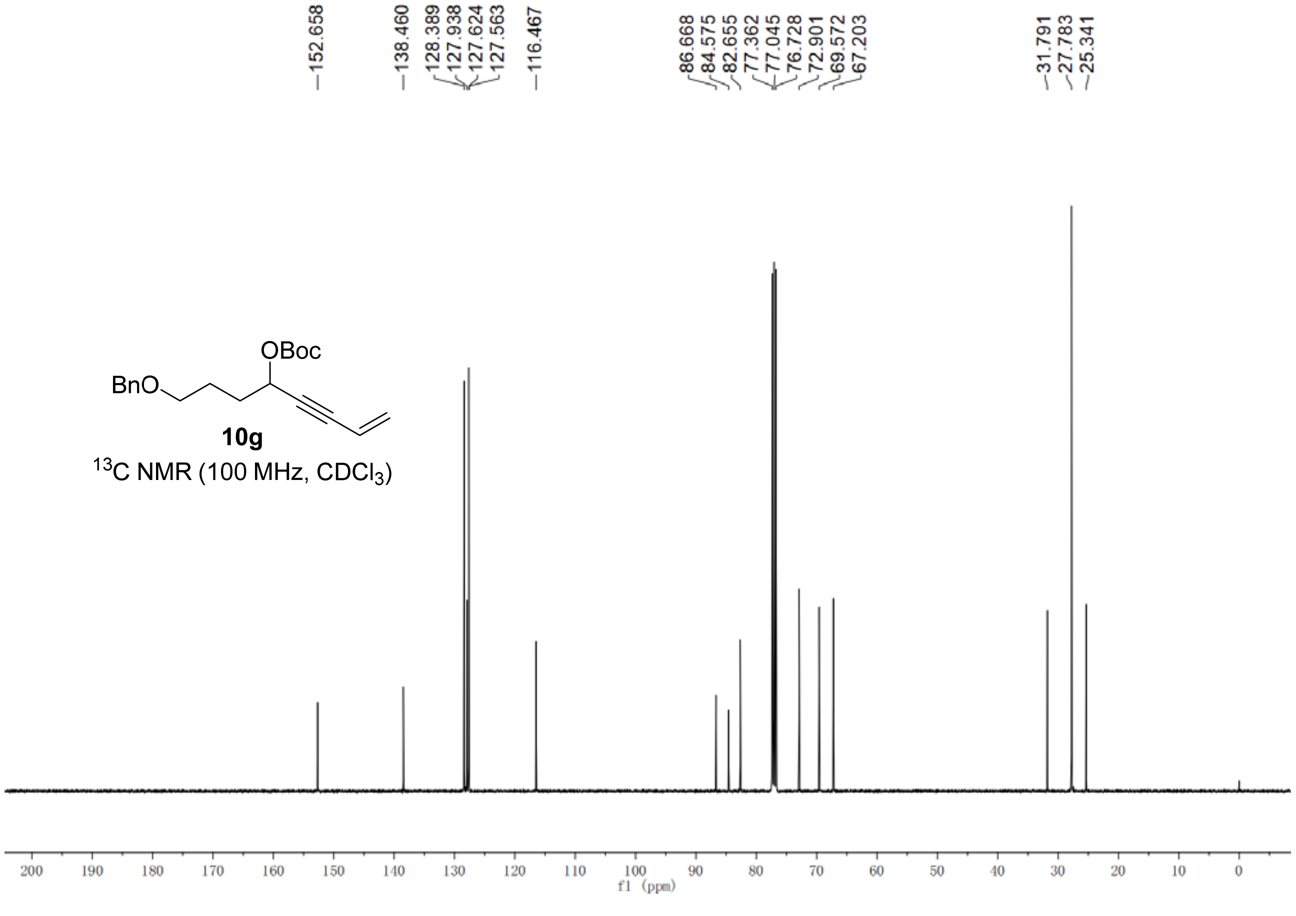


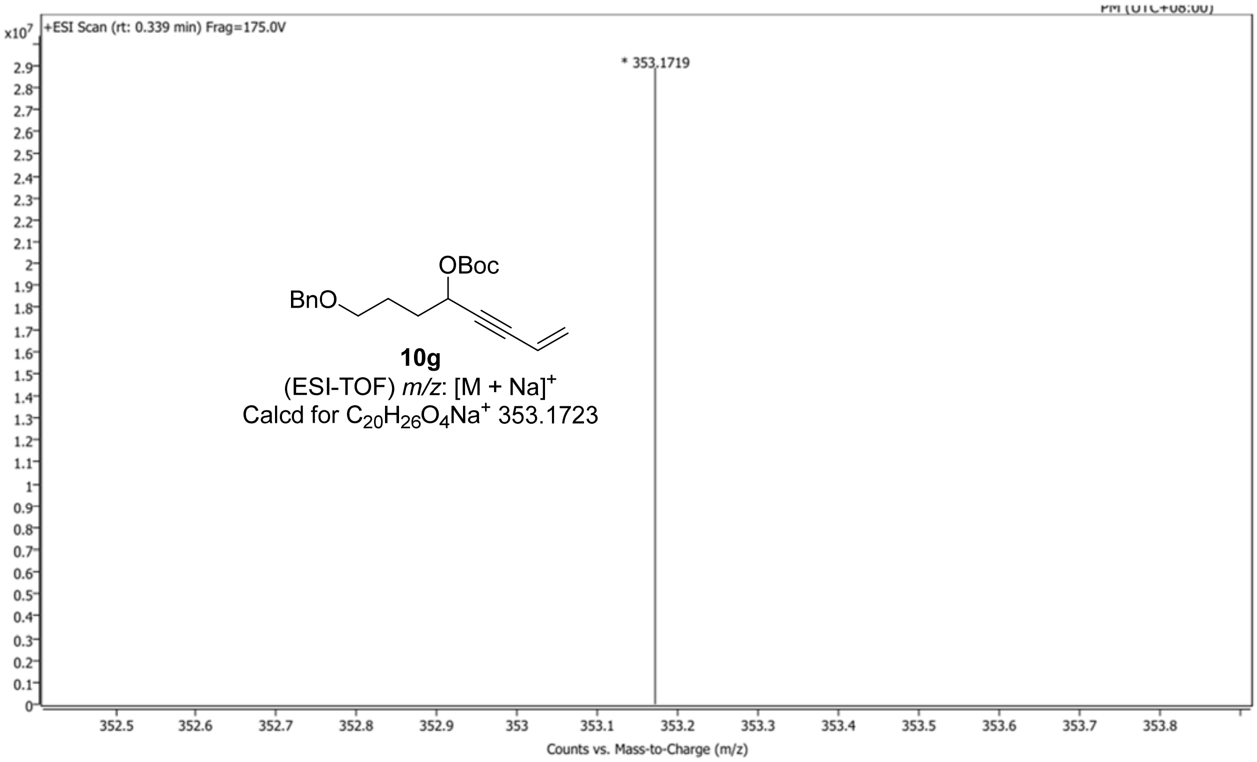
10f

(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{27}H_{31}NO_3Na^+$ 440.2196


7.349
7.344
7.342
7.339
7.331
7.322
7.318
7.295
7.288
7.285
7.283
7.276
7.274
7.258
5.807
5.803
5.791
5.786
5.763
5.759
5.672
5.667
5.628
5.623
5.510
5.504
5.482
5.477
5.350
5.346
5.334
5.329
5.317
5.313
4.503
3.531
3.515
3.500
1.942
1.940
1.934
1.929
1.927
1.924
1.917
1.914
1.911
1.902
1.898
1.817
1.812
1.807
1.801
1.796
1.791
1.780
1.776
1.492
0.000
OBoc
BnO
10g
¹H NMR (400 MHz, CDCl₃)
5.00
1.00
1.01
1.00
1.02
2.00
2.01
2.00
2.01
9.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

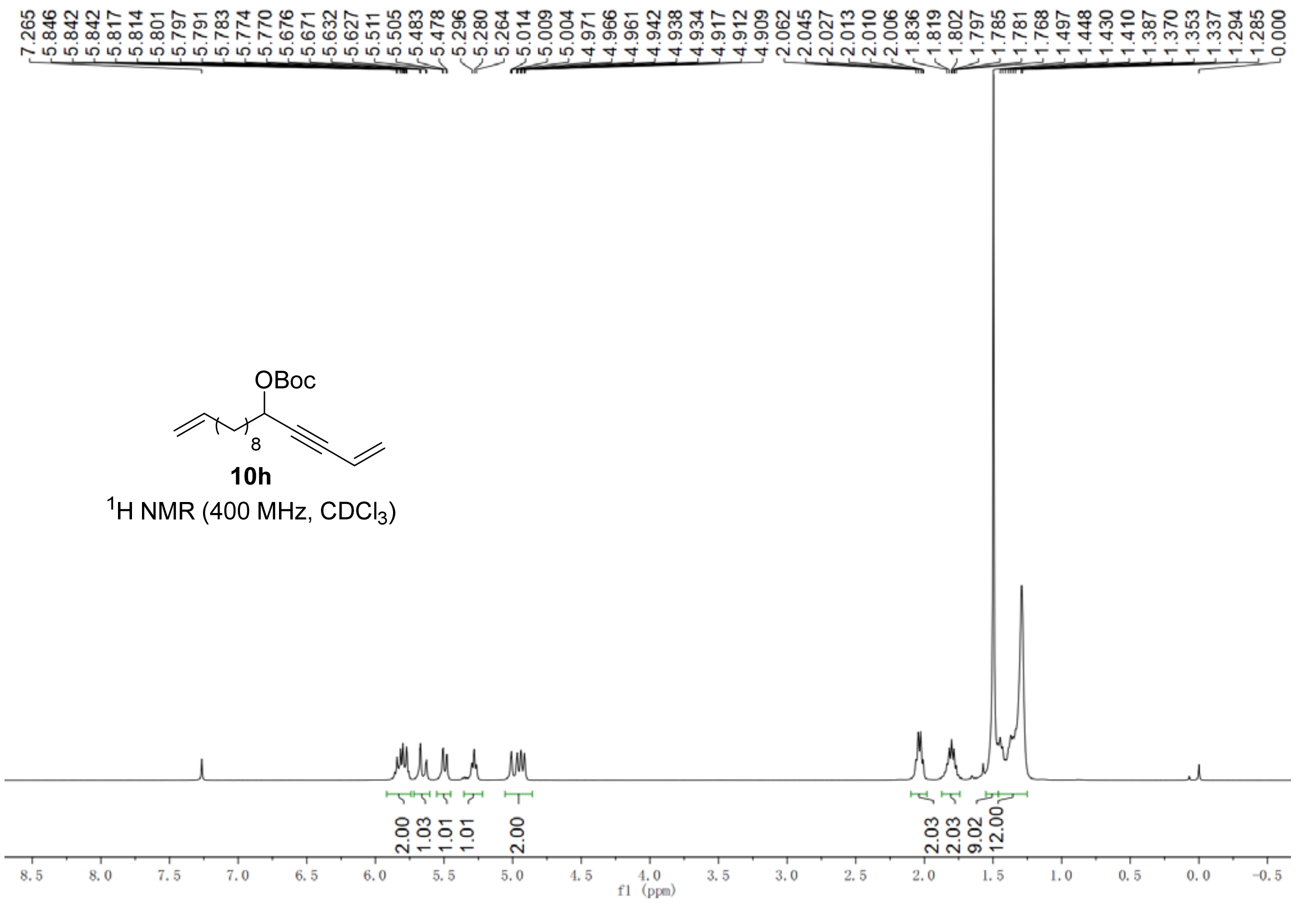

152.658
138.460
128.389
127.938
127.624
127.563
116.467
86.668
84.575
82.655
77.362
77.045
76.728
72.901
69.572
67.203
31.791
27.783
25.341
OBoc
BnO
10g
¹³C NMR (100 MHz, CDCl₃)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



10g

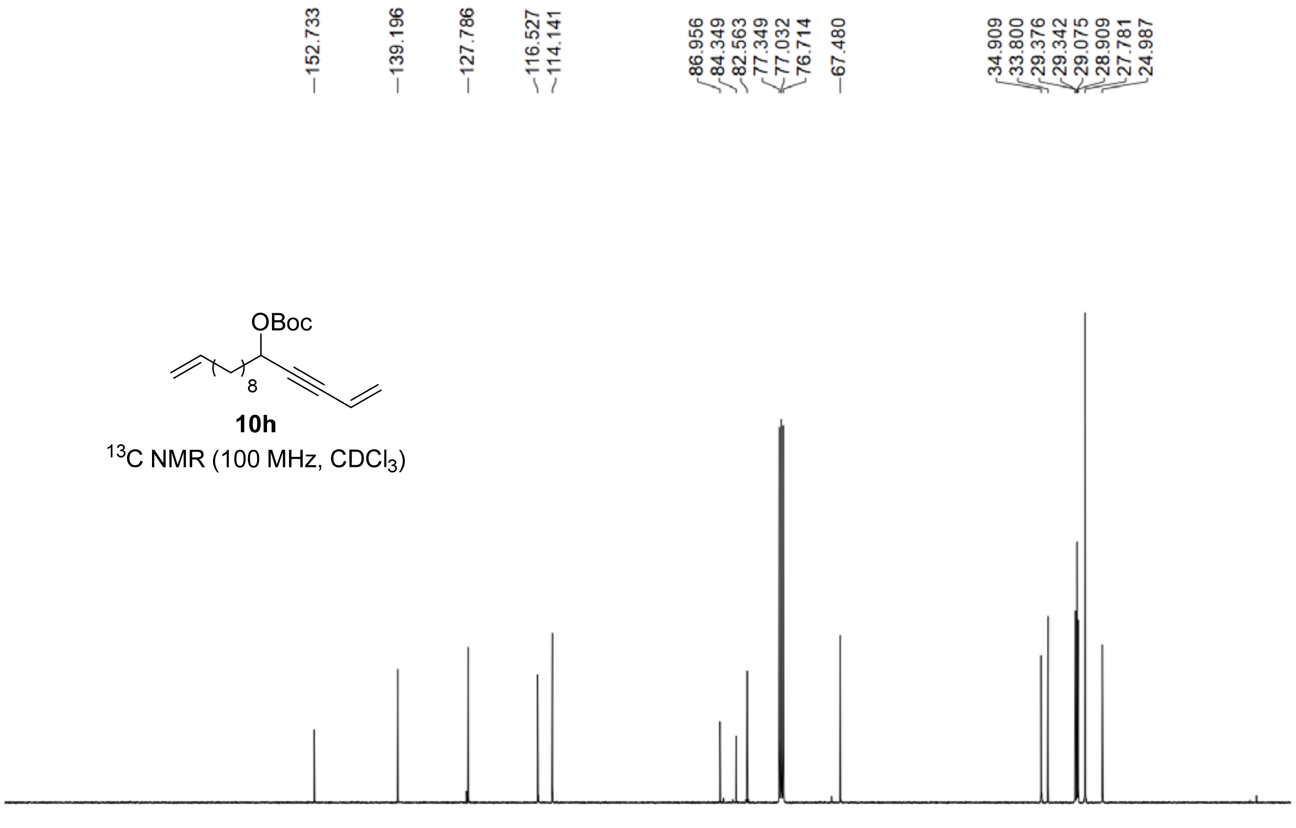
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{20}H_{26}O_4Na^+$ 353.1723



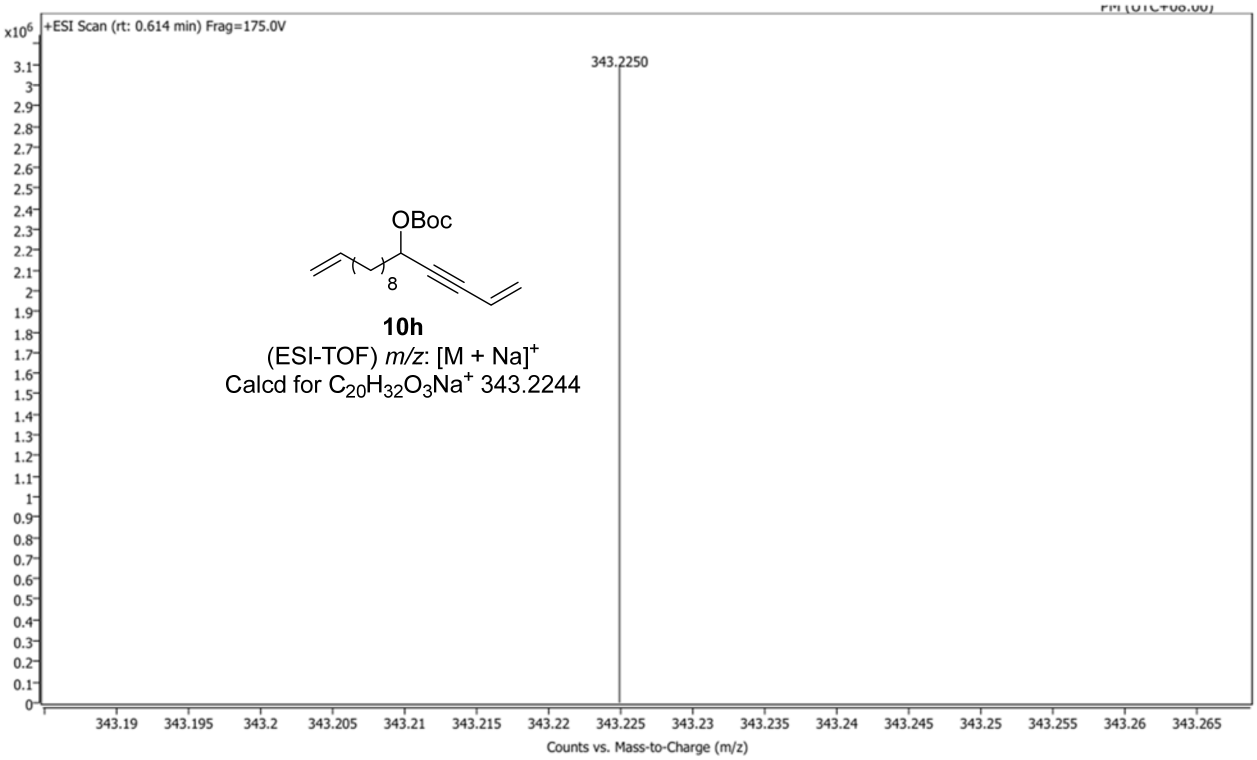
10h

^{1}H NMR (400 MHz, CDCl$_3$)



10h

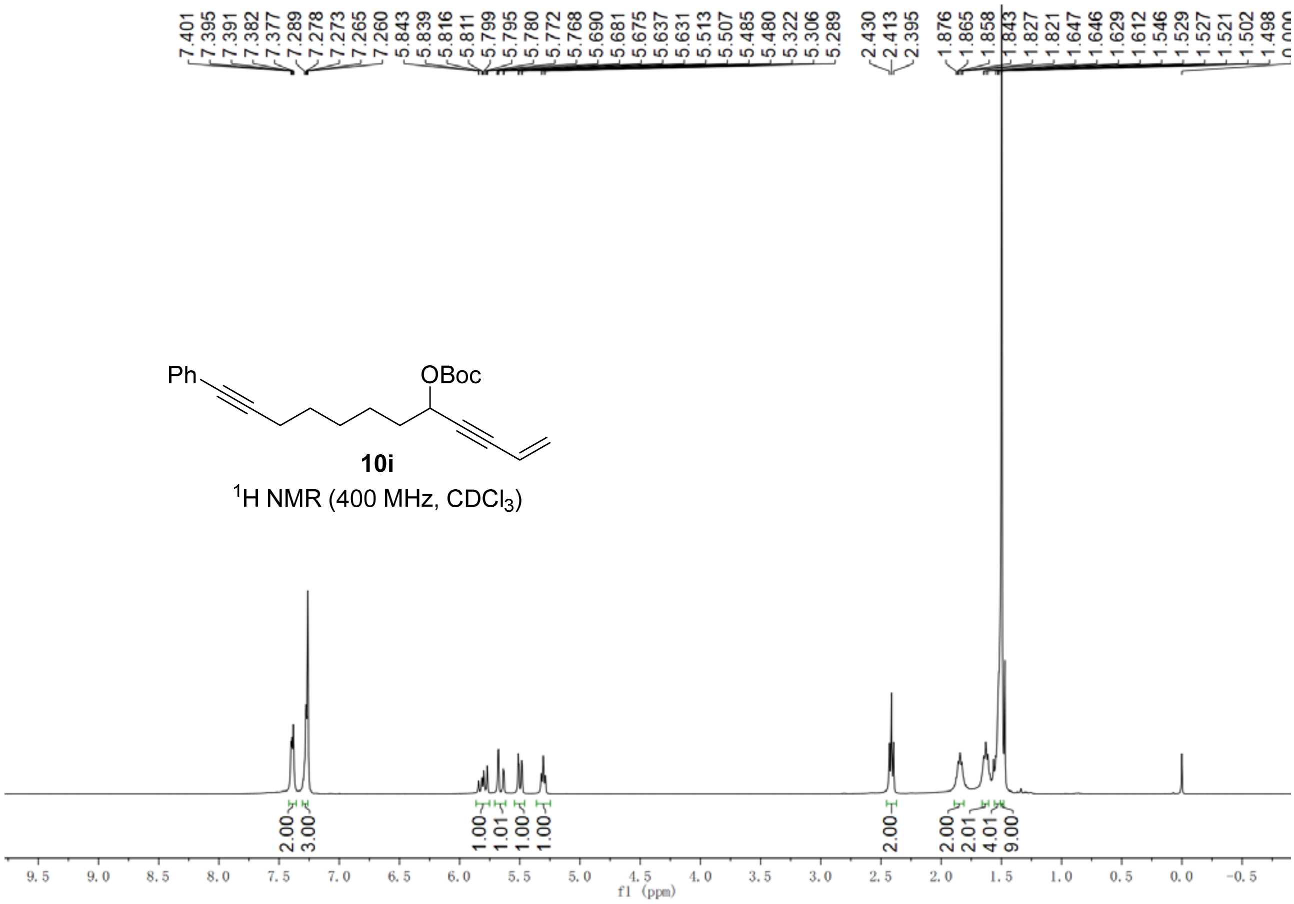
^{13}C NMR (100 MHz, CDCl$_3$)



10h

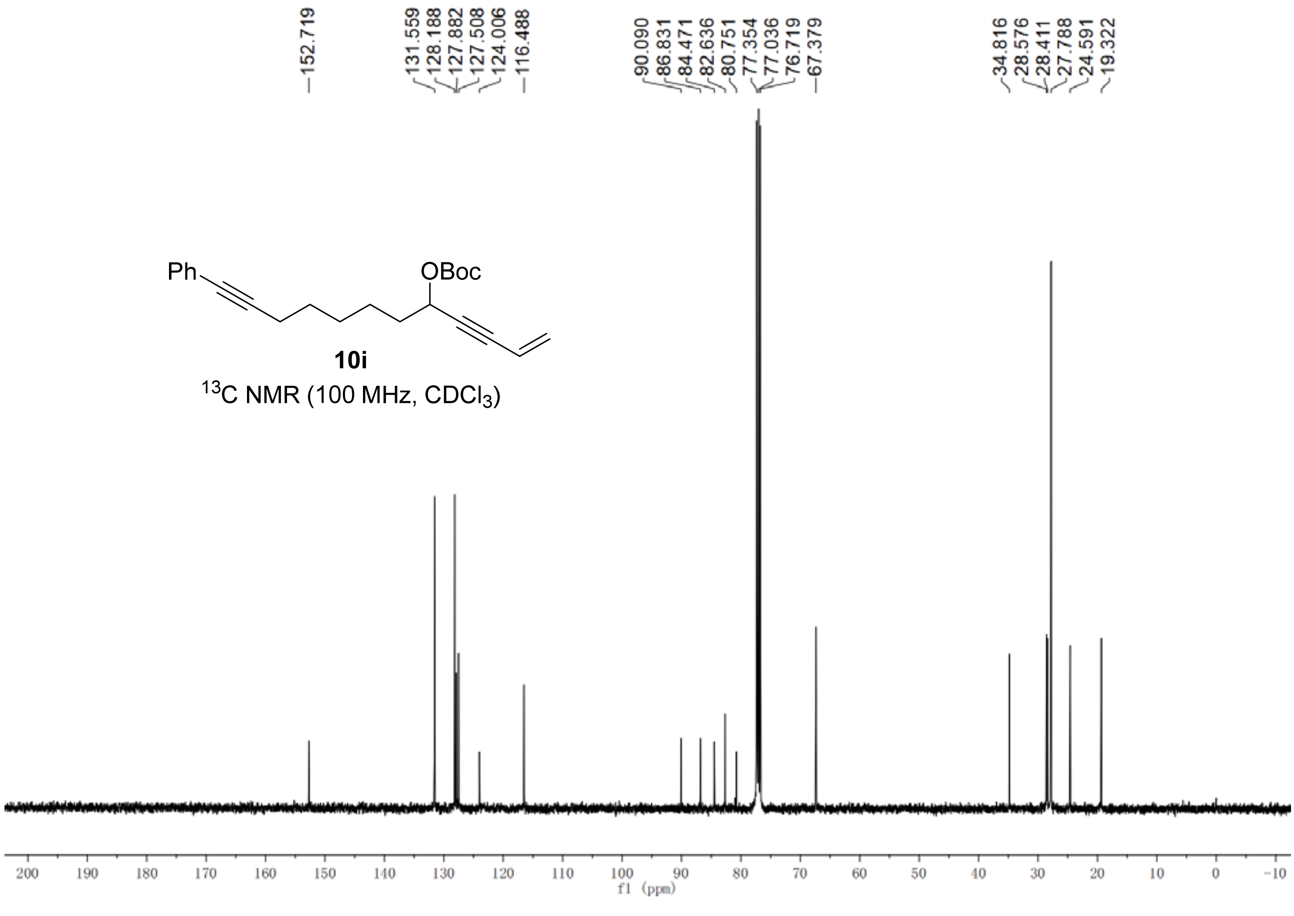
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{20}H_{32}O_3Na^+$ 343.2244



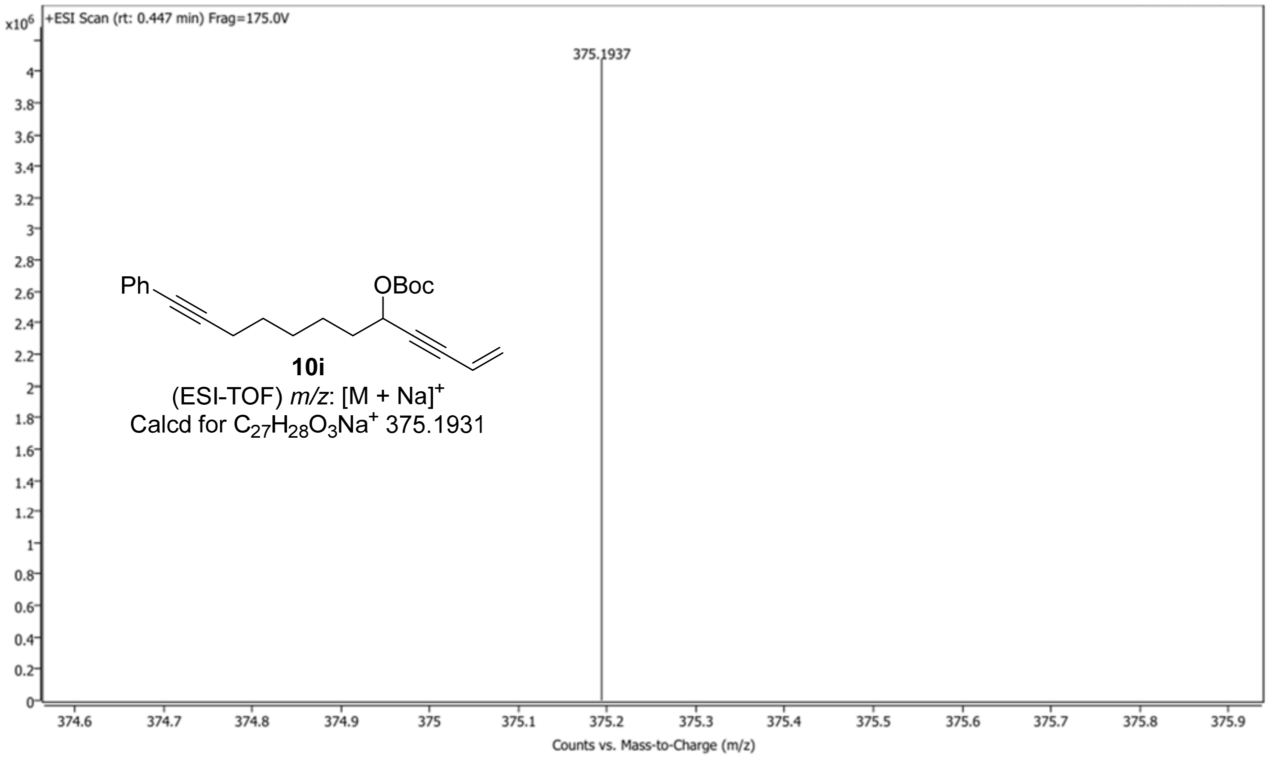
10i

^{1}H NMR (400 MHz, $CDCl_3$)



10i

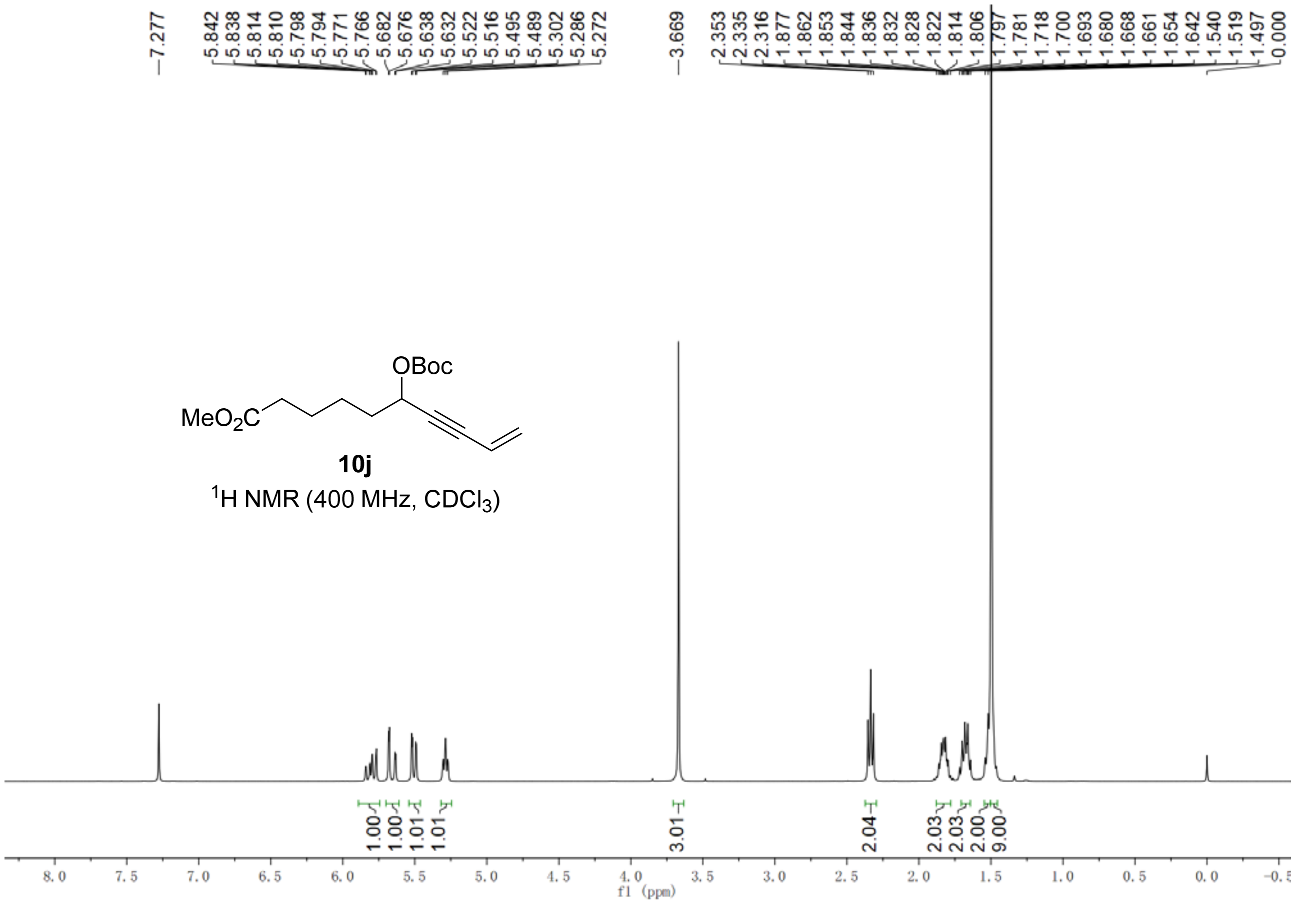
^{13}C NMR (100 MHz, $CDCl_3$)



10i

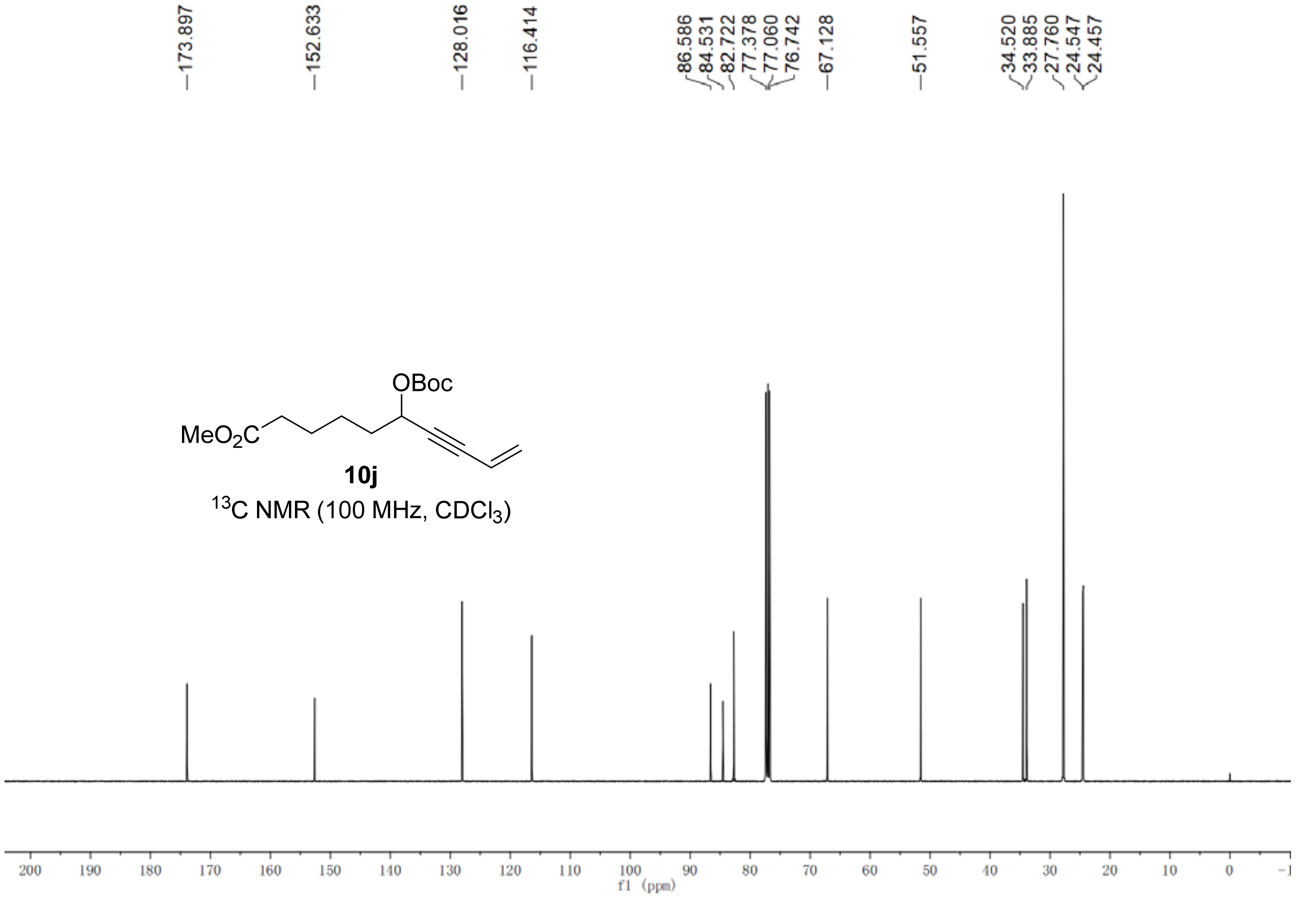
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{27}H_{28}O_3Na^+$ 375.1931



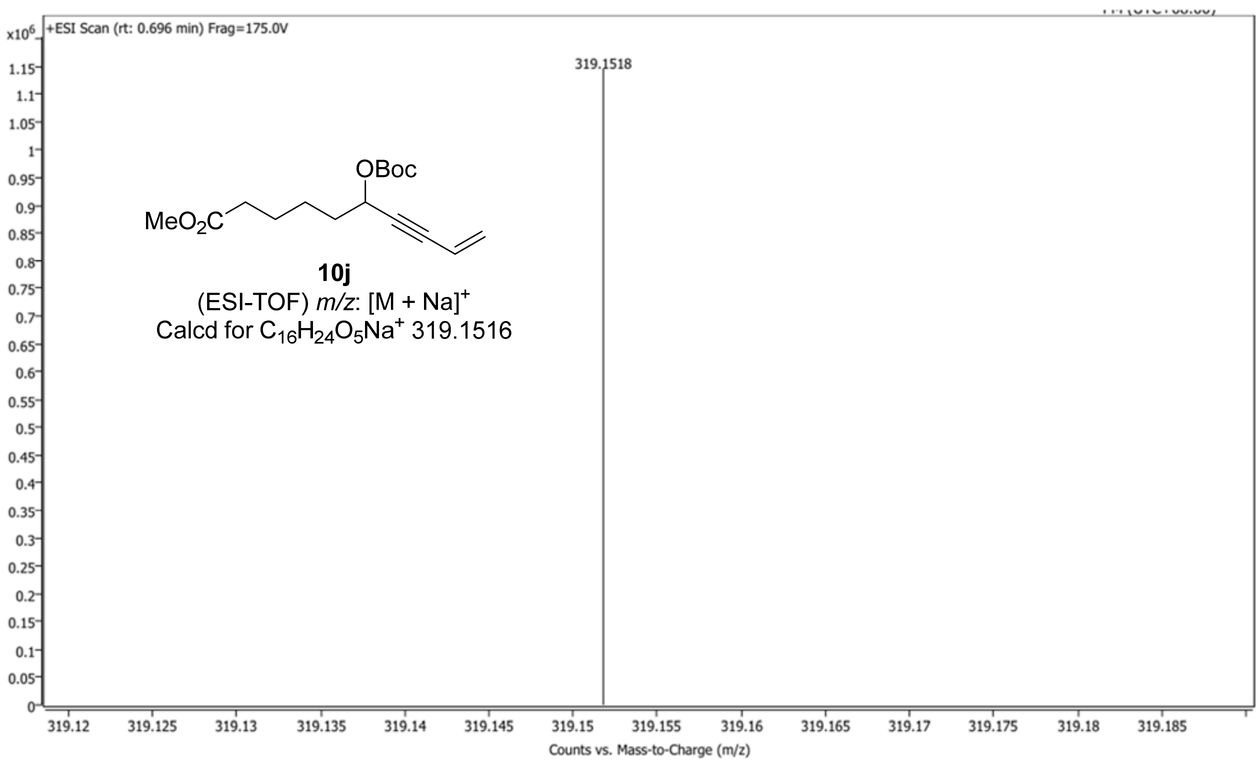
10j

^{1}H NMR (400 MHz, $CDCl_3$)



10j

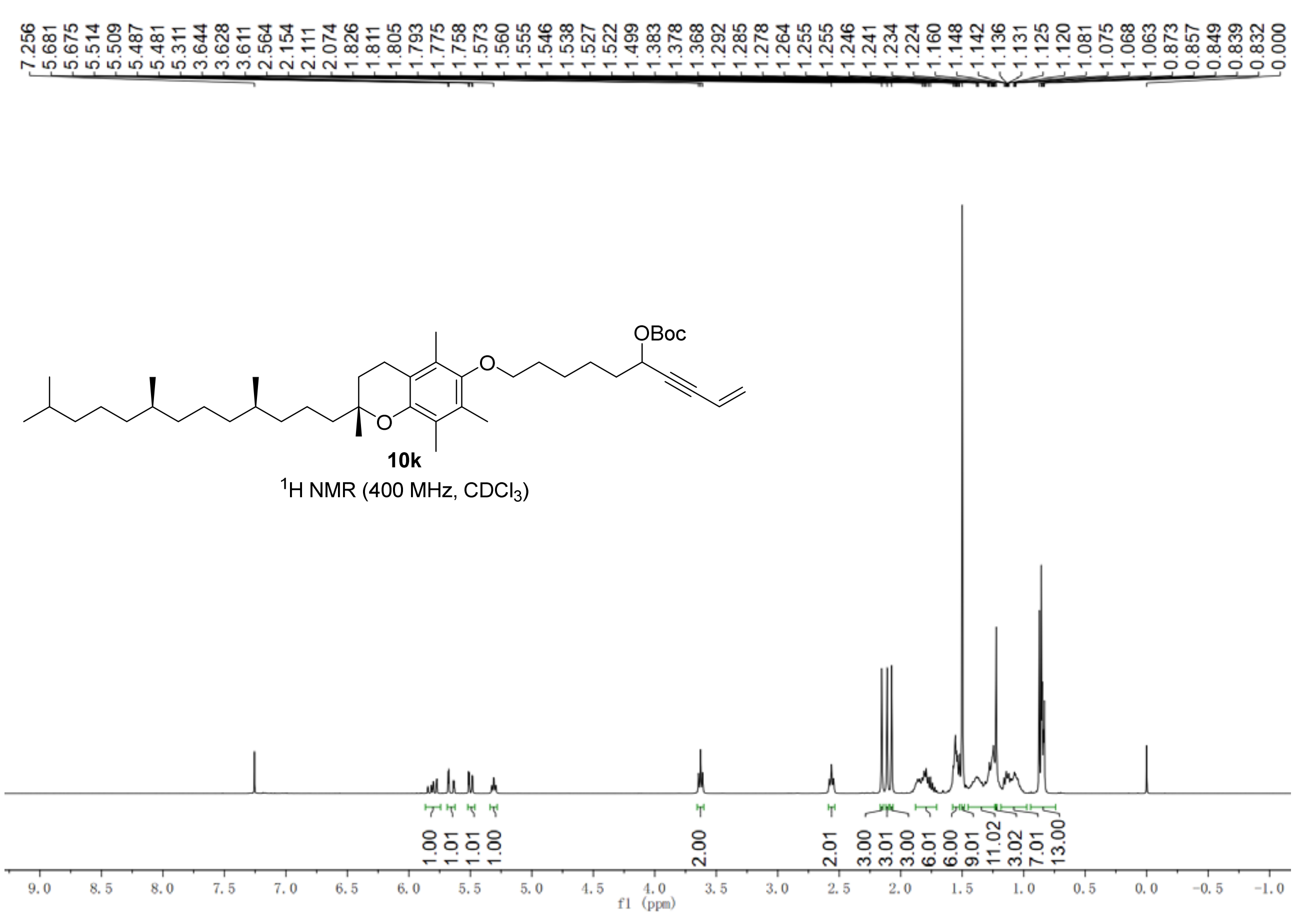
^{13}C NMR (100 MHz, $CDCl_3$)



10j

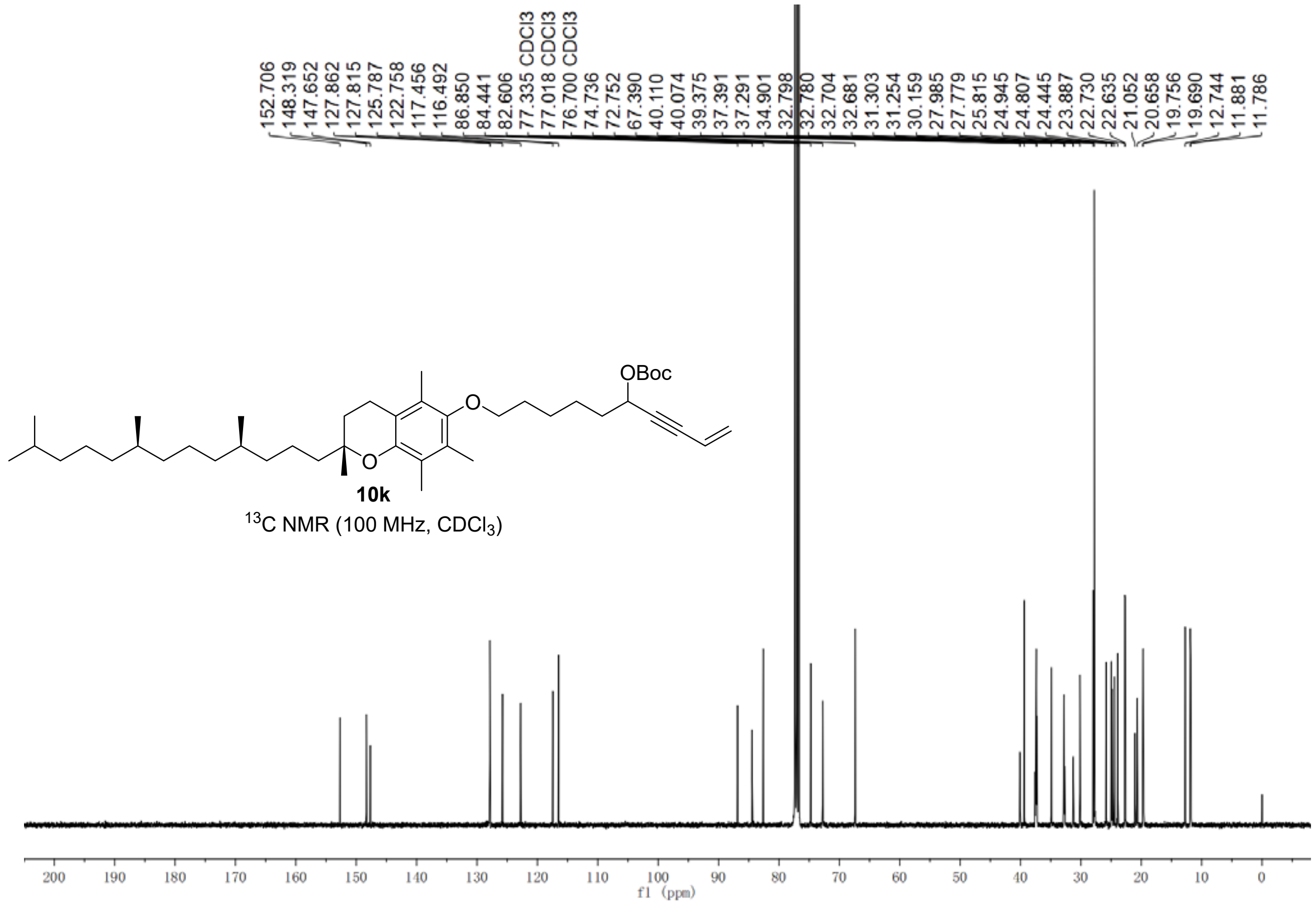
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{16}H_{24}O_5Na^+$ 319.1516



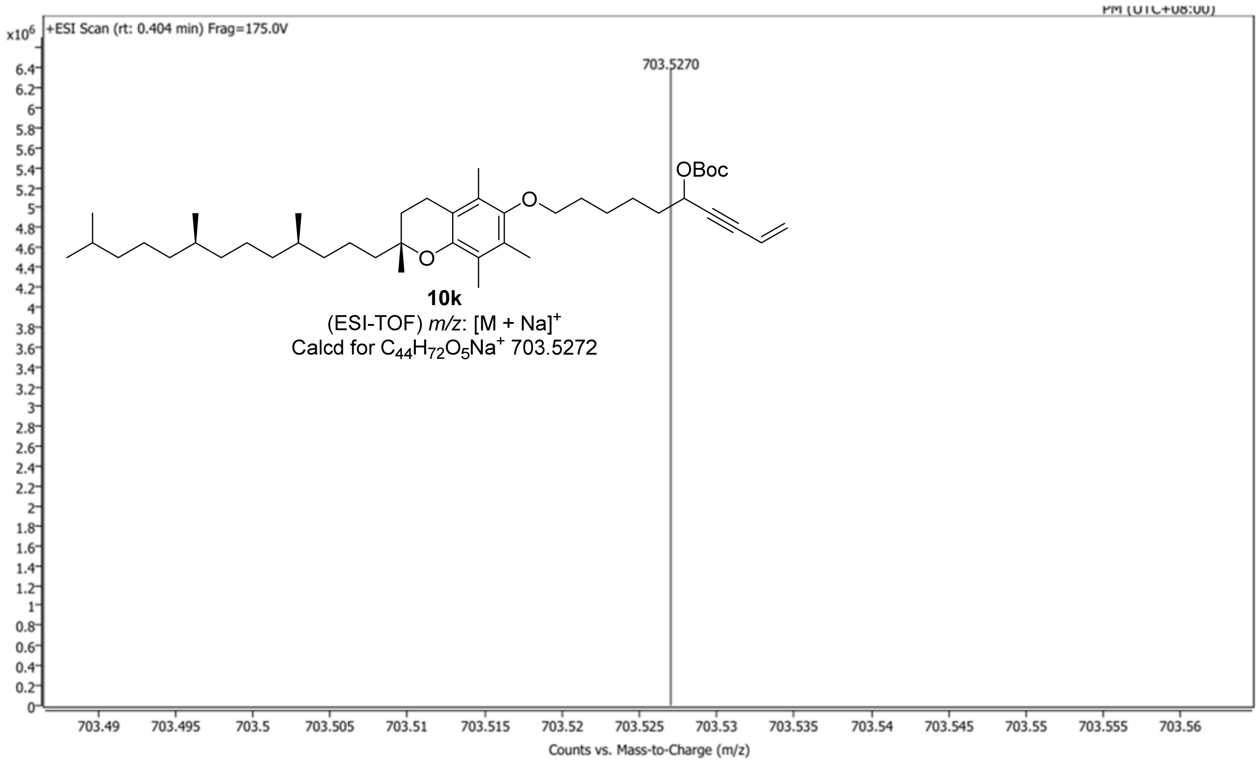
10k

^{1}H NMR (400 MHz, CDCl$_3$)



10k

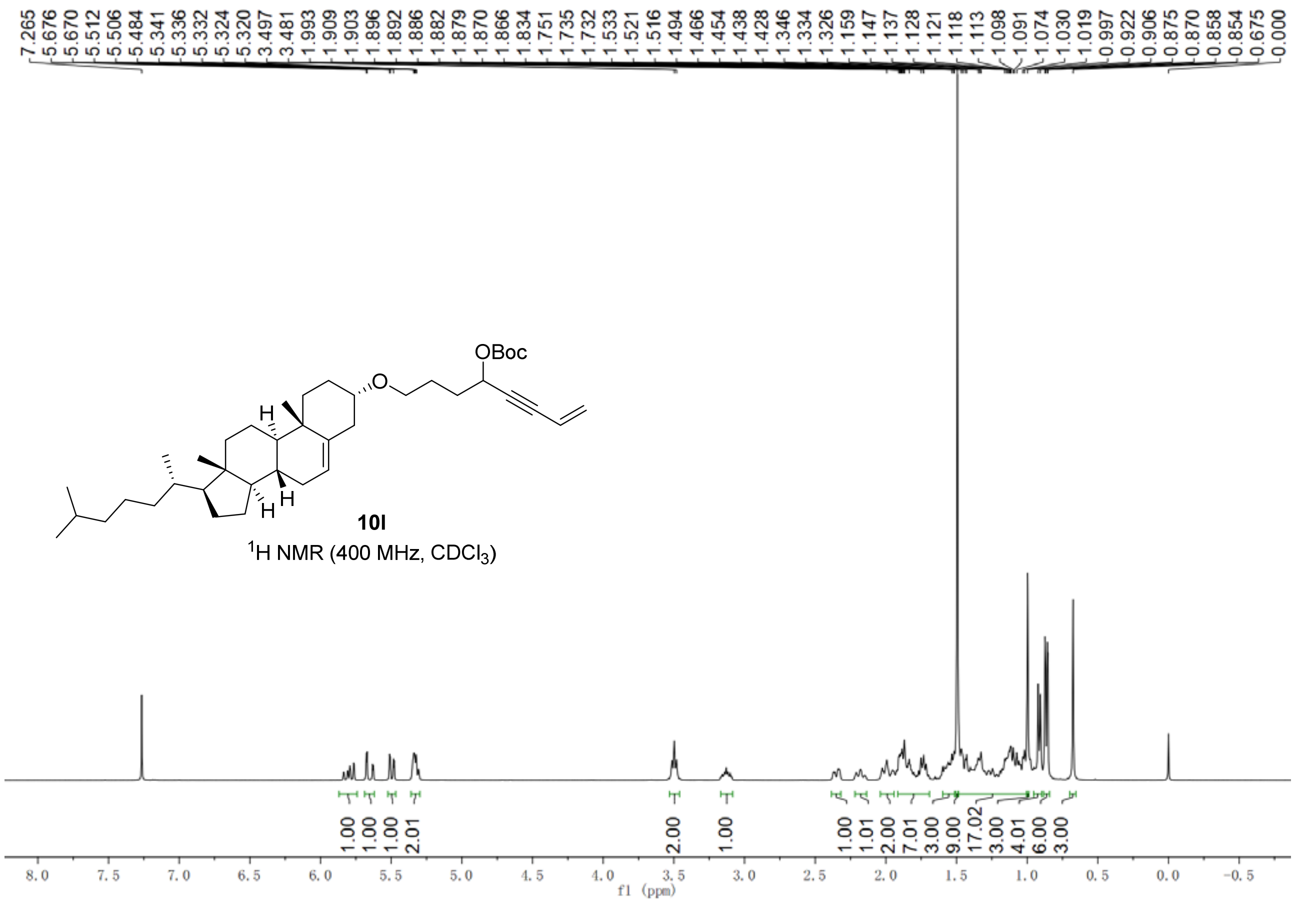
^{13}C NMR (100 MHz, CDCl$_3$)



10k

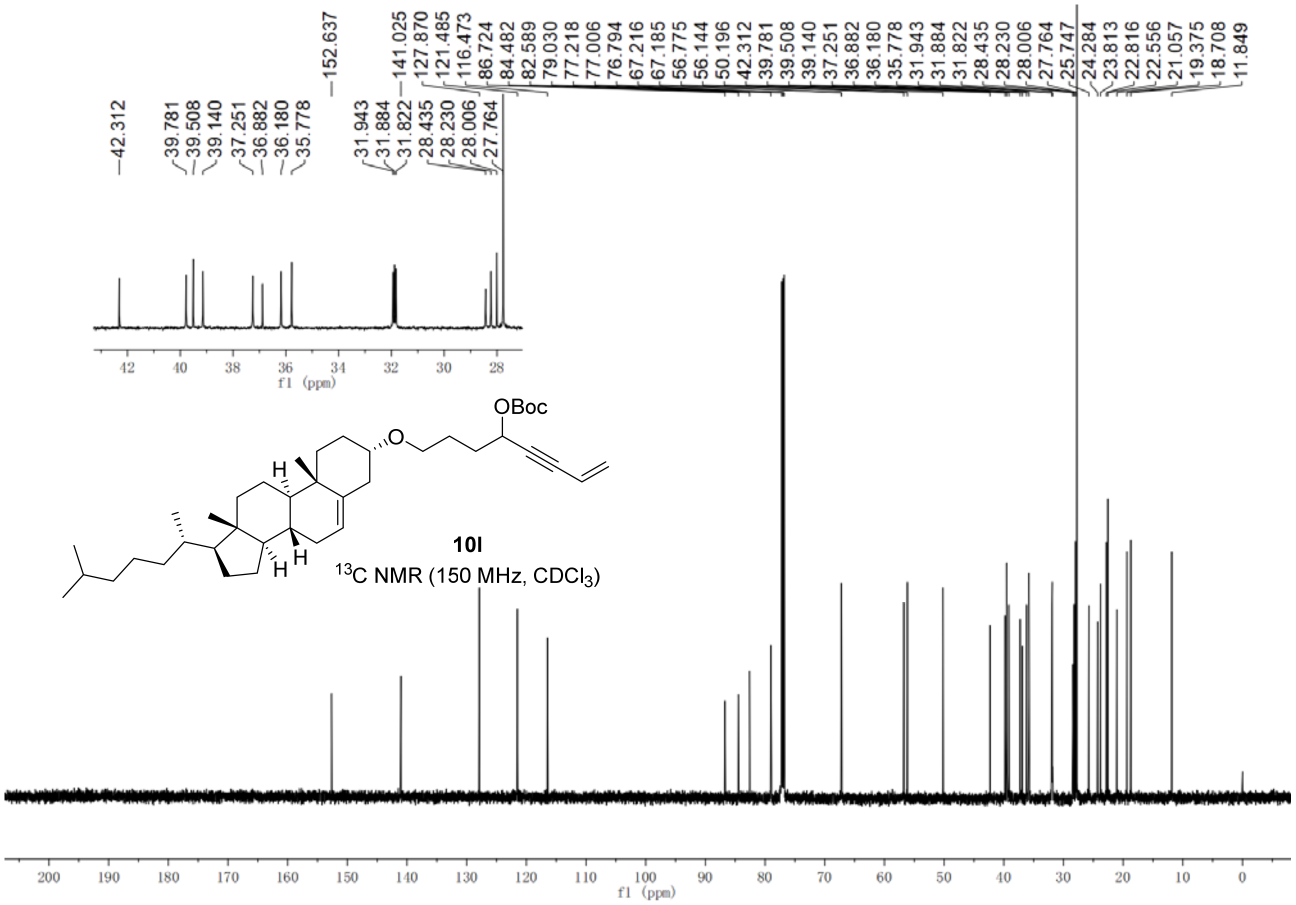
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{44}H_{72}O_5Na^+$ 703.5272



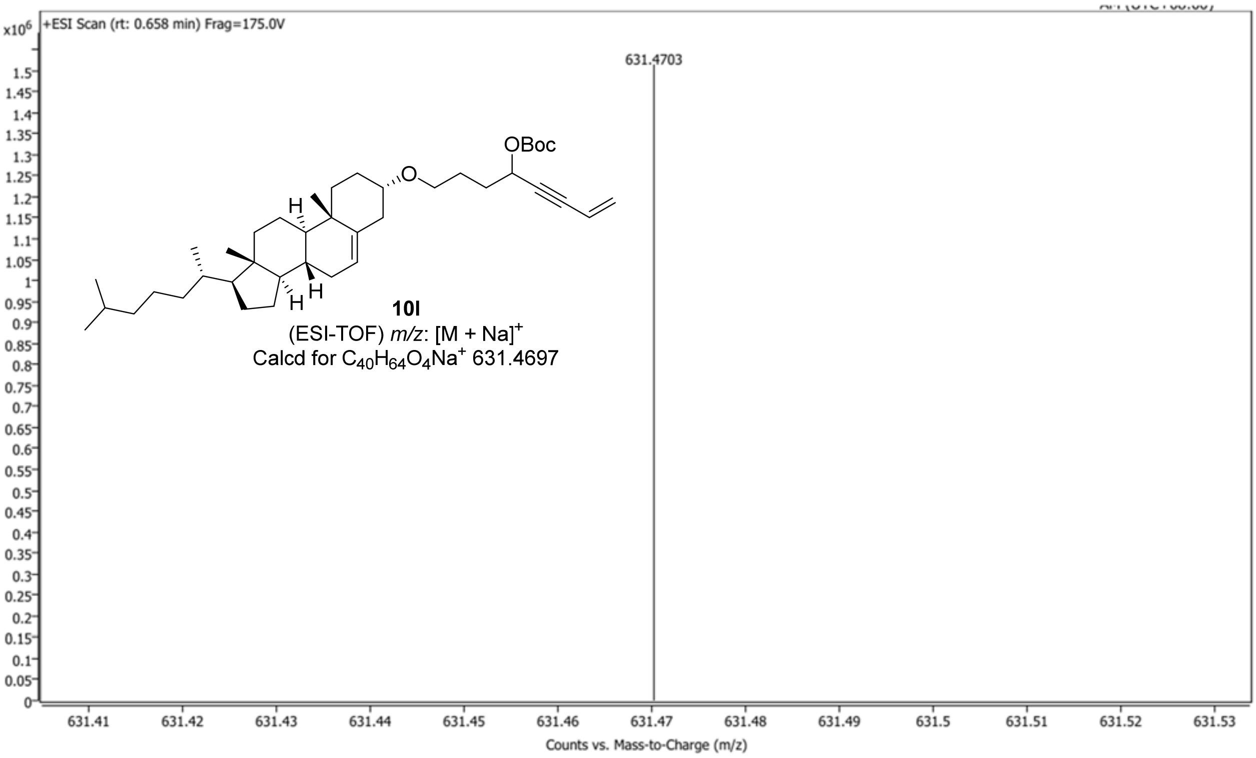
10l

^{1}H NMR (400 MHz, CDCl$_3$)



10l

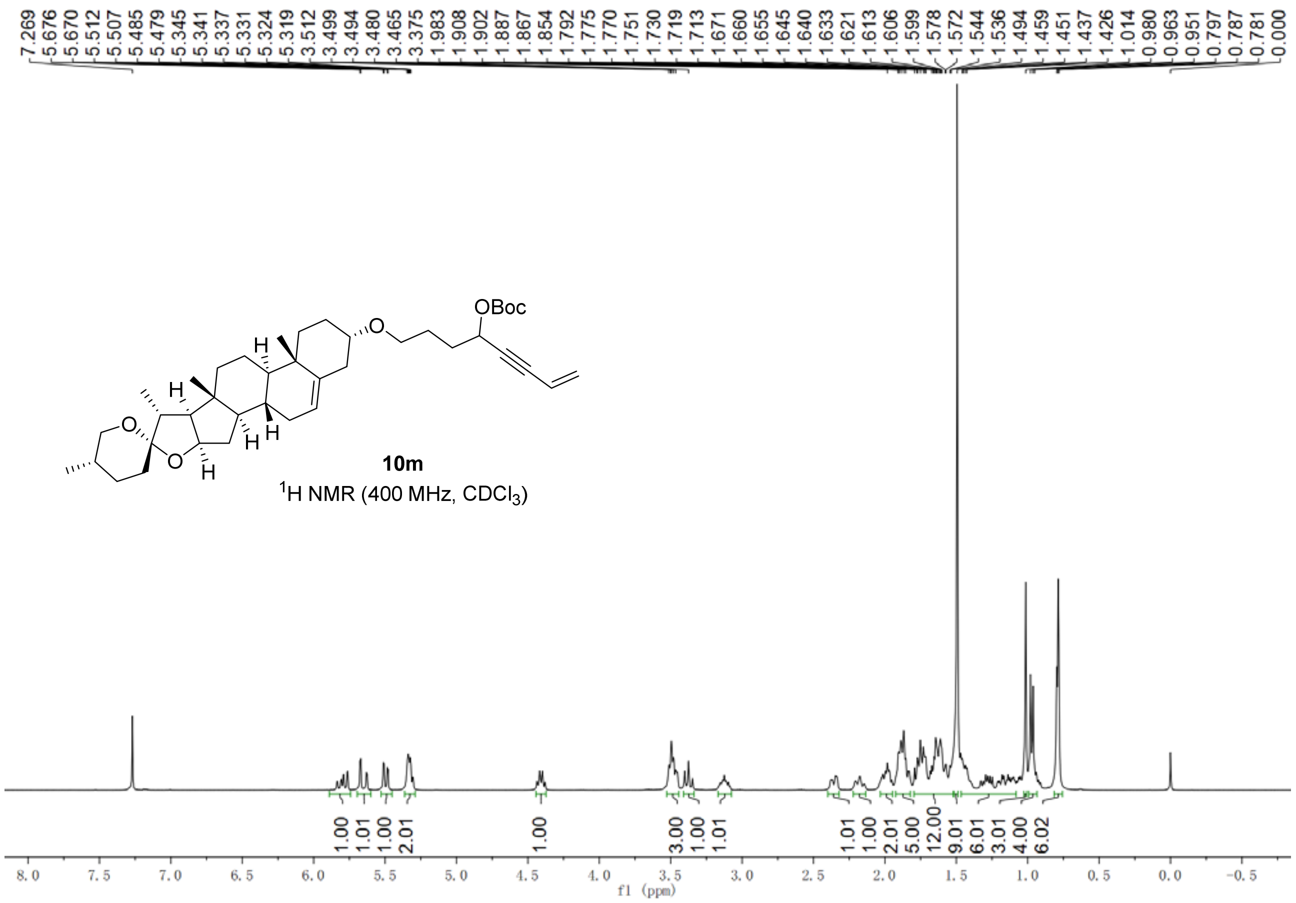
^{13}C NMR (150 MHz, CDCl$_3$)



10l

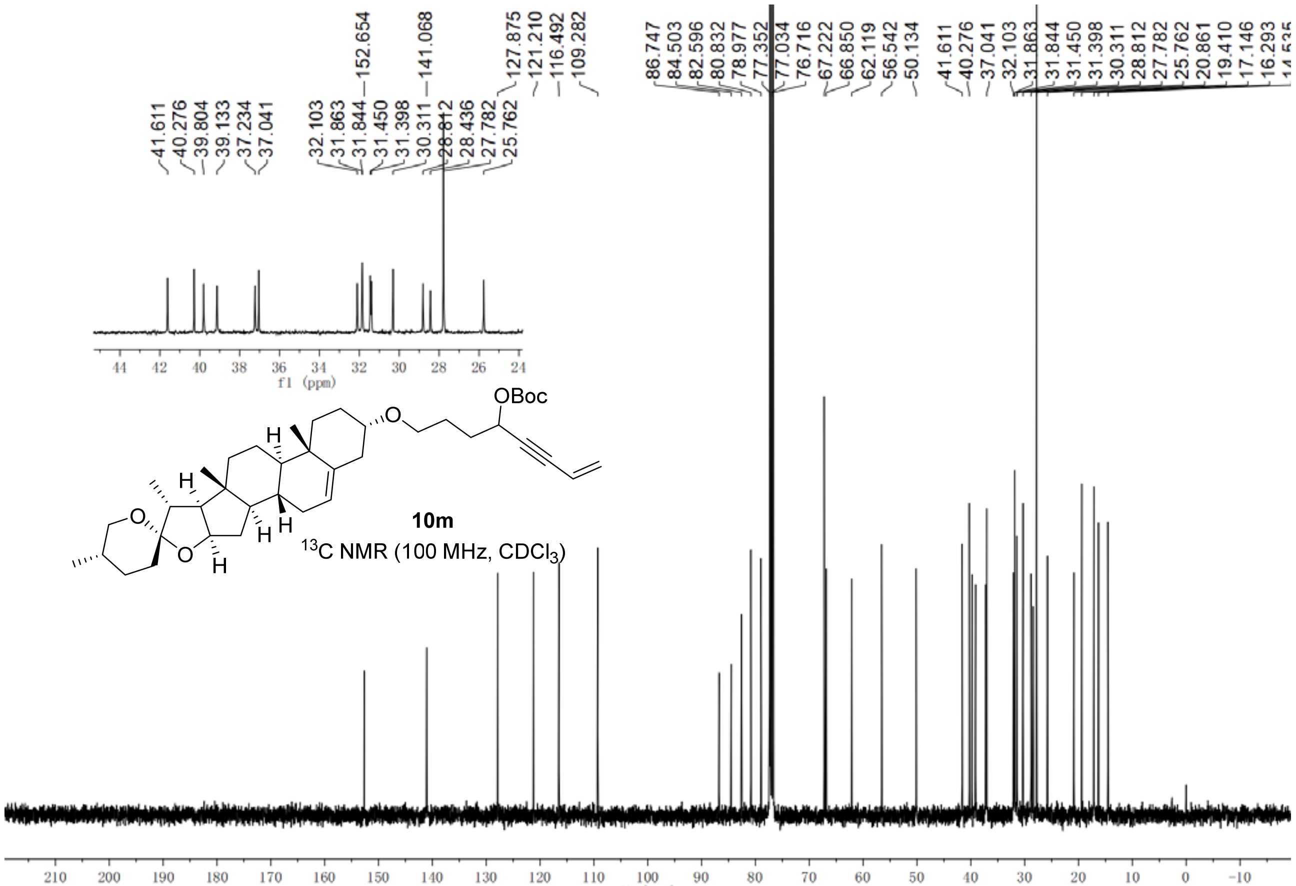
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{40}H_{64}O_4Na^+$ 631.4697



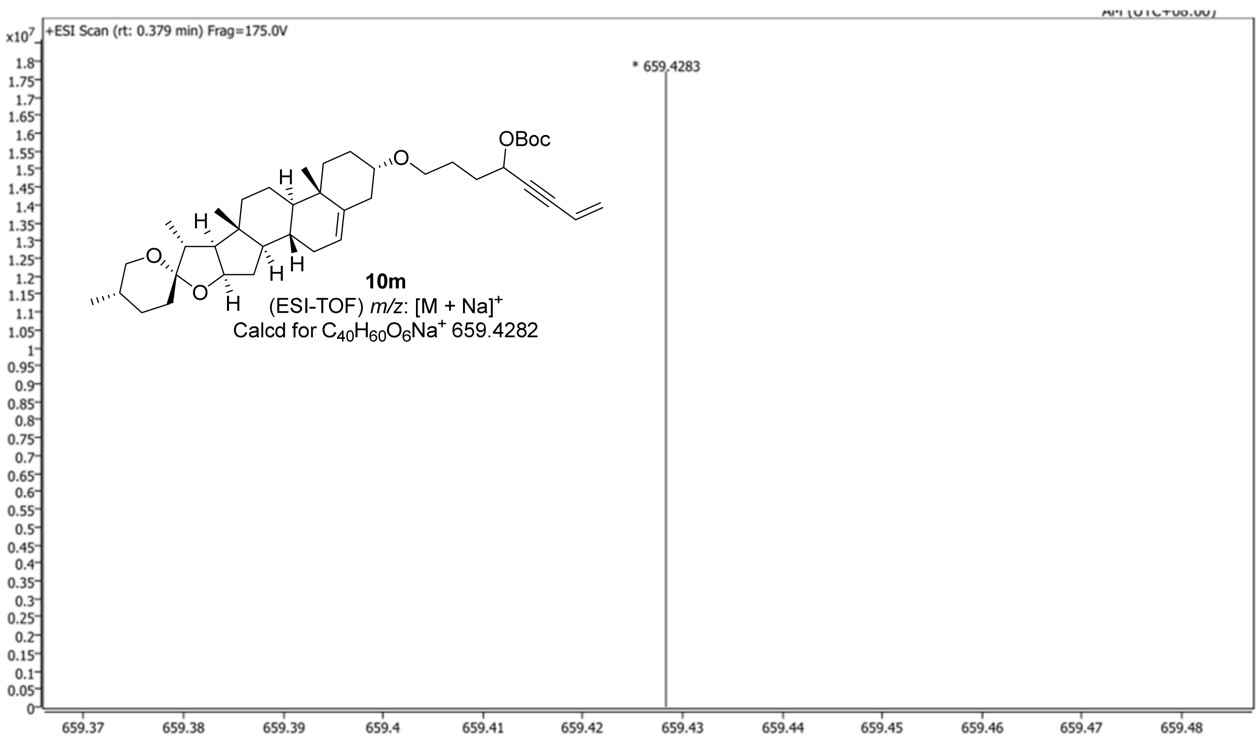
10m

^{1}H NMR (400 MHz, $CDCl_3$)



10m

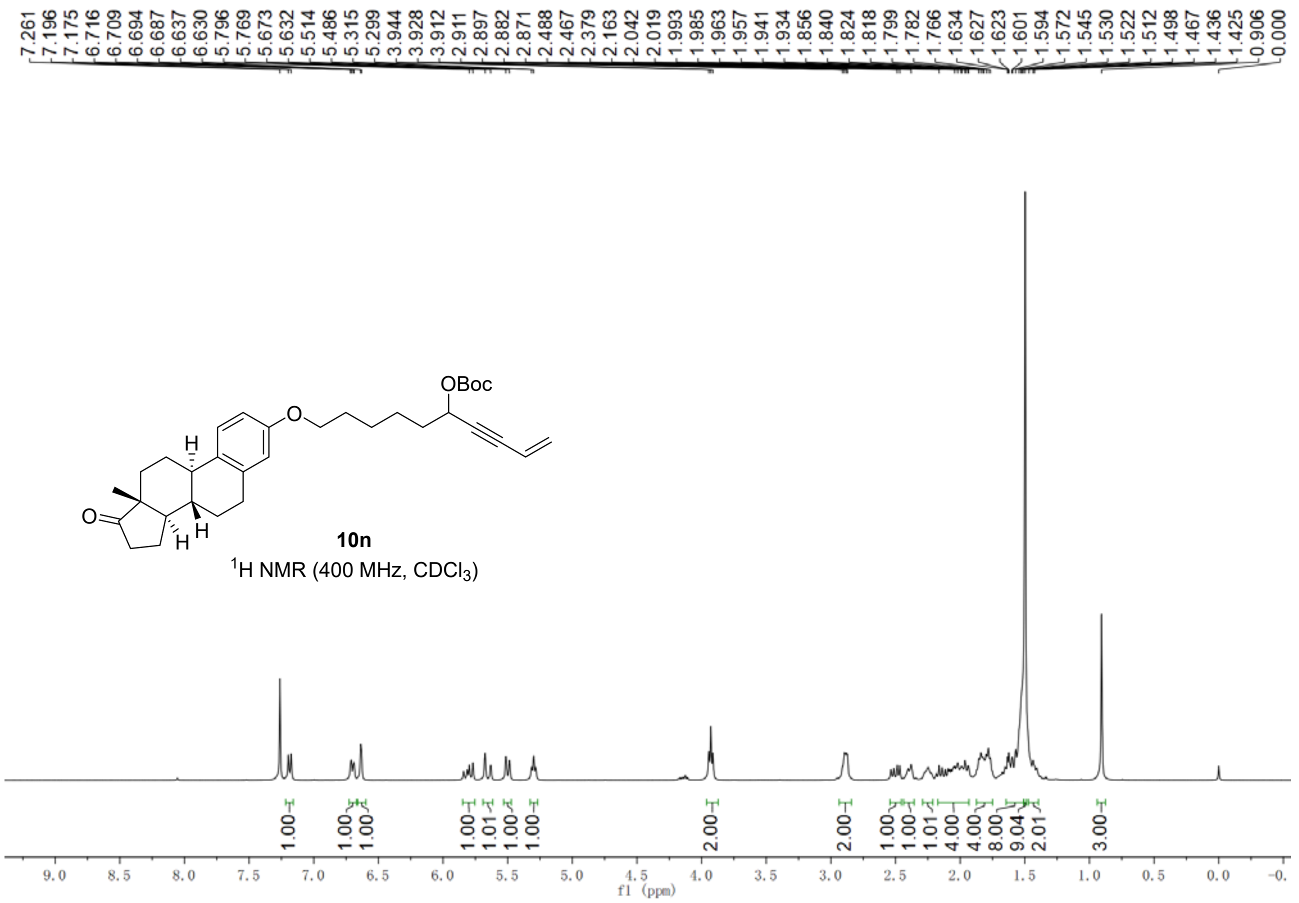
^{13}C NMR (100 MHz, $CDCl_3$)



10m

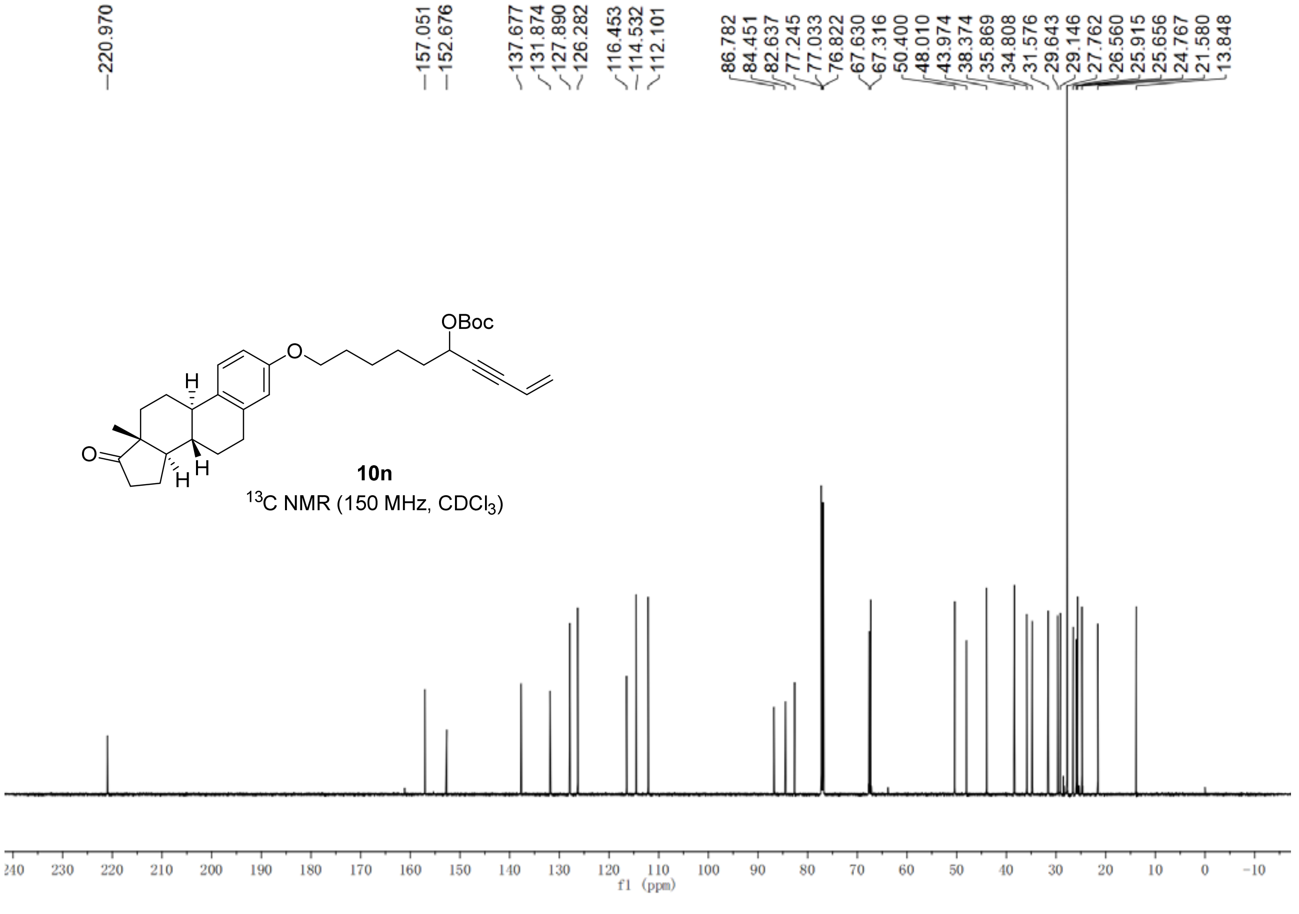
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{40}H_{60}O_6Na^+$ 659.4282



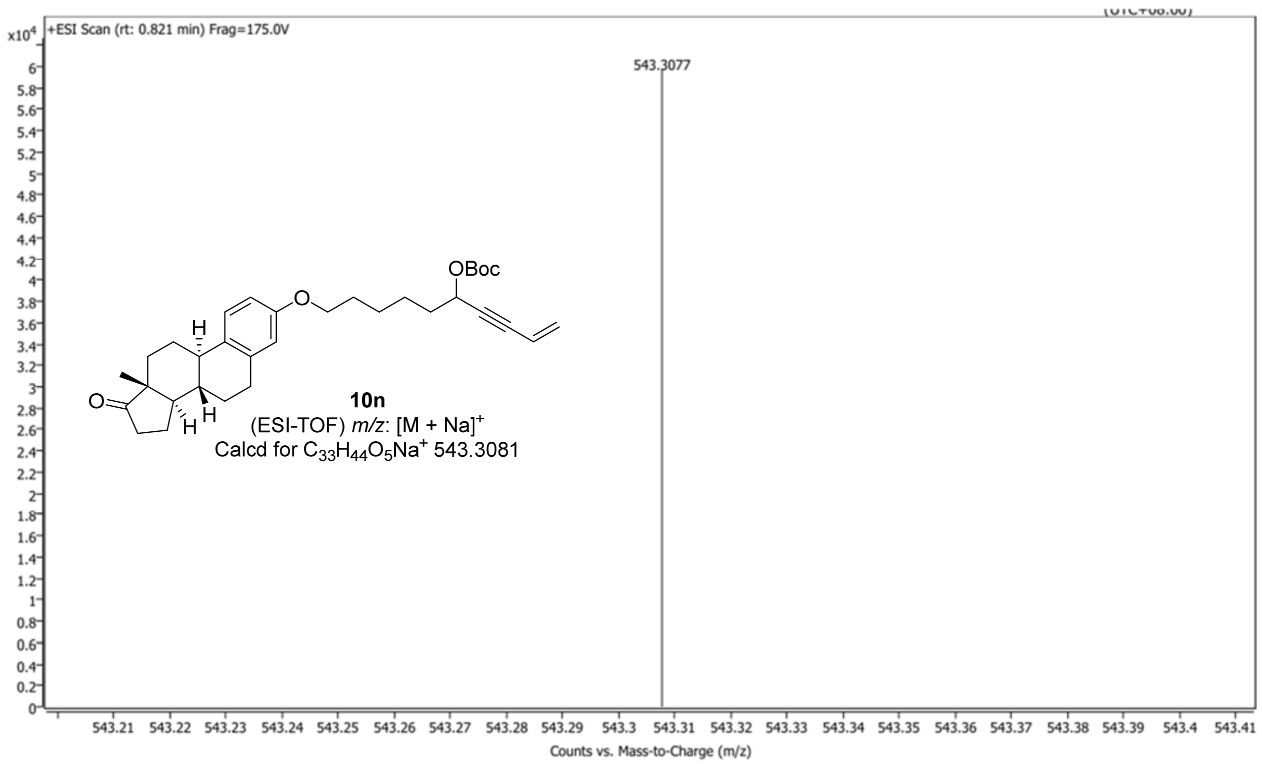
10n

^{1}H NMR (400 MHz, CDCl$_3$)



10n

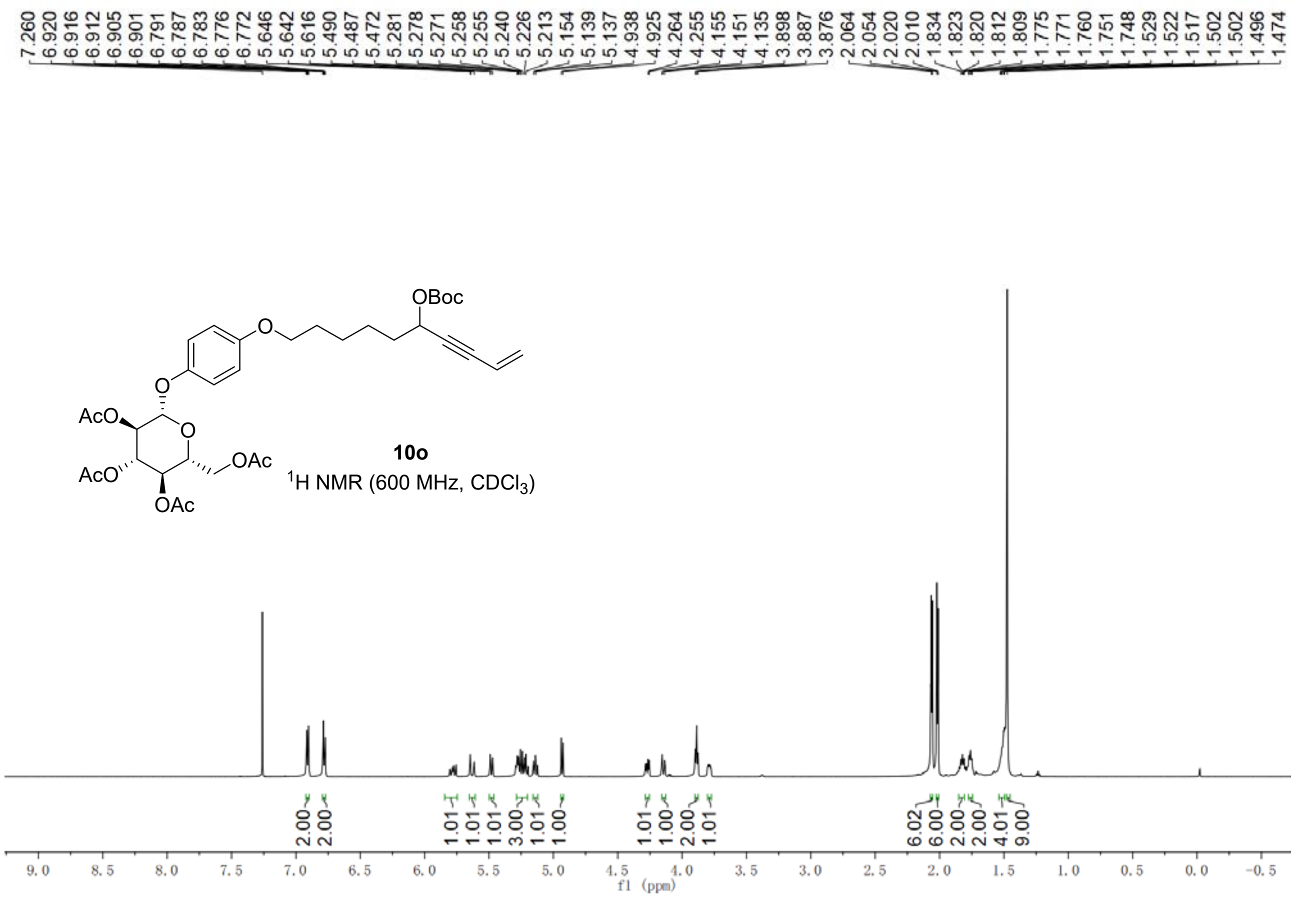
^{13}C NMR (150 MHz, CDCl$_3$)



10n

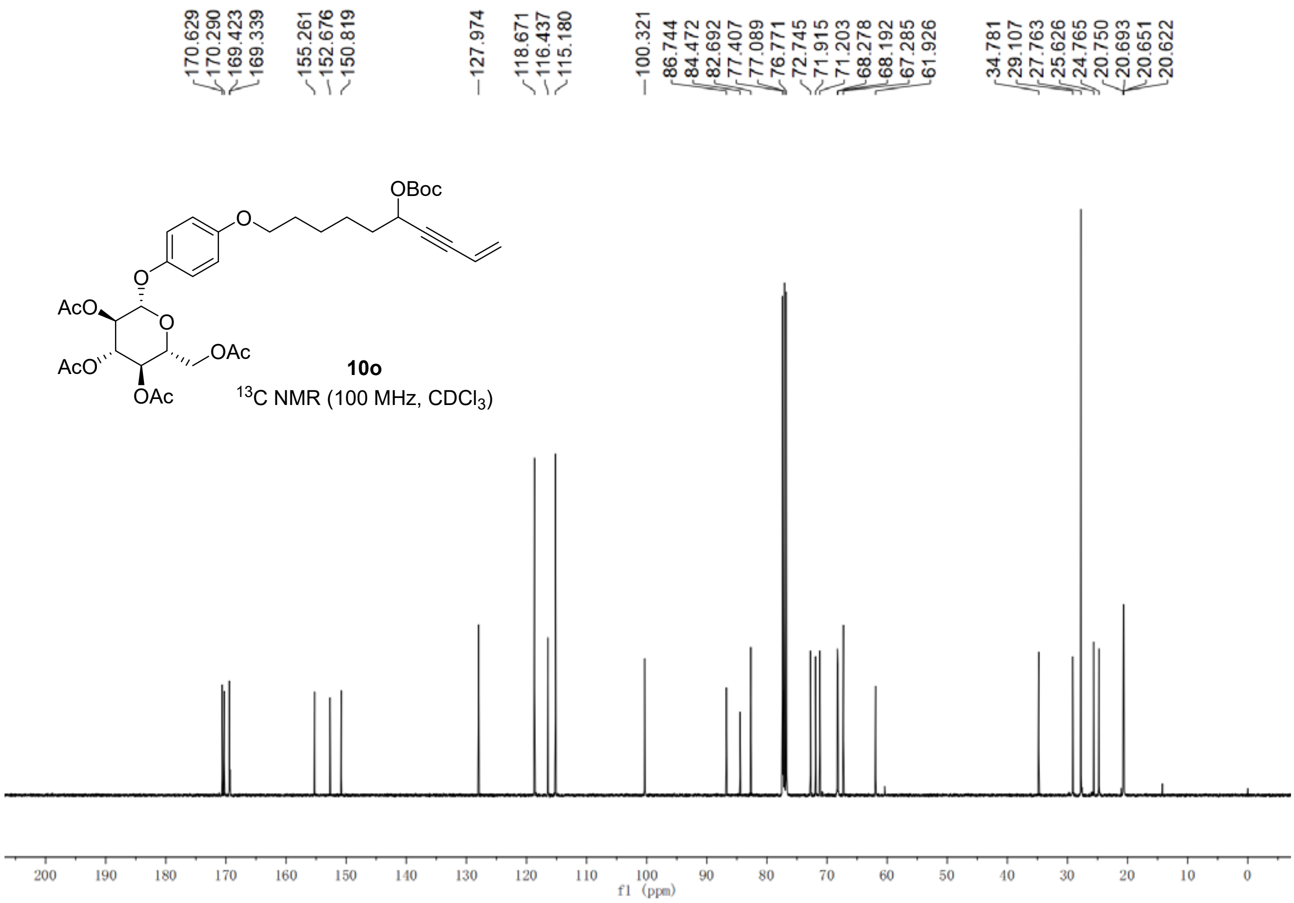
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{33}H_{44}O_5Na^+$ 543.3081



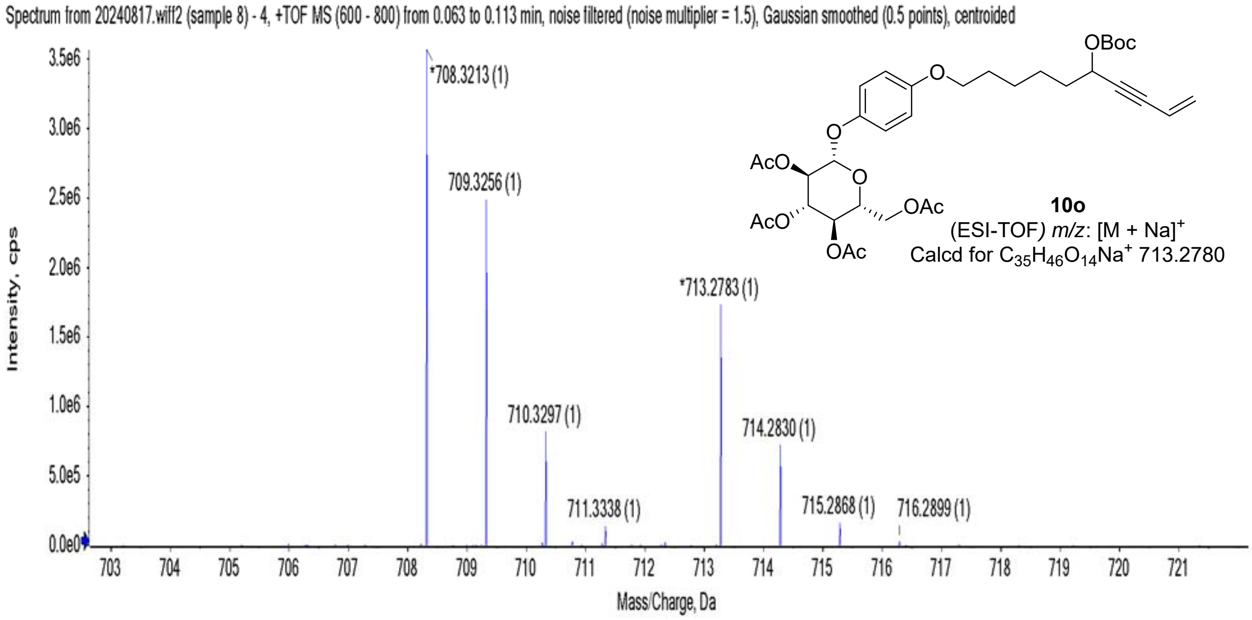
10o

^{1}H NMR (600 MHz, CDCl$_3$)



10o

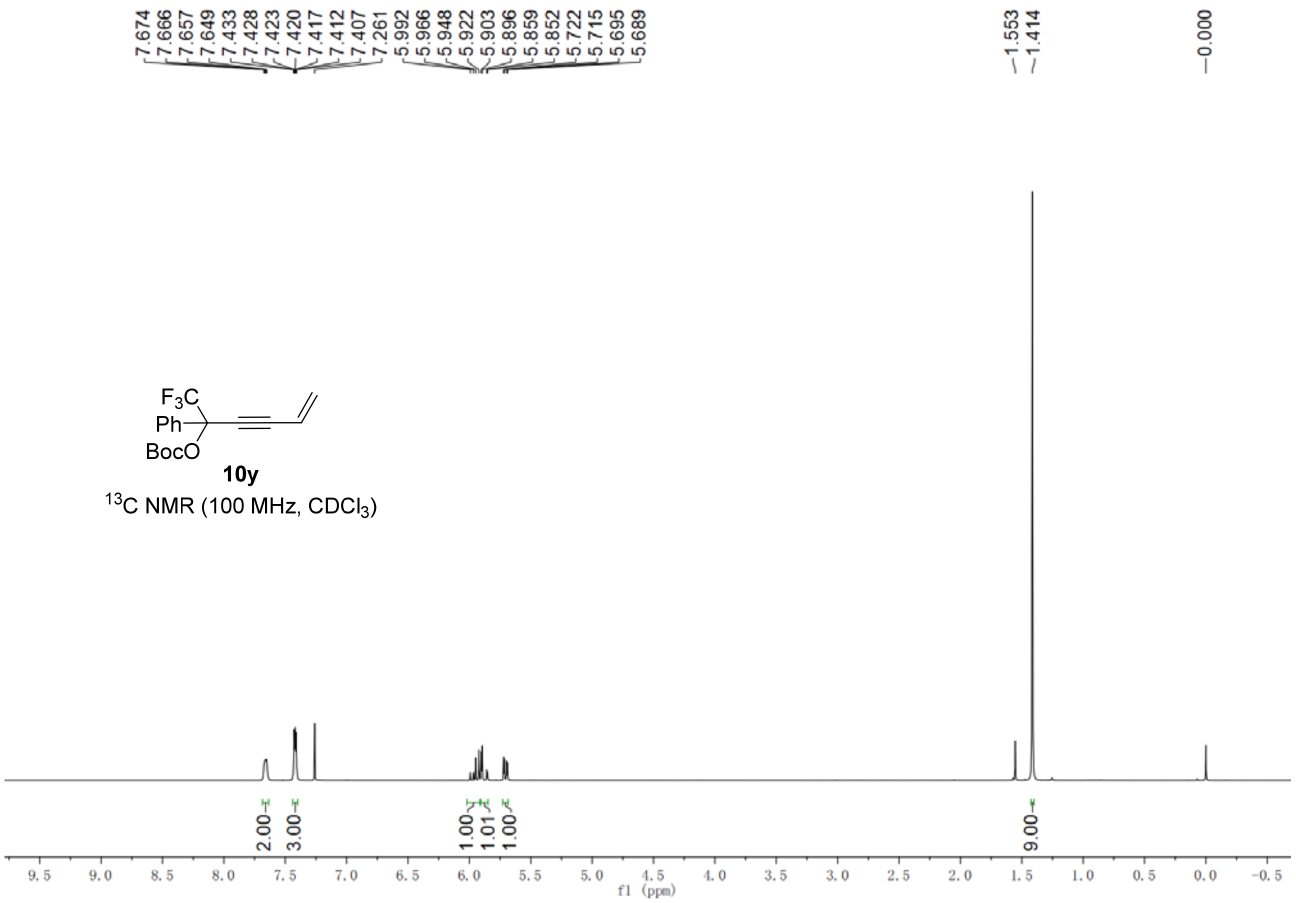
^{13}C NMR (100 MHz, CDCl$_3$)



10o

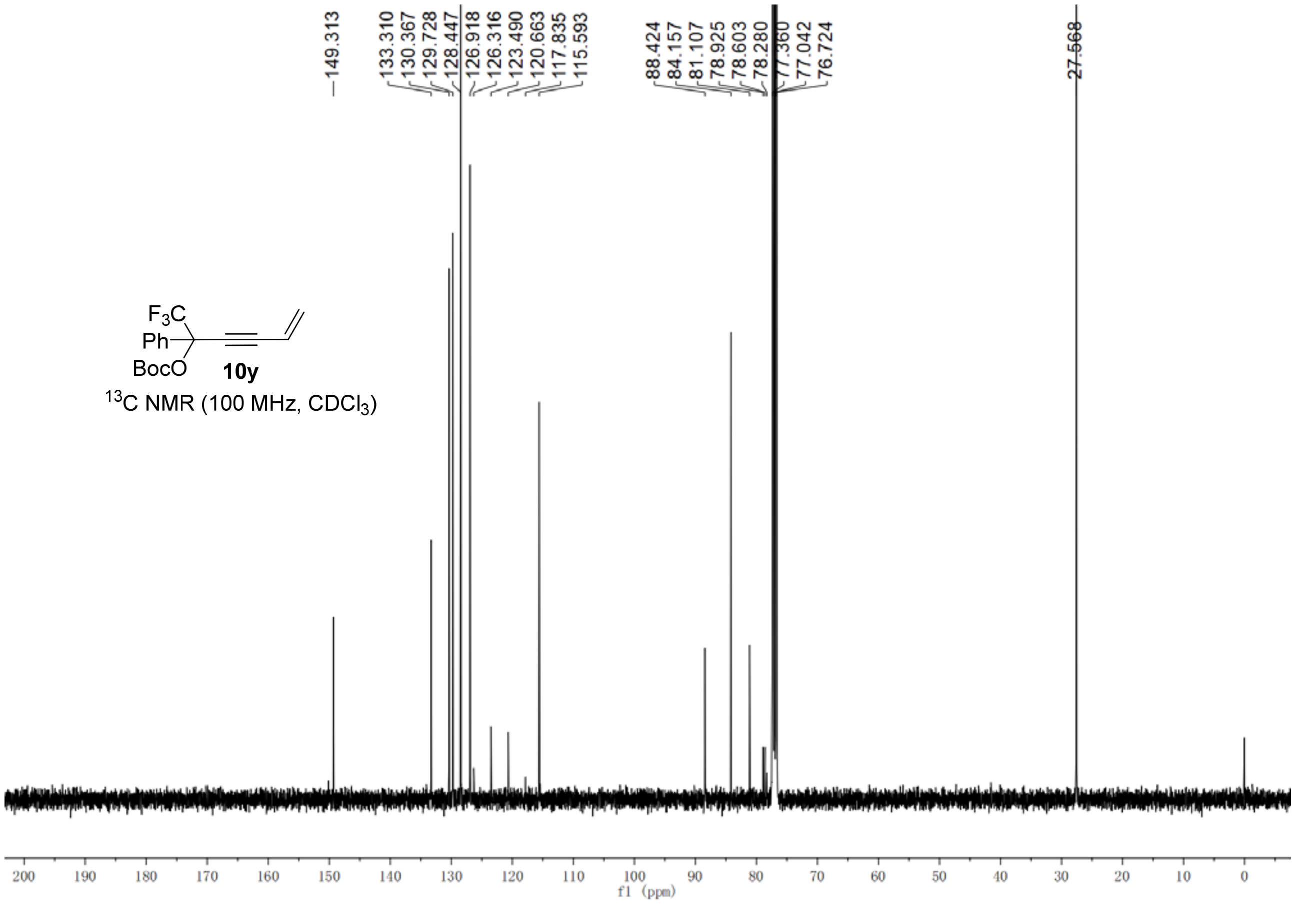
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{35}H_{46}O_{14}Na^+$ 713.2780



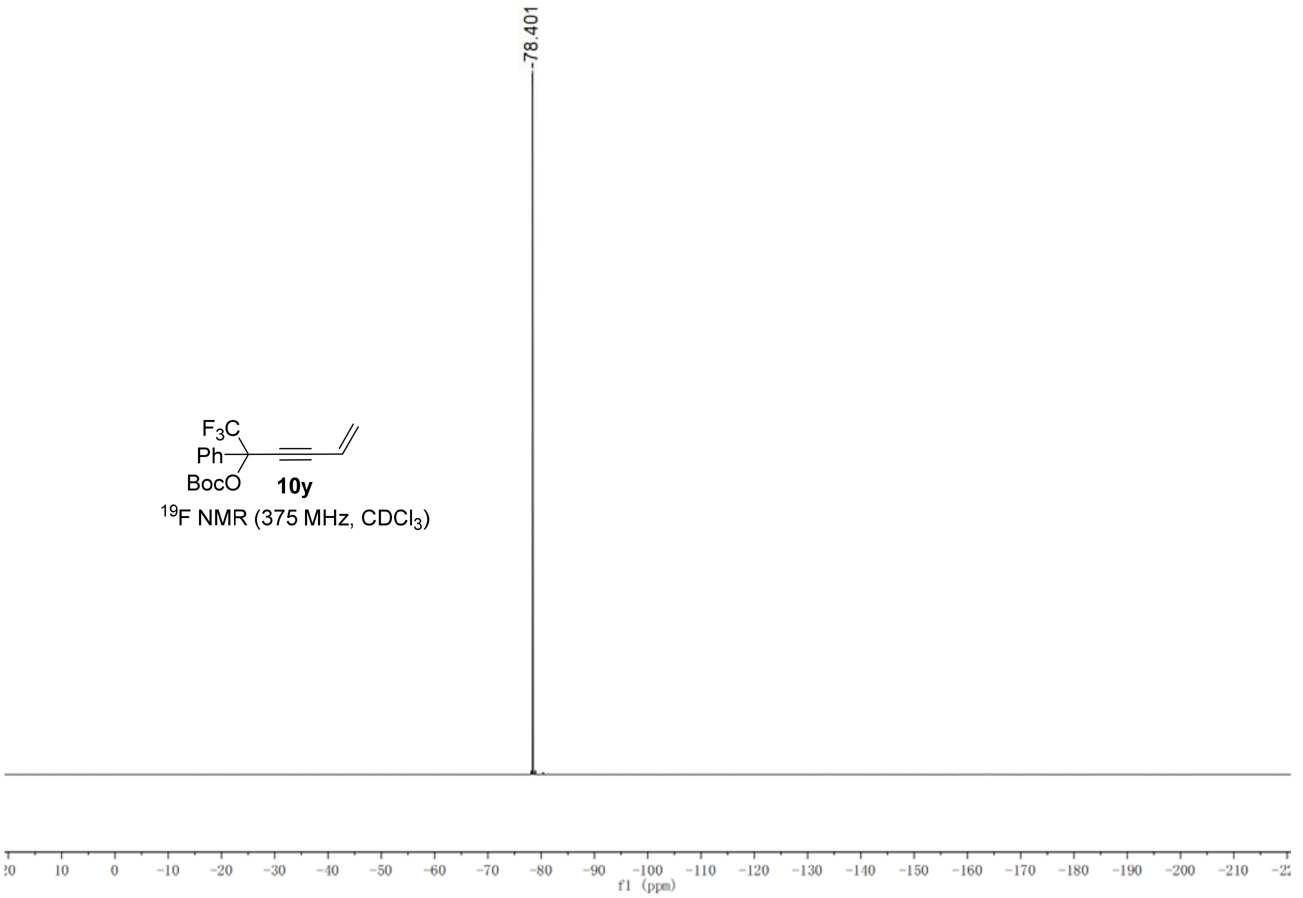
10y

^{13}C NMR (100 MHz, CDCl$_3$)



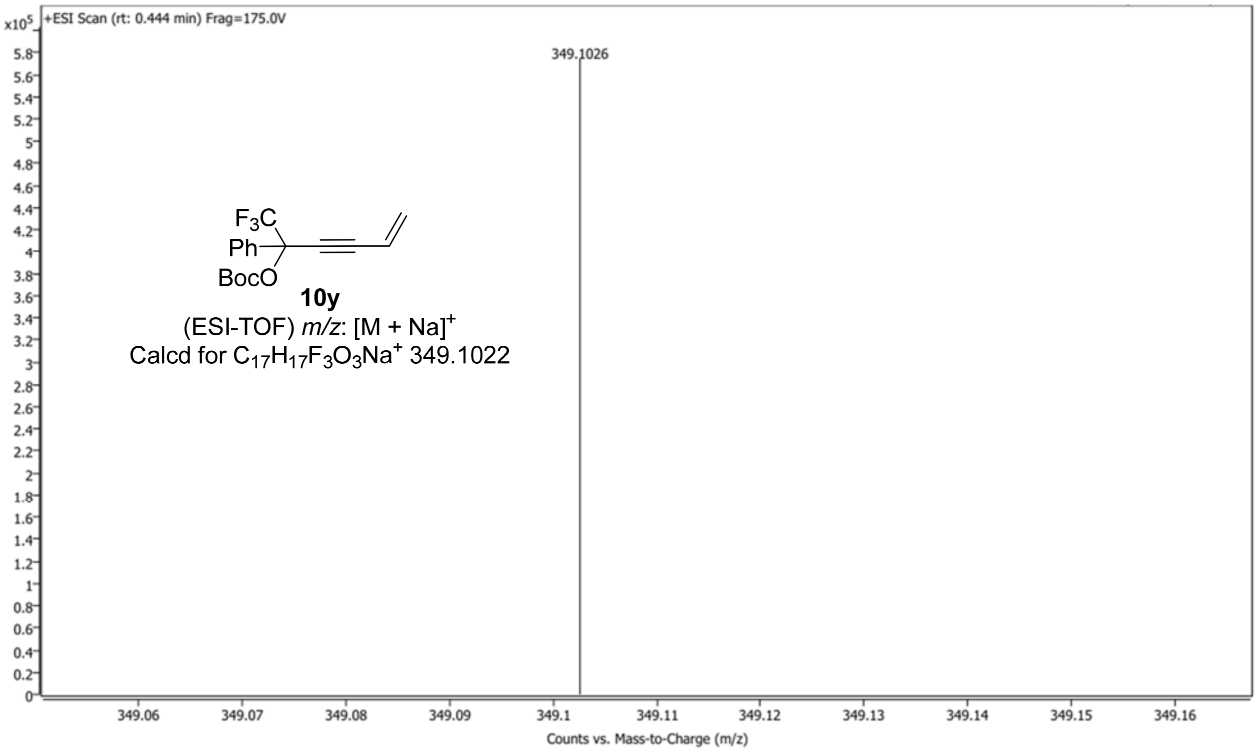
10y

^{13}C NMR (100 MHz, CDCl$_3$)



10y

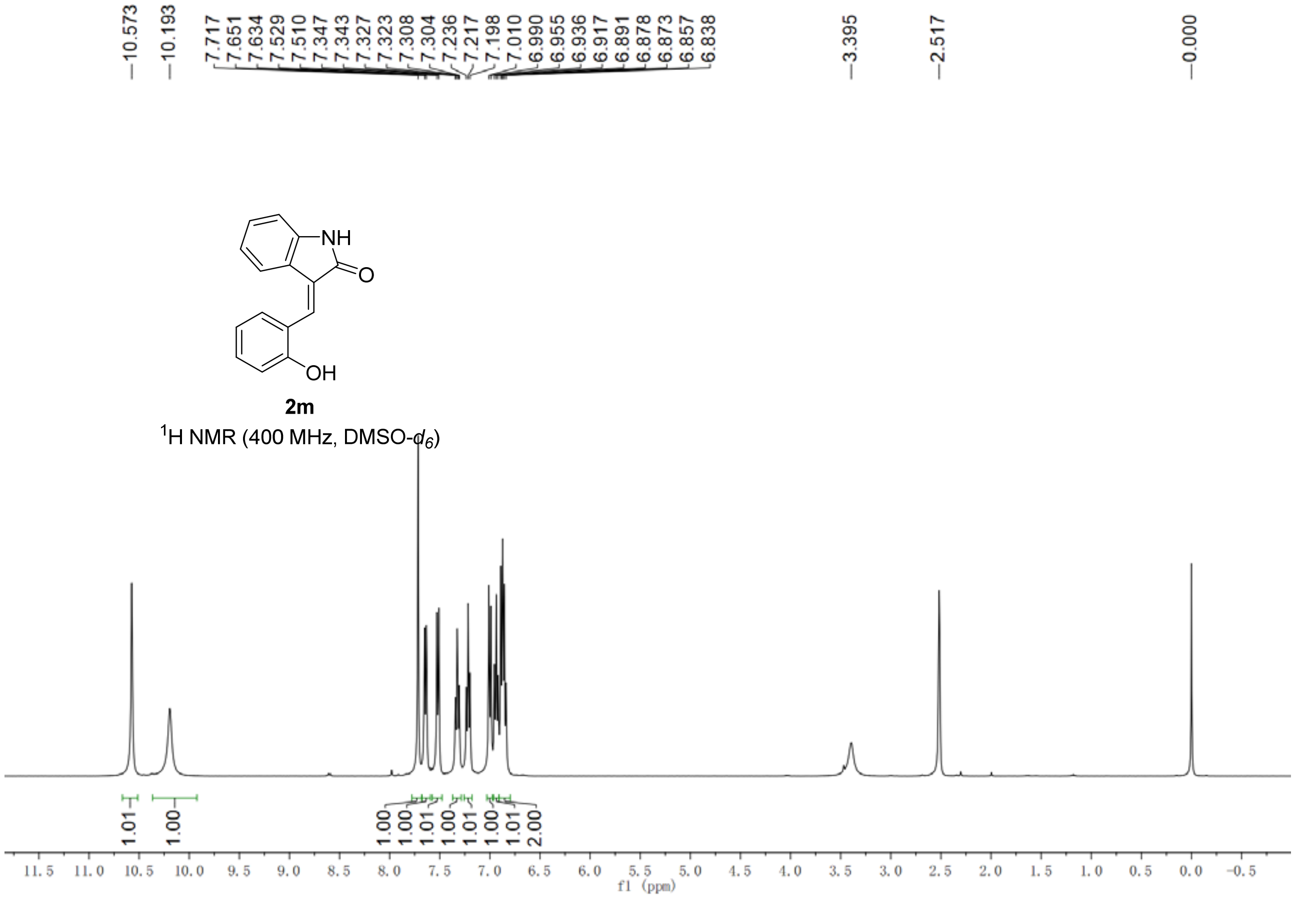
^{19}F NMR (375 MHz, $CDCl_3$)



10y

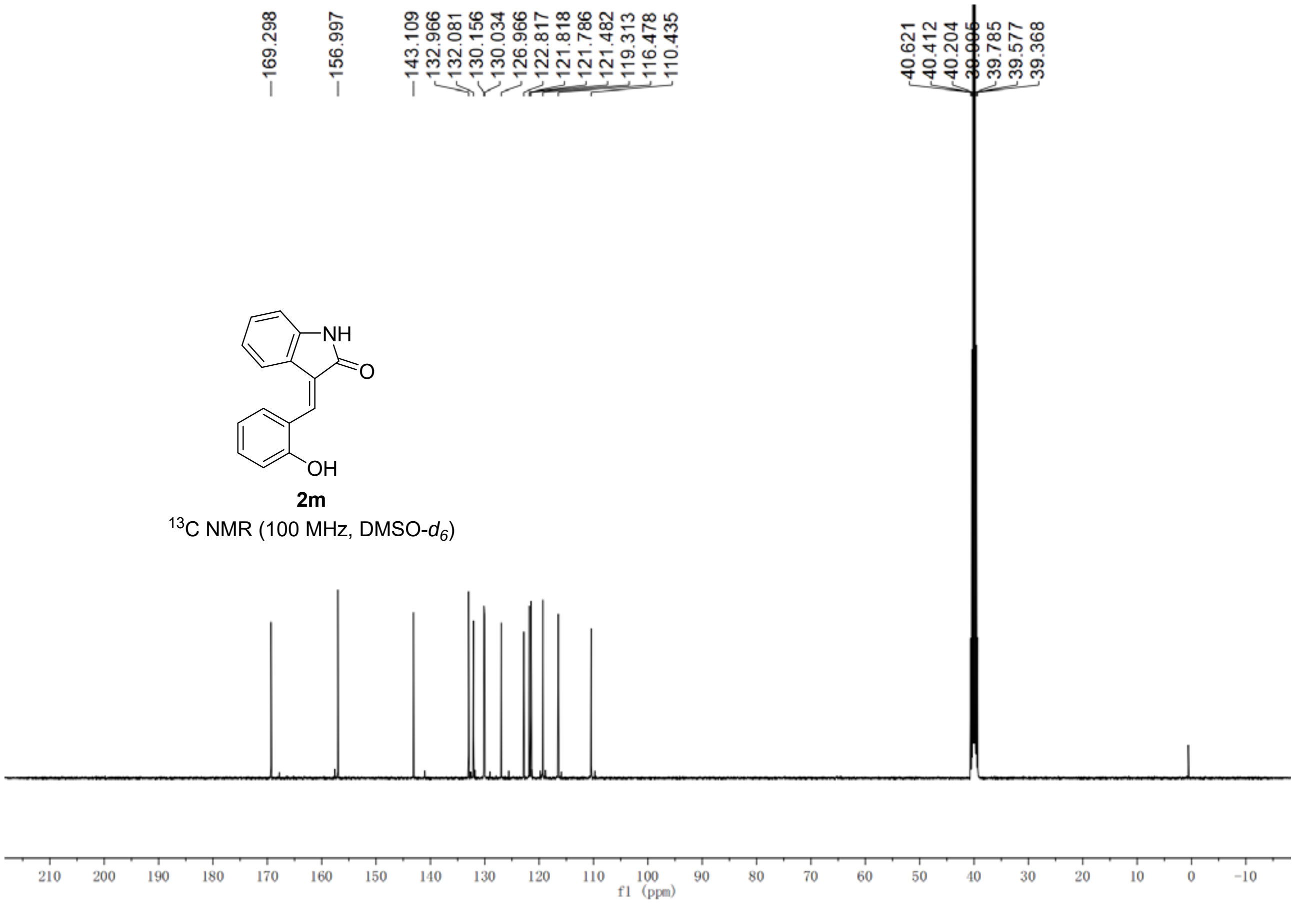
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{17}H_{17}F_3O_3Na^+$ 349.1022



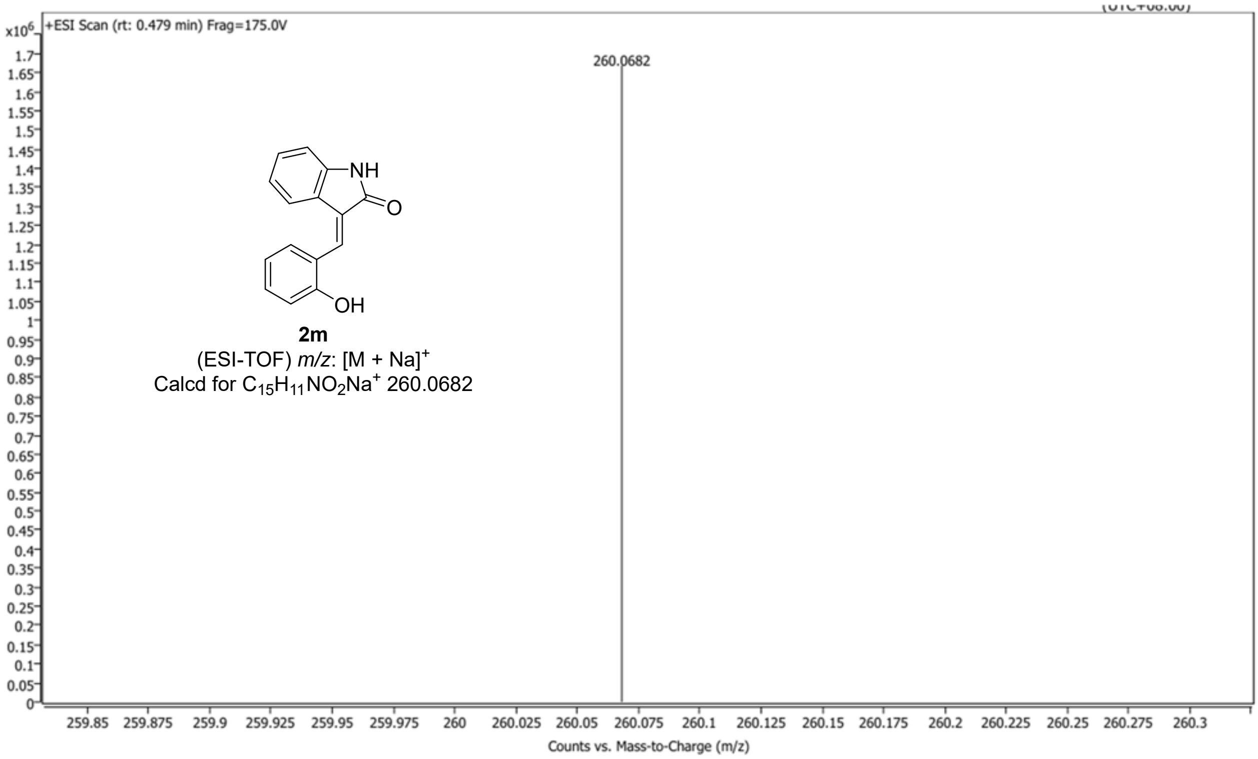
2m

^{1}H NMR (400 MHz, DMSO-d_6)



2m

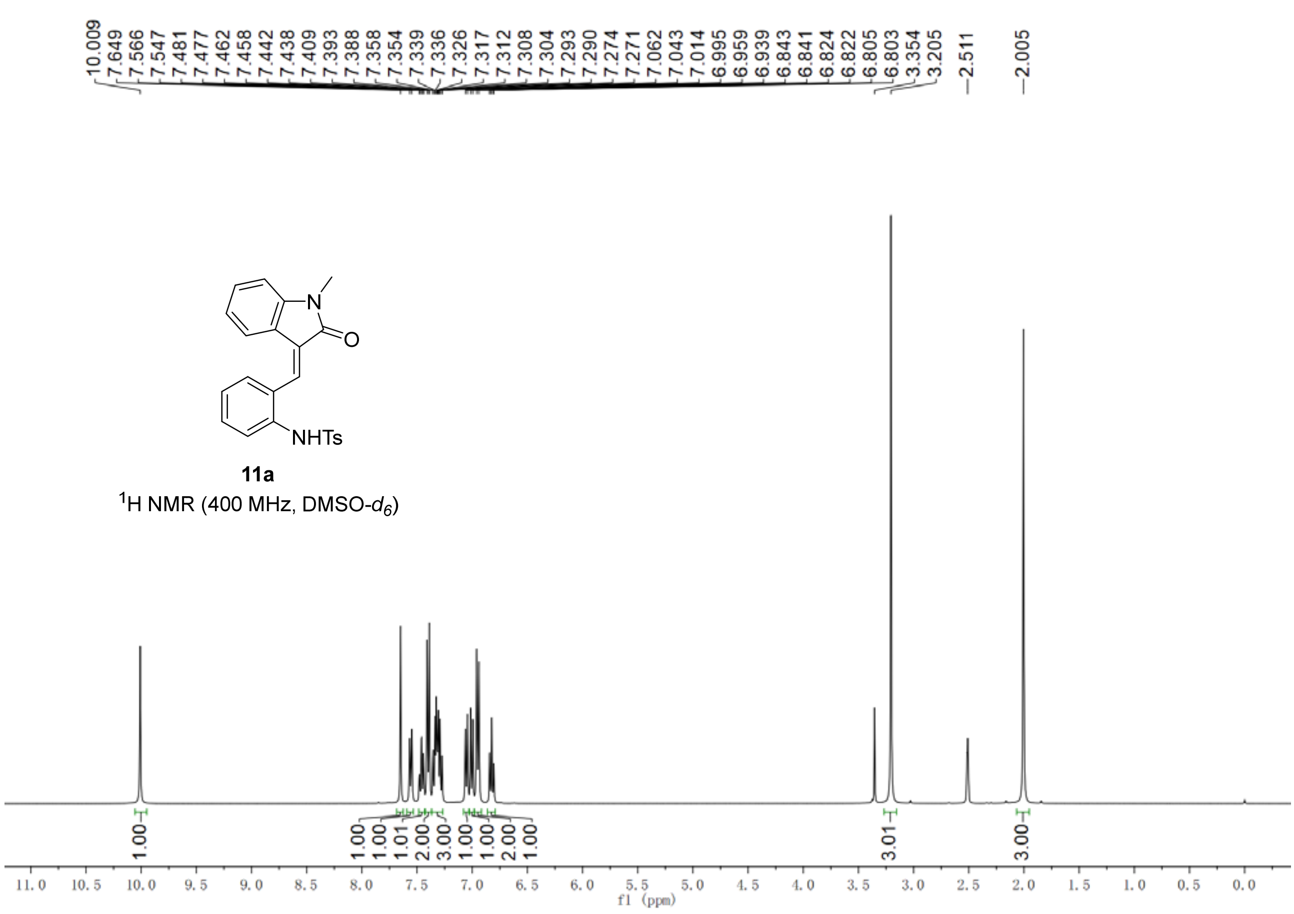
^{13}C NMR (100 MHz, DMSO-d_6)



2m

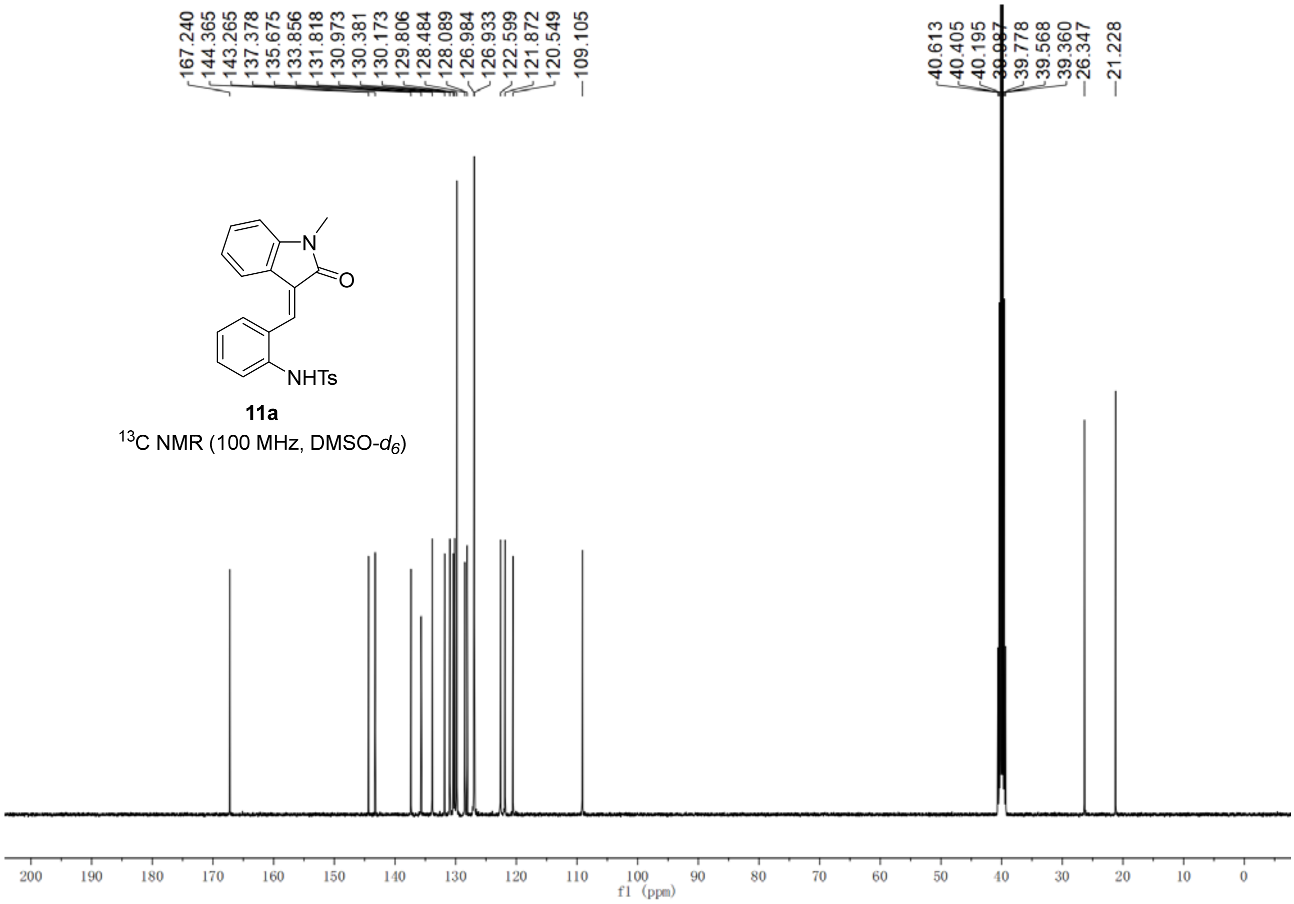
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{15}H_{11}NO_2Na^+$ 260.0682



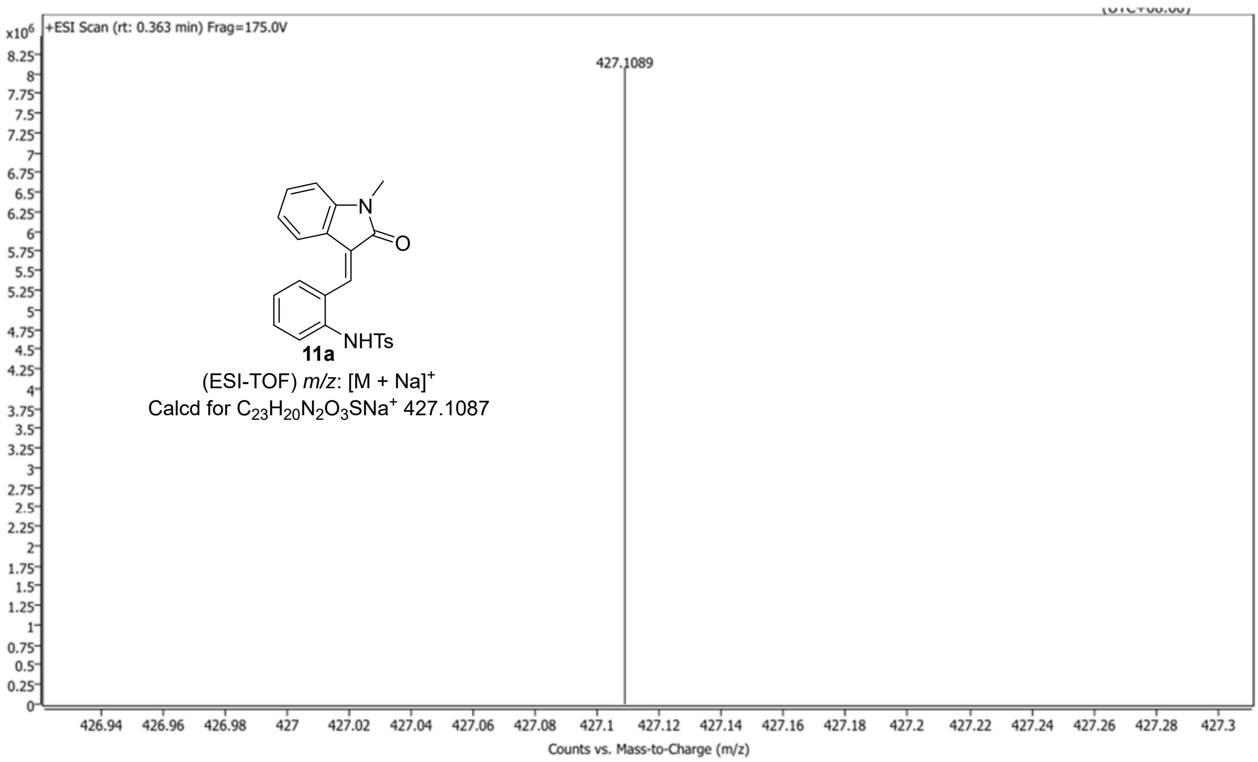
11a

^{1}H NMR (400 MHz, DMSO-d_6)



11a

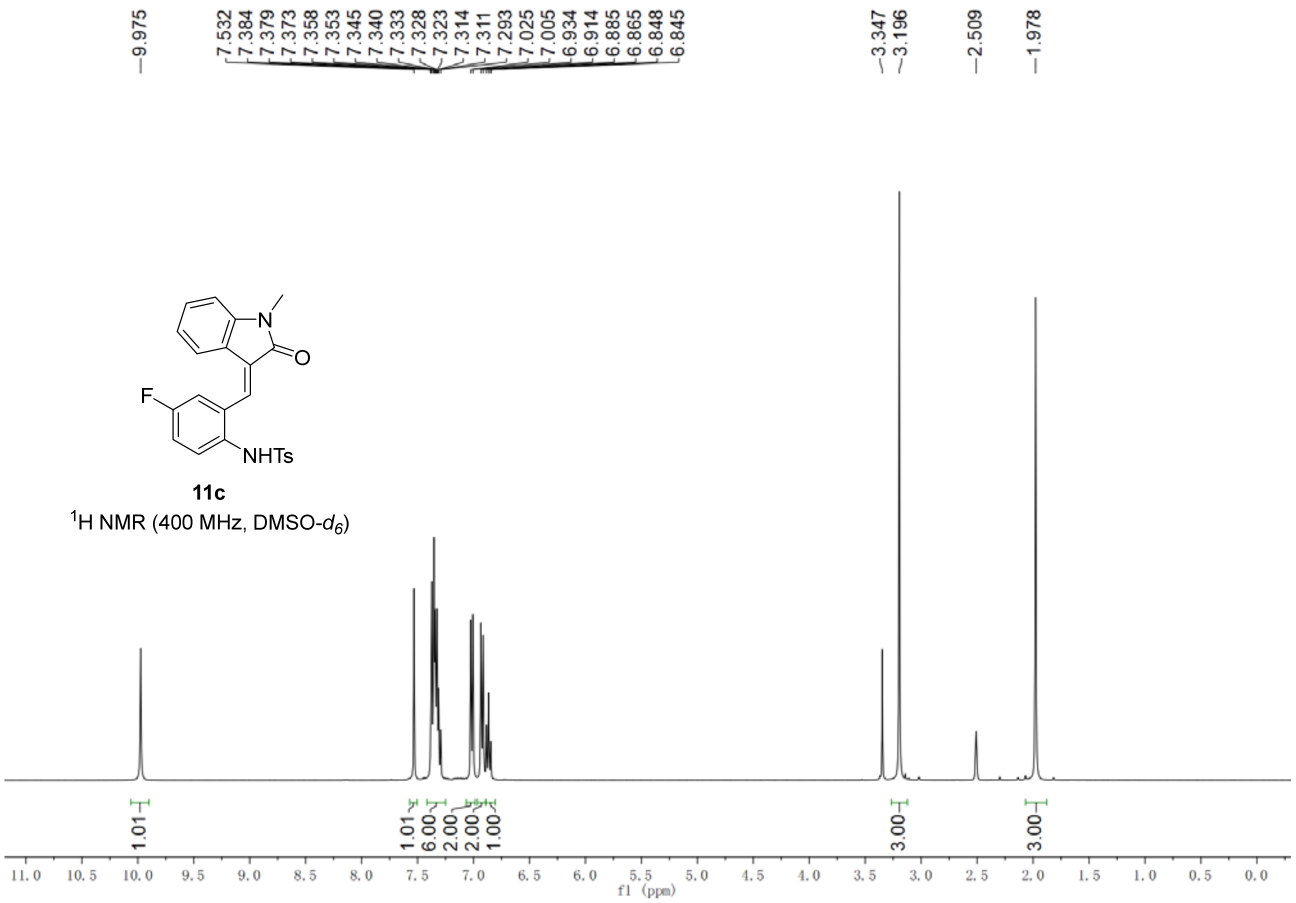
^{13}C NMR (100 MHz, DMSO-d_6)



11a

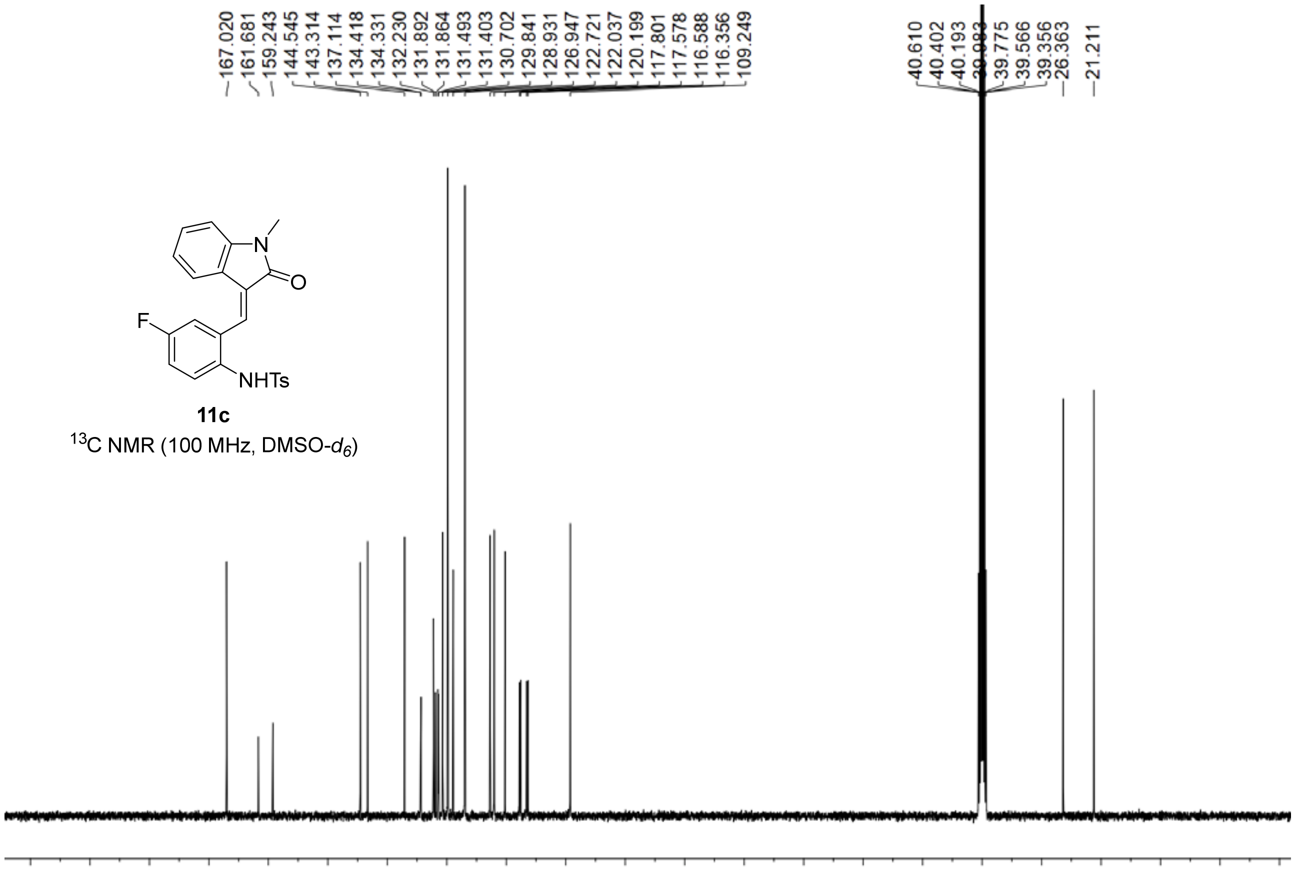
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{23}H_{20}N_2O_3SNa^+$ 427.1087



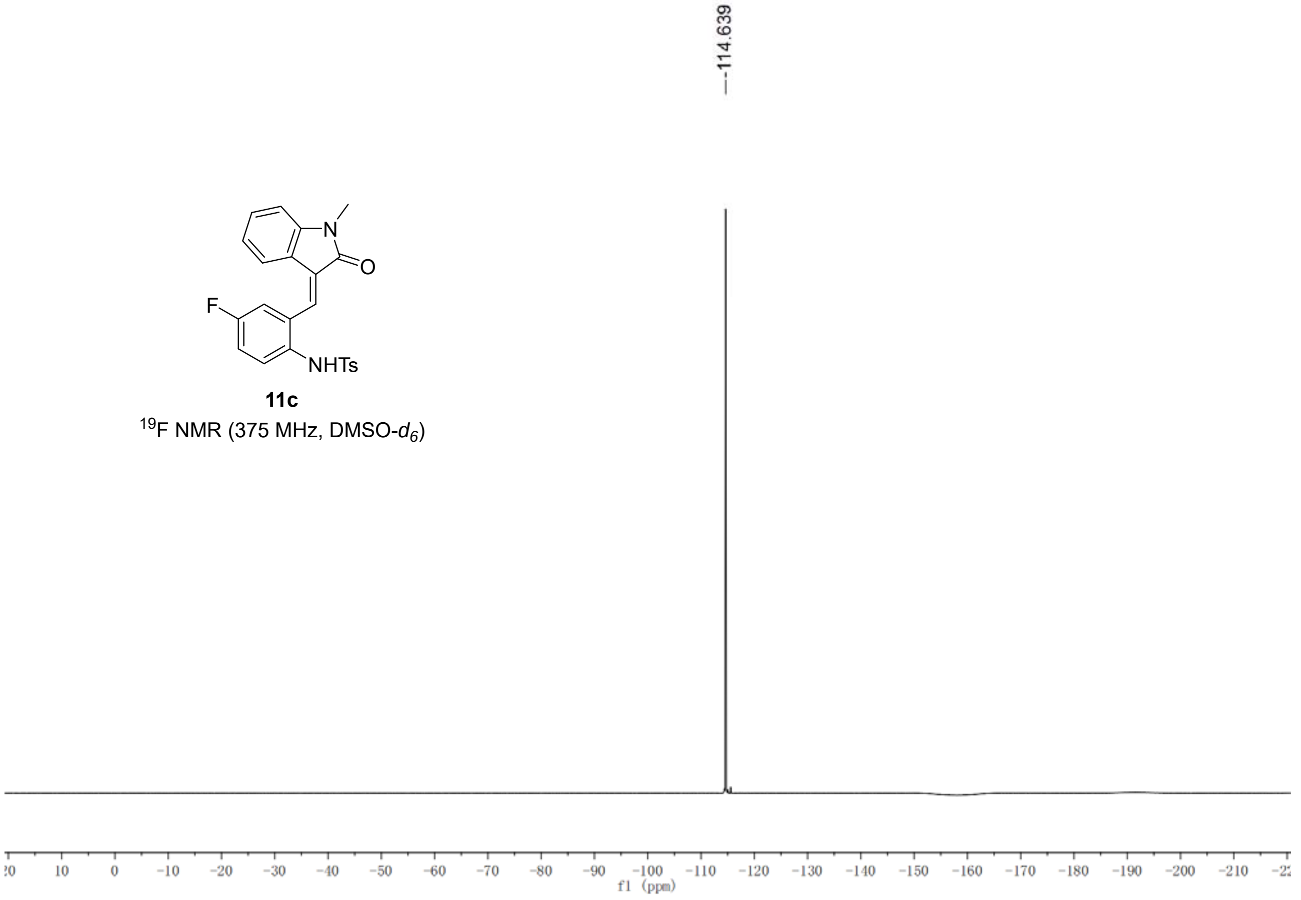
11c

^{1}H NMR (400 MHz, DMSO-d_6)



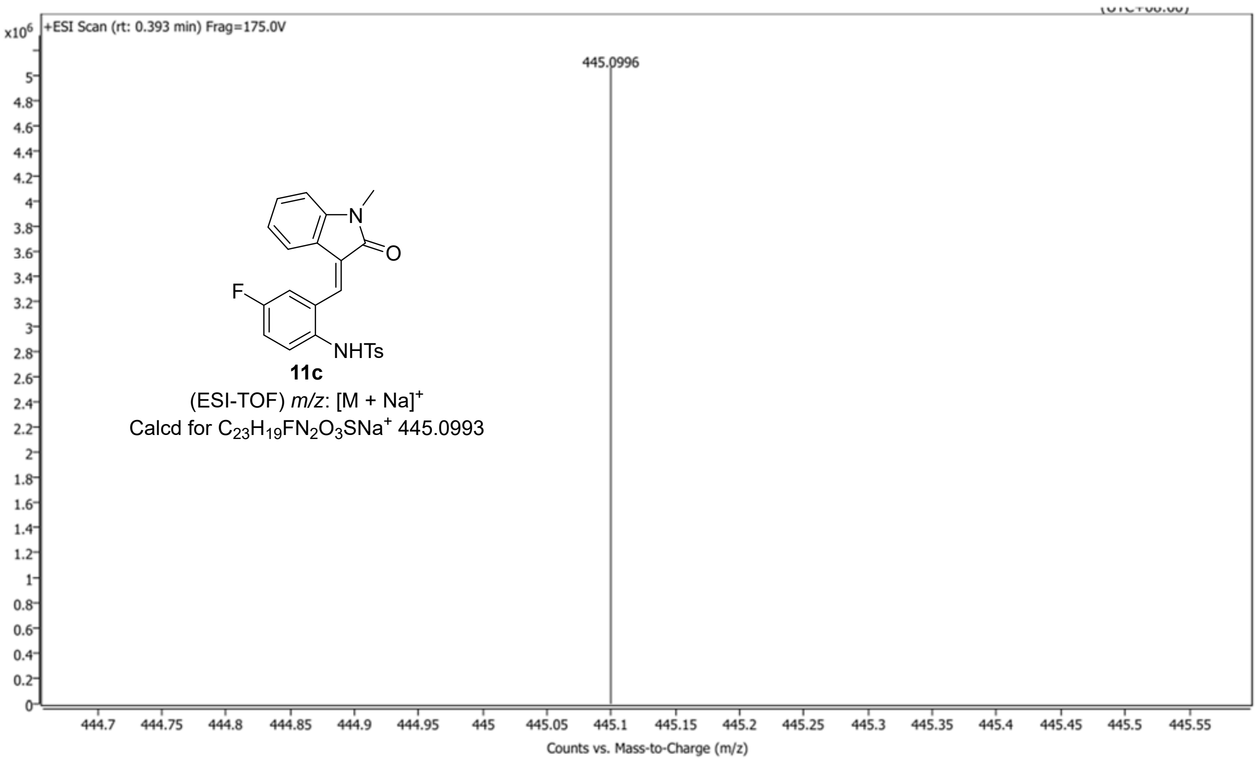
11c

^{13}C NMR (100 MHz, DMSO-d_6)



11c

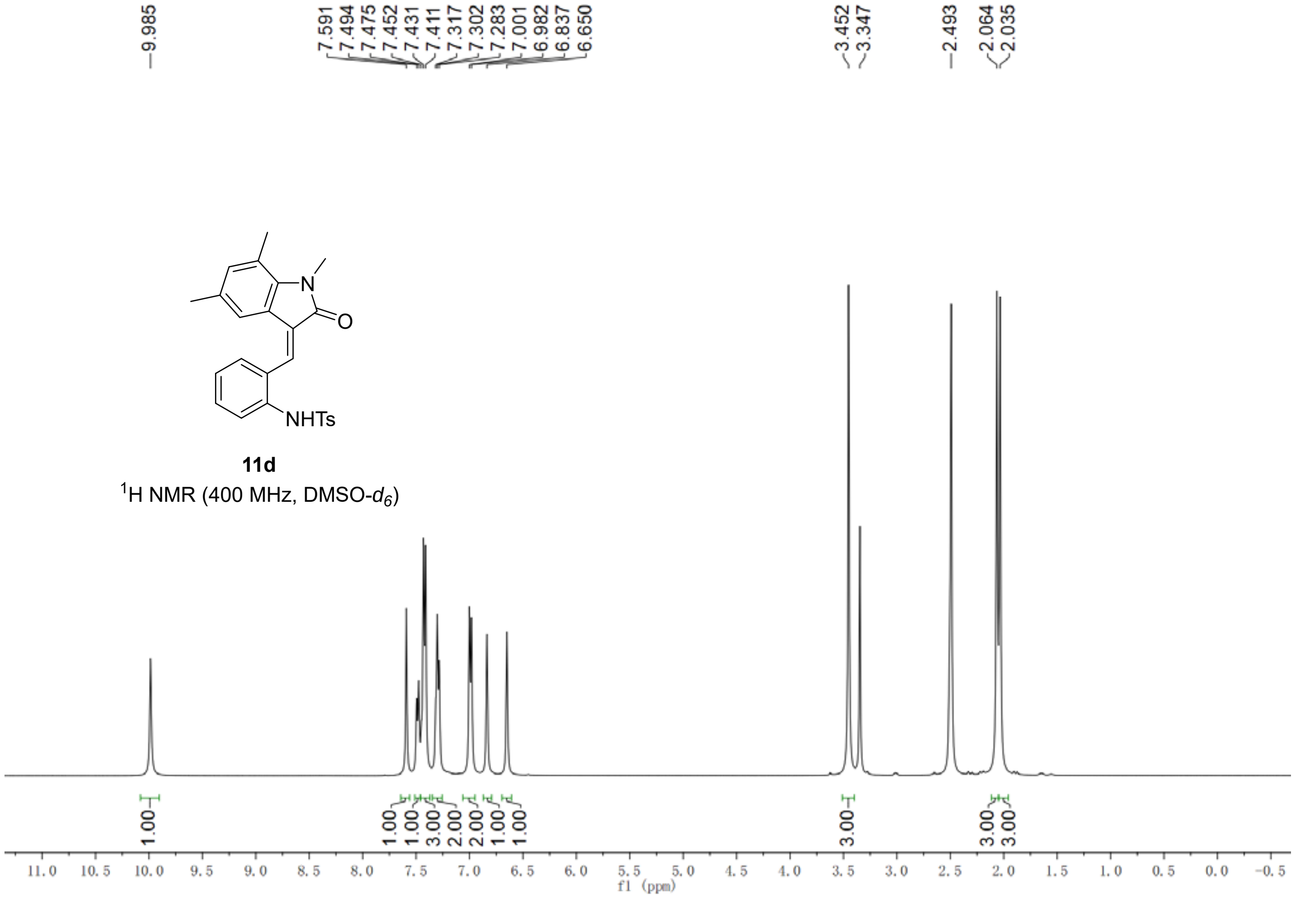
^{19}F NMR (375 MHz, DMSO-d_6)



11c

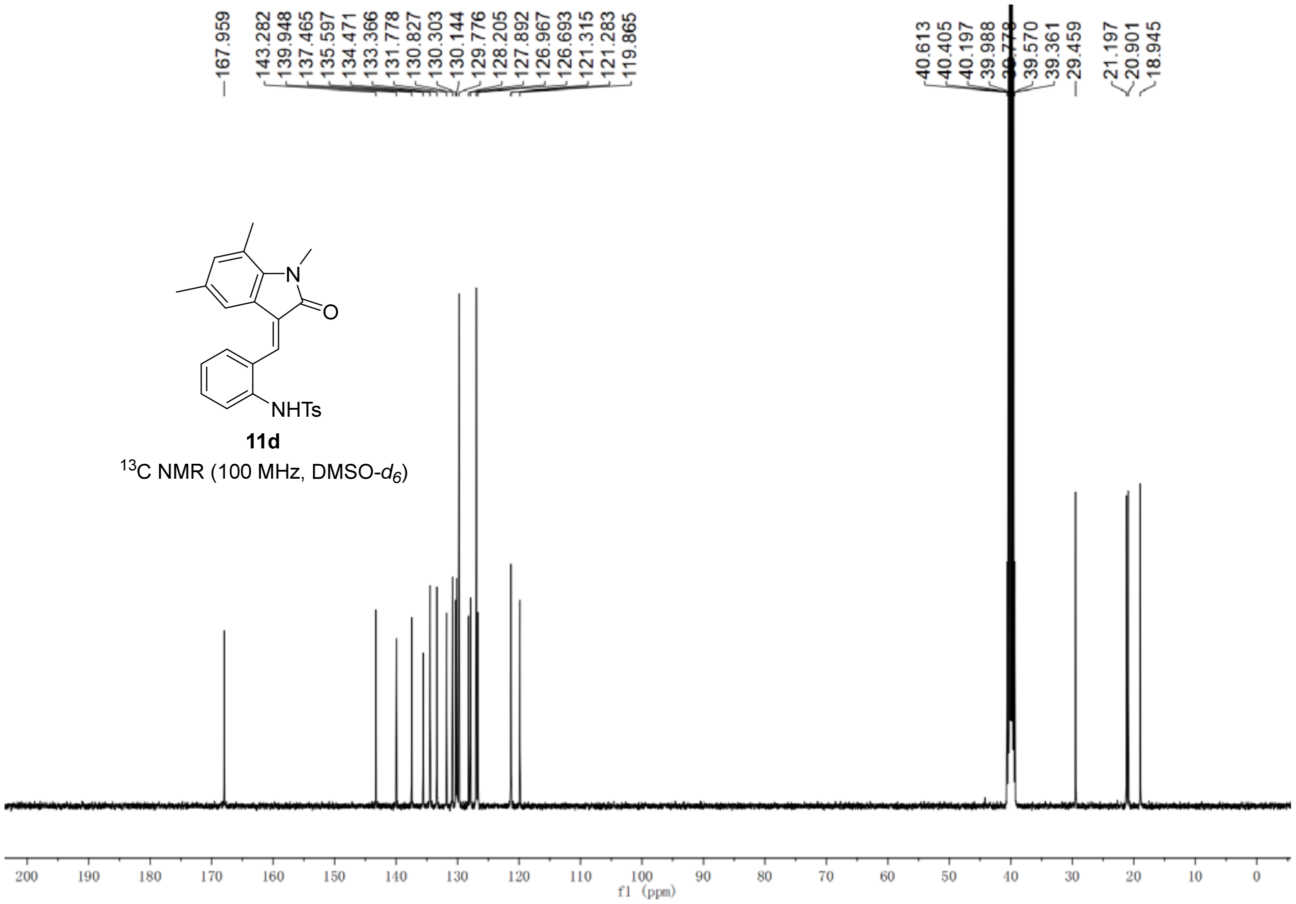
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{23}H_{19}FN_2O_3SNa^+$ 445.0993



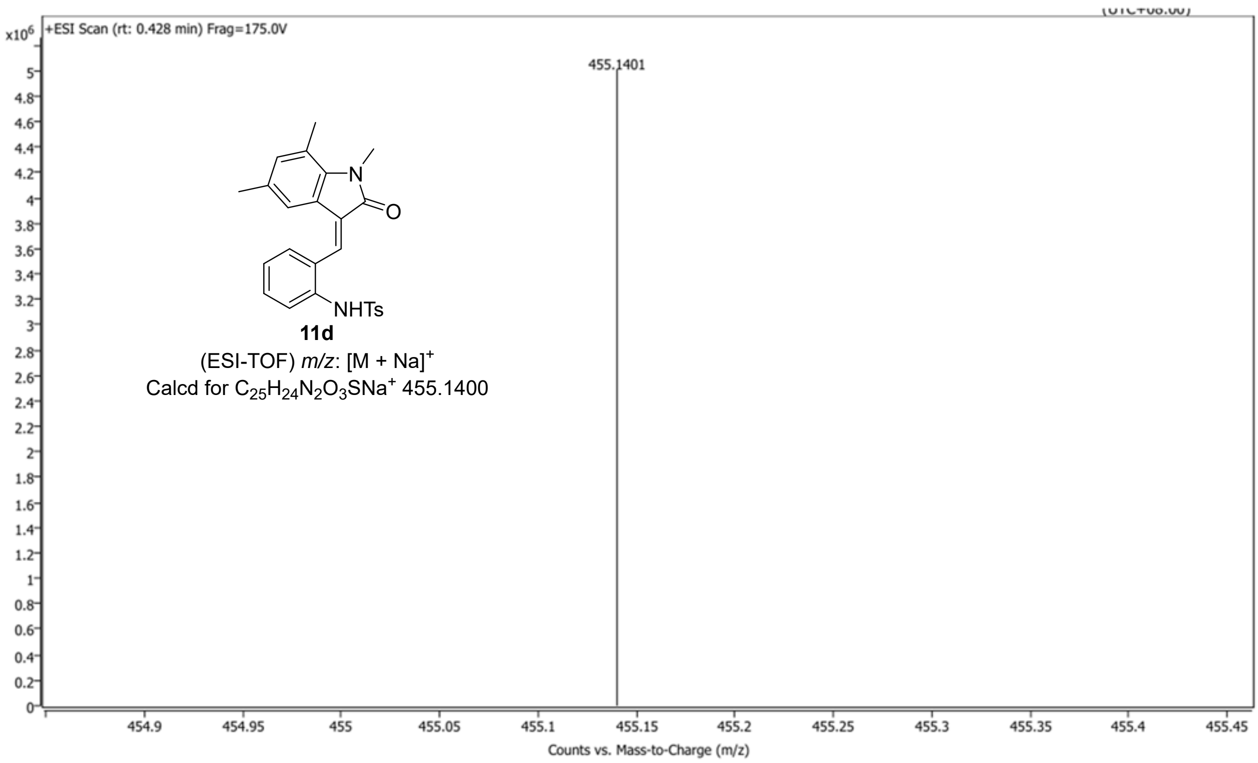
11d

^{1}H NMR (400 MHz, DMSO-d_6)



11d

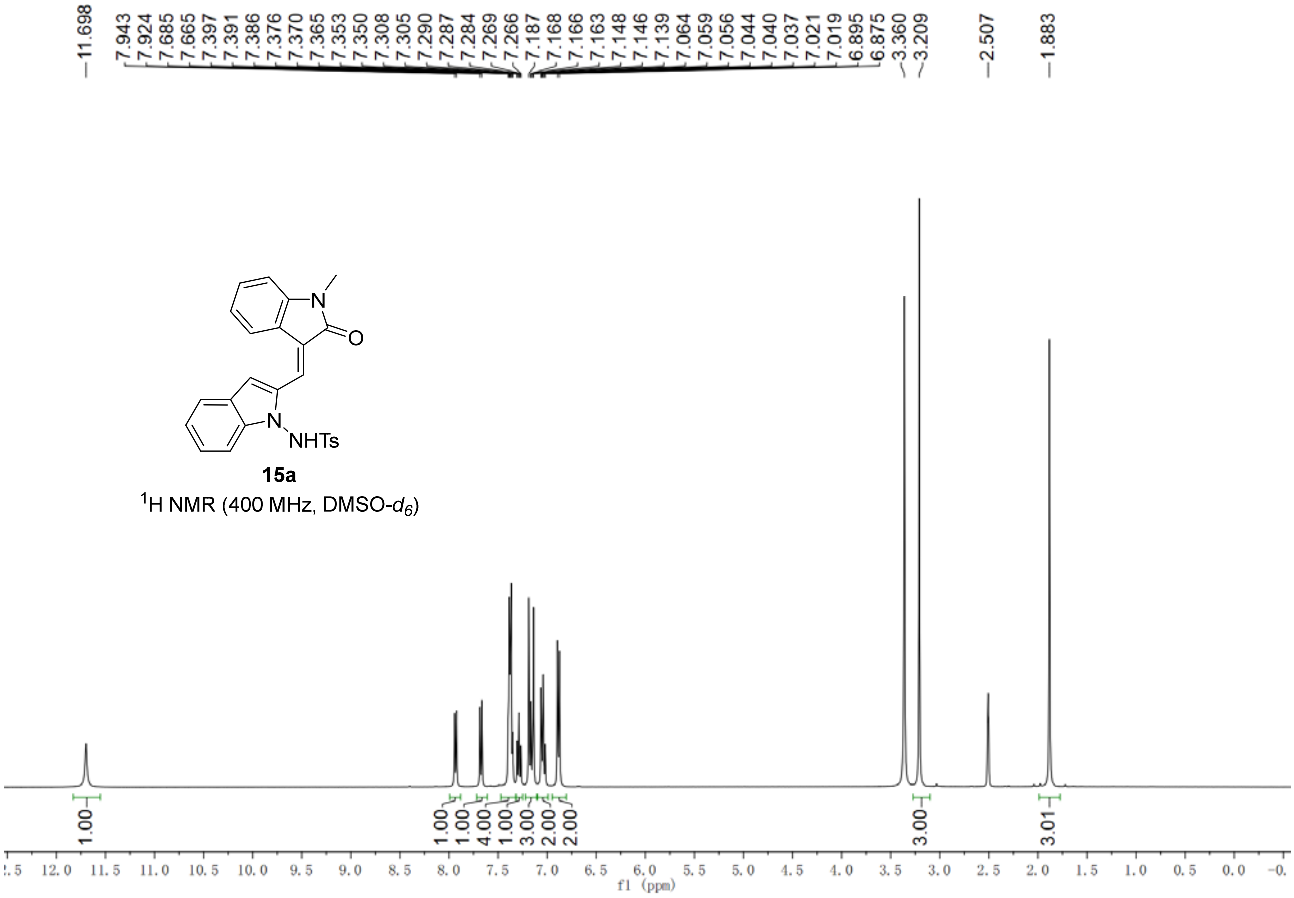
^{13}C NMR (100 MHz, DMSO-d_6)



11d

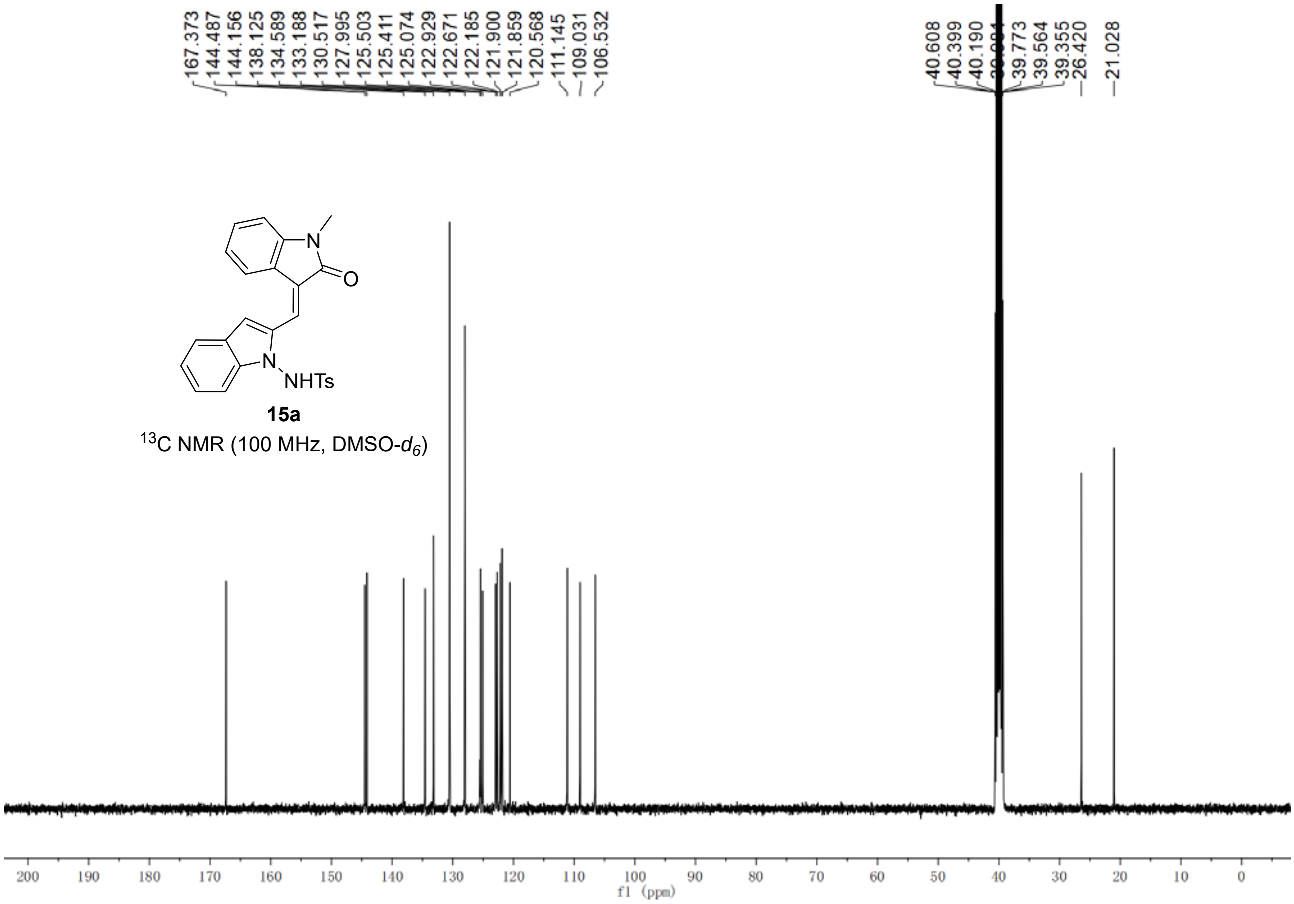
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{25}H_{24}N_2O_3SNa^+$ 455.1400



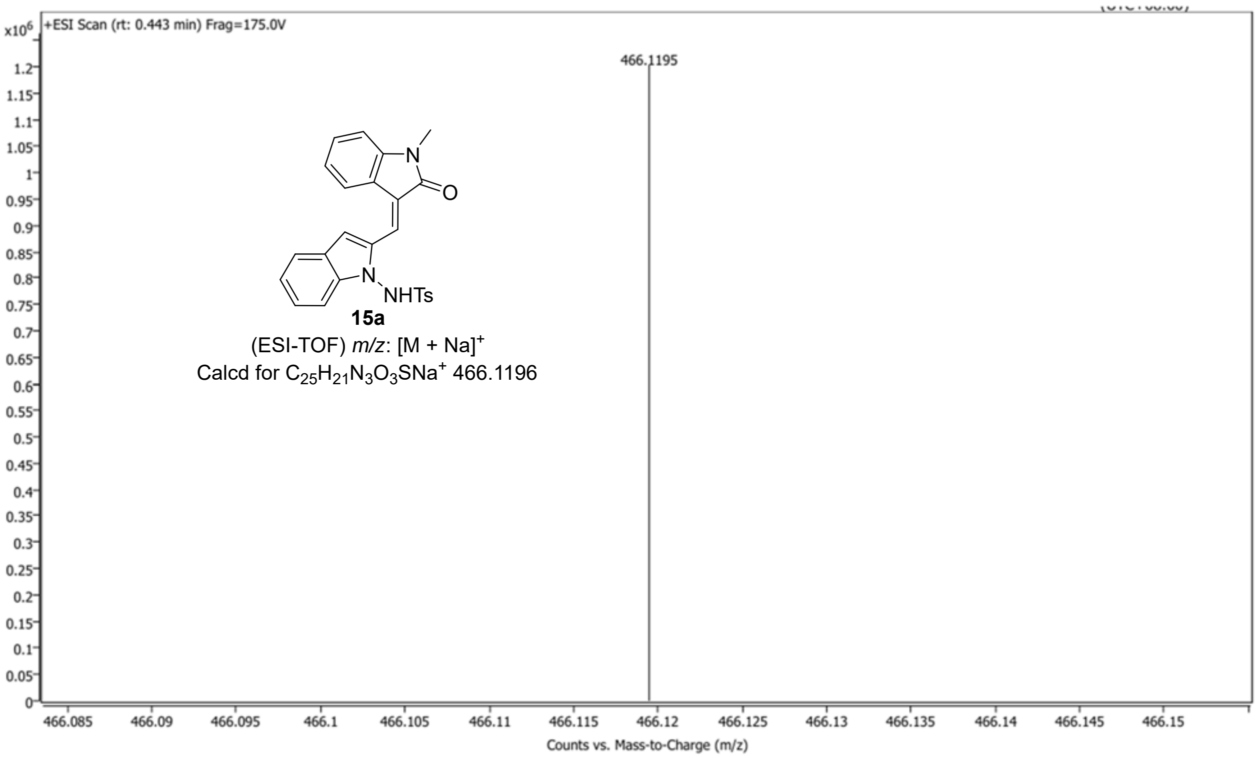
15a

^{1}H NMR (400 MHz, DMSO-d_6)



15a

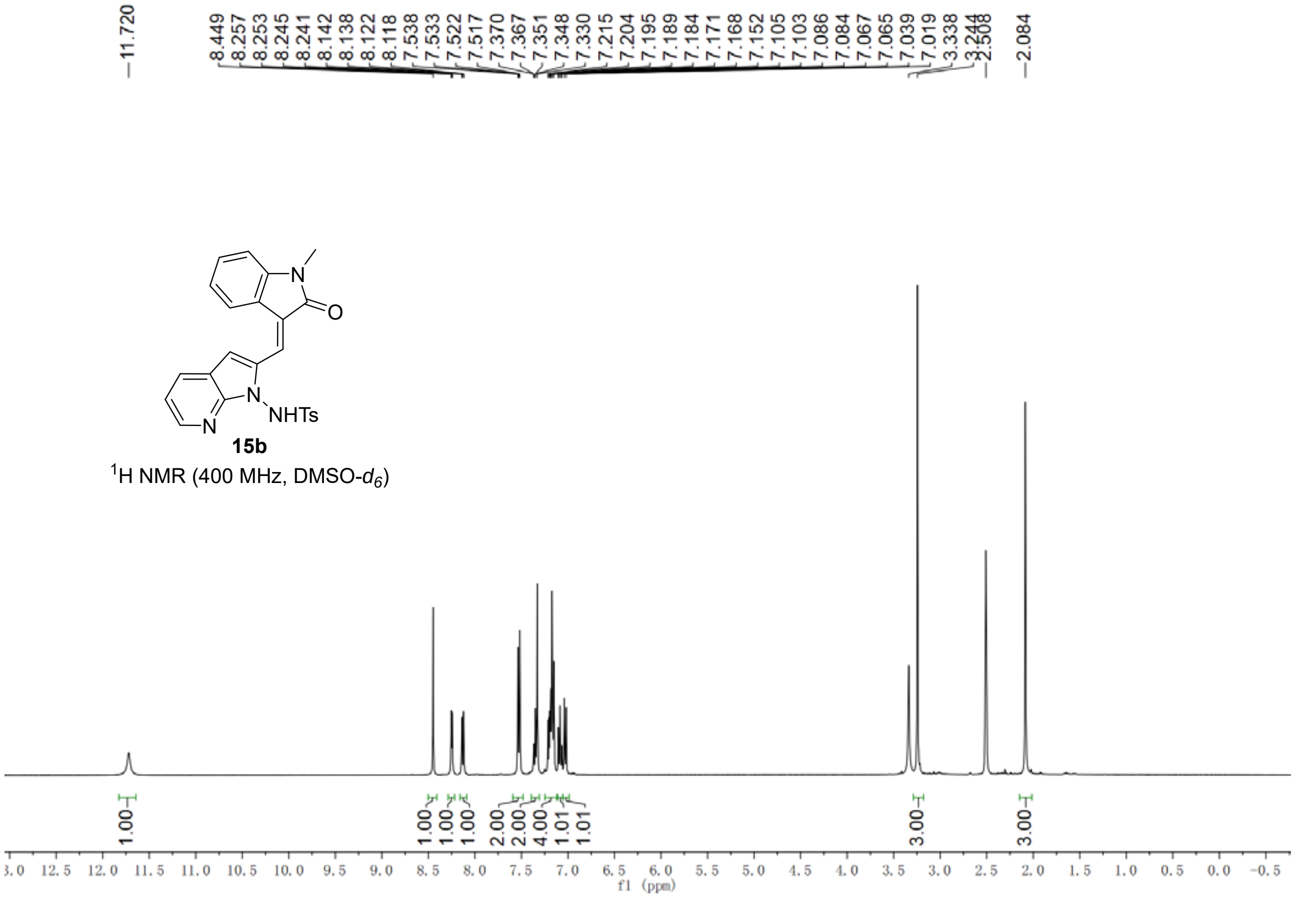
^{13}C NMR (100 MHz, DMSO-d_6)



15a

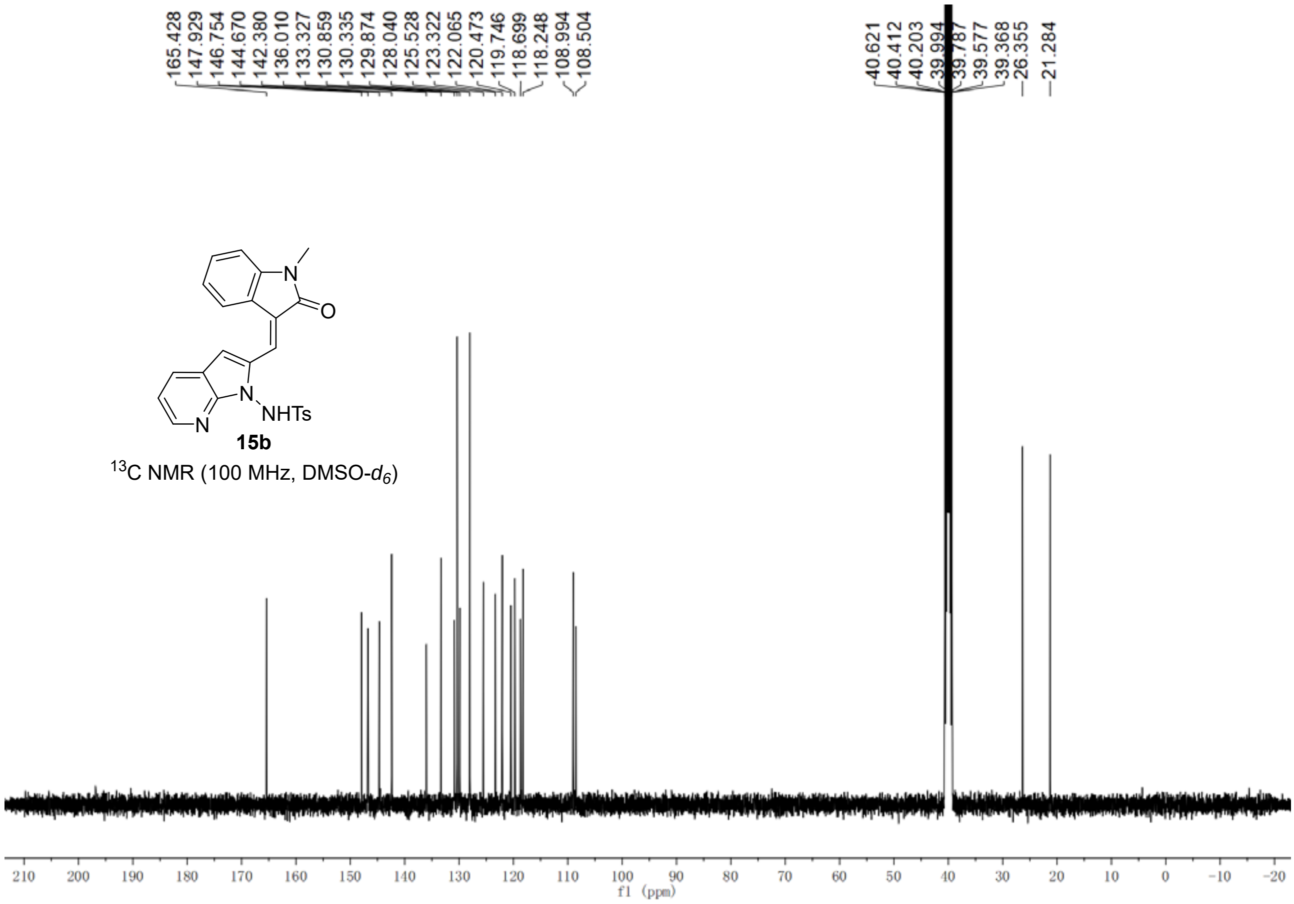
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{25}H_{21}N_3O_3SNa^+$ 466.1196



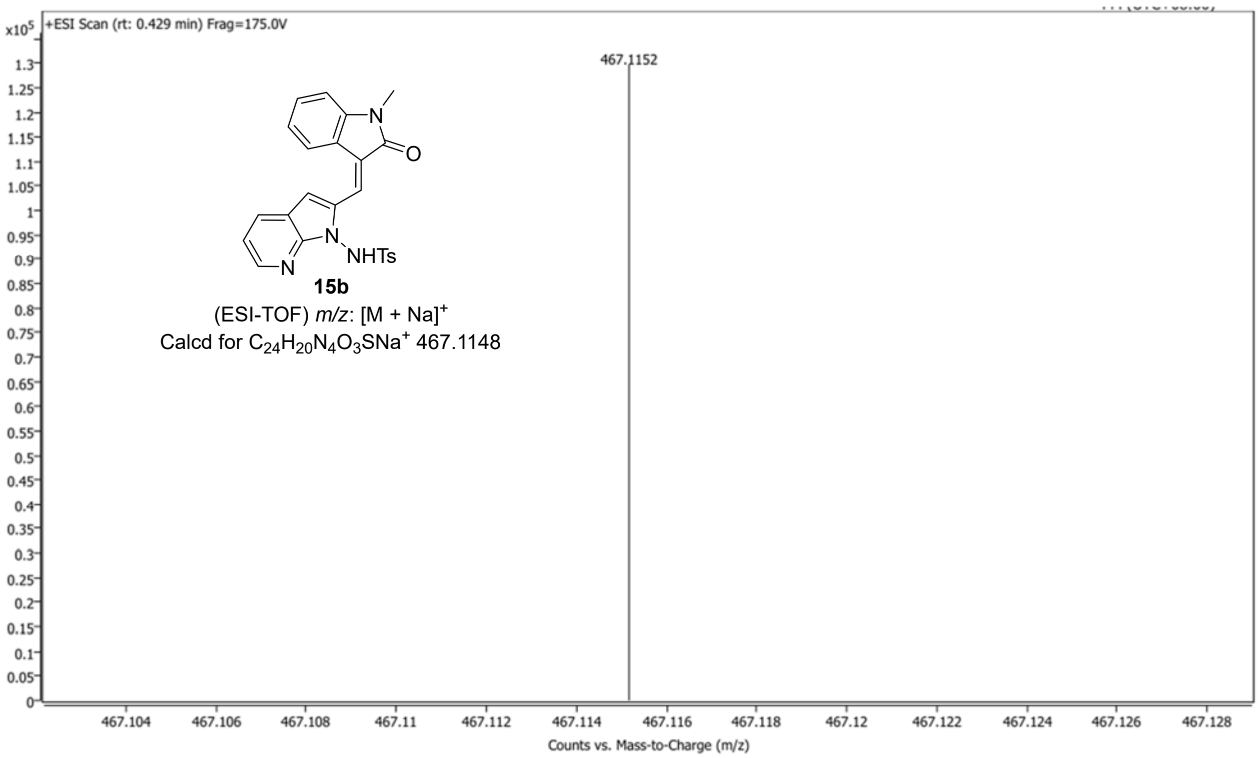
15b

^{1}H NMR (400 MHz, DMSO-d_6)



15b

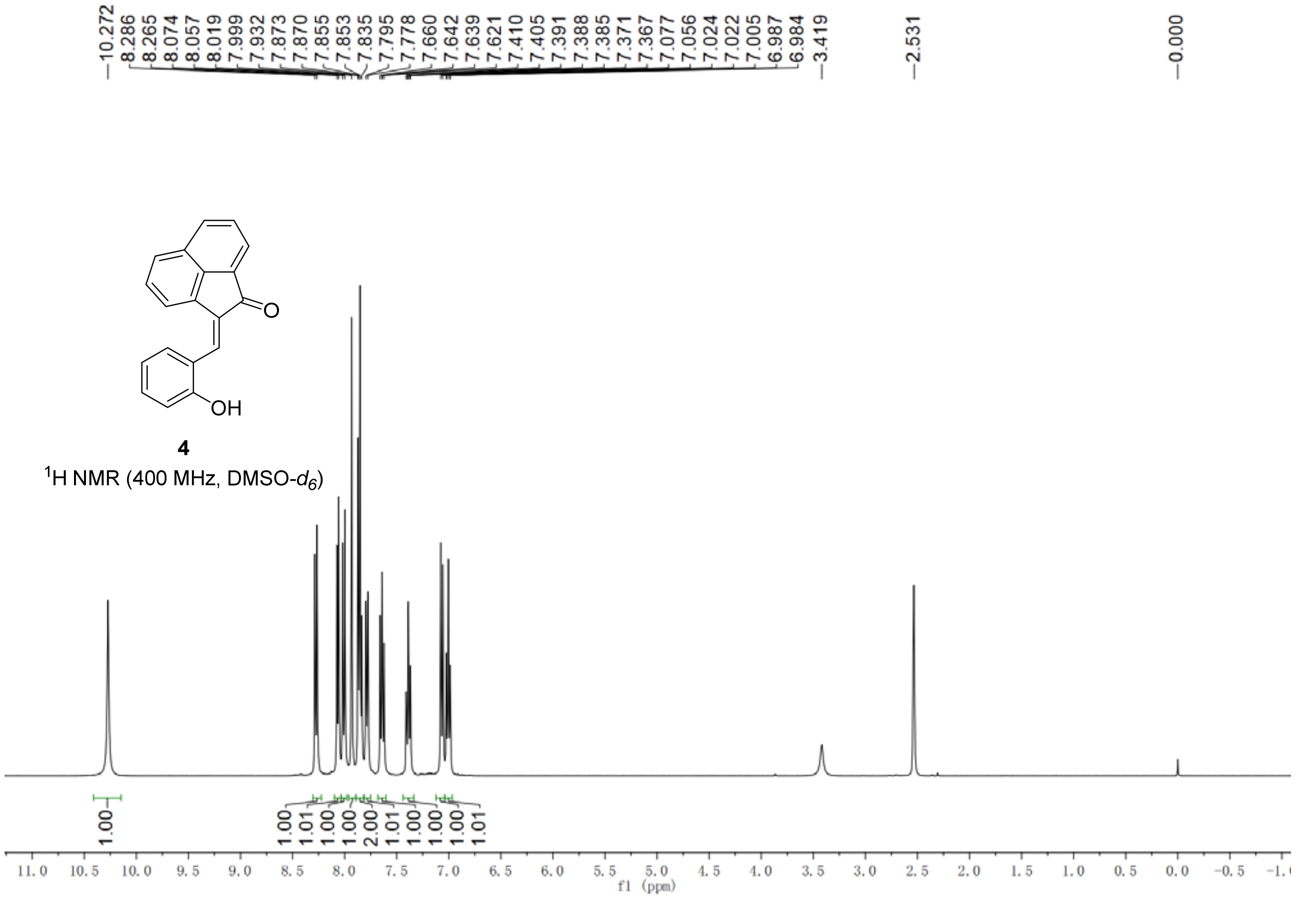
^{13}C NMR (100 MHz, DMSO-d_6)



15b

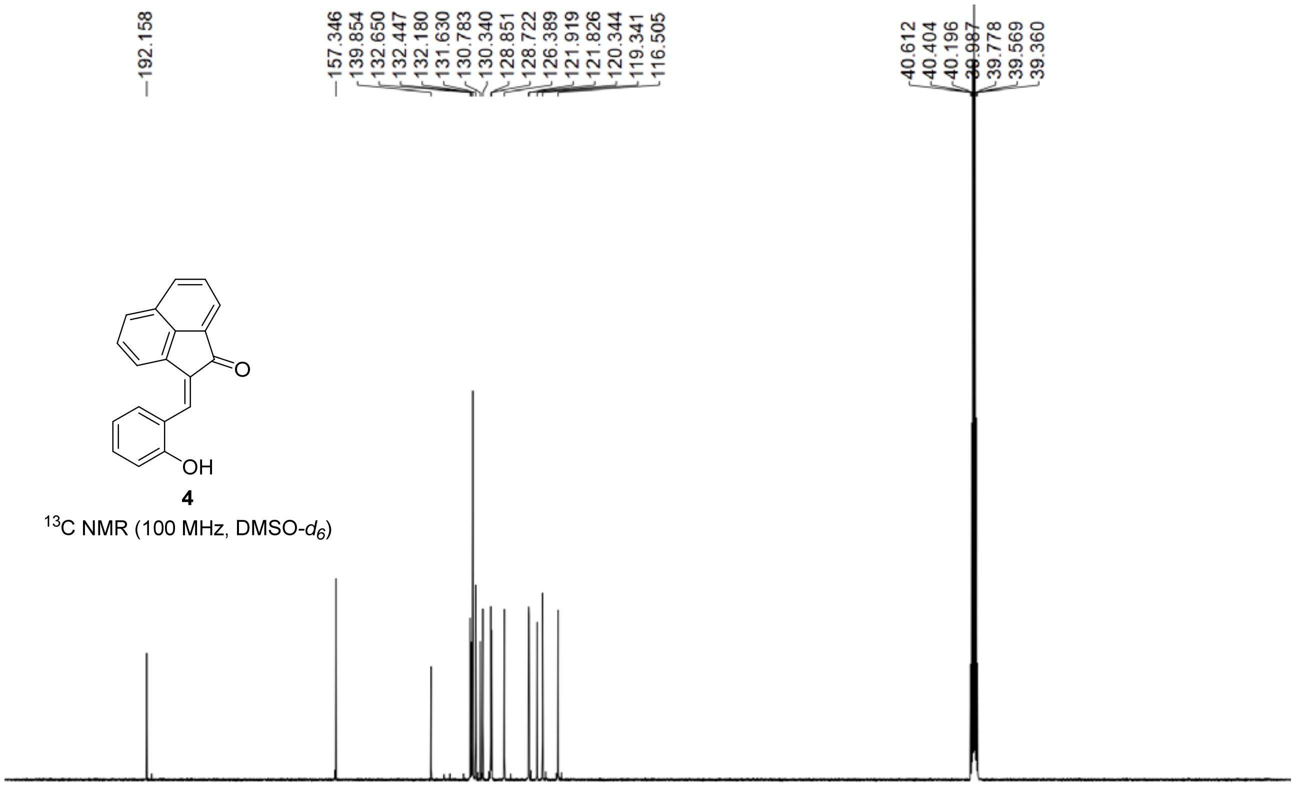
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{24}H_{20}N_4O_3SNa^+$ 467.1148



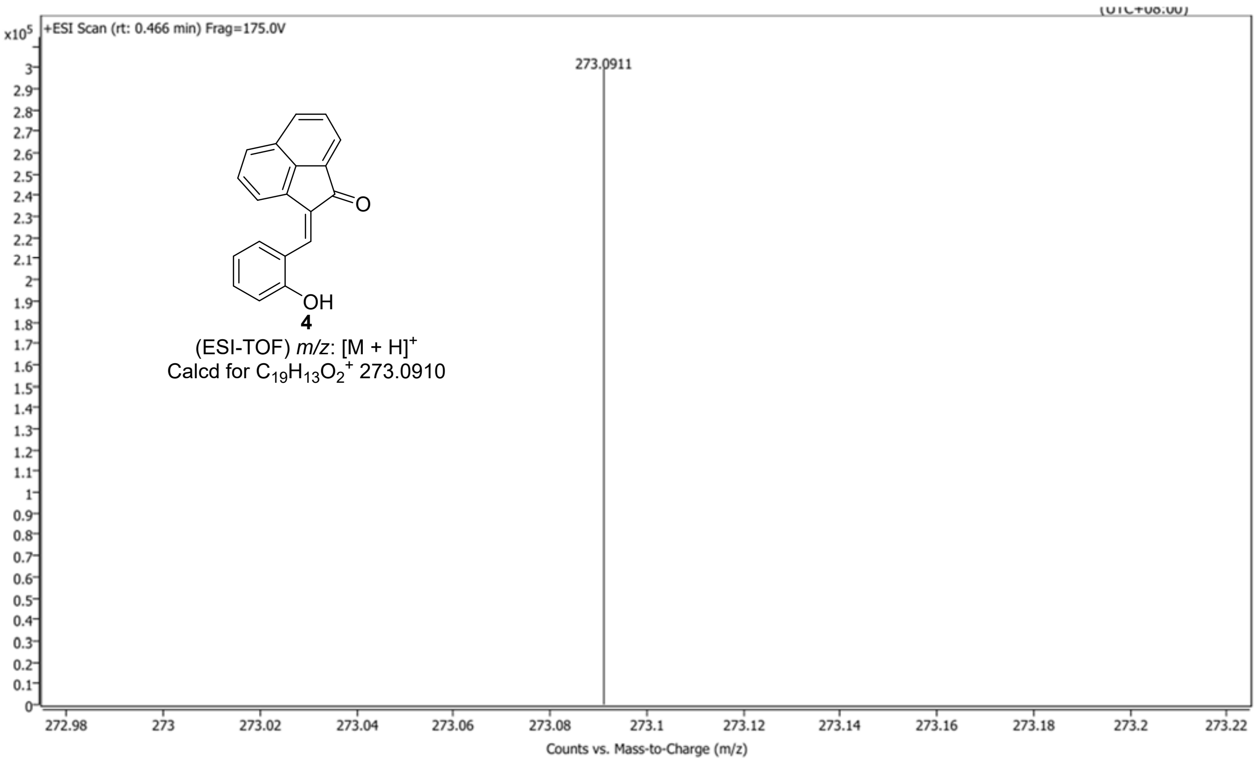
4

^{1}H NMR (400 MHz, DMSO-d_6)



4

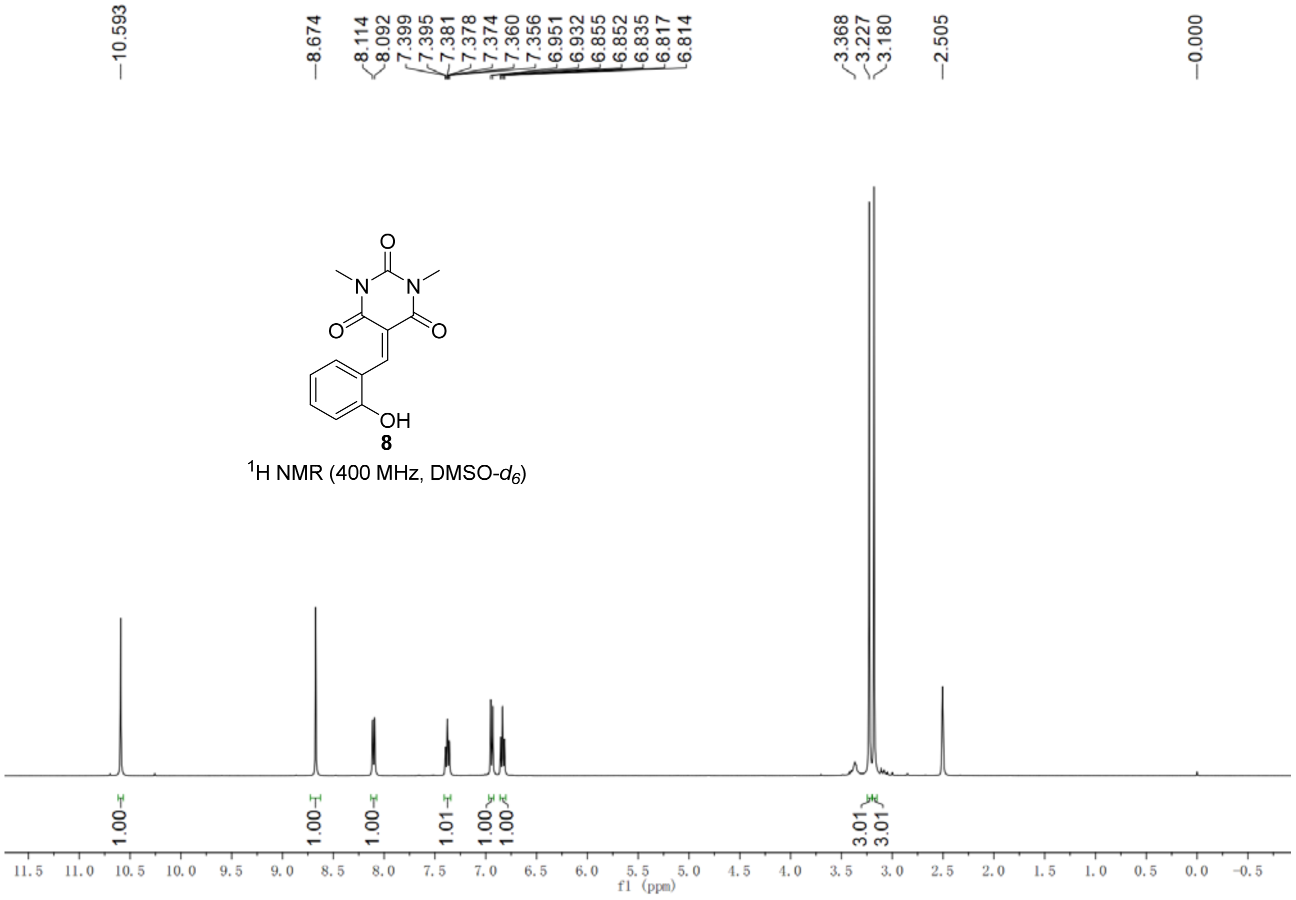
^{13}C NMR (100 MHz, DMSO-d_6)



4

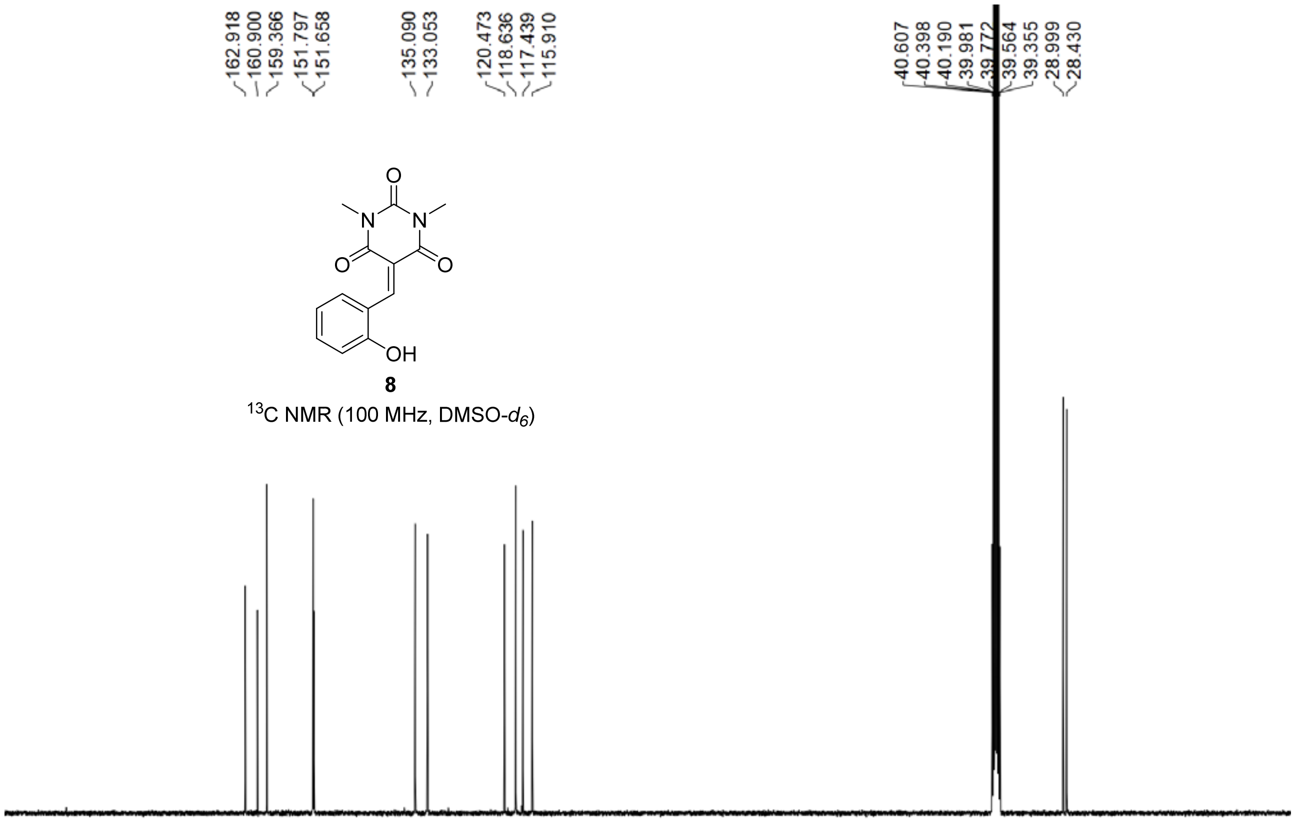
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{19}H_{13}O_2^+$ 273.0910



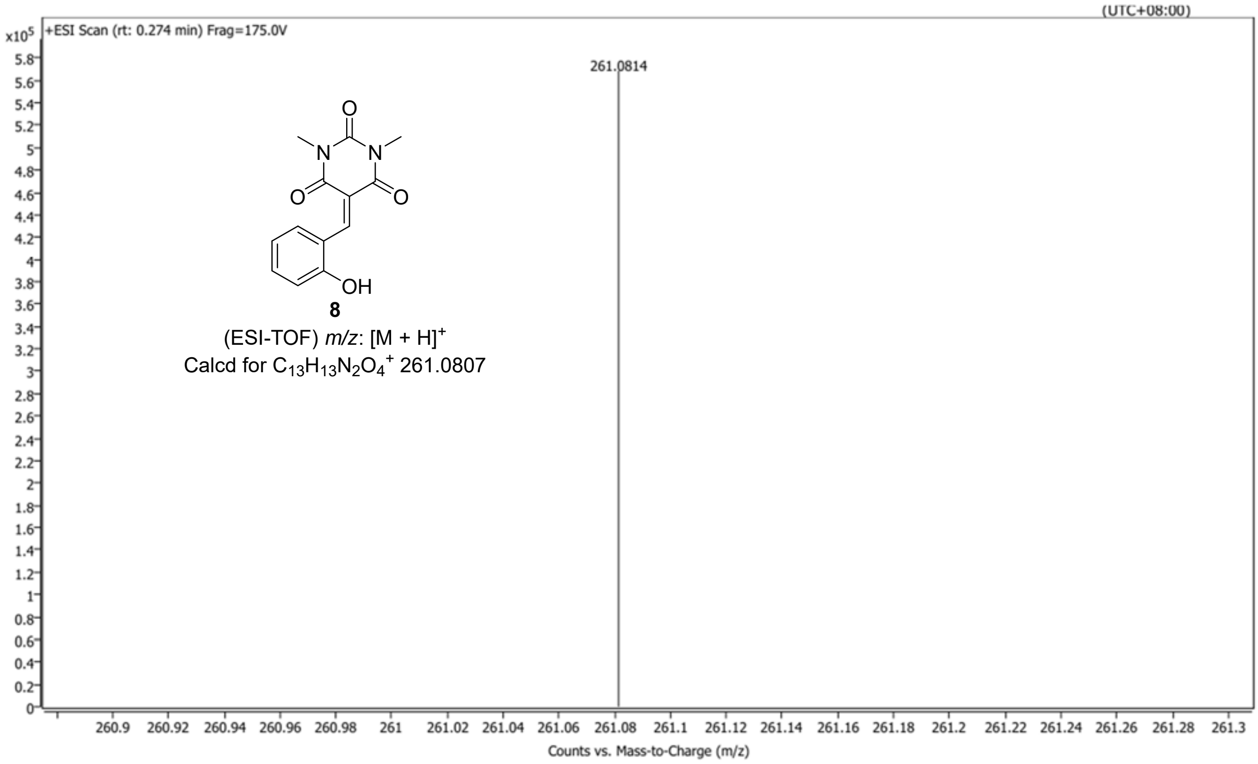
8

^{1}H NMR (400 MHz, DMSO-d_6)



8

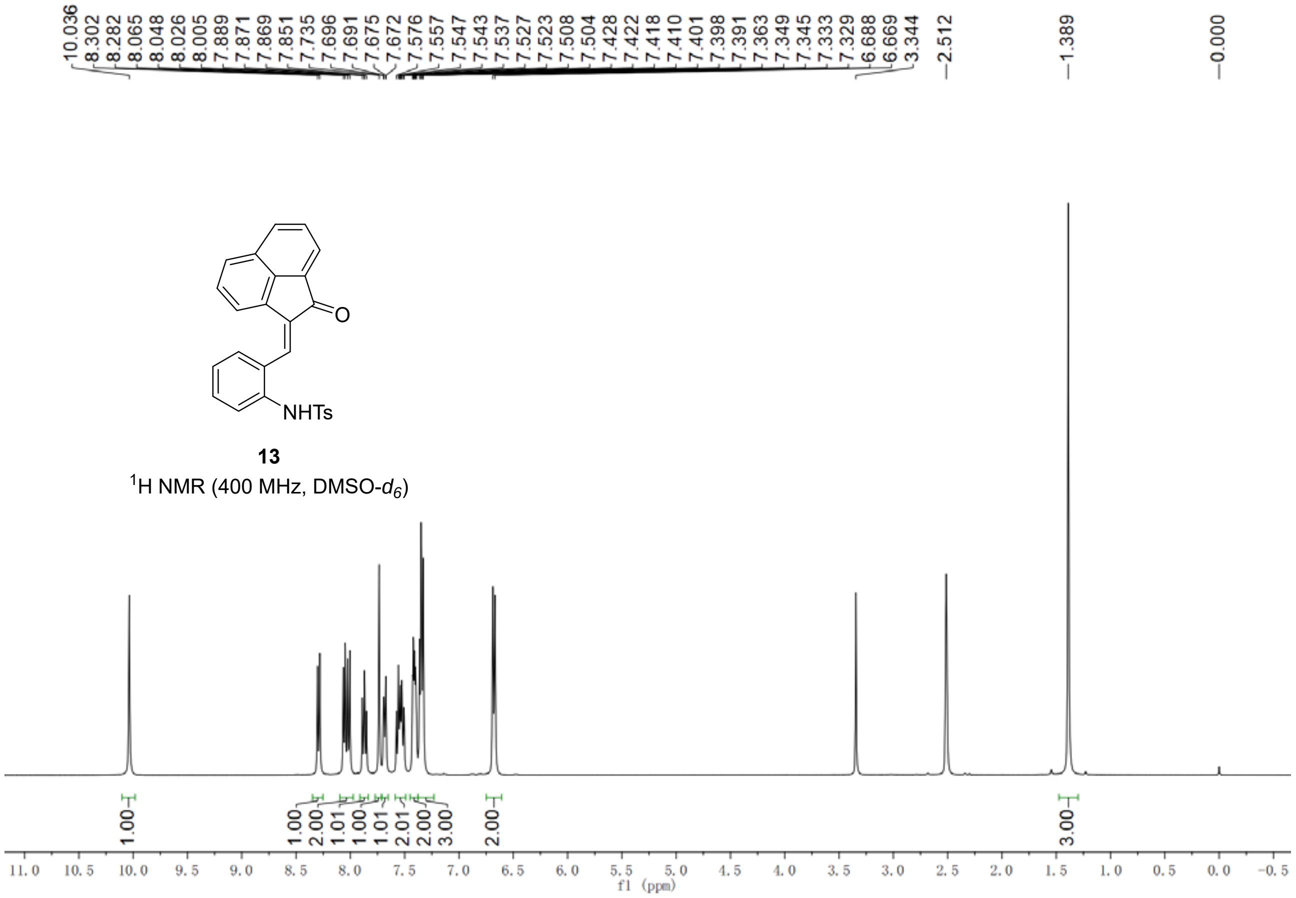
^{13}C NMR (100 MHz, DMSO-d_6)



8

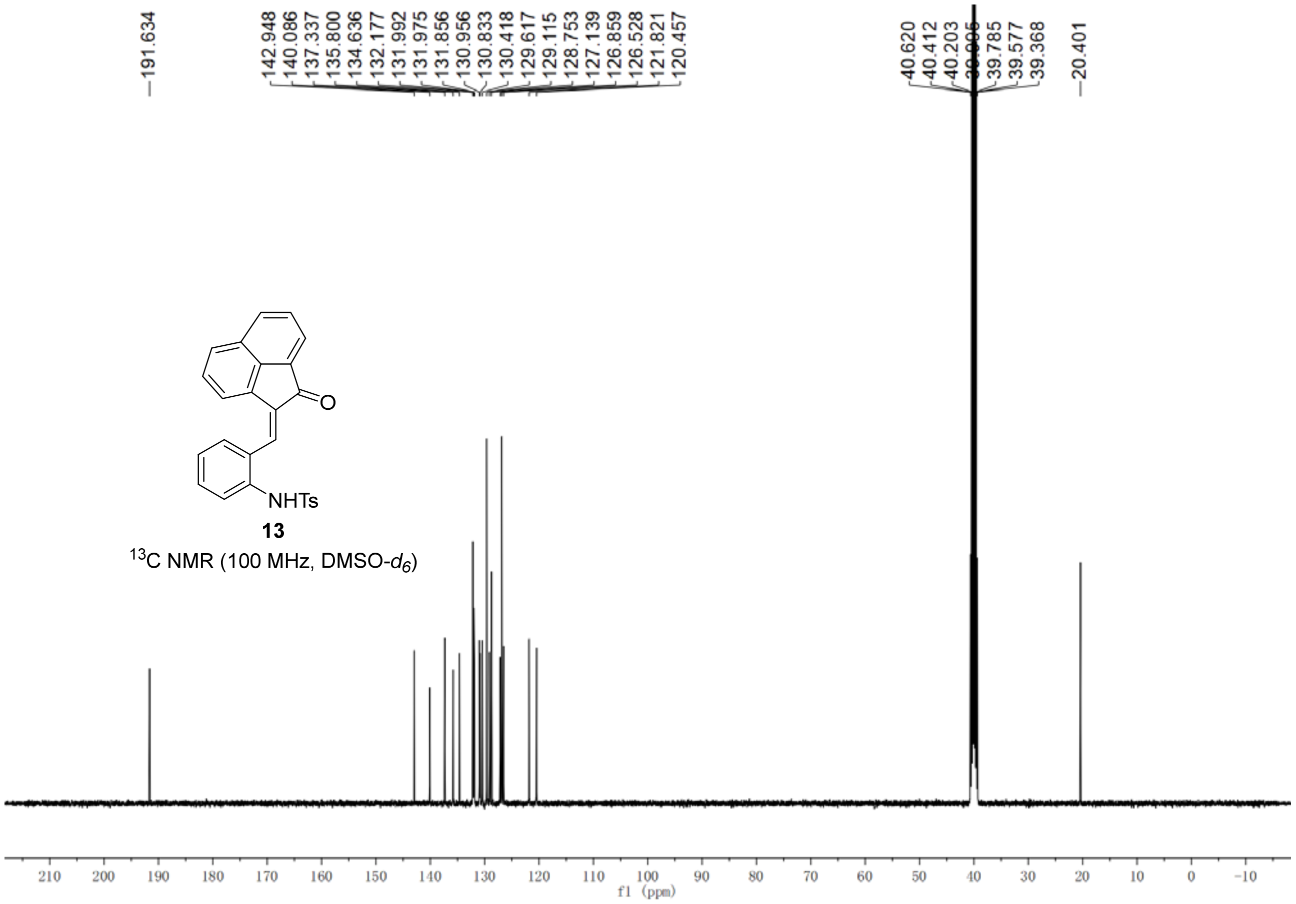
(ESI-TOF) *m/z*: [M + H]$^+$

Calcd for $C_{13}H_{13}N_2O_4^+$ 261.0807



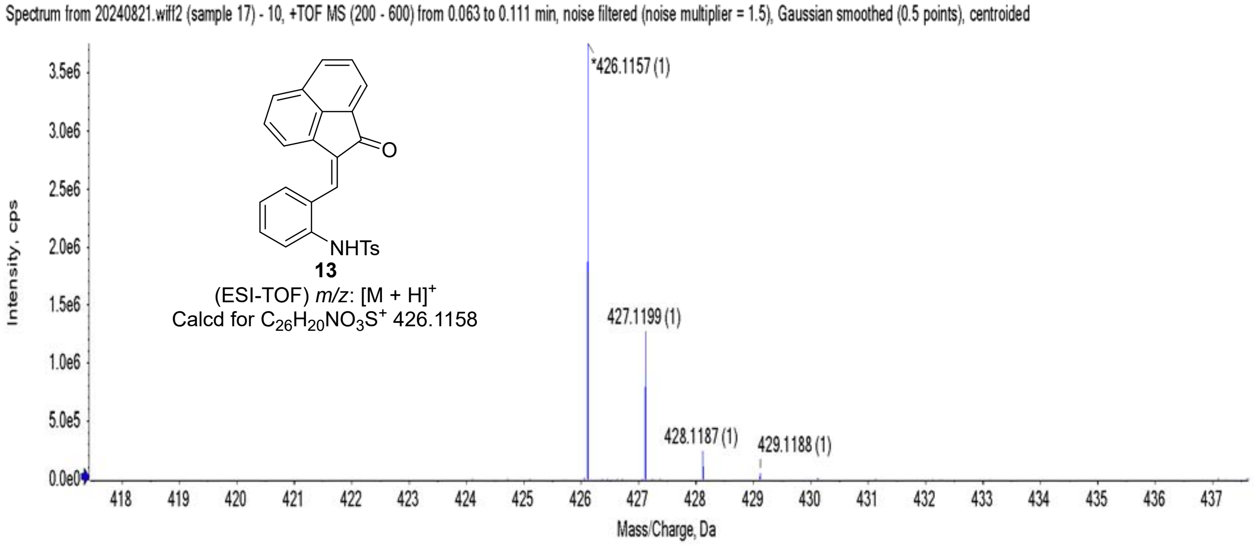
13

^{1}H NMR (400 MHz, DMSO-d_6)



13

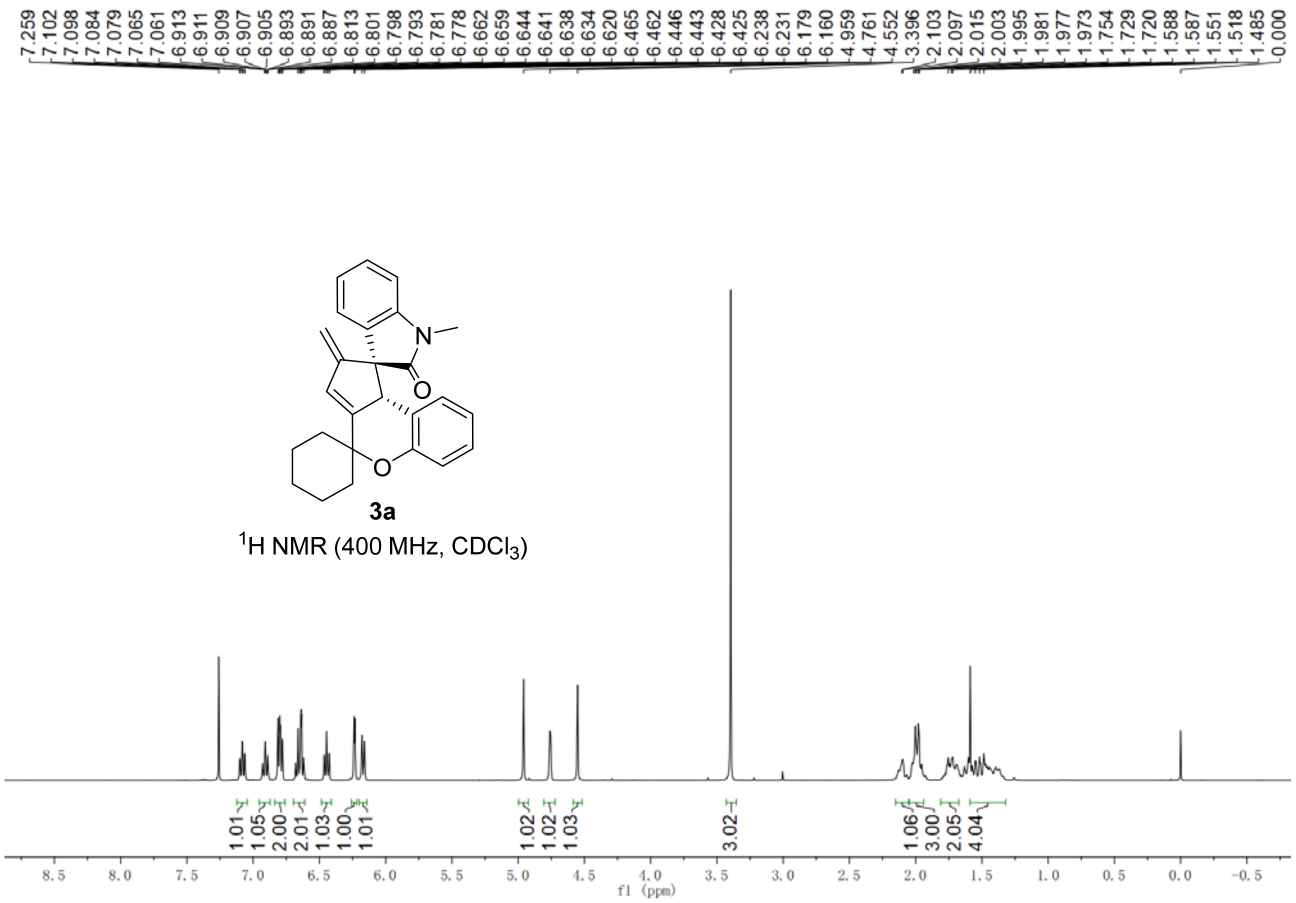
^{13}C NMR (100 MHz, DMSO-d_6)


Spectrum from 20240821.wiff2 (sample 17) - 10, +TOF MS (200 - 600) from 0.063 to 0.111 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points), centroided

13

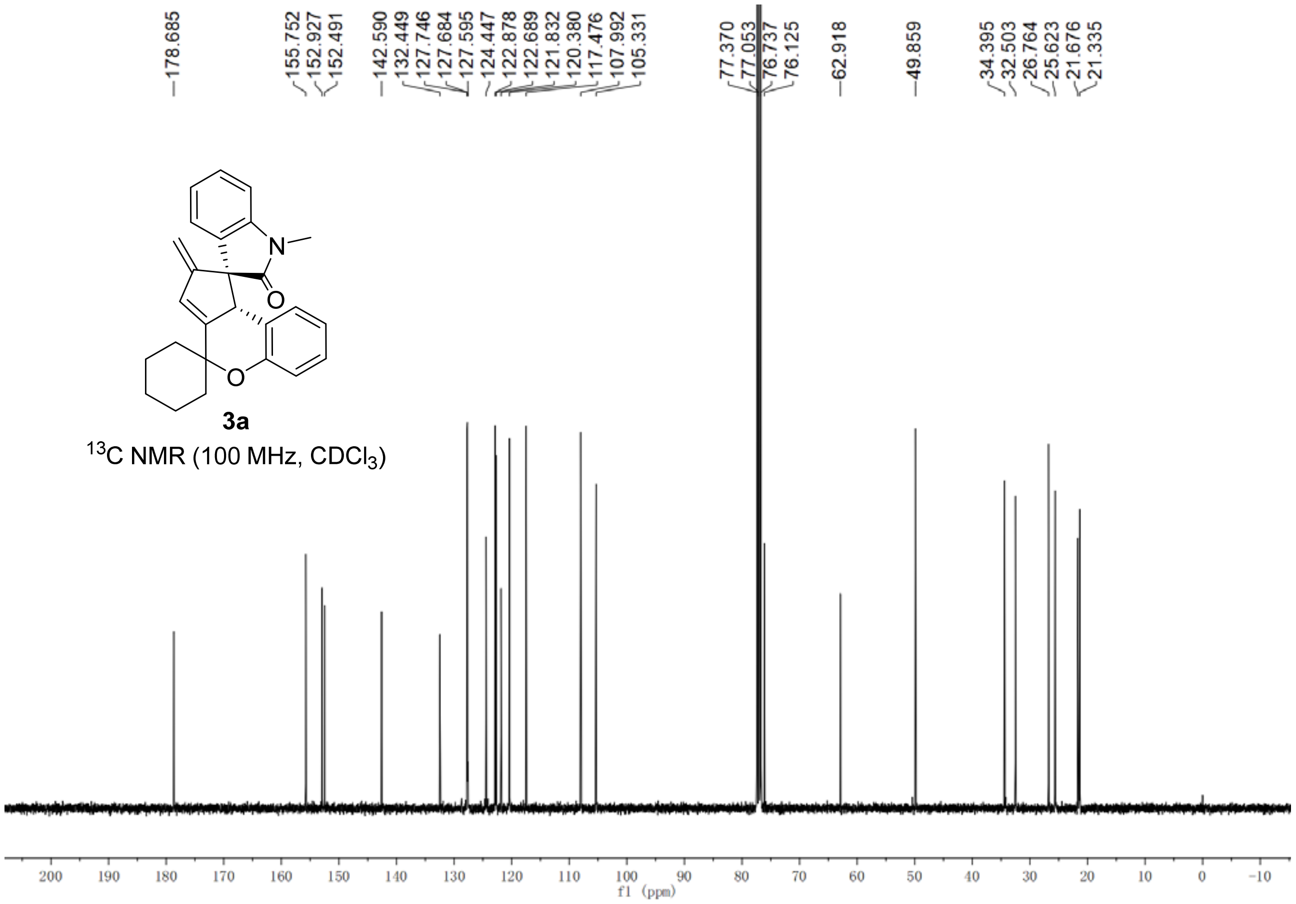
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{26}H_{20}NO_3S^+$ 426.1158



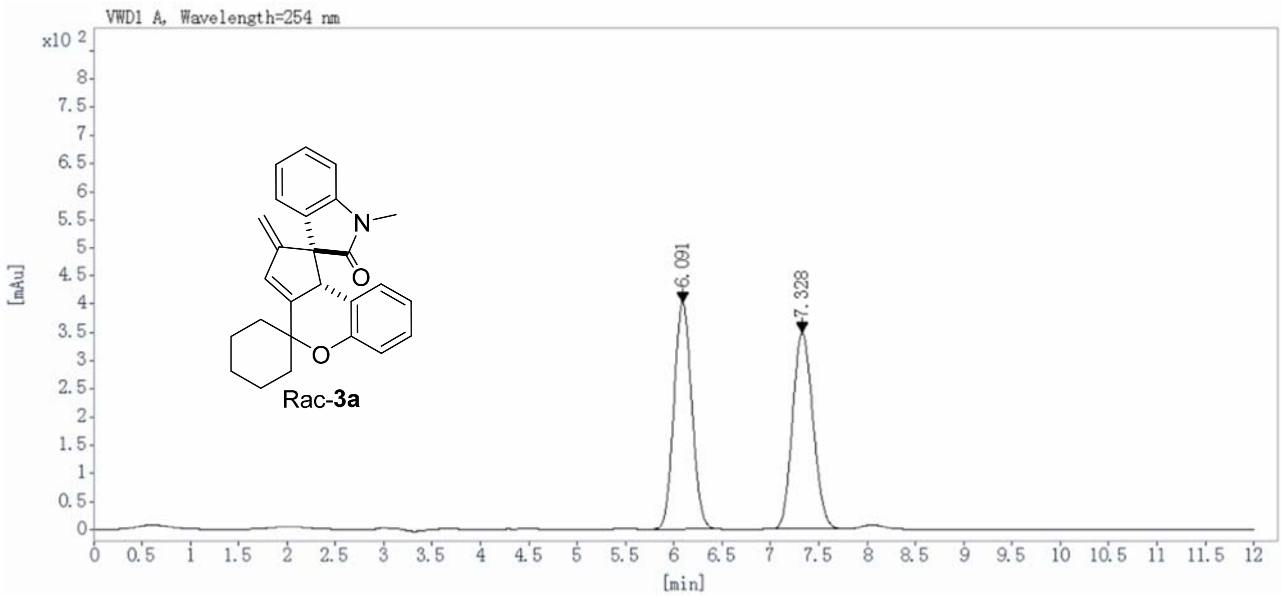
3a

^{1}H NMR (400 MHz, $CDCl_3$)

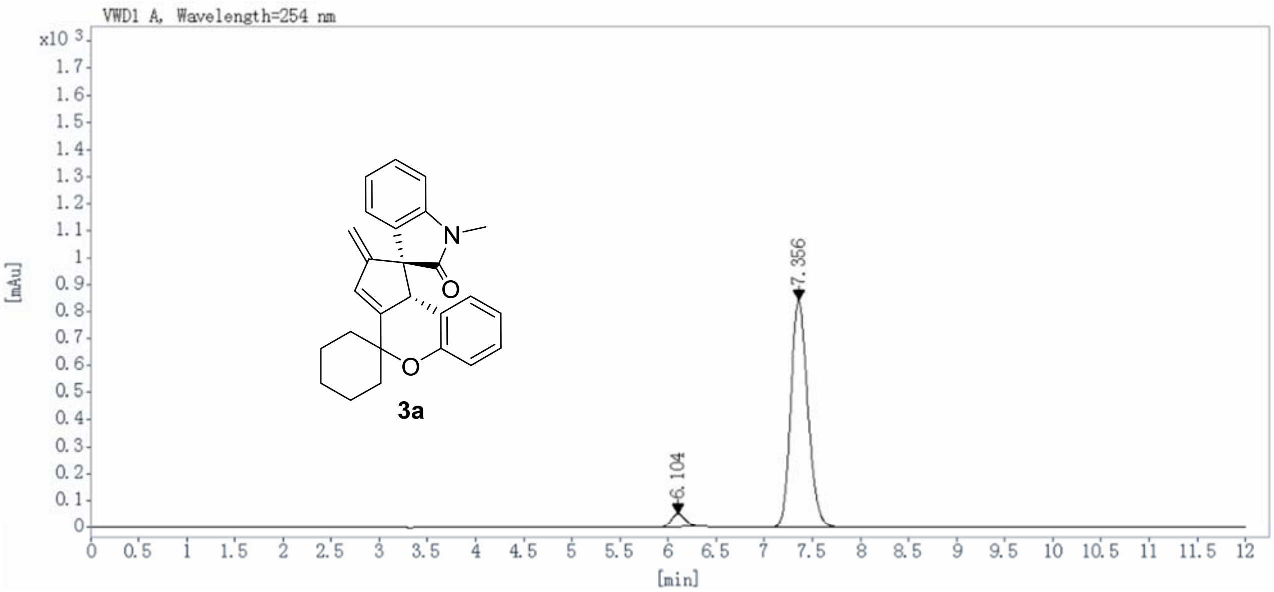


3a

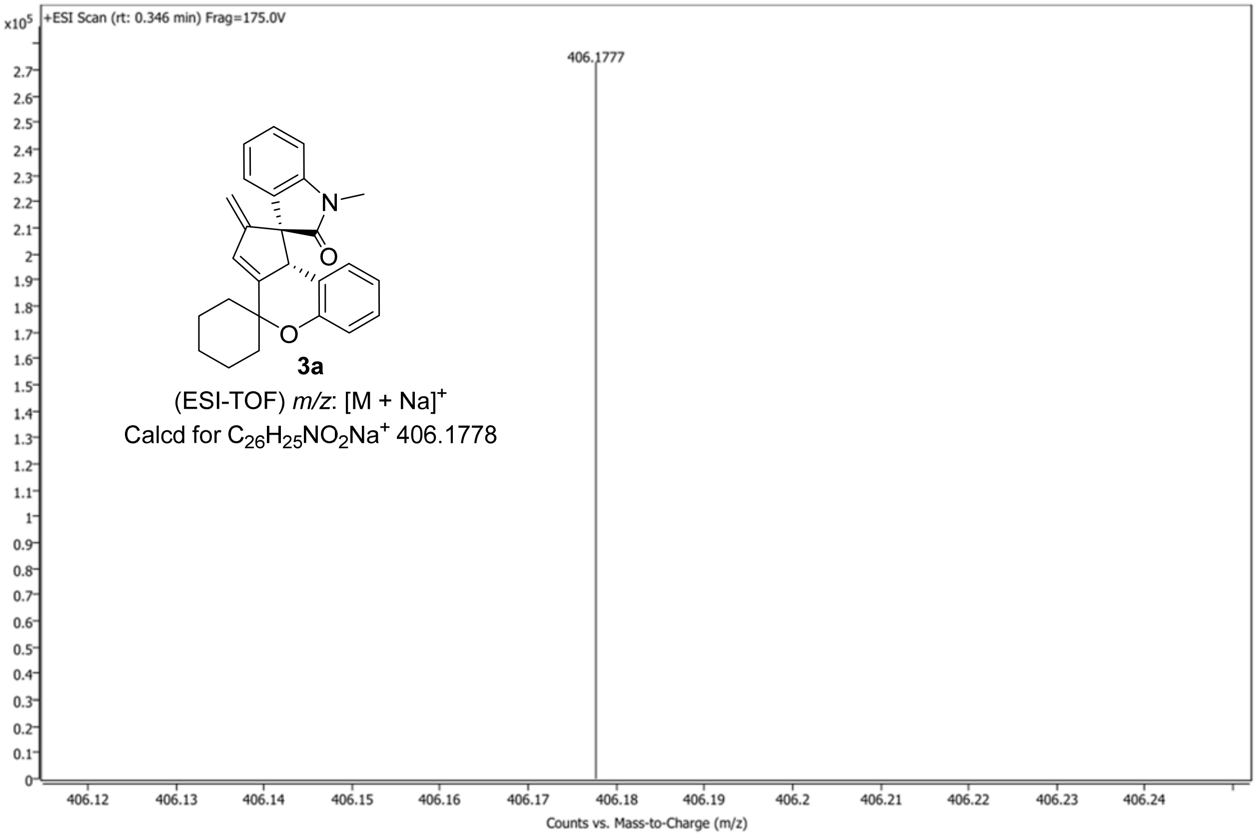
^{13}C NMR (100 MHz, $CDCl_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.091	BBA	0.20	402.5508	5172.2280	50.0206
7.328	BBA	0.23	347.8087	5167.9780	49.9794
			Totals:	10340.2061	100.0000



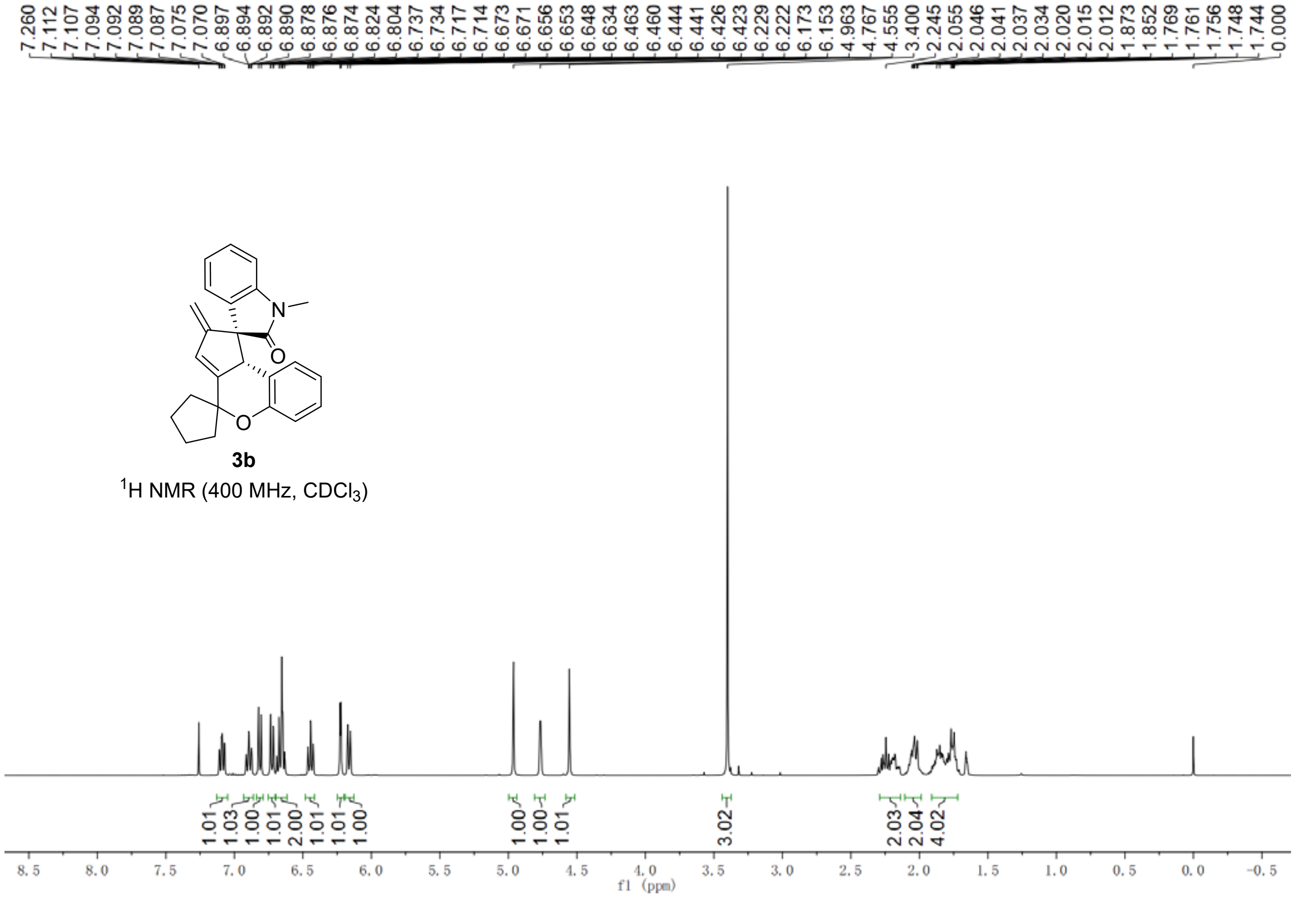
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.104	BBA	0.15	49.1703	488.3062	4.5169
7.356	BBA	0.19	841.7538	10322.3574	95.4831
			Totals:	10810.6636	100.0000



3a

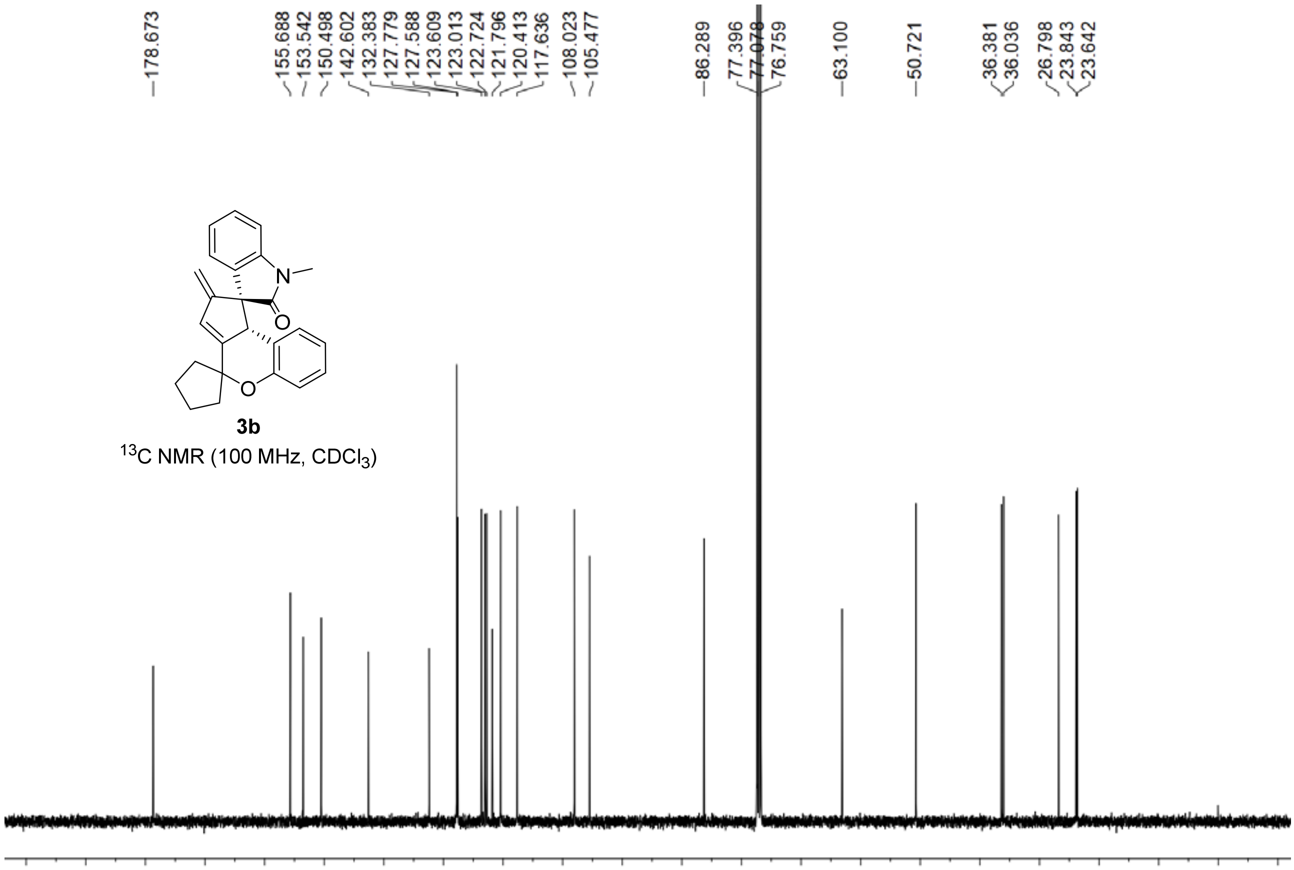
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{26}H_{25}NO_2Na^+$ 406.1778



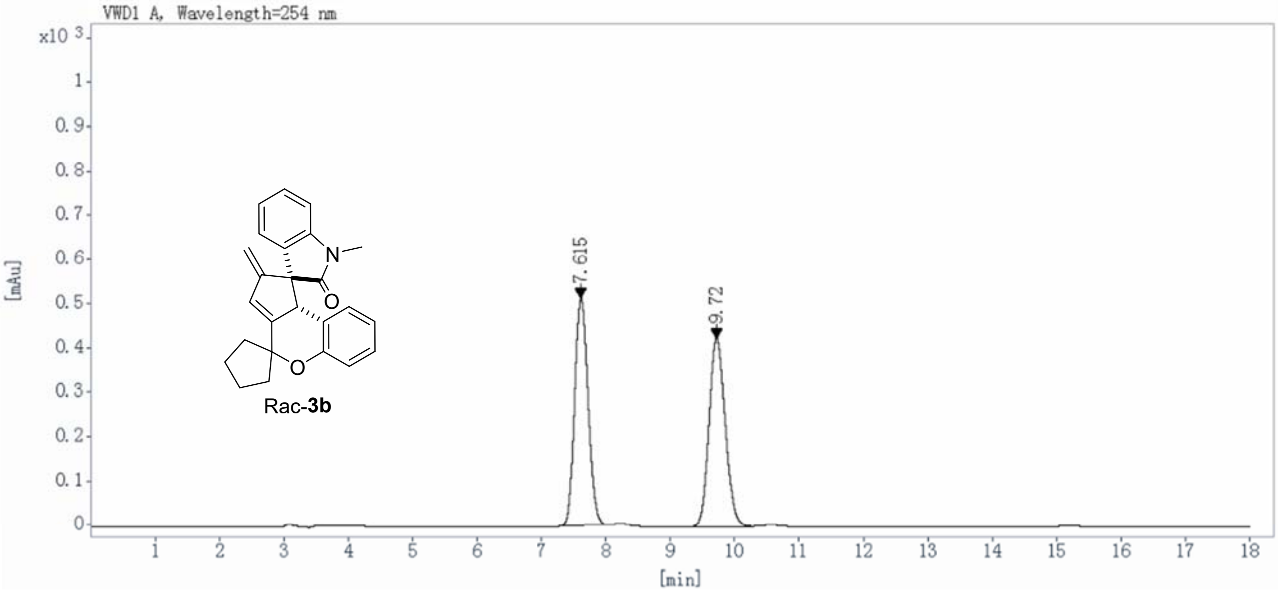
3b

^{1}H NMR (400 MHz, CDCl$_3$)

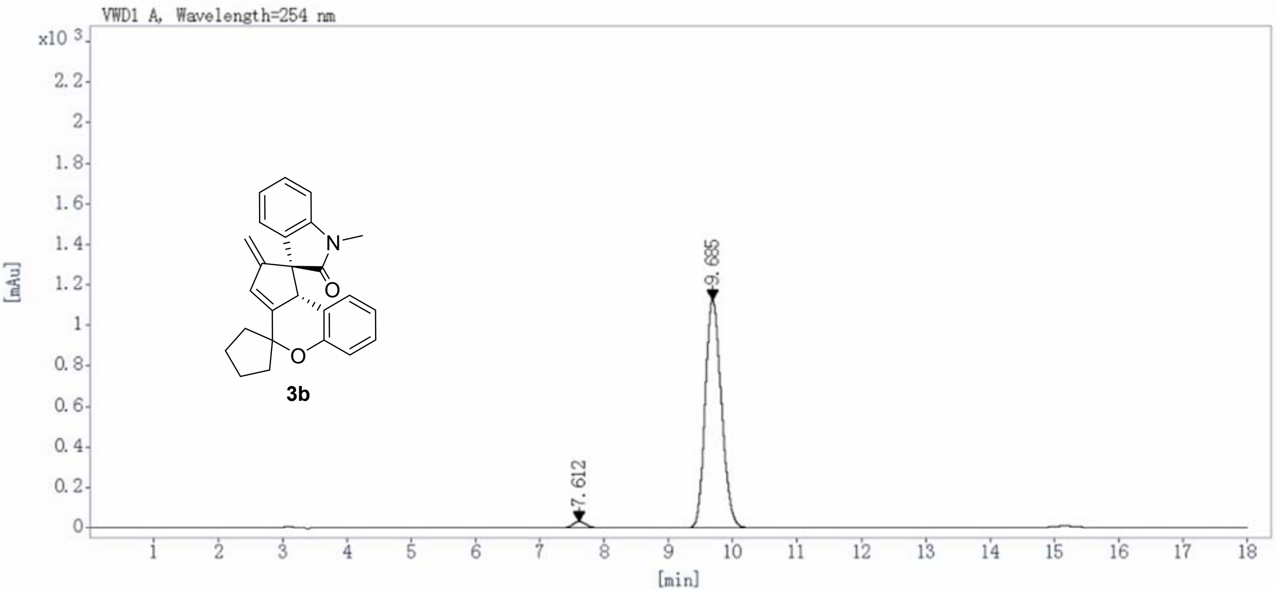


3b

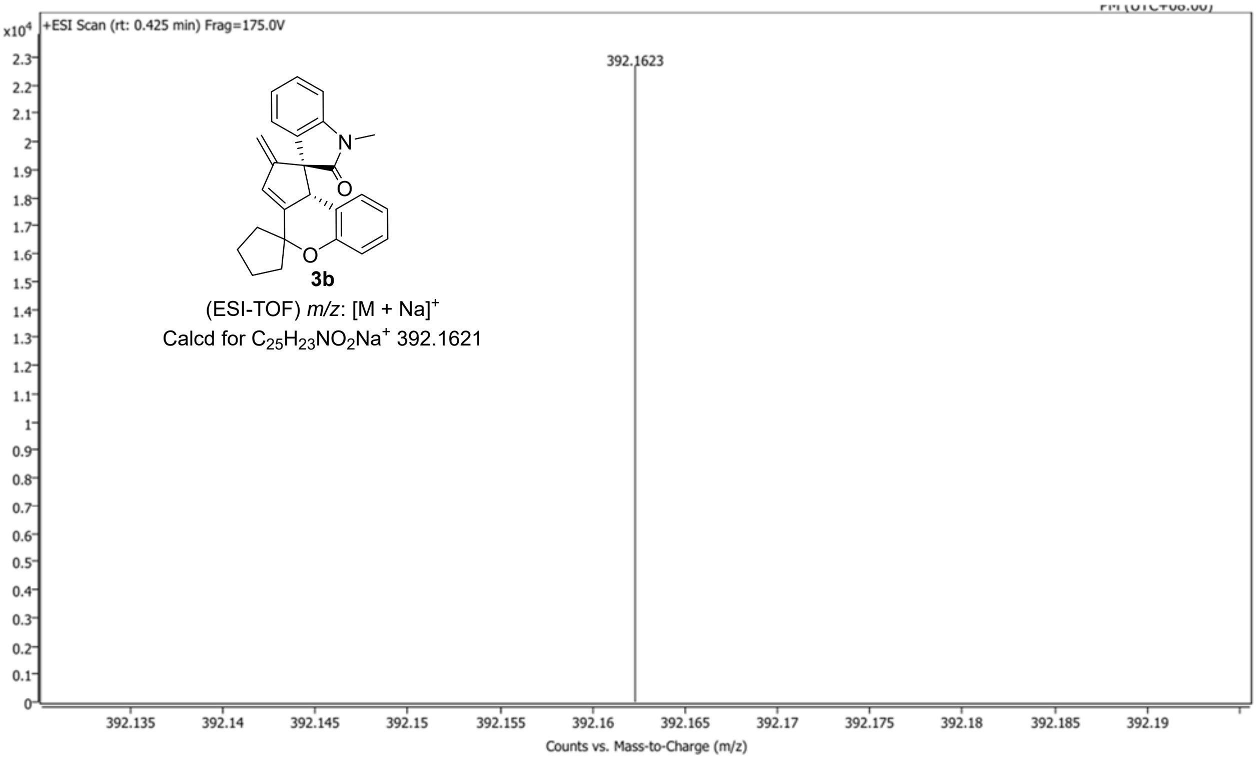
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
7.615	BB	0.23	513.2851	7421.3164	50.0775
9.720	BB	0.27	423.6620	7398.3569	49.9225
			Totals:	14819.6733	100.0000



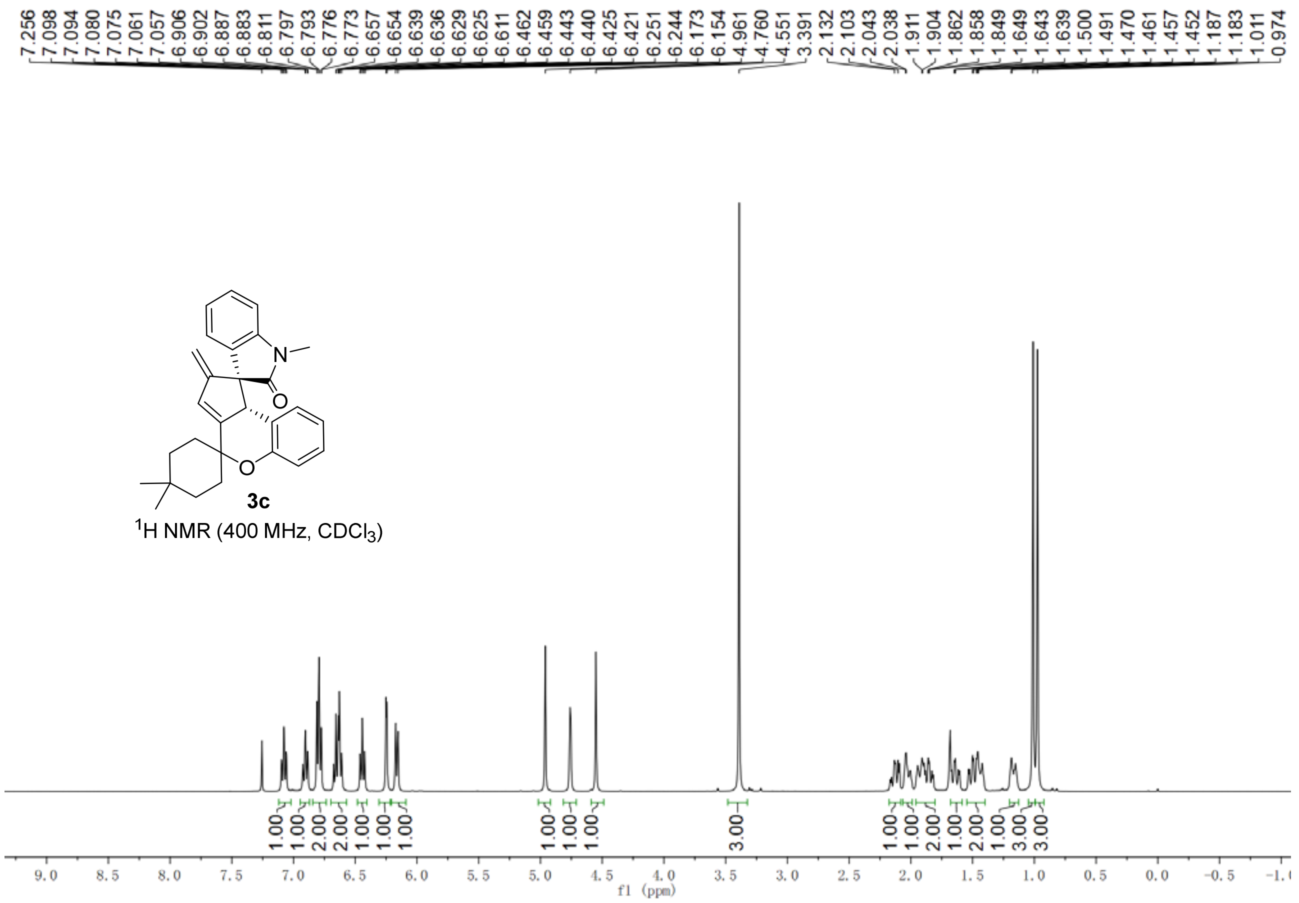
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
7.612	BBA	0.22	32.6851	465.2503	2.3032
9.685	BB	0.27	1125.0988	19734.8965	97.6968
			Totals:	20200.1468	100.0000



3b

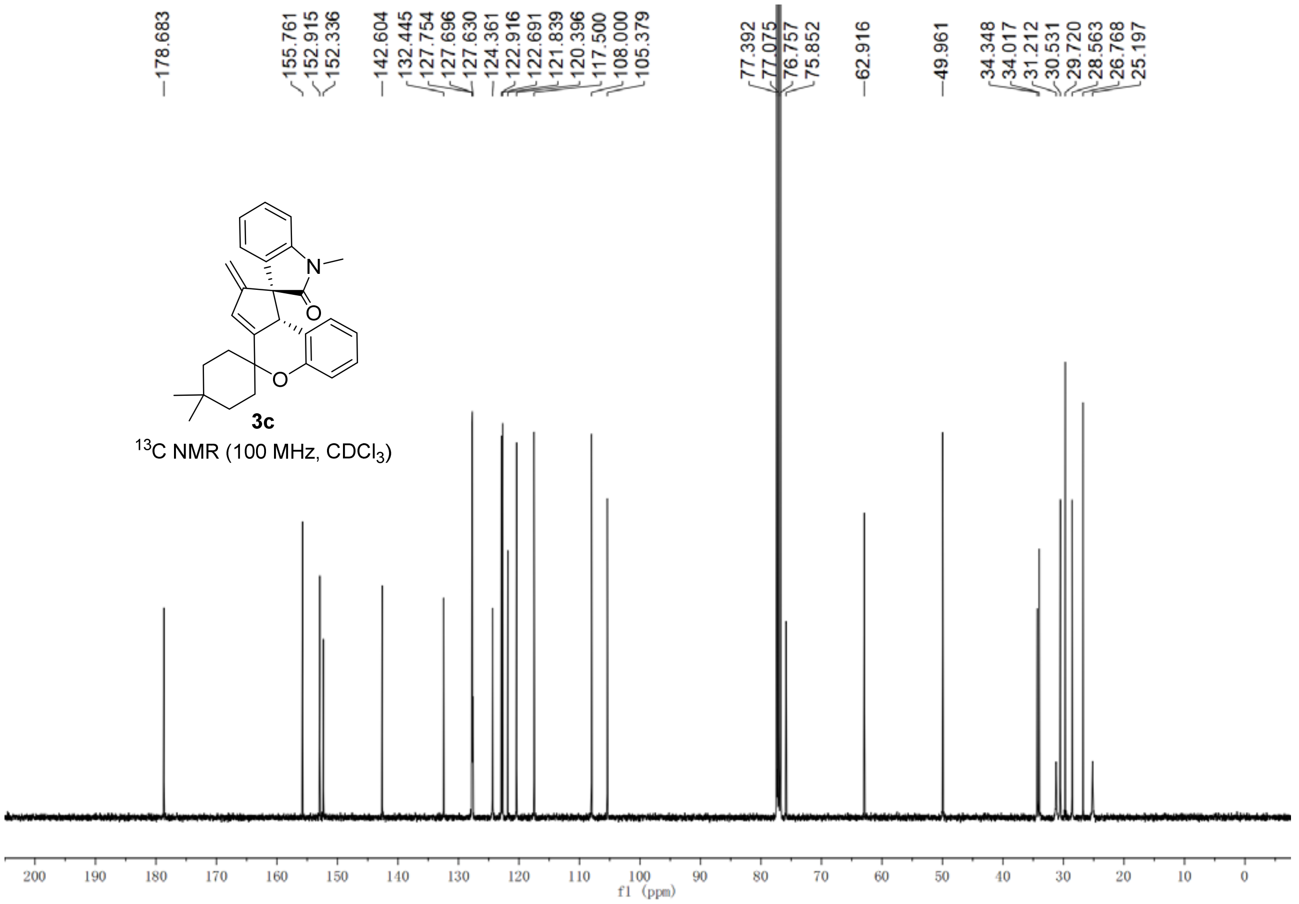
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{25}H_{23}NO_2Na^+$ 392.1621



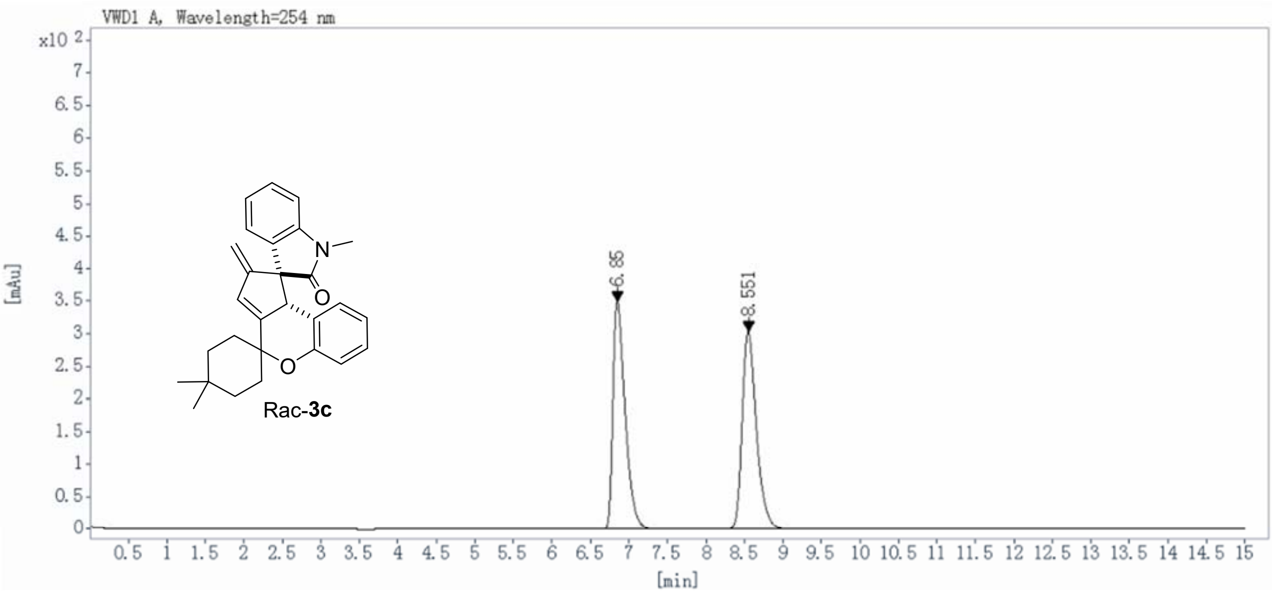
3c

^1H NMR (400 MHz, $CDCl_3$)

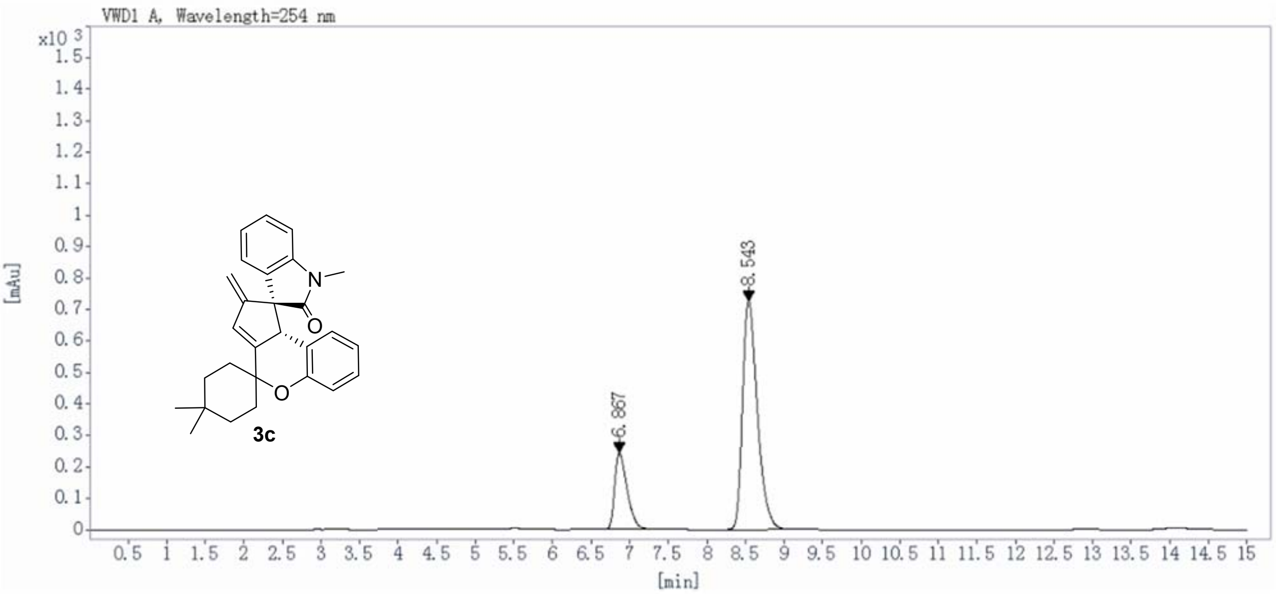


3c

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

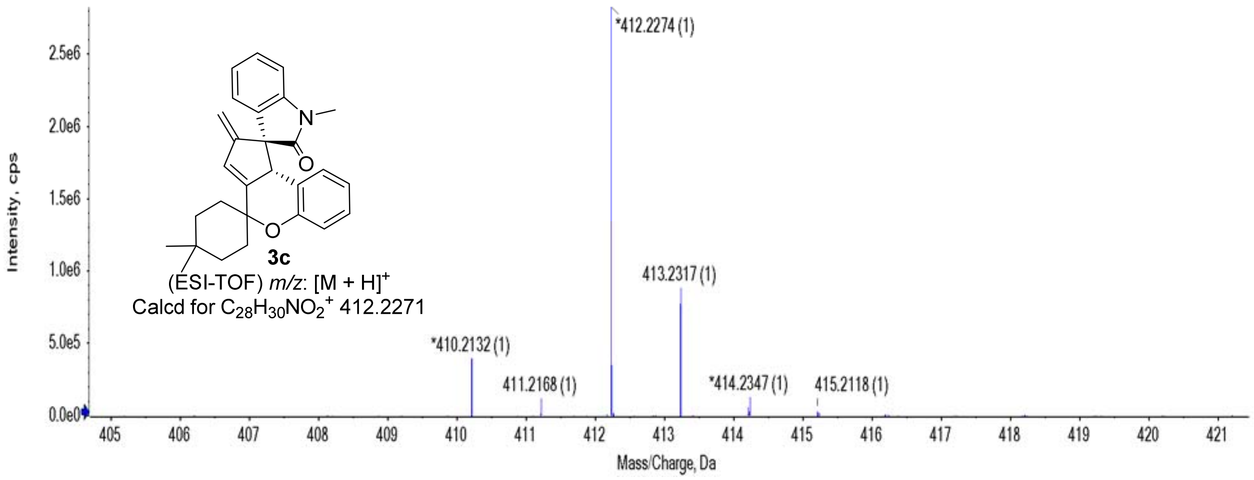


Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.850	BBA	0.17	349.2123	3864.9224	49.8809
8.551	BBA	0.20	302.6716	3883.3809	50.1191
			Totals:	7748.3032	100.0000



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.867	BBA	0.18	243.2090	2777.2302	22.1981
8.543	BBA	0.20	727.0814	9733.8750	77.8019
			Totals:	12511.1052	100.0000

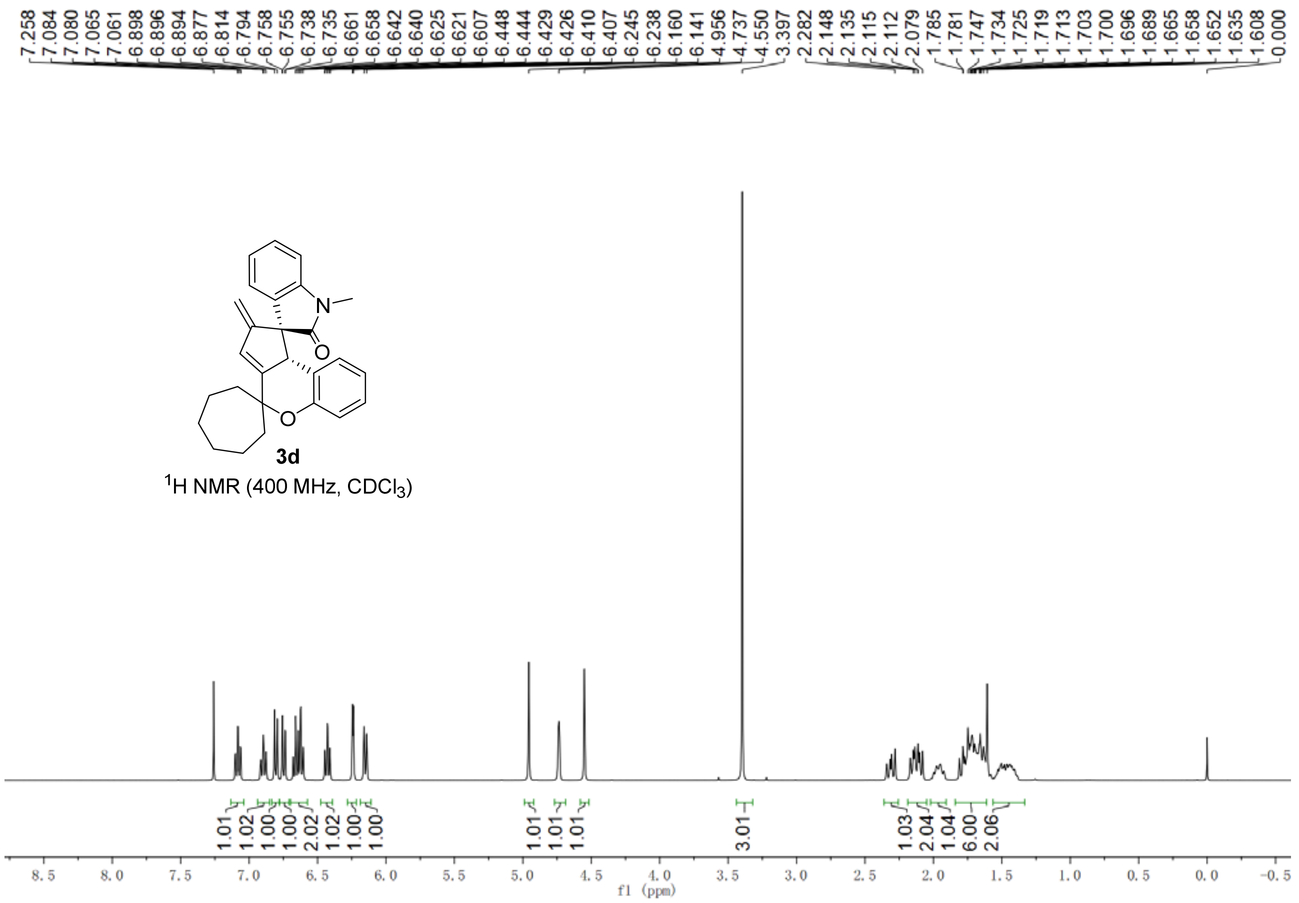
Spectrum from 20240821.wiff2 (sample 15) - 8, +TOF MS (200 - 600) from 0.063 to 0.111 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points), centroided



3c

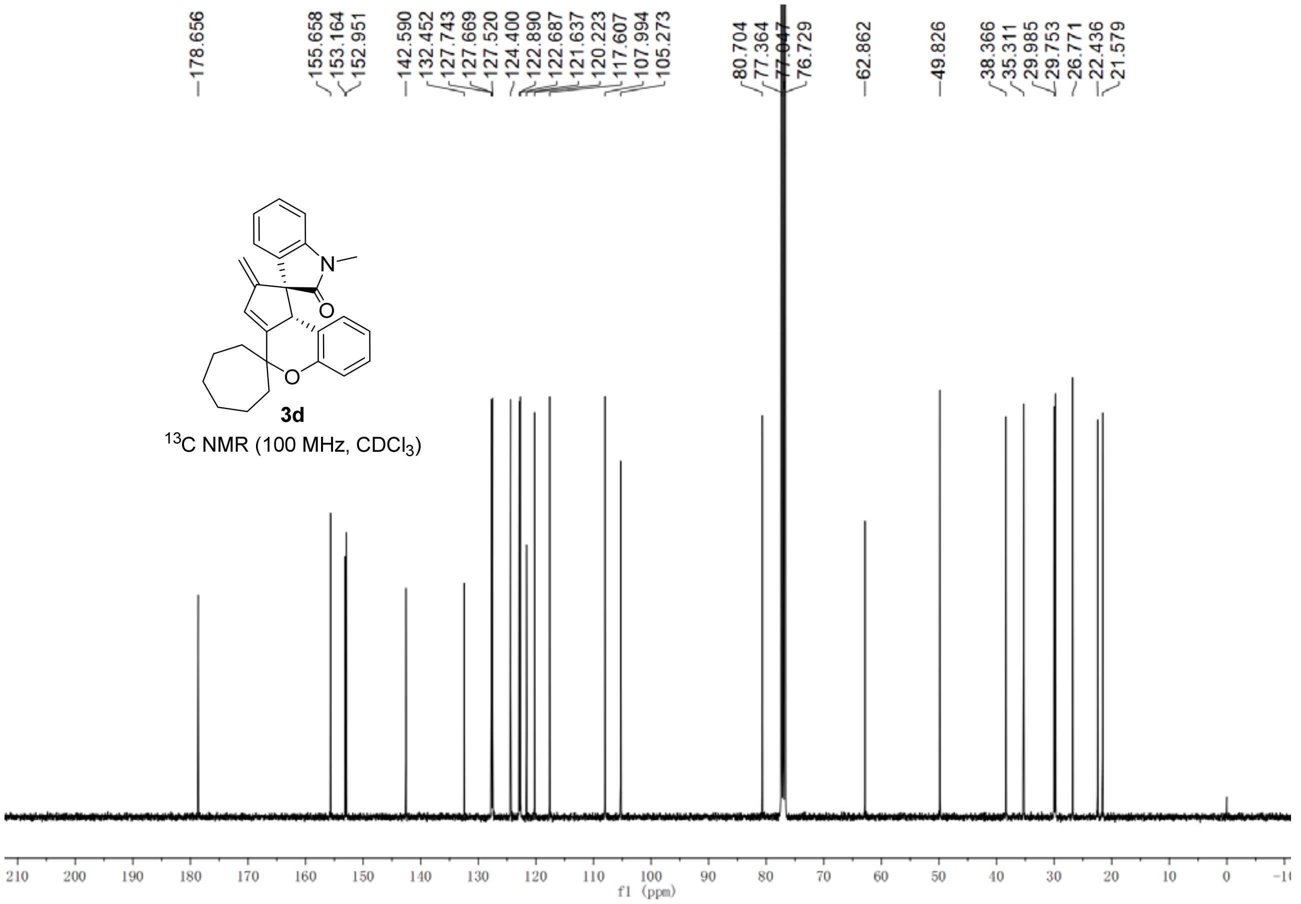
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{28}H_{30}NO_2^+$ 412.2271



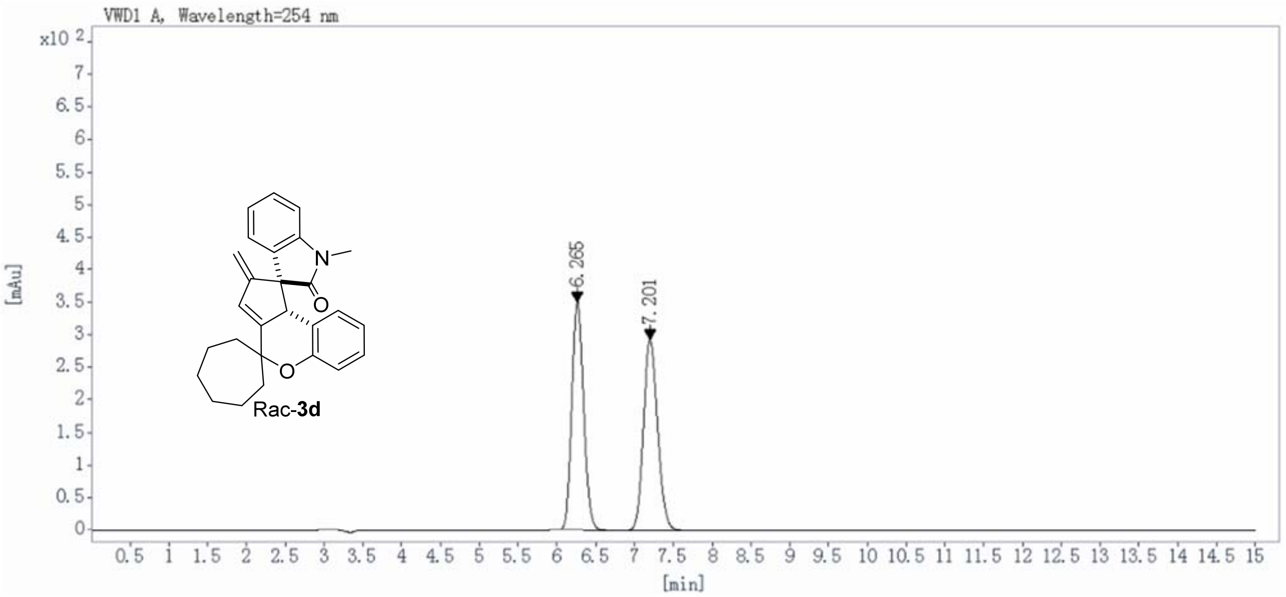
3d

^{1}H NMR (400 MHz, CDCl$_3$)

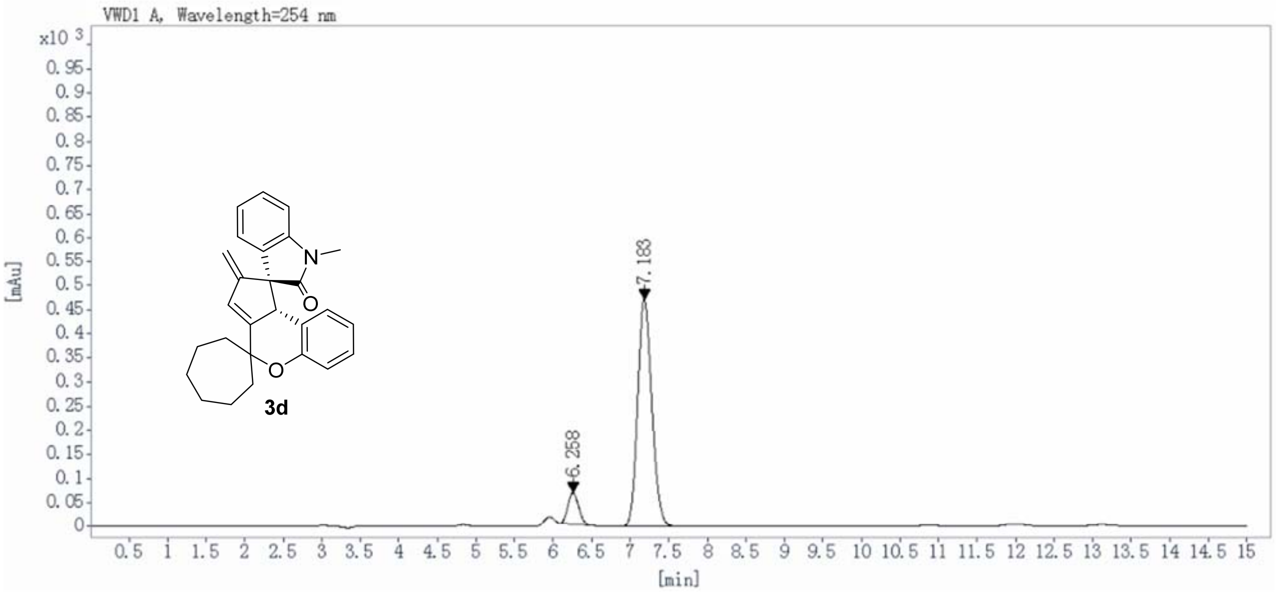


3d

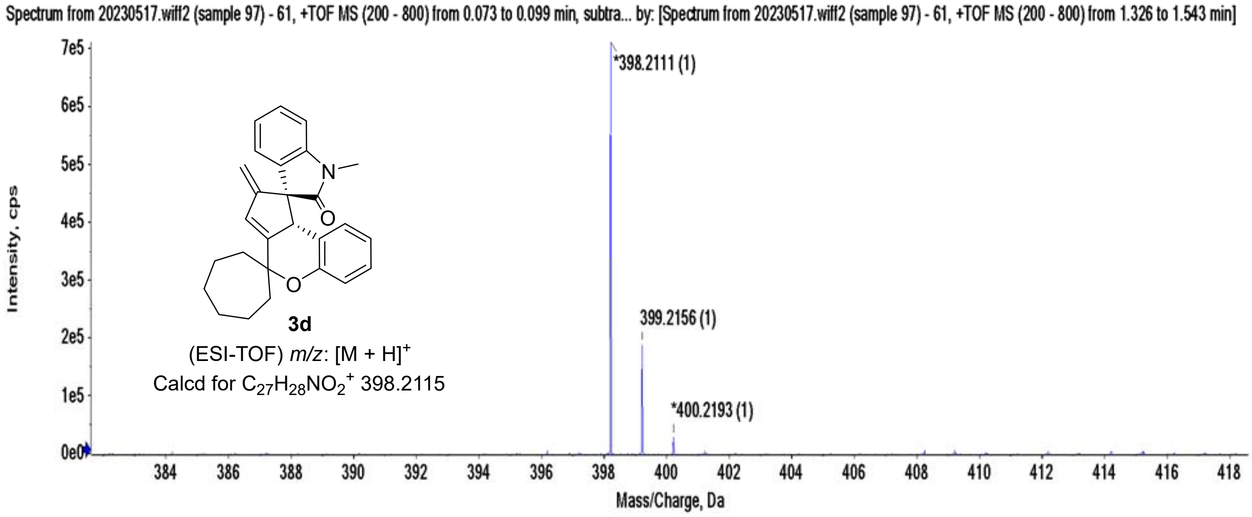
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.265	BBA	0.16	349.9322	3710.8174	49.8768
7.201	BBA	0.20	291.8110	3729.1545	50.1232
			Totals:	7439.9719	100.0000



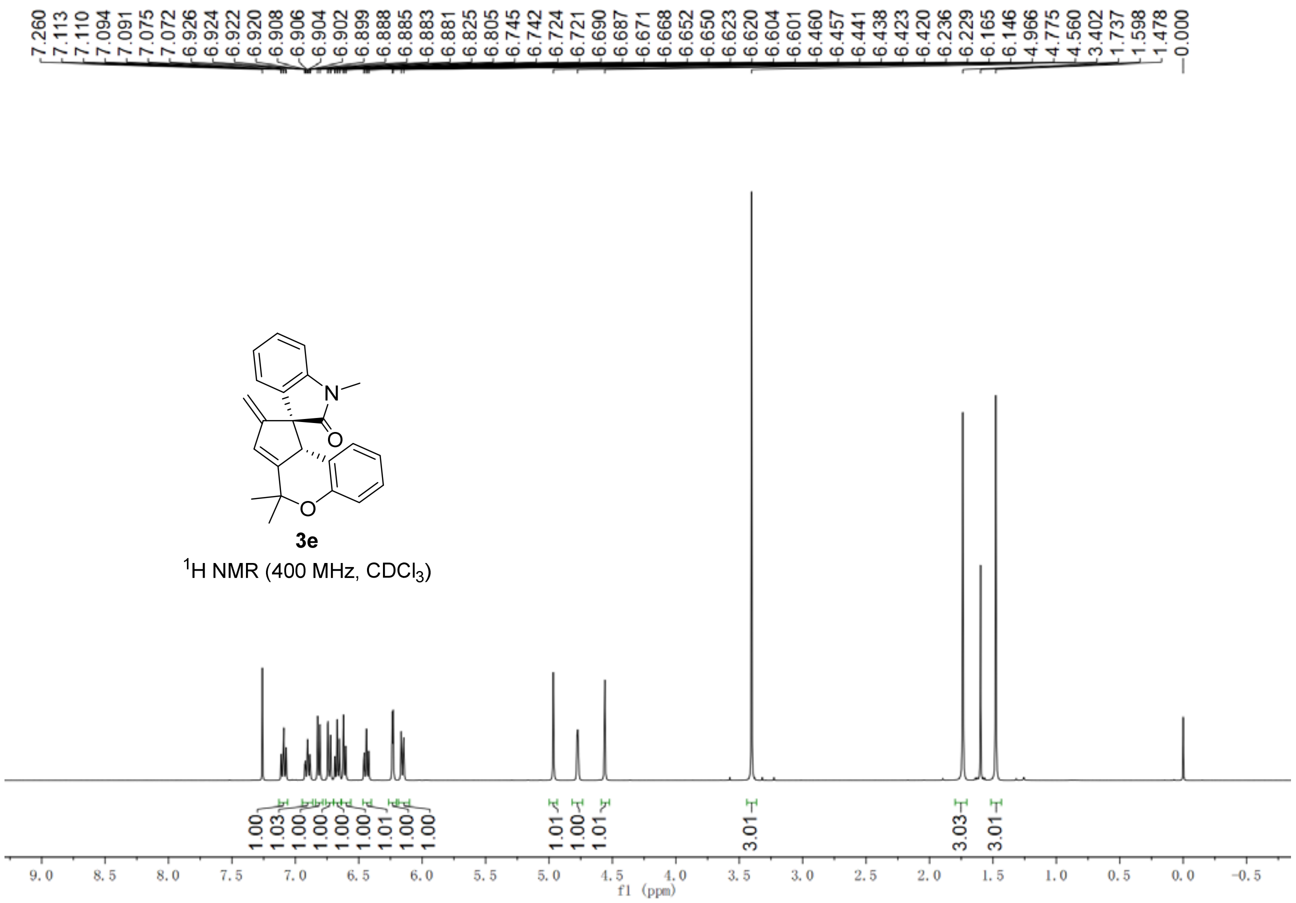
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.258	BBA	0.15	65.9337	642.6335	9.5210
7.183	BBA	0.20	471.5378	6107.0034	90.4790
			Totals:	6749.6369	100.0000



3d

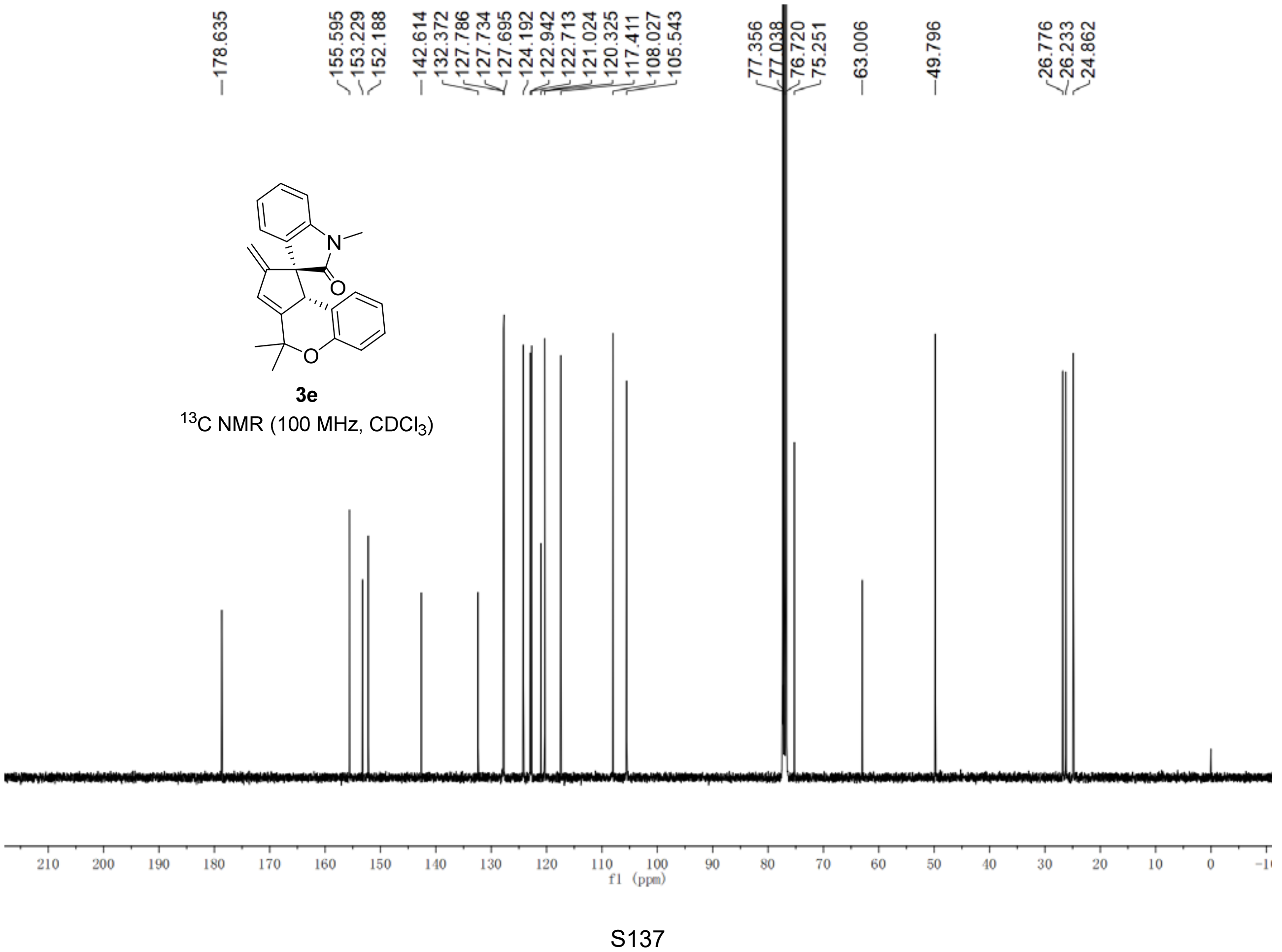
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{27}H_{28}NO_2^+$ 398.2115



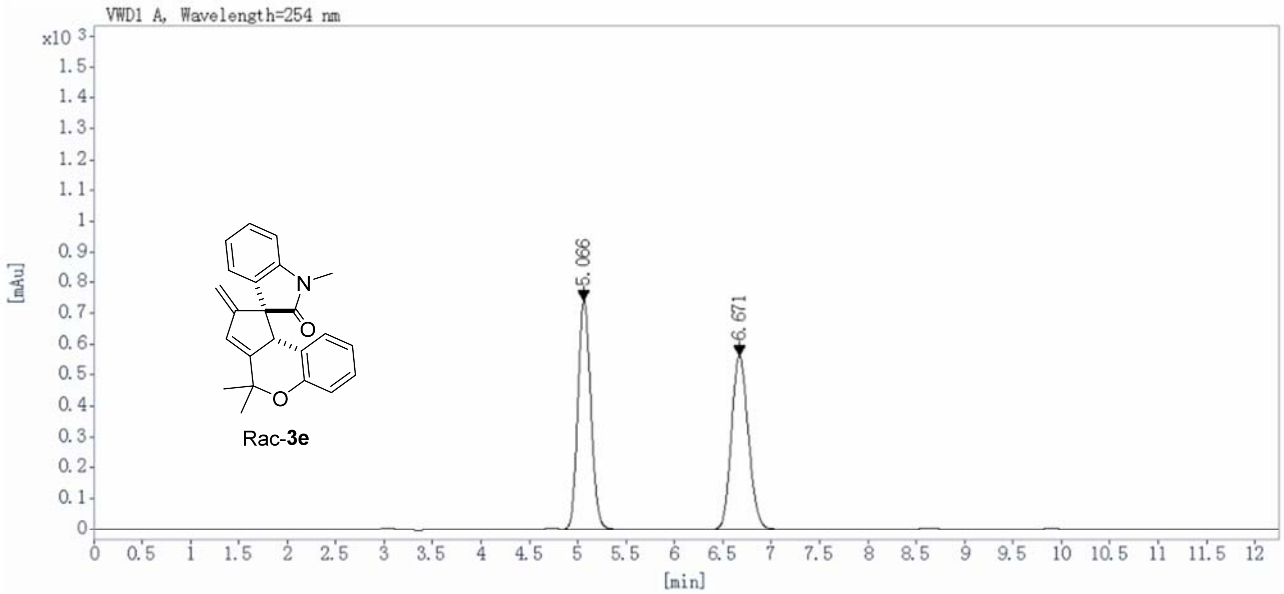
3e

^{1}H NMR (400 MHz, CDCl$_3$)

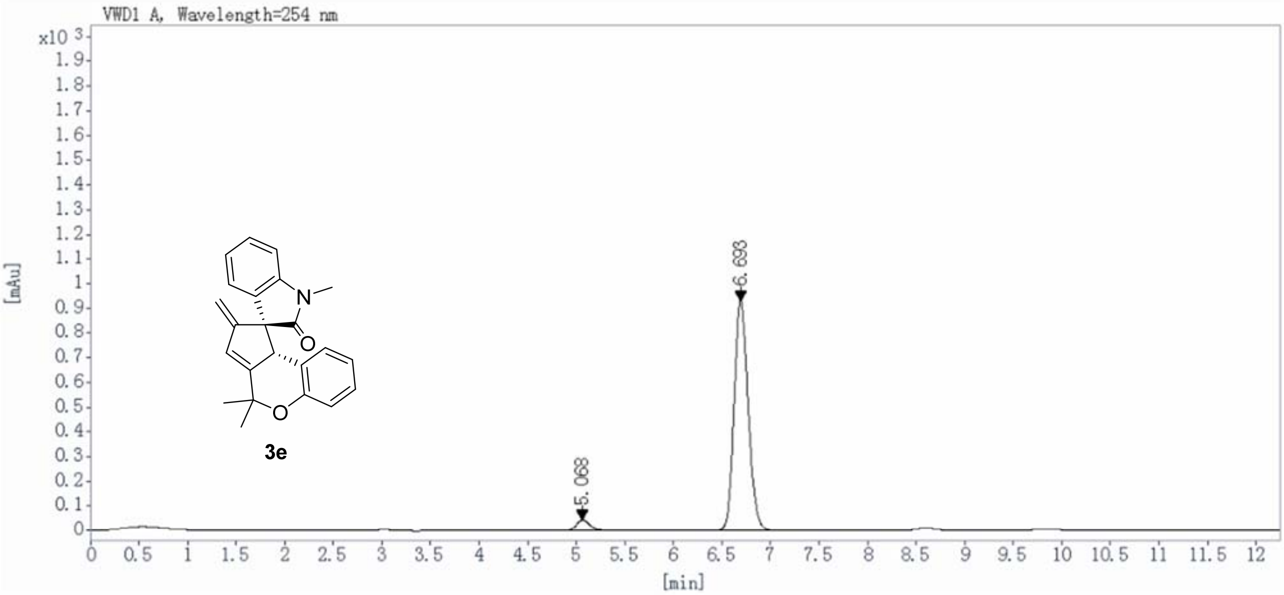


3e

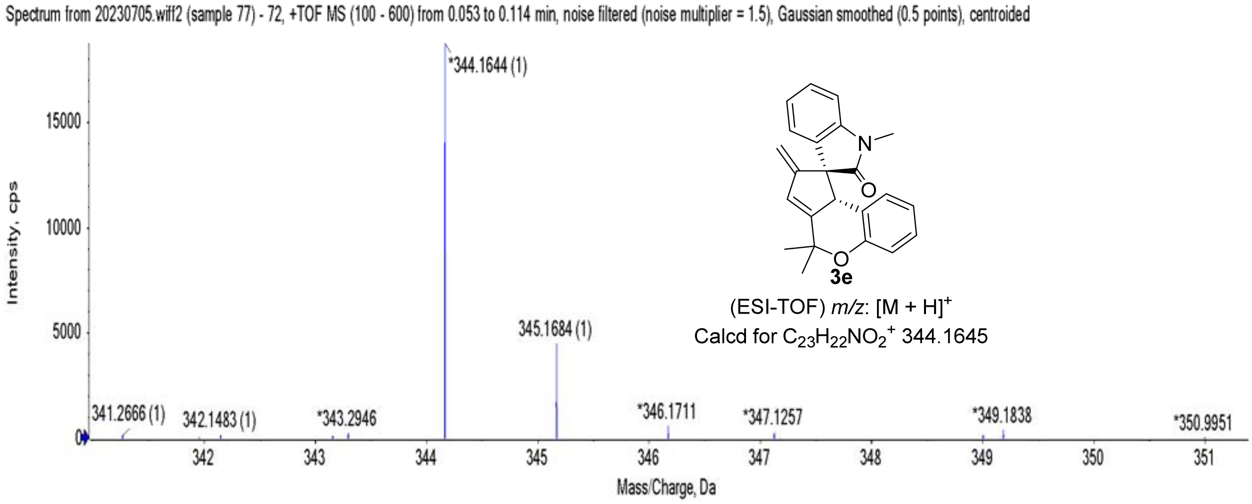
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.066	BBA	0.15	741.8915	6873.9385	50.0958
6.671	BBA	0.19	561.2289	6847.6372	49.9042
			Totals:	13721.5757	100.0000



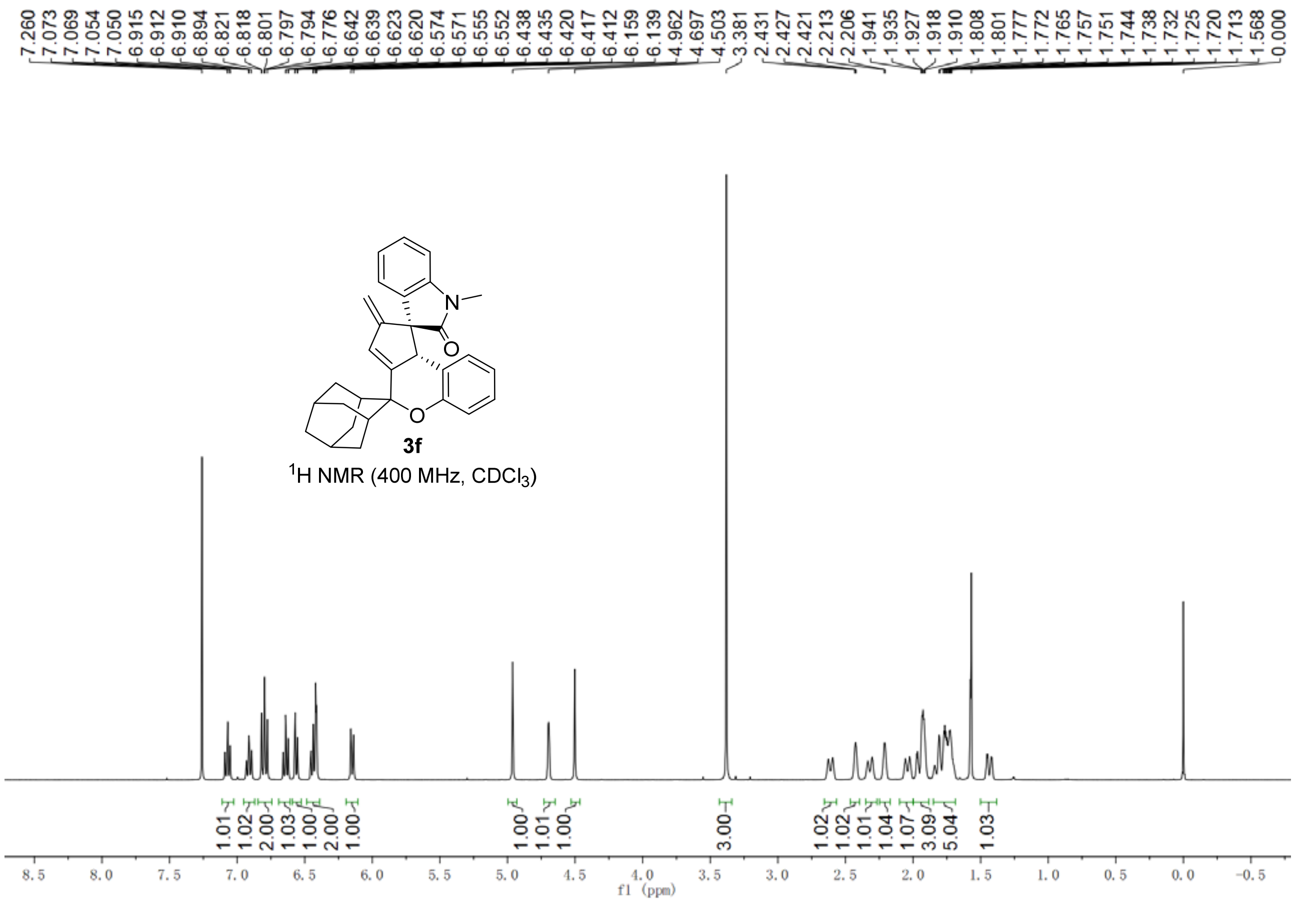
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.068	BBA	0.15	41.3812	384.0868	3.9358
6.693	BBA	0.16	929.2313	9374.7246	96.0642
			Totals:	9758.8114	100.0000



3e

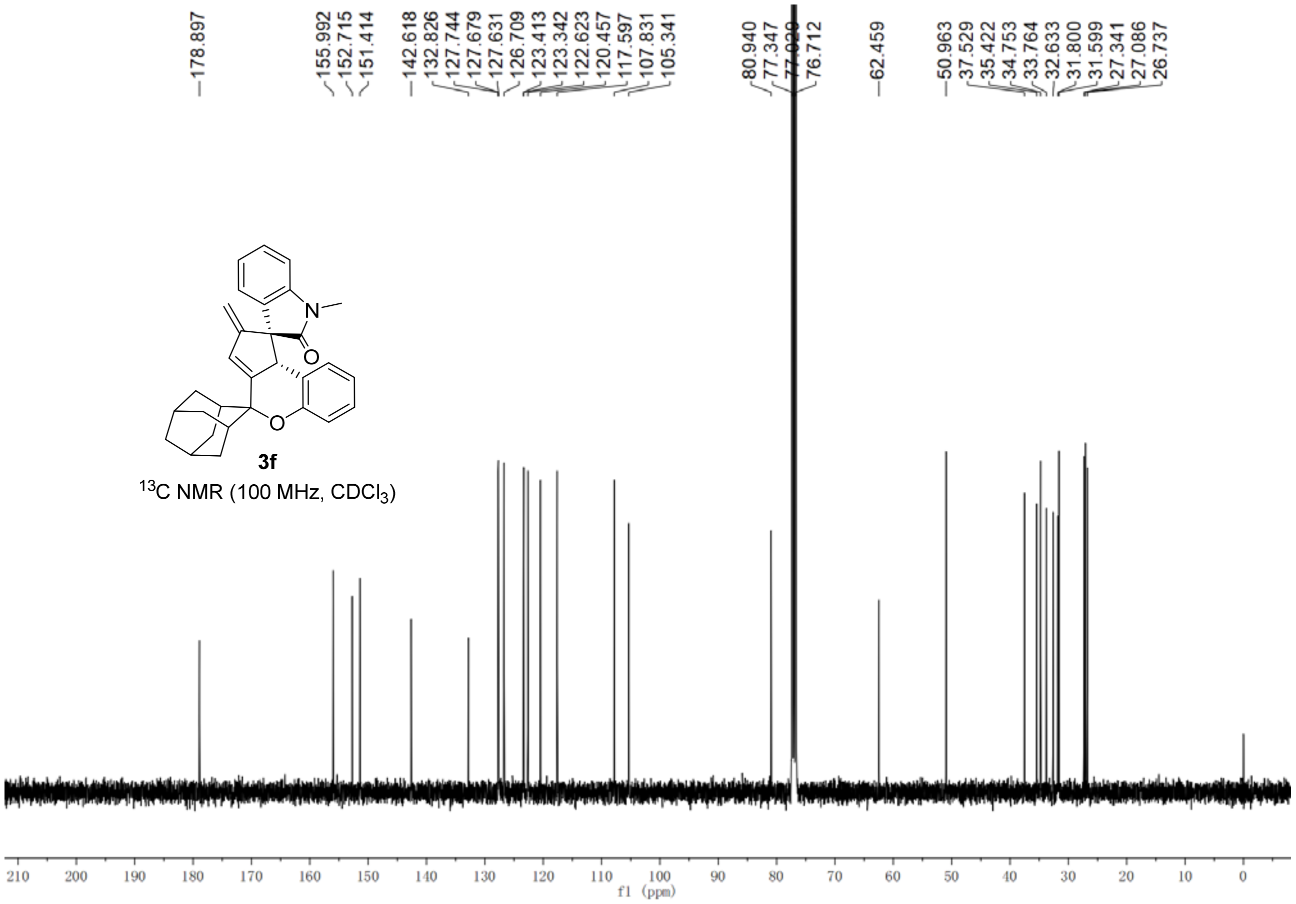
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{23}H_{22}NO_2^+$ 344.1645



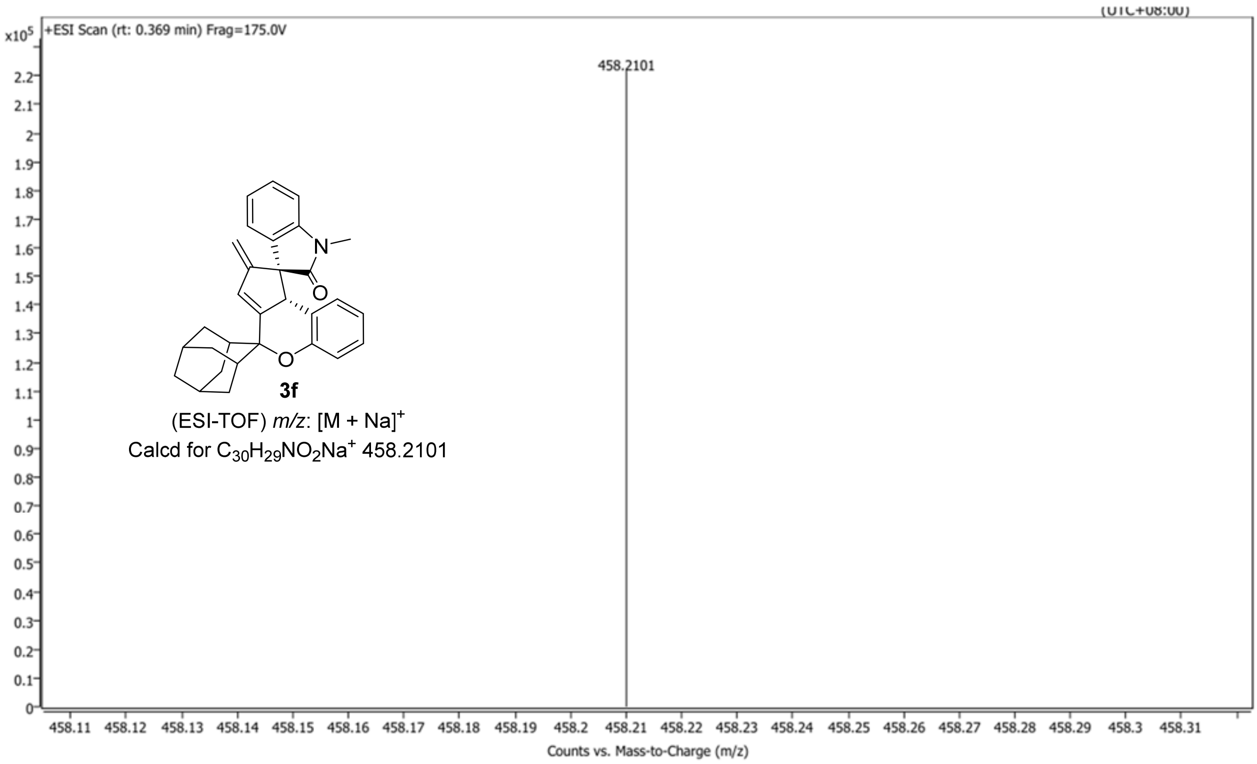
3f

^{1}H NMR (400 MHz, CDCl$_3$)



3f

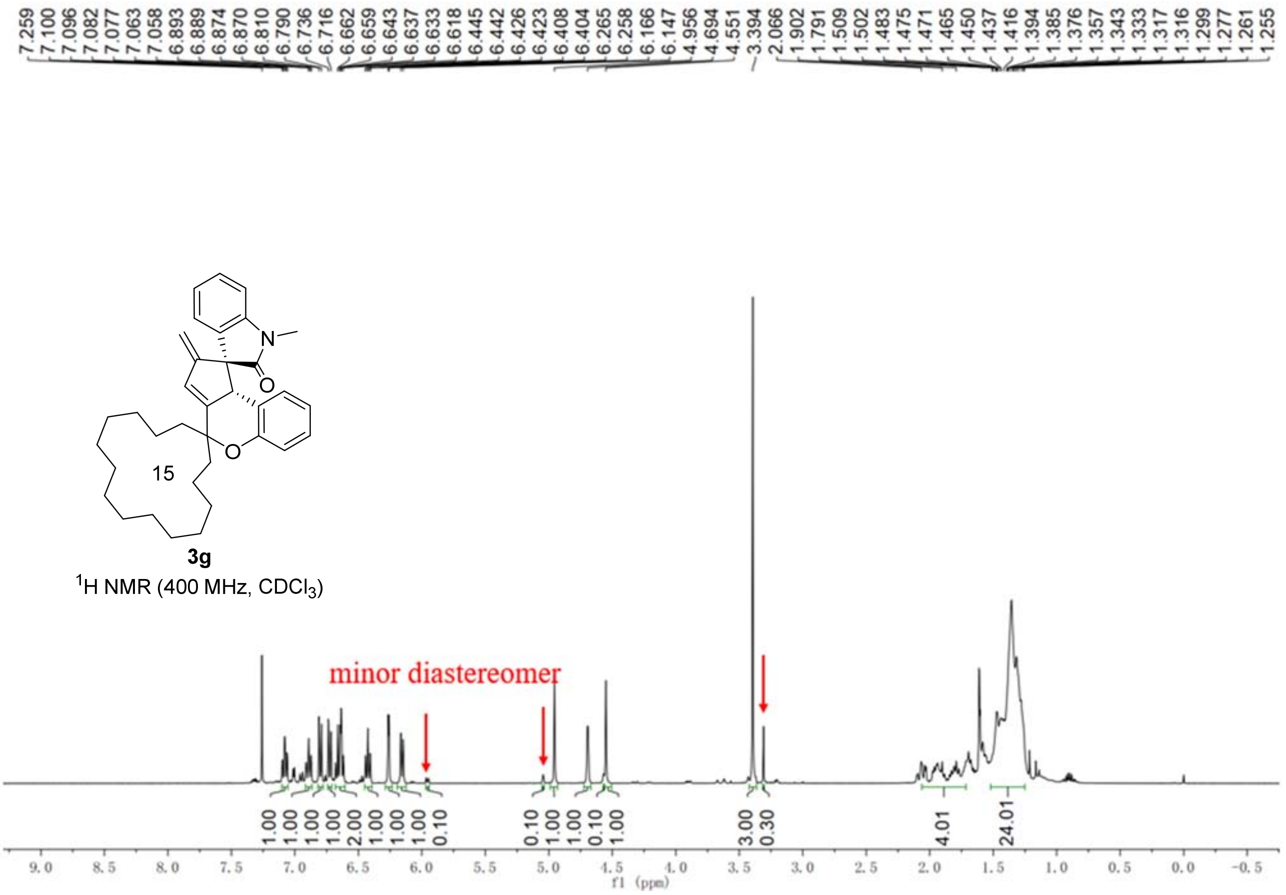
^{13}C NMR (100 MHz, CDCl$_3$)



3f

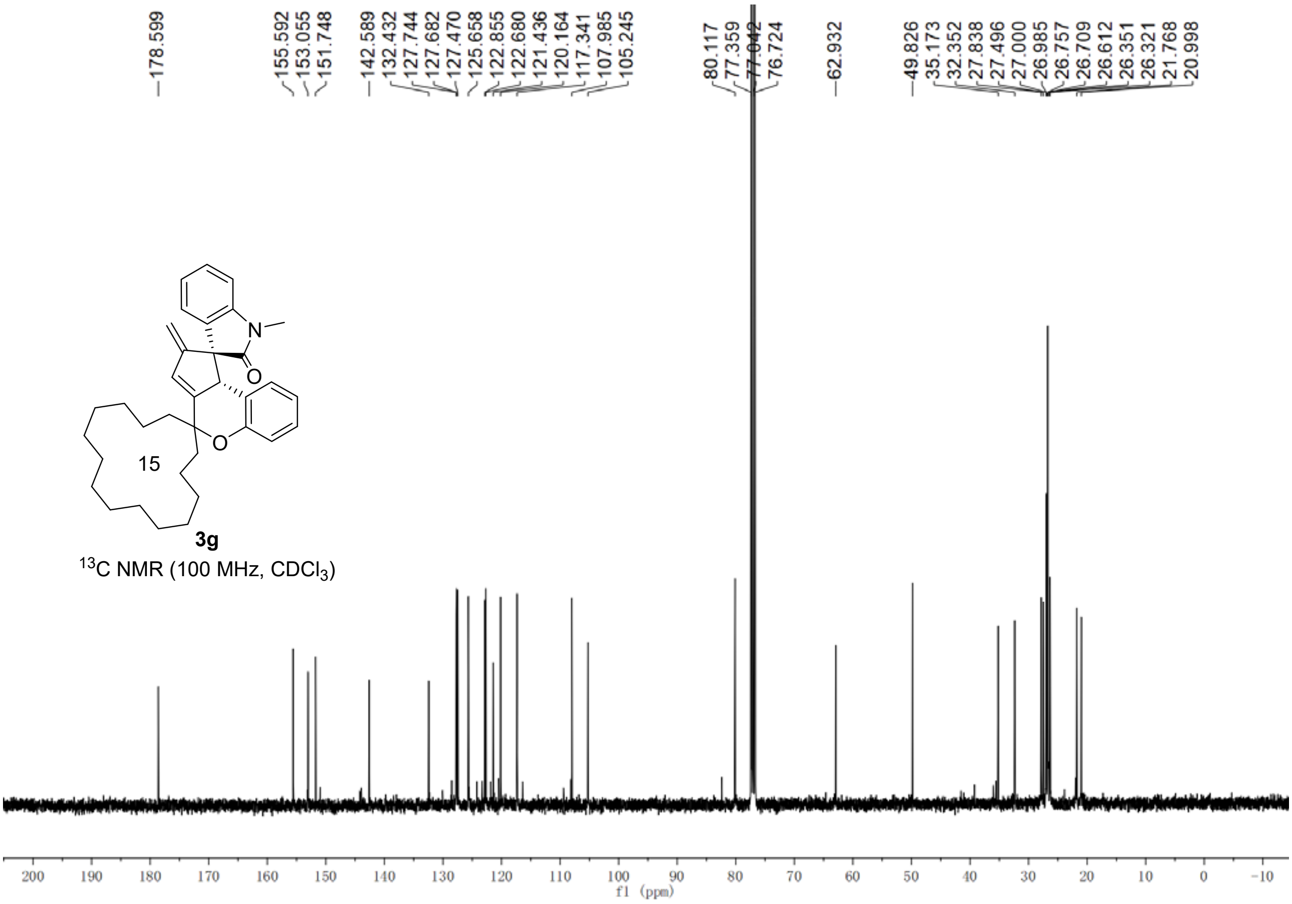
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{30}H_{29}NO_2Na^+$ 458.2101



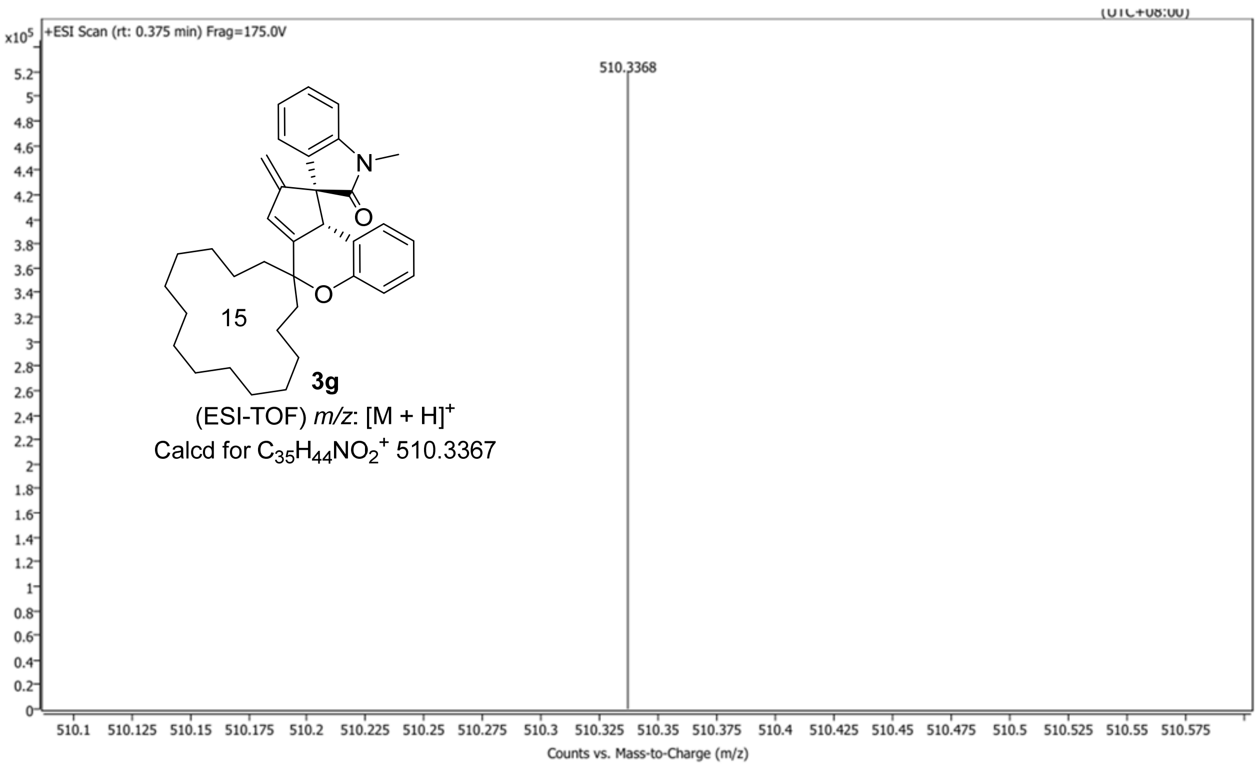
3g

^{1}H NMR (400 MHz, CDCl$_3$)



3g

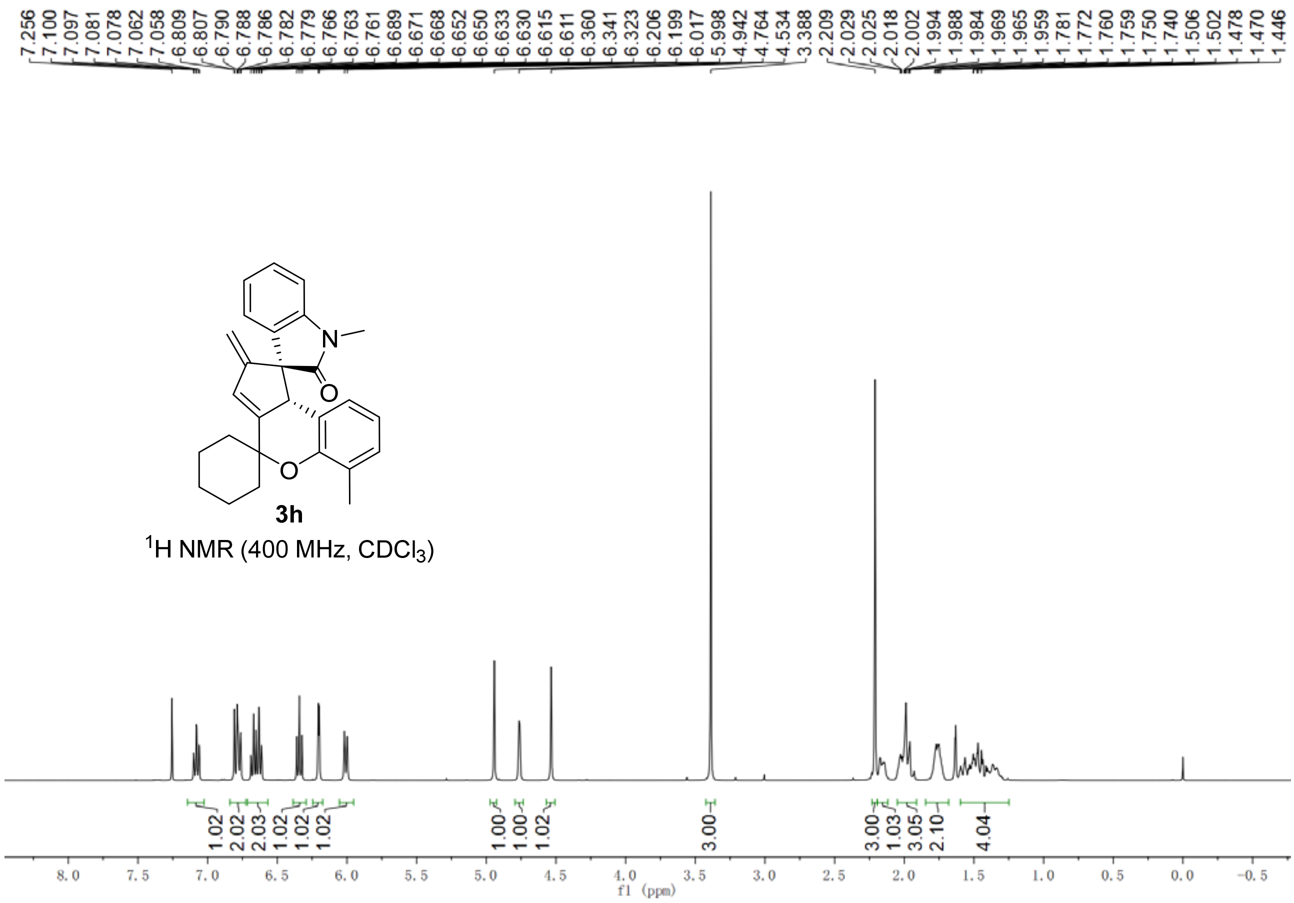
^{13}C NMR (100 MHz, CDCl$_3$)



3g

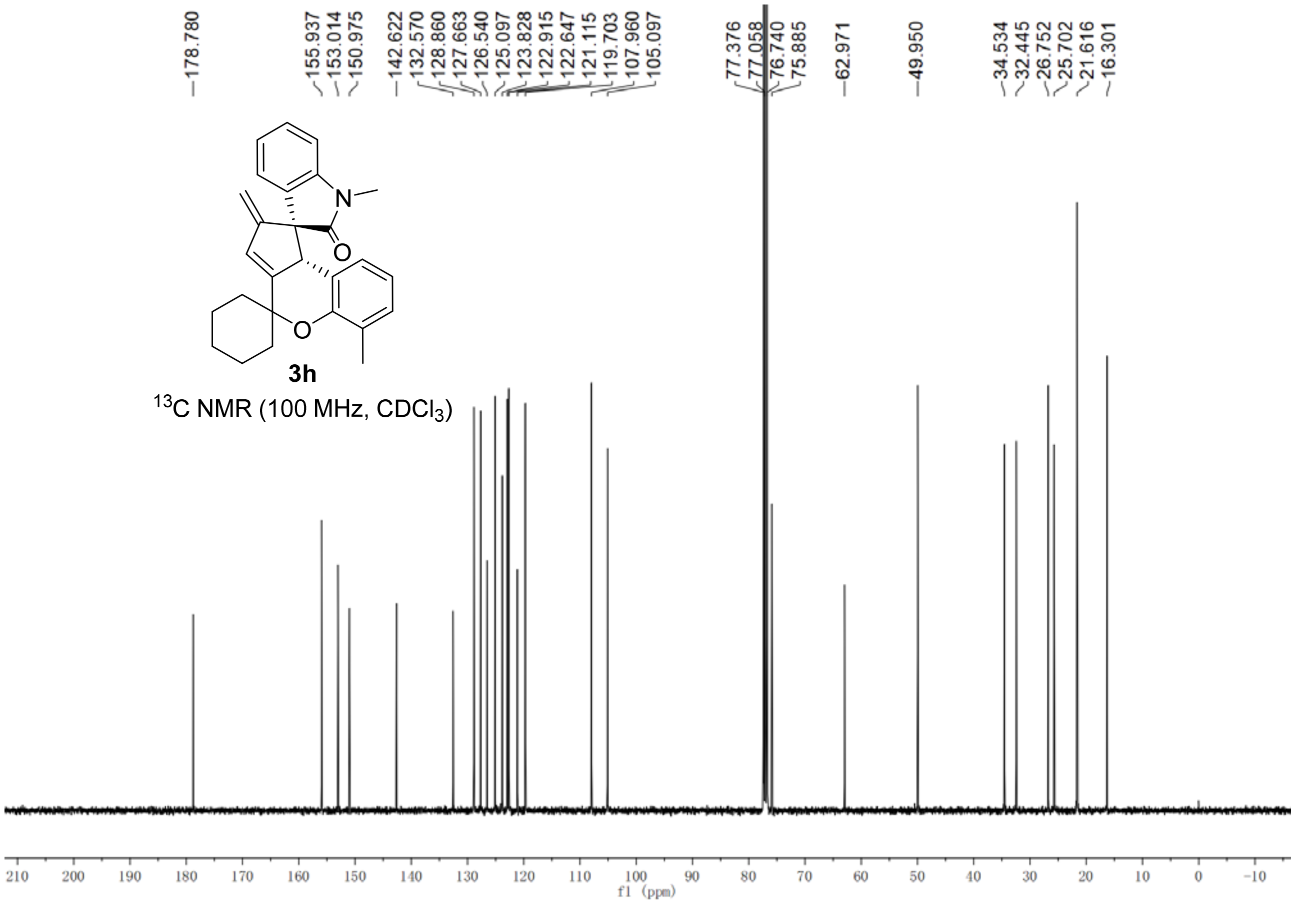
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{35}H_{44}NO_2^+$ 510.3367



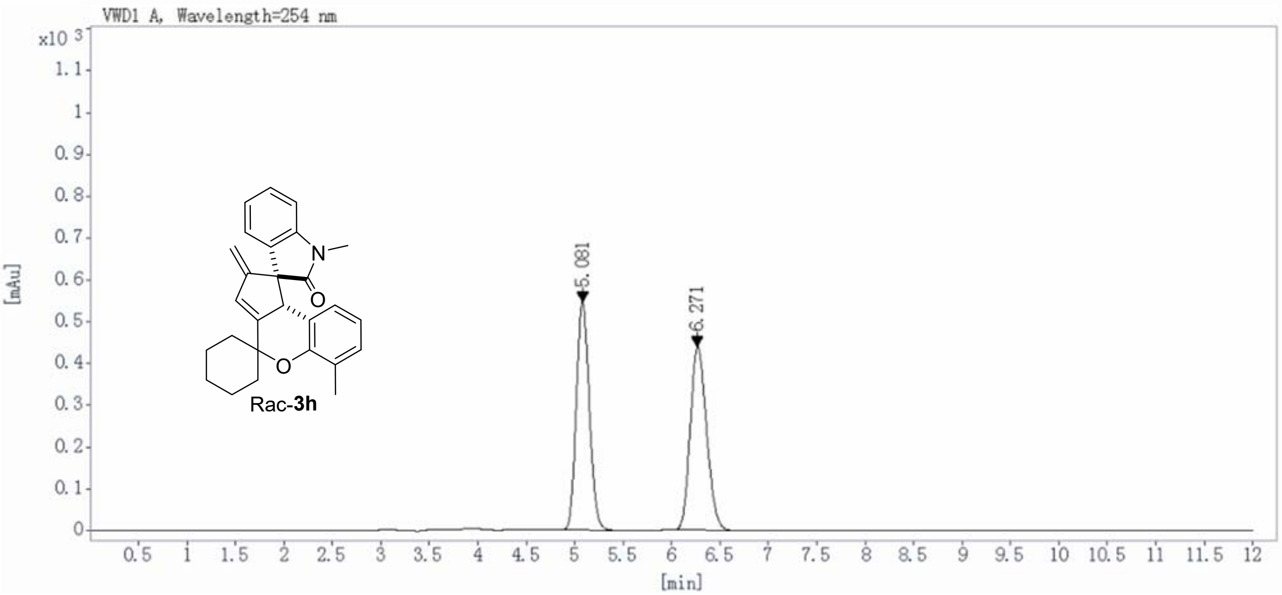
3h

^{1}H NMR (400 MHz, CDCl$_3$)

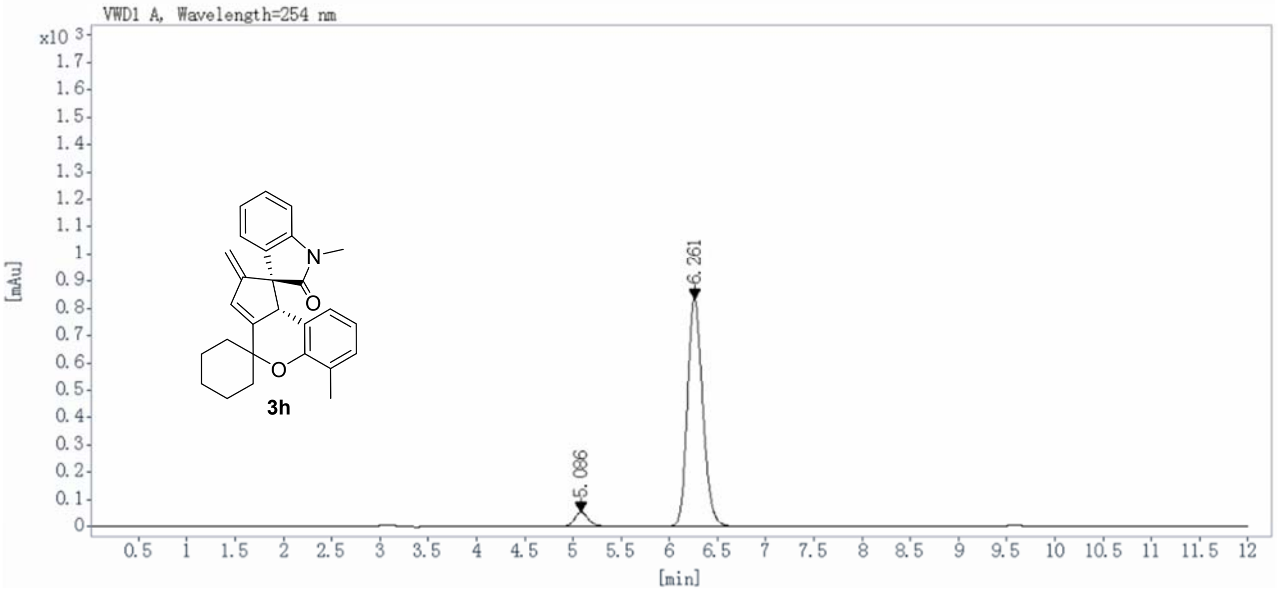


3h

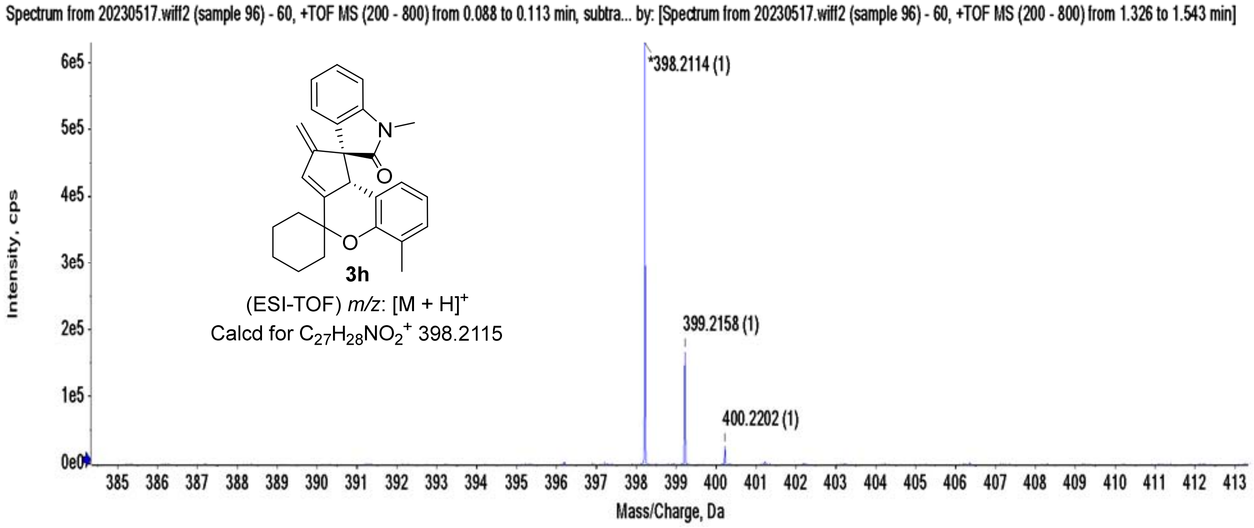
^{13}C NMR (100 MHz, CDCl$_3$)

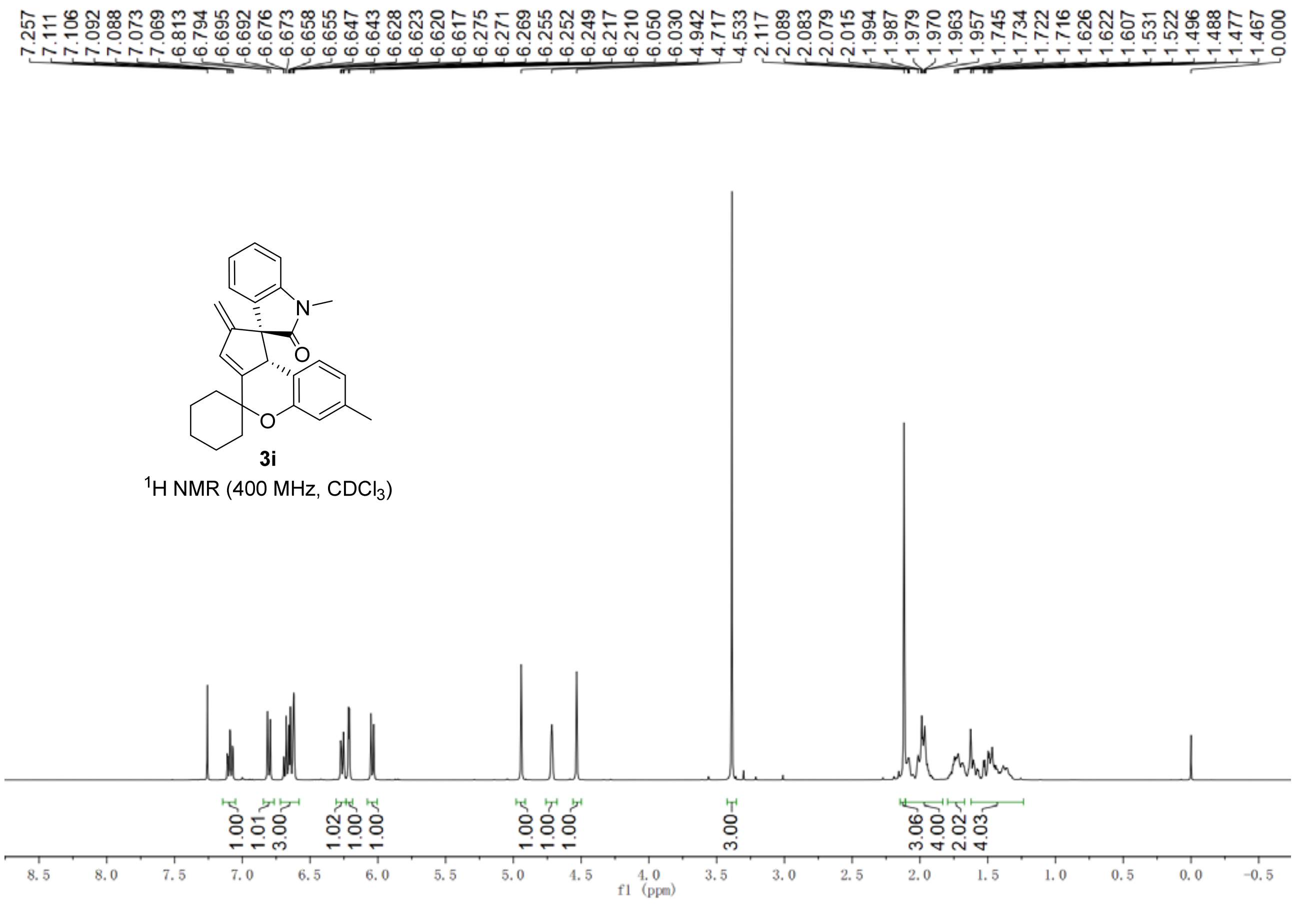


Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.081	BBA	0.15	546.0235	5105.6519	49.6539
6.271	BBA	0.18	438.4892	5176.8340	50.3461
			Totals:	10282.4858	100.0000



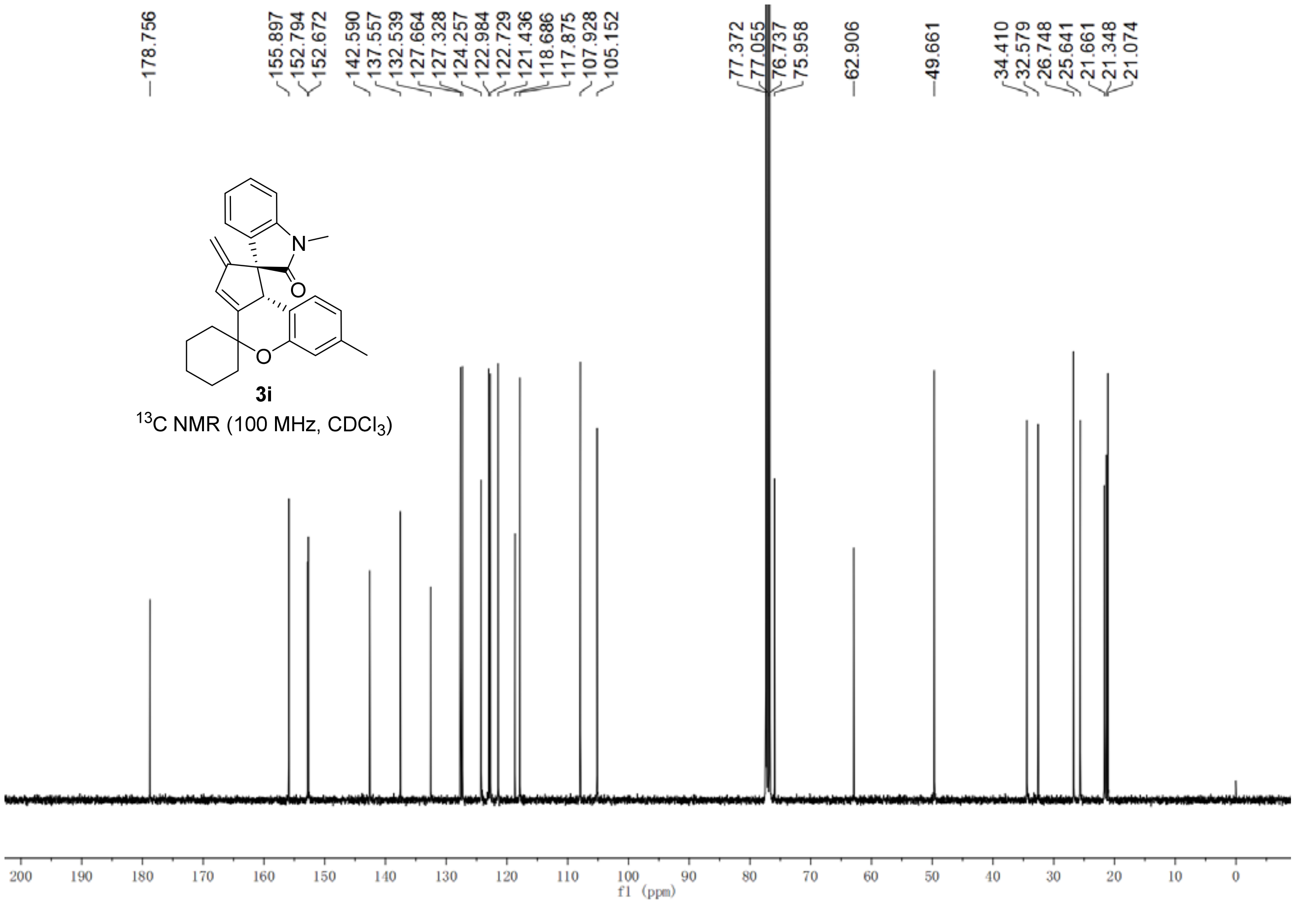
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.086	BBA	0.15	52.6610	507.6499	5.2306
6.261	BBA	0.17	833.6223	9197.7656	94.7694
			Totals:	9705.4156	100.0000


Spectrum from 20230517.wiff2 (sample 96) - 60, +TOF MS (200 - 800) from 0.088 to 0.113 min, subtra... by: [Spectrum from 20230517.wiff2 (sample 96) - 60, +TOF MS (200 - 800) from 1.326 to 1.543 min]
Intensity, cps
6e5
5e5
4e5
3e5
2e5
1e5
0e0
*398.2114 (1)
399.2158 (1)
400.2202 (1)
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
Mass/Charge, Da
N
O
O
3h
(ESI-TOF) m/z: [M + H]+
Calcd for C27H28NO2+ 398.2115



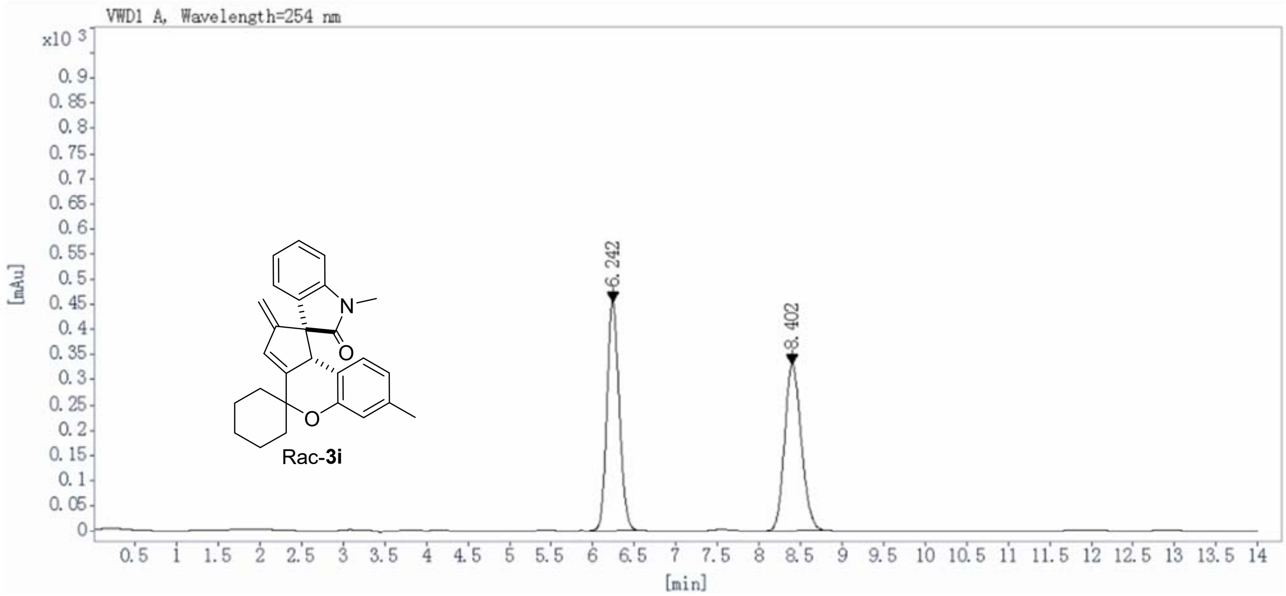
3i

^{1}H NMR (400 MHz, CDCl$_3$)



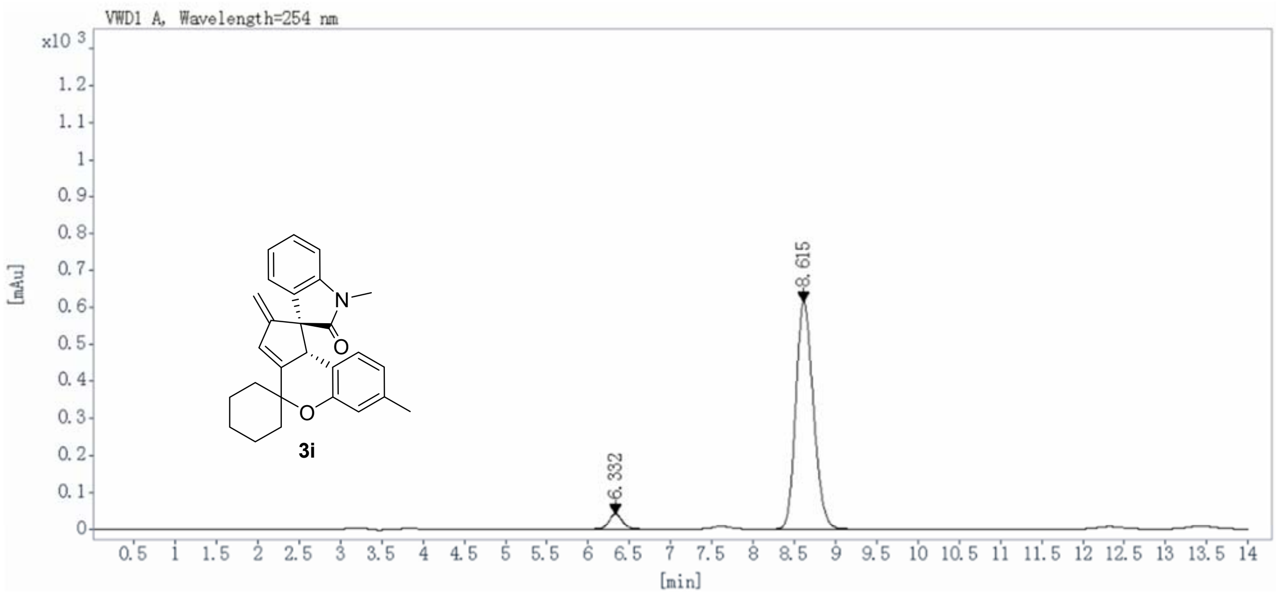
3i

^{13}C NMR (100 MHz, CDCl$_3$)



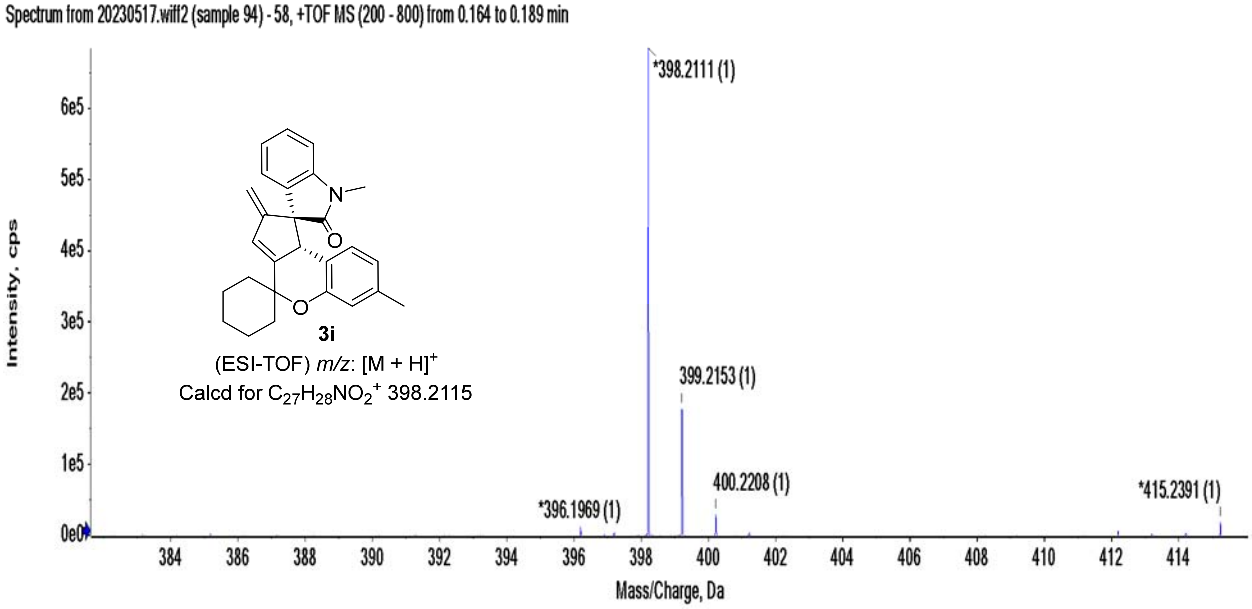
Rac-**3i**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.242	BBA	0.16	454.1411	4702.7432	50.2738
8.402	BBA	0.22	330.2756	4651.5200	49.7262
			Totals:	9354.2632	100.0000



3i

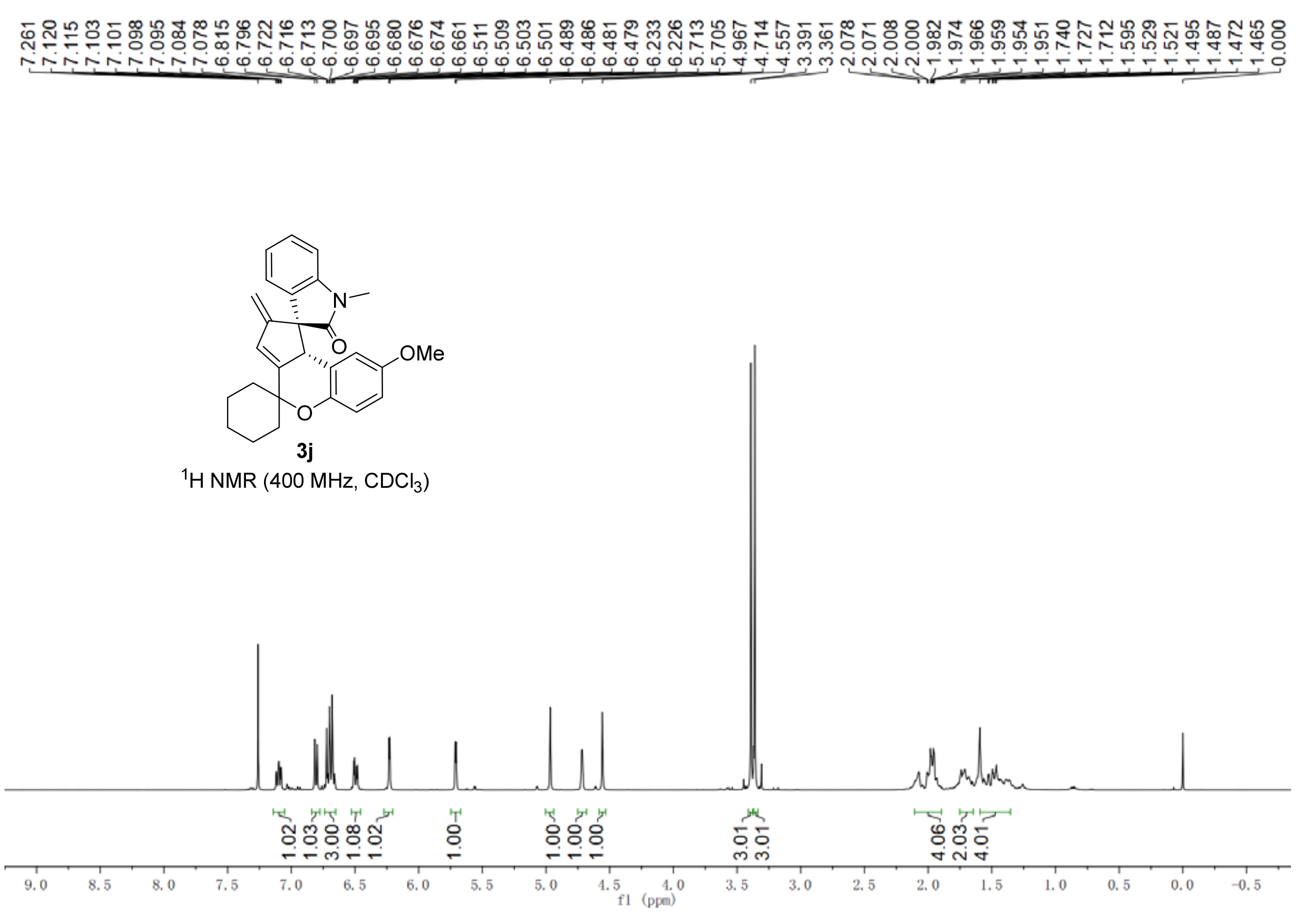
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.332	BBA	0.17	41.2327	461.6652	4.8121
8.615	BBA	0.23	614.2065	9132.0762	95.1879
			Totals:	9593.7414	100.0000



3i

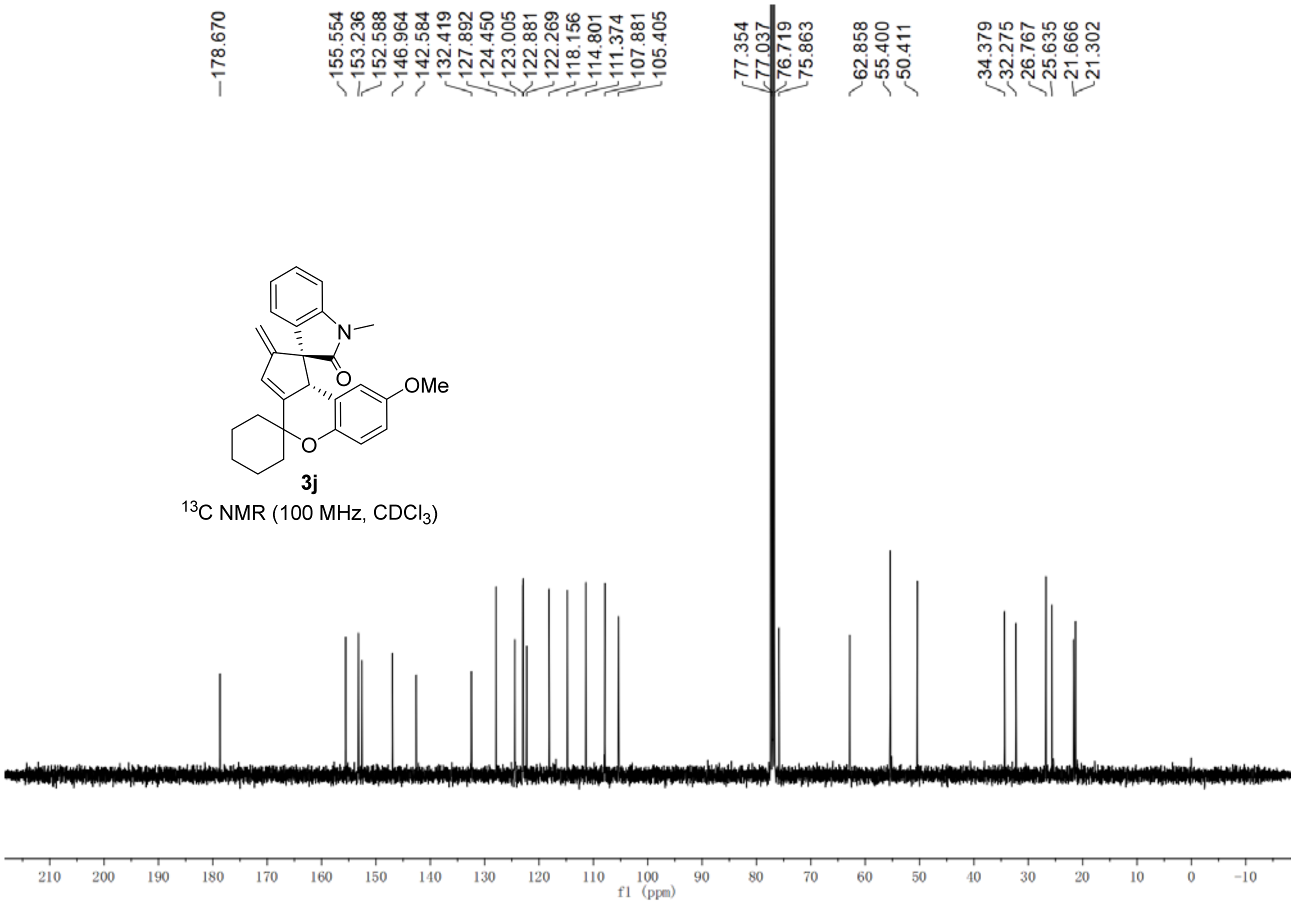
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{27}H_{28}NO_2^+$ 398.2115



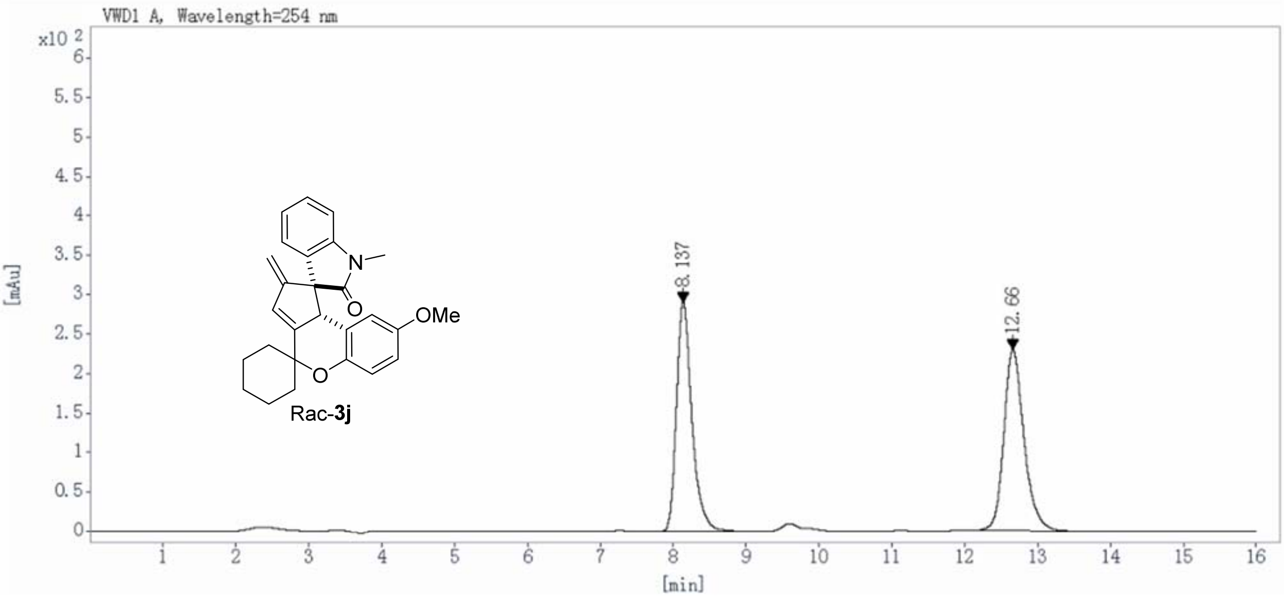
3j

^{1}H NMR (400 MHz, CDCl$_3$)

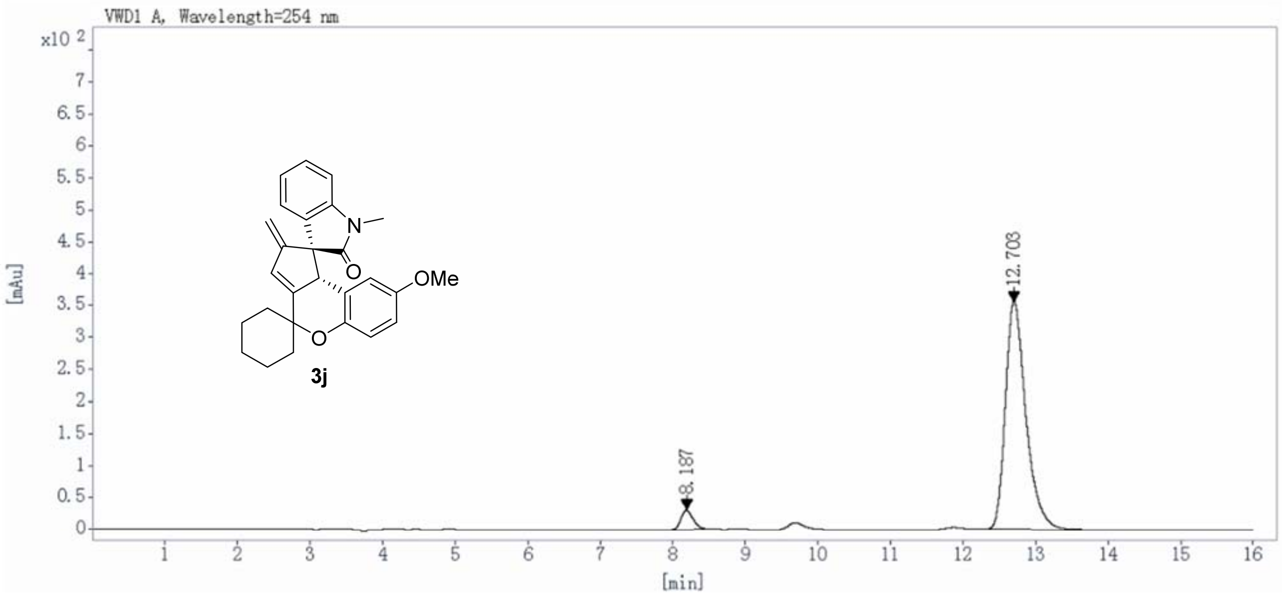


3j

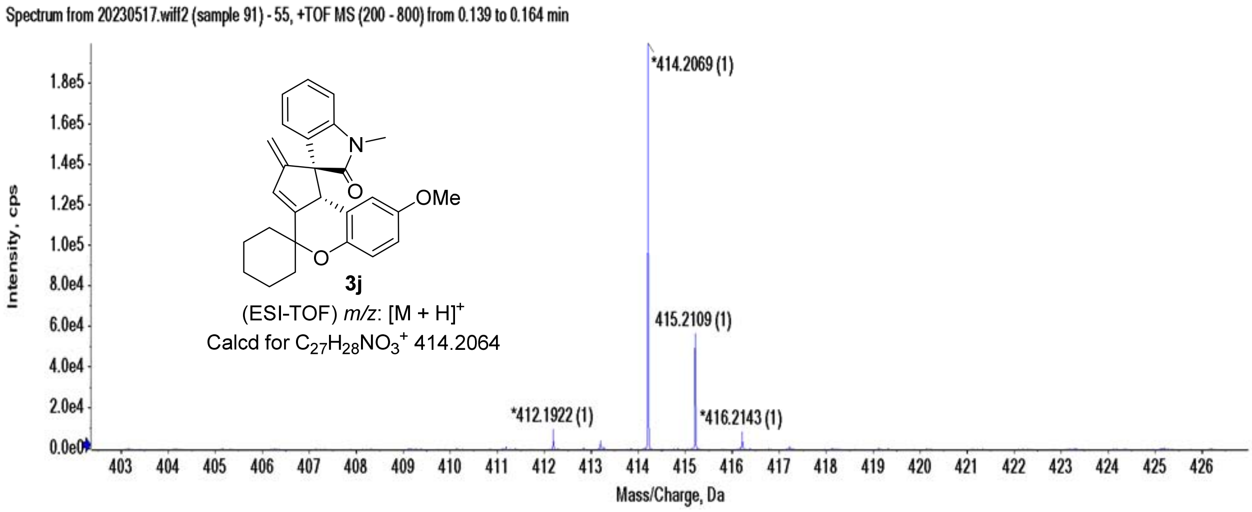
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.137	BBA	0.22	289.9394	4266.7715	49.1870
12.660	BBA	0.29	229.3670	4407.8218	50.8130
			Totals:	8674.5933	100.0000



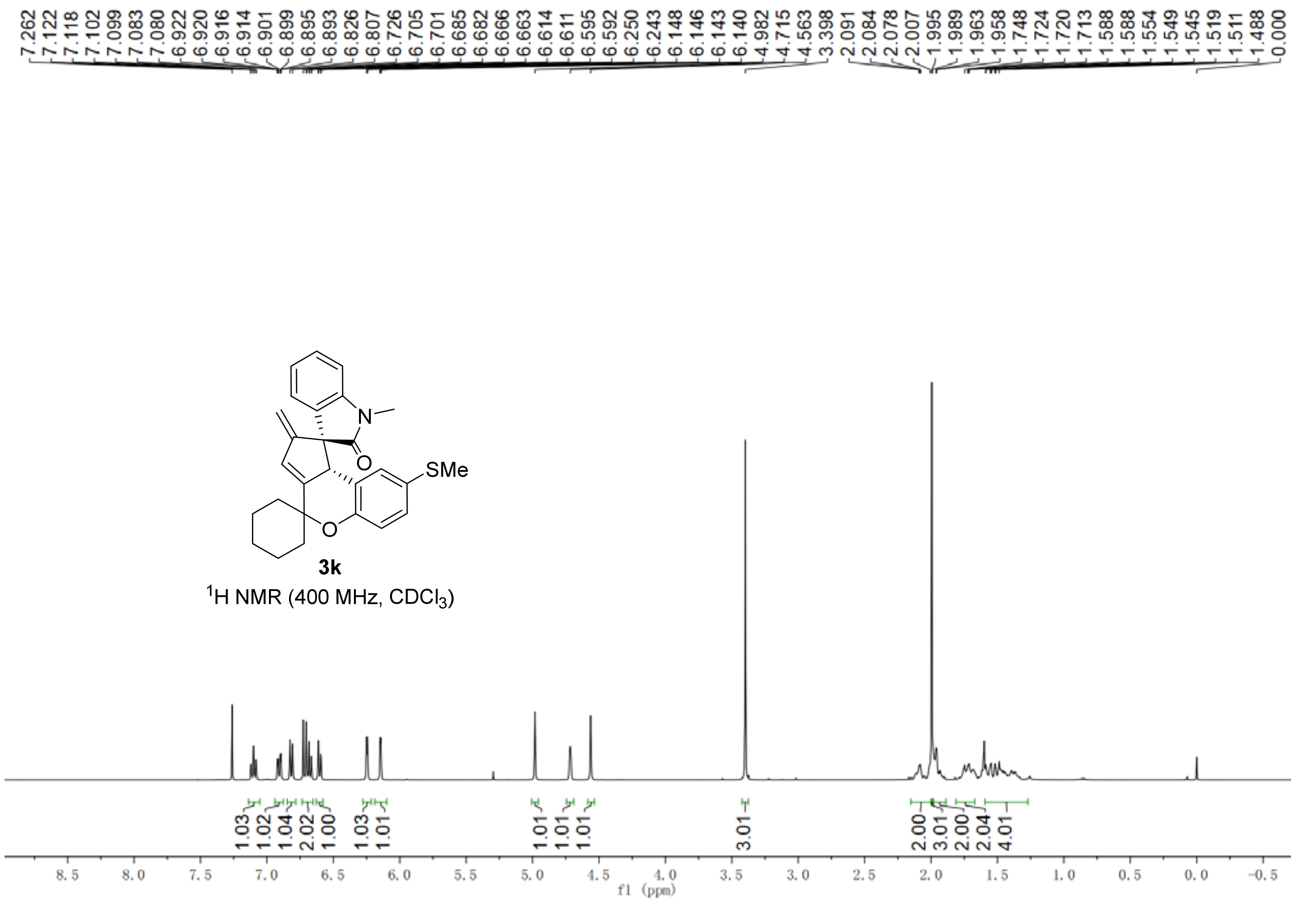
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.187	BBA	0.18	31.2825	376.2105	5.0857
12.703	BBA	0.30	356.7078	7021.1616	94.9143
			Totals:	7397.3722	100.0000



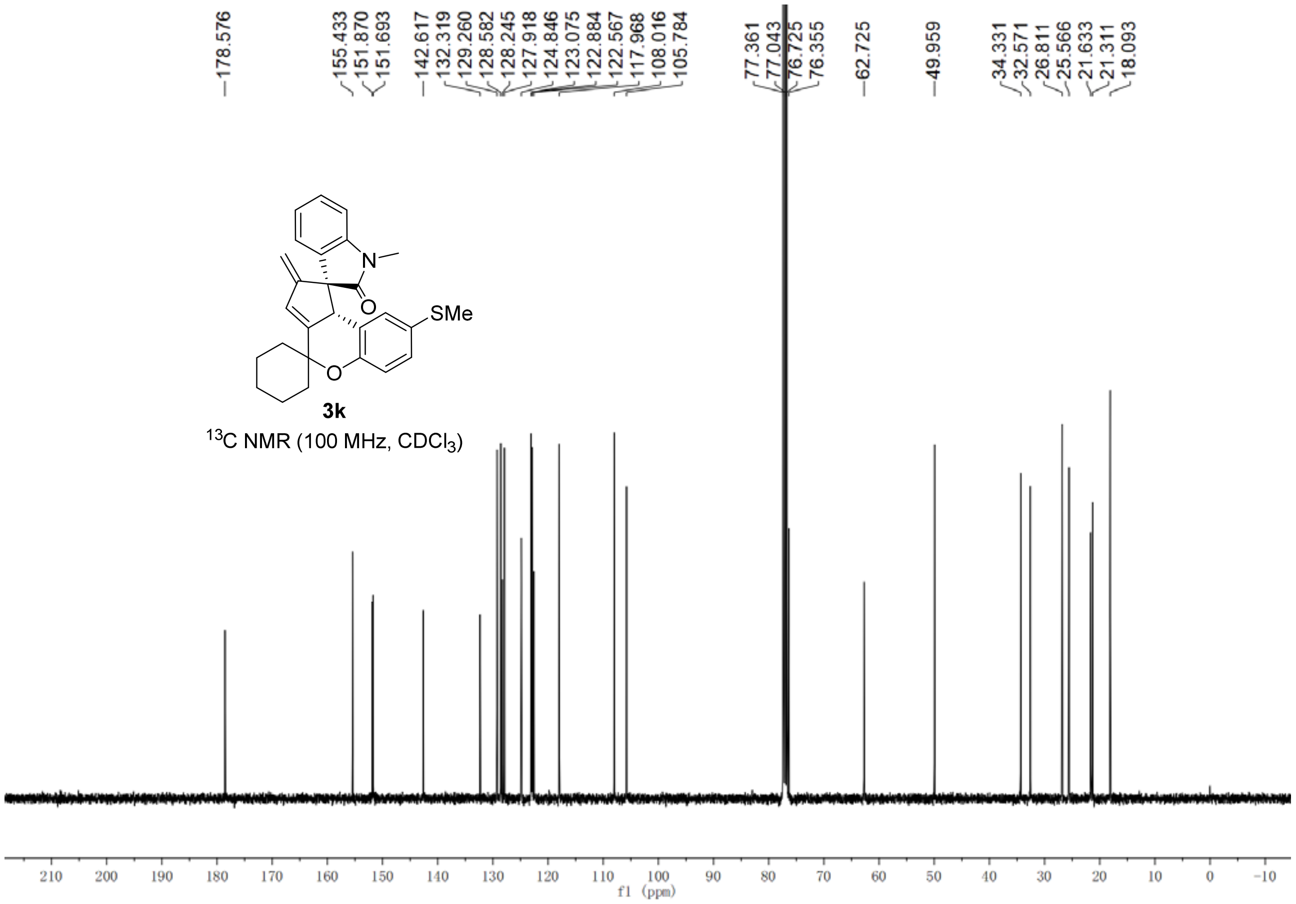
3j

(ESI-TOF) *m/z*: $[M + H]^+$

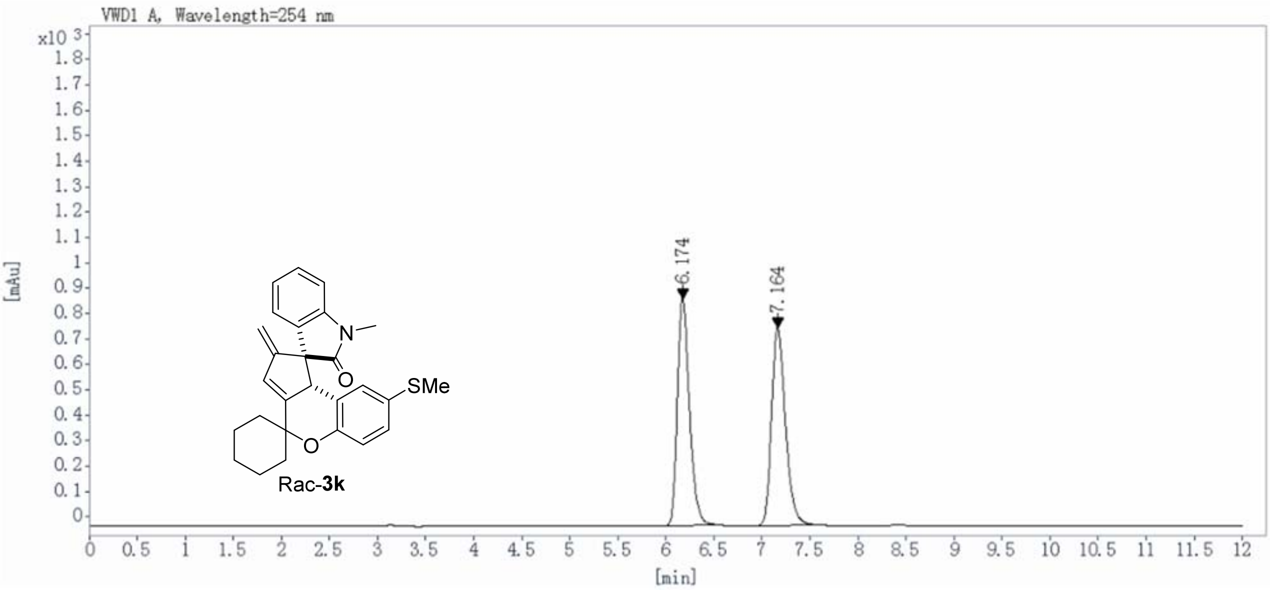
Calcd for $C_{27}H_{28}NO_3^+$ 414.2064


3k

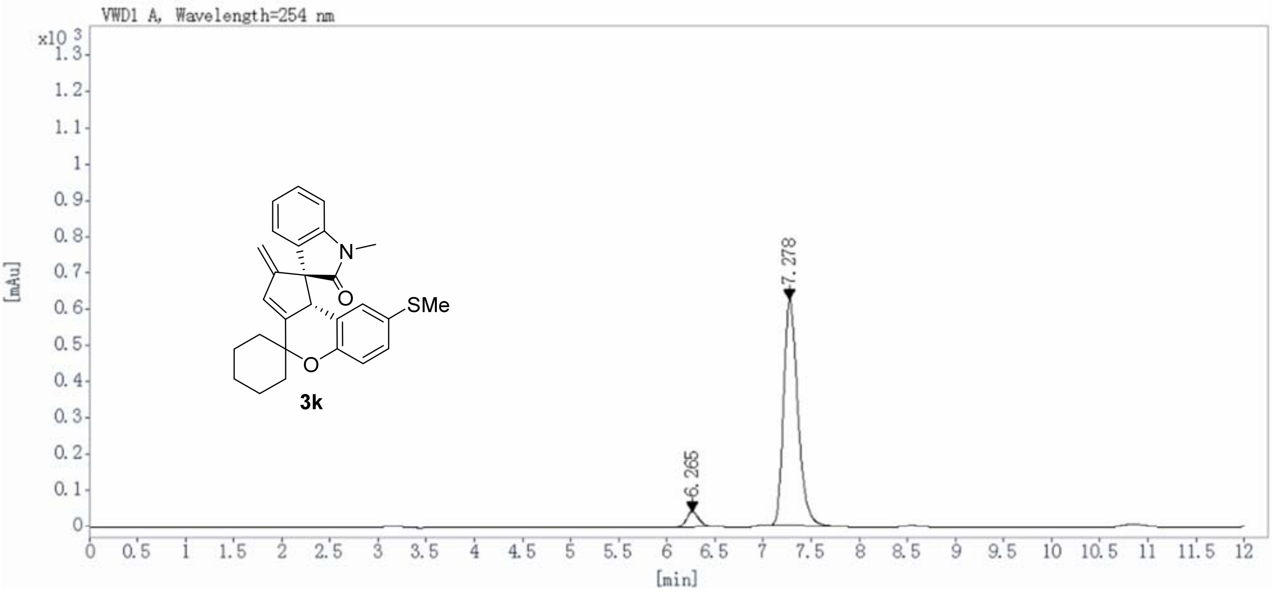
^{1}H NMR (400 MHz, $CDCl_3$)


3k

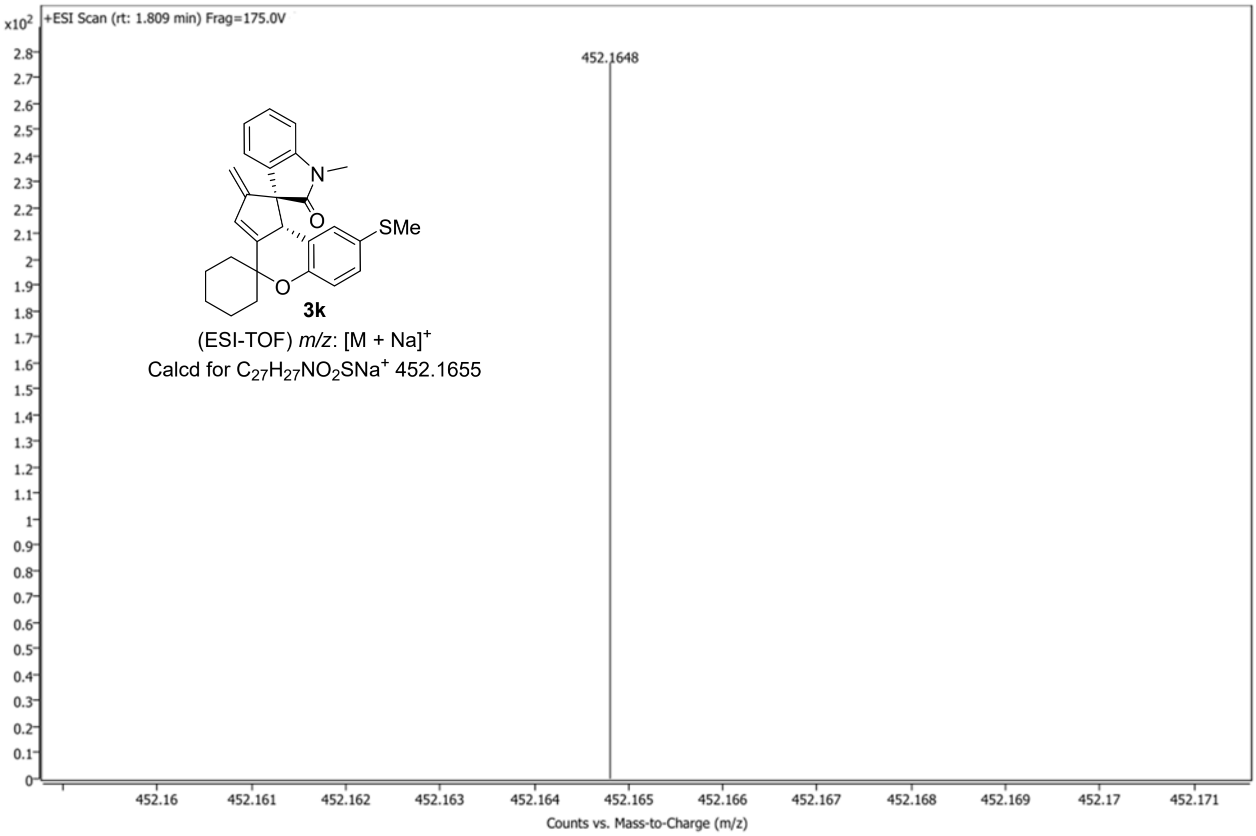
^{13}C NMR (100 MHz, $CDCl_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.174	BBA	0.13	892.4514	7819.1255	49.9049
7.164	BBA	0.15	777.7509	7848.9243	50.0951
			Totals:	15668.0498	100.0000



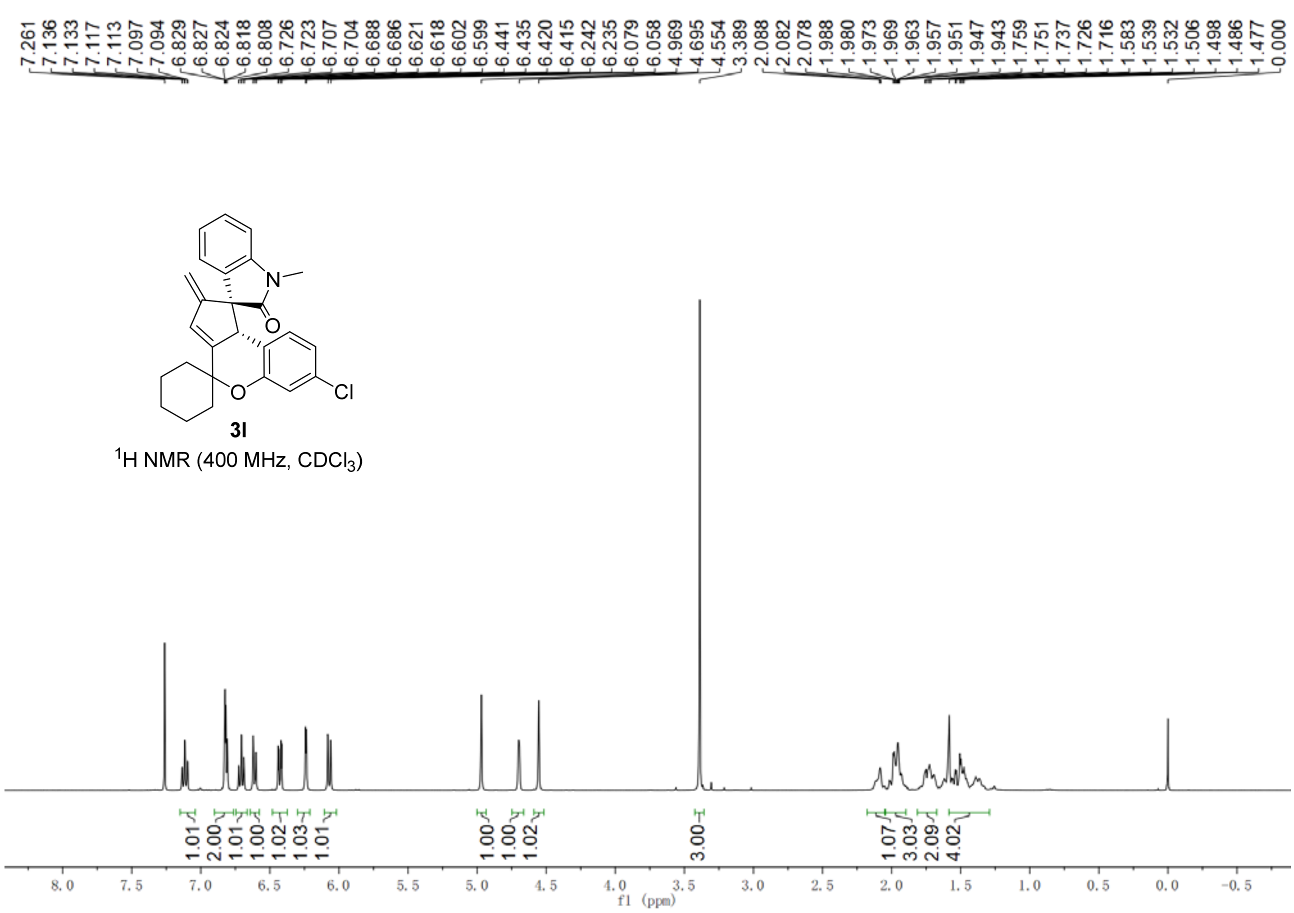
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.265	BBA	0.14	42.4012	373.2176	5.4791
7.278	BBA	0.16	623.3853	6438.4448	94.5209
			Totals:	6811.6624	100.0000



3k

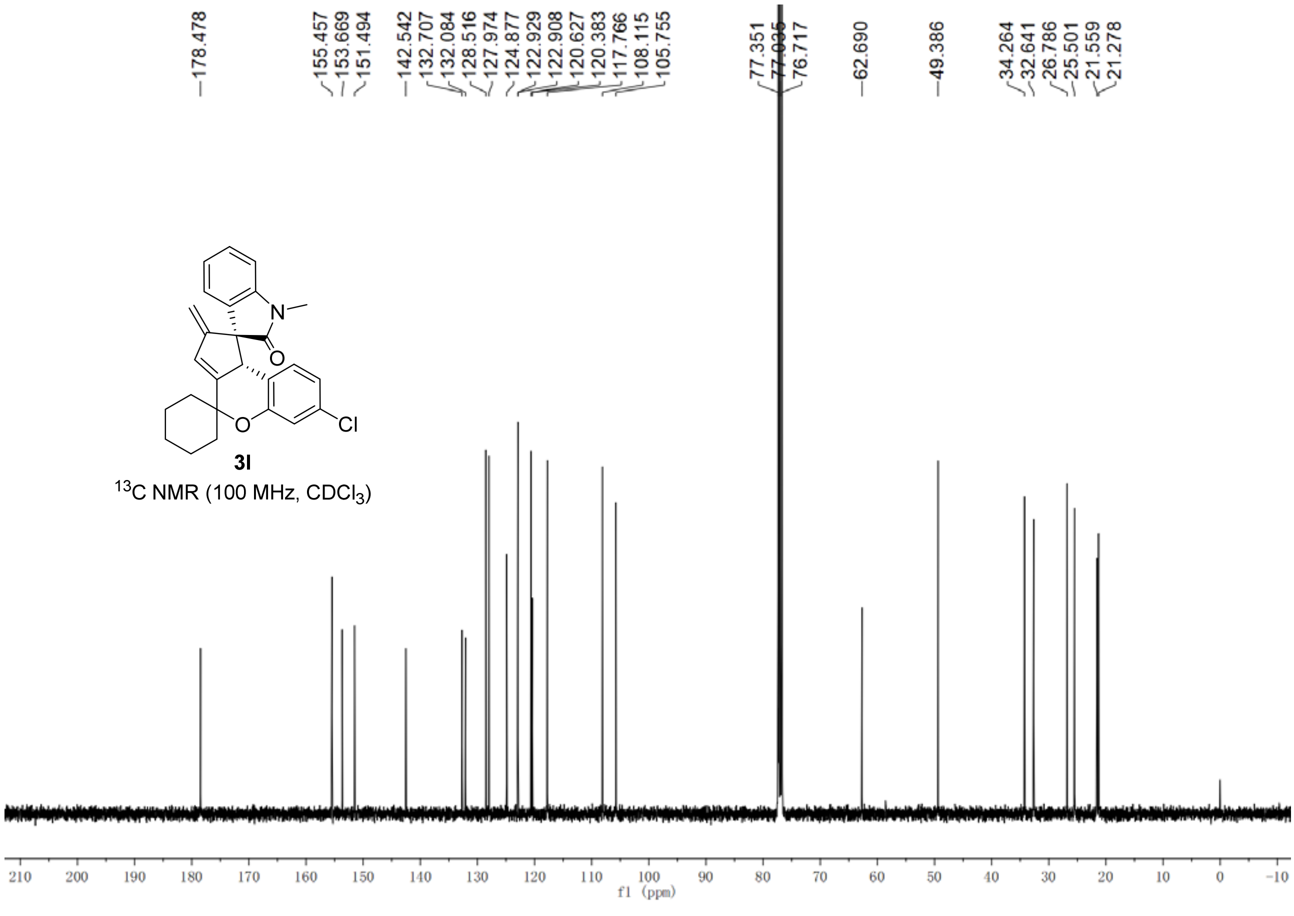
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{27}H_{27}NO_2SNa^+$ 452.1655



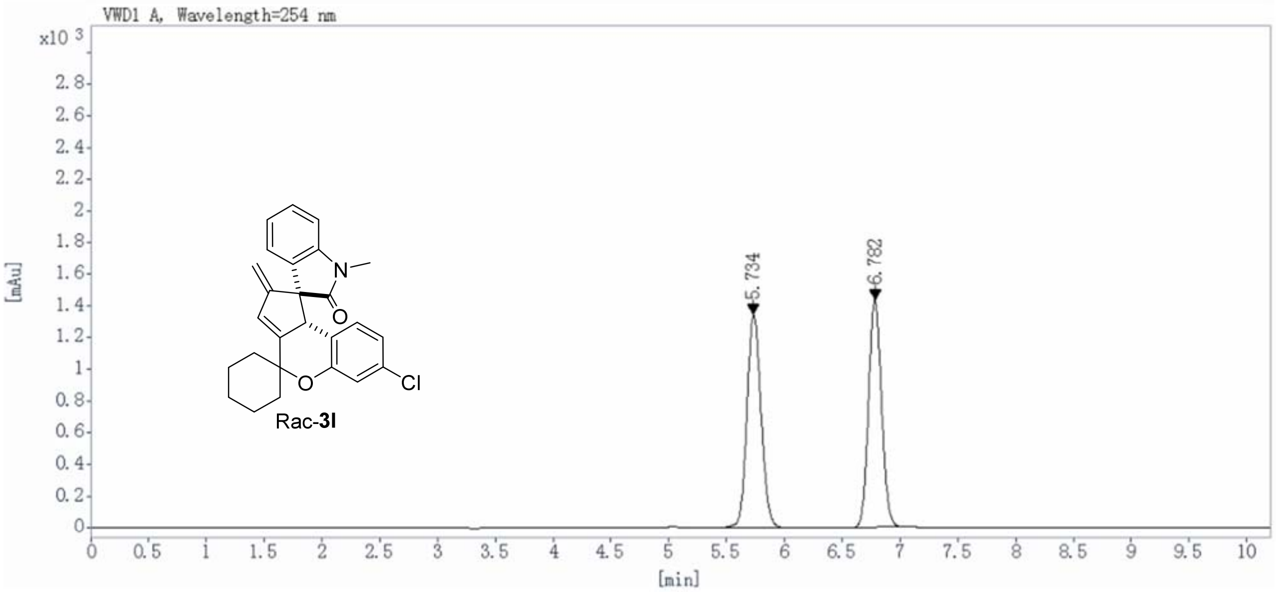
3l

^{1}H NMR (400 MHz, CDCl$_3$)

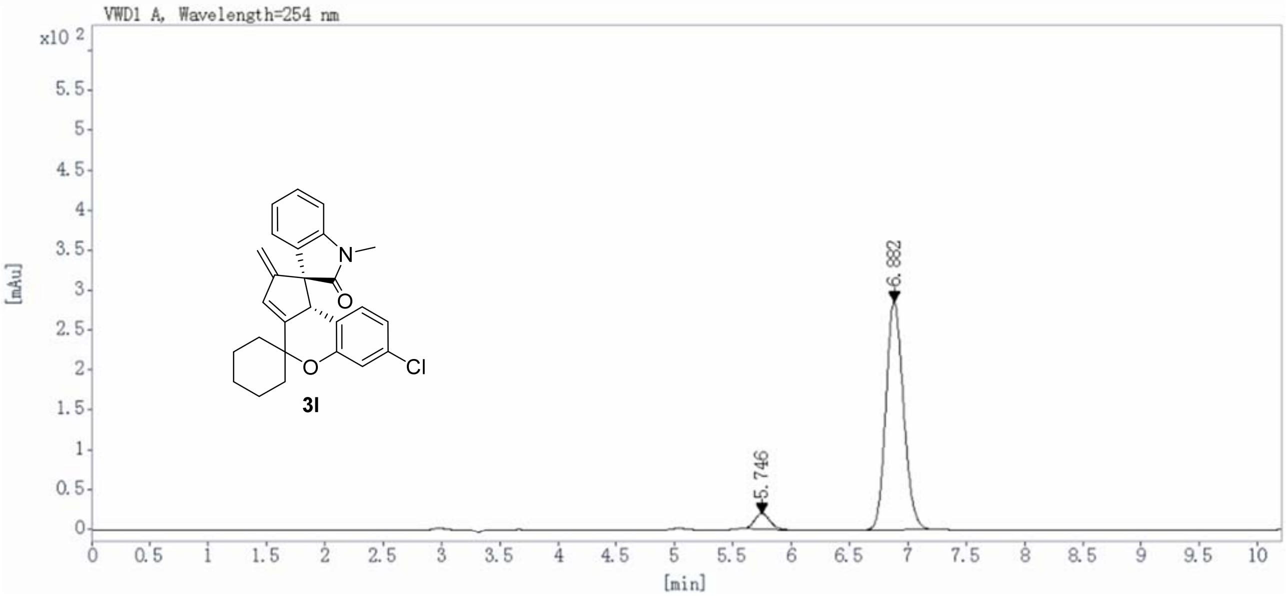


3l

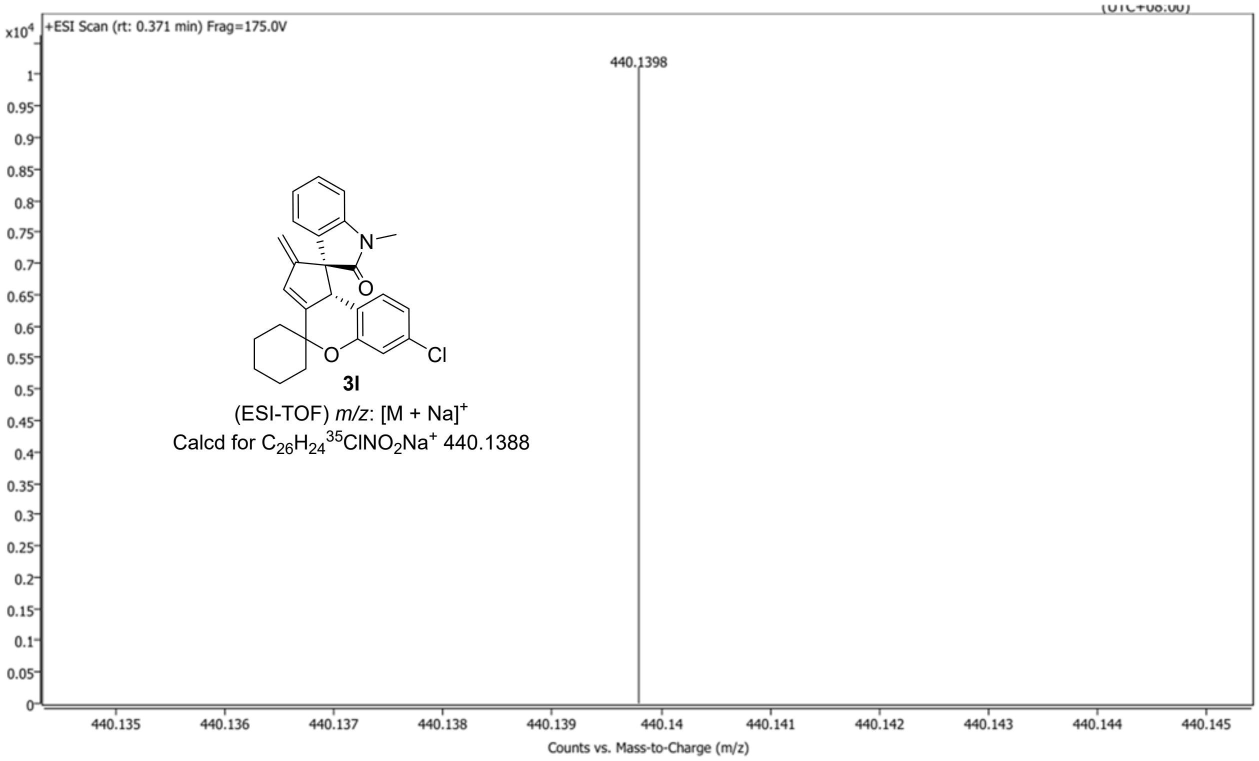
^{13}C NMR (100 MHz, CDCl$_3$)


Rac-**3l**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.734	BBA	0.13	1342.9154	11408.9932	50.4141
6.782	BB	0.12	1436.9625	11221.5811	49.5859
			Totals:	22630.5742	100.0000


3l

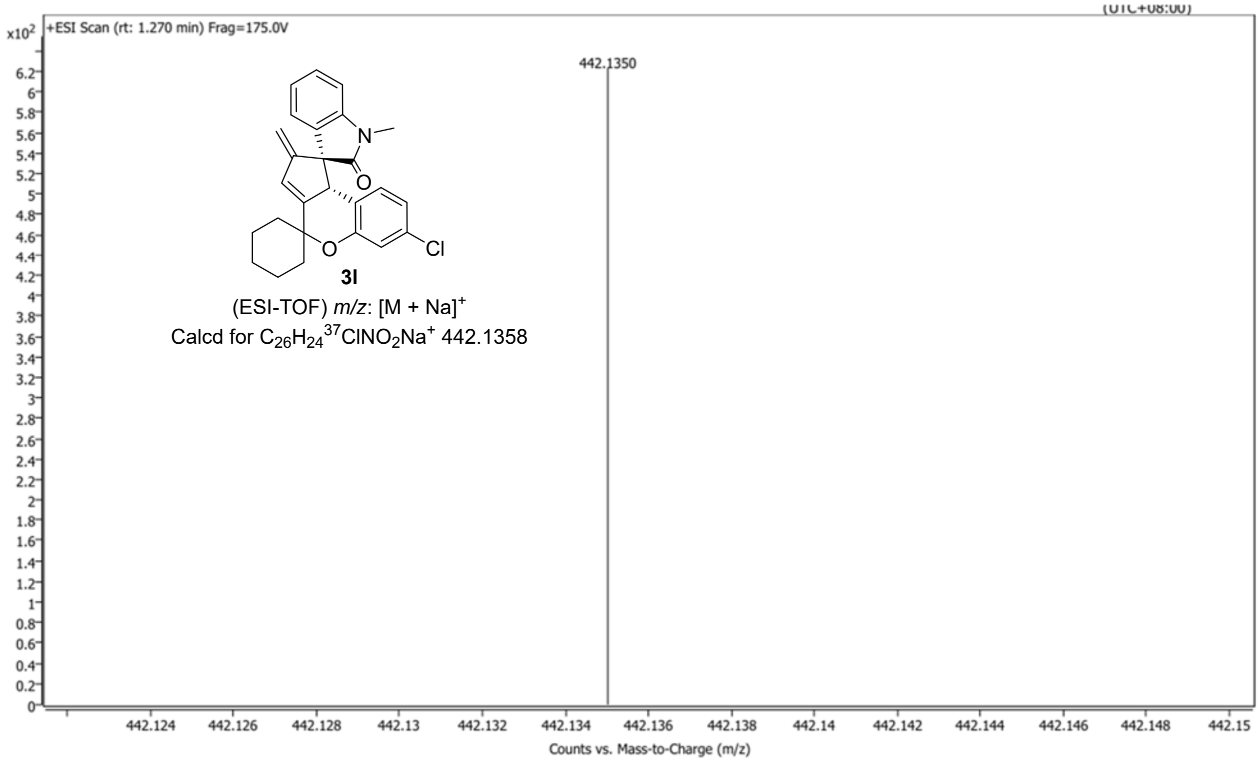
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.746	BBA	0.14	19.8359	184.5714	5.7821
6.882	BBA	0.16	285.8464	3007.5542	94.2179
			Totals:	3192.1256	100.0000



3l

(ESI-TOF) *m/z*: [M + Na]$^+$

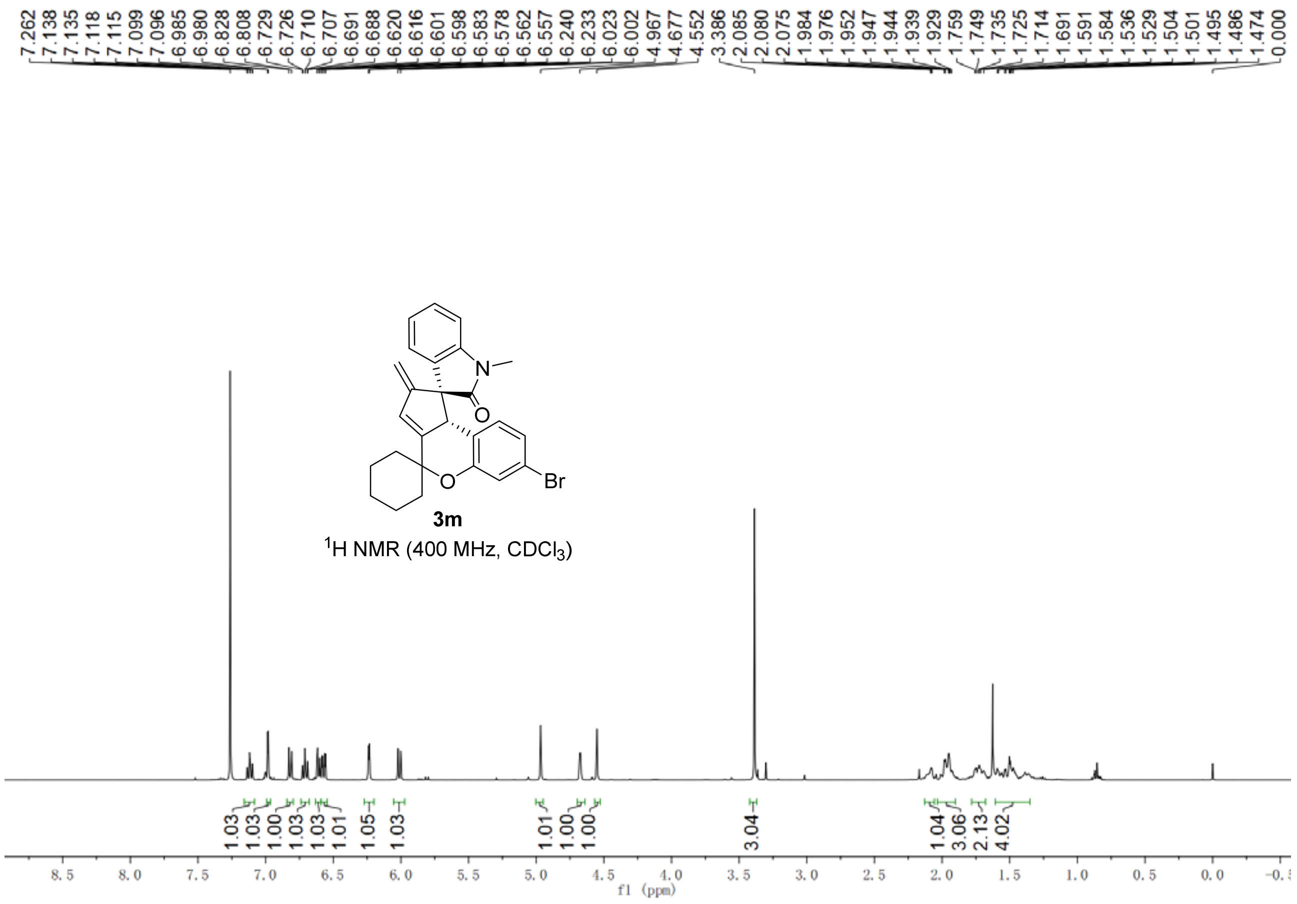
Calcd for $C_{26}H_{24}{}^{35}ClNO_2Na^+$ 440.1388



3l

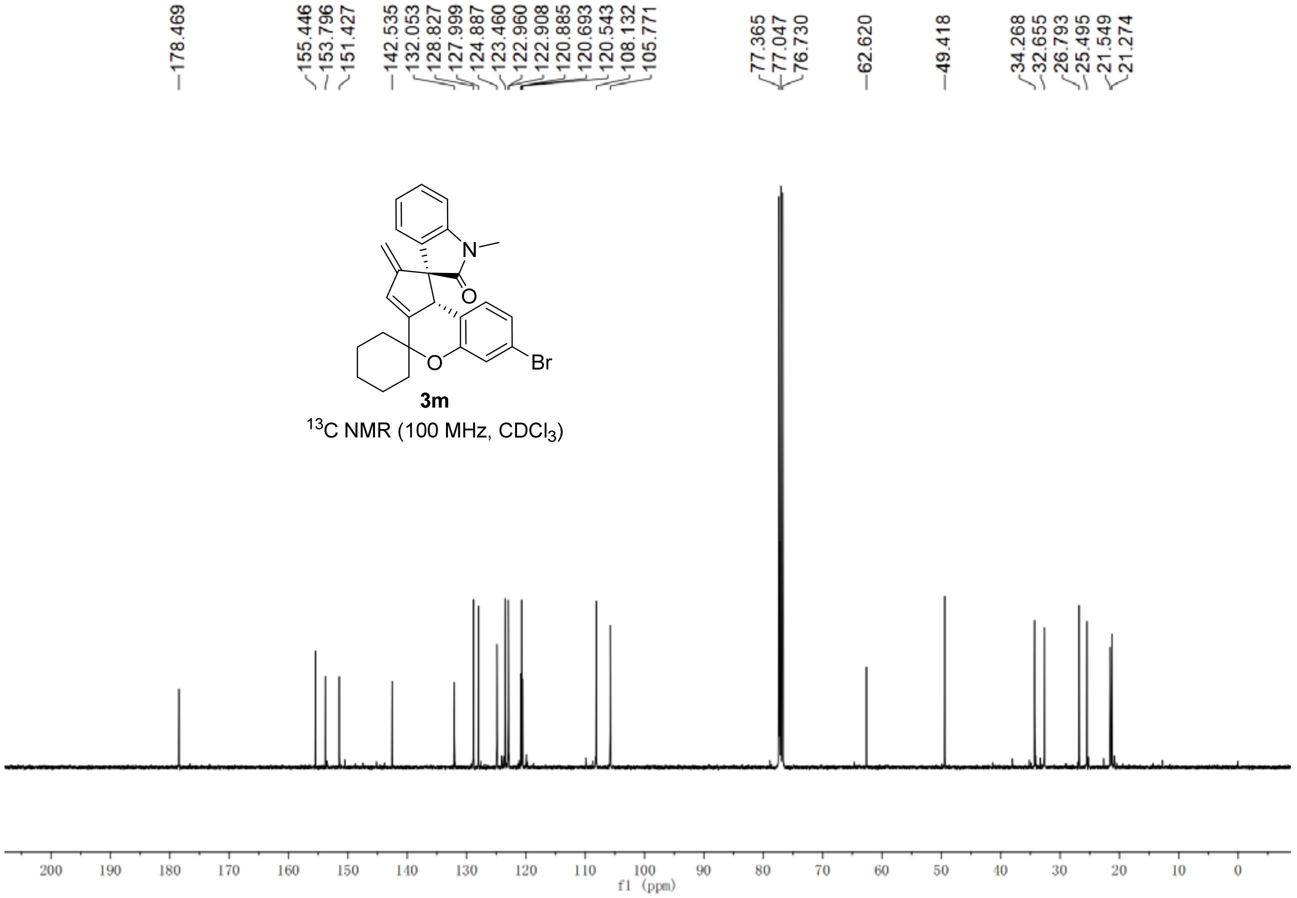
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{26}H_{24}{}^{37}ClNO_2Na^+$ 442.1358



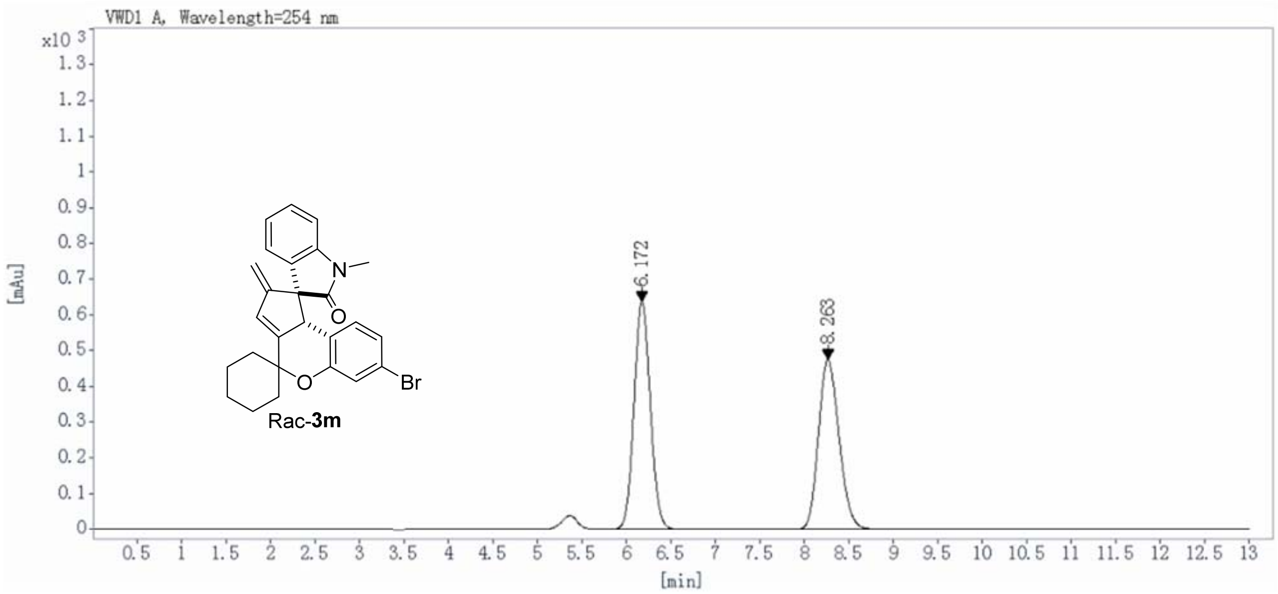
3m

^{1}H NMR (400 MHz, CDCl$_3$)



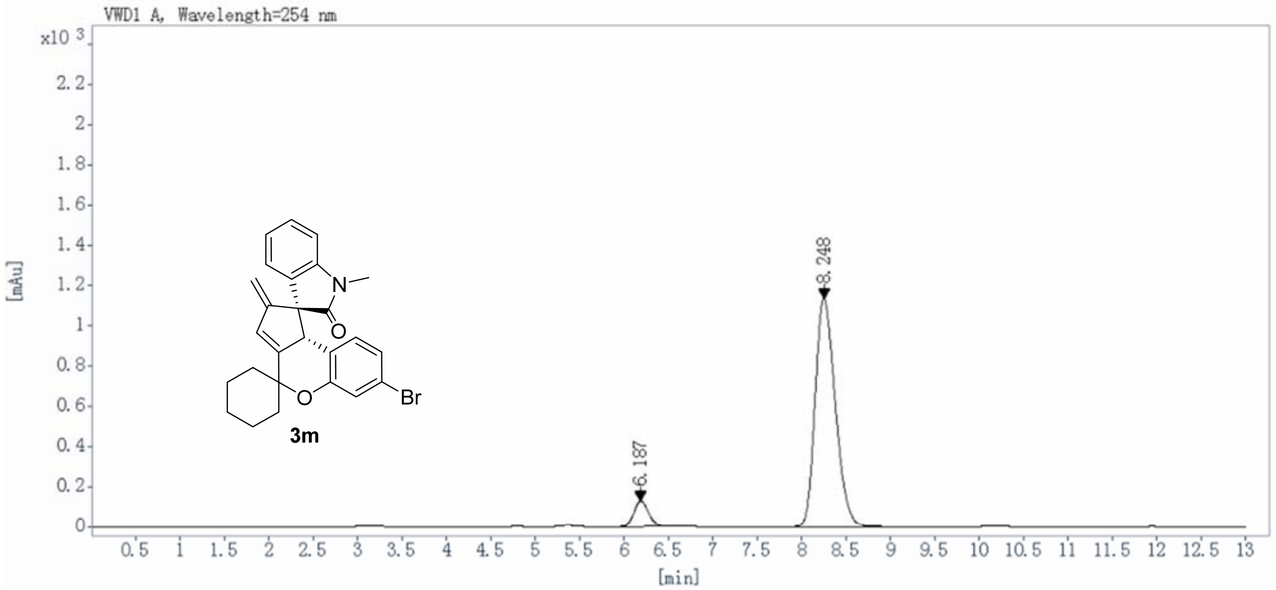
3m

^{13}C NMR (100 MHz, CDCl$_3$)



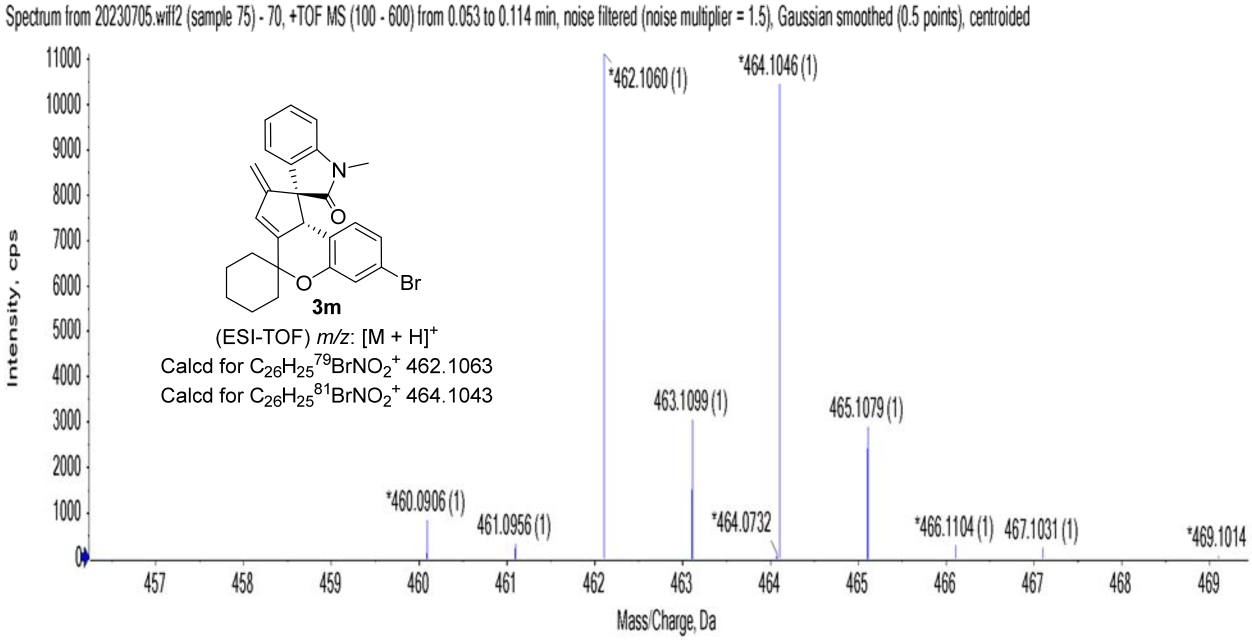
Rac-**3m**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.172	BBA	0.20	636.8077	8103.1338	51.3770
8.263	BB	0.25	474.3646	7668.7861	48.6230
			Totals:	15771.9199	100.0000



3m

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.187	BB	0.17	126.9802	1423.3439	7.4052
8.248	BBA	0.24	1134.6816	17797.6406	92.5948
			Totals:	19220.9845	100.0000

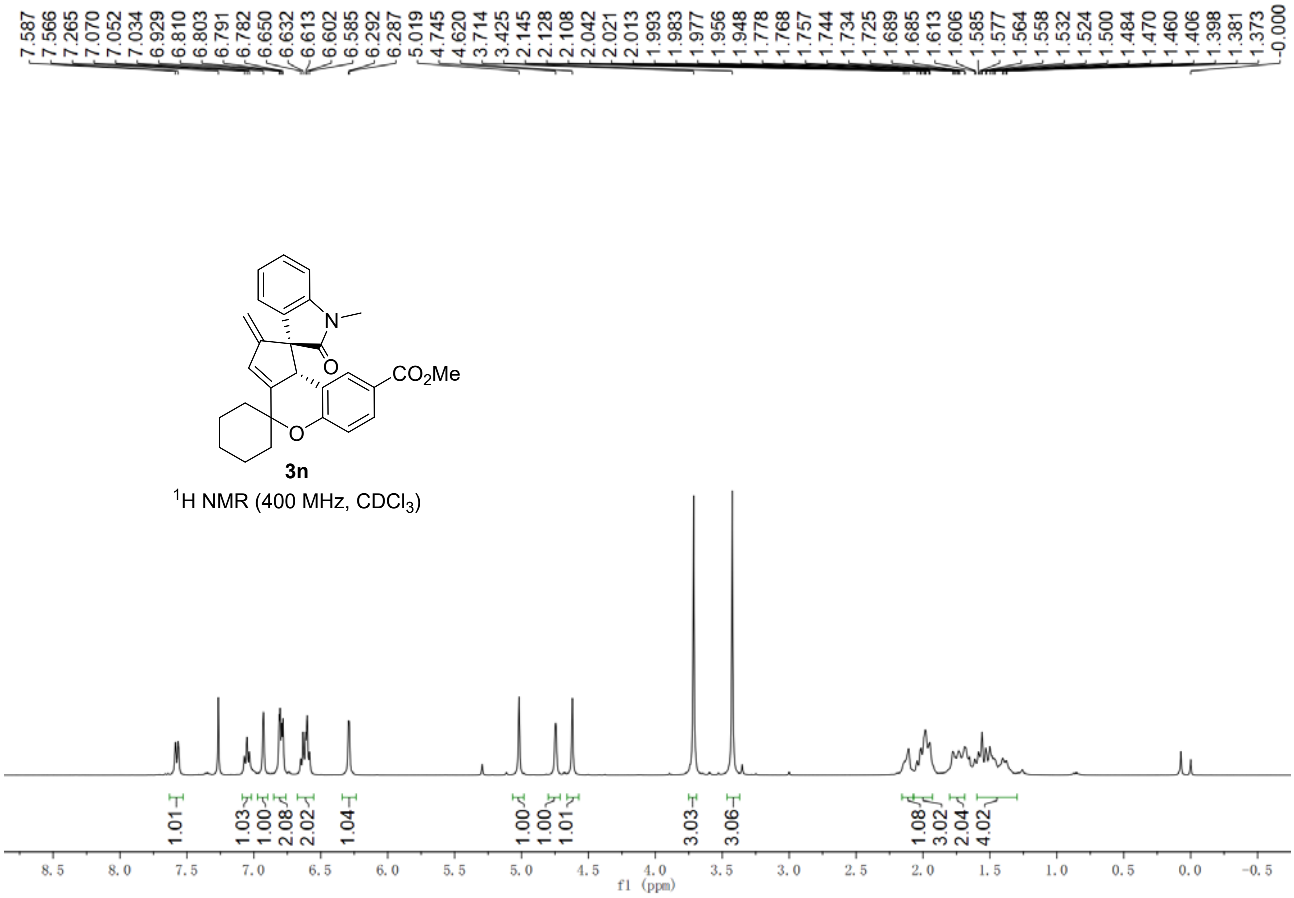


3m

(ESI-TOF) *m/z*: [M + H]$^+$

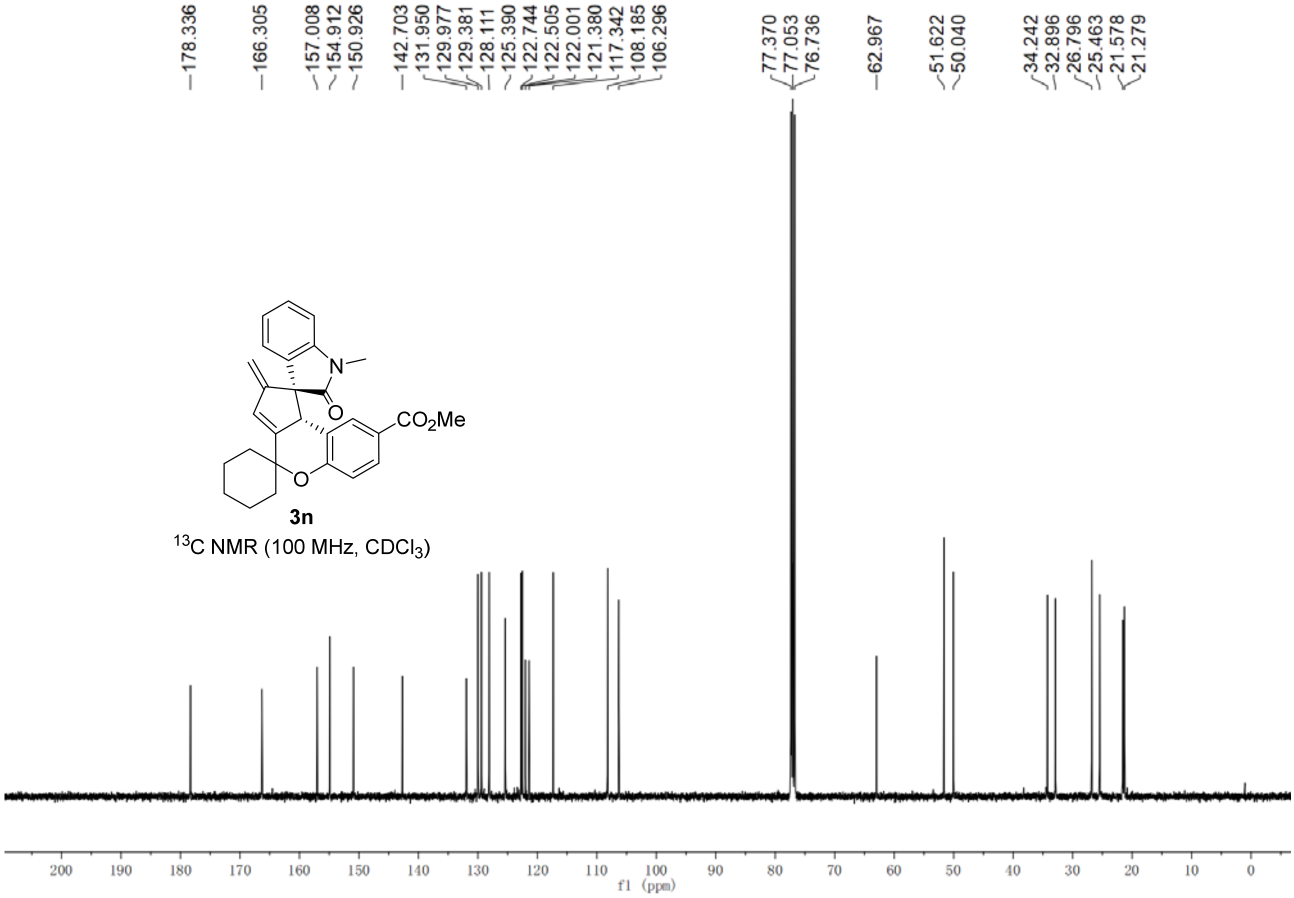
Calcd for $C_{26}H_{25}{}^{79}BrNO_2^+$ 462.1063

Calcd for $C_{26}H_{25}{}^{81}BrNO_2^+$ 464.1043



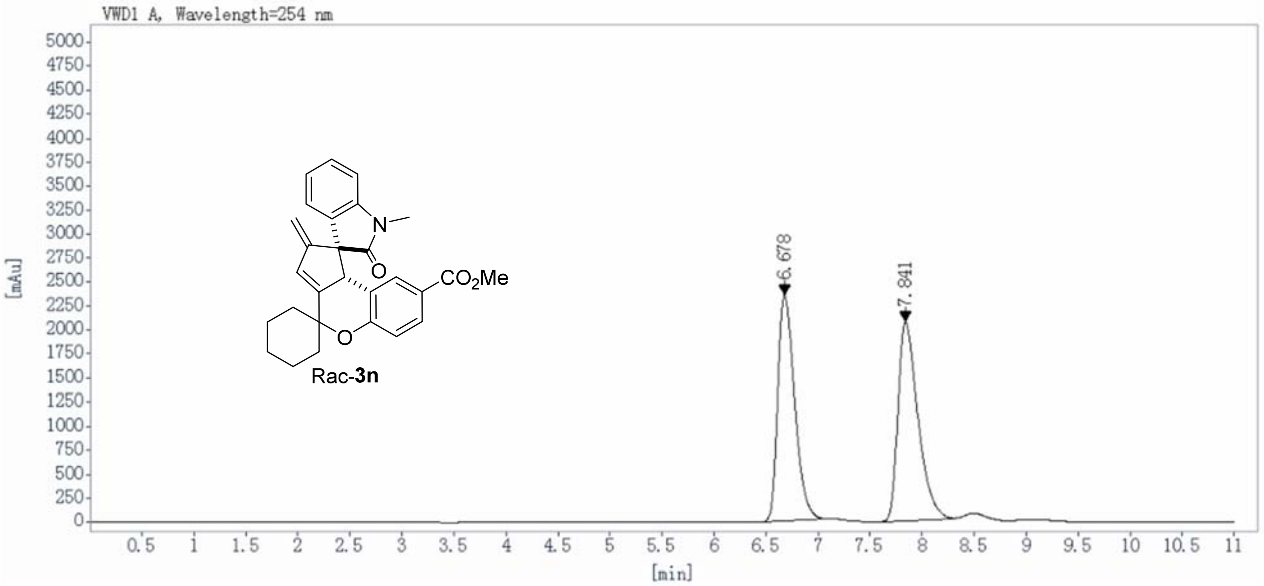
3n

^{1}H NMR (400 MHz, CDCl$_3$)



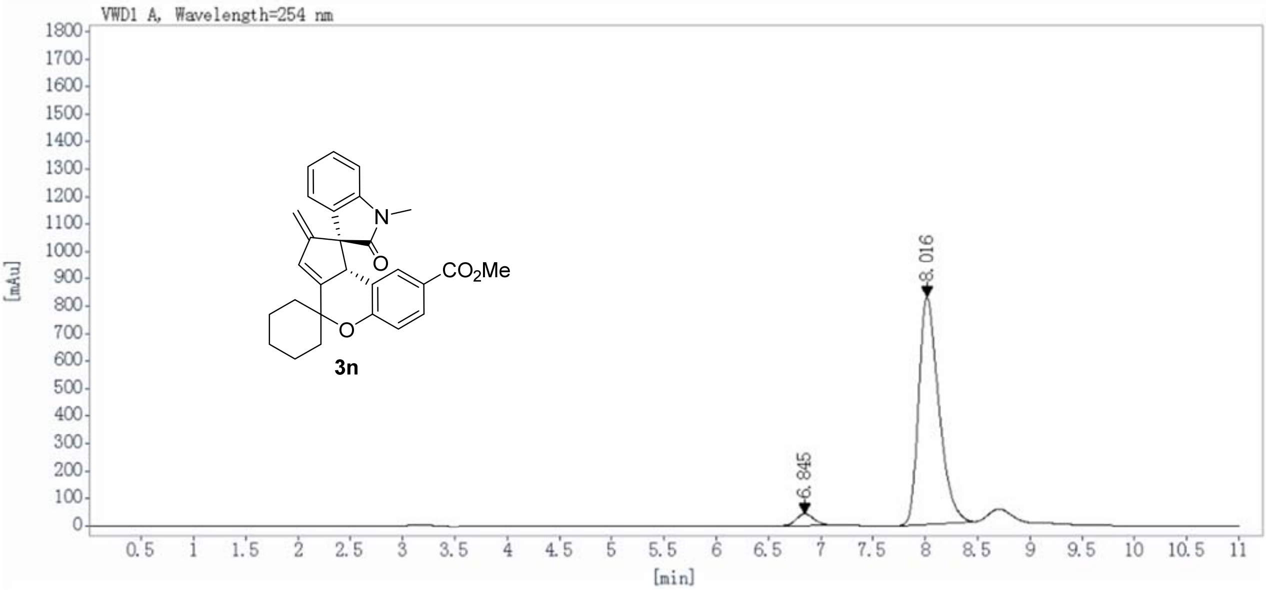
3n

^{13}C NMR (100 MHz, CDCl$_3$)



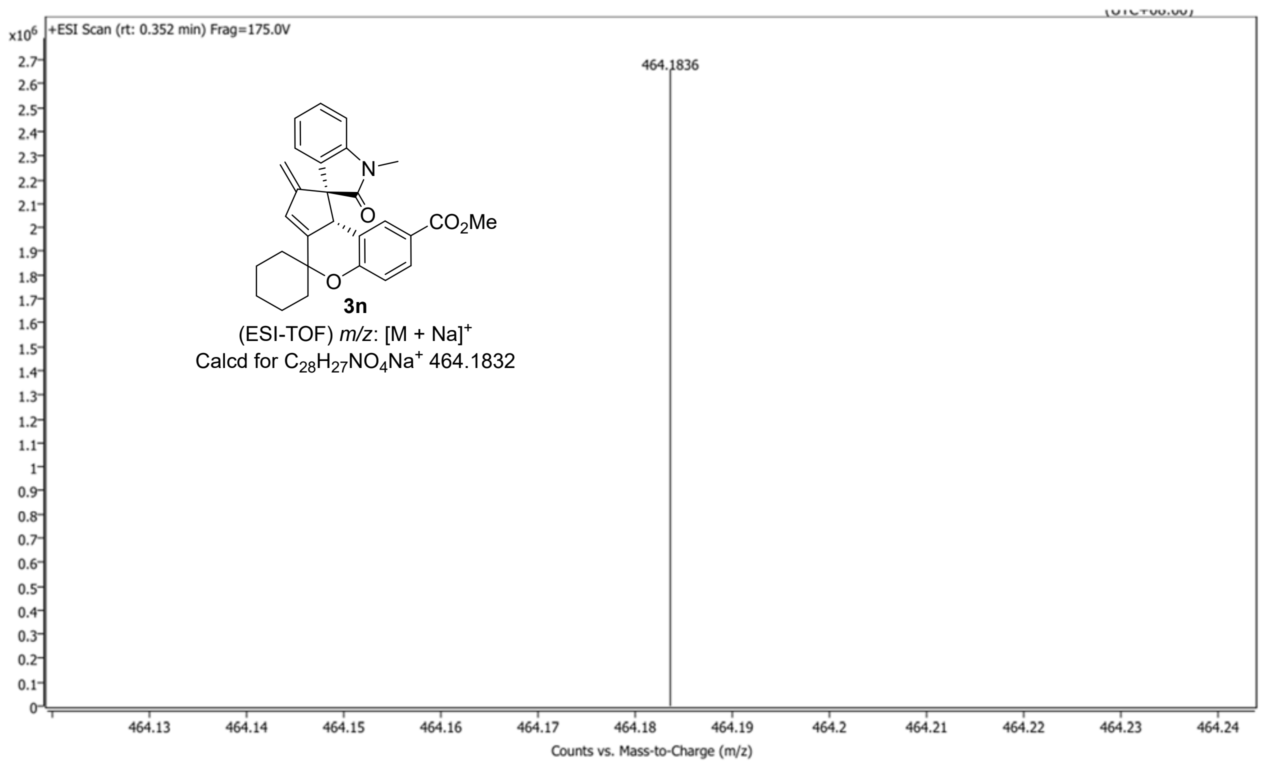
Rac-**3n**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.678	BB	0.17	2350.3589	26511.5176	49.0665
7.841	BB	0.20	2061.8716	27520.2773	50.9335
			Totals:	54031.7949	100.0000



3n

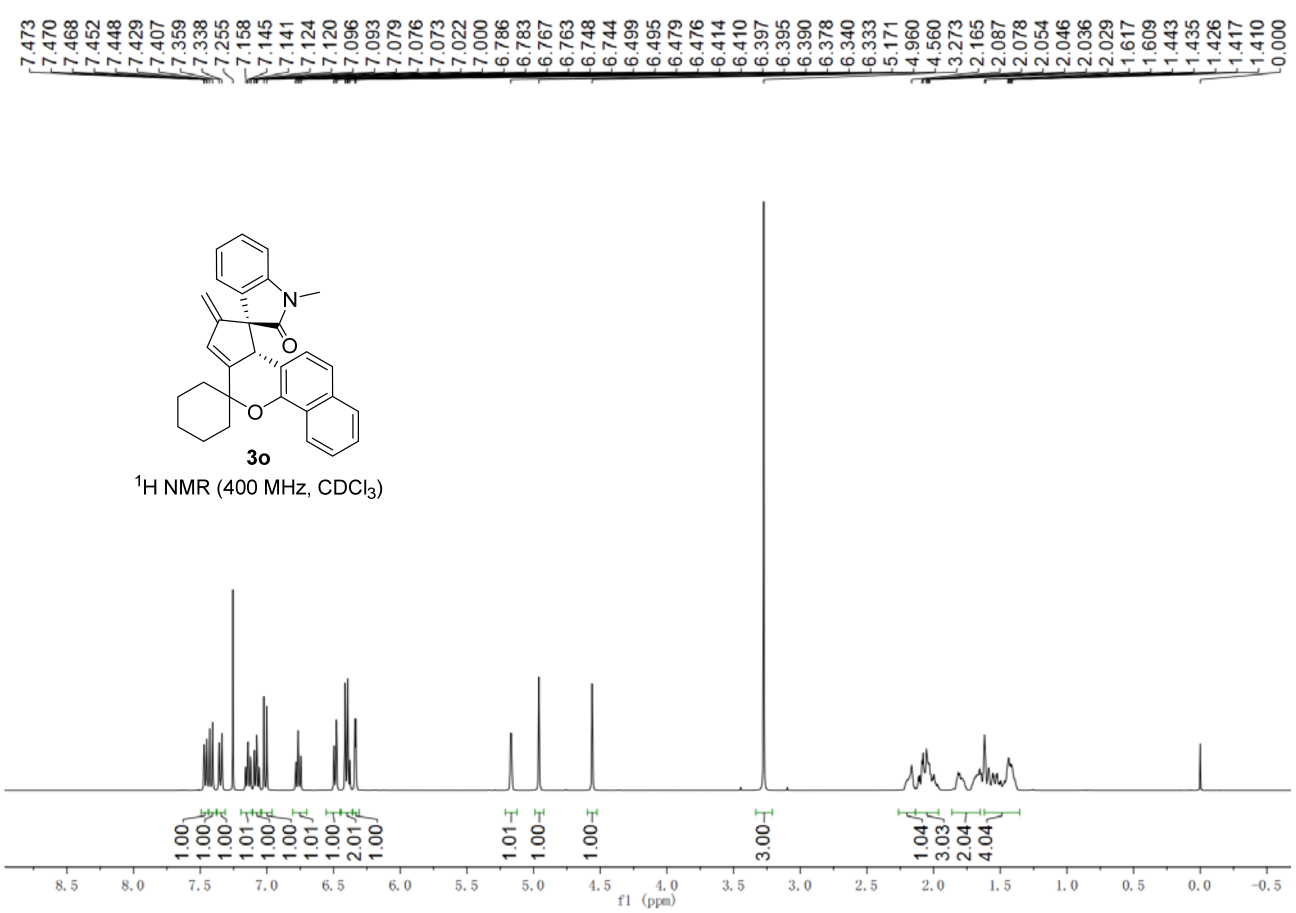
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.845	BBA	0.18	42.4669	508.9646	4.3805
8.016	BB	0.21	825.9418	11109.8457	95.6195
			Totals:	11618.8103	100.0000



3n

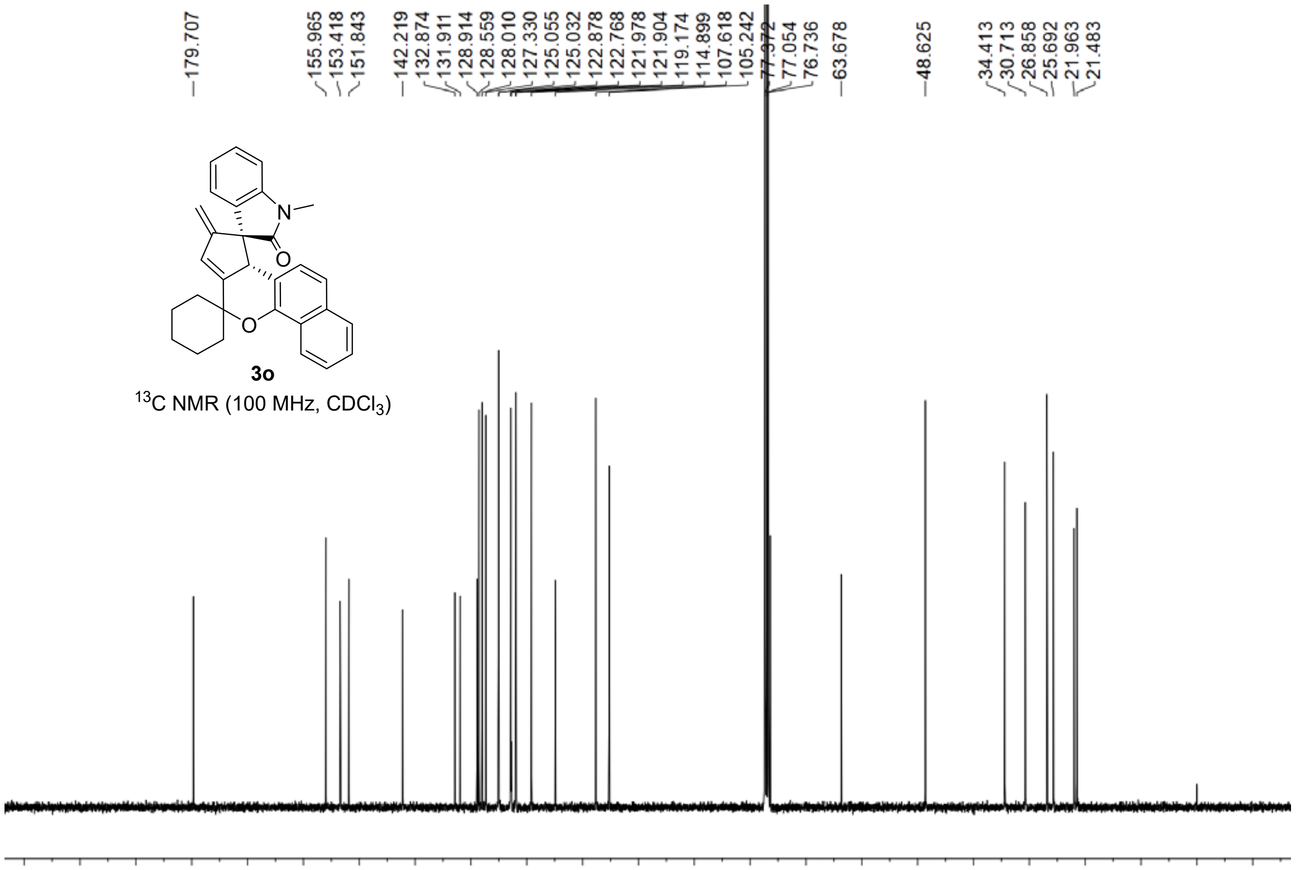
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{28}H_{27}NO_4Na^+$ 464.1832



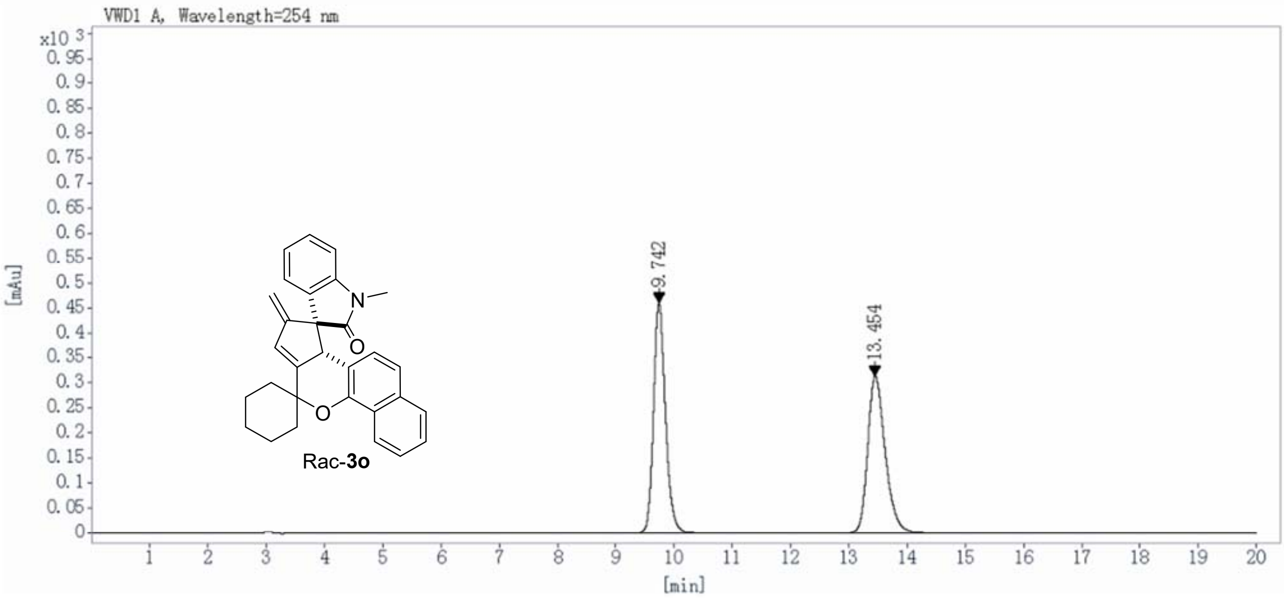
3o

^{1}H NMR (400 MHz, CDCl$_3$)

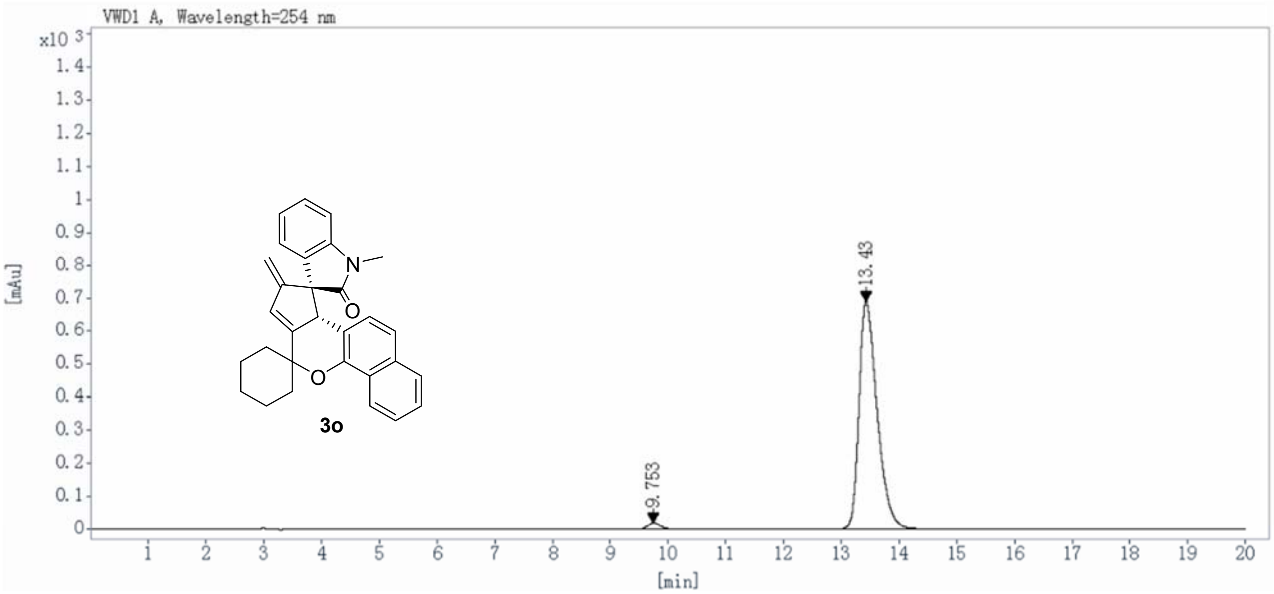


3o

^{13}C NMR (100 MHz, CDCl$_3$)

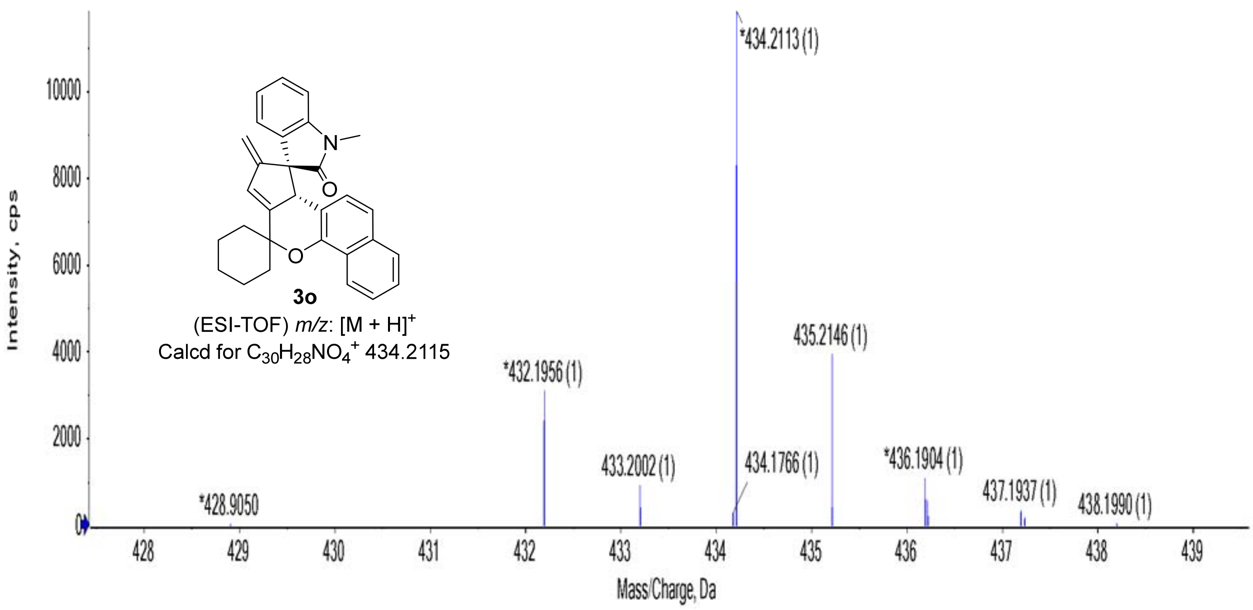


Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
9.742	BBA	0.22	460.1235	6490.4111	49.9937
13.454	BBA	0.32	313.6683	6492.0356	50.0063
			Totals:	12982.4468	100.0000



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
9.753	BBA	0.21	19.0634	265.1130	1.7354
13.430	BBA	0.33	690.0911	15012.0088	98.2646
			Totals:	15277.1218	100.0000

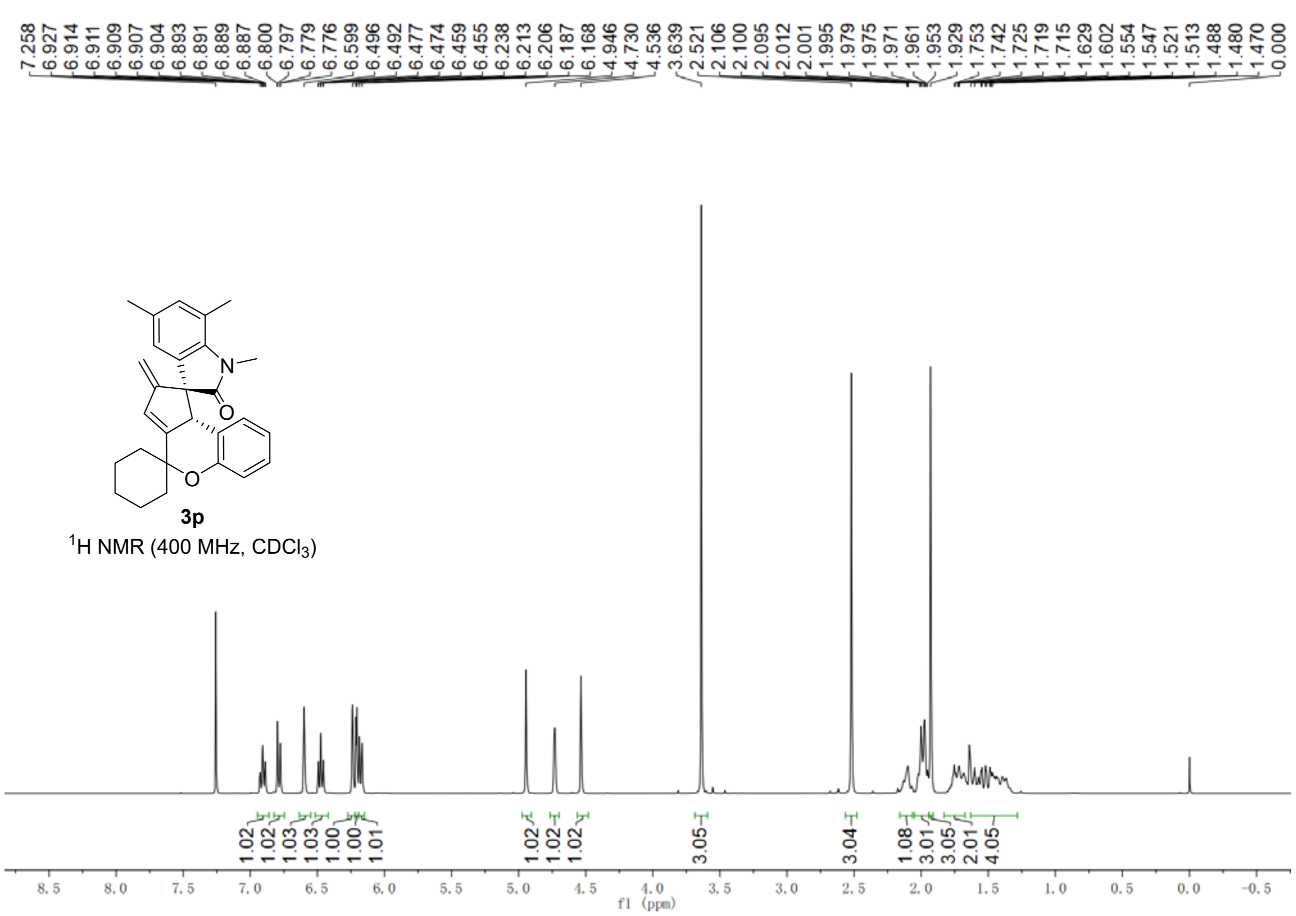
Spectrum from 20230705.wiff2 (sample 79) - 74, +TOF MS (100 - 600) from 0.059 to 0.120 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points), centroided



3o

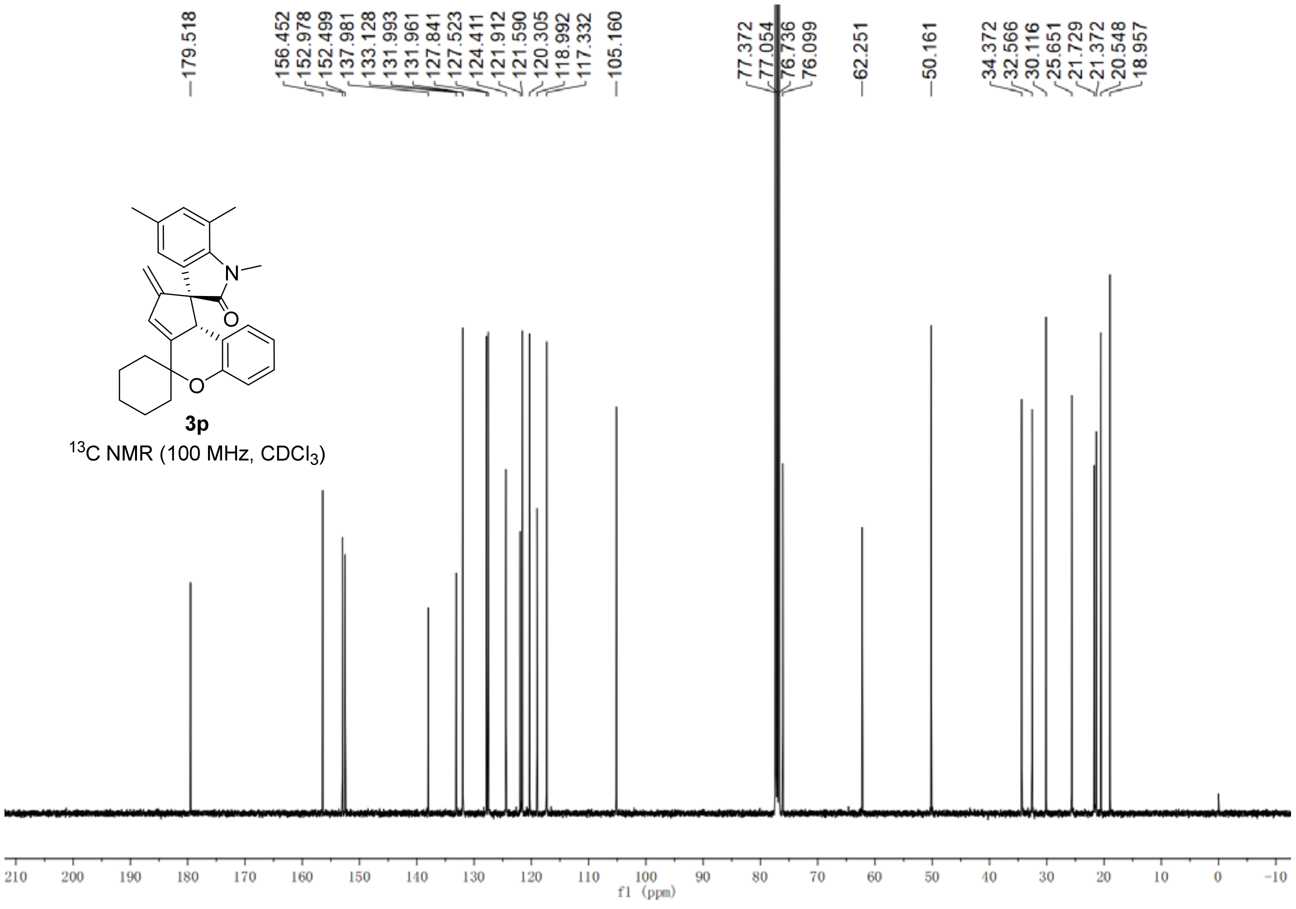
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{30}H_{28}NO_4^+$ 434.2115



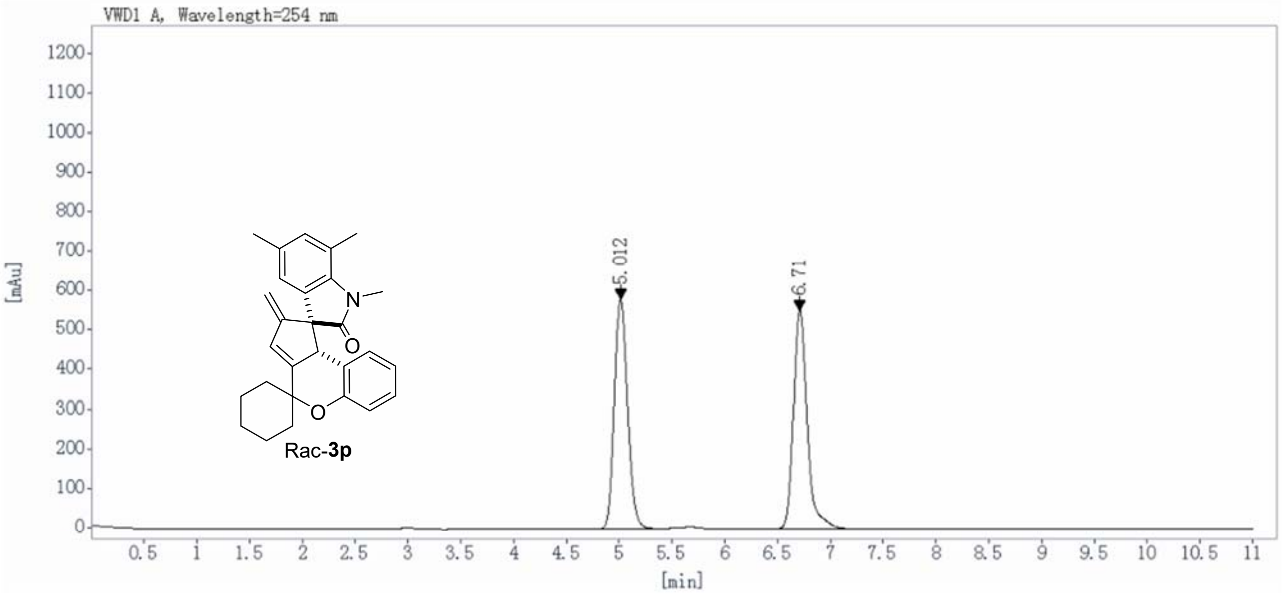
3p

^{1}H NMR (400 MHz, CDCl$_3$)



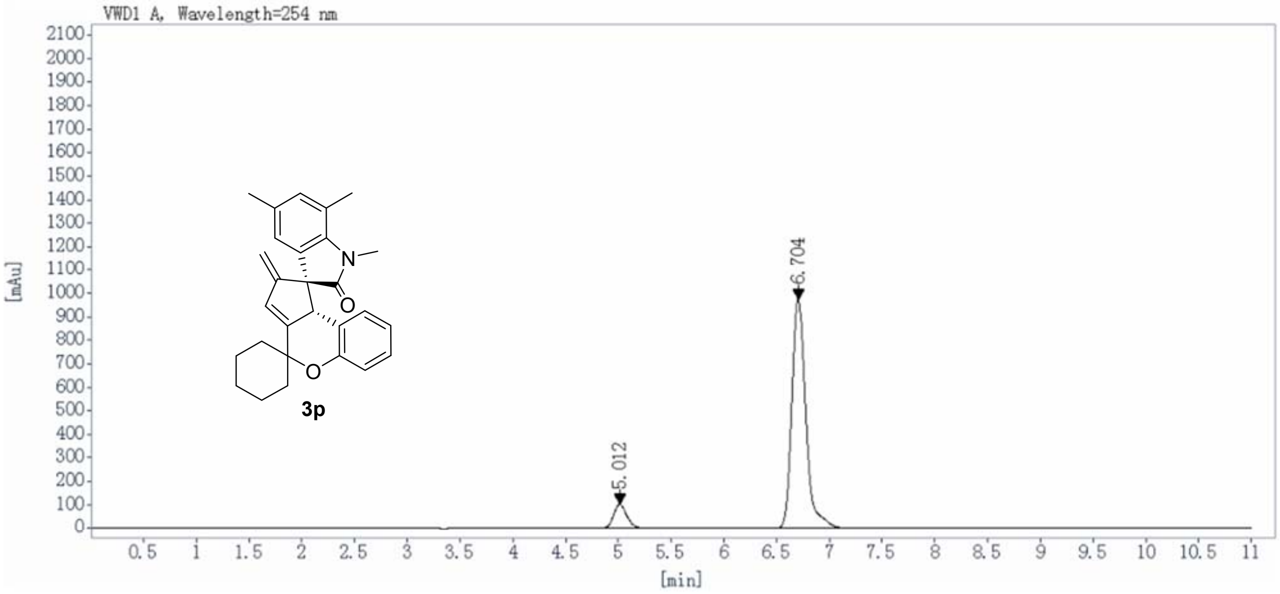
3p

^{13}C NMR (100 MHz, CDCl$_3$)



Rac-**3p**

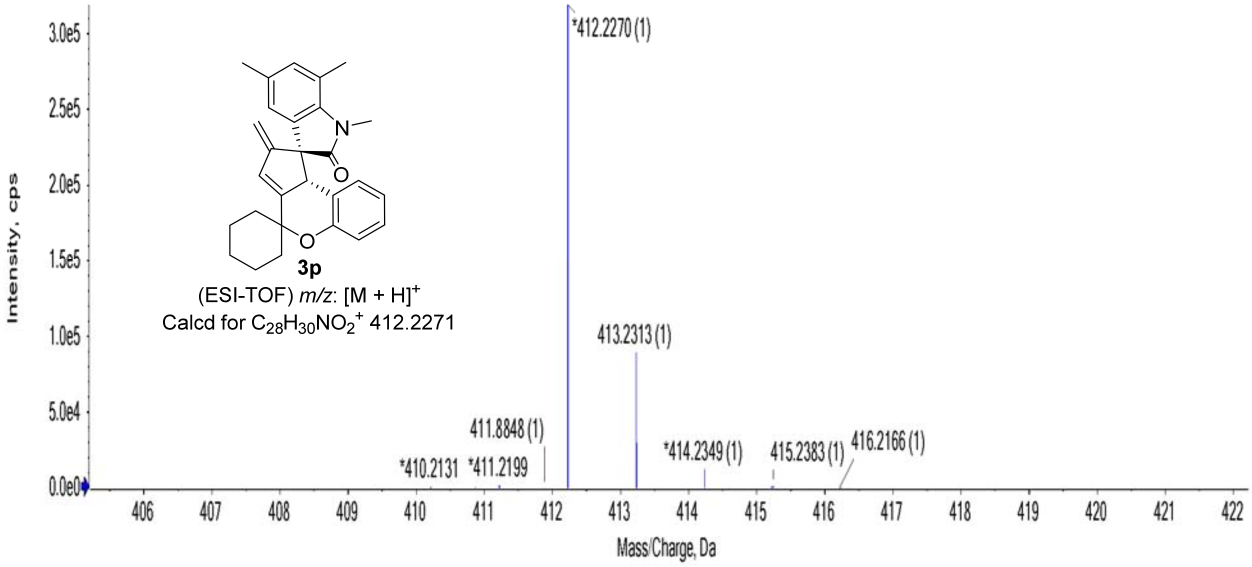
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.012	BBA	0.13	578.7755	5017.1655	50.0194
6.710	BBA	0.14	550.9875	5013.2646	49.9806
			Totals:	10030.4302	100.0000



3p

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.012	BB	0.13	102.0049	887.6588	9.0235
6.704	BBA	0.14	976.2433	8949.5518	90.9765
			Totals:	9837.2106	100.0000

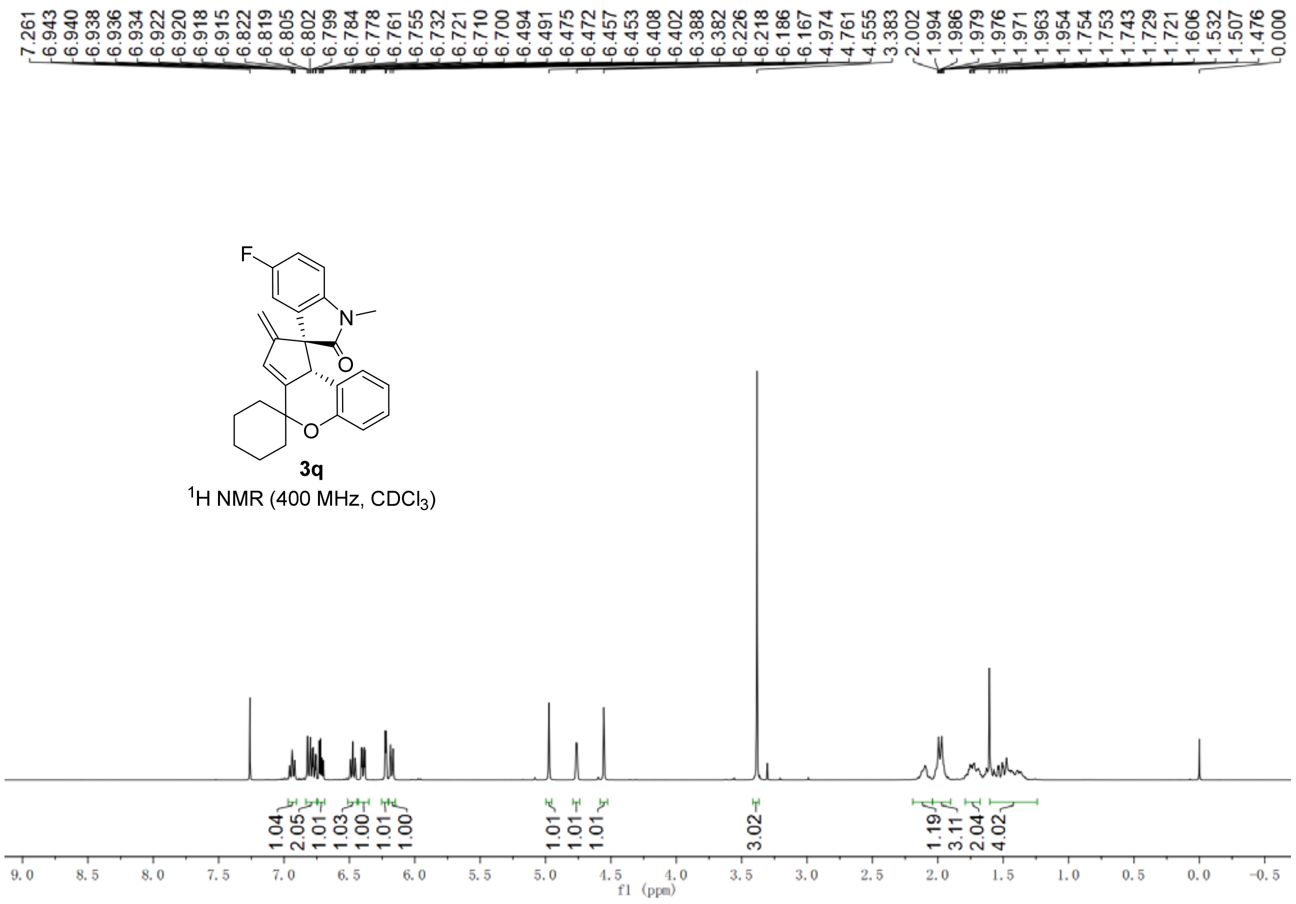
Spectrum from 20230705.wiff2 (sample 72) - 67, +TOF MS (100 - 600) from 0.044 to 0.106 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points), Recalibrated, centroided



3p

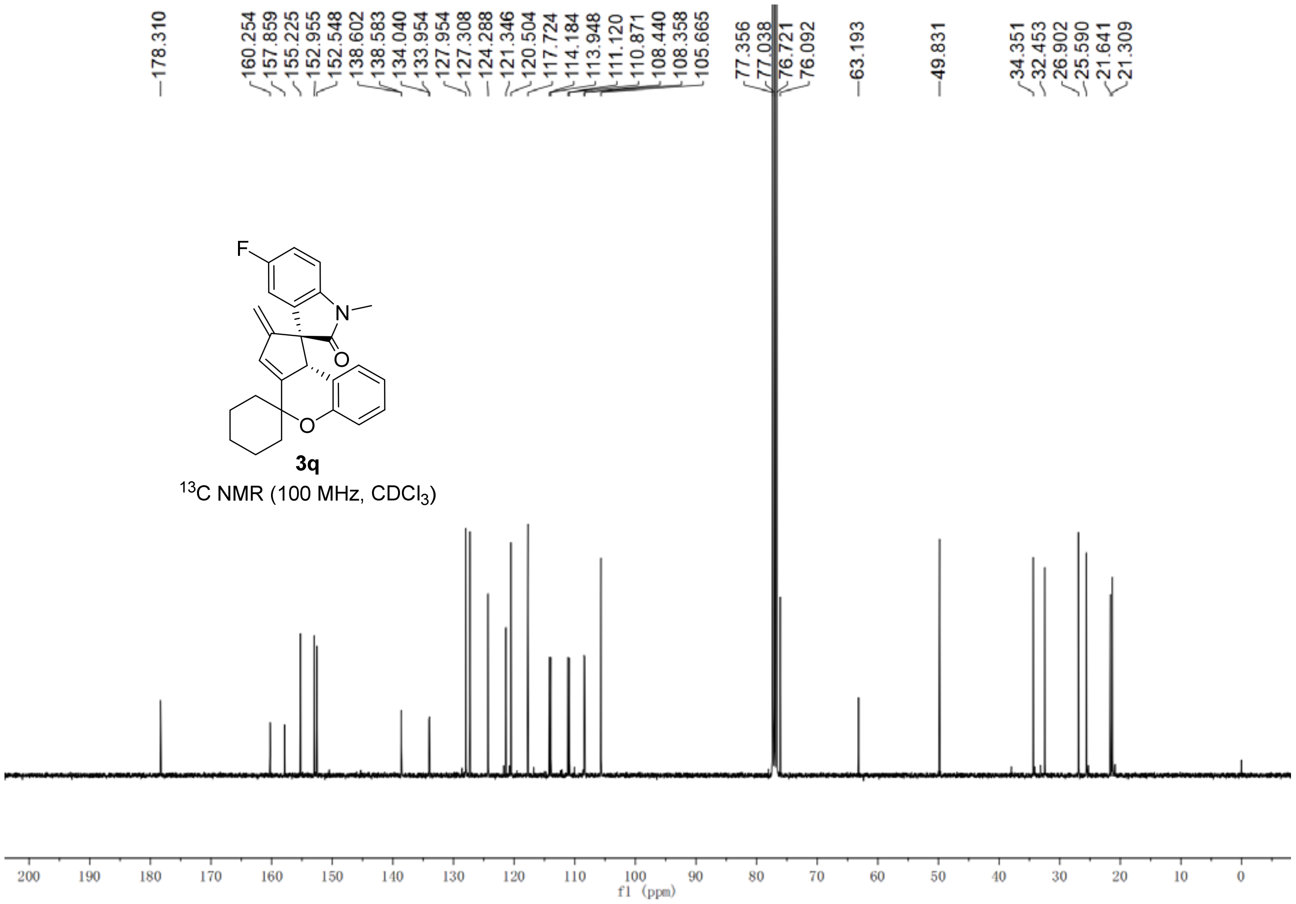
(ESI-TOF) *m/z*: [M + H]$^+$

Calcd for $C_{28}H_{30}NO_2^+$ 412.2271



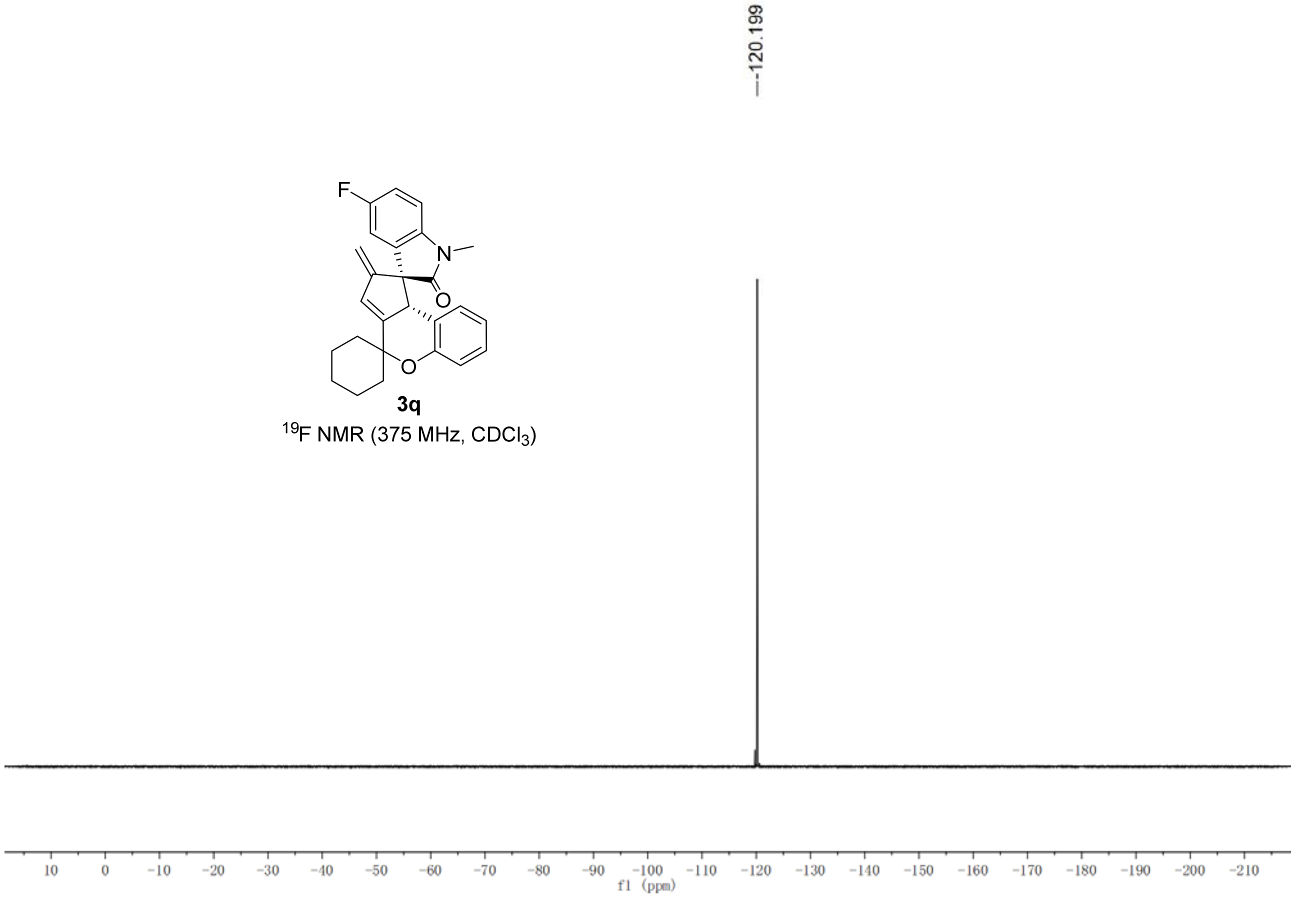
3q

^{1}H NMR (400 MHz, CDCl$_3$)



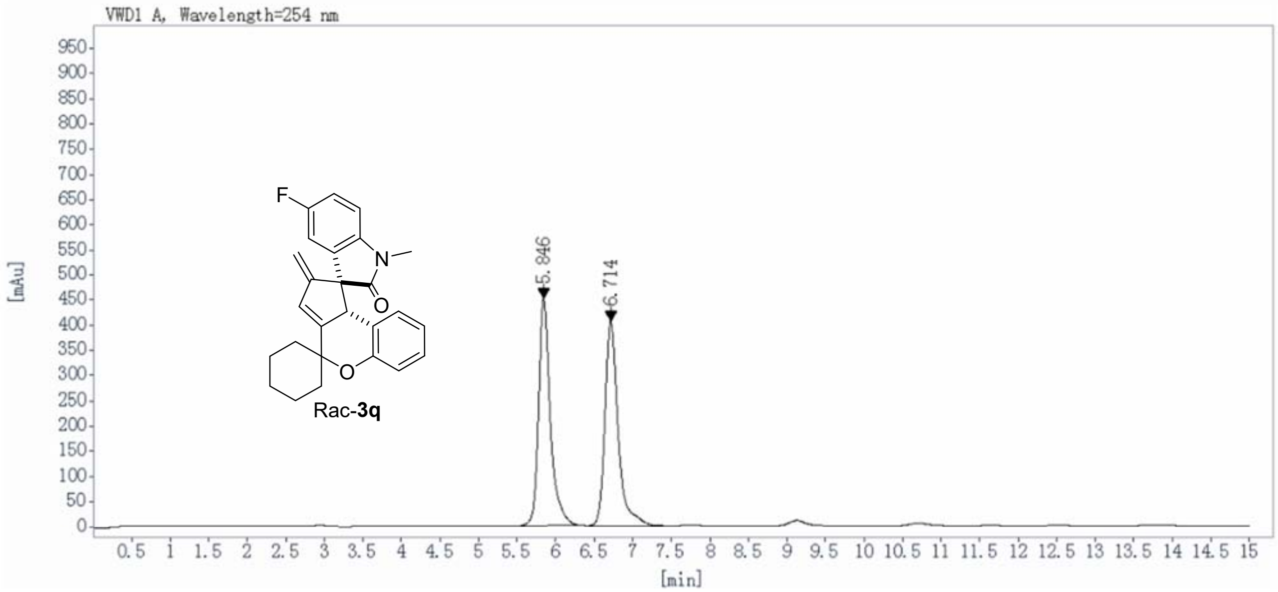
3q

^{13}C NMR (100 MHz, CDCl$_3$)



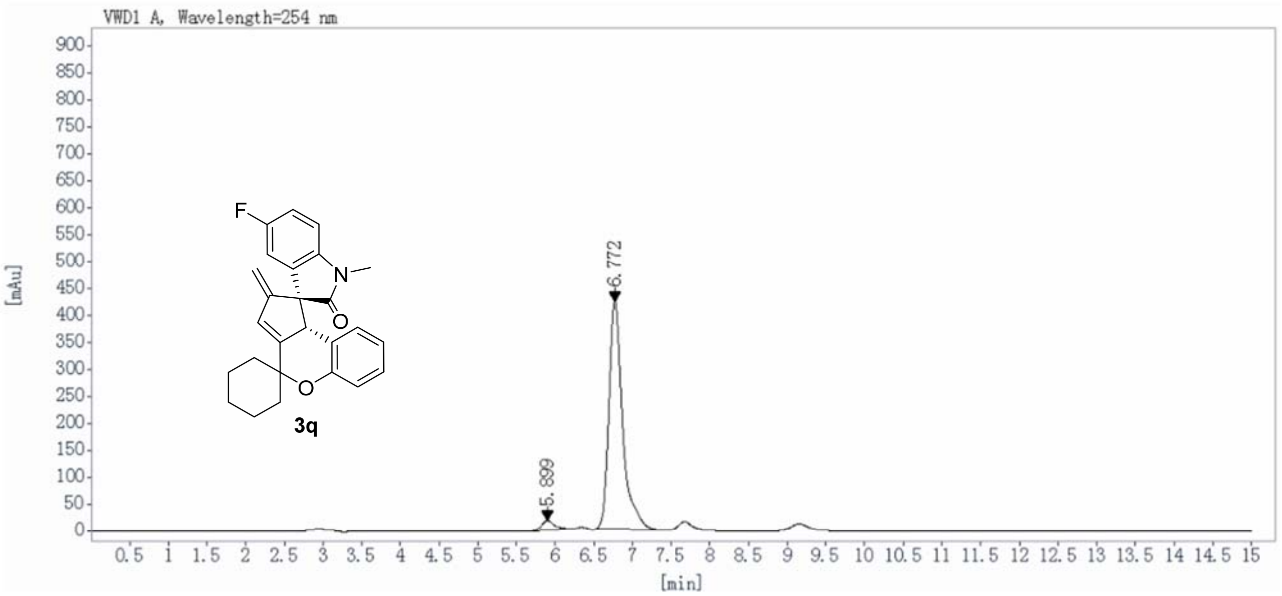
3q

^{19}F NMR (375 MHz, CDCl$_3$)



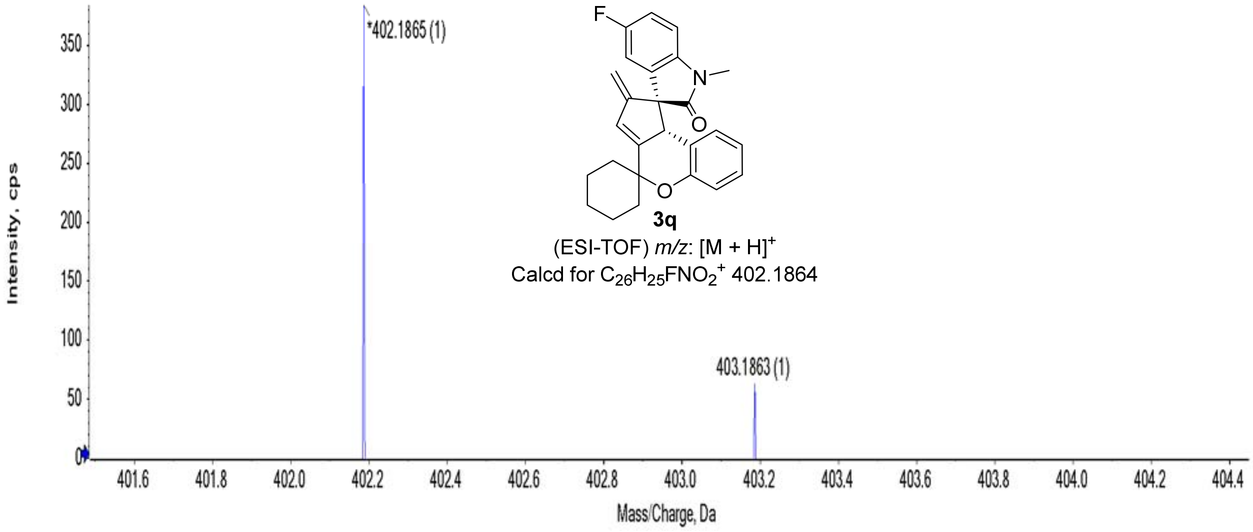
Rac-**3q**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.846	BBA	0.16	451.7264	4895.7183	50.3676
6.714	BBA	0.18	405.9886	4824.2539	49.6324
			Totals:	9719.9722	100.0000



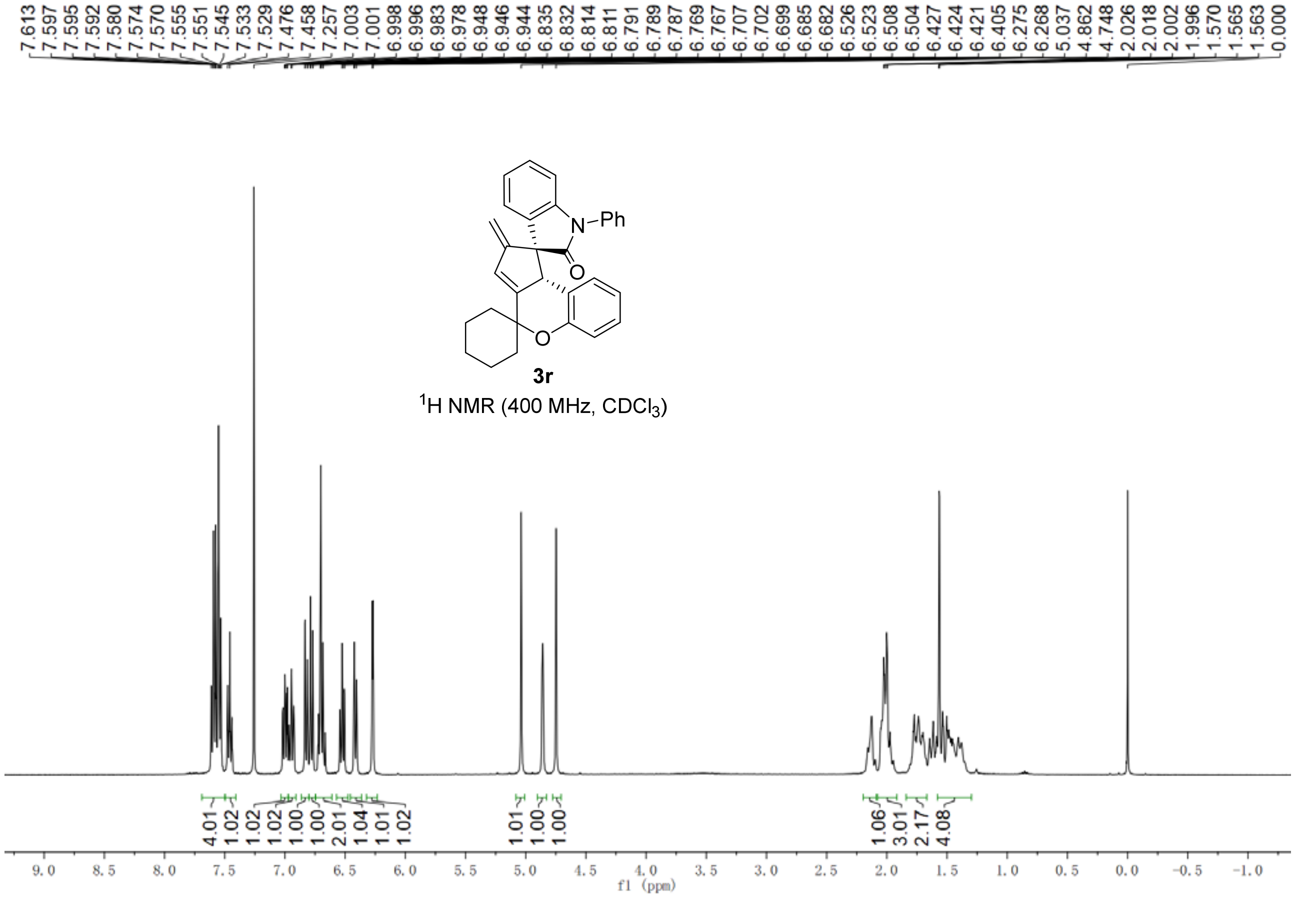
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.899	BBA	0.17	18.3742	204.3898	3.7710
6.772	BB	0.18	423.1734	5215.7002	96.2290
			Totals:	5420.0900	100.0000

Spectrum from 20230705.wiff2 (sample 73) - 68, +TOF MS (100 - 600) from 0.053 to 0.114 min, noise filtere...2 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)], Recalibrated, centroided



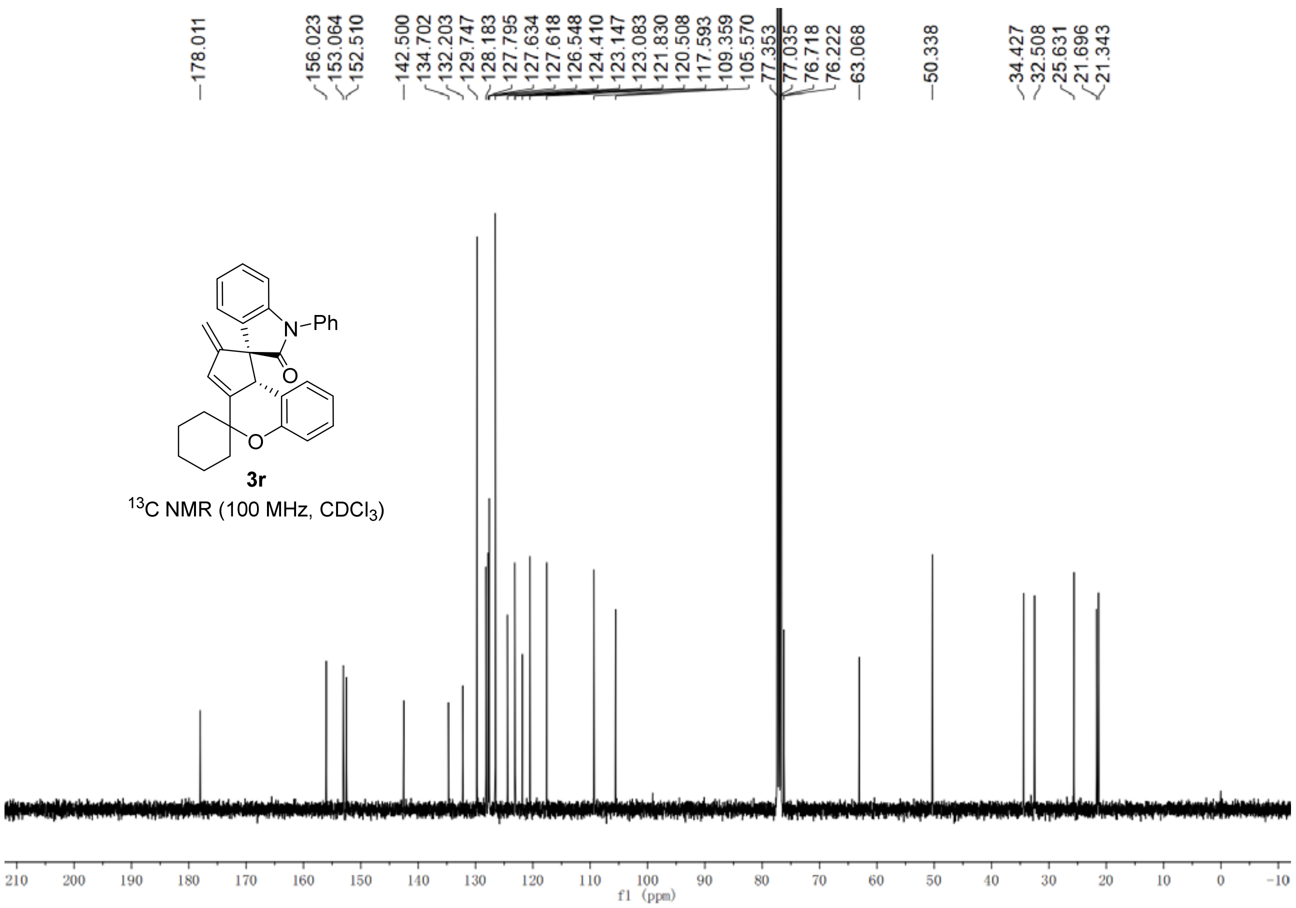
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{26}H_{25}FNO_2^+$ 402.1864



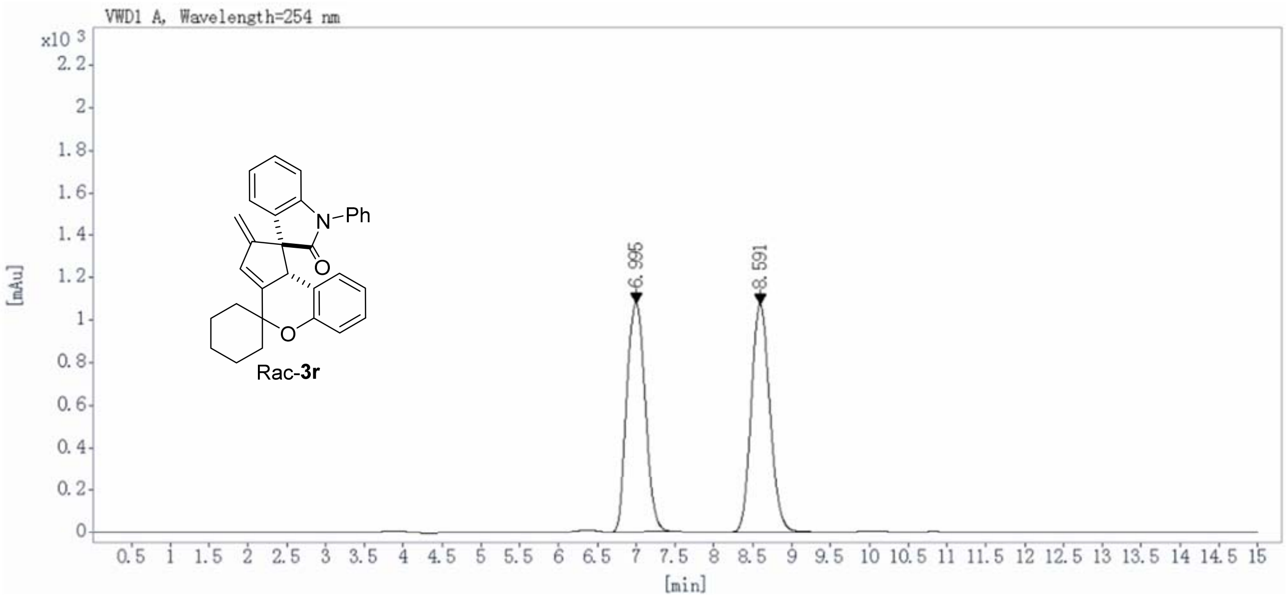
3r

^{1}H NMR (400 MHz, CDCl$_3$)

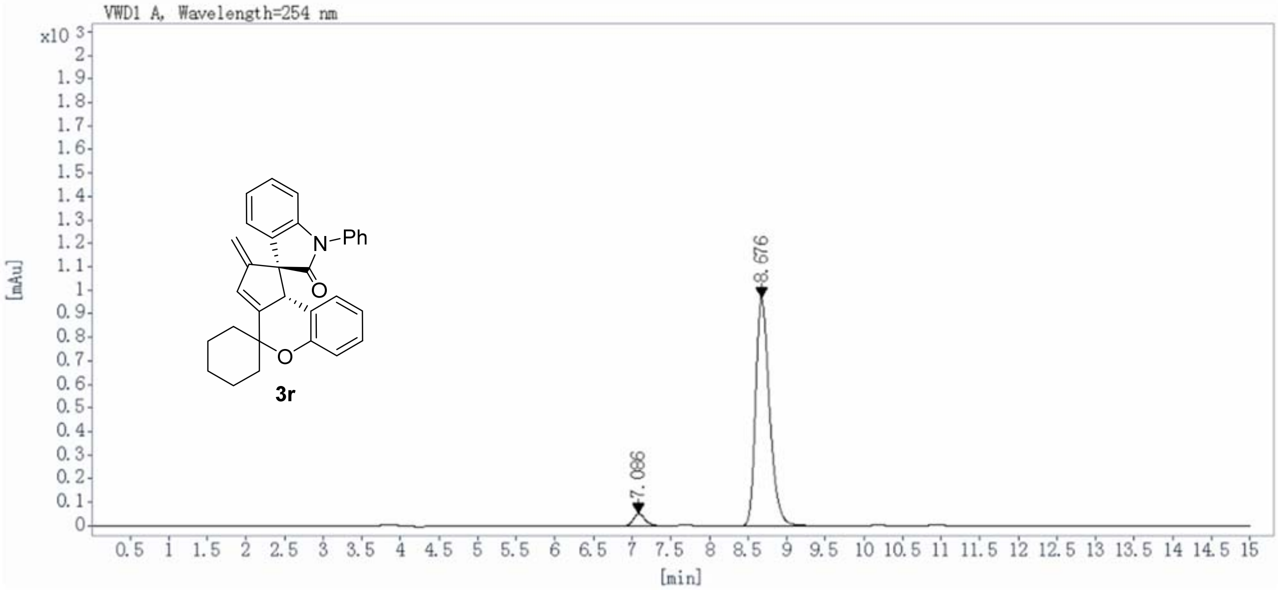


3r

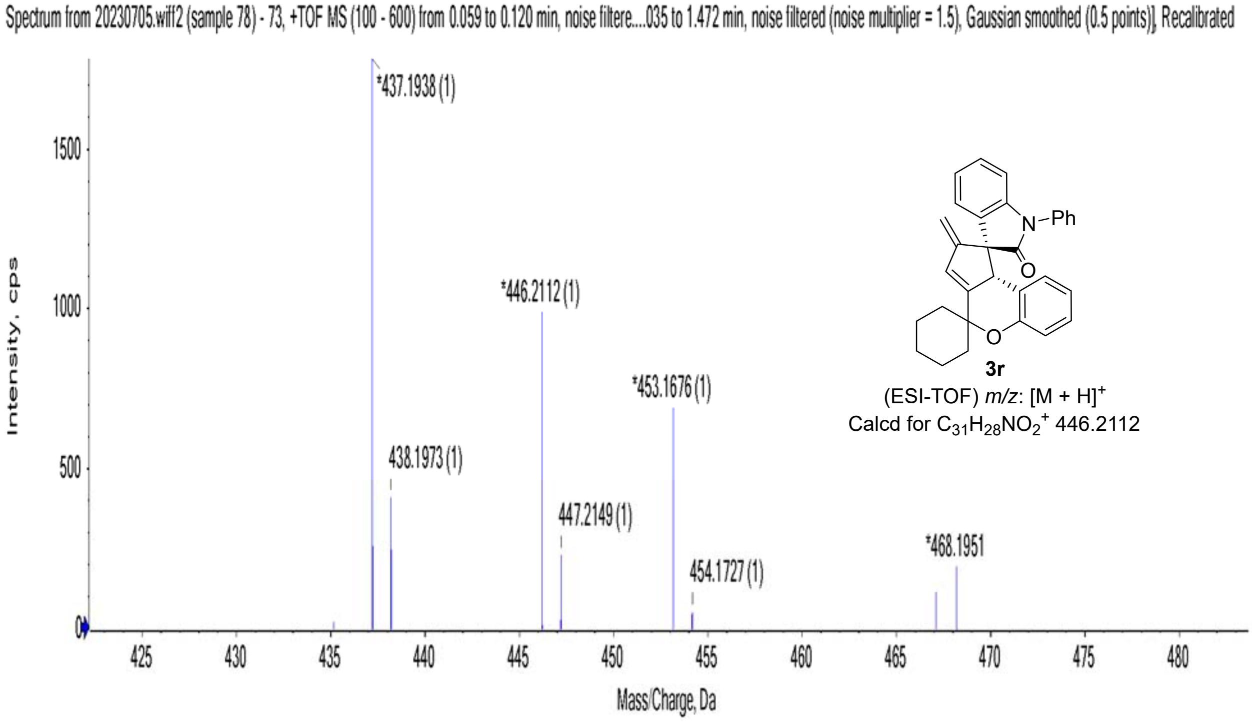
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.995	BBA	0.27	1077.7903	17849.4648	49.7720
8.591	BBA	0.26	1073.0360	18012.9883	50.2280
			Totals:	35862.4531	100.0000



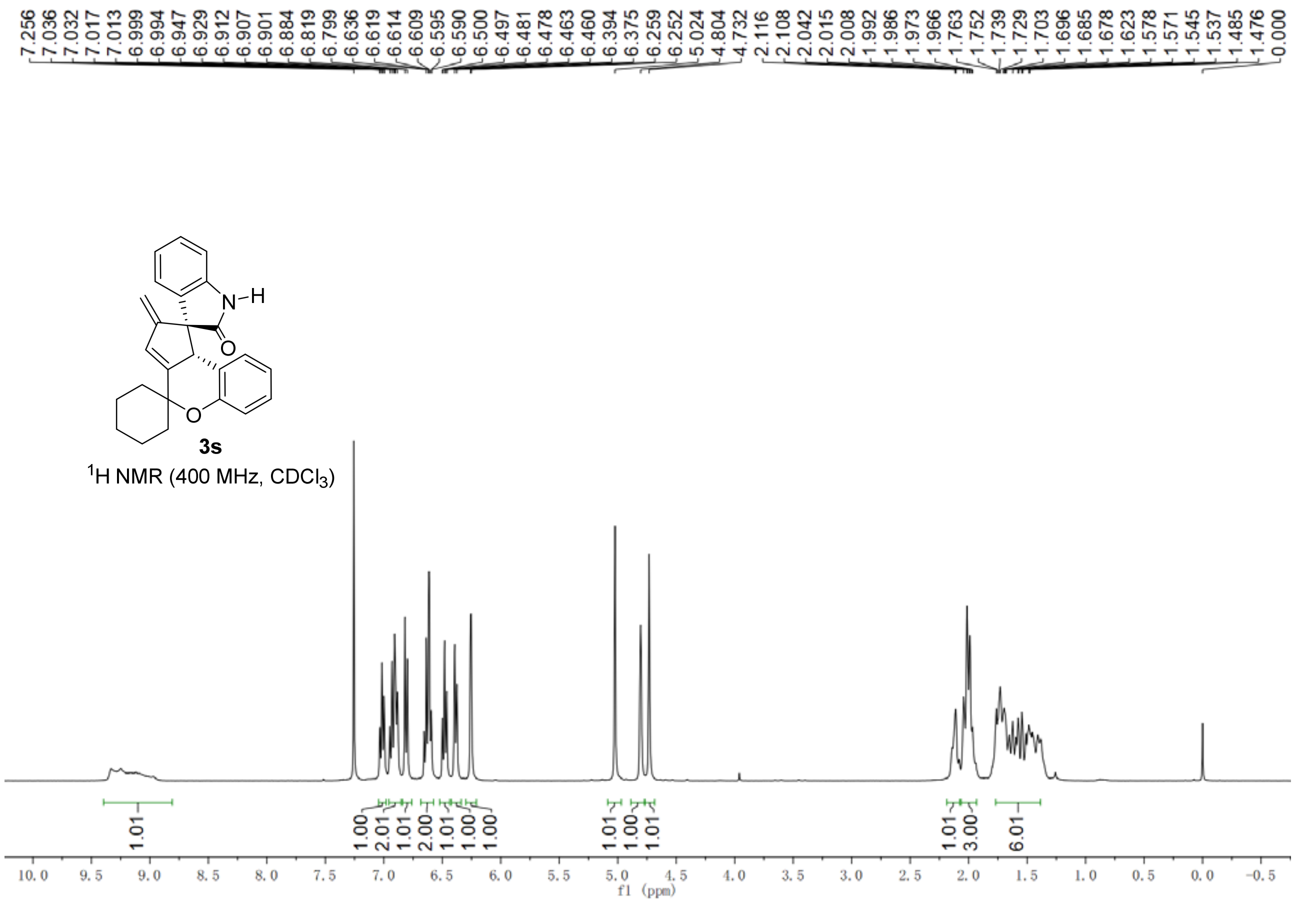
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
7.086	BB	0.16	51.1723	542.4835	4.3210
8.676	BBA	0.19	969.4561	12012.2246	95.6790
			Totals:	12554.7081	100.0000



3r

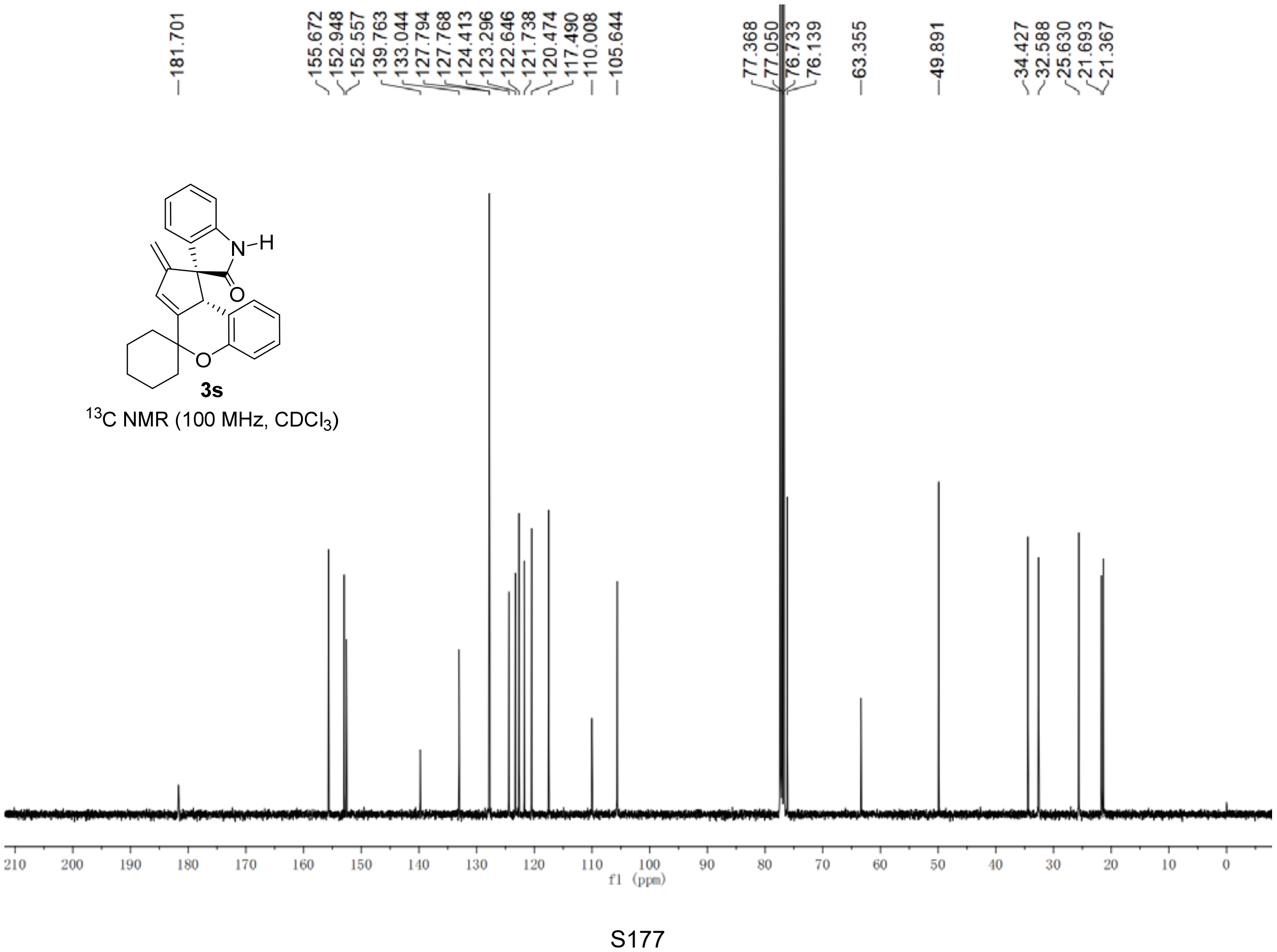
(ESI-TOF) *m/z*: [M + H]$^+$

Calcd for $C_{31}H_{28}NO_2^+$ 446.2112



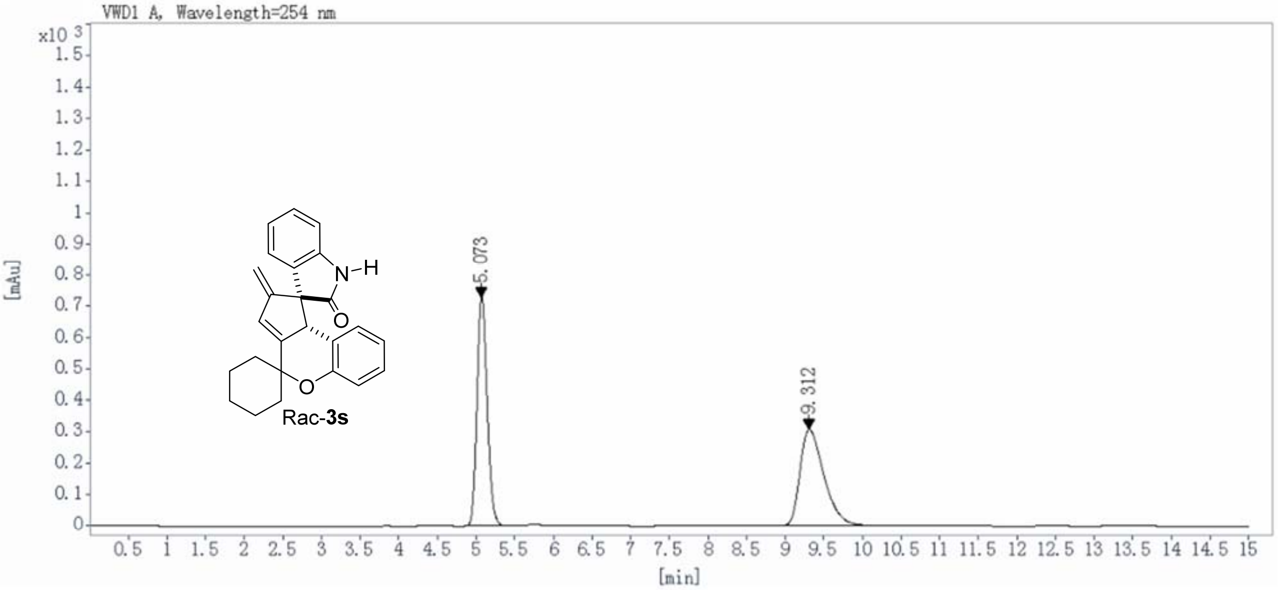
3s

^{1}H NMR (400 MHz, CDCl$_3$)

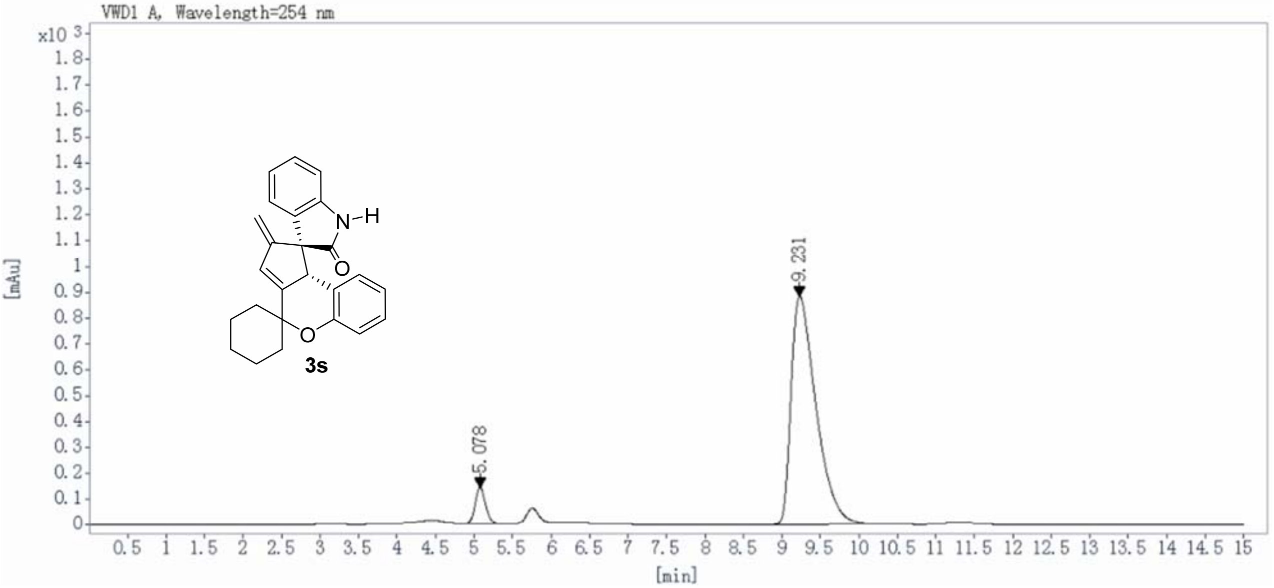


3s

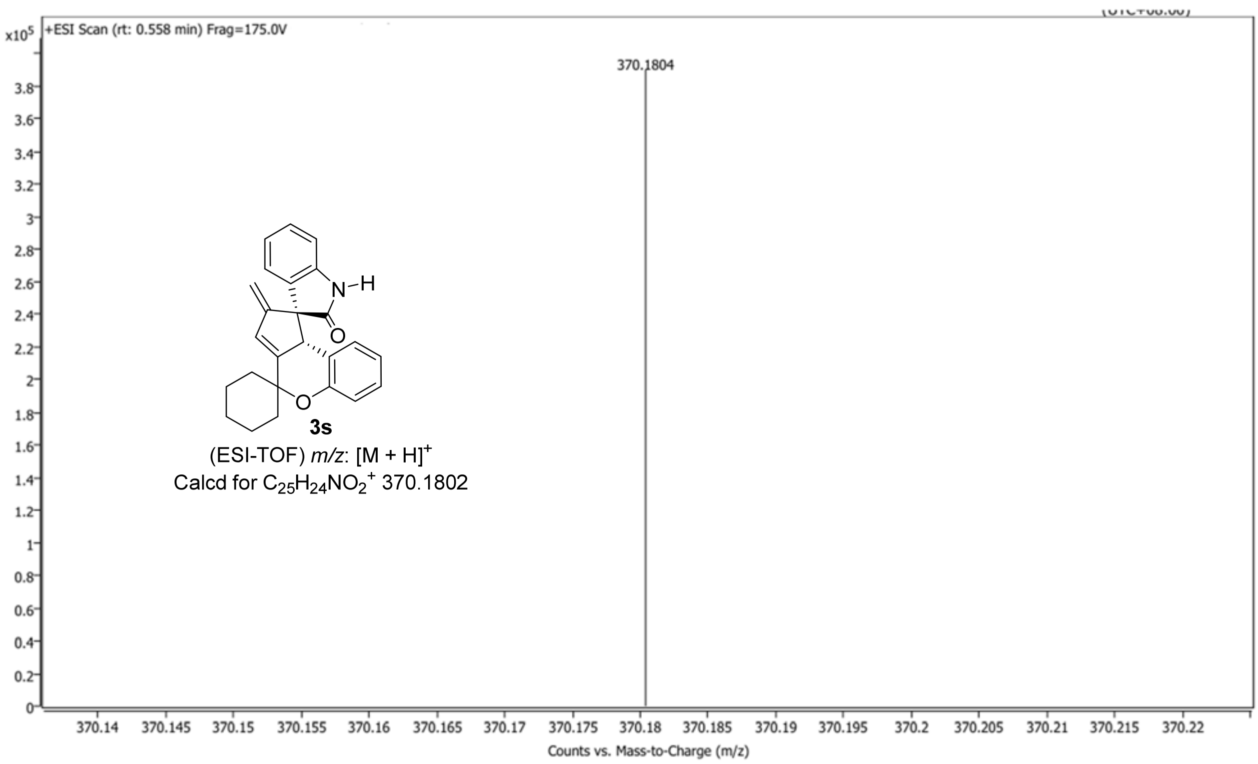
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.073	BBA	0.14	726.8414	6615.3110	49.9077
9.312	BBA	0.33	308.0536	6639.7852	50.0923
			Totals:	13255.0962	100.0000



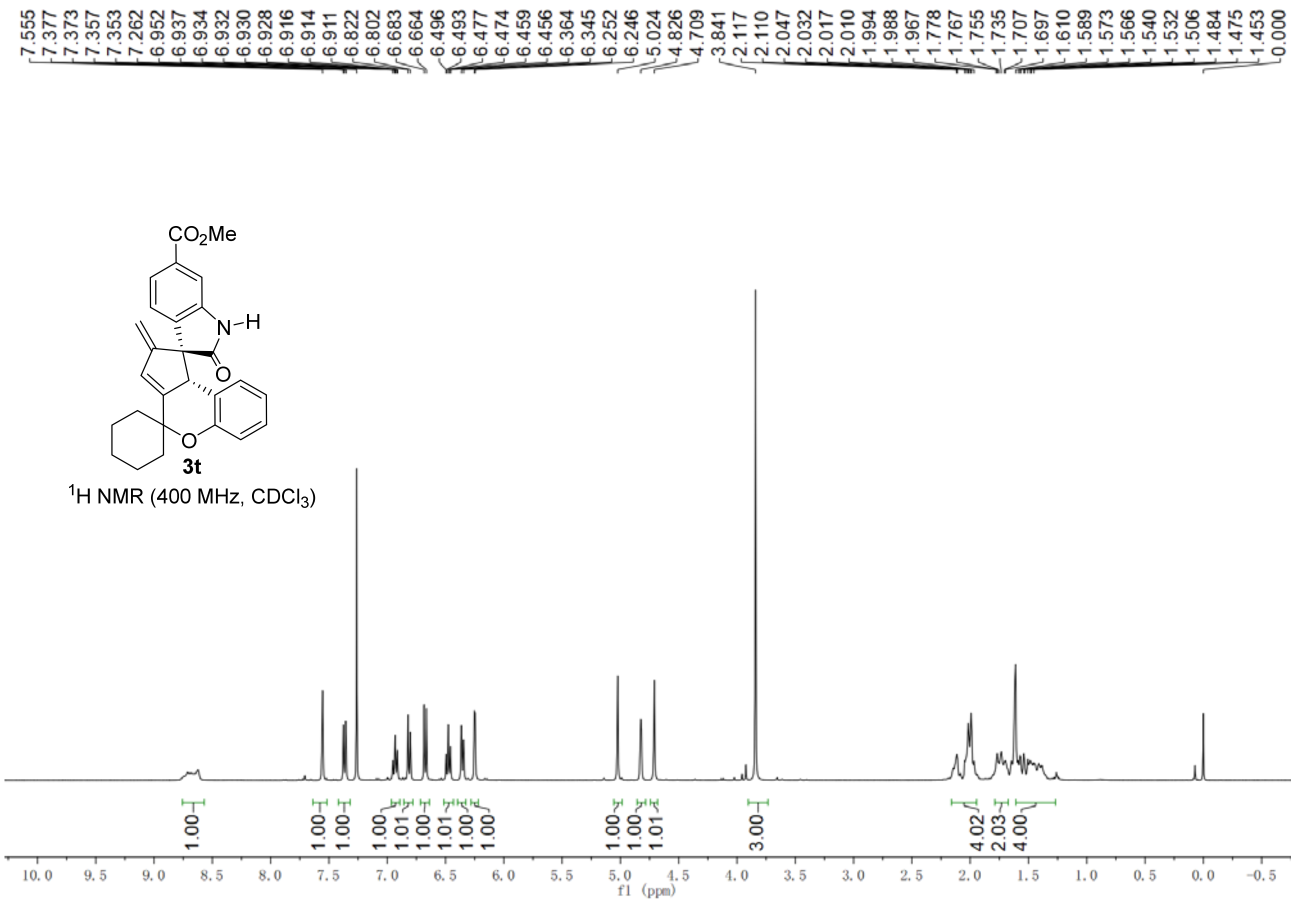
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.078	BBA	0.14	140.4959	1284.6090	6.1001
9.231	BBA	0.34	882.8427	19774.2598	93.8999
			Totals:	21058.8688	100.0000



3s

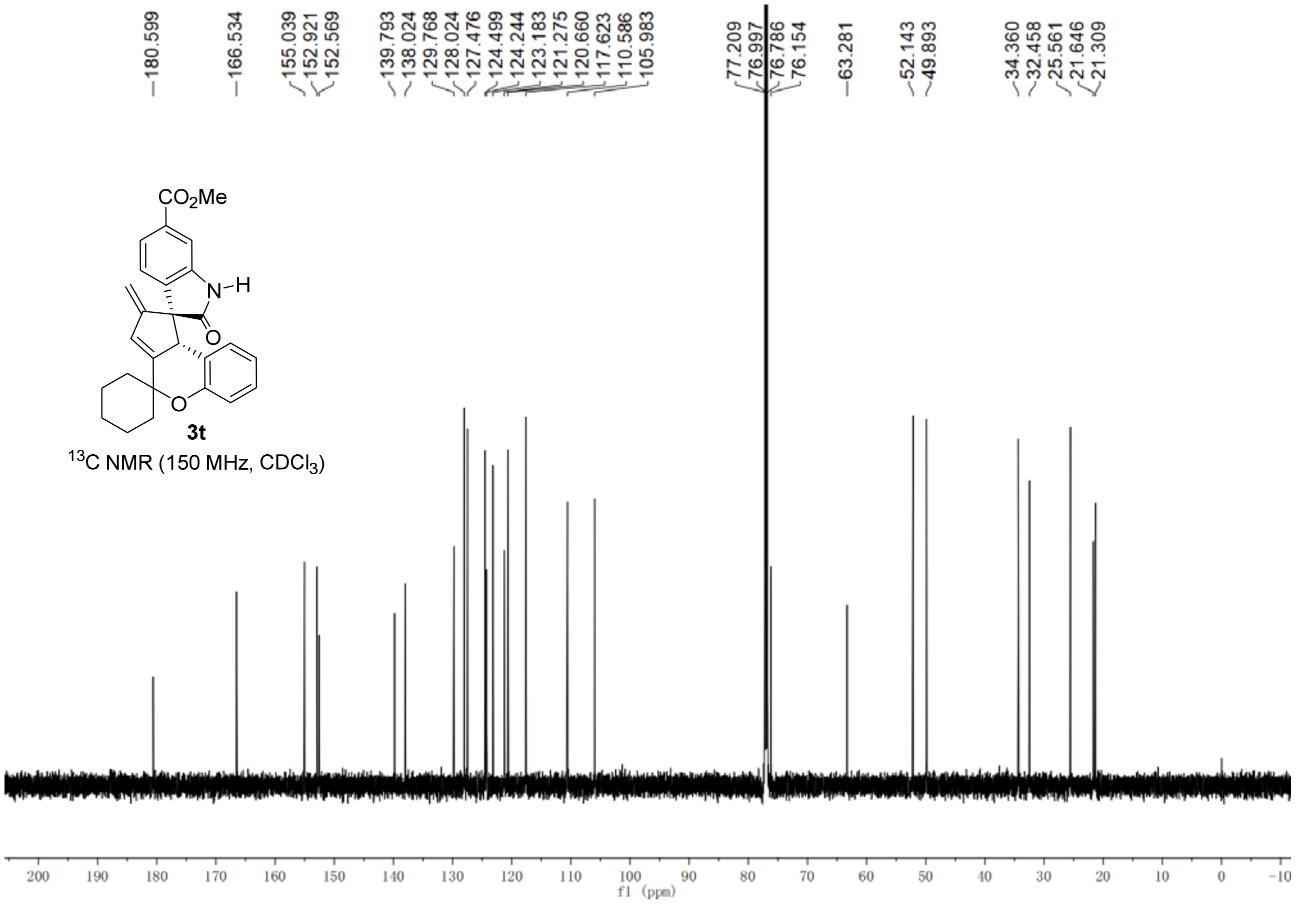
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{25}H_{24}NO_2^+$ 370.1802



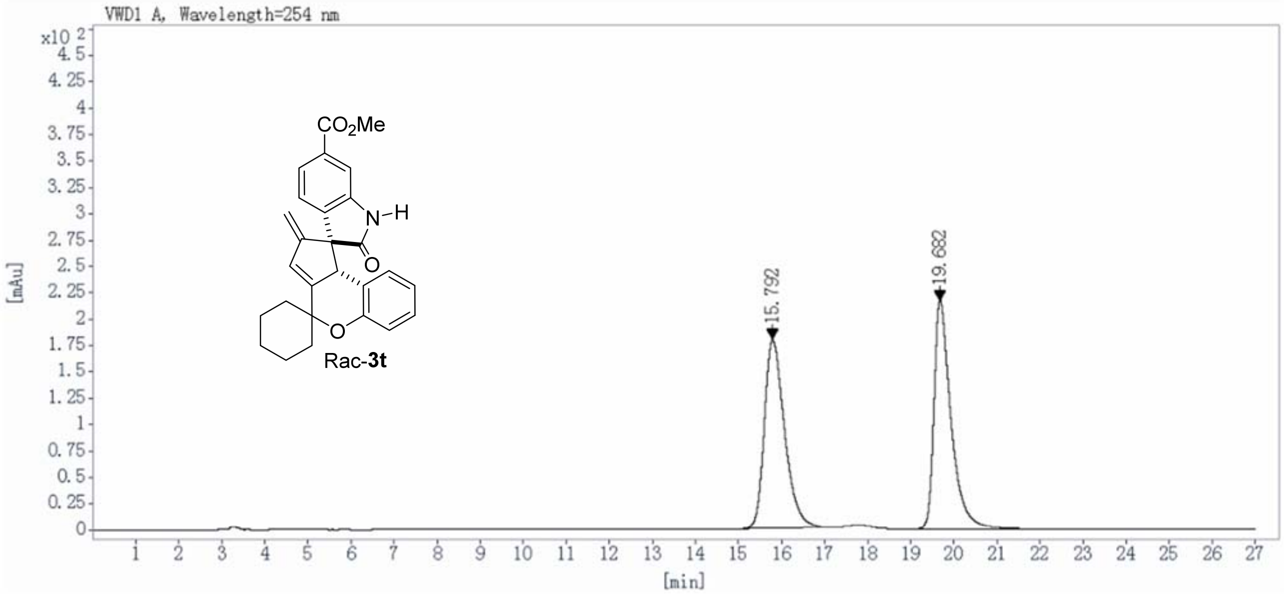
3t

^{1}H NMR (400 MHz, CDCl$_3$)

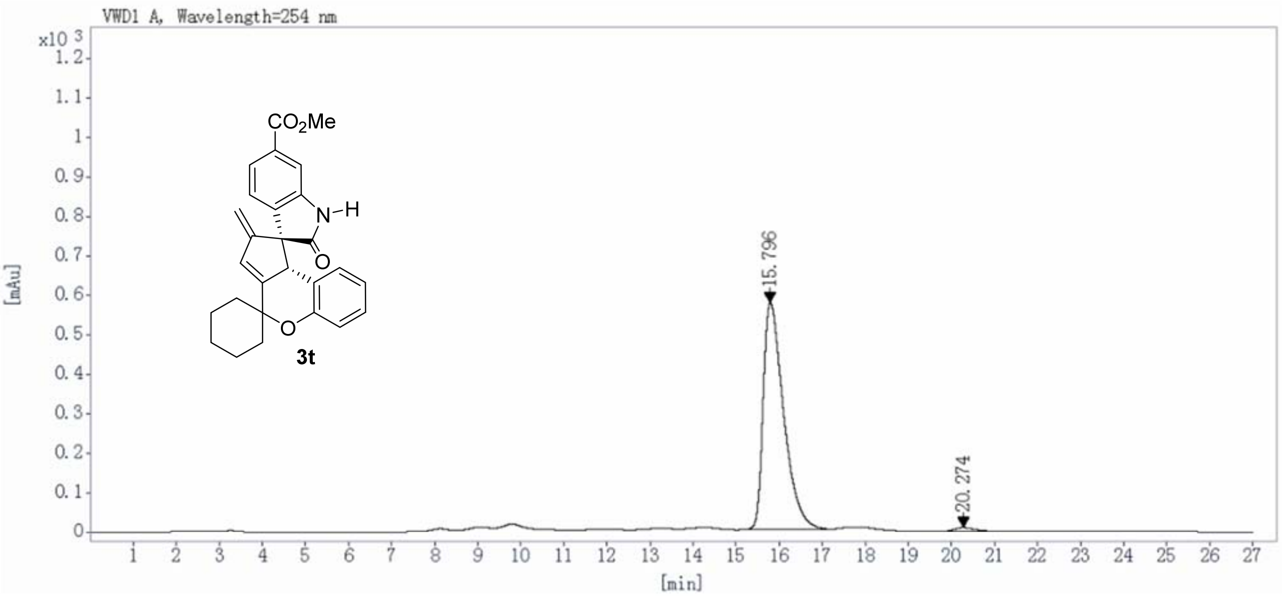


3t

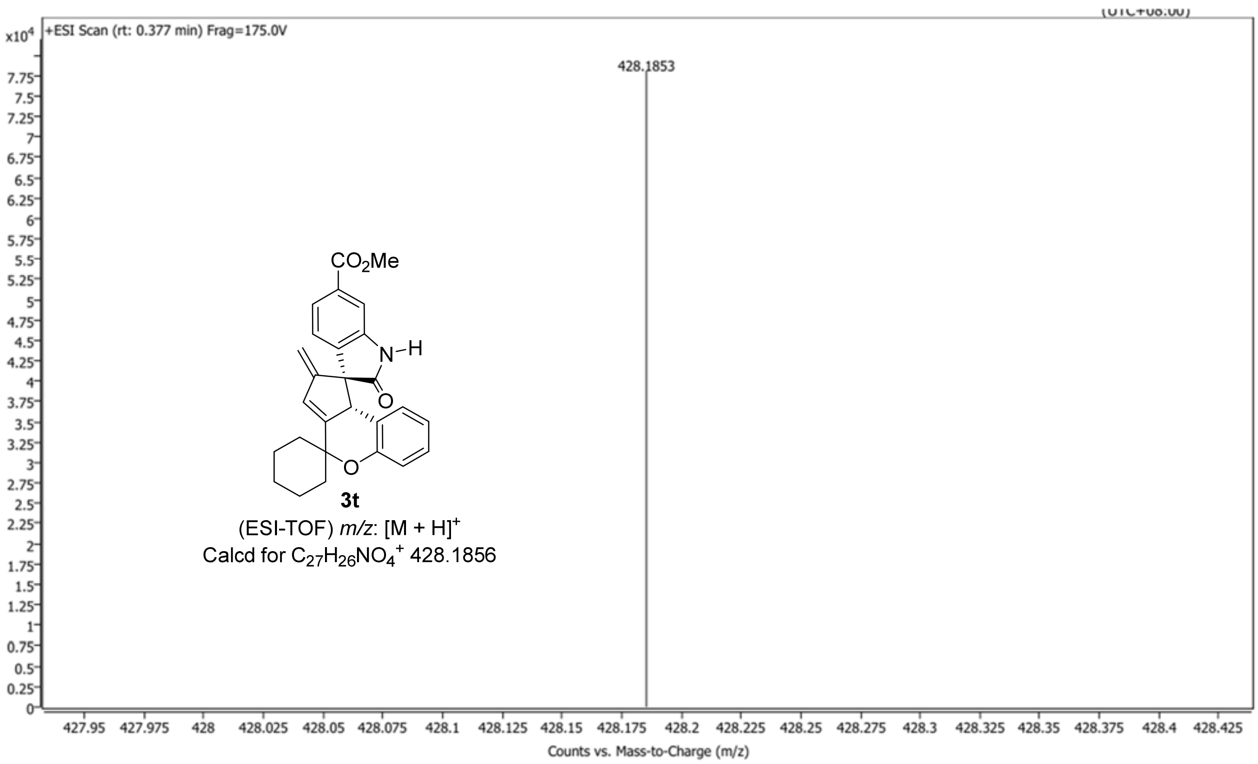
^{13}C NMR (150 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
15.792	BB	0.50	179.2602	5878.5820	49.5607
19.682	BBA	0.41	217.1251	5982.7925	50.4393
			Totals:	11861.3745	100.0000



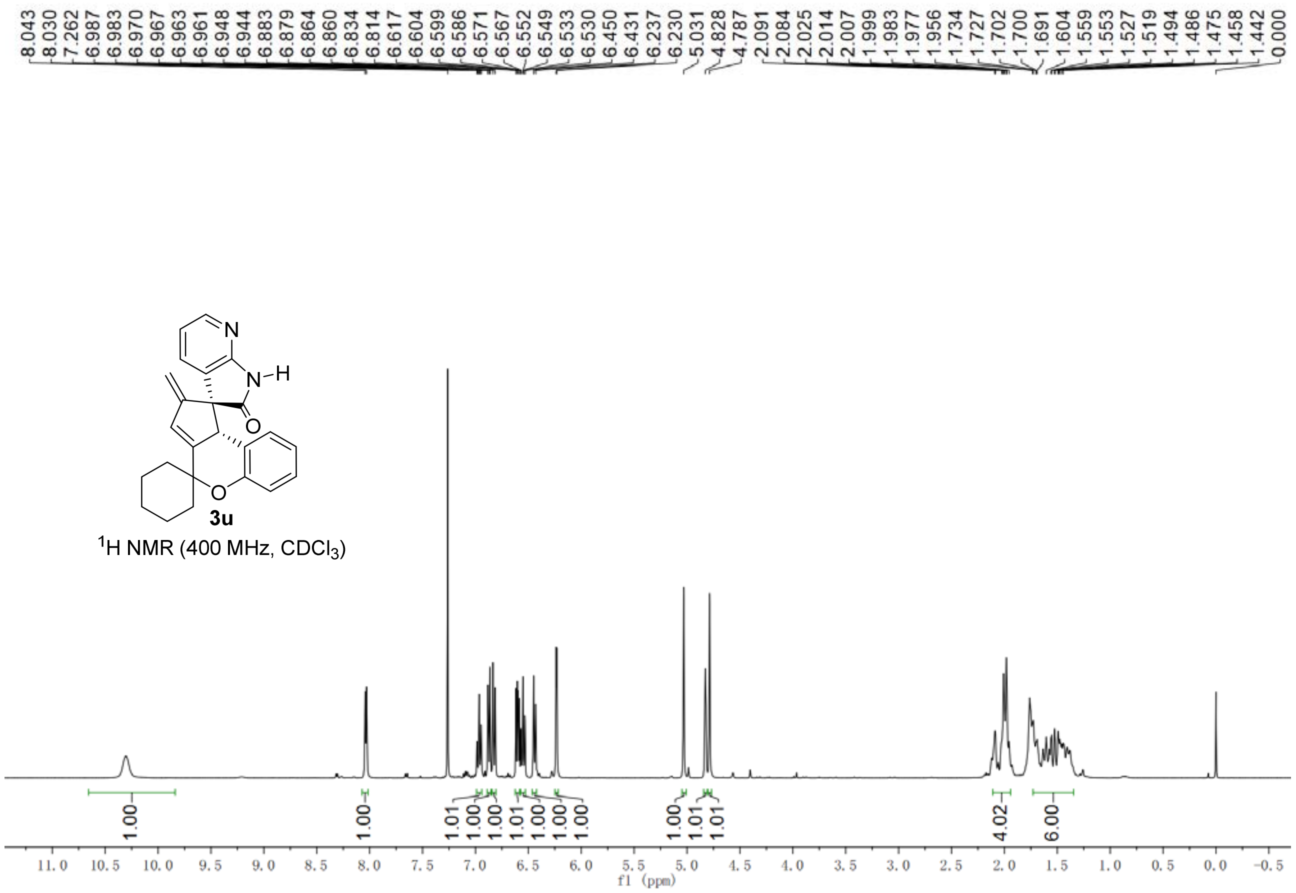
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
15.796	BBA	0.50	575.8636	18961.9141	98.2026
20.274	BBA	0.52	10.0001	347.0662	1.7974
			Totals:	19308.9803	100.0000



3t

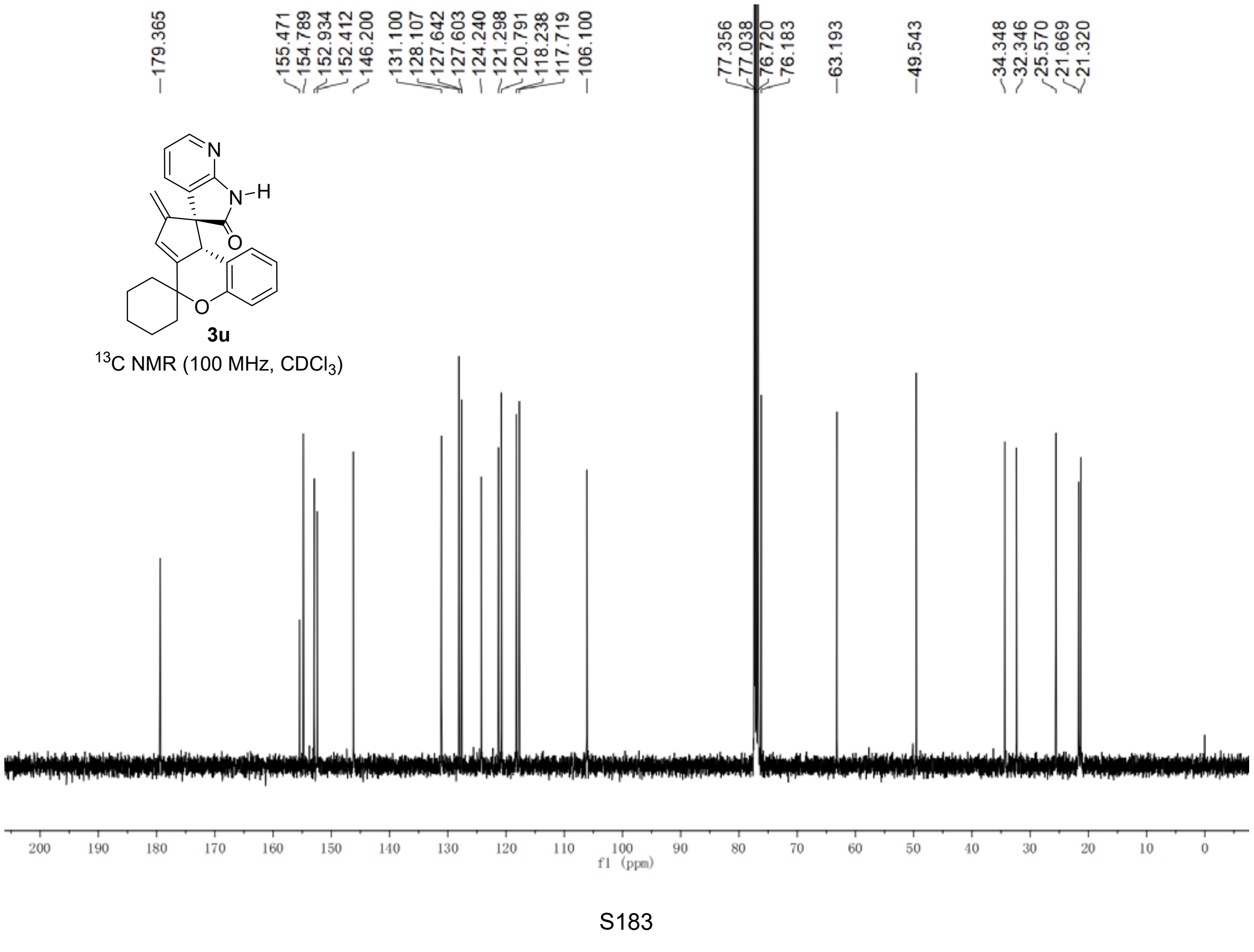
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{27}H_{26}NO_4^+$ 428.1856



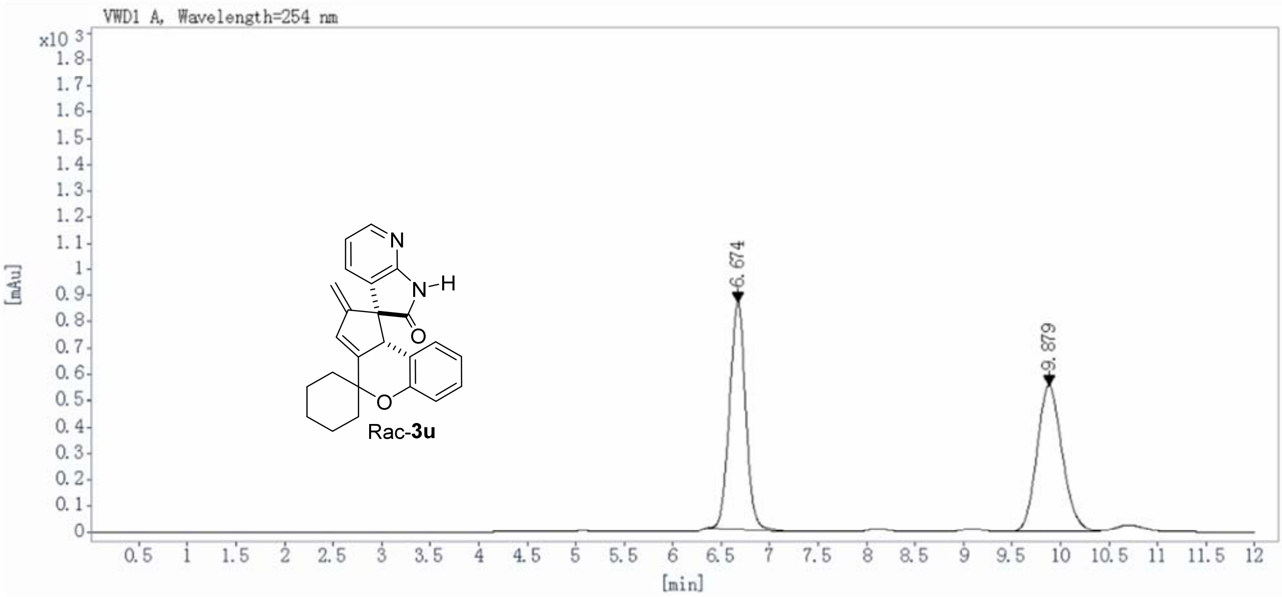
3u

^{1}H NMR (400 MHz, CDCl$_3$)

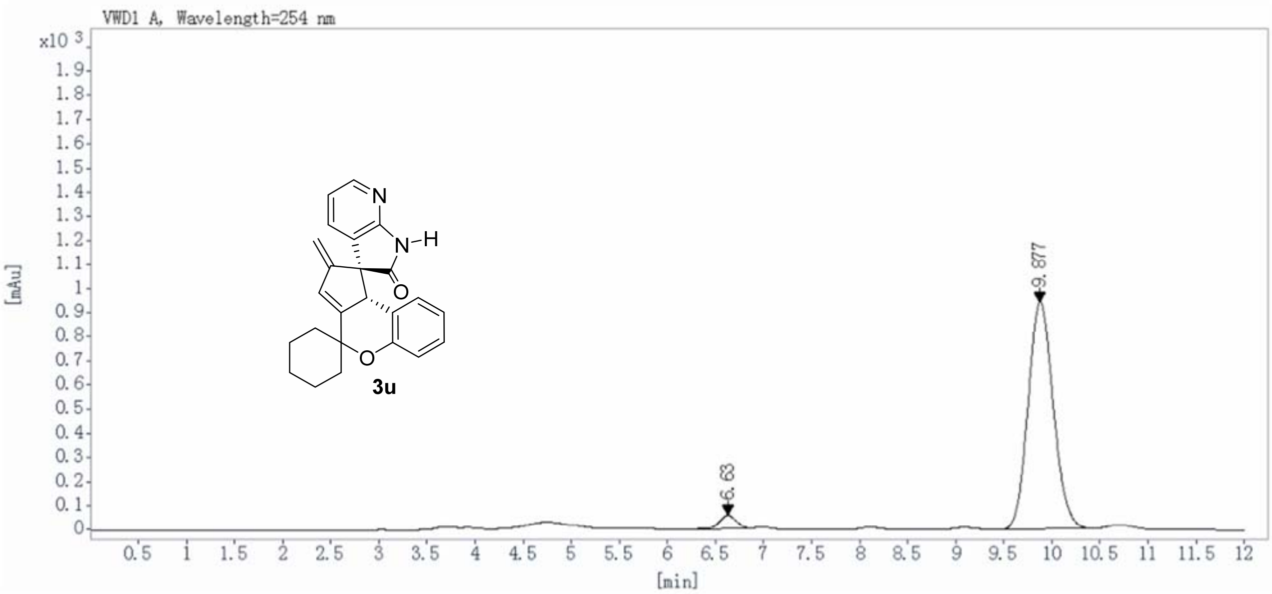


3u

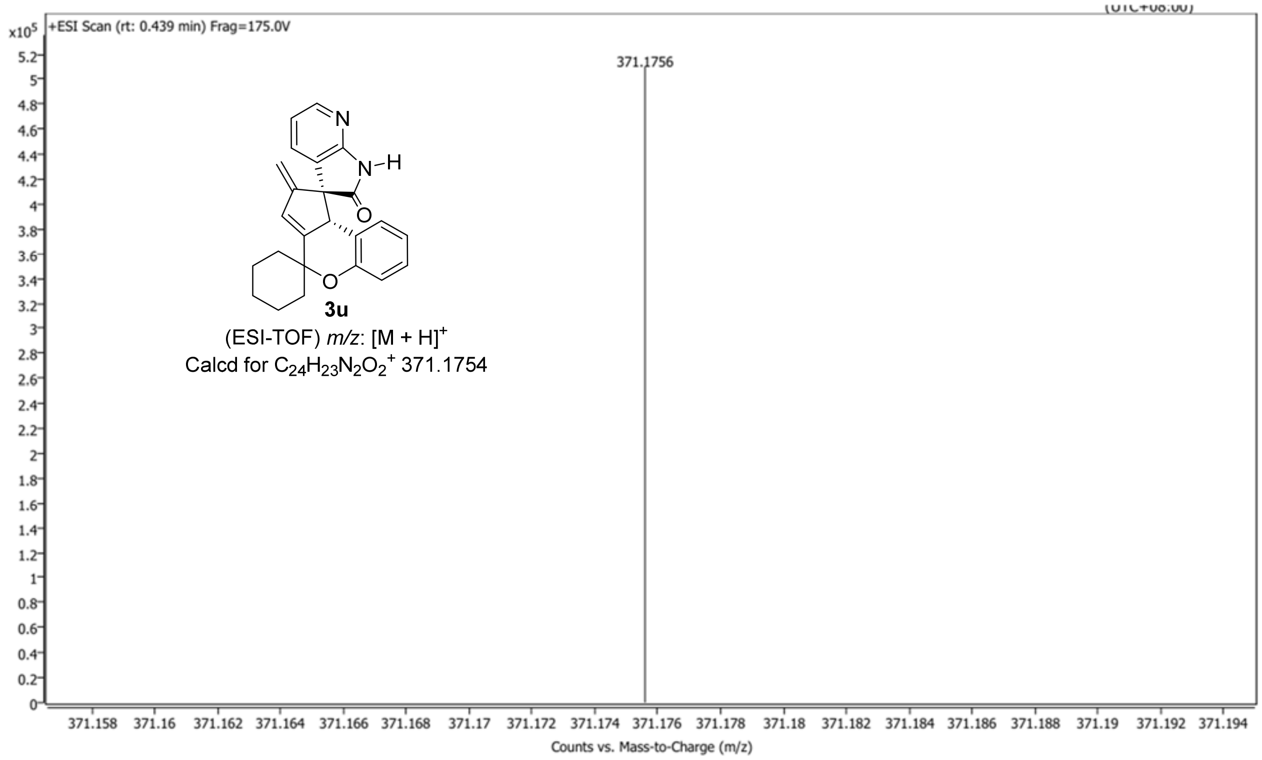
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.674	BBA	0.18	864.6375	10019.2031	49.9140
9.879	BB	0.28	553.8257	10053.7139	50.0860
			Totals:	20072.9170	100.0000



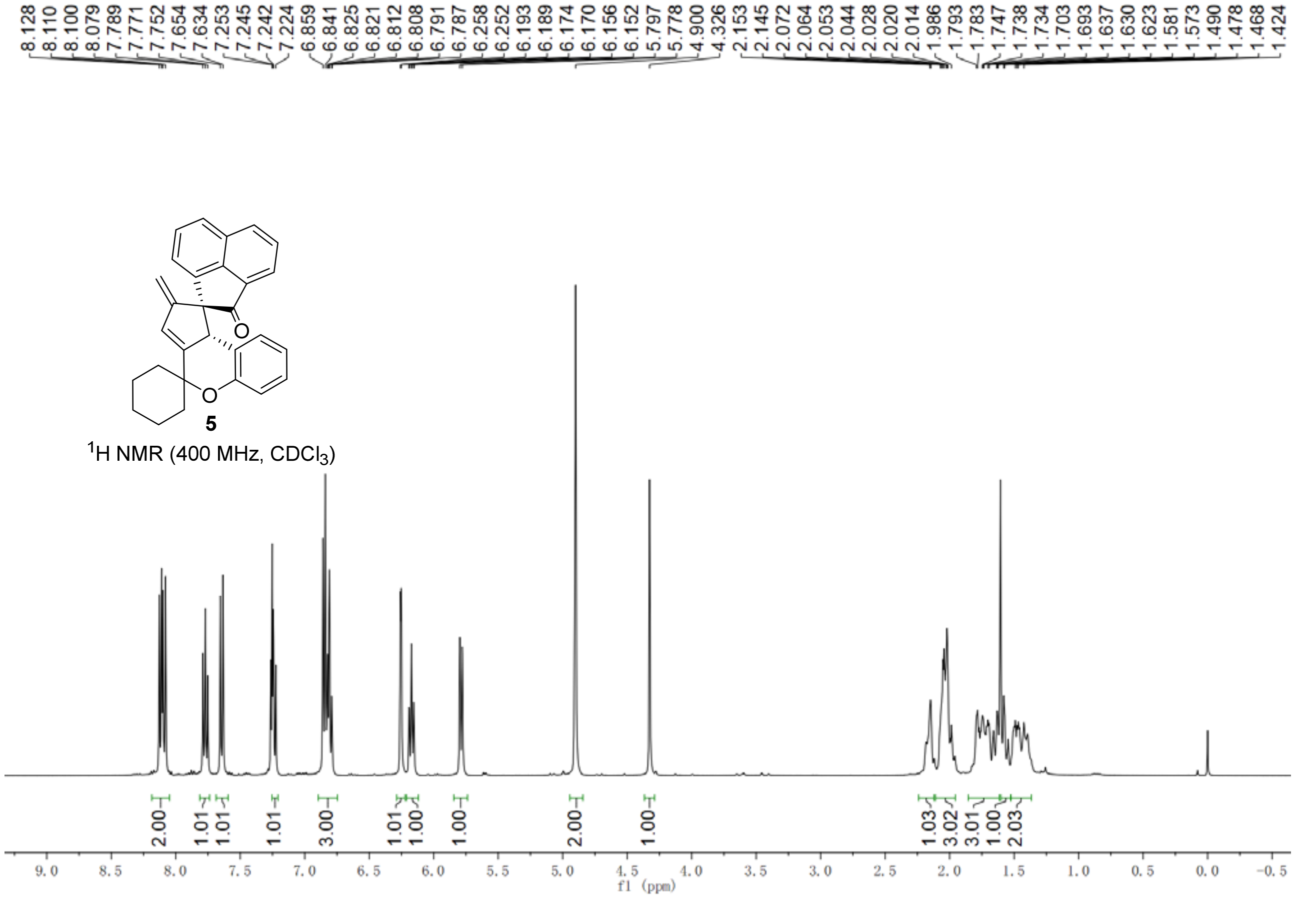
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.630	BB	0.18	54.6443	641.9444	3.5939
9.877	BB	0.29	940.9167	17220.1152	96.4061
			Totals:	17862.0596	100.0000



3u

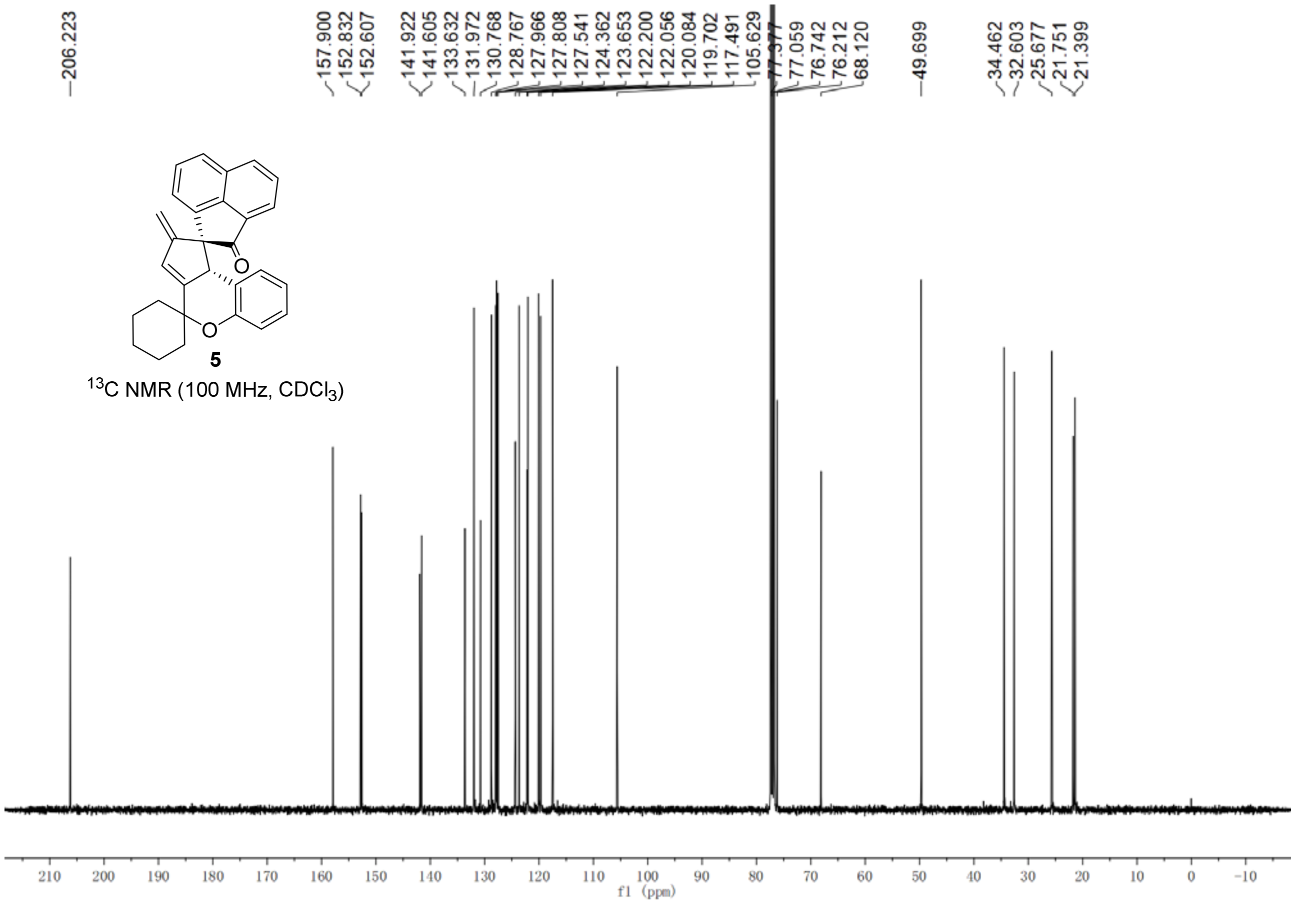
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{24}H_{23}N_2O_2^+$ 371.1754



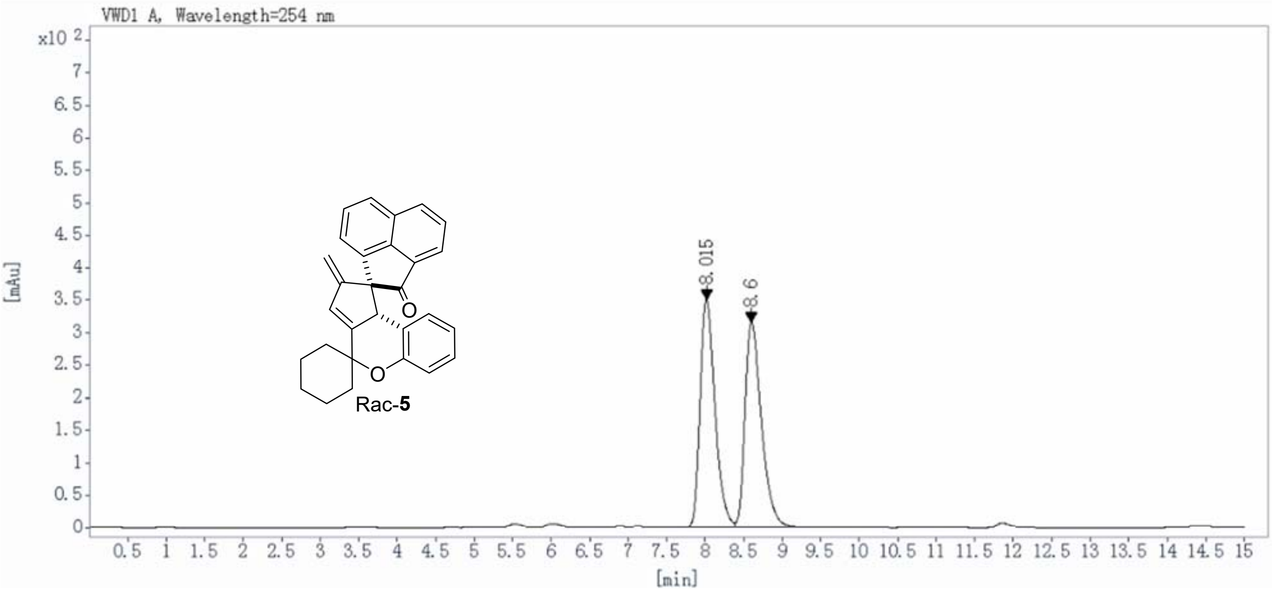
5

^{1}H NMR (400 MHz, CDCl$_3$)

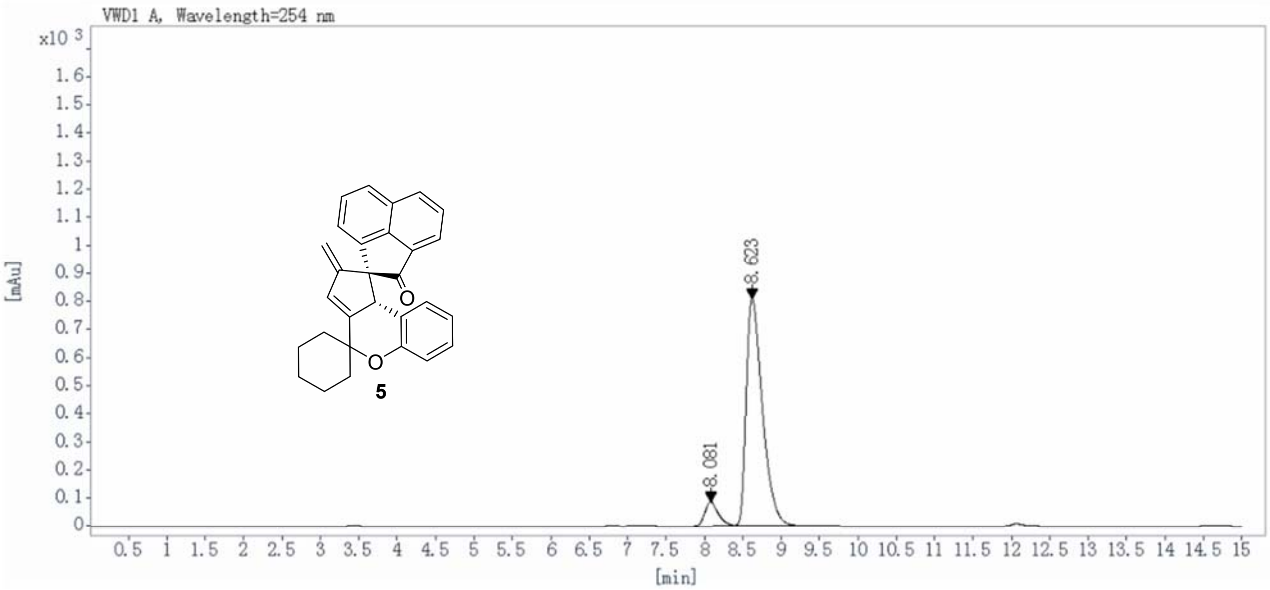


5

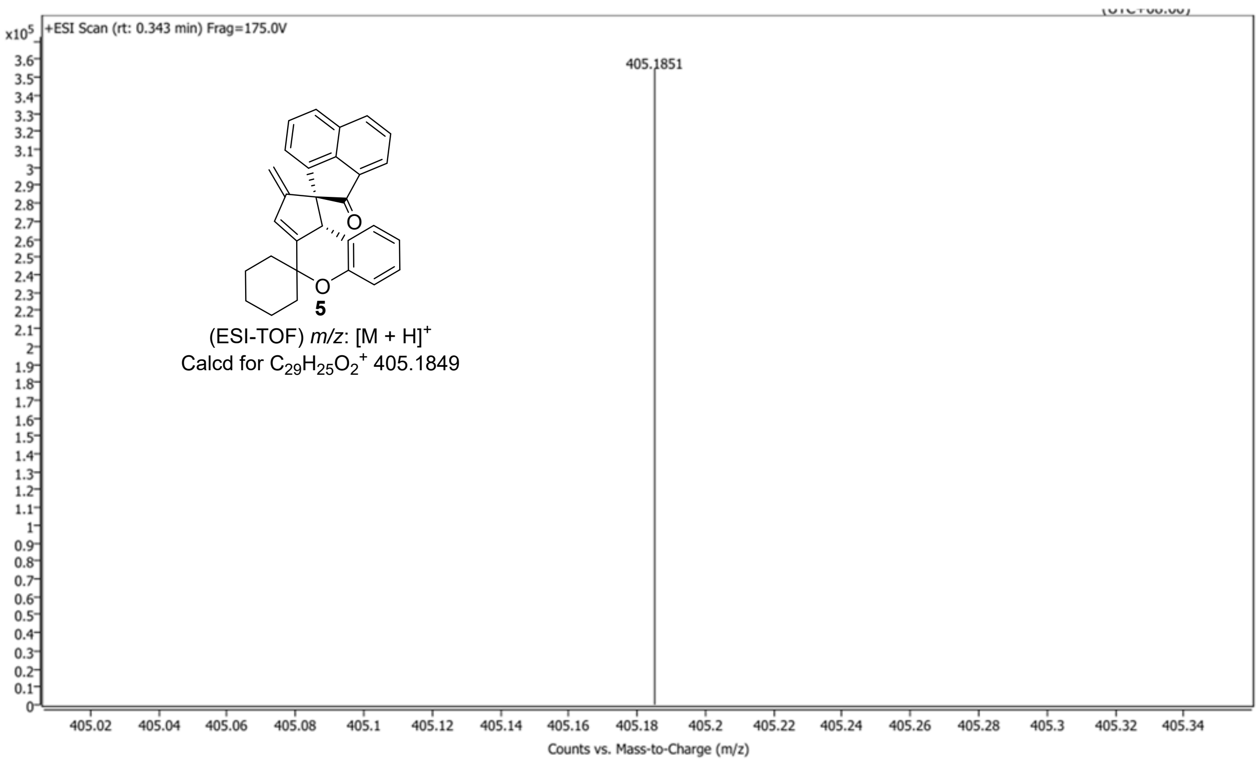
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.015	BV	0.21	350.7008	4718.6255	49.9323
8.600	VBA	0.23	315.7699	4731.4258	50.0677
			Totals:	9450.0513	100.0000

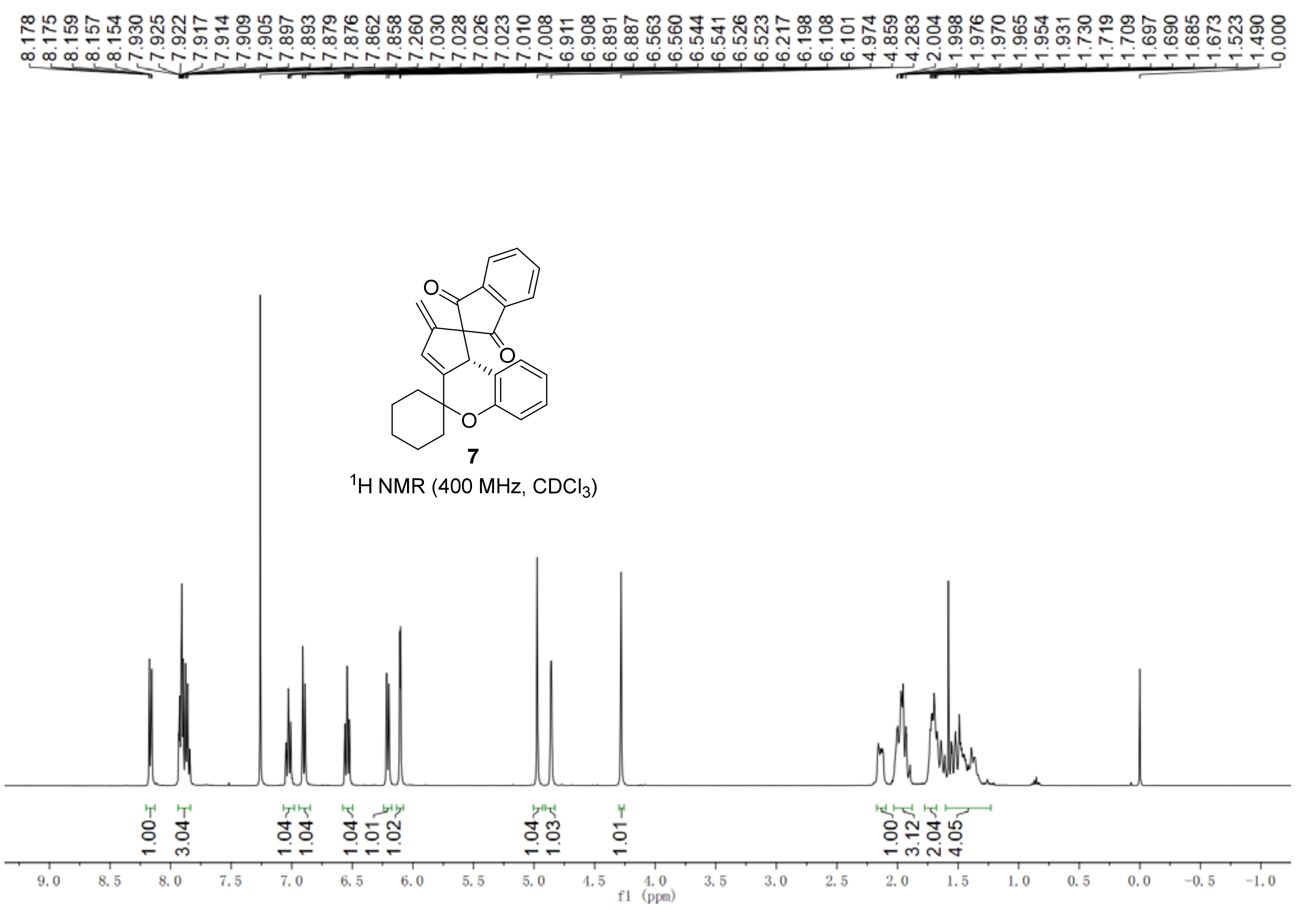


Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.081	BV	0.19	86.4970	1072.3313	8.3051
8.623	VBA	0.22	809.1938	11839.3779	91.6949
			Totals:	12911.7092	100.0000



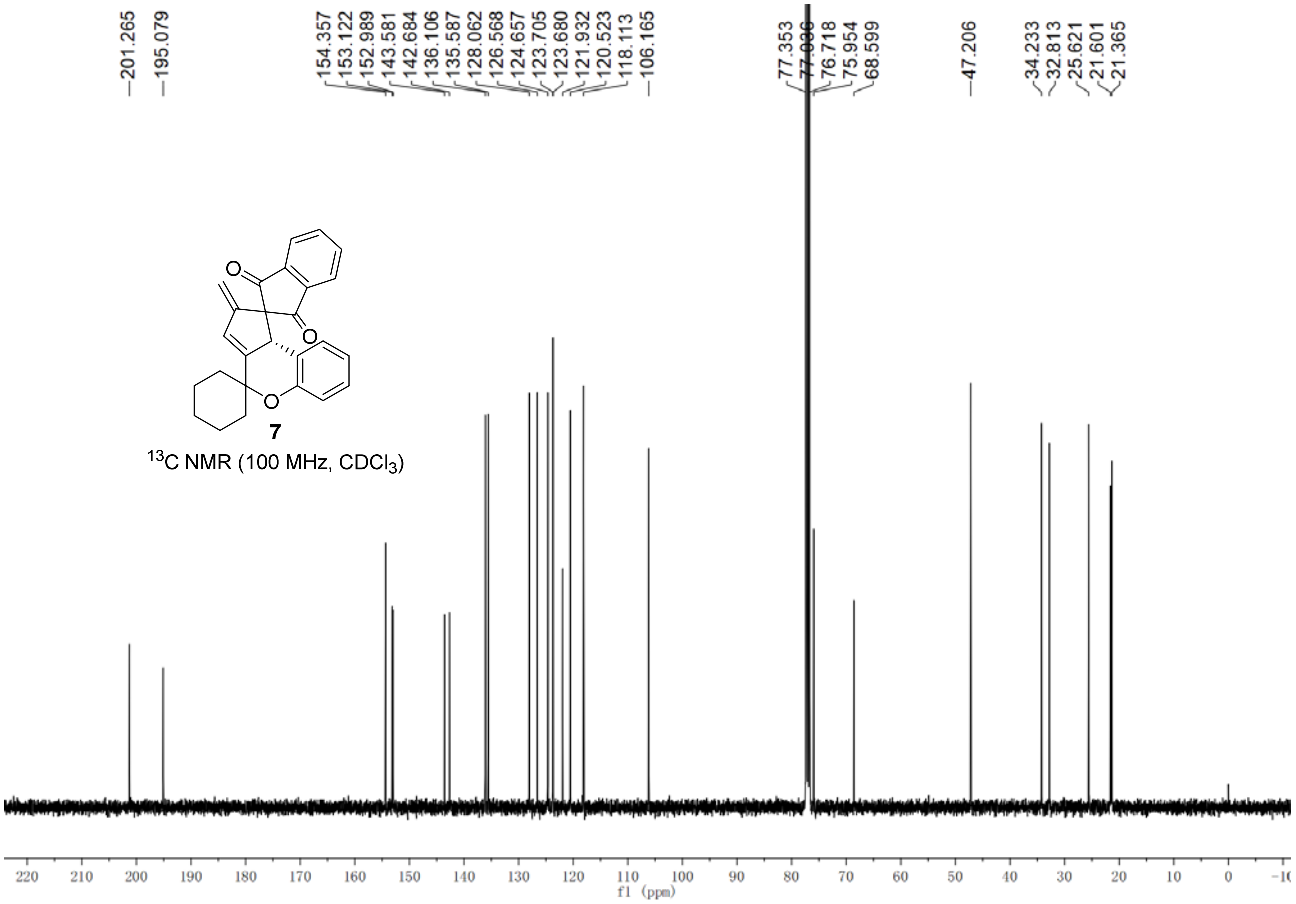
5

(ESI-TOF) *m/z*: $[M + H]^+$
Calcd for $C_{29}H_{25}O_2^+$ 405.1849



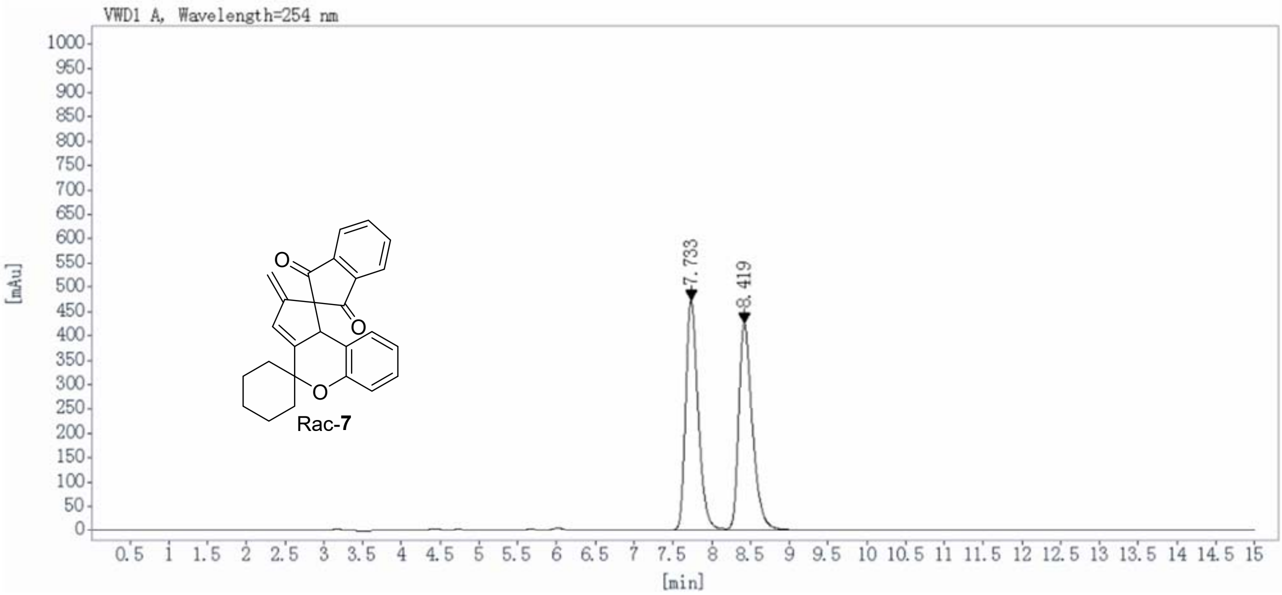
7

^{1}H NMR (400 MHz, CDCl$_3$)

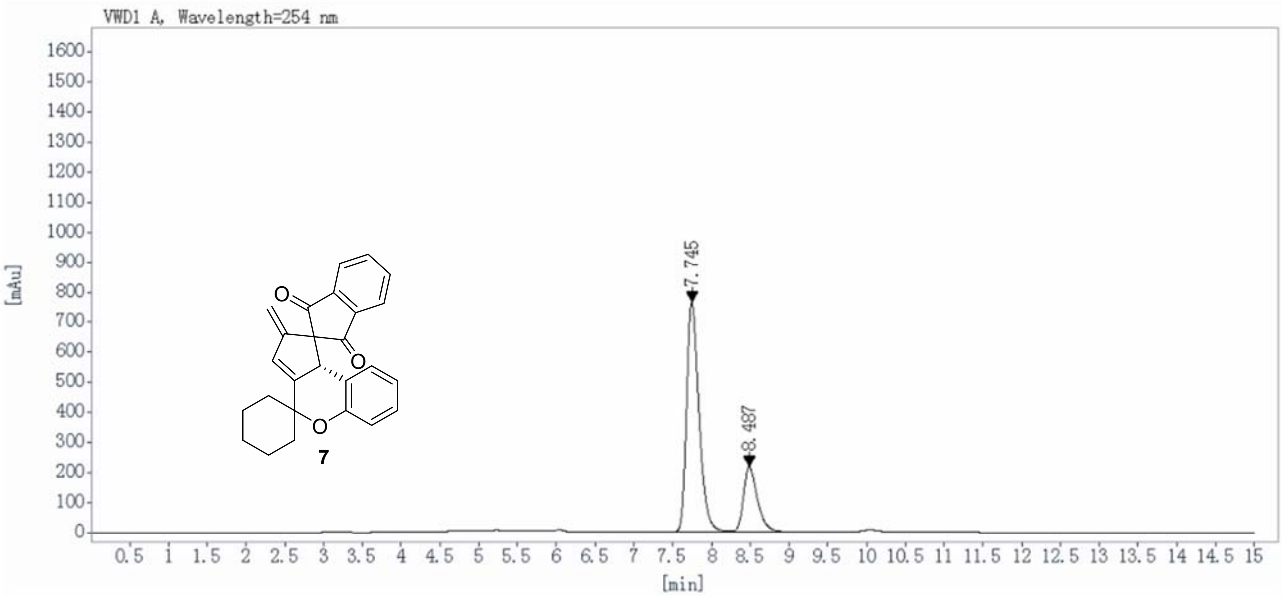


7

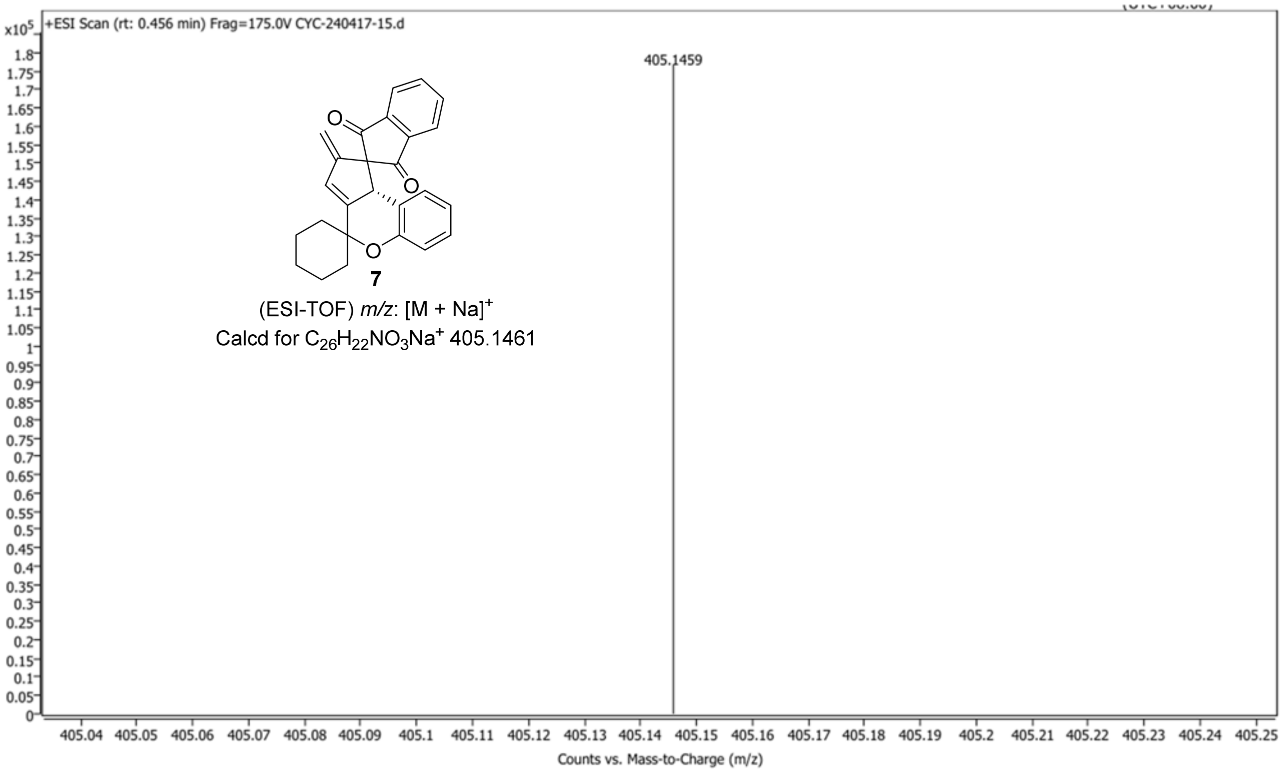
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
7.733	BV	0.17	471.3006	5264.4287	50.0551
8.419	VBA	0.19	425.1812	5252.8433	49.9449
			Totals:	10517.2720	100.0000



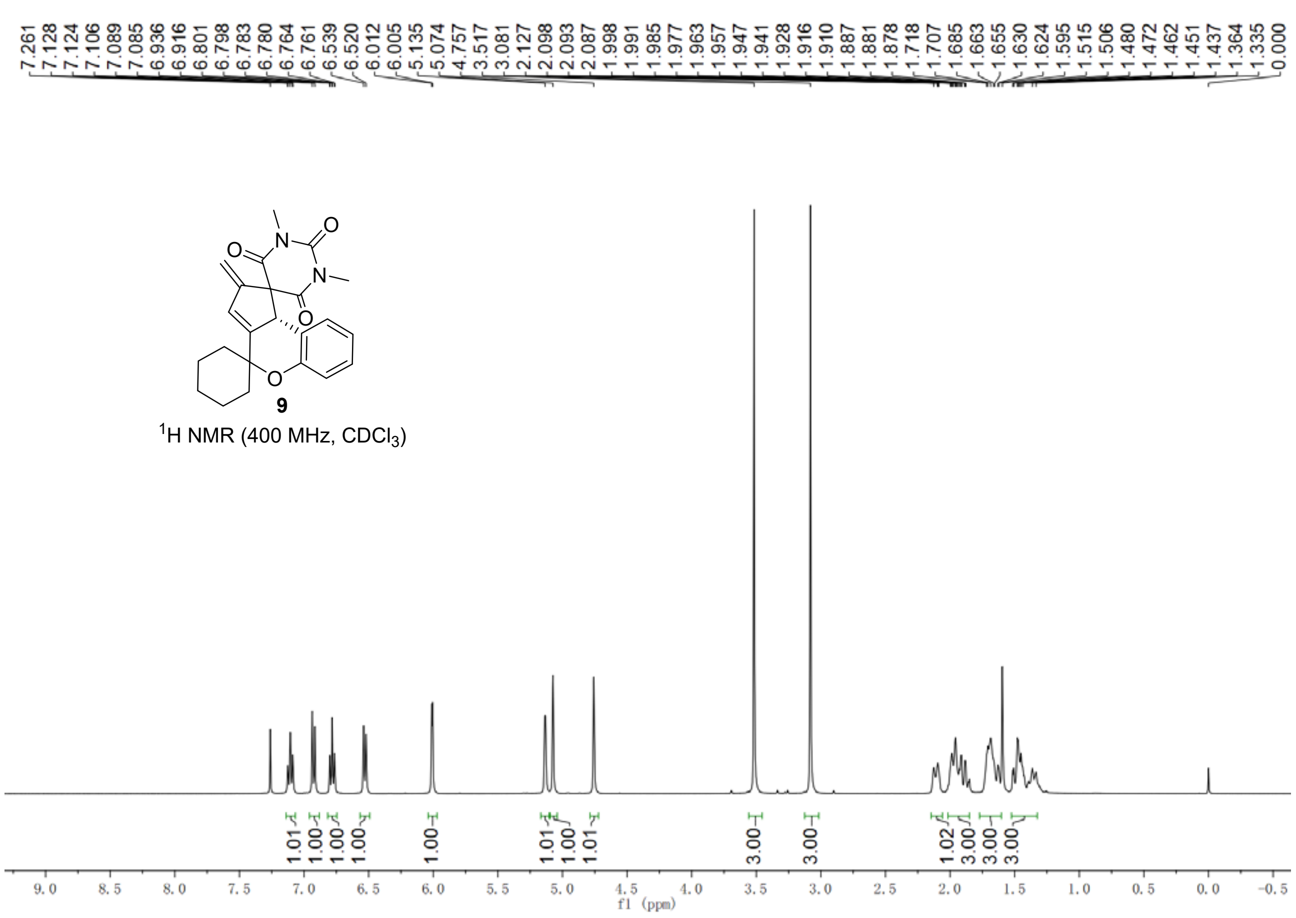
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
7.745	BV	0.17	764.2188	8462.1875	75.5785
8.487	VBA	0.19	217.0580	2734.3687	24.4215
			Totals:	11196.5562	100.0000



7

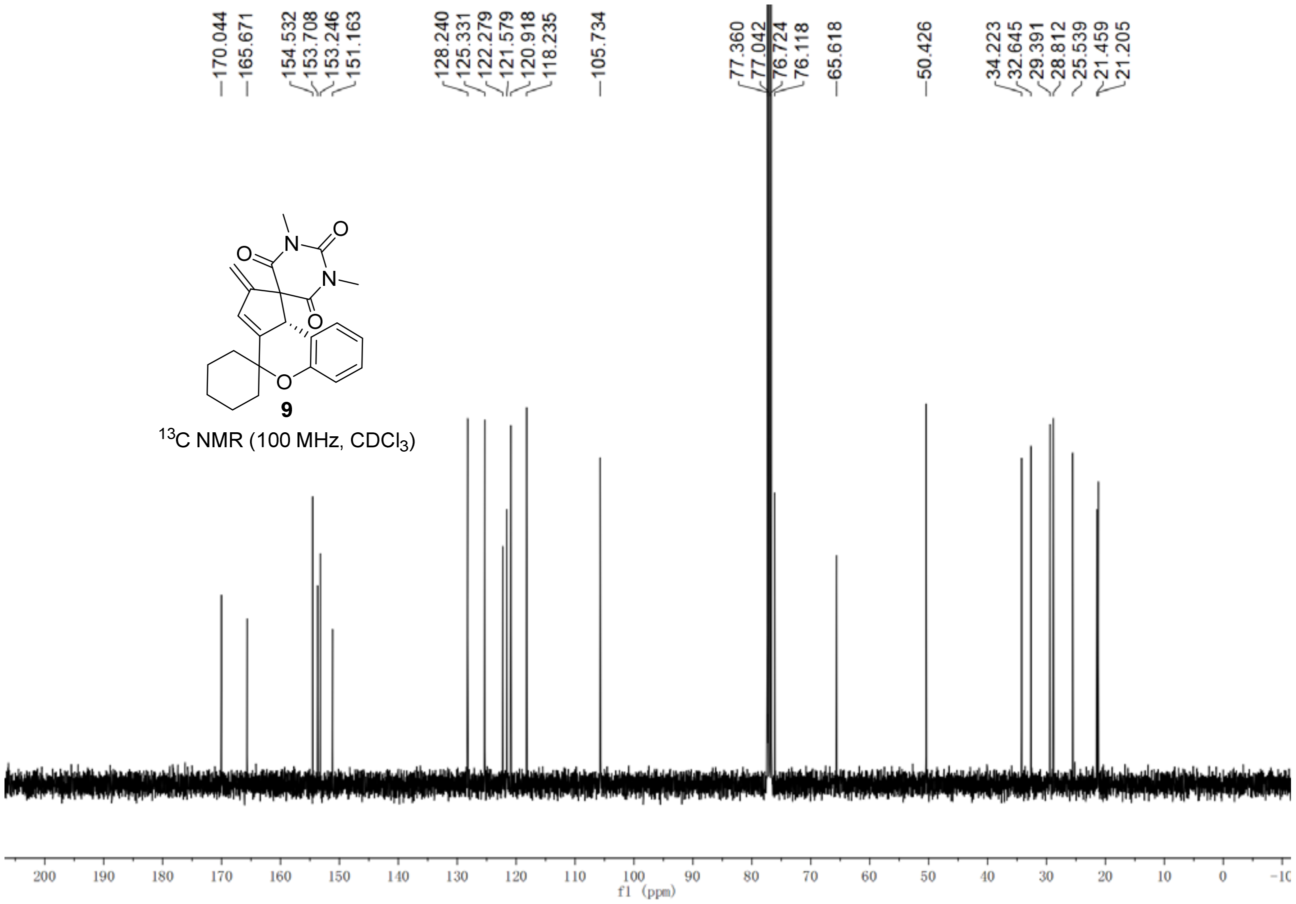
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{26}H_{22}NO_3Na^+$ 405.1461



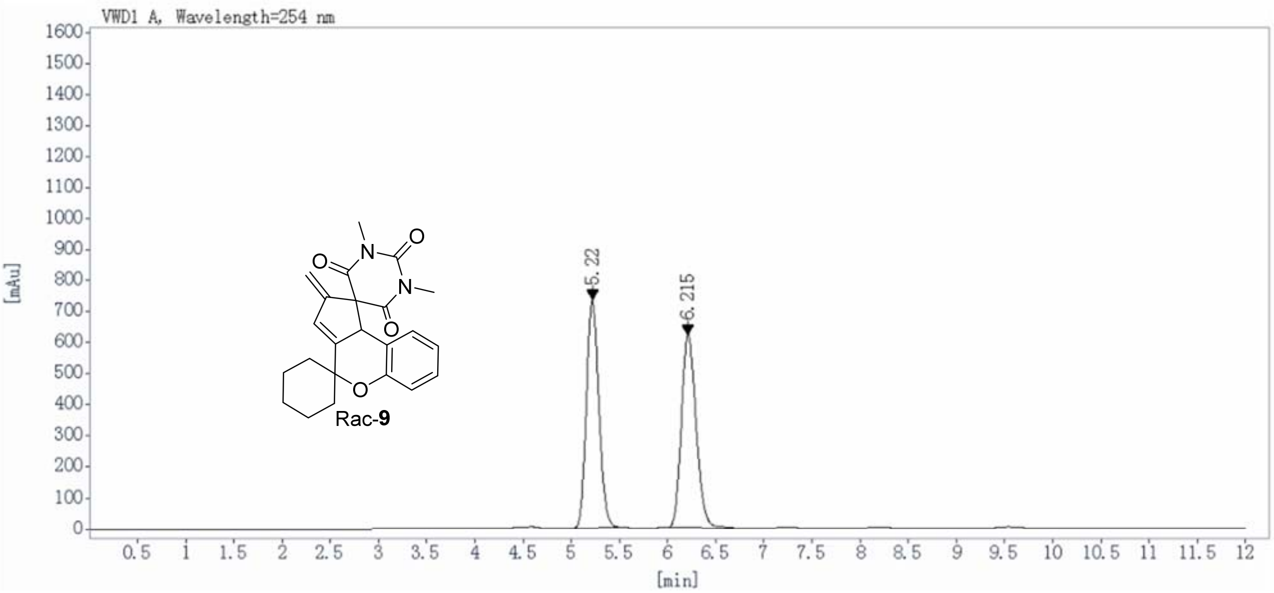
9

^{1}H NMR (400 MHz, CDCl$_3$)

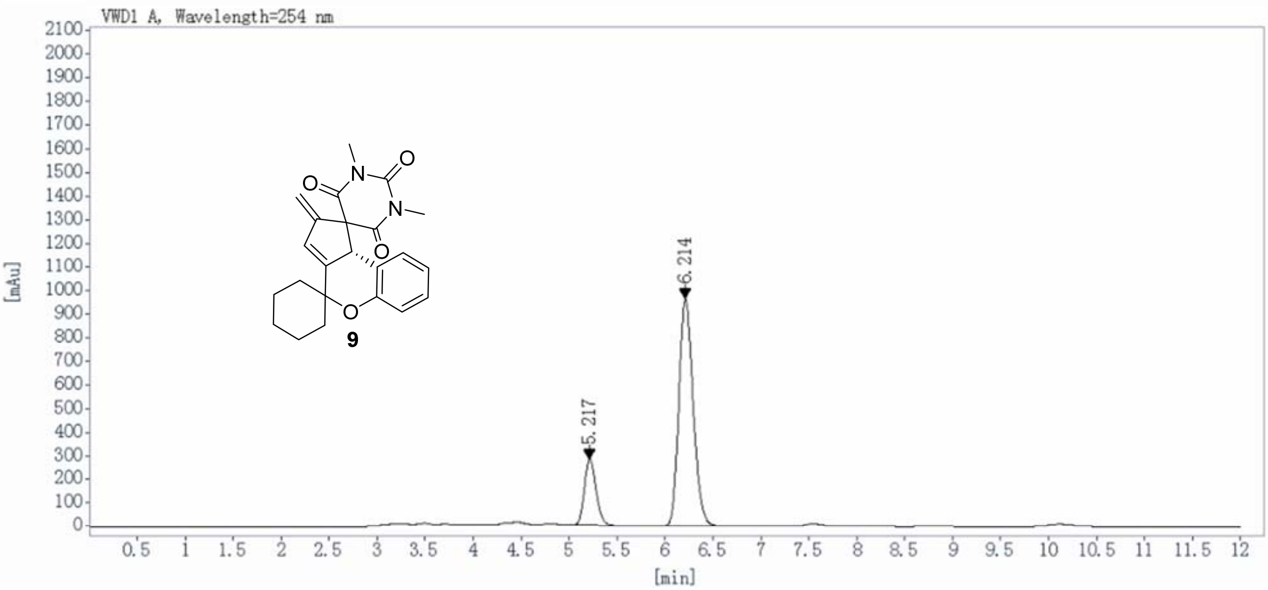


9

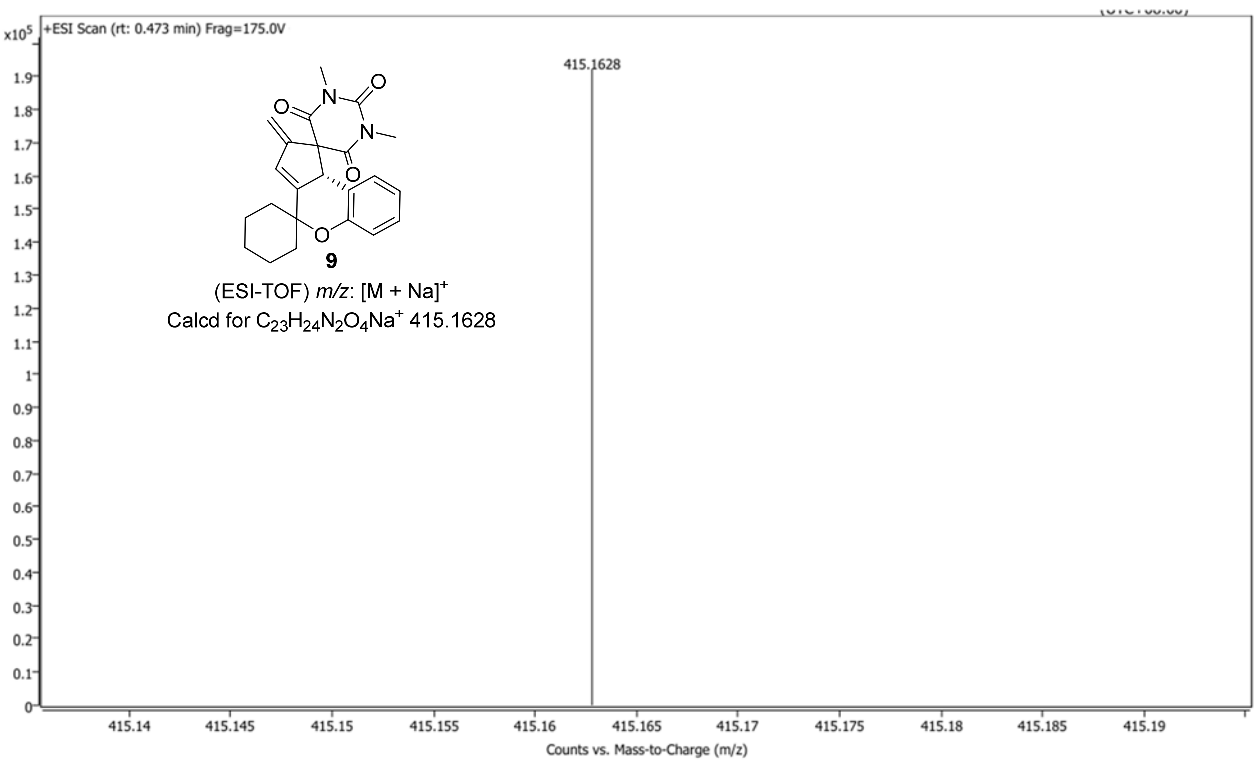
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.220	BBA	0.14	733.8380	6613.3145	49.8825
6.215	BBA	0.17	622.2565	6644.4639	50.1175
			Totals:	13257.7783	100.0000



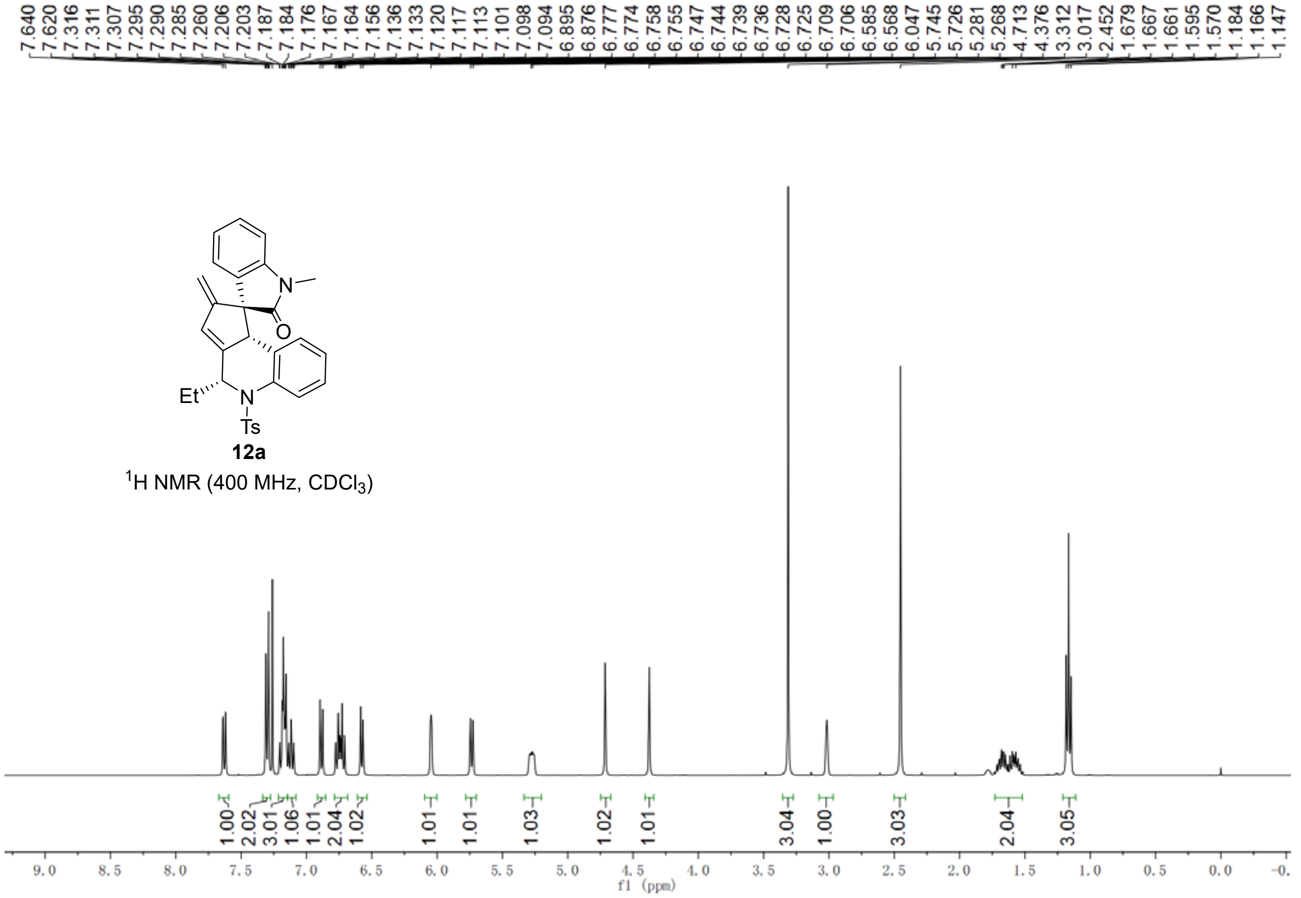
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.217	BBA	0.13	283.1979	2408.3604	19.3641
6.214	BBA	0.16	961.2004	10028.8535	80.6359
			Totals:	12437.2139	100.0000



9

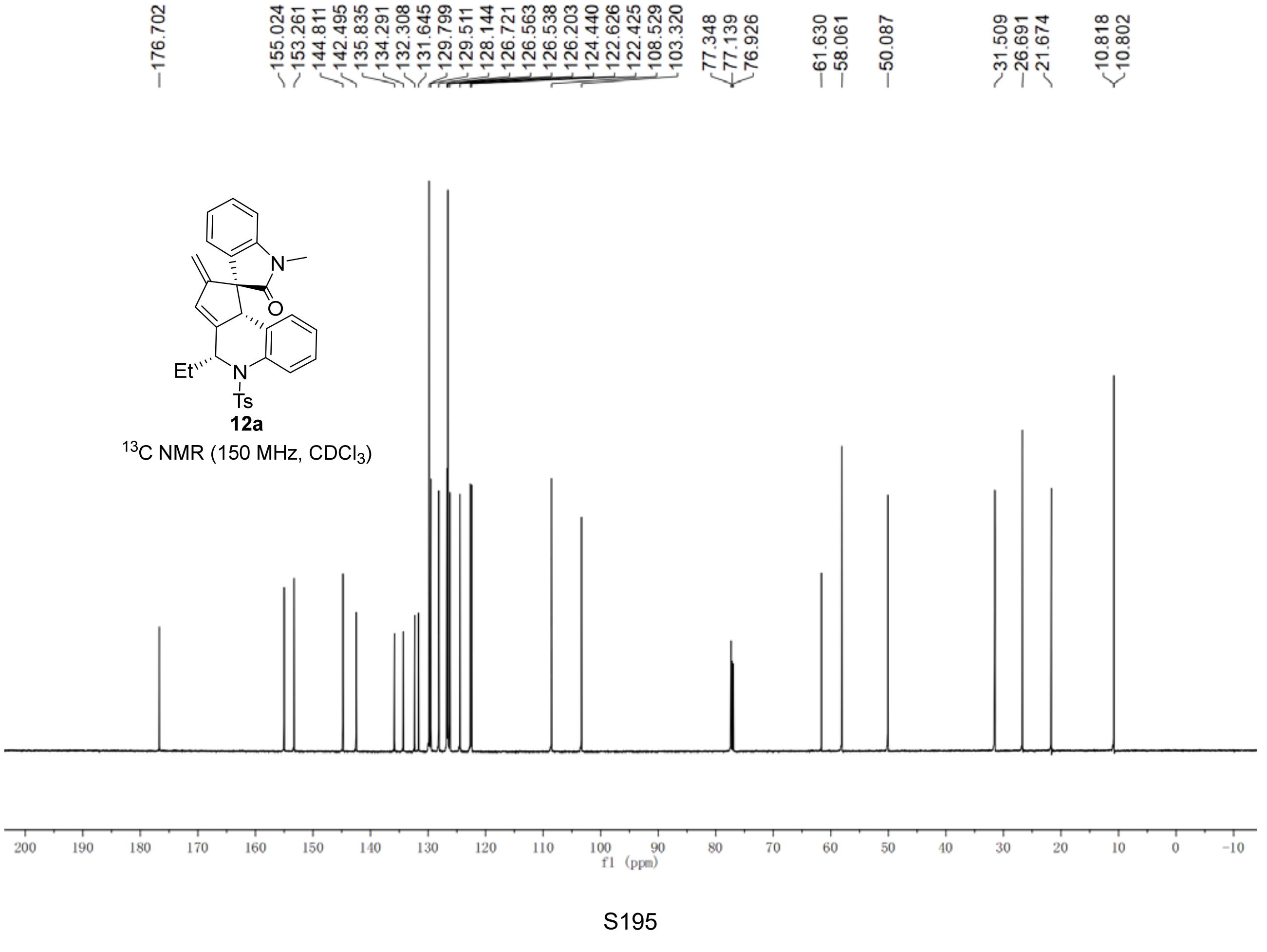
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{23}H_{24}N_2O_4Na^+$ 415.1628



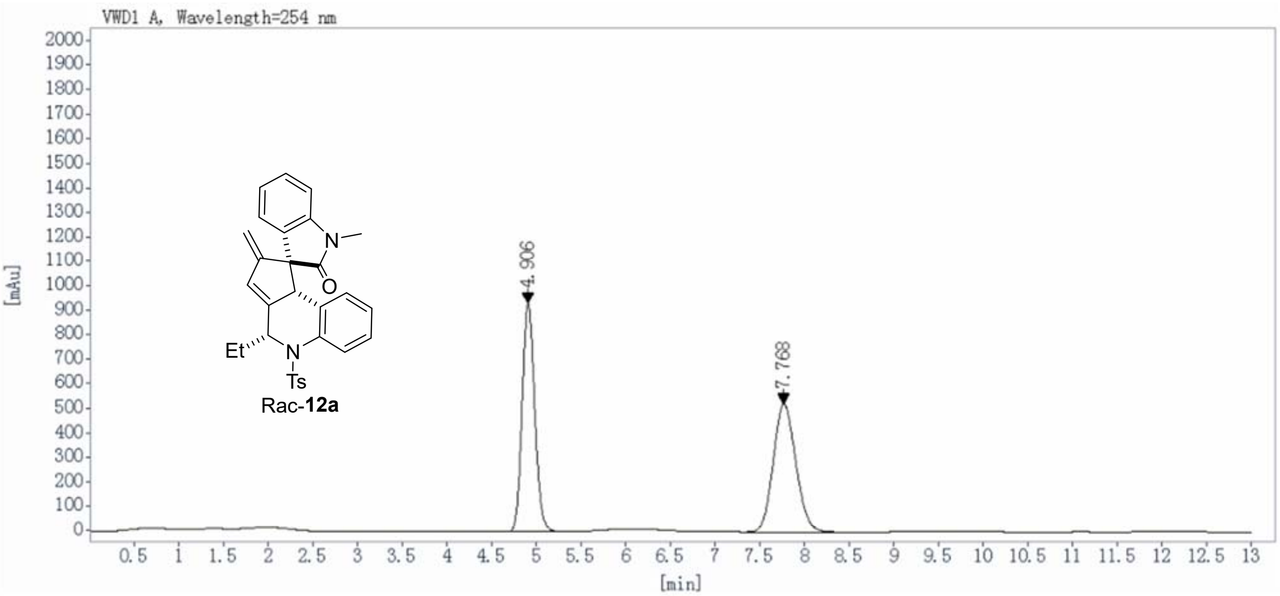
12a

^{1}H NMR (400 MHz, CDCl$_3$)

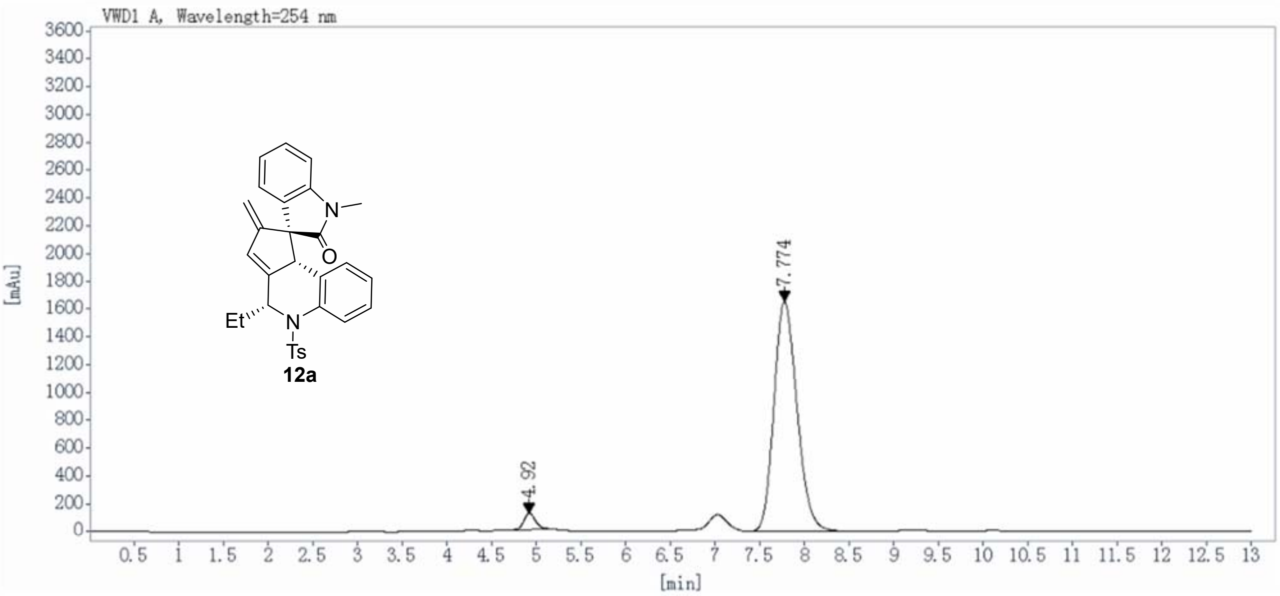


12a

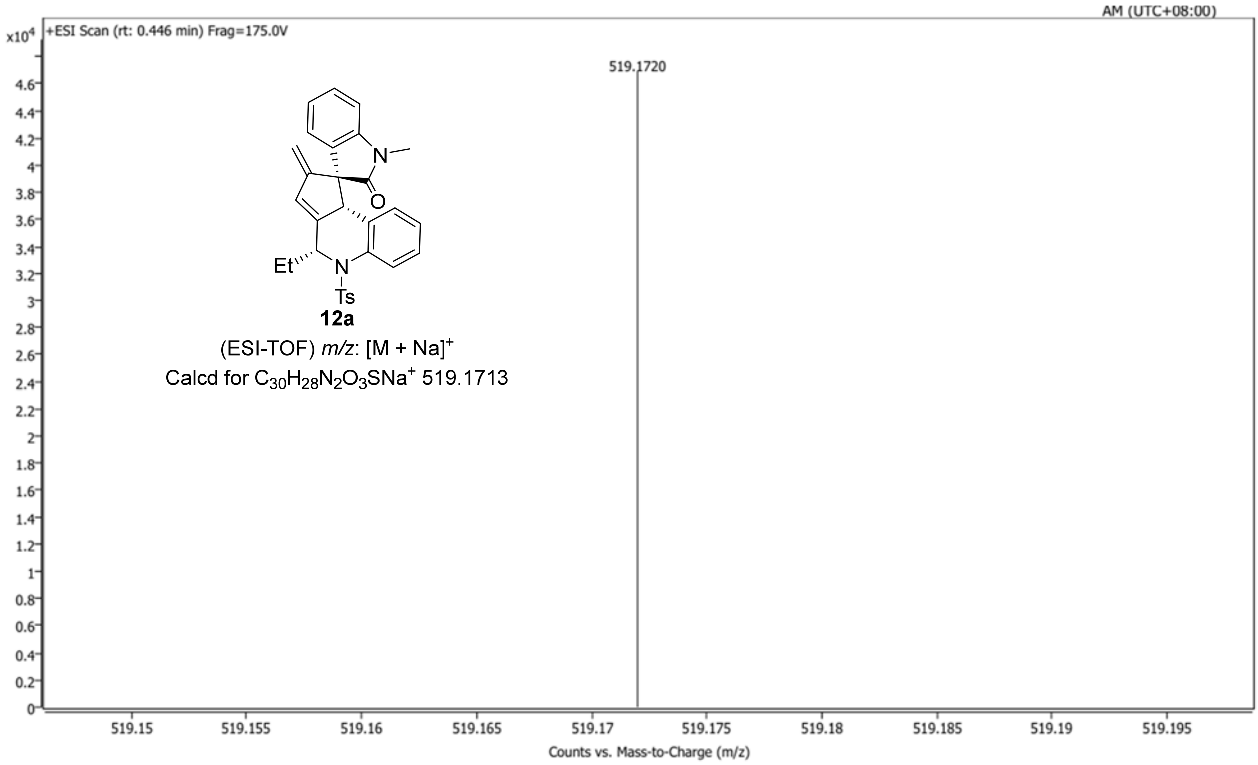
^{13}C NMR (150 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.906	BBA	0.15	935.4191	9221.7646	49.9052
7.768	BBA	0.28	524.1456	9256.7979	50.0948
			Totals:	18478.5625	100.0000



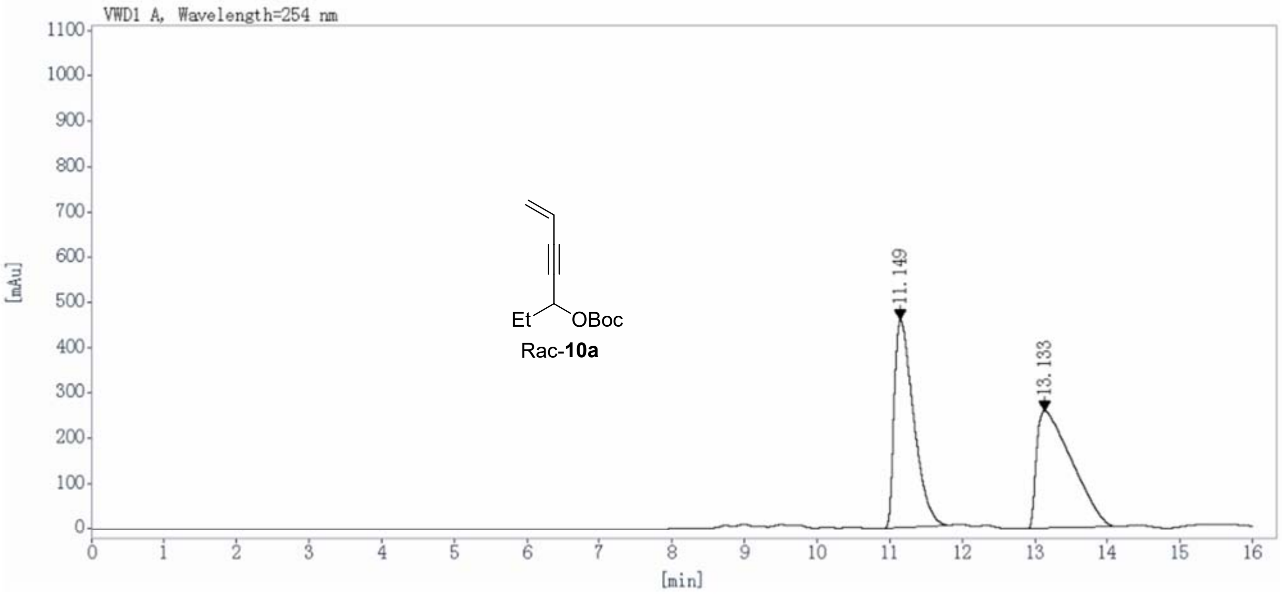
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.920	BBA	0.14	117.5743	1106.3406	3.5979
7.774	BBA	0.28	1648.6512	29643.4590	96.4021
			Totals:	30749.7996	100.0000



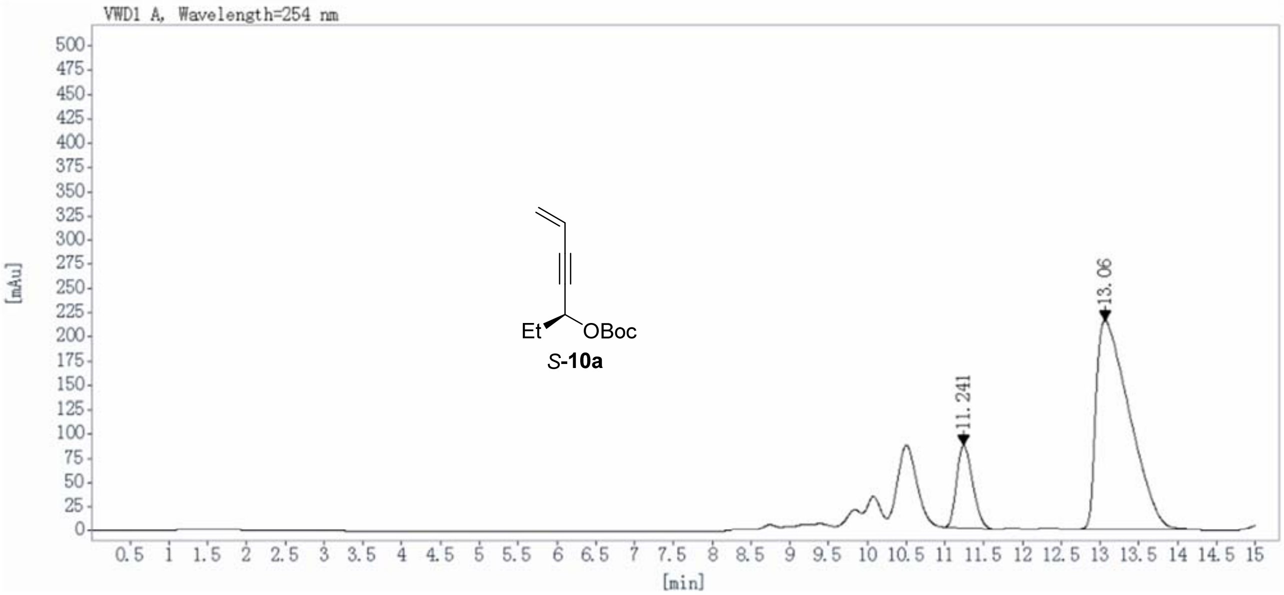
12a

(ESI-TOF) *m/z*: [M + Na]$^+$

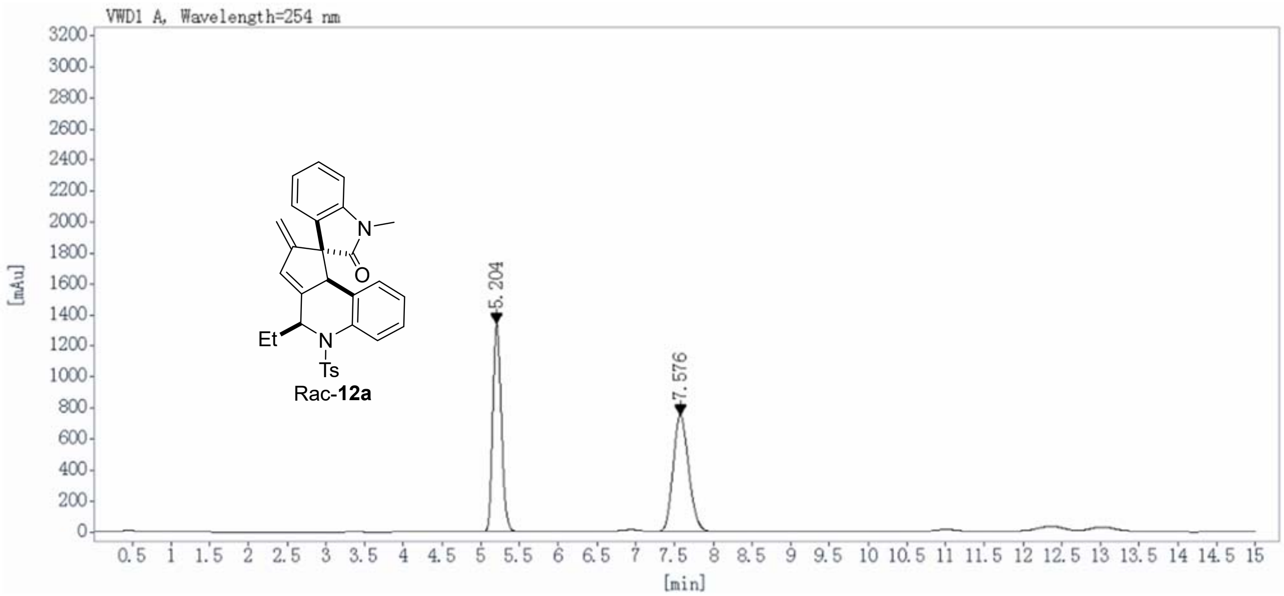
Calcd for $C_{30}H_{28}N_2O_3SNa^+$ 519.1713



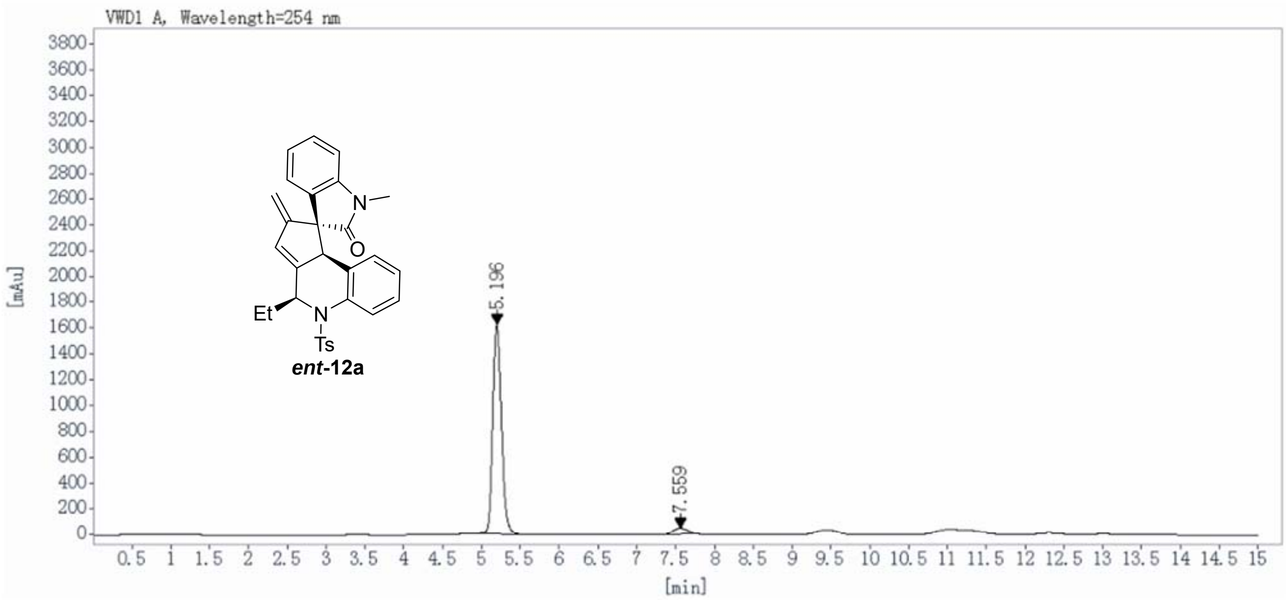
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
11.149	BB	0.28	458.2355	8487.8613	49.3090
13.133	BB	0.51	258.5074	8725.7383	50.6910
			Totals:	17213.5996	100.0000



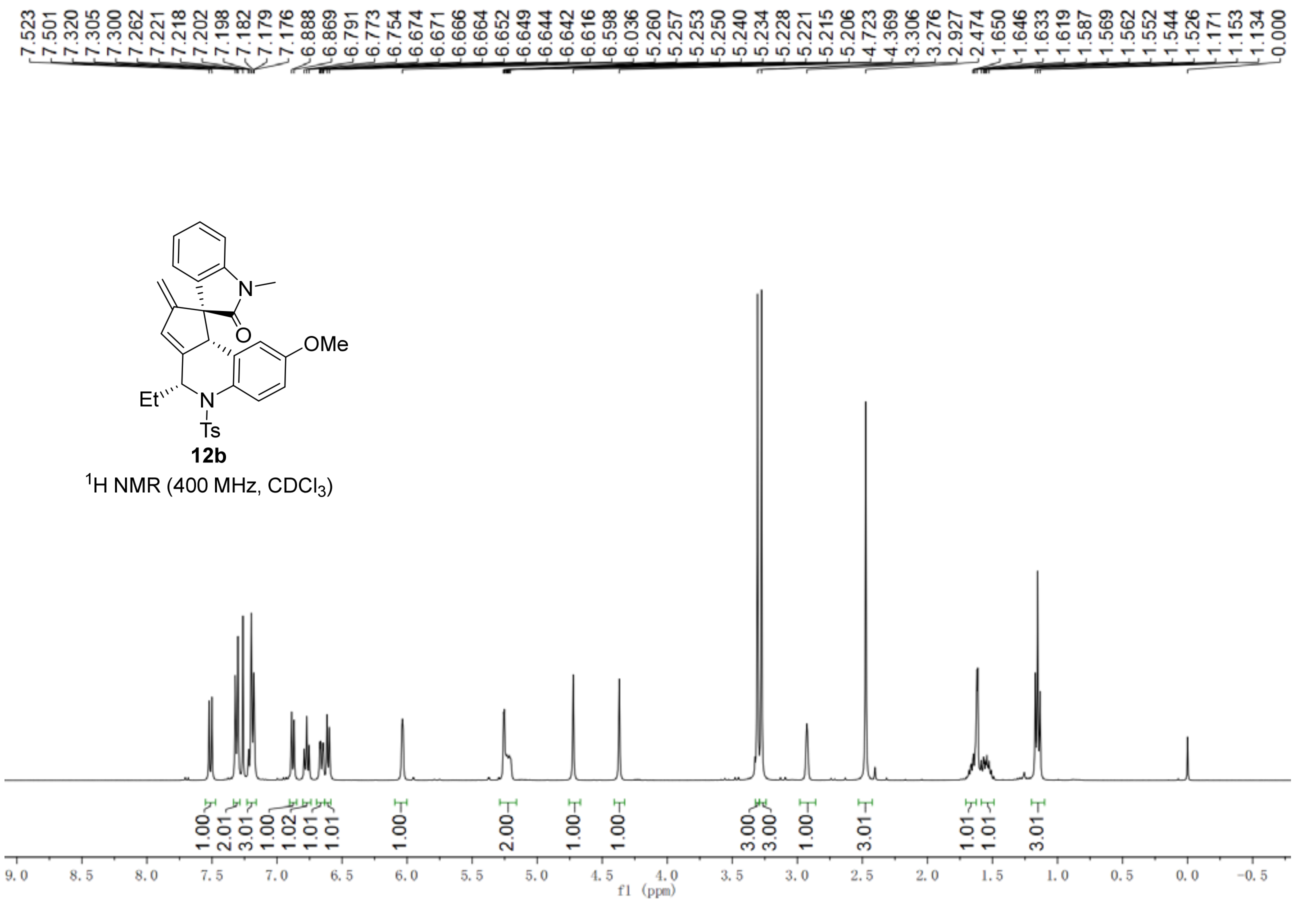
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
11.241	BB	0.23	85.3246	1229.3444	15.9744
13.060	BBA	0.47	215.0339	6466.3936	84.0256
			Totals:	7695.7379	100.0000



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.204	BBA	0.12	1345.2666	10414.7266	49.8143
7.576	BBA	0.22	752.3749	10492.3945	50.1857
			Totals:	20907.1211	100.0000

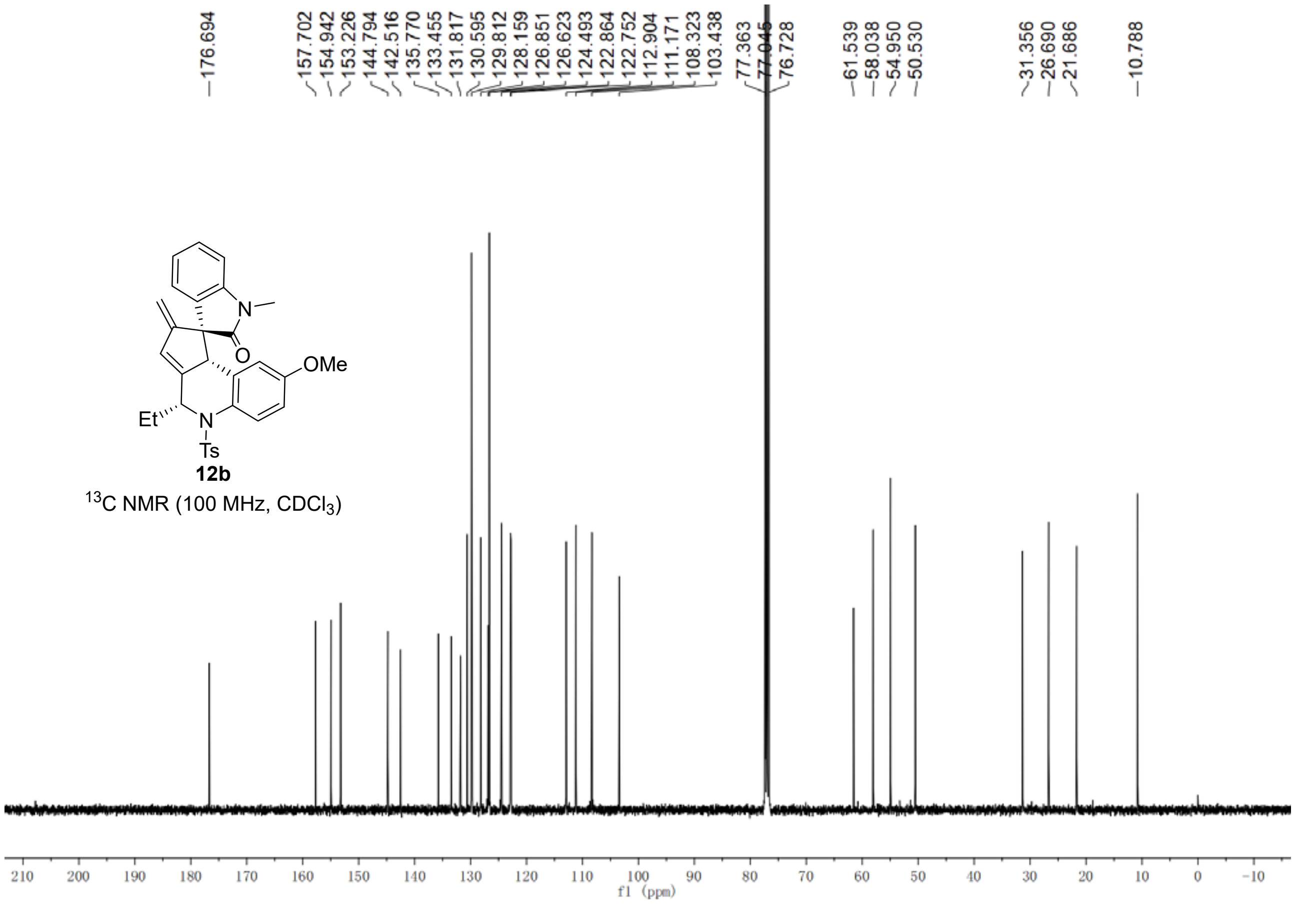


Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.196	BBA	0.12	1618.7483	12679.8691	95.4738
7.559	BBA	0.20	46.7730	601.1260	4.5262
			Totals:	13280.9952	100.0000



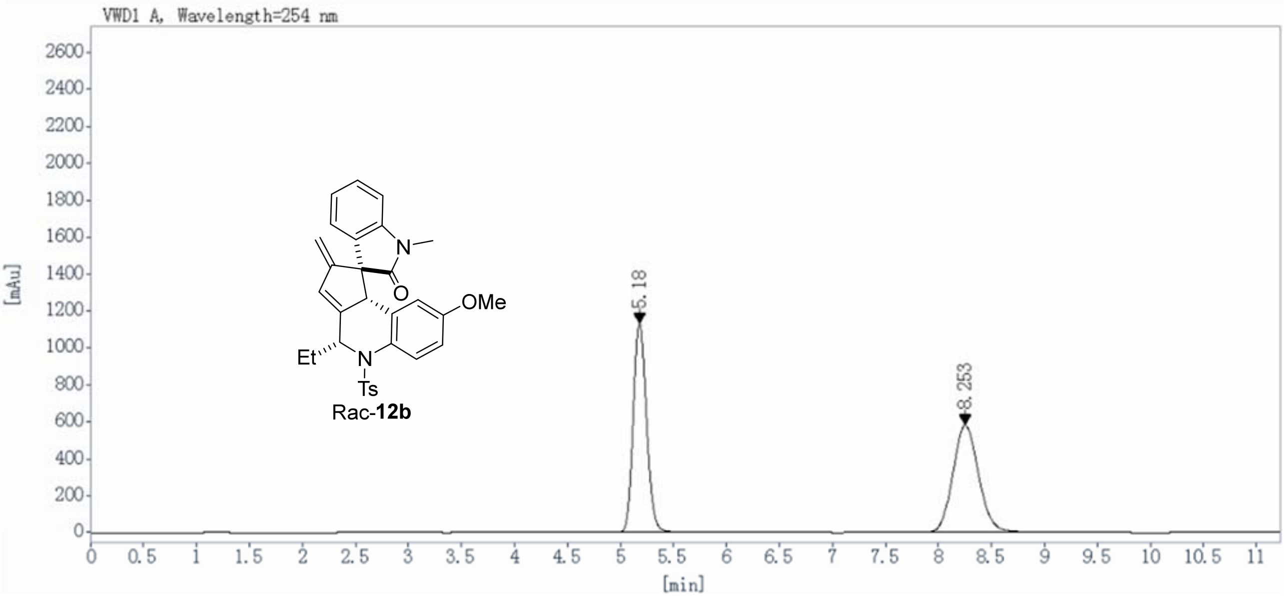
12b

^{1}H NMR (400 MHz, CDCl$_3$)

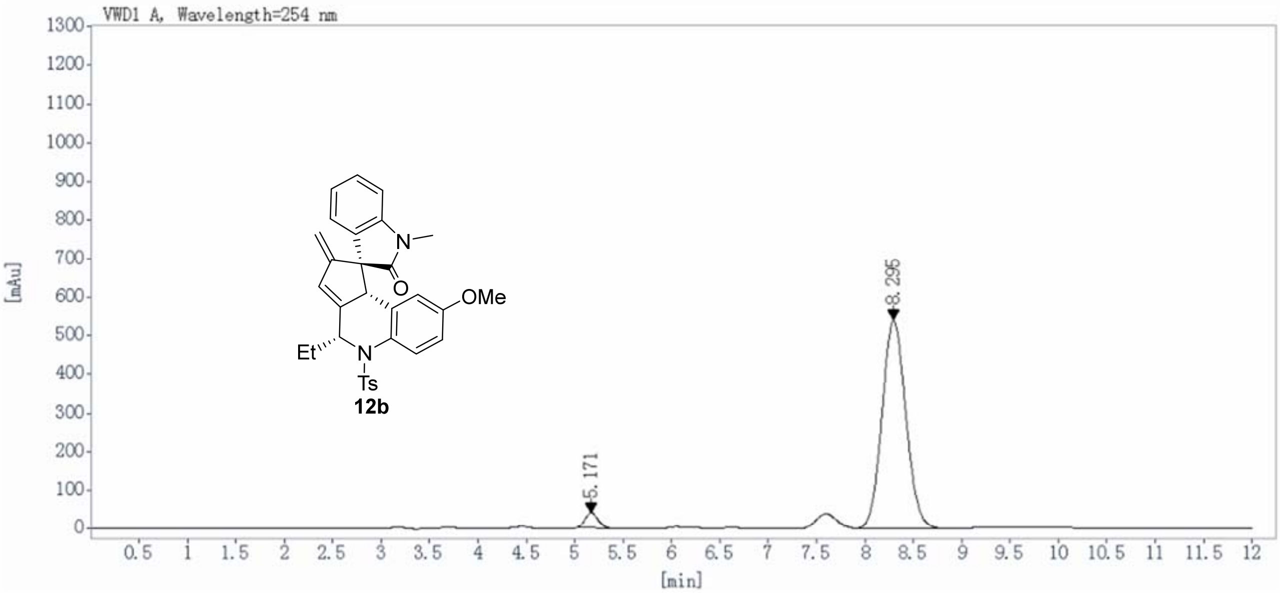


12b

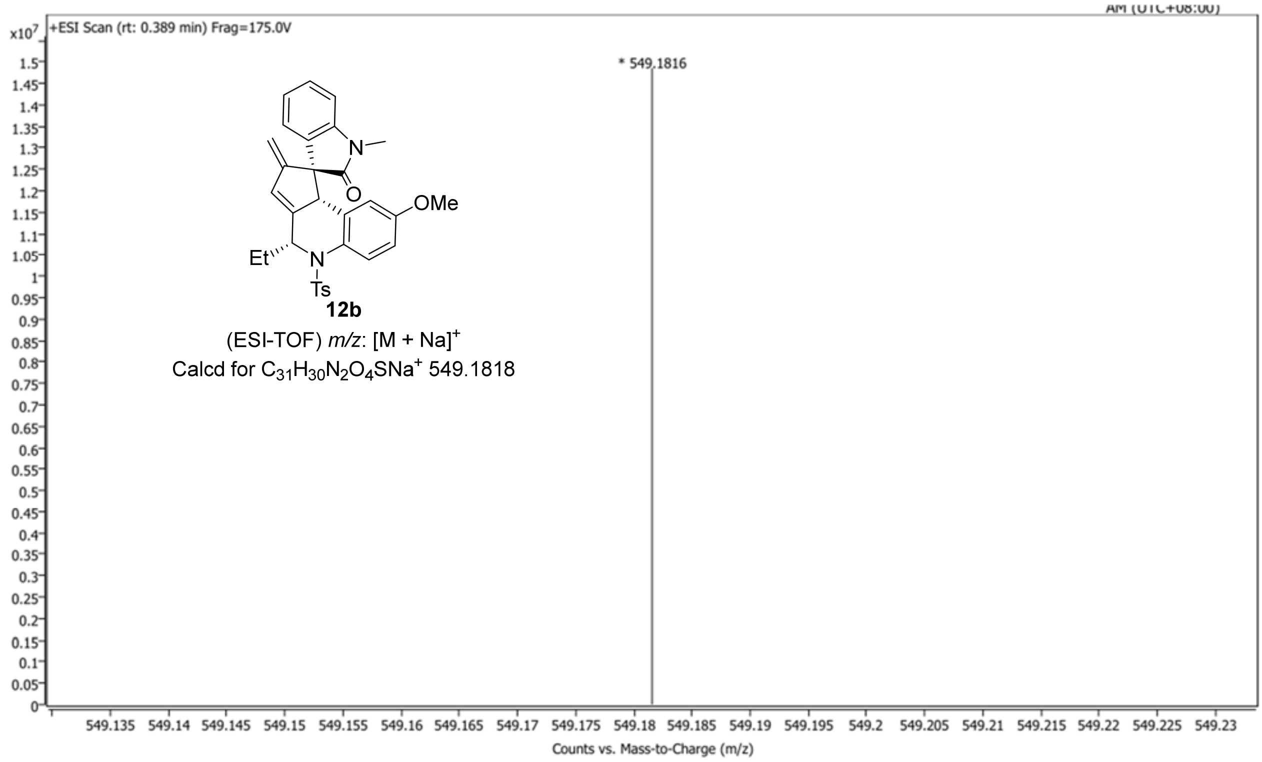
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.180	BBA	0.13	1133.0798	9818.5264	49.8066
8.253	BBA	0.26	580.9495	9894.7607	50.1934
			Totals:	19713.2871	100.0000



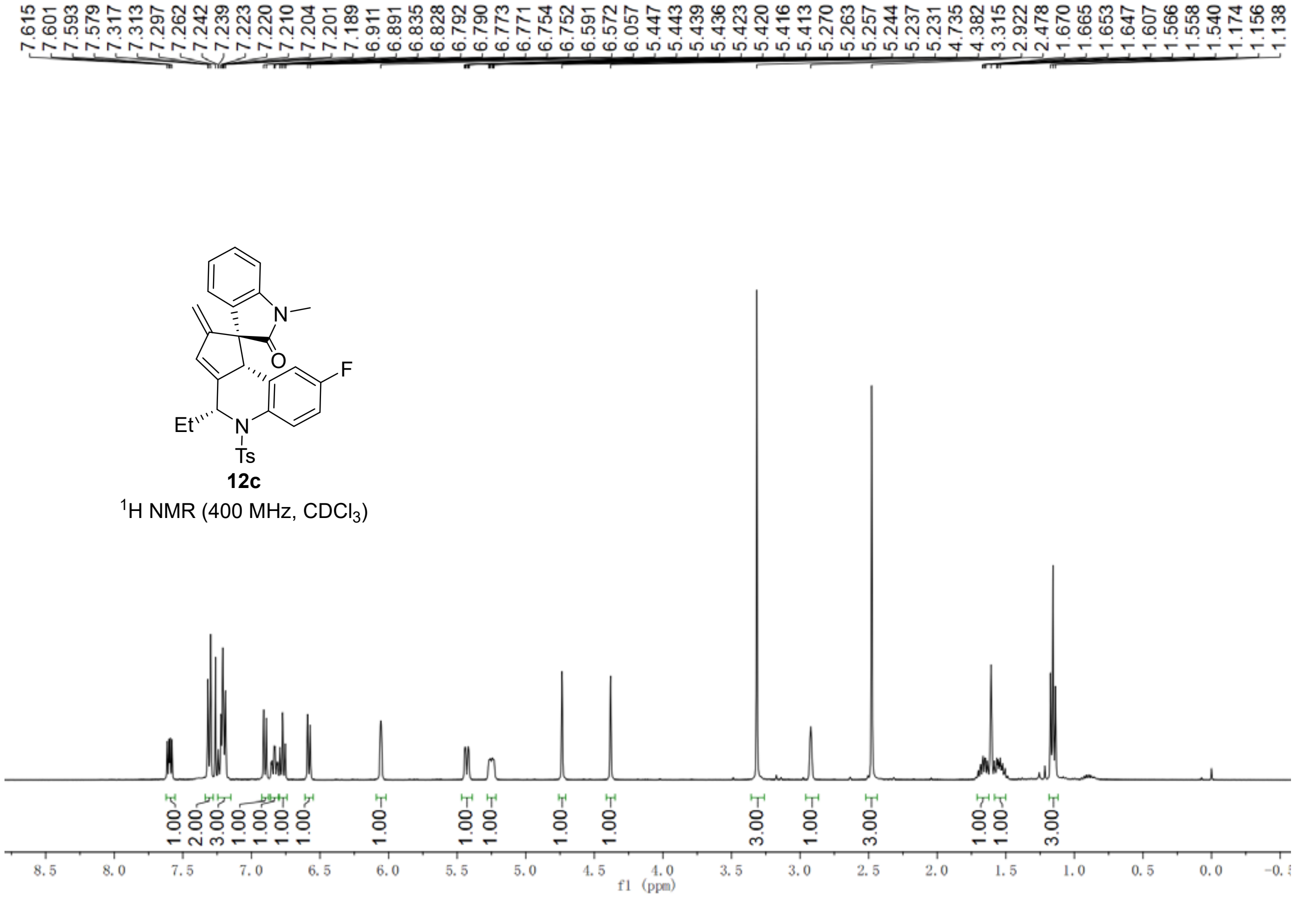
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.171	BBA	0.14	38.6503	352.1087	3.6790
8.295	BBA	0.27	538.2534	9218.6953	96.3210
			Totals:	9570.8040	100.0000



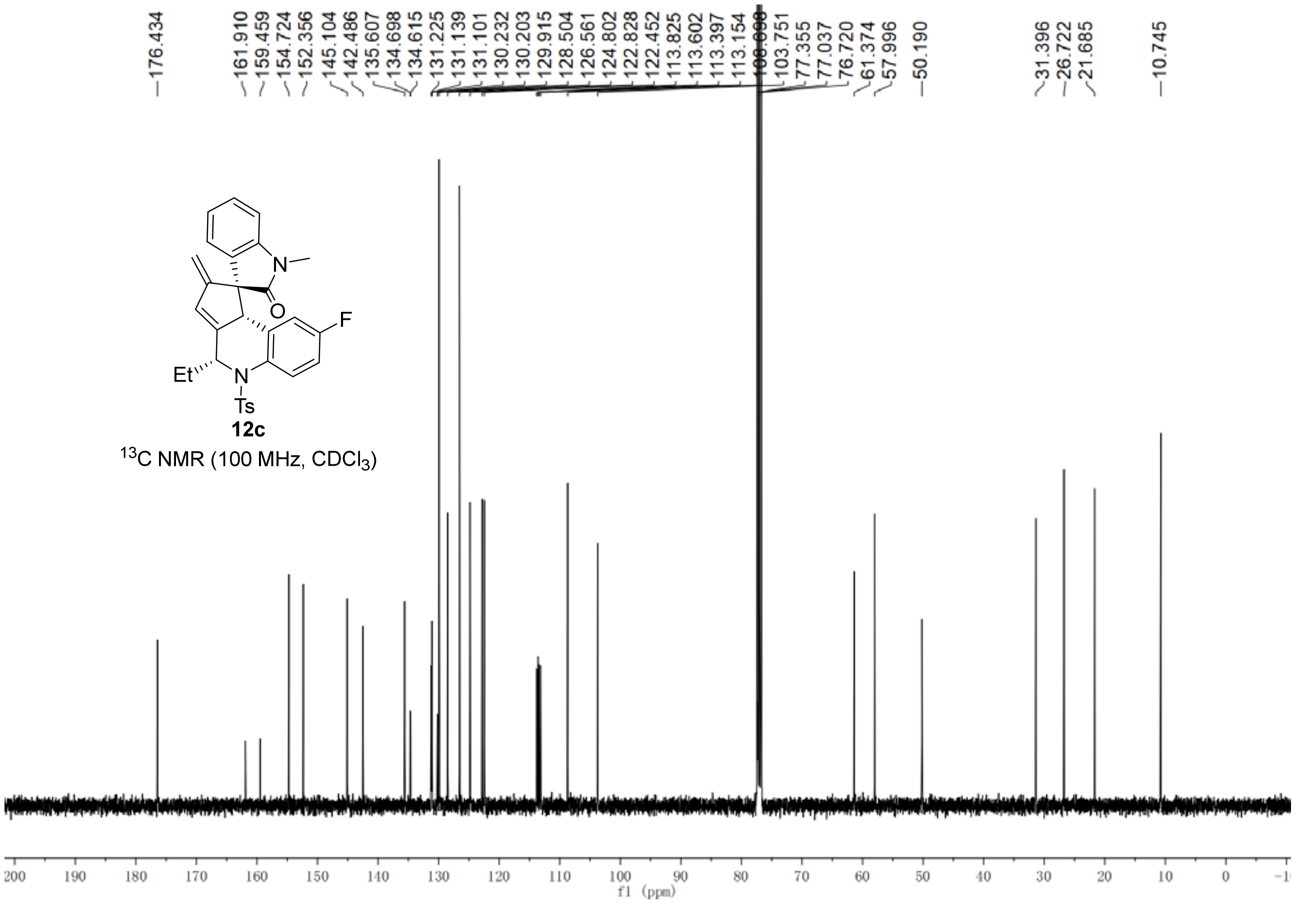
12b

(ESI-TOF) *m/z*: $[M + Na]^+$

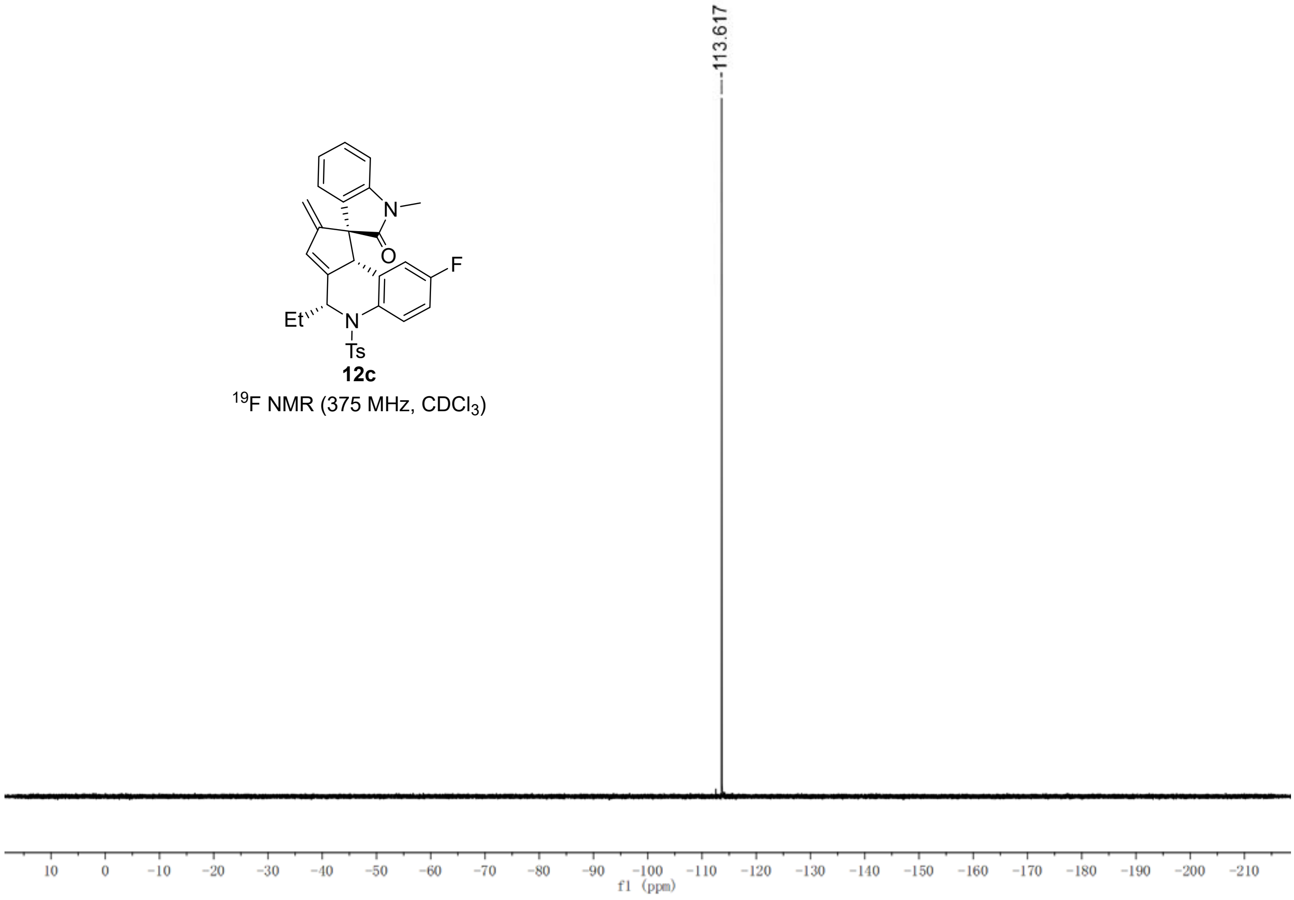
Calcd for $C_{31}H_{30}N_2O_4SNa^+$ 549.1818


12c

^{1}H NMR (400 MHz, CDCl$_3$)

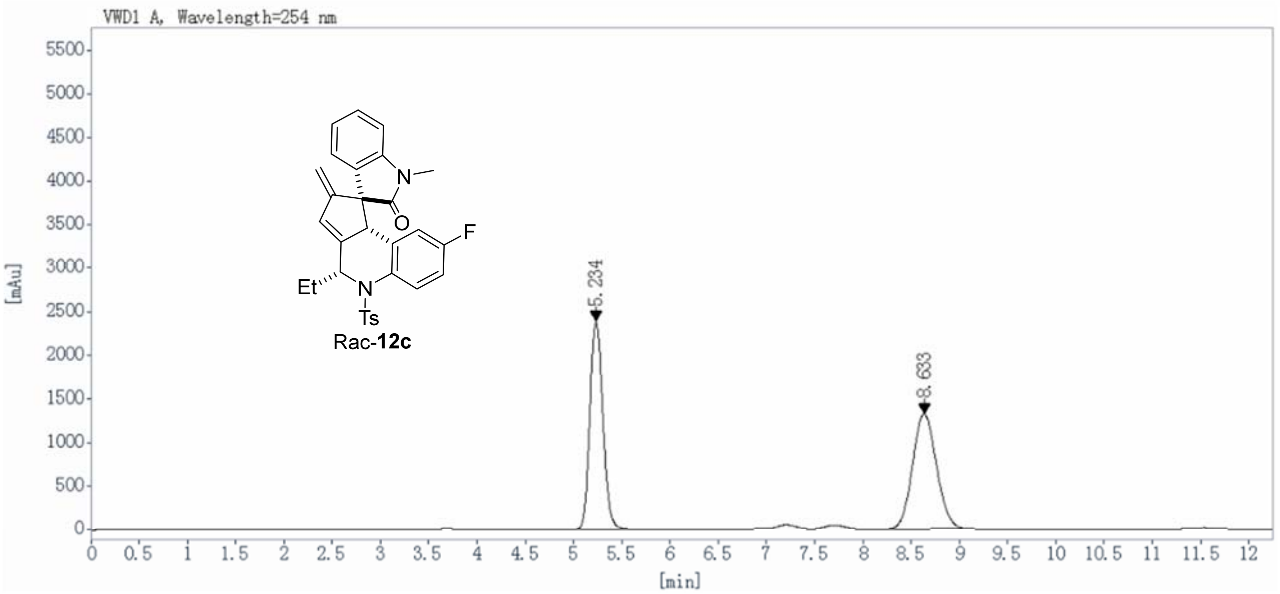

12c

^{13}C NMR (100 MHz, CDCl$_3$)



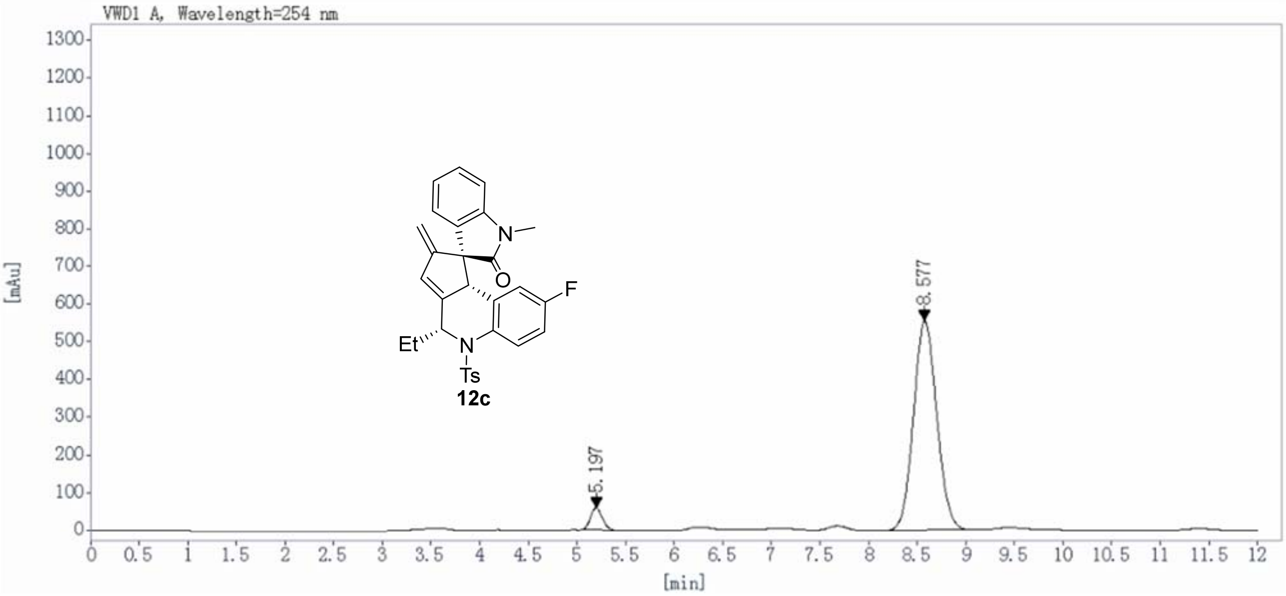
12c

^{19}F NMR (375 MHz, $CDCl_3$)



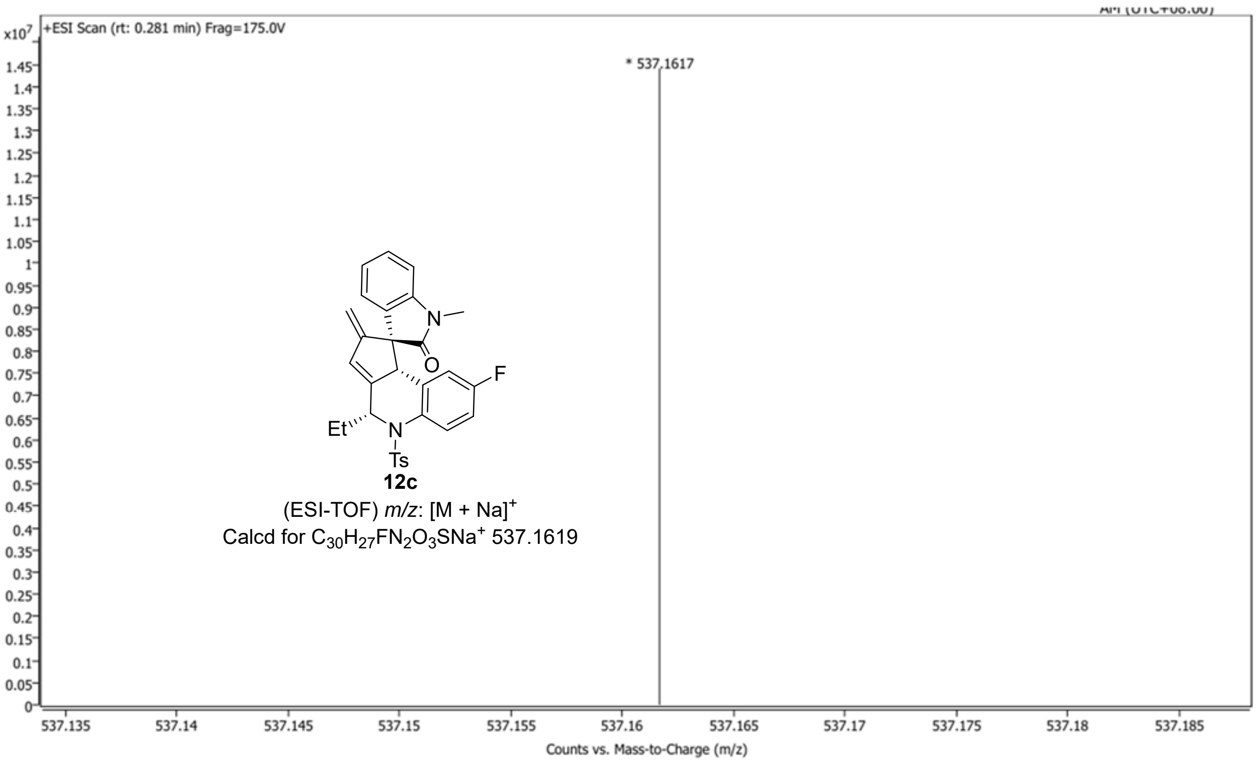
Rac-**12c**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.234	BBA	0.15	2381.8638	22391.8848	49.2868
8.633	BBA	0.27	1325.9989	23039.9160	50.7132
			Totals:	45431.8008	100.0000



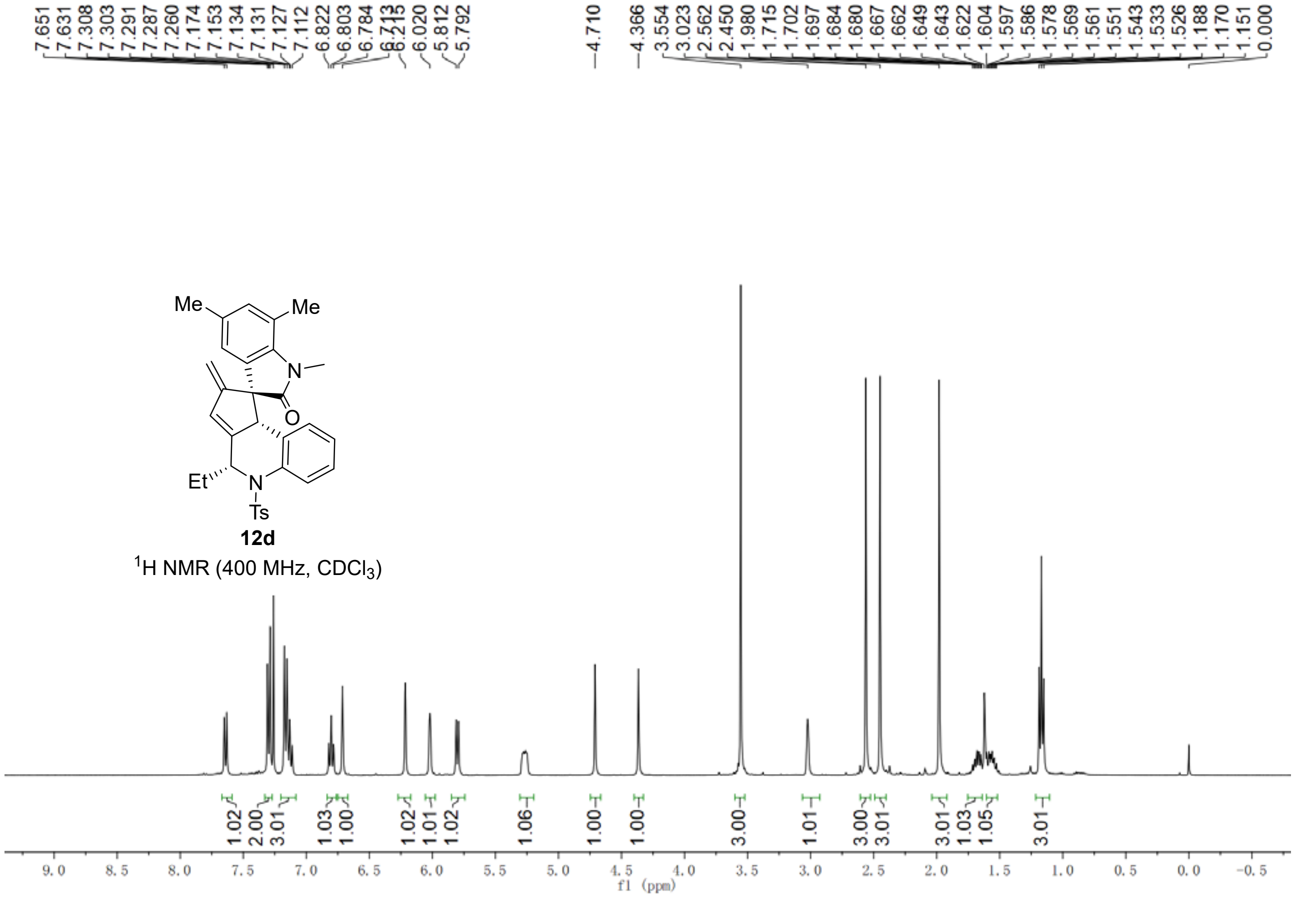
12c

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.197	BBA	0.13	58.9124	498.6888	5.0997
8.577	BB	0.26	555.4326	9280.1836	94.9003
			Totals:	9778.8724	100.0000



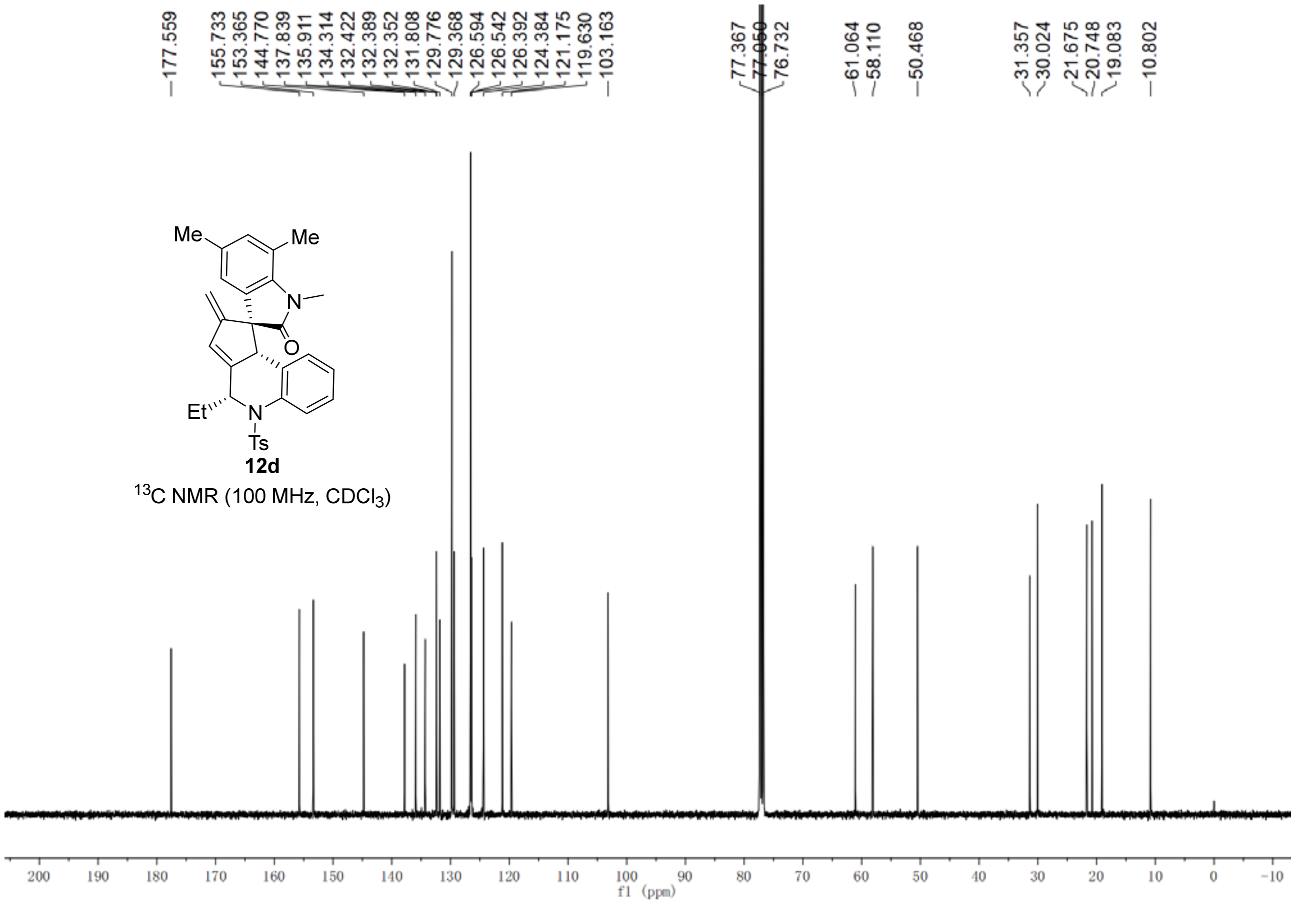
12c

(ESI-TOF) *m/z*: $[M + Na]^+$
Calcd for $C_{30}H_{27}FN_2O_3SNa^+$ 537.1619



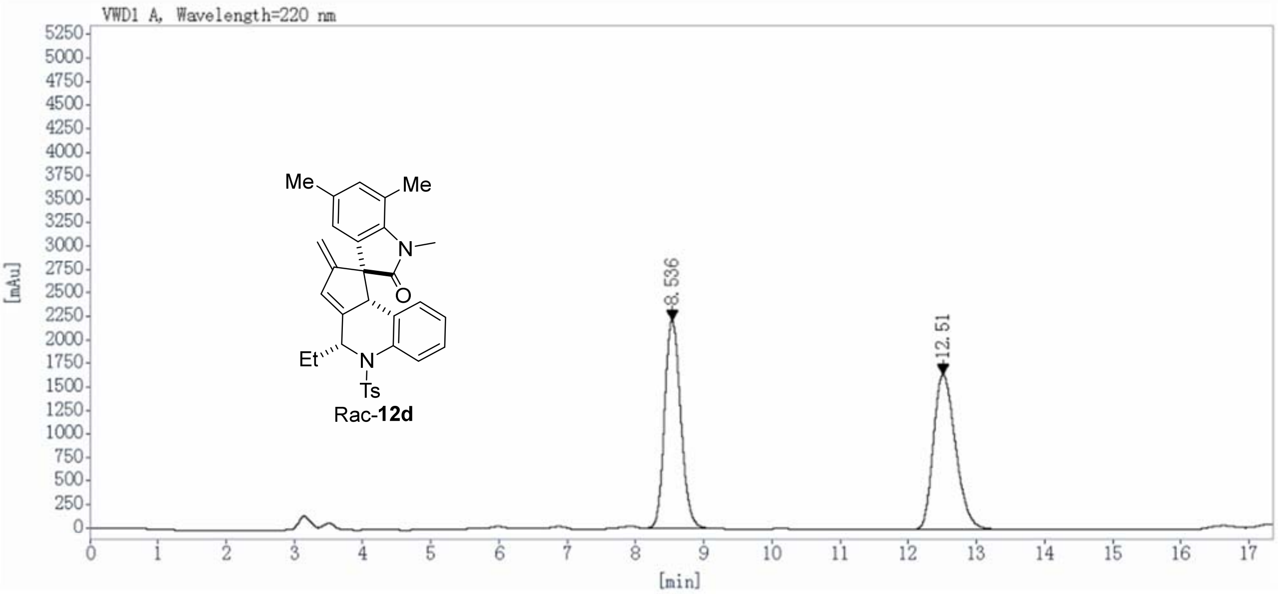
12d

^{1}H NMR (400 MHz, CDCl$_3$)

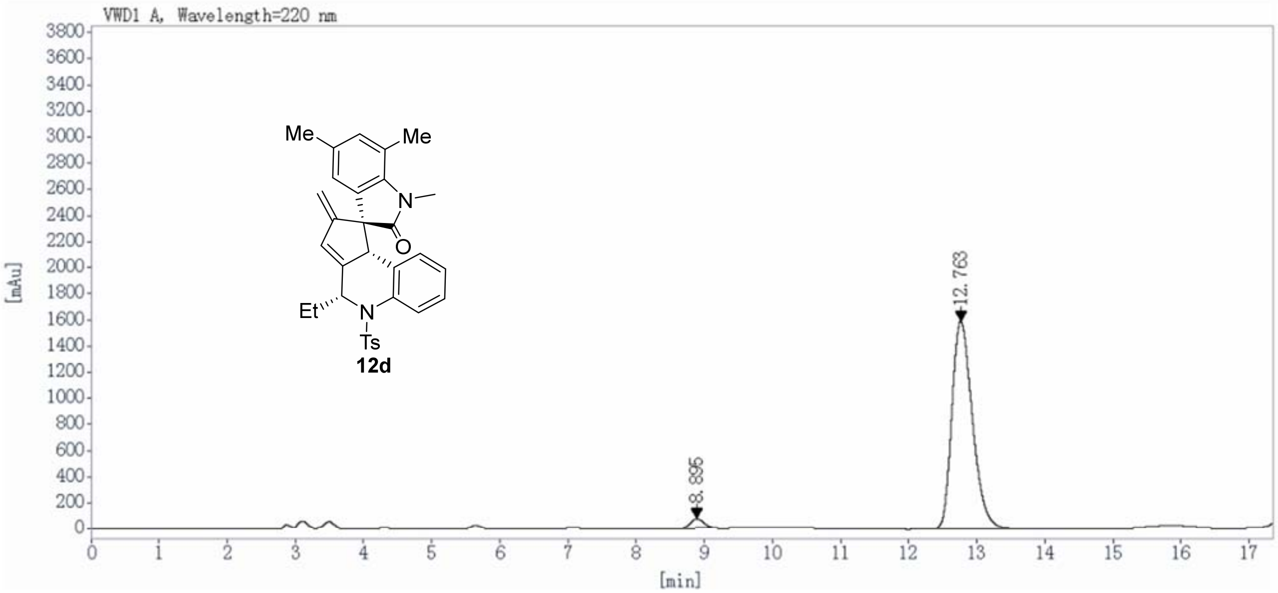


12d

^{13}C NMR (100 MHz, CDCl$_3$)

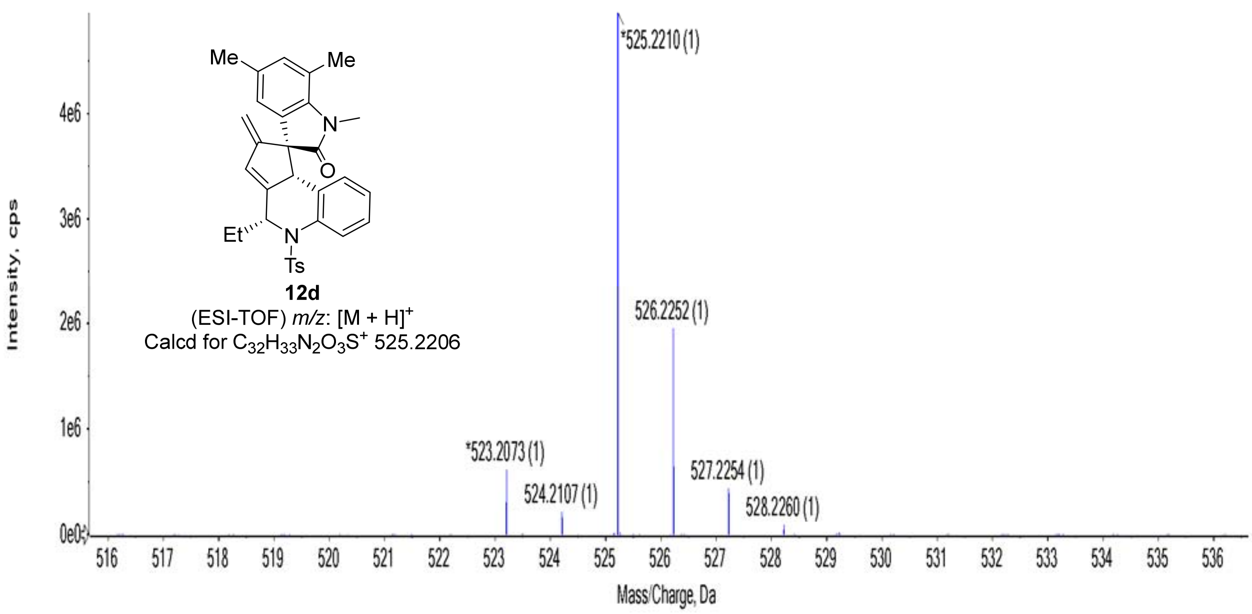


Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.536	BBA	0.26	2210.6050	36334.6484	49.2347
12.510	BBA	0.35	1650.5771	37464.1758	50.7653
			Totals:	73798.8242	100.0000



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.895	BBA	0.21	72.8597	991.8591	2.8952
12.763	BBA	0.32	1591.7700	33266.9531	97.1048
			Totals:	34258.8123	100.0000

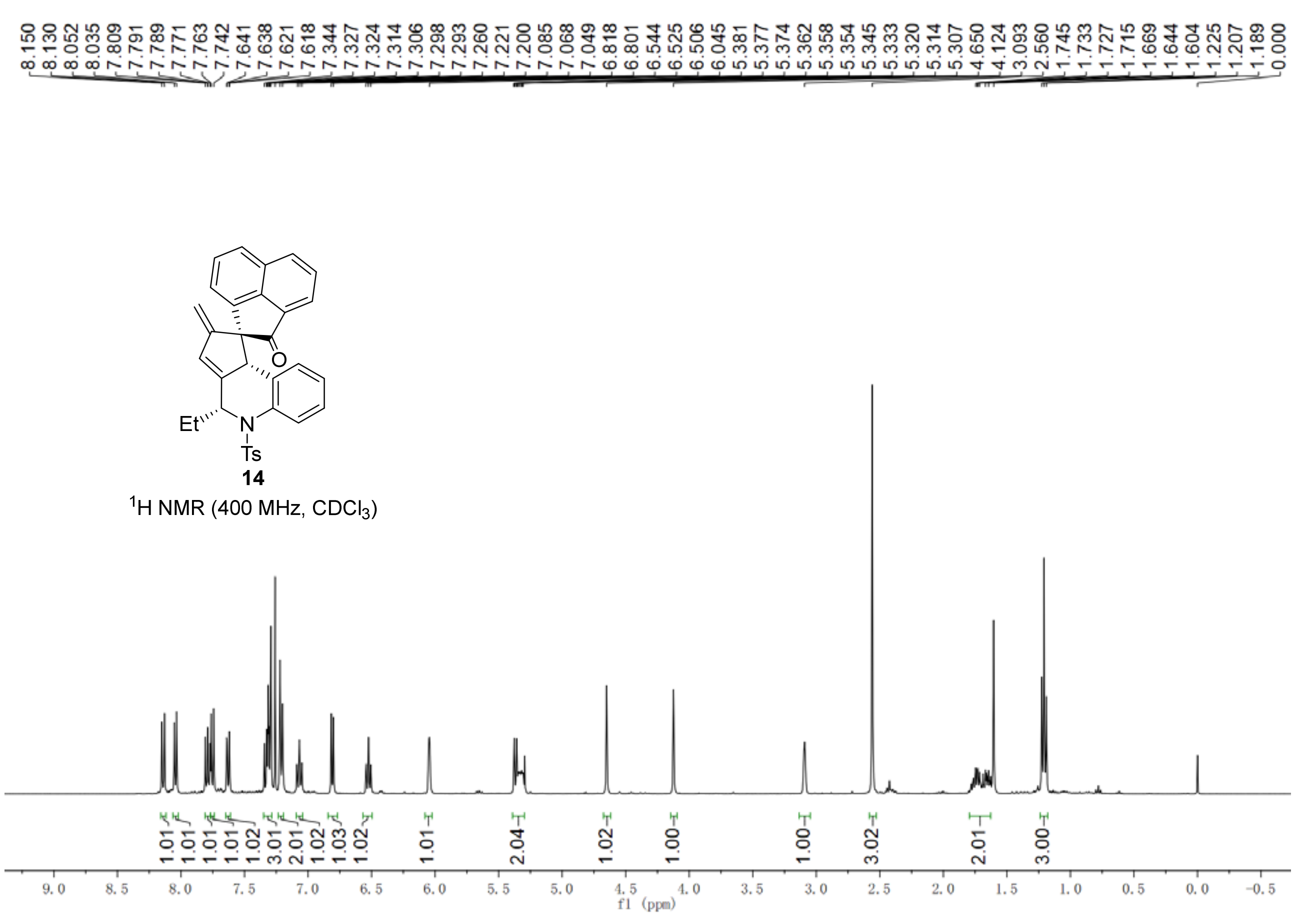
Spectrum from 20240817.wiff2 (sample 9) - 5, +TOF MS (400 - 700) from 0.063 to 0.113 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points), centroided



12d

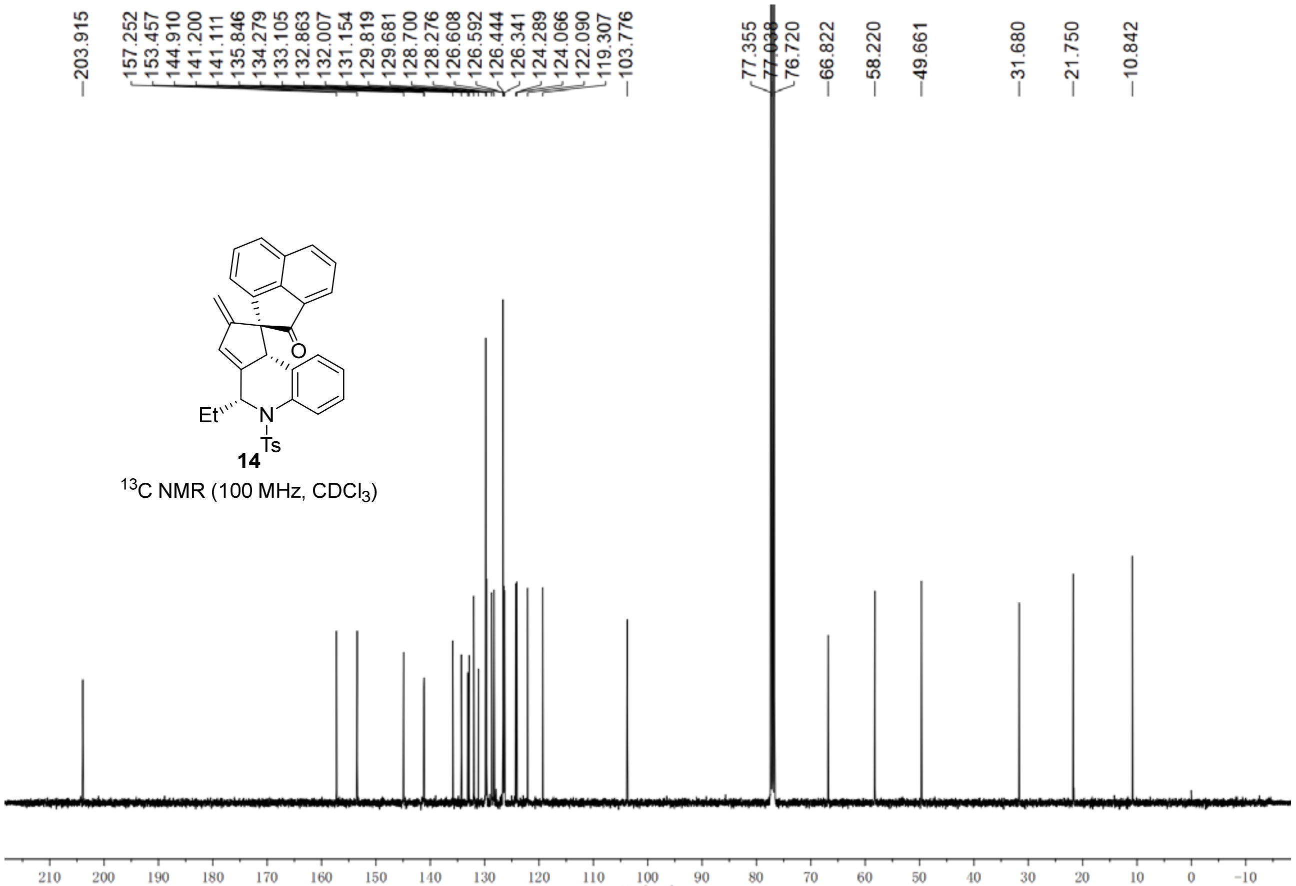
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{32}H_{33}N_2O_3S^+$ 525.2206



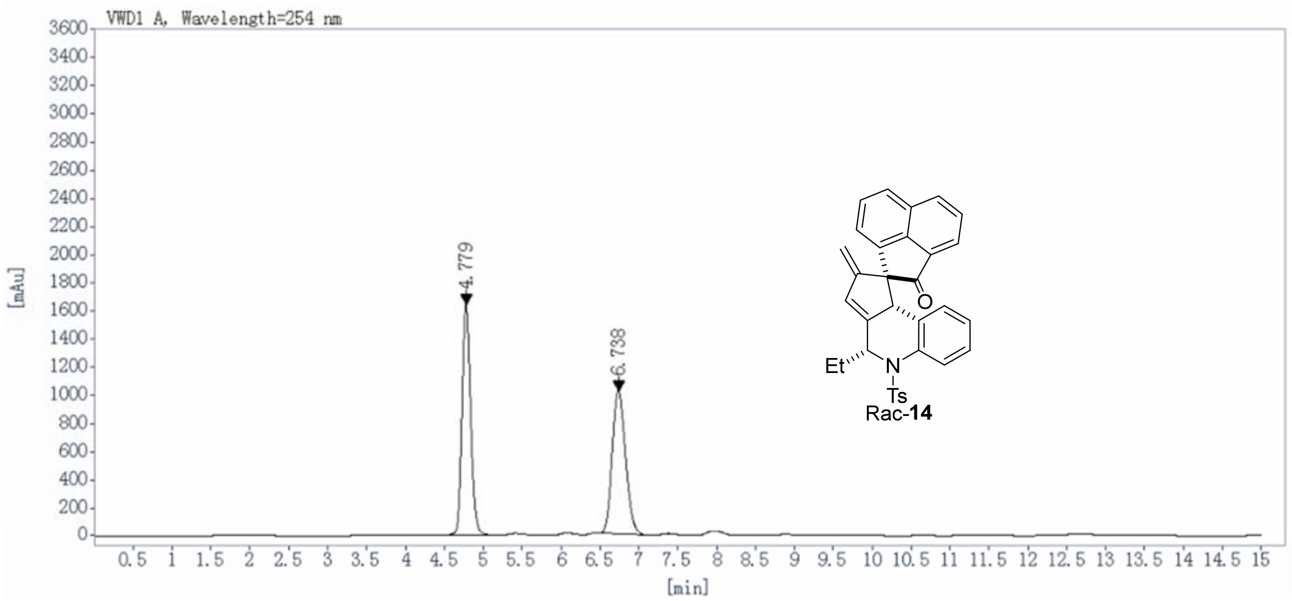
14

^{1}H NMR (400 MHz, CDCl$_3$)

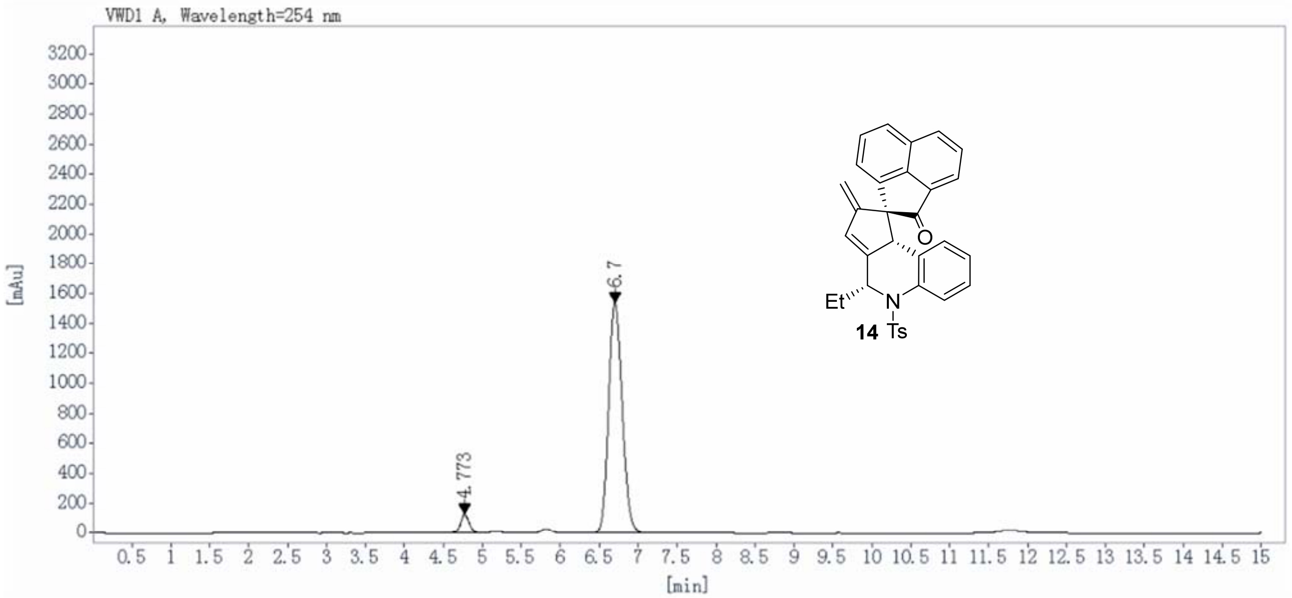


14

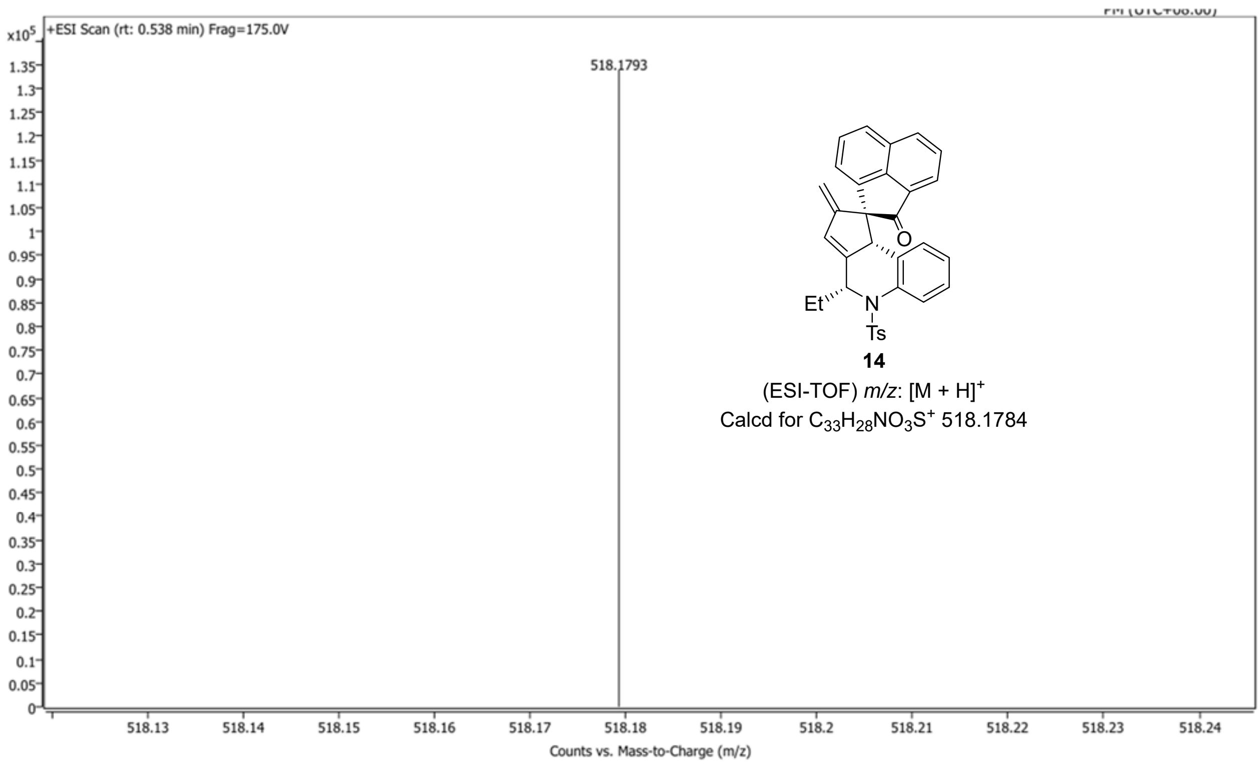
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.779	BBA	0.12	1636.8729	12525.2695	50.5571
6.738	BBA	0.19	1018.9764	12249.2441	49.4429
			Totals:	24774.5137	100.0000



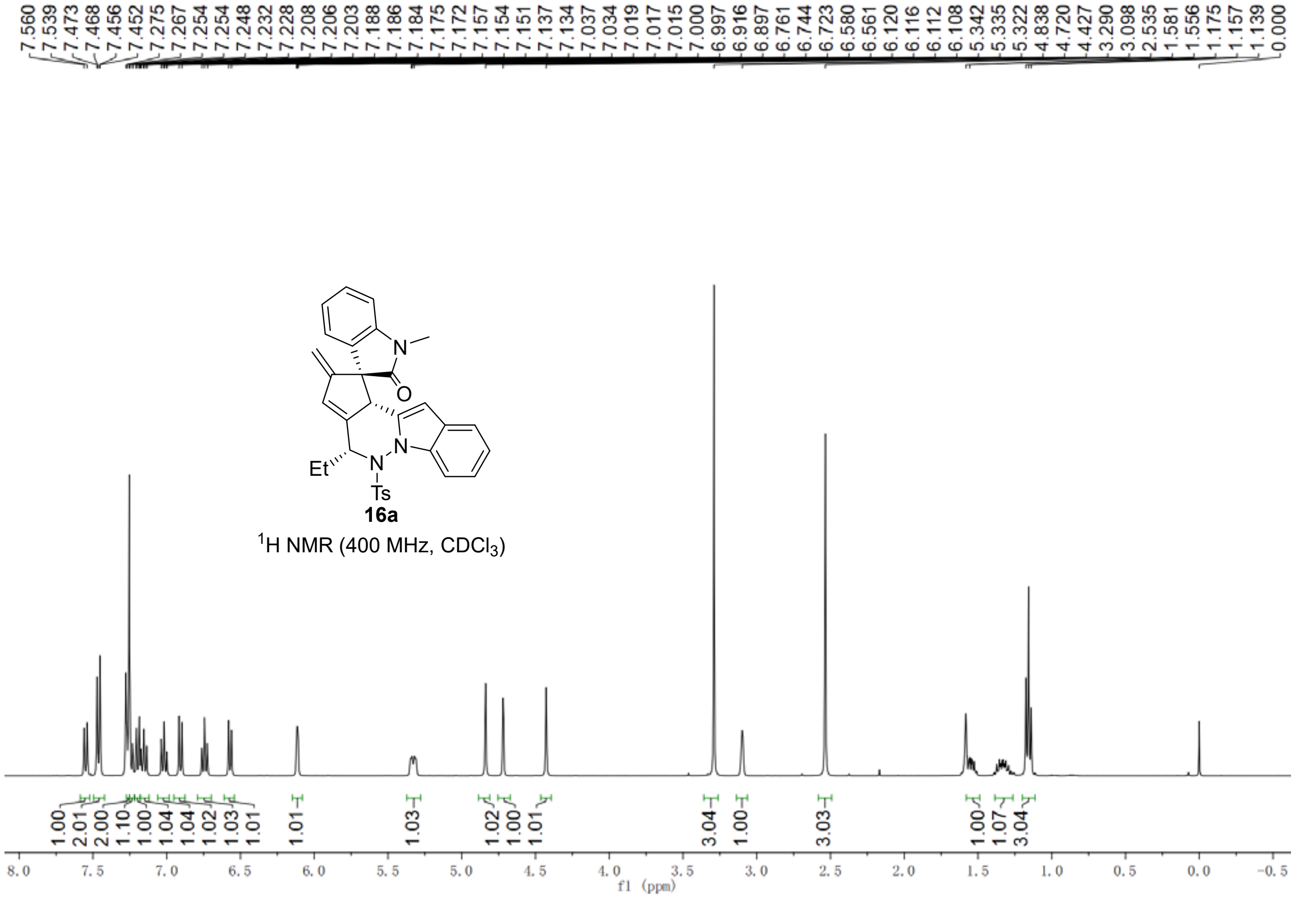
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.773	BB	0.12	124.6385	955.9208	4.8654
6.700	BBA	0.19	1540.2458	18691.2891	95.1346
			Totals:	19647.2099	100.0000



14

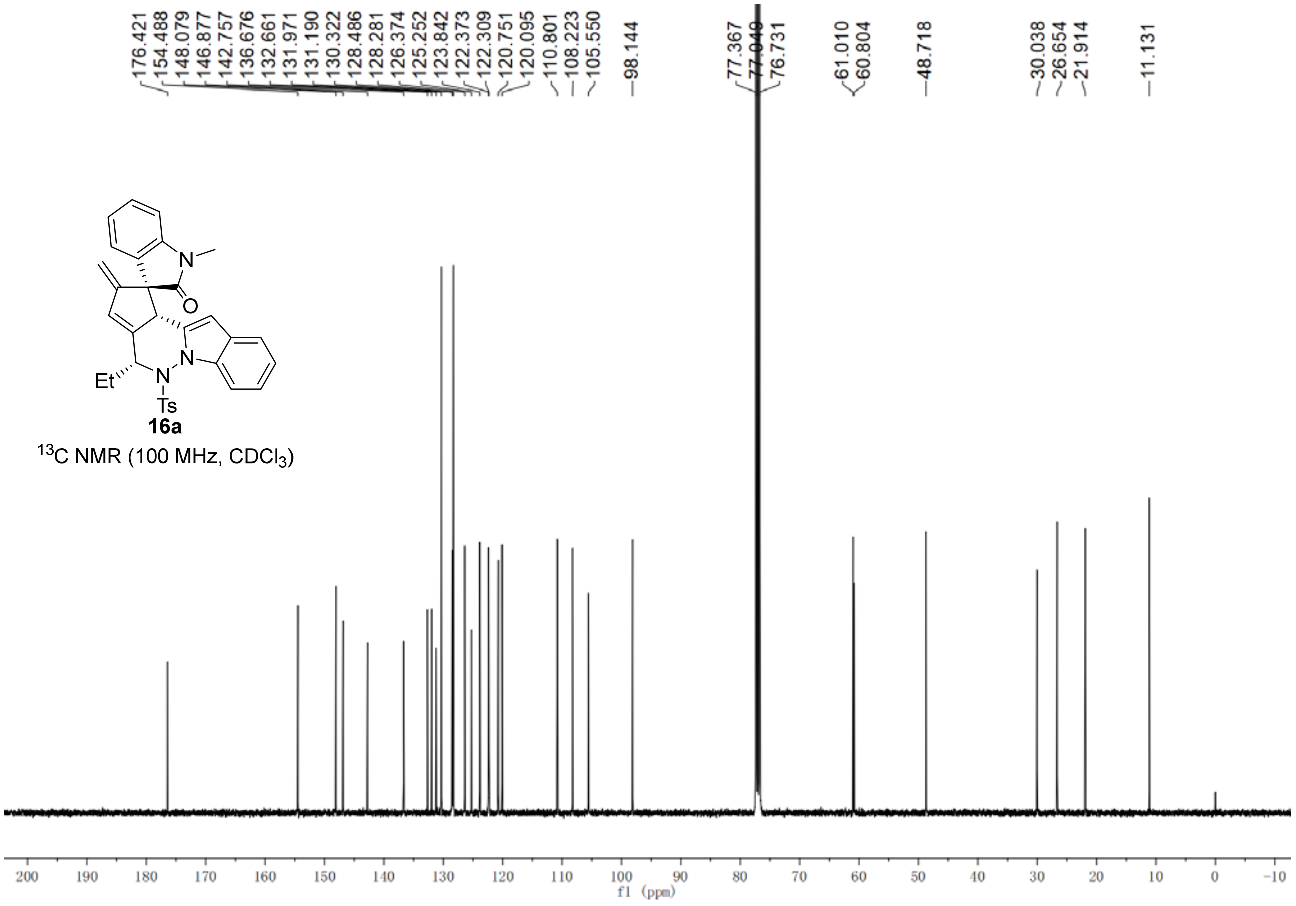
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{33}H_{28}NO_3S^+$ 518.1784



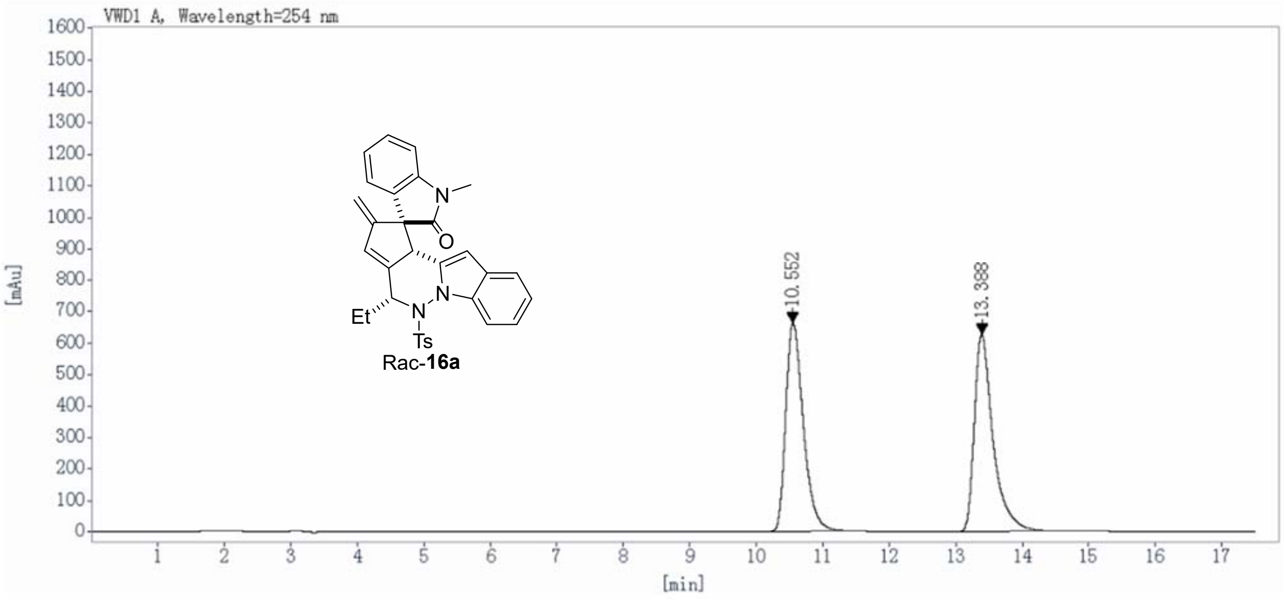
16a

^{1}H NMR (400 MHz, CDCl$_3$)

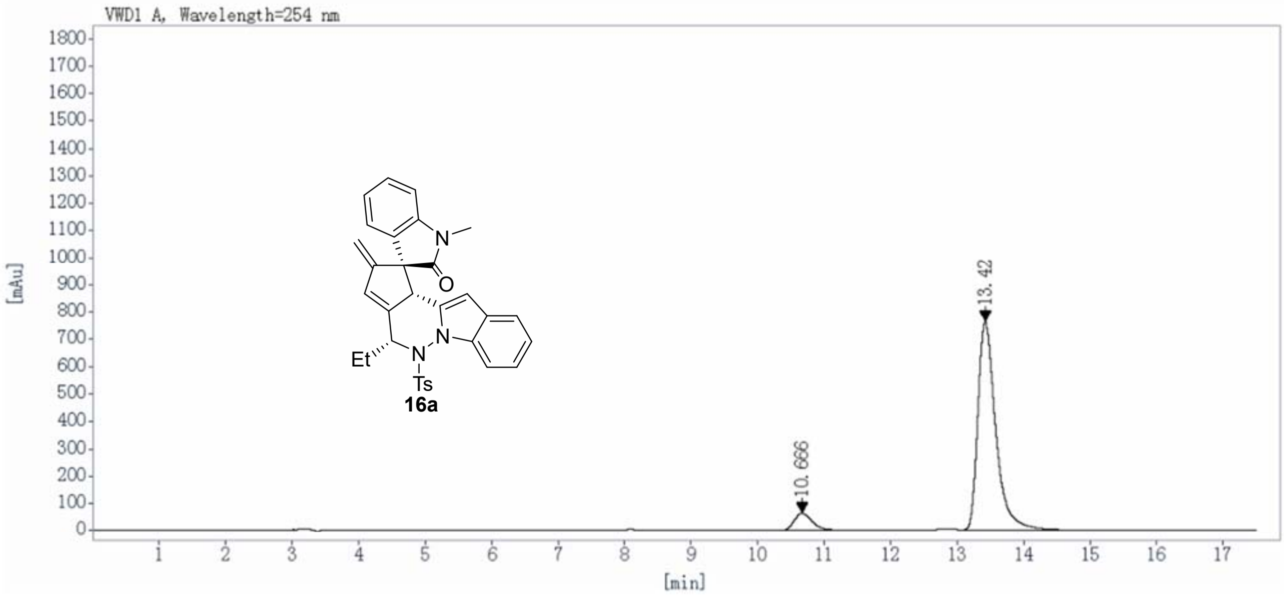


16a

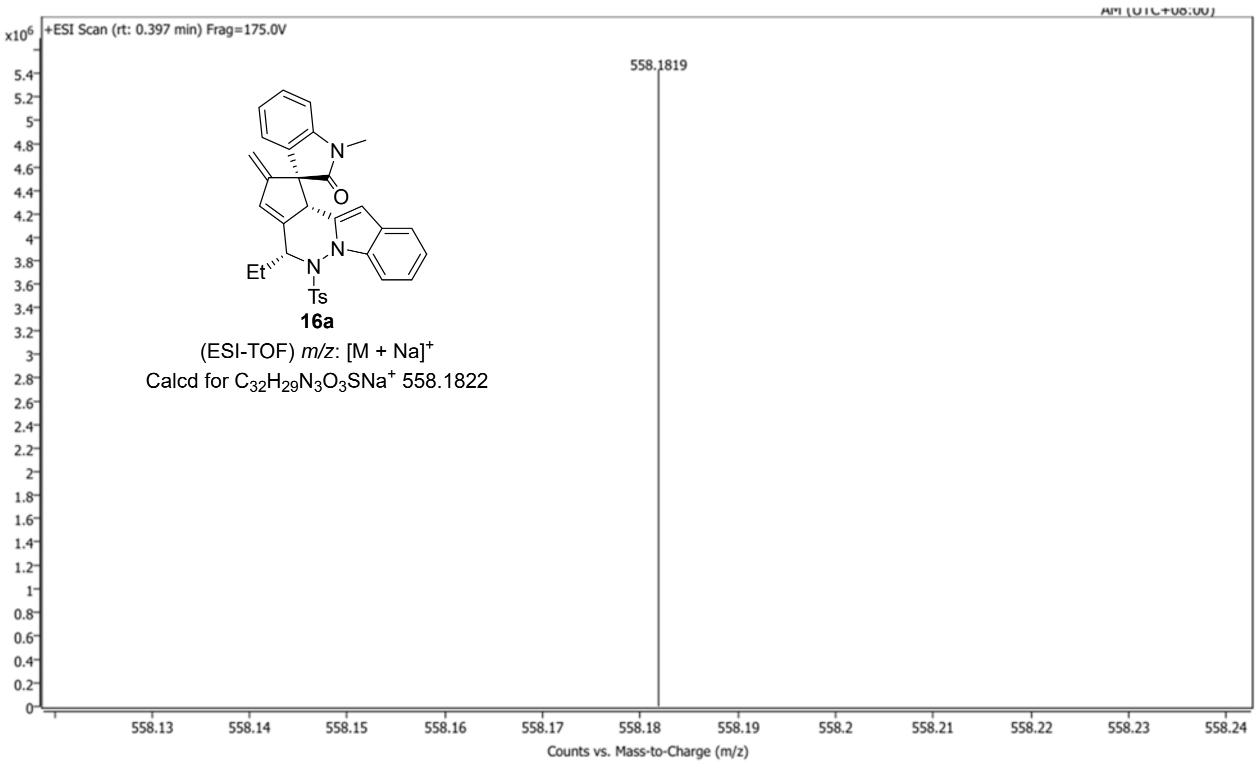
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
10.552	BBA	0.28	663.3882	12264.3691	49.8749
13.388	BBA	0.29	626.3311	12325.8848	50.1251
			Totals:	24590.2539	100.0000



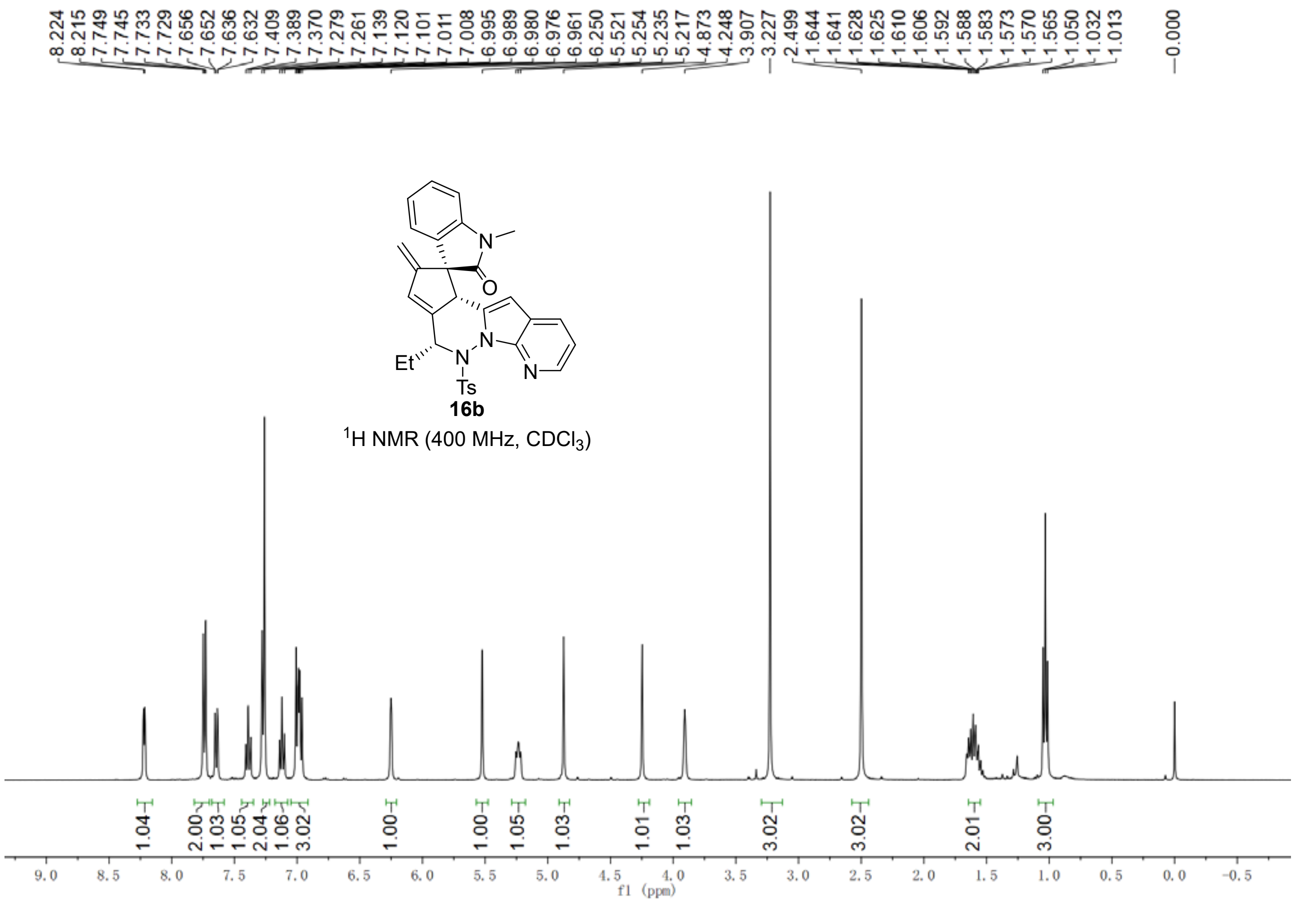
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
10.666	BB	0.29	63.5017	1185.3958	7.6949
13.420	BBA	0.28	763.5140	14219.4668	92.3051
			Totals:	15404.8625	100.0000



16a

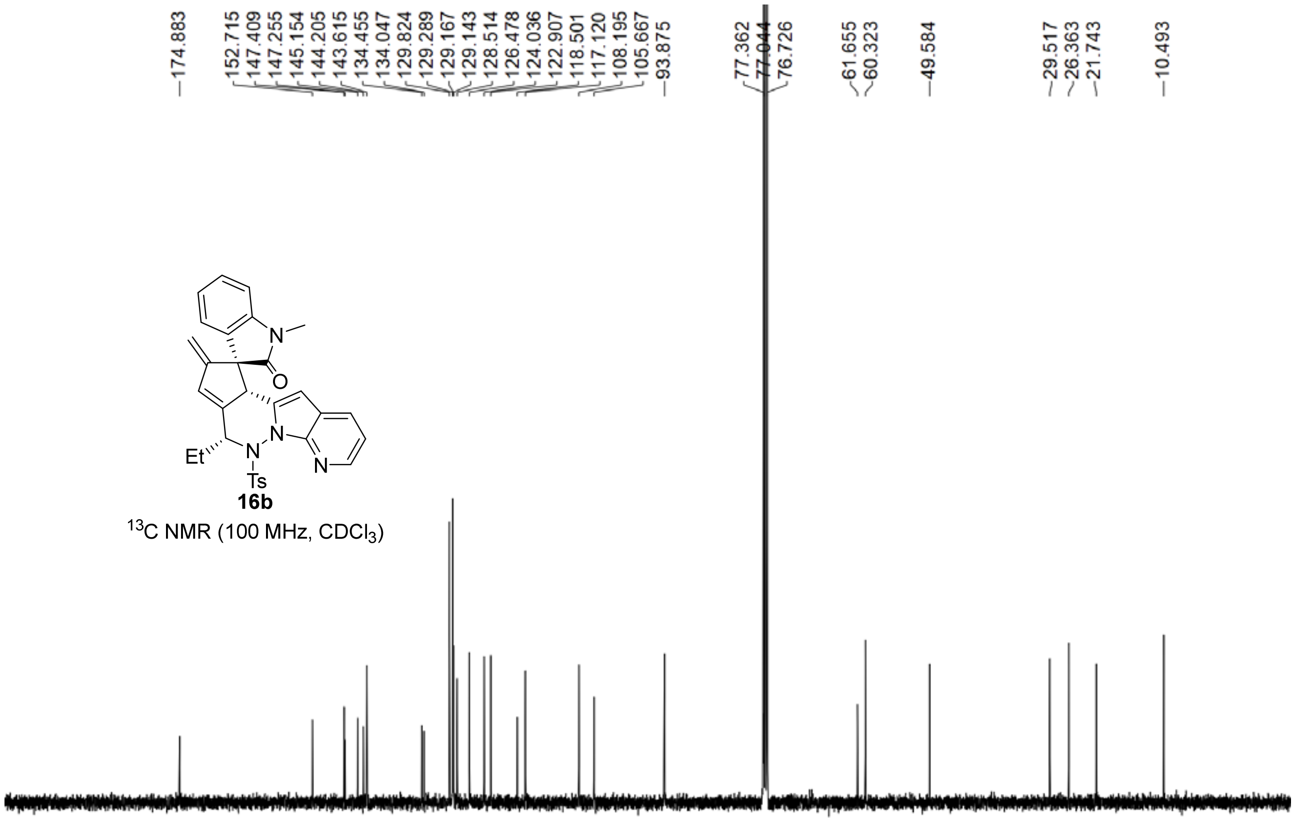
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{32}H_{29}N_3O_3SNa^+$ 558.1822



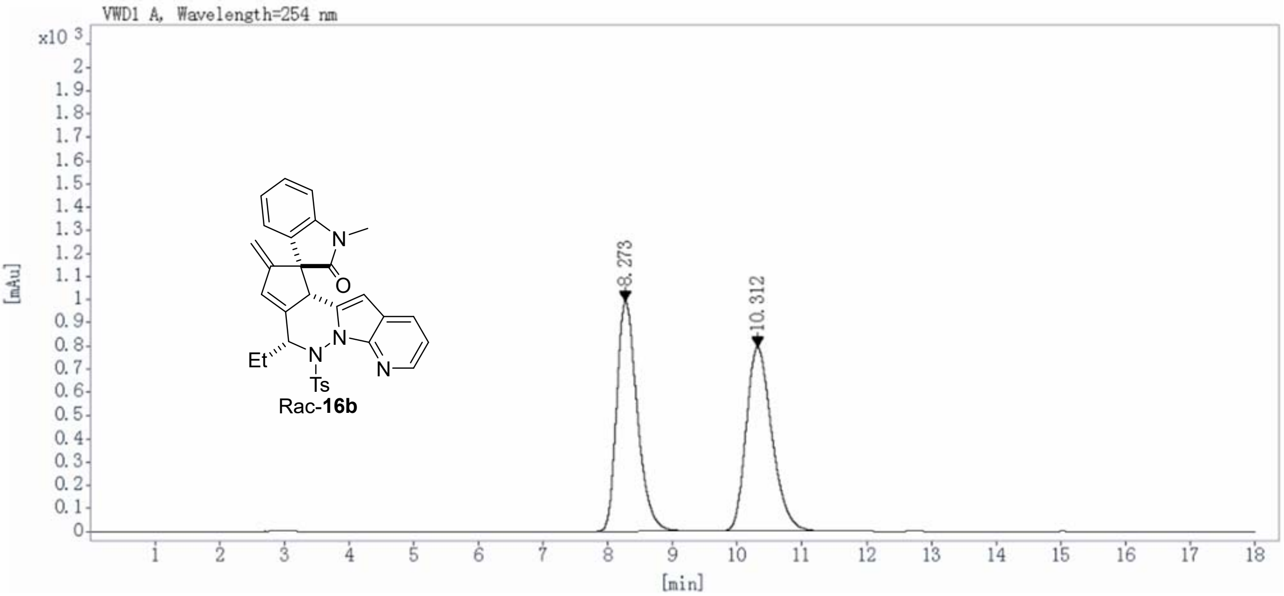
16b

^{1}H NMR (400 MHz, CDCl$_3$)



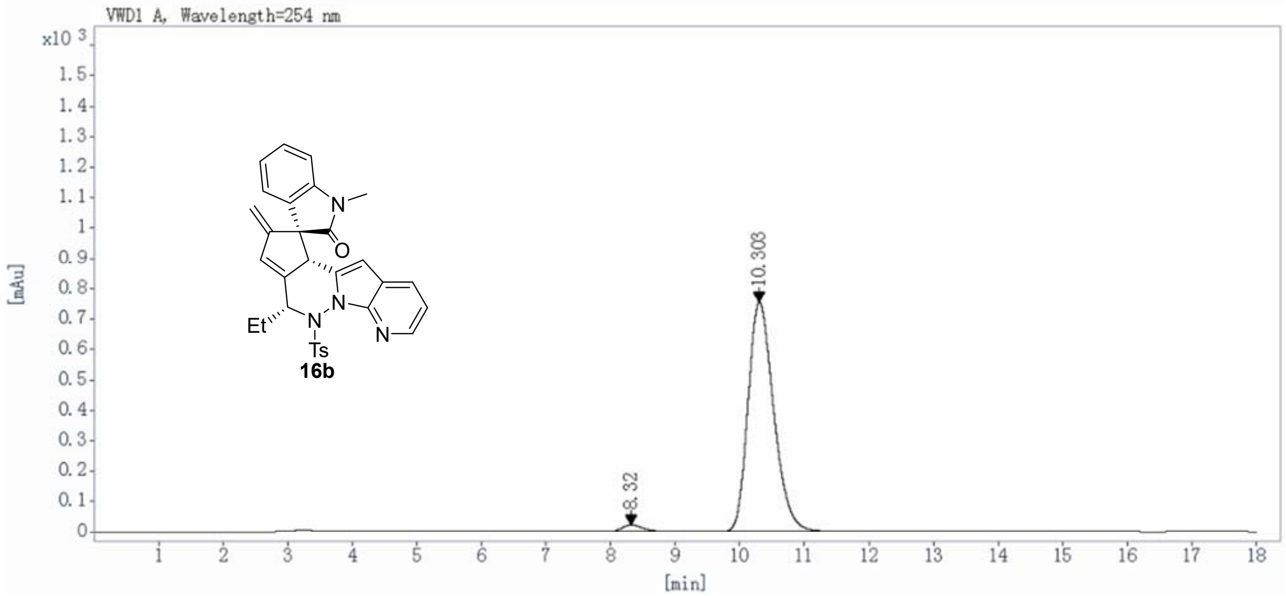
16b

^{13}C NMR (100 MHz, CDCl$_3$)



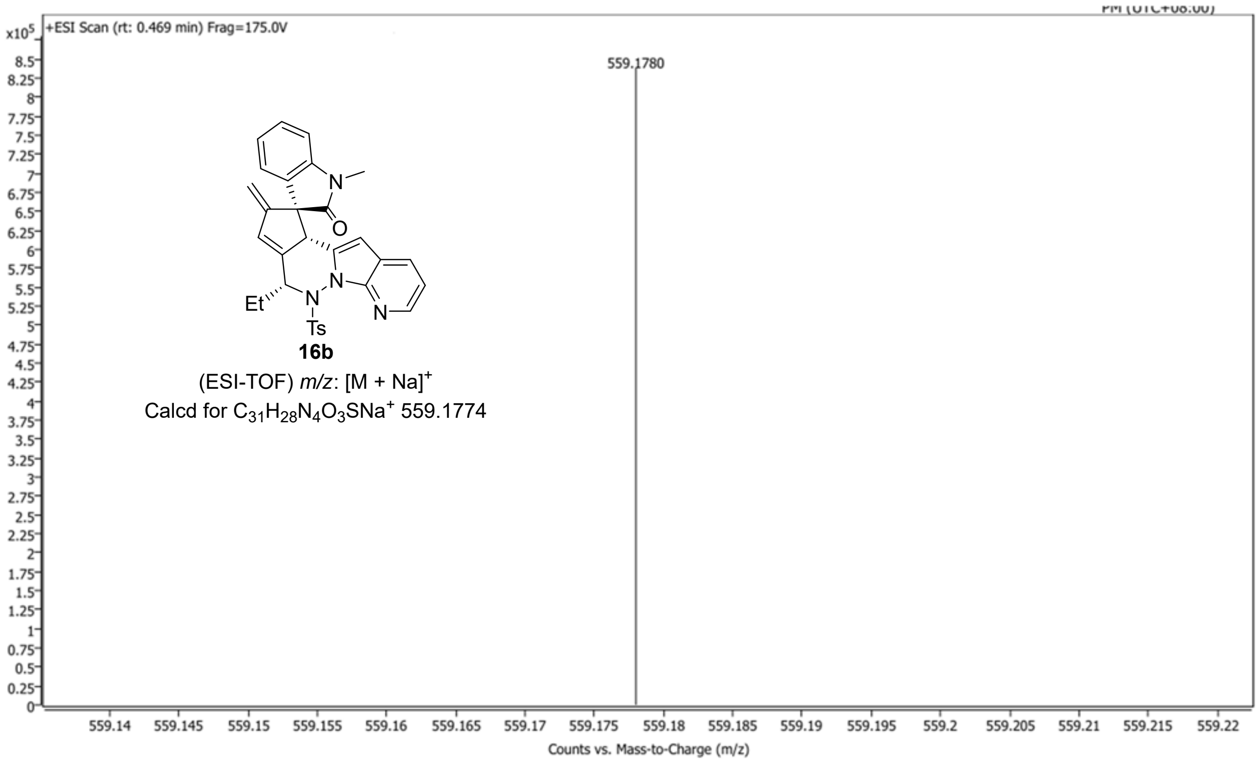
Rac-**16b**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.273	BBA	0.34	991.5527	21815.1191	49.8887
10.312	BBA	0.43	793.1179	21912.4746	50.1113
			Totals:	43727.5938	100.0000



16b

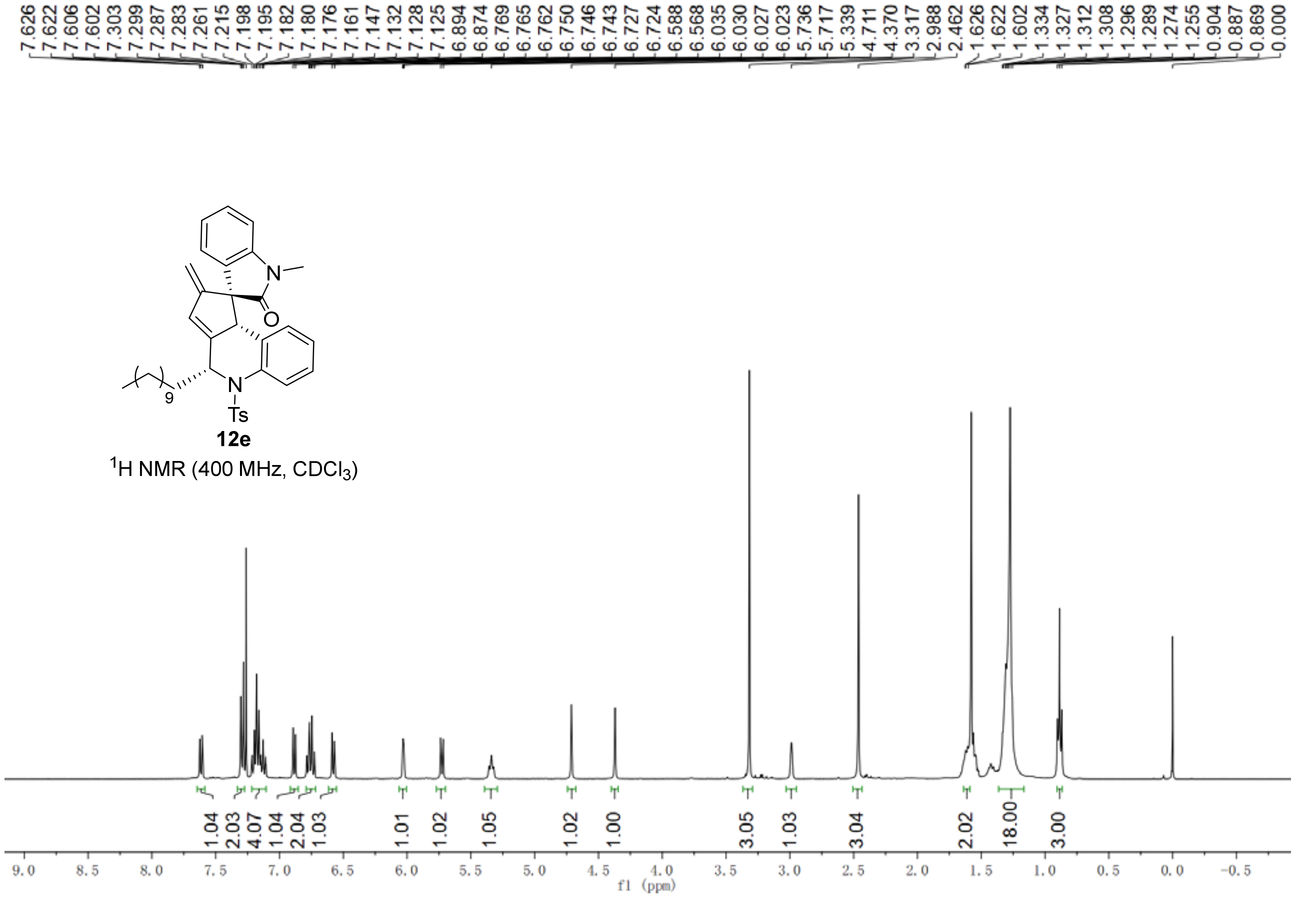
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
8.320	BBA	0.33	22.4122	476.5341	2.2473
10.303	BBA	0.43	753.7796	20728.4980	97.7527
			Totals:	21205.0321	100.0000



16b

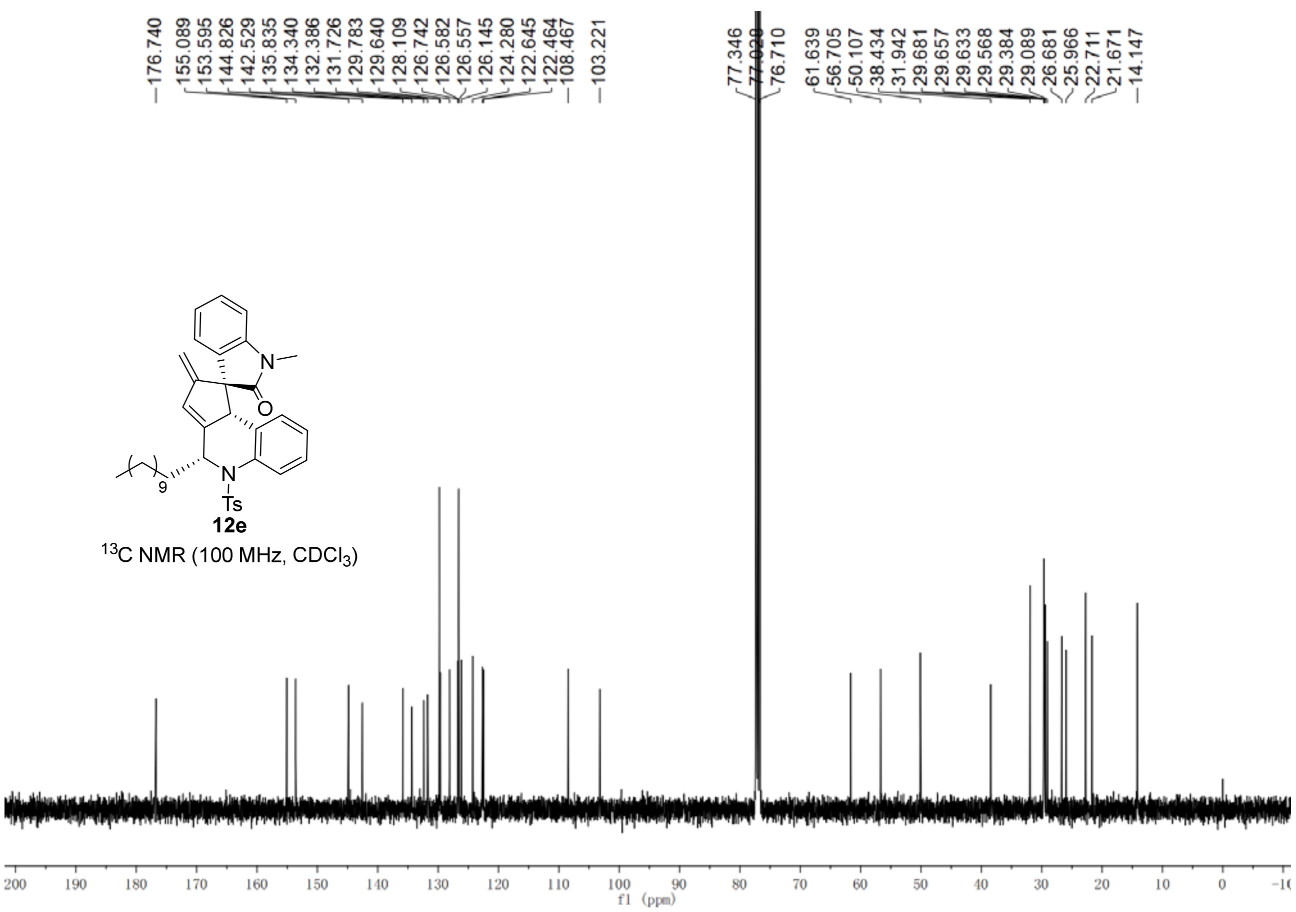
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{31}H_{28}N_4O_3SNa^+$ 559.1774



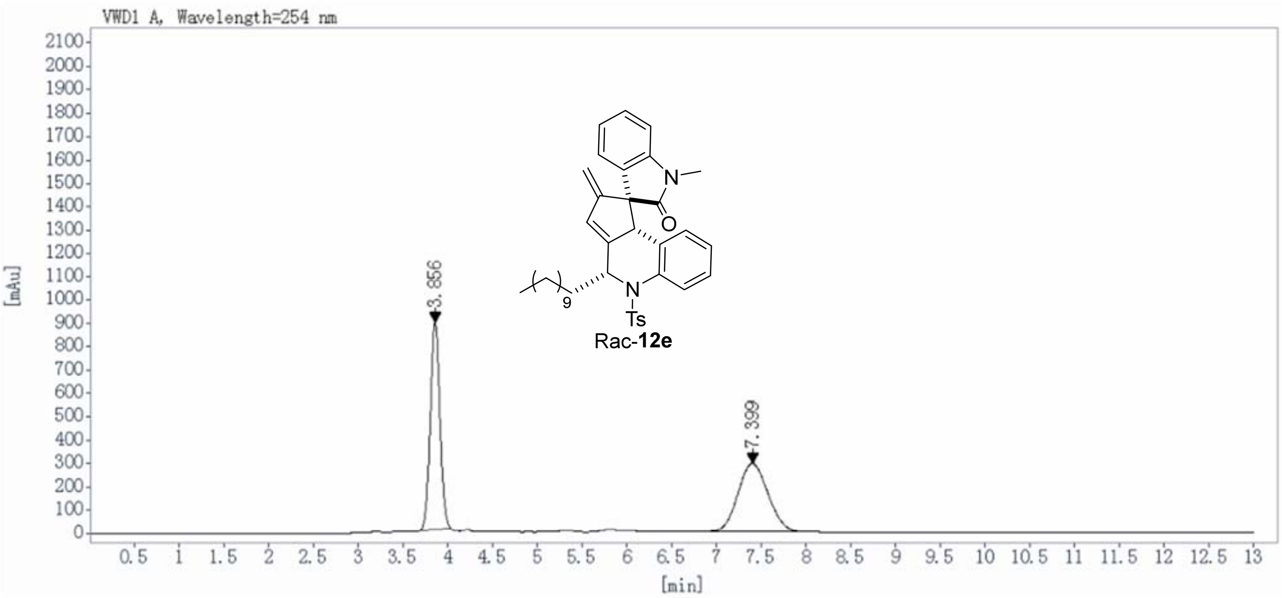
12e

^{1}H NMR (400 MHz, CDCl$_3$)

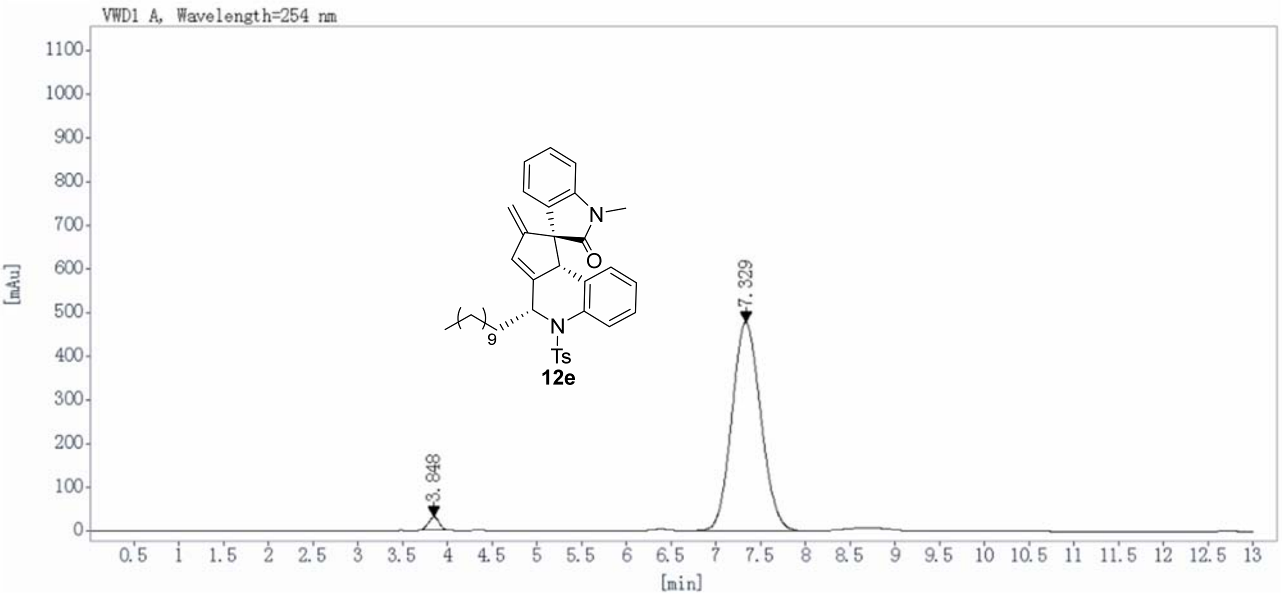


12e

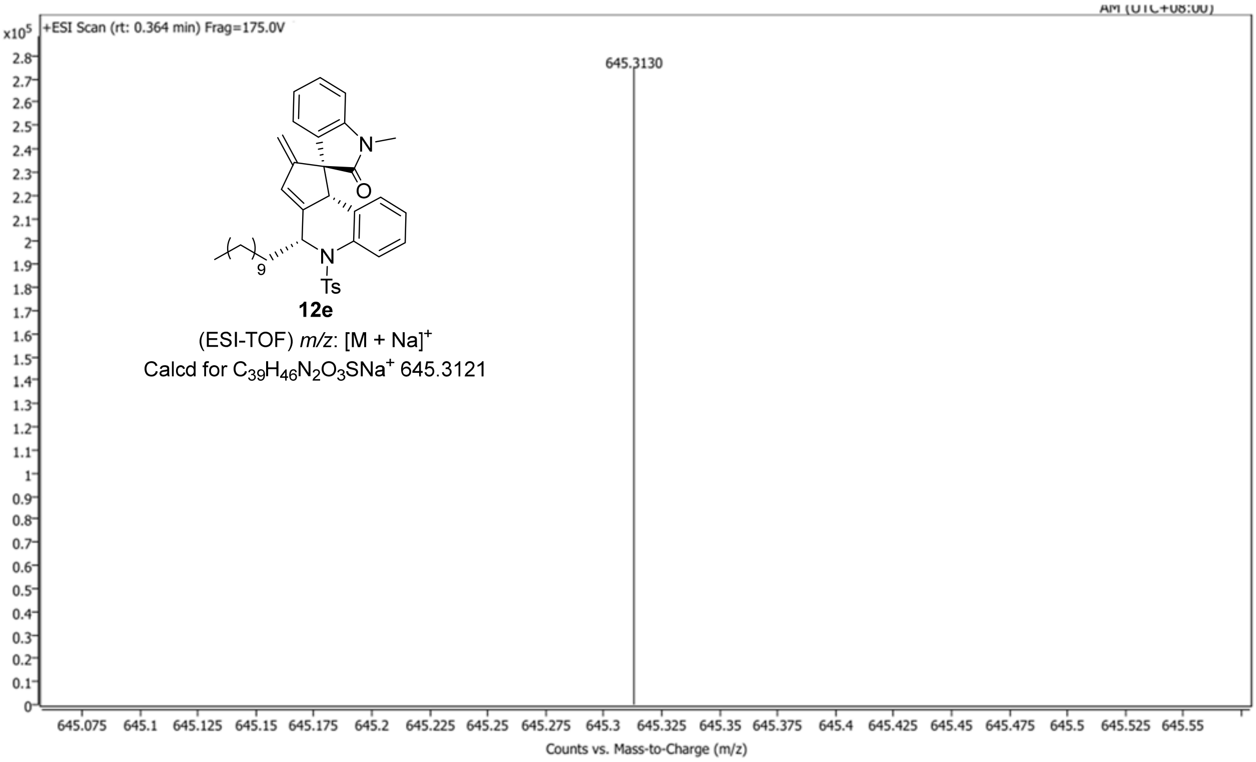
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
3.856	BBA	0.12	888.1533	6696.6675	49.0735
7.399	BB	0.37	294.7439	6949.5410	50.9265
			Totals:	13646.2085	100.0000



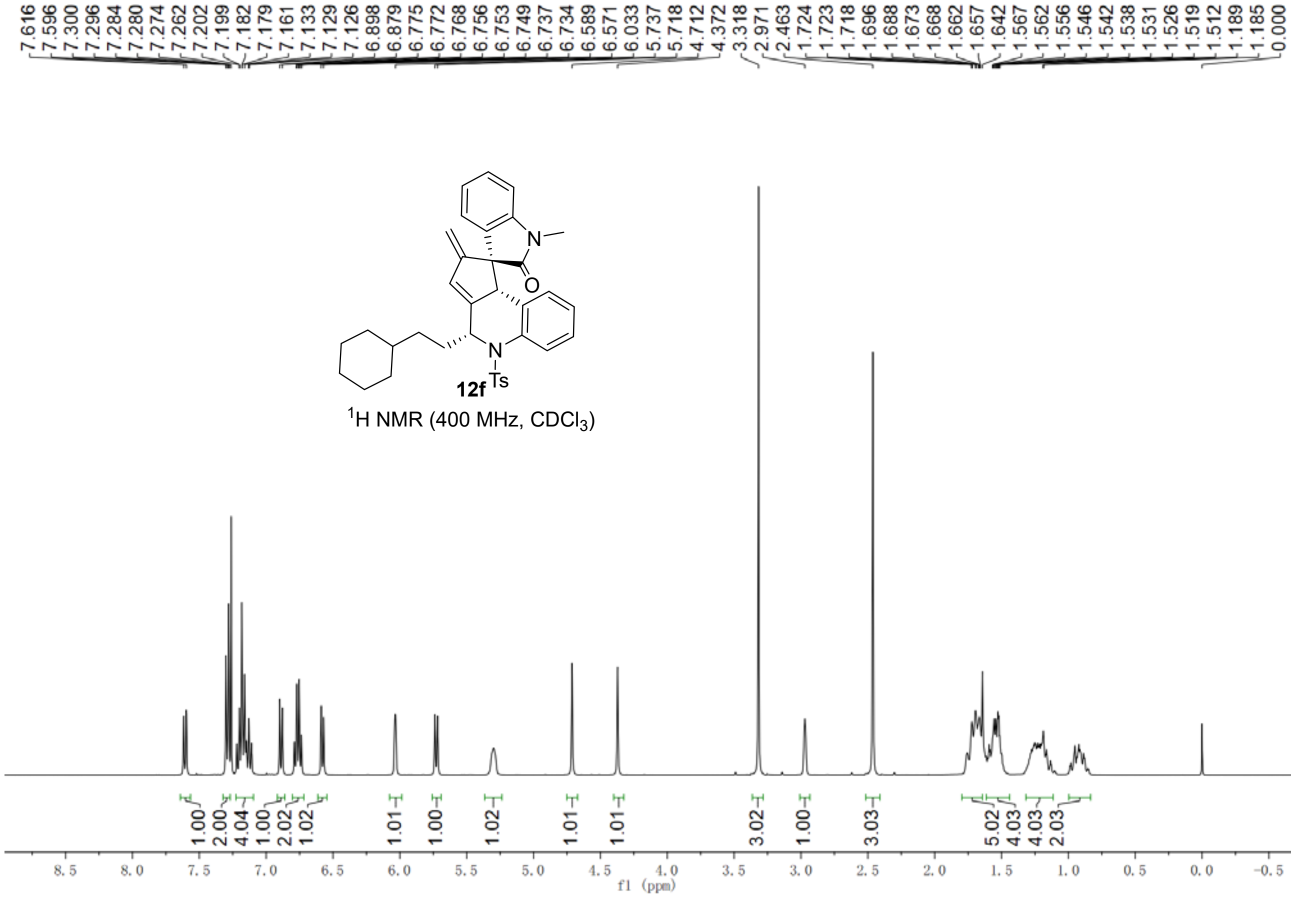
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
3.848	BBA	0.13	30.5947	259.3460	2.3498
7.329	BBA	0.35	477.0155	10777.4502	97.6502
			Totals:	11036.7962	100.0000



12e

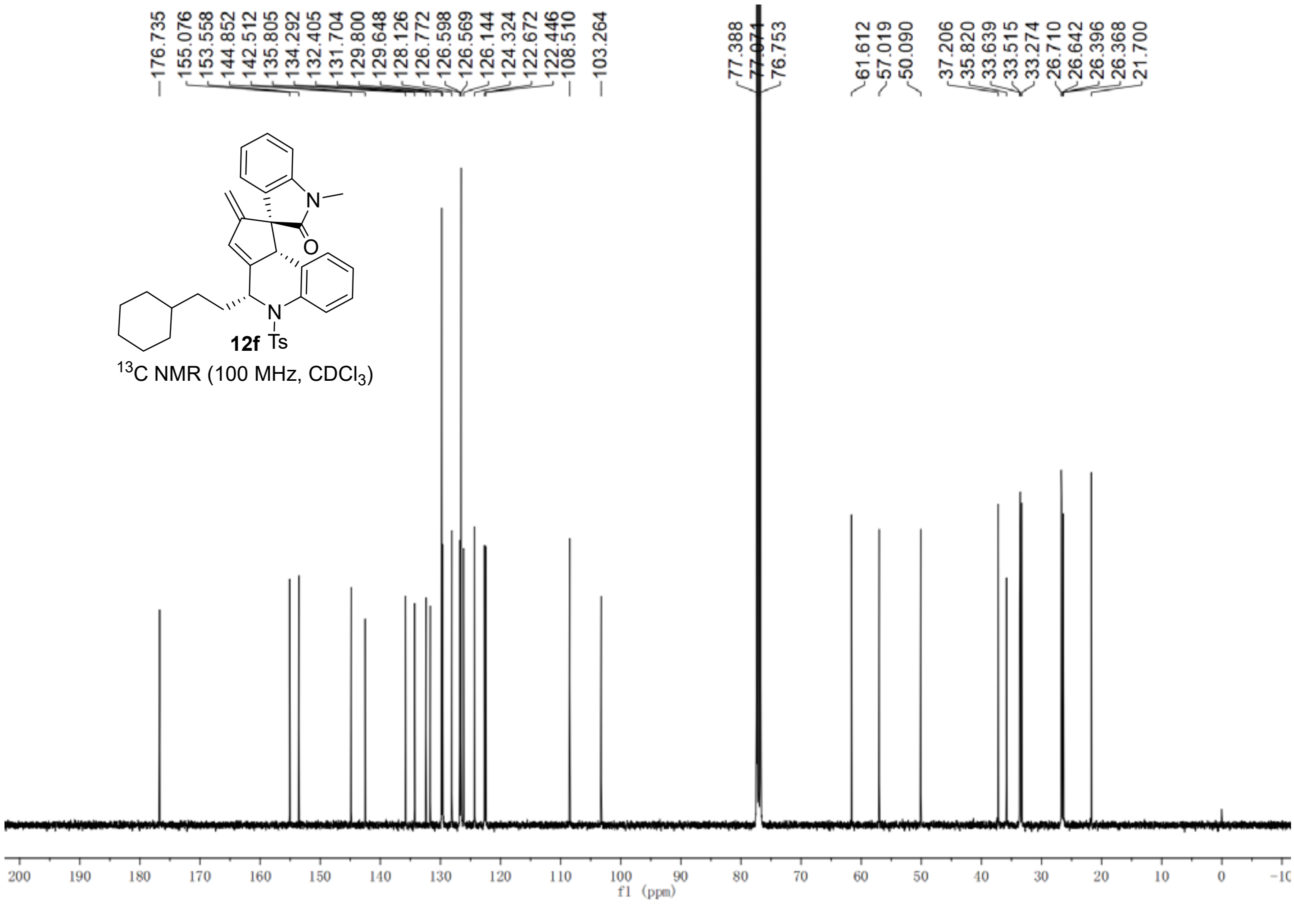
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{39}H_{46}N_2O_3SNa^+$ 645.3121



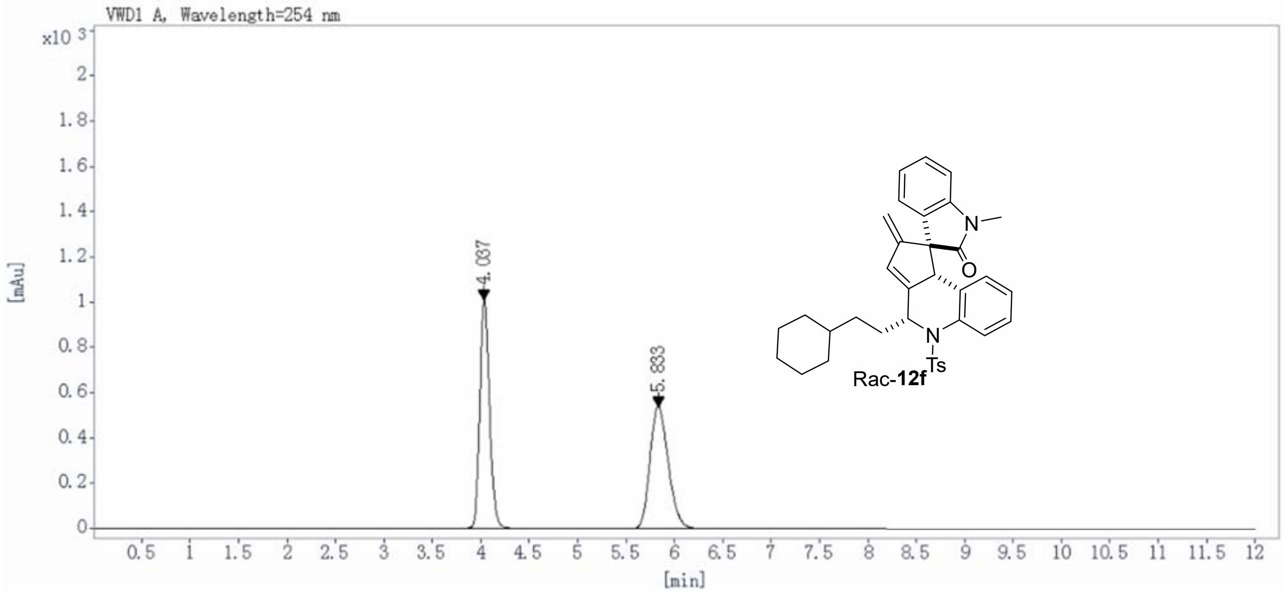
12f

^{1}H NMR (400 MHz, $CDCl_3$)

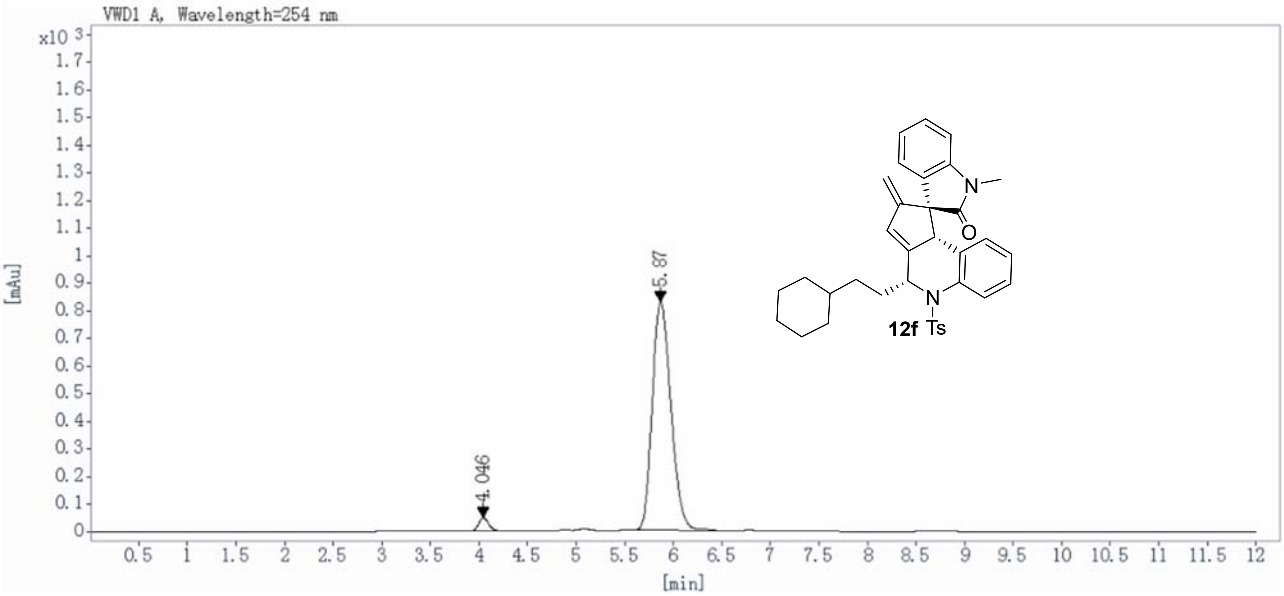


12f

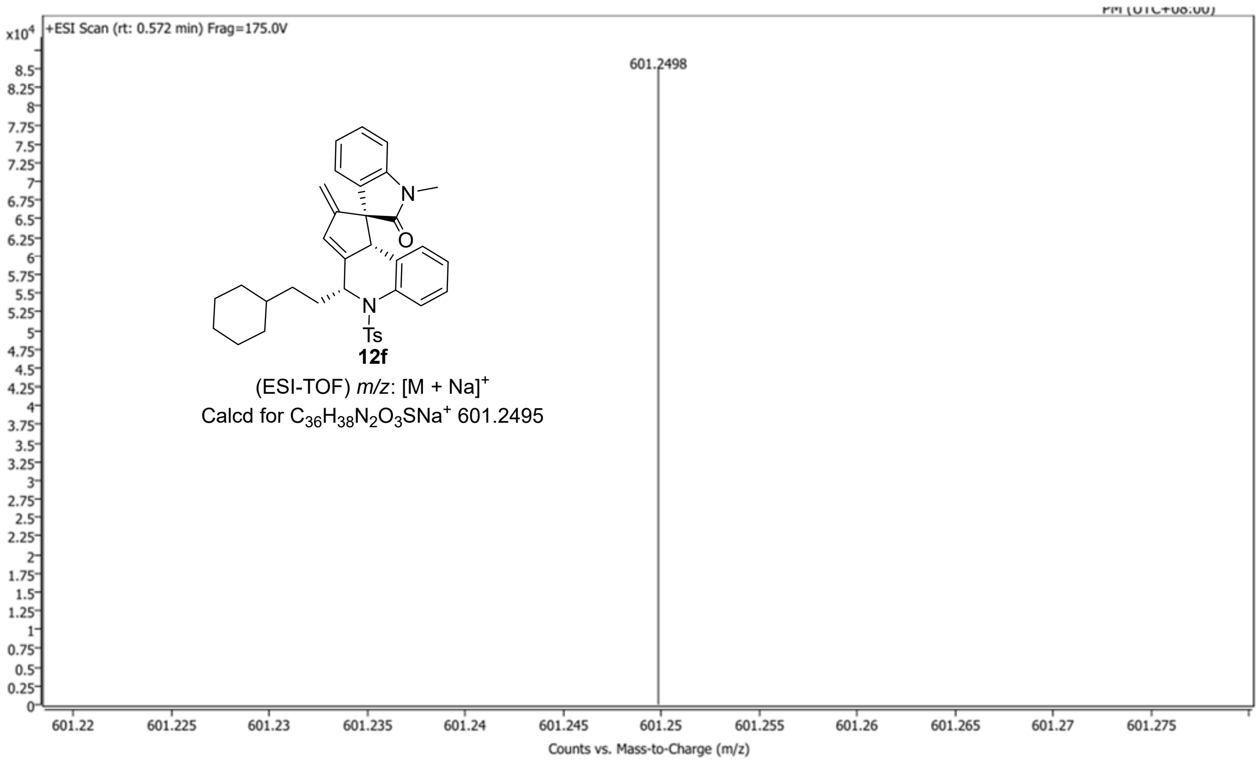
^{13}C NMR (100 MHz, $CDCl_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.037	BBA	0.11	1008.1496	7035.1875	49.8210
5.833	BBA	0.21	538.7615	7085.7324	50.1790
			Totals:	14120.9199	100.0000



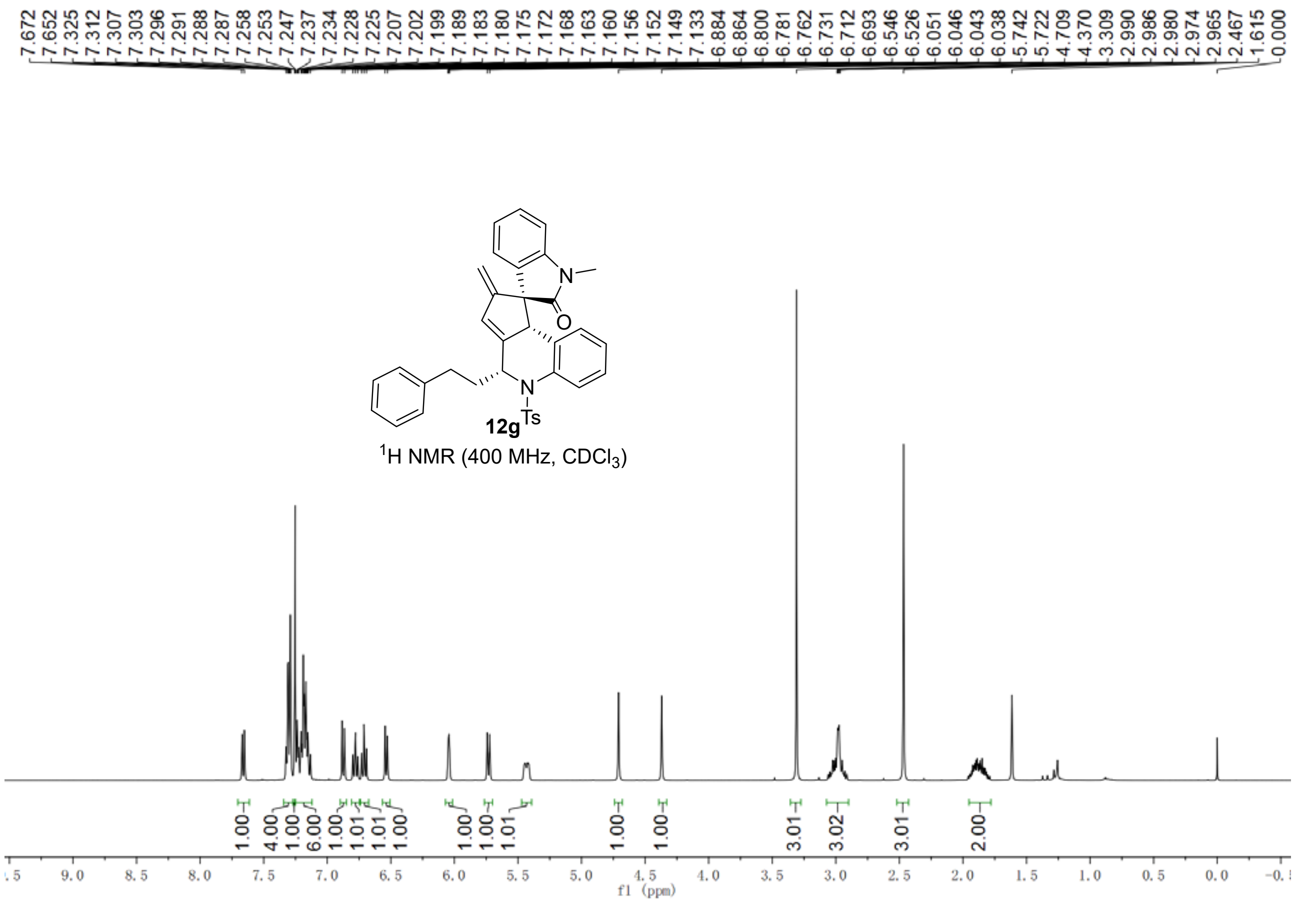
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.046	BBA	0.11	48.3694	348.9897	3.0585
5.870	BBA	0.21	829.1635	11061.6025	96.9415
			Totals:	11410.5922	100.0000



12f

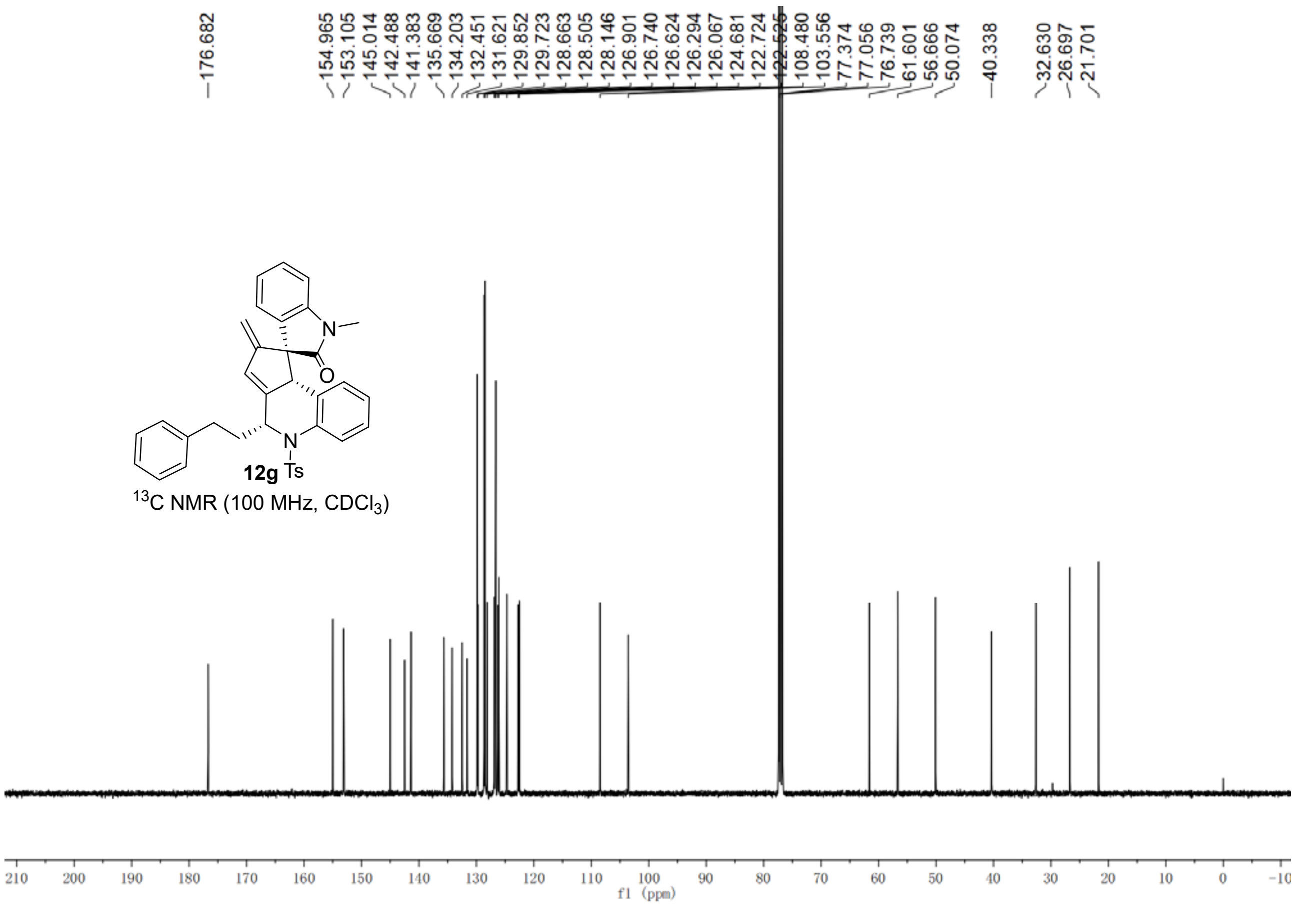
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{36}H_{38}N_2O_3SNa^+$ 601.2495



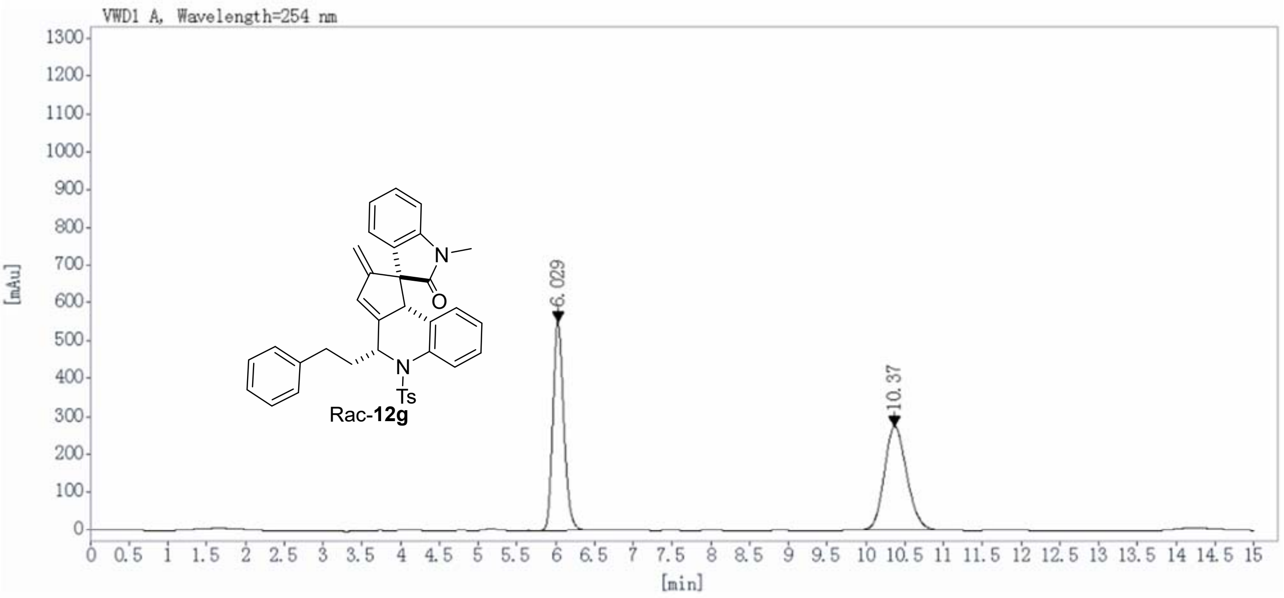
12g

^{1}H NMR (400 MHz, CDCl$_3$)

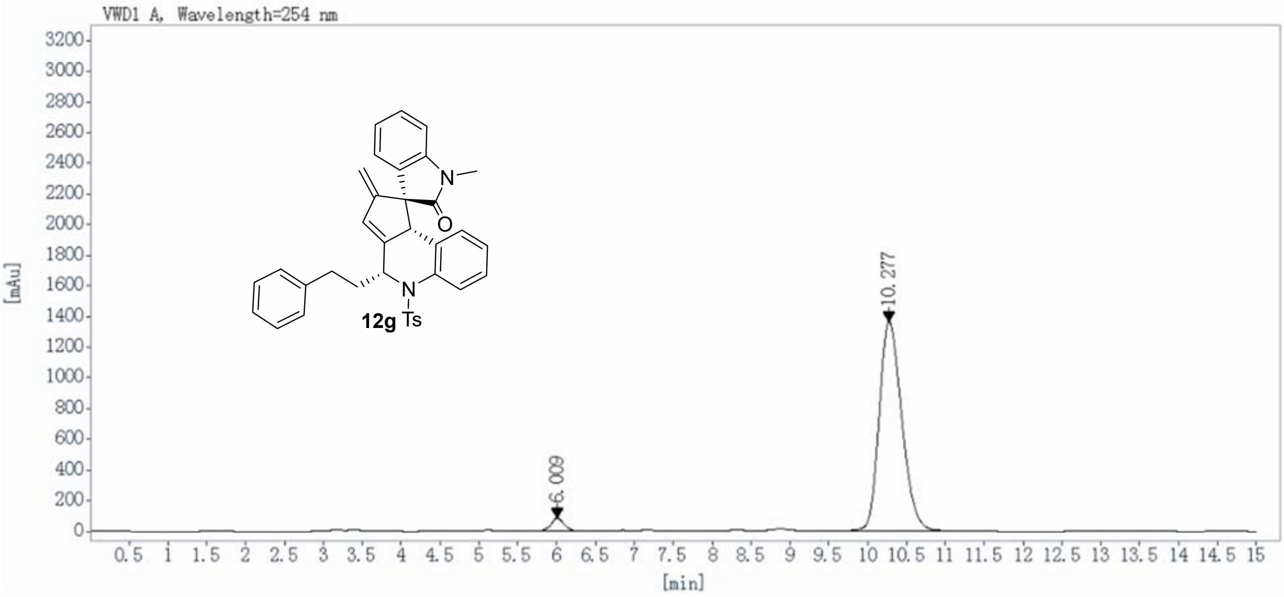


12g

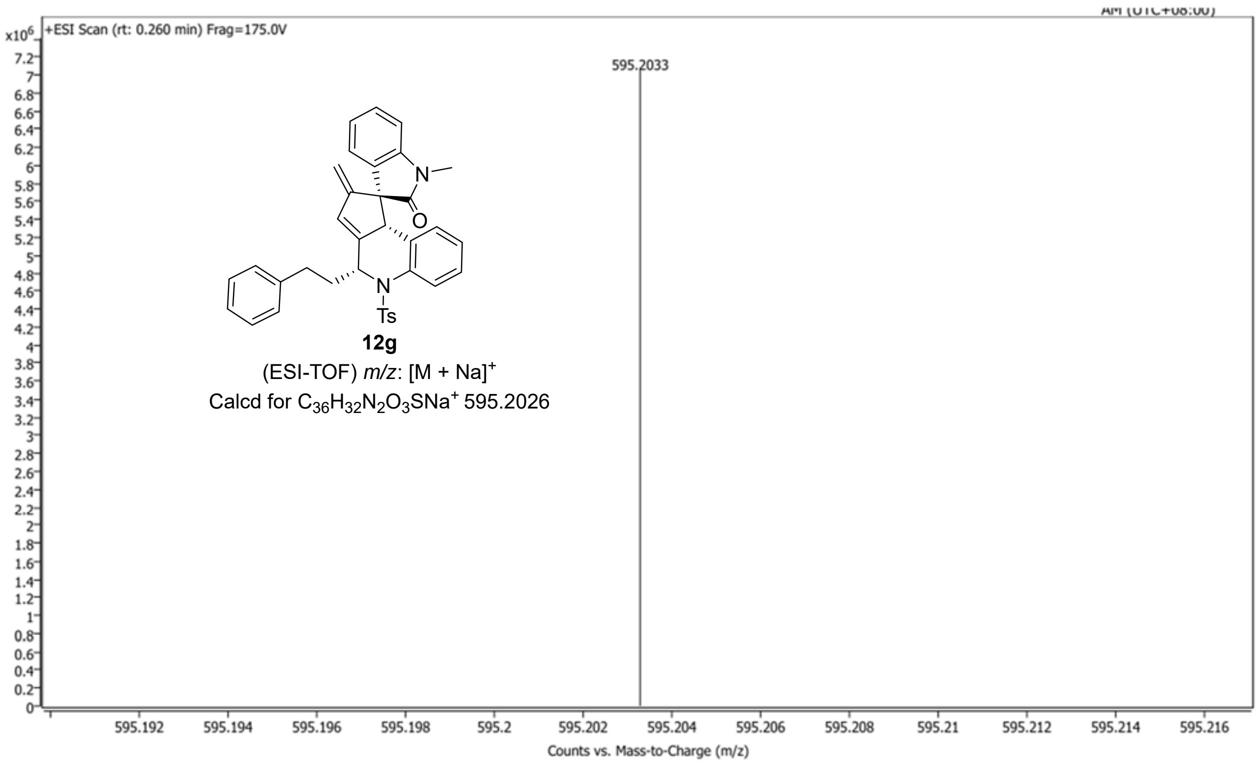
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.029	BBA	0.15	551.4871	5511.3047	49.7055
10.370	BBA	0.31	276.2112	5576.6040	50.2945
			Totals:	11087.9087	100.0000



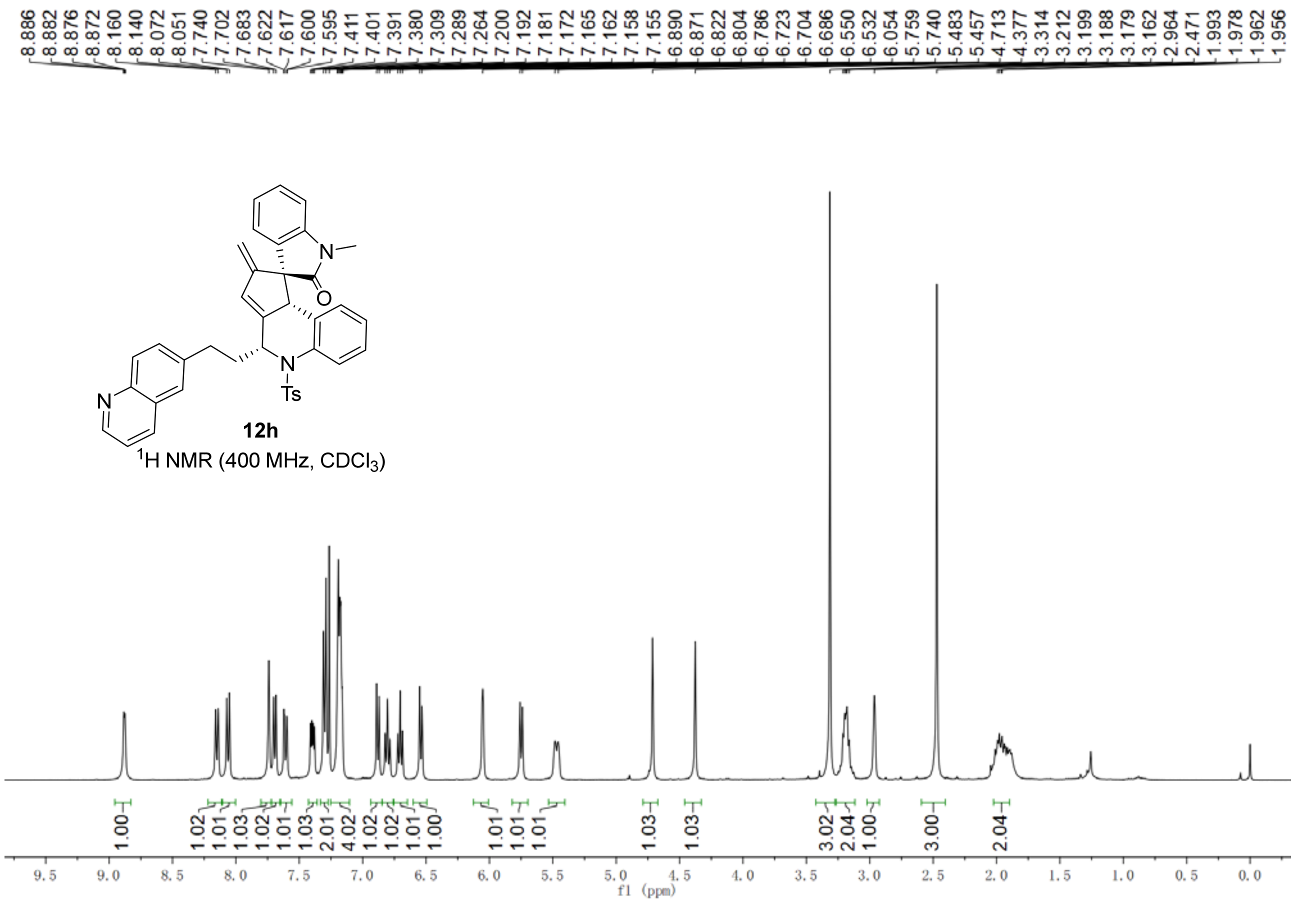
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.009	BBA	0.17	85.6434	1001.8586	3.5056
10.277	BBA	0.31	1364.2518	27576.8809	96.4944
			Totals:	28578.7395	100.0000



12g

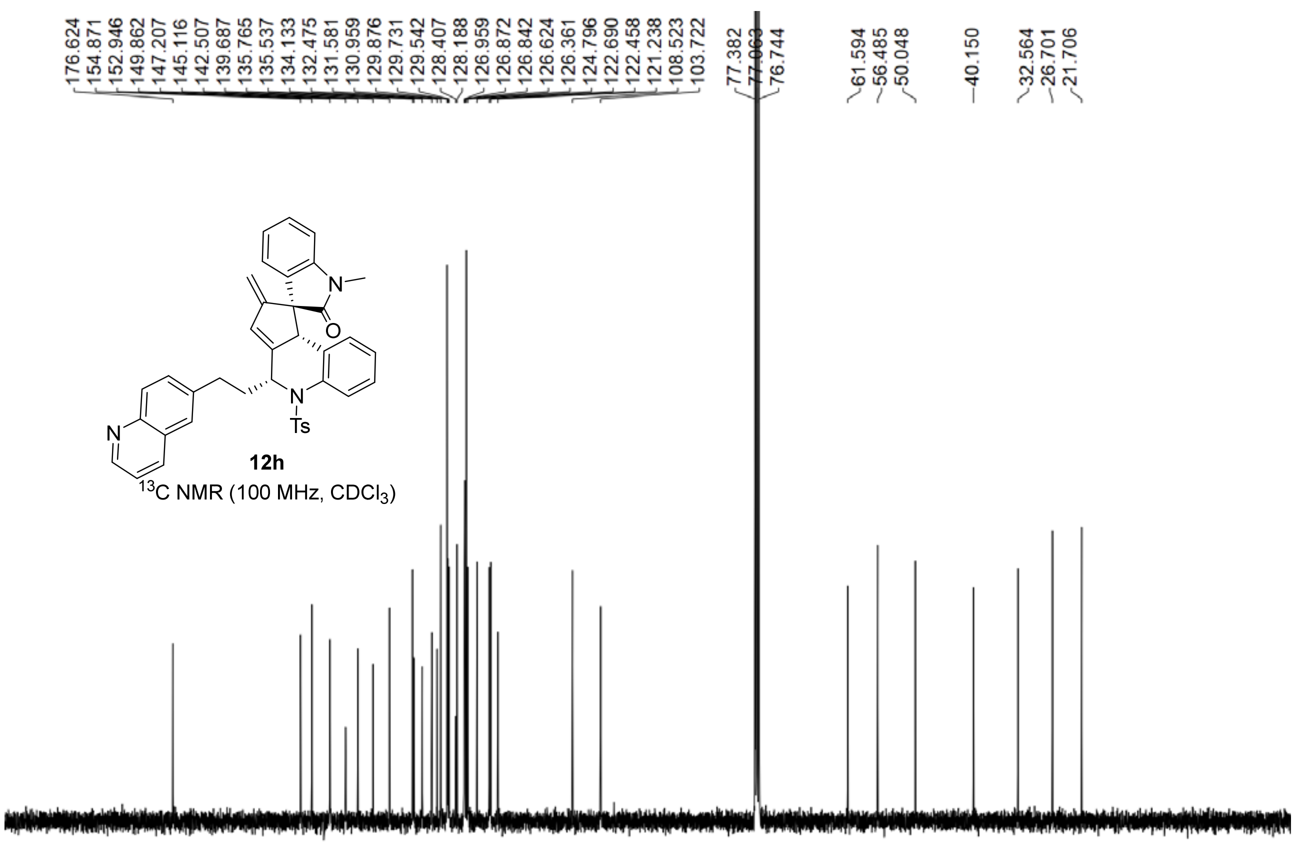
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{36}H_{32}N_2O_3SNa^+$ 595.2026



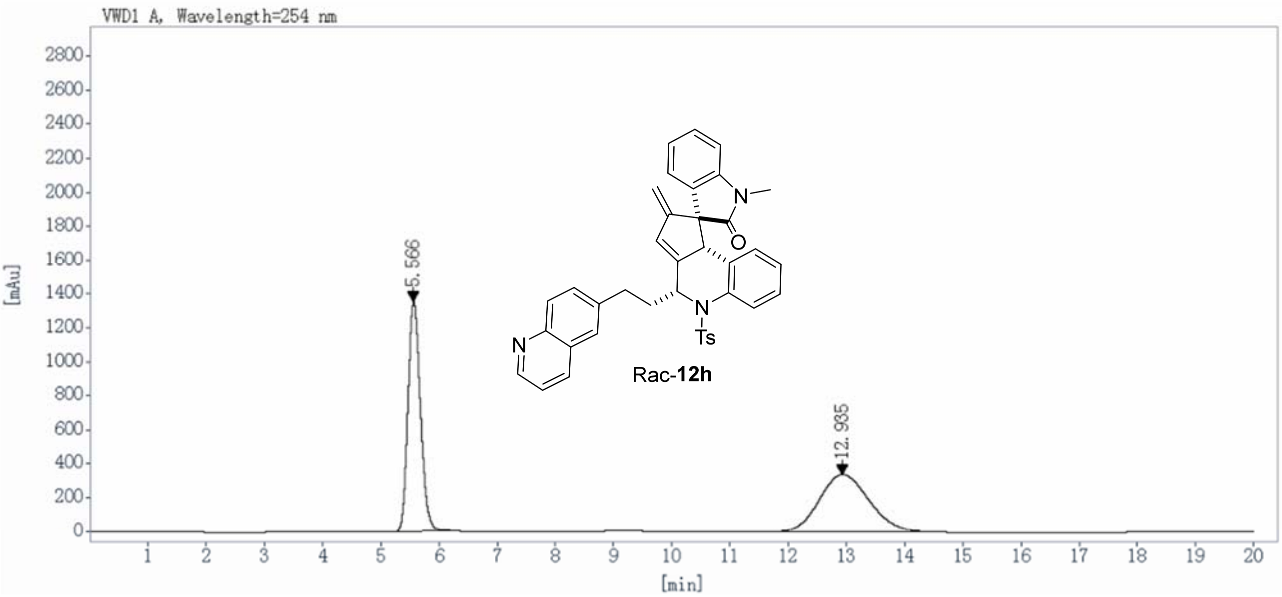
12h

^{1}H NMR (400 MHz, CDCl$_3$)

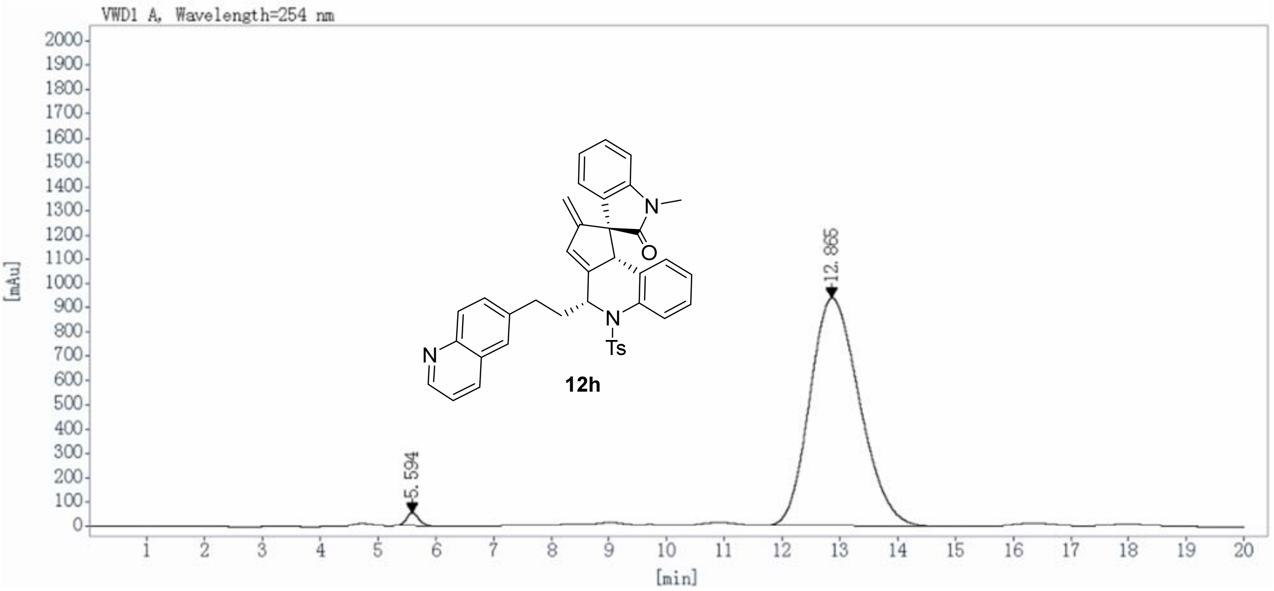


12h

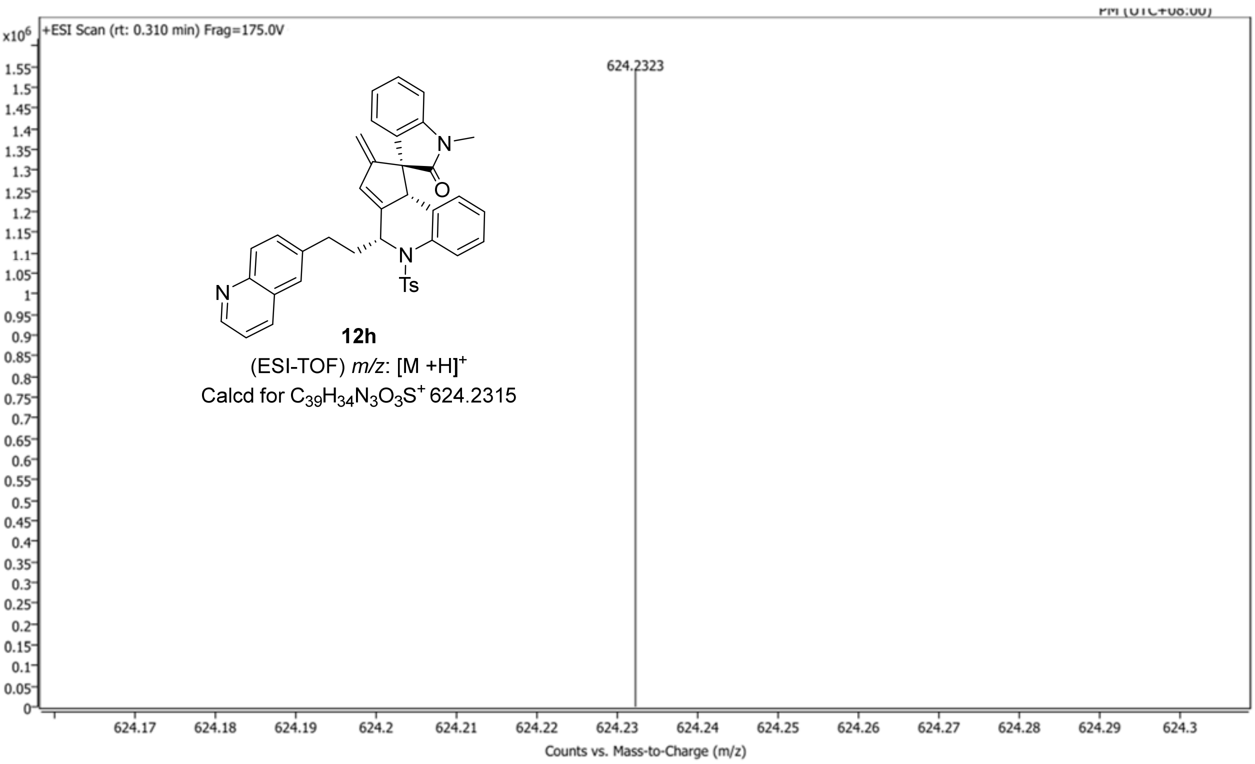
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.566	BBA	0.23	1352.6578	20139.9414	50.0449
12.935	BBA	0.93	338.6057	20103.8398	49.9551
			Totals:	40243.7813	100.0000



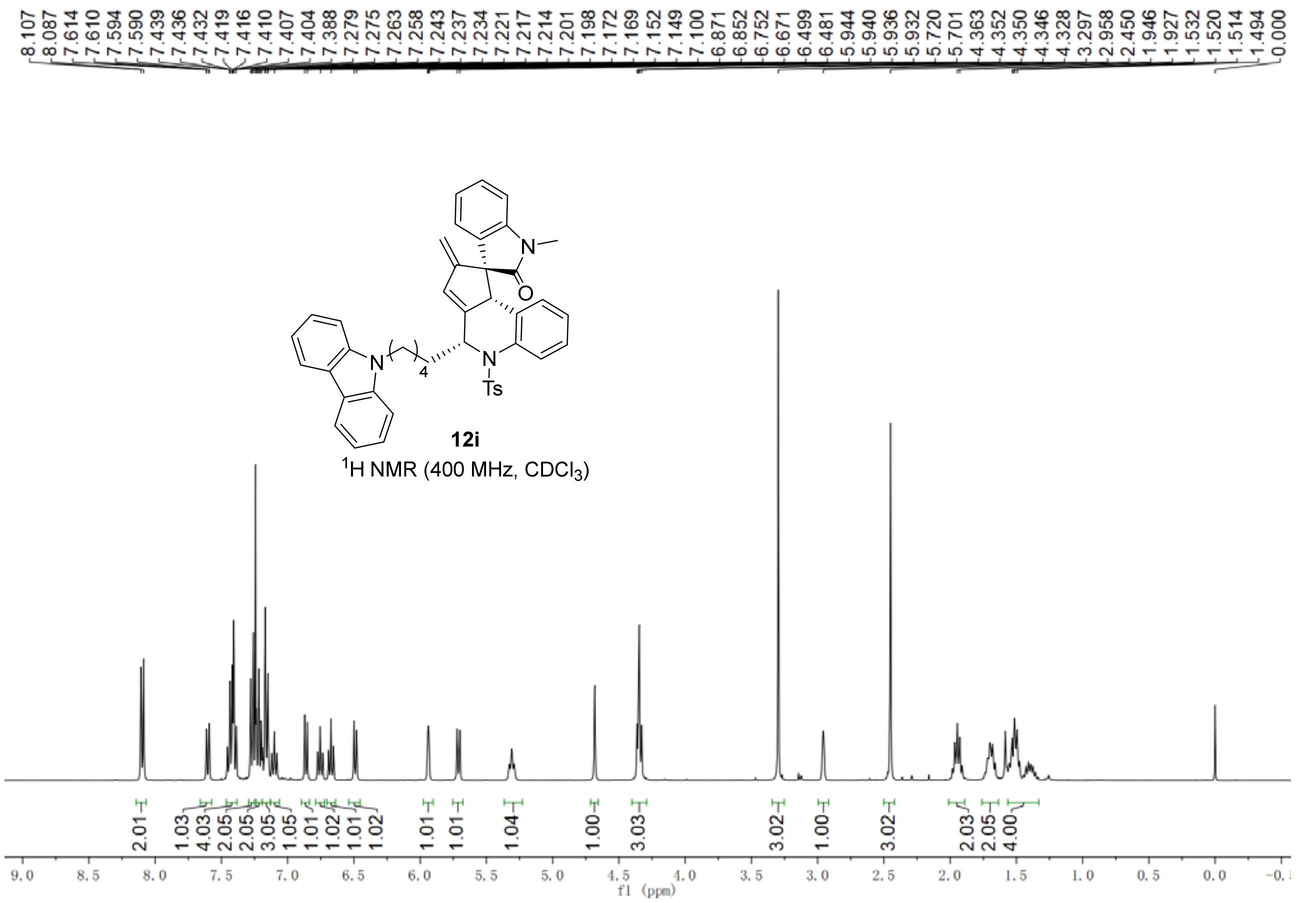
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.594	BBA	0.24	53.7615	821.4728	1.4394
12.865	BBA	0.94	937.7807	56249.4727	98.5606
			Totals:	57070.9454	100.0000



12h

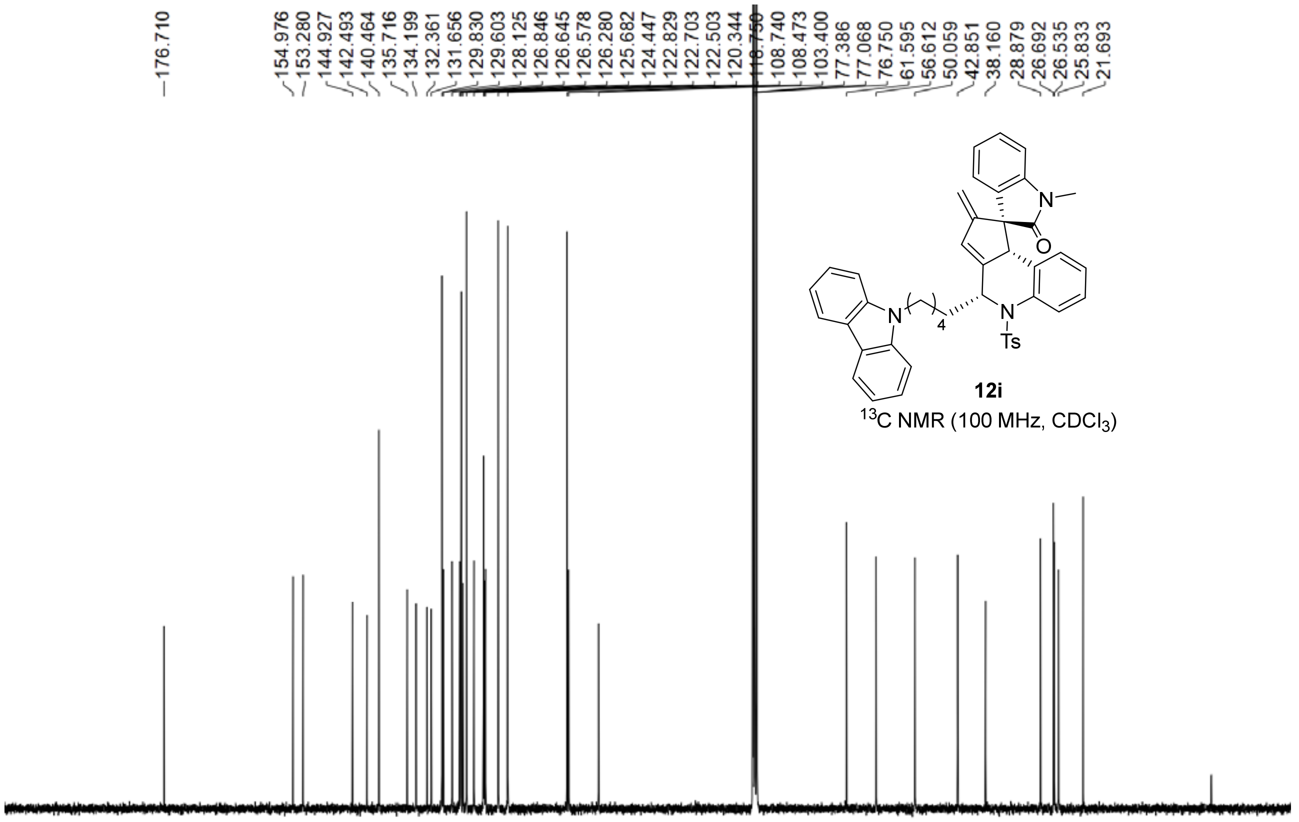
(ESI-TOF) *m/z*: [M +H]$^+$

Calcd for $C_{39}H_{34}N_3O_3S^+$ 624.2315



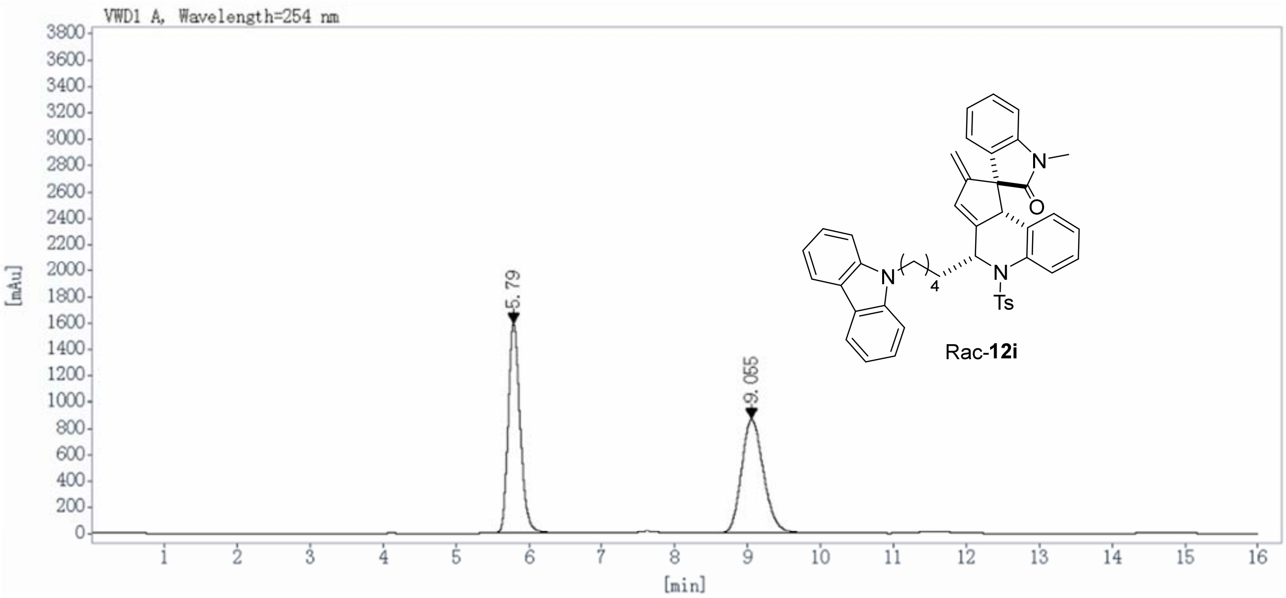
12i

^{1}H NMR (400 MHz, CDCl$_3$)



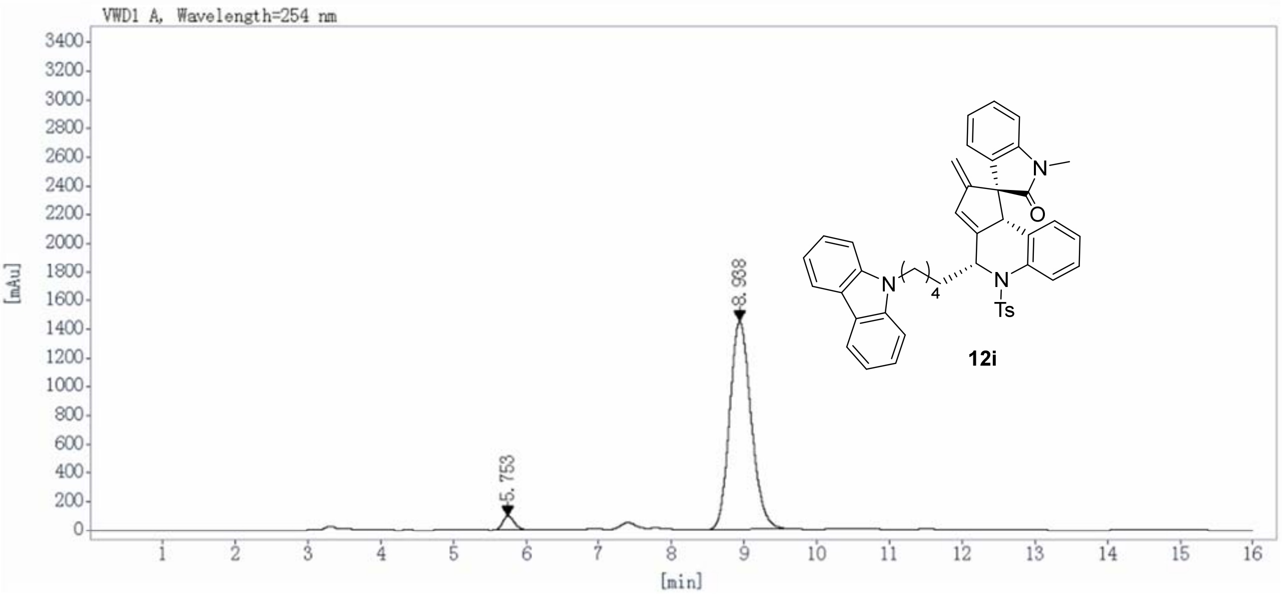
12i

^{13}C NMR (100 MHz, CDCl$_3$)



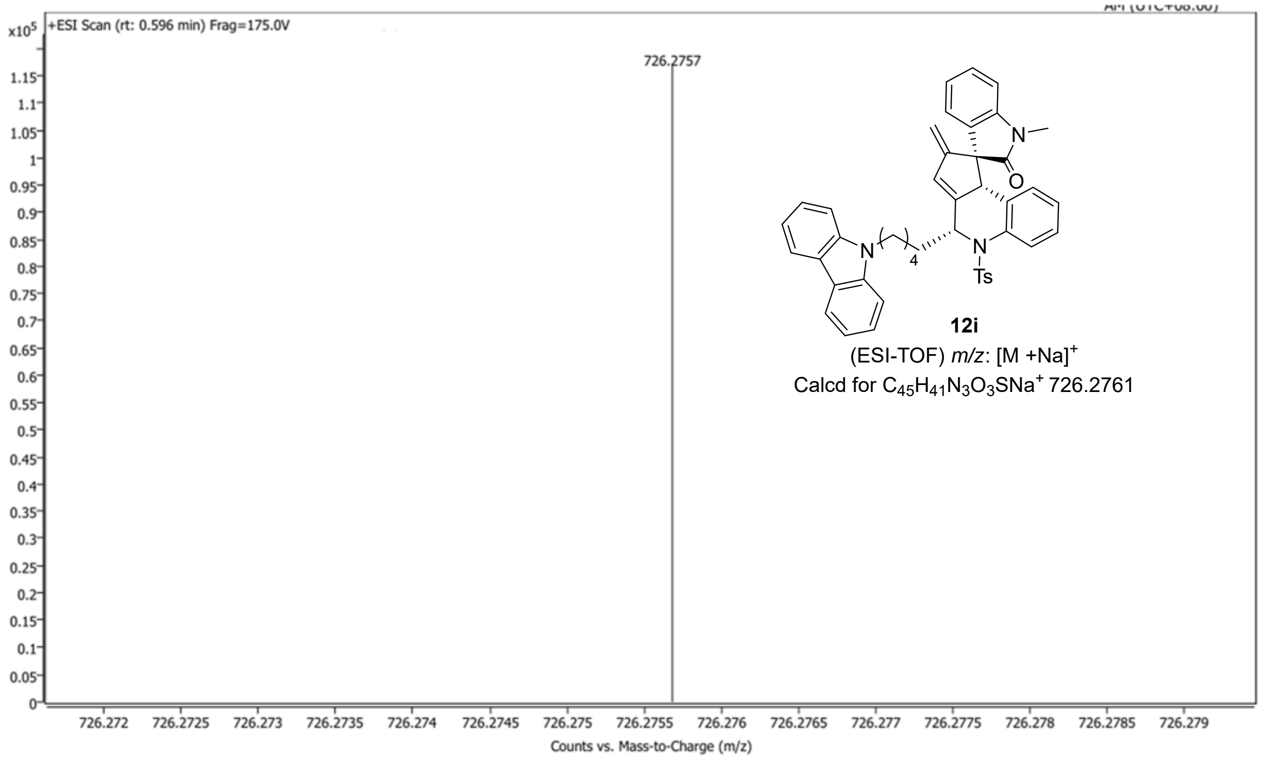
Rac-**12i**

Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.790	BBA	0.18	1591.1262	18135.9199	49.7910
9.055	BBA	0.33	869.1802	18288.1602	50.2090
			Totals:	36424.0801	100.0000



12i

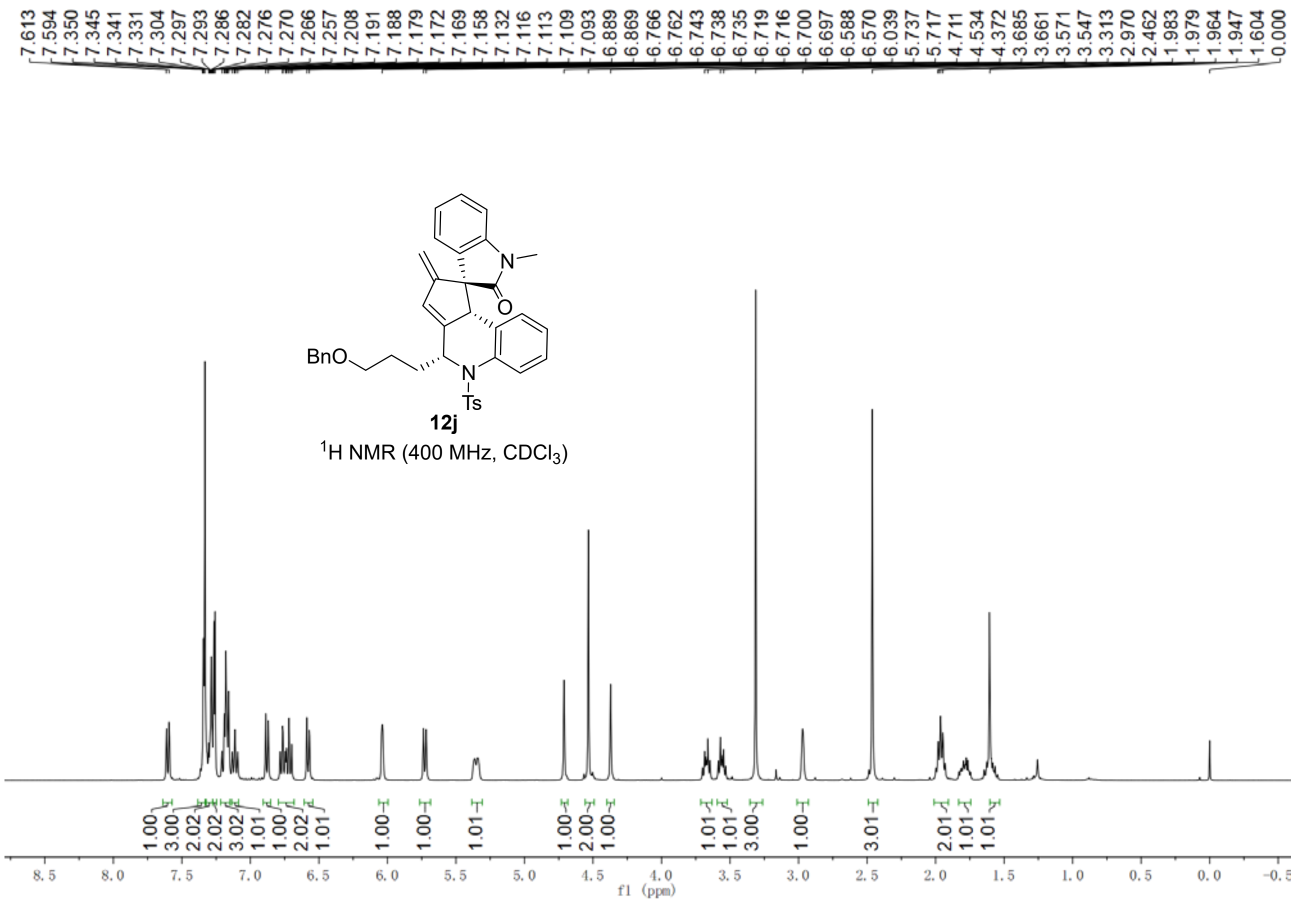
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.753	BBA	0.17	99.4315	1099.3254	3.5334
8.938	BBA	0.32	1450.0912	30013.2988	96.4666
			Totals:	31112.6243	100.0000



12i

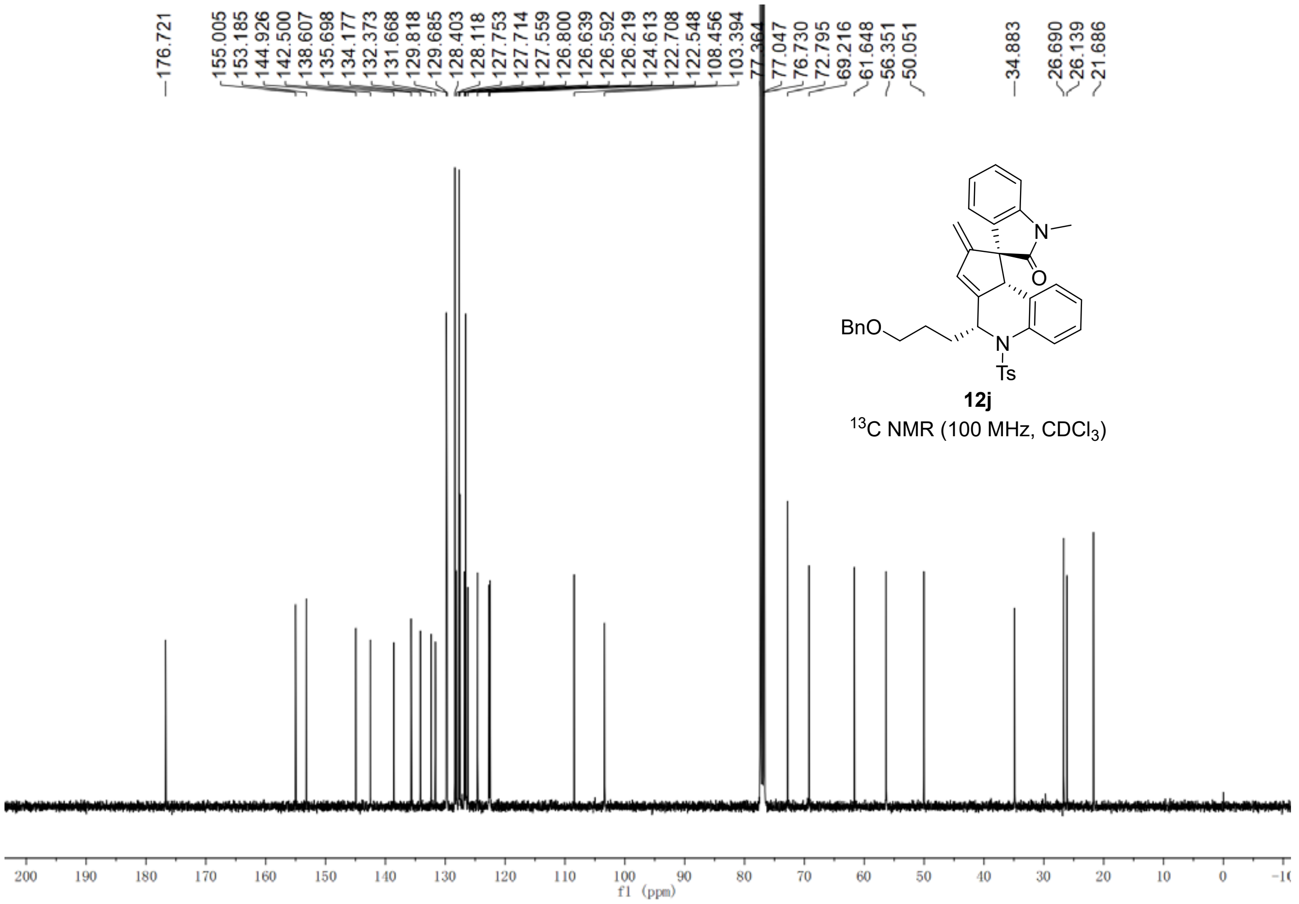
(ESI-TOF) *m/z*: [M +Na]$^+$

Calcd for $C_{45}H_{41}N_3O_3SNa^+$ 726.2761



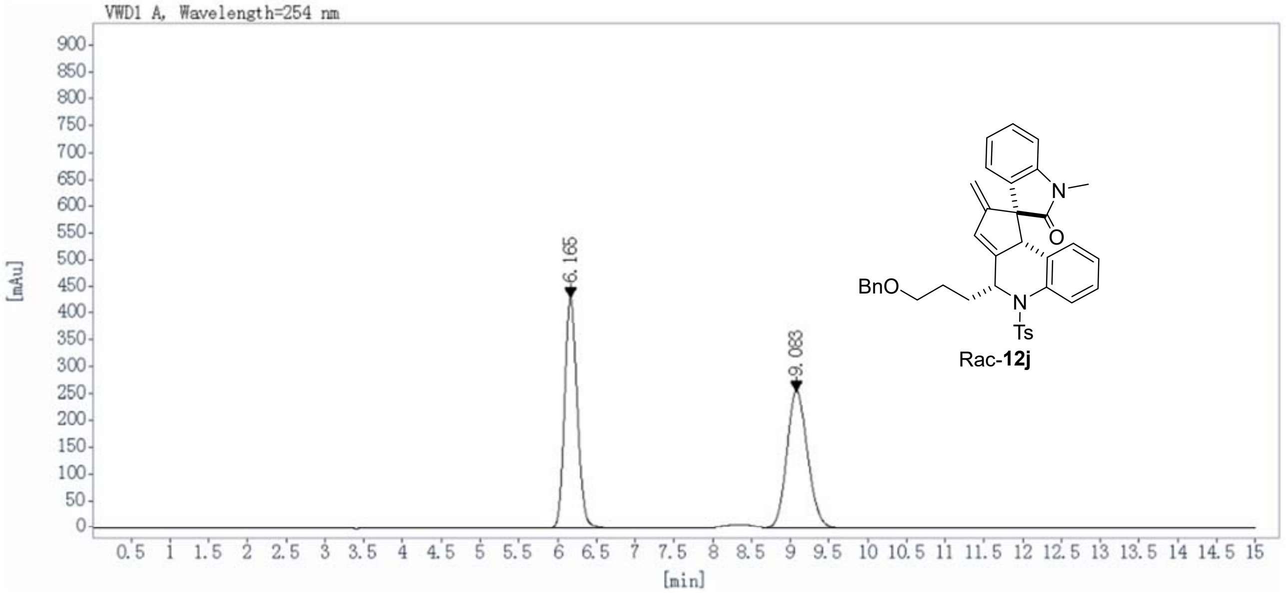
12j

^{1}H NMR (400 MHz, $CDCl_3$)

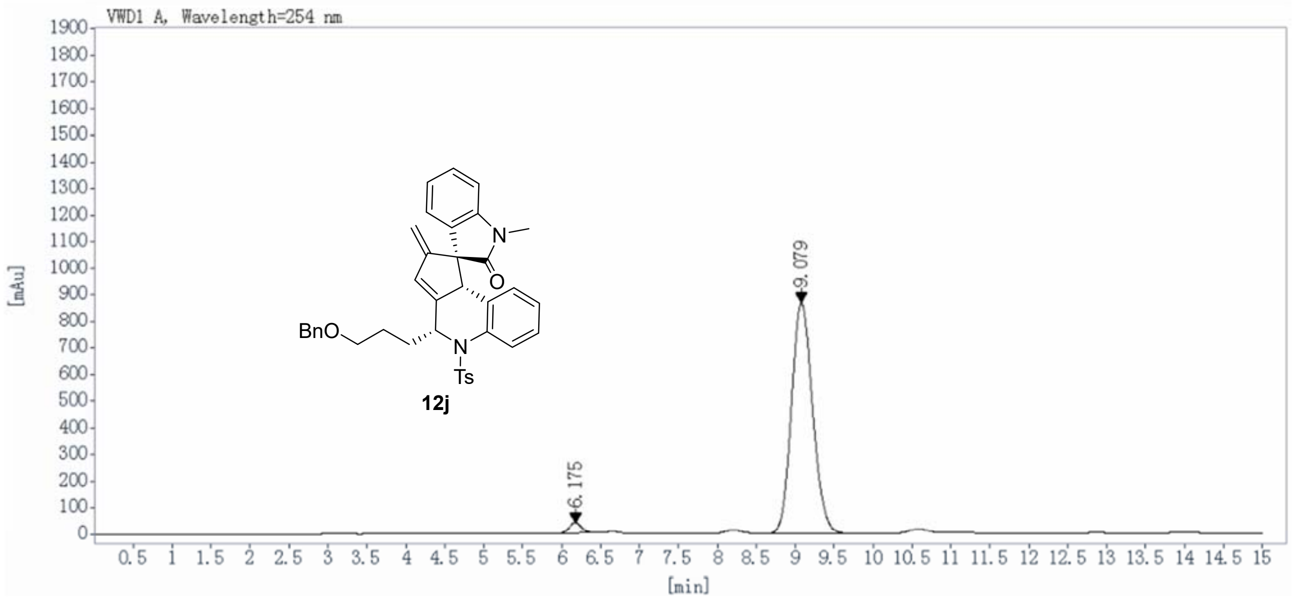


12j

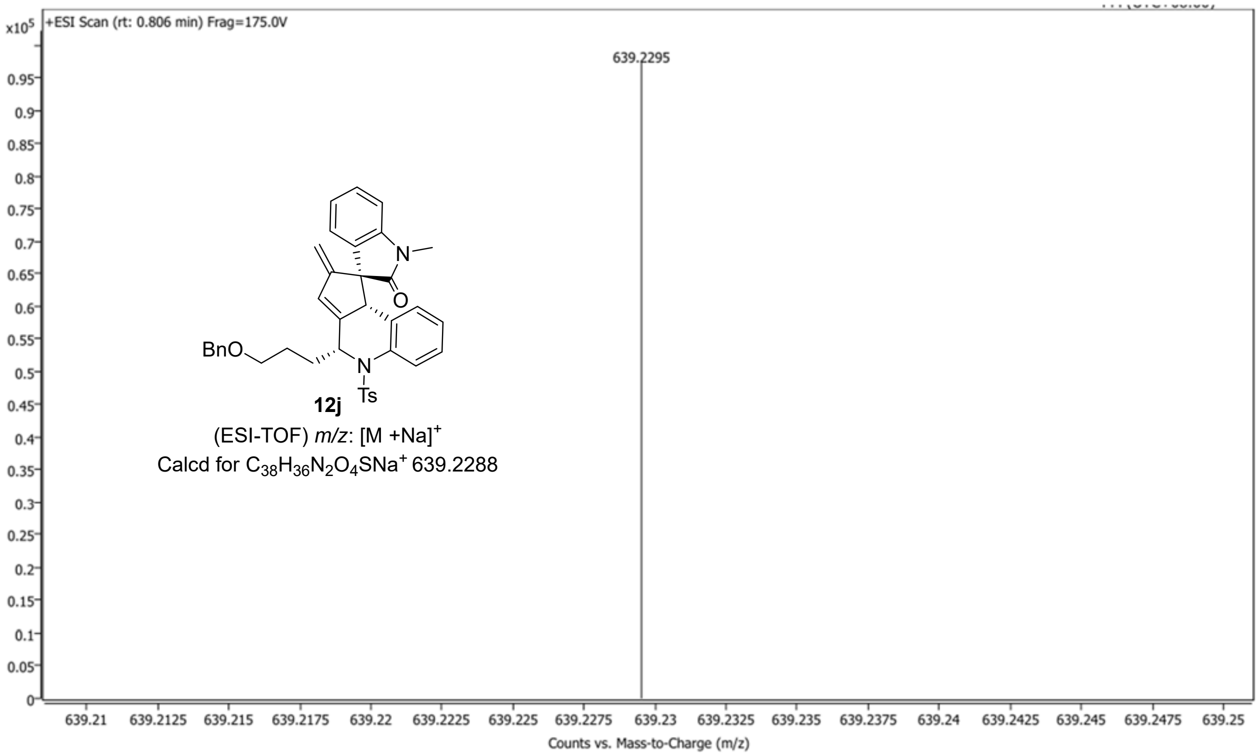
^{13}C NMR (100 MHz, $CDCl_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.165	BBA	0.17	428.2721	4798.7588	50.1795
9.083	BBA	0.29	254.8855	4764.4277	49.8205
			Totals:	9563.1865	100.0000



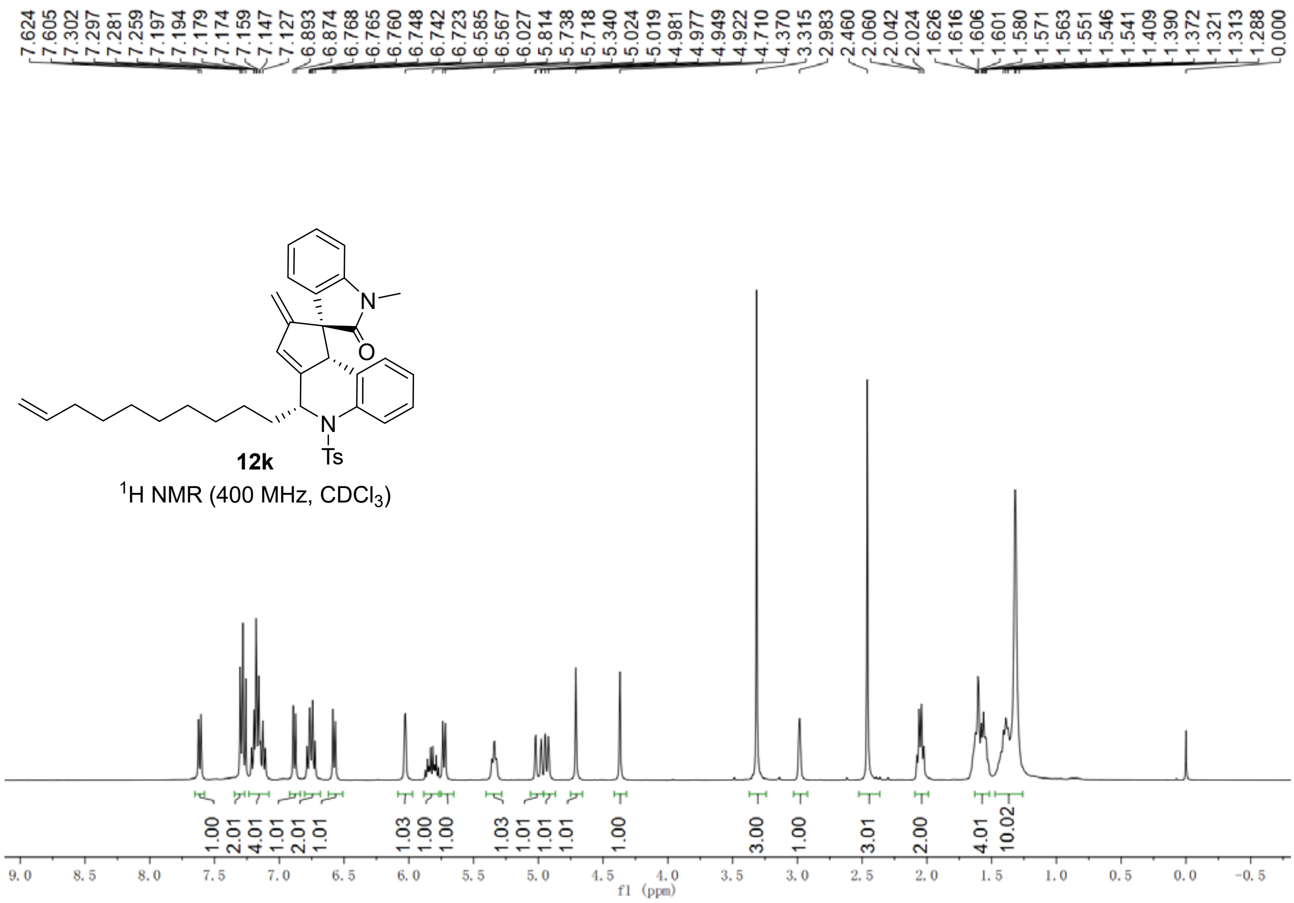
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.175	BB	0.17	39.0287	438.8946	2.6057
9.079	BBA	0.30	865.3759	16404.4570	97.3943
			Totals:	16843.3516	100.0000

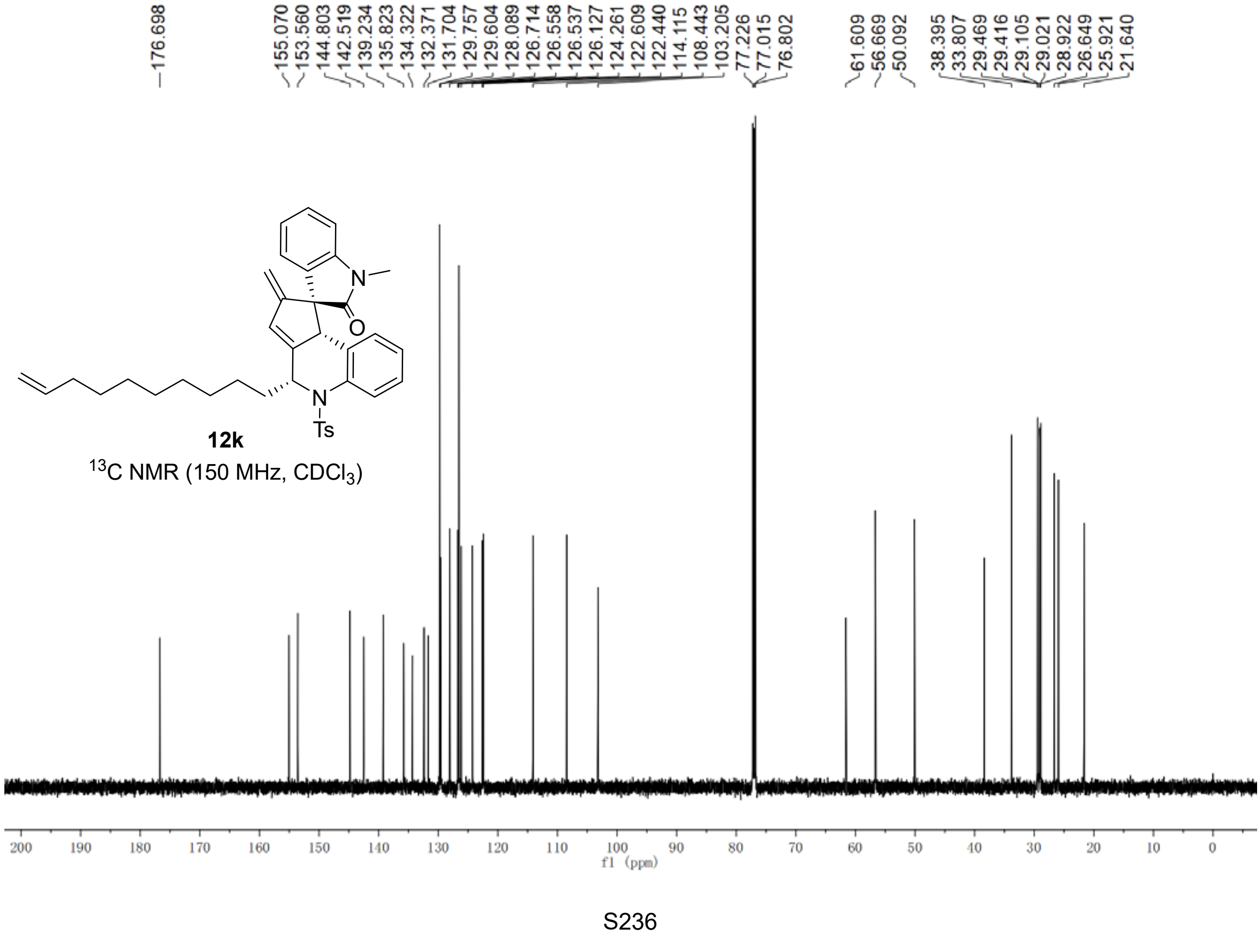


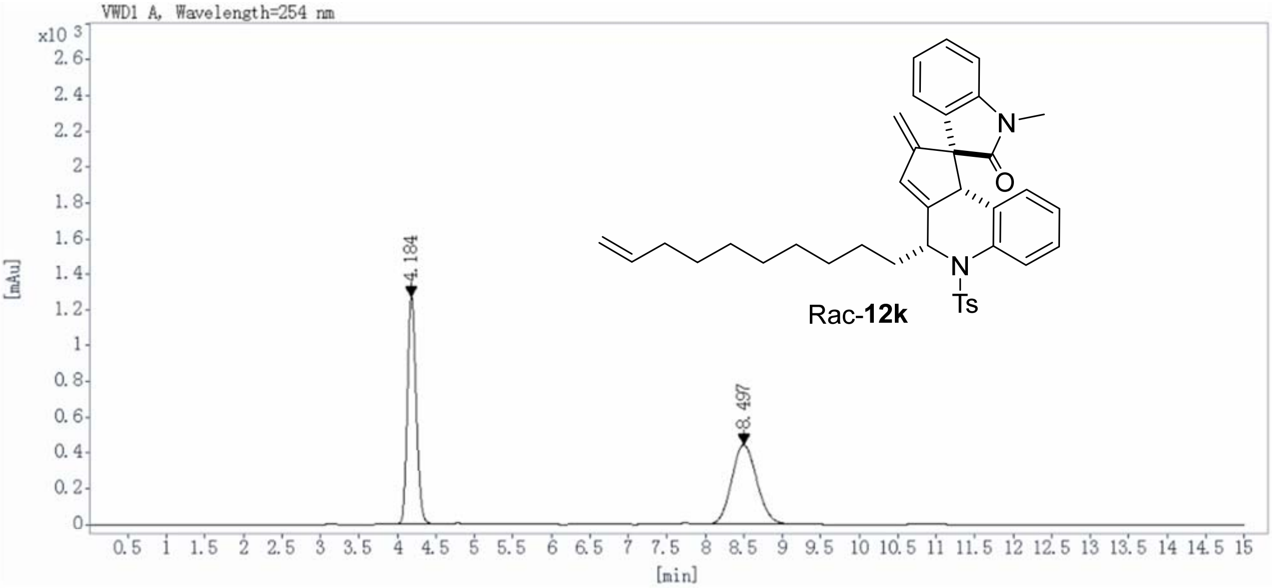
12j

(ESI-TOF) *m/z*: $[M + Na]^+$

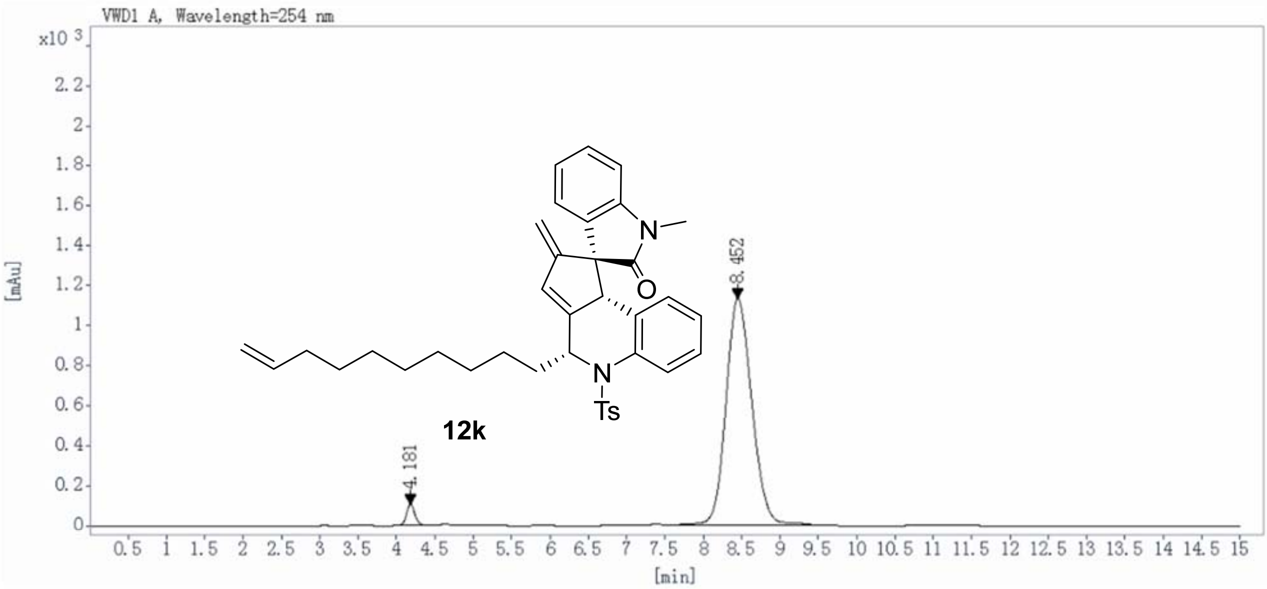
Calcd for $C_{38}H_{36}N_2O_4SNa^+$ 639.2288


7.624
7.605
7.302
7.297
7.281
7.259
7.197
7.179
7.174
7.159
7.147
7.127
6.893
6.874
6.768
6.765
6.760
6.748
6.742
6.723
6.585
6.567
6.027
5.814
5.738
5.718
5.340
5.024
5.019
4.981
4.977
4.949
4.922
4.710
4.370
3.315
2.983
2.460
2.060
2.042
2.024
1.626
1.616
1.606
1.601
1.580
1.571
1.563
1.551
1.546
1.541
1.409
1.390
1.372
1.321
1.313
1.288
0.000
N
O
N
Ts
12k
¹H NMR (400 MHz, CDCl₃)
1.00
2.01
4.01
1.01
2.01
1.01
1.03
1.00
1.00
1.03
1.01
1.01
1.01
1.00
3.00
1.00
3.01
2.00
4.01
10.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

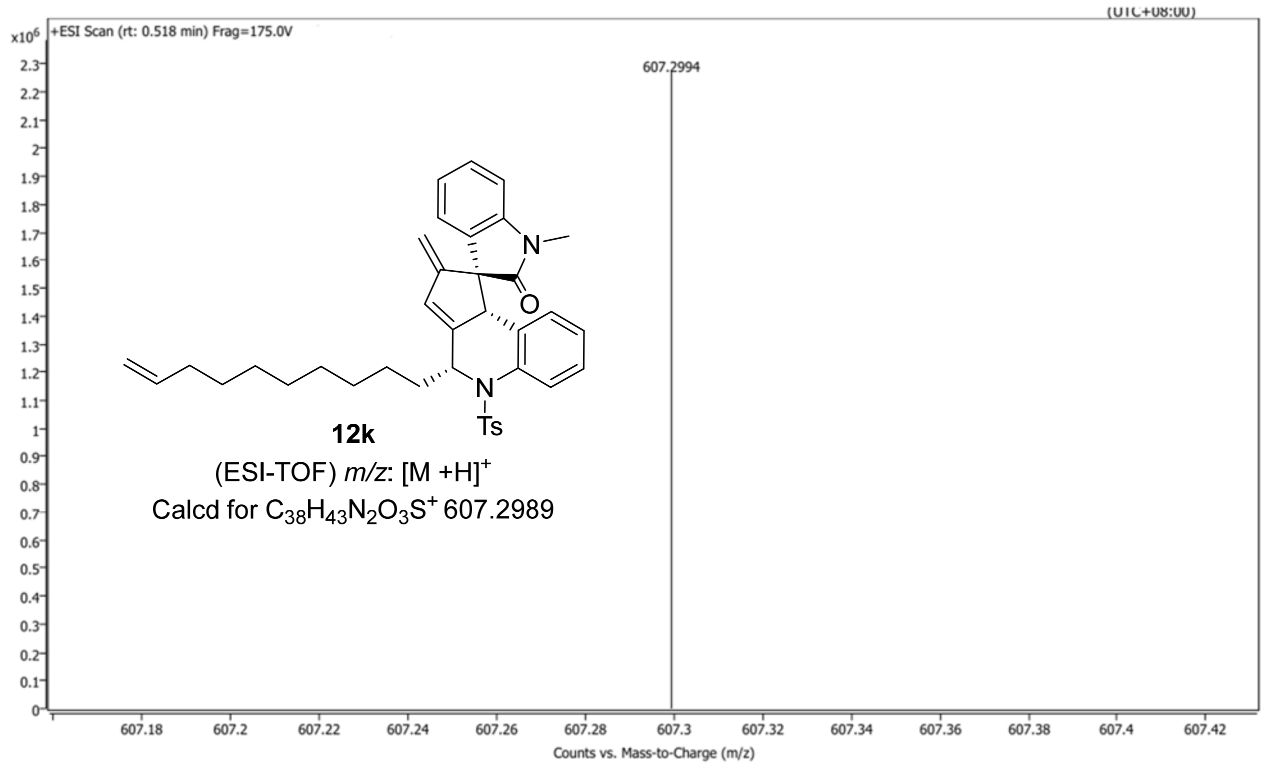

176.698
155.070
153.560
144.803
142.519
139.234
135.823
134.322
132.371
131.704
129.757
129.604
128.089
126.714
126.558
126.537
126.127
124.261
122.609
122.440
114.115
108.443
103.205
77.226
77.015
76.802
61.609
56.669
50.092
38.395
33.807
29.469
29.416
29.105
29.021
28.922
26.649
25.921
21.640
N
O
N
Ts
12k
¹³C NMR (150 MHz, CDCl₃)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.184	BBA	0.12	1273.7031	10044.6152	49.9861
8.497	BBA	0.35	443.9998	10050.2139	50.0139
			Totals:	20094.8291	100.0000



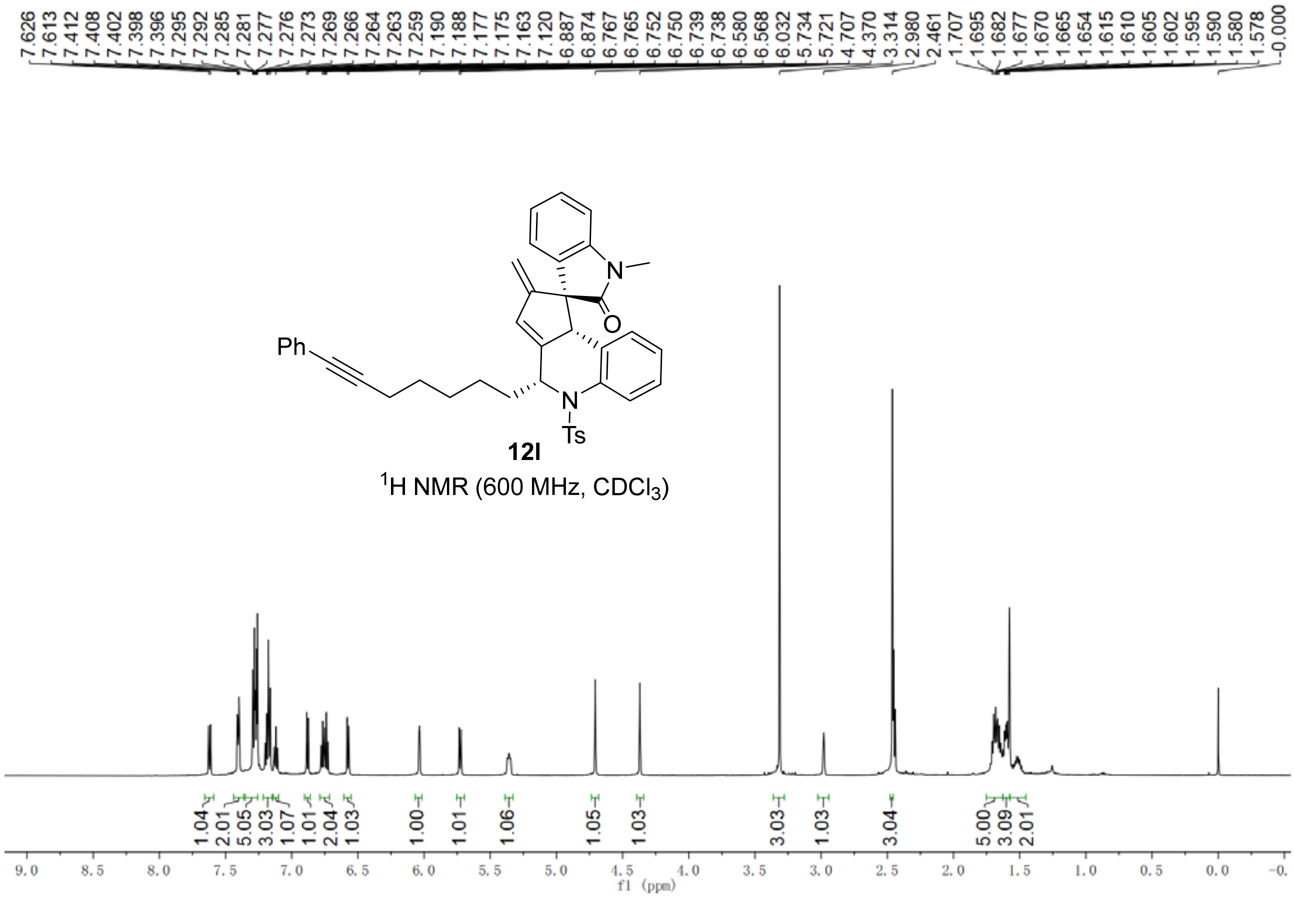
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.181	BB	0.12	104.9507	822.0416	2.9815
8.452	BB	0.37	1132.7063	26749.0391	97.0185
			Totals:	27571.0807	100.0000



12k

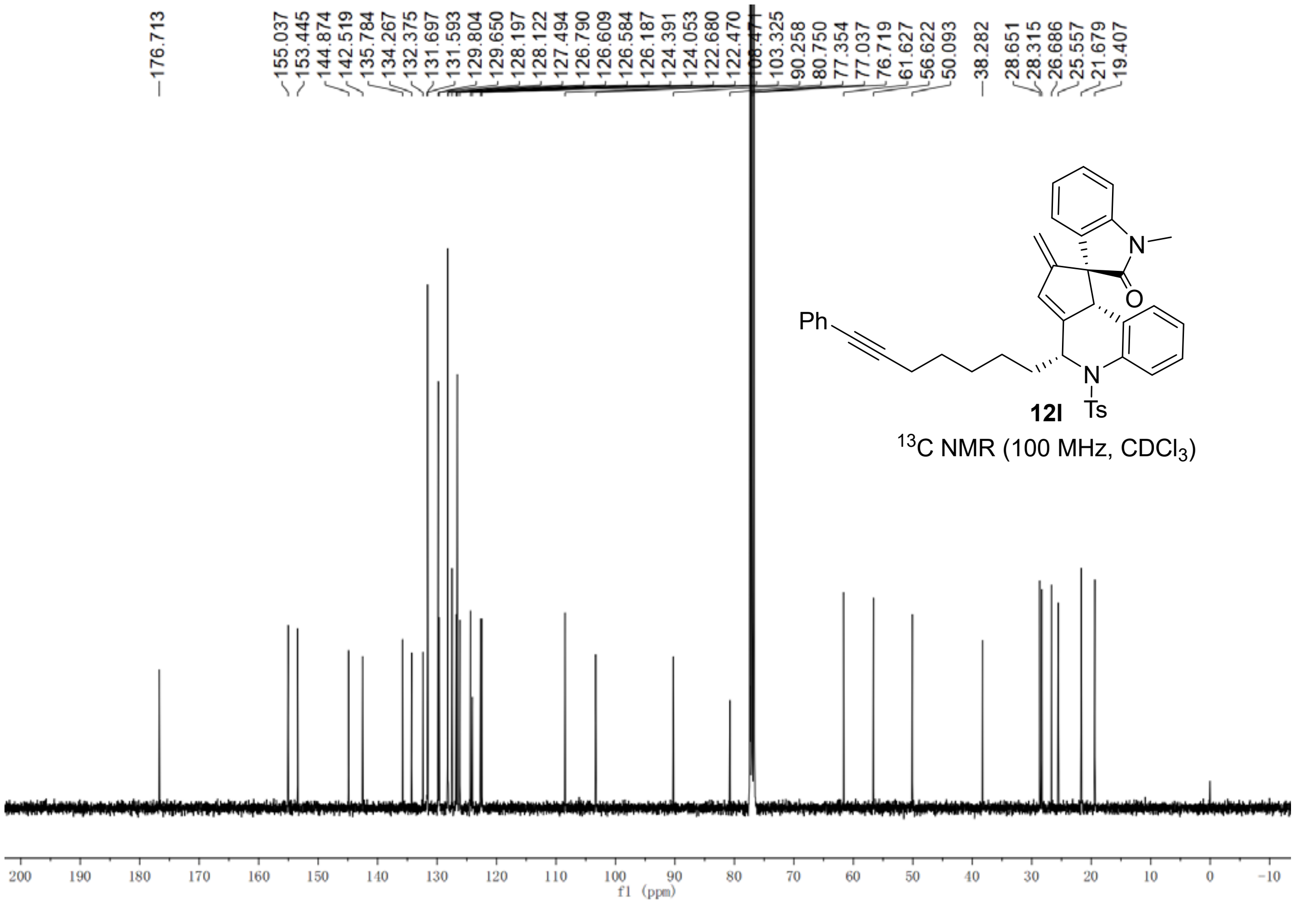
(ESI-TOF) *m/z*: $[M+H]^+$

Calcd for $C_{38}H_{43}N_2O_3S^+$ 607.2989



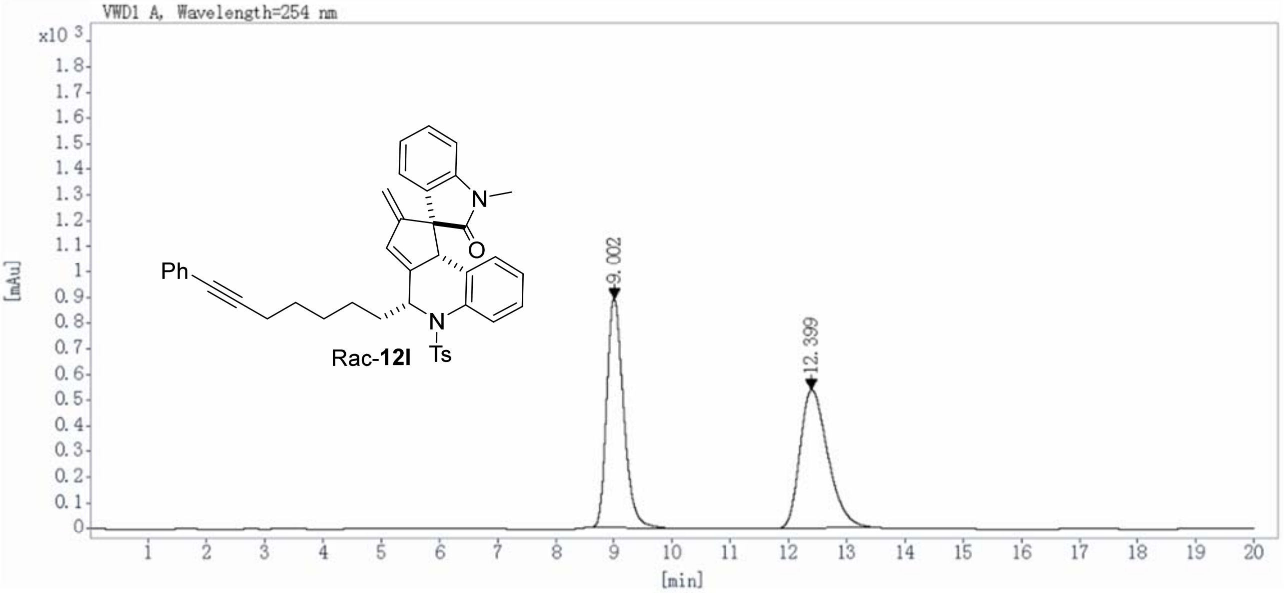
12l

^{1}H NMR (600 MHz, CDCl$_3$)

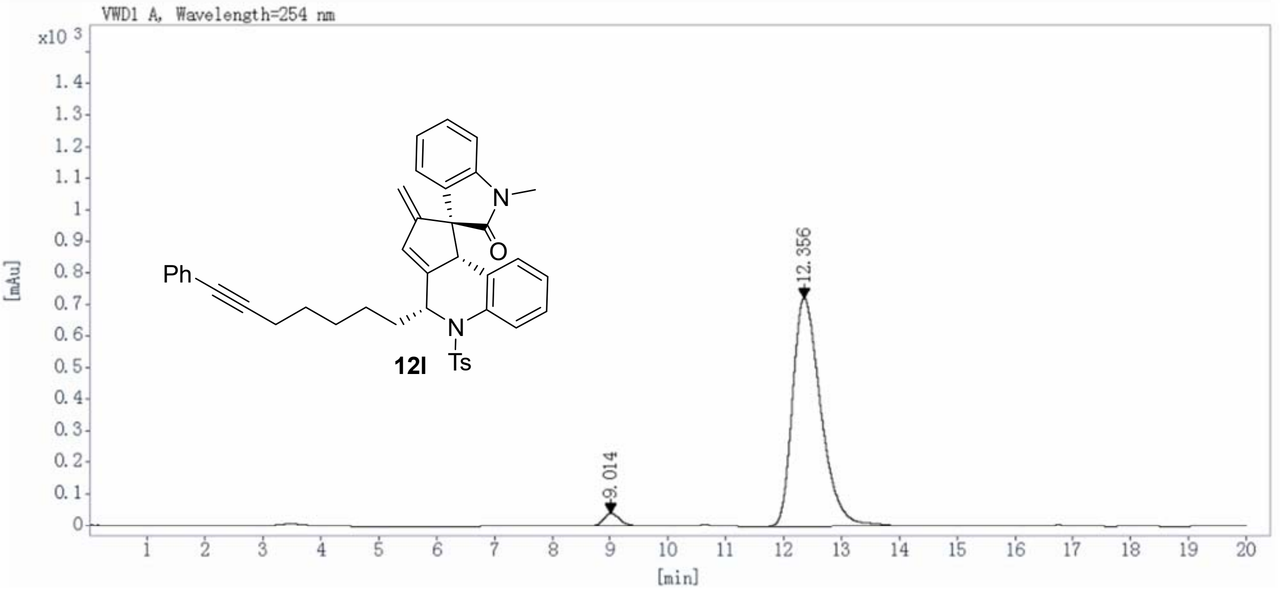


12l

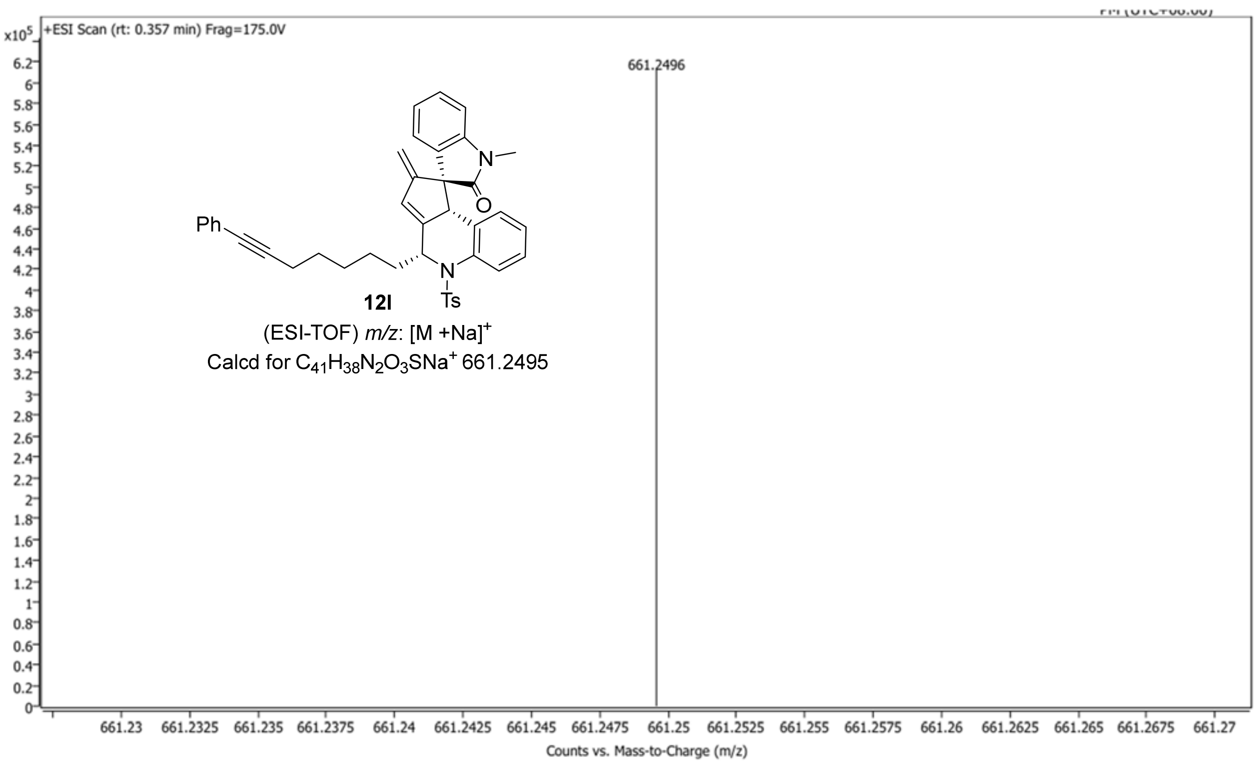
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
9.002	BBA	0.31	891.9315	17841.7578	49.6578
12.399	BBA	0.52	540.7164	18087.6445	50.3422
			Totals:	35929.4023	100.0000



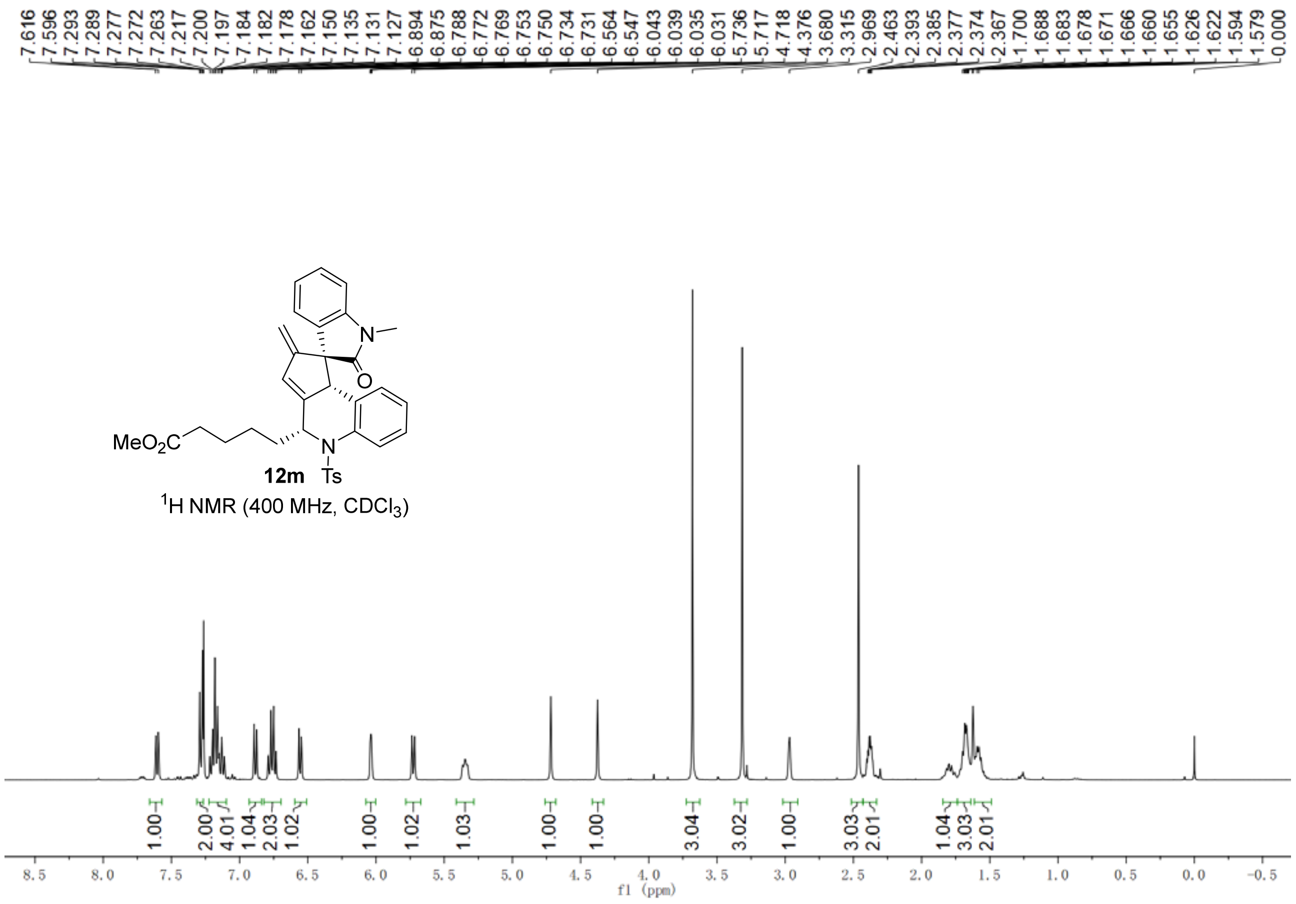
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
9.014	BBA	0.29	40.3394	763.8903	3.0236
12.356	BBA	0.52	721.9957	24500.3711	96.9764
			Totals:	25264.2614	100.0000

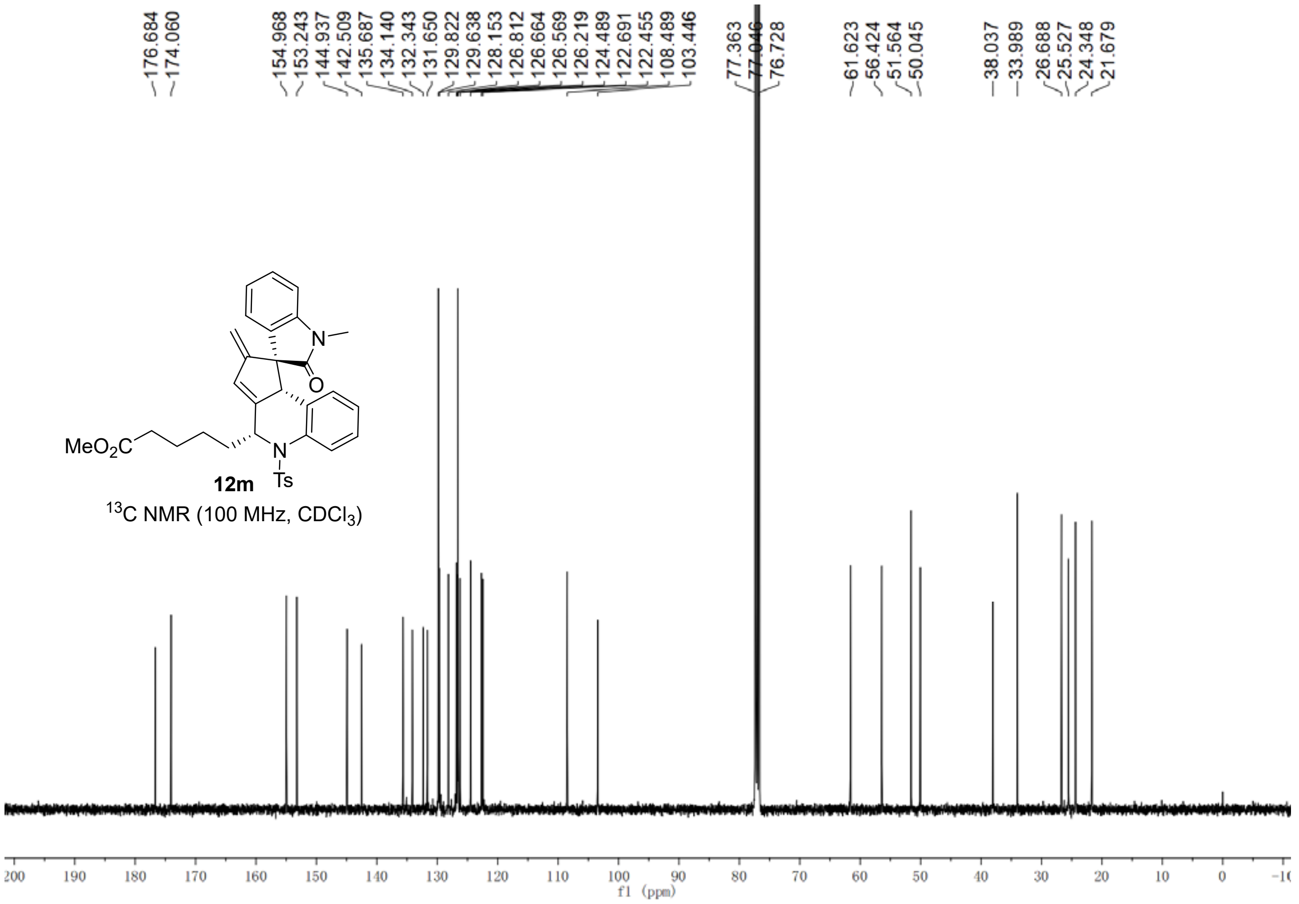


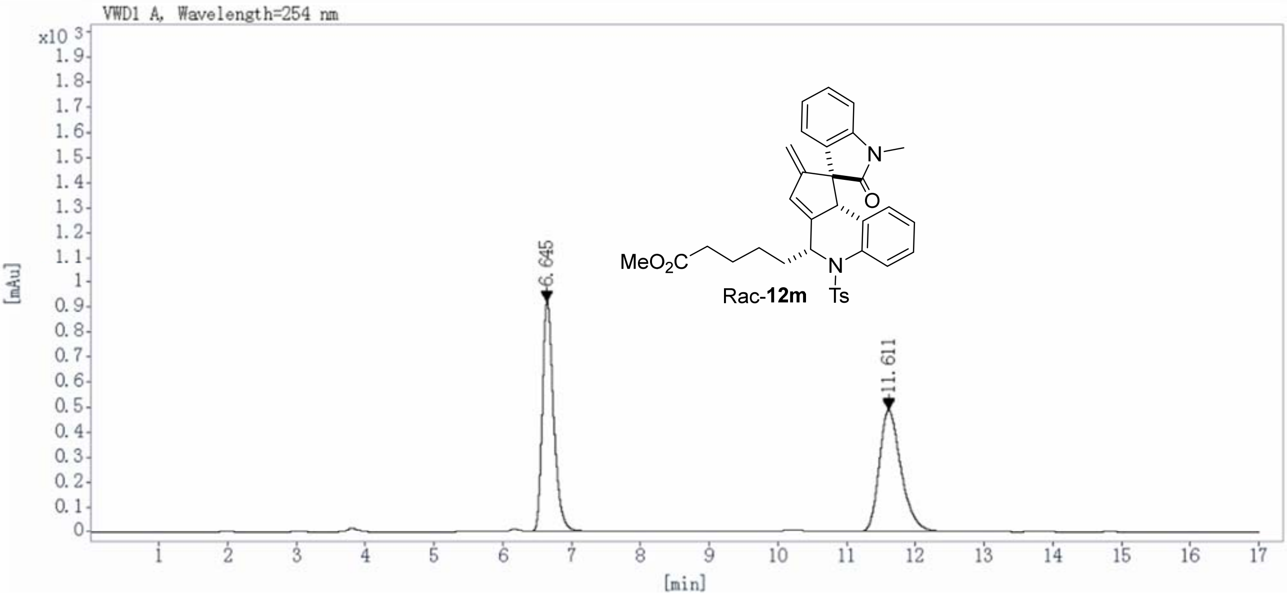
12l

(ESI-TOF) *m/z*: [M +Na]$^+$

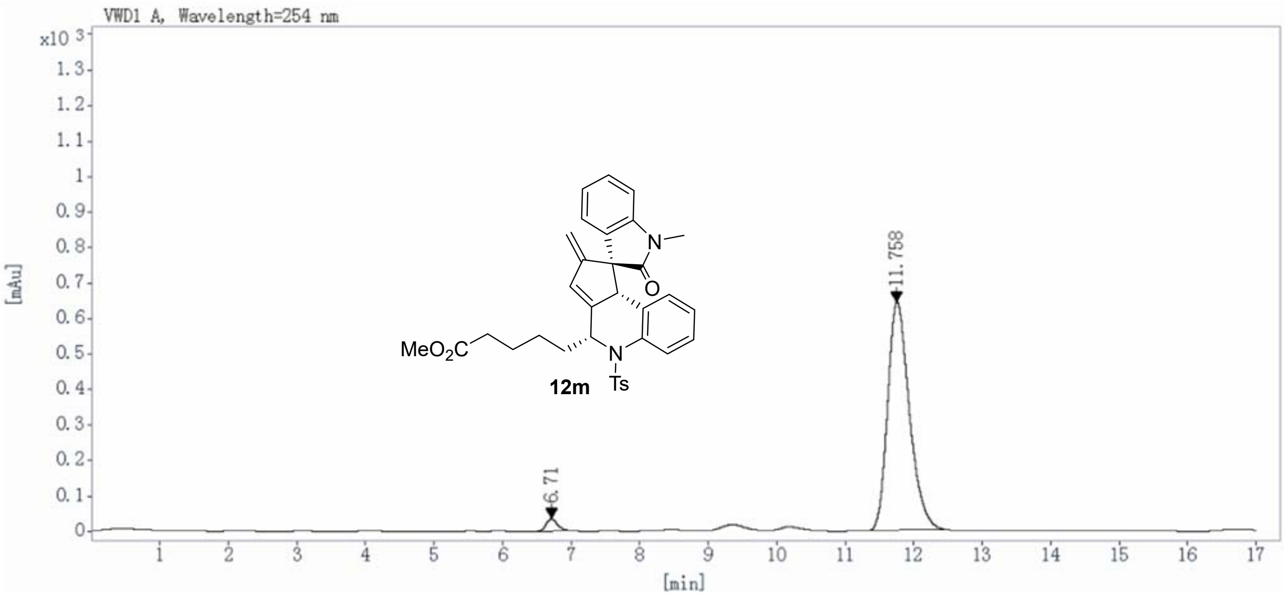
Calcd for $C_{41}H_{38}N_2O_3SNa^+$ 661.2495


7.616
7.596
7.293
7.289
7.277
7.272
7.263
7.217
7.200
7.197
7.184
7.182
7.178
7.162
7.150
7.135
7.131
7.127
6.894
6.875
6.788
6.772
6.769
6.753
6.750
6.734
6.731
6.564
6.547
6.043
6.039
6.035
6.031
5.736
5.717
4.718
4.376
3.680
3.315
2.969
2.463
2.393
2.385
2.377
2.374
2.367
1.700
1.688
1.683
1.678
1.671
1.666
1.660
1.655
1.626
1.622
1.594
1.579
0.000
MeO2C
N
O
N
Ts
12m
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
2.00
4.01
1.04
2.03
1.02
1.00
1.02
1.03
1.00
1.00
3.04
3.02
1.00
3.03
2.01
1.04
3.03
2.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

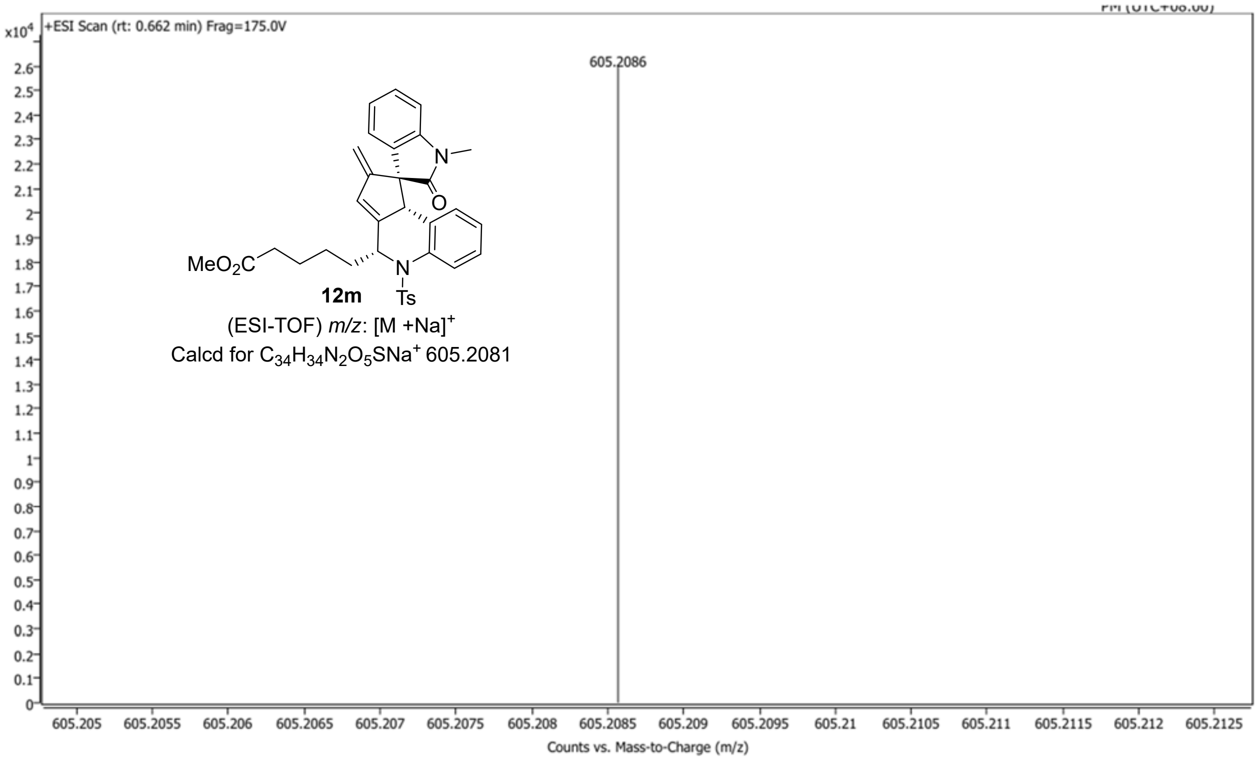

176.684
174.060
154.968
153.243
144.937
142.509
135.687
134.140
132.343
131.650
129.822
129.638
128.153
126.812
126.664
126.569
126.219
124.489
122.691
122.455
108.489
103.446
77.363
77.046
76.728
61.623
56.424
51.564
50.045
38.037
33.989
26.688
25.527
24.348
21.679
MeO2C
N
O
N
Ts
12m
^{13}C NMR (100 MHz, CDCl$_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.645	BV R	0.17	922.2198	10522.9707	49.3114
11.611	BBA	0.34	489.4550	10816.8643	50.6886
			Totals:	21339.8350	100.0000



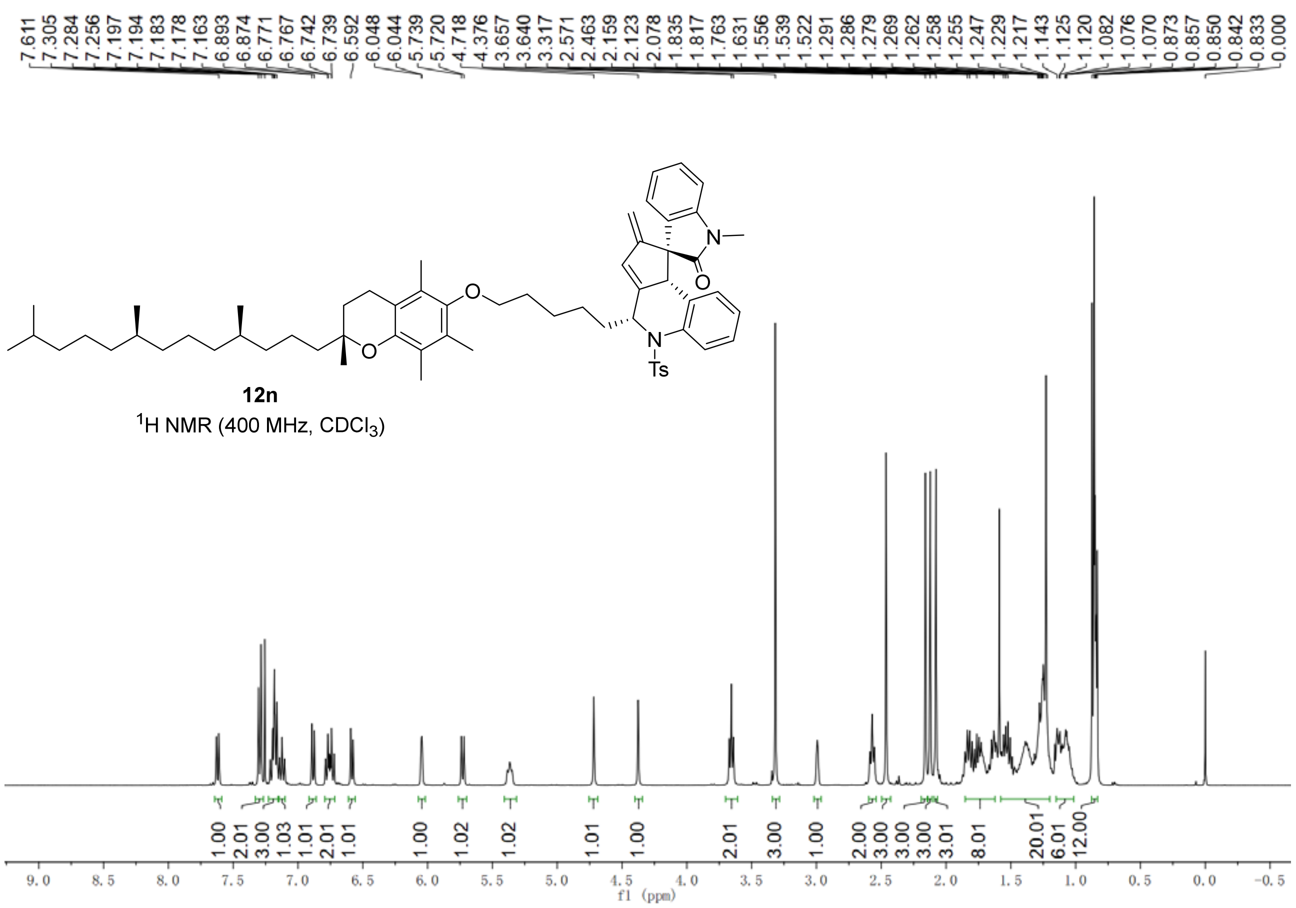
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.710	BBA	0.17	34.9625	388.7296	2.6562
11.758	BBA	0.34	644.5510	14246.2002	97.3438
			Totals:	14634.9298	100.0000



12m

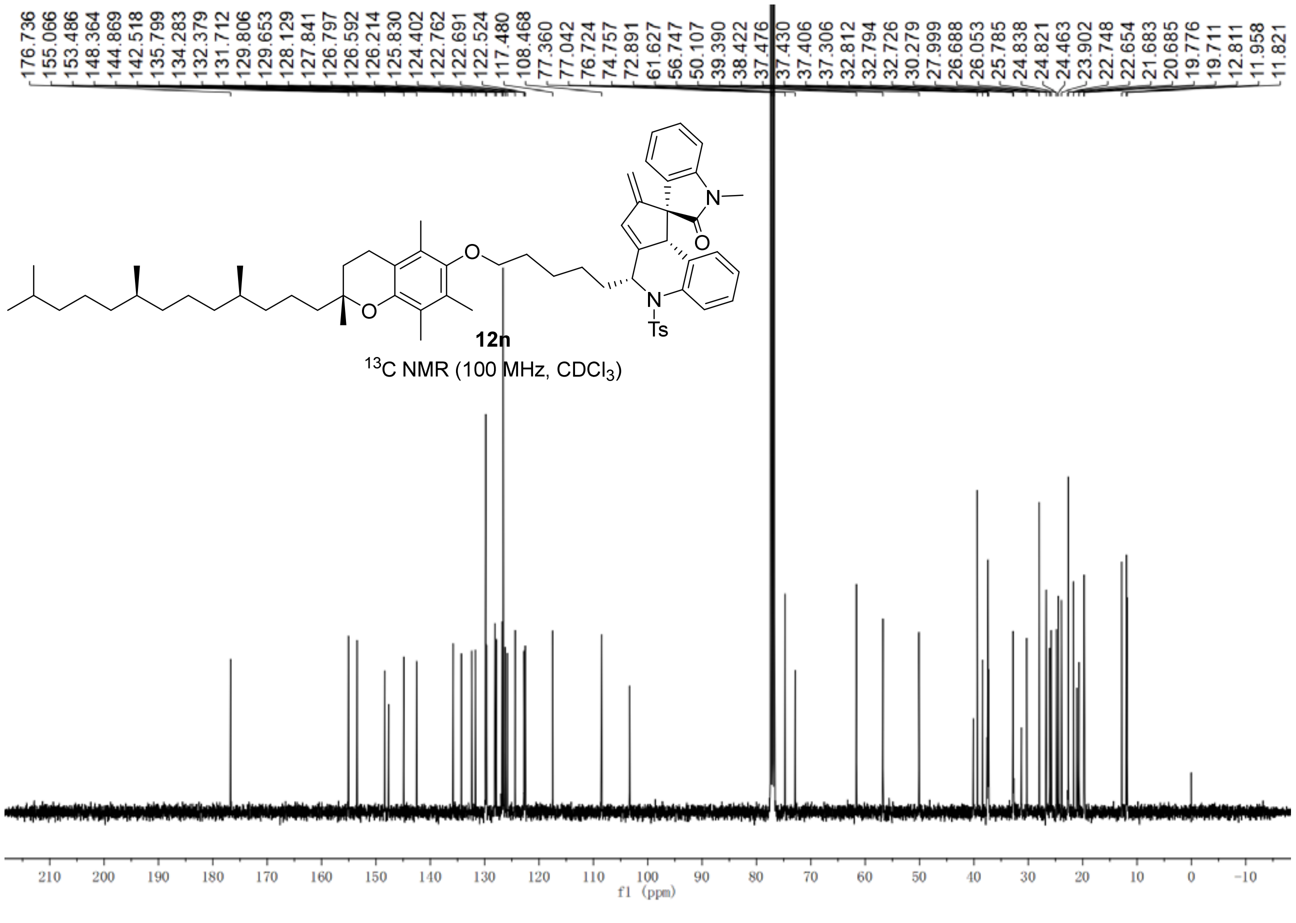
(ESI-TOF) *m/z*: [M +Na]$^+$

Calcd for $C_{34}H_{34}N_2O_5SNa^+$ 605.2081



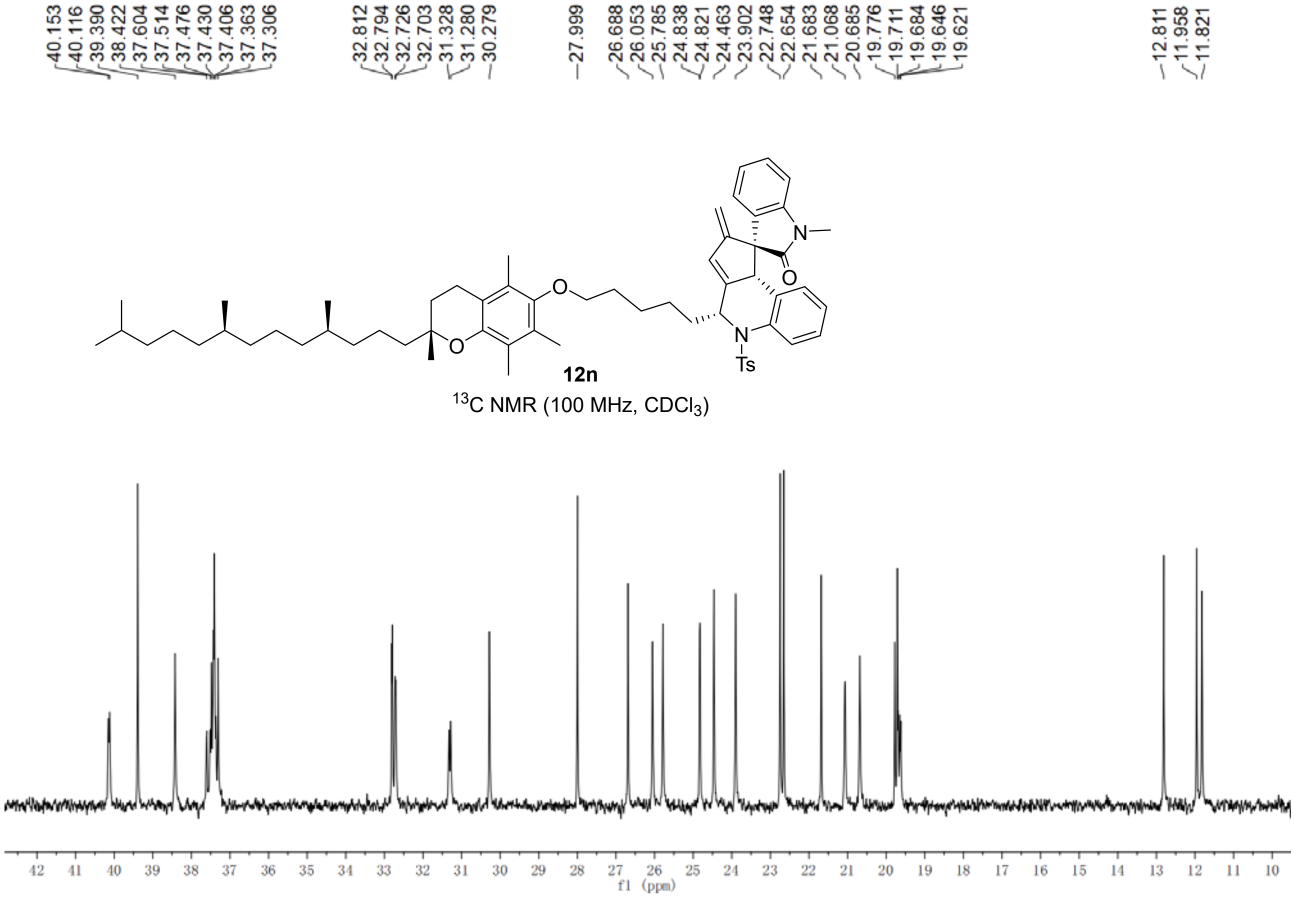
12n

^{1}H NMR (400 MHz, CDCl$_3$)



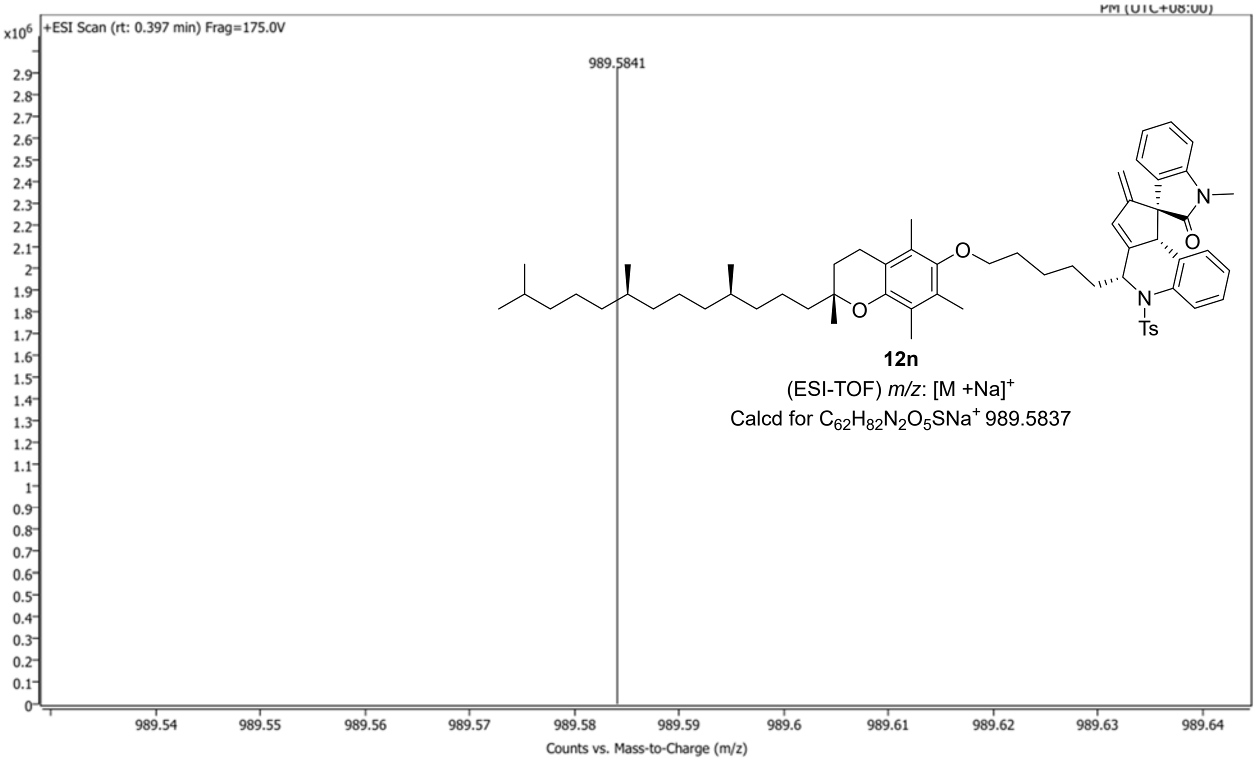
12n

^{13}C NMR (100 MHz, CDCl$_3$)



12n

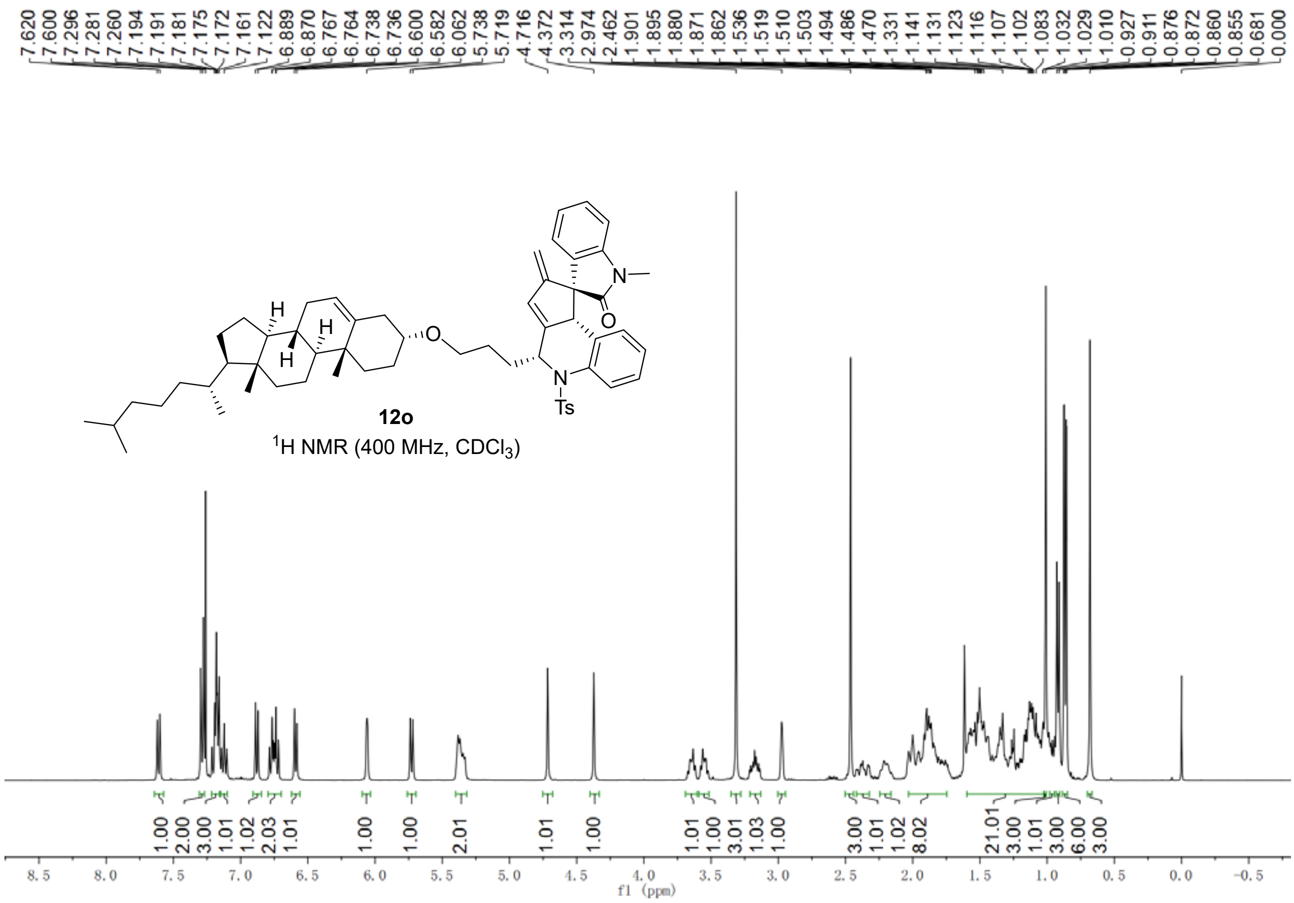
^{13}C NMR (100 MHz, CDCl$_3$)



12n

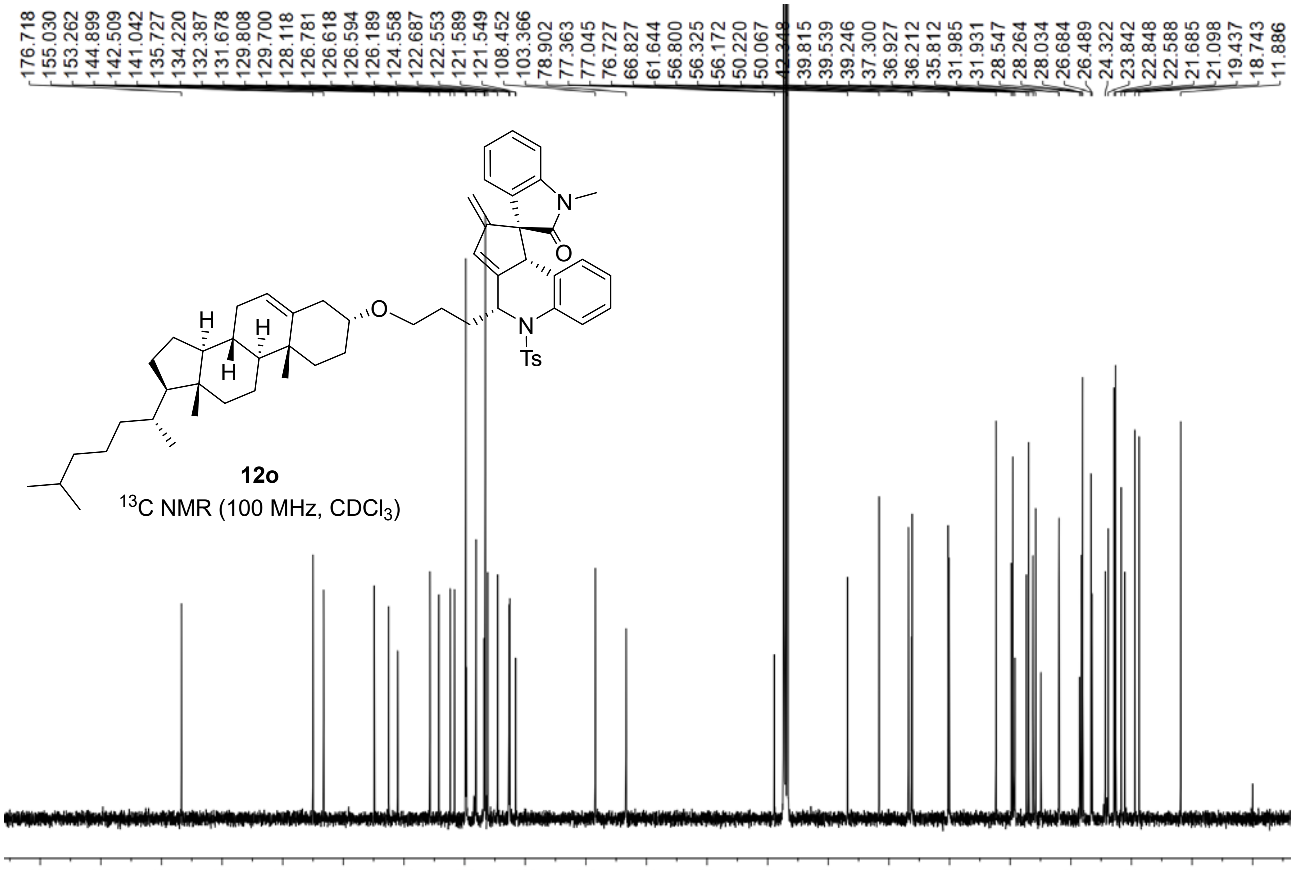
(ESI-TOF) *m/z*: [M +Na]$^+$

Calcd for $C_{62}H_{82}N_2O_5SNa^+$ 989.5837



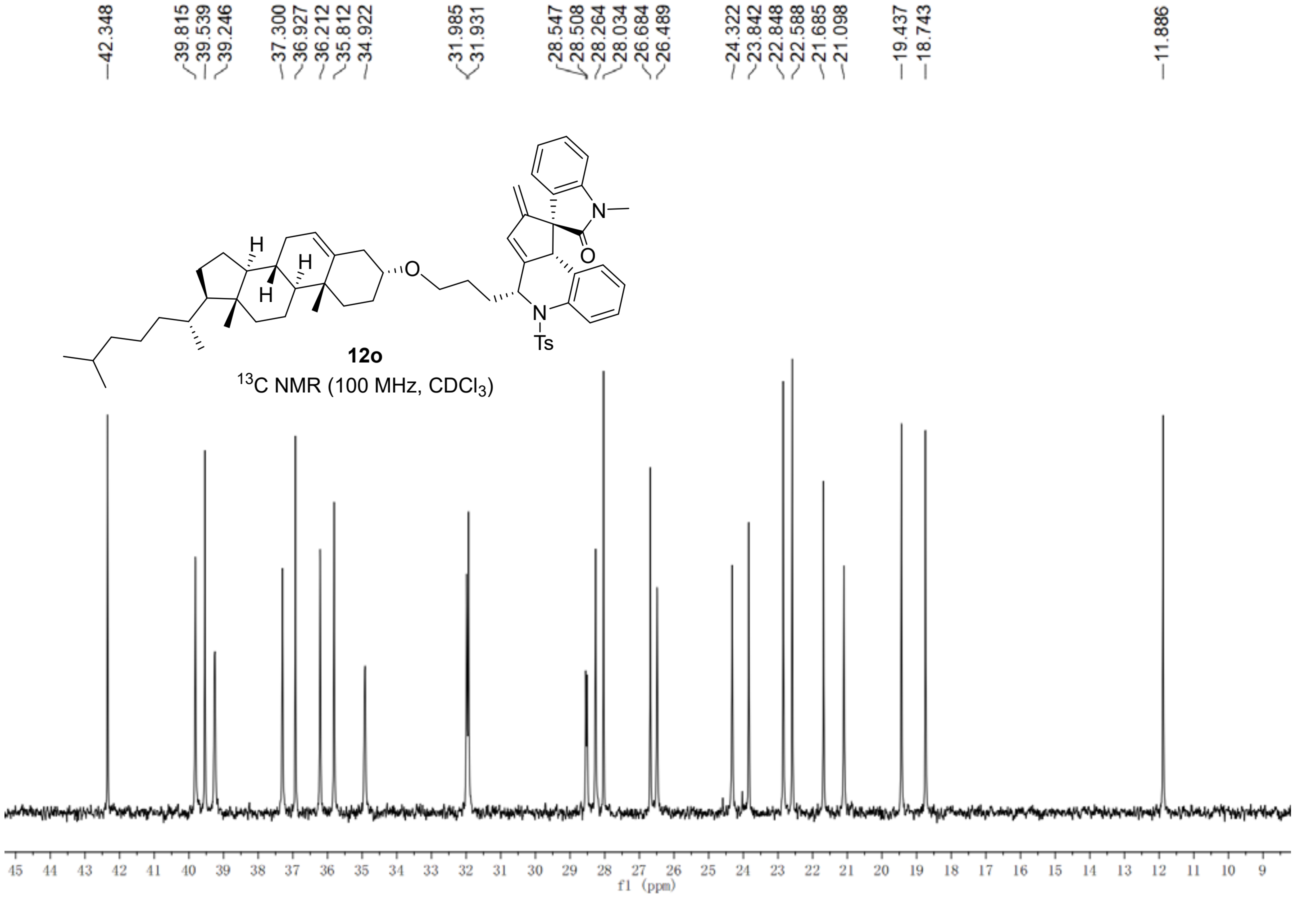
12o

^{1}H NMR (400 MHz, CDCl$_3$)



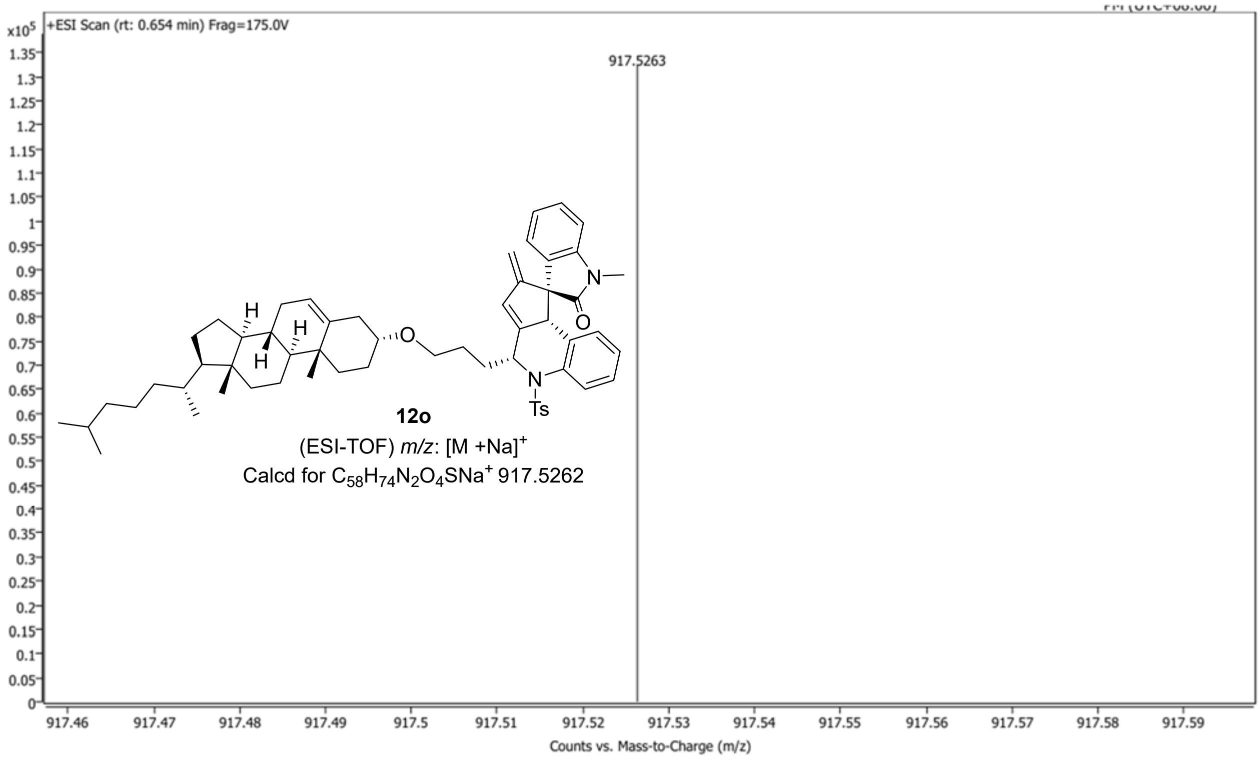
12o

^{13}C NMR (100 MHz, CDCl$_3$)



12o

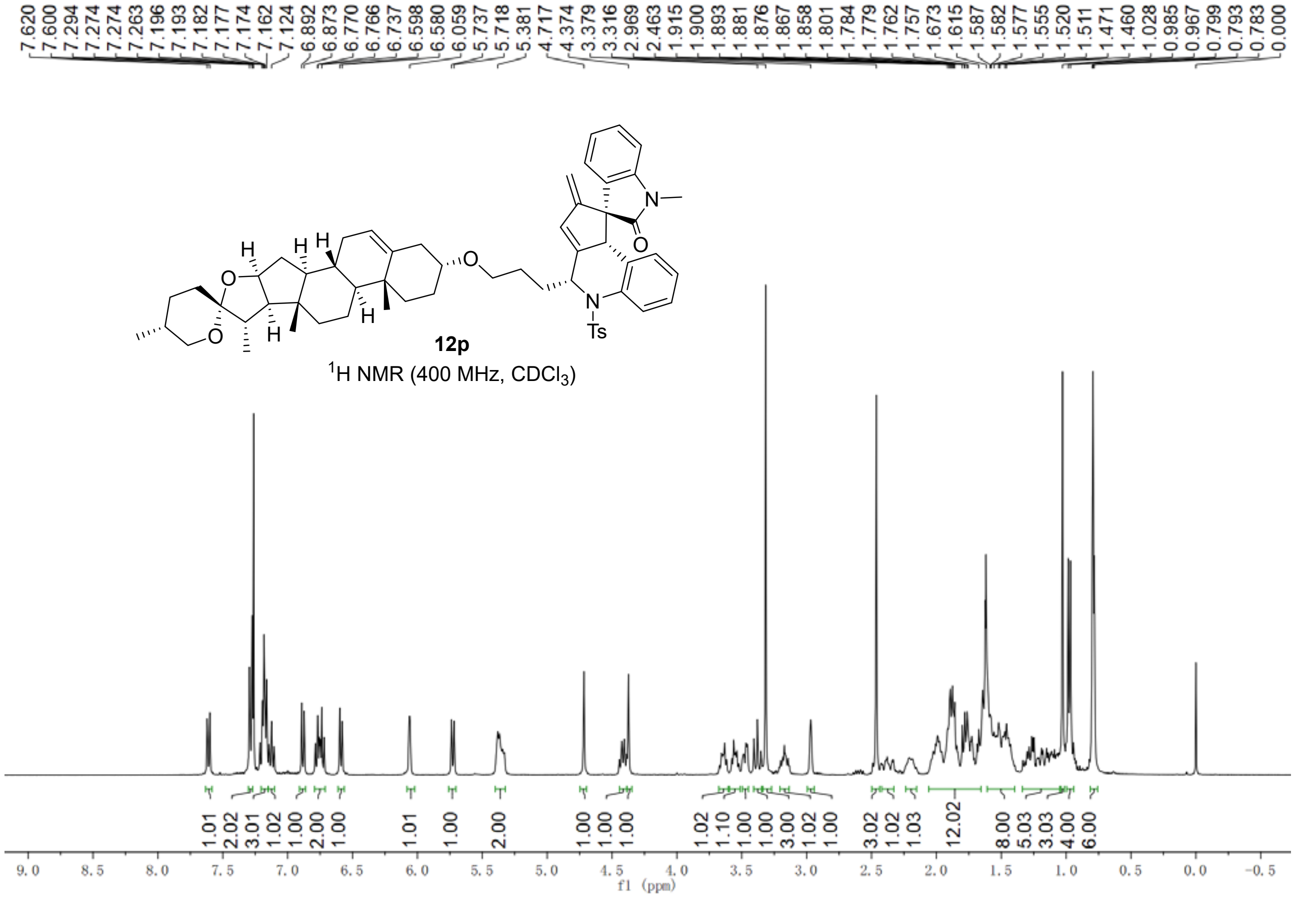
^{13}C NMR (100 MHz, CDCl$_3$)



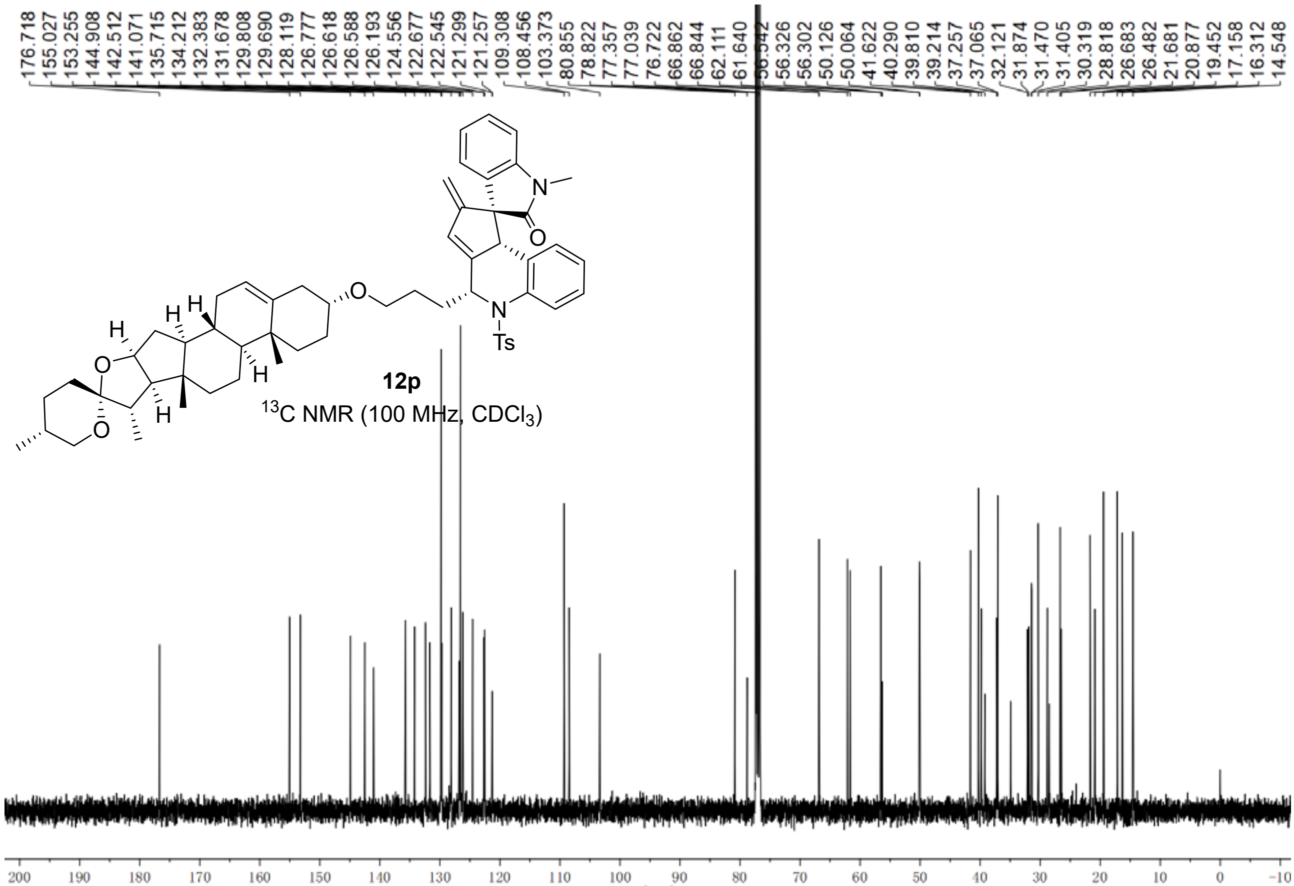
12o

(ESI-TOF) *m/z*: [M +Na]$^+$

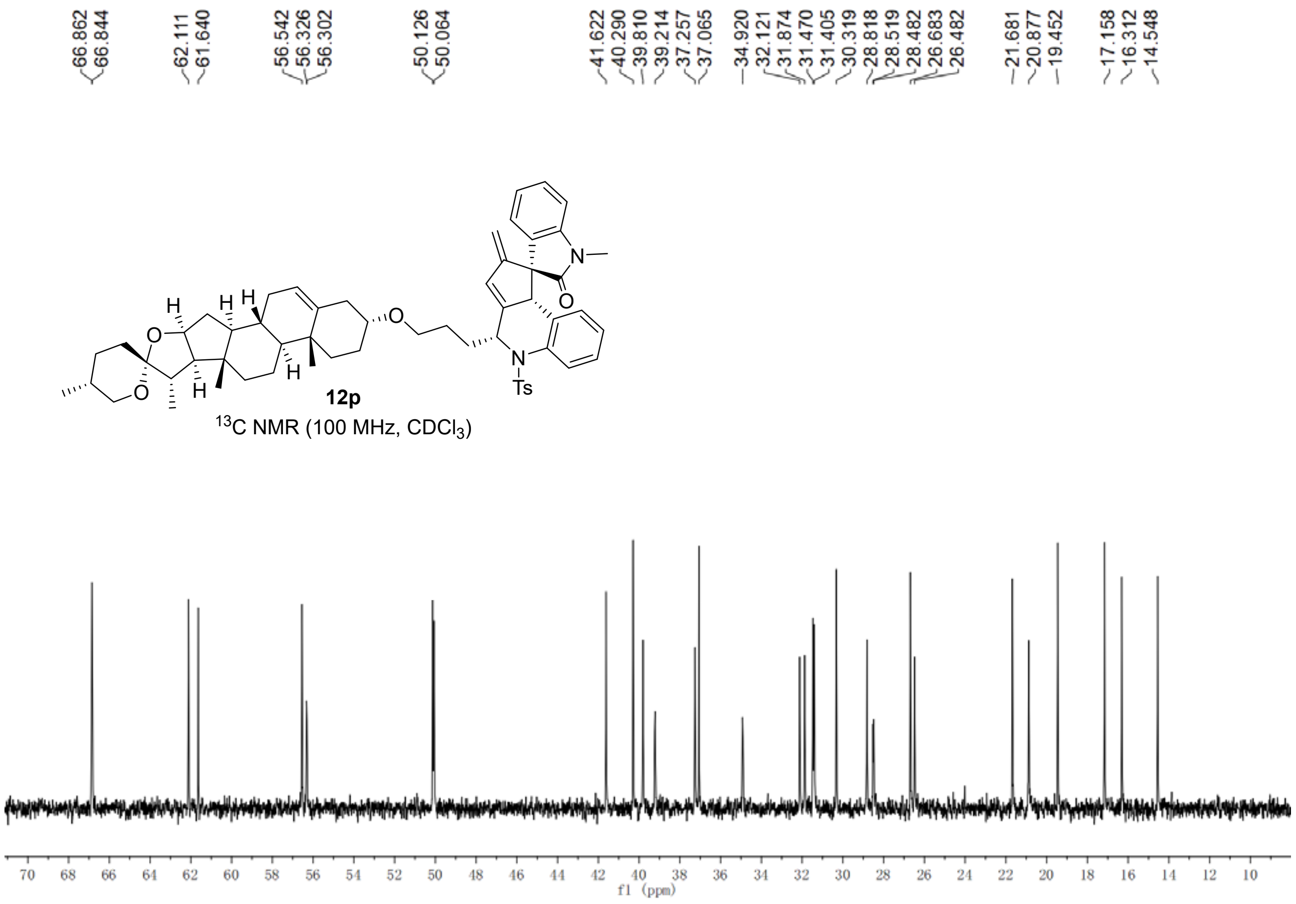
Calcd for $C_{58}H_{74}N_2O_4SNa^+$ 917.5262


12p

^{1}H NMR (400 MHz, CDCl$_3$)

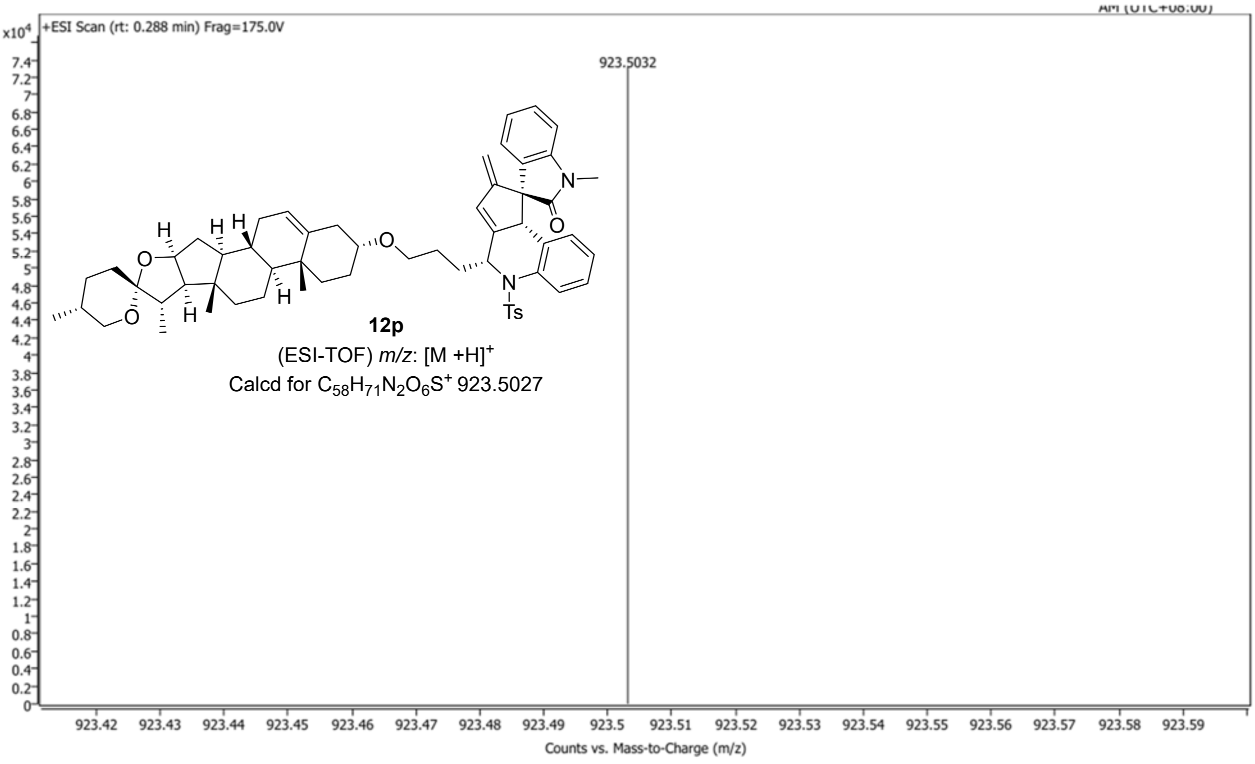

12p

^{13}C NMR (100 MHz, CDCl$_3$)



12p

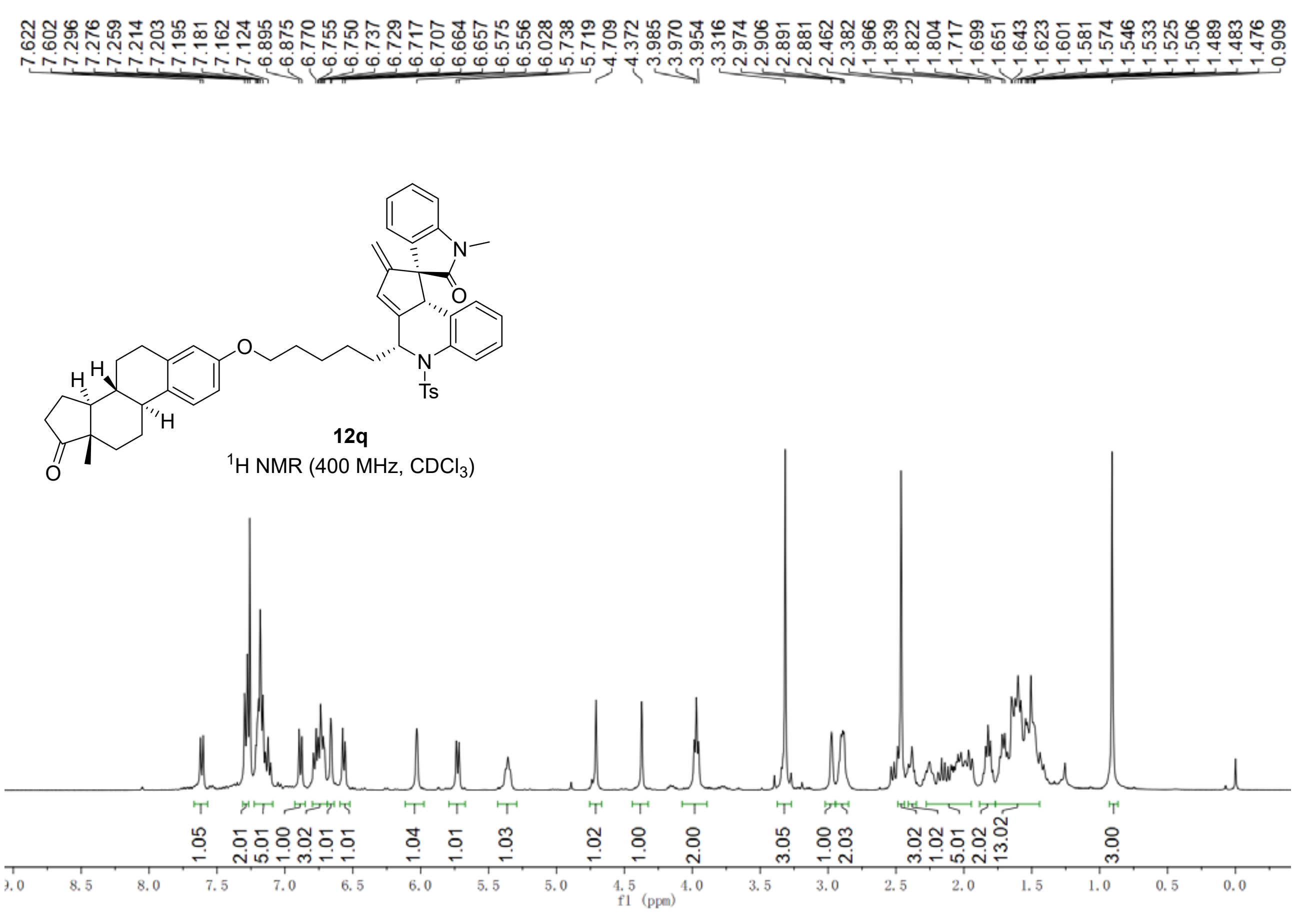
^{13}C NMR (100 MHz, CDCl$_3$)



12p

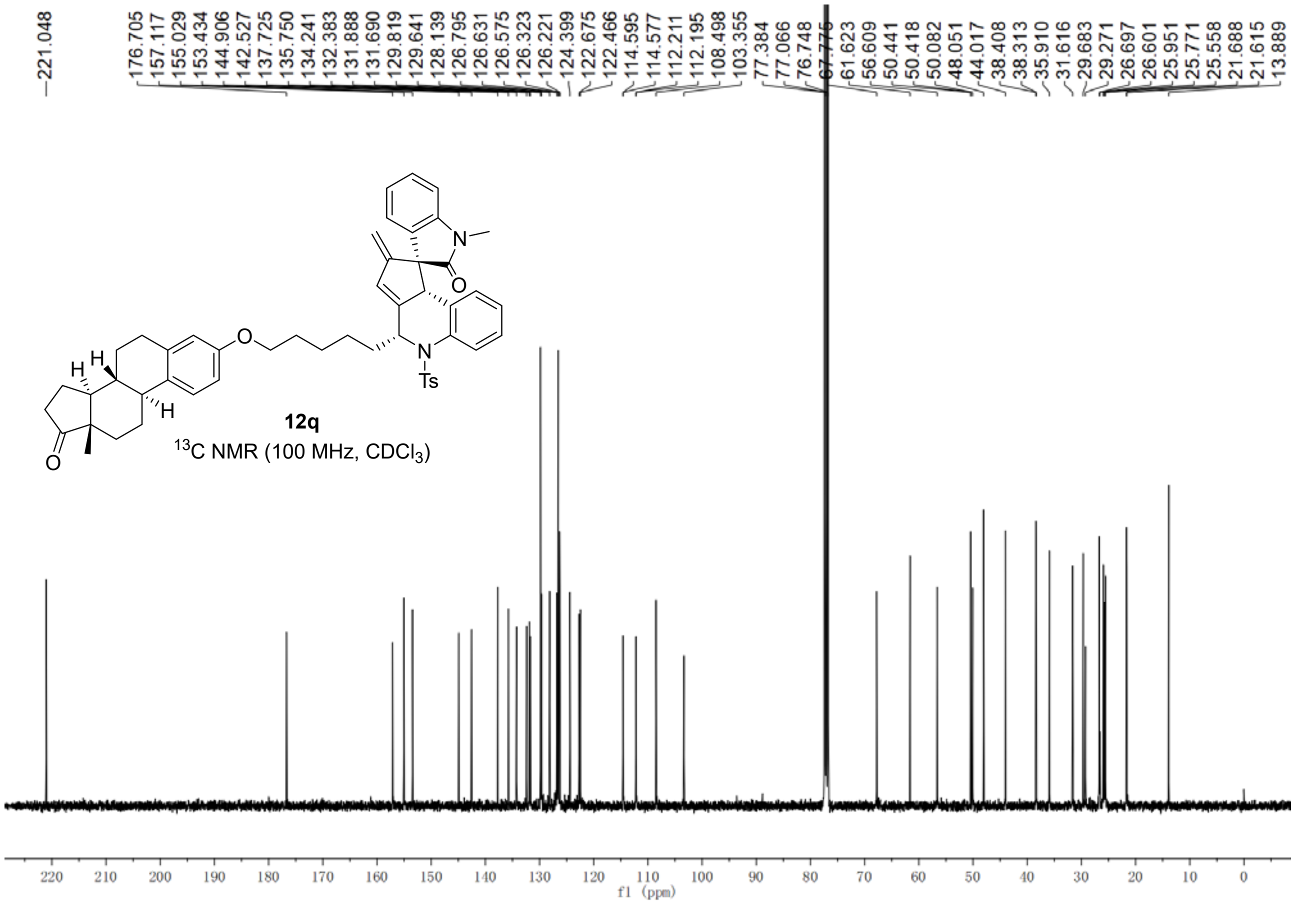
(ESI-TOF) *m/z*: [M +H]$^+$

Calcd for $C_{58}H_{71}N_2O_6S^+$ 923.5027



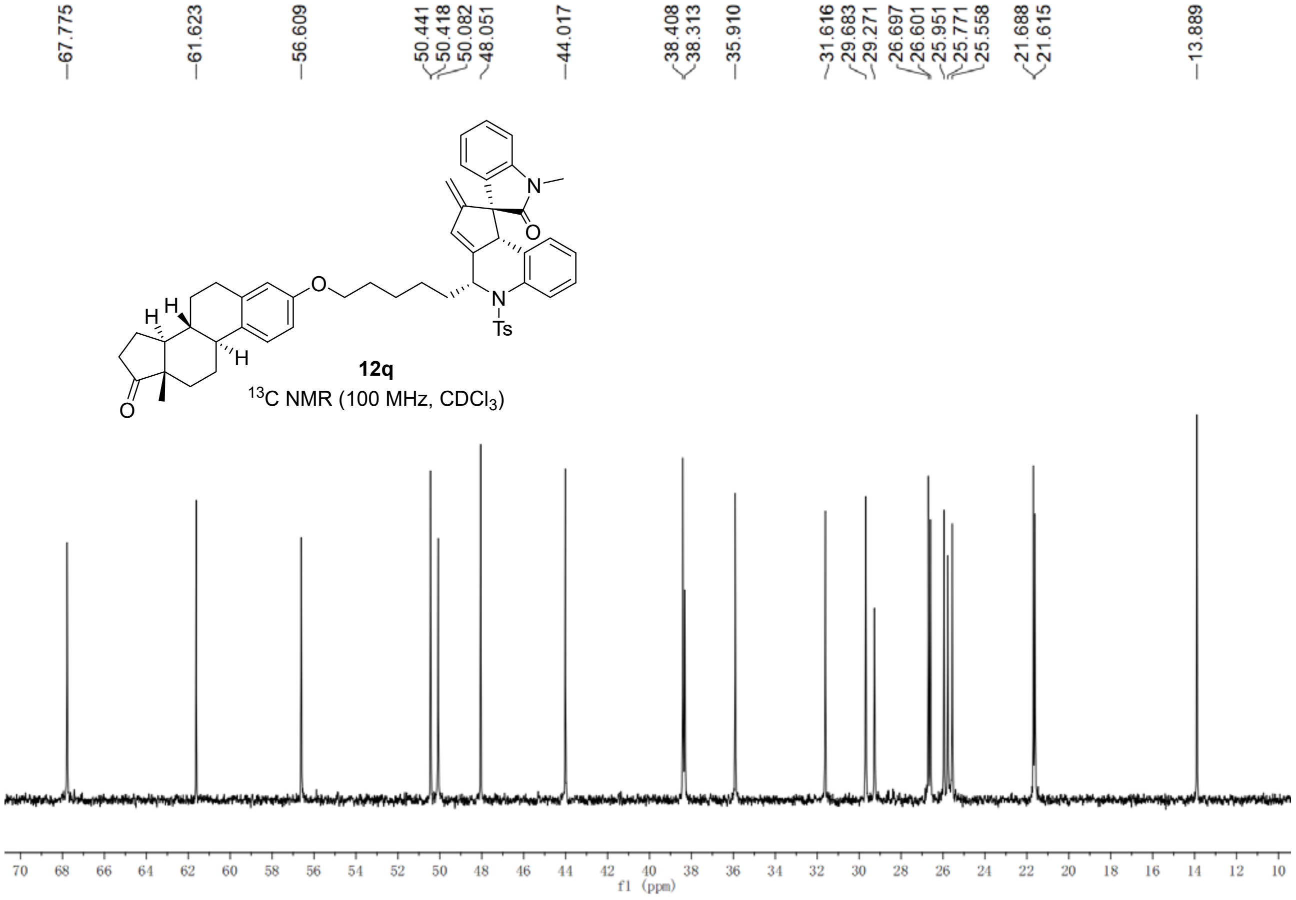
12q

^{1}H NMR (400 MHz, CDCl$_3$)



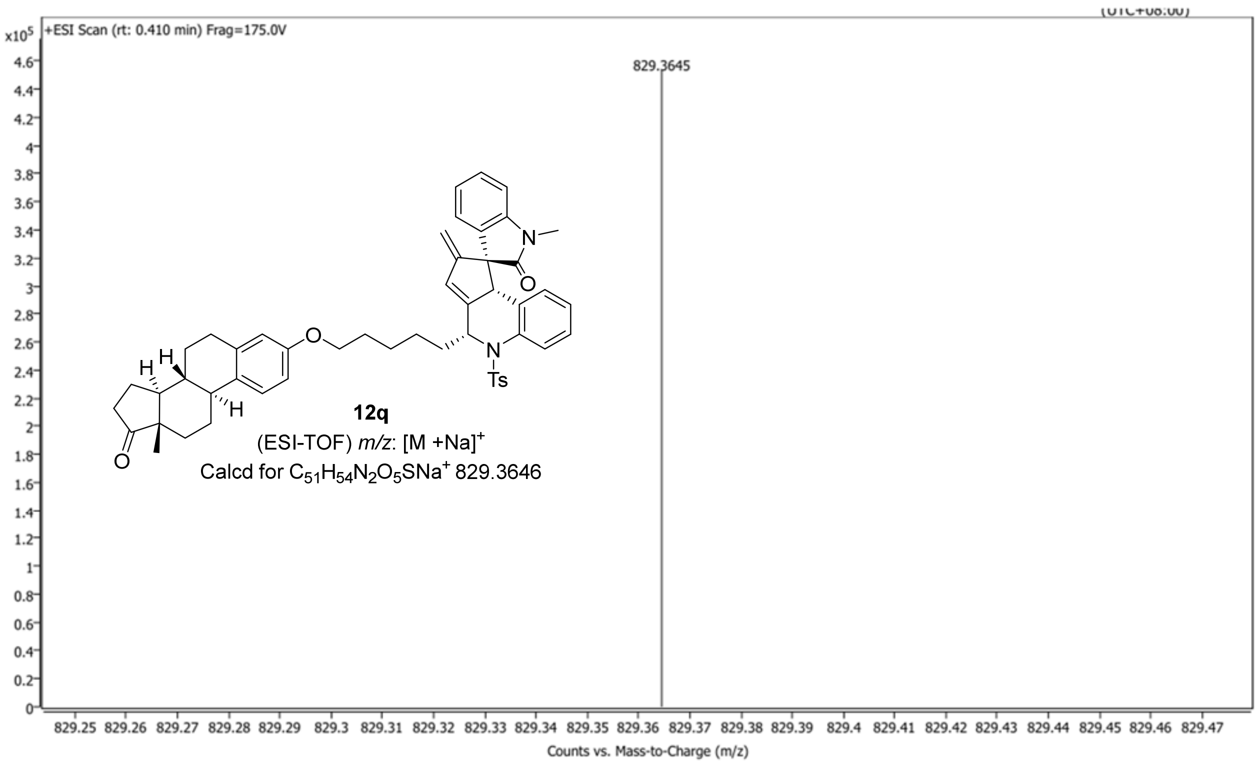
12q

^{13}C NMR (100 MHz, CDCl$_3$)



12q

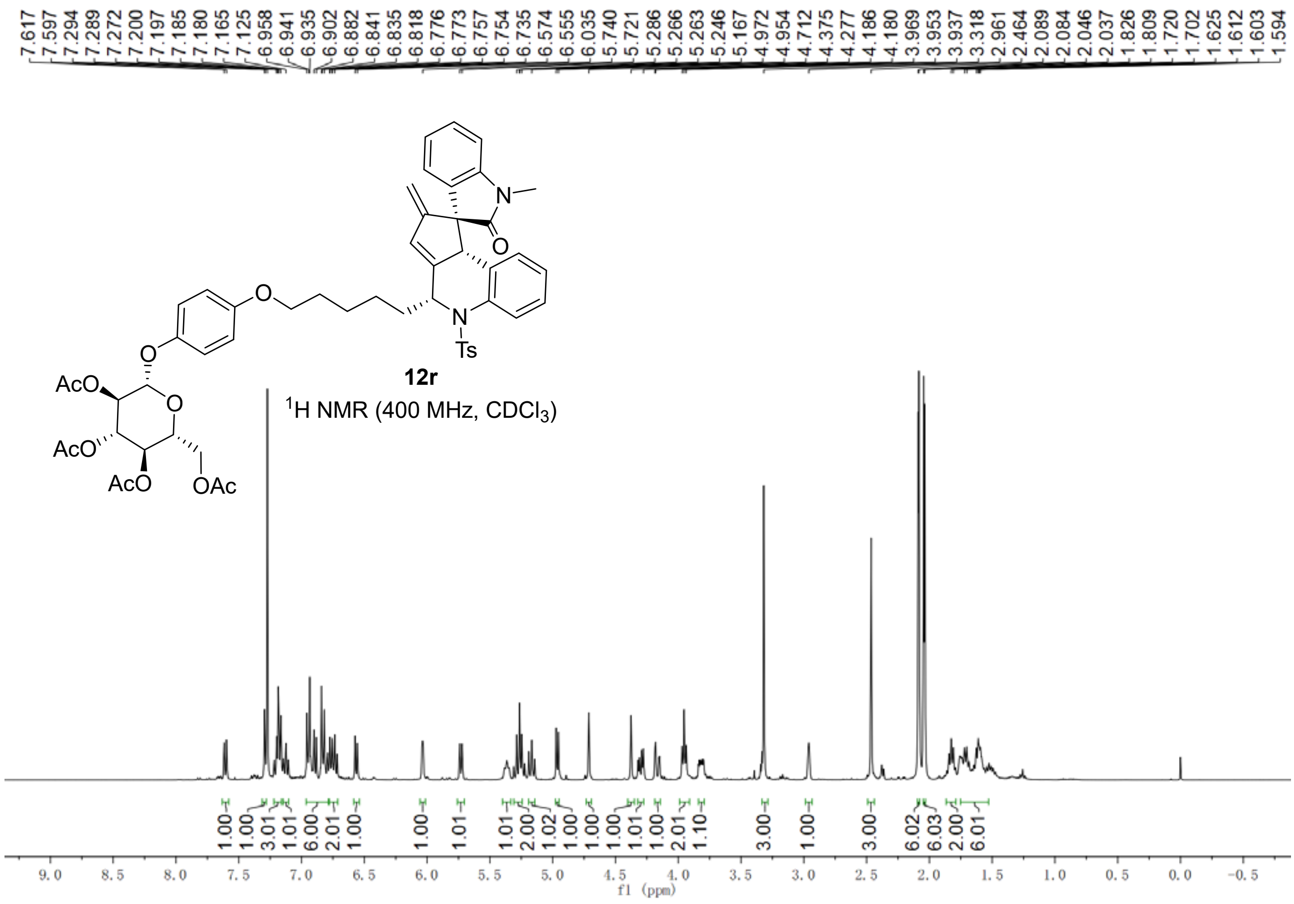
^{13}C NMR (100 MHz, $CDCl_3$)



12q

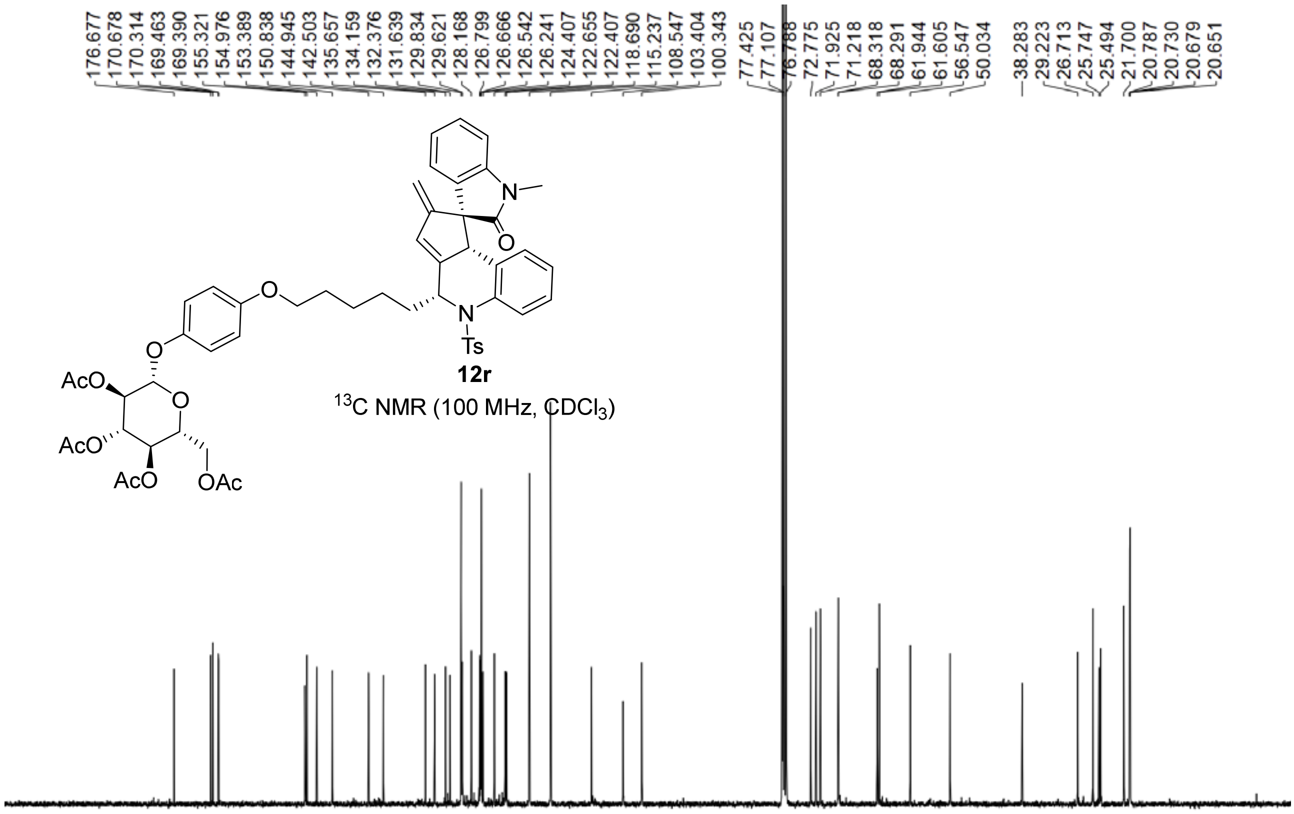
(ESI-TOF) *m/z*: $[M+Na]^+$

Calcd for $C_{51}H_{54}N_2O_5SNa^+$ 829.3646



12r

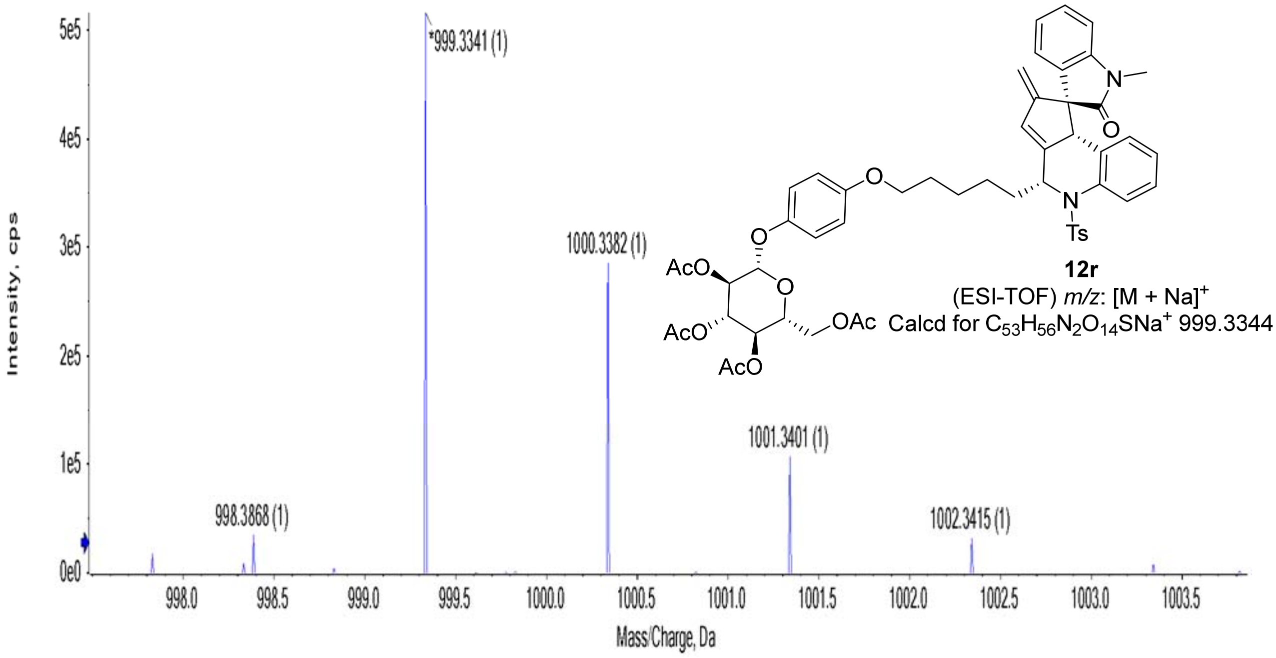
^{1}H NMR (400 MHz, CDCl$_3$)



12r

^{13}C NMR (100 MHz, CDCl$_3$)

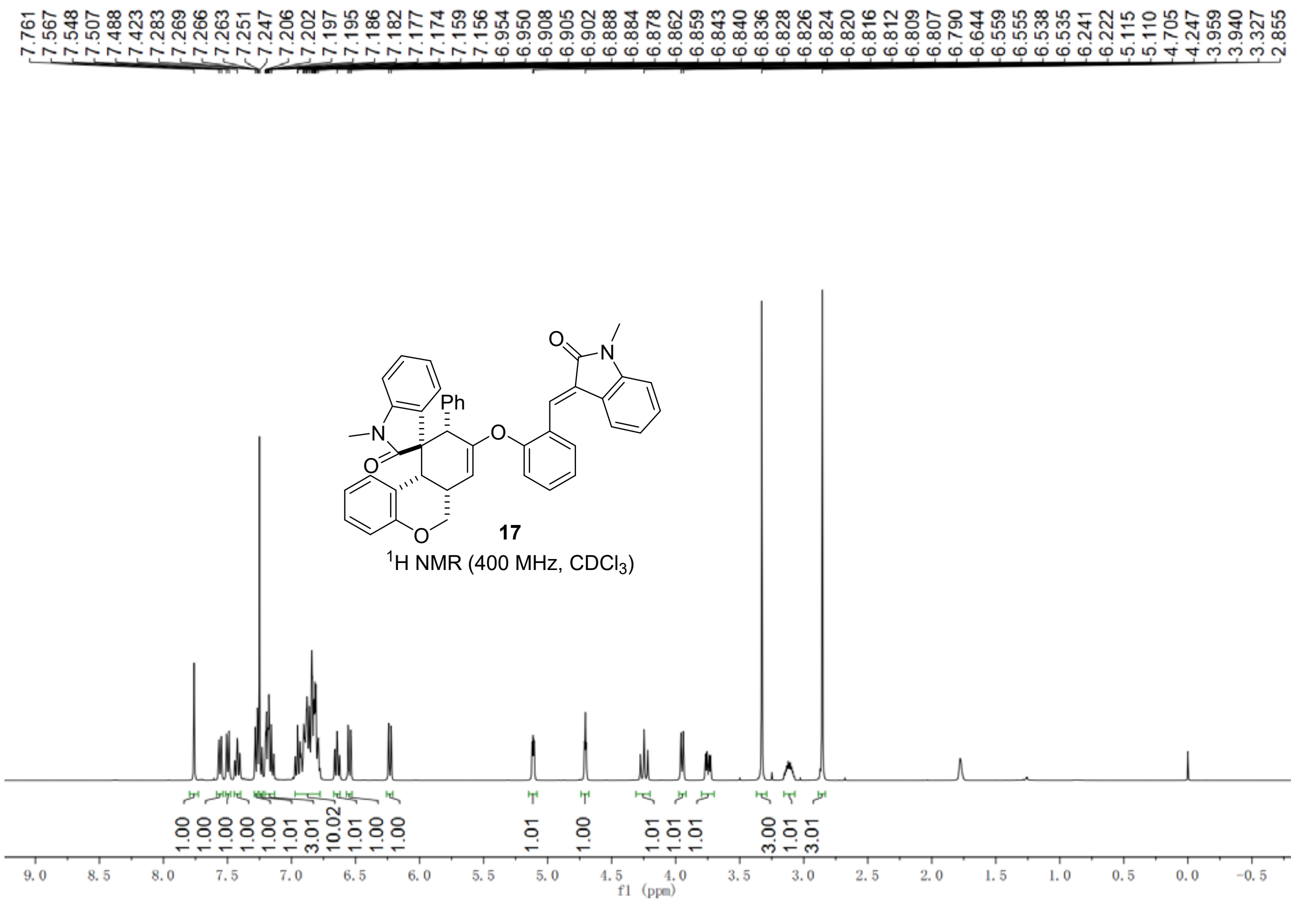
Spectrum from 20240817.wiff2 (sample 10) - 6, +TOF MS (800 - 1100) from 0.037 to 0.086 min, noise filtere... 1.154 to 1.354 min, noise filtered (noise multiplier = 1.5), Gaussian smoothed (0.5 points)], centroided



12r

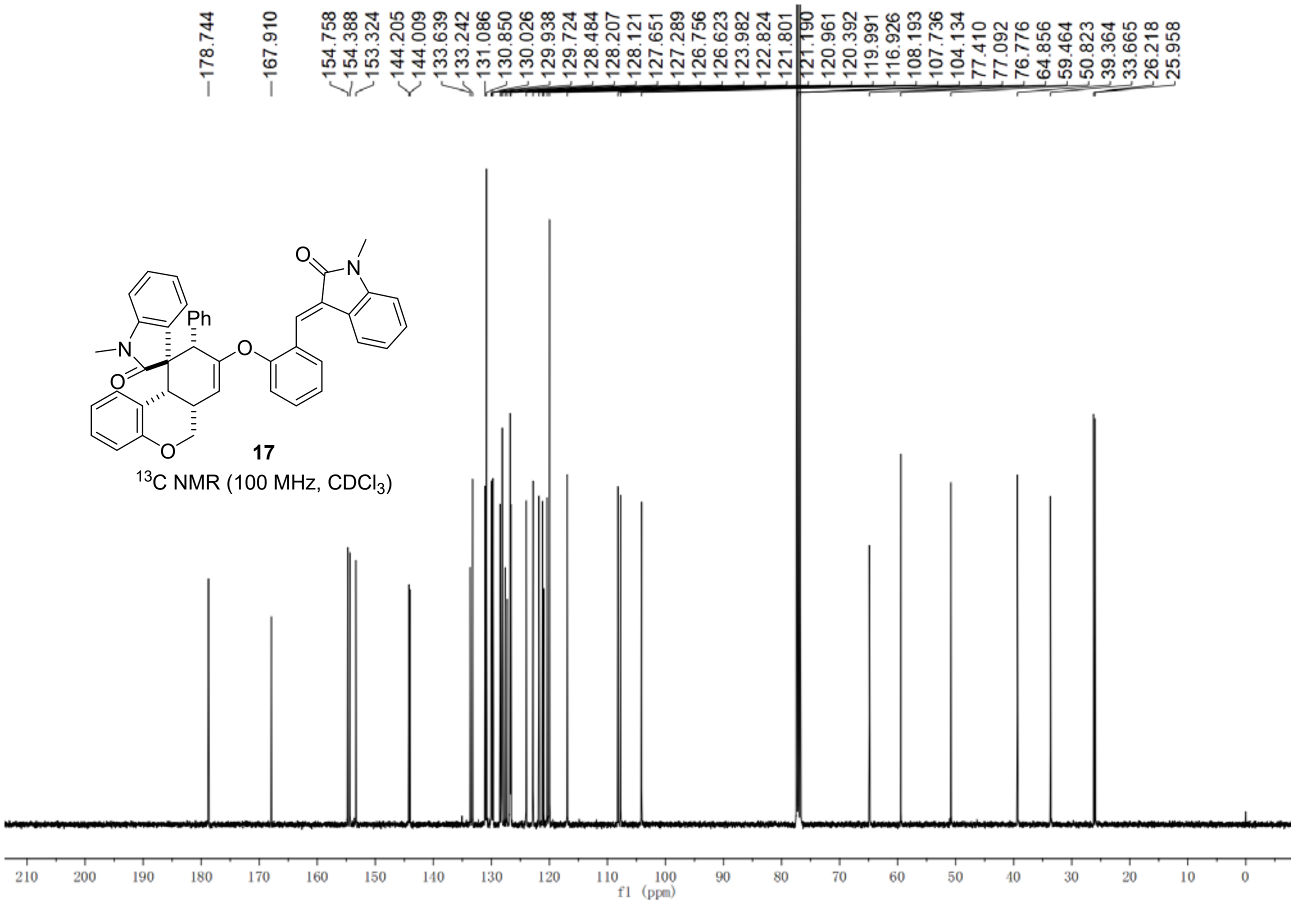
(ESI-TOF) *m/z*: [M + Na]$^+$

Calcd for $C_{53}H_{56}N_2O_{14}SNa^+$ 999.3344



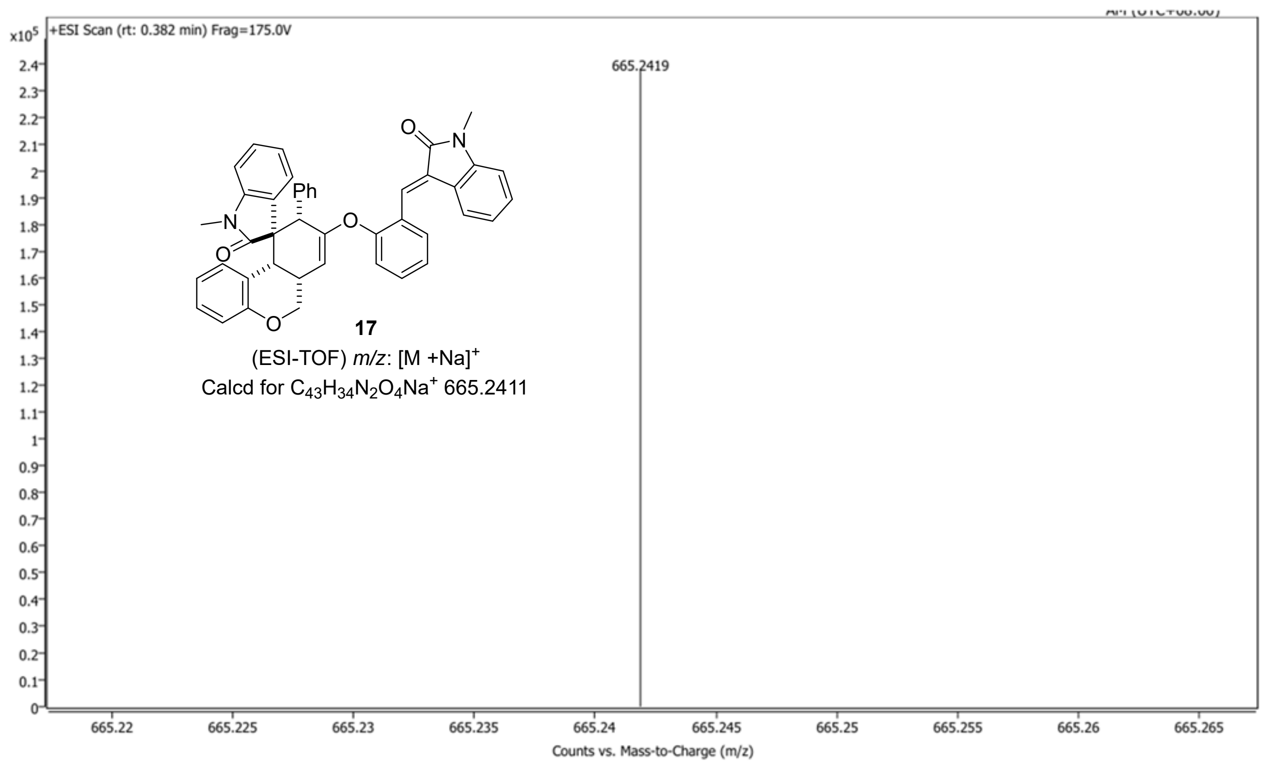
17

^{1}H NMR (400 MHz, $CDCl_3$)



17

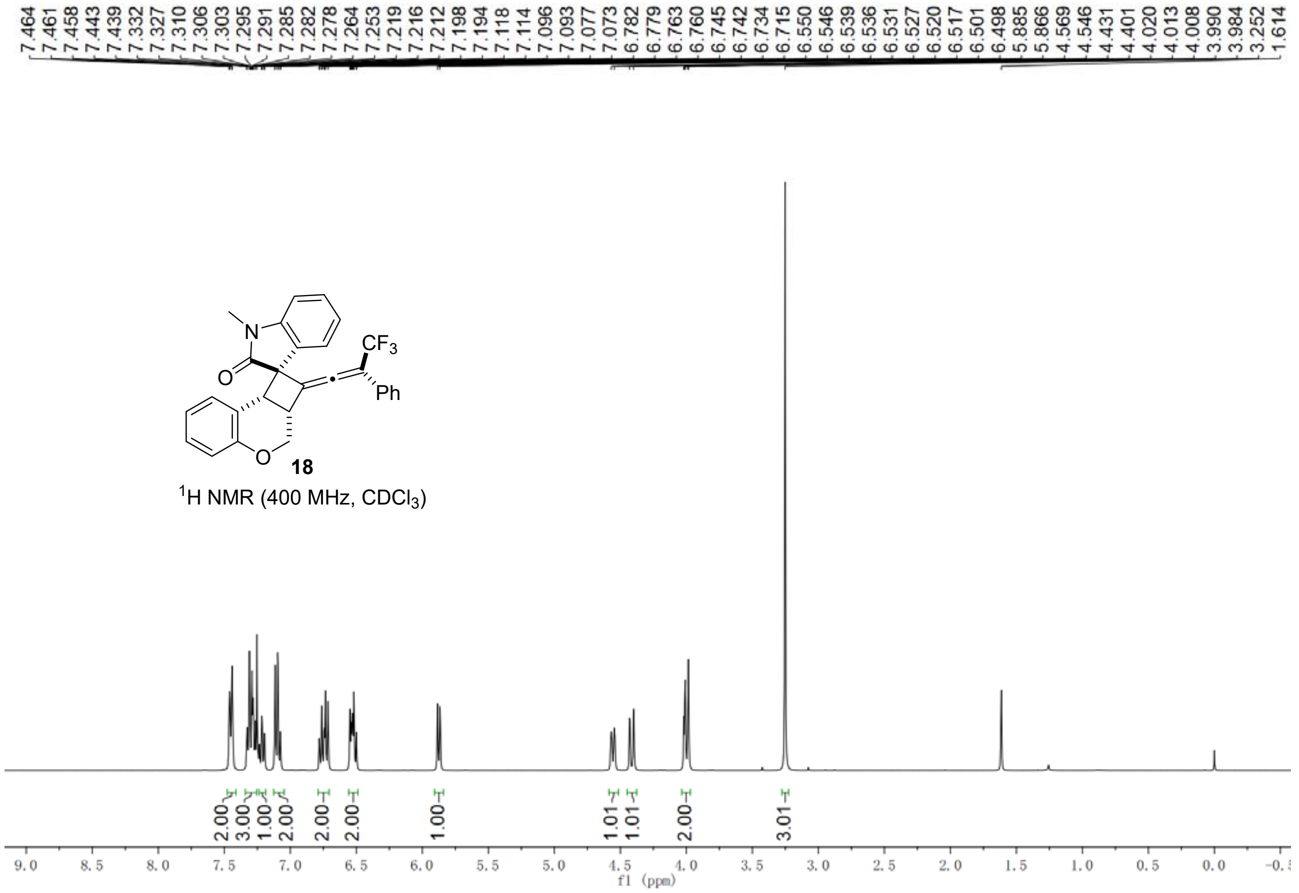
^{13}C NMR (100 MHz, $CDCl_3$)

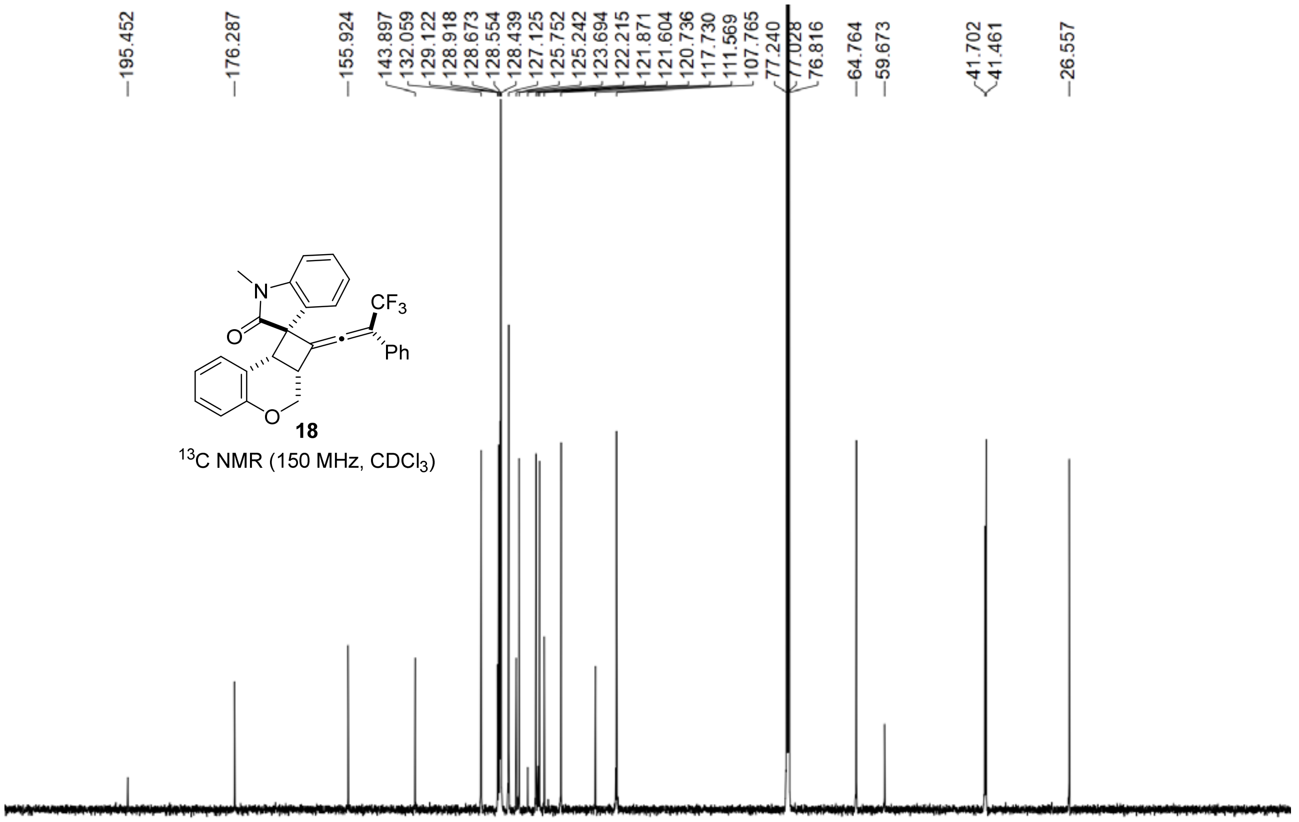


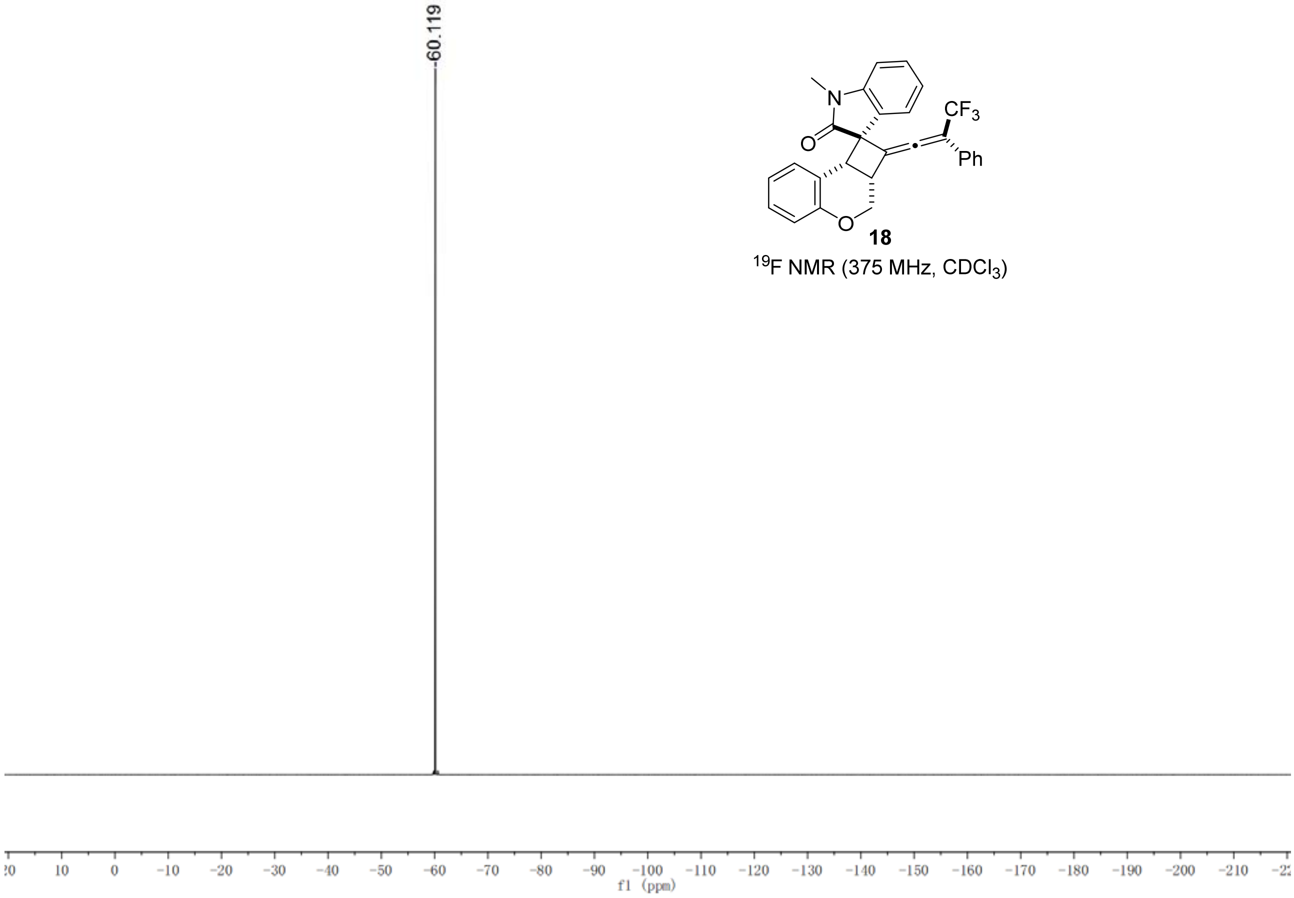
17

(ESI-TOF) *m/z*: [M +Na]$^+$

Calcd for $C_{43}H_{34}N_2O_4Na^+$ 665.2411

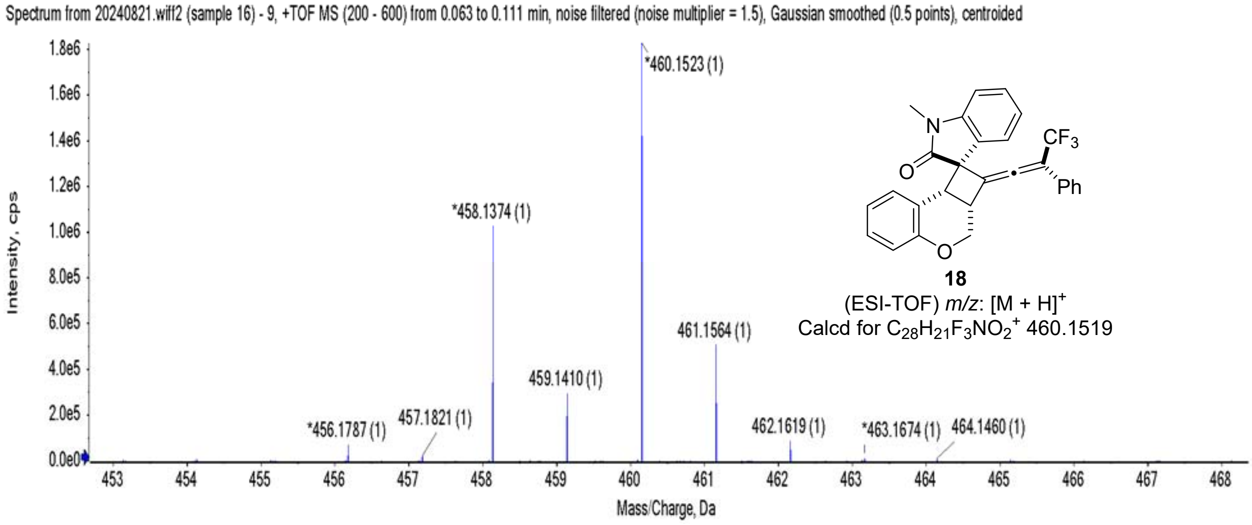

7.464
7.461
7.458
7.443
7.439
7.332
7.327
7.310
7.306
7.303
7.295
7.291
7.285
7.282
7.278
7.264
7.253
7.219
7.216
7.212
7.198
7.194
7.118
7.114
7.096
7.093
7.077
7.073
6.782
6.779
6.763
6.760
6.745
6.742
6.734
6.715
6.550
6.546
6.539
6.536
6.531
6.527
6.520
6.517
6.501
6.498
5.885
5.866
4.569
4.546
4.431
4.401
4.020
4.013
4.008
3.990
3.984
3.252
1.614
N
O
CF3
Ph
O
18
1H NMR (400 MHz, CDCl3)
2.00
3.00
1.00
2.00
2.00
2.00
1.00
1.01
1.01
2.00
3.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


195.452
176.287
155.924
143.897
132.059
129.122
128.918
128.673
128.554
128.439
127.125
125.752
125.242
123.694
122.215
121.871
121.604
120.736
117.730
111.569
107.765
77.240
77.028
76.816
64.764
59.673
41.702
41.461
26.557
N
O
CF3
Ph
O
18
13C NMR (150 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



18

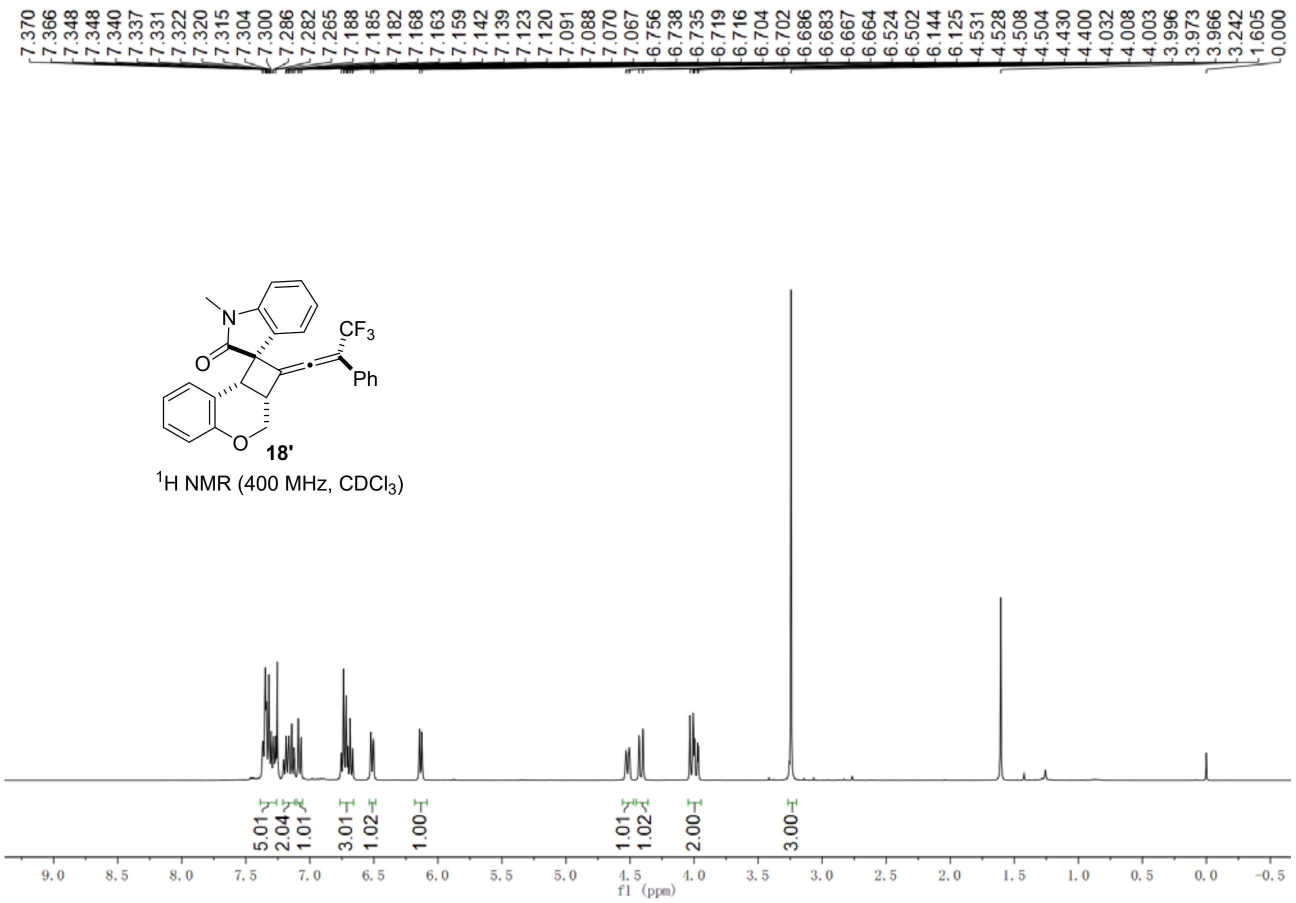
^{19}F NMR (375 MHz, $CDCl_3$)



18

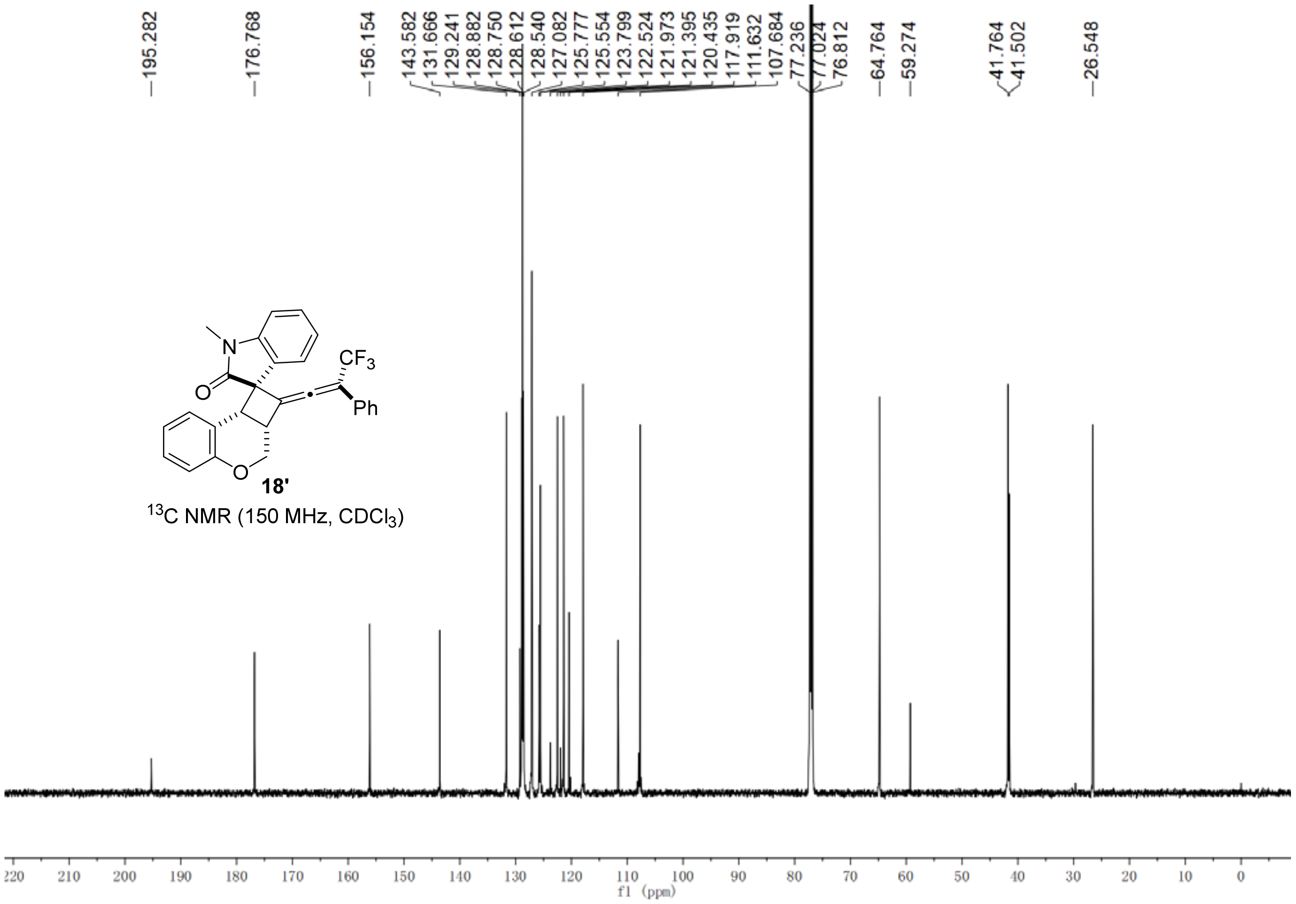
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{28}H_{21}F_3NO_2^+$ 460.1519



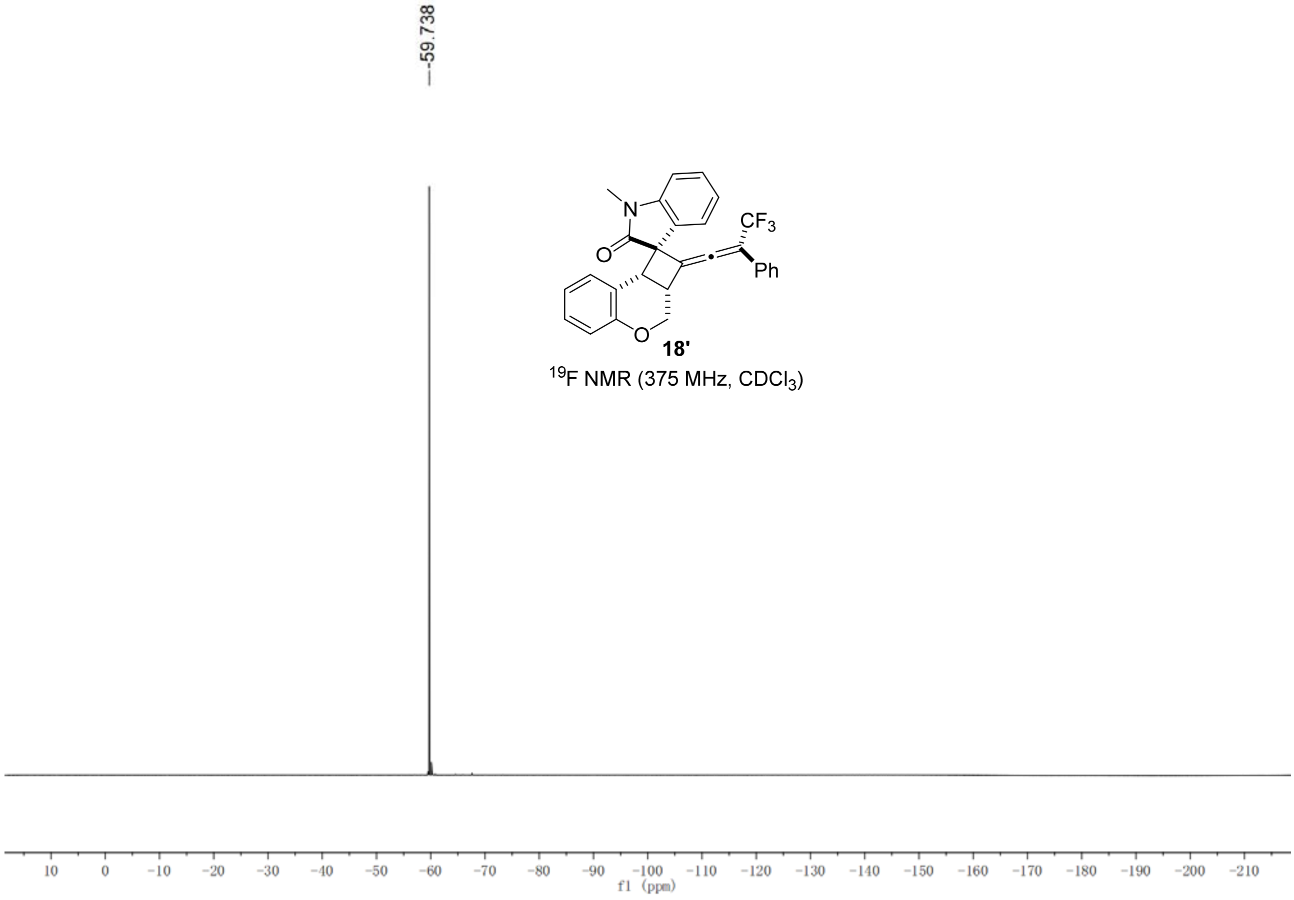
18'

^{1}H NMR (400 MHz, CDCl$_3$)



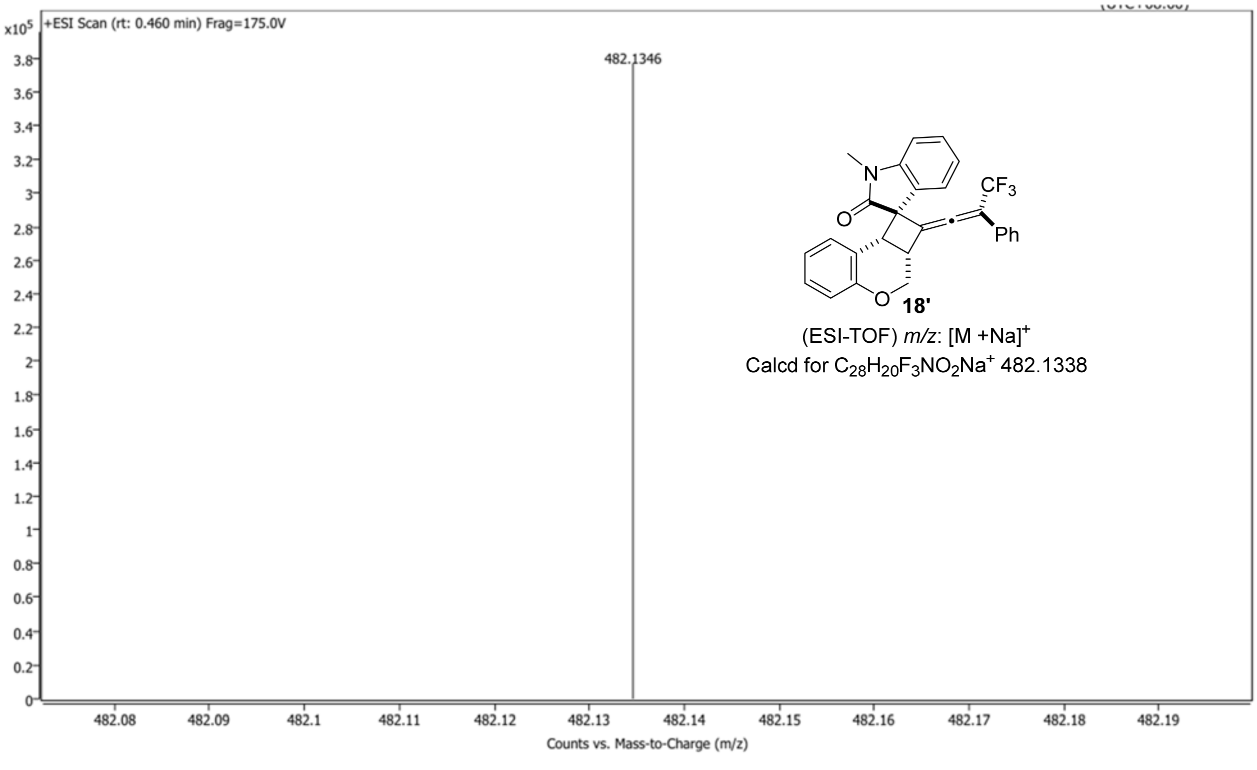
18'

^{13}C NMR (150 MHz, CDCl$_3$)



18'

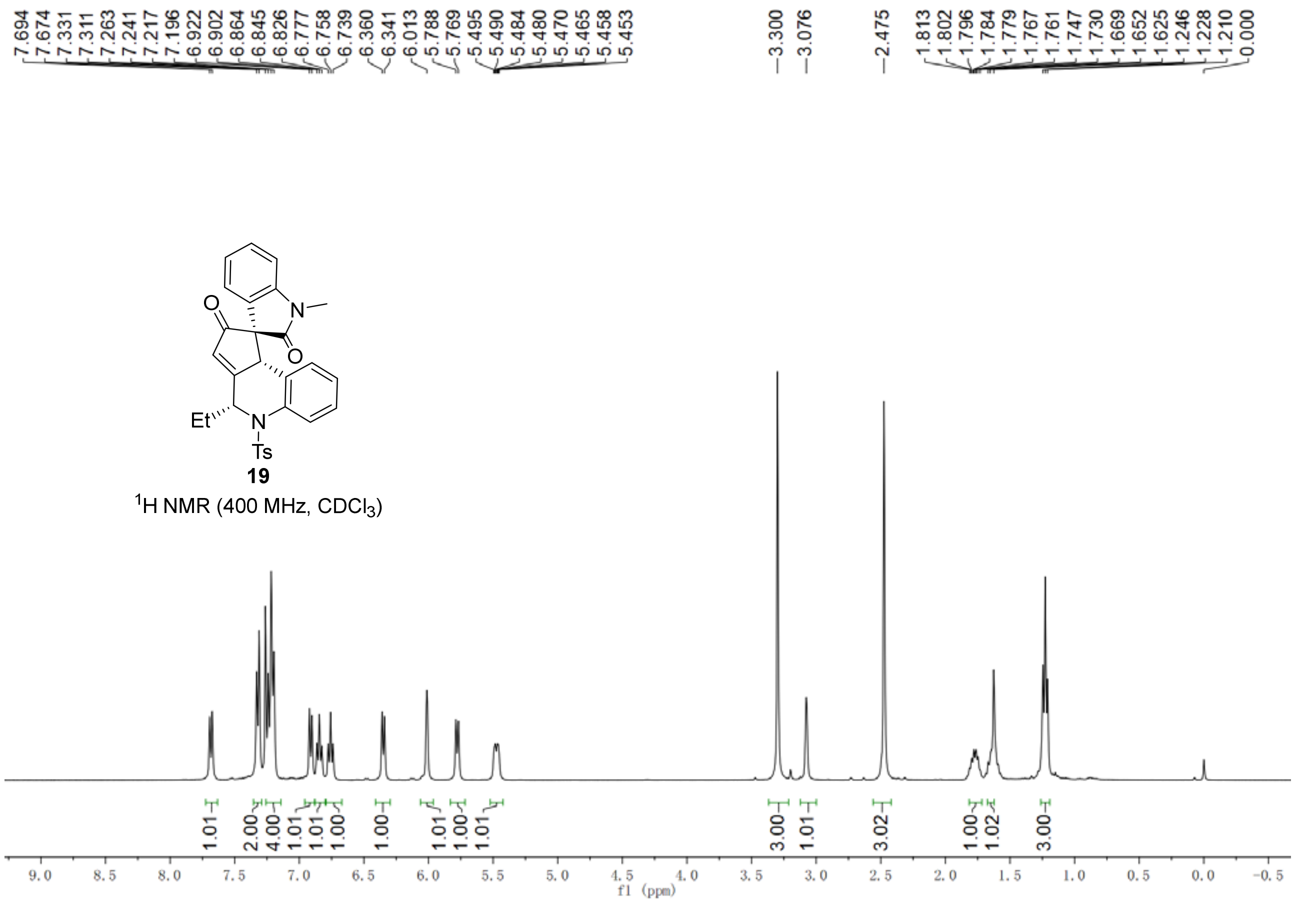
^{19}F NMR (375 MHz, CDCl$_3$)



18'

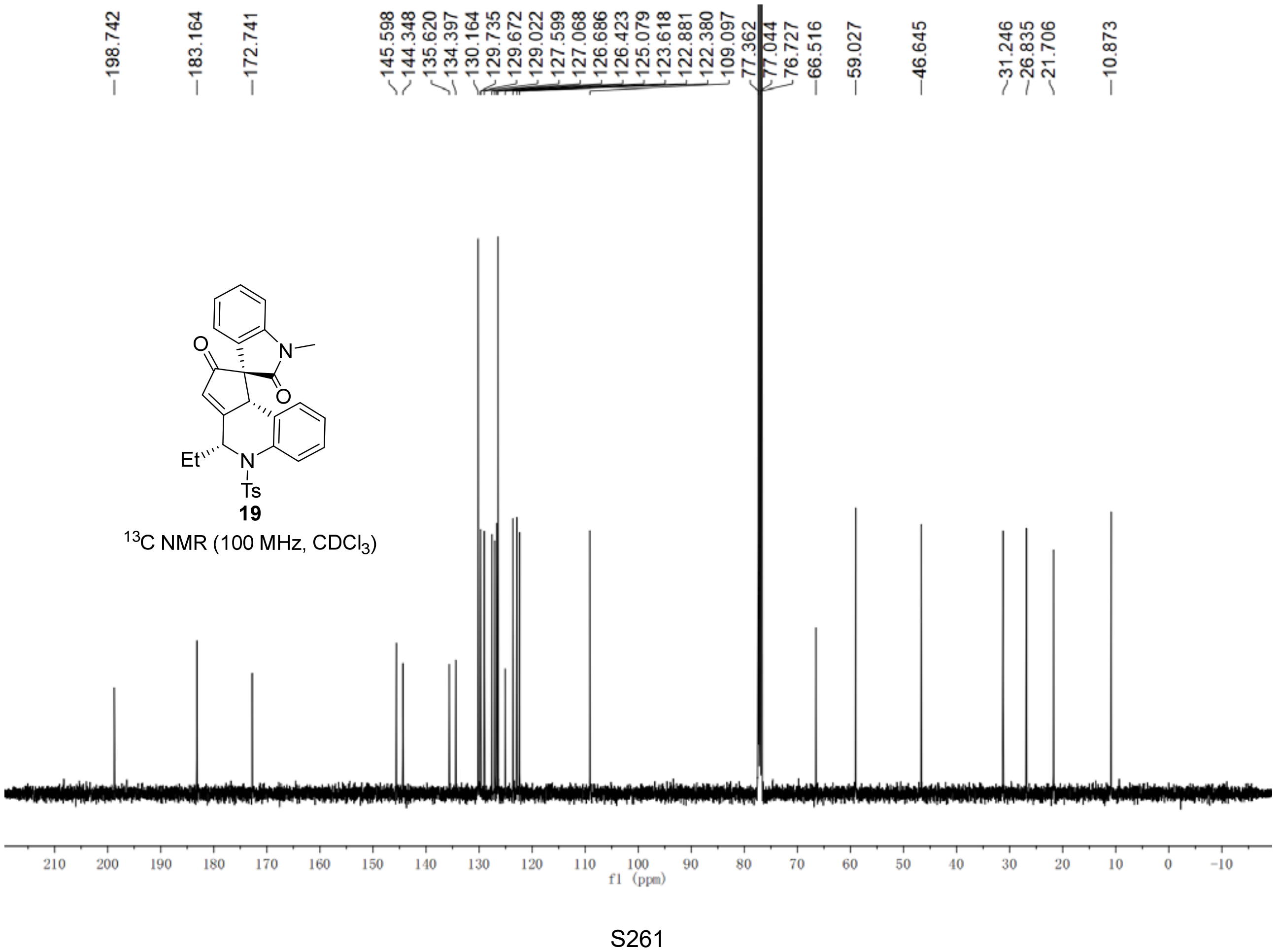
(ESI-TOF) *m/z*: [M +Na]$^+$

Calcd for $C_{28}H_{20}F_3NO_2Na^+$ 482.1338



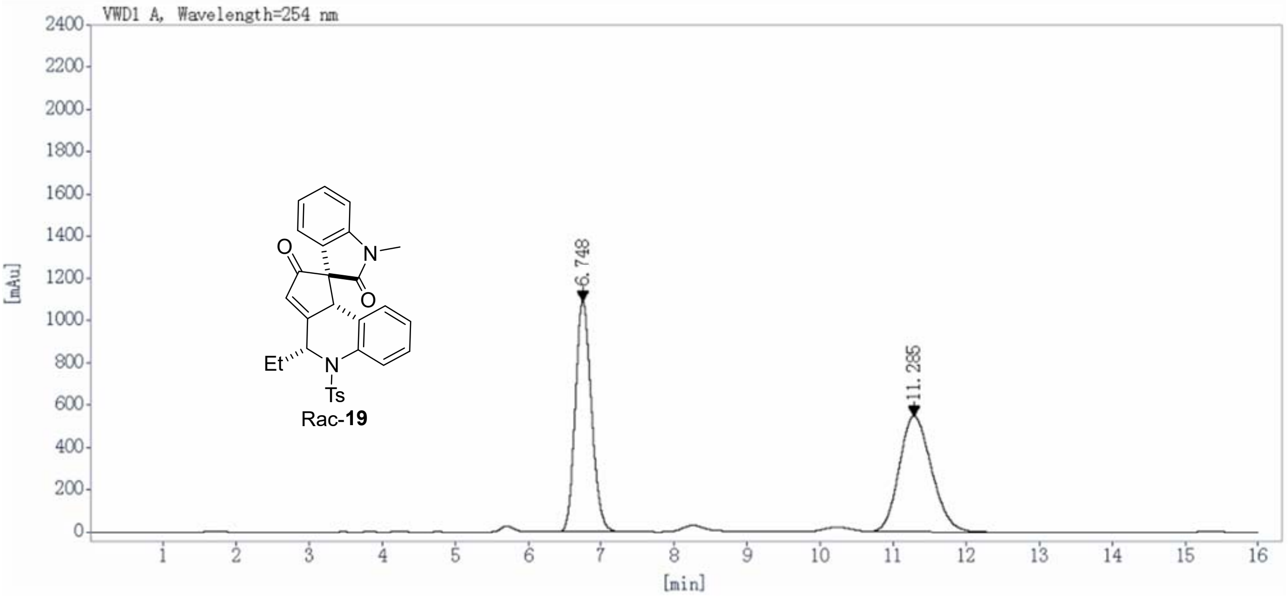
19

^{1}H NMR (400 MHz, CDCl$_3$)

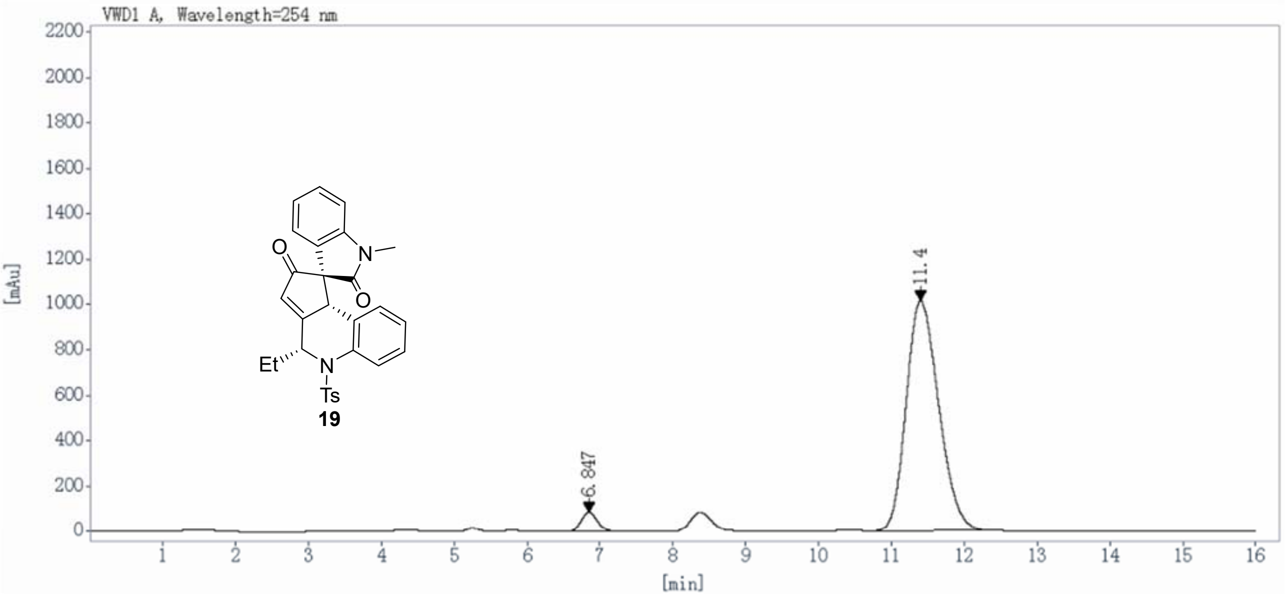


19

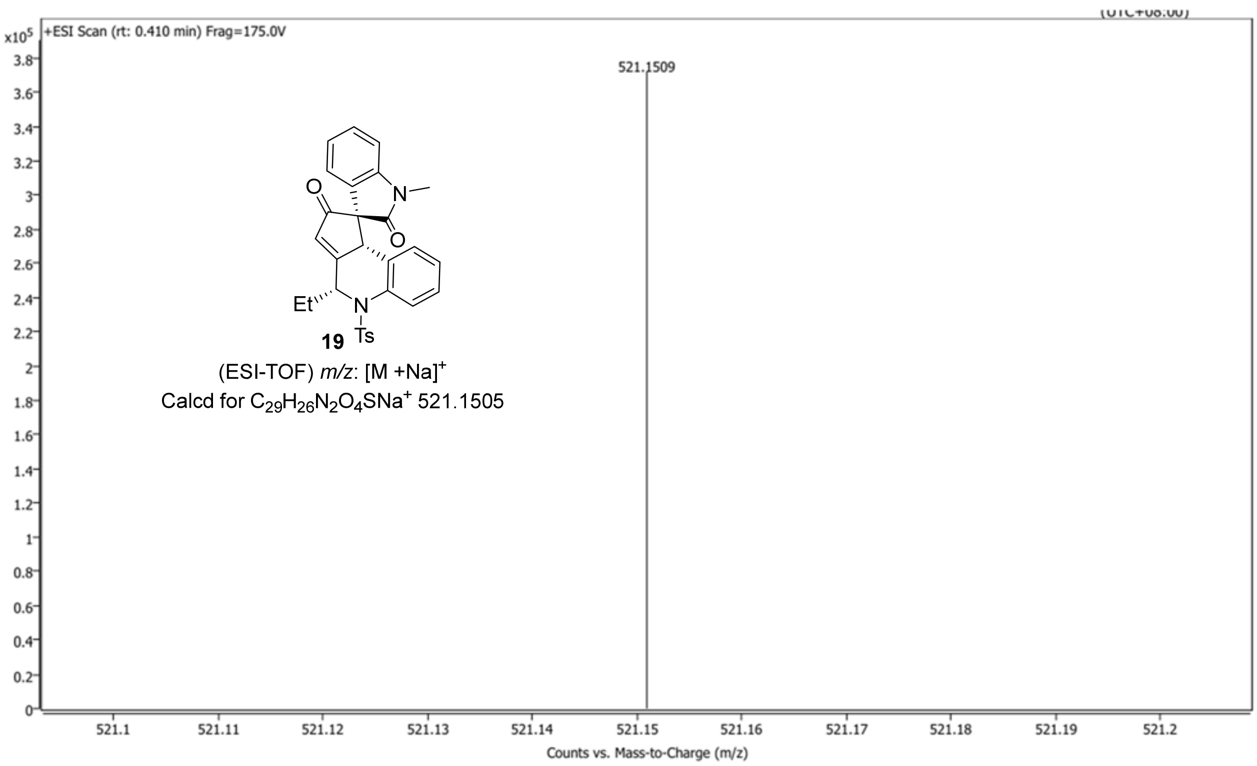
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.748	BBA	0.24	1091.5602	16755.7148	50.0150
11.285	BBA	0.48	545.9031	16745.6582	49.9850
			Totals:	33501.3730	100.0000



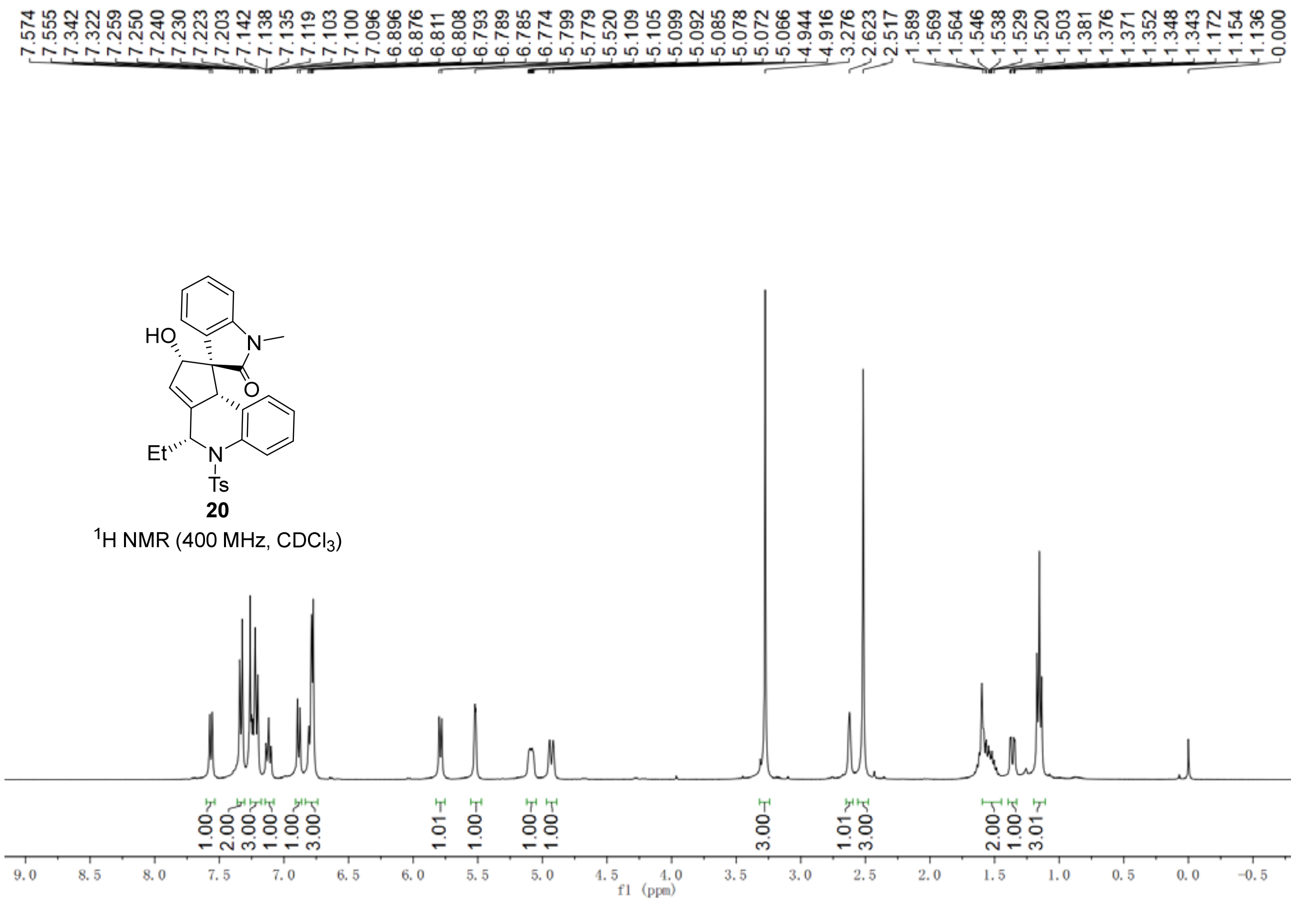
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.847	BBA	0.24	85.6540	1293.7821	3.9508
11.400	BBA	0.48	1013.0538	31453.7012	96.0492
			Totals:	32747.4833	100.0000



19

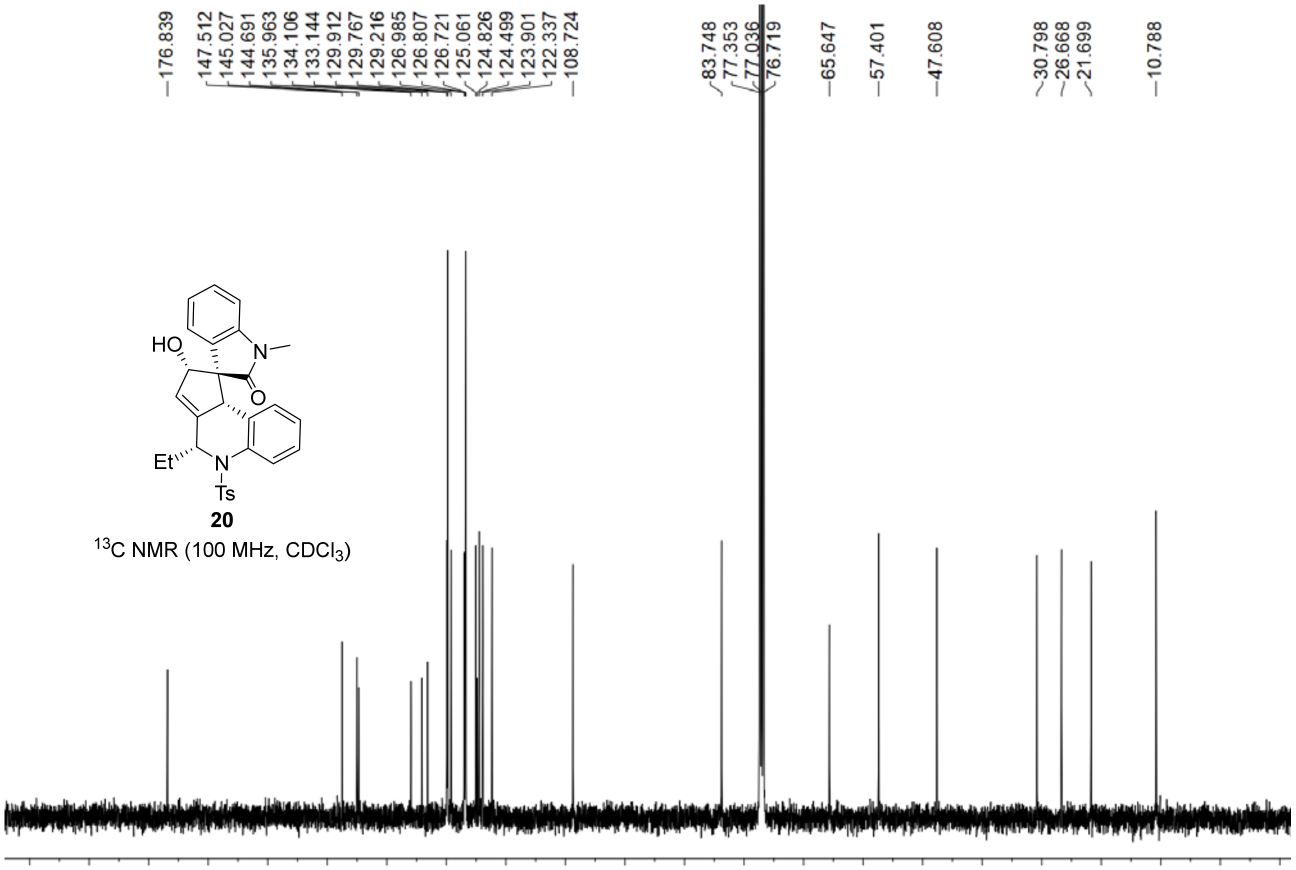
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{29}H_{26}N_2O_4SNa^+$ 521.1505



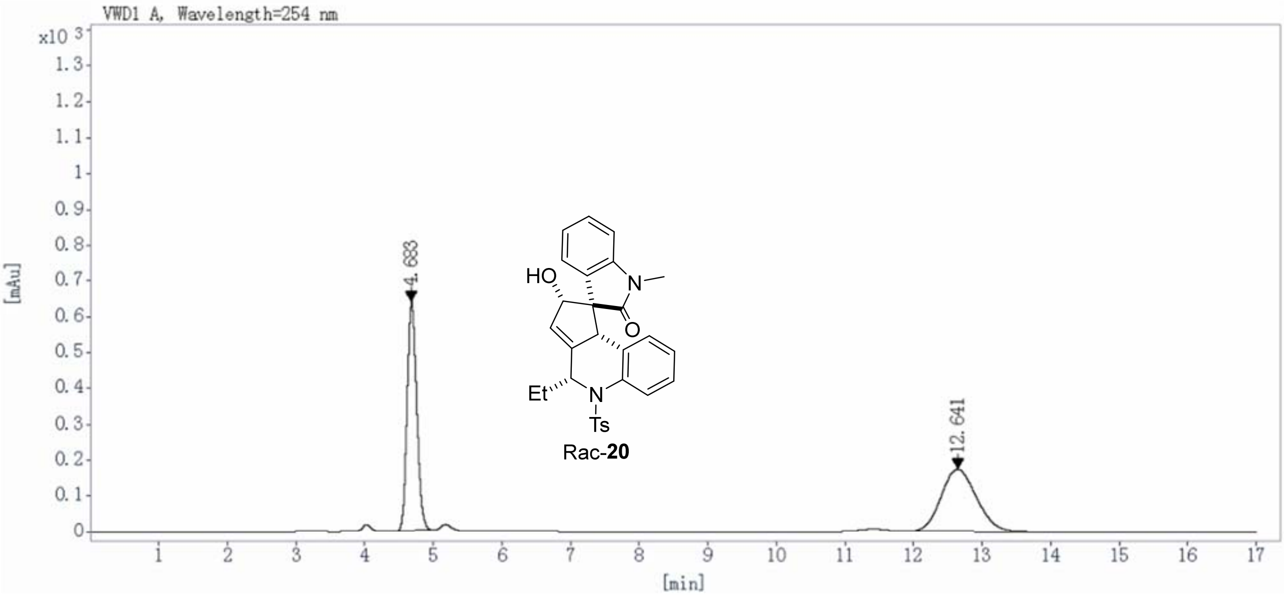
20

^{1}H NMR (400 MHz, CDCl$_3$)

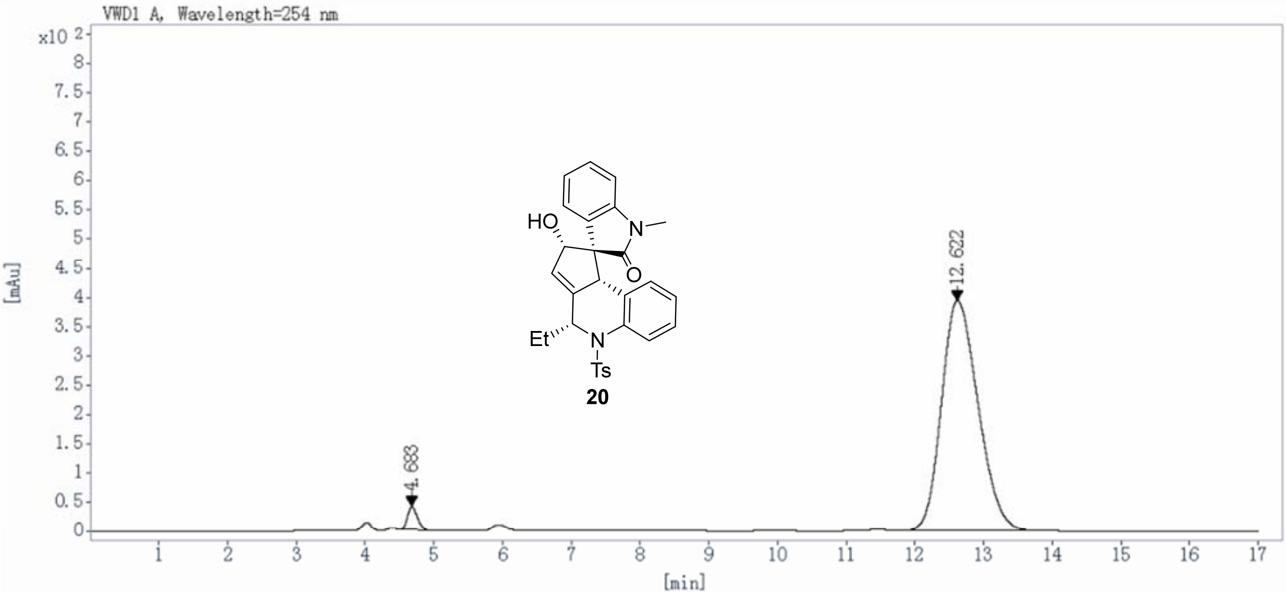


20

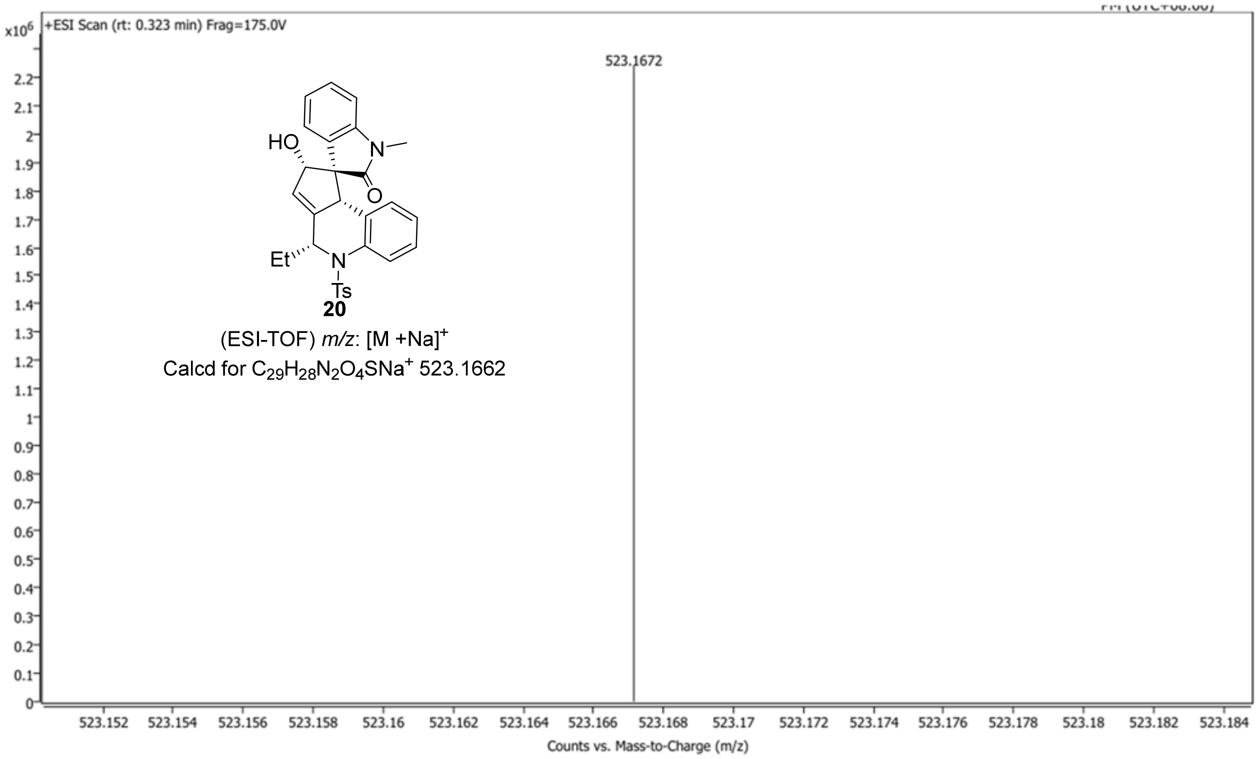
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.683	BBA	0.15	641.1805	6237.6953	49.9388
12.641	BB	0.56	174.5945	6252.9819	50.0612
			Totals:	12490.6772	100.0000



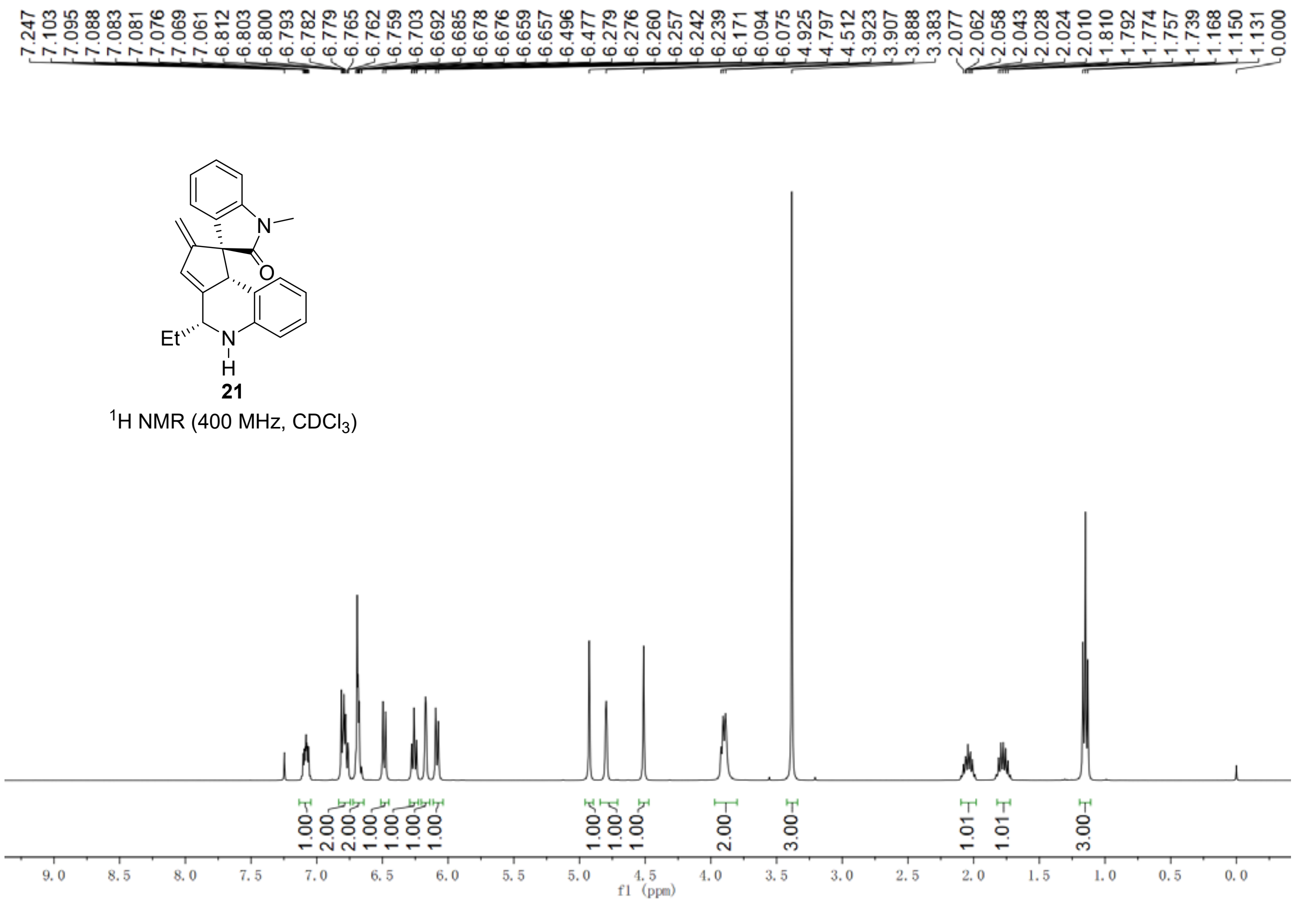
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
4.683	BB	0.15	39.5163	392.4263	2.6313
12.622	BBA	0.58	393.7119	14521.3232	97.3687
			Totals:	14913.7496	100.0000



20

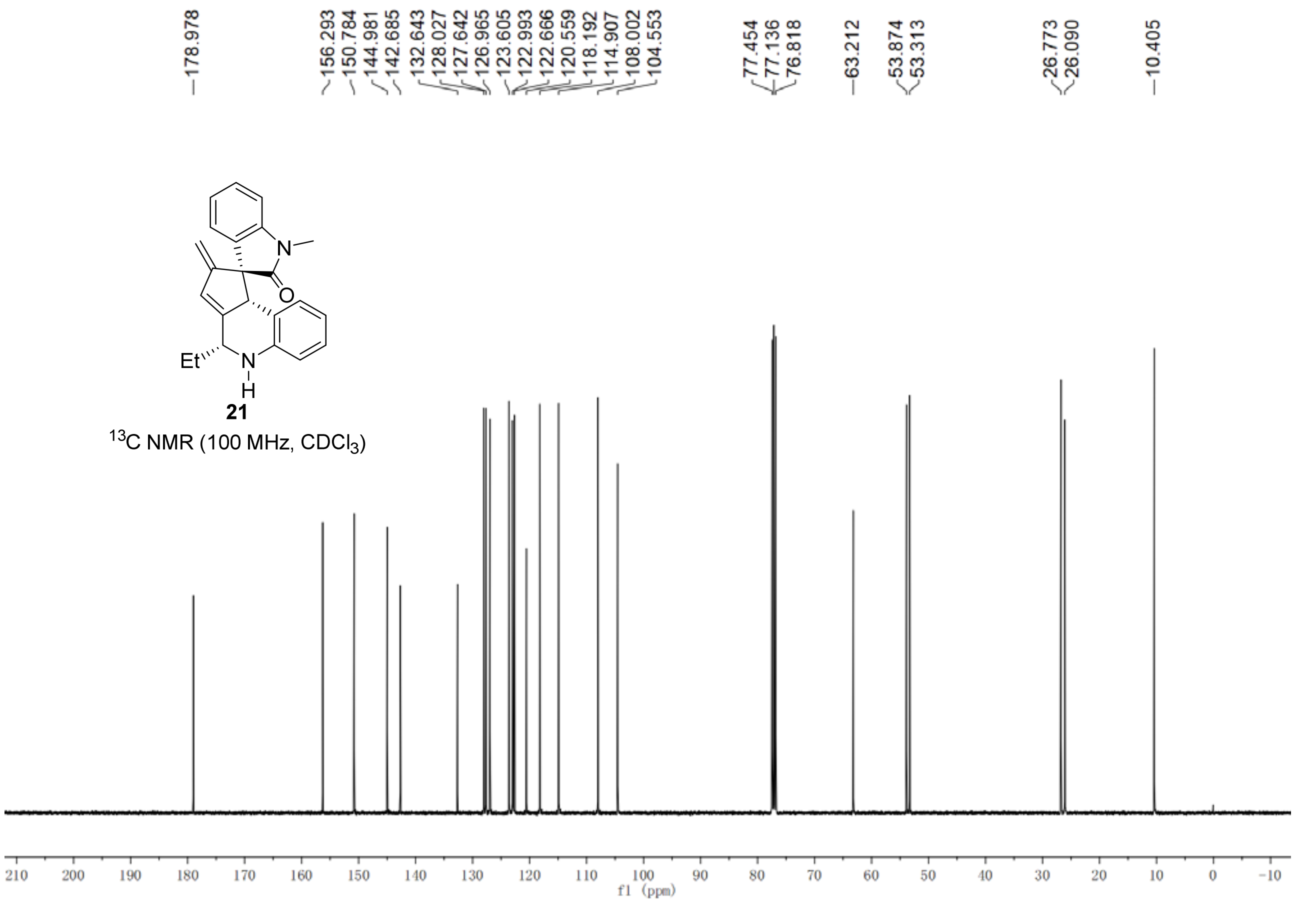
(ESI-TOF) *m/z*: $[M + Na]^+$

Calcd for $C_{29}H_{28}N_2O_4SNa^+$ 523.1662



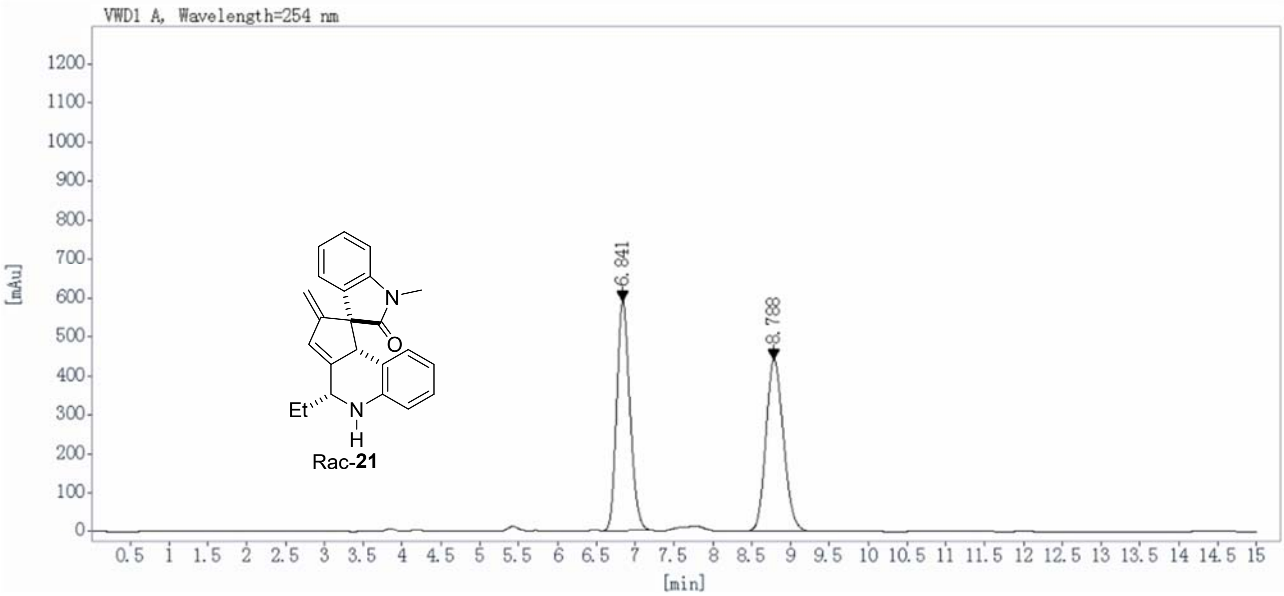
21

^{1}H NMR (400 MHz, CDCl$_3$)

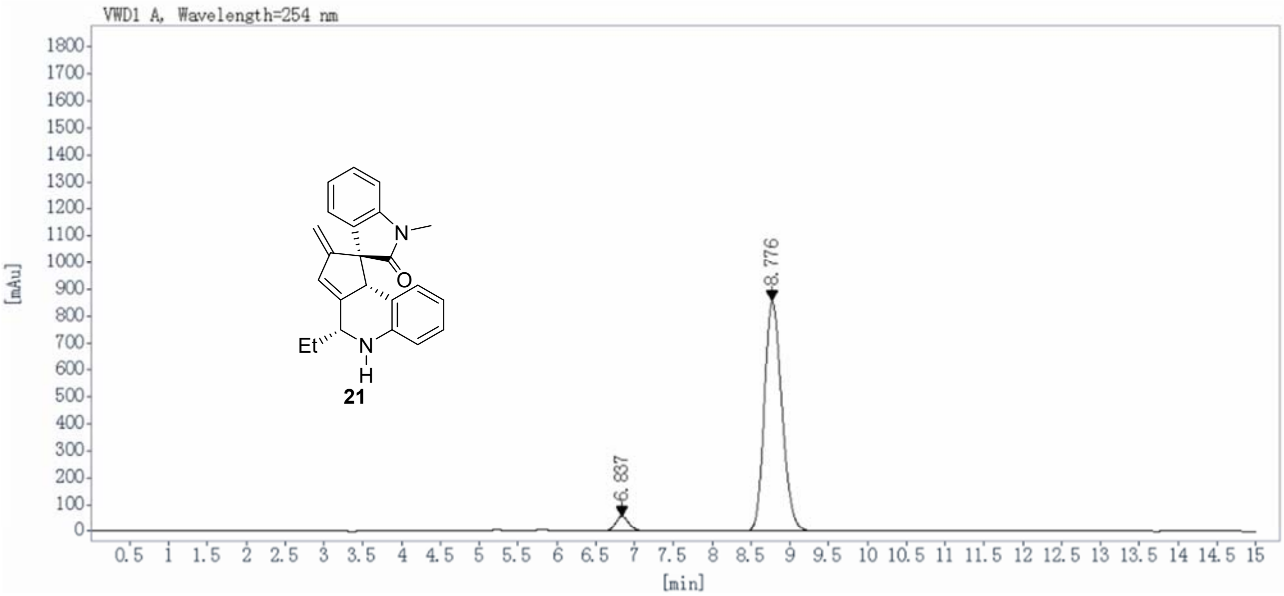


21

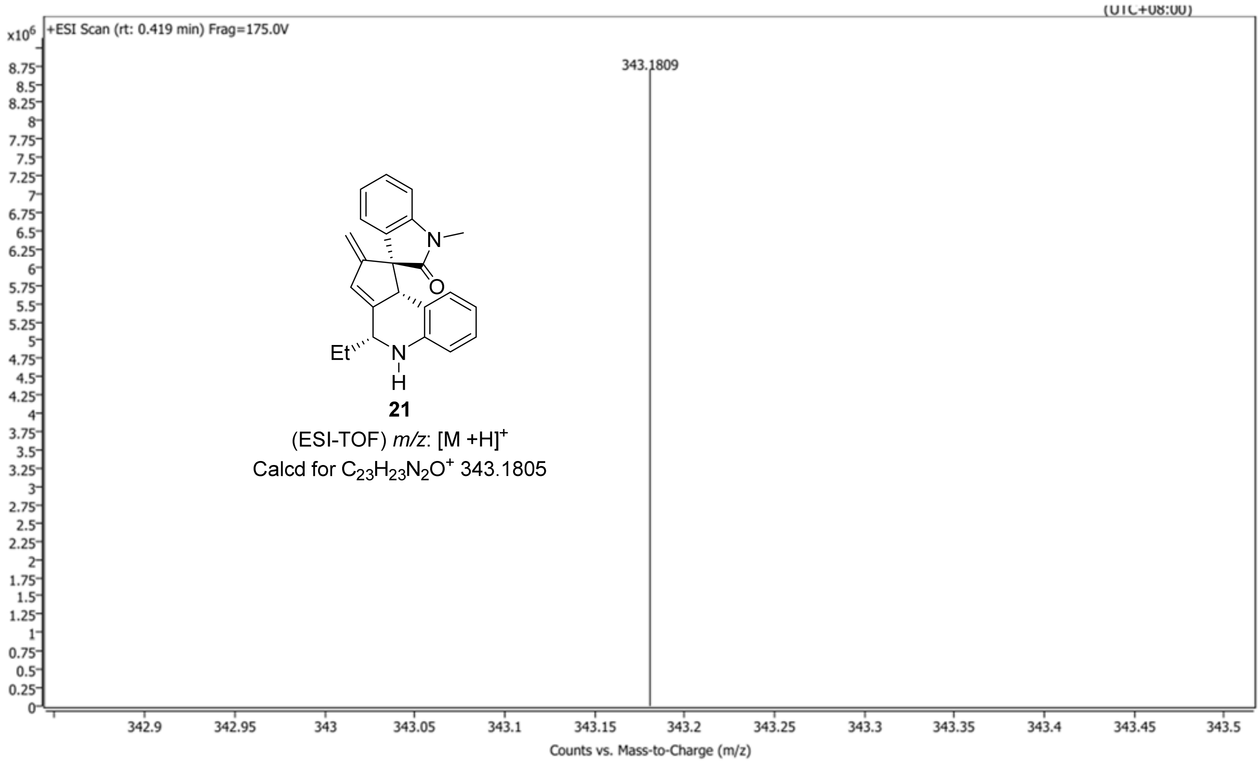
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.841	BBA	0.19	588.1586	7042.9995	50.4276
8.788	BBA	0.24	441.0534	6923.5688	49.5724
			Totals:	13966.5684	100.0000



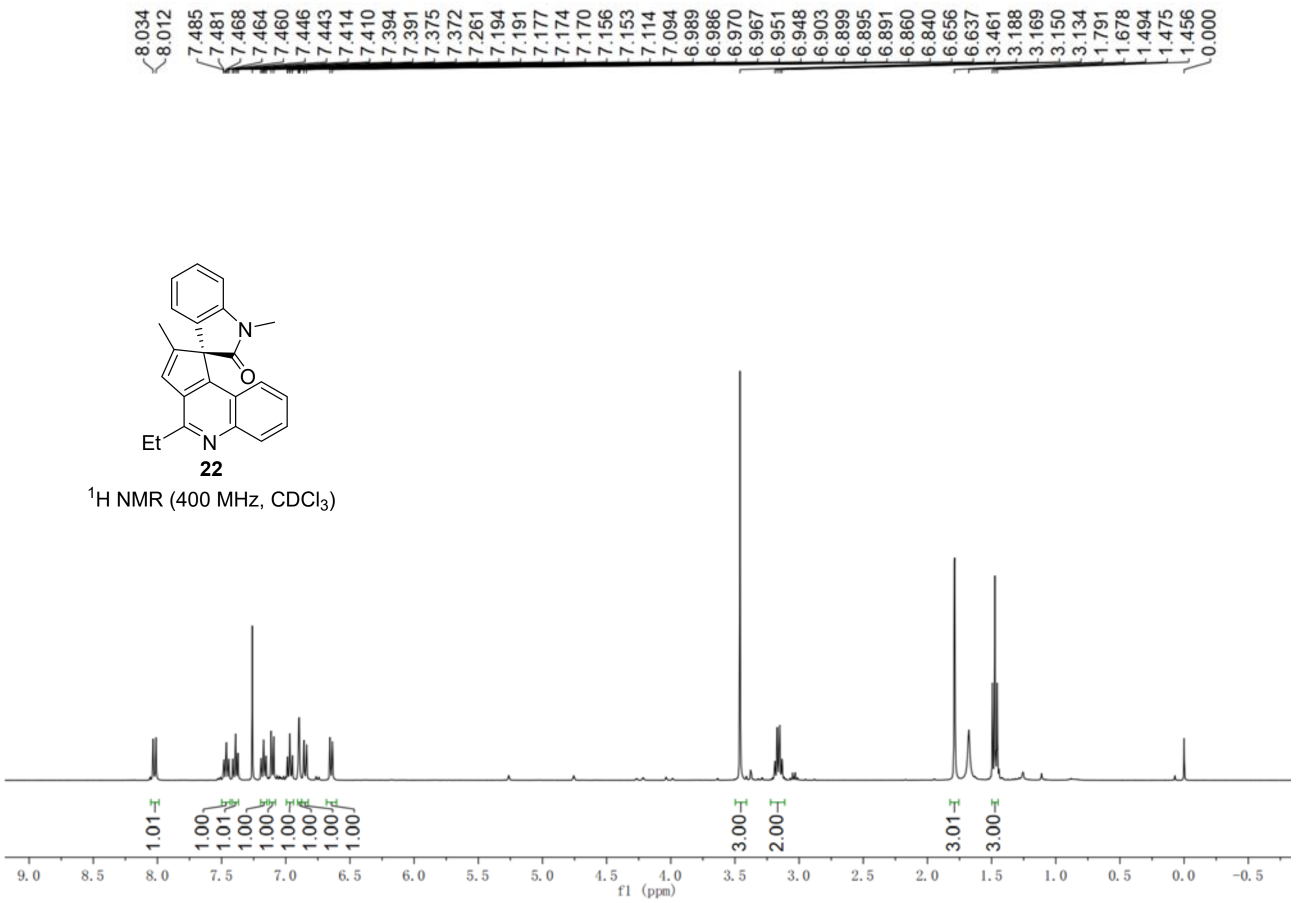
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
6.837	BB	0.18	53.7135	608.9911	4.3398
8.776	BBA	0.24	854.6207	13423.7334	95.6602
			Totals:	14032.7245	100.0000



21

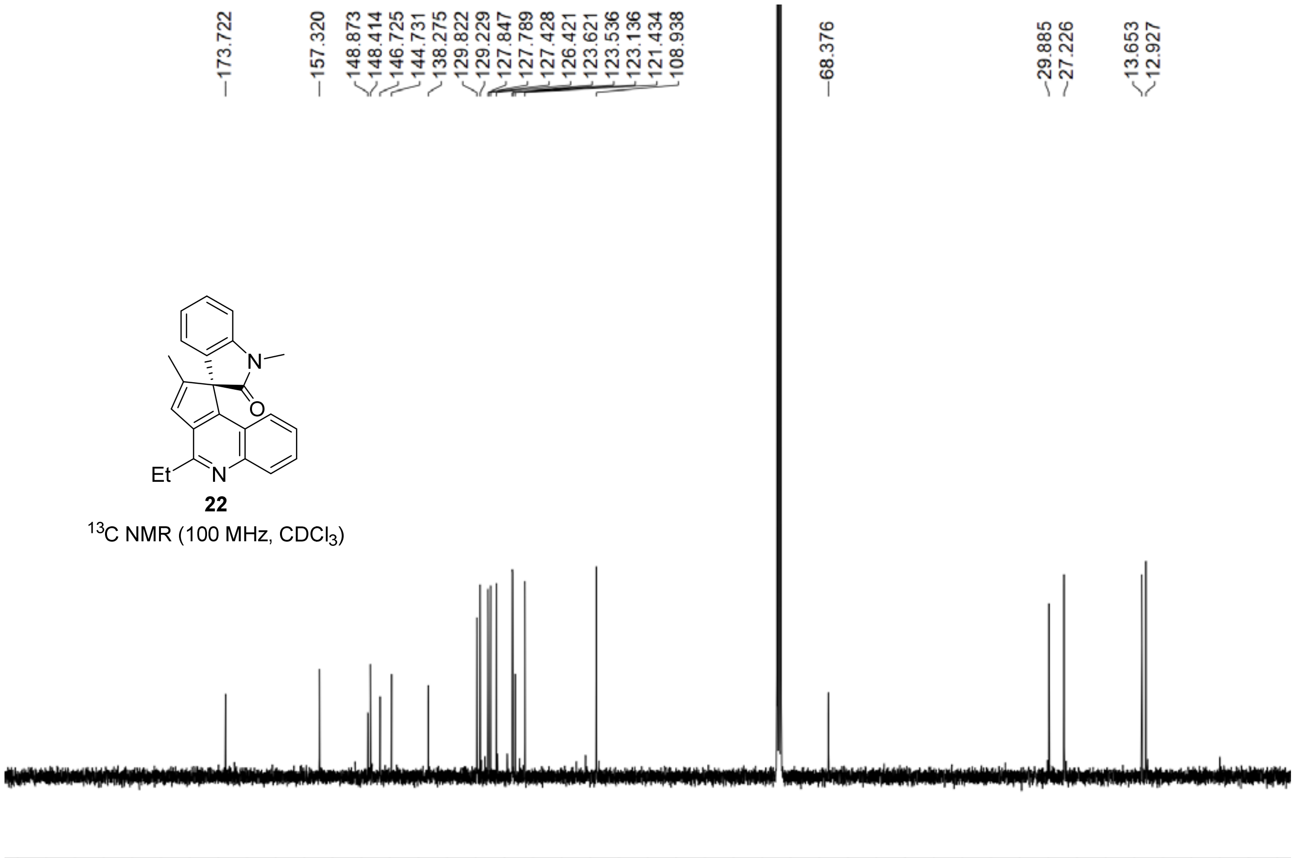
(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{23}H_{23}N_2O^+$ 343.1805



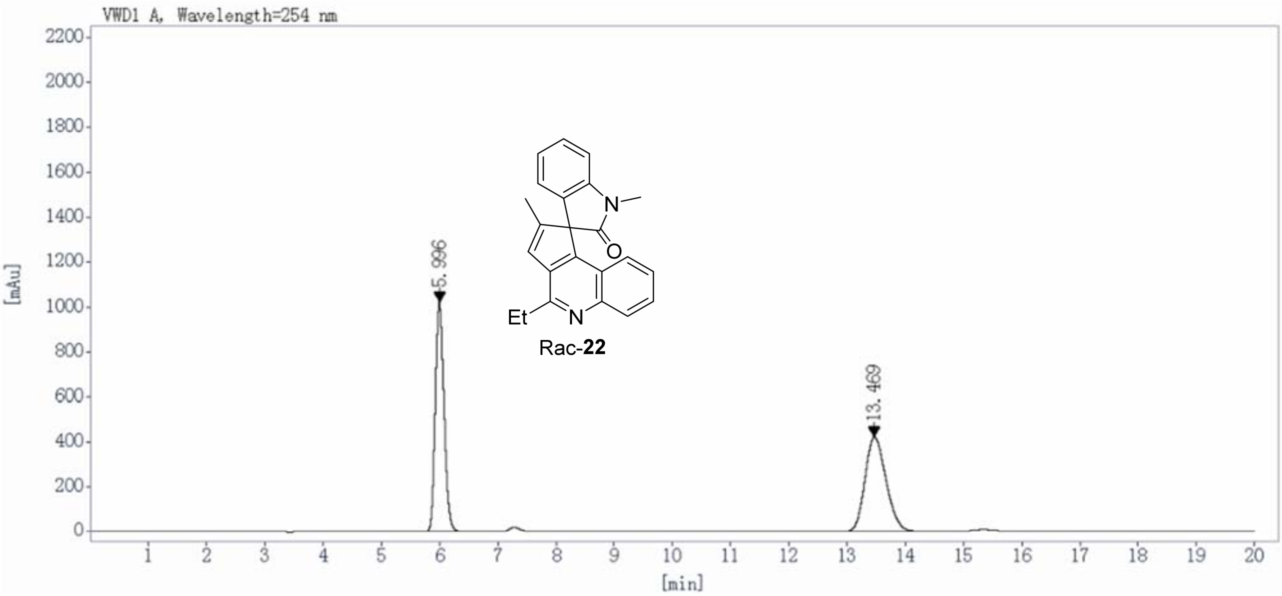
22

^{1}H NMR (400 MHz, CDCl$_3$)

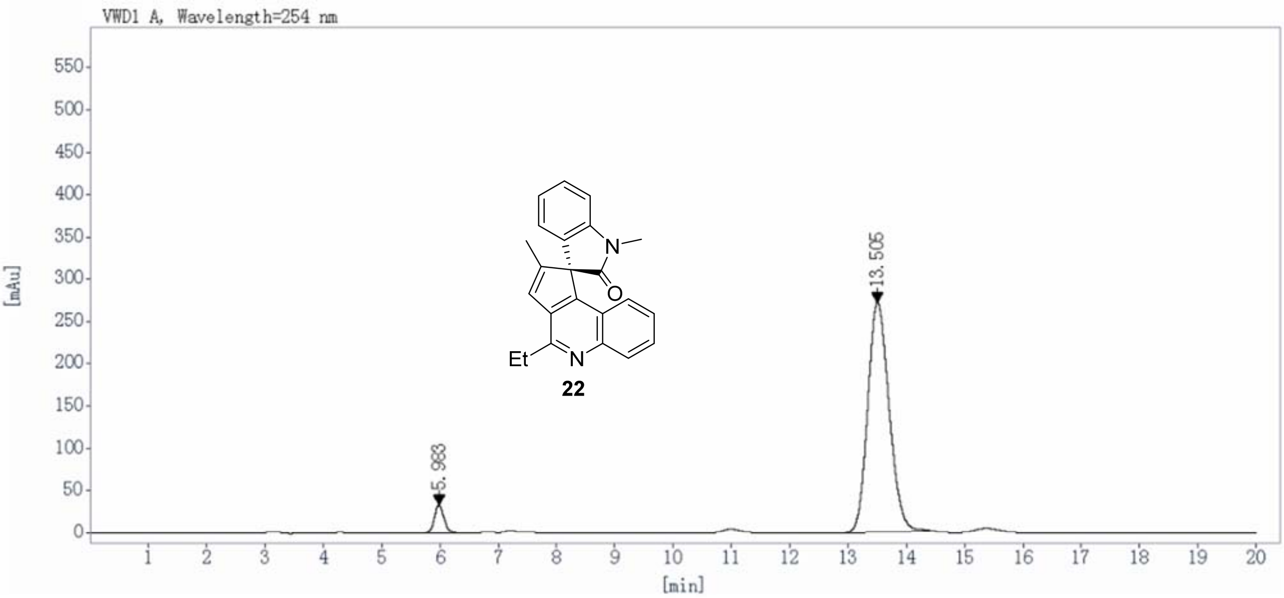


22

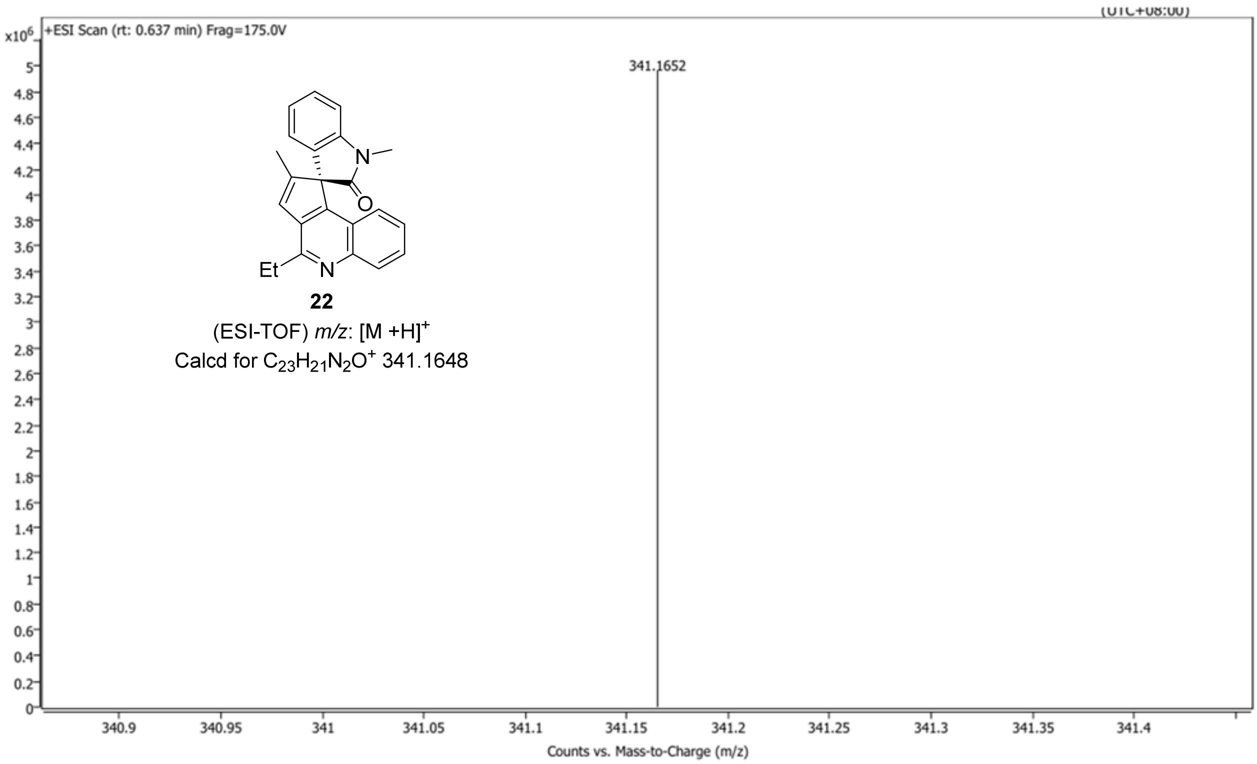
^{13}C NMR (100 MHz, CDCl$_3$)



Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.996	BBA	0.16	1023.4622	10605.2090	49.9482
13.469	BBA	0.39	422.5282	10627.2080	50.0518
			Totals:	21232.4170	100.0000



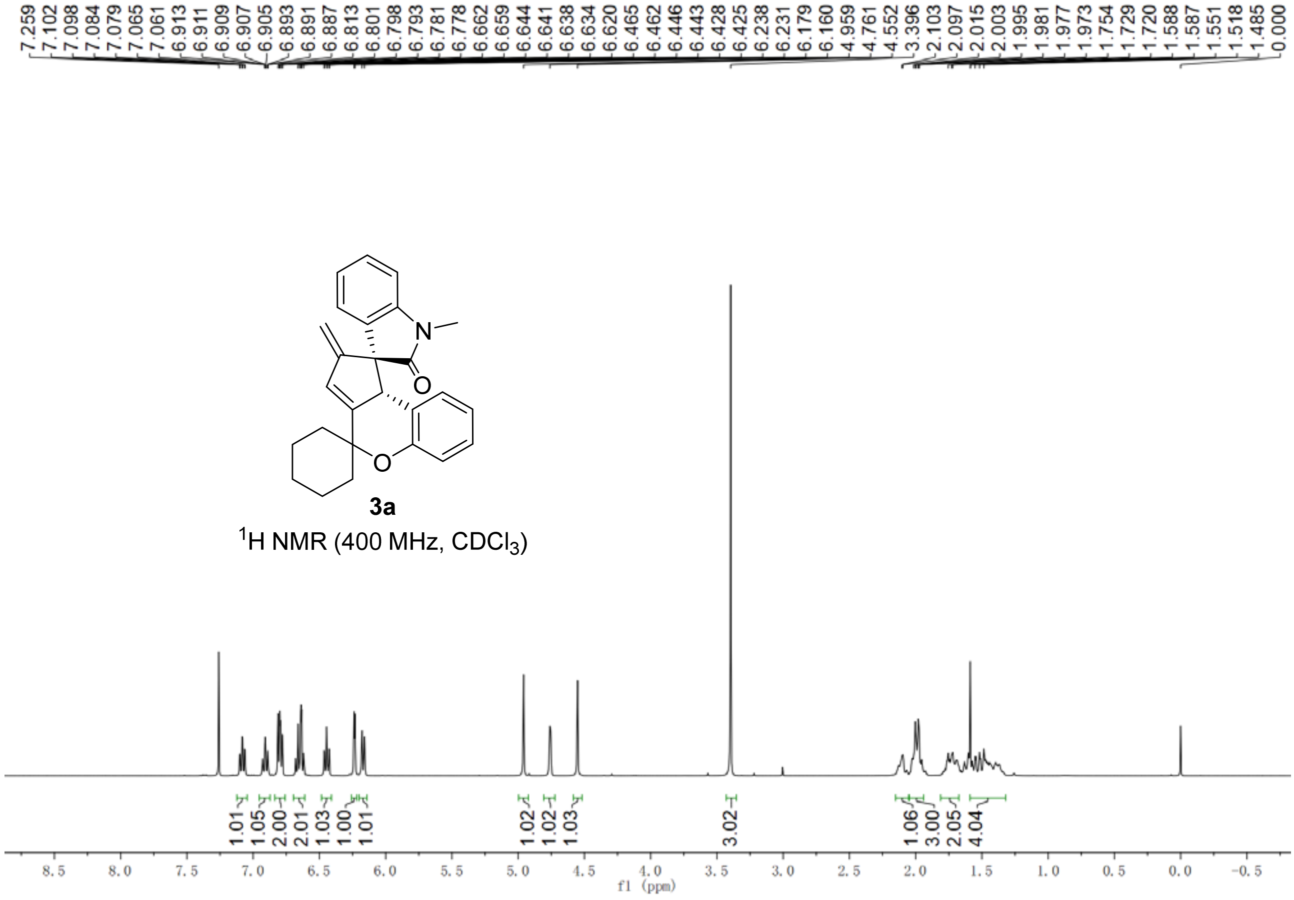
Ret Time [min]	Peak Type	Width [min]	Height [mAU]	Area [mAU*s]	Area [%]
5.983	BBA	0.17	32.8479	365.9035	5.0099
13.505	BBA	0.40	271.3038	6937.6753	94.9901
			Totals:	7303.5788	100.0000

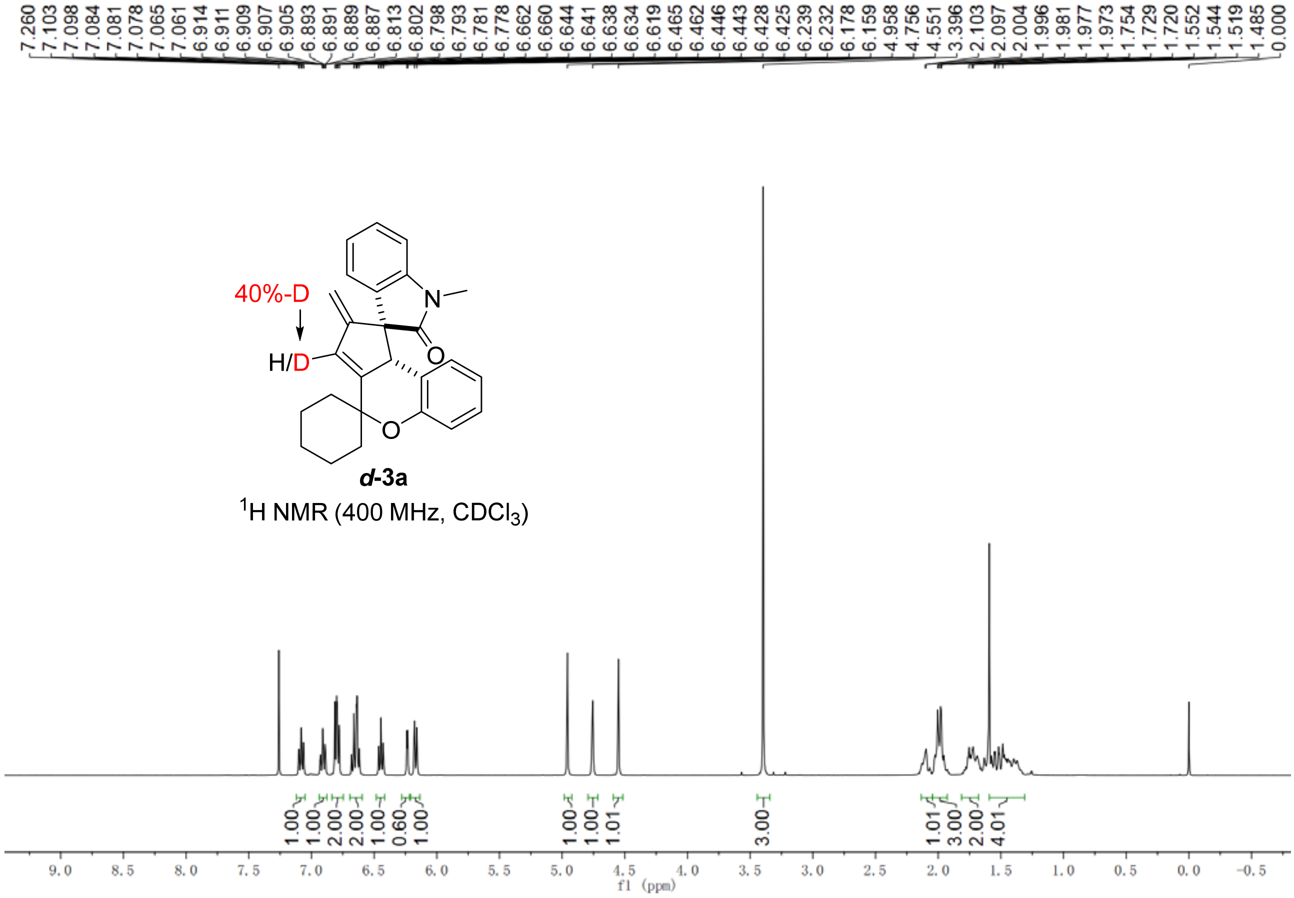


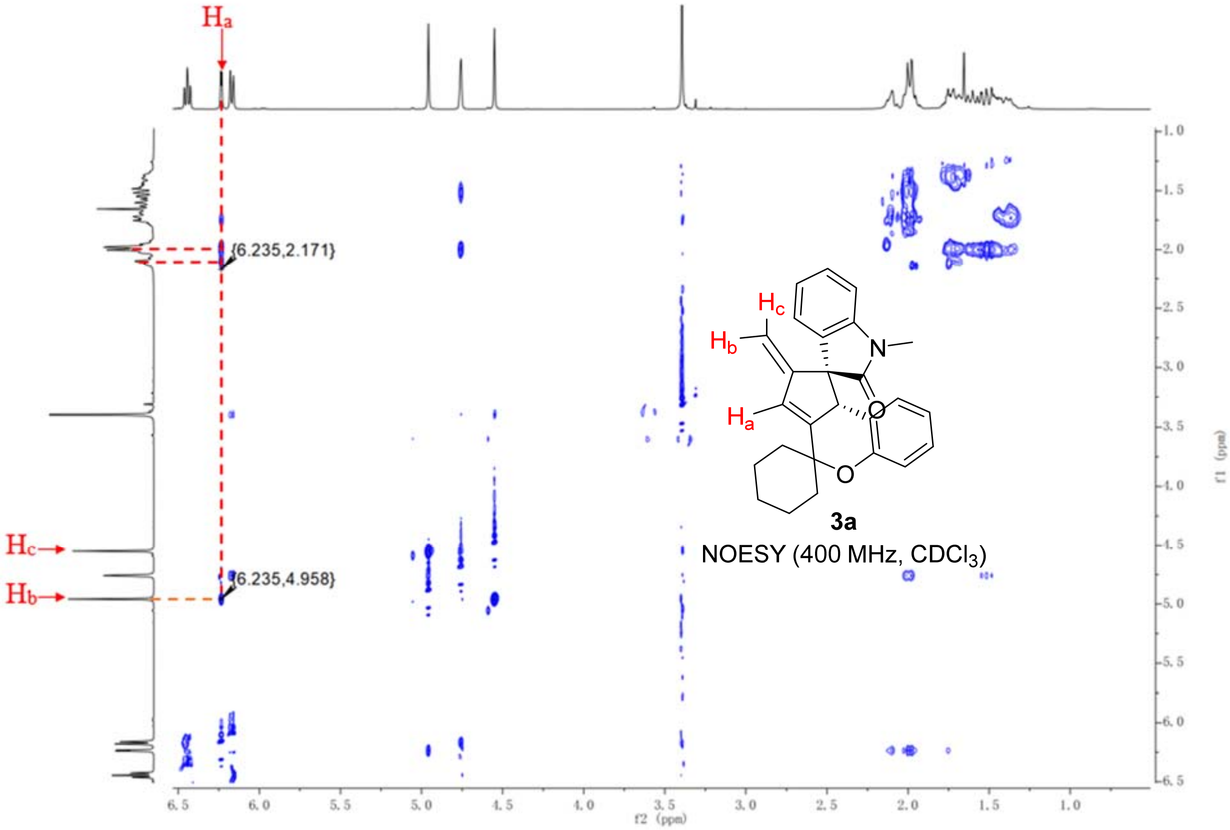
22

(ESI-TOF) *m/z*: $[M + H]^+$

Calcd for $C_{23}H_{21}N_2O^+$ 341.1648


7.259
7.102
7.098
7.084
7.079
7.065
7.061
6.913
6.911
6.909
6.907
6.905
6.893
6.891
6.887
6.813
6.801
6.798
6.793
6.781
6.778
6.662
6.659
6.644
6.641
6.638
6.634
6.620
6.465
6.462
6.446
6.443
6.428
6.425
6.238
6.231
6.179
6.160
4.959
4.761
4.552
3.396
2.103
2.097
2.015
2.003
1.995
1.981
1.977
1.973
1.754
1.729
1.720
1.588
1.587
1.551
1.518
1.485
0.000
N
O
O
3a
^{1}H NMR (400 MHz, CDCl$_3$)
1.01
1.05
2.00
2.01
1.03
1.00
1.01
1.02
1.02
1.03
3.02
1.06
3.00
2.05
4.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


7.260
7.103
7.098
7.084
7.081
7.078
7.065
7.061
6.914
6.911
6.909
6.907
6.905
6.893
6.891
6.889
6.887
6.813
6.802
6.798
6.793
6.781
6.778
6.662
6.660
6.644
6.641
6.638
6.634
6.619
6.465
6.462
6.446
6.443
6.428
6.425
6.239
6.232
6.178
6.159
4.958
4.756
4.551
3.396
2.103
2.097
2.004
1.996
1.981
1.977
1.973
1.754
1.729
1.720
1.552
1.544
1.519
1.485
0.000
40%-D
H/D
N
O
O
d-3a
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.00
2.00
2.00
1.00
0.60
1.00
1.00
1.00
1.01
3.00
1.01
3.00
2.00
4.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



3a

NOESY (400 MHz, $CDCl_3$)