Supplementary Materials for

Asymmetric synthesis of chiral (thio)chromanes and exploration on their structure-activity relationship in macrophages

Xiao Zhang [# a, b], Qian Zhou [# c], Yue Zhou [c], Zihao Wang [e, f *], Jun Wang [b, d] and Mingfu Wang [a, c *]

a School of Biological Science, The University of Hong Kong, Hong Kong 999077, China

b Department of Chemistry, Southern University of Science and Technology, Shenzhen 518055, China

c Shenzhen Key Laboratory of Food Nutrition and Health, Institute for Advanced Study, Shenzhen University, Shenzhen 518060, China

d Department of Chemistry, Hong Kong Baptist University, Hong Kong 999077, China

e School of Chinese Medicine, Hong Kong Baptist University, Hong Kong 999077, China

f. Centre for Chinese Herbal Medicine Drug Development, Hong Kong Baptist University, Hong Kong 999077, China

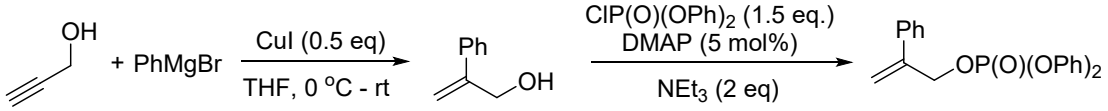
This PDF file includes:

1. General information

All the air or moisture sensitive reactions and manipulations were performed under an atmosphere of argon by using standard Schlenk techniques and Drybox (Mikrouna, Supper 1220/750). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-Avance 400 or 500 MHz spectrometer. $CDCl_3$ was used as solvent. Chemical shifts (δ) were reported in ppm with tetramethylsilane as internal standard, and *J* values were given in Hz. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, dd = double of doublets, t = triplet, q = quartet, m = multiplet. Flash column chromatograph was carried out using 200-300 mesh silica gel at medium pressure. High resolution mass spectra (HRMS) were recorded on a LC-TOF spectrometer. ESI-HRMS data were acquired using a Thermo LTQ Orbitrap XL Instrument equipped with an ESI source. Optical rotation was obtained on a Rudolph Research Analytical (Atopol I). HPLC analysis was performed on Agilent 1260 series, UV detection monitored at 230 or 220 nm. Tetrahydrofuran was distilled over sodium.

2. Preparation of substrates

The substrate allyl phosphate was prepared according to the literature [1].



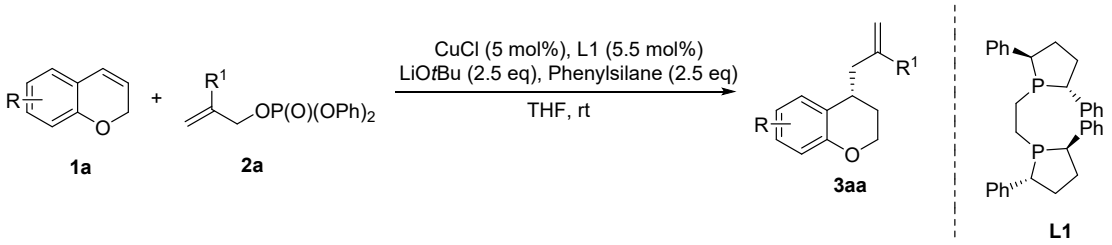
Reaction procedure: To add CuI (10 mmol, 1.95 g) to a 250 mL two-mouth flask, and the flask was evacuated and backfilled with nitrogen for three times, then to add 30 mL THF to the flask and add phenyl magnesium bromide (PhMgBr, 50 mmol, 50 mL) at 0 °C. After stirring for half an hour, propargyl alcohol (20 mmol, 2.9 mL) solution was added dropwise at 0 °C. Then the mixture was allowed to stir at rt for 20 h. The reaction was quenched carefully by aqueous saturated NH_4Cl solution in ice-water bath. The biphase system was extracted by ethyl acetate for three times (100 mL x 3) and then the combined organic phase was washed by brine for three times (100 mL x 3). The organic phase was dried over $MgSO_4$, concentrated in vacuo and the residue was purified by

silica gel column chromatography (pe/ea = 20/1, v/v)) to provide allyl alcohol (17.2 mmol, 2.3 g).

To add DCM (30 mL) to a 100 mL round-bottom flask containing the substrate allyl alcohol and stir. And then to add phenyl chlorophosphate (25.8 mmol, 5.5 mL) and DMAP (0.86 mmol, 0.235 g). Then triethylamine (34.4 mol, 4.5 mL) was added dropwise at 0 ℃ and then stirred at rt for 2 h. The reaction was quenched carefully by aqueous saturated $NaHCO_3$ solution. The biphase system was extracted by DCM for three times (100 mL x 3) and then the combined organic phase was washed by brine for three times (100 mL x 3). The organic phase was dried over $MgSO_4$, concentrated in vacuo and the residue was purified by silica gel column chromatography (PE/EA = 10/1, v/v) to provide allyl phosphate (15.3 mmol, 5.6 g).

3. Preparation for 4-allyl chromanes compounds

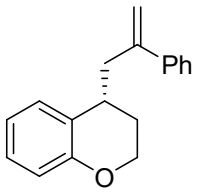
The specific operation of copper(I) hydride-catalyzed hydroallylation was as follows:



CuCl (0.01 mmol, 1.0 mg), L1 (0.011mmol, 5.6 mg) and THF (0.5 mL) were added into the reaction tube (10.0 mL) in a glove box filled with argon atmosphere. After stirring for 10 min at room temperature, phenylsilane (0.5 mol) was added, followed by stirring for 10 min at room temperature, followed by allyl phosphate (0.5 mmol), LiO*t*Bu (0.5 mmol, 40.0 mg), and chromene (0.2 mmol). The reaction tube was removed from the glove box and stirred at rt for 24 h. At the end of the reaction, the reaction was filtered through the funnel with EA and concentrated in vacuo and the residue was purified by silica gel column chromatography (PE) to provide chromane compound. The ee value of the product was determined by HPLC. Diastereomeric ratio was determined by ^{1}H NMR.

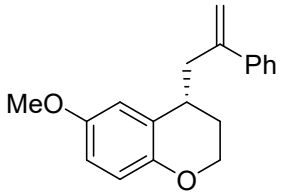
4. Characterization data (^{1}H NMR, ^{13}C NMR, ^{19}F NMR, HRMS, and HPLC) of the products

(*R*)-4-(2-phenylallyl)chromane (3aa)



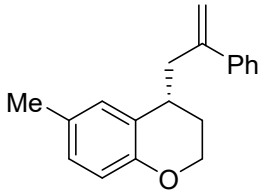
Colorless oil, 91% yield; $[a]^{20}_{D}$ = -4.6 (c = 7.4, **$CHCl_3$**); ee was determined to be 99% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm); tr (major) = 5.389 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.1 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 9.3 Hz, 1H), 7.11 (d, *J* = 7.0 Hz, 1H), 6.90 (d, *J* = 7.4 Hz, 1H), 6.86 - 6.79 (m, 1H), 5.40 (s, 1H), 5.11 (s, 2H), 4.33 - 4.04 (m, 2H), 3.21 (dd, *J* = 14.0, 3.9 Hz, 1H), 2.88 (dq, *J* = 10.1, 4.9 Hz, 1H), 2.60 (dd, *J* = 14.3, 10.8 Hz, 1H), 2.00 - 1.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ154.18, 146.30, 141.21, 140.56, 133.35, 128.76, 128.64, 127.79, 127.78, 126.81, 126.63, 126.37, 117.23, 115.21, 63.35, 42.77, 31.61, 26.06. **HRMS (ESI) m/z: calcd for $C_{18}H_{18}O$ M250.1358, found 250.1350.**

(*R*)-6-methoxy-4-(2-phenylallyl)chromane (3ab)



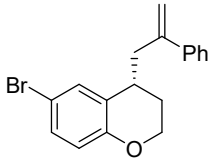
Colorless oil, 64% yield; $[a]^{20}_{D}$ = -117.2 (c = 5, **$CHCl_3$**); ee was determined to be 95% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 7.465 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.46 (m, 2H), 7.43 - 7.35 (m, 2H), 7.35 - 7.29 (m, 1H), 6.78 - 6.66 (m, 3H), 5.38 (d, *J* = 1.8 Hz, 1H), 5.10 (td, *J* = 1.6, 0.8 Hz, 1H), 4.19 - 4.03 (m, 2H), 3.77 (s, 3H), 3.18 (ddd, *J* = 14.5, 4.7, 1.5 Hz, 1H), 2.84 (dq, *J* = 10.4, 5.1 Hz, 1H), 2.64 - 2.54 (m, 1H), 1.90 (dddd, *J* = 14.7, 9.3, 5.8, 3.7 Hz, 1H), 1.79 (dtd, *J* = 13.9, 5.4, 3.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.18, 148.60, 146.31, 140.53, 128.58, 127.73, 126.84, 126.31,117.25, 115.10, 114.08, 113.11, 63.20, 55.80, 42.79, 31.71, 26.16. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O_2$ M280.1463, found 280.1450.**

(*R*)-6-methyl-4-(2-phenylallyl)chromane (3ac)



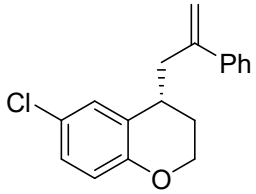
Colorless oil, 67% yield; $[a]^{20}_{D}$ = -270.6 (c = 4.1, **$CHCl_3$**); ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 4.544 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 - 7.50 (m, 2H), 7.47 - 7.39 (m, 2H), 7.38 - 7.32 (m, 1H), 7.01 (d, *J* = 2.1 Hz, 1H), 6.94 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 5.41 (d, *J* = 1.5 Hz, 1H), 5.13 (d, *J* = 1.6 Hz, 1H), 4.25 - 4.00 (m, 2H), 3.23 (ddd, *J* = 14.3, 4.4, 1.4 Hz, 1H), 2.86 (dq, *J* = 10.2, 5.0 Hz, 1H), 2.60 (dd, *J* = 14.3, 11.0 Hz, 1H), 2.32 (s, 3H), 1.88 (dtd, *J* = 25.2, 5.5, 3.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ152.30, 146.38, 140.63, 129.27, 128.55, 128.08, 127.69, 126.33, 125.84, 116.56, 114.99, 63.14, 42.73, 31.39, 25.97, 20.65. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O$ M264.1514, found 264.1509.**

(*R*)-6-bromo-4-(2-phenylallyl)chromane (3ad)



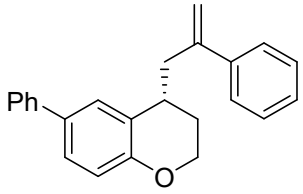
Colorless oil, 66% yield; $[a]^{20}_{D}$ = +43.3 (c = 5, **$CHCl_3$**); ee was determined to be 99% by HPLC analysis with a Chiralcel IC column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm); tr (major) = 5.194 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.47 (m, 2H), 7.45 - 7.38 (m, 2H), 7.38 - 7.31 (m, 1H), 7.28 (s, 2H), 7.19 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.70 (d, *J* = 8.7 Hz, 1H), 5.39 (s, 1H), 5.11 (s, 1H), 4.21 - 4.08 (m, 2H), 3.16 (dd, *J* = 14.1, 4.0 Hz, 1H), 2.84 (dd, *J* = 10.5, 5.2 Hz, 1H), 2.58 (dd, *J* = 14.2, 10.7 Hz, 1H), 1.96 - 1.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.63, 145.92, 140.31, 131.51, 130.26, 128.63, 128.25, 127.81, 126.29, 118.66, 115.38, 112.09, 63.27, 42.56, 31.37, 25.52. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}OBr$ M328.0463, found 328.0448; calcd for $C_{18}H_{17}O^{81}Br$ M330.0442, found 330.0430.**

(*R*)-6-chloro-4-(2-phenylallyl)chromane (3ae)



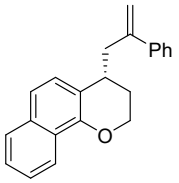
Colorless oil, 70% yield; $[a]^{20}_{D}$ = -14.1 (c = 5, **$CHCl_3$**); ee was determined to be 97% by HPLC analysis with a Chiralcel ODH column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 4.963 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 - 7.47 (m, 2H), 7.42 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.38 - 7.32 (m, 1H), 7.16 - 7.12 (m, 1H), 7.06 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 1H), 5.40 (d, *J* = 1.3 Hz, 1H), 5.11 (d, *J* = 1.5 Hz, 1H), 4.22 - 4.09 (m, 2H), 3.17 (ddd, *J* = 14.3, 4.7, 1.4 Hz, 1H), 2.84 (dq, *J* = 10.3, 5.1 Hz, 1H), 2.58 (dd, *J* = 14.3, 10.7 Hz, 1H), 1.97 - 1.77 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ153.12, 145.94, 140.33, 128.63, 128.56, 127.80, 127.66, 127.38, 126.29, 124.75, 118.17, 115.36, 63.30, 42.57, 31.42, 25.58. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}OCl$ M284.0968, found 284.0961; calcd for $C_{18}H_{17}O^{37}Cl$ M286.0938, found 286.0933.**

(*R*)-6-phenyl-4-(2-phenylallyl)chromane (3af)



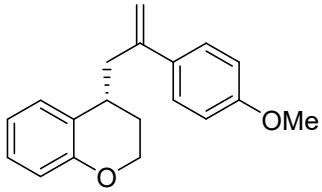
Colorless oil, 72% yield; $[a]^{20}$D = +33.1 (c = 5, $CHCl_3$); ee was determined to be 75% by HPLC analysis with a Chiralcel AD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 9.055 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 - 7.51 (m, 2H), 7.51 - 7.47 (m, 2H), 7.43 - 7.38 (m, 3H), 7.37 - 7.35 (m, 3H), 7.32 - 7.29 (m, 2H), 6.88 - 6.85 (m, 1H), 5.37 (s, 1H), 5.09 (s, 1H), 4.16 (dddd, J = 24.2, 11.0, 5.3, 3.4 Hz, 2H), 3.22 (ddd, J = 14.3, 4.8, 1.5 Hz, 1H), 2.92 (dq, J = 10.3, 5.0 Hz, 1H), 2.62 (dd, J = 14.4, 10.6 Hz, 1H), 1.97 - 1.88 (m, 1H), 1.85 – 1.80 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.21, 146.32, 141.23, 140.58, 135.82, 133.37, 128.79, 128.67, 127.82, 127.80, 126.83, 126.69, 126.66, 126.40, 117.26, 115.24, 63.37, 42.78, 31.63, 26.08. **HRMS (ESI) m/z: calcd for $C_{24}H_{22}O$ M326.1671, found 326.1668.**

(*R*)-4-(2-phenylallyl)-3,4-dihydro-2H-benzo[h]chromene (3ag)



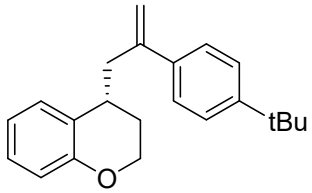
Colorless oil, 70% yield; $[a]^{20}_{D}$ = -42.1 (c = 5, **$CHCl_3$**); ee was determined to be 97% by HPLC analysis with a Chiralcel IC column (hexane/2-propanol = 99/1, 0.5 mL/min, 254 nm); tr (major) = 9.040 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 - 8.19 (m, 1H), 7.83 - 7.75 (m, 1H), 7.60 - 7.56 (m, 2H), 7.51 - 7.47 (m, 2H), 7.47 - 7.42 (m, 2H), 7.42 - 7.35 (m, 2H), 7.31 (d, *J* = 8.5 Hz, 1H), 5.44 (d, *J* = 1.4 Hz, 1H), 5.16 (q, *J* = 1.2 Hz, 1H), 4.45 - 4.31 (m, 2H), 3.32 (ddd, *J* = 14.4, 4.3, 1.4 Hz, 1H), 3.01 (dq, *J* = 9.8, 4.4 Hz, 1H), 2.65 (dd, *J* = 14.4, 10.9 Hz, 1H), 2.12 - 1.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ149.53, 146.42, 140.68, 133.19, 128.62, 127.75, 127.38, 127.11, 126.41, 125.84, 125.27, 125.24, 121.70, 119.65, 119.53, 115.12, 63.24, 43.03, 31.56, 25.73. **HRMS (ESI) m/z: calcd for $C_{22}H_{20}O$ $[M+H]^+$301.1592, found 301.1586.**

(*R*)-4-(2-(4-methoxyphenyl)allyl)chromane (3ah)



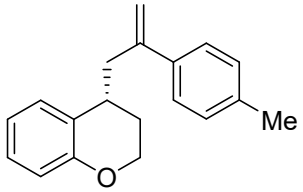
Colorless oil, 86% yield; $[a]^{20}_{D}$ = -59.9 (c = 5, **$CHCl_3$**); ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 7.624 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.7 Hz, 2H), 7.24 - 7.19 (m, 1H), 7.16 - 7.11 (m, 1H), 6.98 - 6.94 (m, 2H), 6.91 (td, *J* = 7.5, 1.3 Hz, 1H), 6.84 (dd, *J* = 8.2, 1.3 Hz, 1H), 5.34 (s, 1H), 5.04 (s, 1H), 4.33 - 4.09 (m, 2H), 3.87 (s, 3H), 3.19 (ddd, *J* = 14.3, 4.6, 1.4 Hz, 1H), 2.91 (dq, *J* = 10.2, 5.0 Hz, 1H), 2.58 (dd, *J* = 14.3, 10.8 Hz, 1H), 1.99 - 1.78 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.27, 154.51, 145.53, 132.89, 129.02, 127.41, 126.28, 120.17, 116.82, 113.92, 113.55, 63.19, 55.33, 42.80, 31.41, 25.87. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O_2$ M280.1463, found 280.1459.**

(*R*)-4-(2-(4-(tert-butyl)phenyl)allyl)chromane (3ai)



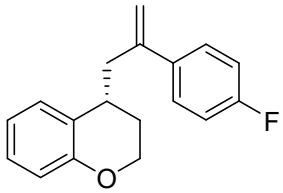
Colorless oil, 60% yield; $[a]^{20}_{D}$ = -24.4 (c = 6.2, **$CHCl_3$**); ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 10.784 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 - 7.46 (m, 2H), 7.46 - 7.42 (m, 2H), 7.23 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.16 - 7.10 (m, 1H), 6.92 (td, *J* = 7.4, 1.3 Hz, 1H), 6.84 (dd, *J* = 8.2, 1.3 Hz, 1H), 5.41 (s, 1H), 5.08 (s, 1H), 4.26 - 4.10 (m, 2H), 3.22 (ddd, *J* = 14.3, 4.4, 1.4 Hz, 2H), 2.92 (dq, *J* = 10.2, 5.0 Hz, 1H), 2.60 (dd, *J* = 14.3, 10.8 Hz, 1H), 1.98 - 1.82 (m, 2H), 1.38 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.52, 150.72, 145.85, 137.40, 129.06, 127.37, 126.31, 125.92, 125.46, 120.16, 116.81, 114.34, 63.20, 42.70, 34.57, 31.35 (d, *J* = 3.2 Hz), 25.92. **HRMS (ESI) m/z: calcd for $C_{22}H_{26}O$ M306.1984, found 306.1971.**

(*R*)-4-(2-(p-tolyl)allyl)chromane (3aj)



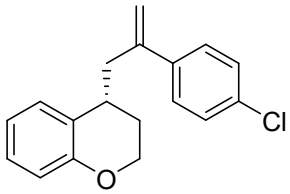
Colorless oil, 76% yield; $[a]^{20}_{D}$ = -99.6 (c = 5, **$CHCl_3$**); ee was determined to be 94% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 5.427 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.22 (t, *J* = 8.6 Hz, 3H), 7.14 - 7.11 (m, 1H), 6.92 - 6.89 (m, 1H), 6.83 (d, *J* = 8.1 Hz, 1H), 5.38 (s, 1H), 5.07 (s, 1H), 4.27 - 4.08 (m, 2H), 3.20 (ddd, *J* = 14.4, 4.6, 1.4 Hz, 1H), 2.89 (dq, *J* = 10.2, 5.0 Hz, 1H), 2.58 (dd, *J* = 14.3, 10.8 Hz, 1H), 5.40 (s, 3H), 2.05- 1.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.51, 146.05, 137.58, 137.51, 129.26, 129.02, 127.37, 126.19, 120.15, 116.80, 114.29, 63.18, 42.75, 31.38, 25.87, 21.14. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O$ M264.1514, found 264.1507.**

(*R*)-4-(2-(4-fluorophenyl)allyl)chromane (3ak)



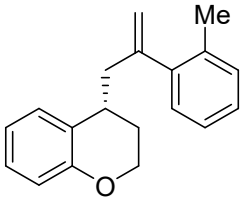
Colorless oil, 80% yield; $[a]^{20}_{D}$ = -7.8 (c = 5, **$CHCl_3$**); ee was determined to be 97% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 6.564 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 - 7.44 (m, 2H), 7.21 - 7.06 (m, 4H), 6.92 - 6.89 (m, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 5.35 (s, 1H), 5.11 (s, 1H), 4.25 - 4.10 (m, 1H), 3.17 (ddd, *J* = 14.4, 4.5, 1.4 Hz, 1H), 2.89 - 2.84 (m, 1H), 2.60 (dd, *J* = 14.4, 10.7 Hz, 1H), 1.97 - 1.90 (m, 1H), 1.85 - 1.80 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.42, 161.46, 154.51, 145.29, 136.62 (d, *J* = 3.5 Hz), 128.95, 127.91 (d, *J* = 7.9 Hz), 127.50, 125.99, 120.21, 116.89, 115.45 (d, *J* = 21.3 Hz), 115.06, 63.12, 42.85, 31.37, 25.88. ^{19}F NMR (376 MHz, $CDCl_{33ay}$) δ -114.71. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}OF$ M268.1263, found 268.1255.**

(*R*)-4-(2-(4-chlorophenyl)allyl)chromane (3al)



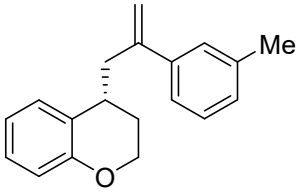
Colorless oil, 51% yield; $[a]^{20}_{D}$ = -63.7 (c = 5.8, **$CHCl_3$**); ee was determined to be 97% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 7.192 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 - 7.42 (m, 2H), 7.40 - 7.36 (m, 2H), 7.18 - 7.10 (m, 2H), 6.90 (td, *J* = 7.4, 1.3 Hz, 1H), 6.83 (dd, *J* = 8.2, 1.3 Hz, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 5.13 (d, *J* = 1.5 Hz, 1H), 4.24 - 4.12 (m, 2H), 3.16 (ddd, *J* = 14.4, 4.6, 1.4 Hz, 1H), 2.85 (dq, *J* = 10.3, 5.0 Hz, 1H), 2.59 (dd, *J* = 14.4, 10.8 Hz, 1H), 1.99 - 1.76 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.48, 145.19, 139.00, 133.52, 128.93, 128.74, 127.62, 127.51, 125.89, 120.21, 116.89, 115.60, 63.09, 42.63, 31.38, 25.89. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}OCl$ M284.0968, found 284.0962; calcd for $C_{18}H_{17}O^{37}Cl$ M286.0938, found 286.0930.**

(*R*)-4-(2-(o-tolyl)allyl)chromane (3am)



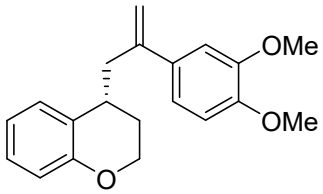
Colorless oil, 82% yield; $[a]^{20}_{D}$ = -82.8 (c = 5.5, **$CHCl_3$**); ee was determined to be 99% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 5.066 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 - 7.17 (m, 4H), 7.13 - 7.08 (m, 1H), 7.08 - 7.06 (m, 1H), 6.88 - 6.85 (m, 1H), 6.84 - 6.81 (m, 1H), 5.29 (s, 1H), 5.08 (s, 1H), 4.25 - 4.15 (m, 2H), 3.05 - 2.97 (m, 1H), 2.84 - 2.73 (m, 1H), 2.56 (dd, *J* = 14.4, 11.2 Hz, 1H), 2.42 (s, 3H), 2.11 - 1.91 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.65, 147.67, 141.92, 134.89, 130.50, 129.13, 128.45, 127.35, 127.16, 126.23, 125.70, 120.25, 116.81 (d), 63.04, 45.22, 31.26, 25.94, 20.16. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O$ M264.1514, found 264.1513.**

(*R*)-4-(2-(m-tolyl)allyl)chromane (3an)



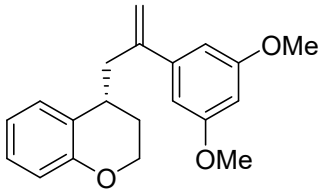
Colorless oil, 82% yield; $[a]^{20}_{D}$ = -9.8 (c = 5, **$CHCl_3$**); ee was determined to be >99% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 5.517 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 - 7.24 (m, 3H), 7.17 (d, *J* = 7.7 Hz, 1H), 7.13 - 7.07 (m, 2H), 6.87 (q, *J* = 10.2, 7.4 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.35 (s, 1H), 5.05 (s, 1H), 4.21 - 4.08 (m, 2H), 3.21 - 3.05 (m, 1H), 2.92 - 2.82 (m, 1H), 2.59 - 2.52 (m, 1H), 2.38 (s, 3H), 1.95 - 1.74 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.57, 146.44, 140.60, 138.15, 129.06, 128.53, 128.49, 127.44, 127.15, 126.31, 123.44, 120.22, 116.87, 114.90, 63.23, 42.82, 31.43, 25.94, 21.65. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O$ M264.1514, found 264.1508.**

(*R*)-4-(2-(3,4-dimethoxyphenyl)allyl)chromane (3ao)



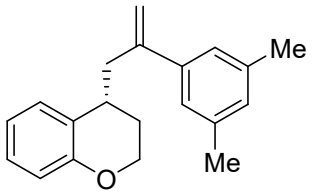
Colorless oil, 50% yield; $[a]^{20}_{D}$ = -49.7 (c = 5.2, **$CHCl_3$**); ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 12.089 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 - 8.14 (m, 3H), 7.86 - 7.76 (m, 2H), 7.31 - 7.26 (m, 2H), 7.12 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.03 (ddd, *J* = 8.1, 7.0, 1.0 Hz, 1H), 3.50 (s, 3H), 1.75 - 1.67 (m, 2H), 1.61 - 1.57 (m, 1H), 1.35 (s, 3H), 1.29 (s, 3H), 0.84 - 0.75 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.68, 182.10, 164.45, 143.87 (d), 141.39, 134.62, 134.18 (d), 132.06 (d), 128.13, 127.23, 126.55, 121.98, 119.96, 118.72, 110.22, 102.76, 52.27, 37.22 (d), 27.41 (d), 9.21. **HRMS (ESI) m/z: calcd for $C_{20}H_{22}O_3$ M310.1569, found 310.1565.**

(*R*)-4-(2-(3,5-dimethoxyphenyl)allyl)chromane (3ap)



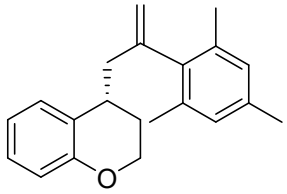
Colorless oil, 85% yield; $[a]^{20}_{D}$ = -39.9 (c = 5.4, **$CHCl_3$**); ee was determined to be 92% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 4.317 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 - 7.15 (m, 1H), 7.11 - 7.06 (m, 3H), 6.95 (s, 1H), 6.87 (td, *J* = 7.4, 1.3 Hz, 1H), 6.79 (dd, *J* = 8.1, 1.3 Hz, 1H), 5.33 (d, *J* = 1.7 Hz, 1H), 5.03 (s, 1H), 4.21 - 4.03 (m, 2H), 3.16 (ddd, *J* = 14.4, 4.5, 1.5 Hz, 1H), 2.86 (dq, *J* = 10.2, 5.0 Hz, 1H), 2.53 (dd, *J* = 14.3, 10.9 Hz, 1H), 2.34 (s, 6H), 1.95 - 1.73 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.59, 146.52, 140.64, 138.01, 129.44, 129.04, 127.42, 126.39, 124.25, 120.21, 116.87, 114.68, 63.28, 42.83, 31.43, 25.96, 21.52. **HRMS (ESI) m/z: calcd for $C_{20}H_{22}O_3$ M310.1569, found 310.1566.**

(*R*)-4-(2-(3,5-dimethylphenyl)allyl)chromane (3aq)



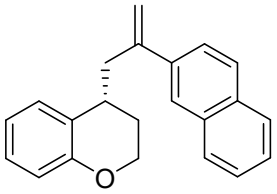
Colorless oil, 85% yield; $[a]^{20}_{D}$ = -59.2 (c = 5.4, **$CHCl_3$**); ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 4.411 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 - 7.07 (m, 4H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 5.28 (s, 1H), 5.07 (s, 1H), 4.23 - 4.18 (m, 2H), 3.01 (d, *J* = 14.3 Hz, 1H), 2.82 - 2.77 (m, 1H), 2.61 - 2.52 (m, 1H), 2.41 (s, 3H), 2.39 (s, 3H), 2.08 - 2.01 (m, 1H), 1.99 - 1.92 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.64, 147.55, 138.94, 136.73, 134.74, 131.32, 129.15, 128.39, 127.31, 126.36 (d, *J* = 9.6 Hz), 120.23, 116.75, 63.06, 45.34, 31.28, 25.94, 21.08, 20.15. **HRMS (ESI) m/z: calcd for $C_{20}H_{22}O$ M278.1671, found 278.1665.**

(*R*)-4-(2-mesitylallyl)chromane (3ar)



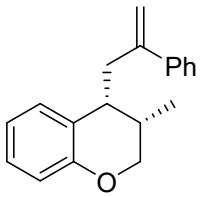
Colorless oil, 46% yield; $[a]^{20}_{D}$ = -121.9 (c = 5, **$CHCl_3$**); ee was determined to be 53% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 3.989 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 - 7.04 (m, 2H), 6.92 (s, 2H), 6.89 - 6.81 (m, 2H), 5.40 (q, *J* = 1.6 Hz, 1H), 5.03 (d, *J* = 1.6 Hz, 1H), 4.32 - 4.14 (m, 2H), 3.04 - 3.00 (m, 1H), 2.78 - 2.69 (m, 1H), 2.53 - 2.48 (m, 1H), 2.36 - 2.26 (m, 9H), 2.24 - 2.15 (m, 1H), 2.12 - 2.07 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.70, 146.54, 139.40, 136.13, 134.98, 134.77, 129.41, 128.47, 128.39, 127.34, 126.40, 120.35, 116.79, 115.45, 63.05, 44.82, 31.05, 26.45, 20.96, 20.18, 19.92. **HRMS (ESI) m/z: calcd for $C_{21}H_{24}O$ M292.1827, found 292.1821.**

(*R*)-4-(2-(naphthalen-2-yl)allyl)chromane (3as)



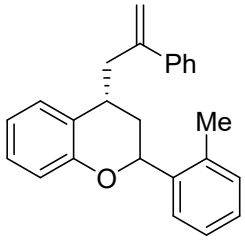
Colorless oil, 50% yield; $[a]^{20}_{D}$ = -36.4 (c = 5, **$CHCl_3$**); ee was determined to be 96% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 6.226 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.8 Hz, 1H), 7.91 - 7.84 (m, 3H), 7.66 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.55 - 7.46 (m, 2H), 7.26 - 7.21 (m, 1H), 7.16 - 7.07 (m, 1H), 6.94 - 6.87 (m, 1H), 6.83 (dd, *J* = 8.2, 1.3 Hz, 1H), 5.54 (d, *J* = 1.4 Hz, 1H), 5.21 (s, 1H), 4.26 - 4.08 (m, 2H), 3.33 (ddd, *J* = 14.2, 4.5, 1.4 Hz, 1H), 3.00 - 2.88 (m, 1H), 2.75 - 2.62 (m, 1H), 2.00 - 1.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.54, 146.17, 137.88, 133.45, 132.95, 129.00, 128.18 (d), 127.63, 127.46, 126.35, 126.19, 126.06, 125.07, 124.67, 120.21, 116.87, 115.60, 63.22, 42.73, 31.56, 25.99. **HRMS (ESI) m/z: calcd for $C_{22}H_{20}O$ M300.1514, found 300.1509.**

(3*S*,4*R*)-3-methyl-4-(2-phenylallyl)chromane (3at)



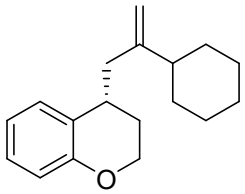
Colorless oil, 42% yield, >25:1 dr; $[a]^{20}_{D}$ = +1.7 (c = 5, **$CHCl_3$**); ee was determined to be 99% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 7.192 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.46 (m, 1H), 7.43 - 7.37 (m, 2H), 7.36 - 7.30 (m, 1H), 7.13 - 7.09 (m, 2H), 6.91 - 6.79 (m, 2H), 5.36 (d, *J* = 1.4 Hz, 1H), 5.06 (s, 1H), 4.19 (dd, *J* = 11.0, 2.3 Hz, 1H), 3.94 (ddd, *J* = 11.0, 2.7, 1.4 Hz, 1H), 3.03 (dd, *J* = 14.6, 4.5 Hz, 1H), 2.69 (dd, *J* = 14.6, 10.2 Hz, 1H), 2.51 (dd, *J* = 10.1, 4.5 Hz, 1H), 2.08 - 2.01 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ153.73, 146.50, 140.86, 130.56, 128.55, 127.65, 127.29, 126.38, 124.97, 120.34, 116.51, 114.90, 66.78, 44.62, 38.57, 29.00, 17.34. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}O$ M264.1514, found 264.1506.**

(4*R*)-4-(2-phenylallyl)-2-(o-tolyl)chromane (3au)



Colorless oil, 40% yield, 2.8:1 dr; $[a]^{20}_{D}$ = -103.6 (c = 6, **$CHCl_3$**); ee was determined to be 98%/96% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 99/1, 0.8 mL/min, 254 nm); tr (major) = 19.091 and 23.480 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 - 7.48 (m, 12H), 7.46 - 7.39 (m, 8H), 7.36 - 7.28 (m, 8H), 7.24 - 7.15 (m, 13H), 7.01 - 6.92 (m, 8H), 5.40 - 5.31 (m, 7H), 5.18 - 5.01 (m, 5H), 3.60 - 3.14 (m, 4H), 3.16 - 3.14 (m, 4H), 2.89 - 2.82 (m, 3H), 2.41 (s, 9H), 2.25 (s, 3H), 2.17 - 2.09 (m, 4H), 1.91 - 1.68 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ155.48, 154.95, 146.48, 146.37, 140.53, 140.43, 139.78, 139.54, 134.83, 134.43, 130.46, 130.42, 129.60, 128.63, 128.54, 127.78, 127.73, 127.64, 127.57, 127.47, 127.02, 126.46, 126.37, 126.28, 125.97, 125.92, 125.72, 125.56, 120.62, 120.36, 117.25, 117.11, 115.50, 115.11, 74.82, 70.21, 44.10, 41.58, 35.16, 32.96, 32.37, 31.59, 19.17, 18.95. **HRMS (ESI) m/z: calcd for $C_{25}H_{24}O$ M340.1827, found 340.1823.**

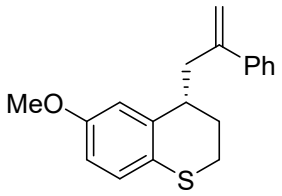
(*R*)-4-(2-cyclohexylallyl)chromane (3av)



Colorless oil, 85% yield; $[a]^{20}_{D}$ = +143.0 (c = 5, **$CHCl_3$**); ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 4.277 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 - 7.17 (m, 1H), 7.15 - 7.10 (m, 1H), 6.92 - 6.87 (m, 1H), 6.86 - 6.82 (m, 1H), 4.91 (s, 1H), 4.79 (s, 1H), 4.23 - 4.14 (m, 2H), 3.05 - 2.97 (m, 1H), 2.66 (dd, *J* = 14.7, 4.4 Hz, 1H), 2.26 - 2.17 (m, 1H), 2.08 - 1.98 (m, 1H), 1.98 - 1.91 (m, 2H), 1.89 - 1.77 (m, 4H), 1.77 - 1.71 (m, 1H), 1.39 - 1.24 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.57, 152.45, 129.16, 127.32, 126.56, 120.14, 116.81, 109.63, 63.22, 43.52, 42.60, 32.95, 32.21,

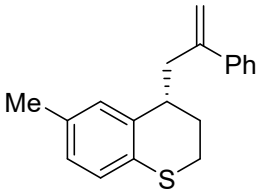
31.40, 26.97, 26.76, 26.42, 25.97. **HRMS (ESI) m/z: calcd for $C_{18}H_{24}O$ M256.1827, found 256.1819.**

(*R*)-6-methoxy-4-(2-phenylallyl)thiochromane (3aw)



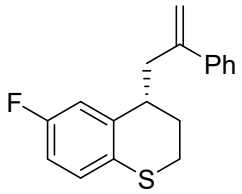
Colorless oil, 57% yield; $[a]^{20}_D$ = +61.7 (c = 5.1, **$CHCl_3$**); ee was determined to be 91% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 7.819 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 -7.45 (m, 2H), 7.43 - 7.36 (m, 2H), 7.36 - 7.29 (m, 1H), 7.05 - 7.02 (m, 1H), 6.72 - 6.69 (m, 1H), 6.62 - 6.61 (m, 1H), 5.35 (s, 1H), 5.07 (s, 1H), 3.77 (m, 3H), 3.21 - 3.15 (m, 1H), 3.01 - 2.96 (m, 1H), 2.92 - 2.82(m, 2H), 2.76 - 2.70 (m, 1H), 2.21 - 2.06 (m, 1H), 1.90 - 1.82 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ156.52, 146.21, 140.56, 138.57, 128.58, 127.70. 127.43, 126.38, 123.13, 112.71, 55.38, 40.79, 35.91, 25.32, 22.61. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}SO$ M296.1235, found 296.1229.**

(*R*)-6-methyl-4-(2-phenylallyl)thiochromane (3ax)



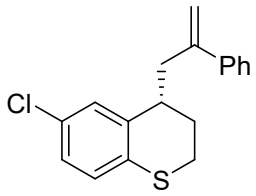
Colorless oil, 61% yield; $[a]^{20}_D$ = +52.2 (c = 5.3, **$CHCl_3$**). ee was determined to be 94% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 99/1, 0.5 mL/min, 254 nm); tr (major) = 9.127 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 2H), 7.44 (s, 2H), 7.38 - 7.31 (m, 1H), 7.05 - 7.00 (m, 1H), 6.92 (m, 1H), 6.86 (m, 1H), 5.36 (m, 1H), 5.11 - 5.05 (m, 1H), 3.26 (s, 1H), 2.99 (m, 1H), 2.93 (m, 2H), 2.77 - 2.67 (m, 1H), 2.29 (m, 3H), 2.16 - 2.06 (m, 1H), 1.90 - 1.78 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.27, 140.63, 137.02, 133.34, 130.54, 128.57, 127.68, 127.55, 126.42, 115.15, 40.92, 35.4, 24.89, 22.43, 20.92. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}S$ $[M+H]^+$281.1364, found 281.1357.**

(*R*)-6-fluoro-4-(2-phenylallyl)thiochromane (3ay)



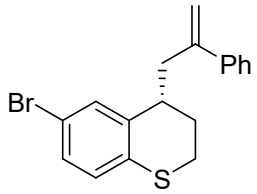
Colorless oil, 80% yield; $[a]^{20}_{D}$ = +11.2 (c = 5.1, **$CHCl_3$**); ee was determined to be 85% by HPLC analysis with a Chiralcel OJ-3 column (hexane/2-propanol = 99/1, 0.5 mL/min, 254 nm); tr (major) = 24.720 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.51 - 7.49 (m, 2H), 7.45 - 7.42 (m, 2H), 7.38 -7.36 (m, 1H), 7.09 - 7.07 (m, 1H), 6.86 - 6.82 (m, 1H), 6.80 - 6.78 (m, 1H), 5.38 (s, 1H), 5.08 (s, 1H), 3.24 - 3.19 (m, 1H), 3.00 - 2.96 (m, 1H), 2.94 - 2.86 (m, 2H), 2.75 - 2.71 (m, 1H), 2.15 - 2.09 (m, 1H), 1.87 - 1.84 (m, 1H). ^{13}C NMR (125 MHz, CDCl3) δ 145.87, 140.36, 128.66, 127.81, 127.70 (d, *J* = 7.6 Hz), 126.37, 116.46, 116.29, 115.46, 114.08, 113.91, 40.74, 35.76, 24.92, 22.54. ^{19}F NMR (376 MHz, $CDCl_3$): δ -119.51. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}SF$ M284.1035, found 284.1030.**

(*R*)-6-chloro-4-(2-phenylallyl)thiochromane (3az)



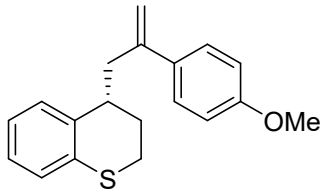
Colorless oil, 66% yield; $[a]^{20}_{D}$ = +75.3 (c = 5.8, **$CHCl_3$**); ee was determined to be 84% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 99/1, 0.5 mL/min, 254 nm); tr (major) = 10.670 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.48 - 7.47 (m, 2H), 7.43 - 7.40 (m, 2H), 7.36 - 7.32 (m, 1H), 7.04 (s, 2H), 6.99 (s, 1H), 5.35 (s, 1H), 5.06 (s, 1H), 3.24 - 3.17 (m, 2H), 2.96 - 2.83 (m, 3H), 2.72 - 2.67 (m, 1H), 2.14 - 2.08 (m, 1H), 1.86 - 1.78 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ145.81, 140.35, 138.68,129.58, 129.05, 128.66, 127.81, 127.68, 126.71, 126.38, 115.49, 40.69, 35.5, 24.59, 22.44. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}SCl$ M300.0739, found 300.0731; calcd for $C_{19}H_{20}S^{37}Cl$ M302.0710, found 302.0699.**

(*R*)-6-bromo-4-(2-phenylallyl)thiochromane (3ba):



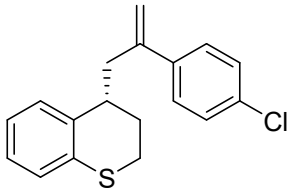
Colorless oil, 82% yield; $[a]^{20}_{D}$ = +27.0 (c = 5.2, **$CHCl_3$**); ee was determined to be 85% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 5.416 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.48 - 7.46 (m, 2H), 7.43 -7.39 (m, 2H), 7.36 - 7.32 (m, 1H), 7.19 - 7.16 (m, 1H), 7.13 -7.12 (d, *J* = 1.8 Hz, 1H), 6.98 - 6.96 (d, *J* = 8.4 Hz, 1H), 5.35 (s, 1H), 5.05 (s, 1H), 7.30 -7.32 (m, 1H), 3.23 - 3.16 (m, 1H), 2.95 - 2.83 (m, 3H), 2.71 - 2.66 (m, 1H), 2.14 - 2.08 (m, 1H), 1.85 - 1.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ145.80, 140.34,139.03, 131.56, 129.53, 128.66, 127.98, 127.80, 126.38, 116.76, 115.51, 40.68, 35.44, 24.52, 22.39. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}SBr$ M344.0234, found 344.0232; calcd for $C_{18}H_{17}S^{81}Br$ M346.0214, found 346.0211.**

(*R*)-4-(2-(4-methoxyphenyl)allyl)thiochromane (3bb)



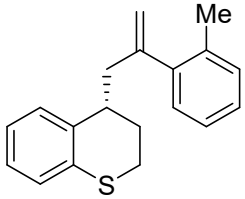
Colorless oil, 35% yield; $[a]^{20}_{D}$ = +49.2 (c = 5.3, **$CHCl_3$**); ee was determined to be 81% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 6.947 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.44 - 7.42 (m, 2H), 7.12 - 6.99 (m, 4H), 6.95 - 6.93 (m, 2H), 0.86 (s, 1H), 4.97 (s, 1H), 3.85 (s, 3H), 3.27 - 3.19 (m, 1H), 2.95 - 2.87 (m, 3H), 2.86 - 2.83 (m, 1H), 2.14 - 2.10 (m, 1H), 1.89 - 1.80 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ159.24, 145.38, 137.2, 132.89, 132.24, 129.91, 127.49, 126.57, 126.51, 123.78, 113.91, 55.33, 41.04, 35.40, 24.71, 22.44. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}OS$ $[M+H]^+$297.1313, found 297.1304.**

(*R*)-4-(2-(4-chlorophenyl)allyl)thiochromane (3bc)



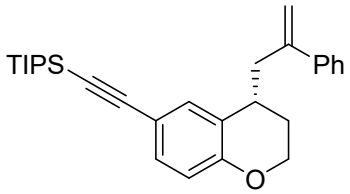
Colorless oil, 50% yield; $[a]^{20}_{D}$ = -20.6 (c = 4, **$CHCl_3$**); ee was determined to be 89% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 7.556 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.35 (m, 4H), 7.12 - 7.05 (m, 2H), 7.01 - 6.96 (m, 2H), 5.35 (s, 1H), 5.07 (s, 1H), 3.24 - 3.17 (m, 1H), 2.92 - 2.85 (m, 3H), 2.72 - 2.65 (m, 1H), 2.13 - 2.06 (m, 1H), 1.90 - 1.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ145.05, 139.00, 136.83, 133.47, 132.24, 129.83, 128.73, 127.68, 126.68, 126.58, 123.82, 115.72, 40.76, 35.49, 24.82, 22.41. **HRMS (ESI) m/z: calcd for $C_{18}H_{17}SCl$ M300.0739, found 300.0731; calcd for $C_{18}H_{17}S^{37}Cl$ M302.0710, found 302.0703.**

(*R*)-4-(2-(o-tolyl)allyl)thiochromane (3bd)



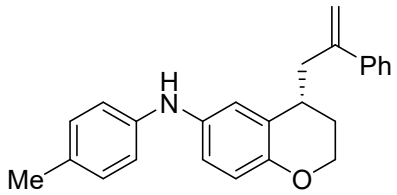
Colorless oil, 65% yield; $[a]^{20}_{D}$ = -119.6 (c = 5, **$CHCl_3$**); ee was determined to be 96% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 98/2, 1.0 mL/min, 254 nm); tr (major) = 4.922 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.27 - 7.24 (m, 4H), 7.16 - 7.14 (m, 1H), 7.11 - 7.07 (m, 1H), 7.03 - 6.98 (m, 1H), 5.30 (s, 1H), 5.10 (s, 1H), 3.28 - 3.21 (m, 1H), 2.94 - 2.82 (m, 3H), 2.73 - 2.66 (m, 1H), 2.74 (s, 3H), 2.30 - 2.25 (m, 1H), 2.01 - 1.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ147.44, 141.83, 137.50, 134.95, 132.49, 130.61, 129.82, 128.56, 127.21, 126.59, 125.74, 123.97, 117.00, 43.12, 35.53, 24.92, 22.63, 20.30. **HRMS (ESI) m/z: calcd for $C_{19}H_{20}S$ M280.1286, found 280.1278.**

(*R*)-triisopropyl((4-(2-phenylallyl)chroman-6-yl)ethynyl)silane (3be)



Colorless oil, 40% yield; $[a]^{20}_{D}$ = -76.8 (c = 5.2, **$CHCl_3$**). ee was determined to be 99% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 99/1, 0.2 mL/min, 254 nm); tr (major) = 18.134 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 - 7.46 (m, 2H), 7.41 - 7.36 (m, 2H), 7.34 - 7.29 (m, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.21 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 5.36 (s, 1H), 5.08 (s, 1H), 4.24 - 4.04 (m, 2H), 3.16 (ddd, *J* = 14.4, 4.9, 1.5 Hz, 1H), 2.89 - 2.75 (m, 1H), 2.66 - 2.50 (m, 1H), 1.96 - 1.72 (m, 2H), 1.14 (s, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.77, 146.07, 140.44, 132.90, 131.51, 128.61, 127.78, 126.36, 126.02, 116.87, 115.29, 115.07, 107.49, 88.21, 63.41, 42.42, 31.18, 25.76, 18.75, 11.41. **HRMS (ESI) m/z: calcd for $C_{29}H_{38}OSi$ $[M+H]^+$431.2770, found 431.2761.**

(*R*)-4-(2-phenylallyl)-N-(p-tolyl)chroman-6-amine (3bf)



Colorless oil, 40% yield; $[a]^{20}_{D}$ = 7.6 (c = 5.1, **$CHCl_3$**). ee was determined to be 98% by HPLC analysis with a Chiralcel OD-H column (hexane/2-propanol = 95/5, 1.0 mL/min, 254 nm); tr (major) = 17.573 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 - 7.40 (m, 2H), 7.37 - 7.31 (m, 2H), 7.31 - 7.26 (m, 1H), 7.06 - 7.01 (m, 2H), 6.93 - 6.88 (m, 1H), 6.86 - 6.80 (m, 3H), 6.75 - 6.71 (m, 1H), 5.36 (s, 1H), 5.09 (s, 1H), 4.18 - 4.05 (m, 2H), 3.13 (ddd, *J* = 14.3, 4.6, 1.5 Hz, 1H), 2.84 - 2.73 (m, 1H), 2.63 - 2.51 (m, 1H), 2.28 (s, 3H), 1.94 - 1.83 (m, 1H), 1.82 - 1.74 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.78, 146.20, 142.66, 140.45, 135.81, 129.80, 129.05, 128.53, 127.67, 126.75, 126.28, 120.71, 120.11, 117.34, 116.25, 115.08, 63.18, 42.76, 31.52, 26.10, 20.56. **HRMS (ESI) m/z: calcd for $C_{25}H_{25}ON$ $[M+H]^+$356.2014, found 356.2004.**

5. Crystal data and structure refinement of compound 3ao

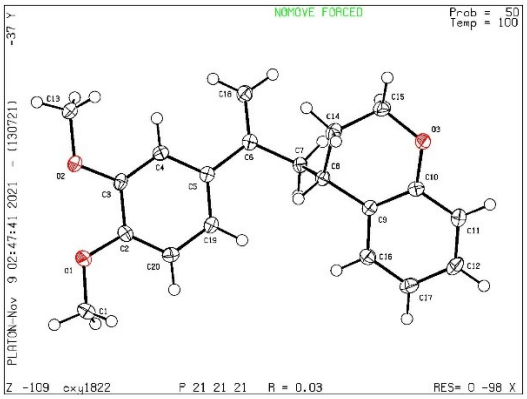


Table S1 Crystal data and structure refinement for compound 3ao.

Identification code	3ao
Empirical formula	$C_{20}H_{22}O_3$
Formula weight	310.37
Temperature/K	100
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.4702(3)
b/Å	9.9613(4)
c/Å	25.6312(11)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1651.97(12)
Z	4
ρ_{calc}g/cm^3	1.248
μ/mm^{-1}	0.660
F(000)	664.0
Crystal size/mm^3	0.41 × 0.35 × 0.33
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.898 to 137.206
Index ranges	-7 ≤ h ≤ 7, -10 ≤ k ≤ 12, -30 ≤ l ≤ 30
Reflections collected	19161
Independent reflections	3041 [R_{int} = 0.0370, R_{sigma} = 0.0217]
Data/restraints/parameters	3041/0/211
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0252, wR_2 = 0.0639
Final R indexes [all data]	R_1 = 0.0261, wR_2 = 0.0645
Largest diff. peak/hole / e Å^{-3}	0.16/-0.14
Flack parameter	-0.12(6)

Table S2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for compound 3ao. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	-7735.9(18)	-5095.8(12)	-4714.8(4)	24.8(3)
O2	-4537.1(18)	-3596.8(11)	-4555.0(4)	22.6(3)
O3	-8212.8(18)	-3287.8(11)	-981.5(4)	21.9(3)
C1	-9477(3)	-5936.4(19)	-4821.5(7)	30.9(4)
C2	-7077(2)	-5033.1(16)	-4209.2(5)	18.4(3)
C3	-5314(2)	-4222.3(15)	-4122.6(6)	17.5(3)
C4	-4530(2)	-4083.0(14)	-3625.7(6)	17.2(3)
C5	-5452(2)	-4725.8(14)	-3194.0(5)	15.7(3)
C6	-4565(2)	-4549.1(14)	-2661.5(5)	16.3(3)
C7	-5761(2)	-5080.5(15)	-2198.7(5)	16.4(3)
C8	-7698(2)	-4232.1(14)	-2064.8(6)	16.5(3)
C9	-9008(2)	-4928.4(15)	-1656.8(6)	16.0(3)
C10	-9215(2)	-4421.7(15)	-1151.1(6)	17.6(3)
C11	-10515(3)	-5041.7(17)	-788.5(6)	21.8(3)
C12	-11603(3)	-6180.3(17)	-928.3(6)	24.0(3)
C13	-2841(3)	-2693.4(17)	-4472.1(6)	26.7(4)
C14	-7142(3)	-2819.3(15)	-1875.3(6)	21.1(3)
C15	-6523(3)	-2853.0(16)	-1304.6(6)	22.6(3)
C16	-10121(2)	-6087.9(15)	-1783.0(6)	19.2(3)
C17	-11399(3)	-6716.9(17)	-1427.5(6)	22.9(3)
C18	-2771(3)	-3928.7(16)	-2579.4(6)	20.9(3)
C19	-7185(2)	-5511.1(14)	-3287.5(6)	18.0(3)
C20	-7993(3)	-5668.7(15)	-3790.7(6)	19.8(3)

Table S3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for compound 3ao. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	27.8(6)	30.0(6)	16.7(5)	1.5(4)	-3.8(4)	-8.6(5)
O2	26.4(6)	25.2(6)	16.2(5)	3.9(4)	0.8(4)	-8.3(5)
O3	26.3(6)	20.4(5)	18.9(5)	-3.0(4)	3.8(4)	-5.4(5)
C1	30.8(9)	39.9(10)	21.8(8)	-2.8(7)	-5.0(7)	-12.7(8)
C2	20.0(7)	18.6(7)	16.5(7)	-0.6(5)	-1.7(6)	1.7(6)
C3	20.0(7)	15.7(7)	16.7(7)	2.7(5)	3.1(6)	1.2(6)
C4	16.7(7)	14.4(7)	20.4(7)	0.4(6)	0.6(6)	0.3(6)

C5	16.1(7)	13.5(6)	17.5(7)	0.7(5)	0.8(5)	3.4(6)
C6	17.9(7)	13.0(7)	18.0(7)	1.8(5)	0.5(6)	3.7(6)
C7	17.8(7)	15.7(7)	15.8(7)	1.4(5)	-0.4(5)	1.3(6)
C8	17.1(7)	16.1(7)	16.2(7)	2.1(5)	0.0(6)	0.9(6)
C9	14.6(7)	16.2(7)	17.4(7)	3.1(6)	-0.1(5)	2.4(6)
C10	17.5(7)	15.3(7)	20.0(7)	0.9(6)	-0.6(6)	0.6(6)
C11	22.9(7)	24.3(8)	18.3(7)	2.5(6)	2.5(6)	1.2(7)
C12	21.2(8)	25.6(8)	25.2(8)	8.4(6)	4.3(7)	-2.6(7)
C13	30.6(9)	29.2(8)	20.1(8)	3.2(6)	2.6(7)	-12.6(7)
C14	24.6(8)	15.8(7)	22.8(8)	2.0(6)	5.1(6)	0.2(6)
C15	23.7(8)	19.1(8)	25.0(8)	-3.8(6)	4.0(6)	-5.3(7)
C16	19.3(7)	19.2(7)	19.1(7)	0.2(6)	-1.2(6)	0.7(6)
C17	20.6(7)	20.8(8)	27.4(8)	4.1(6)	-2.3(6)	-4.2(6)
C18	18.3(7)	25.7(8)	18.8(7)	4.0(6)	-1.7(6)	-0.1(6)
C19	18.6(7)	17.8(7)	17.6(7)	2.6(5)	2.4(6)	0.5(6)
C20	19.4(7)	17.9(7)	22.2(7)	-0.4(6)	-0.1(6)	-2.3(6)

Table S4 Bond Lengths for compound 3ao.

Atom	Atom	Length/Å		Atom	Atom	Length/Å
O1	C1	1.430(2)		C6	C18	1.332(2)
O1	C2	1.3655(17)		C7	C8	1.550(2)
O2	C3	1.3672(18)		C8	C9	1.514(2)
O2	C13	1.435(2)		C8	C14	1.532(2)
O3	C10	1.3731(19)		C9	C10	1.397(2)
O3	C15	1.4384(19)		C9	C16	1.399(2)
C2	C3	1.415(2)		C10	C11	1.397(2)
C2	C20	1.379(2)		C11	C12	1.382(2)
C3	C4	1.378(2)		C12	C17	1.393(2)
C4	C5	1.411(2)		C14	C15	1.517(2)
C5	C6	1.491(2)		C16	C17	1.381(2)
C5	C19	1.388(2)		C19	C20	1.401(2)
C6	C7	1.5118(19)				

Table S5 Bond Angles for compound 3ao.

Atom	Atom	Atom	Angle/°		Atom	Atom	Atom	Angle/°
C2	O1	C1	117.00(12)		C9	C8	C7	110.84(11)
C3	O2	C13	116.55(12)		C9	C8	C14	109.47(12)
C10	O3	C15	115.12(12)		C14	C8	C7	112.41(13)
O1	C2	C3	115.24(13)		C10	C9	C8	121.93(13)
O1	C2	C20	125.66(14)		C10	C9	C16	117.60(13)

C20	C2	C3	119.09(13)		C16	C9	C8	120.44(13)
O2	C3	C2	115.43(13)		O3	C10	C9	123.06(13)
O2	C3	C4	124.60(14)		O3	C10	C11	115.93(13)
C4	C3	C2	119.95(13)		C11	C10	C9	121.00(14)
C3	C4	C5	121.57(14)		C12	C11	C10	119.79(14)
C4	C5	C6	120.12(13)		C11	C12	C17	120.32(14)
C19	C5	C4	117.52(13)		C15	C14	C8	110.34(12)
C19	C5	C6	122.36(13)		O3	C15	C14	111.18(13)
C5	C6	C7	118.69(13)		C17	C16	C9	122.03(14)
C18	C6	C5	122.32(14)		C16	C17	C12	119.26(15)
C18	C6	C7	118.98(13)		C5	C19	C20	121.58(14)
C6	C7	C8	113.36(12)		C2	C20	C19	120.29(14)

Table S6 Torsion Angles for compound 3ao.

A	B	C	D	Angle/°		A	B	C	D	Angle/°
O1	C2	C3	O2	1.1(2)		C8	C9	C10	C11	176.70(14)
O1	C2	C3	C4	179.58(13)		C8	C9	C16	C17	-177.23(14)
O1	C2	C20	C19	-179.12(15)		C8	C14	C15	O3	-62.91(17)
O2	C3	C4	C5	177.93(13)		C9	C8	C14	C15	43.23(17)
O3	C10	C11	C12	179.27(14)		C9	C10	C11	C12	0.6(2)
C1	O1	C2	C3	178.20(14)		C9	C16	C17	C12	0.4(2)
C1	O1	C2	C20	-2.6(2)		C10	O3	C15	C14	47.98(18)
C2	C3	C4	C5	-0.4(2)		C10	C9	C16	C17	0.5(2)
C3	C2	C20	C19	0.0(2)		C10	C11	C12	C17	0.4(2)
C3	C4	C5	C6	-179.81(13)		C11	C12	C17	C16	-0.9(2)
C3	C4	C5	C19	0.1(2)		C13	O2	C3	C2	175.68(14)

Table S7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for compound 3ao.

Atom	*x*	*y*	*z*	U(eq)
H1A	-10672.52	-5619.65	-4621.61	46
H1B	-9154.99	-6862.27	-4720.93	46
H1C	-9796.46	-5903.37	-5195	46
H4	-3340.13	-3541.24	-3572.52	21
H7A	-4837.17	-5102.65	-1890.92	20
H7B	-6197.51	-6013.74	-2272.94	20
H8	-8545.5	-4140.78	-2389.12	20
H11	-10650.21	-4681.81	-446.93	26
H12	-12493.68	-6599.08	-682.68	29
H13A	-1638.44	-3198.51	-4347.78	40

H13B	-3230.76	-2020.59	-4211.04	40
H13C	-2496.28	-2243.92	-4800.89	40
H14A	-5984.95	-2461.38	-2086.3	25
H14B	-8344.57	-2216.3	-1921.04	25
H15A	-5339.62	-3471.91	-1258.86	27
H15B	-6076.84	-1945.66	-1194.31	27
H16	-9994.53	-6453.61	-2123.81	23
H17	-12130.88	-7506.84	-1522.31	28
H18A	-2008.62	-3580.33	-2865.72	25
H18B	-2253.5	-3834.62	-2234.42	25
H19	-7838.56	-5952.2	-3003.32	22
H20	-9176.87	-6215.78	-3844.03	24

Experimental

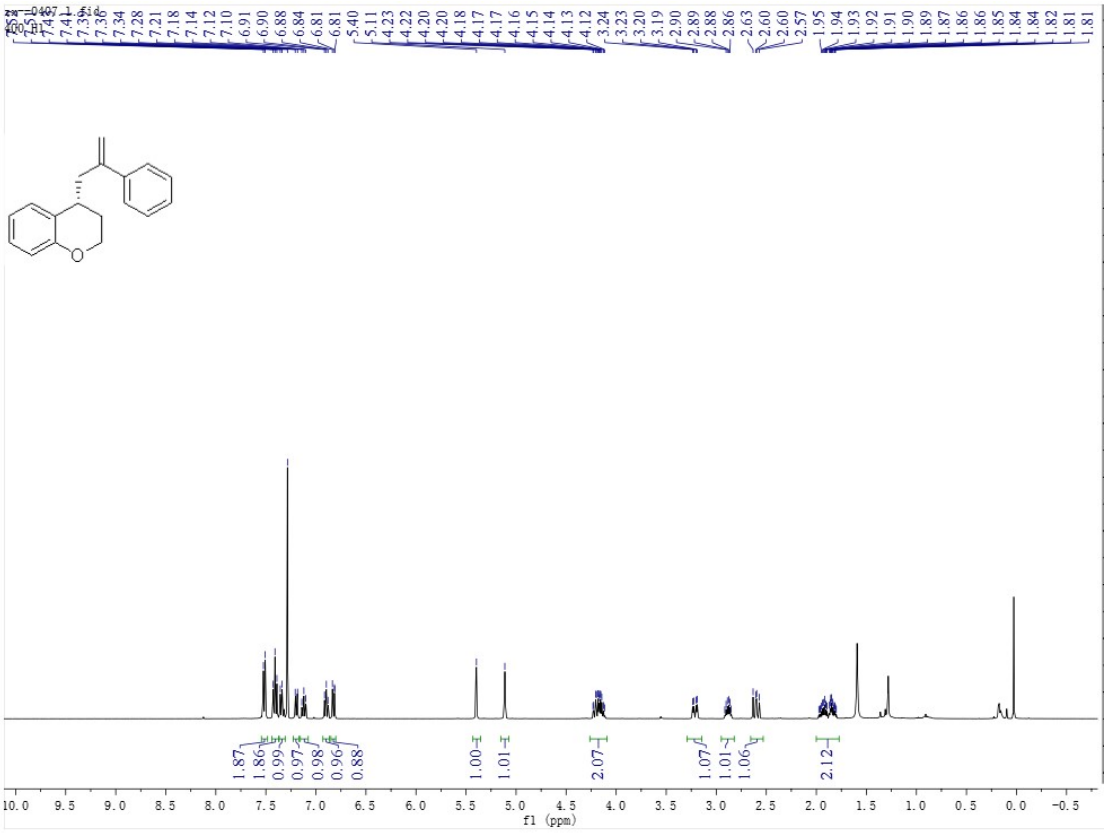
Single crystals of $C_{20}H_{22}O_3$ **[compound 3ao]** were **[]**. A suitable crystal was selected and **[]** on a **Bruker CMOS area detector** diffractometer. The crystal was kept at 100 K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

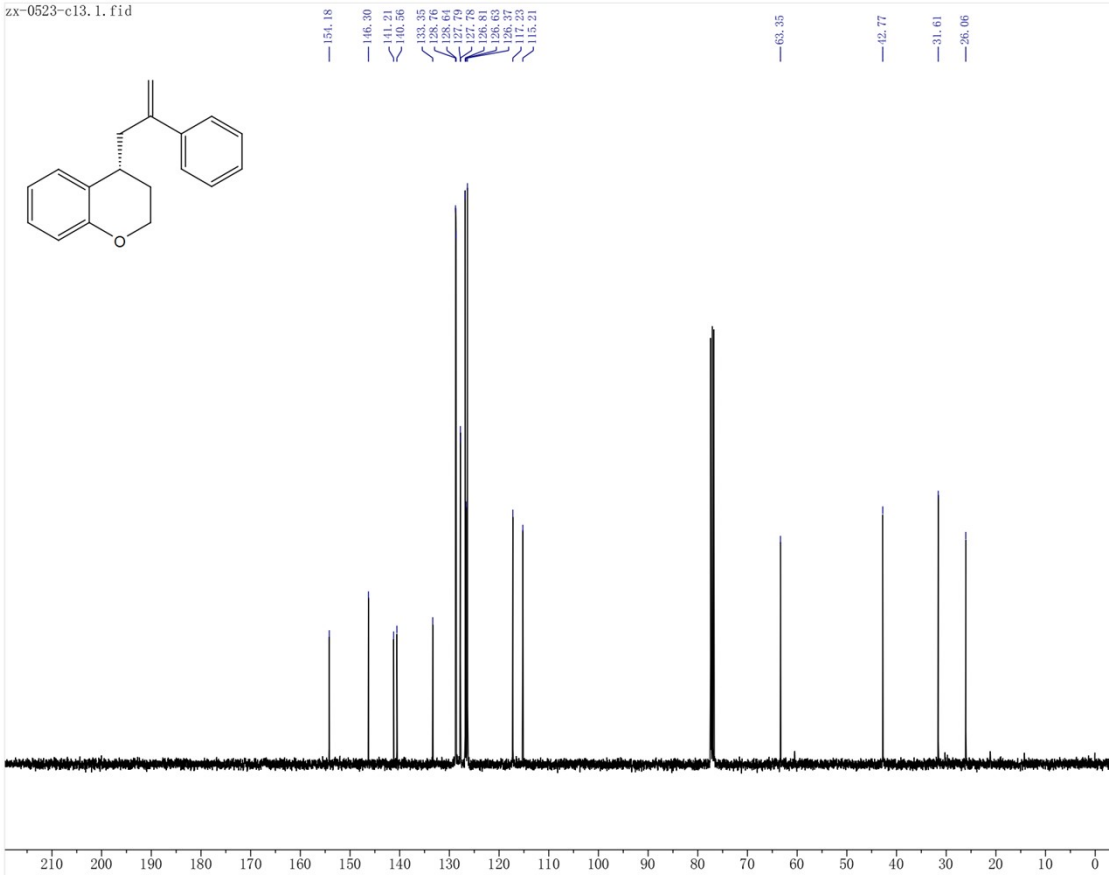
Crystal structure determination of [compound 3ao]

Crystal Data for $C_{20}H_{22}O_3$ (M =310.37 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 6.4702(3) Å, b = 9.9613(4) Å, c = 25.6312(11) Å, V = 1651.97(12) Å^3, Z = 4, T = 100 K, μ(CuKα) = 0.660 mm^{-1}, *Dcalc* = 1.248 g/cm^3, 19161 reflections measured (6.898° ≤ 2Θ ≤ 137.206°), 3041 unique (R_{int} = 0.0370, R_{sigma} = 0.0217) which were used in all calculations. The final R_1 was 0.0252 (I > 2σ(I)) and wR_2 was 0.0645 (all data).

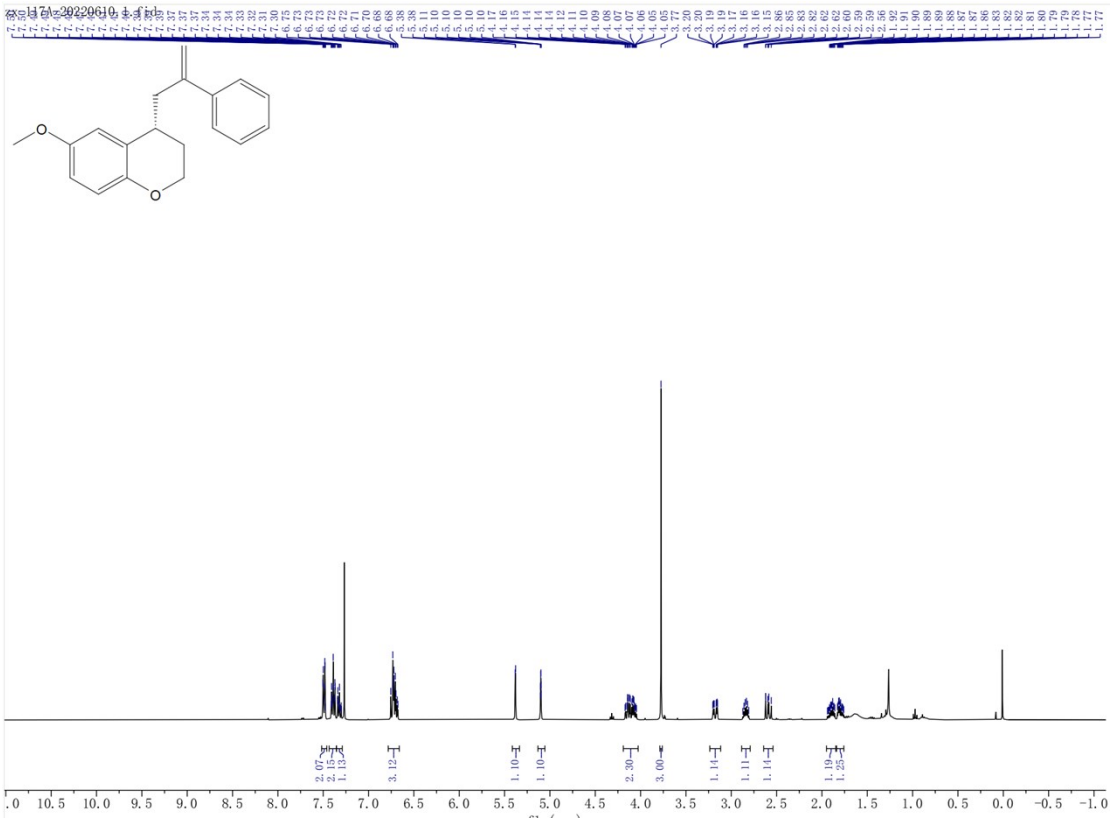
6. Copies of ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HPLC spectra of the products

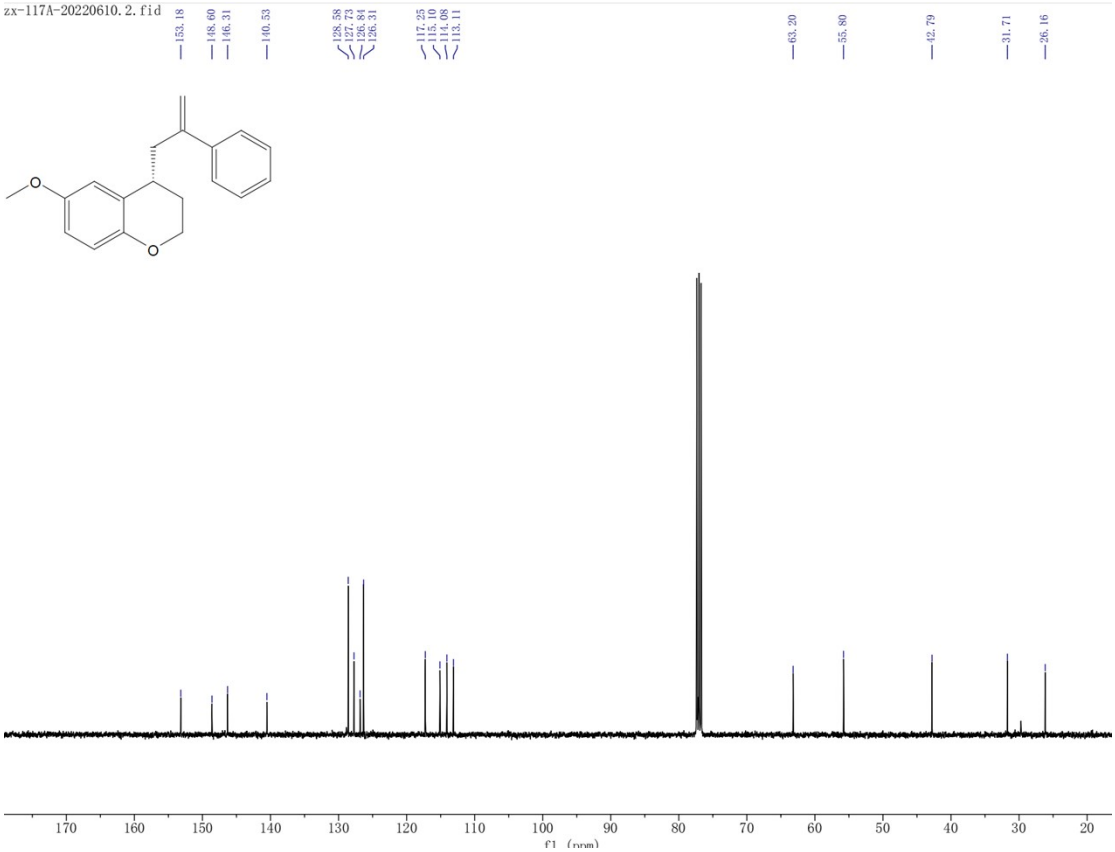
Compound 3aa



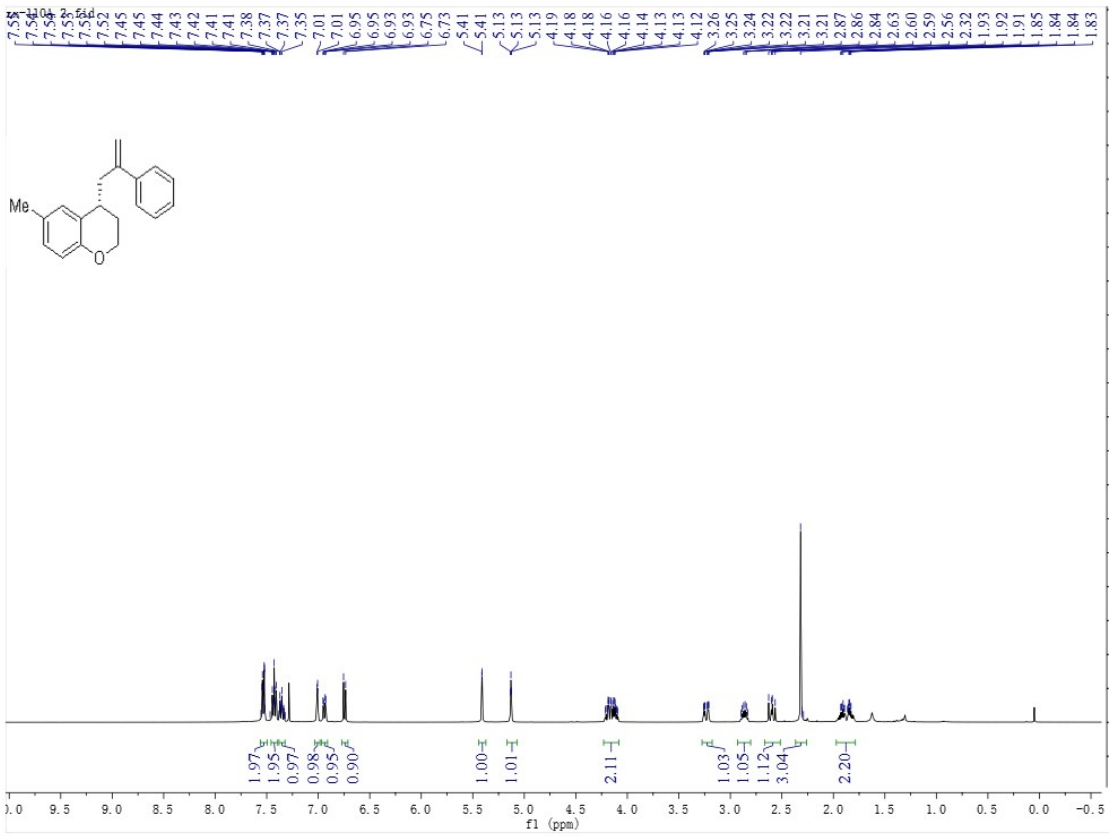


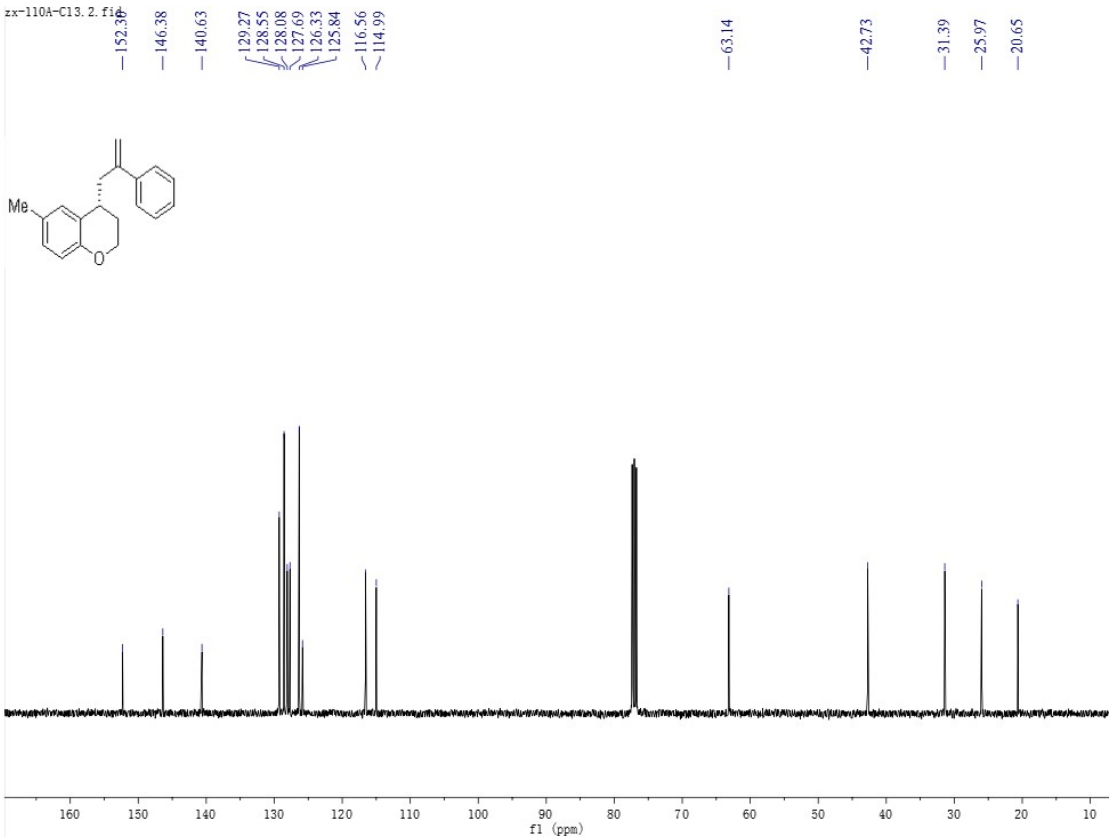
Compound 3ab



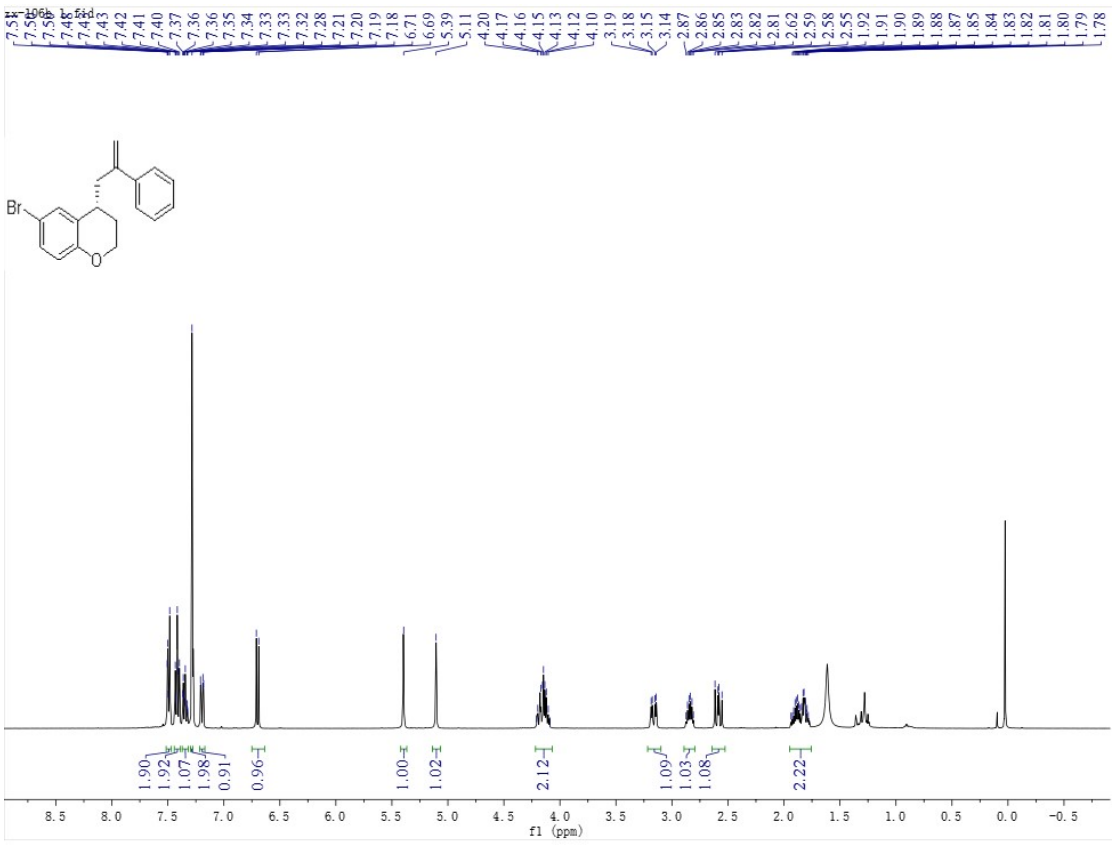


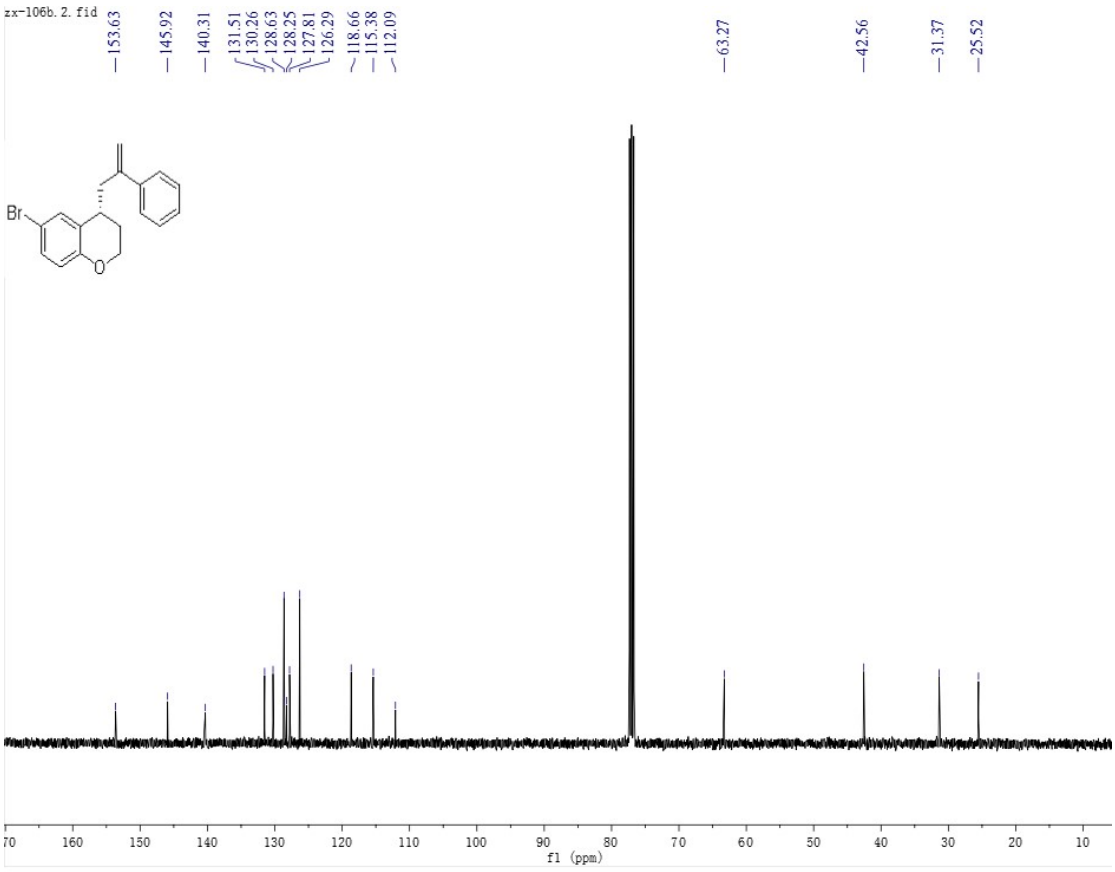
Compound 3ac



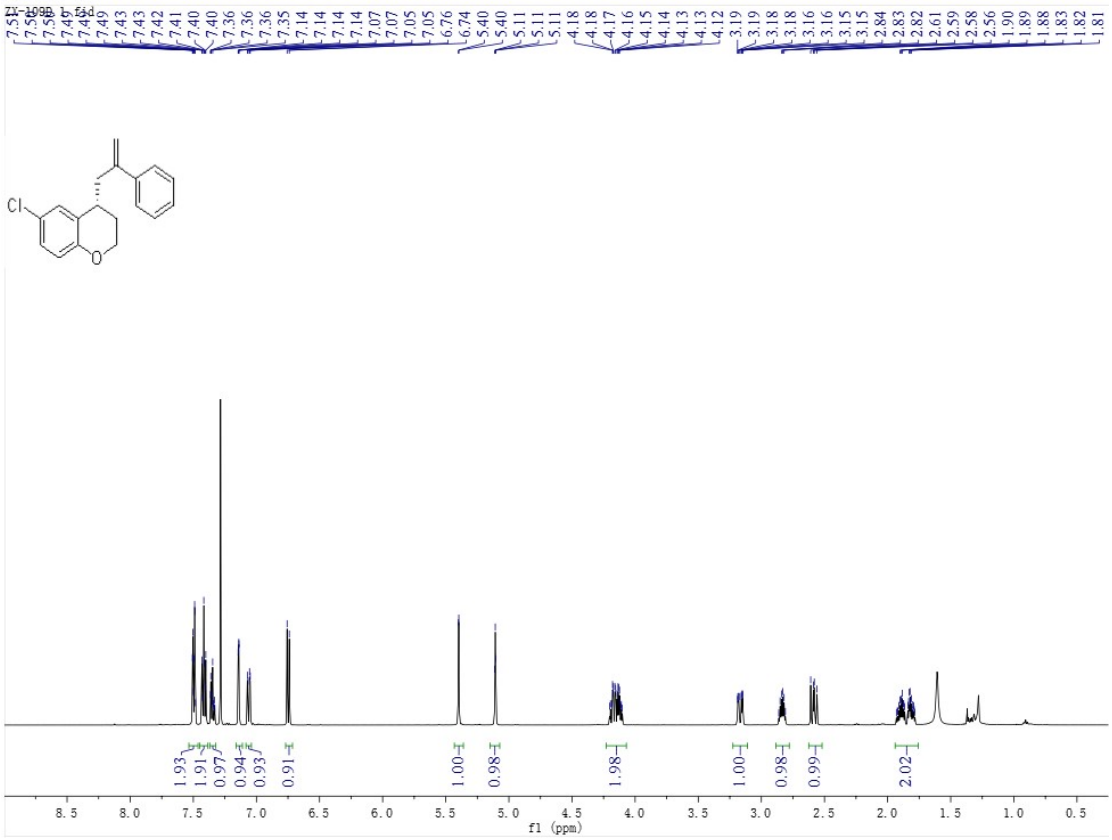


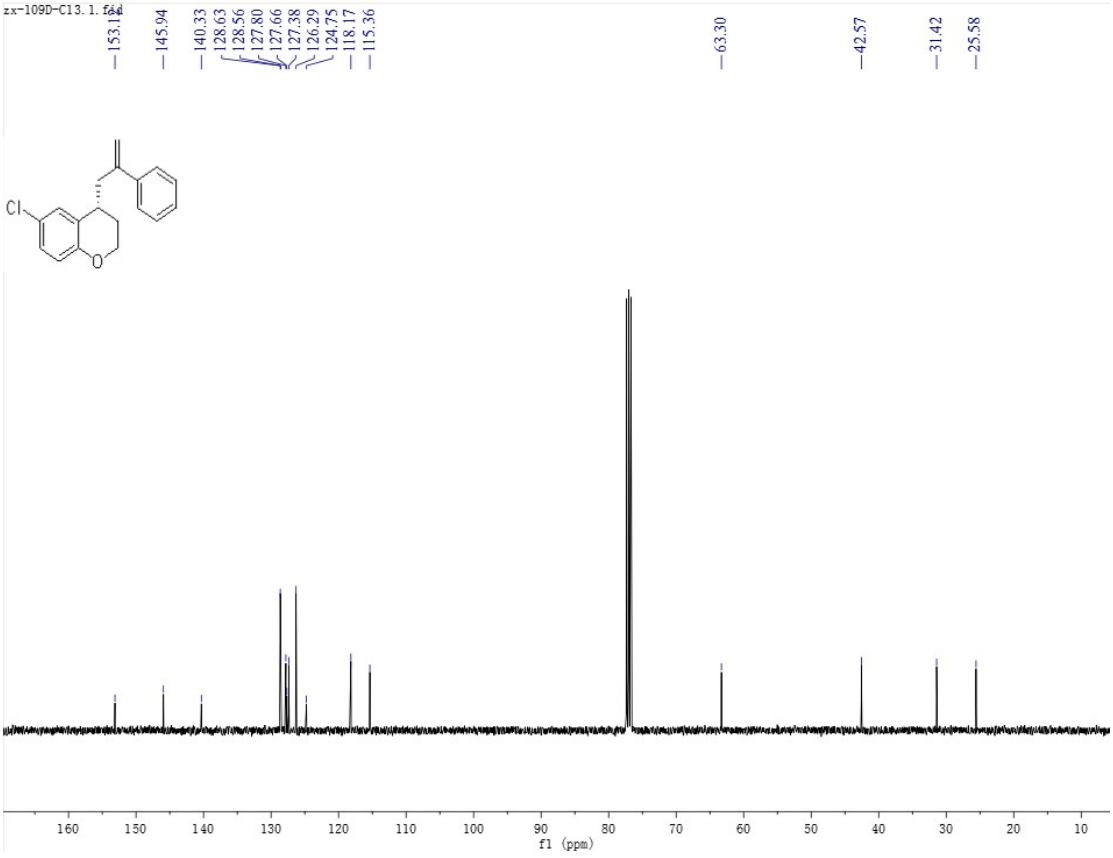
Compound 3ad



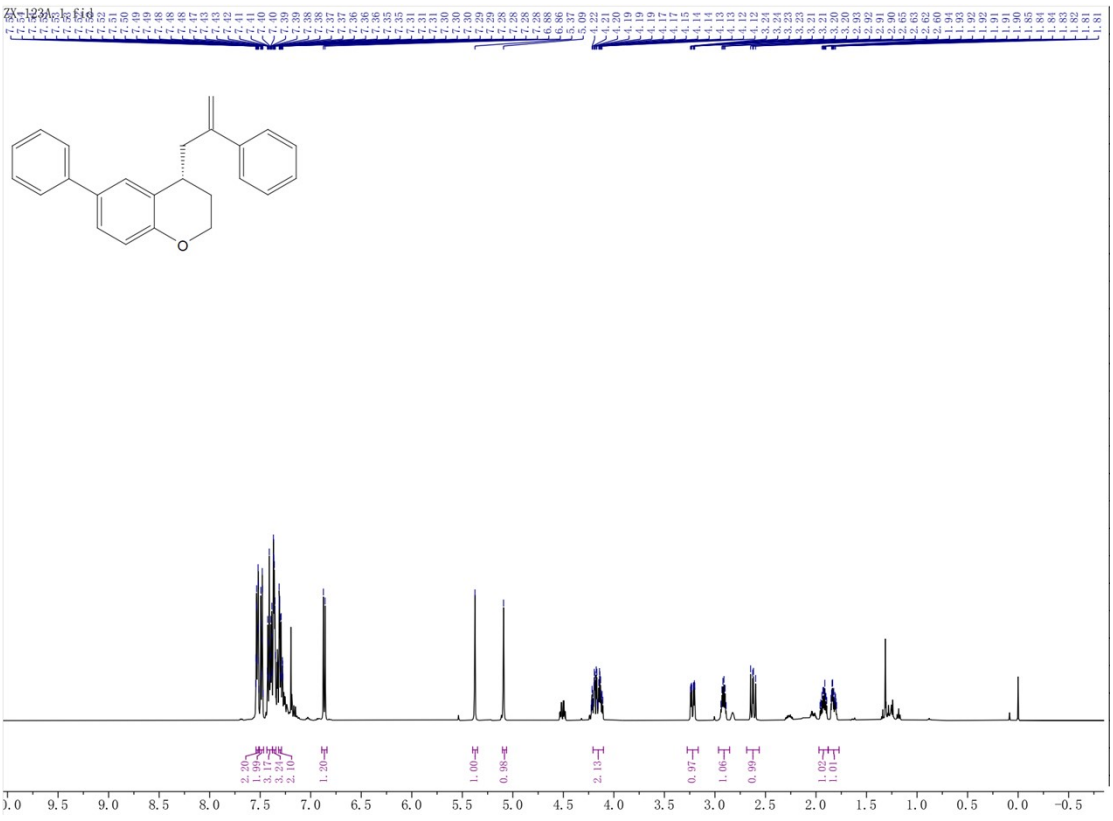


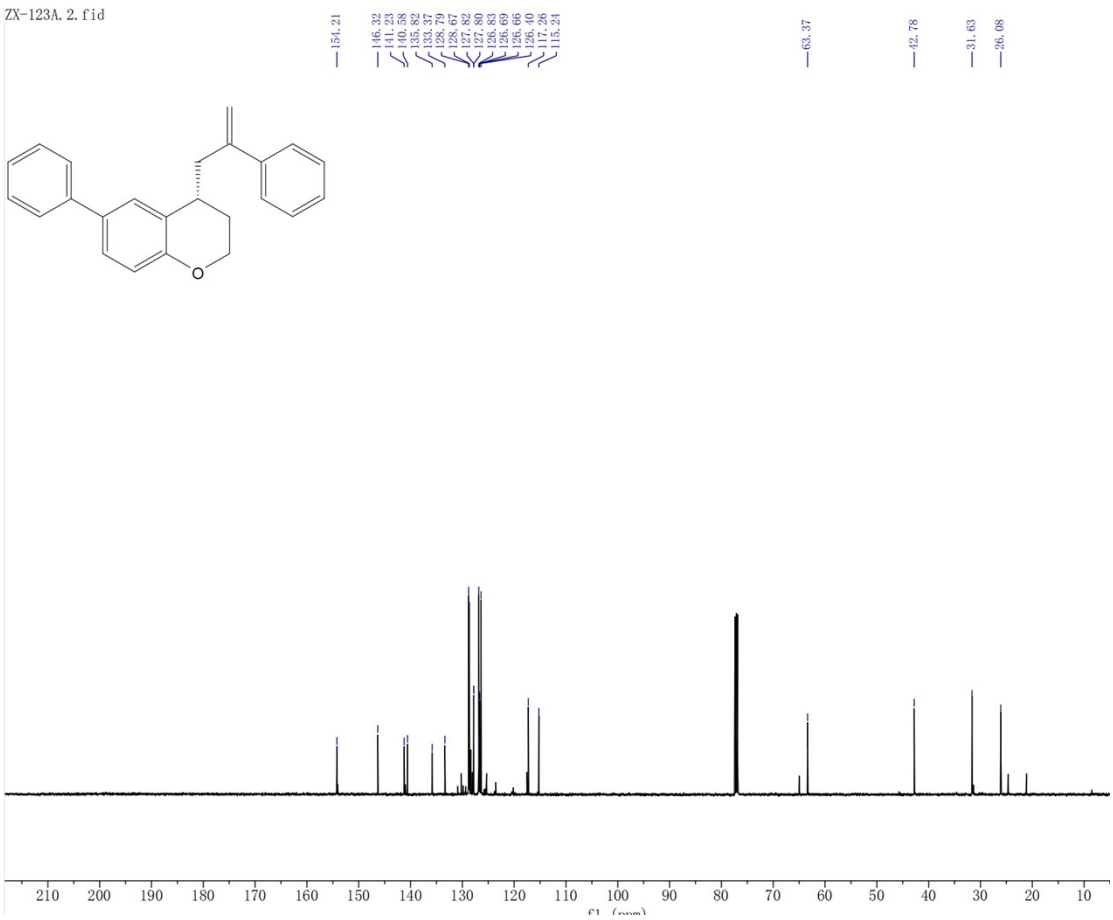
Compound 3ae



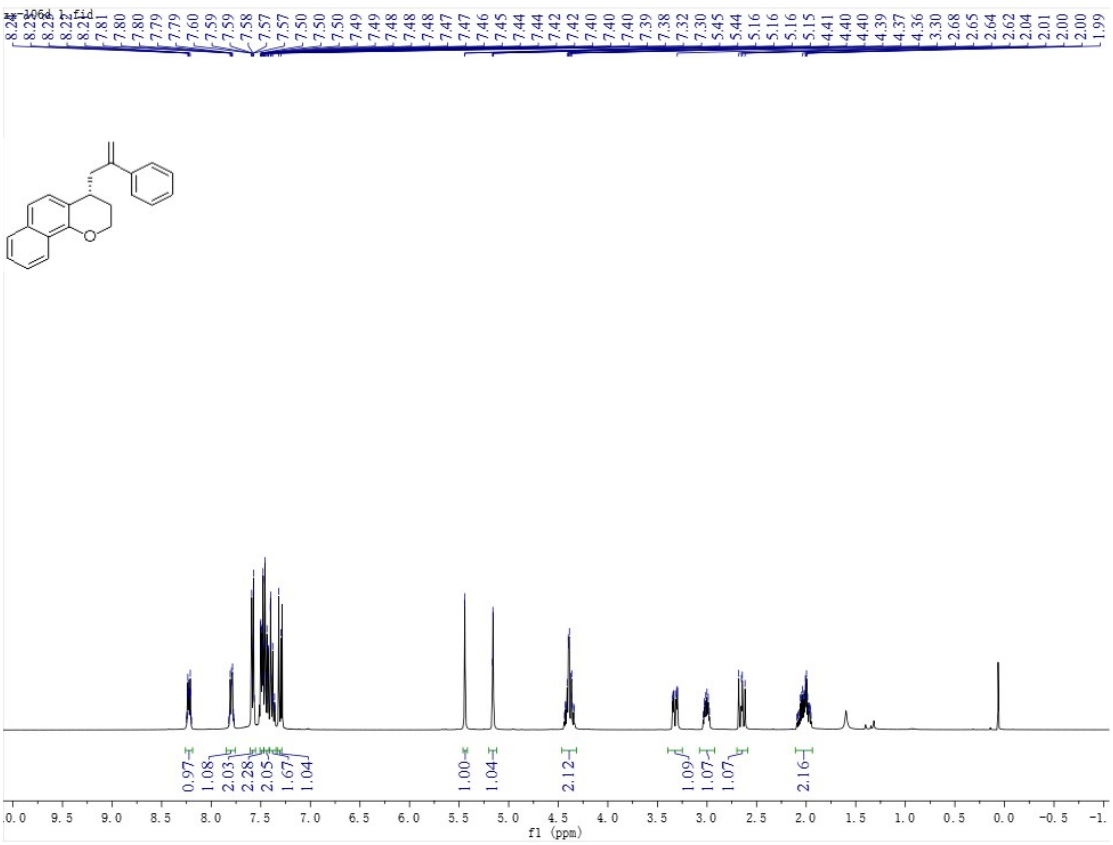


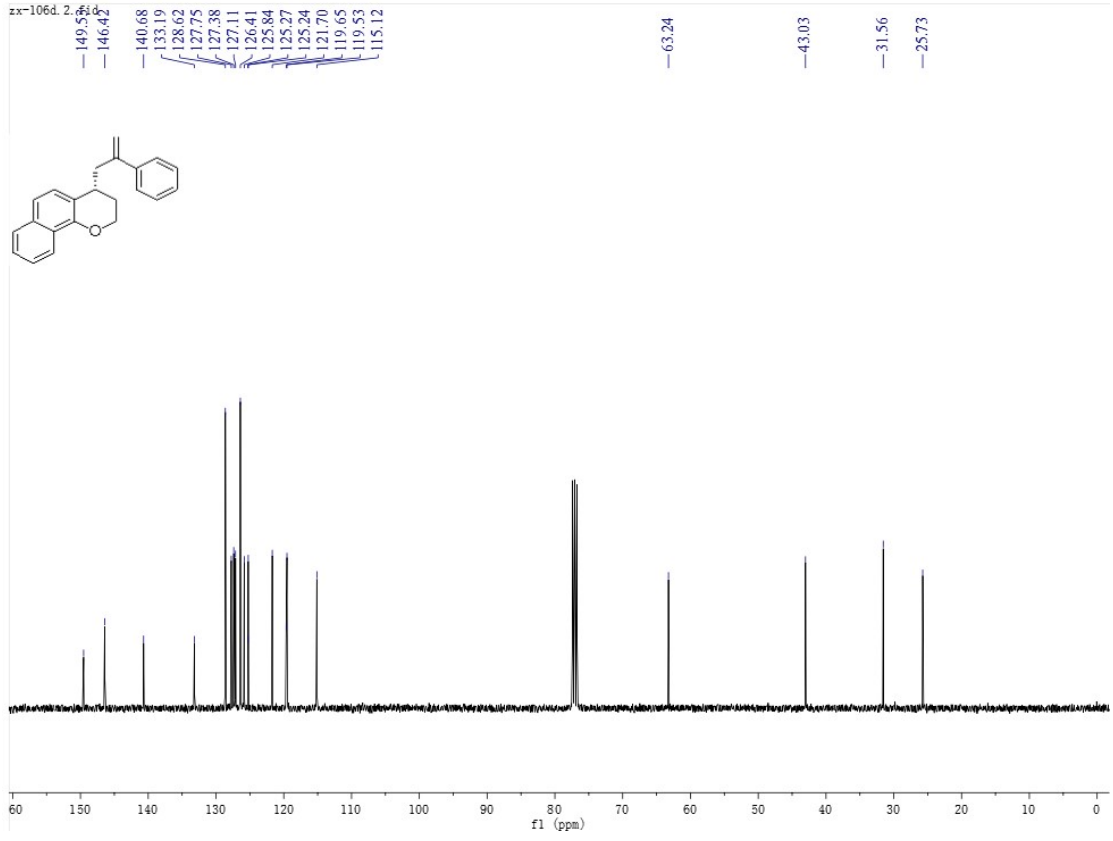
Compound 3af



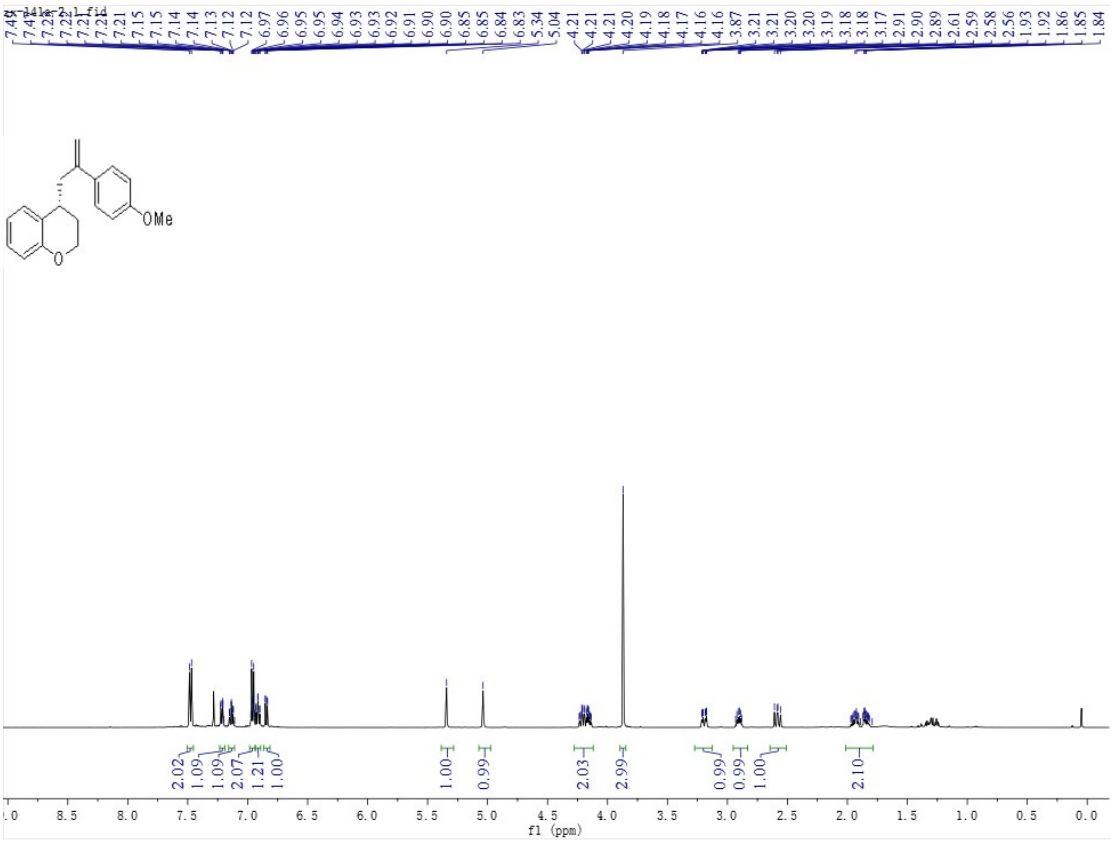


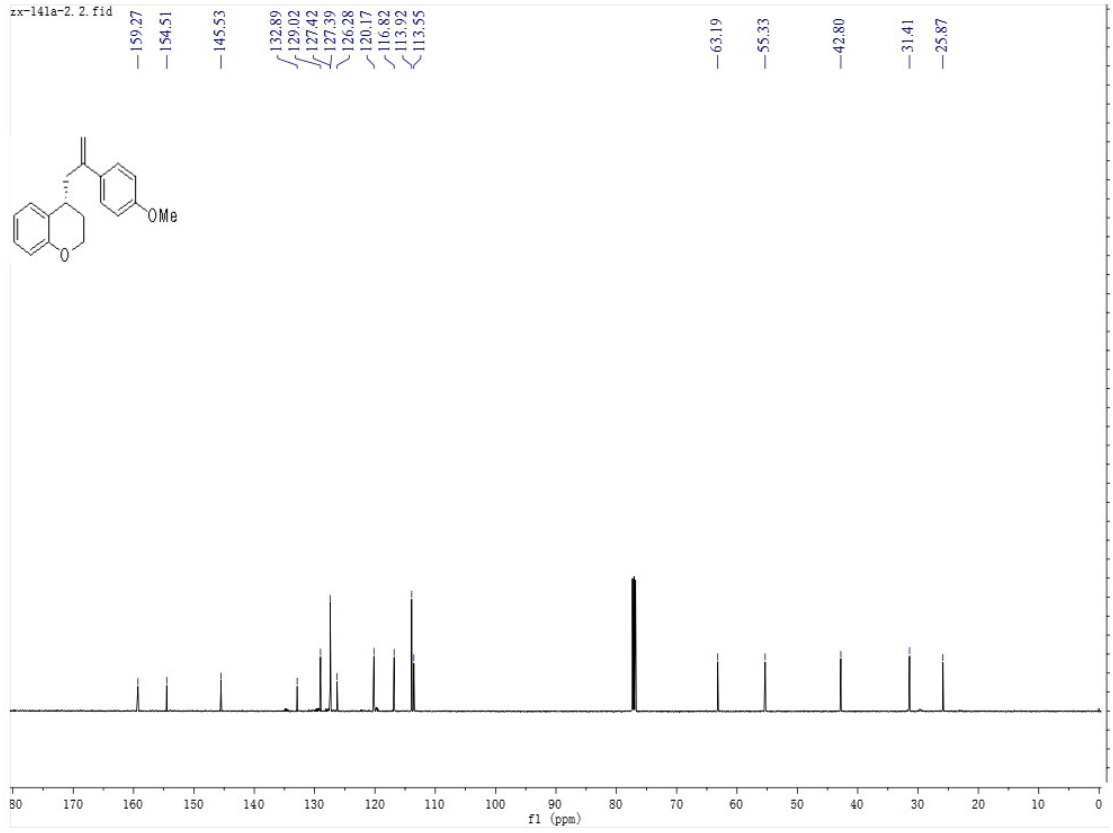
Compound 3ag



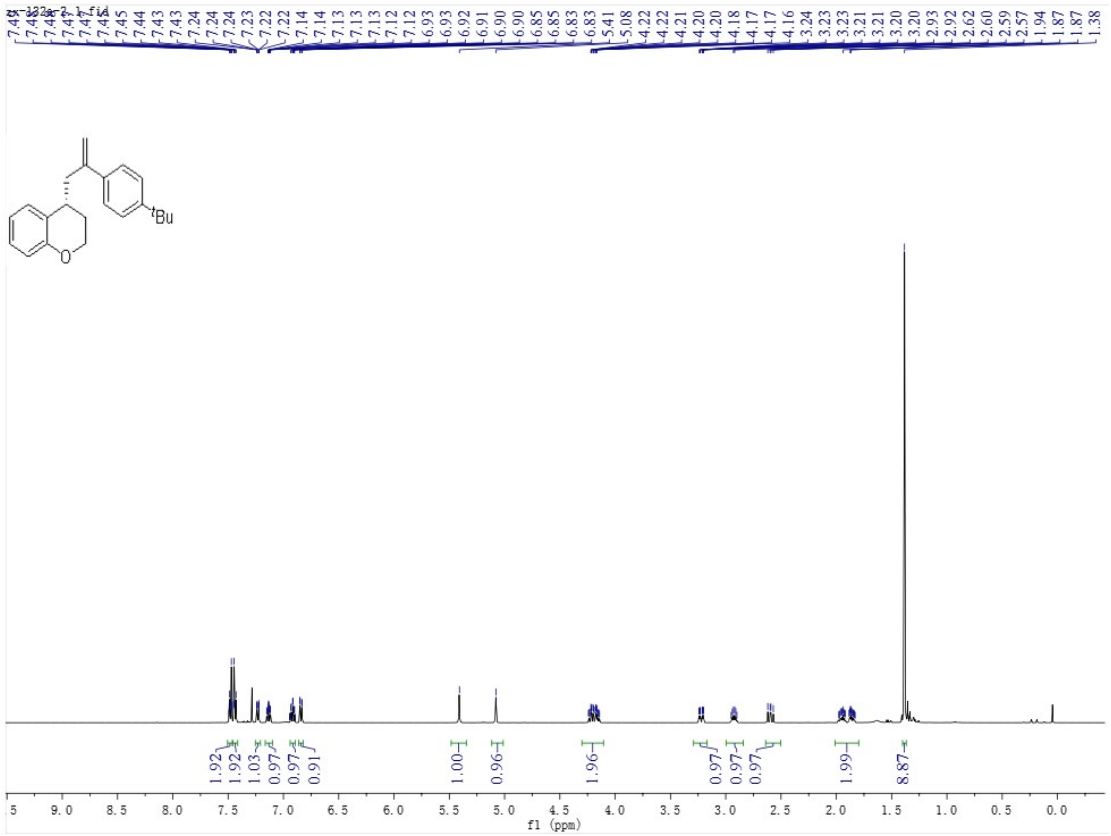


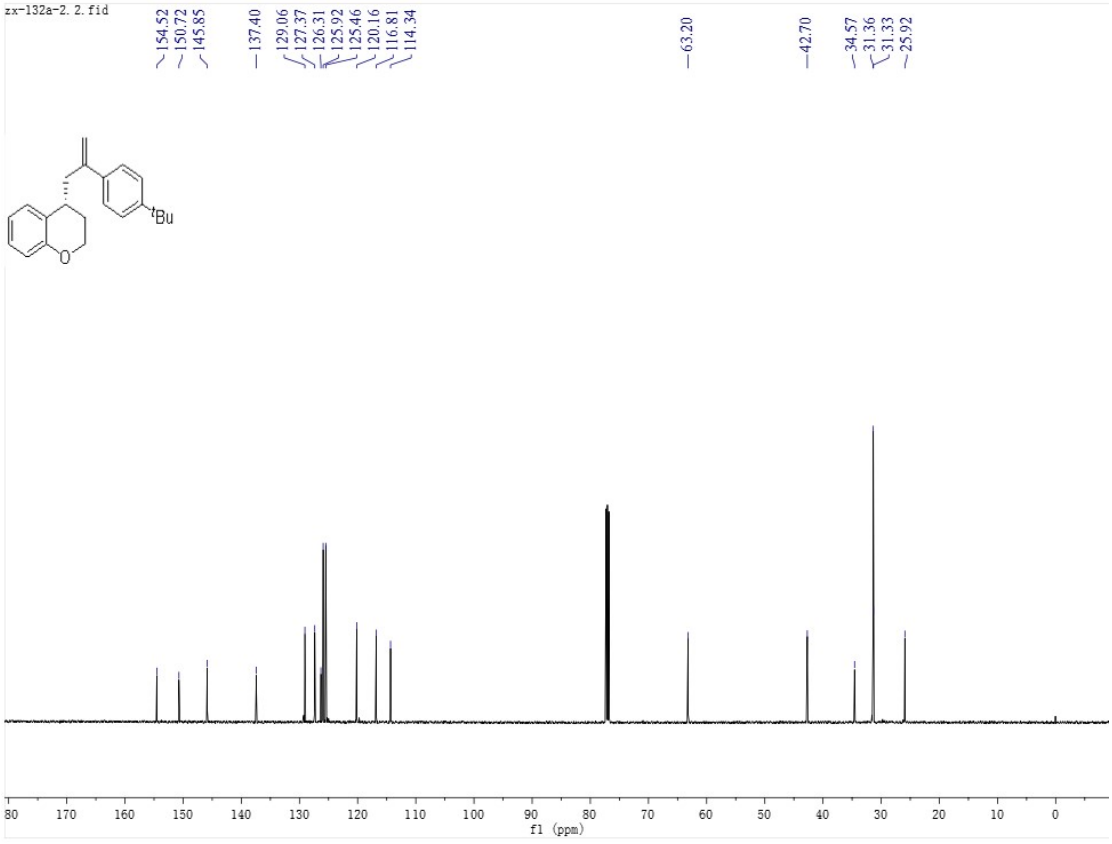
Compound 3ah



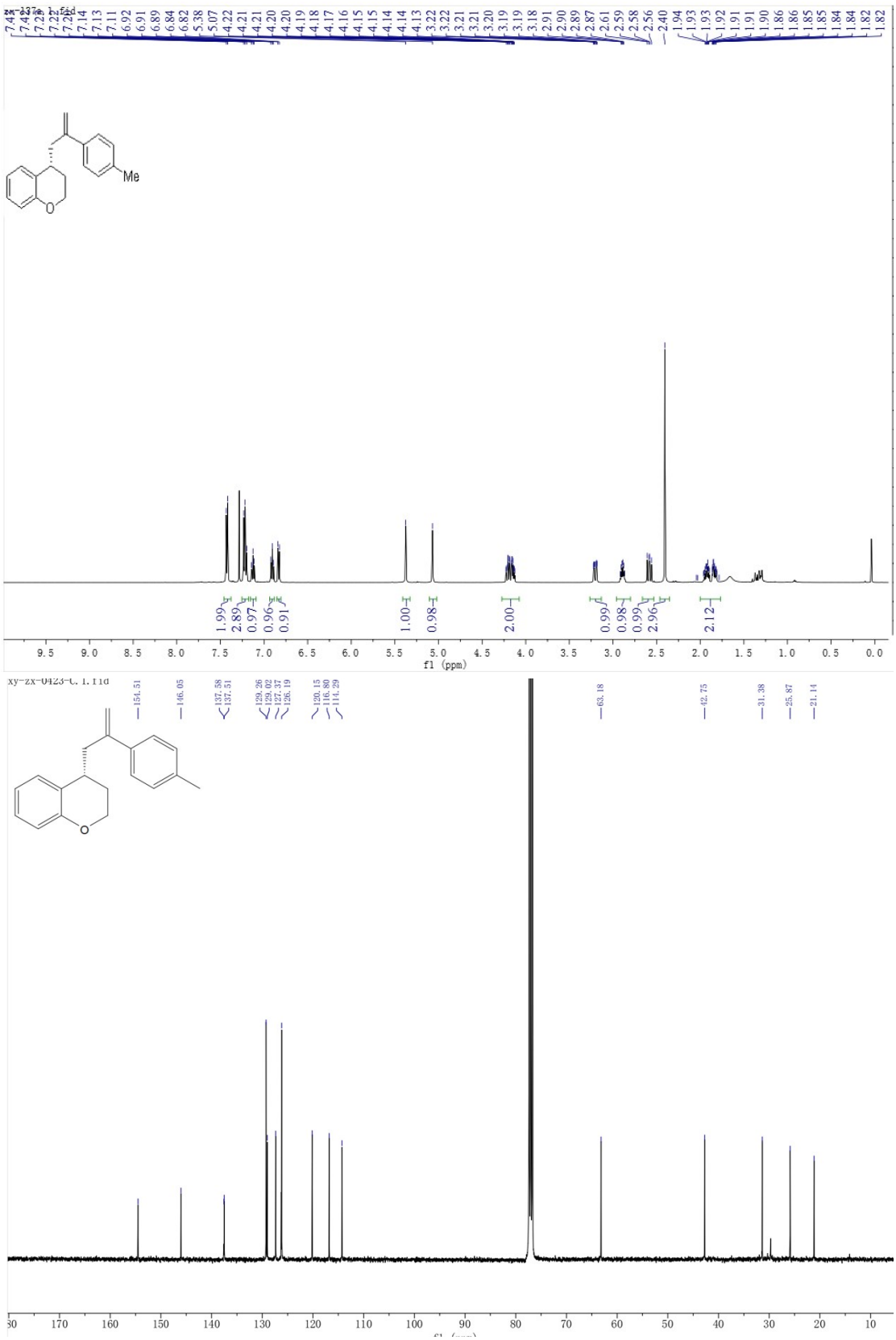


Compound 3ai

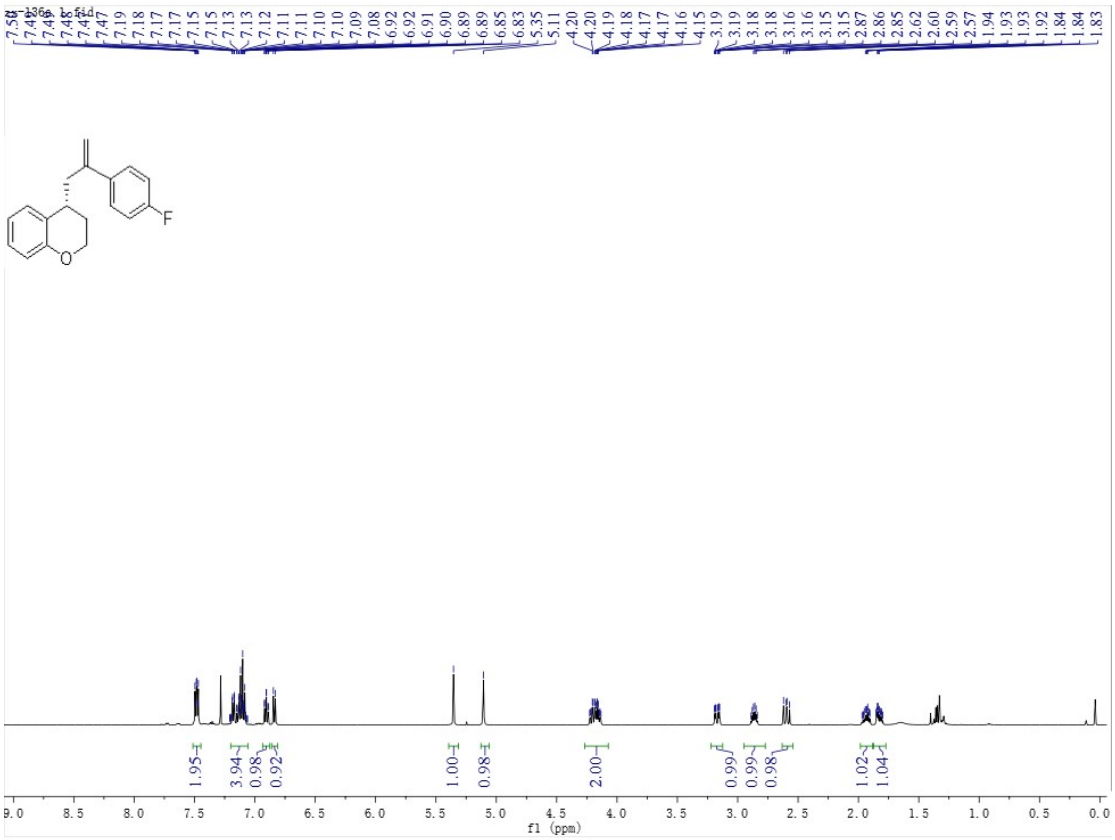




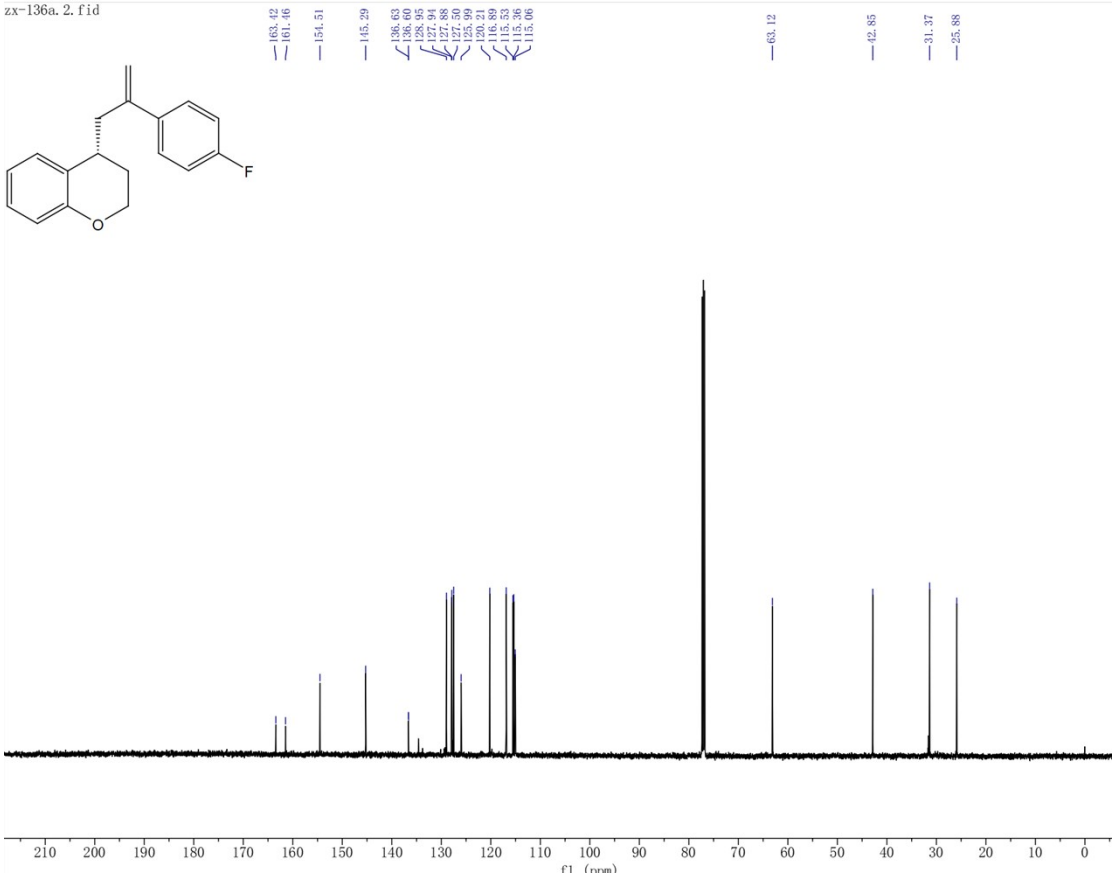
Compound 3aj

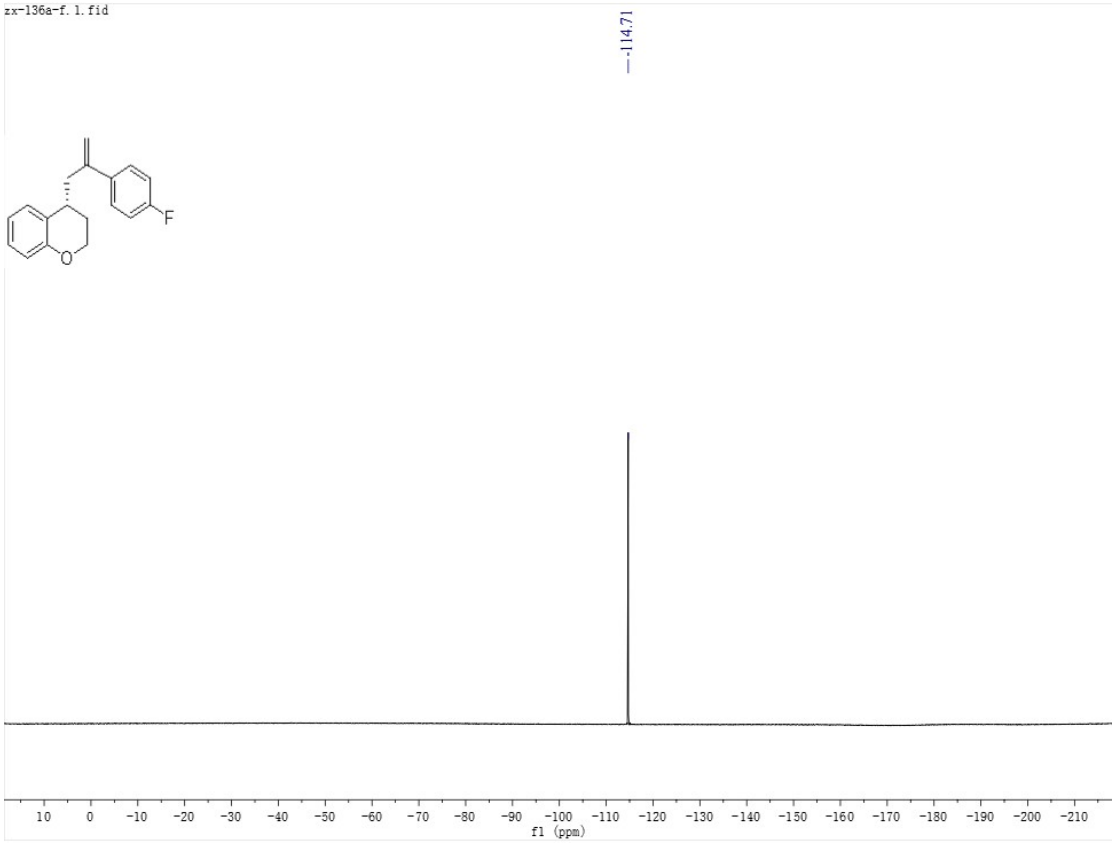


Compound 3ak

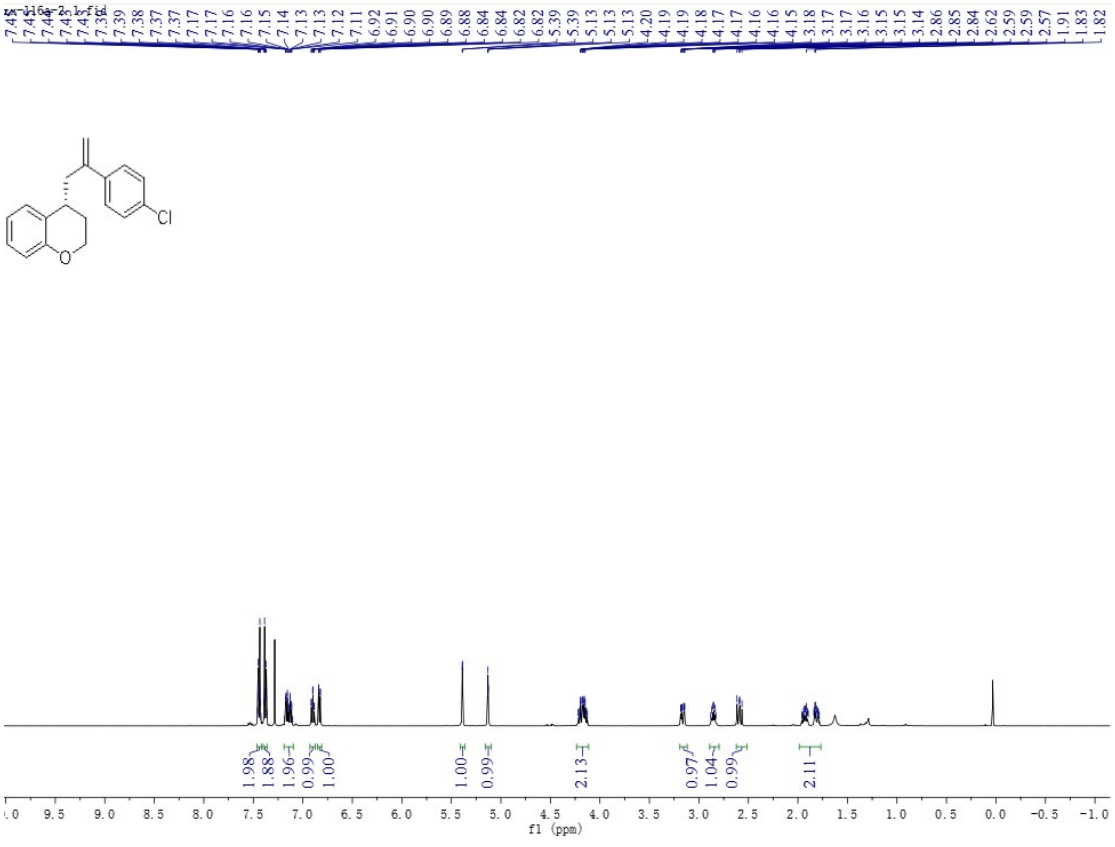

F
O
1.95
3.94
0.98
0.92
1.00
0.98
2.00
0.99
0.99
0.98
1.02
1.04
f1 (ppm)

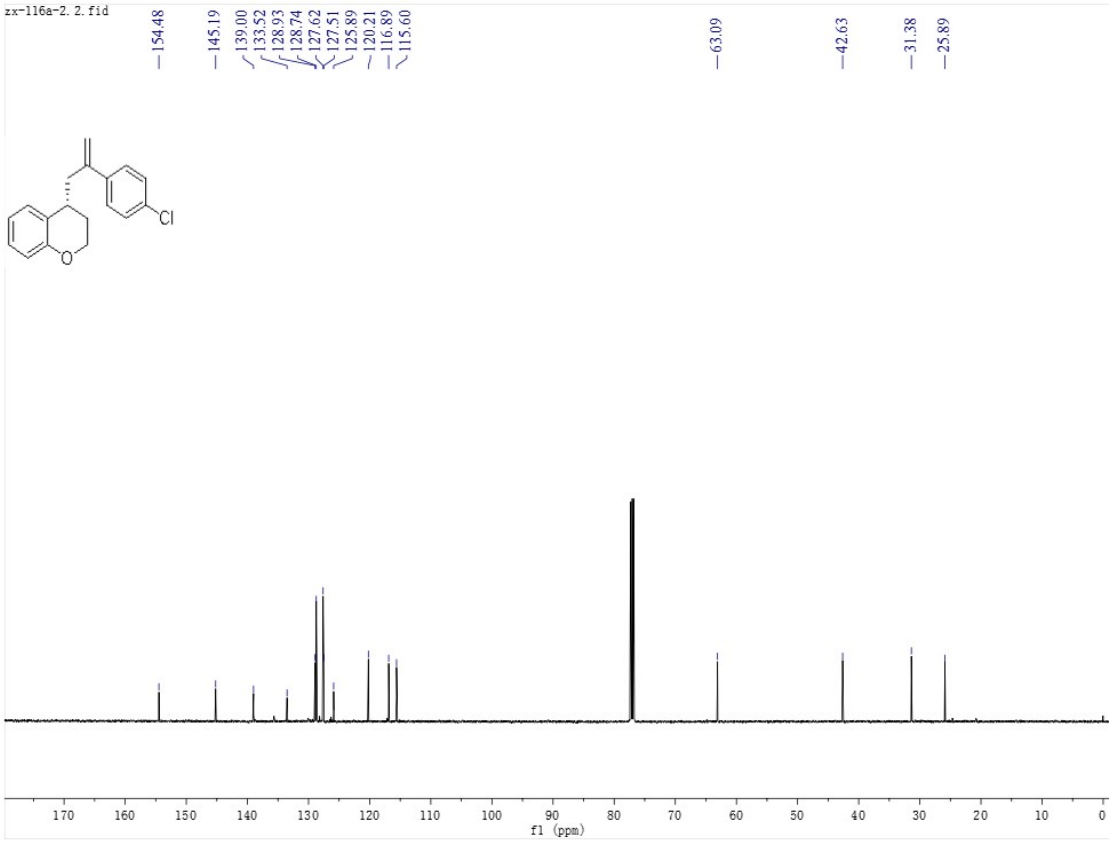
zx-136a.2.fid


163.42
161.46
154.51
145.29
136.63
136.60
128.95
127.94
127.88
127.50
125.99
120.21
116.89
115.53
115.36
115.06
63.12
42.85
31.37
25.88
F
O
f1 (ppm)

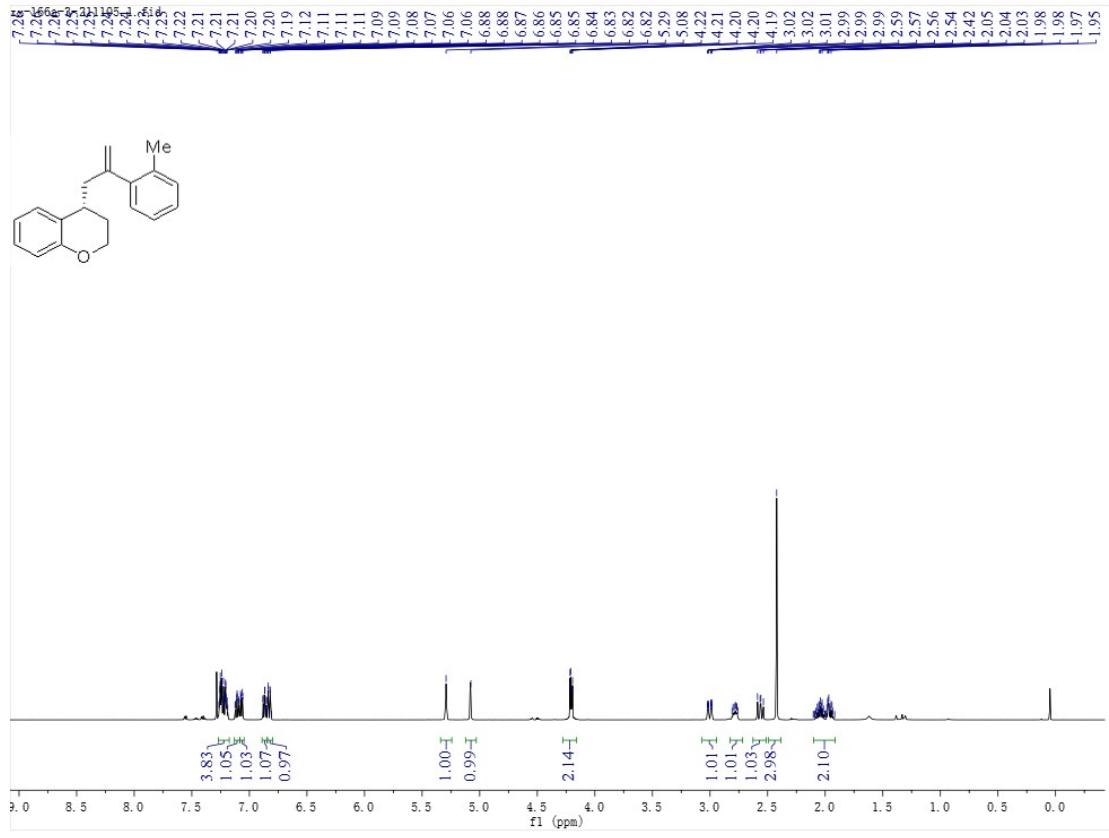


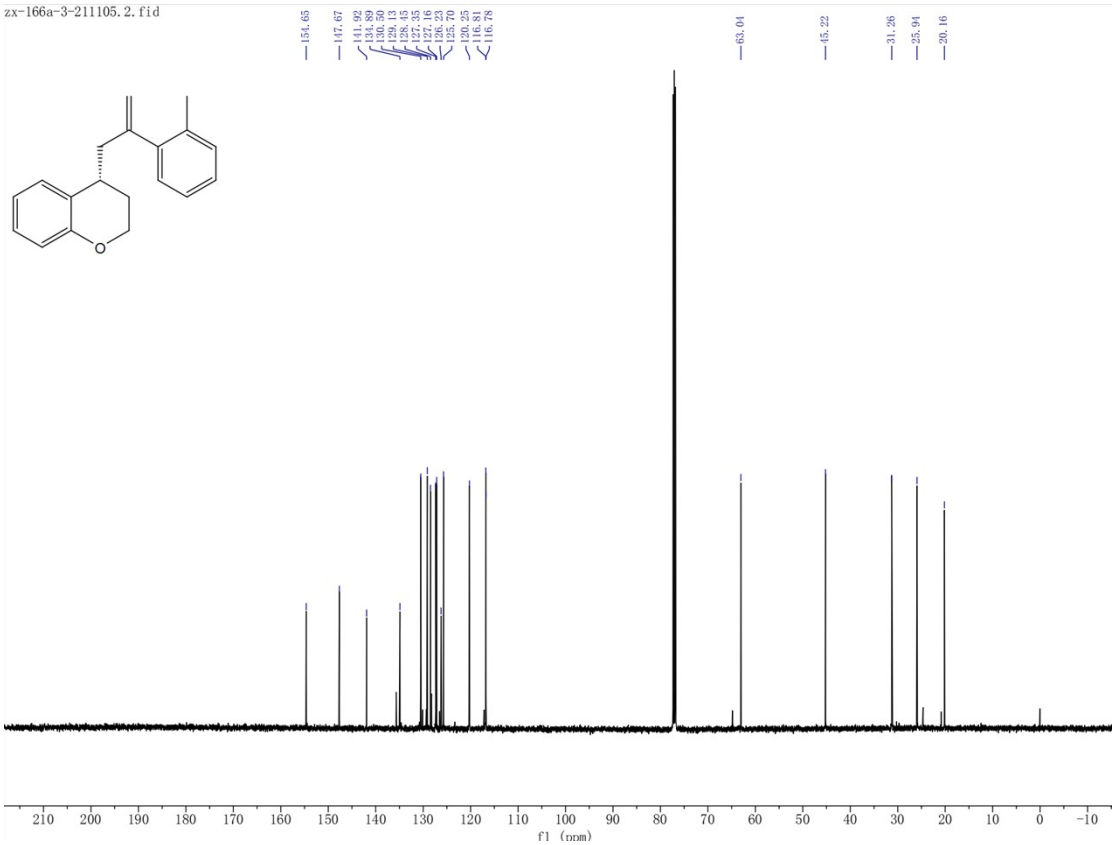
Compound 3al



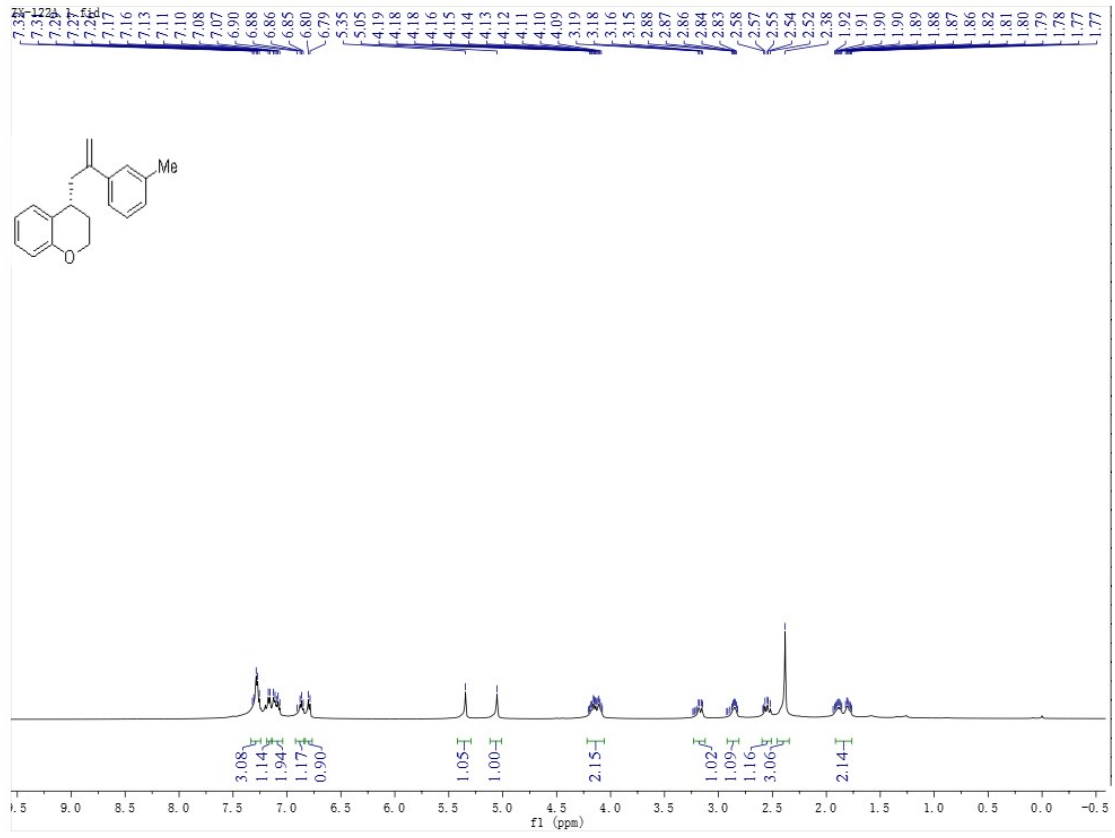


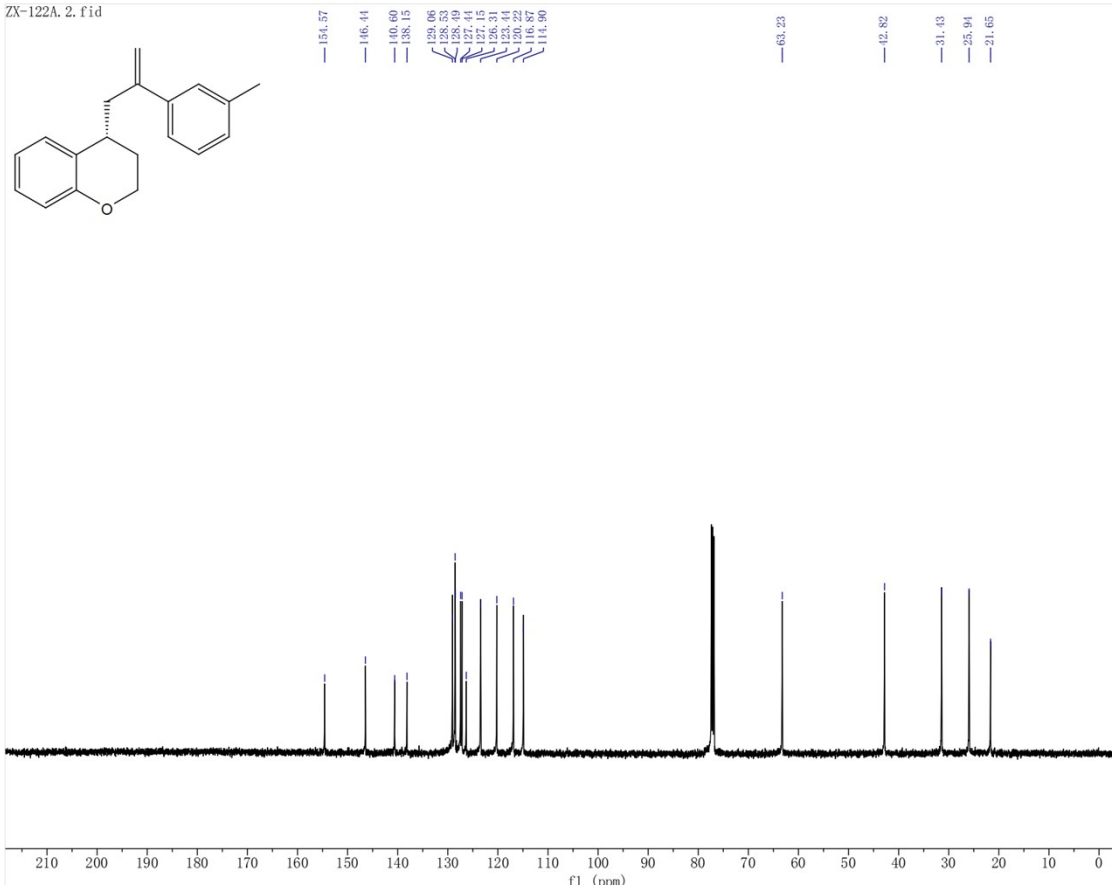
Compound 3am



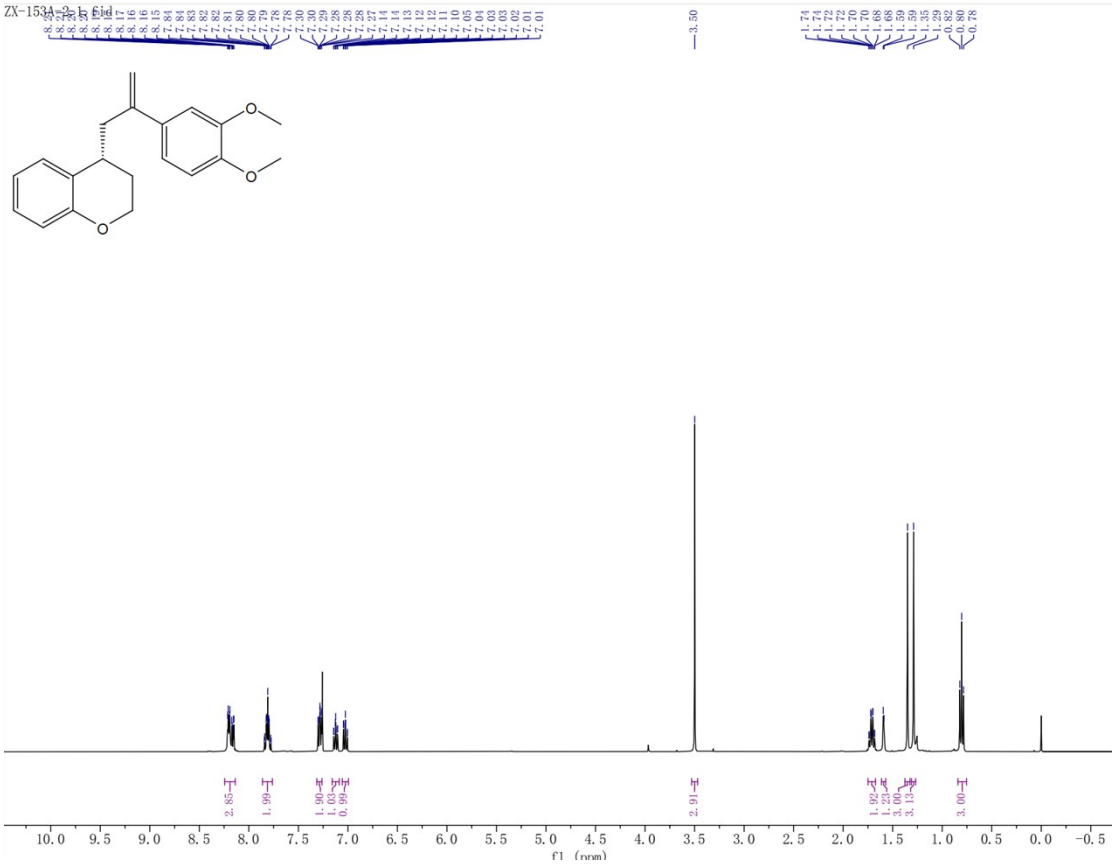


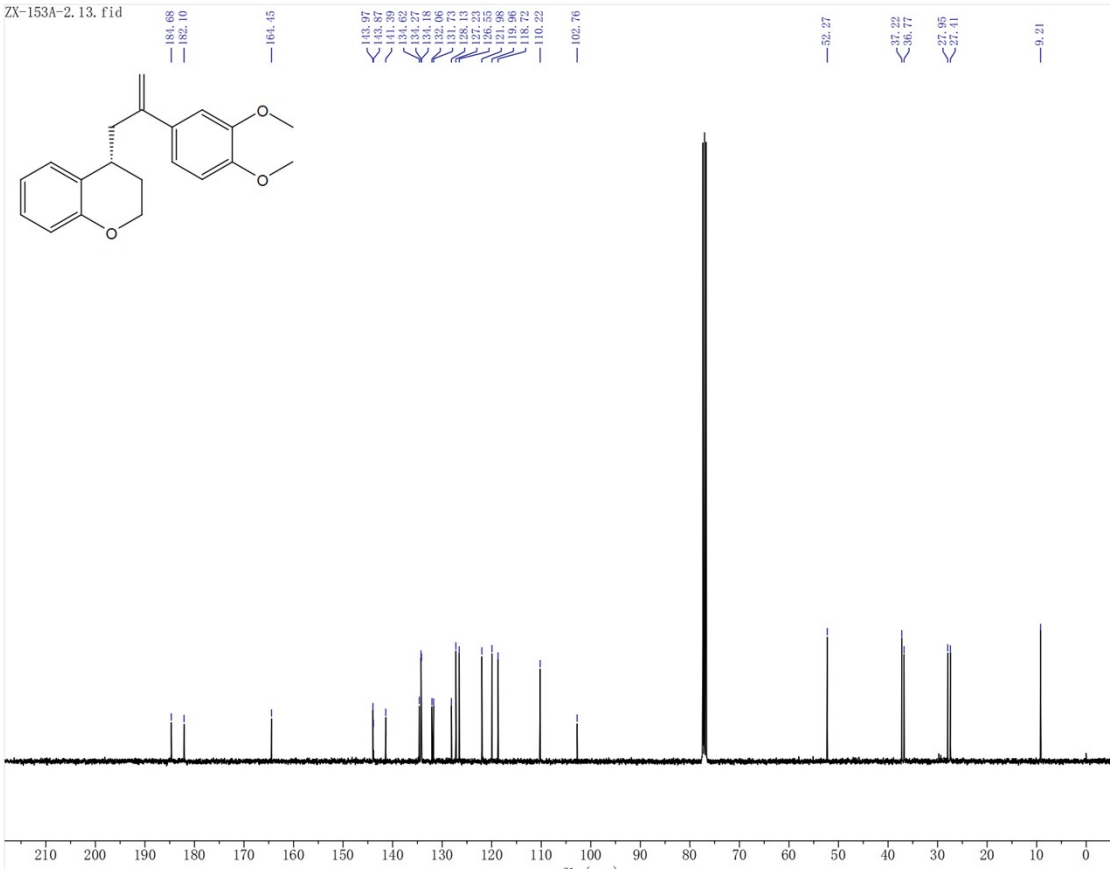
Compound 3an



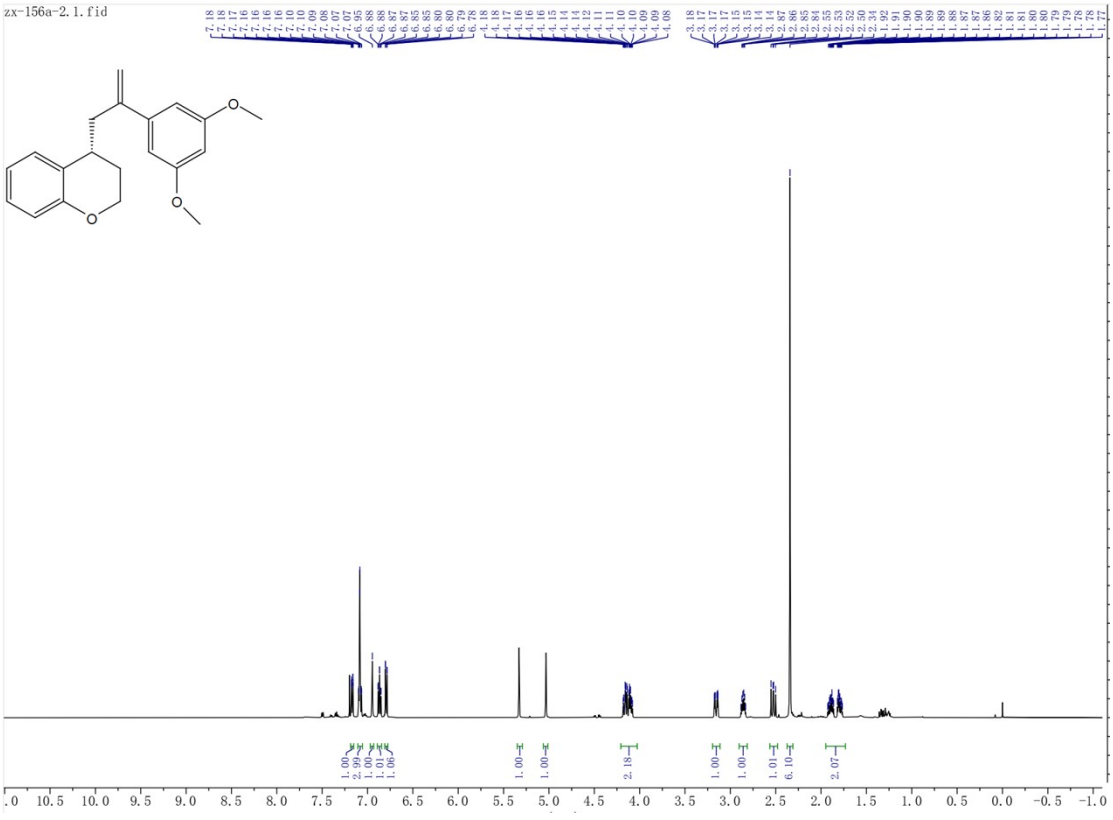


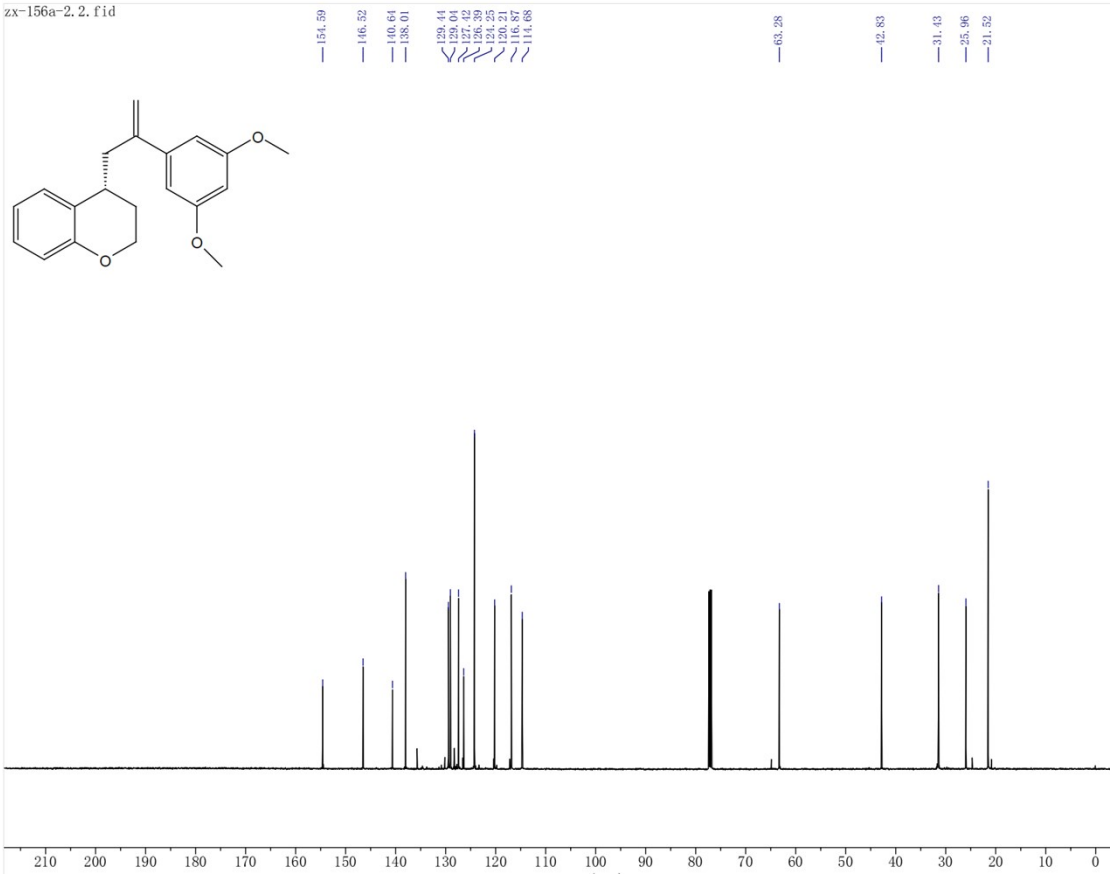
Compound 3ao



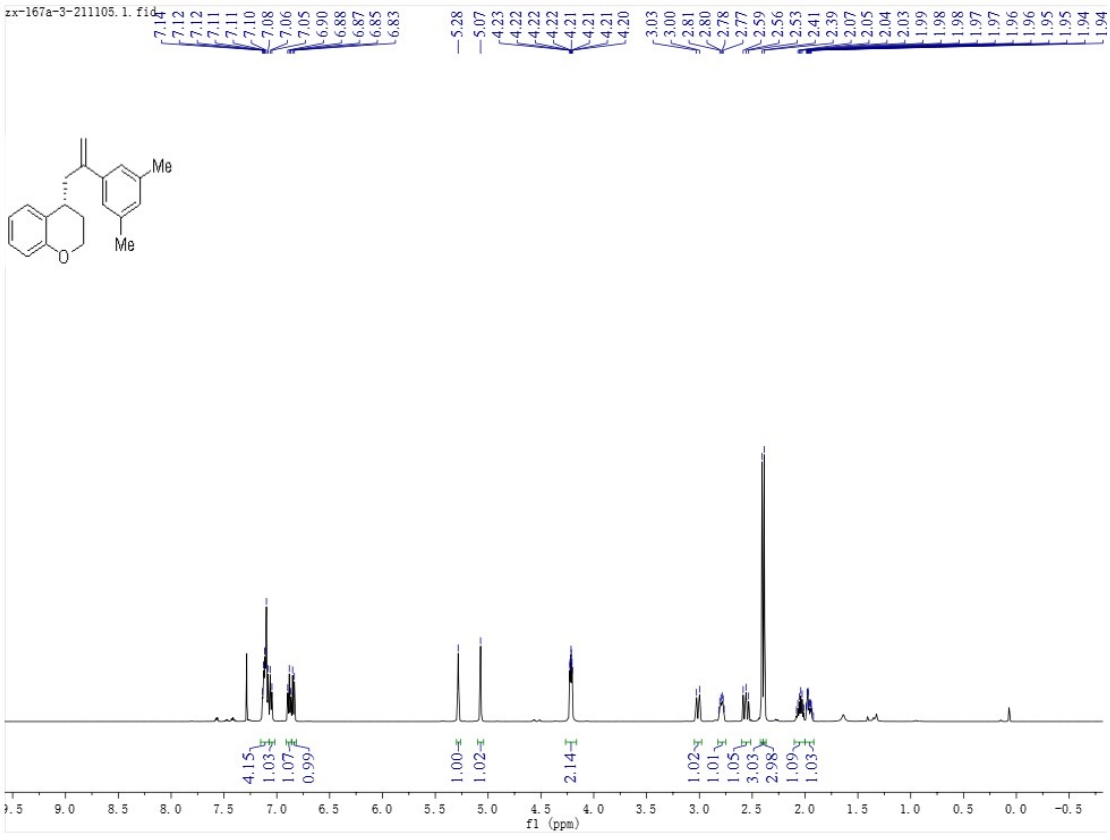


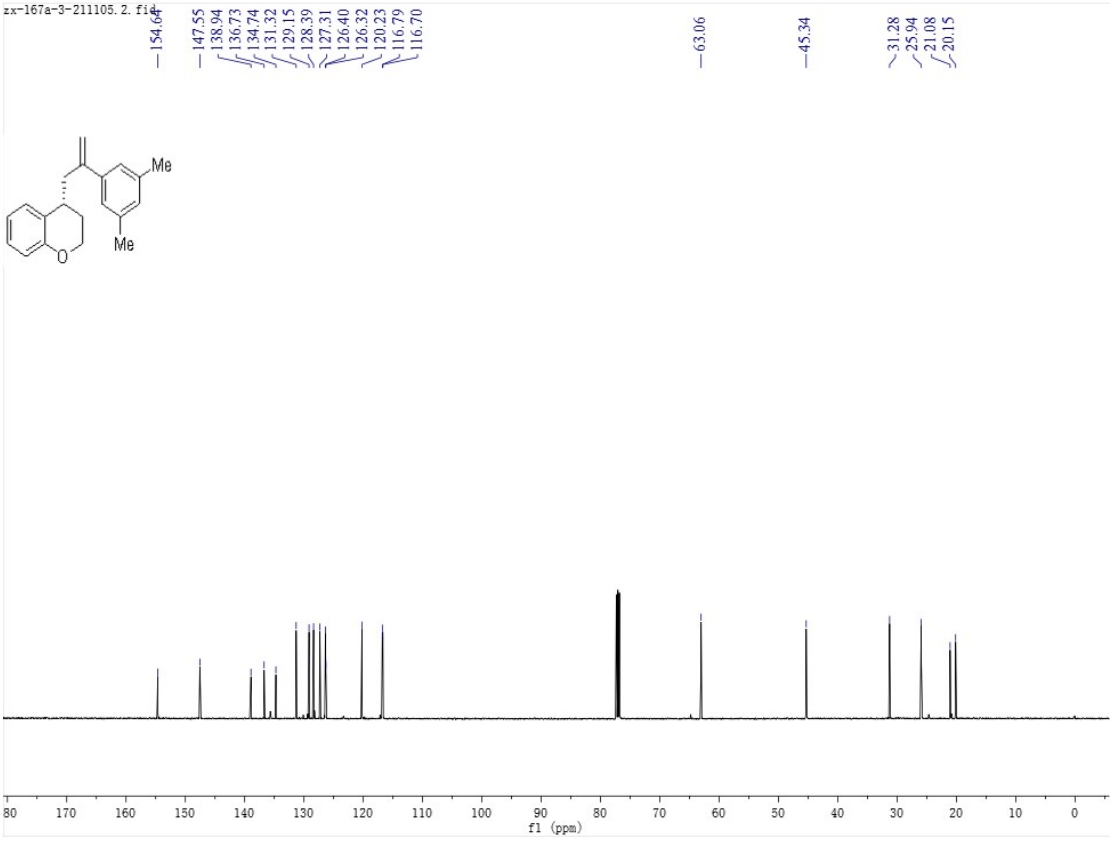
Compound 3ap



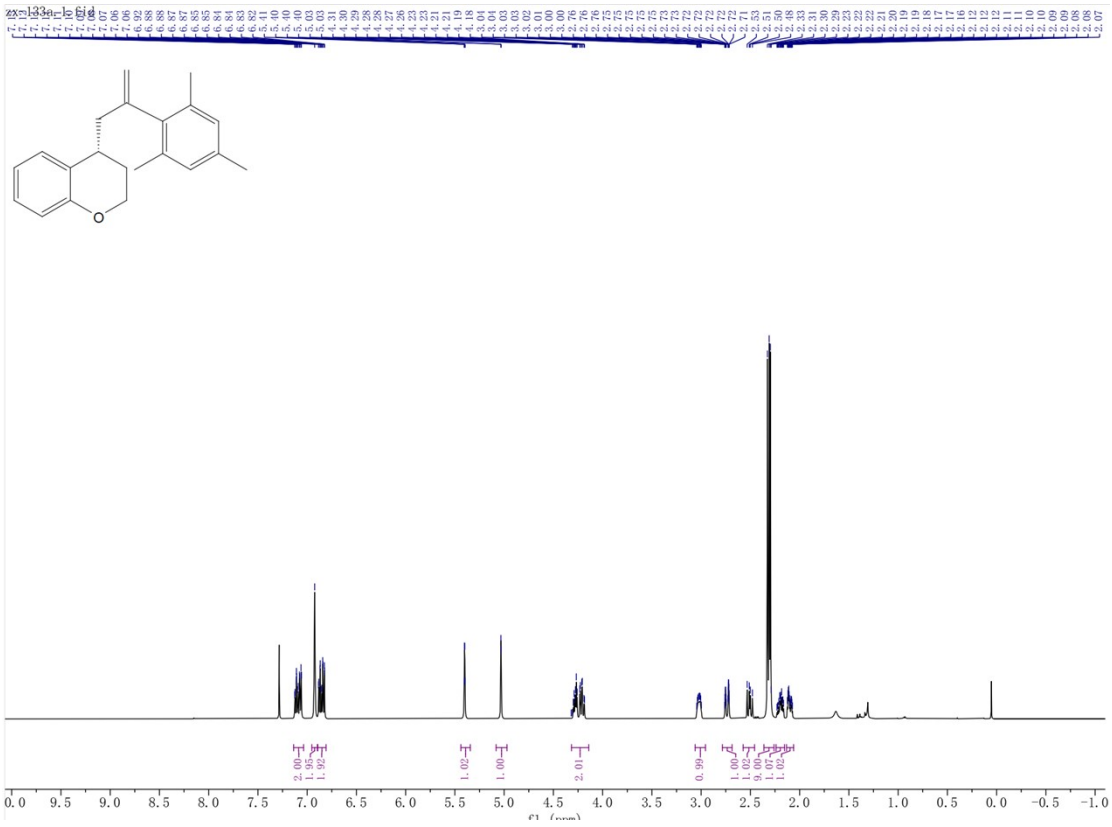


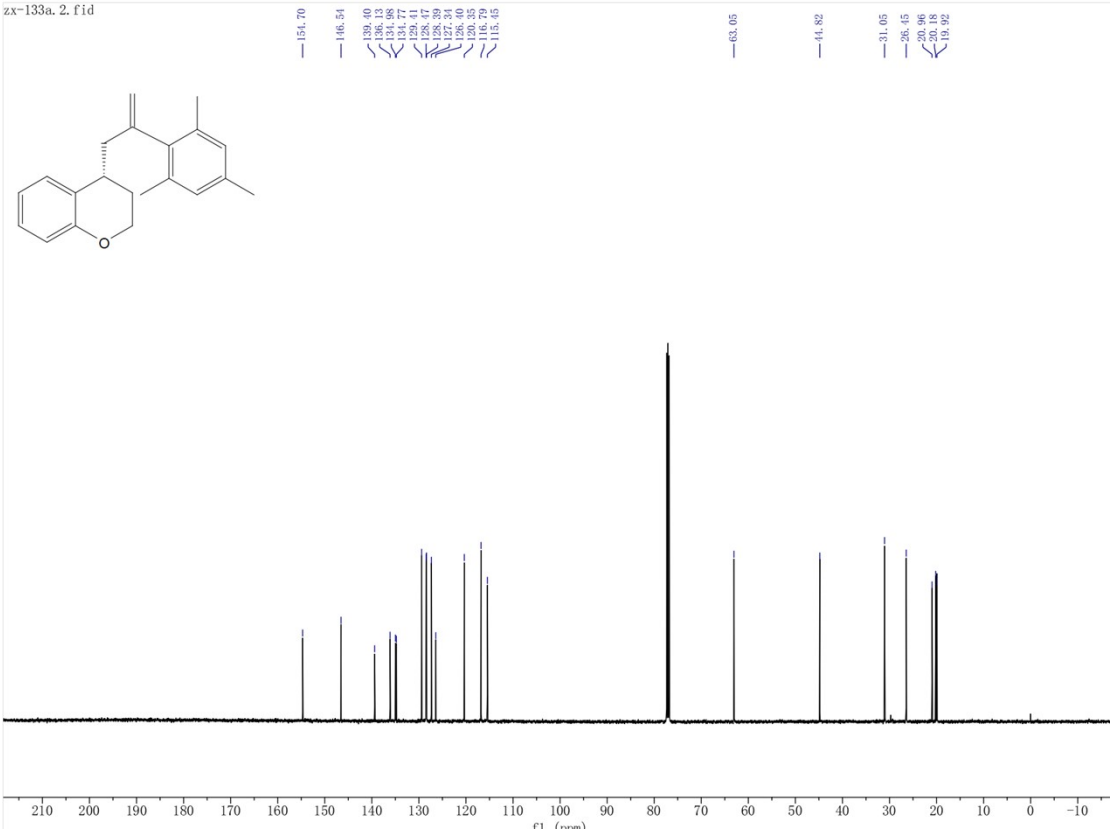
Compound 3aq



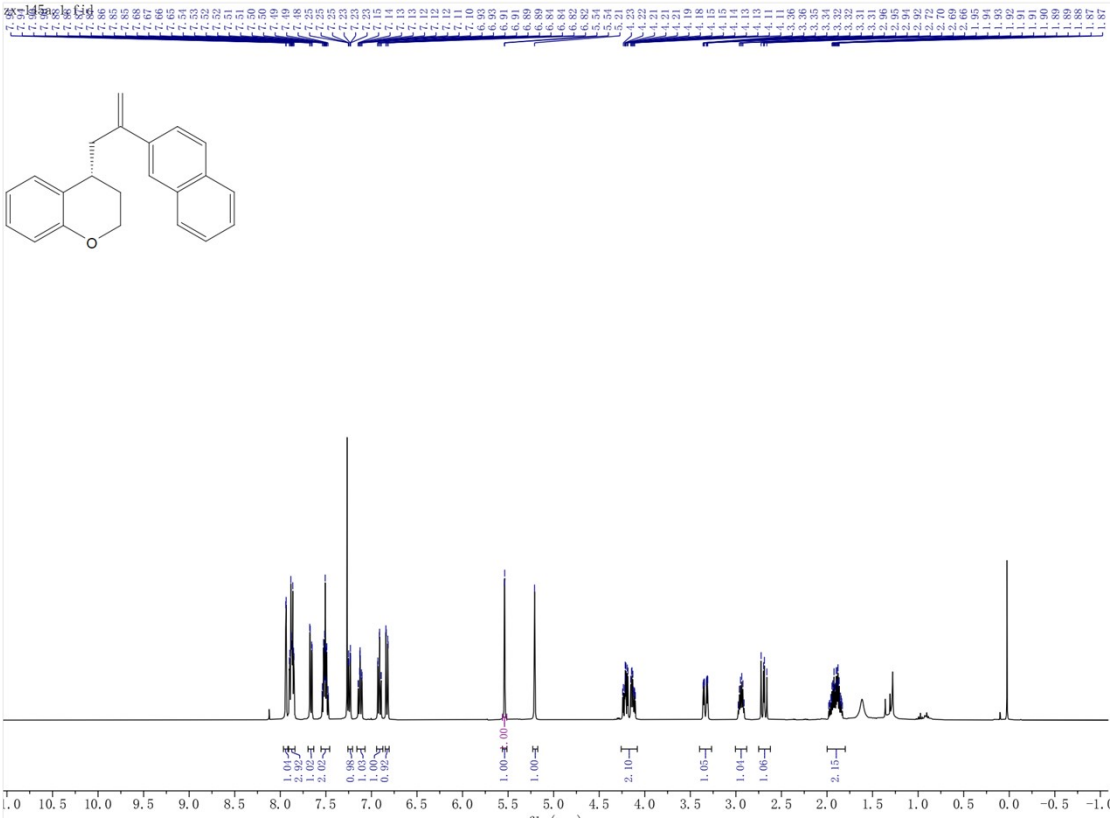


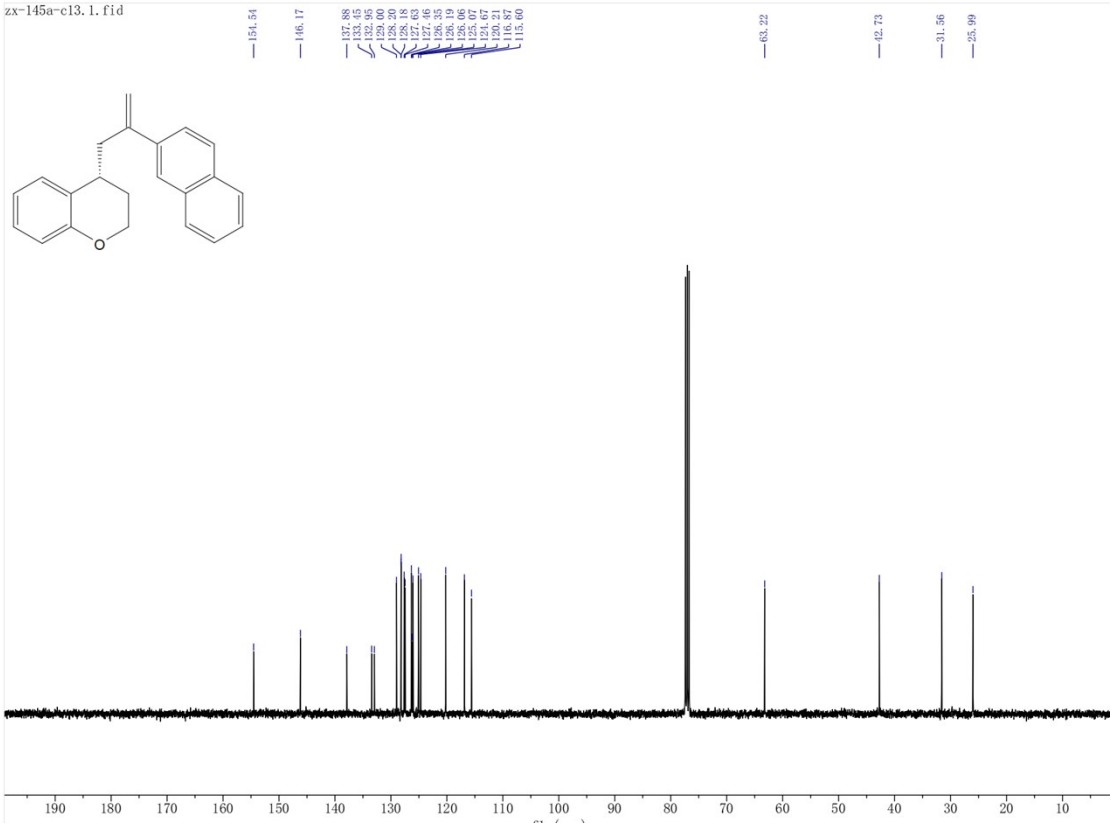
Compound 3ar



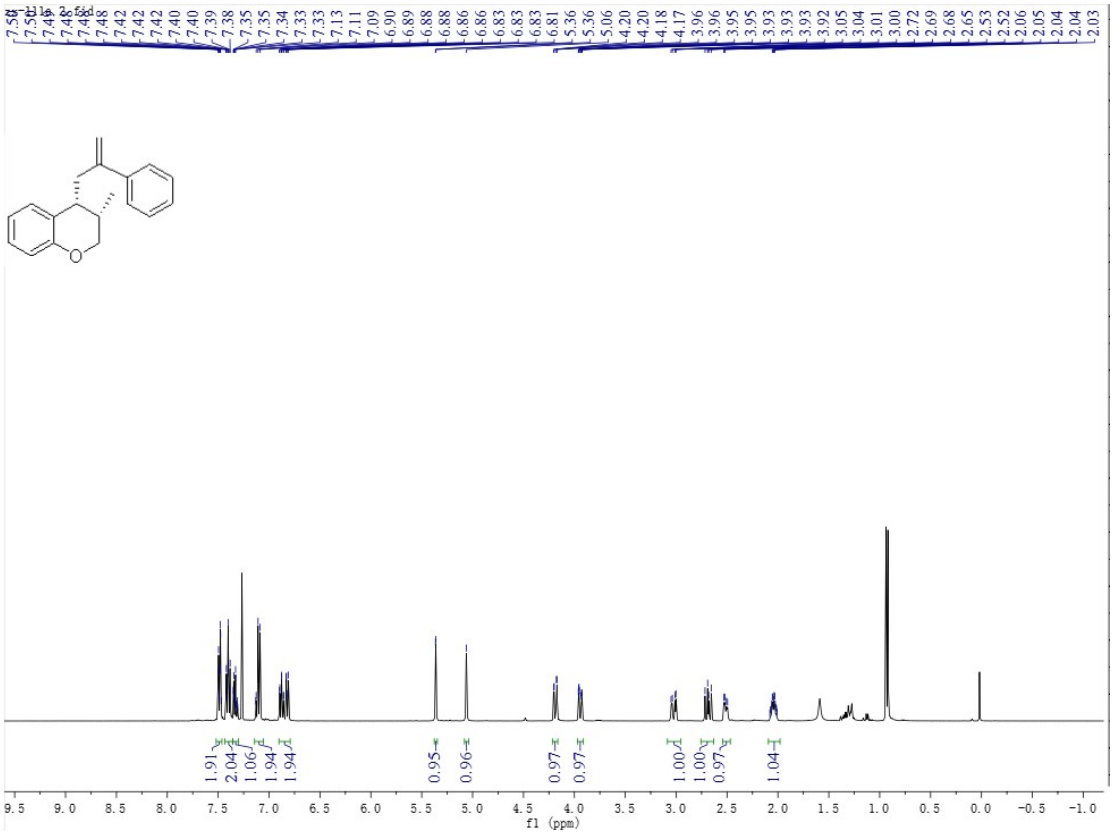


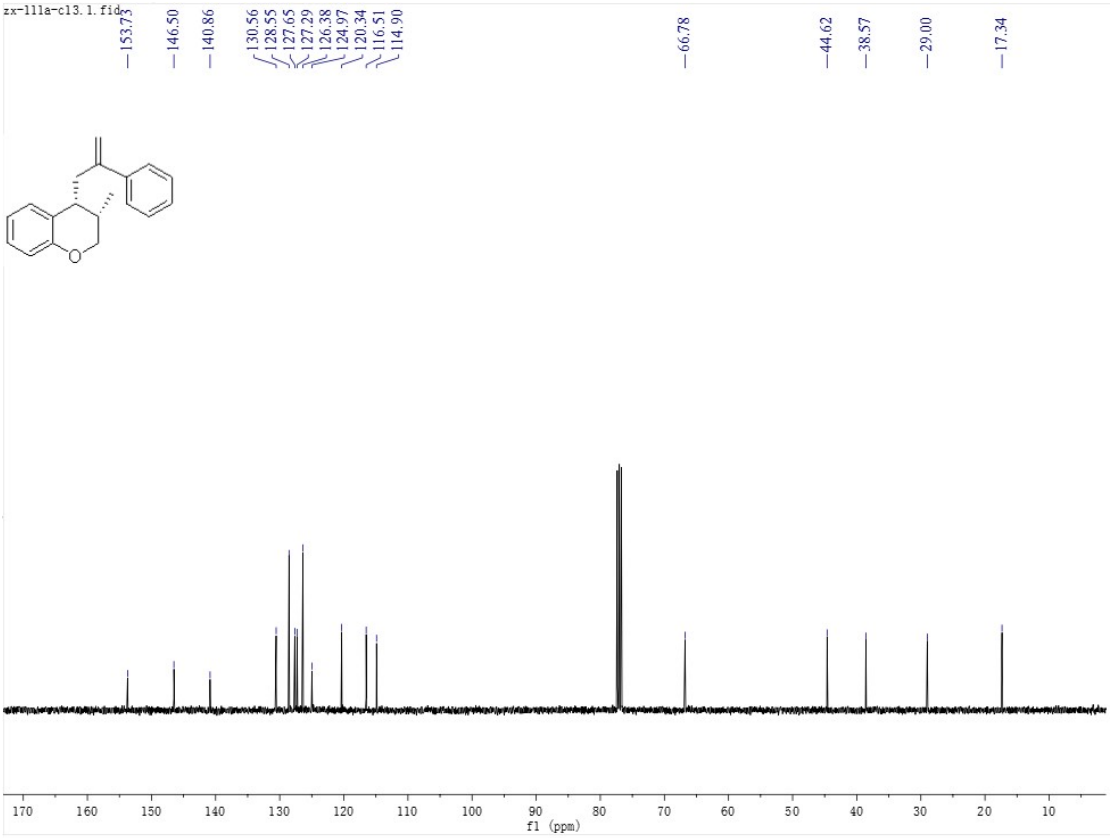
Compound 3as



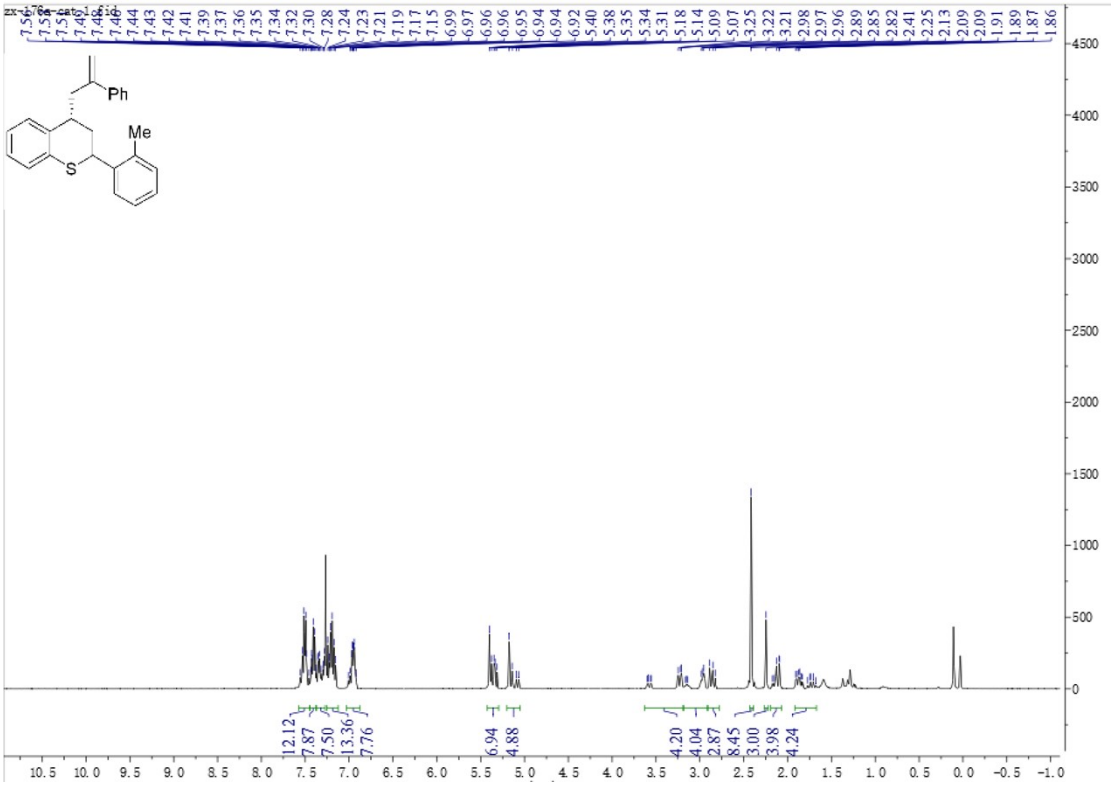


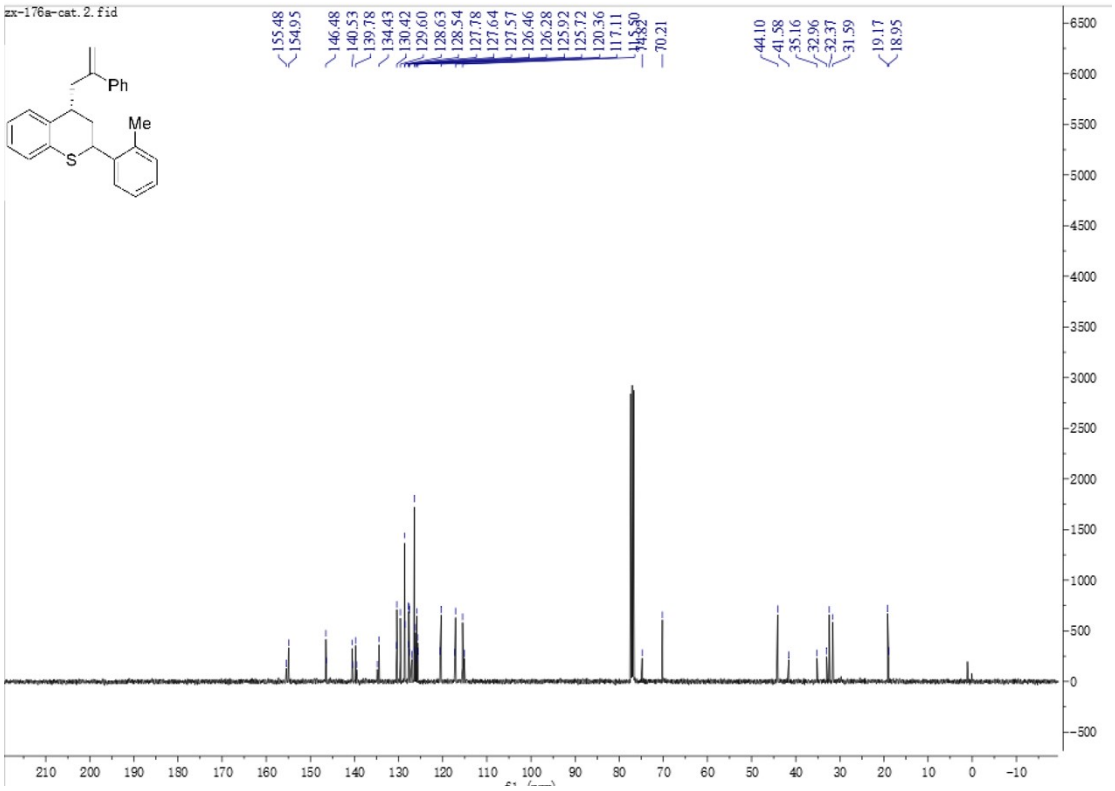
Compound 3at



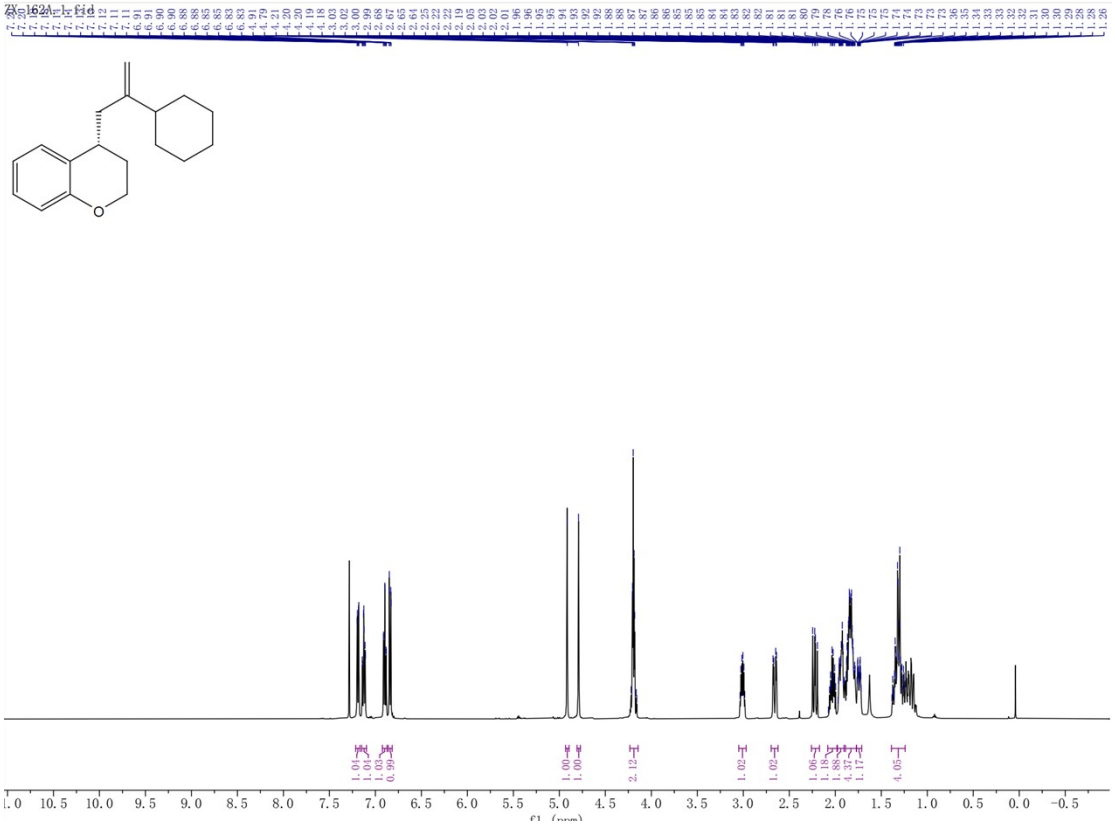


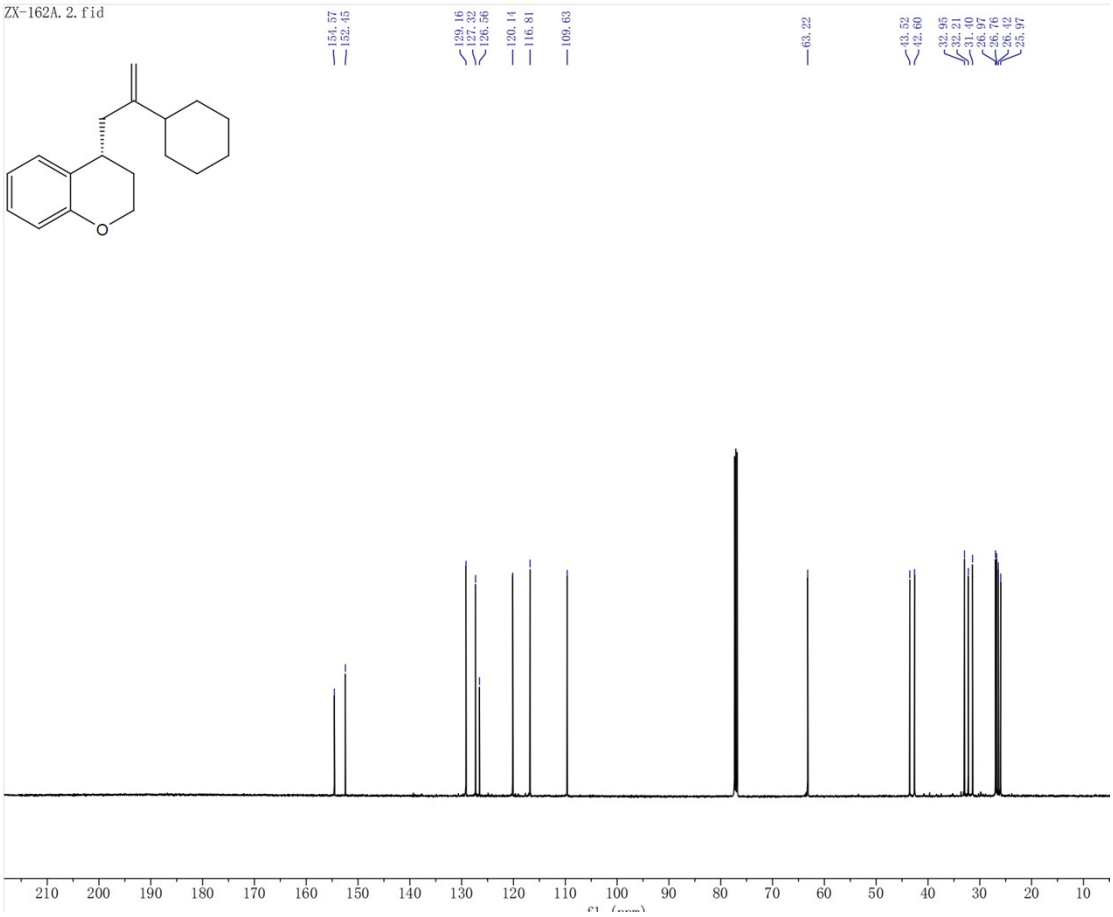
Compound 3au



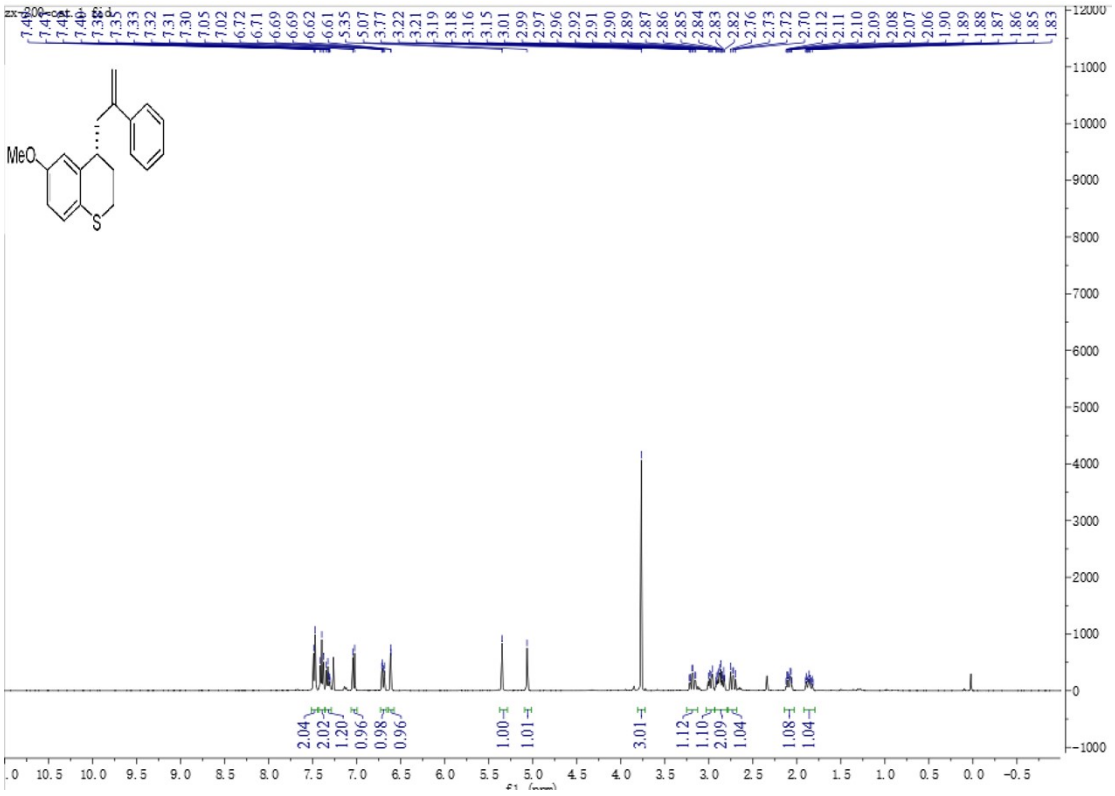


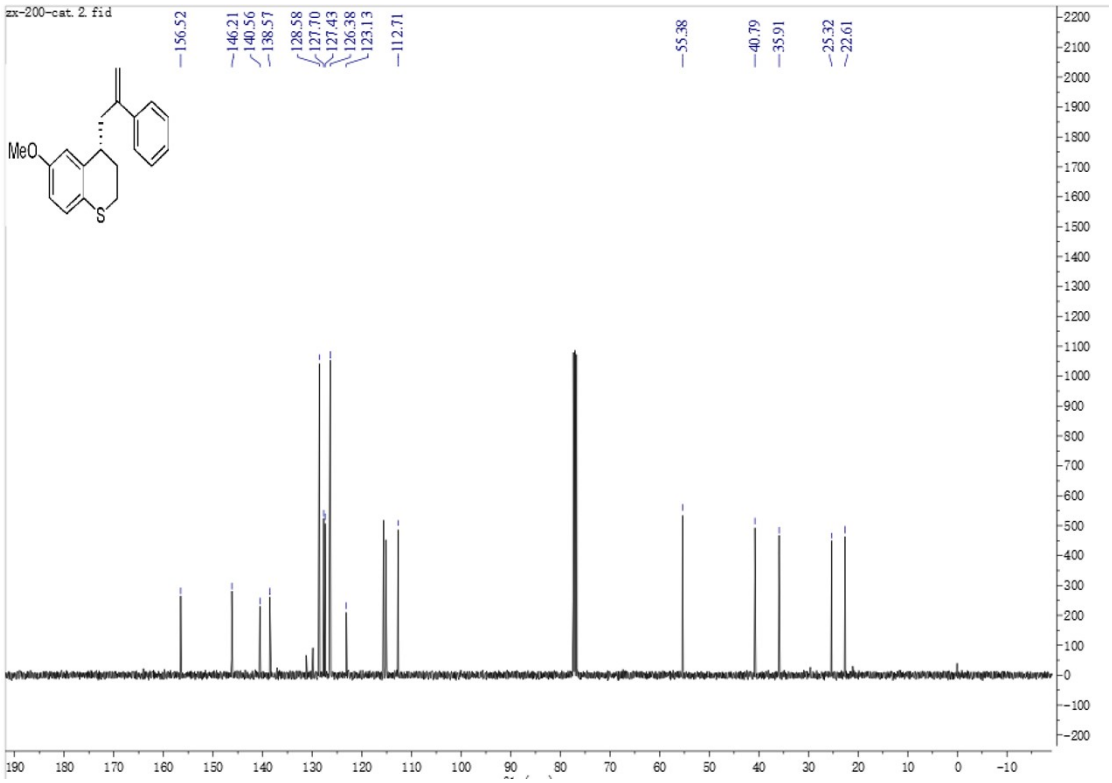
Compound 3av



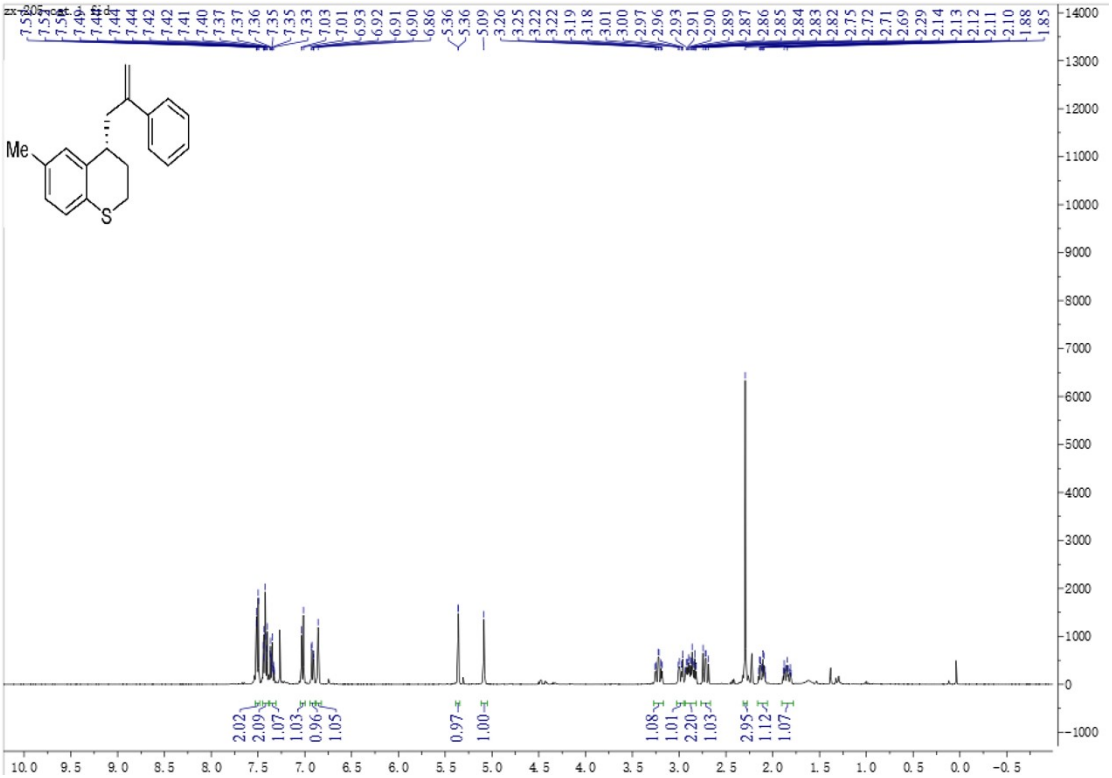


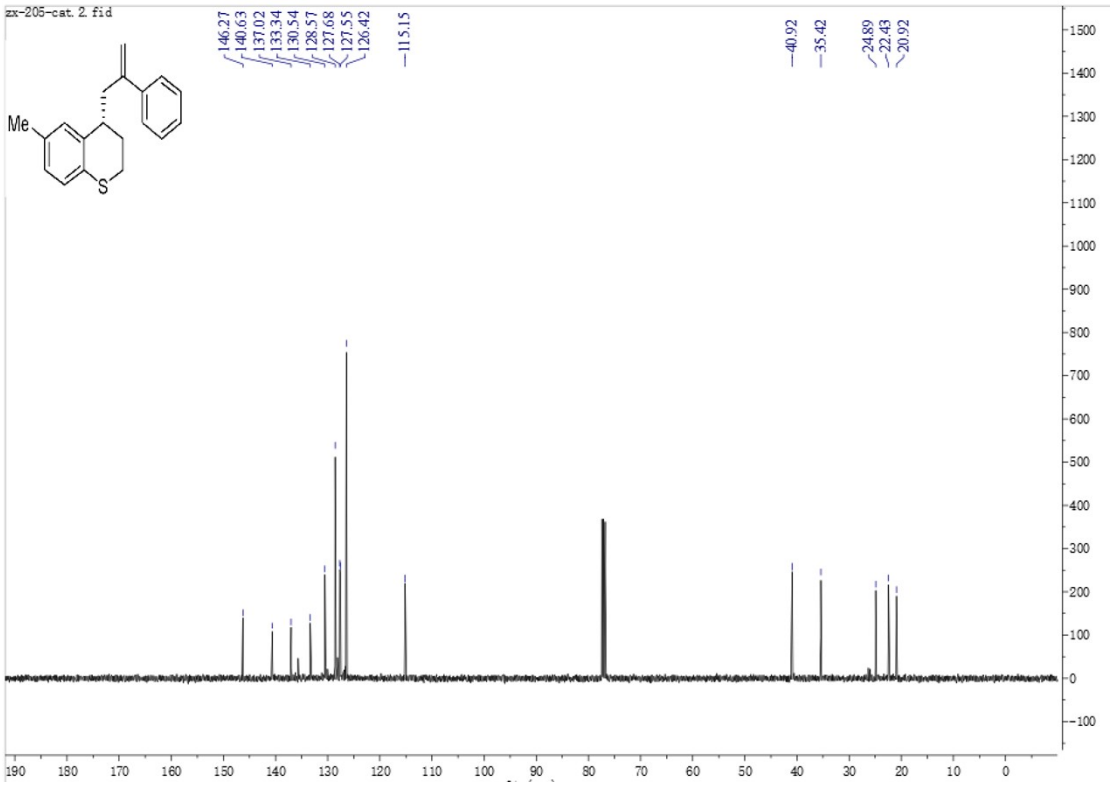
Compound 3aw



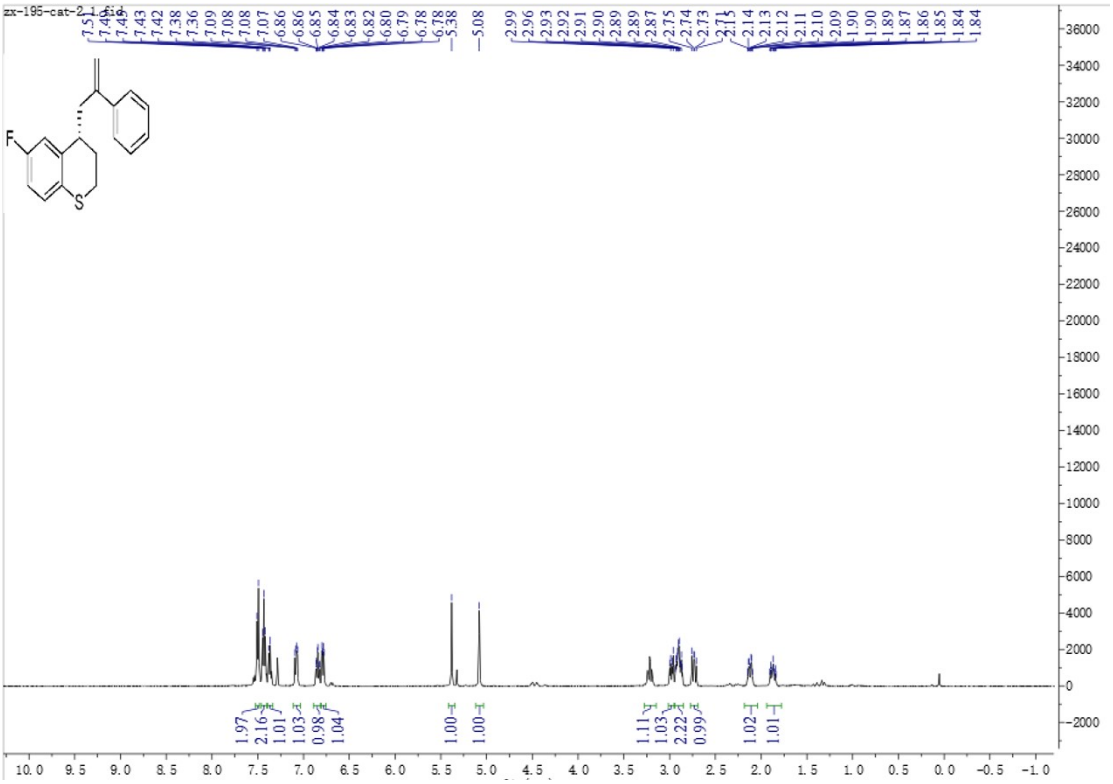


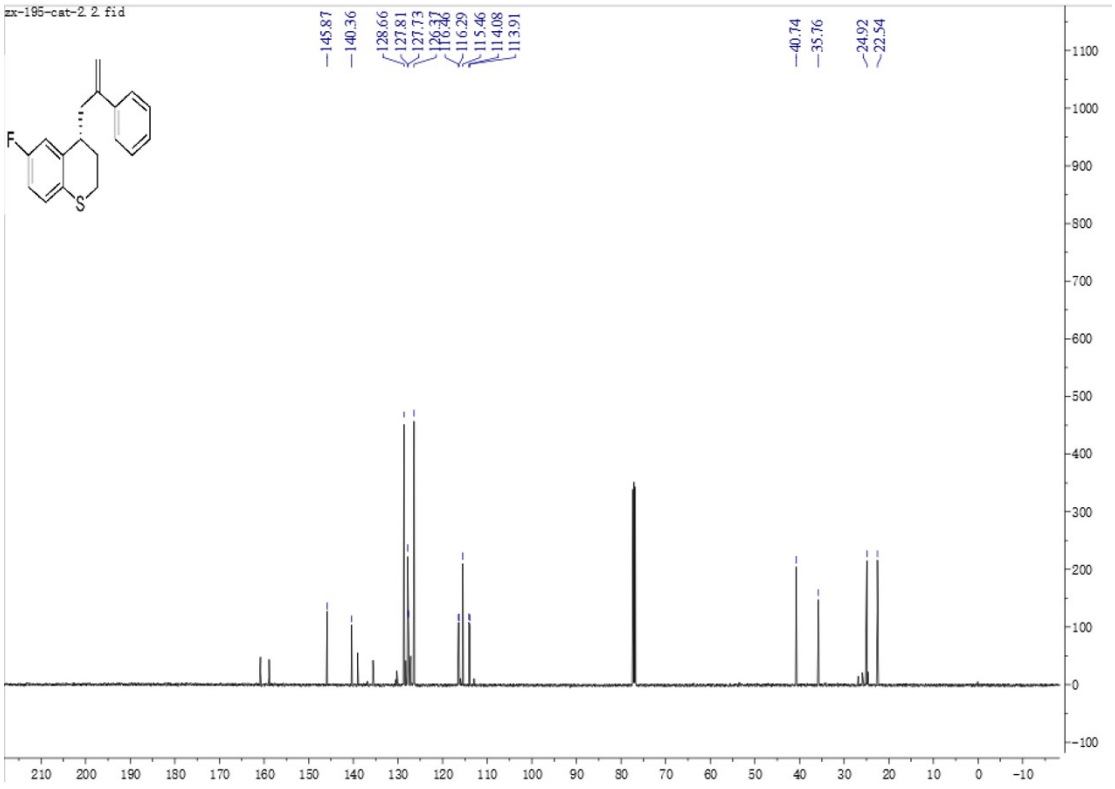
Compound 3ax

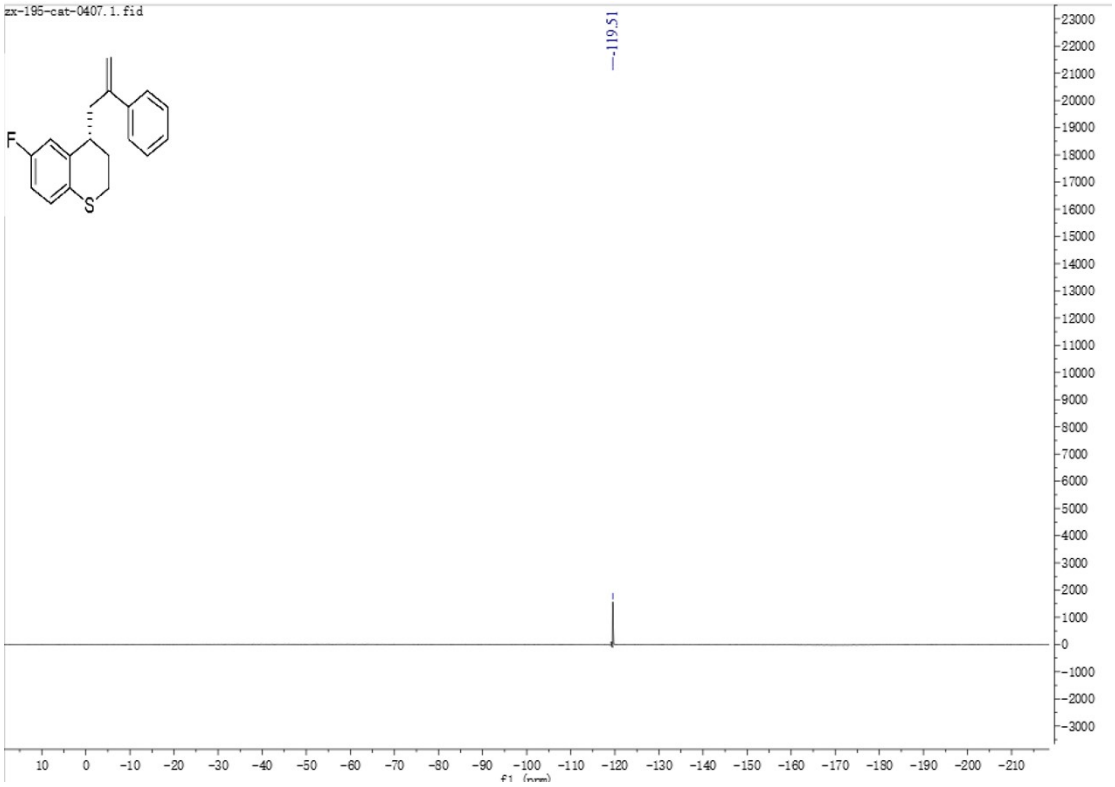




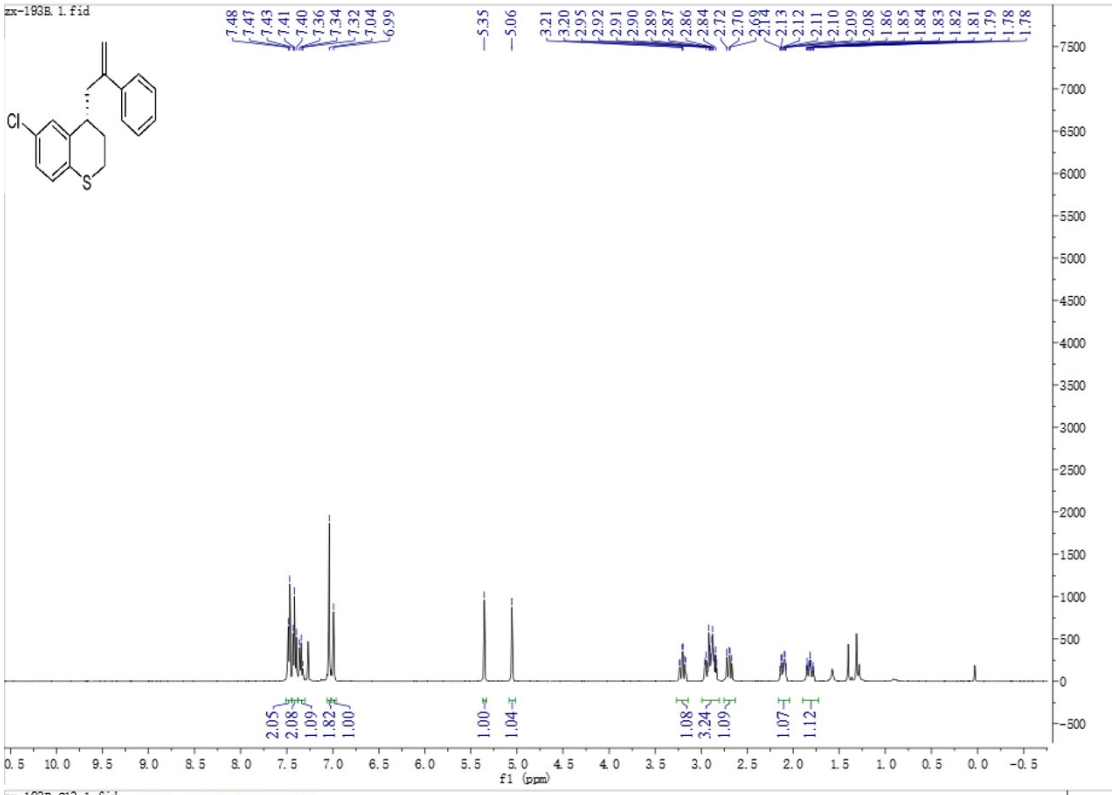
Compound 3ay

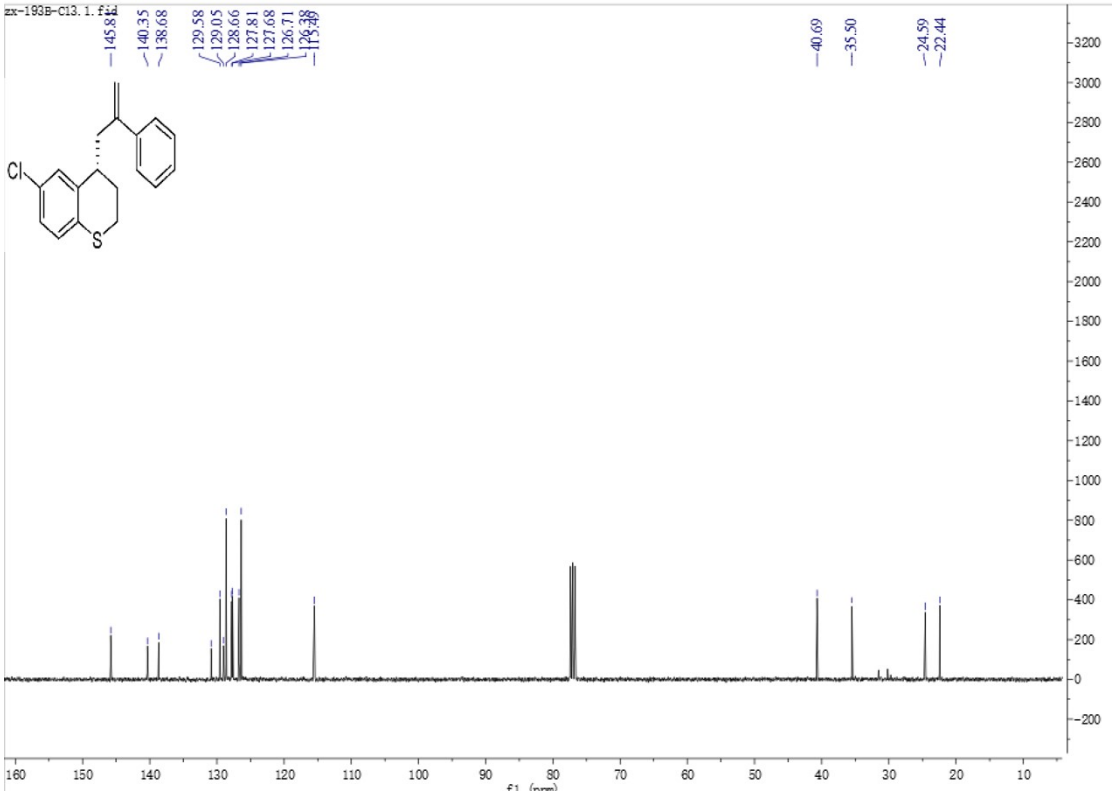




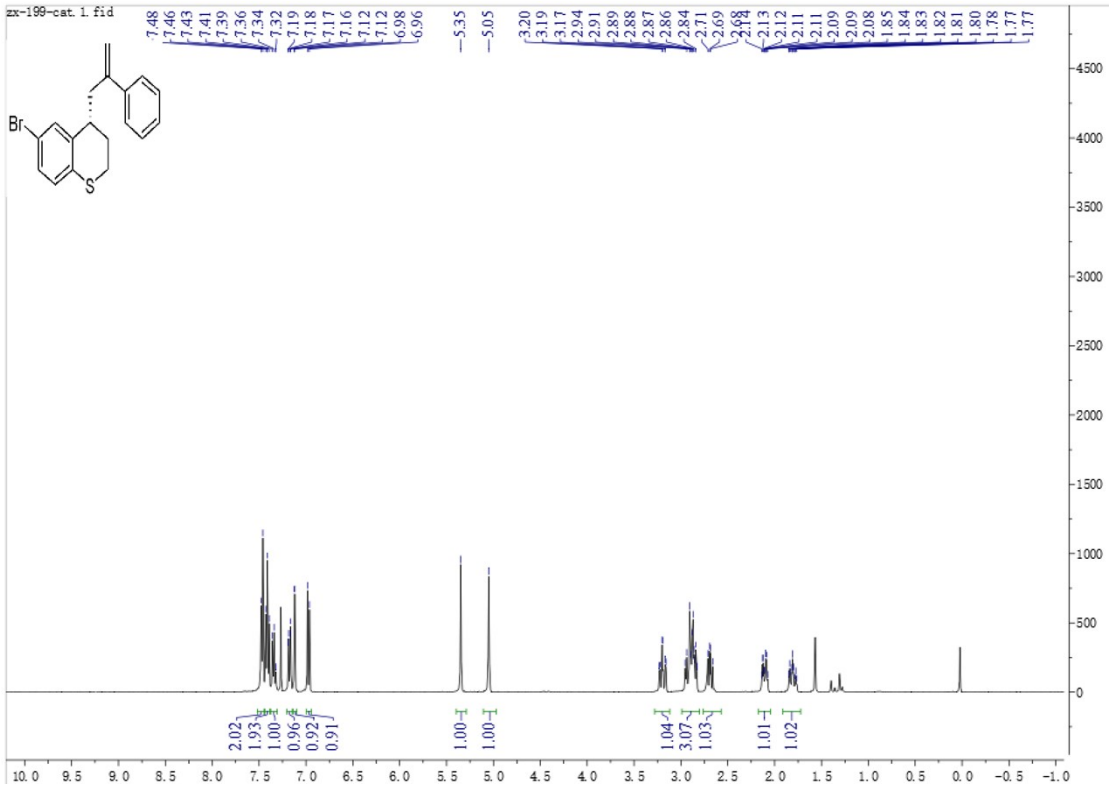


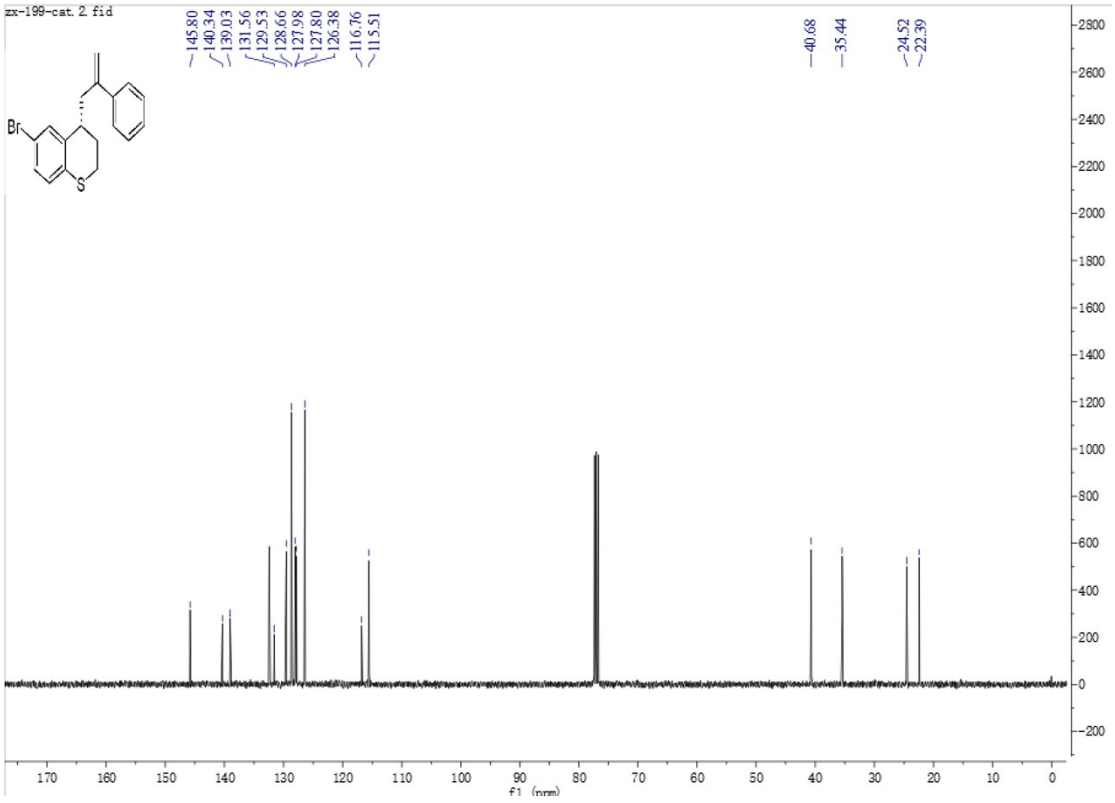
Compound 3az



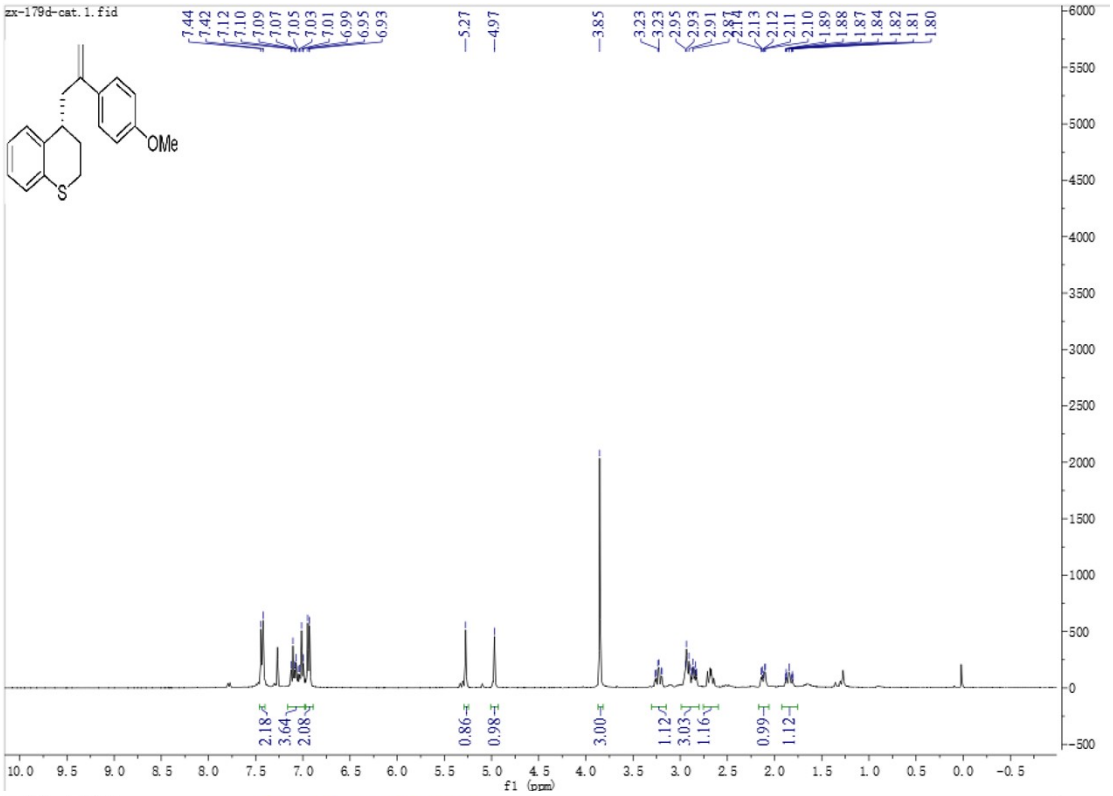


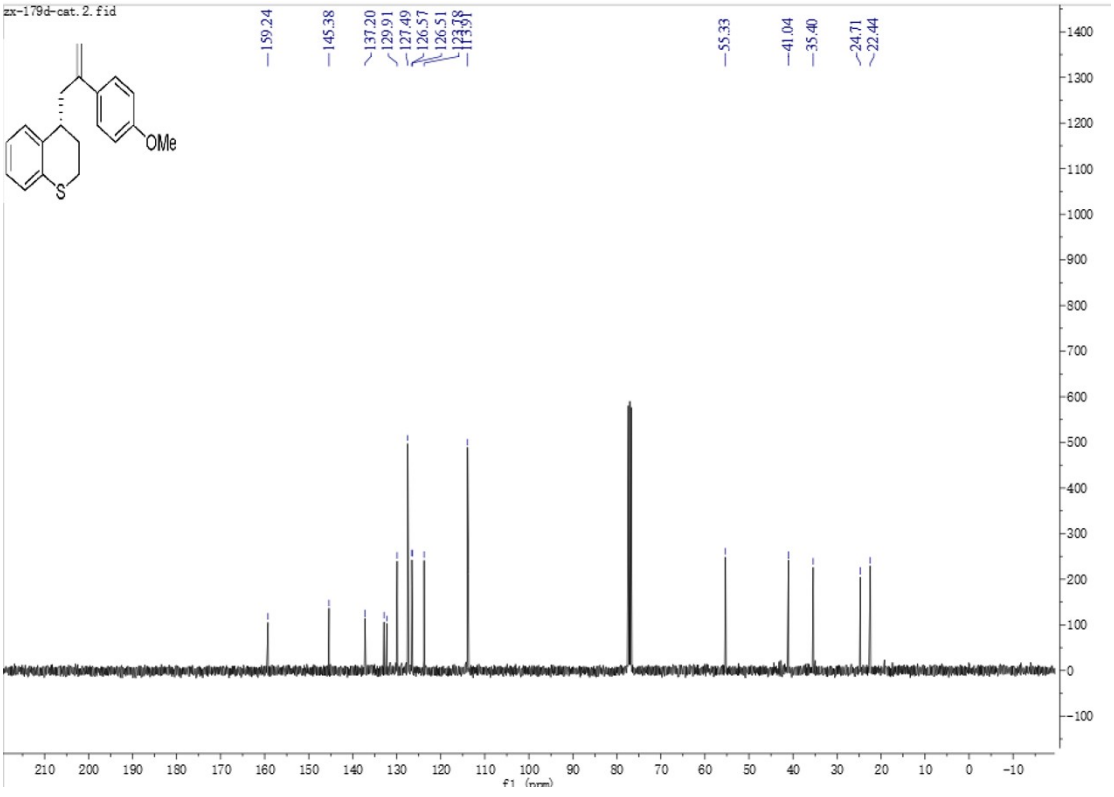
Compound 3ba



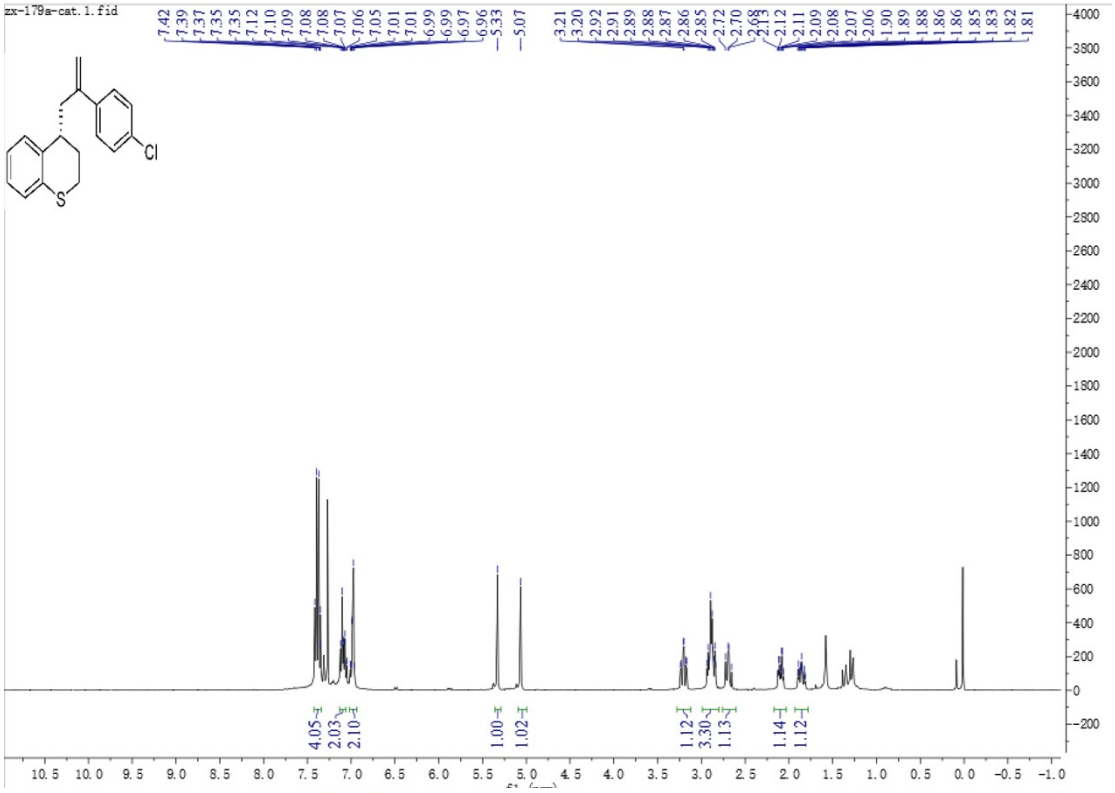


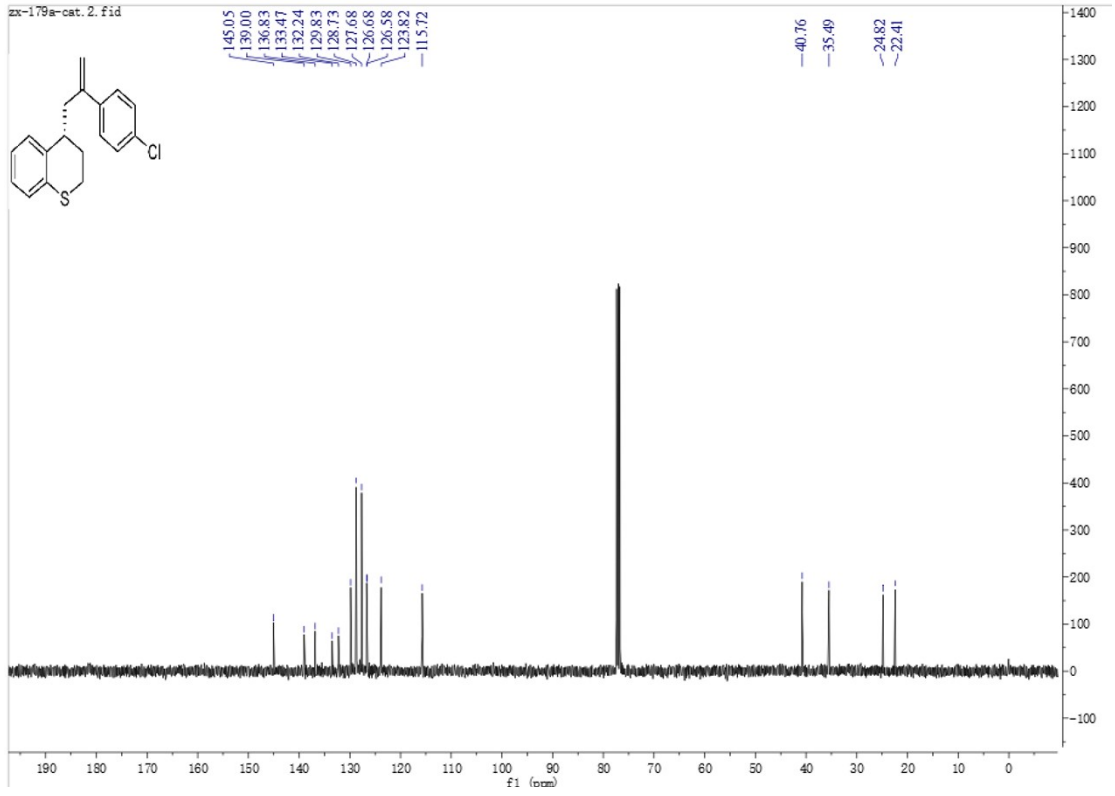
Compound 3bb



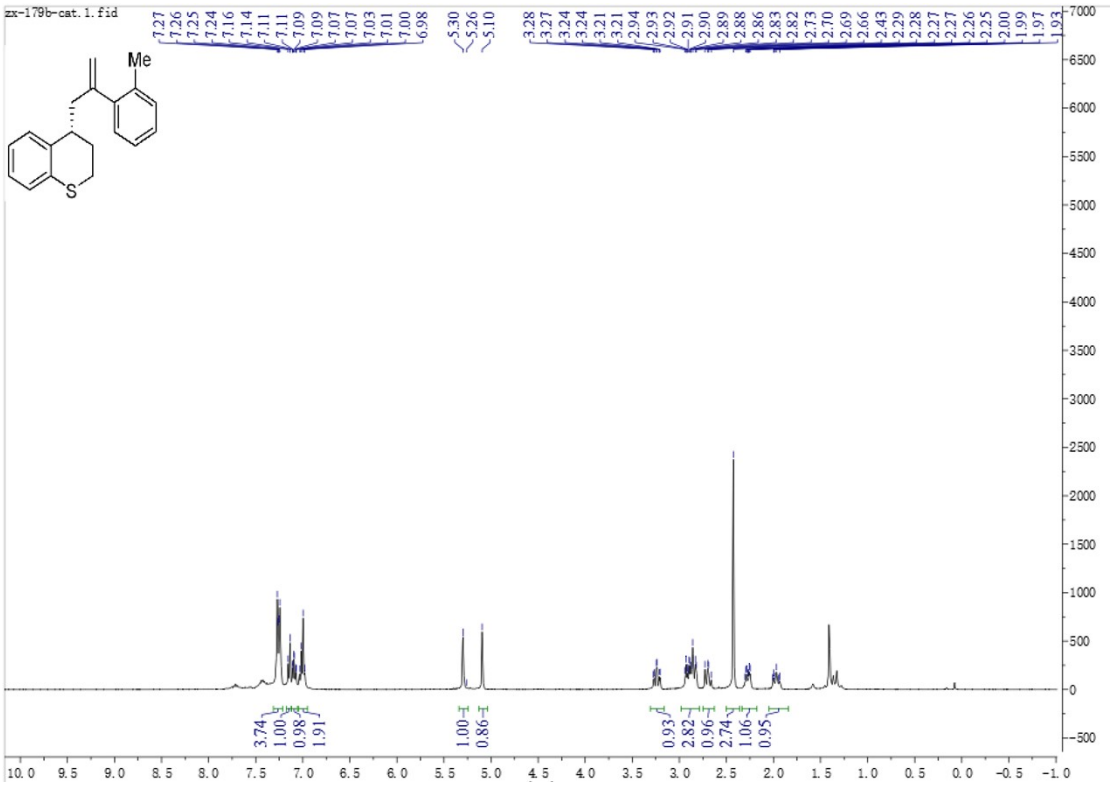


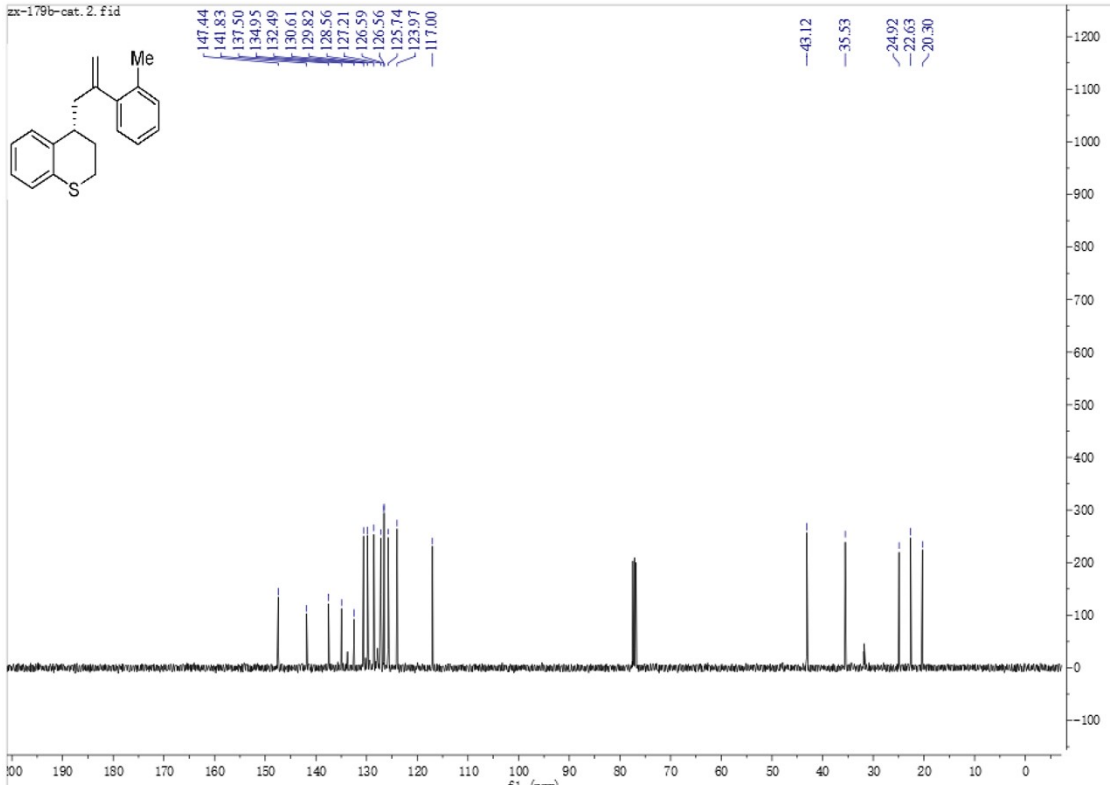
Compound 3bc



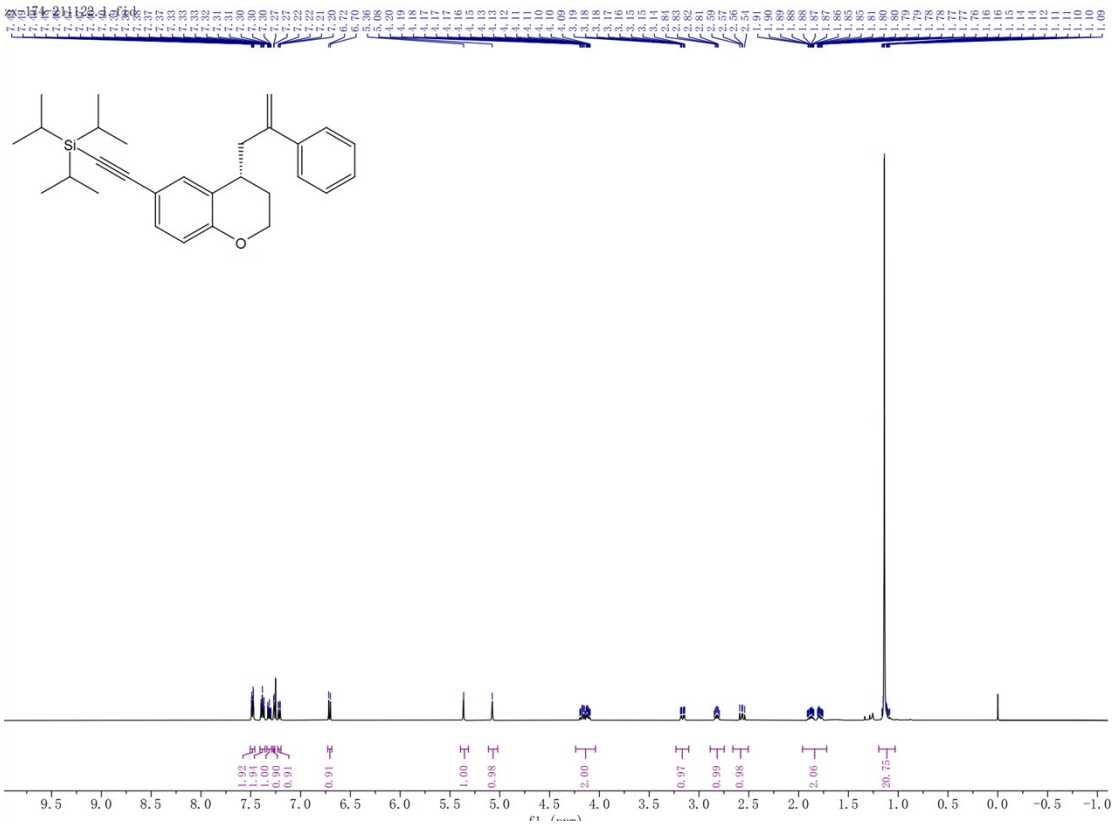


Compound 3bd

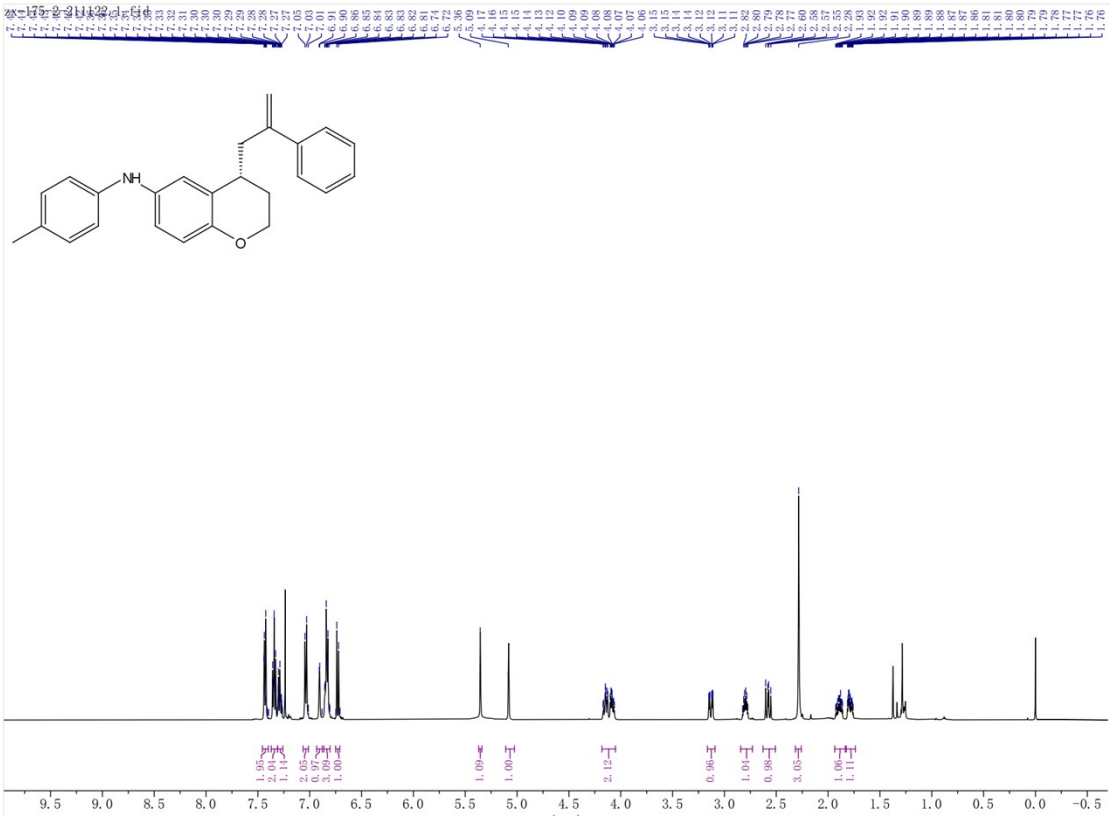


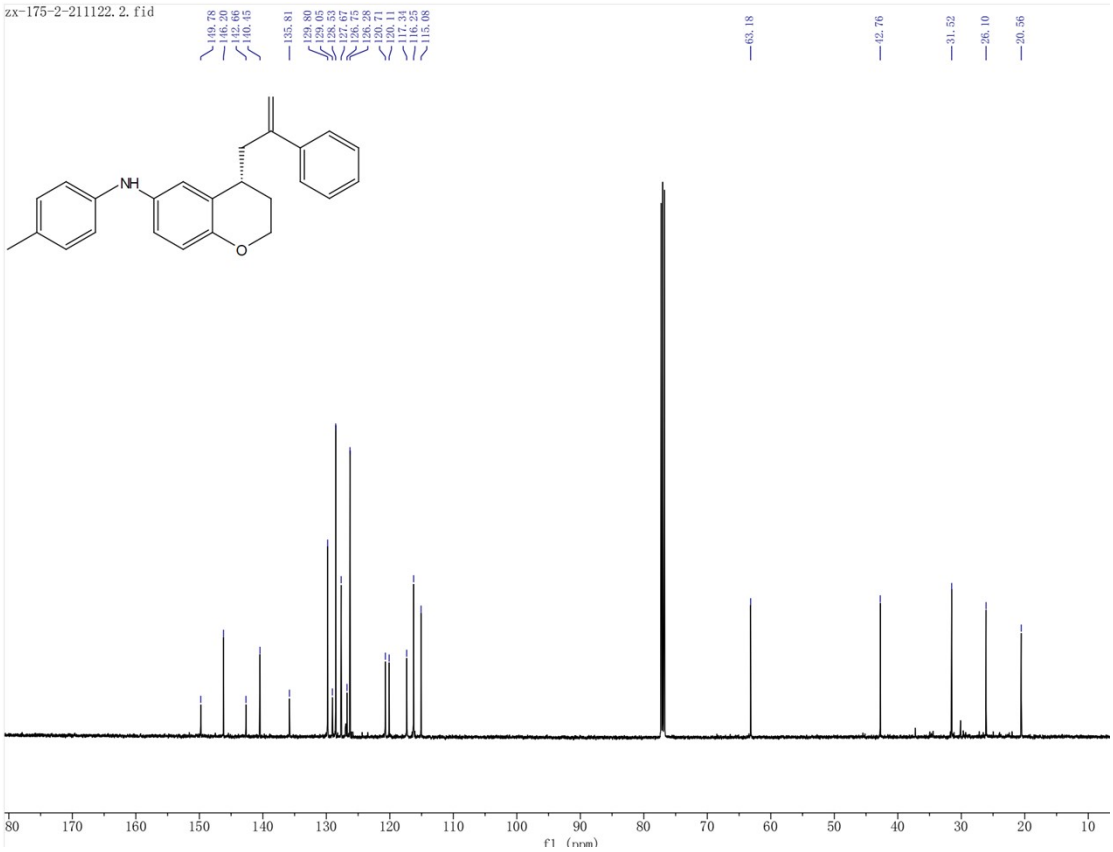


Compound 3be

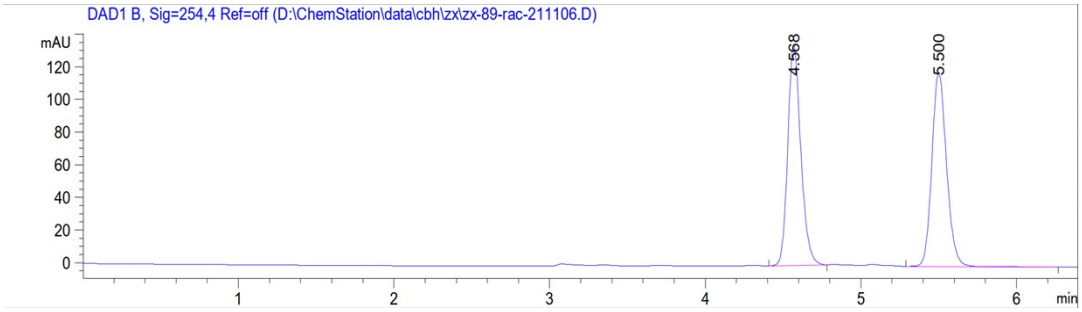


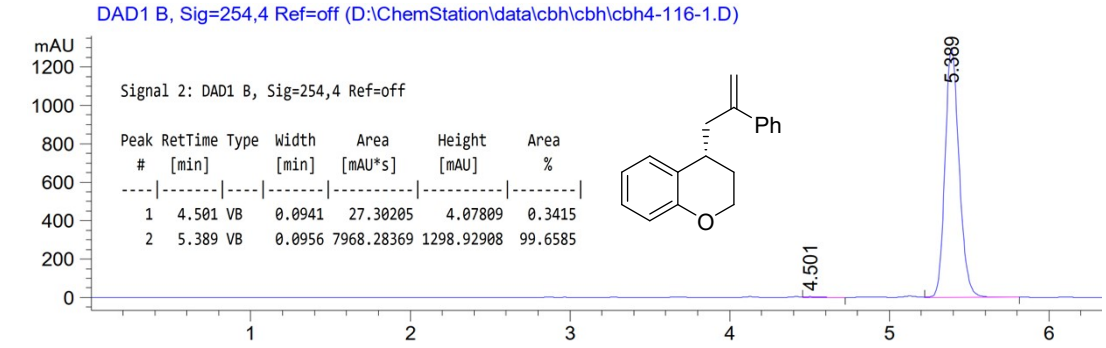
Compound 3bf



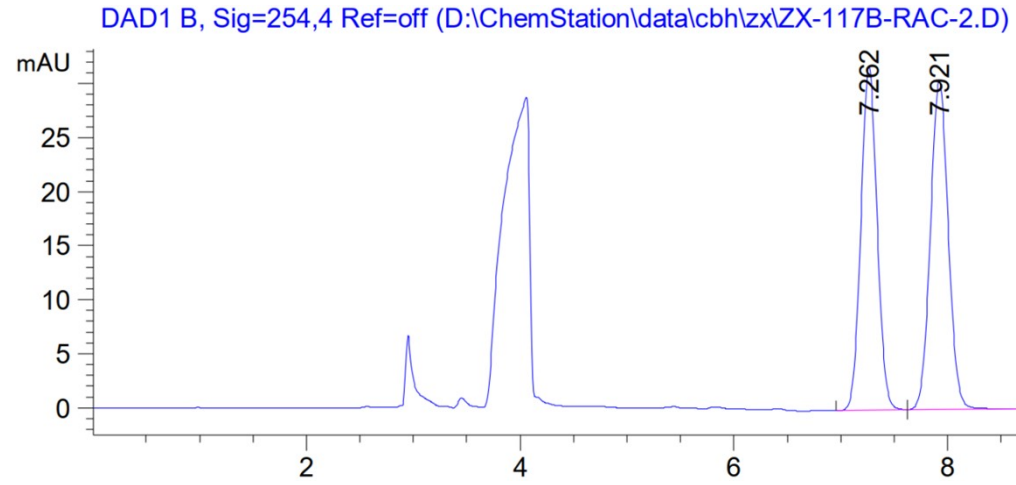


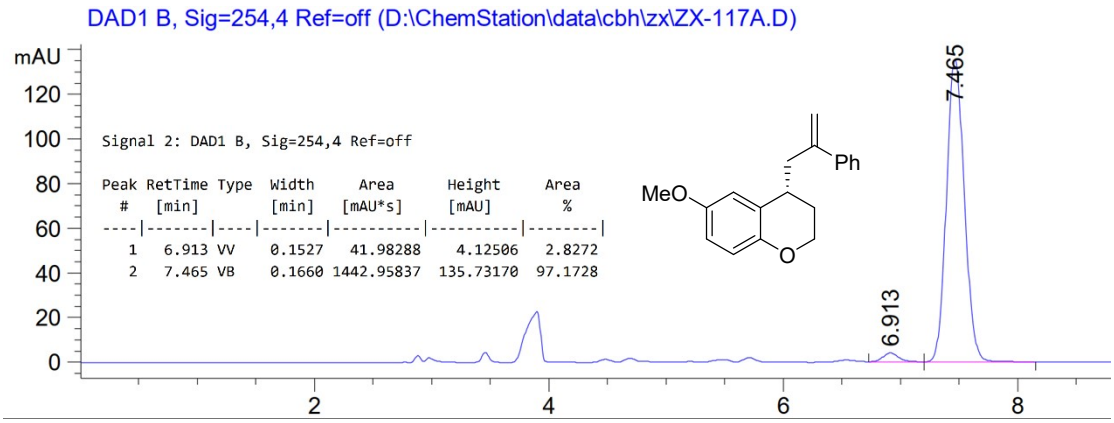
Compound 3aa



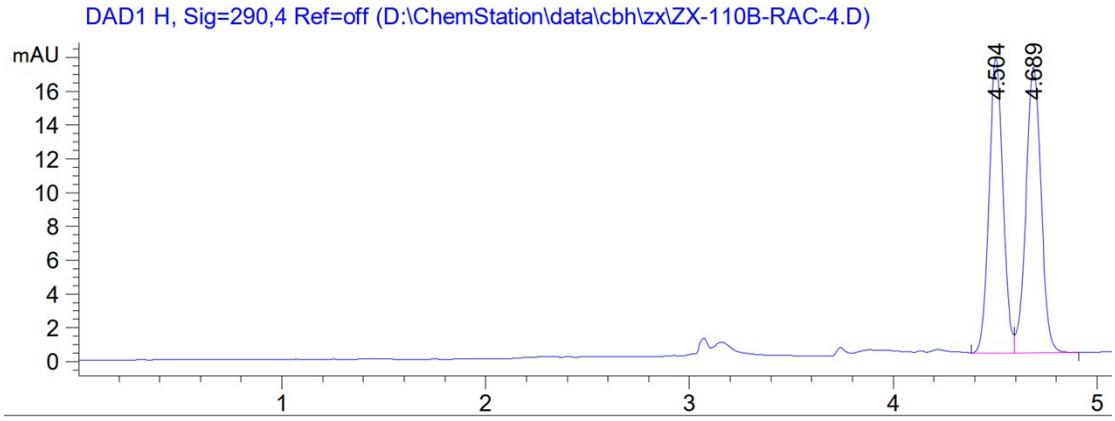


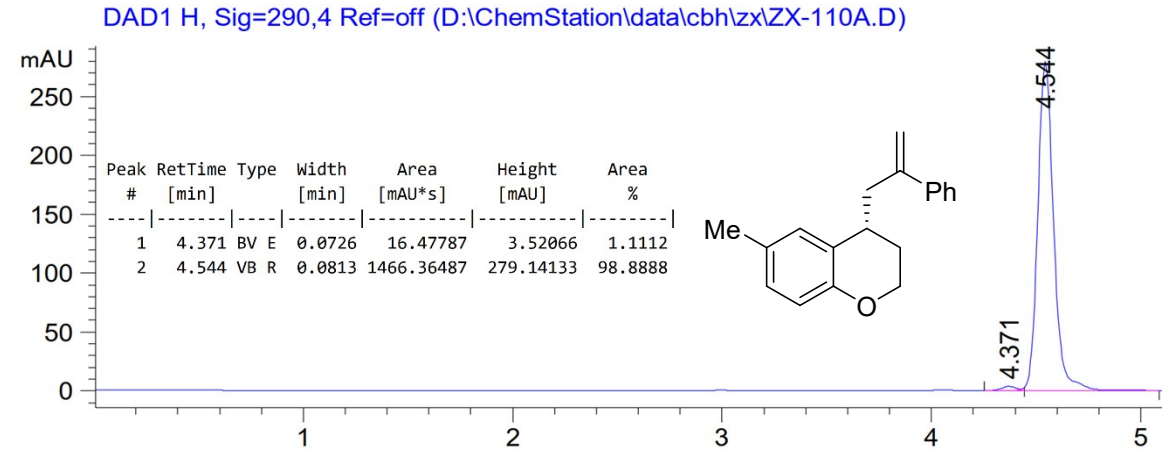
Compound 3ab



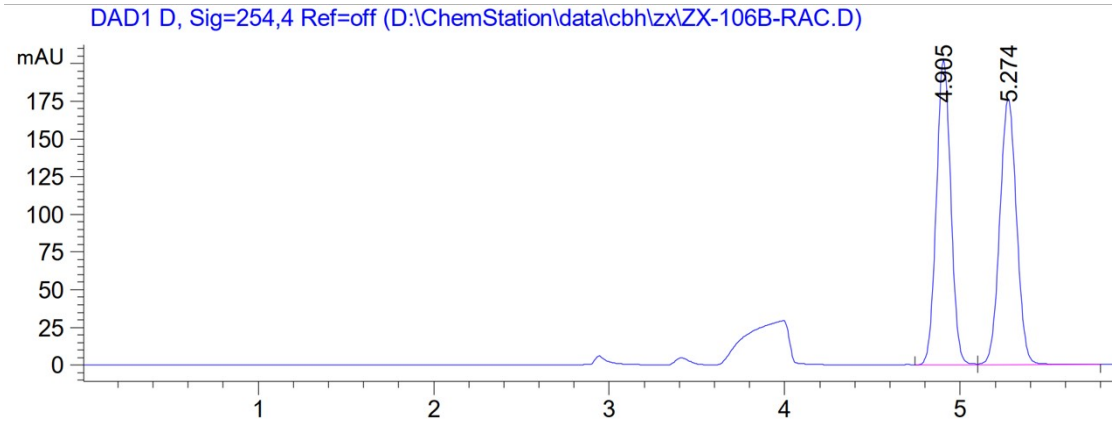


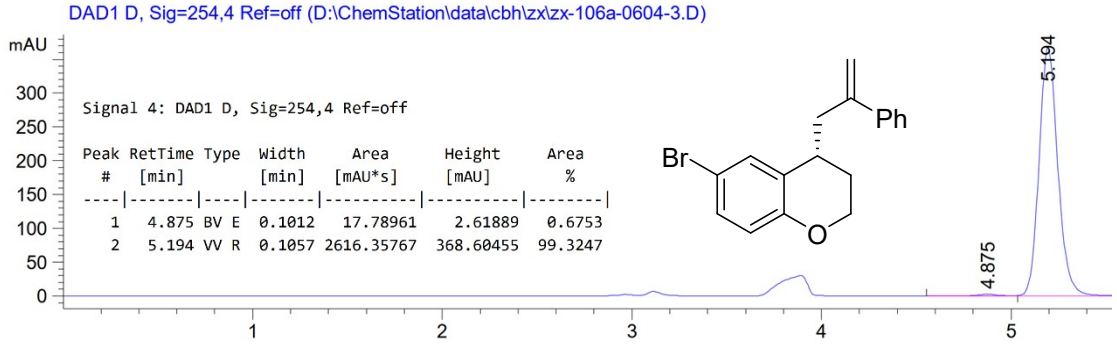
Compound 3ac



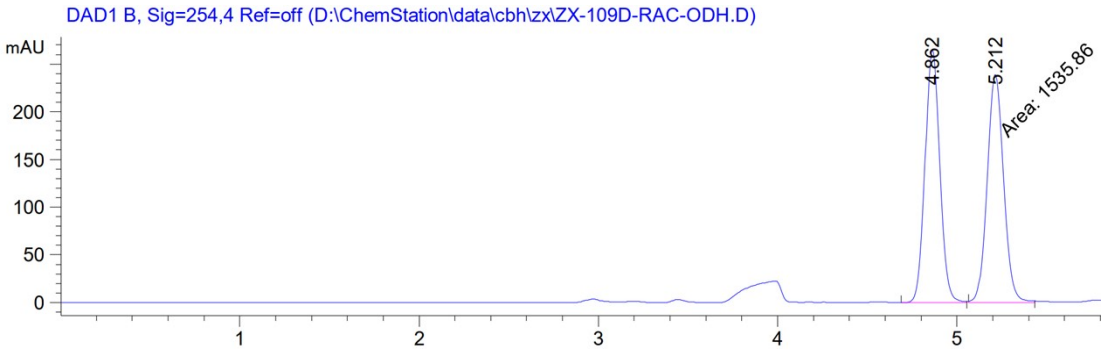


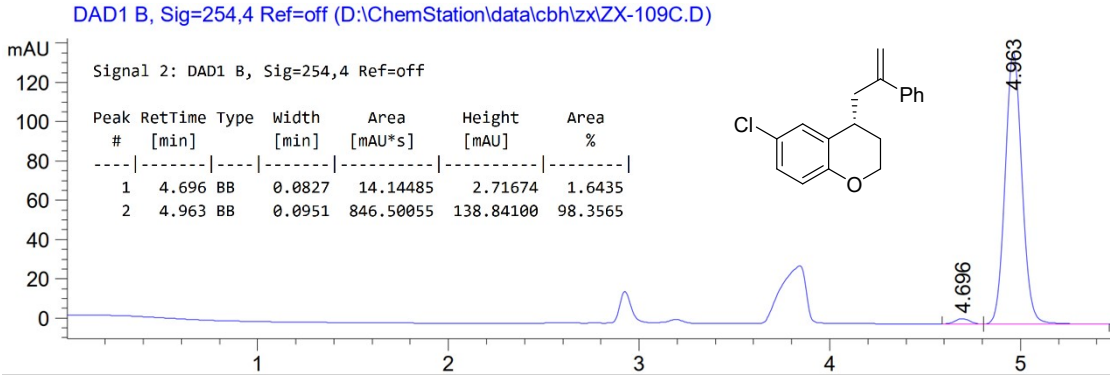
Compound 3ad



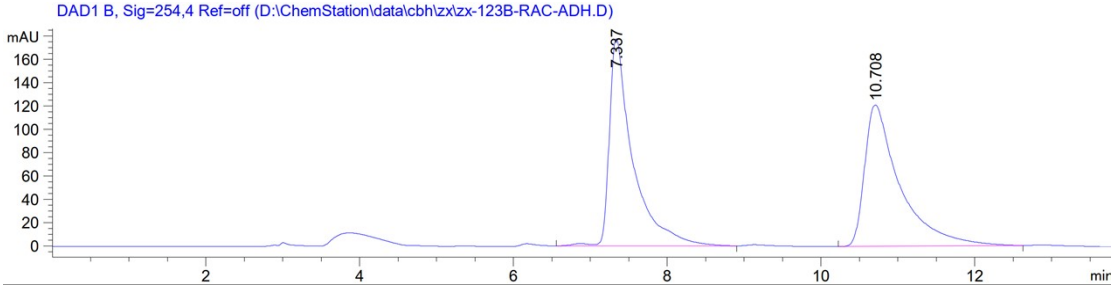


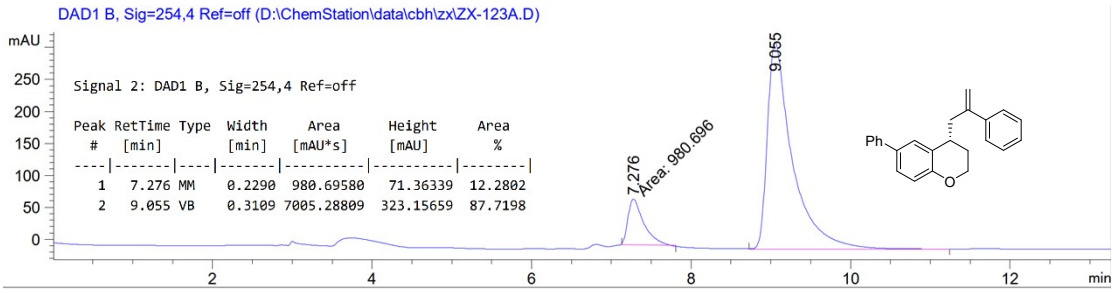
Compound 3ae



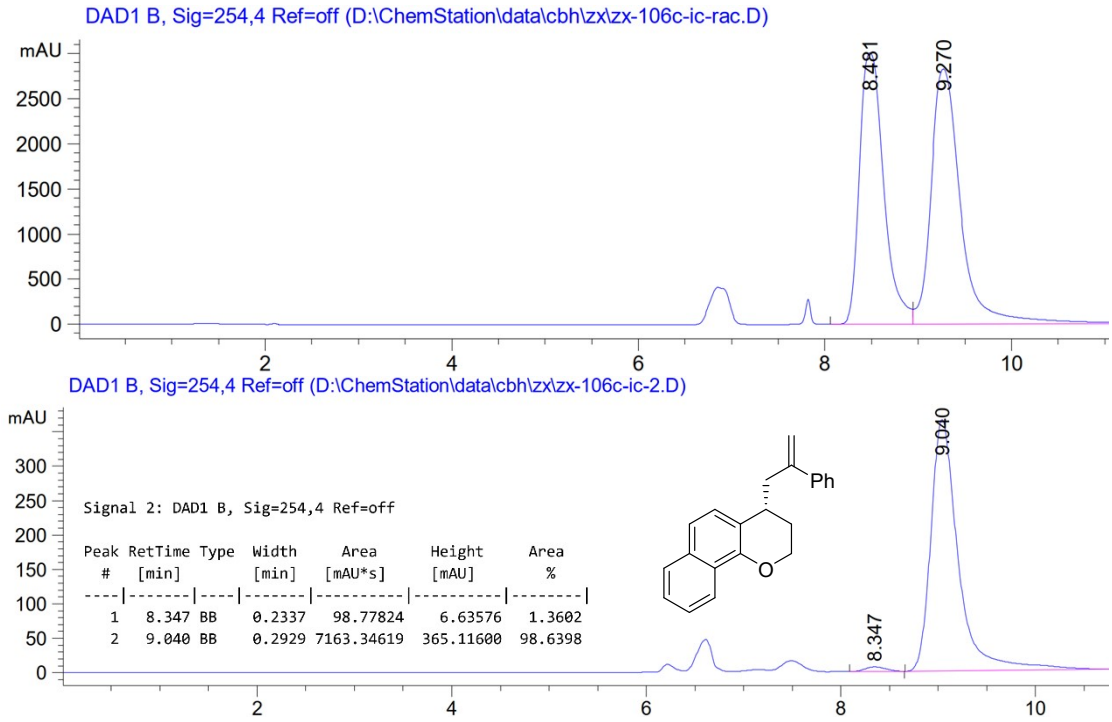


Compound 3af

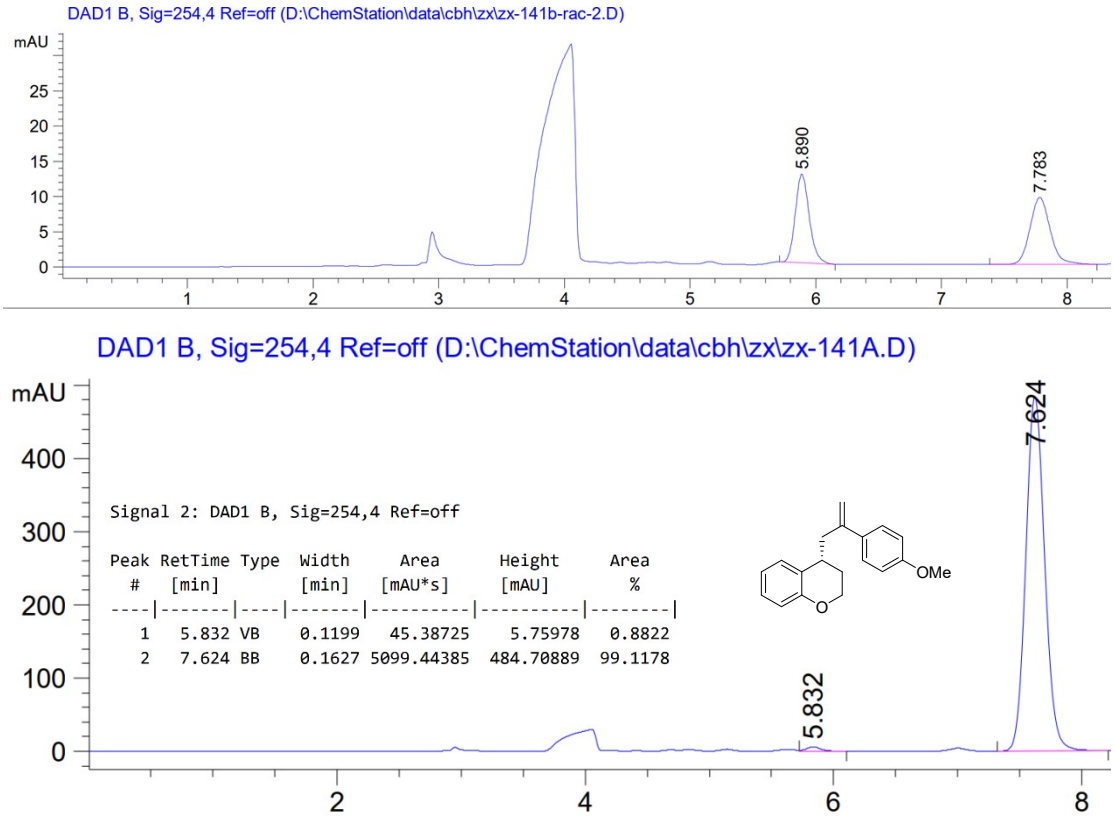




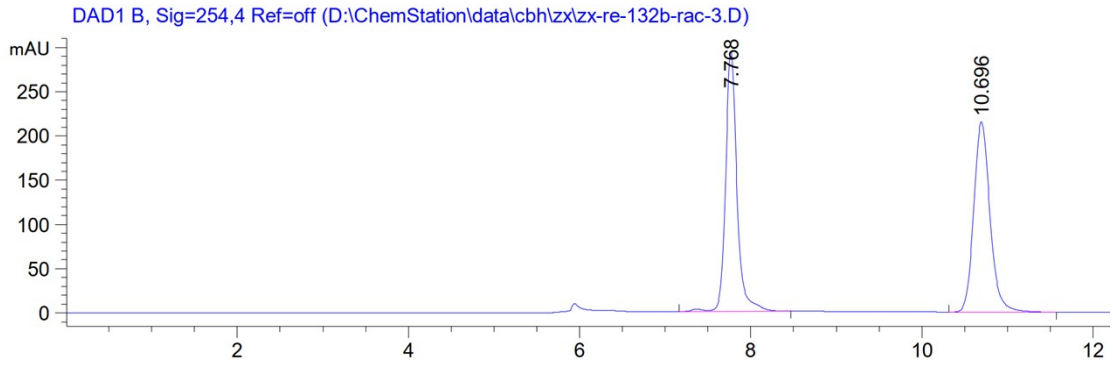
Compound 3ag

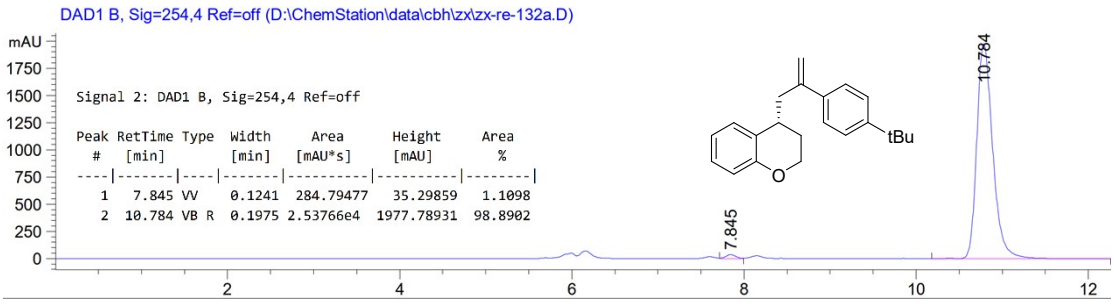


Compound 3ah

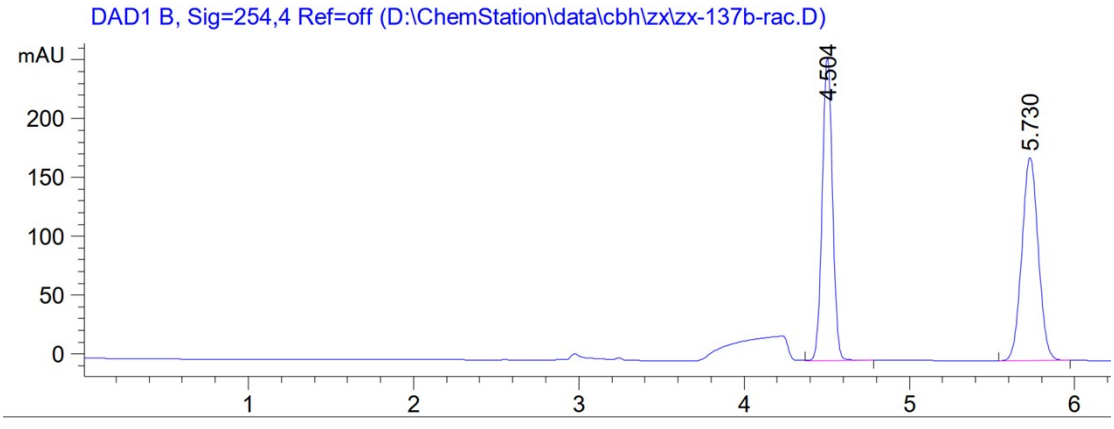


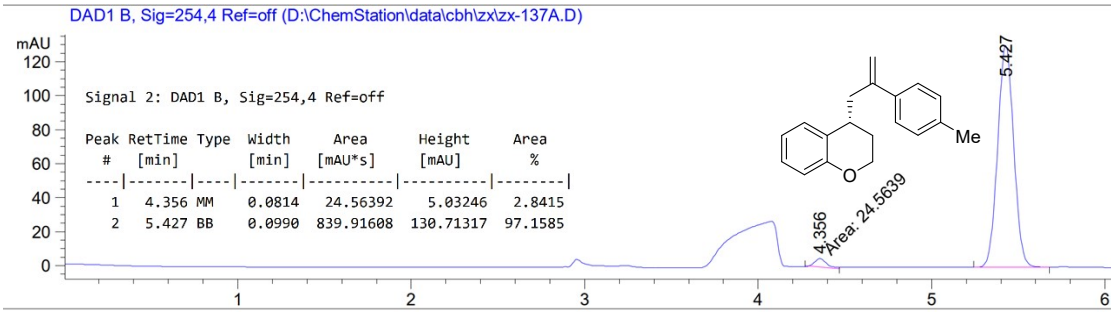
Compound 3ai



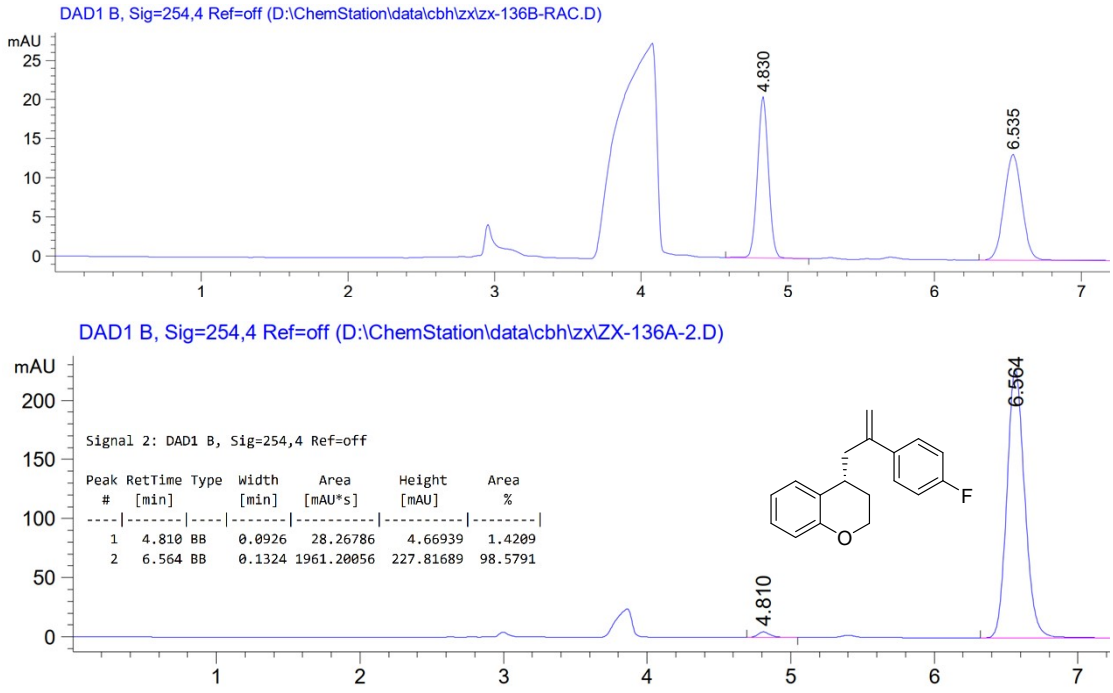


Compound 3aj

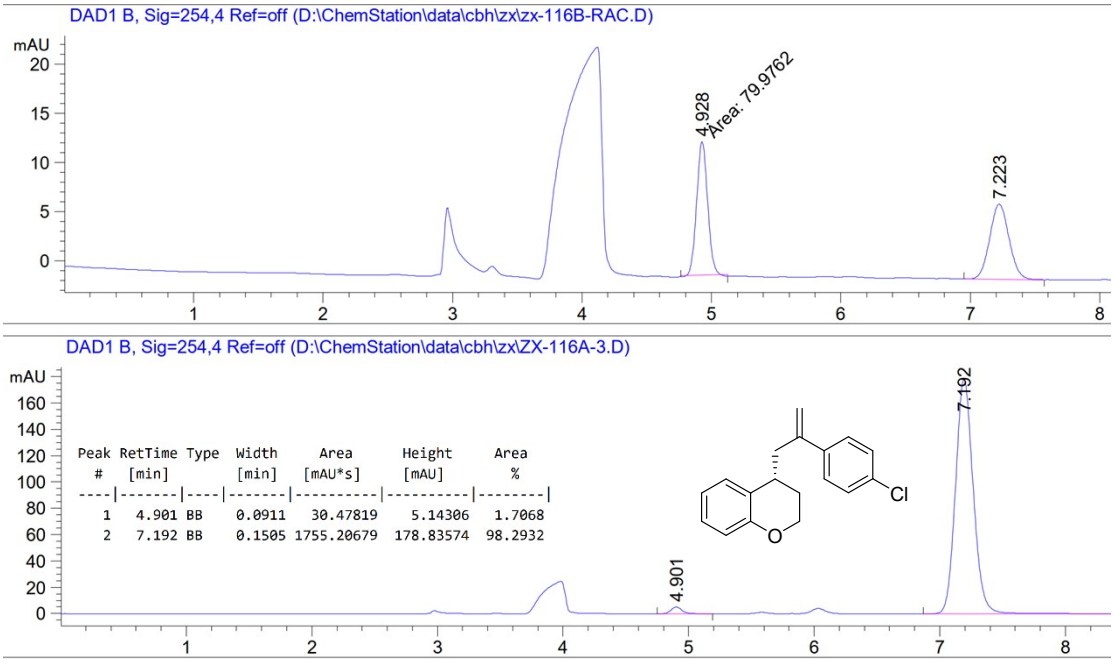




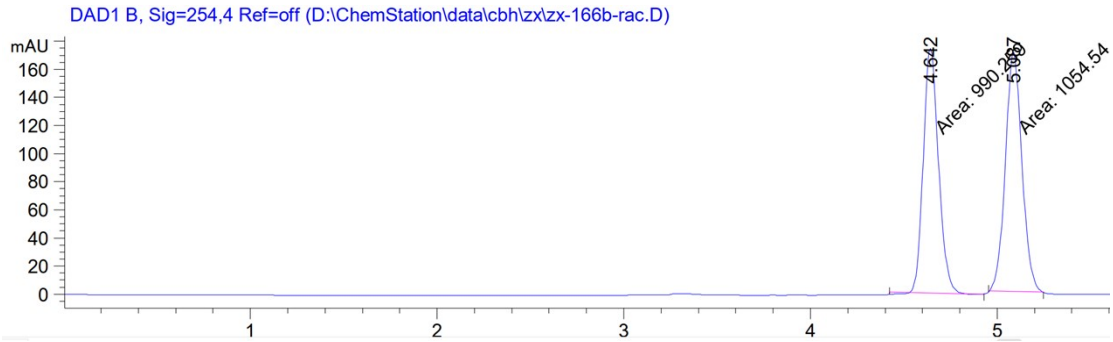
Compound 3ak

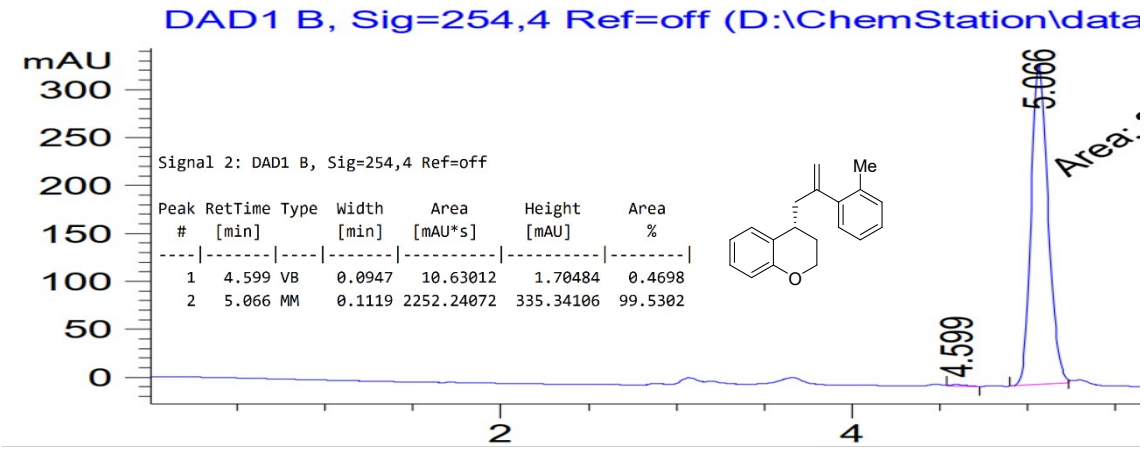


Compound 3al

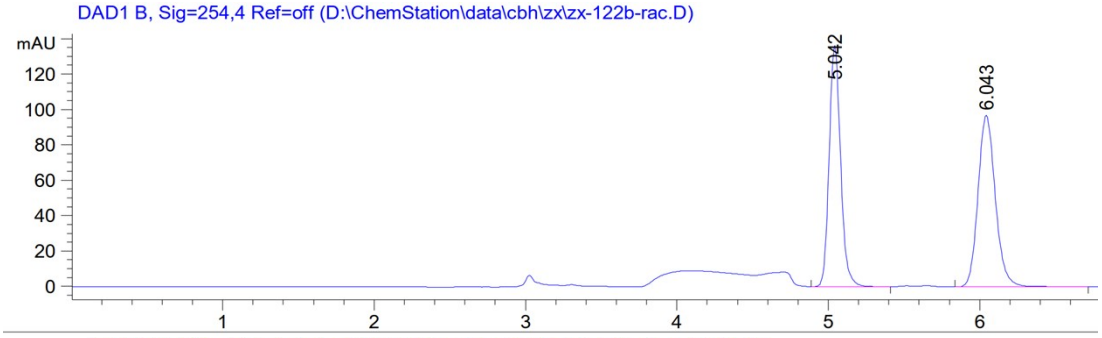


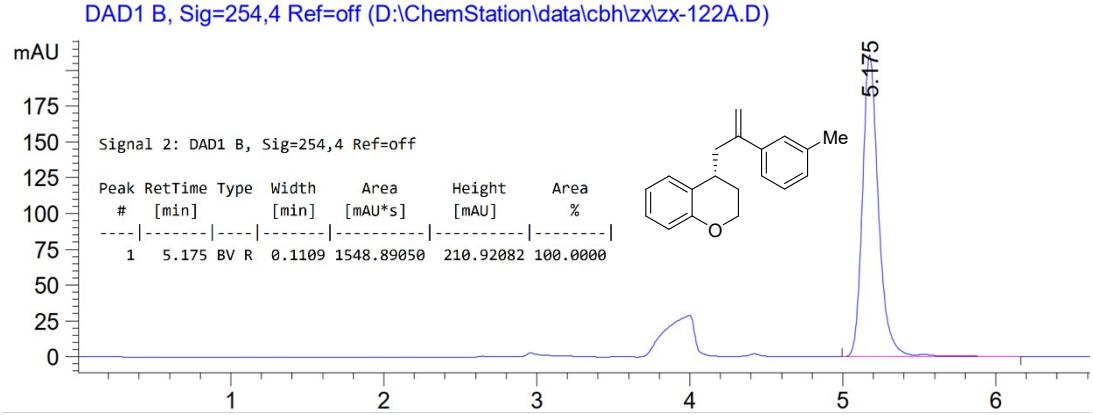
Compound 3am



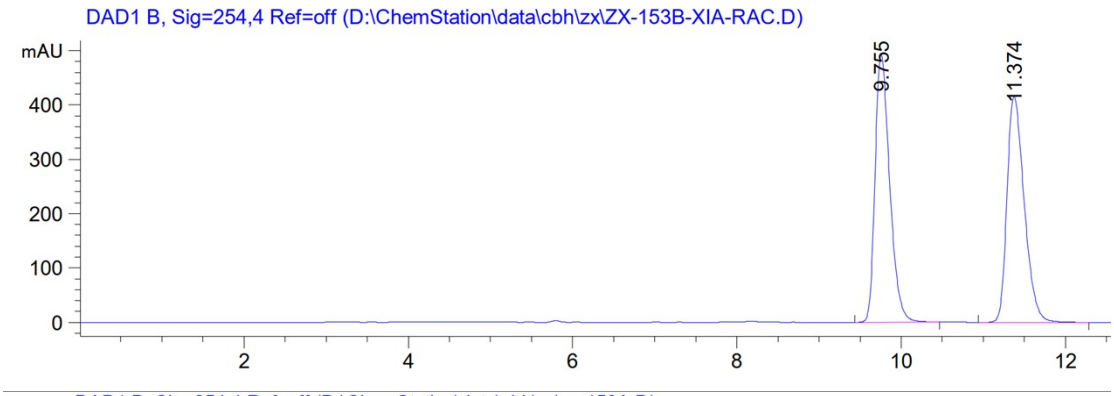


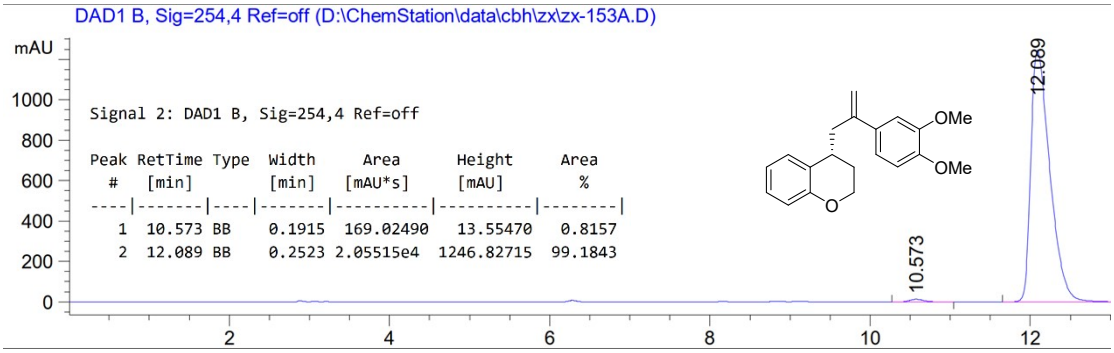
Compound 3an





Compound 3ao

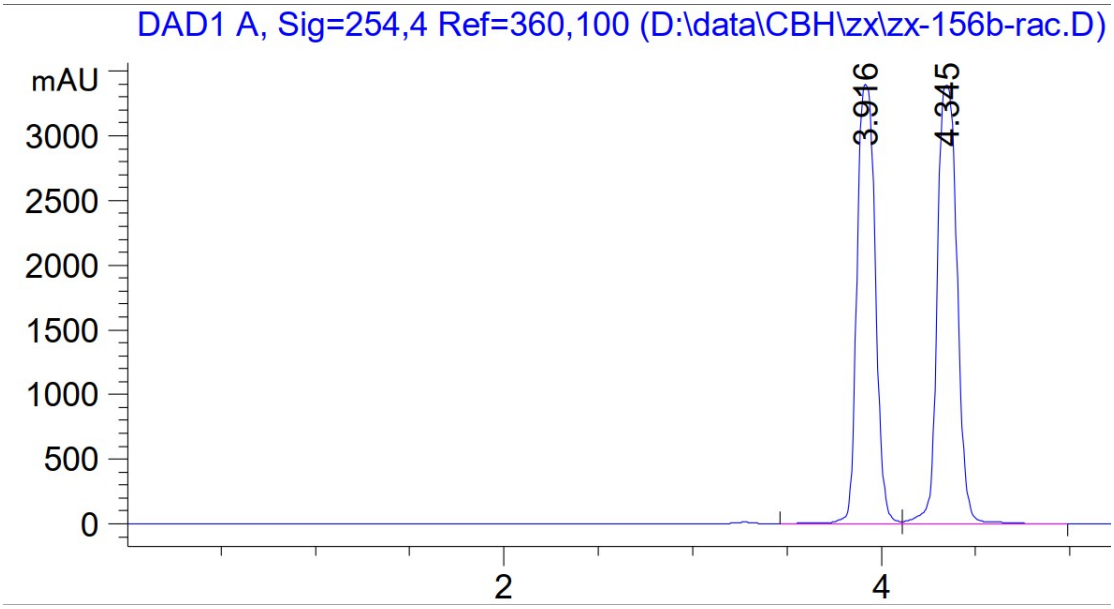




Signal 2: DAD1 B, Sig=254,4 Ref=off

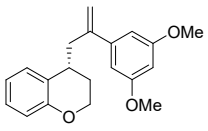
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.573	BB	0.1915	169.02490	13.55470	0.8157
2	12.089	BB	0.2523	2.05515e4	1246.82715	99.1843

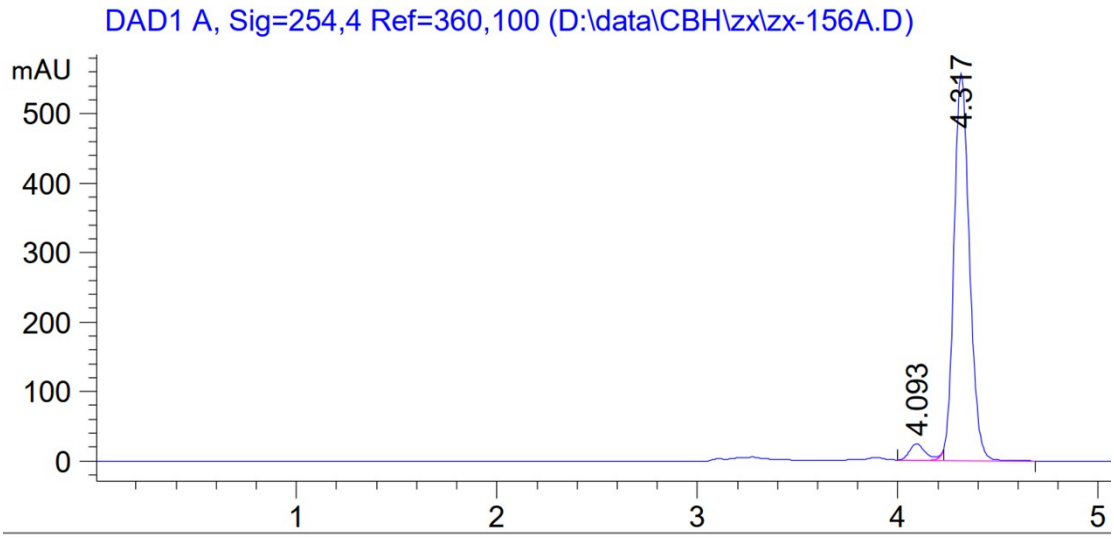
Compound 3ap



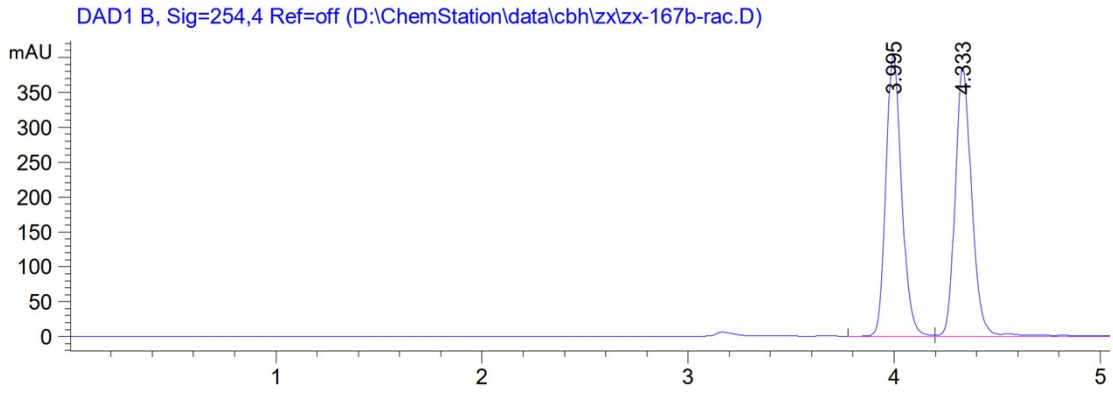
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

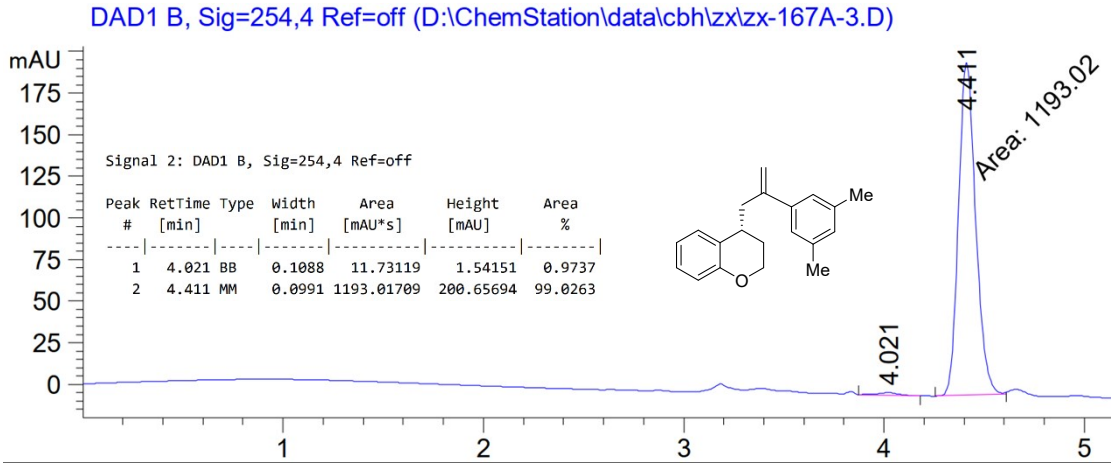
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.093	BV E	0.0825	125.71877	23.46672	4.0441
2	4.317	VB R	0.0823	2982.98145	558.38873	95.9559



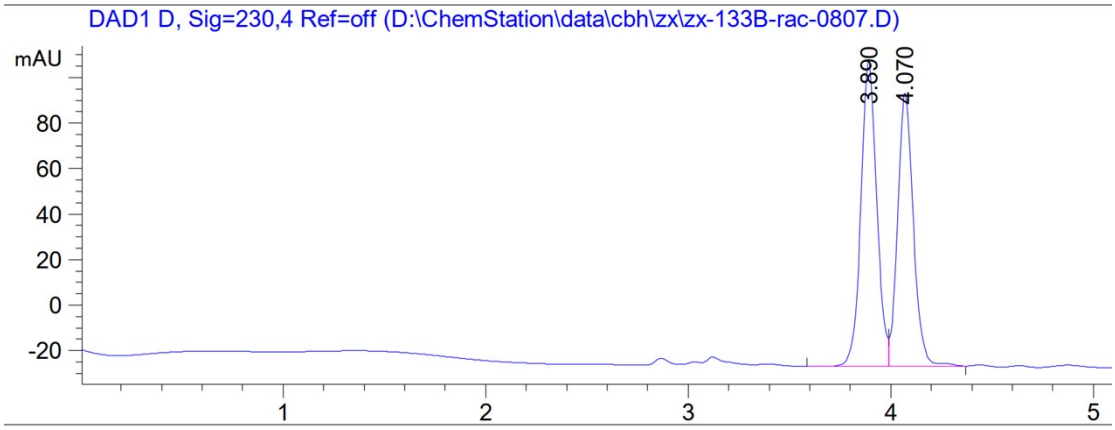


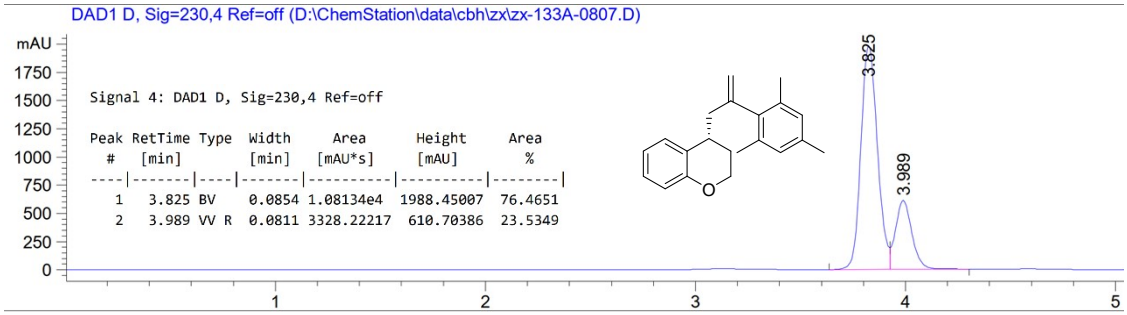
Compound 3aq



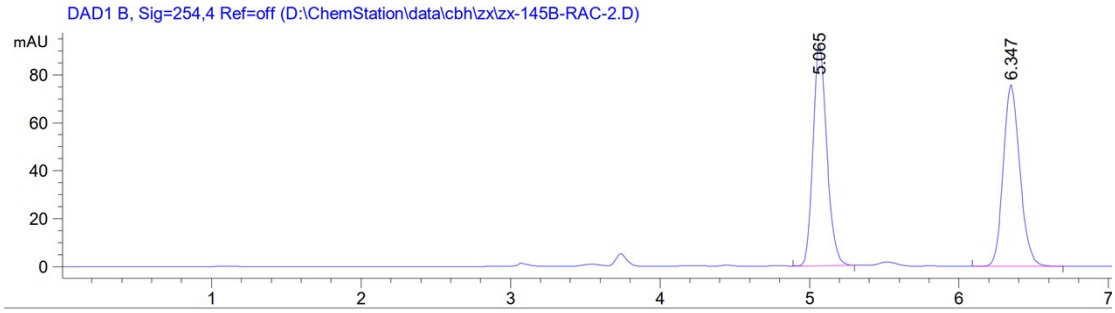


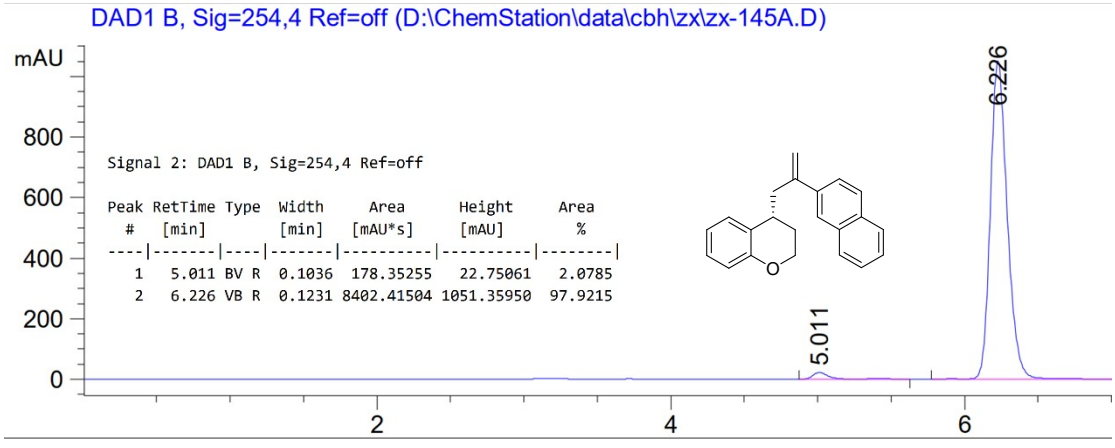
Compound 3ar



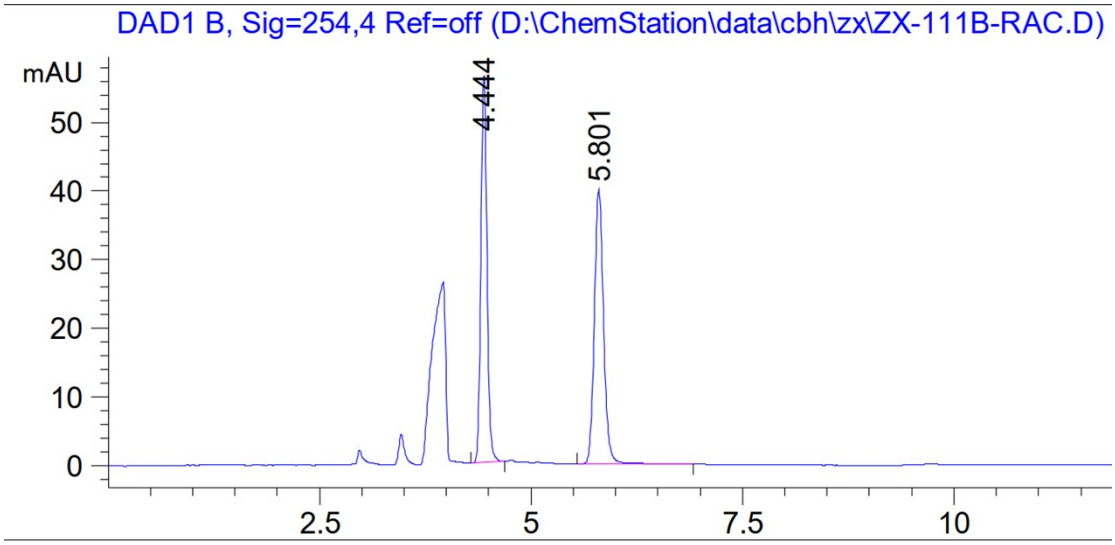


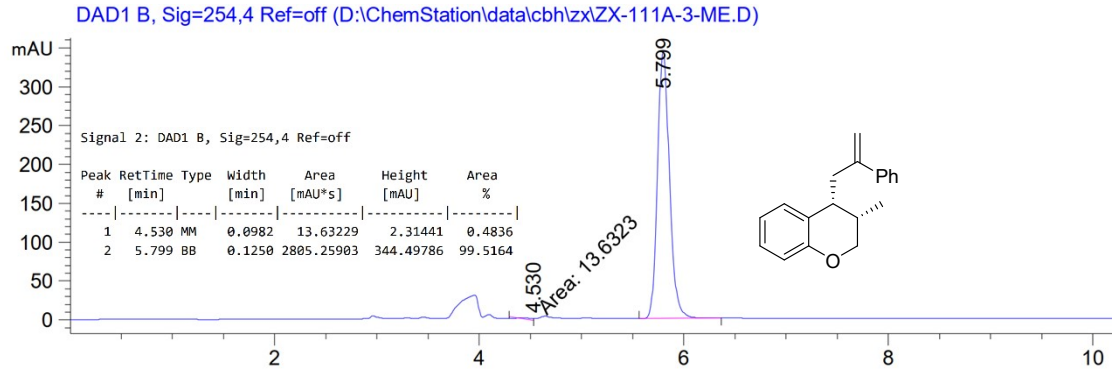
Compound 3as



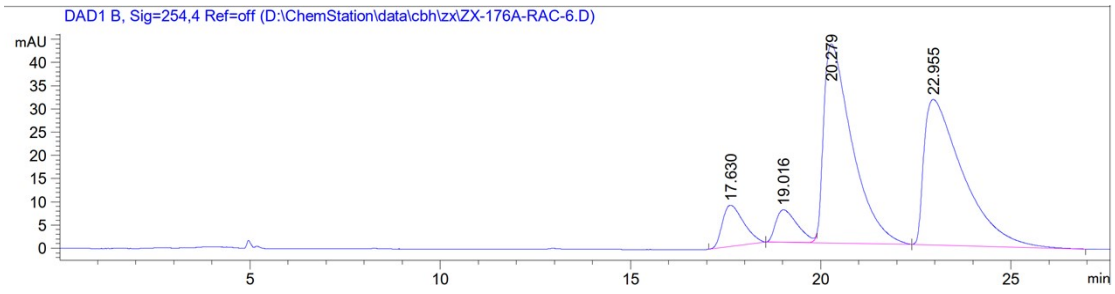


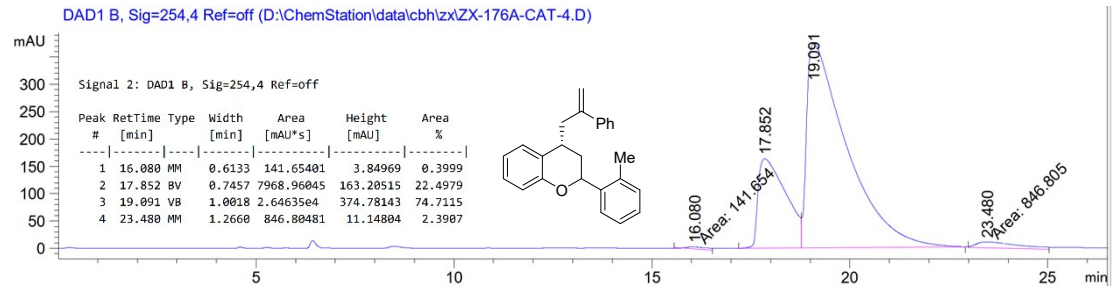
Compound 3at



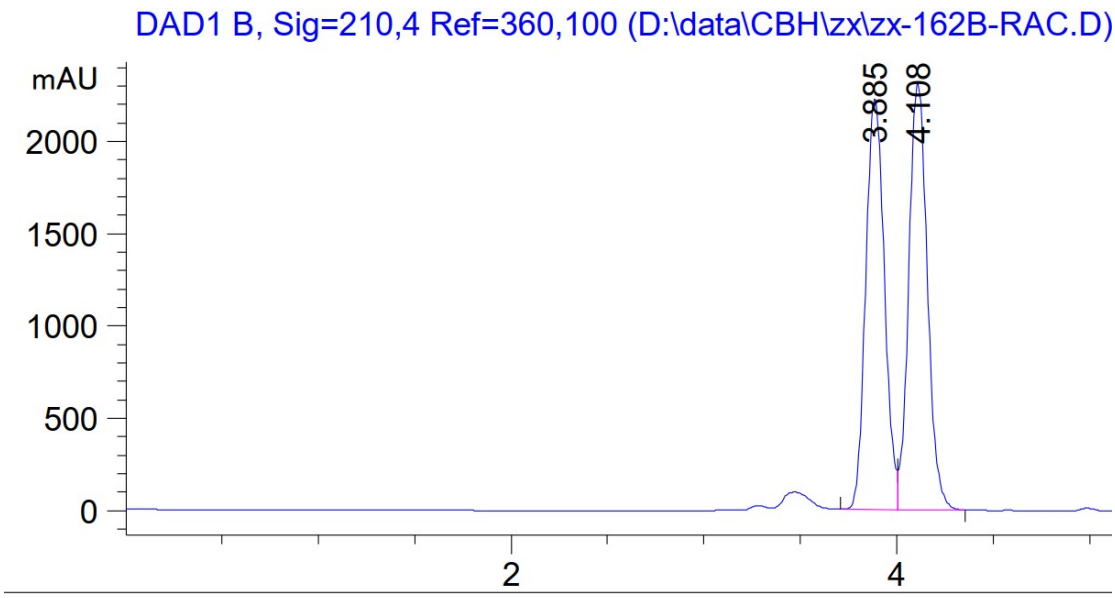


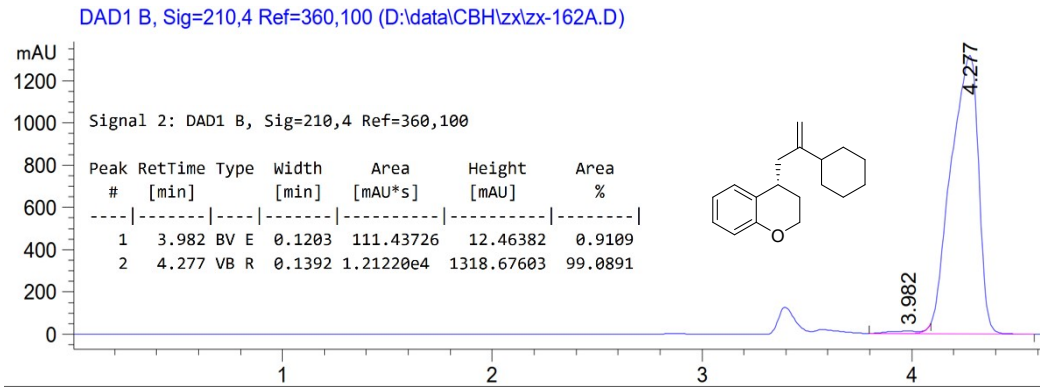
Compound 3au



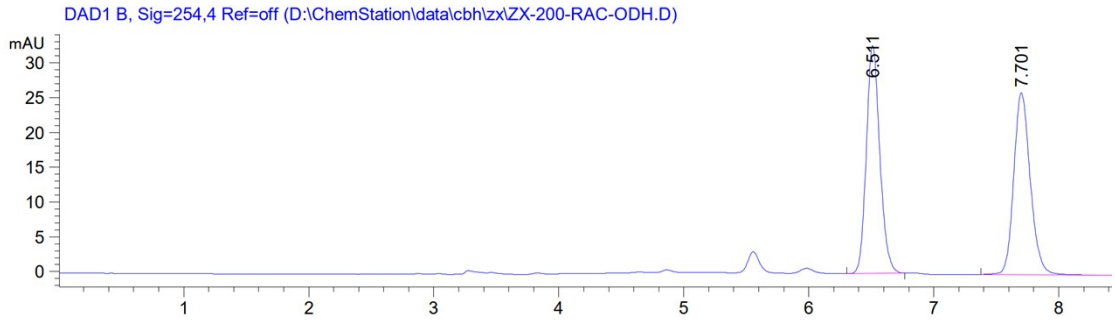


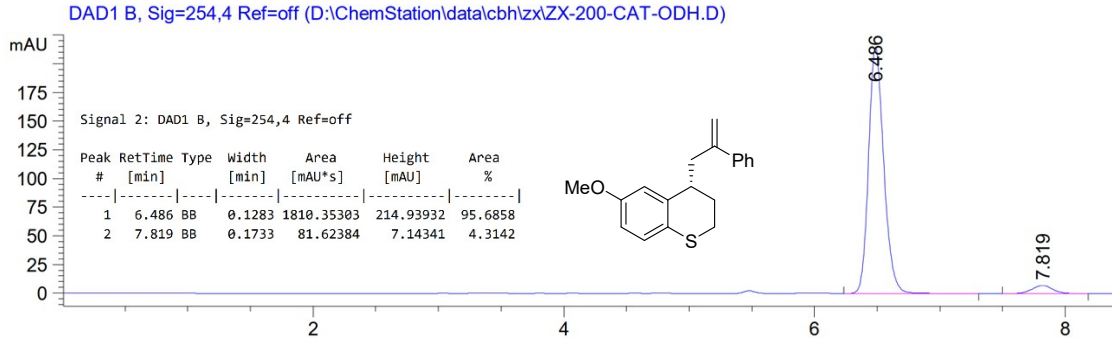
Compound 3av



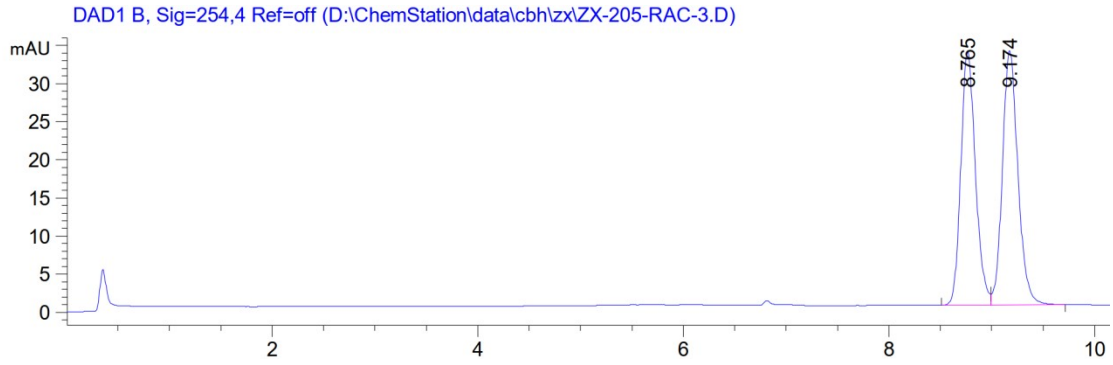


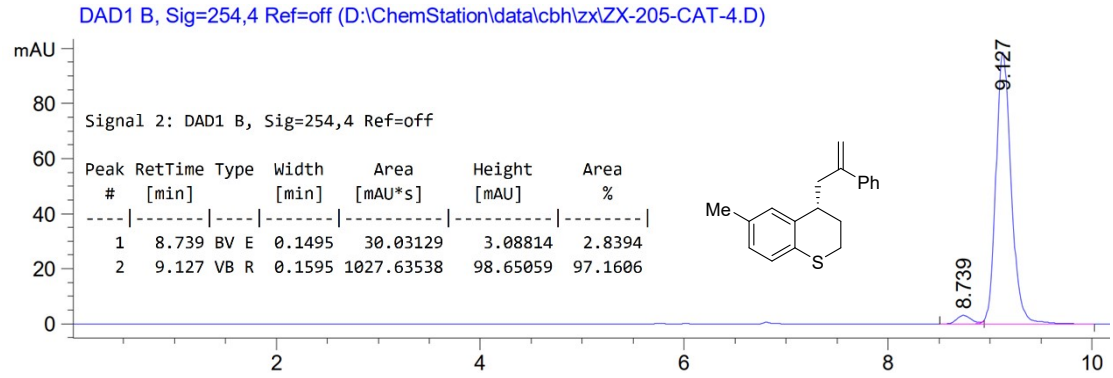
Compound 3aw



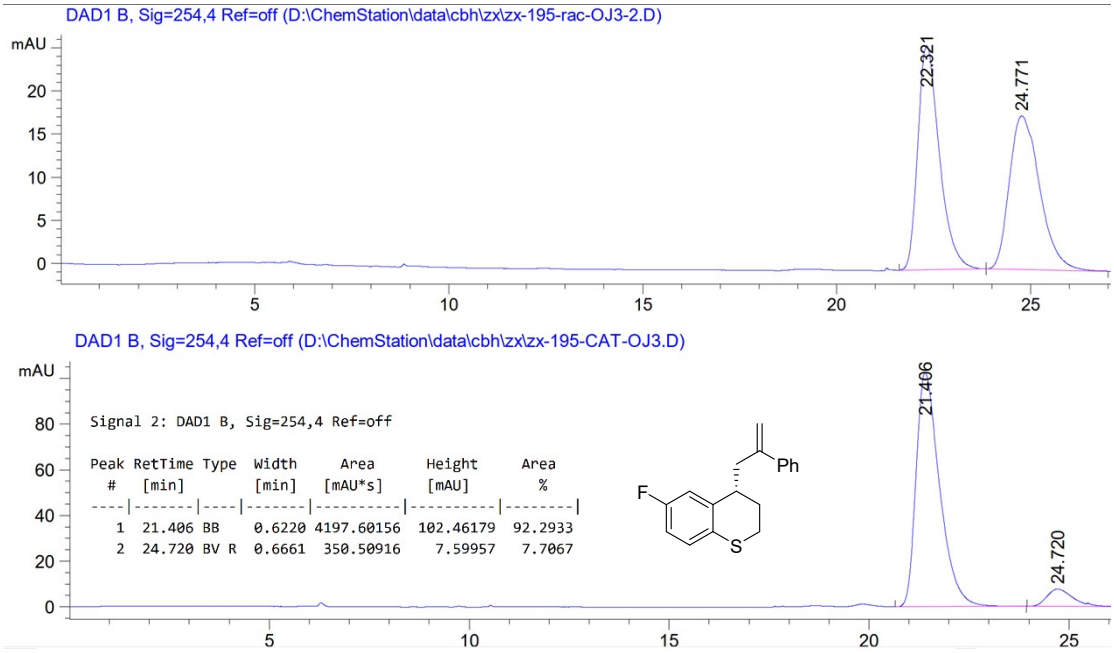


Compound 3ax

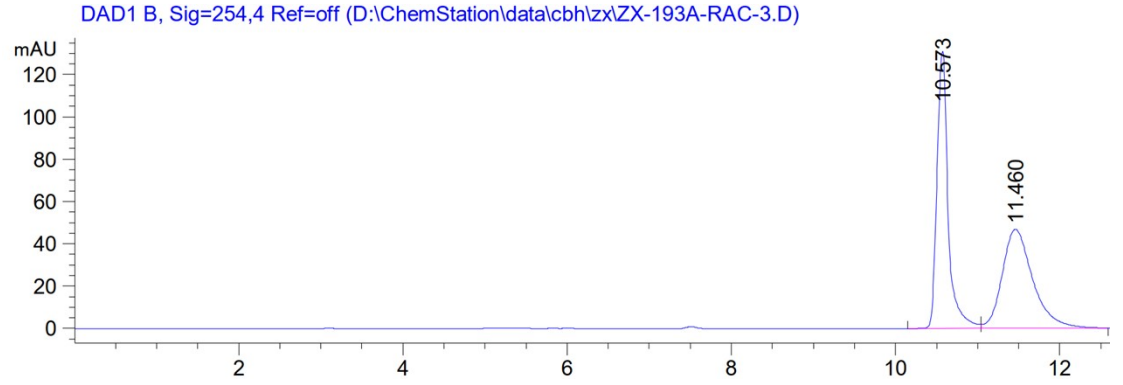


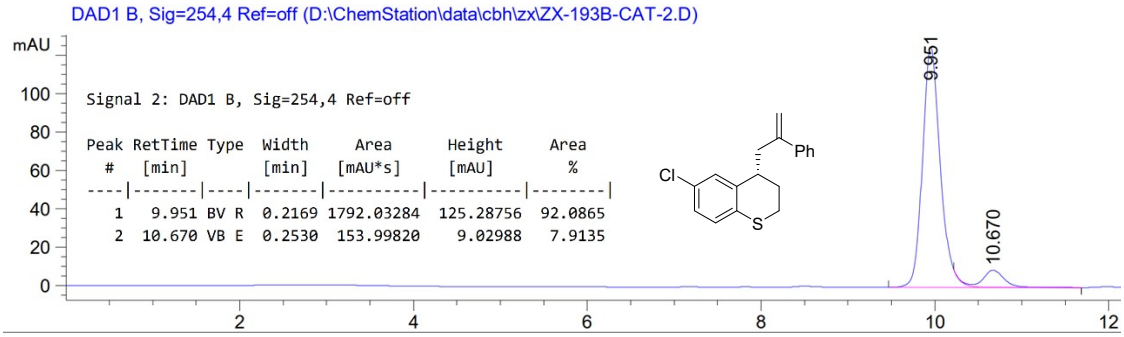


Compound 3ay



Compound 3az

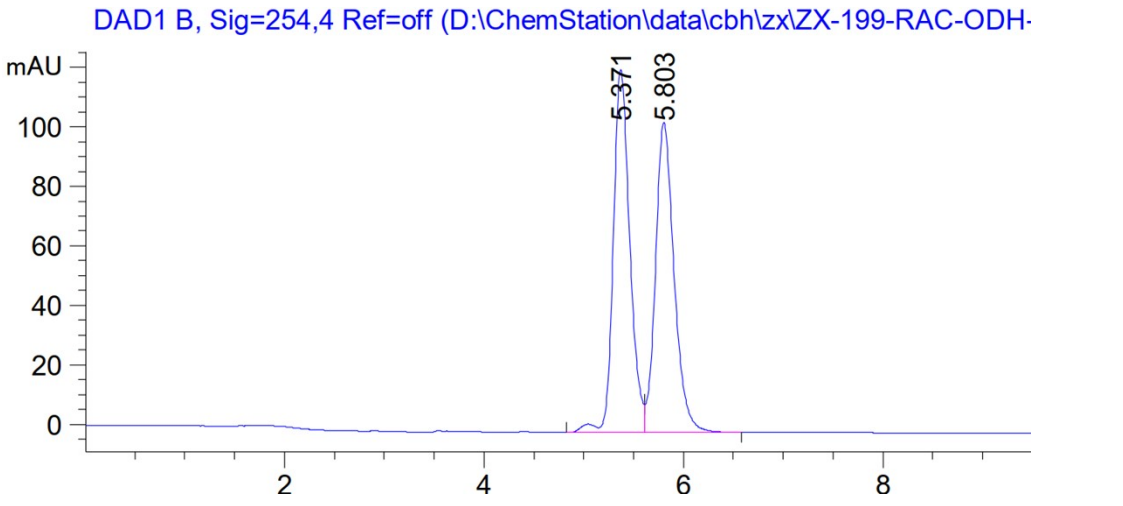


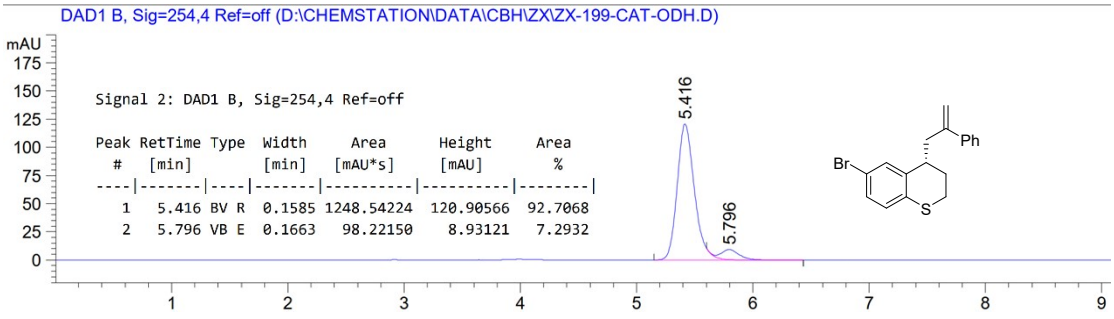


Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.951	BV R	0.2169	1792.03284	125.28756	92.0865
2	10.670	VB E	0.2530	153.99820	9.02988	7.9135

Compound 3ba

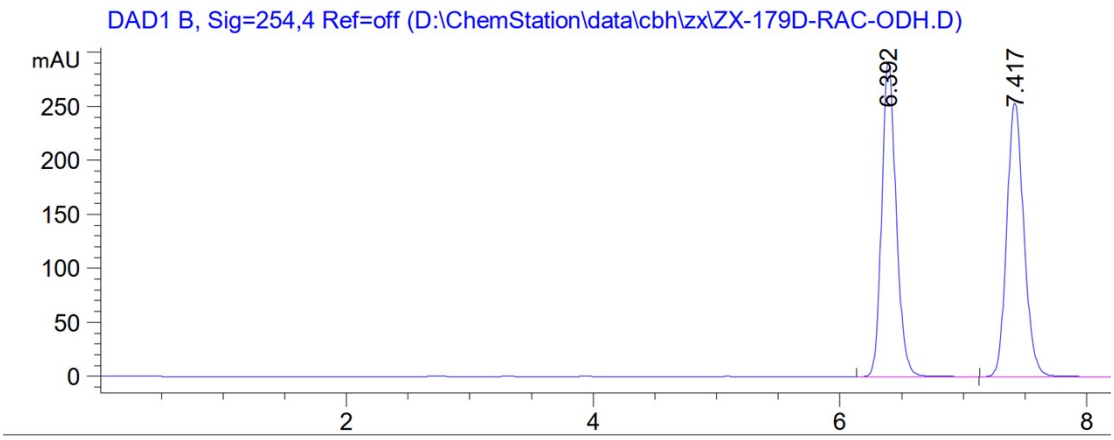


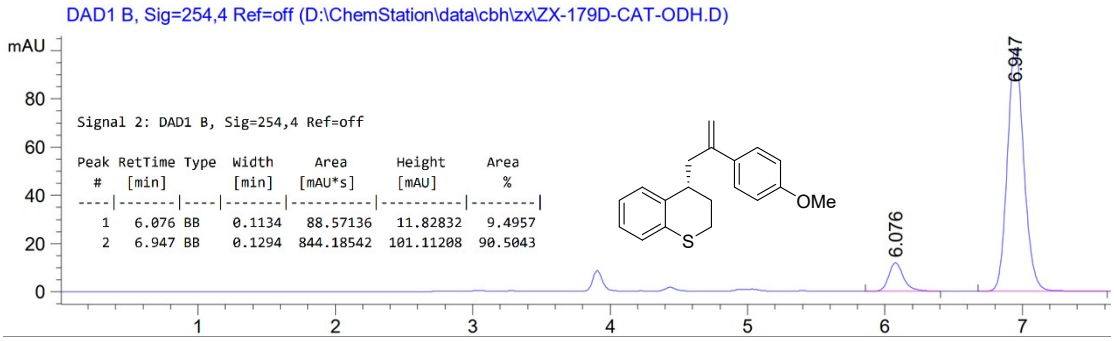


Signal 2: DAD1 B, Sig=254,4 Ref=off

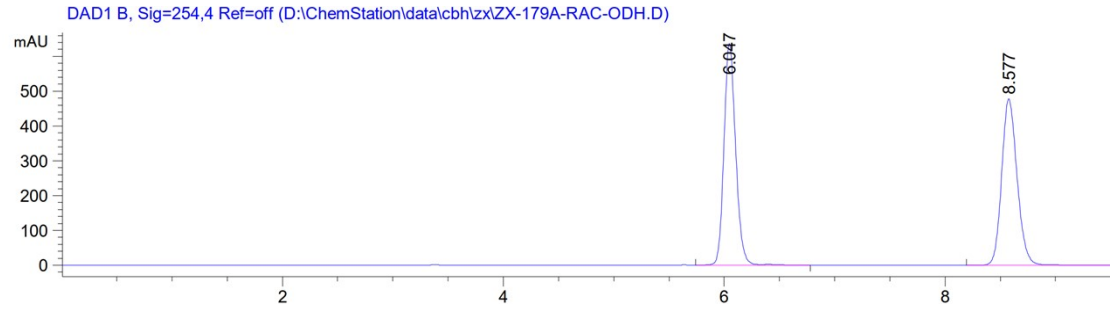
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.416	BV R	0.1585	1248.54224	120.90566	92.7068
2	5.796	VB E	0.1663	98.22150	8.93121	7.2932

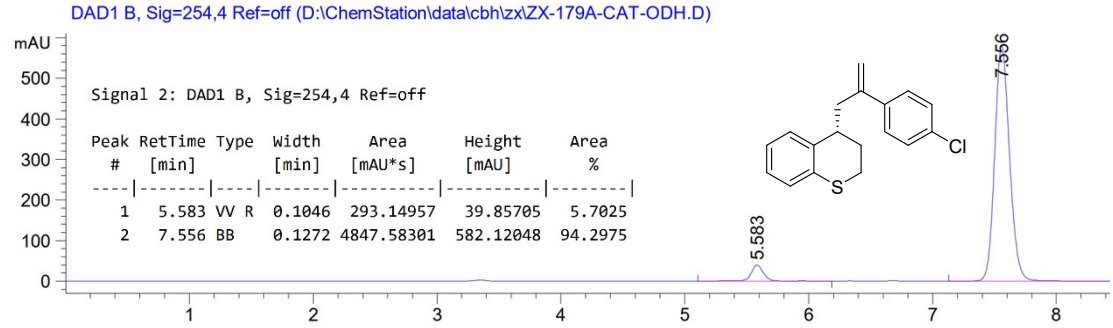
Compound 3bb



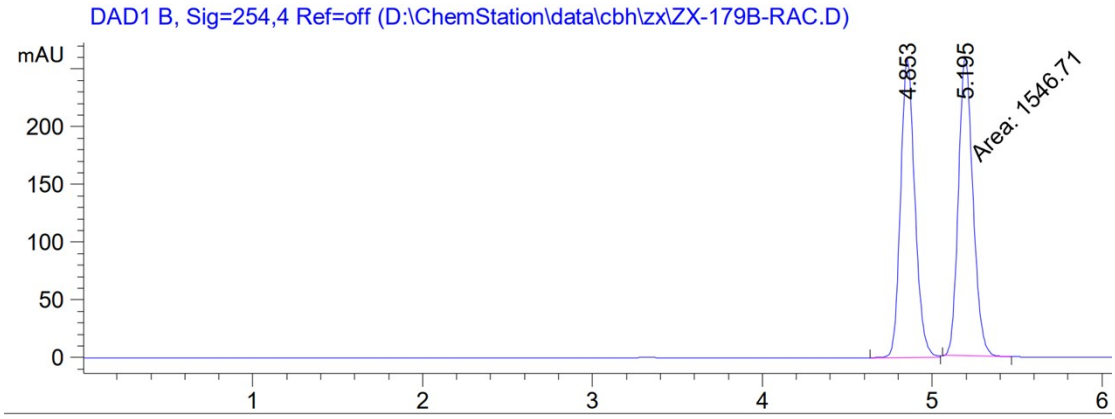


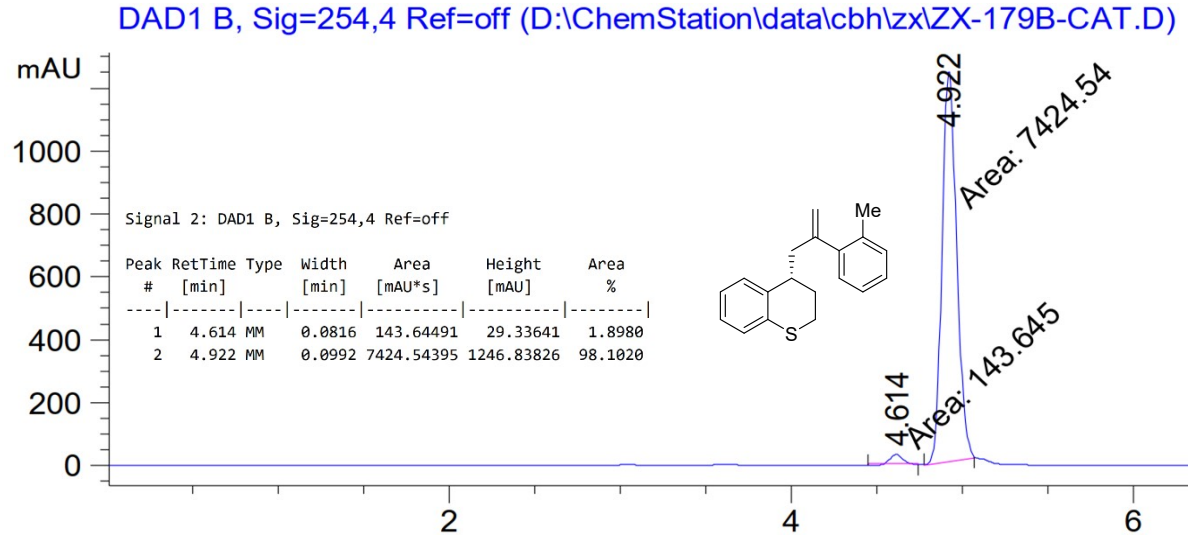
Compound 3bc



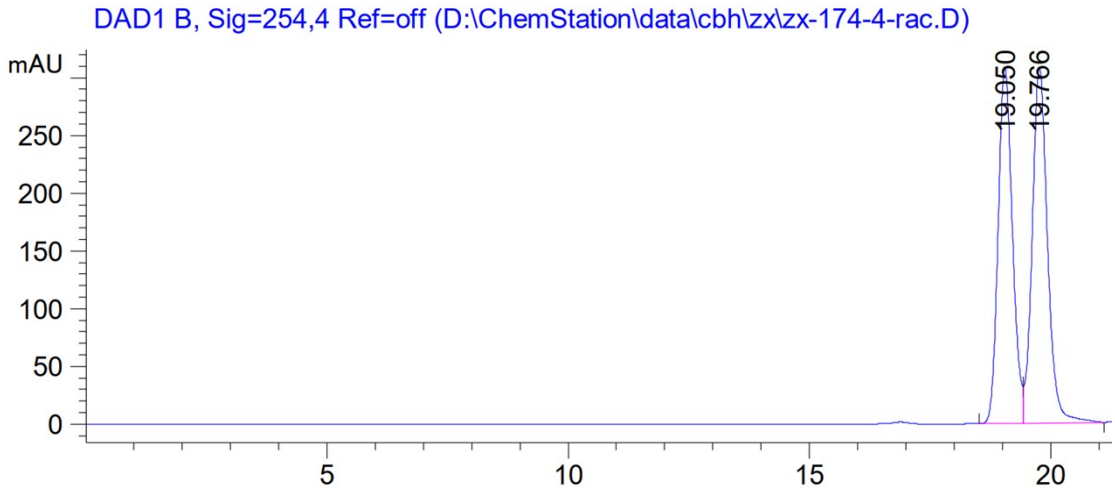


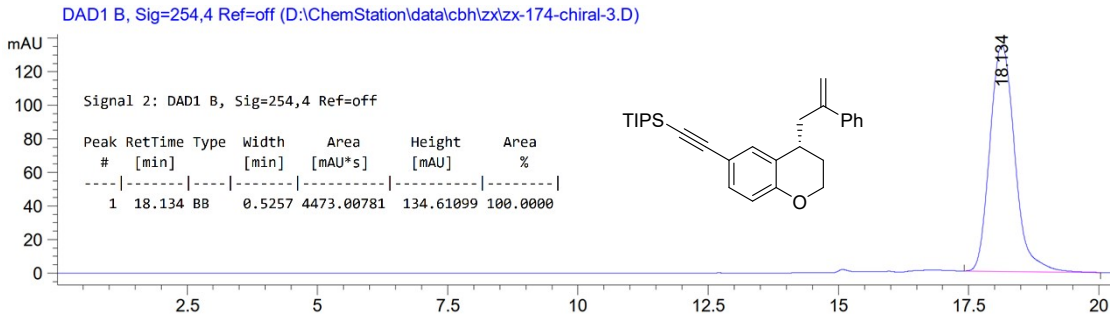
Compound 3bd



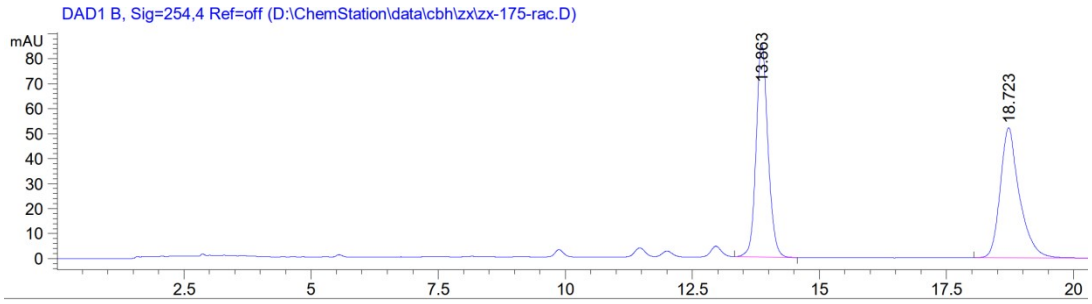


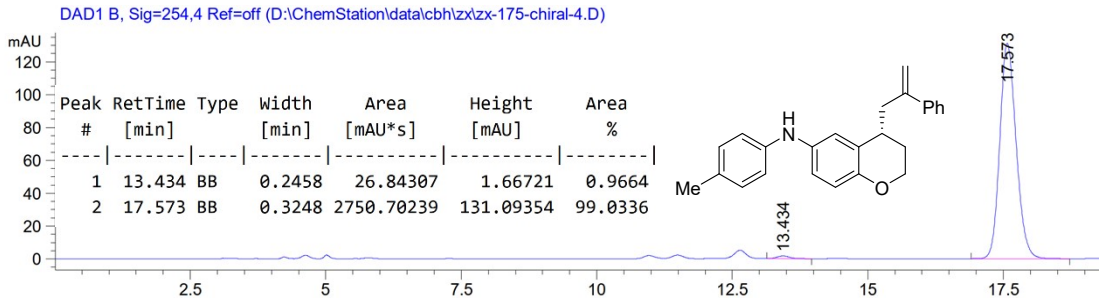
Compound 3be



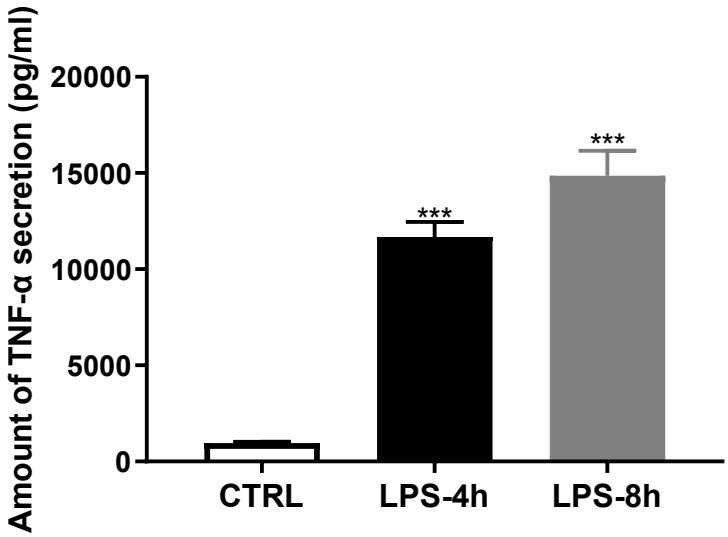


Compound 3bf





7. Study of time of LPS on RAW 264.7 cell



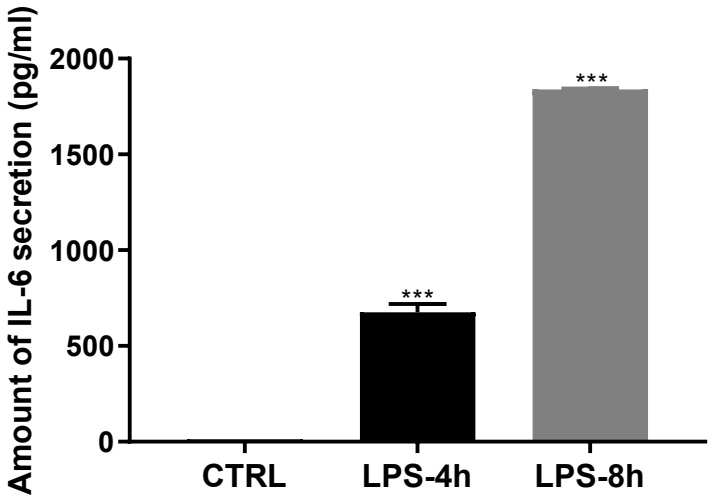


Figure S1. Different time and concentration of LPS on ELISA assay experiments. RAW 264.7 cells were plated in a 96-well plate and treated with LPS. The culture supernatant was collected. The concentrations of IL-6 and TNF-α in the culture supernatant of RAW 264.7 cells were determined according to the manufacturer's instructions of the Duo-set ELISA kits, purchased from Jonln Co. Ltd. (Shanghai, China). The absorbance was measured at 450 nm. Data from three times independent experiments were expressed as means ± SD. $^{*}p < 0.05$ compared with the control group.

References

1. M. V. Vita, P. Caramenti and J. Waser, *Organic Letters*, 2015, **17**, 5832-5835.