Supporting Information

Synthesis of Chiral Chromanols via a RuPHOX-Ru Catalyzed Asymmetric Hydrogenation of Chromones

Yujie Ma,[a] Jing Li,[a] Jianxun Ye,[a] Delong Liu,*[,a] and Wanbin Zhang[a,b]

[a] Shanghai Key Laboratory for Molecular Engineering of Chiral Drugs, School of Pharmacy, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China

[b] School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China

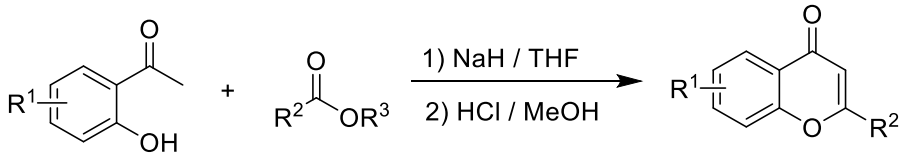
Fax: (+)86-21-54743265; Phone: (+)86-21-34207176; E-mail: dlliu@sjtu.edu.cn

Contents

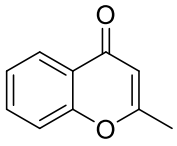
1. General Details

All reactions were performed in flame-dried glassware under an atmosphere of dry nitrogen, and the workup was carried out in air, unless otherwise noted. Solvents were dried and degassed by standard procedures. All commercially available reagents were used without further purification. ^{1}H NMR spectra were recorded on a Bruker Ascend^{TM} 400 (400 MHz), and Bruker Ascend^{TM} 500 (500 MHz). ^{13}C NMR spectra were recorded on a Bruker Ascend^{TM} 400 (100 MHz), and Bruker Ascend^{TM} 500 (125 MHz). Enantioselectivity was measured by high performance liquid chromatography (HPLC) using Daicel Chiralcel OD-H, AD-H and AS-H columns with *n*-hexane/*i*-PrOH as an eluent. Column chromatography was performed using 100 – 200 mesh silica gel.

2. Synthesis and Characterization of Chromones[1]



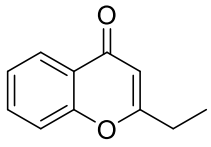
General procedure: Sodium hydride (60% dispersion in mineral oil, 3.53 g, 88.2 mmol) was rinsed three times with hexane and suspended in THF (9 mL). A mixture of 2-hydroxyacetophenone (22.0 mmol) and corresponding ester (55.1 mmol) in THF (2.5 mL) was added dropwise to the above suspension at room temperature. A vigorous reaction was observed, and the temperature rose to reflux. After complete addition, the reaction mixture was stirred for a further 5 min, quenched by pouring onto ice and further acidified to pH 6 with 6 M HCl (aq). The solution was extracted with EtOAc (10 mL×3) and the combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was evaporated to yield the crude 1,3-dione. Without further purification, a solution of the crude 1,3-dione product (2.50 g, 14.0 mmol) in methanol (30 mL) was treated conc. HCl (1 mL), and the mixture was allowed to stirring at room temperature for 14 h. The mixture was concentrated under reduced pressure and the residue was diluted with ethyl acetate (50 mL), then washed successively with solutions of saturated $NaHCO_3$ (aq), water, and brine. The organic layer was then dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified via flash column chromatography (silica gel, ethyl acetate/hexanes 1:3 as eluent) to give the desired products **1**.



1a

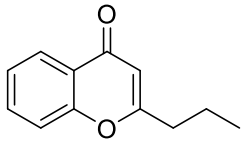
2-Methyl-4*H*-chromen-4-one (1a):[2] A white solid (1.68 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18

(d, J = 7.6 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.43–7.36 (m, 2H), 6.17 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 166.1, 156.5, 133.4, 125.6, 124.9, 123.5, 117.7, 110.5, 20.5.



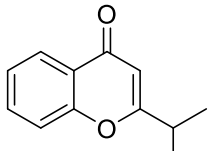
1b

2-Ethyl-4*H*-chromen-4-one (1b):[2] A white oil (1.4 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 6.17 (s, 1H), 2.65 (q, J = 7.6 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 170.8, 156.5, 133.4, 125.6, 124.8, 123.7, 117.8, 108.9, 27.5, 10.9.



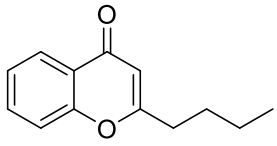
1c

2-Propyl-4*H*-chromen-4-one (1c):[3] A white oil (1.2 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 6.17 (s, 1H), 2.59 (t, J = 7.6 Hz, 2H), 1.82–1.72 (m, 2H), 1.02 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 169.5, 156.5, 133.4, 125.6, 124.8, 123.7, 117.8, 109.9, 36.2, 20.2, 13.5.



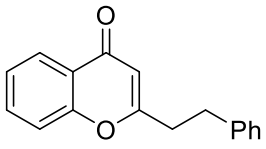
1d

2-Isopropyl-4*H*-chromen-4-one (1d):[2] A white oil (0.9 g, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.0 Hz, 1H), 7.65–7.61 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 6.19 (s, 1H), 2.91–2.81 (m, 1H), 1.32 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 174.2, 156.5, 133.4, 125.6, 124.8, 123.7, 117.8, 107.5, 33.2, 20.1.



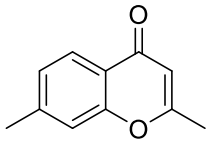
1e

2-Butyl-4*H*-chromen-4-one (1e):[2] A white oil (1.3 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 1.2, 8.0 Hz, 1H), 7.65–7.60 (m, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 7.2 Hz, 1H) 6.17 (s, 1H), 2.61 (t, J = 7.6 Hz, 2H), 1.75–1.68 (m, 2H), 1.47–1.38 (m, 1H), 0.95 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 169.8, 156.5, 133.3, 125.6, 124.8, 123.7, 117.8, 109.7, 34.0, 28.8, 22.1, 13.7.



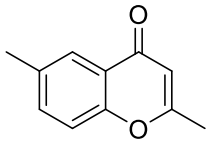
1f

2-Phenethyl-4*H*-chromen-4-one (1f):[2] A white solid (1.8 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 7.6 Hz, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.28 (q, J = 7.2 Hz, 2H), 7.21 (t, J = 6.8 Hz, 3H), 6.15 (s, 1H), 3.06 (t, J = 7.6 Hz, 2H), 2.93 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 168.4, 156.4, 139.7, 133.5, 128.6, 128.2, 126.5, 125.7, 124.9, 123.7, 117.8, 110.2, 36.1, 33.0.



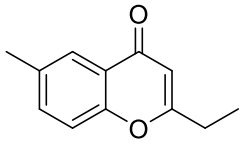
1g

2,7-Dimethyl-4*H*-chromen-4-one (1g):[2] A yellow solid (1.2 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 1H), 7.20–7.17 (m, 2H), 6.13 (s, 1H), 2.47 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 166.1, 156.8, 144.9, 126.6, 125.6, 121.5, 117.8, 110.7, 22.0, 20.8.



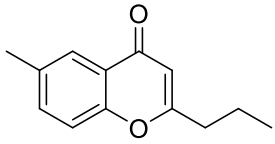
1h

2,6-Dimethyl-4*H*-chromen-4-one (1h):[2] A yellow solid (1.8 g, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.39 (d, J = 8.8 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 6.09 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 166.2, 154.9, 135.0, 134.8, 125.1, 123.4, 117.7, 110.6, 21.1, 20.8.



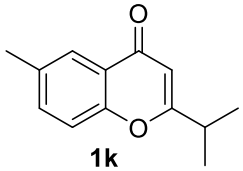
1i

2-Ethyl-6-methyl-4*H*-chromen-4-one (1i): A white solid (1.4 g, 95%). Mp 44-45 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 5.0 Hz, 1H), 7.43 (dd, J = 2.0, 8.5 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 6.16 (s, 1H), 2.64 (q, J = 7.5 Hz, 2H), 2.43 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 170.7, 154.8, 134.8, 134.6, 125.0, 123.3, 117.6, 108.7, 27.5, 20.9, 11.0; IR (KBr) cm^{-1}: 3041, 2934, 1701, 1681, 1611, 1580, 1502, 1462, 813; HRMS (ESI): calcd for $C_{12}H_{12}O_2$ $[M+H]^+$: 189.0916, found 189.0923.



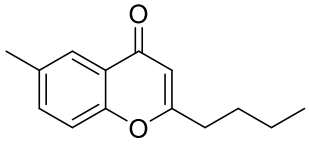
1j

6-Methyl-2-propyl-4*H*-chromen-4-one (1j): Yellow oil (1.5 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 1.2 Hz, 1H), 7.44 (dd, J = 6.0, 8.4 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 6.15 (s, 1H), 2.58 (t, J = 7.2 Hz, 2H), 2.43 (s, 3H), 1.81–1.72 (m, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 169.4, 154.8, 134.8, 134.6, 125.0, 123.3, 117.6, 109.7, 36.2, 20.9, 20.2, 13.5; IR (KBr) cm^{-1}: 3022, 2944, 1721, 1681, 1601, 1580, 1501, 1464, 810; HRMS (ESI): calcd for $C_{13}H_{14}O_2$ $[M+H]^+$: 203.1072, found 203.1079.



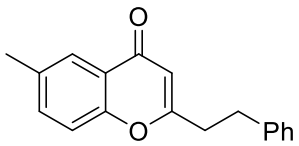
1k

2-Isopropyl-6-methyl-4*H*-chromen-4-one (1k): Yellow oil (3.0 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 0.8 Hz, 1H), 7.47 (dd, J = 2.0, 8.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.20 (s, 1H), 2.93–2.83 (m, 1H), 2.46 (s, 3H), 1.34 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 174.0, 154.8, 134.7, 134.6, 125.0, 123.4, 117.6, 107.4, 33.2, 20.9, 20.1; IR (KBr) cm^{-1}: 3010, 2904, 1701, 1682, 1589, 1580, 1501, 1454, 1385, 1368, 800; HRMS (ESI): calcd for $C_{13}H_{14}O_2$ $[M+H]^+$: 203.1072, found 203.1070.



1l

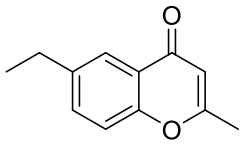
2-Butyl-6-methyl-4*H*-chromen-4-one (1l):[4] Yellow oil (1.3 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 1.2 Hz, 1H), 7.44 (dd, J = 2.4, 8.8 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 6.15 (s, 1H), 2.61 (t, J = 7.6 Hz, 2H), 2.44 (s, 3H), 1.75–1.67 (m, 2H), 1.47–1.38 (m, 2H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 169.7, 154.8, 134.8, 134.6, 125.0, 123.4, 117.6, 109.6, 34.0, 28.8, 22.1, 13.7.



1m

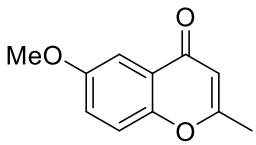
6-Methyl-2-phenethyl-4*H*-chromen-4-one (1m):[5] A white powder (1.3 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 1.2 Hz, 1H), 7.46 (dd, J = 2.4, 8.8 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.29 (t, J = 7.2 Hz, 2H), 7.21 (t, J = 7.6 Hz, 3H), 6.13 (s, 1H), 3.06 (t, J = 7.2 Hz, 2H), 2.92 (t, J = 7.2 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.4, 168.3, 154.7, 139.8, 134.9, 134.7, 128.6, 126.5, 123.4, 117.6,

110.1, 36.1, 33.0, 20.9.



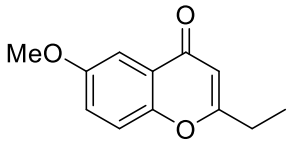
1n

6-Ethyl-2-methyl-4*H*-chromen-4-one (1n): A white solid (1.6 g, 78%). Mp 63–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.46 (dd, J = 2.0, 8.5 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H), 6.14 (s, 1H), 2.73 (q, J = 7.5 Hz, 2H), 2.36 (s, 3H), 1.26 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.5, 166.0, 154.9, 141.2, 133.6, 123.8, 123.3, 117.6, 110.4, 28.3, 20.6, 15.5; IR (KBr) cm^{-1}: 3006, 2924, 1701, 1672, 1599, 1580, 1491, 1454, 1375, 820; HRMS (ESI): calcd for $C_{12}H_{12}O_2$ $[M+H]^+$: 189.0916, found 189.0906



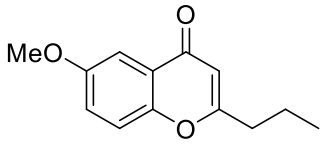
1o

6-Methoxy-2-methyl-4*H*-chromen-4-one (1o):[6] A white solid (1.5 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 3.2 Hz, 1H), 7.29 (d, J = 9.2 Hz, 1H), 7.17 (dd, J = 3.2, 8.4 Hz, 1H), 6.11 (s, 1H), 3.84 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 166.1, 156.9, 151.5, 124.3, 123.6, 119.4, 110.0, 105.0, 56.1, 20.7.



1p

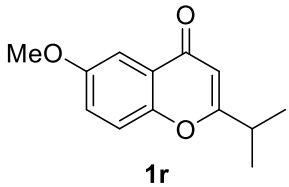
2-Ethyl-6-methoxy-4*H*-chromen-4-one (1p): A white solid (2.4 g, 90%). Mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 2.8 Hz, 1H), 7.34 (d, J = 9.2 Hz, 1H), 7.21 (dd, J = 3.2, 9.2 Hz, 1H), 6.16 (s, 1H), 3.87 (s, 3H), 2.64 (q, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 170.5, 156.7, 151.3, 124.2, 123.4, 119.2, 108.2, 104.8, 55.9, 27.5, 11.0; IR (KBr) cm^{-1}: 3001, 2944, 1721, 1652, 1619, 1580, 1501, 1454, 1371, 836; HRMS (ESI): calcd for $C_{12}H_{12}O_3$ $[M+H]^+$: 205.0865, found 205.0867.



1q

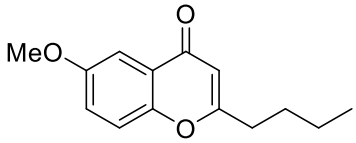
6-Methoxy-2-propyl-4*H*-chromen-4-one (1q): A white solid (1.9 g, 88%). Mp 60–61 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 2.8 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 7.22 (dd, J = 2.8, 8.8 Hz, 1H), 6.16

(s, 1H), 3.88 (s, 3H), 2.58 (t, J = 7.6 Hz, 2H), 1.81–1.72 (m, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 169.3, 156.7, 151.4, 124.3, 123.4, 119.2, 109.2, 104.8, 55.9, 36.2, 20.2, 13.5; IR (KBr) cm^{-1}: 3006, 2954, 1701, 1682, 1598, 1580, 1501, 1444, 1369, 812; HRMS (ESI): calcd for $C_{13}H_{14}O_3$ $[M+H]^+$: 219.1021, found 219.1023.



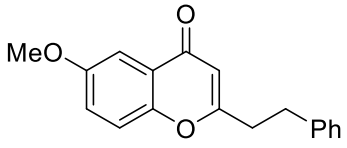
1r

2-Isopropyl-6-methoxy-4*H*-chromen-4-one (1r): Yellow oil (0.8 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 3.2 Hz, 1H), 7.37 (d, J = 6.8 Hz, 1H), 7.22 (dd, J = 3.2, 9.2 Hz, 1H), 6.18 (s, 1H), 3.88 (s, 3H), 2.91–2.80 (m, 1H), 1.31 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 173.9, 156.7, 151.3, 124.3, 123.5, 119.3, 106.8, 104.8, 55.9, 33.2, 20.2; IR (KBr) cm^{-1}: 3006, 2934, 1701, 1682, 1599, 1580, 1501, 1454, 1381, 1363, 828; HRMS (ESI): calcd for $C_{13}H_{14}O_3$ $[M+H]^+$: 219.1021, found 219.1026.



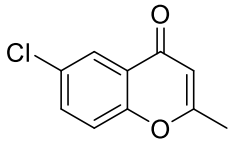
1s

2-Butyl-6-methoxy-4*H*-chromen-4-one (1s):[7] A white solid (1.7 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 9.2 Hz, 1H), 7.24 (dd, J = 2.8, 8.8 Hz, 1H), 6.17 (s, 1H), 3.90 (s, 3H), 2.63 (t, J = 7.2 Hz, 2H), 1.77–1.69 (m, 2H), 1.49–1.39 (m, 2H), 0.97 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 169.5, 156.7, 151.3, 124.3, 123.4, 119.2, 109.1, 104.8, 55.9, 34.0, 28.9, 22.1, 13.7.



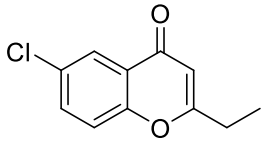
1t

6-Methoxy-2-phenethyl-4*H*-chromen-4-one (1t):[5] A white solid (1.8 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 3.2 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 7.33–7.21 (m, 6H), 6.16 (s, 1H), 3.90 (s, 3H), 3.08 (t, J = 7.2 Hz, 2H), 2.94 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 168.1, 156.8, 151.3, 139.8, 128.6, 128.3, 126.5, 124.3, 123.5, 119.2, 109.5, 104.9, 55.9, 36.1, 33.0.



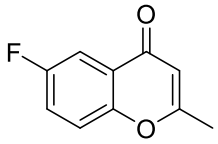
1u

6-Chloro-2-methyl-4*H*-chromen-4-one (1u):[8] A white solid (2.4 g, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 1.5 Hz, 1H), 7.57 (dd, J = 2.5, 9.0 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.17 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 166.5, 154.8, 133.6, 130.9, 125.1, 124.5, 119.5, 110.5, 20.6.



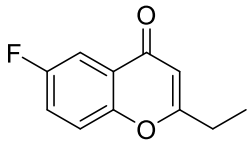
1v

6-Chloro-2-ethyl-4*H*-chromen-4-one (1v):[8] A white solid (2.4 g, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 2.5 Hz, 1H), 7.57 (dd, J = 2.5, 9.0 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 6.18 (s, 1H), 2.66 (q, J = 7.5 Hz, 2H), 1.31 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 171.1, 154.8, 133.6, 130.8, 125.1, 124.7, 119.6, 108.9, 27.5, 10.9.



1w

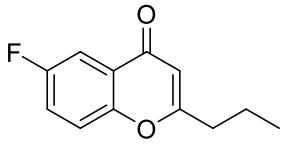
6-Fluoro-2-methyl-4*H*-chromen-4-one (1w): A white solid (1.3 g, 70%). Mp 95–96 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, J = 2.0, 3.0 Hz, 1H), 7.41 (dd, J = 3.5, 8.5 Hz, 1H), 7.37–7.33 (m, 1H), 6.15 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4 (d, J = 2.1 Hz), 166.5, 159.4 (d, J = 244.8 Hz), 152.7 (d, J = 1.6 Hz), 124.7 (d, J = 7.3 Hz), 121.6 (d, J = 25.3 Hz), 119.8 (d, J = 8.0 Hz), 110.5 (d, J = 23.5 Hz), 109.9, 20.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ −115.7; IR (KBr) cm^{-1}: 3016, 2954, 1701, 1662, 1601, 1580, 1491, 1454, 1379, 1280, 812; HRMS (ESI): calcd for $C_{10}H_7FO_2$ $[M+H]^+$: 179.0508, found 179.0516.



1x

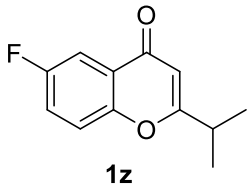
2-Ethyl-6-fluoro-4*H*-chromen-4-one (1x): A white solid (2.4 g, 85%). Mp 50–52 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 4.0, 10.5 Hz, 1H), 7.46 (dd, J = 5.5, 11.5 Hz, 1H), 7.41–7.36 (m, 1H), 6.21 (s, 1H), 2.69 (q, J = 9.0 Hz, 2H), 1.62 (s, 3H), 1.34 (t, J = 9.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 171.1, 159.4 (d, J = 244.9 Hz), 152.7, 124.9 (d, J = 7.3 Hz), 121.6 (d, J = 25.3 Hz), 119.9 (d, J = 8.0 Hz),

110.5 (d, J = 23.5 Hz), 108.3, 27.5, 10.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ −115.7; IR (KBr) cm^{-1}: 3001, 2954, 1701, 1652, 1598 1580, 1491, 1460, 1375, 1280, 822; HRMS (ESI): calcd for $C_{11}H_9FO_2$ $[M+H]^+$: 193.0665, found 193.0667.



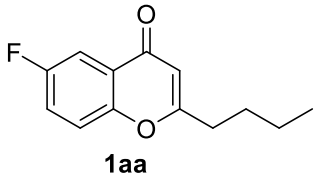
1y

6-Fluoro-2-propyl-4*H*-chromen-4-one (1y): A white solid (1.5 g, 80%). Mp 36–38 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 3.2, 8.4 Hz, 1H), 7.44 (dd, J = 4.0, 8.8 Hz, 1H), 7.39–7.34 (m, 1H), 6.18 (s, 1H), 2.61 (t, J = 7.2 Hz, 2H), 1.83–1.74 (m, 2H), 1.04 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5 (d, J = 2.2 Hz), 169.9, 159.4 (d, J = 244.7 Hz), 152.7 (d, J = 1.7 Hz), 124.9 (d, J = 7.3 Hz), 121.5 (d, J = 25.2 Hz), 119.9 (d, J = 8.0 Hz), 110.5 (d, J = 23.4 Hz), 109.2 , 36.2, 20.2, 13.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.7; IR (KBr) cm^{-1}: 3012, 2944, 1711, 1658, 1601, 1580, 1501, 1454, 1380, 1280, 823; HRMS (ESI): calcd for $C_{12}H_{11}FO_2$ $[M+H]^+$: 207.0821, found 207.0826.



1z

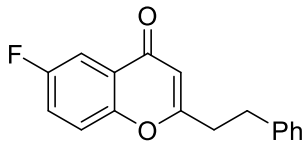
6-Fluoro-2-isopropyl-4*H*-chromen-4-one (1z): A white solid (1.4 g, 76%). Mp 51–52 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 3.2, 8.4 Hz, 1H), 7.46 (dd, J = 0.4, 8.8 Hz, 1H), 7.41–7.36 (m, 1H), 6.21 (s, 1H), 2.94–2.84 (m, 1H), 1.34 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8 (d, J = 2.2 Hz), 174.4, 159.4 (d, J = 244.7 Hz), 152.7, 124.9 (d, J = 7.3 Hz), 121.5 (d, J = 25.3 Hz), 119.9 (d, J = 8.0 Hz), 110.5 (d, J = 23.5 Hz), 107.0, 33.3, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.8; IR (KBr) cm^{-1}: 3007, 2924, 1699, 1668, 1601, 1580, 1500, 1454, 1385, 1369, 1280, 812; HRMS (ESI): calcd for $C_{12}H_{11}FO_2$ $[M+H]^+$: 207.0821, found 207.0818.



1aa

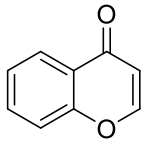
2-Butyl-6-fluoro-4*H*-chromen-4-one (1aa): Yellow oil (1.7 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 2.8, 8.0 Hz, 1H), 7.41 (dd, J = 4.0, 8.8 Hz, 1H), 7.34 (td, J = 3.2, 8.0 Hz, 1H), 6.15 (s, 1H), 2.61 (t, J = 7.6 Hz, 2H), 1.75–1.67 (m, 2H), 1.47–1.37 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 170.1, 159.4 (d, J = 244.9 Hz), 152.7, 124.9 (d, J = 7.3 Hz), 121.5 (d, J = 25.3 Hz),

119.9 (d, J = 7.0 Hz), 110.5 (d, J = 23.5 Hz), 109.1, 34.0, 28.8, 22.1, 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.7; IR (KBr) cm^{-1}: 3006, 2934, 1701, 1632, 1601, 1580, 1498, 1454, 1382, 1280, 832; HRMS (ESI): calcd for $C_{13}H_{13}FO_2$ $[M+H]^+$: 221.0978, found 221.0981.



1ab

6-Fluoro-2-phenethyl-4*H*-chromen-4-one (1ab): A white solid (1.7 g, 79%). Mp 65–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 2.8, 8.0 Hz, 1H), 7.46 (dd, J = 4.0, 8.8 Hz, 1H), 7.42–7.37 (m, 1H), 7.34–7.21 (m, 5H), 6.16 (s, 1H), 3.08 (t, J = 6.8 Hz, 2H), 2.96 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4 (d, J = 2.2 Hz), 168.7, 159.4 (d, J = 245.0 Hz), 152.7, 139.6, 128.5 (d, J = 43.3 Hz), 126.6, 124.9 (d, J = 7.3 Hz), 121.6 (d, J = 25.3 Hz), 119.9 (d, J = 8.0 Hz), 110.6 (d, J = 23.4 Hz), 109.6, 36.1, 33.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.5; IR (KBr) cm^{-1}: 3008, 2914, 1711, 1652, 1601, 1580, 1491, 1454, 1384, 1280, 822; HRMS (ESI): calcd for $C_{17}H_{13}FO_2$ $[M+H]^+$: 269.0978, found 269.0986.



1ac

4*H*-Chromen-4-one (1ac):[1b] A white solid (1.6 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, J = 0.8, 8.0 Hz, 1H), 7.82 (d, J = 6.0 Hz, 1H), 7.65–7.60 (m, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.38–7.34 (m, 1H), 6.30 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 156.5, 155.3, 133.7, 125.7, 125.2, 124.8, 118.1, 112.9.

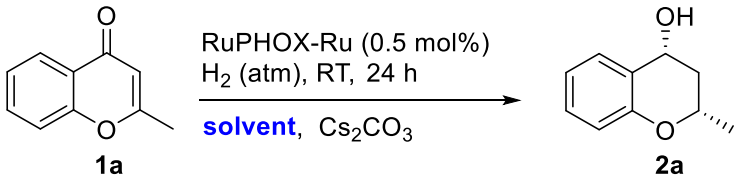
3. Asymmetric Synthesis of Chromanols 2

3.1 Solvent and Hydrogen Pressure Screening

As shown in Table 1, MeOH was first used as a solvent and the desired product (2*S*,4*R*)-2-methyl-4*H*-chroman-4-ol (chromanol **2a**) was obtained in full conversion and 99% ee (entry 1). The use of EtOH provided the same conversion but a slightly lower enantioselectivity than that of MeOH (entry 2). However, almost no reaction occurred when *i*-PrOH was used as a solvent (entry 3). As a comparison, aprotic solvents, such as DCM and toluene, were used and both provided the desired product **2a** with excellent enantioselectivities (entries 4 and 5). However, only 90% conversion was obtained when the reaction was conducted in DCM (entry 5). Next, the asymmetric hydrogenation was carried out under a low hydrogen pressure in either MeOH or toluene as a solvent. Similar conversion and enantioselectivities

were obtained when 20 bar hydrogen pressure was used (entries 6 and 7). However, only 94% conversion was observed in MeOH and only a trace amount of product was obtained in toluene when the reaction was carried out under a hydrogen pressure of 10 bar (entries 8 and 9).

Table S1 Solvent and hydrogen pressure screening.[a]



1a **2a**

Entry	Solvent	H_2 (bar)	Conv (%)[b]	ee (%)[c]	*dr*[d]
1	MeOH	50	>99	99	>20:1
2	EtOH	50	>99	98	>20:1
3	*i*-PrOH	50	trace	-	-
4	toluene	50	>99	99.6	>20:1
5	DCM	50	90	99.9	>20:1
6	MeOH	20	>99	98	>20:1
7	toluene	20	>99	99.7	>20:1
8	MeOH	10	94	97	>20:1
9	toluene	10	trace	-	-

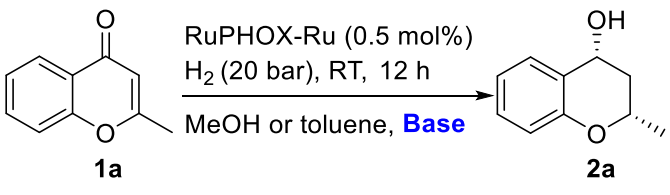
[a] Conditions: **1a** (0.30 mmol), (*S*,*S*p)-RuPHOX-Ru (0.5 mol %) and Cs_2CO_3 (0.5 equiv) in a suitable solvent (3 mL) under a certain hydrogen pressure at rt for 12 h. [b] By using ^{1}H NMR analysis of the crude product to determine the consumption of **1a** and the formation of **2a** by comparison of ^{1}H NMR integrals corresponding to methyl groups. [c] Determined by chiral HPLC analysis of **2a** using an OD-H column; The absolute configuration of **2a** was determined by single crystal. [d] Determined by ^{1}H NMR.

3.2 Base Screening

Subsequently, we chose both MeOH and toluene as the solvents to examine the impact of different bases on the reaction when it was carried out at 20 bar hydrogen pressure over 12 h (Table S2). First, the reaction was carried out with MeOH as a solvent. Three frequently used sodium containing bases and salts were first examined with Na_2CO_3 giving the best results (entries 1-3). As a comparison, potassium containing bases and salts were also examined, and somewhat inferior results were obtained (entries 4-6). The organic base DIPEA was also examined and **2a** was obtained in 91% conversion and with 95% ee (entry 7). Next, the above reactions were carried out using toluene as a solvent instead of MeOH (entries 8-14). It was found that the reaction activity in toluene was affected significantly by base. Full conversions and excellent enantioselectivities were obtained when the reactions were carried out in the presence of KOH or K_2CO_3 (entries 11 and 12). Considering reaction activity, subsequent reactions were carried out

using Na_2CO_3 as a suitable base in MeOH under 20 bar hydrogen pressure at room temperature for 12 h (entry 2).

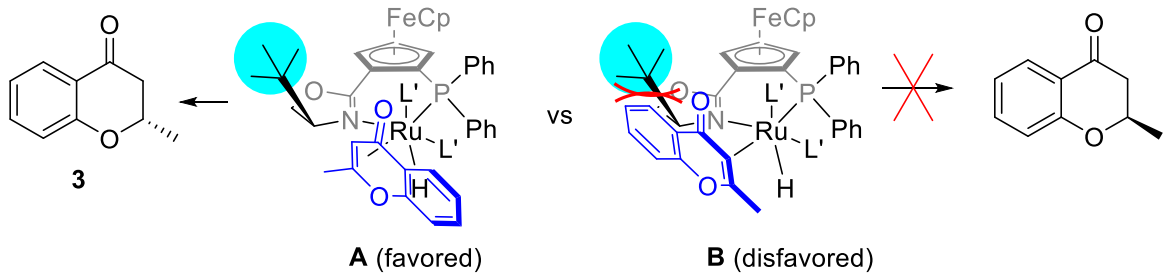
Table S2 Screening of base.[a]



Entry	Solvent	Base	Conv (%)[b]	ee (%)[c]	*dr*[d]
1	MeOH	NaOH	>99	97	>20:1
2	MeOH	Na_2CO_3	>99	99.9	>20:1
3	MeOH	$NaHCO_3$	95	98	>20:1
4	MeOH	KOH	>99	97	>20:1
5	MeOH	K_2CO_3	>99	97	>20:1
6	MeOH	*t*-BuOK	89	95	>20:1
7	MeOH	DIPEA	91	95	>20:1
8	toluene	NaOH	48	99.6	>20:1
9	toluene	Na_2CO_3	NR	-	-
10	toluene	$NaHCO_3$	NR	-	-
11	toluene	KOH	>99	99.7	>20:1
12	toluene	K_2CO_3	>99	99.4	>20:1
13	toluene	*t*-BuOK	NR	-	-
14	toluene	DIPEA	NR	-	-

[a] Conditions: **1a** (0.30 mmol), (*S*,*Sp*)-RuPHOX-Ru (0.5 mol%) and base (0.5 equiv) in MeOH or toluene (3 mL) under a 20 bar hydrogen pressure at rt for 12 h. [b] By using ^{1}H NMR analysis of the crude product to determine the consumption of **1a** and the formation of **2a** by comparison of ^{1}H NMR integrals corresponding to methyl groups. [c] Determined by chiral HPLC analysis of **2a** using an OD-H column; The absolute configuration of **2a** was determined by single crystal. [d] Determined by ^{1}H NMR.

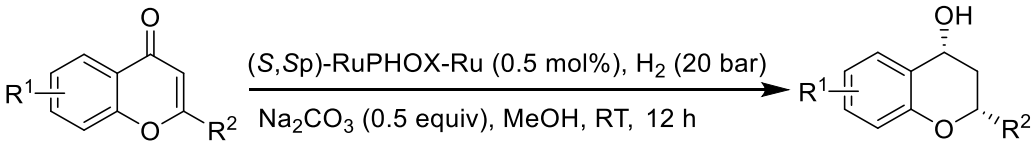
3.3 Proposed steric control pathway



According to the X-ray crystal structure of **2a** (Table S2), the chiral induction process in the asymmetric

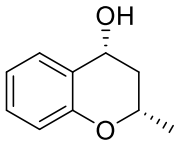
hydrogenation of C=C double bond of **1a** can be speculated. Due to the steric hindrance between the bulky *t*-Bu group of the chiral oxazoline ring and the phenyl ring of **1a**, the Ru-complex **A** is prone to form via the coordination of the Ru metal center to the C=C bond, thus leading to the major enantiomer (*S*)-**3**. As for Ru-complex **B**, the steric interaction is stronger than that in **A** and so is more difficult to form. Subsequently, **3** was further hydrogenated under the same reaction conditions, affording the terminal product **2a** with the indicated absolute configuration.

3.4 General procedure for the RuPHOX-Ru catalyzed asymmetric hydrogenation



General Procedure: In a nitrogen-filled glovebox, a hydrogenation tube was charged with a stirring bar, substituted chromones (0.30 mmol), RuPHOX-Ru (2.6 mg, 0.5 mol%) and Na_2CO_3 (15.9 mg, 0.5 equiv, 0.15 mmol). MeOH (3 mL) was then injected into the hydrogenation tube by a syringe. The hydrogenation tube was then put into an autoclave. The system was evacuated and filled with hydrogen 3 times. The autoclave was then charged with hydrogen to 20 bar hydrogen pressure, and the reaction mixture was stirred at RT for 12 h before releasing the hydrogen. After the completion of reaction, the solvent was evaporated to afford the crude product. The conversion of substrate was determined by ^{1}H NMR analysis. HPLC with a chiral column was used to determine the ee value.

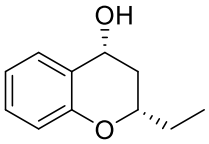
Gram scale synthesis of **2a**: To a 50 mL round-bottom flask was charged with a stir bar, compound **1a** (1.87 g, 11.7 mmol), RuPhOX-Ru (20 mg, 0.1 mol%), Na_2CO_3 (1.2 g, 5.8 mmol) in an argon-filled glovebox. Then, MeOH (20 mL) was injected into the flask by a syringe with stirring and the reaction flask was then put into an autoclave. The autoclave was evacuated and filled hydrogen for 3 times and then charged with hydrogen to 50 bar. After vigorous stirring at room temperature for 72 hours, the solvent was evaporated under reduced pressure to afford the crude product, which was determined by ^{1}H NMR analysis to determine the conversion of substrate. The crude product was passed through a short column of silicon (PE/EA = 20/1 as the eluent) to afford **2a** as a white soild (1.81 g, 94%, 96% *ee*).



2a

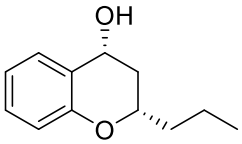
(2*S*,4*R*)-2-Methylchroman-4-ol (2a):[2] A white solid (48.6 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.93 (t, J = 7.2 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H),

4.95–4.89 (m, 1H), 4.29–4.21 (m, 1H), 2.86 (dd, J = 6.4, 12.8 Hz, 1H), 1.92 (d, J = 8.0 Hz, 1H), 1.78–1.69 (m, 1H), 1.42 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 129.0, 126.9, 125.7, 120.6, 116.4, 71.2, 65.5, 39.8, 21.4; $[\alpha]_D^{26}$ = −131.82 (*c* 0.50, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 21.982 min (minor) and t_{R2} = 26.669 min (major), ee = 99.9%.



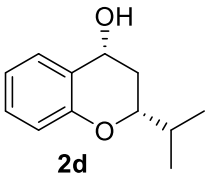
2b

(2*S*,4*R*)-2-Ethylchroman-4-ol (2b):[2] A white solid (52.78 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 4.95-4.91 (m, 1H), 4.07-4.00 (m, 1H), 2.30 (ddd, J = 1.6, 6.4, 13.2 Hz, 1H), 1.84–1.69 (m, 4H), 1.05 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 129.2, 127.1, 126.2, 120.7, 116.7, 76.3, 65.9, 37.7, 29.9, 28.7, 9.7; $[\alpha]_D^{26}$ = −130.94 (*c* 0.54, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 20.598 min (minor) and t_{R2} = 22.228 min (major), ee = 99%.



2c

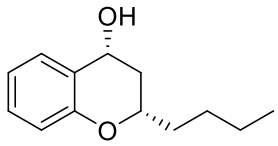
(2*S*,4*R*)-2-Propylchroman-4-ol (2c): A white solid (54.8 mg, 96%). Mp 59-60 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H), 6.79 (d, J = 8.4 Hz,1H), 4.95–4.91 (m, 1H), 4.15–4.08 (m, 1H), 2.30 (ddt, J = 1.2, 6.4, 12.8 Hz, 1H), 1.82–1.72 (m, 3H), 1.66–1.52 (m, 3H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 129.2, 127.1, 126.2, 120.7, 116.7, 74.9, 65.9, 38.3, 37.9, 18.6, 14.2; HRMS (ESI): calcd for $C_{12}H_{16}O_2$ $[M+Na]^+$: 215.1048, found 215.1059; IR (KBr) cm^{-1}: 3580, 2914, 1601, 1580, 1491, 1465, 1384, 750; HRMS (ESI): calcd for $C_{12}H_{16}O_2$ $[M+Na]^+$:215.1048, found 215.1057; $[\alpha]_D^{26}$ = −131.49 (*c* 0.48, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 99/1, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 33.254 min (minor) and t_{R2} = 35.837 min (major), ee = 99.7%.



2d

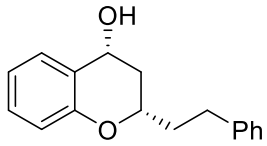
(2*R*,4*R*)-2-Isopropylchroman-4-ol (2d):[2] A white solid (54.1 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.2 Hz, 1H), 7.16 (t, J = 7.6 Hz 1H), 6.93 (t, J = 7.2 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H),

4.95–4.91 (m, 1H), 3.90–3.80 (m, 1H), 2.28 (dd, J = 5.6, 12.4 Hz, 1H), 2.00–1.91 (m, 1H), 1.72 (q, J = 11.6 Hz, 2H), 1.03 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 129.1, 126.9, 126.3, 120.6, 116.7, 79.7, 66.3, 34.9, 32.6, 18.2, 18.1; $[\alpha]_D^{26}$ = −123.92 (*c* 0.49, $CHCl_3$); HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH = 99/1, UV = 210 nm, flow rate = 0.25 mL/min) t_{R1} = 72.981 min (minor) and t_{R2} = 85.516 min (major), ee = 99.1%.



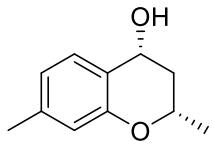
2e

(2*S*,4*R*)-2-Butylchroman-4-ol (2e):[2] A white solid (59.3 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H), 4.93–4.91 (m, 1H), 4.13–4.07 (m, 1H), 2.30 (dd, J = 10.4, 12.8 Hz, 1H), 1.83–1.73 (m, 3H), 1.70–1.60 (m, 2H), 1.45–1.34 (m, 3H), 0.95 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 129.2, 127.1, 126.2, 120.7, 116.7, 75.2, 65.9, 38.2, 35.5, 27.5, 22.9, 14.3; $[\alpha]_D^{26}$ = −119.44 (*c* 0.50, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 98/2, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 22.812 min (minor) and t_{R2} = 24.162 min (major), ee = 99.6%.



2f

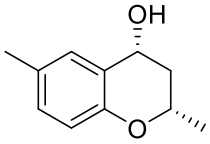
(2*S*,4*R*)-2-Phenethylchroman-4-ol (2f):[2] A white solid (72.5 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 6.0 Hz 1H), 7.33 (t, J = 6.0 Hz, 2H), 7.28–7.20 (m, 4H), 6.98 (t, J = 6.0 Hz, 1H), 6.87 (d, J = 6.4 Hz, 1H), 4.99–4.88 (m, 1H), 4.15–4.10 (m, 1H), 2.96–2.83 (m, 2H), 2.31 (ddd, J = 1.2, 5.2, 10.4 Hz, 1H), 2.18–2.11 (m, 1H), 2.00–1.93 (m, 2H), 1.86–1.79 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 141.6, 129.0, 128.6, 128.5, 127.0, 126.0, 120.7, 116.6, 73.8, 65.5, 38.0, 37.2, 31.3; $[\alpha]_D^{26}$ = –133.55 (*c* 0.51, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 95/5, UV = 210 nm, flow rate = 0.7 mL/min) t_{R1} = 25.283 min (minor) and t_{R2} = 35.795 min (major), ee = 98%.



2g

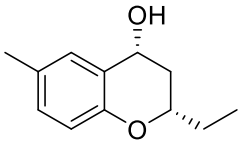
(2*S*,4*R*)-2,7-Dimethylchroman-4-ol (2g):[2] A white solid (53.1 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.0 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.61 (s, 1H), 4.93–4.84 (m, 1H), 4.26–4.18 (m, 1H), 2.28–2.24 (m, 4H), 1.75–1.66 (m, 2H), 1.40 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6,

139.3, 127.0, 123.1, 121.8, 117.0, 71.4, 65.6, 40.2, 21.7, 21.4; $[\alpha]_D^{26}$ = –124.65 (*c* 0.54, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 20.492 min (minor) and t_{R2} = 24.786 min (major), ee = 99.7%.



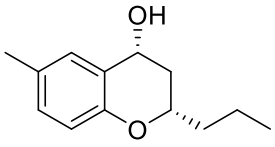
2h

(2*S*,4*R*)-2,6-Dimethylchroman-4-ol (2h):[2] A white solid (52.8 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 4.93-4.82 (m, 1H), 4.24–4.16 (m, 1H), 2.28–2.22 (m, 4H), 1.76–1.67 (m, 2H), 1.40 (dd, *J* = 1.6, 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 130.0, 129.9, 127.4, 125.6, 116.4, 71.4, 65.7, 40.1, 21.7, 20.8; $[\alpha]_D^{26}$ = –130.98 (*c* 0.52, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 19.886 min (minor) and t_{R2} = 23.689 min (major), ee = 99.3%.



2i

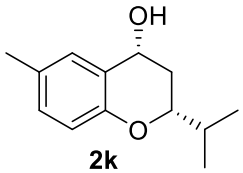
(2*S*,4*R*)-2-ethyl-6-methylchroman-4-ol (2i): A white solid (56.1 mg, 98%). Mp 64–65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 1H), 6.98 (dd, *J* = 1.6, 8.4 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 4.93–4.89 (m, 1H), 4.05–3.98 (m, 1H), 2.32–2.27 (m, 4H), 1.86–1.65 (m, 4H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 129.7, 129.6, 127.1, 125.6, 116.2, 76.0, 65.7, 37.6, 28.4, 20.6, 9.5; IR (KBr) cm^{-1}: 3578, 2924, 1601, 1580, 1499, 1460, 1375, 810; HRMS (ESI): calcd for $C_{12}H_{16}O_2$ $[M+Na]^+$: 215.1048, found 215.1039; $[\alpha]_D^{26}$ = –125.93 (*c* 0.59, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 17.891 min (minor) and t_{R2} = 19.170 min (major), ee = 94%.



2j

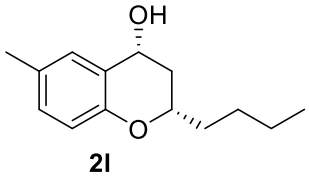
(2*S*,4*R*)-6-Methyl-2-propylchroman-4-ol (2j): A white solid (59.6 mg, 97%). Mp 79–81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (s, 1H), 6.98 (dd, *J* = 2.0, 10.5 Hz, 1H), 6.72 (d, *J* = 10.0 Hz, 1H), 4.93–4.89 (m, 1H), 4.12–4.06 (m, 1H), 2.30–2.26 (m, 4H), 1.83–1.45 (m, 6H), 1.00 (t, *J* = 9.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 129.7, 129.6, 127.2, 125.6, 116.3, 74.6, 65.7, 38.1, 37.6, 20.6, 18.4, 14.0; IR (KBr) cm^{-1}: 3565, 2934, 1599, 1579, 1491, 1460, 1380, 790; HRMS (ESI): calcd for $C_{13}H_{18}O_2$ $[M+Na]^+$: 229.1204, found 229.1214; $[\alpha]_D^{26}$ = –118.21 (*c* 0.49, $CHCl_3$); HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 16.492 min (minor) and t_{R2} = 18.467 min (major), ee =

98%.



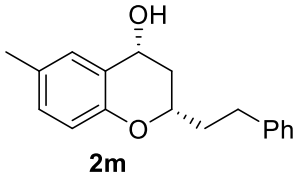
2k

(2*R*,4*R*)-2-Isopropyl-6-methylchroman-4-ol (2k): A white solid (59.3 mg, 97%). Mp 72–73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 1H), 6.98 (dd, J = 1.6, 8.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 4.93–4.89 (m, 1H), 3.88–3.83 (m, 1H), 2.30–2.25 (m, 4H), 2.00-1.91 (m, 2H), 1.78–1.69 (m, 1H), 1.07–1.03 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 129.6, 126.9, 125.7, 116.2, 79.4, 66.1, 34.8, 32.4, 20.6, 18.0, 17.9; IR (KBr) cm^{-1}: 3588, 2904, 1601, 1580, 1501, 1465, 1384, 1368, 744; HRMS (ESI): calcd for $C_{13}H_{18}O_2$ [M+Na]$^+$: 229.1204, found 229.1210; $[\alpha]_D^{26}$ = –131.75 (*c* 0.52, $CHCl_3$); HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH = 99/1, UV = 210 nm, flow rate = 0.25 mL/min) t_{R1} = 65.928 min (minor) and t_{R2} = 74.529 min (major), ee = 99.8%.



2l

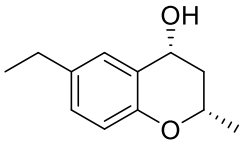
(2*S*,4*R*)-2-Butyl-6-methylchroman-4-ol (2l): A white solid (64.5 mg, 98%). Mp 74–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 6.96 (d, J = 8.0 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 4.93–4.87 (m, 1H), 4.09–4.02 (m, 1H), 2.32–2.27 (m, 4H), 1.81–1.68 (m, 3H), 1.53–1.25 (m, 5H), 0.93 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 129.7, 129.6, 127.1, 125.6, 116.3, 74.9, 65.7, 38.2, 35.2, 27.3, 22.6, 20.6, 14.0; IR (KBr) cm^{-1}: 3563, 2936, 1601, 1580, 1498, 1465, 1386, 721; HRMS (ESI): calcd for $C_{14}H_{20}O_2$ [M+Na]$^+$: 243.1364, found 249.1363; $[\alpha]_D^{26}$ = –113.42 (*c* 0.28, $CHCl_3$); HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.3 mL/min) t_{R1} = 24.493 min (minor) and t_{R2} = 26.637 min (major), ee = 97%.



2m

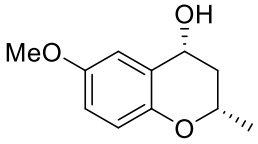
(2*S*,4*R*)-6-Methyl-2-phenethylchroman-4-ol (2m): A white solid (75.7 mg, 95%). Mp 88–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.22 (m, 6H), 7.02 (dd, J = 1.6, 8.0 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 4.98–4.83 (m, 1H), 4.12–4.06 (m, 1H), 2.96–2.89 (m, 2H), 2.32–2.27 (m, 4H), 2.17–2.11 (m, 1H), 2.00–1.91 (m, 2H), 1.85–1.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 141.6, 129.9, 129.7, 128.6, 128.5, 127.2, 126.0, 125.6, 116.3, 73.7, 65.5, 38.2 37.2, 31.4, 20.6; IR (KBr) cm^{-1}: 3579, 2914, 1601, 1579, 1491, 1465, 1384, 768; HRMS (ESI): calcd for $C_{18}H_{20}O_2$ [M+Na]$^+$: 291.1361, found 291.1360; $[\alpha]_D^{26}$ =

−70.65 (*c* 0.54, $CHCl_3$); HPLC (Chiralcel AD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 42.124 min (minor) and t_{R2} = 52.387 min (major), ee = 97%.



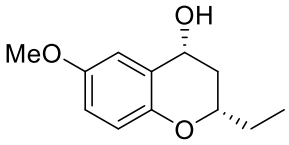
2n

(2*S*,4*R*)-6-Ethyl-2-methylchroman-4-ol (2n): A white solid (57.4 mg, 99%). Mp 49–51 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.01 (d, J = 10.0 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 4.93–4.89 (m, 1H), 4.26–4.18 (m, 1H), 2.58 (q, J = 7.6 Hz, 2H), 2.28 (ddd, J = 1.6, 6.4, 12.8 Hz, 1H), 1.77–1.66 (m, 2H), 1.41 (d, J = 6.0 Hz, 3H), 1.21 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 136.4, 128.5, 126.0, 125.3, 116.3, 71.1, 65.6, 40.0, 28.1, 21.5, 15.9; IR (KBr) cm^{-1}: 3580, 2904, 1599, 1577, 1491, 1465, 1380, 767; HRMS (ESI): calcd for $C_{12}H_{16}O_2$ $[M+Na]^+$: 215.1048, found 215.1054; $[\alpha]_D^{26}$ = −112.25 (*c* 0.50, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 17.067 min (minor) and t_{R2} = 20.204 min (major), ee = 96%.



2o

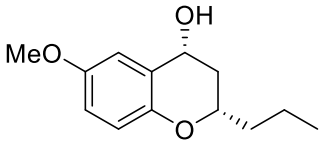
(2*S*,4*R*)-6-Methoxy-2-methylchroman-4-ol (2o): A white solid (57.5 mg, 99%). Mp 74–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.75–6.70 (m, 2H), 4.92–4.86 (m, 1H), 4.22–4.15 (m, 1H), 3.75 (s, 3H), 2.27 (dd, J = 6.8, 13.2 Hz, 1H), 1.75–1.66 (m, 2H), 1.39 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 148.8, 126.3, 117.4, 115.8, 111.3, 71.4, 65.9, 56.0, 40.1, 21.7; IR (KBr) cm^{-1}: 3580, 2934, 1601, 1580, 1501, 1465, 1384, 1215, 780; HRMS (ESI): calcd for $C_{11}H_{14}O_3$ $[M+Na]^+$: 217.0841, found 217.0850; $[\alpha]_D^{26}$ = −119.46 (*c* 0.53, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 32.079 min (minor) and t_{R2} = 40.849 min (major), ee = 99.1%.



2p

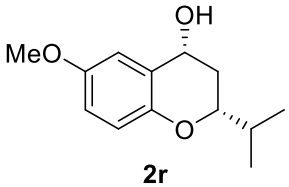
(2*S*,4*R*)-2-Ethyl-6-methoxychroman-4-ol (2p): A white solid (62.1 mg, 99%). Mp 56–58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02–7.00 (m, 1H), 6.78–6.73 (m, 2H), 4.96–4.84 (m, 1H), 4.01–3.96 (m, 1H), 3.77 (s, 3H), 2.31–2.27 (m, 1H), 1.83–1.65 (m, 4H), 1.05 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 148.6, 126.4, 117.2, 115.5, 111.1, 76.1, 65.9, 55.8, 37.6, 28.4, 9.5; HRMS (ESI): calcd for $C_{12}H_{16}O_3$ $[M+Na]^+$: 231.0997, found 231.1005; IR (KBr) cm^{-1}: 3572, 2914, 1601, 1581, 1491, 1465, 1379, 1264, 750;

$[\alpha]_D^{26}$ = –107.06 (*c* 0.50, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 26.736 min (minor) and t_{R2} = 31.238 min (major), ee = 98%.



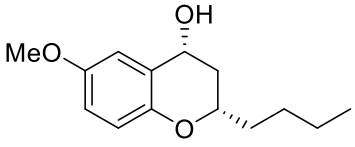
2q

(2*S*,4*R*)-6-Methoxy-2-propylchroman-4-ol (2q): A white solid (63.9 mg, 97%). Mp 62–63 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, *J* = 2.5 Hz, 1H), 6.76–6.72 (m, 2H), 4.95–4.85 (m, 1H), 4.08–4.03 (m, 1H), 3.77 (s, 3H), 2.29–2.26 (m, 1H), 1.80–1.43 (m, 6H), 0.99 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 148.7, 126.4, 117.2, 115.5, 111.1, 74.6, 65.8, 55.8, 38.1, 37.7, 18.4, 14.0; IR (KBr) cm^{-1}: 3580, 2914, 1601, 1580, 1491, 1465, 1384, 1266, 750; HRMS (ESI): calcd for $C_{13}H_{18}O_3$ $[M+Na]^+$: 245.1154, found 245.1164; $[\alpha]_D^{26}$ = –108.58 (*c* 0.55, $CHCl_3$); HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 33.168 min (minor) and t_{R2} = 37.861 min (major), ee = 98%.



2r

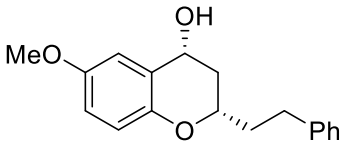
(2*R*,4*R*)-2-Isopropyl-6-methoxychroman-4-ol (2r):[9] A white solid (64.1 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.77–6.73 (m, 2H), 4.96–4.85 (m, 1H), 3.85–3.81 (m, 1H), 3.78 (s, 3H), 2.27 (ddd, *J* = 1.5, 6.5, 12.5 Hz, 1H), 1.98–1.92 (m, 1H), 1.71 (q, *J* = 12.0 Hz, 2H), 1.05 (d, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 148.8, 126.5, 117.2, 115.5, 110.9, 79.5, 66.3, 55.8, 34.8, 32.4, 18.0, 17.9; $[\alpha]_D^{26}$ = –101.72 (*c* 0.54, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 22.162 min (minor) and t_{R2} = 25.229 min (major), ee = 97%.



2s

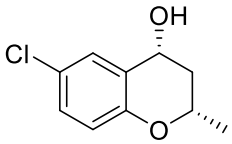
(2*S*,4*R*)-2-Butyl-6-methoxychroman-4-ol (2s): A white solid (68.8 mg, 98%). Mp 62–64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.77–6.73 (m, 2H), 4.95–4.85 (m, 1H), 4.07–4.04 (m, 1H), 3.78 (d, *J* = 2.4 Hz, 3H), 2.31–2.27 (m, 1H), 1.77–1.39 (m, 8H), 0.98–0.92 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 148.7, 126.4, 117.2, 115.5, 111.1, 74.9, 65.9, 55.8, 38.2, 35.3, 27.3, 22.7, 14.0; IR (KBr) cm^{-1}: 3588,

2934, 1611, 1580, 1491, 1465, 1384, 790; HRMS (ESI): calcd for $C_{14}H_{20}O_3$ $[M+Na]^+$: 259.1310, found 259.1317; $[\alpha]_D^{26}$ = −106.11 (*c* 0.48, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 24.062 min (minor) and t_{R2} = 26.916 min (major), ee = 99%.



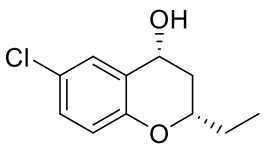
2t

(2*S*,4*R*)-6-Methoxy-2-phenethylchroman-4-ol (2t): A white solid (80.4 mg, 95%). Mp 97–98 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.20 (m, 5H), 7.03 (s, 1H), 6.81–6.76 (m, 2H), 4.96–4.87 (m, 1H), 4.09–4.03 (m, 1H), 3.79 (s, 3H), 2.94–2.80 (m, 2H), 2.31 (dd, *J* = 6.0, 12.5 Hz,), 2.15–2.08 (m, 1H), 1.97–1.90 (m, 1H), 1.83–1.76 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 148.5, 141.6, 128.5, 128.4, 126.3, 125.9, 117.3, 115.6, 111.1, 73.7, 65.8, 55.8, 38.2, 37.2, 31.3; IR (KBr) cm^{-1}: 3578, 2934, 1591, 1580, 1500, 1465, 1380, 790; HRMS (ESI): calcd for $C_{18}H_{20}O_3$ $[M+Na]^+$: 307.1310, found 307.1306; $[\alpha]_D^{26}$ = −116.77 (*c* 0.52, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 95/5, UV = 210 nm, flow rate = 0.8 mL/min) t_{R1} = 26.457 min (minor) and t_{R2} = 40.748 min (major), ee = 98%.



2u

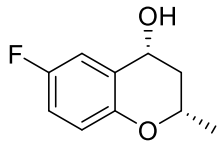
(2*S*,4*R*)-6-Chloro-2-methylchroman-4-ol (2u):[9] A white solid (58.8 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 1.2 Hz, 1H), 7.11–7.08 (m, 1H), 6.73–6.70 (m, 1H), 4.89–4.87 (m, 1H), 4.26–4.21 (m, 1H), 2.30–2.25 (m, 1H), 1.73–1.65 (m, 1H), 1.43–1.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 128.9, 127.1, 126.8, 125.4, 117.8, 71.5, 65.3, 39.4, 21.4; $[\alpha]_D^{26}$ = −131.68 (*c* 0.54, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 21.424 min (minor) and t_{R2} = 25.758 min (major), ee = 98%.



2v

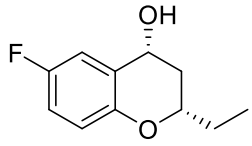
(2*S*,4*R*)-6-Chloro-2-ethylchroman-4-ol (2v): A white solid (60.9 mg, 96%). Mp 113–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.12 (dd, *J* = 2.0, 7.2 Hz, 1H), 6.75 (d, *J* = 7.2 Hz, 1H), 4.91 (s, 1H), 4.07–4.03 (m, 1H), 2.31 (ddd, *J* = 1.2, 4.8, 10.4 Hz, 1H), 1.84–1.64 (m, 4H), 1.06 (t, *J* = 6.0 Hz, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 153.2, 128.9, 127.4, 126.7, 125.3, 117.9, 76.4, 65.4, 37.1, 28.3, 9.4; IR (KBr) cm^{-1}: 3588, 2930, 1598, 1580, 1500, 1465, 1382, 750; HRMS (ESI): calcd for $C_{11}H_{13}ClO_2$ $[M+Na]^+$: 235.0502, found 235.0503; $[\alpha]_D^{26}$ = –119.45 (*c* 0.51, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 19.275 min (minor) and t_{R2} = 21.029 min (major), ee = 87%.



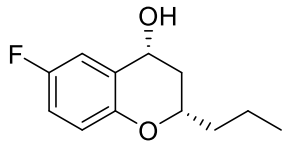
2w

(2*S*,4*R*)-6-Fluoro-2-methylchroman-4-ol (2w): A white solid (54.2mg, 99%). Mp 94–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 2.4, 7.2 Hz, 1H), 6.87 (td, *J* = 2.0, 6.8 Hz, 1H), 6.74 (dd, *J* = 4.0, 7.2 Hz, 1H), 4.95–4.89 (m, 1H), 4.28–4.21 (m, 1H), 2.30 (dd, *J* = 4.8, 10.4 Hz, 1H), 1.74 (q, *J* = 9.2 Hz, 2H), 1.43 (d, *J* = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1 (d, *J* = 189.4 Hz), 150.5 (d, *J* = 1.5 Hz), 126.7 (d, *J* = 5.3 Hz), 117.4 (d, *J* = 6.3 Hz), 115.8 (d, *J* = 18.6 Hz), 113.1 (d, *J* = 18.7 Hz), 71.4, 65.4, 39.5, 21.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.4; IR (KBr) cm^{-1}: 3588, 2934, 1596, 1584, 1500, 1465, 1380, 1217, 780; HRMS (ESI): calcd for $C_{10}H_{11}FO_2$ $[M+Na]^+$:205.0641, found 205.0650; $[\alpha]_D^{26}$ = –97.07 (*c* 0.50, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 22.519 min (minor) and t_{R2} = 27.109 min (major), ee = 99%.



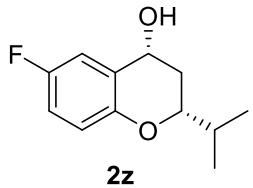
2x

(2*S*,4*R*)-2-Ethyl-6-fluorochroman-4-ol (2x): A white solid (57.1mg, 98%). Mp 77–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.87 (td, *J* = 2.8, 8.4 Hz, 1H), 6.74 (dd, *J* = 4.8, 8.8 Hz, 1H), 4.98–4.85 (m, 1H), 4.06–4.00 (m, 1H), 2.30 (ddd, *J* = 1.2, 6.4, 12.8 Hz, 1H), 1.86–1.65 (m, 4H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0 (d, *J* = 236.6 Hz), 150.6 (d, *J* = 1.9 Hz), 126.9 (d, *J* = 6.6 Hz), 117.4 (d, *J* = 7.7 Hz), 115.7 (d, *J* = 23.2 Hz), 113.0 (d, *J* = 23.4 Hz), 76.2, 65.6, 37.2, 28.4, 9.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −124.0; IR (KBr) cm^{-1}: 3586, 2932, 1598 1584, 1499, 1465, 1218, 1385, 780; HRMS (ESI): calcd for $C_{11}H_{13}FO_2$ $[M+Na]^+$: 219.0797, found 219.0789; $[\alpha]_D^{26}$ = –93.69 (*c* 0.55, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 19.408 min (minor) and t_{R2} = 21.154 min (major), ee = 90%.



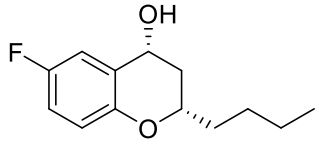
2y

(2*S*,4*R*)-6-Fluoro-2-propylchroman-4-ol (2y): A white solid (62.6 mg, 99%). Mp 65–66 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, J = 2.8, 8.8 Hz, 1H), 6.86 (td, J = 2.8, 8.4 Hz, 1H), 6.73 (dd, J = 4.4, 8.8 Hz, 1H), 4.97–4.83 (m, 1H), 4.12–4.06 (m, 1H), 2.28 (dd, J = 6.4, 12.8 Hz, 1H), 1.81-1.46 (m, 6H), 1.00 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0 (d, J = 236.7 Hz), 150.6 (d, J = 1.9 Hz), 126.9 (d, J = 6.6 Hz), 117.4 (d, J = 7.8 Hz), 115.7 (d, J = 23.3 Hz), 113.0 (d, J = 23.3 Hz), 74.8, 65.6, 37.7, 37.6, 18.3, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.5; IR (KBr) cm^{-1}: 3571, 2934, 1600, 1584, 1498, 1465, 1380, 1218, 768; HRMS (ESI): calcd for $C_{12}H_{15}FO_2$ $[M+Na]^+$: 233.0954, found 233.0961; $[\alpha]_D^{26}$ = −109.08 (*c* 0.52, $CHCl_3$); HPLC (Chiralcel AD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 24.338 min (minor) and t_{R2} = 29.615 min (major), ee = 98%.



2z

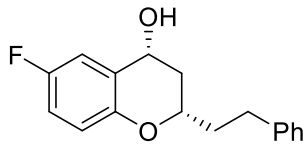
(2*R*,4*R*)-6-Fluoro-2-isopropylchroman-4-ol (2z): A white solid (60.3 mg, 96%). Mp 56–57 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, J = 8.8 Hz, 1H), 6.85 (t, J = 7.2 Hz, 1H), 6.73 (dd, J = 4.4, 8.8 Hz, 1H), 4.93–4.86 (m, 1H), 3.87–3.83 (m, 1H), 2.27 (dd, J = 6.0, 12.8 Hz, 1H), 1.98–1.90 (m, 1H), 1.80–1.67 (m, 2H), 1.02 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0 (d, J = 236.5 Hz), 150.8 (d, J = 2.0 Hz), 127.0 (d, J = 6.0 Hz), 117.4 (d, J = 7.7 Hz), 115.6 (d, J = 23.2 Hz), 112.9 (d, J = 23.4 Hz), 79.7, 66.0, 34.4, 32.3, 18.0, 17.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.7; HRMS (ESI): calcd for $C_{12}H_{15}FO_2$ $[M+Na]^+$: 233.0954, found 233.0950; IR (KBr) cm^{-1}: 3589, 2934, 1596, 1584, 1500, 1465, 1380, 1368, 1217, 780; $[\alpha]_D^{26}$ = −101.90 (*c* 0.59, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 16.768 min (minor) and t_{R2} = 17.871 min (major), ee = 96%.



2aa

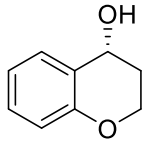
(2*S*,4*R*)-2-Butyl-6-fluorochroman-4-ol (2aa): A white solid (65.1mg, 97%). Mp 76–77 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 2.4, 8.8 Hz, 1H), 6.85 (td, J = 2.4, 8.4 Hz, 1H), 6.72 (dd, J = 4.8, 8.8 Hz, 1H), 4.92–4.86 (m, 1H), 4.10–4.04 (m, 1H), 2.29 (dd, J = 6.4, 13.2 Hz, 1H), 1.78–1.62 (m, 4H), 1.53–1.33

(m, 4H), 0.94 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0 (d, J = 236.7 Hz), 150.6 (d, J = 1.9 Hz), 126.9 (d, J = 6.6 Hz), 117.4 (d, J = 7.8 Hz), 115.7 (d, J = 23.2 Hz), 113.0 (d, J = 23.4 Hz), 75.1, 65.6, 37.7, 35.2, 27.2, 22.6, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.6; HRMS (ESI): calcd for $C_{13}H_{17}FO_2$ $[M+Na]^+$: 247.1110, found 247.1113; IR (KBr) cm^{-1}: 3581, 2942, 1600, 1584, 1500, 1465, 1383, 1217, 769; $[\alpha]_D^{26}$ = –91.31 (*c* 0.49, $CHCl_3$); HPLC (Chiralcel AD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 23.747 min (minor) and t_{R2} = 29.488 min (major), ee = 98%.



2ab

(2*S*,4*R*)-6-Fluoro-2-phenethylchroman-4-ol (2ab): A white solid (77.9 mg, 96%). Mp 91–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.15 (m, 6H), 6.87 (td, J = 2.4, 8.8 Hz, 1H), 6.77 (dd, J = 4.8, 8.8 Hz, 1H), 4.90–4.84 (m, 1H), 4.10–4.04 (m, 1H), 2.92–2.76 (m, 2H), 2.29 (dd, J = 6.4, 13.2 Hz, 1H), 2.14–2.05 (m, 1H), 1.97–1.88 (m, 1H), 1.82–1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1 (d, J = 236.9 Hz), 150.5 (d, J = 2.0 Hz), 141.5, 128.5, 128.4, 126.9 (d, J = 6.6 Hz), 126.0, 117.5 (d, J = 7.8 Hz), 115.8 (d, J = 23.2 Hz), 113.1 (d, J = 23.3 Hz), 74.0, 65.4, 37.7, 37.1, 31.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.3; IR (KBr) cm^{-1}: 3589, 2934, 1599, 1580, 1500, 1465, 1384, 1216, 789; HRMS (ESI): calcd for $C_{17}H_{17}FO_2$ $[M+Na]^+$: 295.1110, found 295.1112; $[\alpha]_D^{26}$ = –124.32 (*c* 0.58, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 84.433 min (minor) and t_{R2} = 89.431 min (major), ee = 98%.

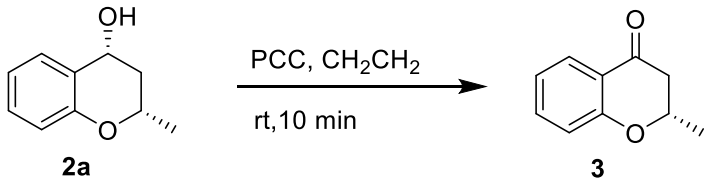


2ac

(*R*)-Chroman-4-ol (2ac):[10] A white solid (44.8 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 7.6 Hz, 1H), 7.21 (t, J = 6.8 Hz, 1H), 6.92 (t, J = 7.2 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 4.81–4.73 (m, 1H), 4.27–4.24 (m, 1H), 2.15–2.00 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 130.0, 129.9, 124.5, 120.8, 117.3, 63.5, 62.1, 31.0; $[\alpha]_D^{26}$ = +56.52 (*c* 0.47, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 24.971 min (minor) and t_{R2} = 29.406 min (major), ee = 99%.

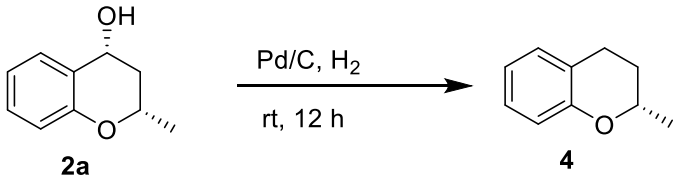
4. Transformation of Chromanol

4.1 Procedure for synthesis of 3[2]



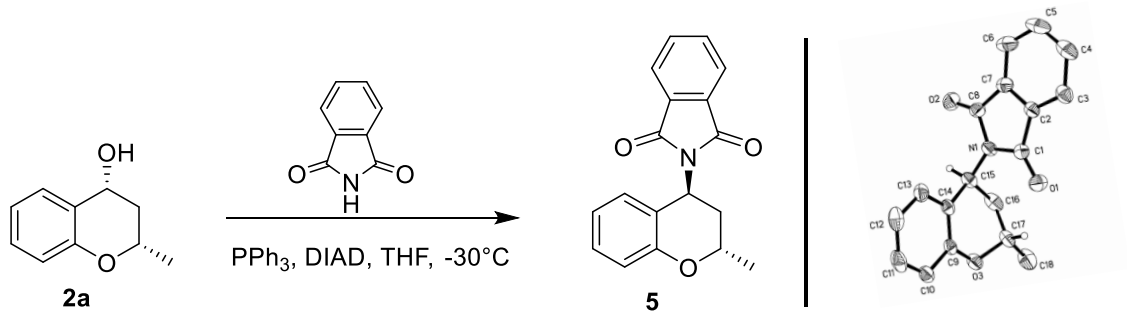
The **2a** (0.15 mmol) was treated with PCC (120 mg) in CH_2Cl_2 (2 mL) at room temperatures for 10 min. Evaporation of DCM gave a residue and then Et_2O was added. The solution was filtered through a plug of silica using Et_2O. The solvent was evaporated to give crude product. Then, it was purified by chromatography (PE:EtOAc = 20:1) to give pure product **3** as a colorless oil (46.3 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 1.6, 8.0 Hz, 1H), 7.49 (td, J = 1.6, 7.2 Hz, 1H), 7.04-6.98 (m, 2H), 4.67–4.57 (m, 1H), 2.70 (d, J = 7.6 Hz, 2H), 1.54 (d, J = 6.4 Hz, 3H); $[\alpha]_D^{26}$ = +26.56 (c 0.47, $CHCl_3$); HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 13.128 min (minor) and t_{R2} = 14.520 min (major), ee = 99.9%.

4.2 Procedure for synthesis of 4[11]



A hydrogenation tube was charged with a stirring bar, **2a** (0.30 mmol), Pd/C (20%). MeOH (3 mL) was then injected into the hydrogenation tube by a syringe. The hydrogenation tube was then put into an autoclave. The autoclave was then charged with hydrogen to 30 bar hydrogen pressure, and the reaction mixture was stirred at RT for 12 h. The solvent was evaporated to afforde the crude product and it was purified by chromatography (PE:EtOAc = 10:1) to give pure product **4** as a colorless oil(44.1 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13–7.06 (m, 2H), 6.87–6.82 (m, 2H), 4.21–4.13 (m, 1H), 2.94–2.85 (m, 1H), 2.81–2.74 (m, 1H), 2.05–1.99 (m, 1H), 1.81–1.70 (m, 1H), 1.43 (d, J = 6.4 Hz, 3H); $[\alpha]_D^{26}$ = +84.20 (c 0.47, $CHCl_3$); HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 8.572 min (minor) and t_{R2} = 9.246 min (major), ee = 99.8%.

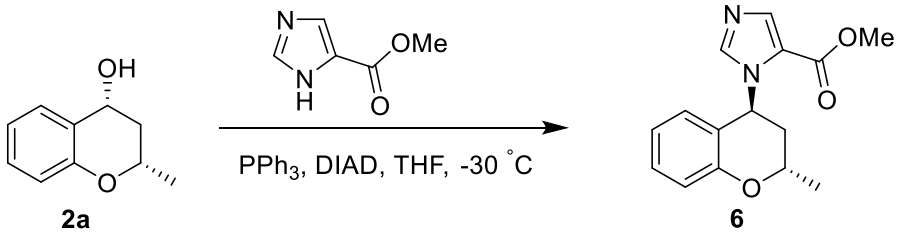
4.3 Procedure for synthesis of 5



Diisopropyl azodicarboxylate (DIAD) (0.54 g, 2.7 mmol) in dry THF (5 ml) was added dropwise to a

stirred solution of **2a** (0.36 g, 2.2 mmol), PPh_3, (0.68 g, 2.6 mmol) and phthalimide (0.33 g, 2.3 mmol) in dry THF (15 ml) at –30 °C before the mixture was warmed to room temperature and stirred for a further 1 h. Then the solvent was evaporated to provide crude product and it was purified by chromatography (PE:EA=10:1) to give pure product **5** as a white soild (0.6 g, 93%). Mp 145–146 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.83 (m, 2H), 7.78–7.74 (m, 2H), 7.23–7.19 (m, 1H), 7.02 (d, J = 7.2 Hz, 1H), 6.94 (dd, J = 0.8, 8.0 Hz, 1H), 6.84 (td, J = 0.8, 7.2 Hz, 1H), 5.55–5.53 (m, 1H), 4.76–4.68 (m, 1H), 2.34–2.29 (m, 1H), 2.19–2.09 (m, 1H), 1.44 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 155.6, 134.1, 131.8, 129.2, 128.0, 123.3, 120.4, 118.8, 117.3, 69.1, 43.8, 35.8, 20.7; IR (KBr) cm^{-1}: 2934, 1651, 1601, 1580, 1500, 1465, 1380, 740; HRMS (ESI): calcd for $C_{18}H_{15}NO_2$ $[M+H]^+$: 294.1130, found 294.1122; $[\alpha]_D^{26}$ = +45.68 (*c* 0.52, $CHCl_3$); HPLC (Chiralcel AD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.3 mL/min) t_{R1} = 19.430 min (minor) and t_{R2} = 22.901 min (major), ee = 98%.

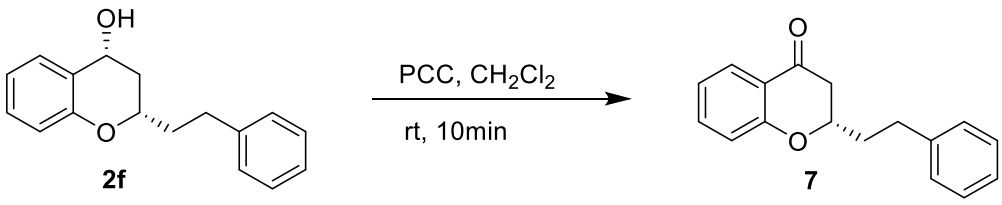
4.4 Procedure for synthesis of 6



2a **6**

Diisopropyl azodicarboxylate (DIAD) (0.54 g, 2.7 mmol) in dry THF (5 ml) was added dropwise to a stirred solution of **1a** (0.36 g, 2.2 mmol), PPh_3, (0.68 g, 2.6 mmol) and methyl-5-imidazolecarboxylate (0.29 g, 2.3 mmol) in dry THF (15 ml) at -30°C before the mixture was warmed to room temperature and stirred for a further 1 h. Then the solvent was evaporated to provide crude product and it was purified by chromatography (PE:EA=10:1) to give pure product **6** as a white soild (0.6 g, 93%). Mp 115–117 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.30–7.26 (m, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.97–6.91 (m, 2H), 6.11 (s, 1H), 4.03–3.96 (m, 1H), 3.90 (s, 3H), 2.19–2.13 (m, 2H), 1.76 (s, 1H), 1.37 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 155.9, 142.1, 138.8, 130.7, 130.6, 122.2, 121.1, 117.6, 117.1, 66.7, 51.6, 51.3, 36.8, 20.7; IR (KBr) cm^{-1}: 3098, 2934, 1725, 1601, 1580, 1500, 1465, 1380, 790; HRMS (ESI): calcd for $C_{18}H_{15}NO_2$ $[M+H]^+$: 273.1239, found 273.1233; $[\alpha]_D^{26}$ = +35.48 (*c* 0.52, $CHCl_3$); HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 97/3, UV = 210 nm, flow rate = 0.5 mL/min) t_{R1} = 42.046 min (major) and t_{R2} = 49.029 min (minor), ee = 99.9%.

4.5 Procedure for synthesis of 7 [2]

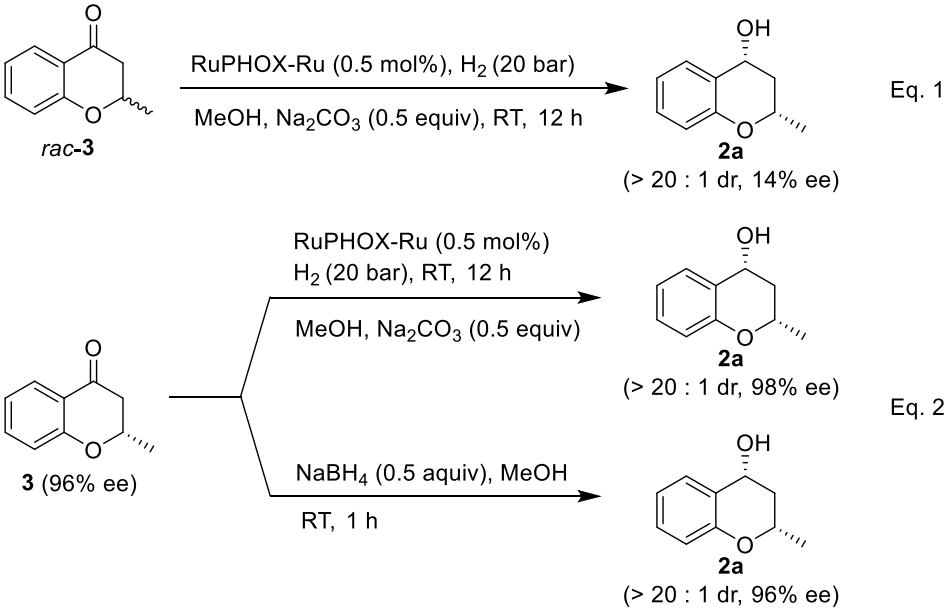


2f **7**

2f (0.15 mmol) was treated with PCC (120 mg) in CH_2Cl_2 (2 mL) at room temperatures for 10 min before evaporation of DCM. Then Et_2O was added to the residue. The resulting mixture was filtered

through a plug of silica using Et_2O. The solvent was evaporated to give crude product which was purified by chromatography (PE:EA = 20:1) to give pure product **7** as colorless oil (36.3 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.34–7.25 (m, 5H), 7.04 (d, J = 7.6 Hz, 2H), 4.49–4.43 (m, 1H), 2.98–2.83 (m, 2H), 2.79–2.69 (m, 2H), 2.30–2.21 (m, 1H), 2.07–1.98 (m, 1H); $[\alpha]_D^{26}$ = +59.89 (c 0.47, $CHCl_3$); HPLC (Chiralcel OD-H, n-hexane/i-PrOH = 90/10, UV = 210 nm, flow rate = 1.0 mL/min) t_{R1} = 15.848 min (minor) and t_{R2} = 28.636 min (major), ee = 98%.

5. Control Experiments to Verify Reaction Pathway



To further explore the reaction pathway, the asymmetric hydrogenation of racemic **3** was carried out under the optimal reaction conditions (Eq. 1). To our surprise, the desired product **2a** was obtained with up to 14% ee and > 20 : 1dr. Subsequently, chiral intermediate **3** (96% ee), obtained via oxidation of chiral **2a** from the above mentioned gram-scale synthesis, was reduced under the same reaction conditions, affording **2a** in quantitative yield, 98% ee and > 20 : 1 dr (Eq. 1, top). These results indicated that the asymmetric catalytic hydrogenation of **3** proceeds together with a dynamic kinetic resolution process. Nevertheless, only a slight effect is observed in our case because the asymmetric catalytic hydrogenation was carried out using a weak base (Na_2CO_3) and the chiral center may be established in the first step. To verify this process, the chiral intermediate **3** (96% ee) used above was also reduced by $NaBH_4$ in MeOH, with **2a** being obtained in high yield, 96% ee and > 20 : 1 dr (Eq. 1, bottom). The results suggested that the subsequent hydrogenation of the C=O double bond can be directed by the previously formed carbon chiral center.

6. Reference

[1] a) T. Patonay, A. Vasas, A. Kiss-Szikszai, A. M. S. Silva and J. A. S. Cavaleiro, *Aust. J. Chem.* 2010, **63**, 1582; b) L. A. Stubbing, F. F. Li, D. P. Furkert, V. E. Caprio and M. A. Brimble, *Tetrahedron* 2012, **68**, 6948.

[2] D. Zhao, B, Beiring and F. Glorius, *Angew. Chem. Int. Ed*. 2013, **52**, 8454.

[3] S.-S. Wen, J. Wang, Y.-M. Luo and H. Yang, *Tetrahedron* 2014, **70**, 9314.

[4] J. Liu, M. Liu, Y. Yue, N. Zhang, Y. Zhang and K. Zhuo, *Tetrahedron Lett.* 2013, **54**, 1802.

[5] S. G. Shashi and J. K. Makrandi, *Indian. J. Chem*. 2006, **45**, 535.

[6] A. Y. Shawa, C.-Y. Chang, H.-H. Liau, P.-J. Lu, H.-L. Chen, C.-N. Yang and H.-Y. Li, *Eur. J. Med. Chem.* 2009, **44**, 2552.

[7] S. Zhang, C. Wan, Q. Wang, B. Zhang, L. Gao, Z. Zha and Z. Wang, *Eur. J. Org. Chem.* 2013, 2080.

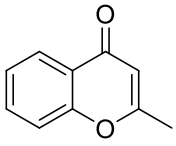
[8] J. Zhao, Y. Zhao and H. Fu, *Angew. Chem. Int. Ed.* 2011, **50**, 3769.

[9] E. R. Ashley, E. C. Sherer, B. Pio, R. K. Orr and R. T. Ruck, *ACS Catal*. 2017, **7**, 1446.

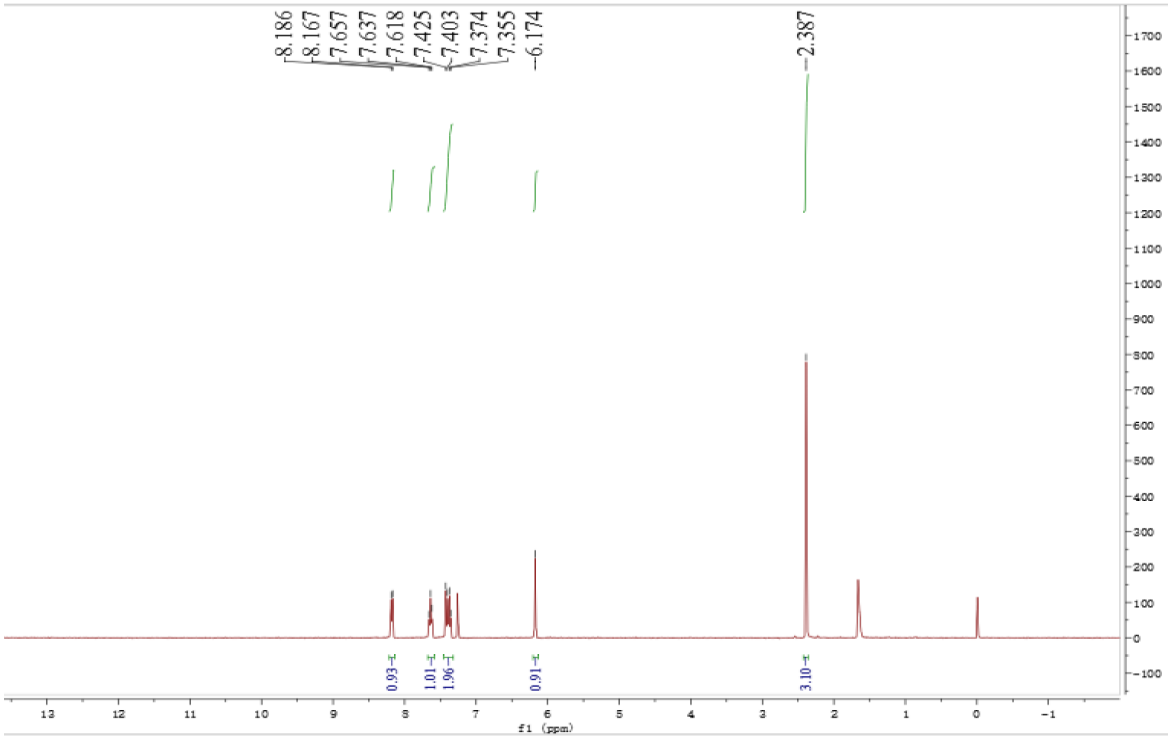
[10] S. Rast, B. Modec, M. Stephan and B. Mohar, *Org. Biomol. Chem.* 2016, **14**, 2112.

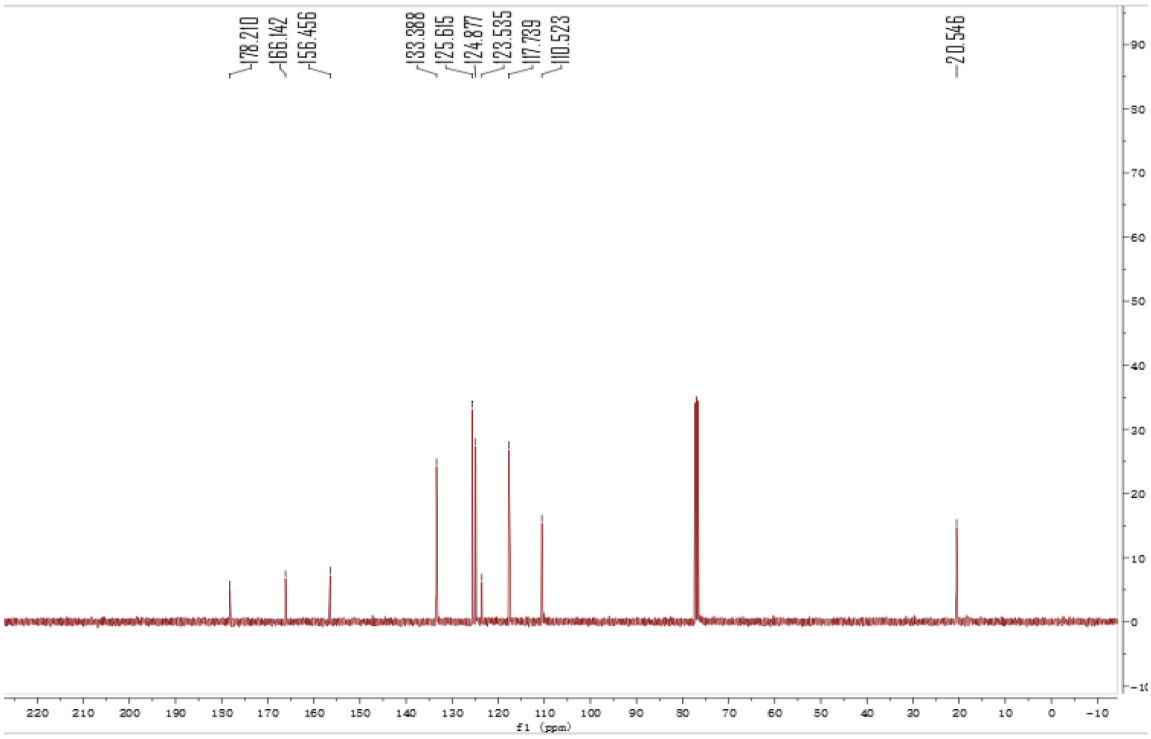
[11] C. Valla, A. Baeza, F. Menges and A. Pfaltz, *Synlett* 2008, 3167.

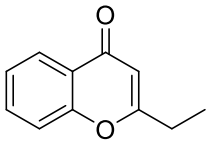
7. NMR spectra



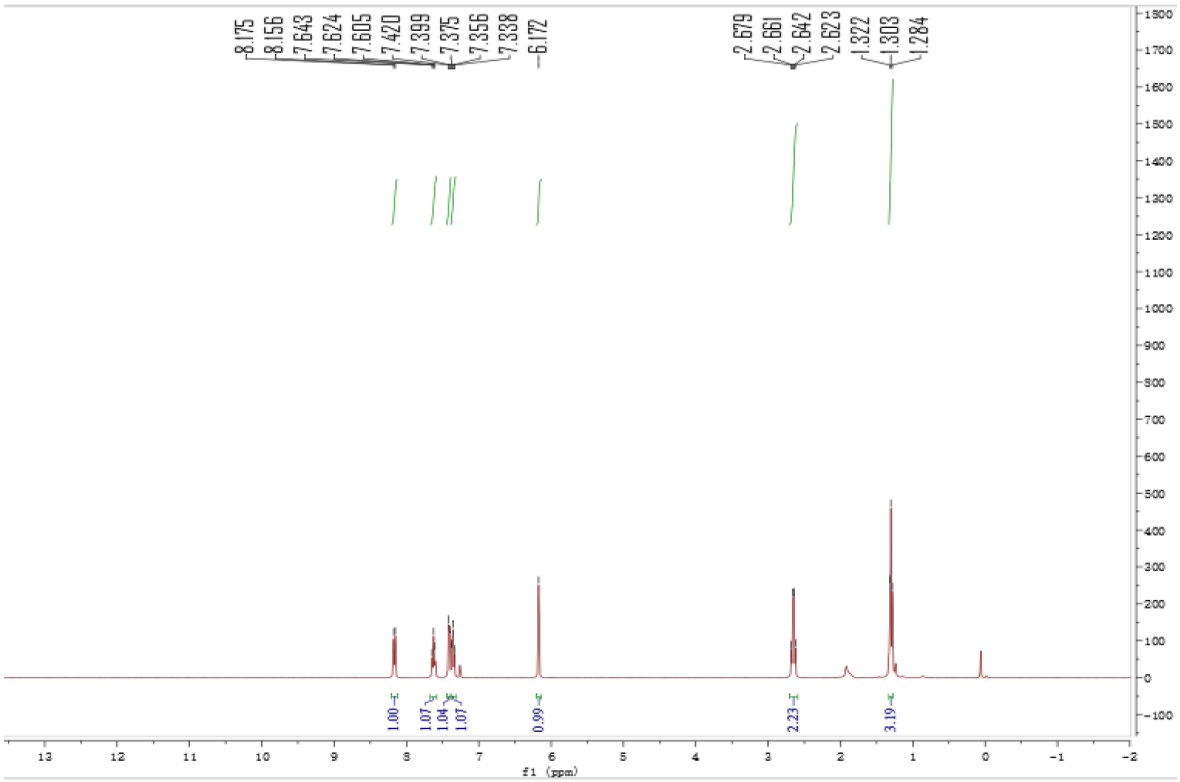
1a

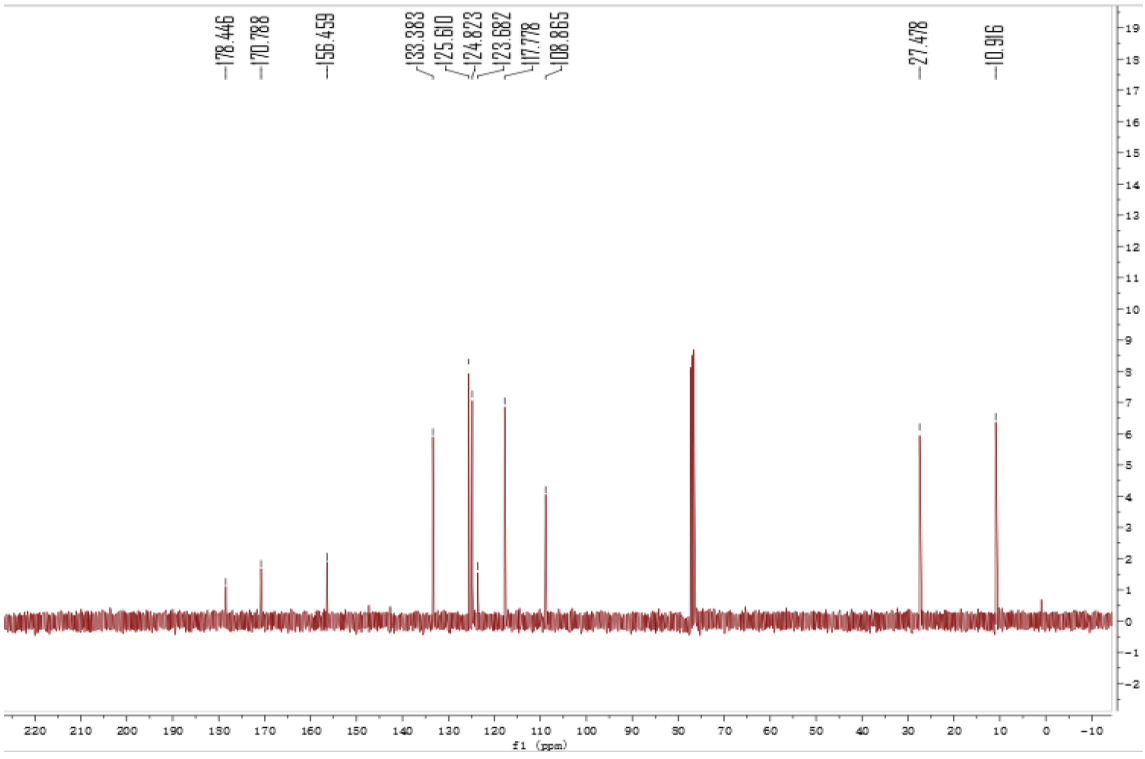


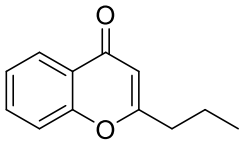




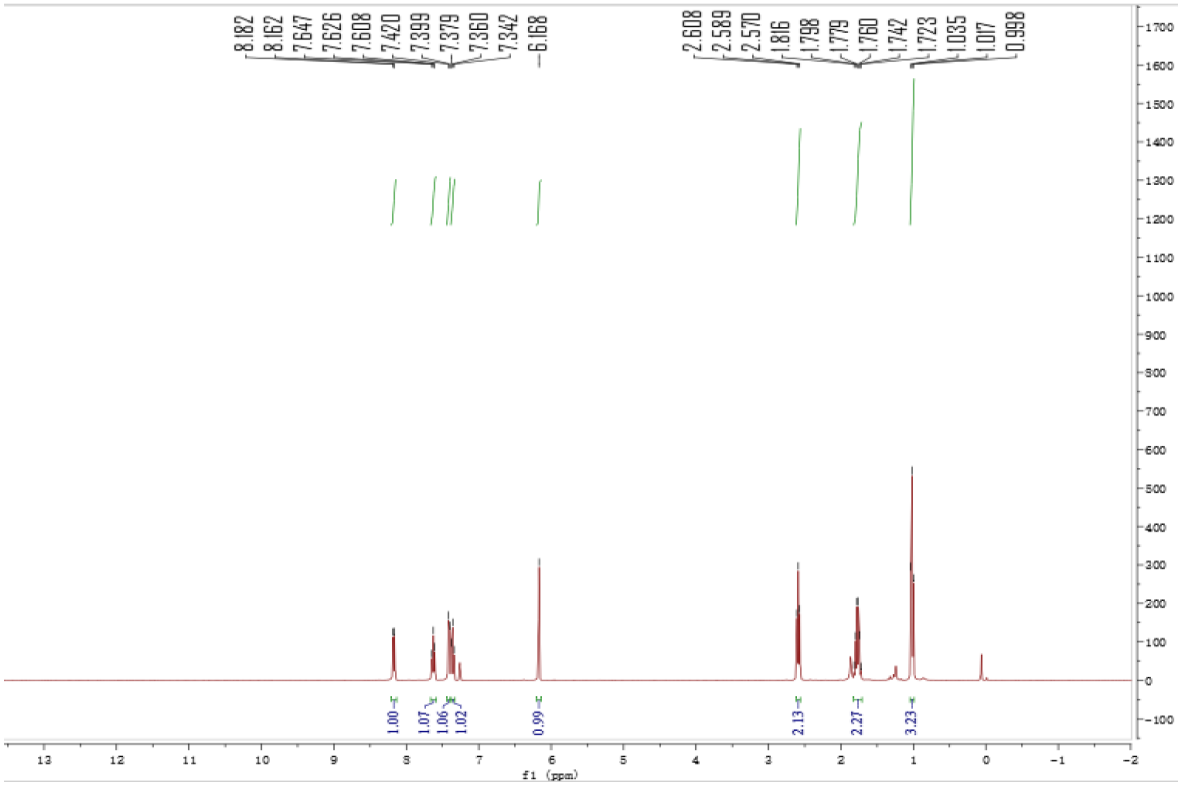
1b

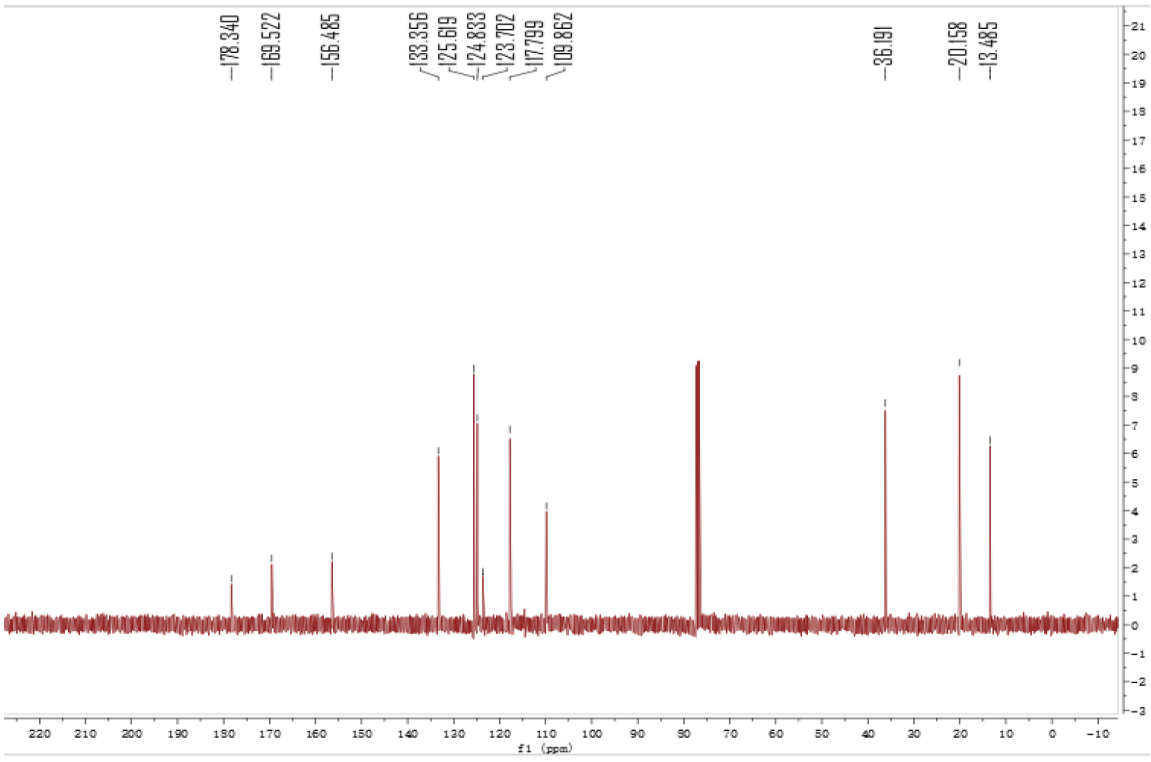

8.175
8.156
7.643
7.624
7.605
7.420
7.399
7.375
7.356
7.338
6.172
2.679
2.661
2.642
2.623
1.322
1.303
1.284
1.00
1.07
1.04
1.07
0.99
2.23
3.19
f1 (ppm)

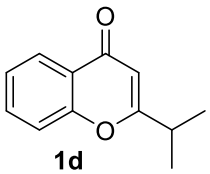

178.446
170.788
156.459
133.383
125.610
124.823
123.682
117.778
108.865
27.478
10.916
f1 (ppm)



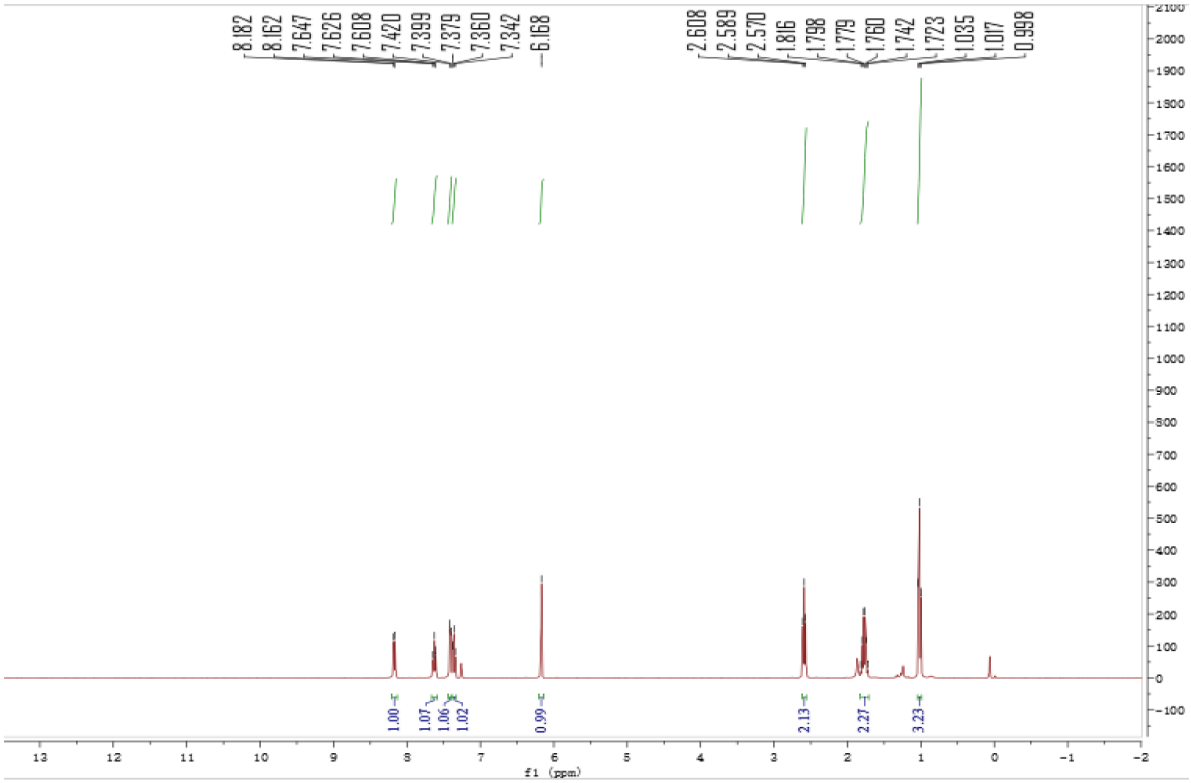
1c

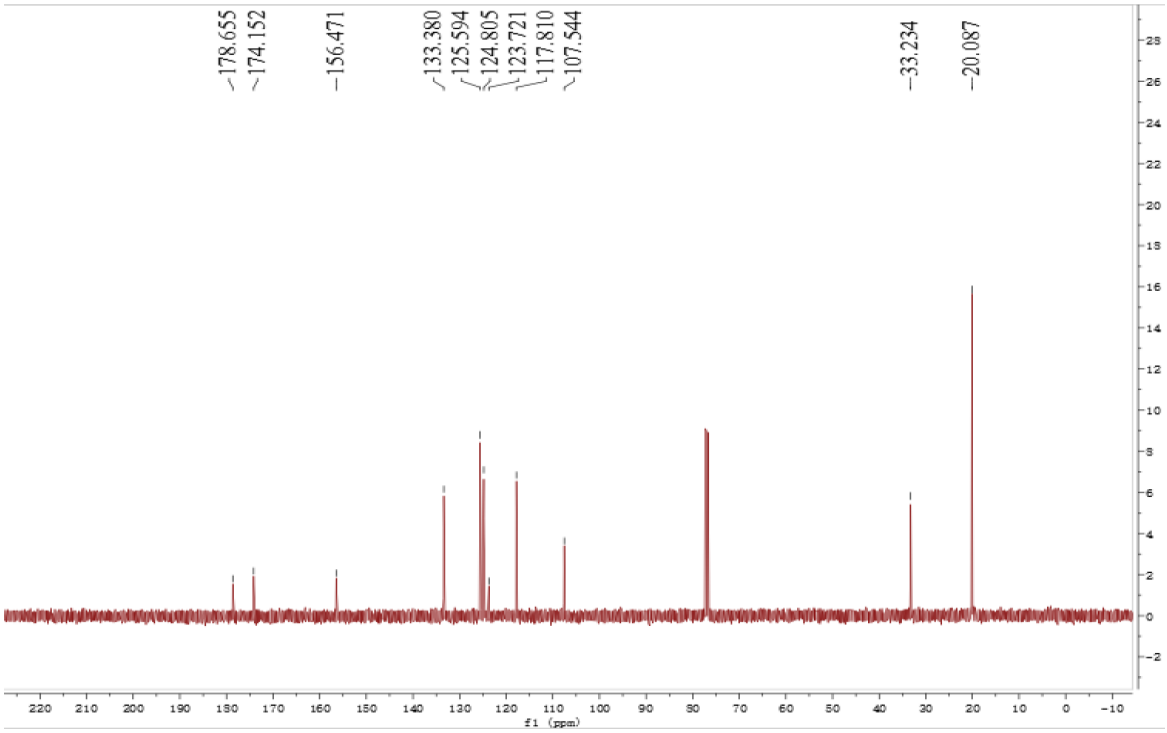

8.182
8.162
7.647
7.626
7.608
7.420
7.399
7.379
7.360
7.342
6.168
2.608
2.589
2.570
1.816
1.798
1.779
1.760
1.742
1.723
1.035
1.017
0.998
1.00
1.07
1.06
1.02
0.99
2.13
2.27
3.23
f1 (ppm)

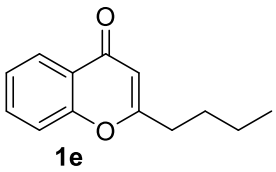

178.340
169.522
156.485
133.356
125.619
124.833
123.702
117.799
109.862
36.191
20.158
13.485
f1 (ppm)



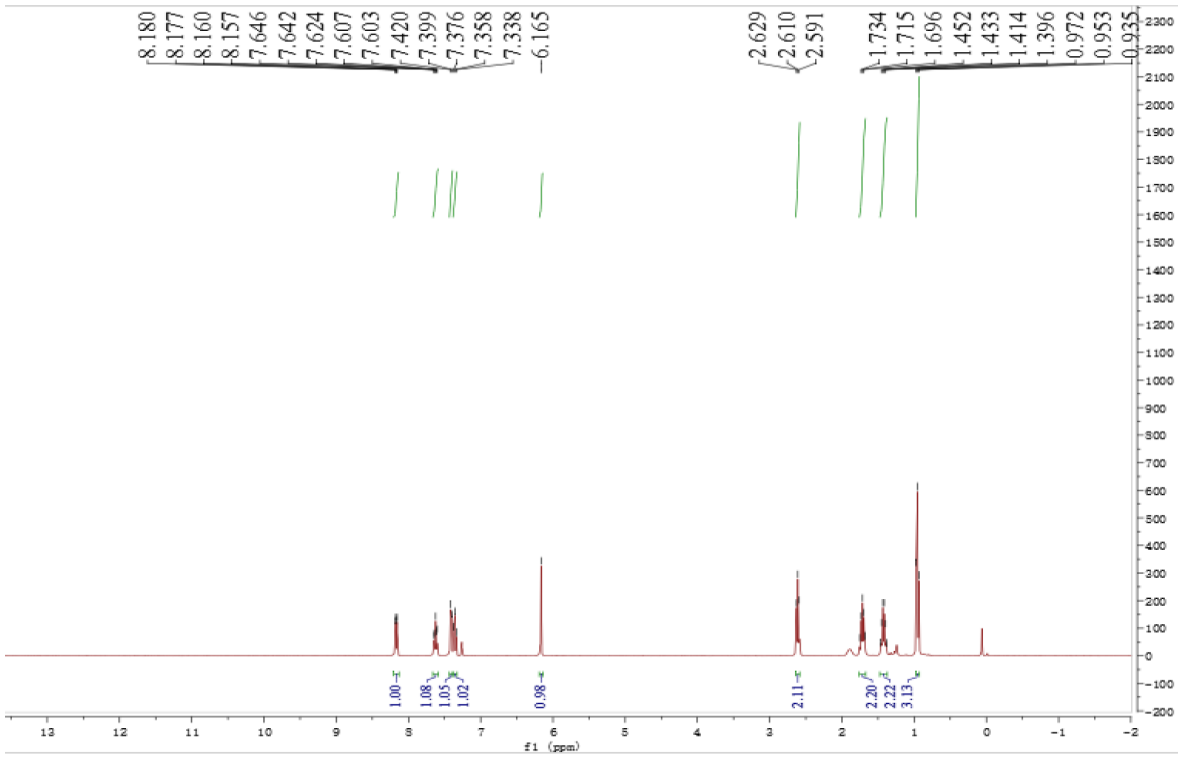
1d

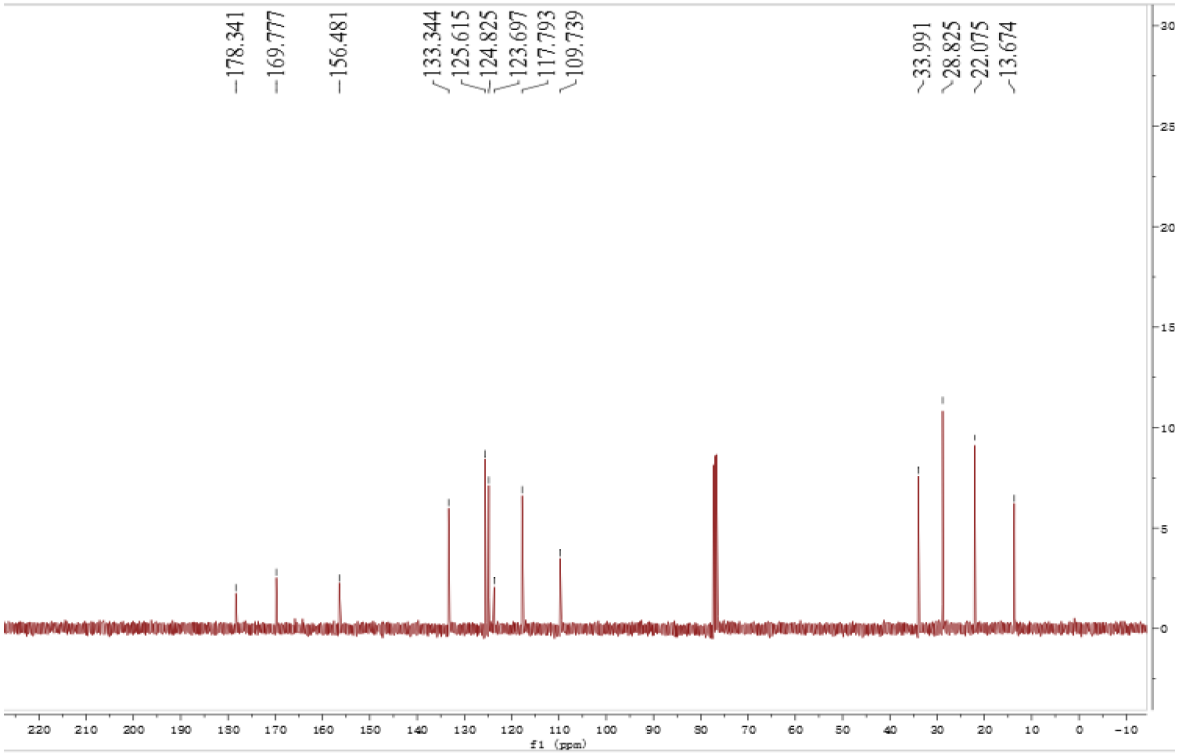

8.182
8.162
7.647
7.626
7.608
7.420
7.399
7.379
7.360
7.342
6.168
2.608
2.589
2.570
1.816
1.798
1.779
1.760
1.742
1.723
1.035
1.017
0.998
1.00
1.07
1.06
1.02
0.99
2.13
2.27
3.23
f1 (ppm)

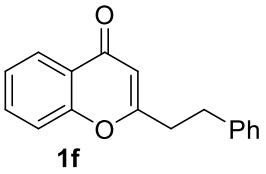

178.655
174.152
156.471
133.380
125.594
124.805
123.721
117.810
107.544
33.234
20.087
f1 (ppm)



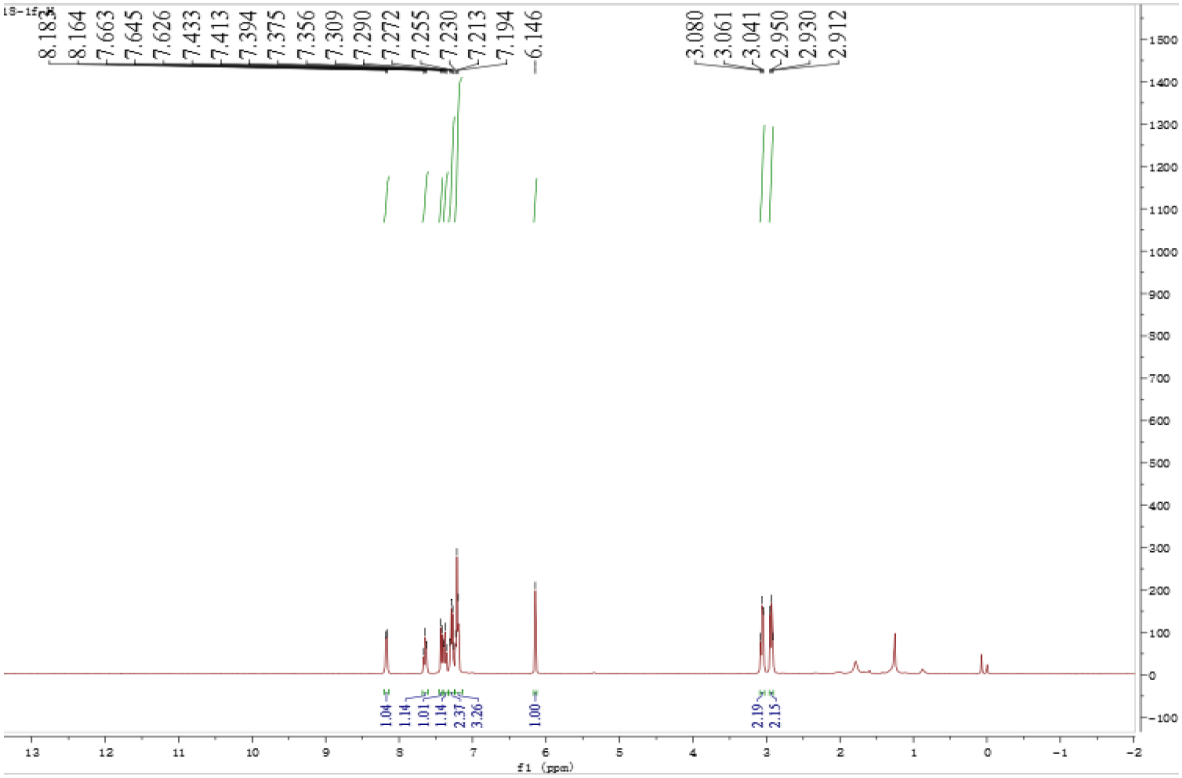
1e

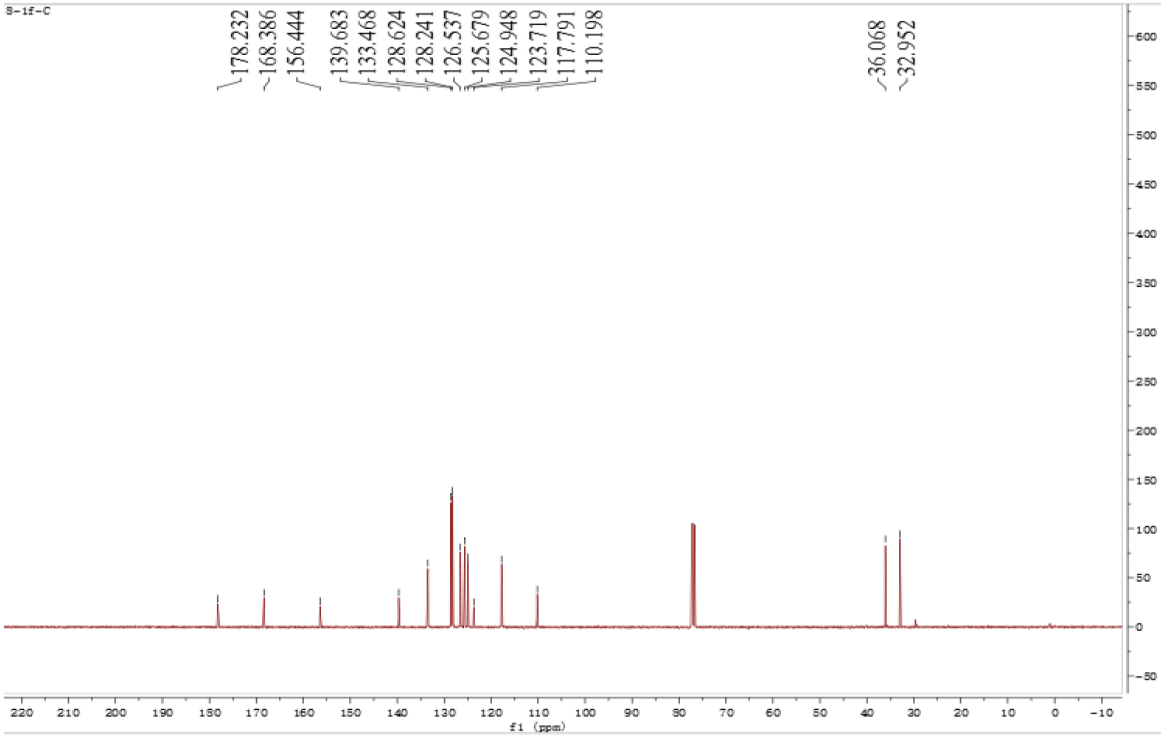

8.180
8.177
8.160
8.157
7.646
7.642
7.624
7.607
7.603
7.420
7.399
7.376
7.358
7.338
6.165
2.629
2.610
2.591
1.734
1.715
1.696
1.452
1.433
1.414
1.396
0.972
0.953
0.935
1.00
1.08
1.05
1.02
0.98
2.11
2.20
2.22
3.13
f1 (ppm)

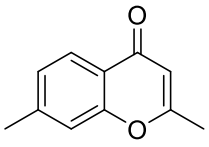

178.341
169.777
156.481
133.344
125.615
124.825
123.697
117.793
109.739
33.991
28.825
22.075
13.674
f1 (ppm)


O
O
Ph

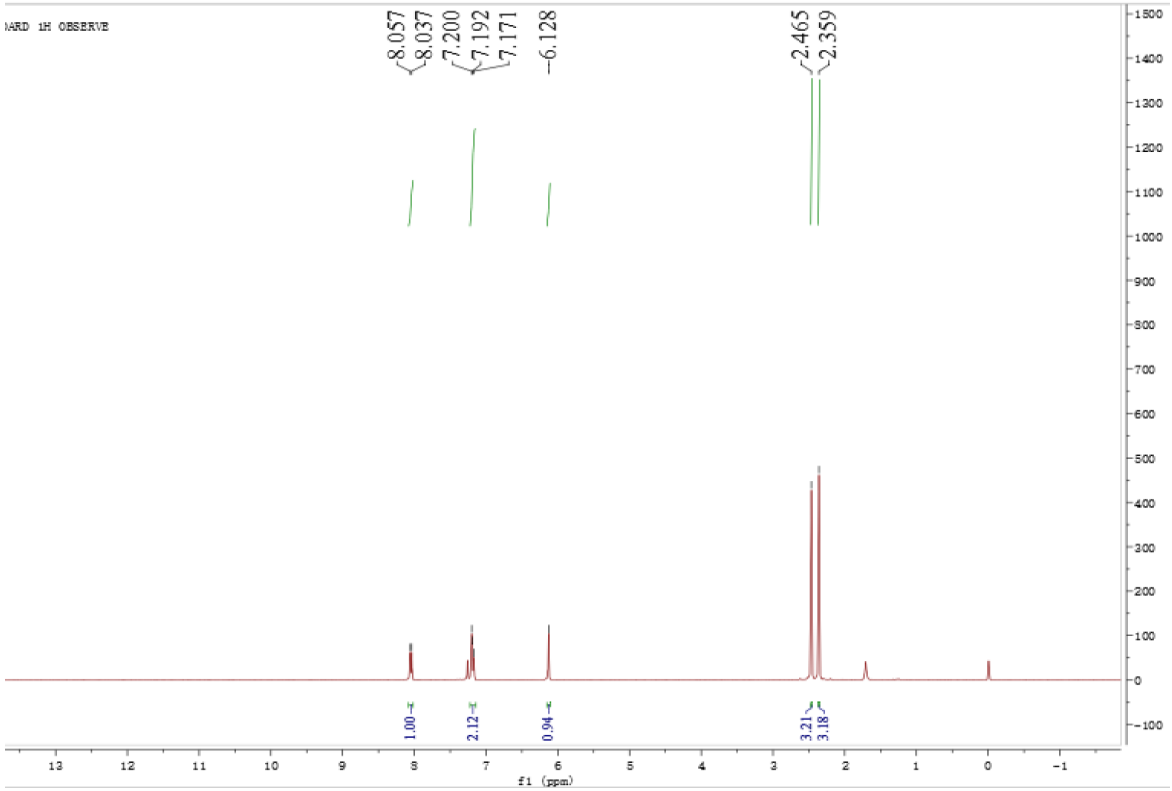
1f

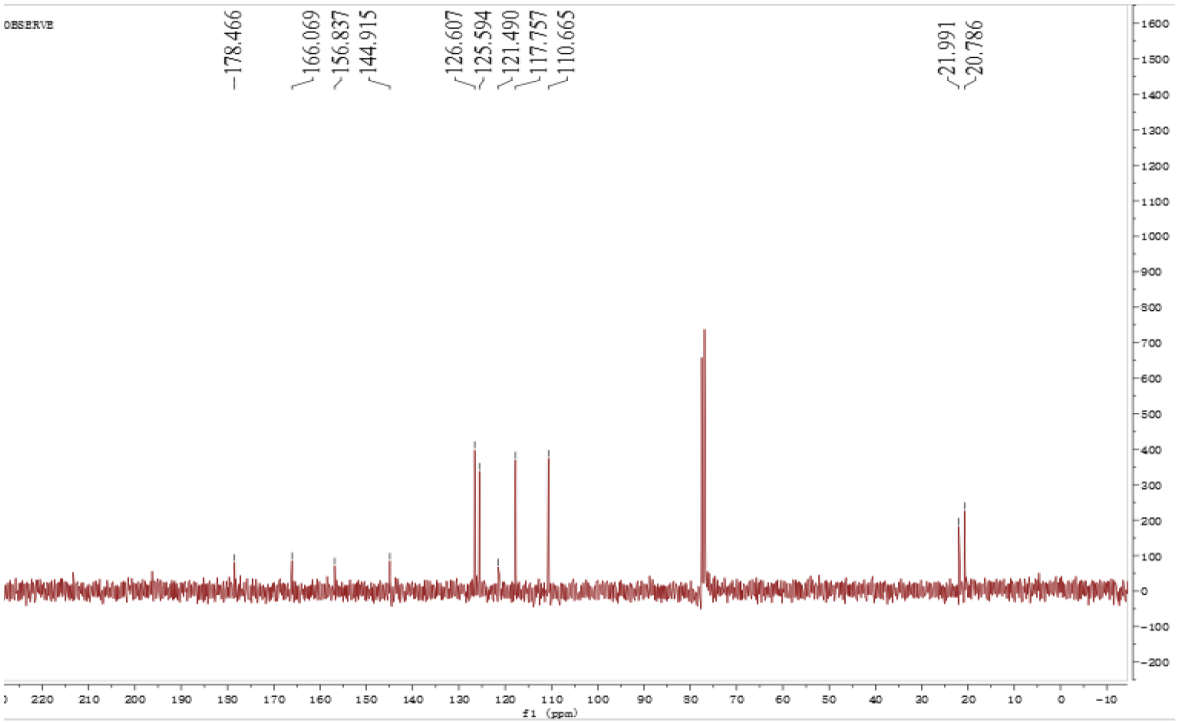

8.183
8.164
7.663
7.645
7.626
7.433
7.413
7.394
7.375
7.356
7.309
7.290
7.272
7.255
7.230
7.213
7.194
6.146
3.080
3.061
3.041
2.950
2.930
2.912
1.04
1.14
1.01
1.14
2.37
3.26
1.00
2.19
2.15
f1 (ppm)

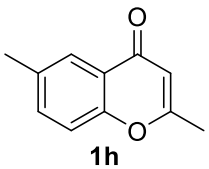

178.232
168.386
156.444
139.683
133.468
128.624
128.241
126.537
125.679
124.948
123.719
117.791
110.198
36.068
32.952
f1 (ppm)



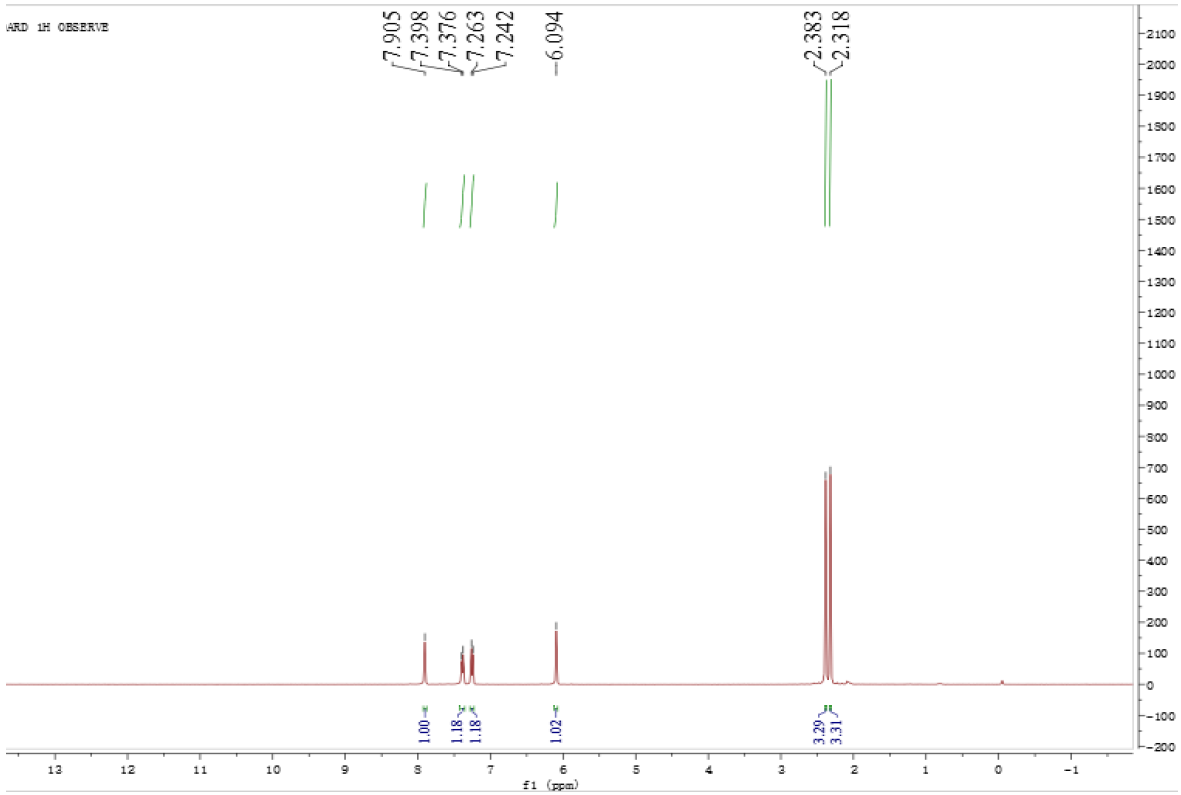
1g

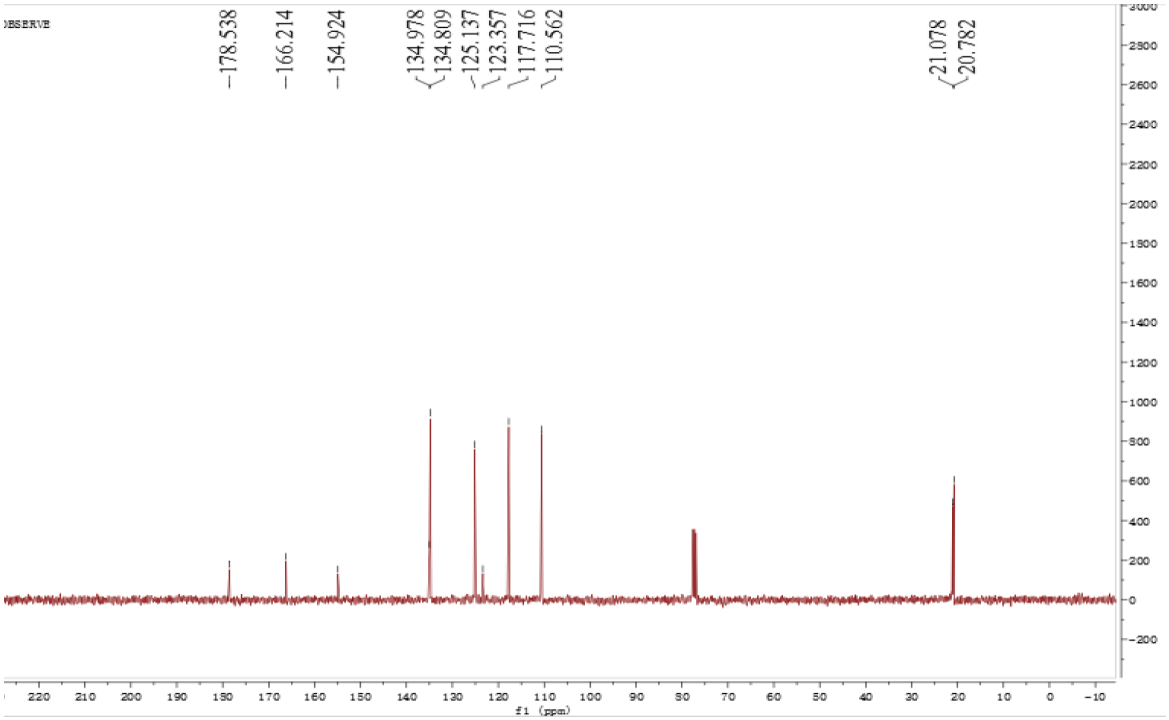

8.057
8.037
7.200
7.192
7.171
6.128
2.465
2.359
1.00
2.12
0.94
3.21
3.18
f1 (ppm)

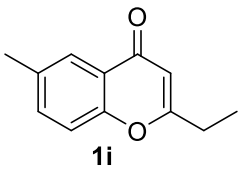

178.466
166.069
156.837
144.915
126.607
125.594
121.490
117.757
110.665
21.991
20.786
f1 (ppm)



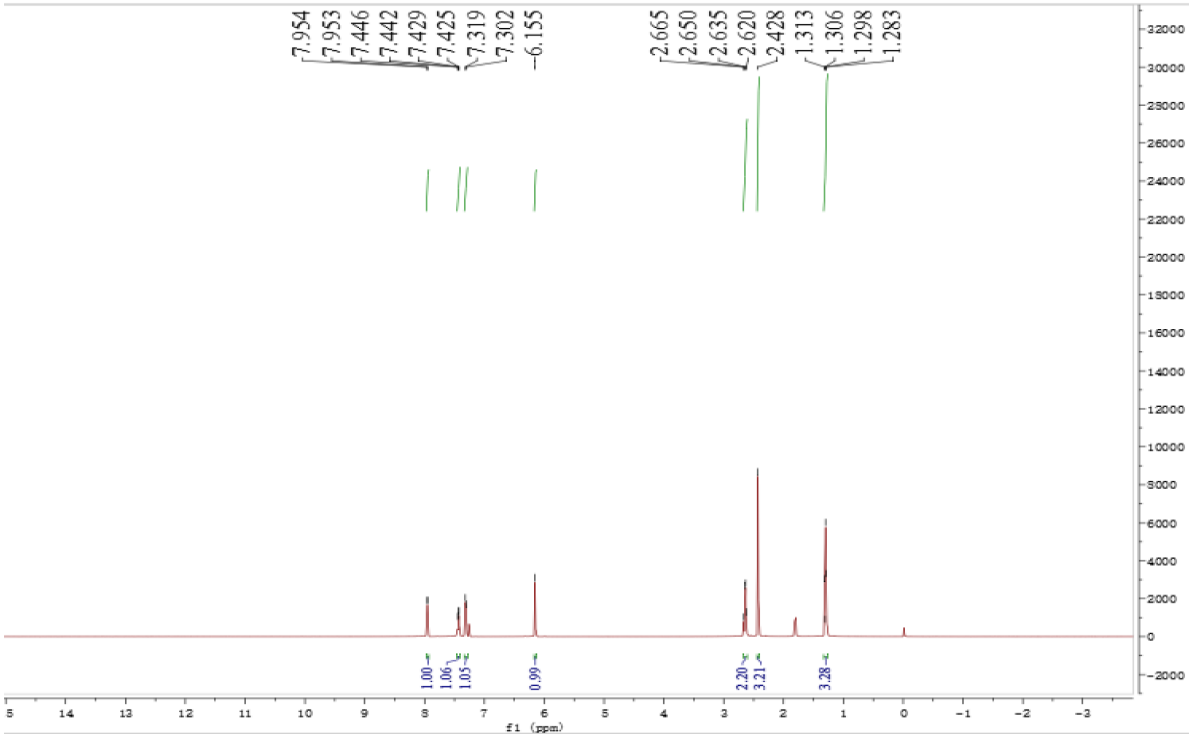
1h

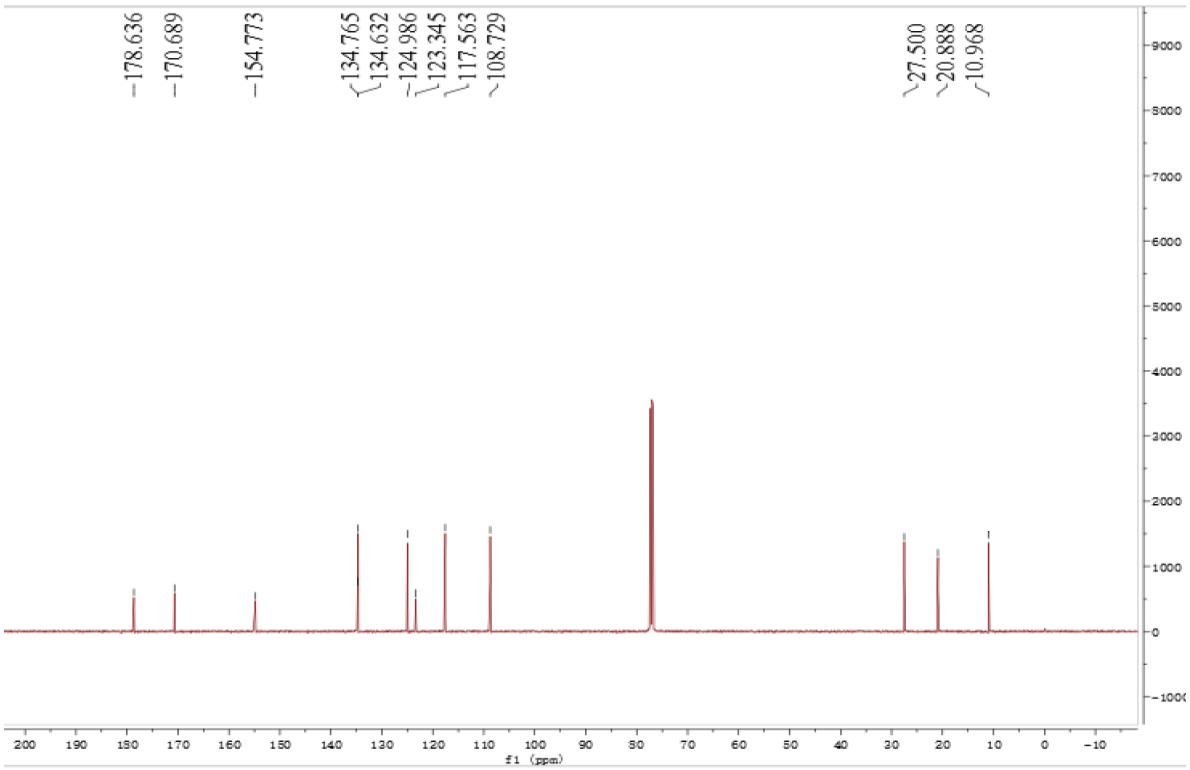

7.905
7.398
7.376
7.263
7.242
6.094
2.383
2.318
1.00
1.18
1.18
1.02
3.29
3.31
f1 (ppm)

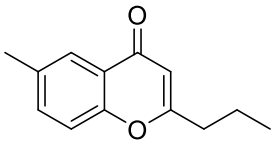

178.538
166.214
154.924
134.978
134.809
125.137
123.357
117.716
110.562
21.078
20.782
f1 (ppm)


O
O

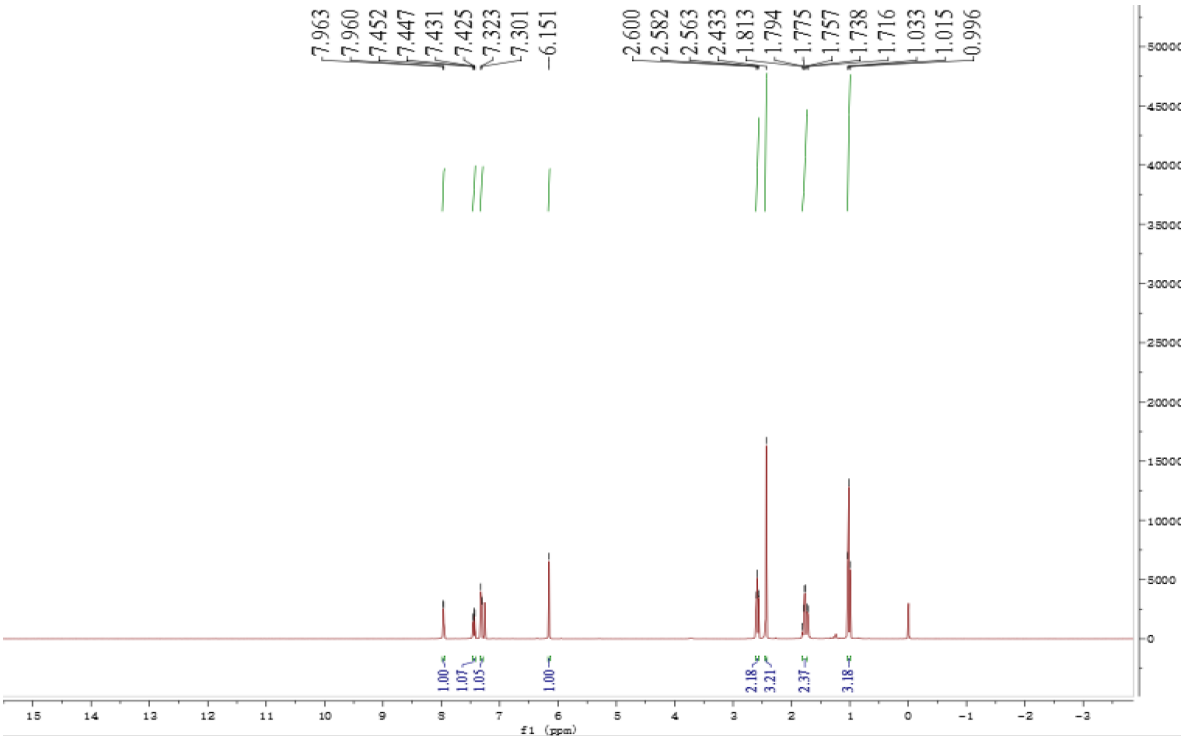
1i

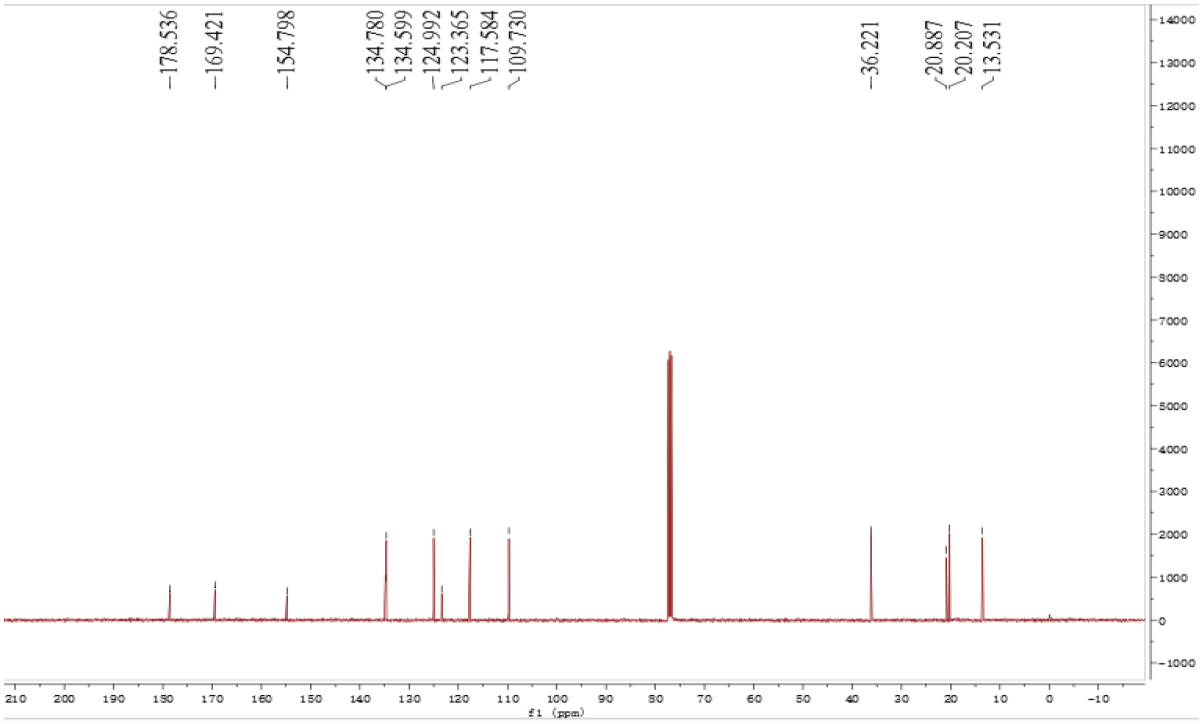

7.954
7.953
7.446
7.442
7.429
7.425
7.319
7.302
6.155
2.665
2.650
2.635
2.620
2.428
1.313
1.306
1.298
1.283
1.00
1.06
1.05
0.99
2.20
3.21
3.28
f1 (ppm)

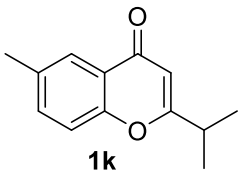

178.636
170.689
154.773
134.765
134.632
124.986
123.345
117.563
108.729
27.500
20.888
10.968
f1 (ppm)



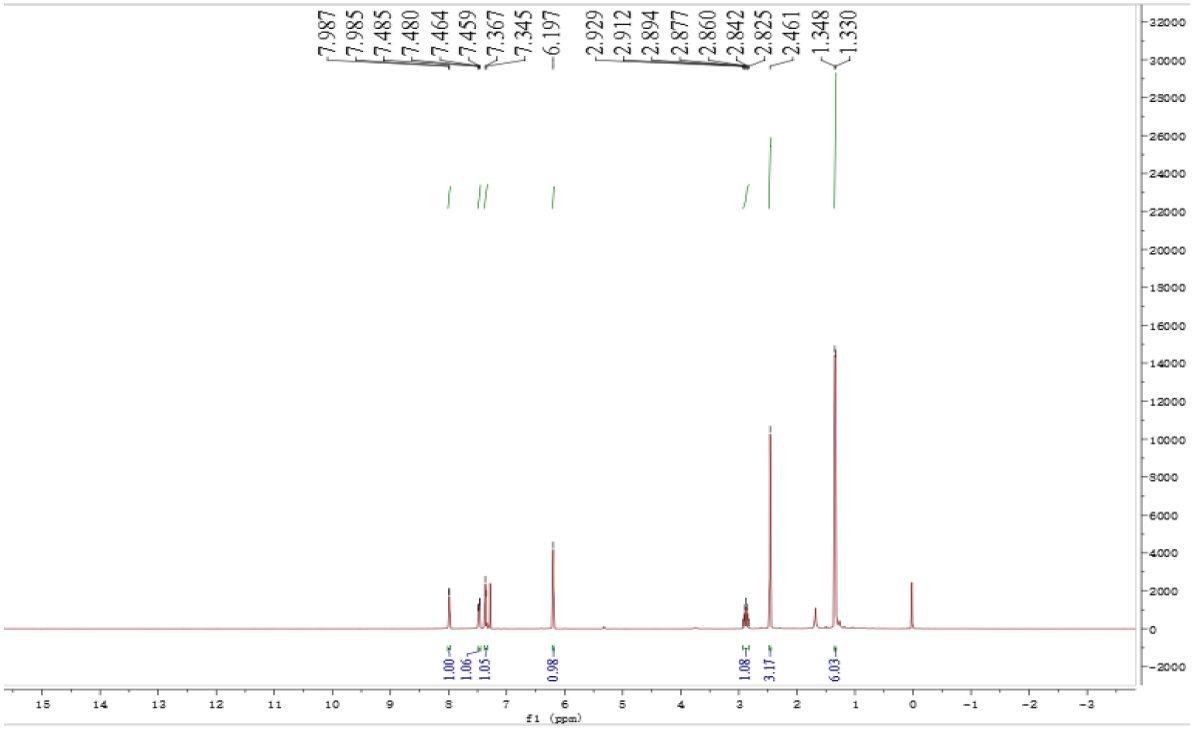
1j

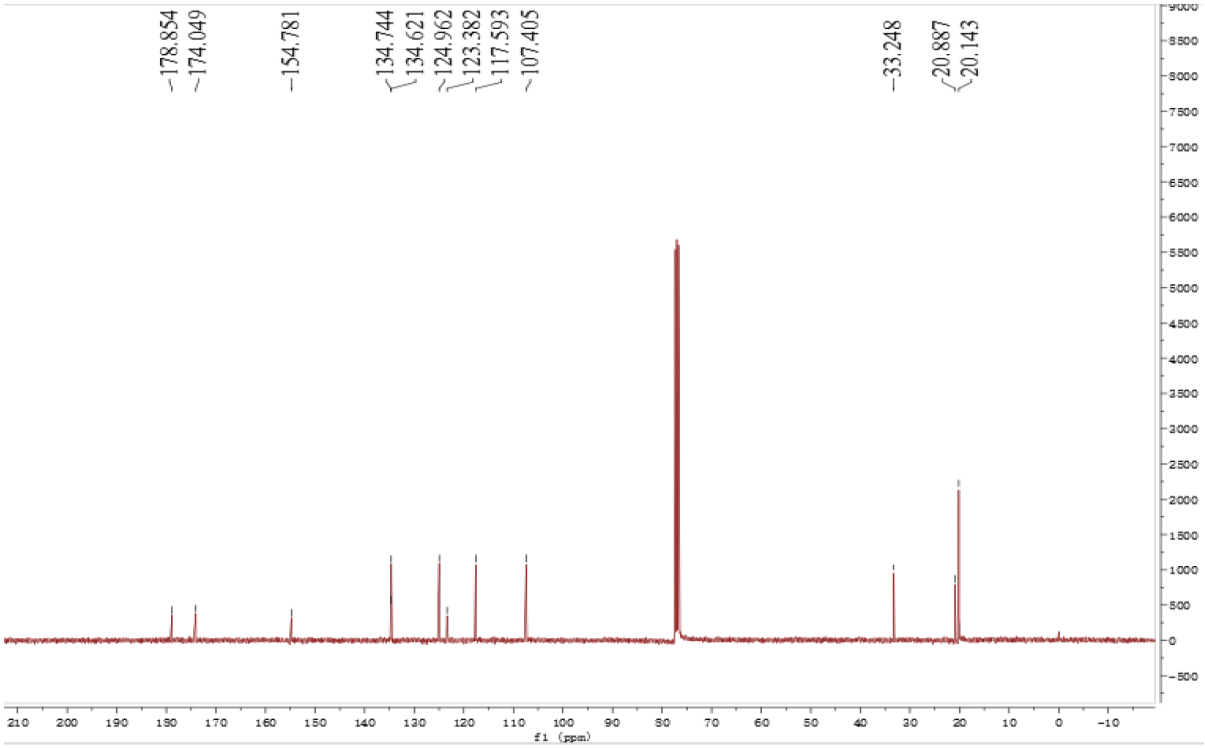

7.963
7.960
7.452
7.447
7.431
7.425
7.323
7.301
6.151
2.600
2.582
2.563
2.433
1.813
1.794
1.775
1.757
1.738
1.716
1.033
1.015
0.996
1.00
1.07
1.05
1.00
2.18
3.21
2.37
3.18
f1 (ppm)

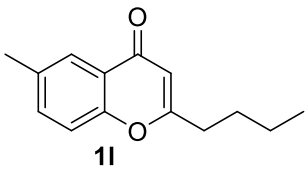

178.536
169.421
154.798
134.780
134.599
124.992
123.365
117.584
109.730
36.221
20.887
20.207
13.531
f1 (ppm)


O
O

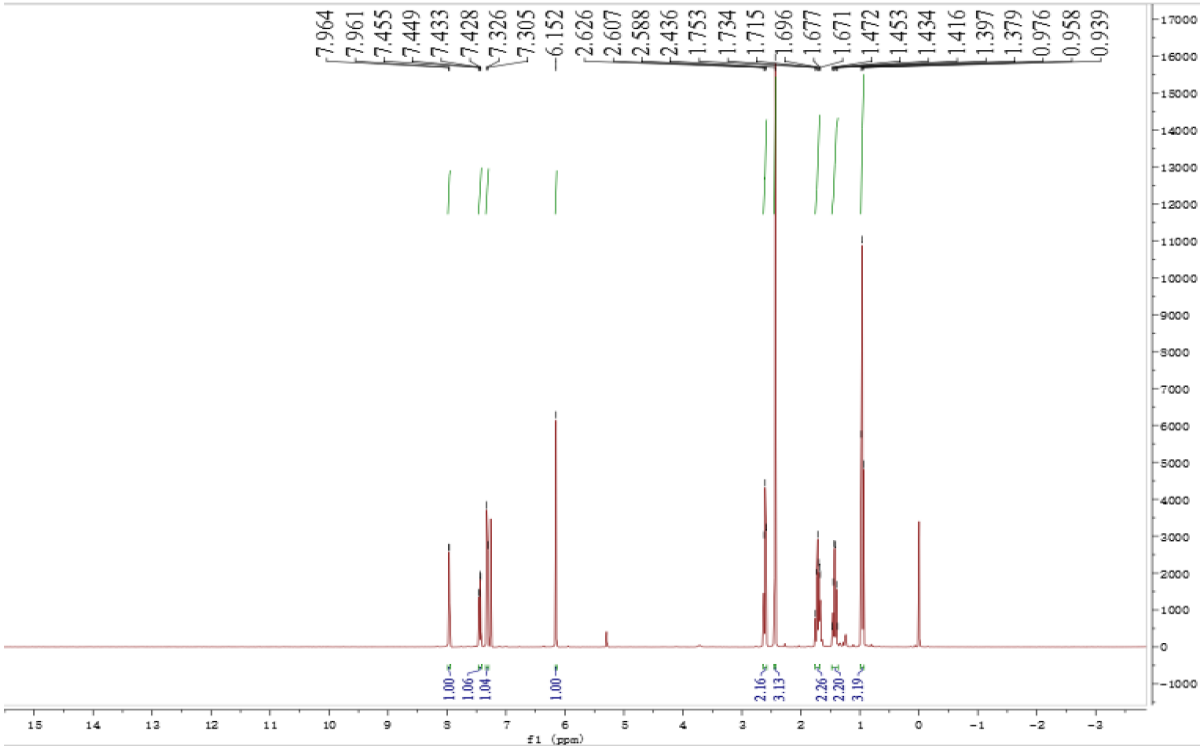
1k

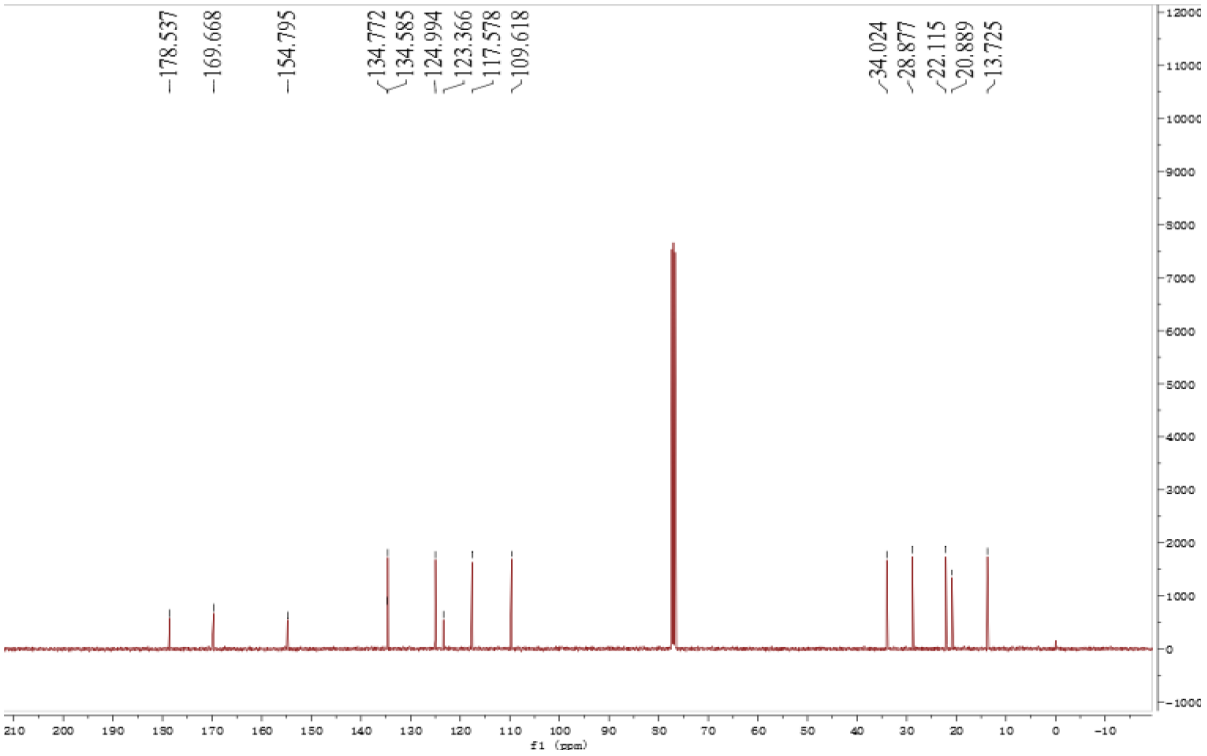

7.987
7.985
7.485
7.480
7.464
7.459
7.367
7.345
6.197
2.929
2.912
2.894
2.877
2.860
2.842
2.825
2.461
1.348
1.330
1.00
1.06
1.05
0.98
1.08
3.17
6.03
f1 (ppm)

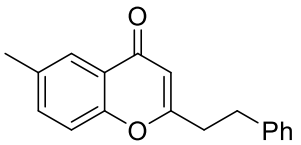

178.854
174.049
154.781
134.744
134.621
124.962
123.382
117.593
107.405
33.248
20.887
20.143
f1 (ppm)



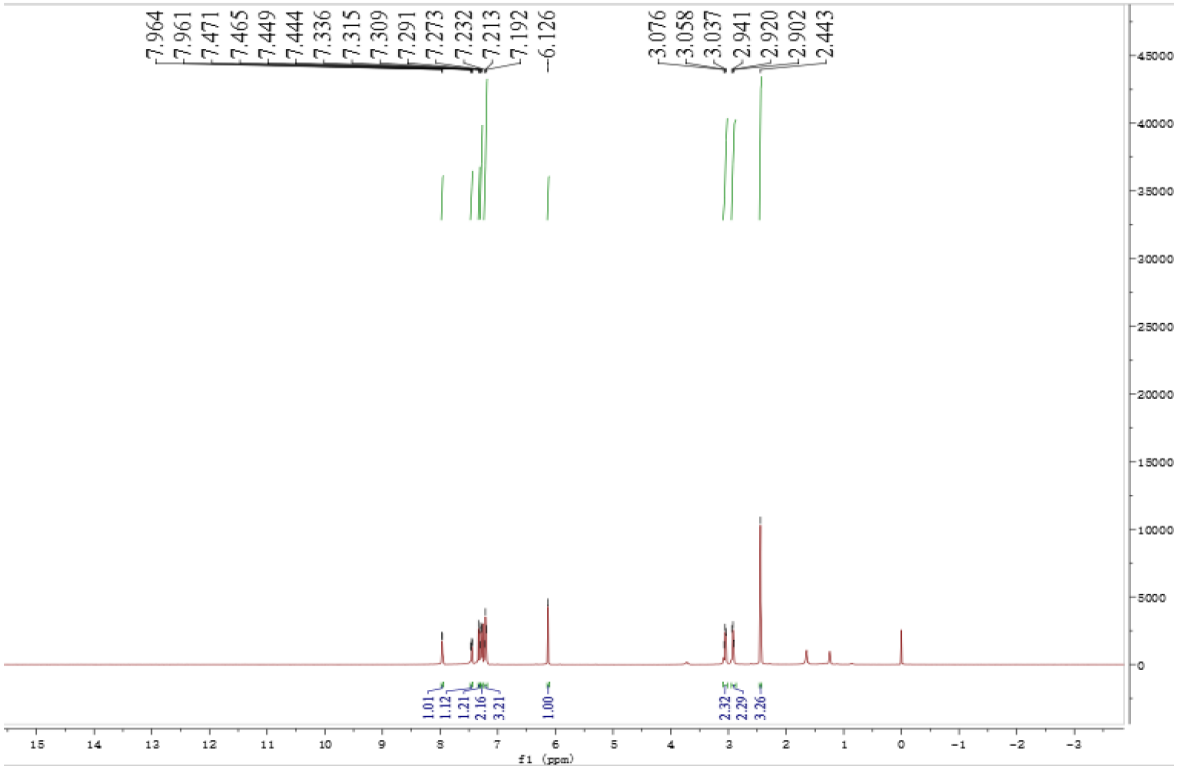
1l

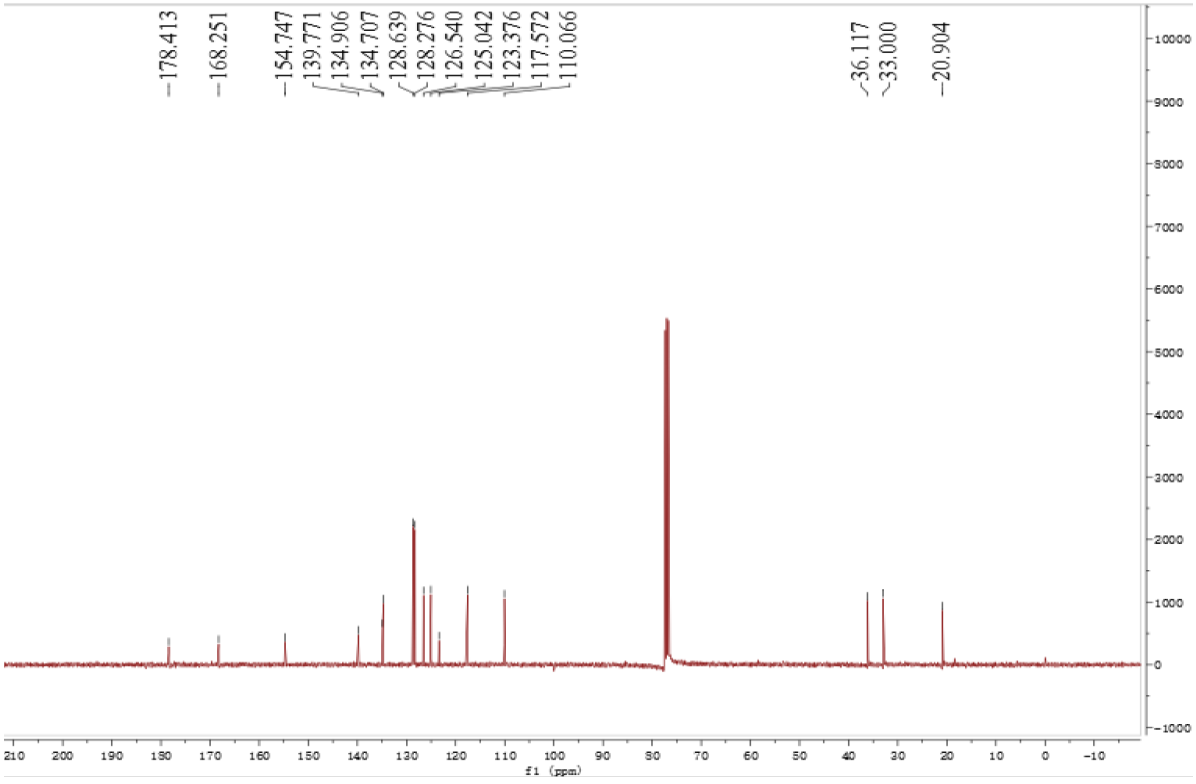

7.964
7.961
7.455
7.449
7.433
7.428
7.326
7.305
6.152
2.626
2.607
2.588
2.436
1.753
1.734
1.715
1.696
1.677
1.671
1.472
1.453
1.434
1.416
1.397
1.379
0.976
0.958
0.939
1.00
1.06
1.04
1.00
2.16
3.13
2.26
2.20
3.19
f1 (ppm)

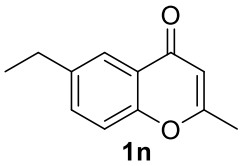

178.537
169.668
154.795
134.772
134.585
124.994
123.366
117.578
109.618
34.024
28.877
22.115
20.889
13.725
f1 (ppm)


O
O
Ph

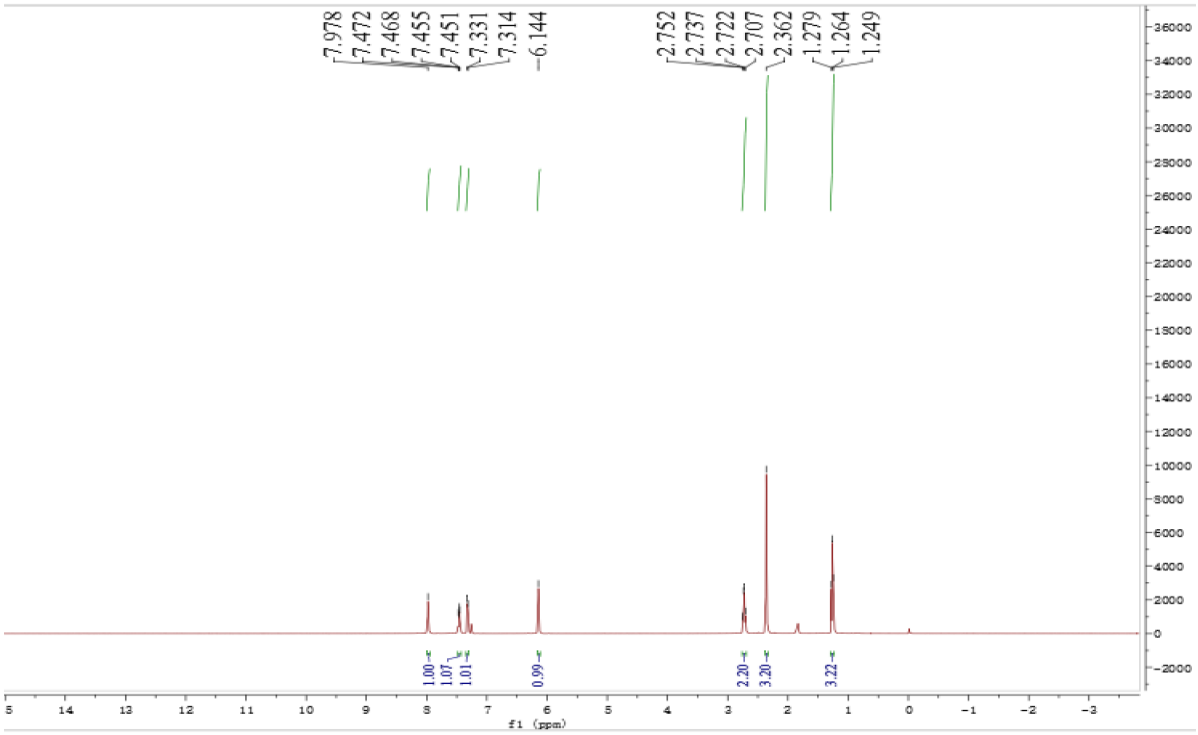
1m

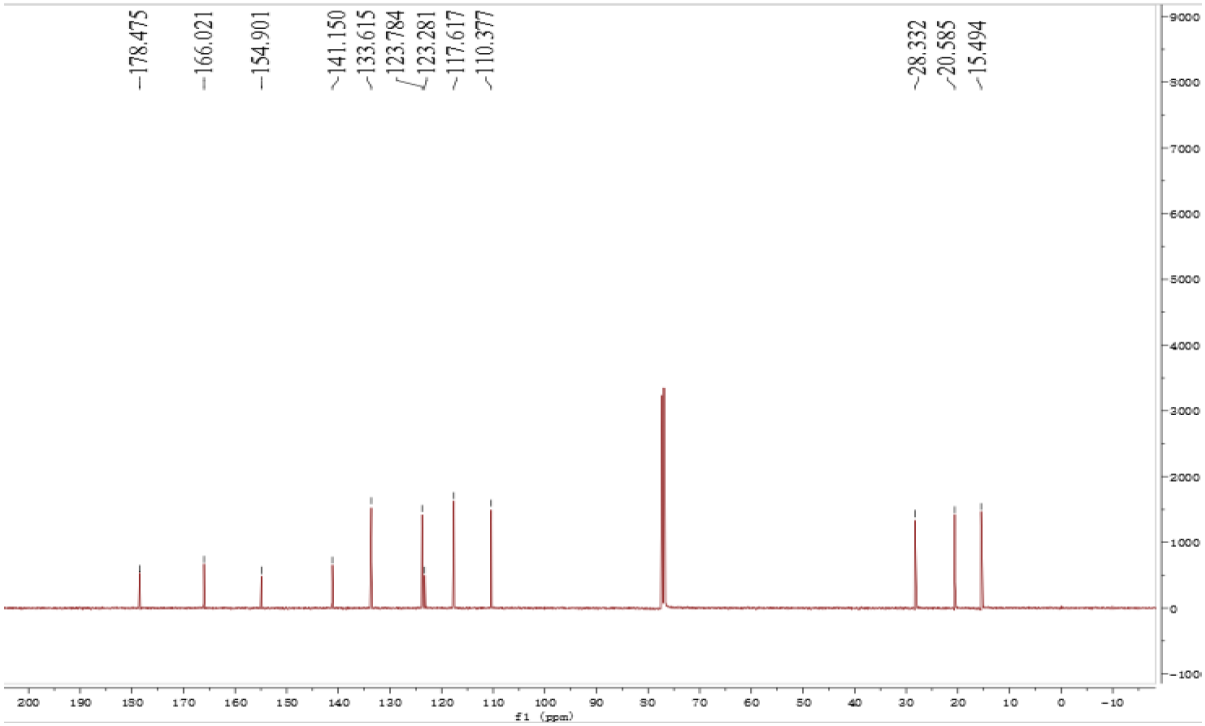

7.964
7.961
7.471
7.465
7.449
7.444
7.336
7.315
7.309
7.291
7.273
7.232
7.213
7.192
6.126
3.076
3.058
3.037
2.941
2.920
2.902
2.443
1.01
1.12
1.21
2.16
3.21
1.00
2.32
2.29
3.26
f1 (ppm)

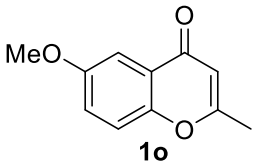

178.413
168.251
154.747
139.771
134.906
134.707
128.639
128.276
126.540
125.042
123.376
117.572
110.066
36.117
33.000
20.904
f1 (ppm)


O
O

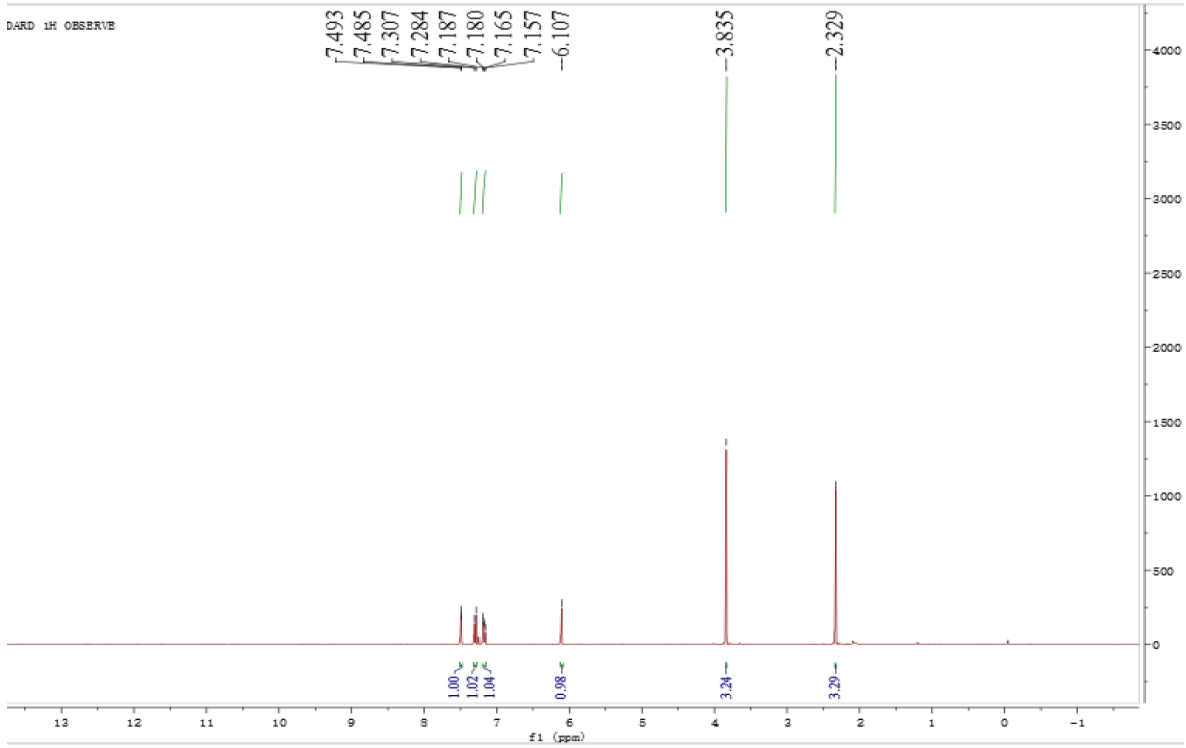
1n

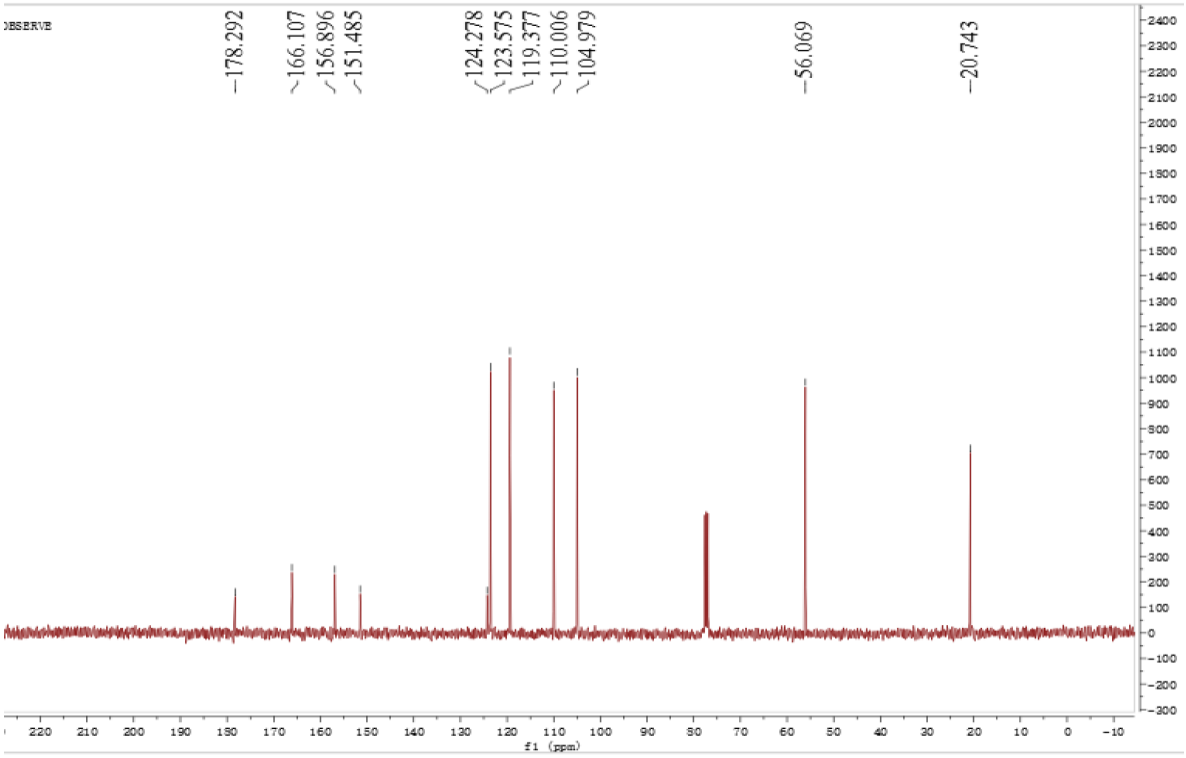

7.978
7.472
7.468
7.455
7.451
7.331
7.314
6.144
2.752
2.737
2.722
2.707
2.362
1.279
1.264
1.249
1.00
1.07
1.01
0.99
2.20
3.20
3.22
f1 (ppm)

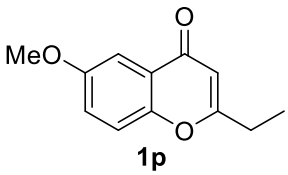

178.475
166.021
154.901
141.150
133.615
123.784
123.281
117.617
110.377
28.332
20.585
15.494
f1 (ppm)


MeO
O
O

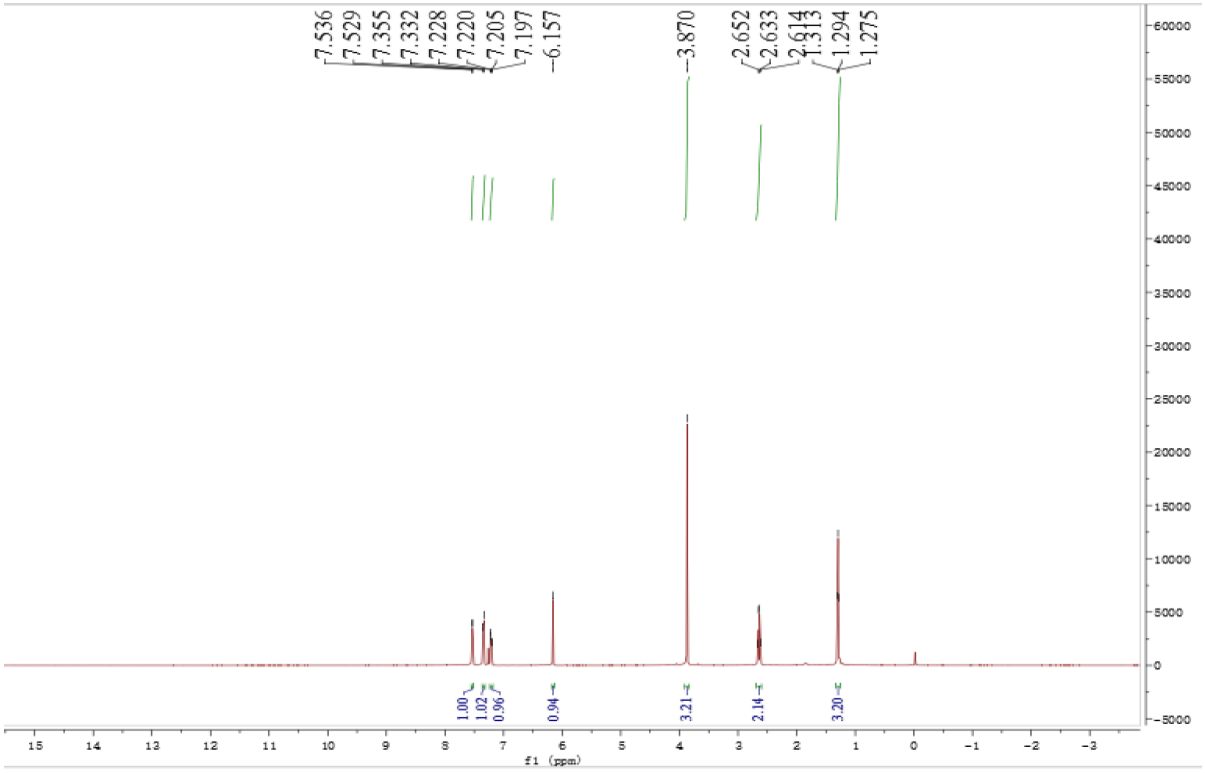
1o

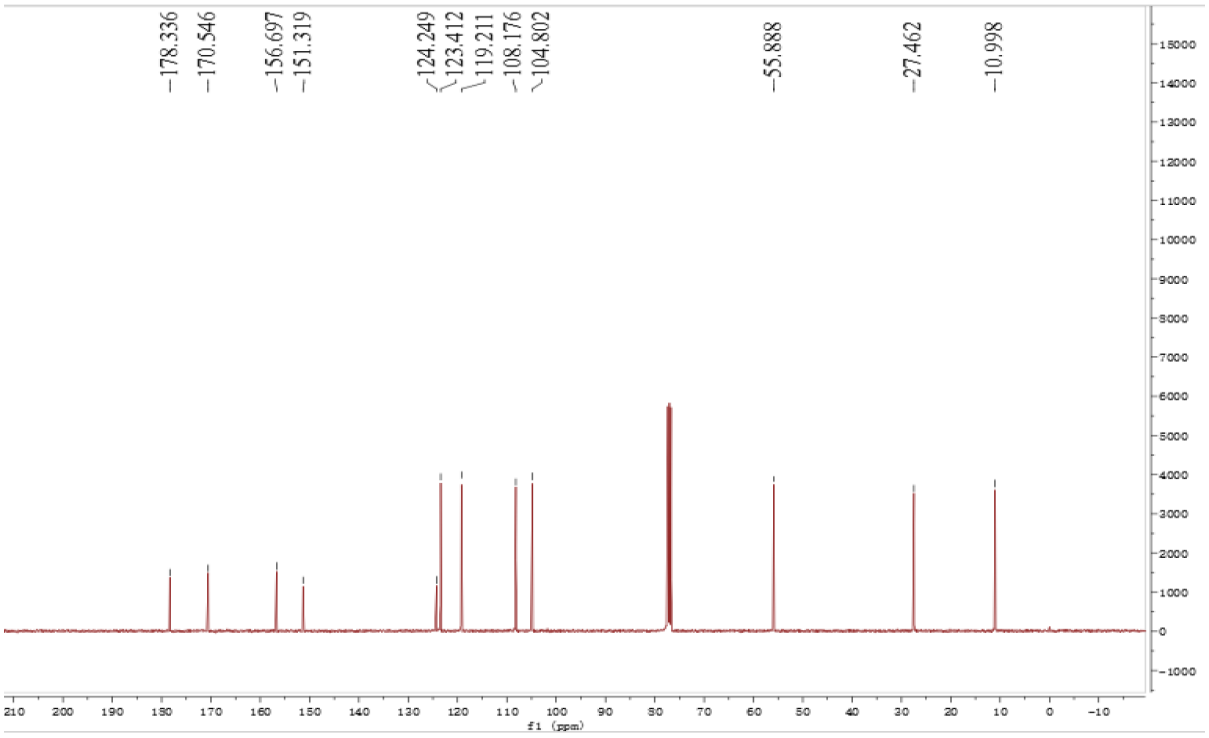

DARD 1H OBSERVE
7.493
7.485
7.307
7.284
7.187
7.180
7.165
7.157
6.107
3.835
2.329
1.00
1.02
1.04
0.98
3.24
3.29
f1 (ppm)

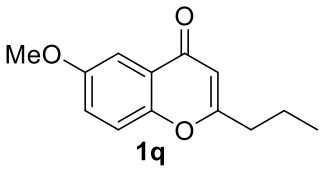

OBSERVE
178.292
166.107
156.896
151.485
124.278
123.575
119.377
110.006
104.979
56.069
20.743
f1 (ppm)


MeO
O
O

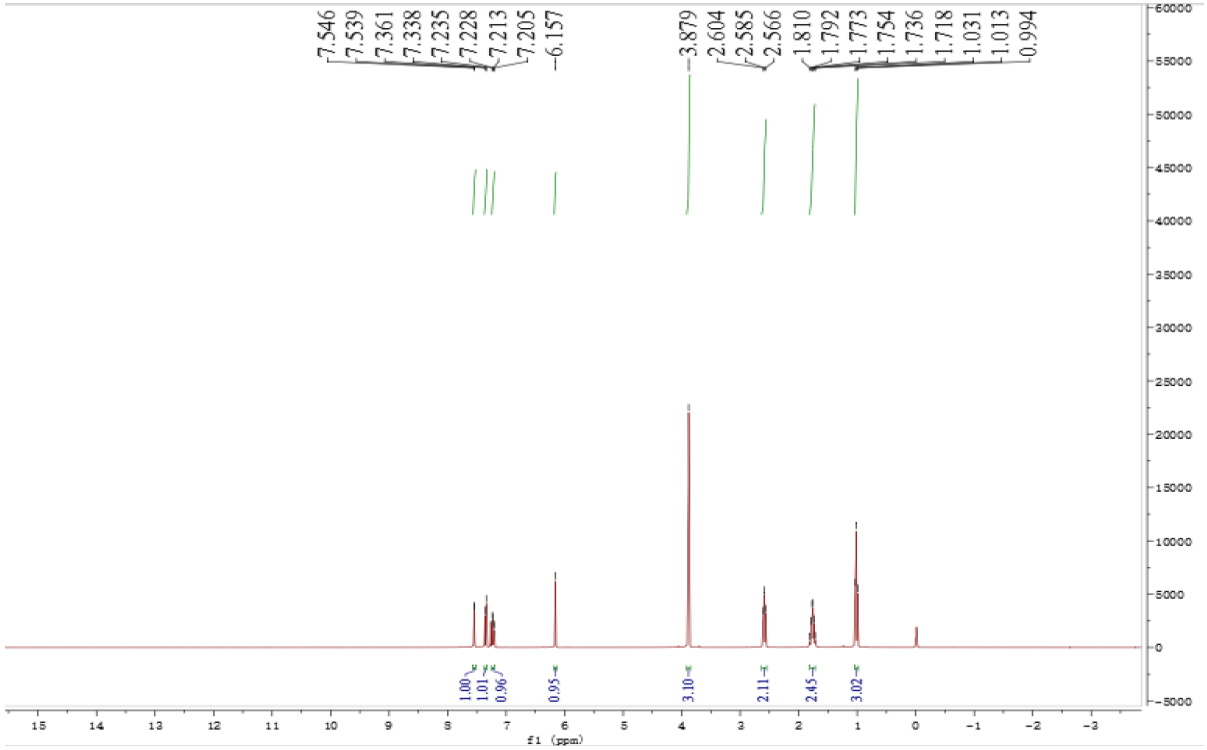
1p

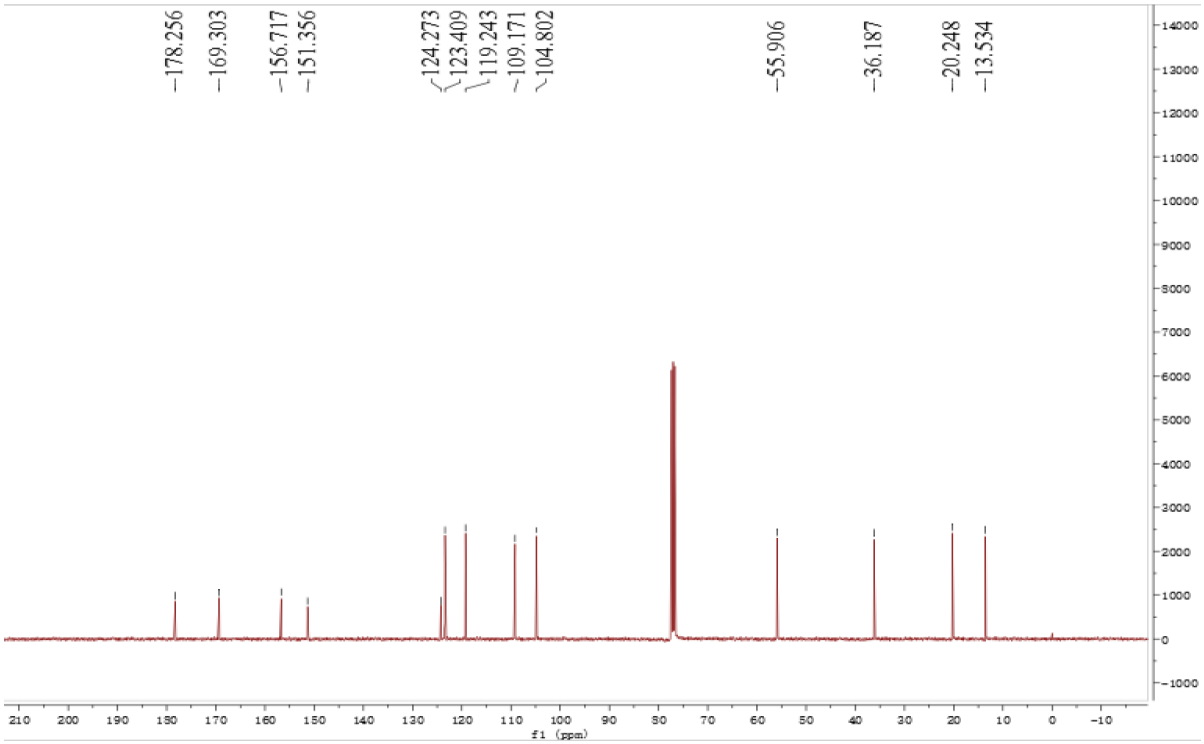

7.536
7.529
7.355
7.332
7.228
7.220
7.205
7.197
6.157
3.870
2.652
2.633
2.614
1.313
1.294
1.275
1.00
1.02
0.96
0.94
3.21
2.14
3.20
f1 (ppm)

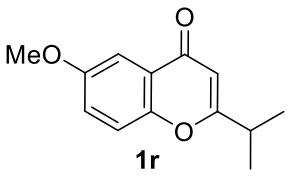

178.336
170.546
156.697
151.319
124.249
123.412
119.211
108.176
104.802
55.888
27.462
10.998
f1 (ppm)


MeO
O
O

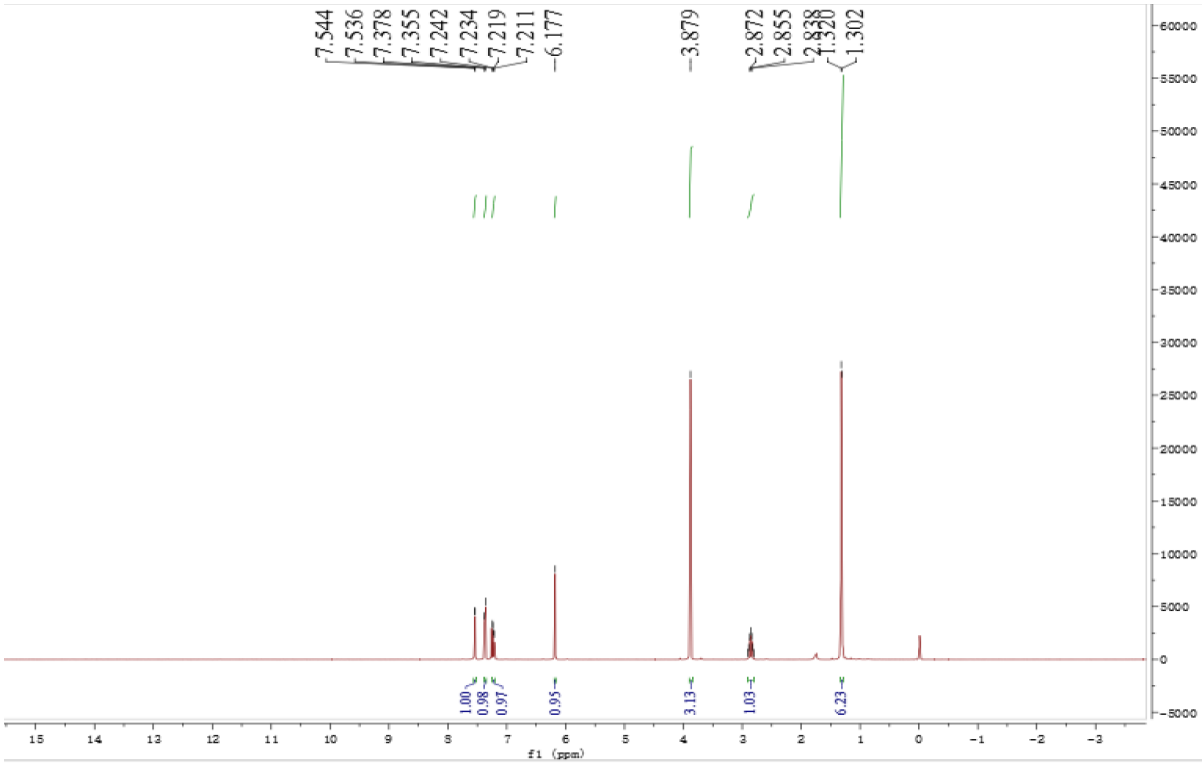
1q

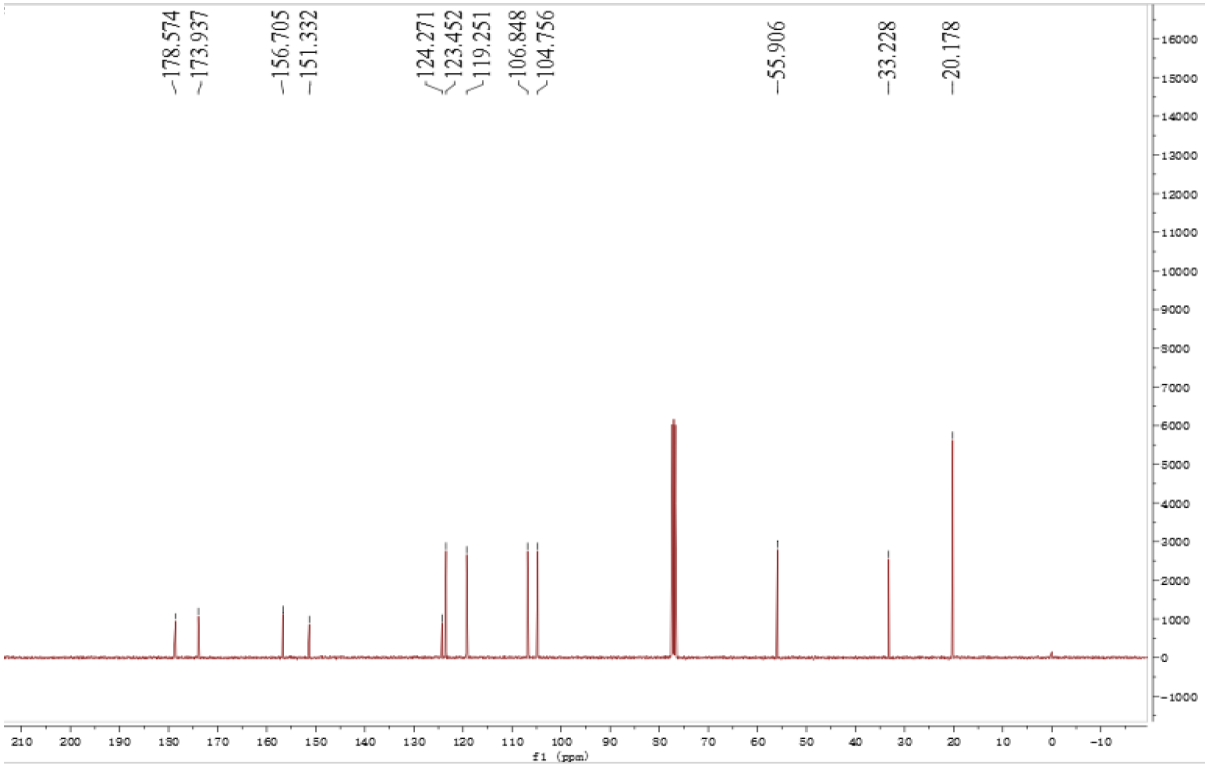

7.546
7.539
7.361
7.338
7.235
7.228
7.213
7.205
6.157
3.879
2.604
2.585
2.566
1.810
1.792
1.773
1.754
1.736
1.718
1.031
1.013
0.994
1.00
1.01
0.96
0.95
3.10
2.11
2.45
3.02
f1 (ppm)

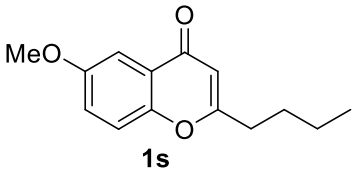

178.256
169.303
156.717
151.356
124.273
123.409
119.243
109.171
104.802
55.906
36.187
20.248
13.534
f1 (ppm)


MeO
O
O

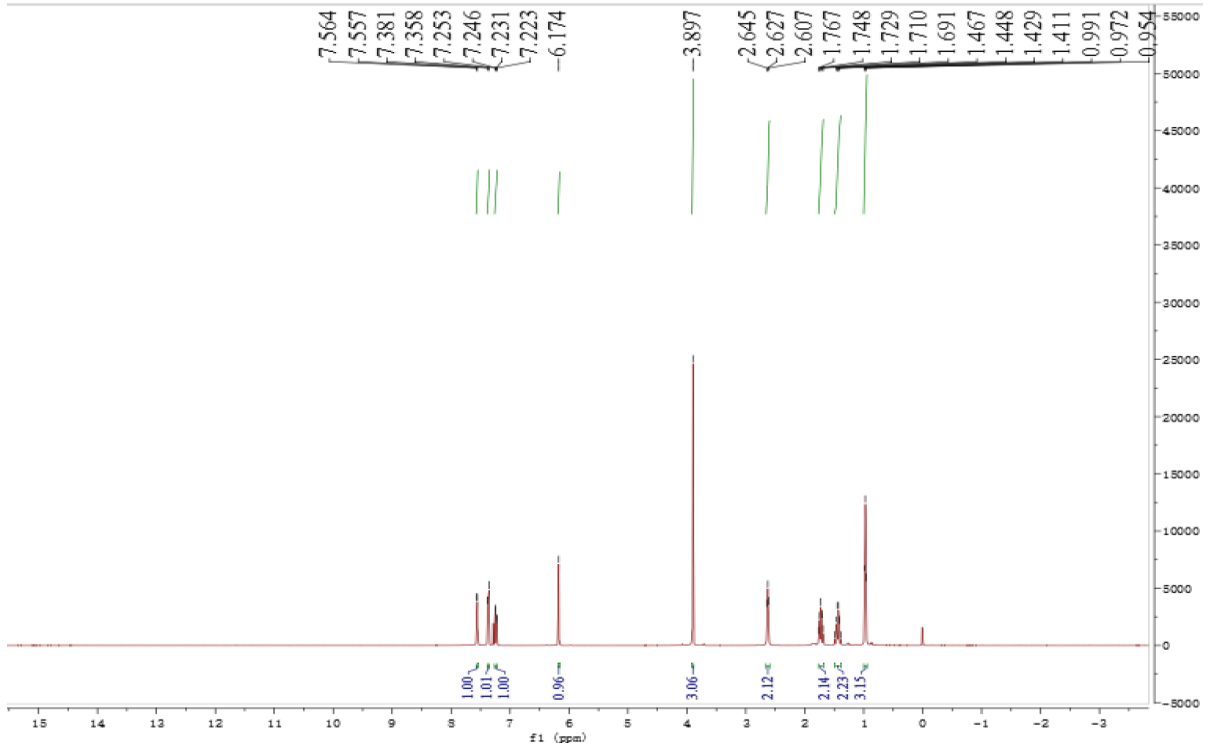
1r

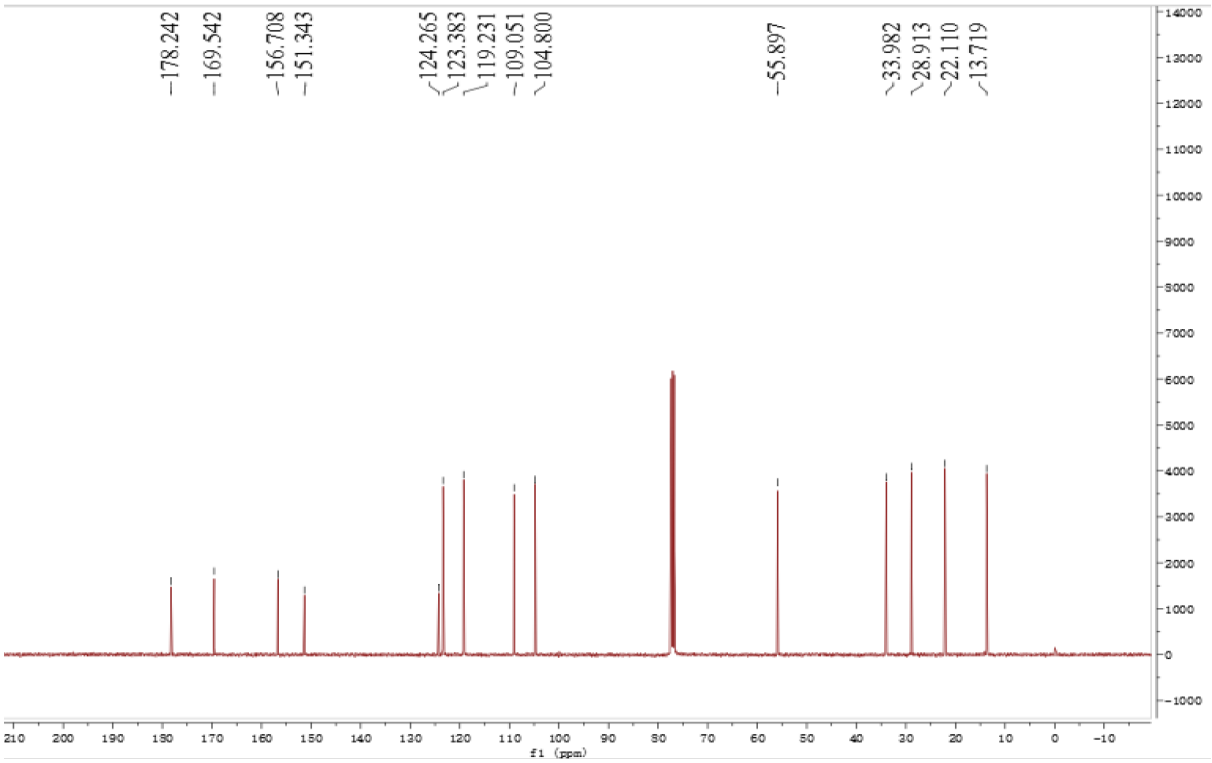

7.544
7.536
7.378
7.355
7.242
7.234
7.219
7.211
6.177
3.879
2.872
2.855
2.838
1.320
1.302
1.00
0.98
0.97
0.95
3.13
1.03
6.23
f1 (ppm)

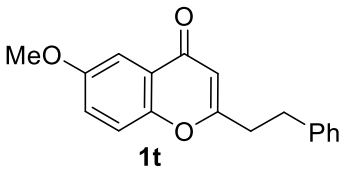

178.574
173.937
156.705
151.332
124.271
123.452
119.251
106.848
104.756
55.906
33.228
20.178
f1 (ppm)


MeO
O
O

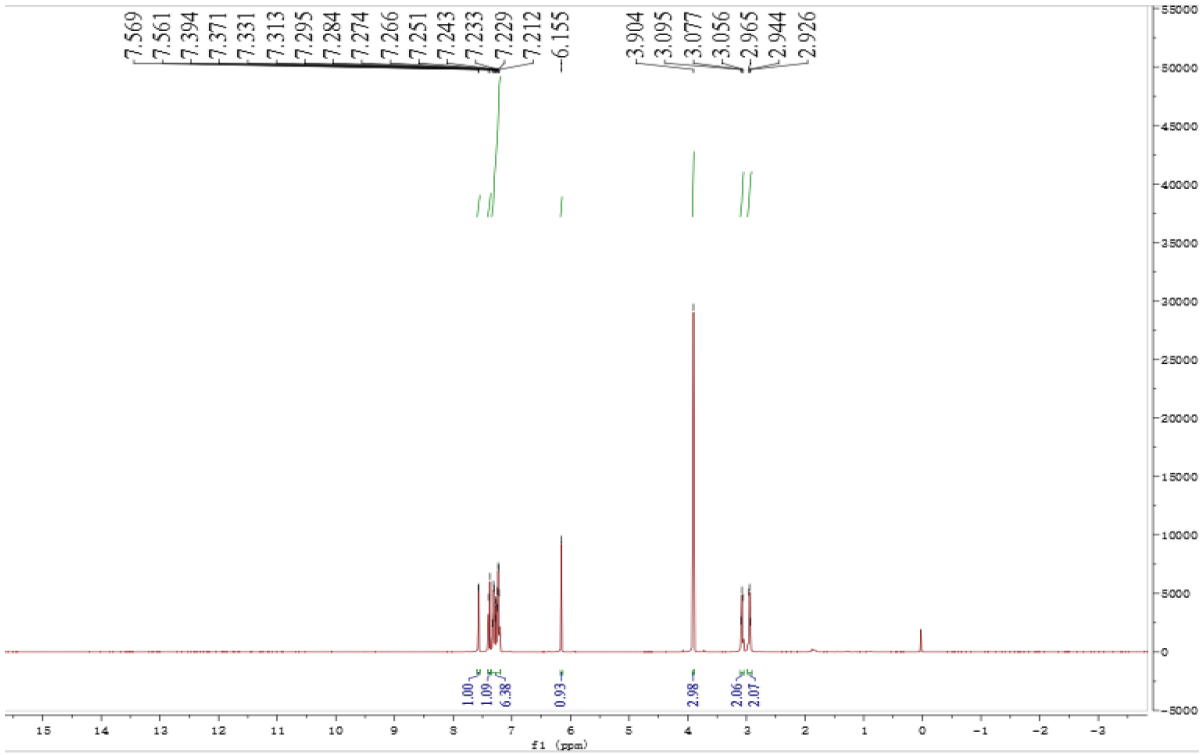
1s

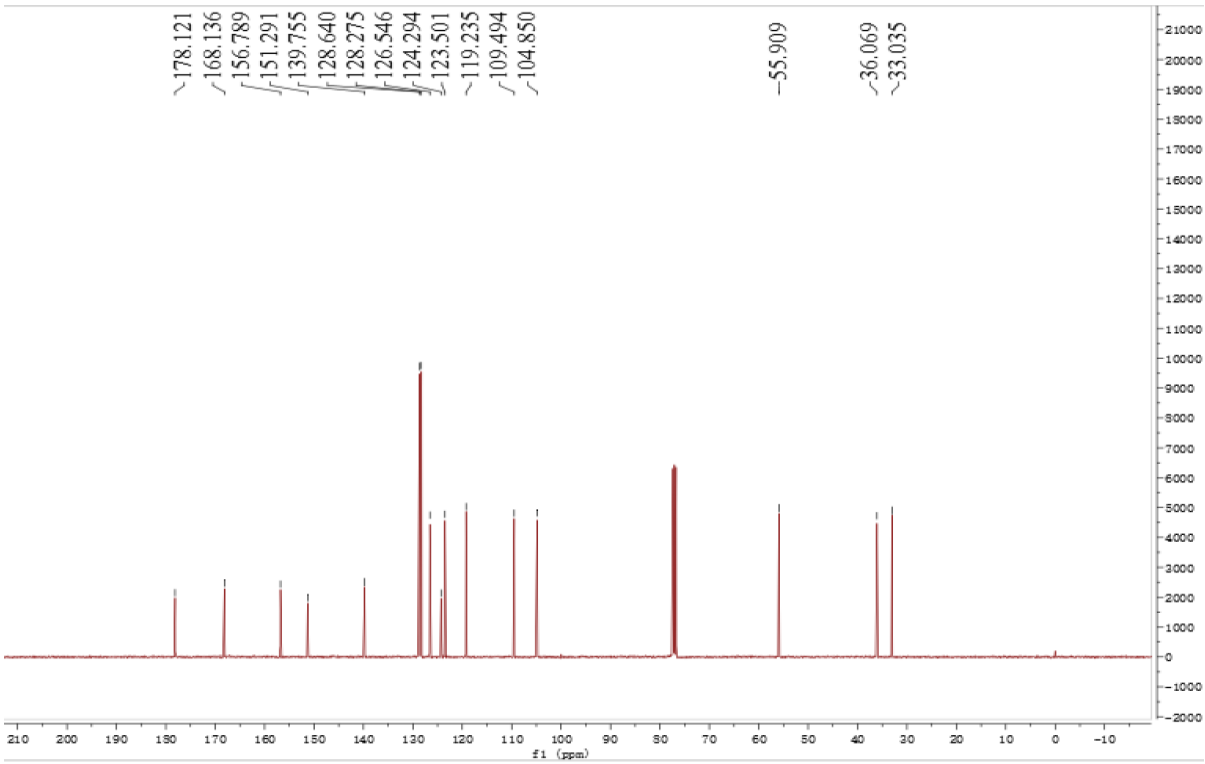

7.564
7.557
7.381
7.358
7.253
7.246
7.231
7.223
6.174
3.897
2.645
2.627
2.607
1.767
1.748
1.729
1.710
1.691
1.467
1.448
1.429
1.411
0.991
0.972
0.954
1.00
1.01
1.00
0.96
3.06
2.12
2.14
2.23
3.15
f1 (ppm)

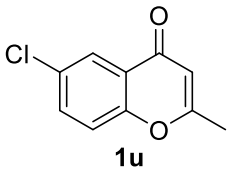

178.242
169.542
156.708
151.343
124.265
123.383
119.231
109.051
104.800
55.897
33.982
28.913
22.110
13.719
f1 (ppm)


O
MeO
O
Ph

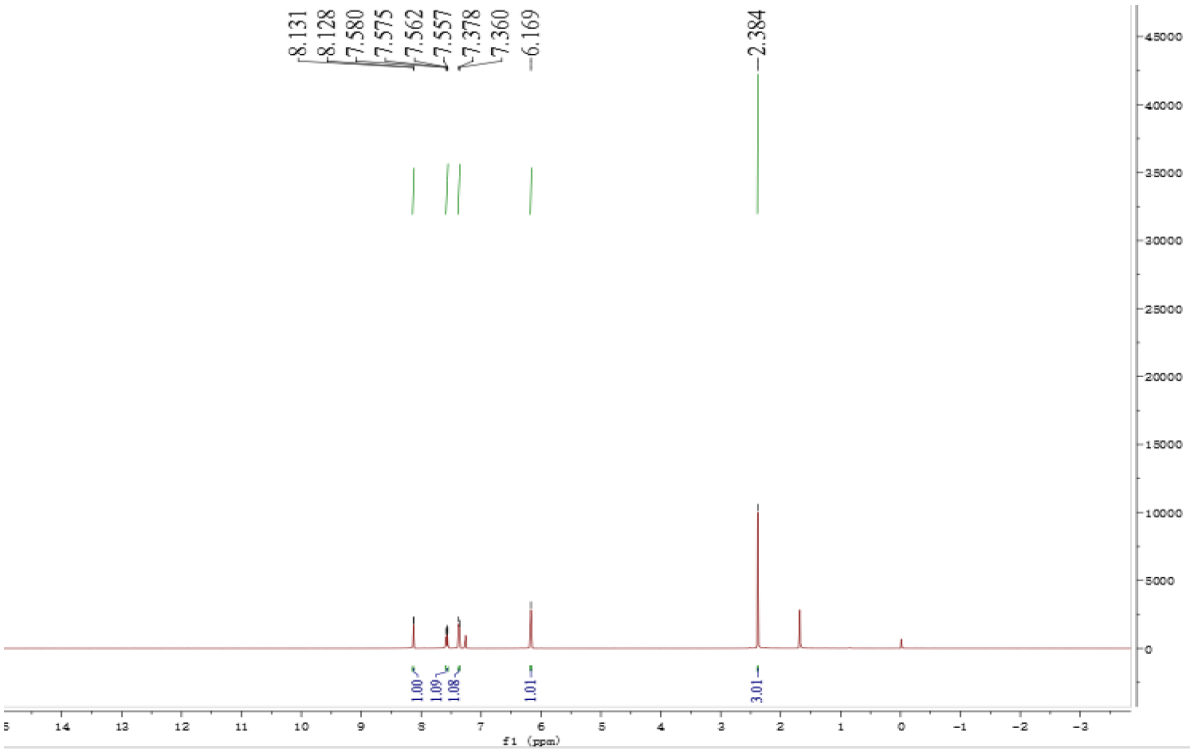
1t

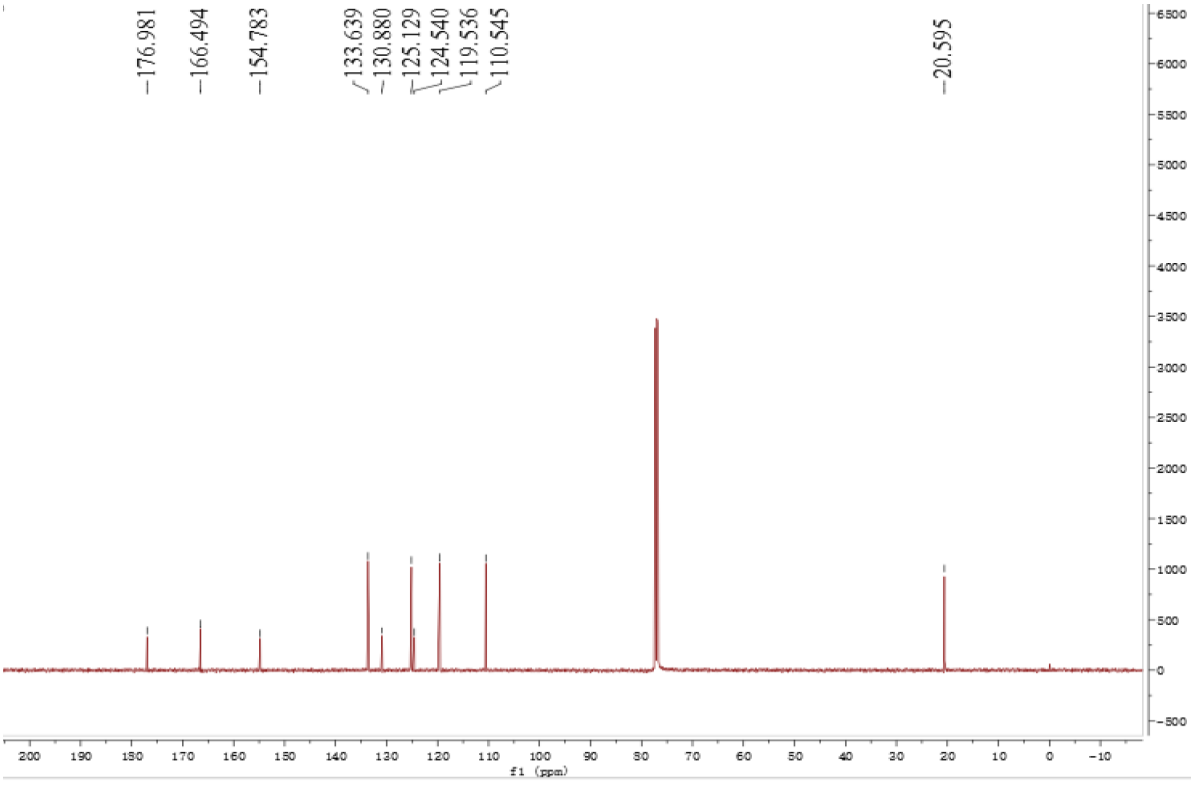

7.569
7.561
7.394
7.371
7.331
7.313
7.295
7.284
7.274
7.266
7.251
7.243
7.233
7.229
7.212
6.155
3.904
3.095
3.077
3.056
2.965
2.944
2.926
1.00
1.09
6.38
0.93
2.98
2.06
2.07
f1 (ppm)

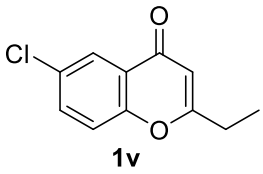

178.121
168.136
156.789
151.291
139.755
128.640
128.275
126.546
124.294
123.501
119.235
109.494
104.850
55.909
36.069
33.035
f1 (ppm)


O
Cl
O

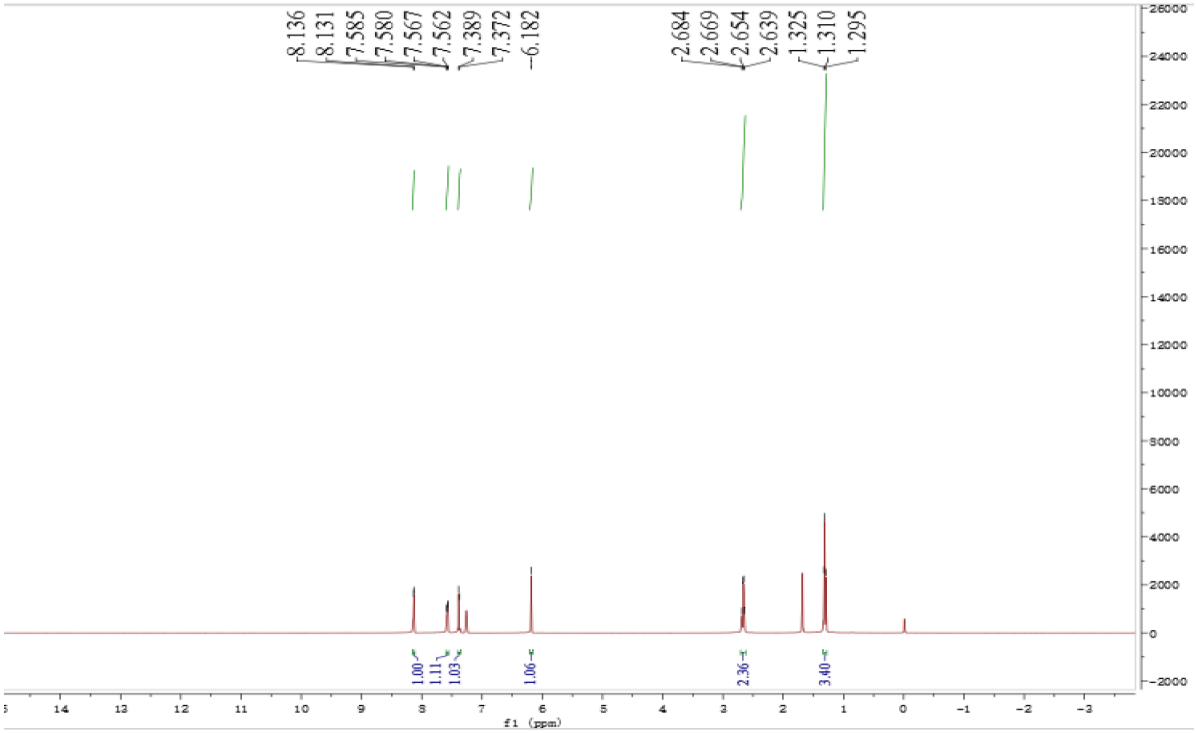
1u

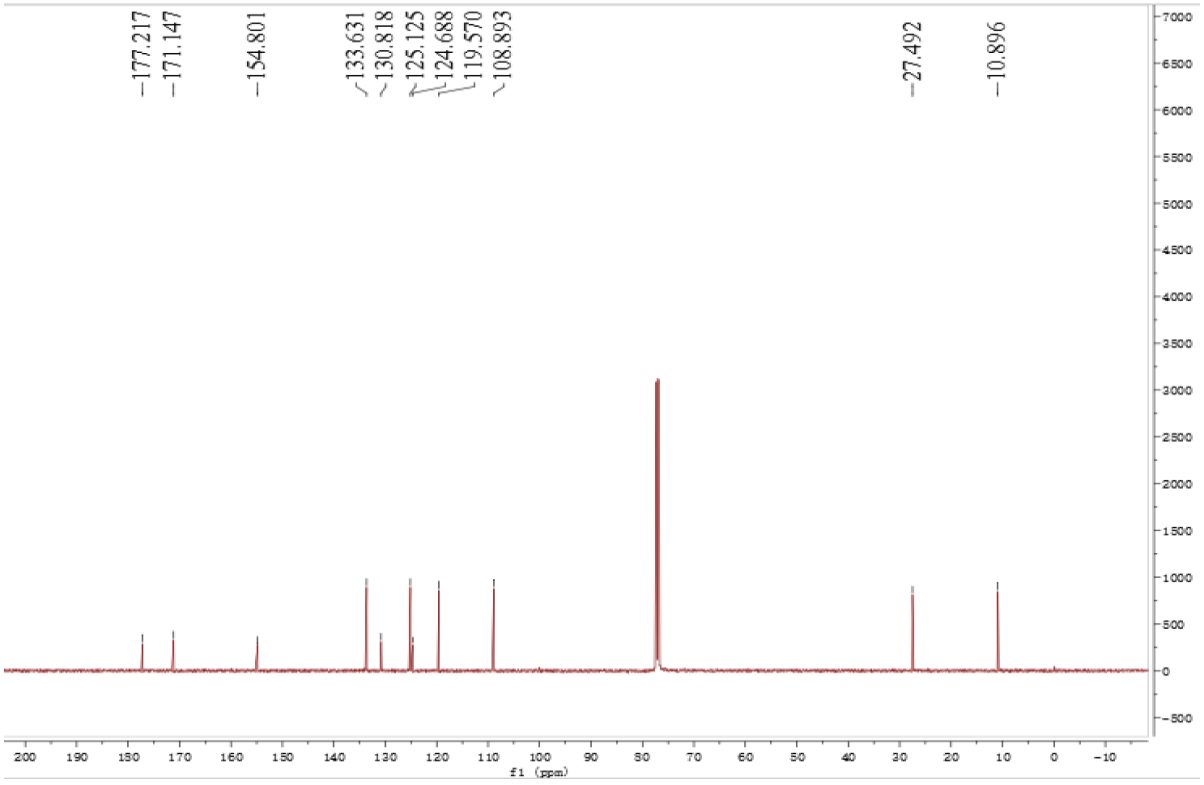

8.131
8.128
7.580
7.575
7.562
7.557
7.378
7.360
6.169
2.384
1.00
1.09
1.08
1.01
3.01
f1 (ppm)

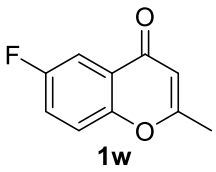

176.981
166.494
154.783
133.639
130.880
125.129
124.540
119.536
110.545
20.595
f1 (ppm)


O
Cl
O

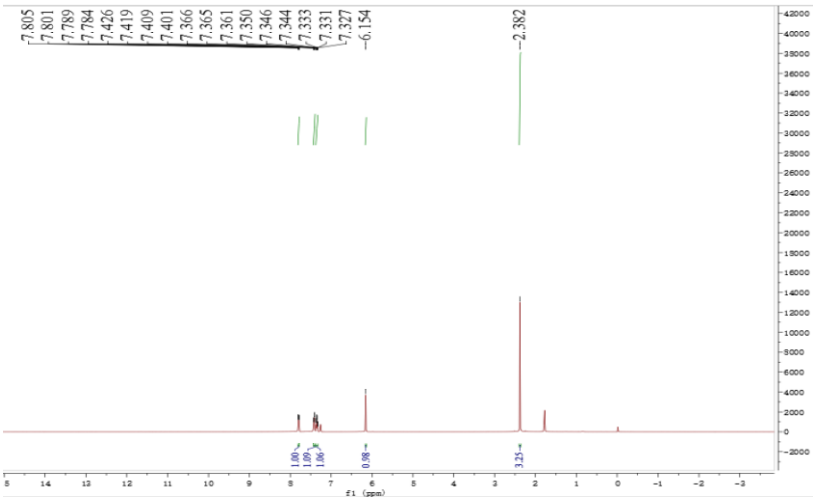
1v

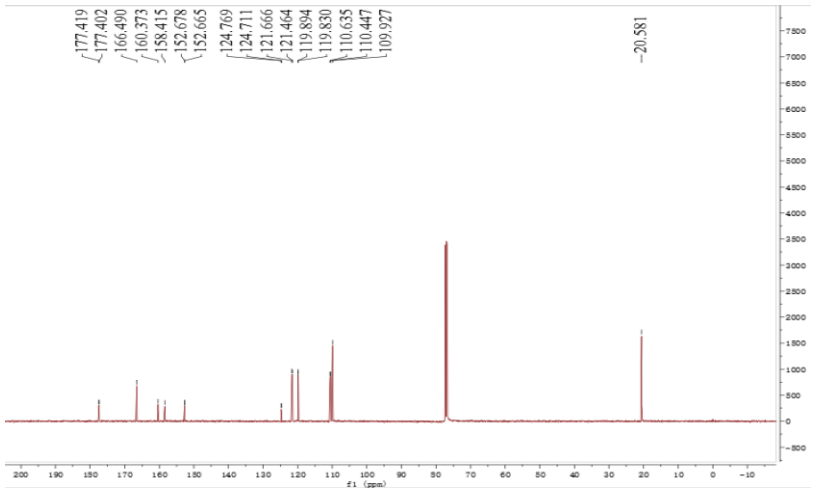

8.136
8.131
7.585
7.580
7.567
7.562
7.389
7.372
6.182
2.684
2.669
2.654
2.639
1.325
1.310
1.295
1.00
1.11
1.03
1.06
2.36
3.40
f1 (ppm)

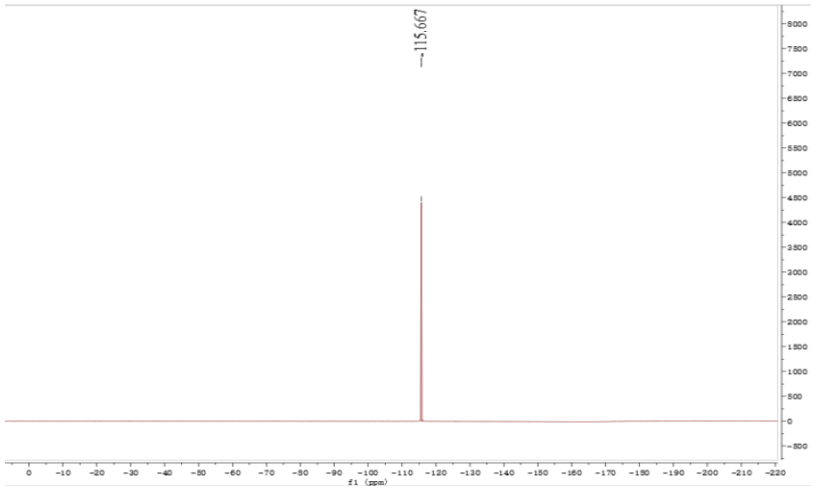

177.217
171.147
154.801
133.631
130.818
125.125
124.688
119.570
108.893
27.492
10.896
f1 (ppm)

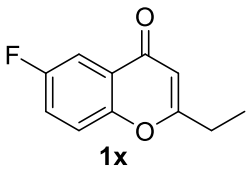

O
F
O

1w

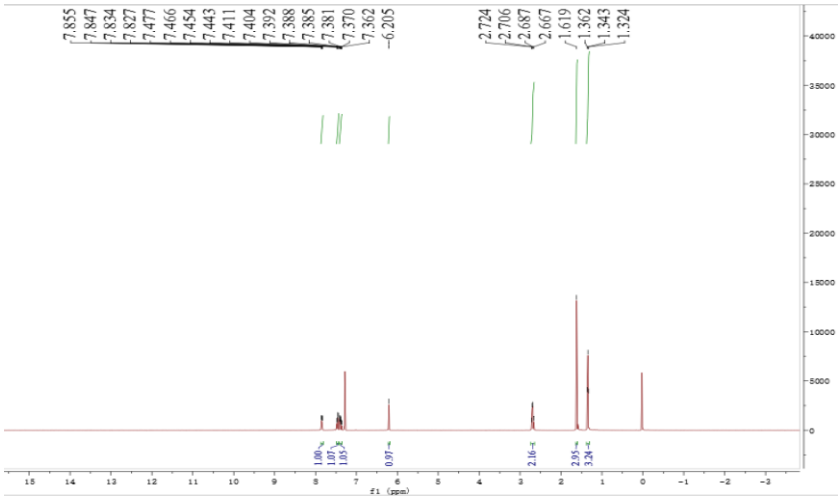

7.805
7.801
7.789
7.784
7.426
7.419
7.409
7.401
7.366
7.365
7.361
7.350
7.346
7.344
7.333
7.331
7.327
6.154
2.382
f1 (ppm)

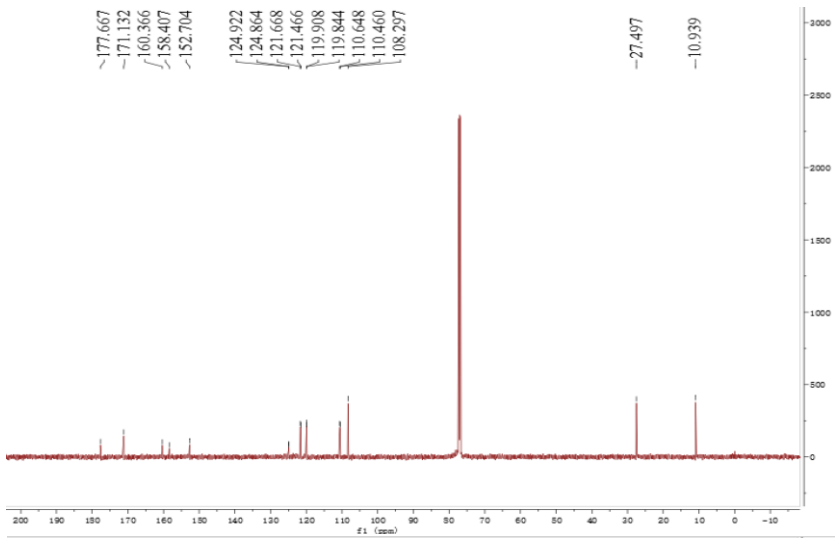

177.419
177.402
166.490
160.373
158.415
152.678
152.665
124.769
124.711
121.666
121.464
119.894
119.830
110.635
110.447
109.927
20.581
f1 (ppm)

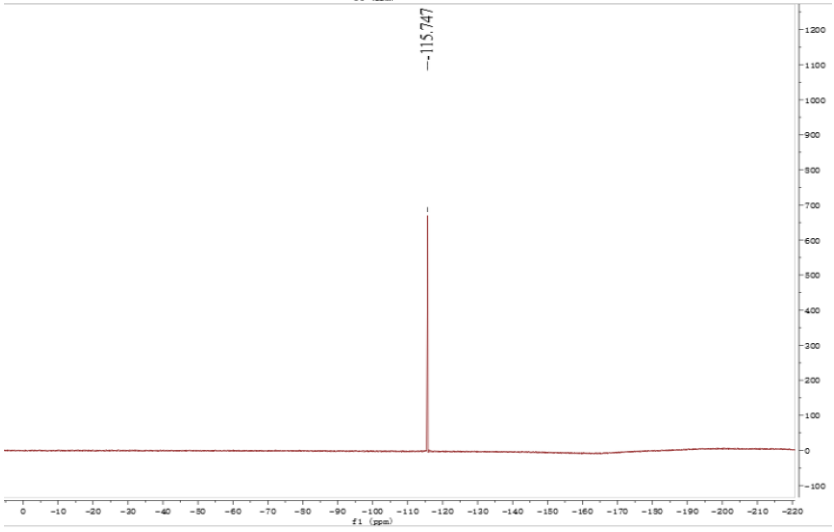

115.667
f1 (ppm)

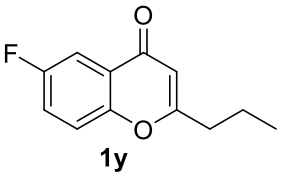

O
F
O

1x

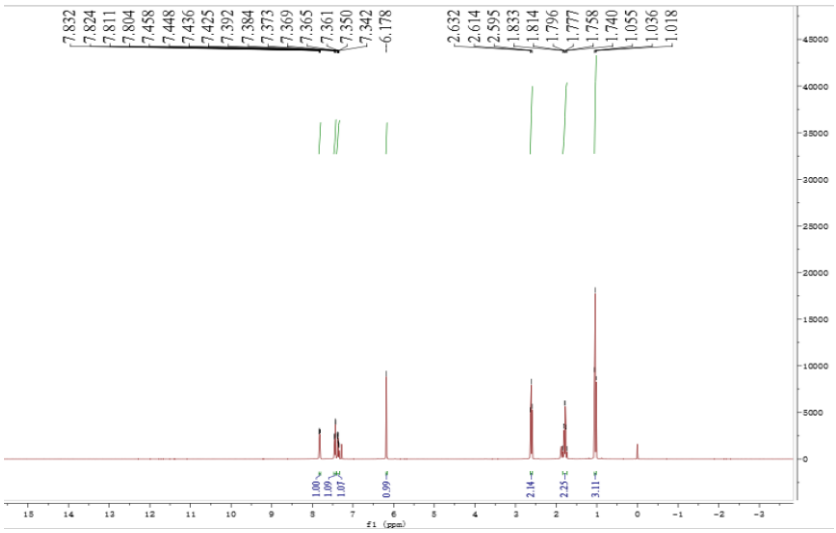

7.855
7.847
7.834
7.827
7.477
7.466
7.454
7.443
7.411
7.404
7.392
7.388
7.385
7.381
7.370
7.362
6.205
2.724
2.706
2.687
2.667
1.619
1.362
1.343
1.324
f1 (ppm)

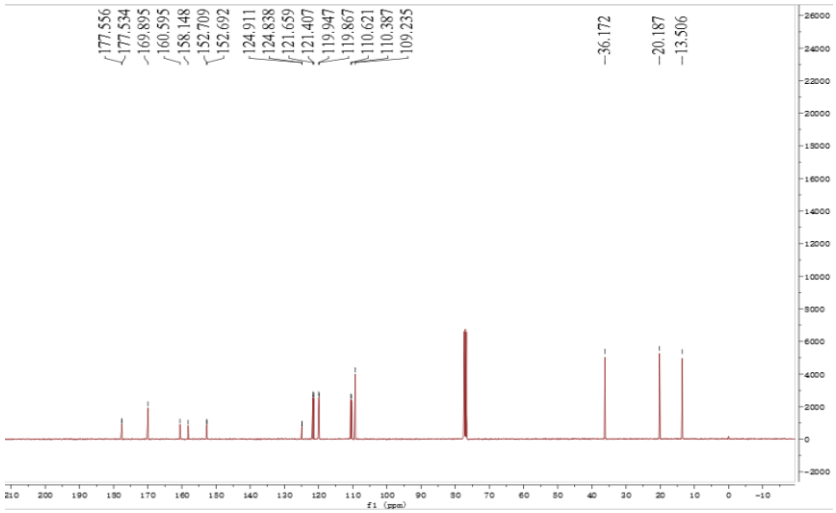

177.667
171.132
160.366
158.407
152.704
124.922
124.864
121.668
121.466
119.908
119.844
110.648
110.460
108.297
27.497
10.939
f1 (ppm)

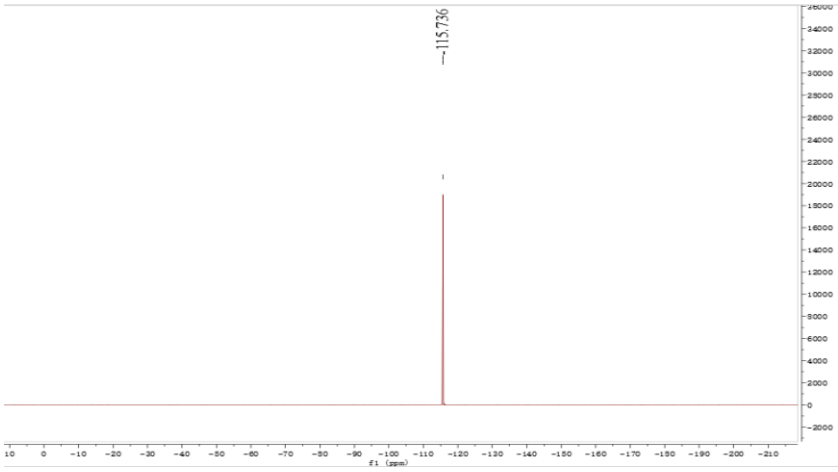

115.747
f1 (ppm)

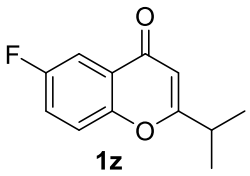

O
F
O

1y

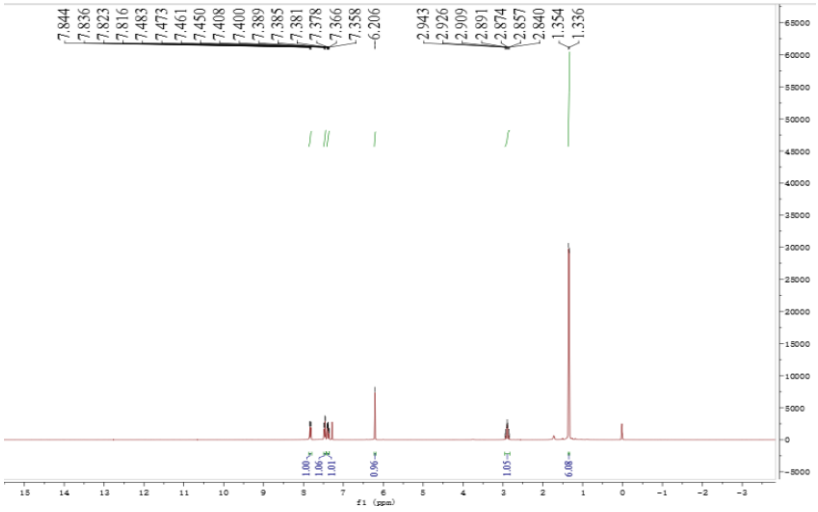

7.832
7.824
7.811
7.804
7.458
7.448
7.436
7.425
7.392
7.384
7.373
7.369
7.365
7.361
7.350
7.342
6.178
2.632
2.614
2.595
1.833
1.814
1.796
1.777
1.758
1.740
1.055
1.036
1.018
1.00
1.09
1.07
0.99
2.14
2.23
3.11
f1 (ppm)

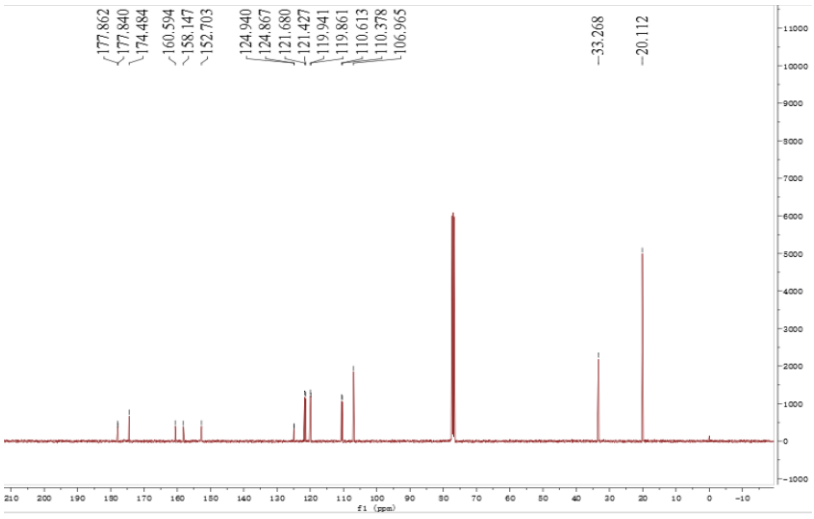

177.556
177.534
169.895
160.595
158.148
152.709
152.692
124.911
124.838
121.659
121.407
119.947
119.867
110.621
110.387
109.235
36.172
20.187
13.506
f1 (ppm)

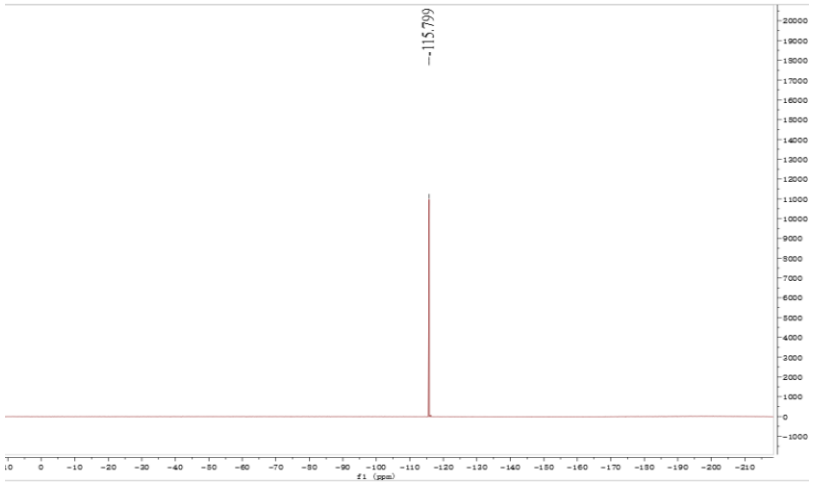

115.736
f1 (ppm)

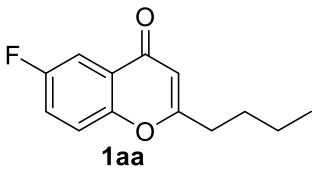

O
F
O

1z

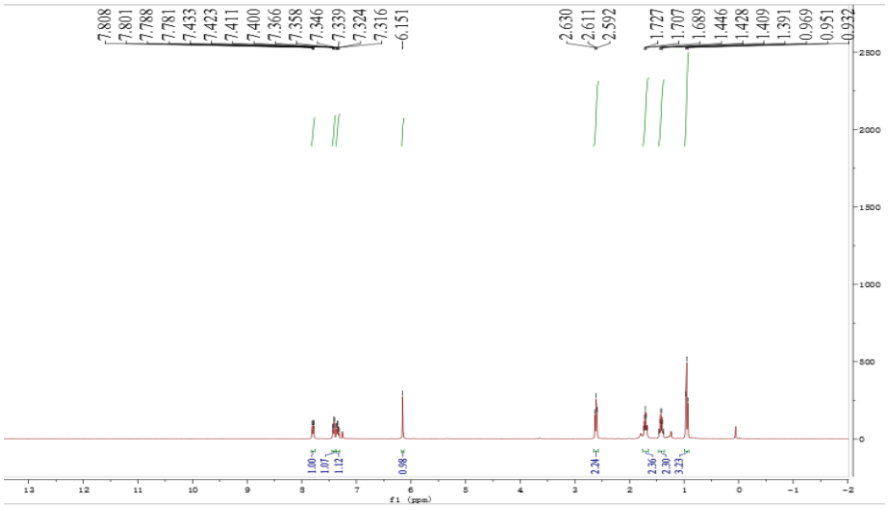

7.844
7.836
7.823
7.816
7.483
7.473
7.461
7.450
7.408
7.400
7.389
7.385
7.381
7.378
7.366
7.358
6.206
2.943
2.926
2.909
2.891
2.874
2.857
2.840
1.354
1.336
1.00
1.06
1.01
0.96
1.05
6.08
f1 (ppm)

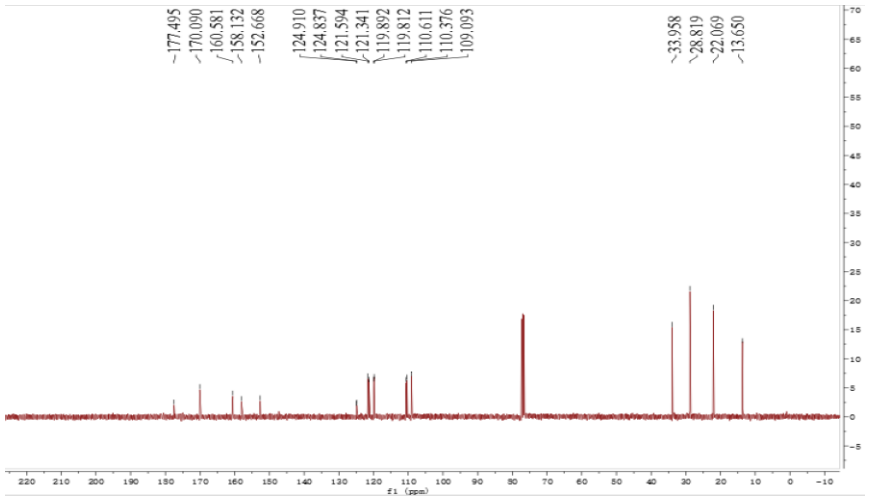

177.862
177.840
174.484
160.594
158.147
152.703
124.940
124.867
121.680
121.427
119.941
119.861
110.613
110.378
106.965
33.268
20.112
f1 (ppm)

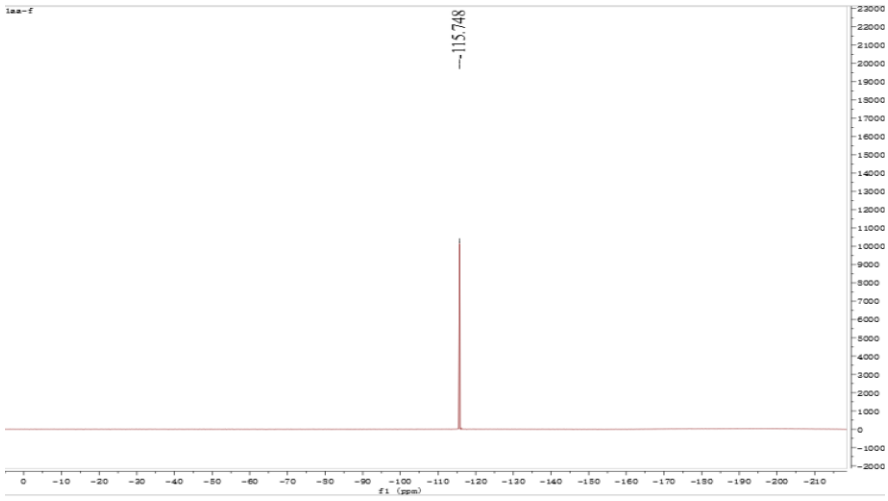

115.799
f1 (ppm)

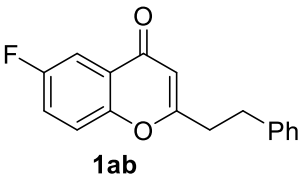

O
F
O

1aa

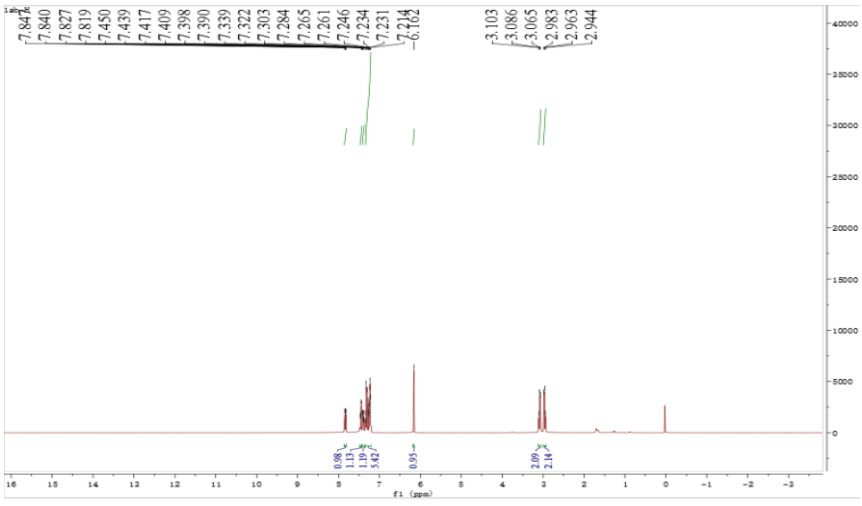

7.808
7.801
7.788
7.781
7.433
7.423
7.411
7.400
7.366
7.358
7.346
7.339
7.324
7.316
6.151
2.630
2.611
2.592
1.727
1.707
1.689
1.446
1.428
1.409
1.391
0.969
0.951
0.932
f1 (ppm)

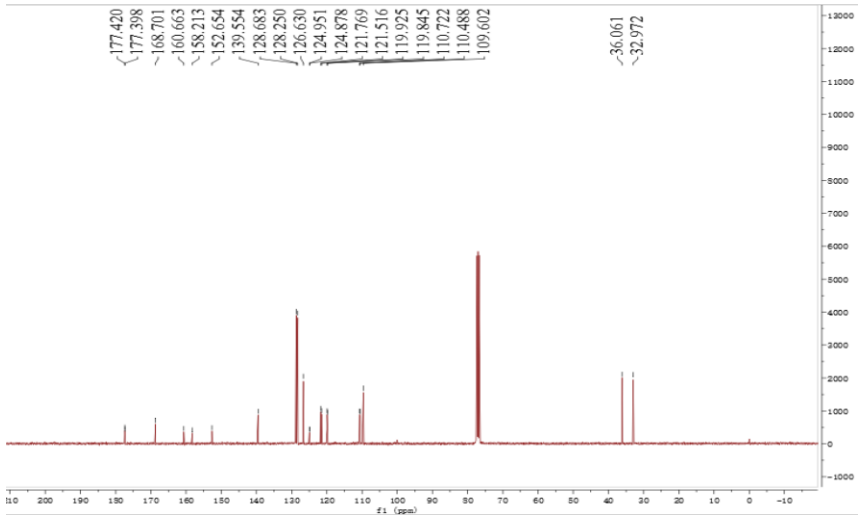

177.495
170.090
160.581
158.132
152.668
124.910
124.837
121.594
121.341
119.892
119.812
110.611
110.376
109.093
33.958
28.819
22.069
13.650
f1 (ppm)

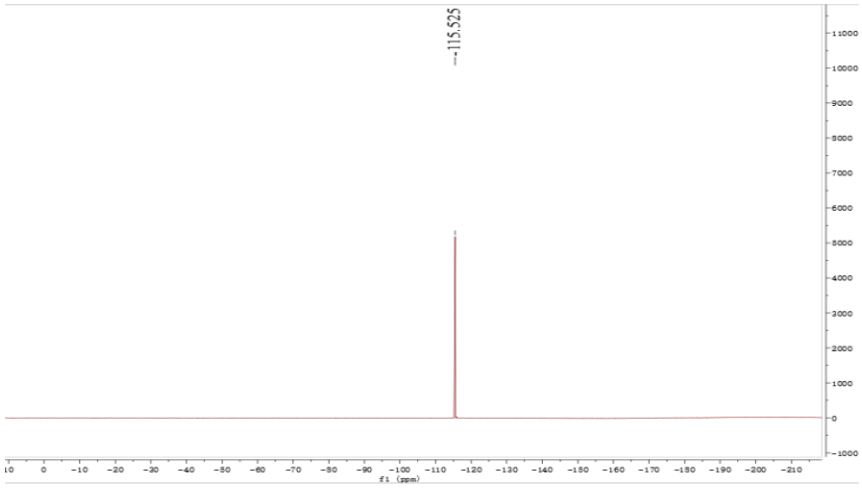

1aa-f
115.748
f1 (ppm)

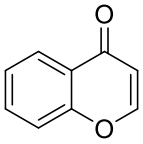

O
F
O
Ph

1ab

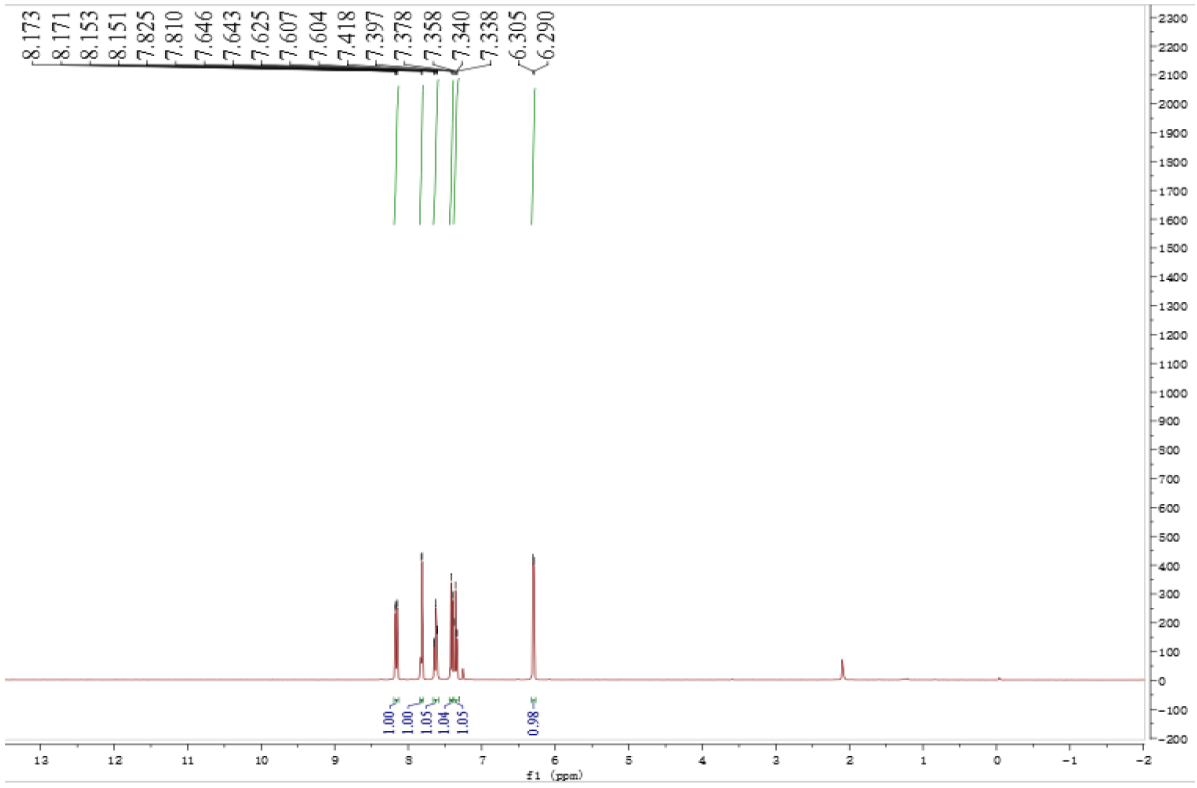

7.847
7.840
7.827
7.819
7.450
7.439
7.417
7.409
7.398
7.390
7.339
7.322
7.303
7.284
7.265
7.261
7.246
7.234
7.231
7.214
6.162
3.103
3.086
3.065
2.983
2.963
2.944
0.98
0.95
1.10
5.42
0.95
2.00
2.14
f1 (ppm)

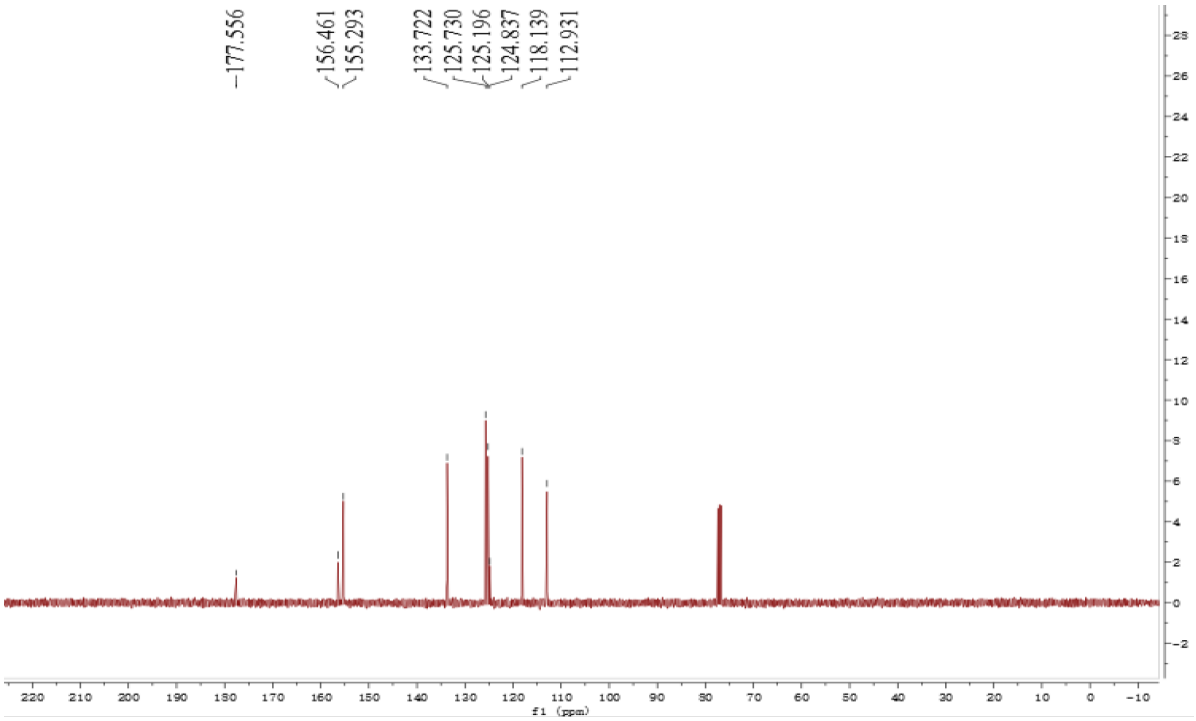

177.420
177.398
168.701
160.663
158.213
152.654
139.554
128.683
128.250
126.630
124.951
124.878
121.769
121.516
119.925
119.845
110.722
110.488
109.602
36.061
32.972
f1 (ppm)

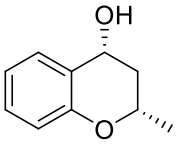

-115.525
f1 (ppm)



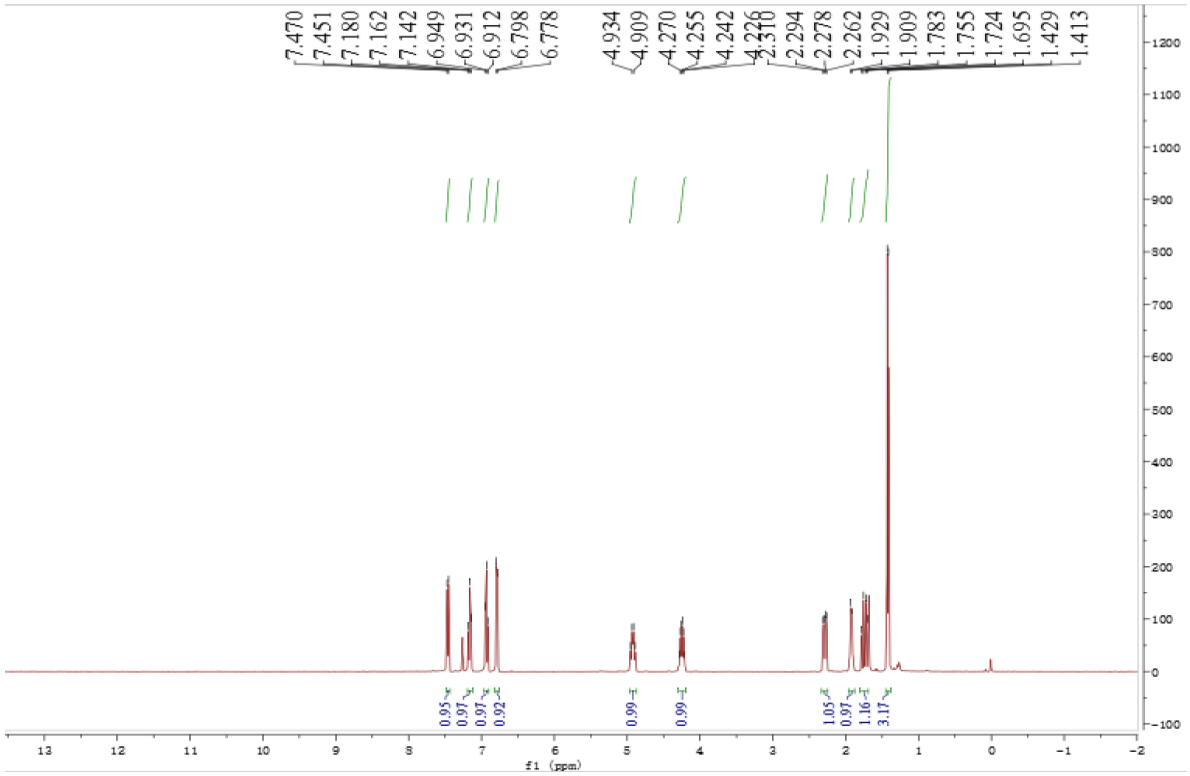
1ac

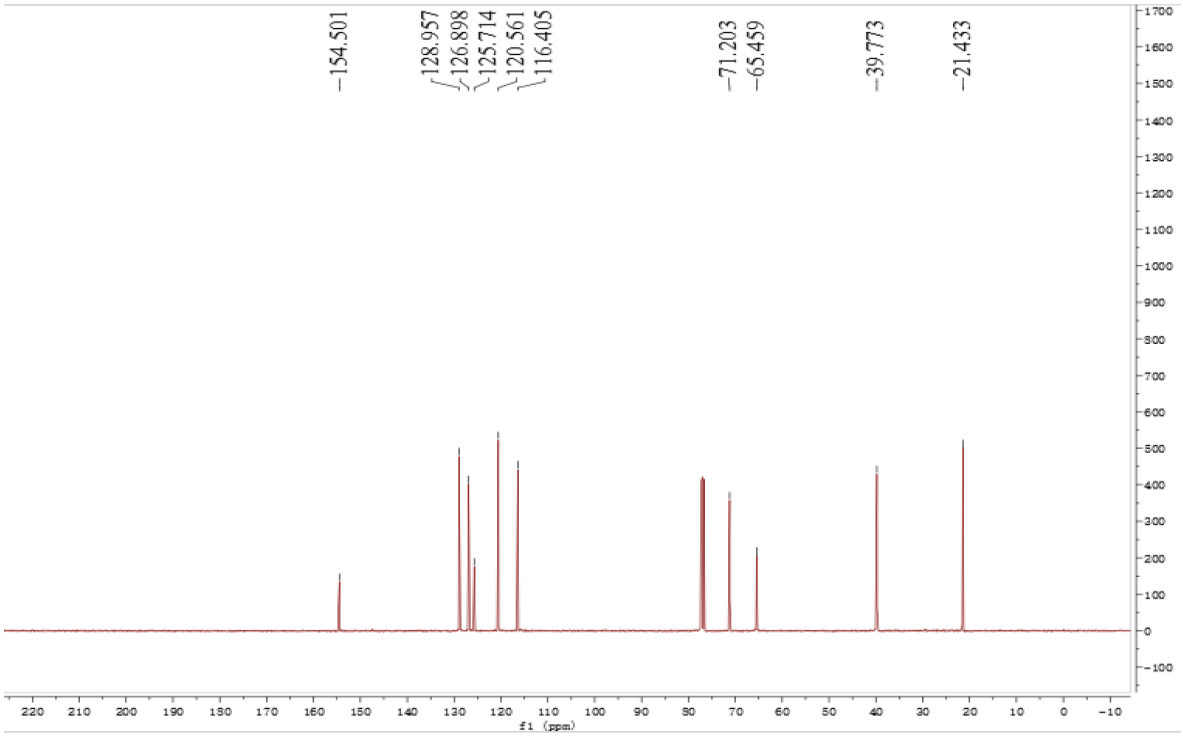

8.173
8.171
8.153
8.151
7.825
7.810
7.646
7.643
7.625
7.607
7.604
7.418
7.397
7.378
7.358
7.340
7.338
6.305
6.290
1.00
1.00
1.05
1.04
1.05
0.98
f1 (ppm)

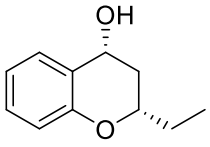

177.556
156.461
155.293
133.722
125.730
125.196
124.837
118.139
112.931
f1 (ppm)


OH
O

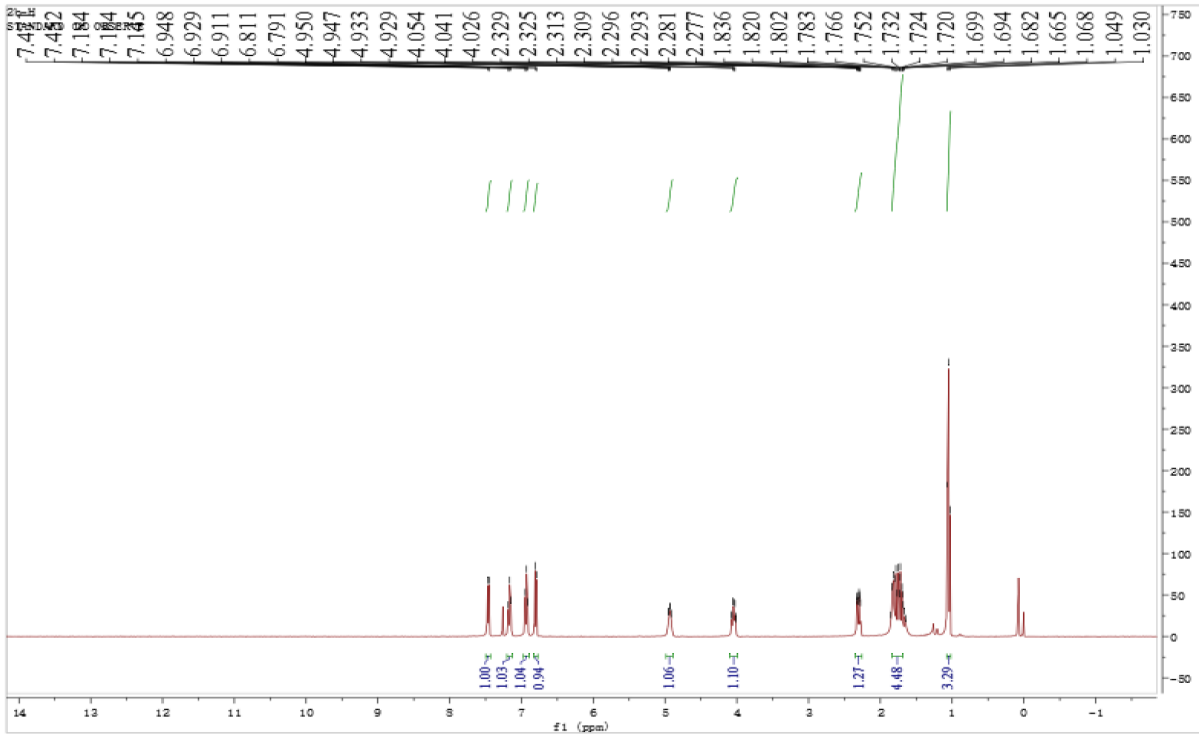
2a

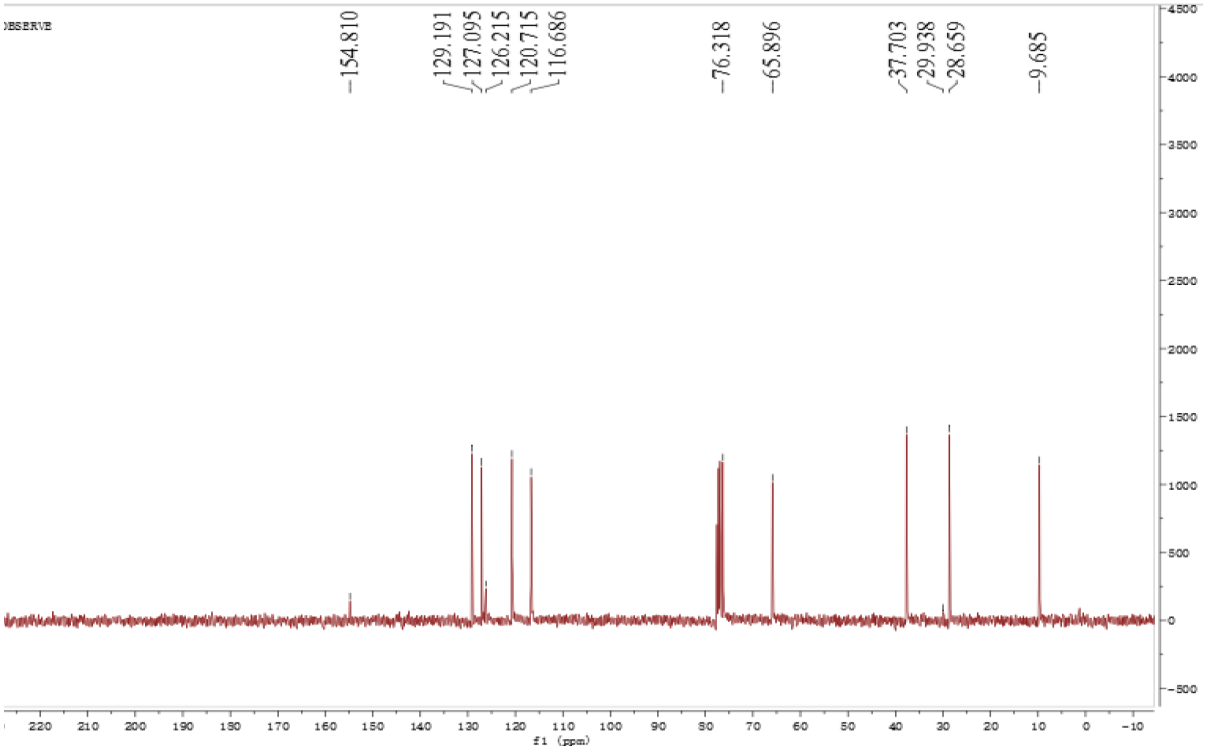

7.470
7.451
7.180
7.162
7.142
6.949
6.931
6.912
6.798
6.778
4.934
4.909
4.270
4.255
4.242
4.226
2.310
2.294
2.278
2.262
1.929
1.909
1.783
1.755
1.724
1.695
1.429
1.413
0.95
0.97
0.97
0.92
0.99
0.99
1.05
0.97
1.16
3.17
f1 (ppm)

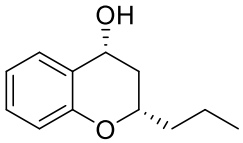

154.501
128.957
126.898
125.714
120.561
116.405
71.203
65.459
39.773
21.433
f1 (ppm)


OH
O

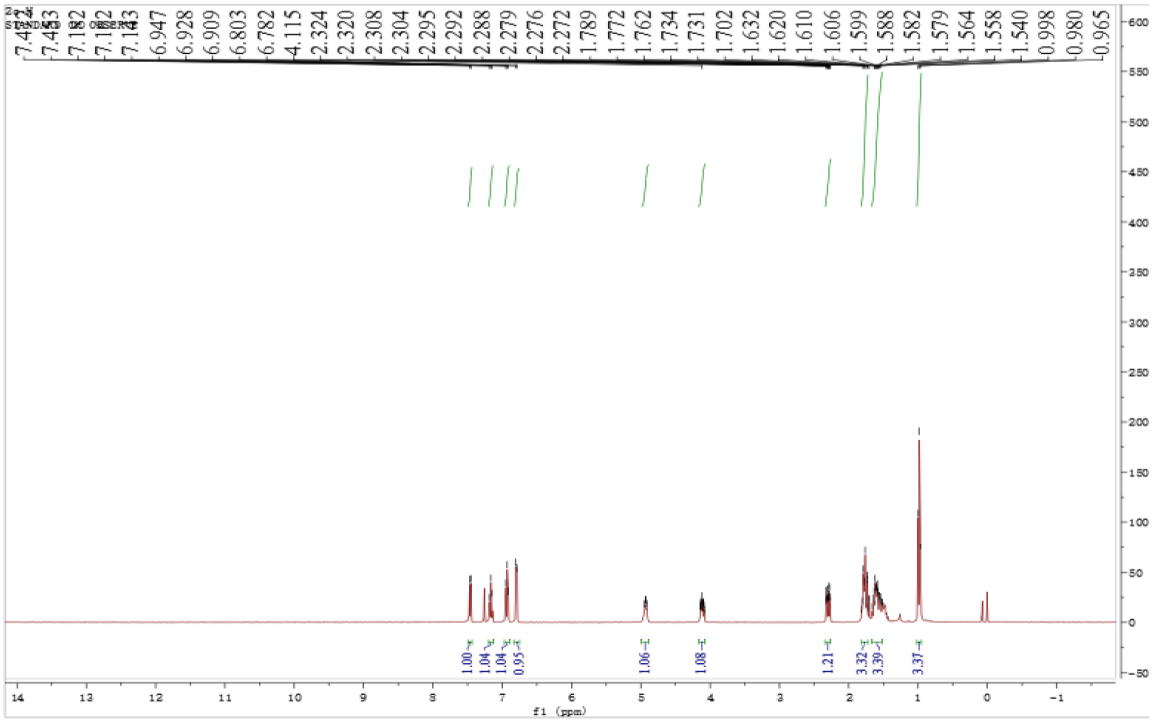
2b

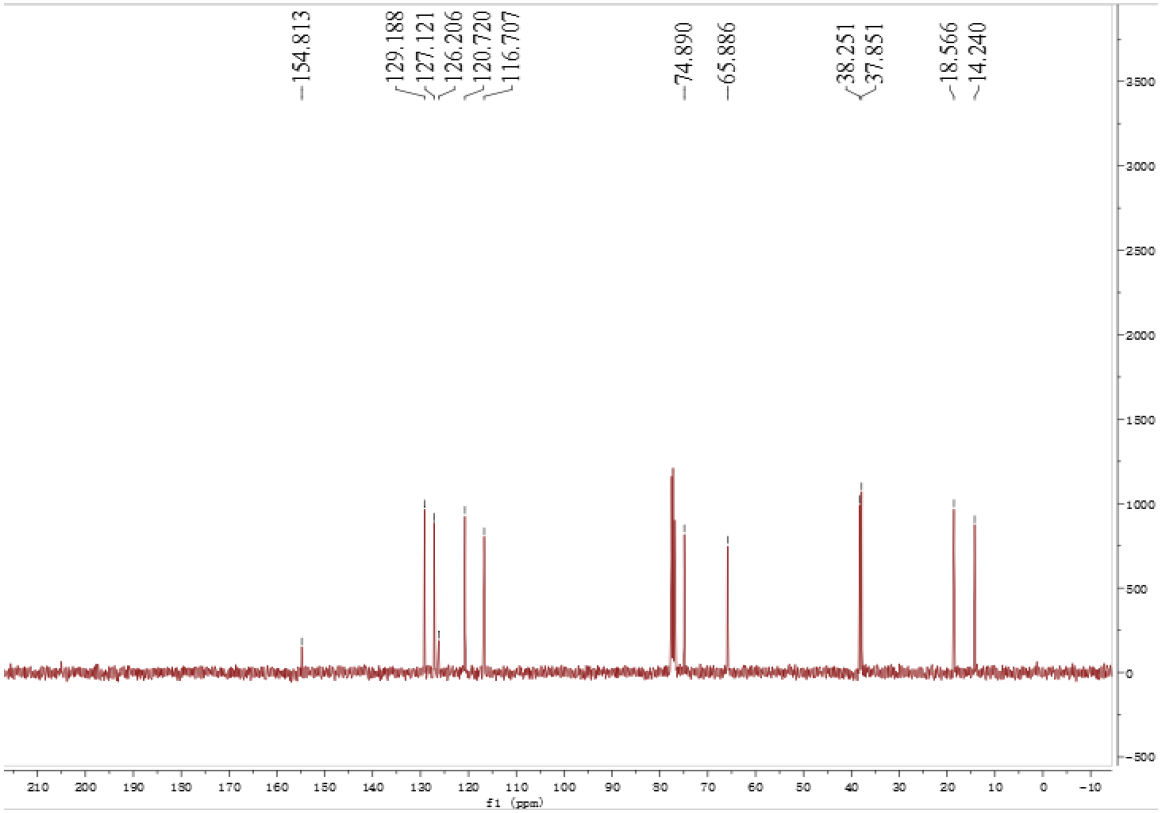

7.402
7.184
7.145
6.948
6.929
6.911
6.811
6.791
4.950
4.947
4.933
4.929
4.054
4.041
4.026
2.329
2.325
2.313
2.309
2.296
2.293
2.281
2.277
1.836
1.820
1.802
1.783
1.766
1.752
1.732
1.724
1.720
1.699
1.694
1.682
1.665
1.068
1.049
1.030
1.00
1.03
1.04
0.94
1.06
1.10
1.27
4.48
3.29
f1 (ppm)

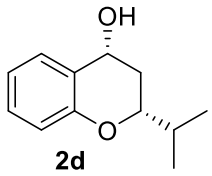

154.810
129.191
127.095
126.215
120.715
116.686
76.318
65.896
37.703
29.938
28.659
9.685
f1 (ppm)


OH
O

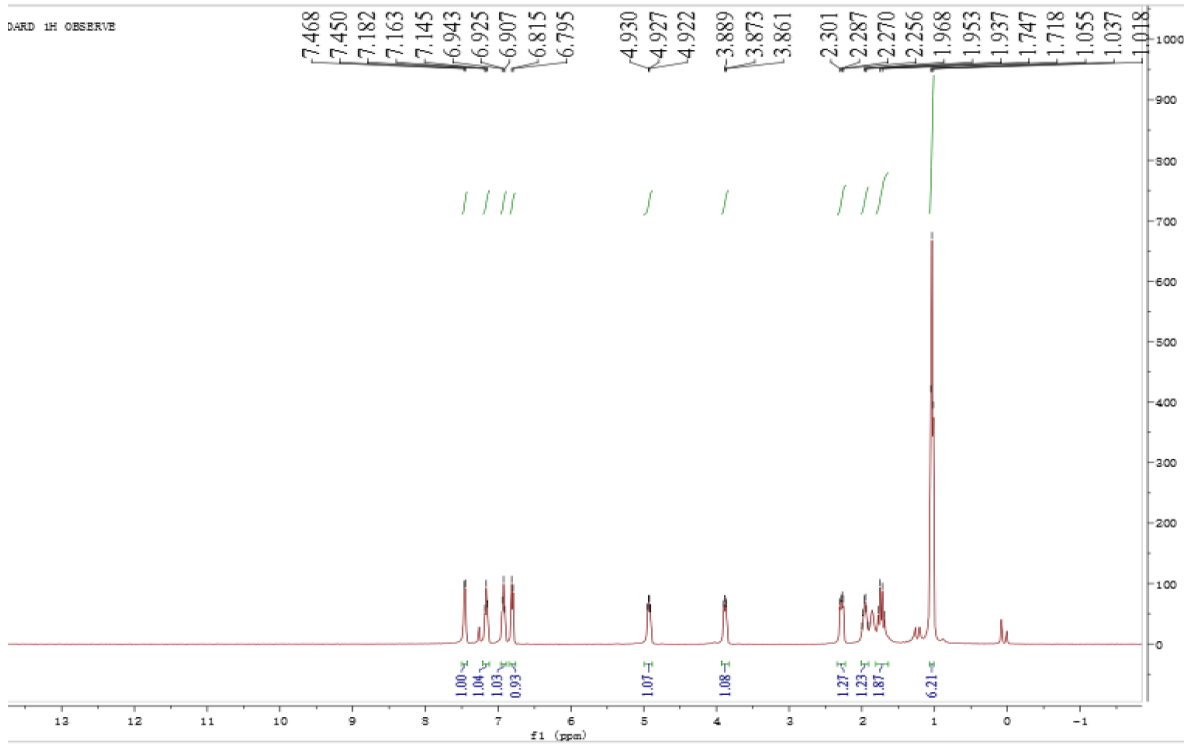
2c

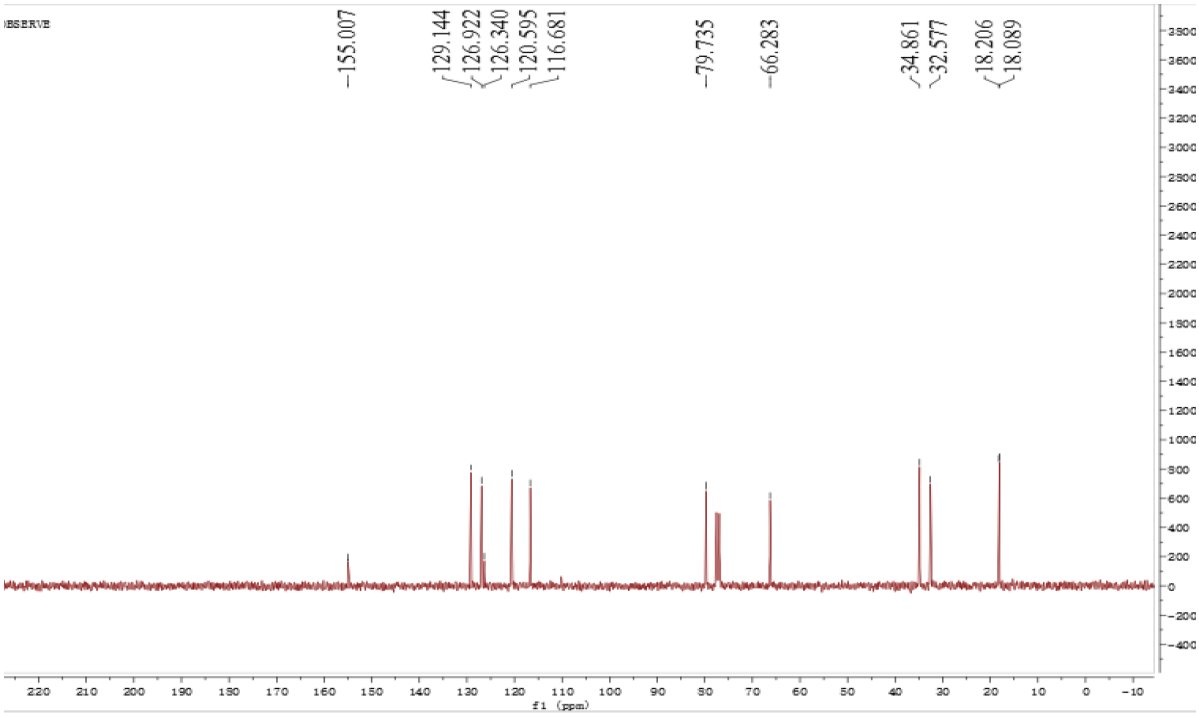

7.422
7.453
7.182
7.143
6.947
6.928
6.909
6.803
6.782
4.115
2.324
2.320
2.308
2.304
2.295
2.292
2.288
2.279
2.276
2.272
1.789
1.772
1.762
1.734
1.731
1.702
1.632
1.620
1.610
1.606
1.599
1.588
1.582
1.579
1.564
1.558
1.540
0.998
0.980
0.965
1.00
1.04
1.04
0.95
1.06
1.08
1.21
3.32
3.39
3.37
f1 (ppm)

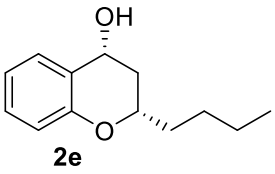

154.813
129.188
127.121
126.206
120.720
116.707
74.890
65.886
38.251
37.851
18.566
14.240
f1 (ppm)


OH
O

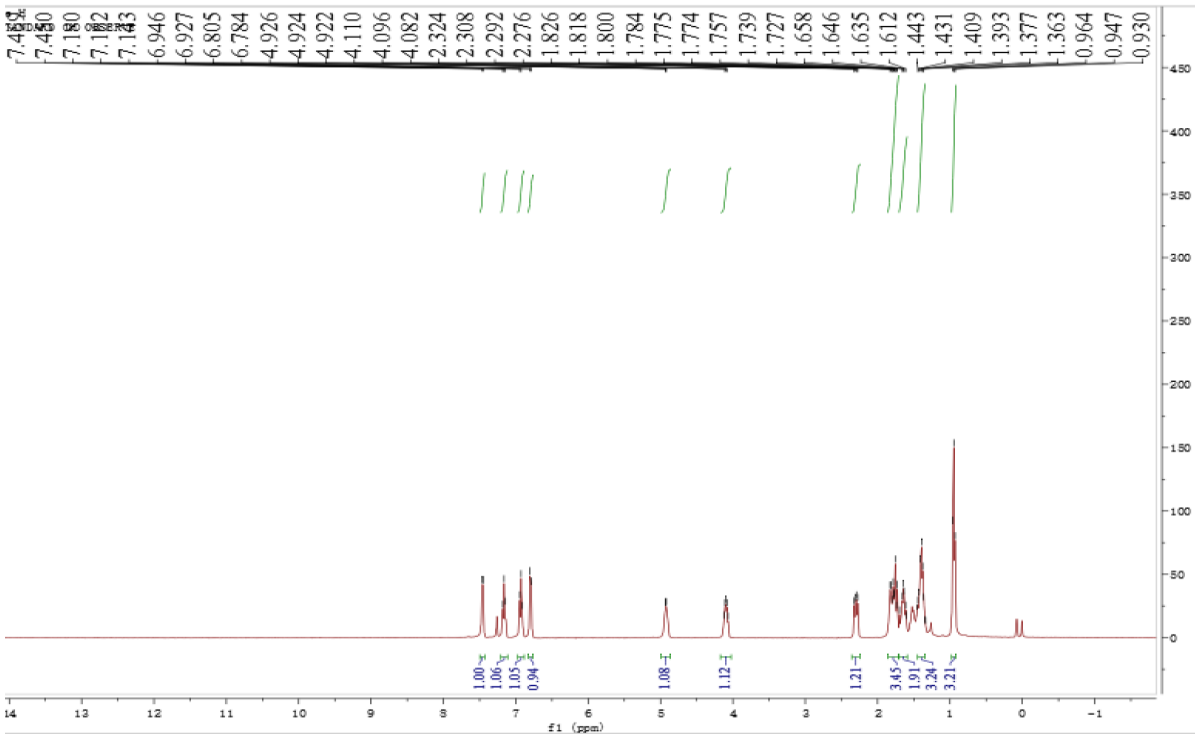
2d

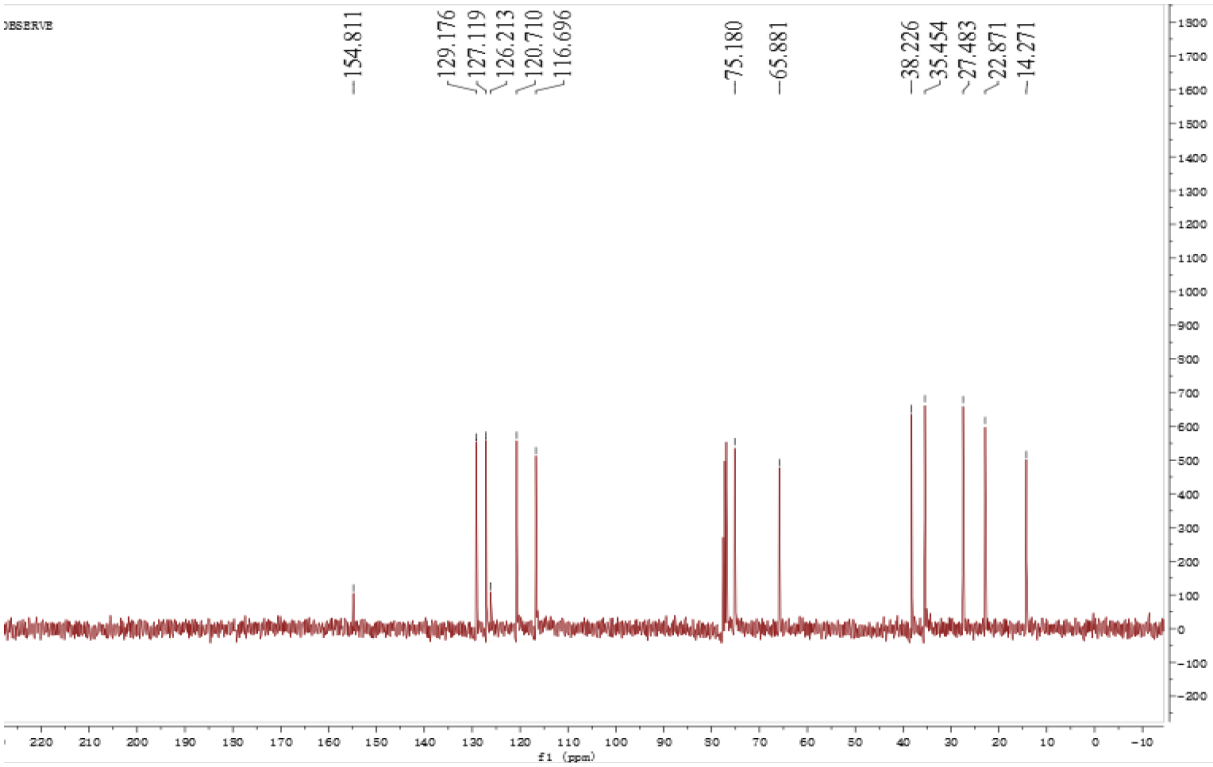

DARD 1H OBSERVE
7.468
7.450
7.182
7.163
7.145
6.943
6.925
6.907
6.815
6.795
4.930
4.927
4.922
3.889
3.873
3.861
2.301
2.287
2.270
2.256
1.968
1.953
1.937
1.747
1.718
1.055
1.037
1.018
1.00
1.04
1.03
0.93
1.07
1.08
1.27
1.23
1.87
6.21
f1 (ppm)

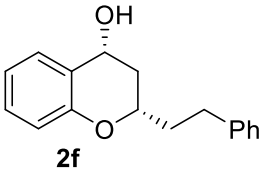

OBSERVE
155.007
129.144
126.922
126.340
120.595
116.681
79.735
66.283
34.861
32.577
18.206
18.089
f1 (ppm)


OH
O

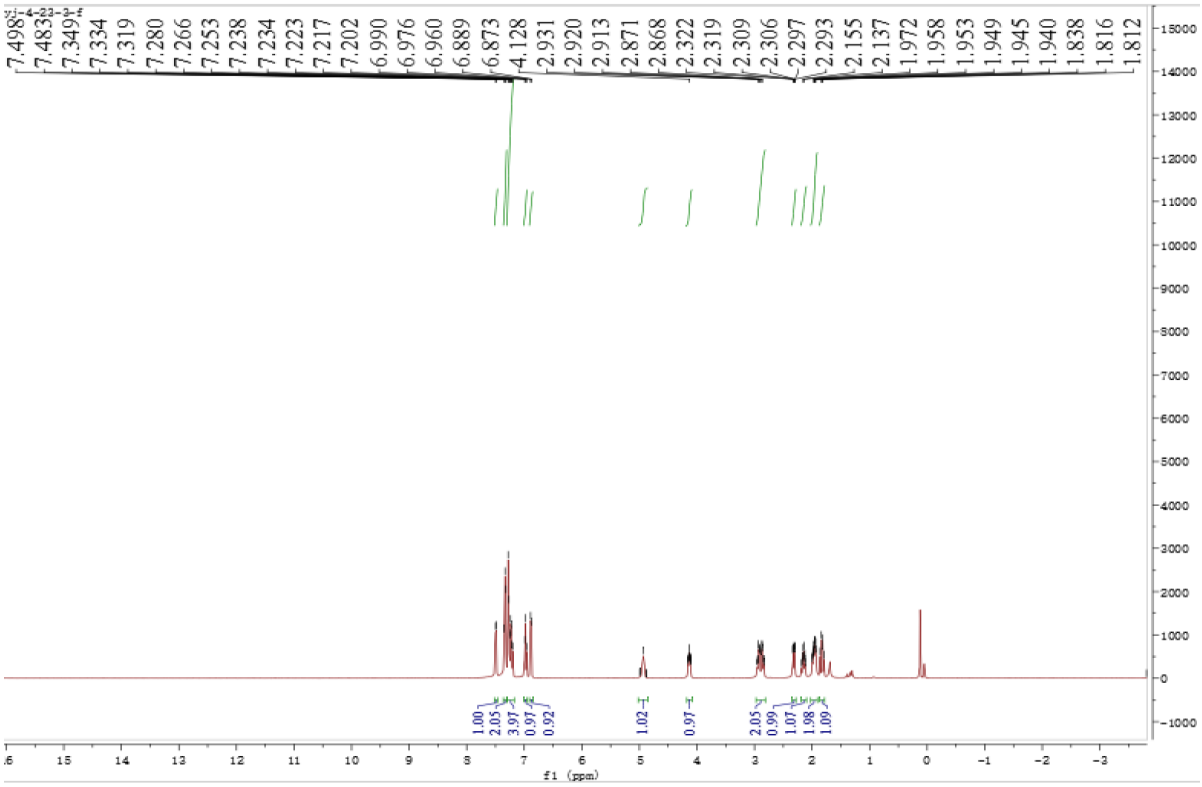
2e

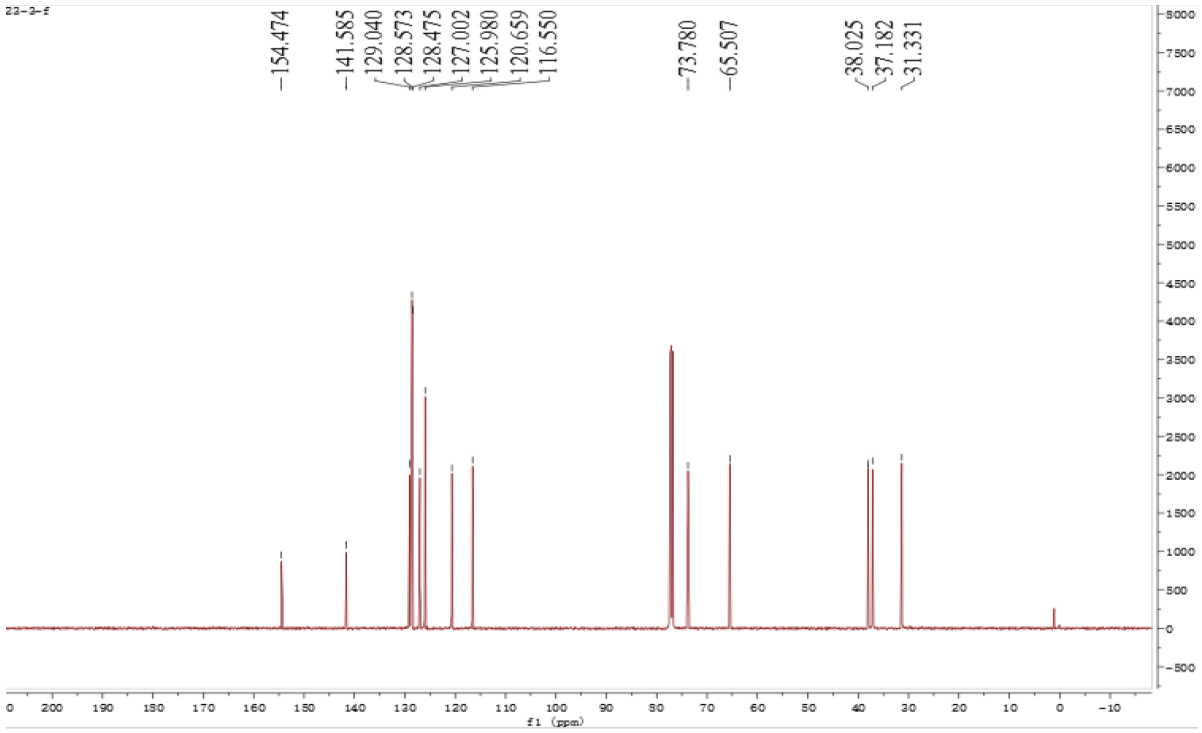

7.400
7.180
7.162
7.143
6.946
6.927
6.805
6.784
4.926
4.924
4.922
4.110
4.096
4.082
2.324
2.308
2.292
2.276
1.826
1.818
1.800
1.784
1.775
1.774
1.757
1.739
1.727
1.658
1.646
1.635
1.612
1.443
1.431
1.409
1.393
1.377
1.363
0.964
0.947
0.930
1.00
1.06
1.05
0.94
1.08
1.12
1.21
3.45
1.91
3.24
3.21
f1 (ppm)

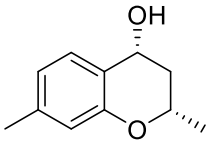

154.811
129.176
127.119
126.213
120.710
116.696
75.180
65.881
38.226
35.454
27.483
22.871
14.271
f1 (ppm)


OH
O
Ph

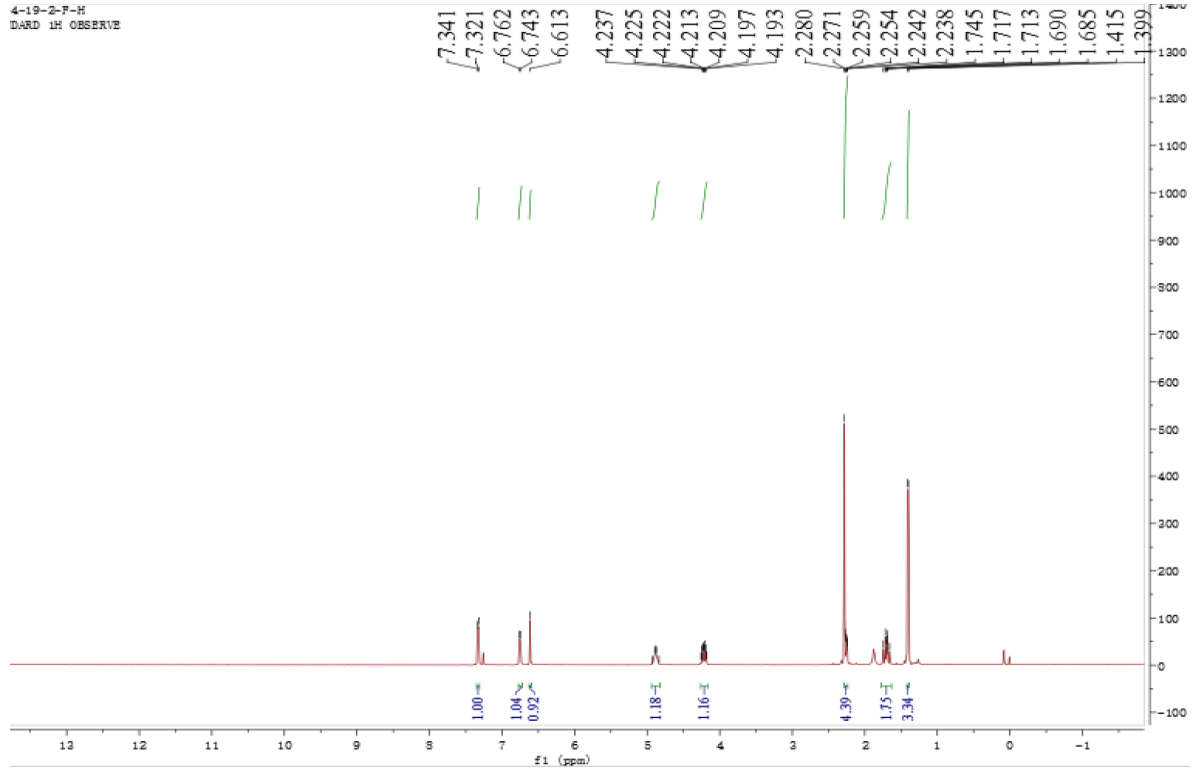
2f

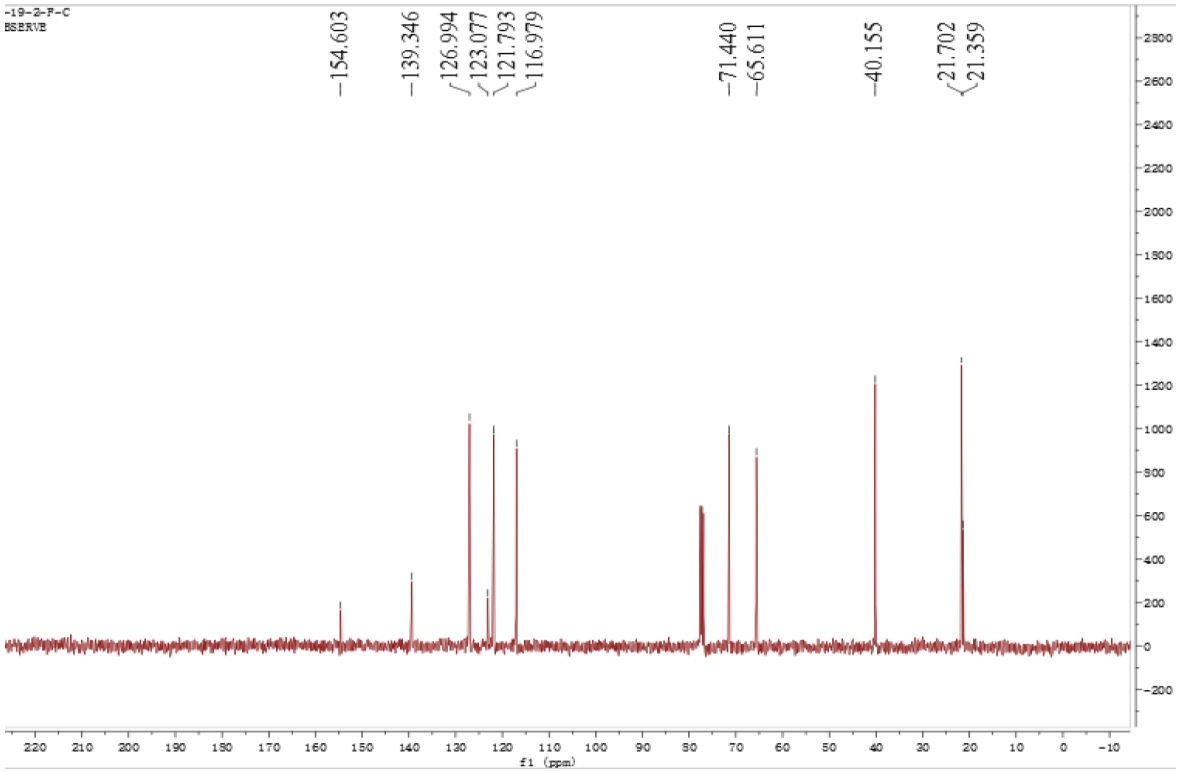

7.498
7.483
7.349
7.334
7.319
7.280
7.266
7.253
7.238
7.234
7.223
7.217
7.202
6.990
6.976
6.960
6.889
6.873
4.128
2.931
2.920
2.913
2.871
2.868
2.322
2.319
2.309
2.306
2.297
2.293
2.155
2.137
1.972
1.958
1.953
1.949
1.945
1.940
1.838
1.816
1.812
1.00
2.05
3.97
0.97
0.92
1.02
0.97
2.05
0.99
1.07
1.98
1.09
f1 (ppm)

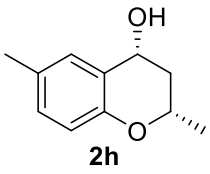

154.474
141.585
129.040
128.573
128.475
127.002
125.980
120.659
116.550
73.780
65.507
38.025
37.182
31.331
f1 (ppm)


OH
O

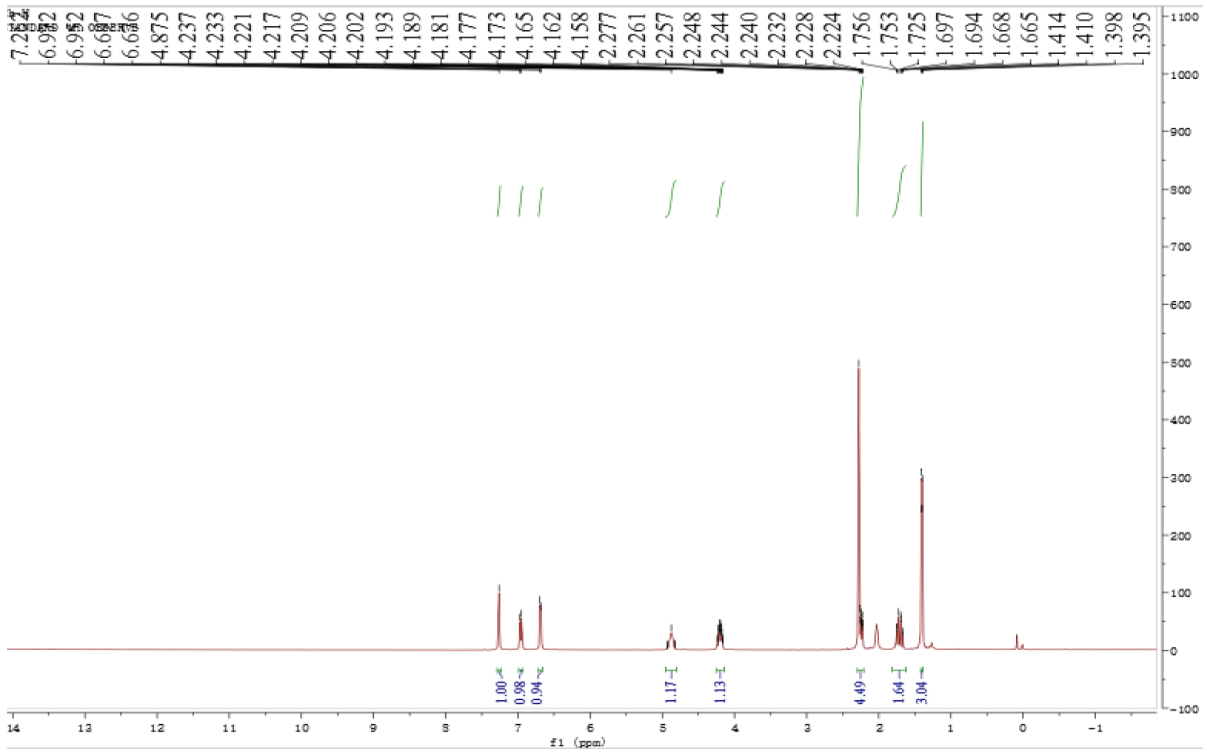
2g

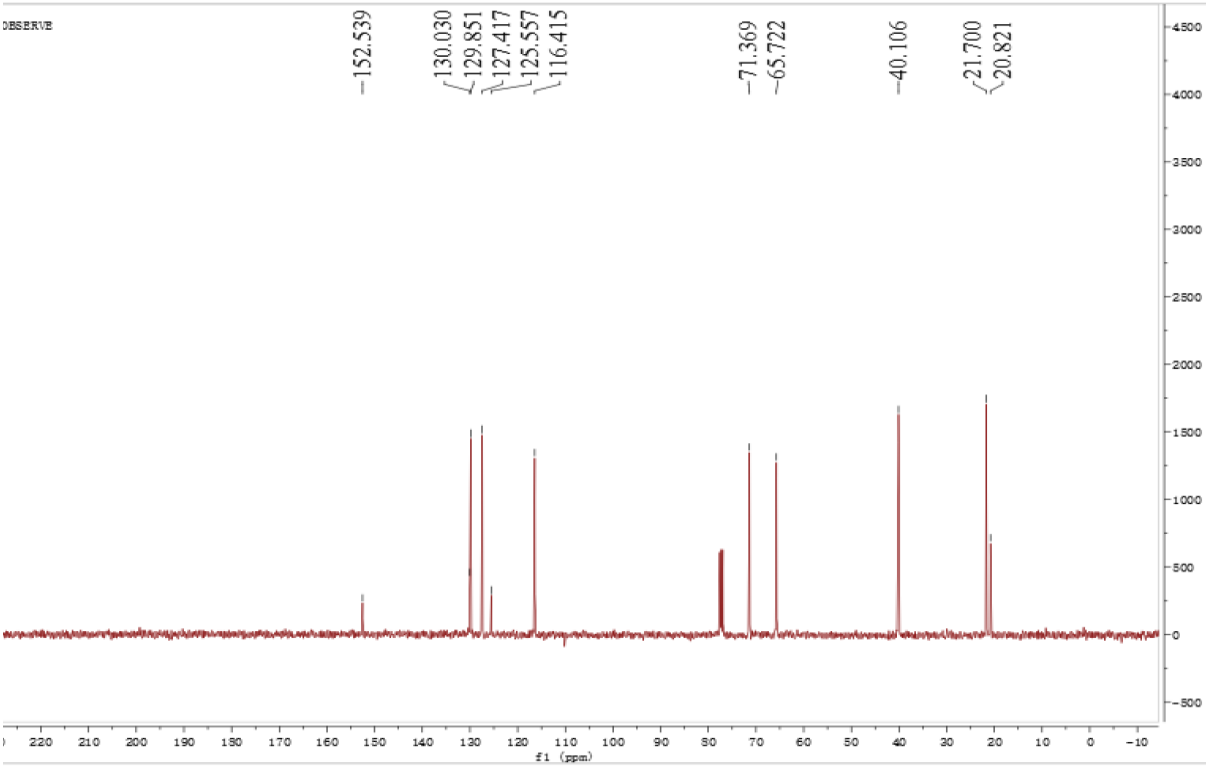

4-19-2-F-H
DARD 1H OBSERVE
7.341
7.321
6.762
6.743
6.613
4.237
4.225
4.222
4.213
4.209
4.197
4.193
2.280
2.271
2.259
2.254
2.242
2.238
1.745
1.717
1.713
1.690
1.685
1.415
1.399
1.00
1.04
0.92
1.18
1.16
4.39
1.75
3.34
f1 (ppm)

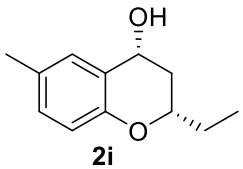

-19-2-F-C
BSERVE
154.603
139.346
126.994
123.077
121.793
116.979
71.440
65.611
40.155
21.702
21.359
f1 (ppm)


OH
O

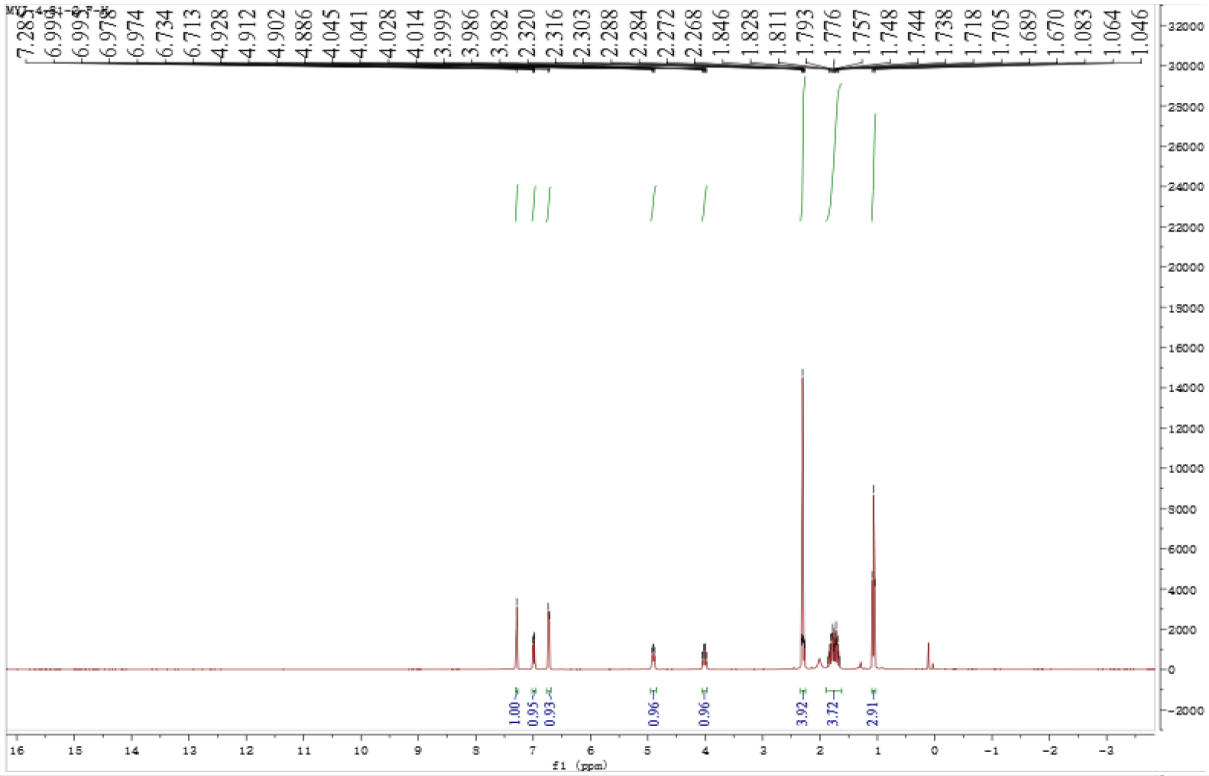
2h

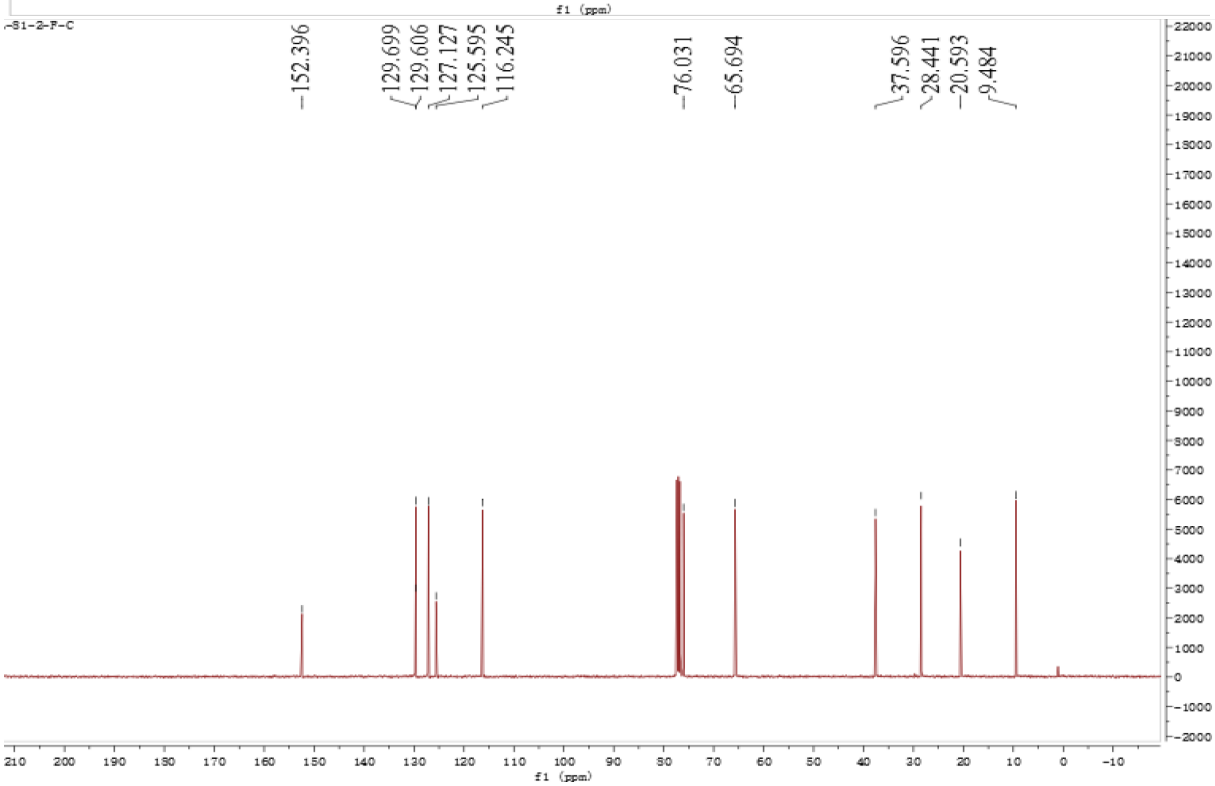

7.260
6.982
6.952
6.687
6.676
4.875
4.237
4.233
4.221
4.217
4.209
4.206
4.202
4.193
4.189
4.181
4.177
4.173
4.165
4.162
4.158
2.277
2.261
2.257
2.248
2.244
2.240
2.232
2.228
2.224
1.756
1.753
1.725
1.697
1.694
1.668
1.665
1.414
1.410
1.398
1.395
1.00
0.98
0.94
1.17
1.13
4.49
1.64
3.04
f1 (ppm)

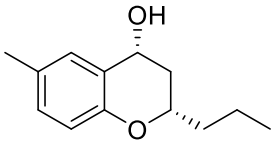

152.539
130.030
129.851
127.417
125.557
116.415
71.369
65.722
40.106
21.700
20.821
f1 (ppm)


OH
O

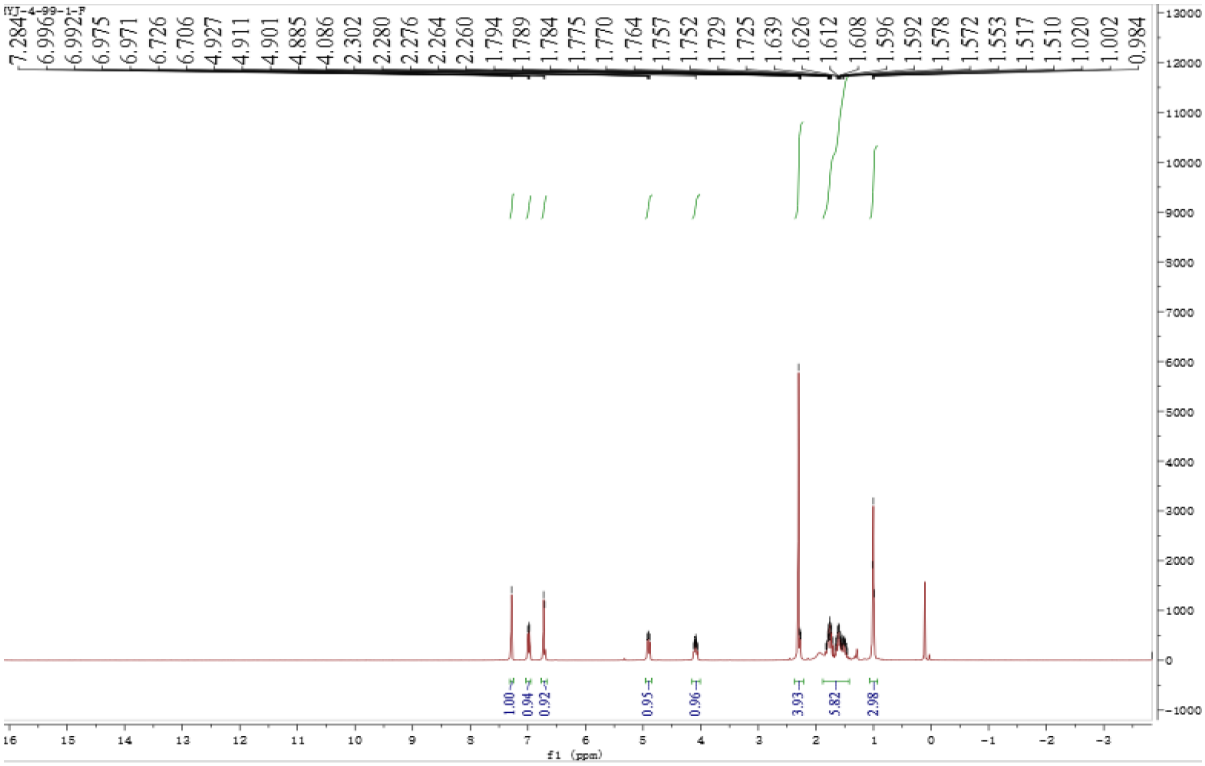
2i

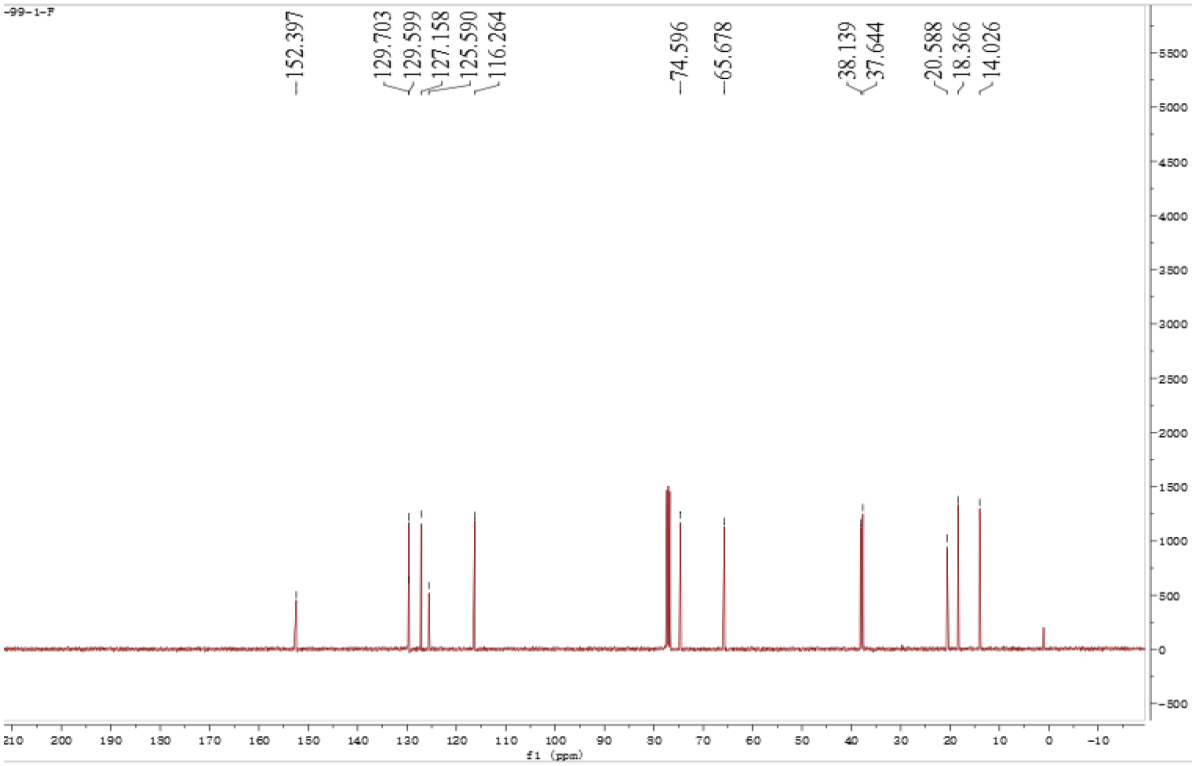

7.285
6.999
6.993
6.978
6.974
6.734
6.713
4.928
4.912
4.902
4.886
4.045
4.041
4.028
4.014
3.999
3.986
3.982
2.320
2.316
2.303
2.288
2.284
2.272
2.268
1.846
1.828
1.811
1.793
1.776
1.757
1.748
1.744
1.738
1.718
1.705
1.689
1.670
1.083
1.064
1.046
1.00
0.95
0.93
0.96
0.96
3.92
3.72
2.91
f1 (ppm)

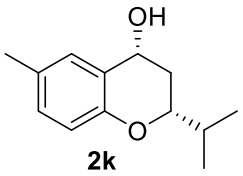

152.396
129.699
129.606
127.127
125.595
116.245
76.031
65.694
37.596
28.441
20.593
9.484
f1 (ppm)


OH
O

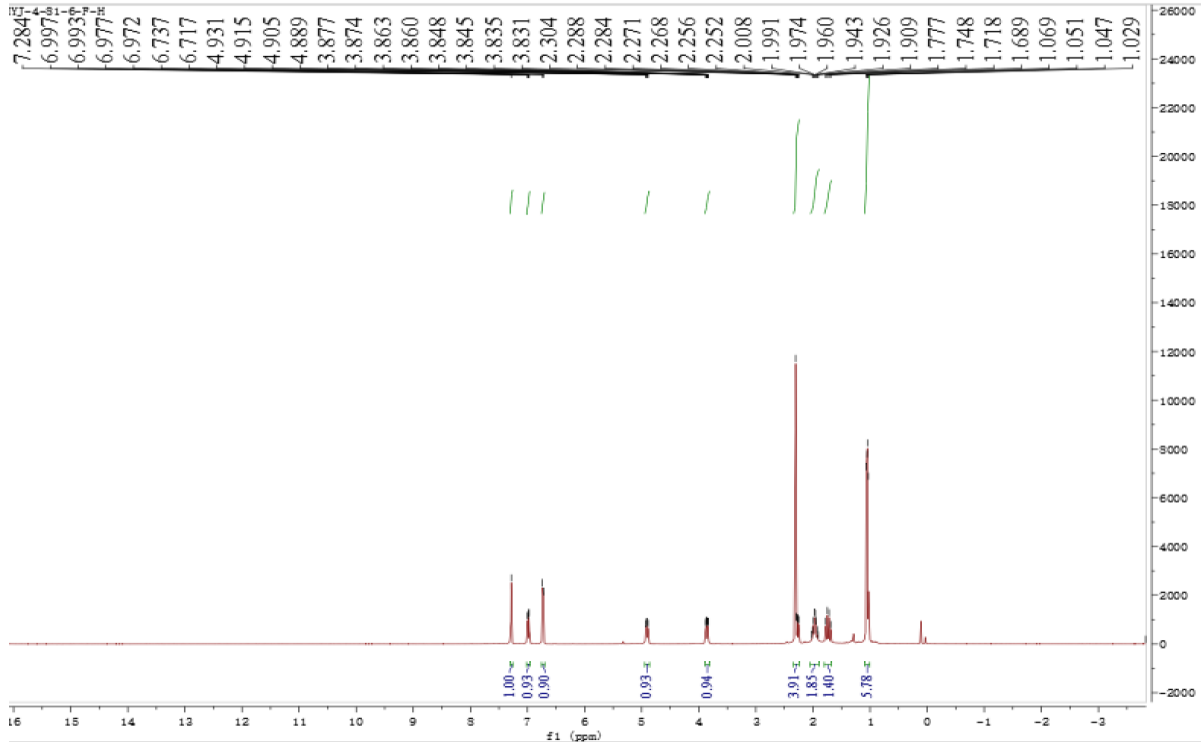
2j

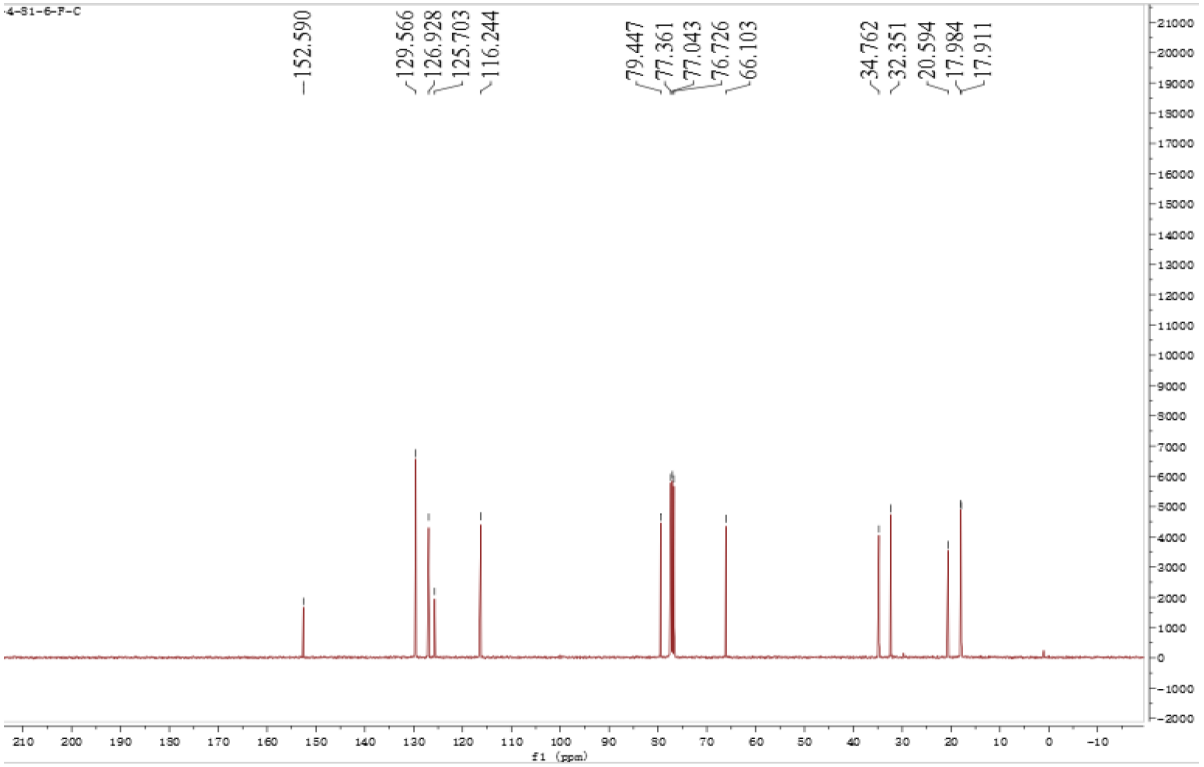

7.284
6.996
6.992
6.975
6.971
6.726
6.706
4.927
4.911
4.901
4.885
4.086
2.302
2.280
2.276
2.264
2.260
1.794
1.789
1.784
1.775
1.770
1.764
1.757
1.752
1.729
1.725
1.639
1.626
1.612
1.608
1.596
1.592
1.578
1.572
1.553
1.517
1.510
1.020
1.002
0.984
1.00
0.94
0.92
0.95
0.96
3.93
5.82
2.98
f1 (ppm)

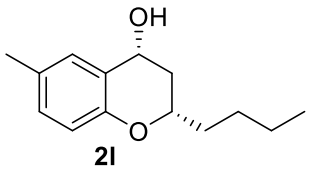

152.397
129.703
129.599
127.158
125.590
116.264
74.596
65.678
38.139
37.644
20.588
18.366
14.026
f1 (ppm)


OH
O

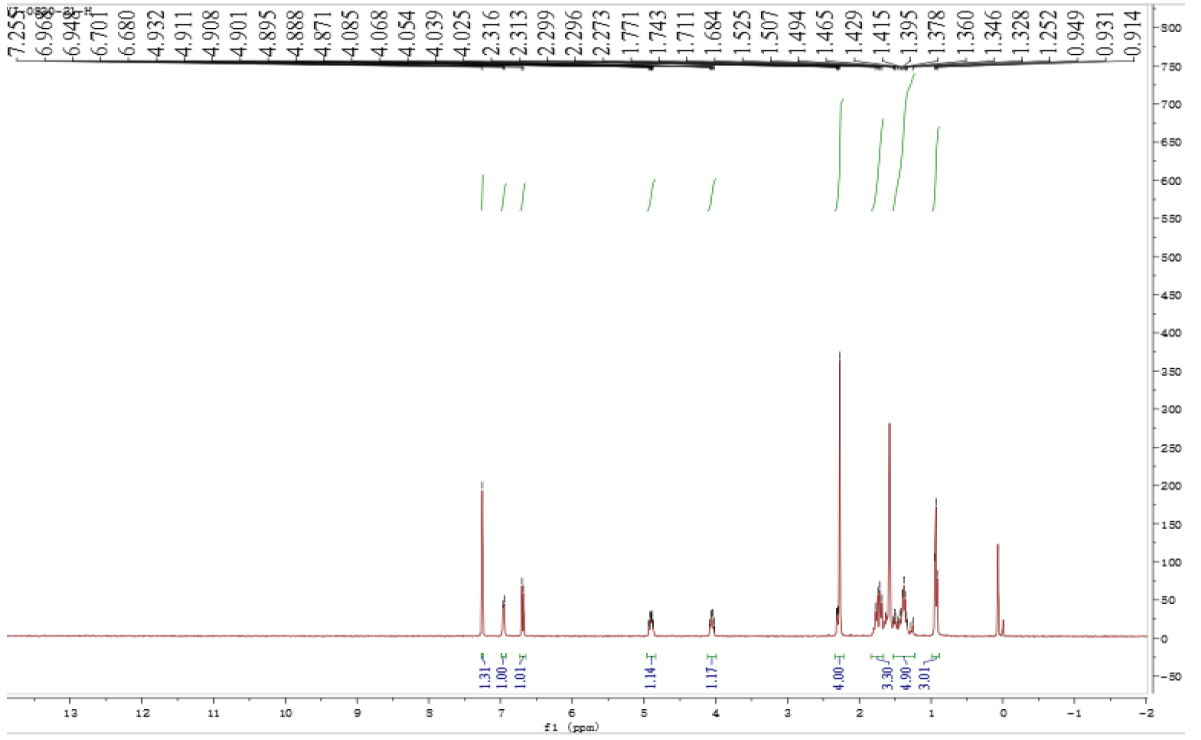
2k

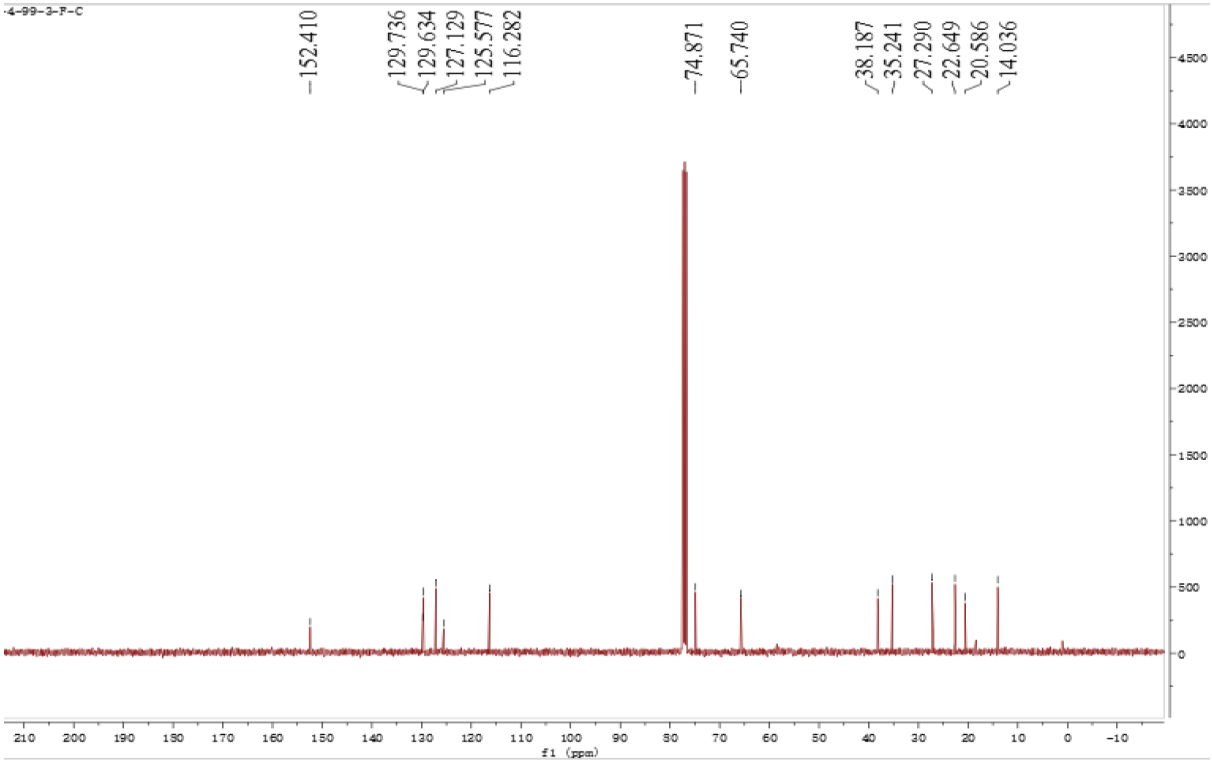

7.284
6.997
6.993
6.977
6.972
6.737
6.717
4.931
4.915
4.905
4.889
3.877
3.874
3.863
3.860
3.848
3.845
3.835
3.831
2.304
2.288
2.284
2.271
2.268
2.256
2.252
2.008
1.991
1.974
1.960
1.943
1.926
1.909
1.777
1.748
1.718
1.689
1.069
1.051
1.047
1.029
1.00
0.93
0.90
0.93
0.94
3.91
1.85
1.40
5.78
f1 (ppm)

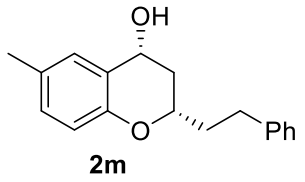

152.590
129.566
126.928
125.703
116.244
79.447
77.361
77.043
76.726
66.103
34.762
32.351
20.594
17.984
17.911
f1 (ppm)


OH
O

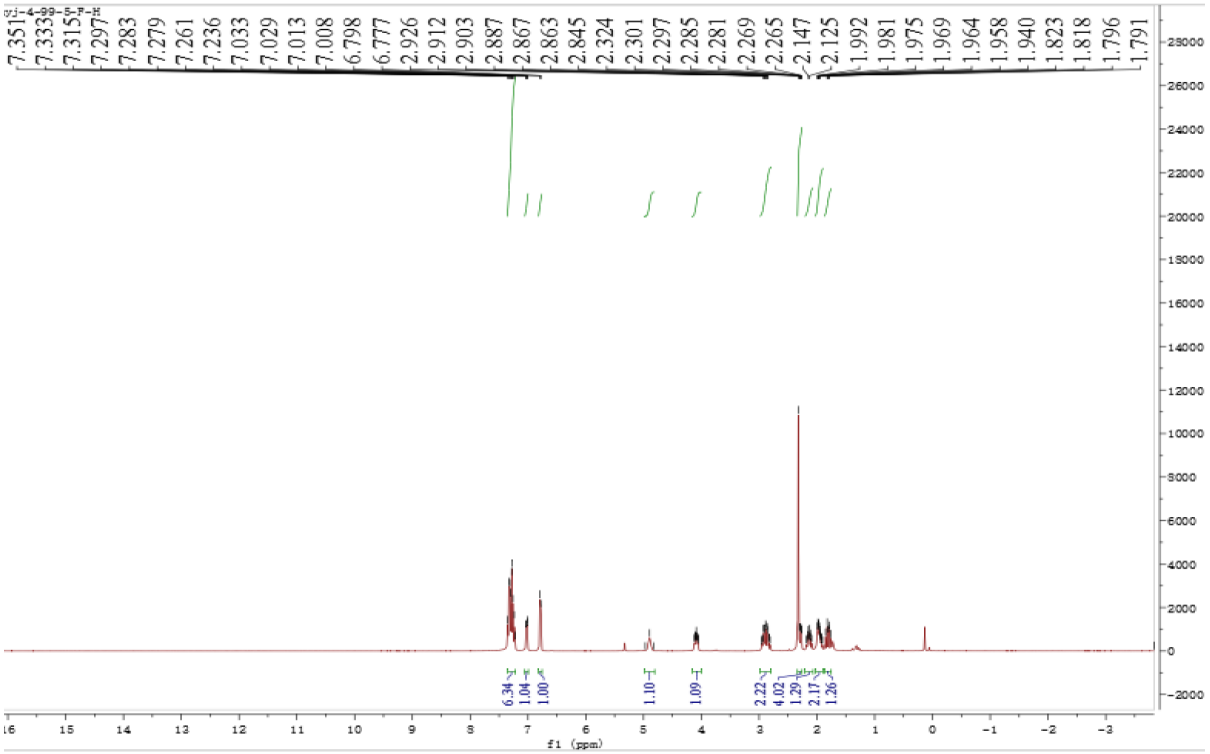
2l

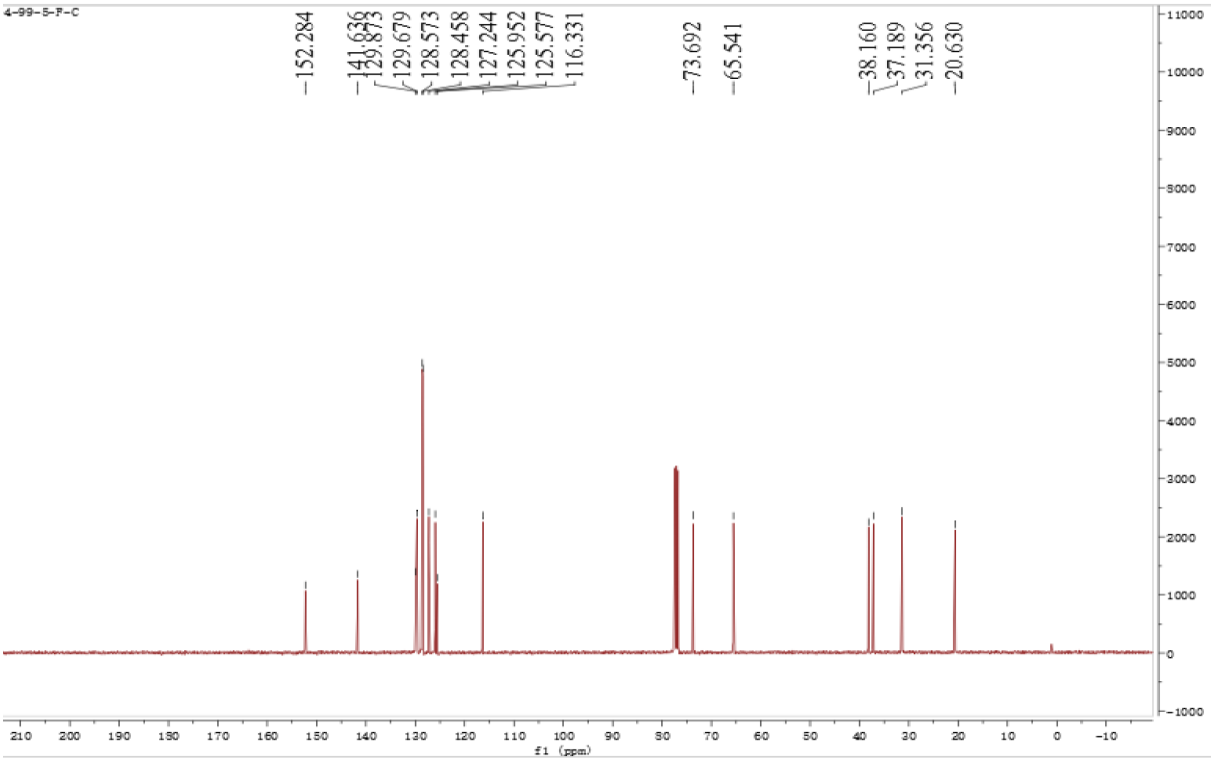

7.255
6.968
6.948
6.701
6.680
4.932
4.911
4.908
4.901
4.895
4.888
4.871
4.085
4.068
4.054
4.039
4.025
2.316
2.313
2.299
2.296
2.273
1.771
1.743
1.711
1.684
1.525
1.507
1.494
1.465
1.429
1.415
1.395
1.378
1.360
1.346
1.328
1.252
0.949
0.931
0.914
1.31
1.00
1.01
1.14
1.17
4.00
3.30
4.90
3.01
f1 (ppm)

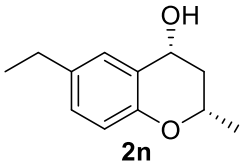

152.410
129.736
129.634
127.129
125.577
116.282
74.871
65.740
38.187
35.241
27.290
22.649
20.586
14.036
f1 (ppm)


OH
O
Ph

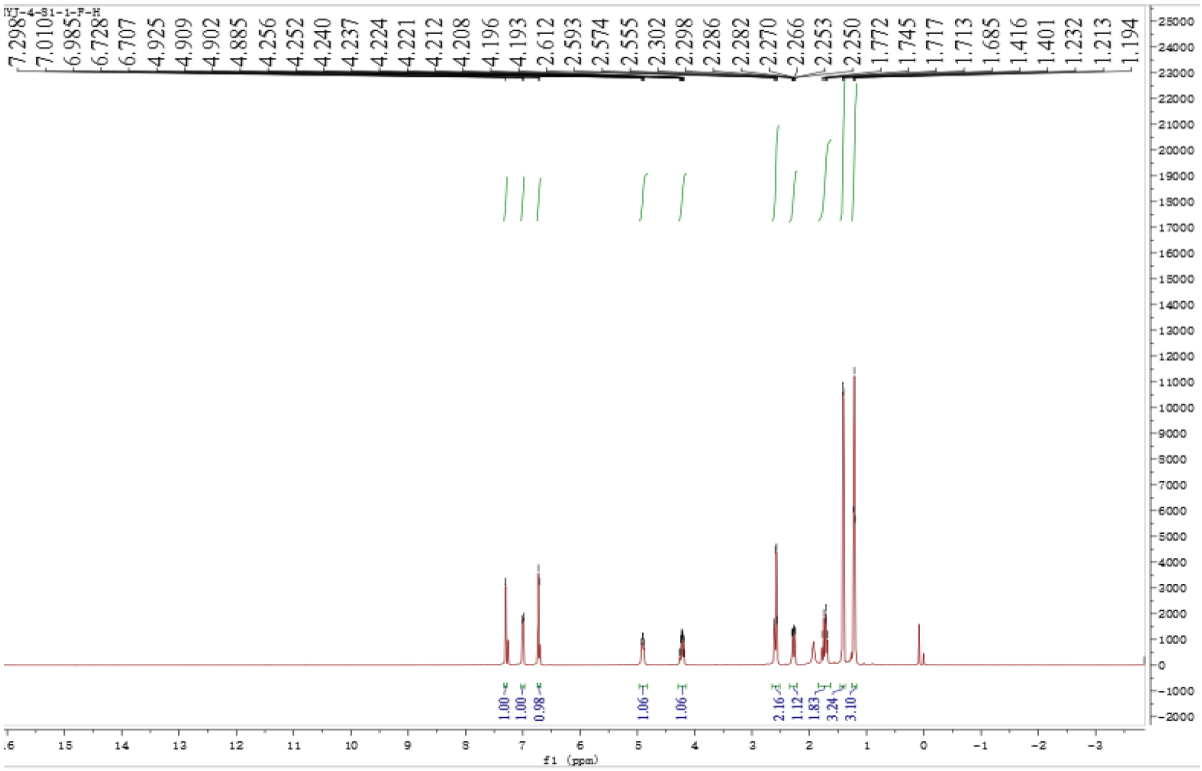
2m

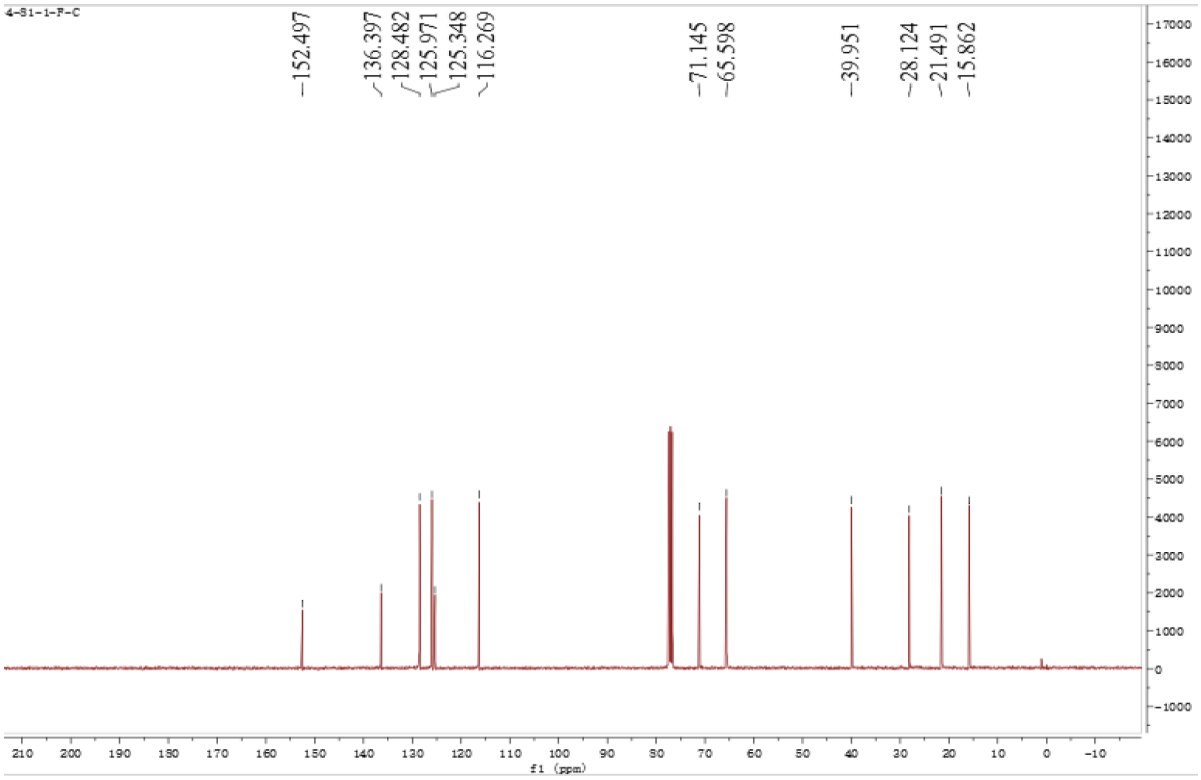

7.351
7.333
7.315
7.297
7.283
7.279
7.261
7.236
7.033
7.029
7.013
7.008
6.798
6.777
2.926
2.912
2.903
2.887
2.867
2.863
2.845
2.324
2.301
2.297
2.285
2.281
2.269
2.265
2.147
2.125
1.992
1.981
1.975
1.969
1.964
1.958
1.940
1.823
1.818
1.796
1.791
6.34
1.04
1.00
1.10
1.09
2.22
4.02
1.29
2.17
1.26
f1 (ppm)

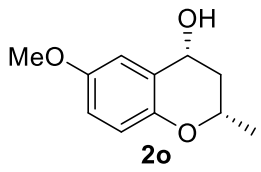

152.284
141.636
129.873
129.679
128.573
128.458
127.244
125.952
125.577
116.331
73.692
65.541
38.160
37.189
31.356
20.630
f1 (ppm)


OH
O

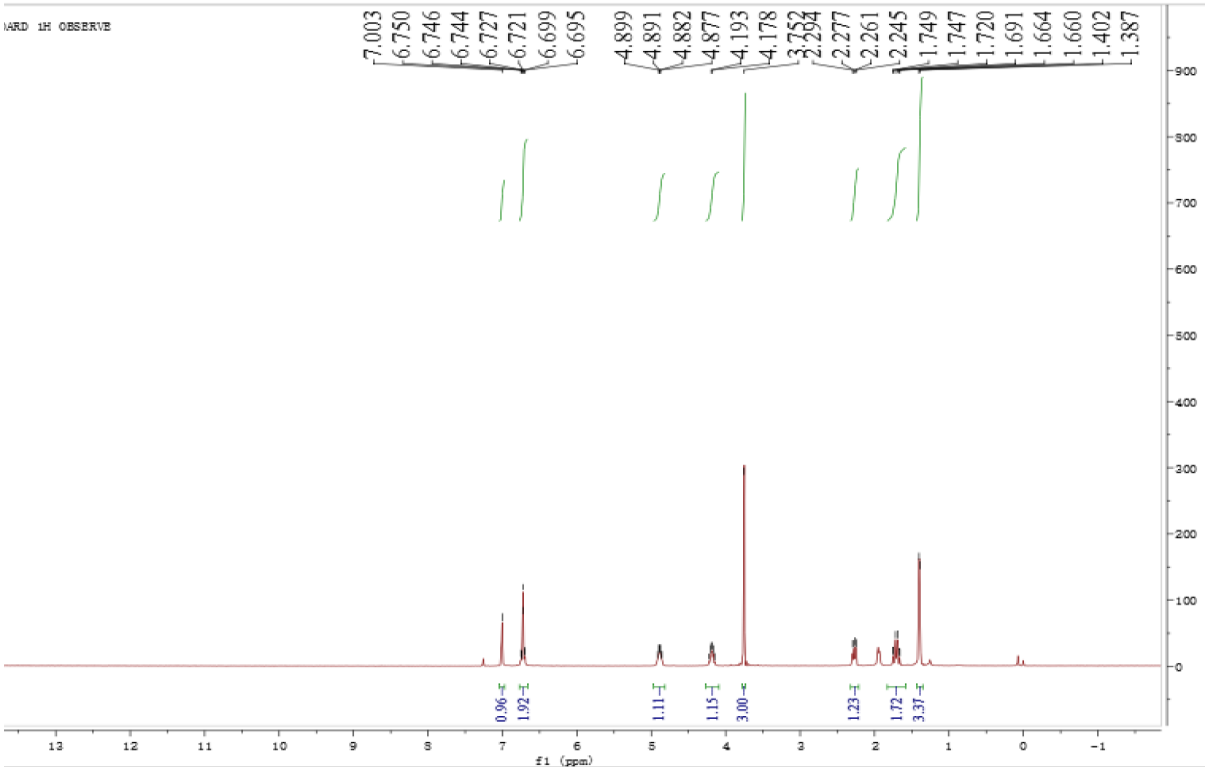
2n

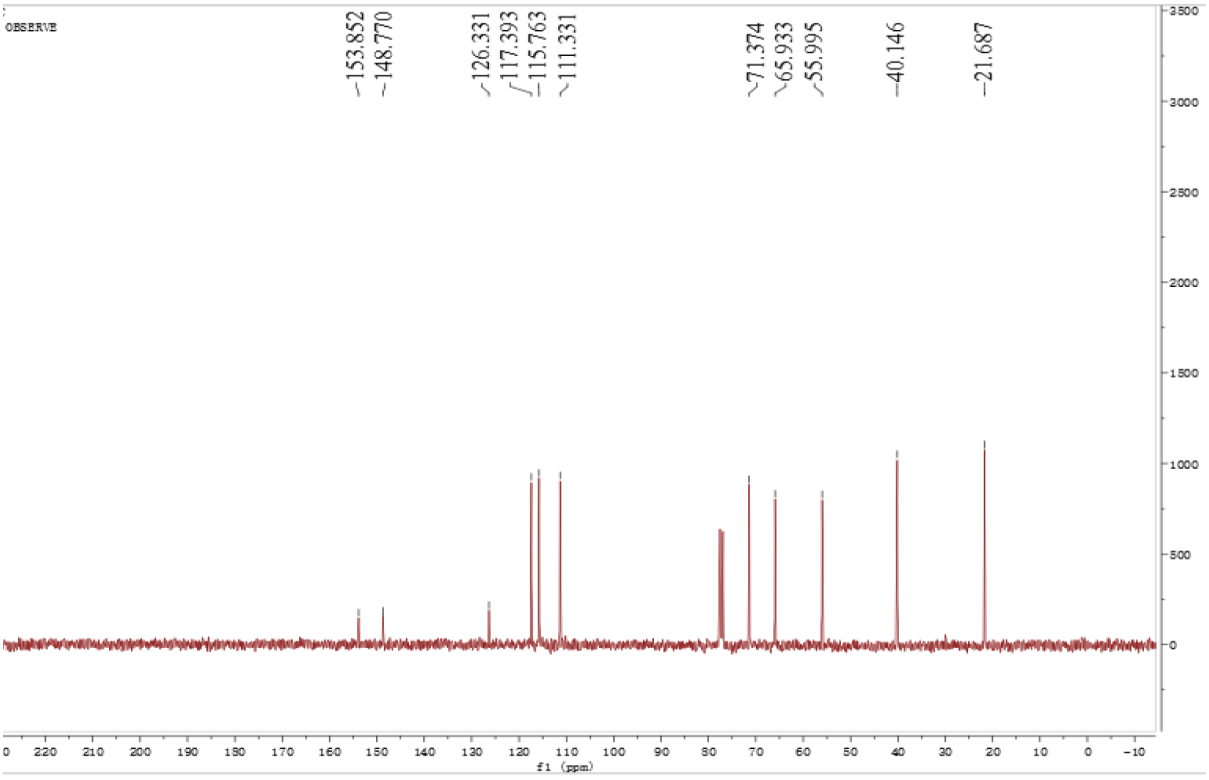

7.298
7.010
6.985
6.728
6.707
4.925
4.909
4.902
4.885
4.256
4.252
4.240
4.237
4.224
4.221
4.212
4.208
4.196
4.193
2.612
2.593
2.574
2.555
2.302
2.298
2.286
2.282
2.270
2.266
2.253
2.250
1.772
1.745
1.717
1.713
1.685
1.416
1.401
1.232
1.213
1.194
1.00
1.00
0.98
1.06
1.06
2.16
1.12
1.83
3.24
3.10
f1 (ppm)

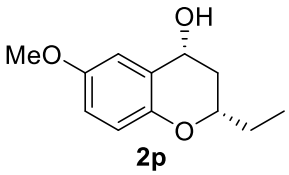

152.497
136.397
128.482
125.971
125.348
116.269
71.145
65.598
39.951
28.124
21.491
15.862
f1 (ppm)


OH
MeO
O

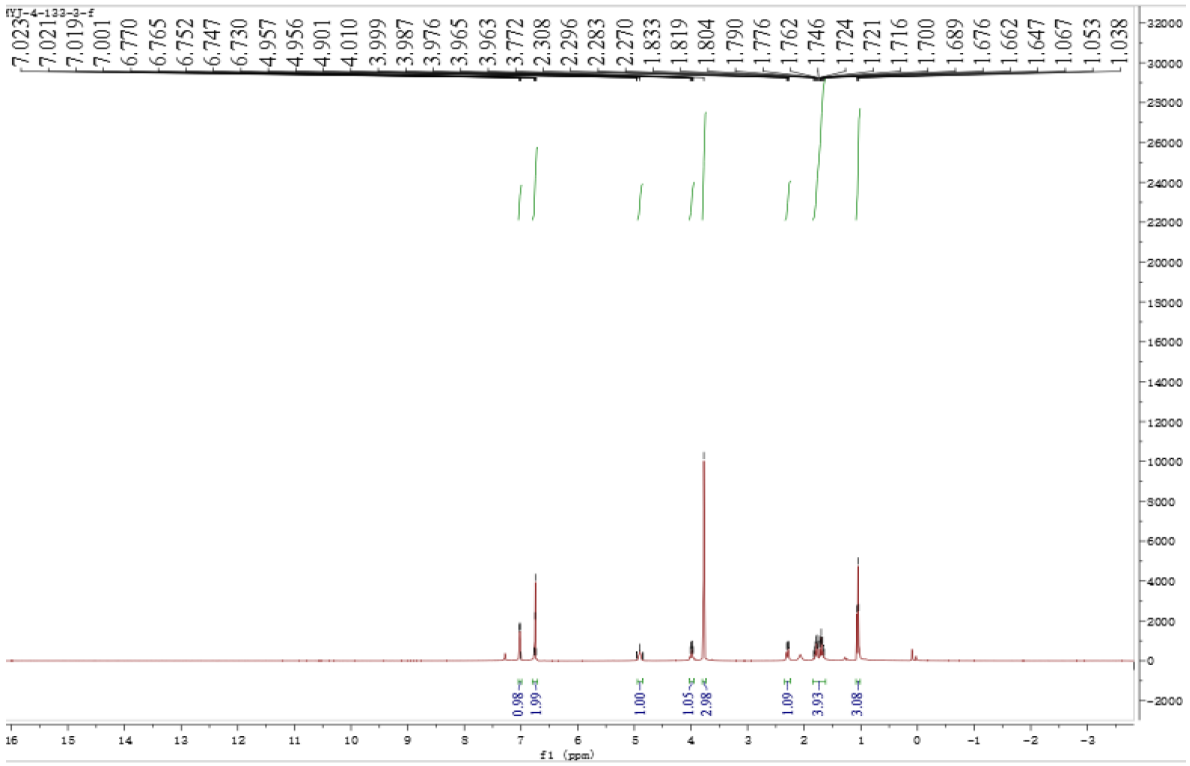
2o

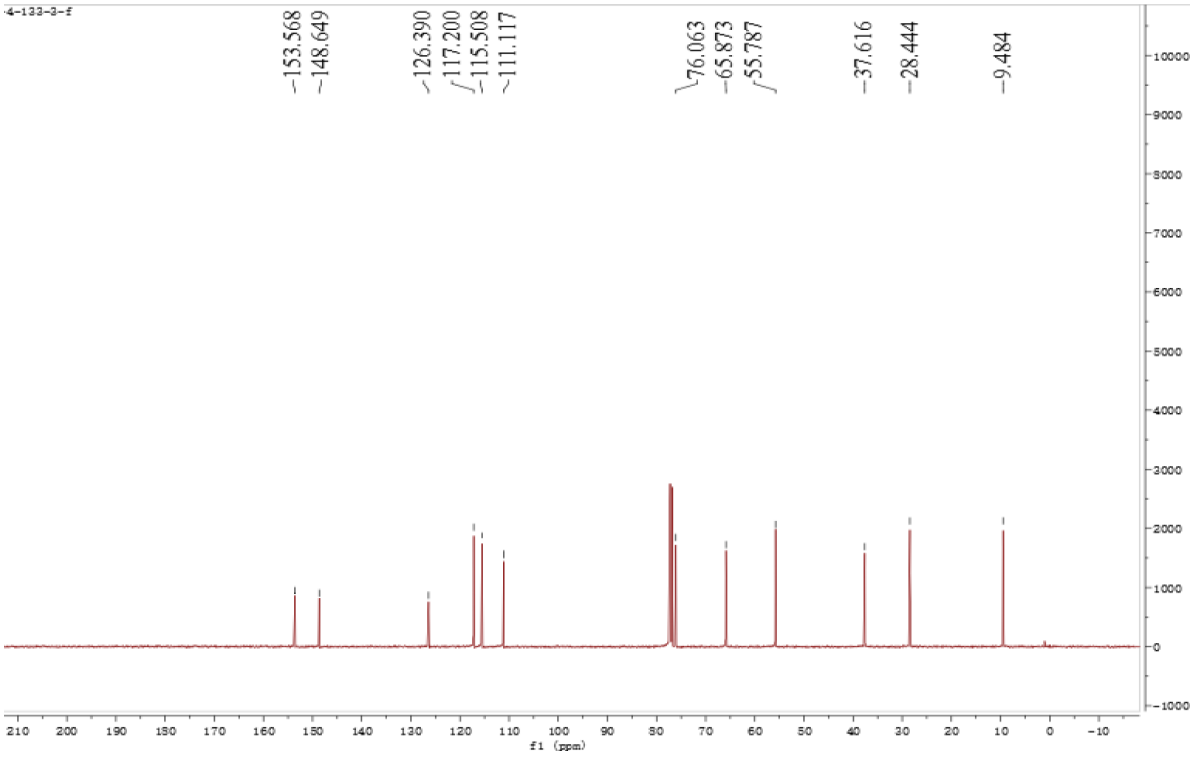

7.003
6.750
6.746
6.744
6.727
6.721
6.699
6.695
4.899
4.891
4.882
4.877
4.193
4.178
3.752
2.294
2.277
2.261
2.245
1.749
1.747
1.720
1.691
1.664
1.660
1.402
1.387
0.96
1.92
1.11
1.15
3.00
1.23
1.72
3.37
f1 (ppm)

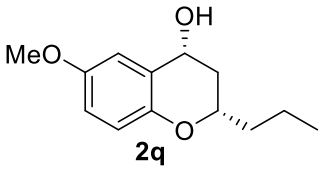

153.852
148.770
126.331
117.393
115.763
111.331
71.374
65.933
55.995
40.146
21.687
f1 (ppm)


OH
MeO
O

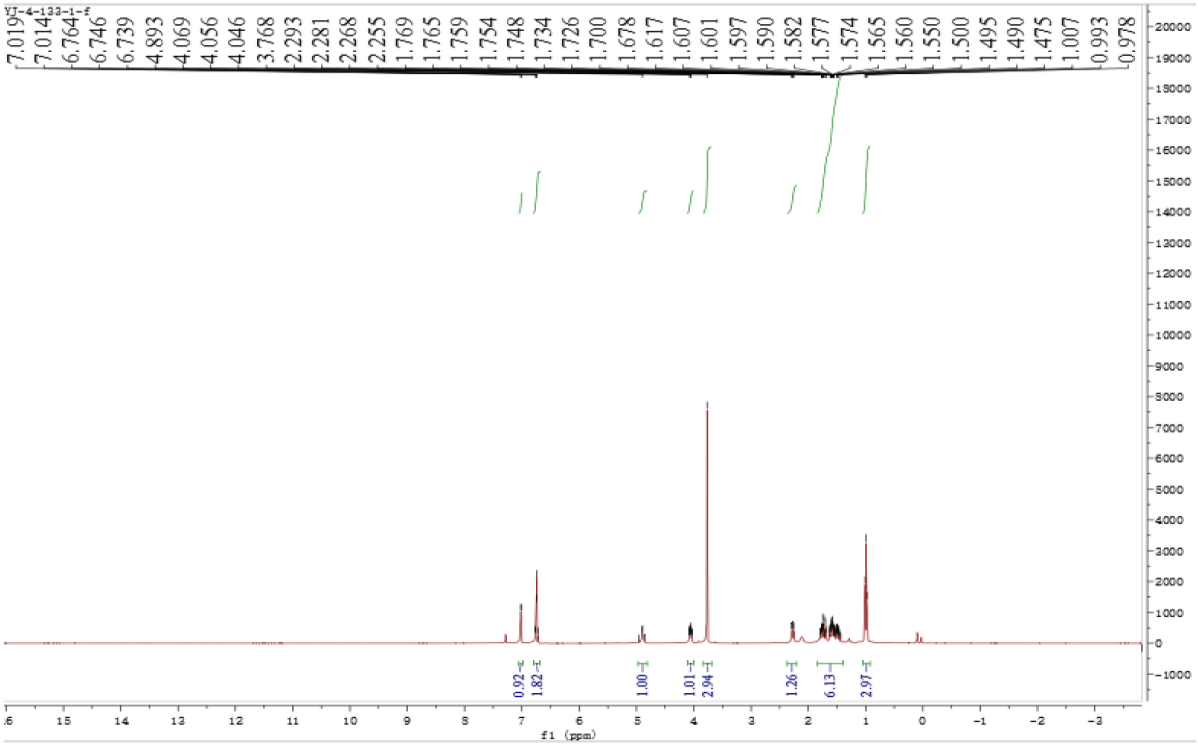
2p

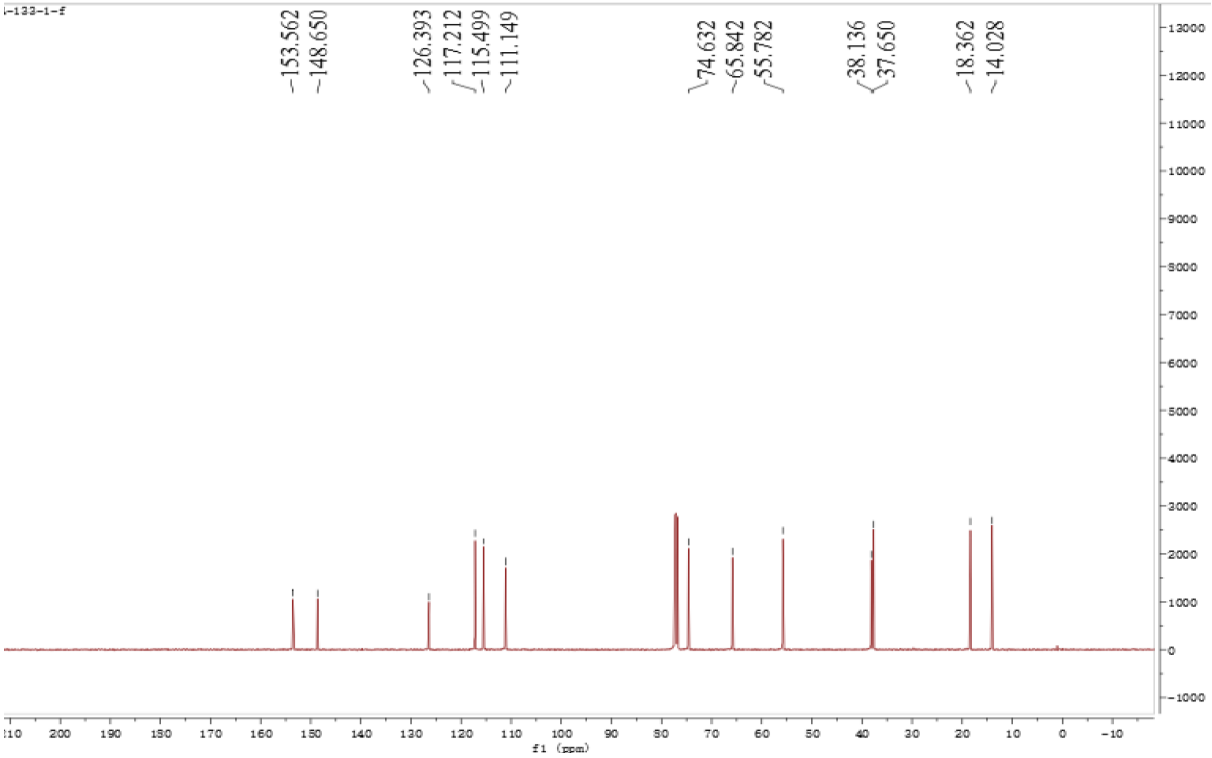

7.023
7.021
7.019
7.001
6.770
6.765
6.752
6.747
6.730
4.957
4.956
4.901
4.010
3.999
3.987
3.976
3.965
3.963
3.772
2.308
2.296
2.283
2.270
1.833
1.819
1.804
1.790
1.776
1.762
1.746
1.724
1.721
1.716
1.700
1.689
1.676
1.662
1.647
1.067
1.053
1.038
0.98
1.99
1.00
1.05
2.98
1.09
3.93
3.08
f1 (ppm)

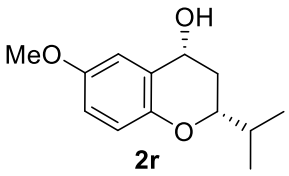

153.568
148.649
126.390
117.200
115.508
111.117
76.063
65.873
55.787
37.616
28.444
9.484
f1 (ppm)


OH
MeO
O

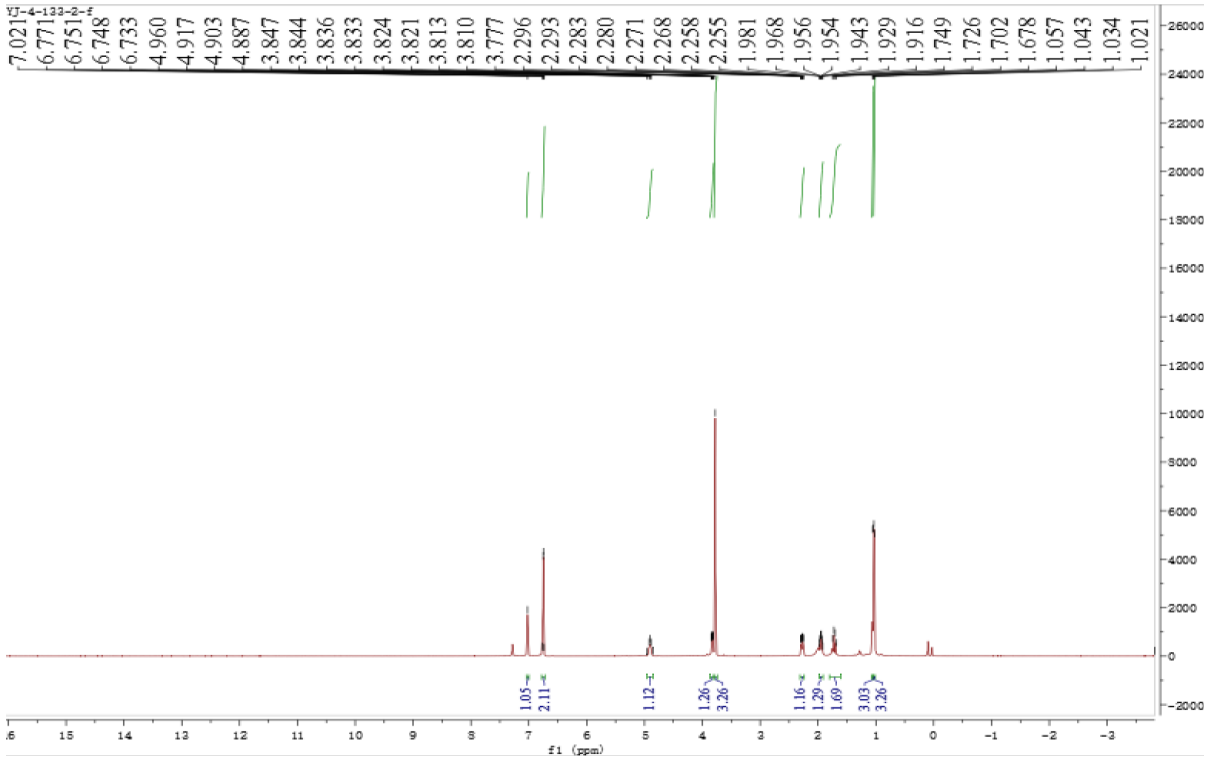
2q

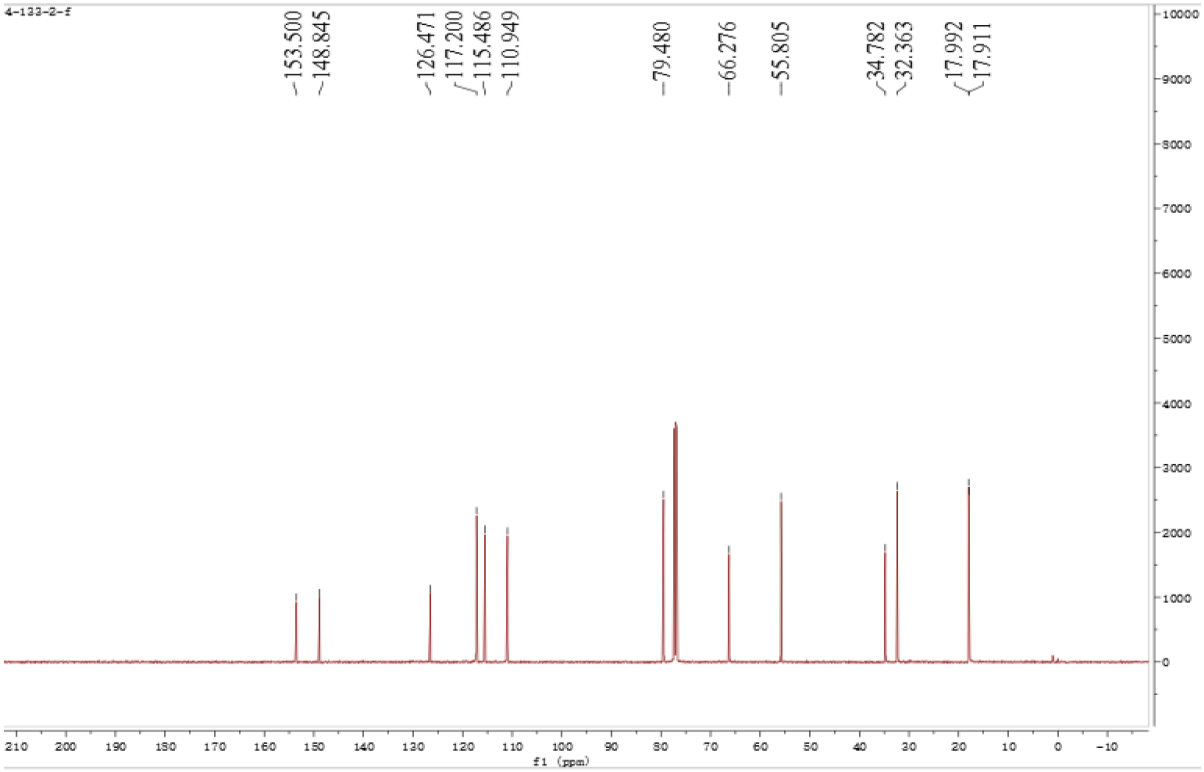

7.019
7.014
6.764
6.746
6.739
4.893
4.069
4.056
4.046
3.768
2.293
2.281
2.268
2.255
1.769
1.765
1.759
1.754
1.748
1.734
1.726
1.700
1.678
1.617
1.607
1.601
1.597
1.590
1.582
1.577
1.574
1.565
1.560
1.550
1.500
1.495
1.490
1.475
1.007
0.993
0.978
0.92
1.82
1.00
1.01
2.94
1.26
6.13
2.97
f1 (ppm)

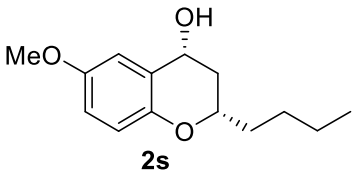

153.562
148.650
126.393
117.212
115.499
111.149
74.632
65.842
55.782
38.136
37.650
18.362
14.028
f1 (ppm)


OH
MeO
O

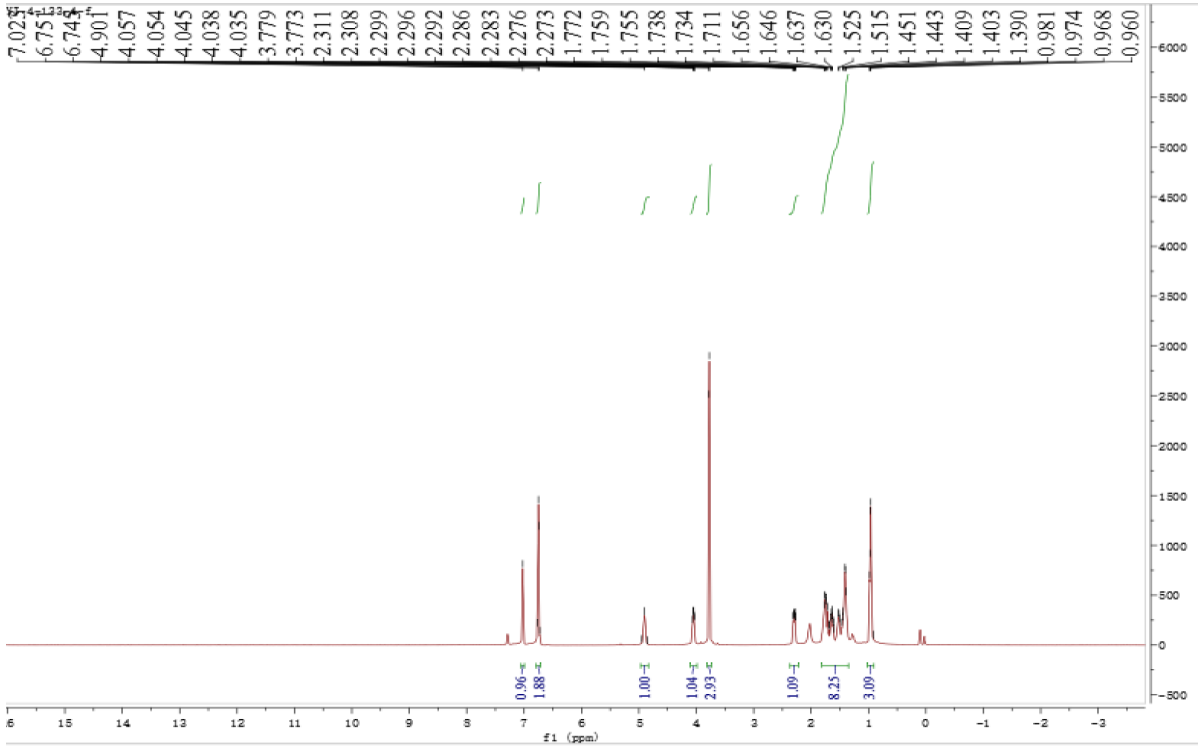
2r

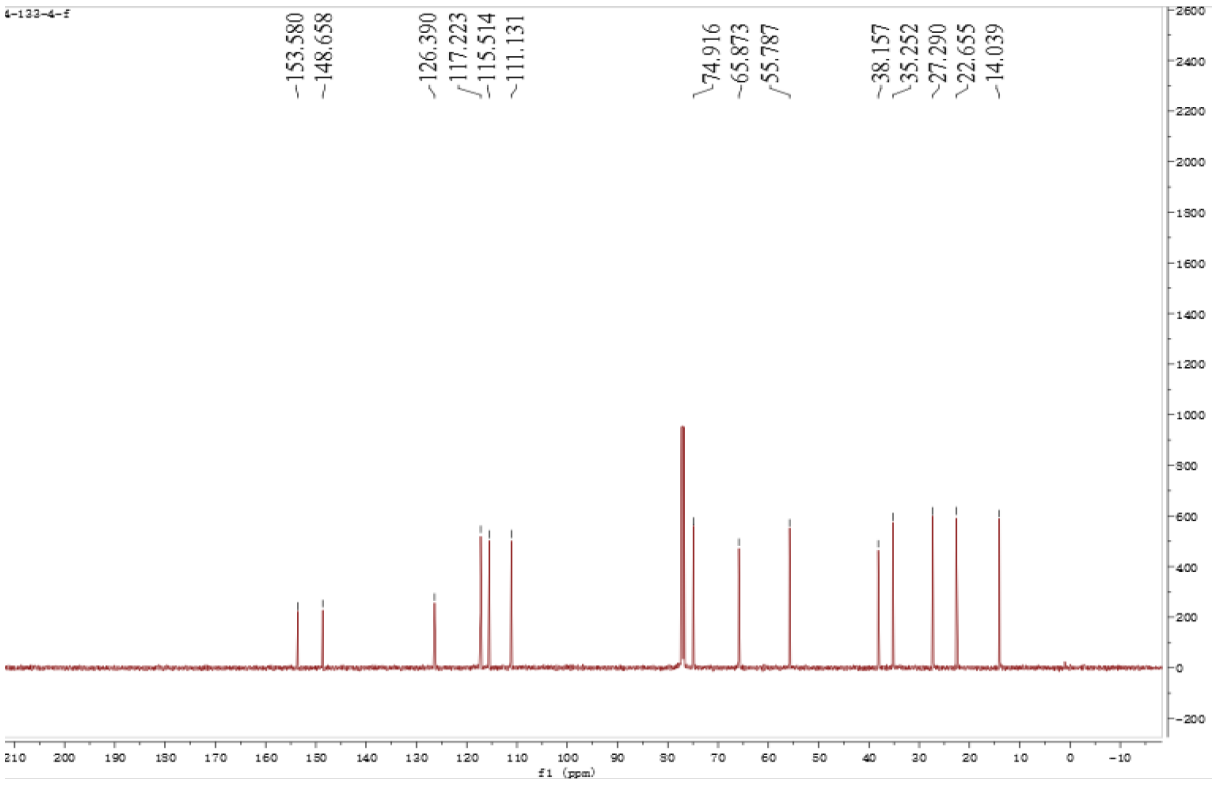

YJ-4-133-2-f
7.021
6.771
6.751
6.748
6.733
4.960
4.917
4.903
4.887
3.847
3.844
3.836
3.833
3.824
3.821
3.813
3.810
3.777
2.296
2.293
2.283
2.280
2.271
2.268
2.258
2.255
1.981
1.968
1.956
1.954
1.943
1.929
1.916
1.749
1.726
1.702
1.678
1.057
1.043
1.034
1.021
1.05
2.11
1.12
1.26
3.26
1.16
1.29
1.69
3.03
3.26
f1 (ppm)

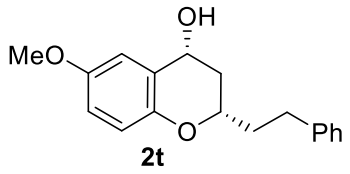

4-133-2-f
153.500
148.845
126.471
117.200
115.486
110.949
79.480
66.276
55.805
34.782
32.363
17.992
17.911
f1 (ppm)


OH
MeO
O

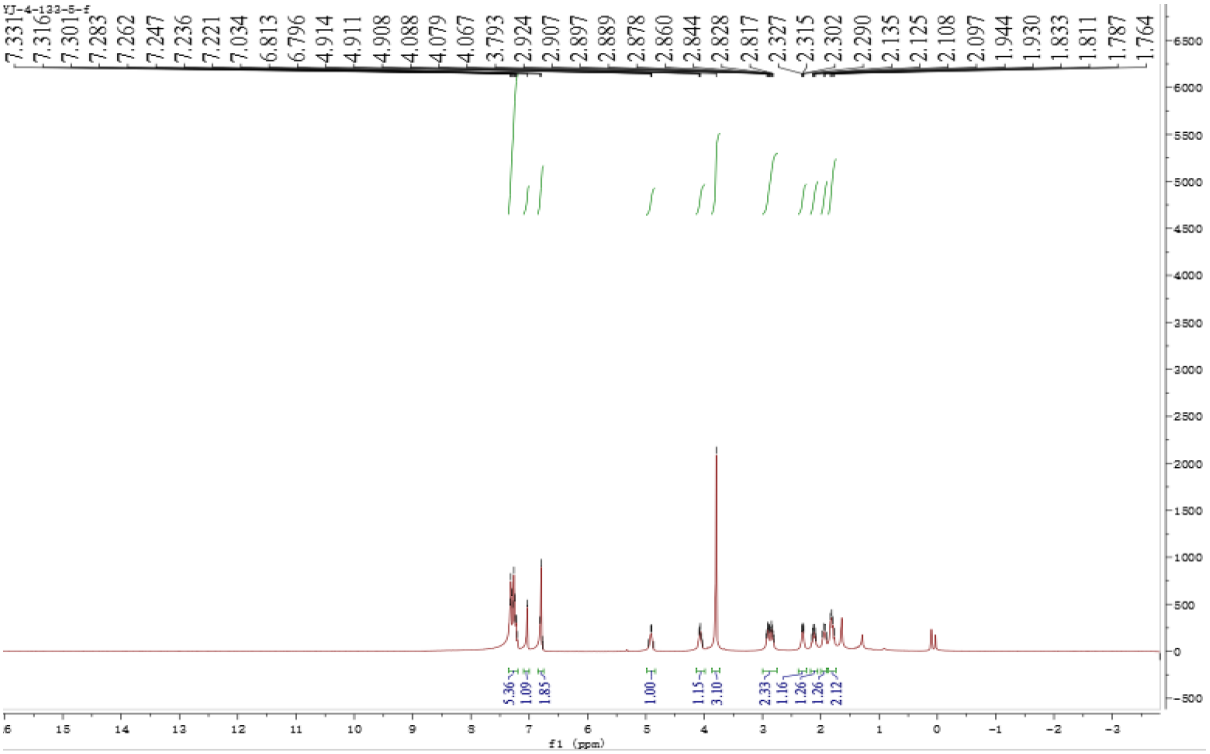
2s

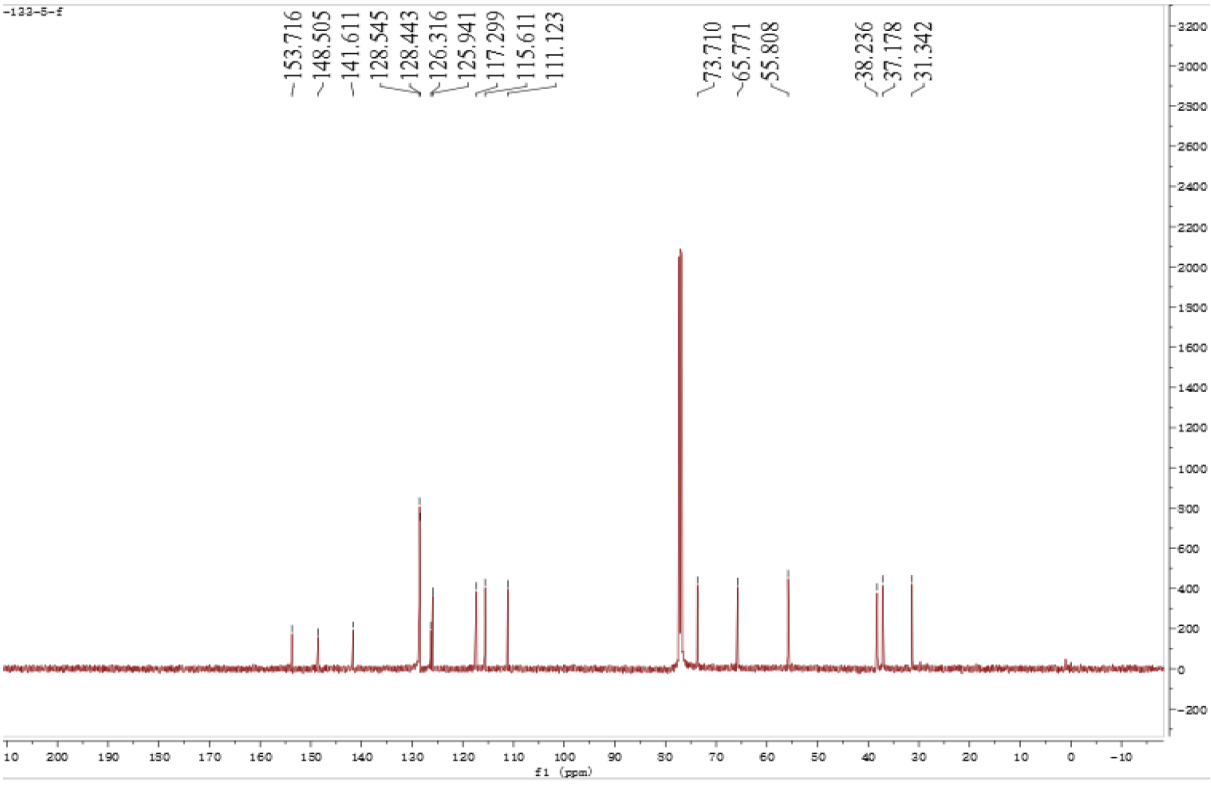

7.023
6.751
6.743
4.901
4.057
4.054
4.045
4.038
4.035
3.779
3.773
2.311
2.308
2.299
2.296
2.292
2.286
2.283
2.276
2.273
1.772
1.759
1.755
1.738
1.734
1.711
1.656
1.646
1.637
1.630
1.525
1.515
1.451
1.443
1.409
1.403
1.390
0.981
0.974
0.968
0.960
0.96
1.88
1.00
1.04
2.93
1.09
8.25
3.09
f1 (ppm)

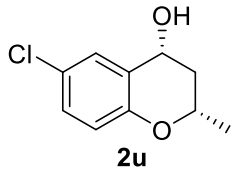

153.580
148.658
126.390
117.223
115.514
111.131
74.916
65.873
55.787
38.157
35.252
27.290
22.655
14.039
f1 (ppm)


OH
MeO
O
Ph

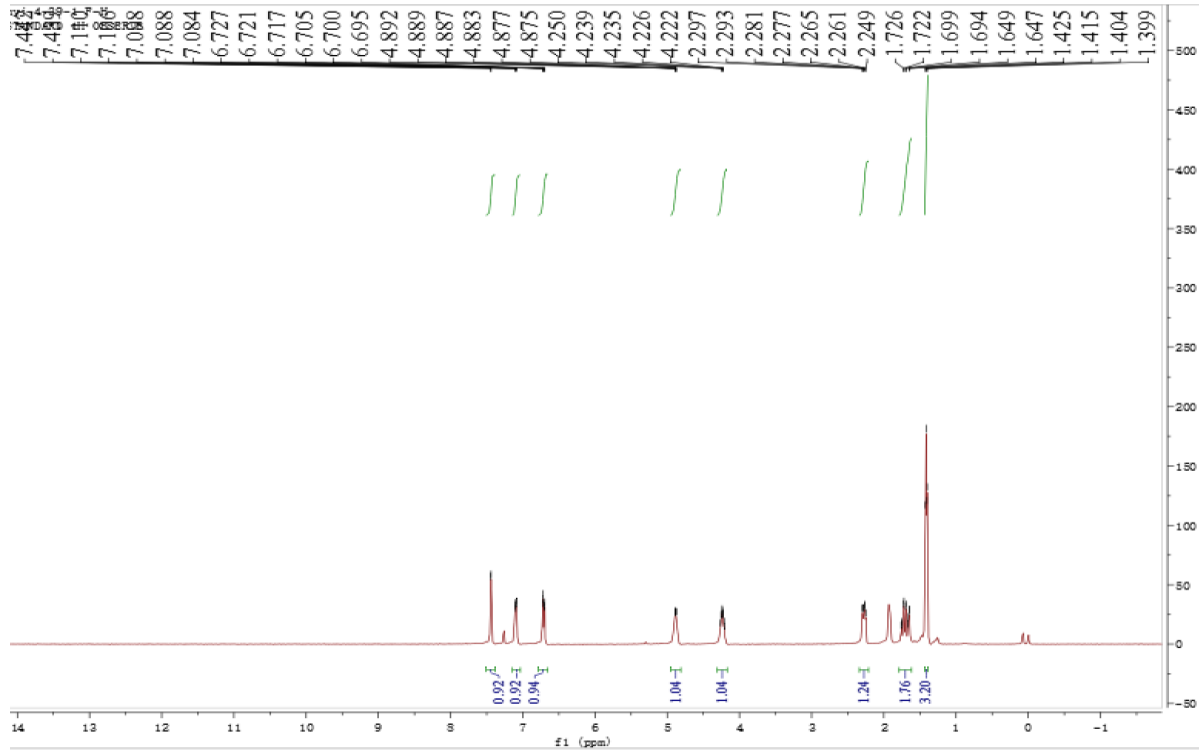
2t

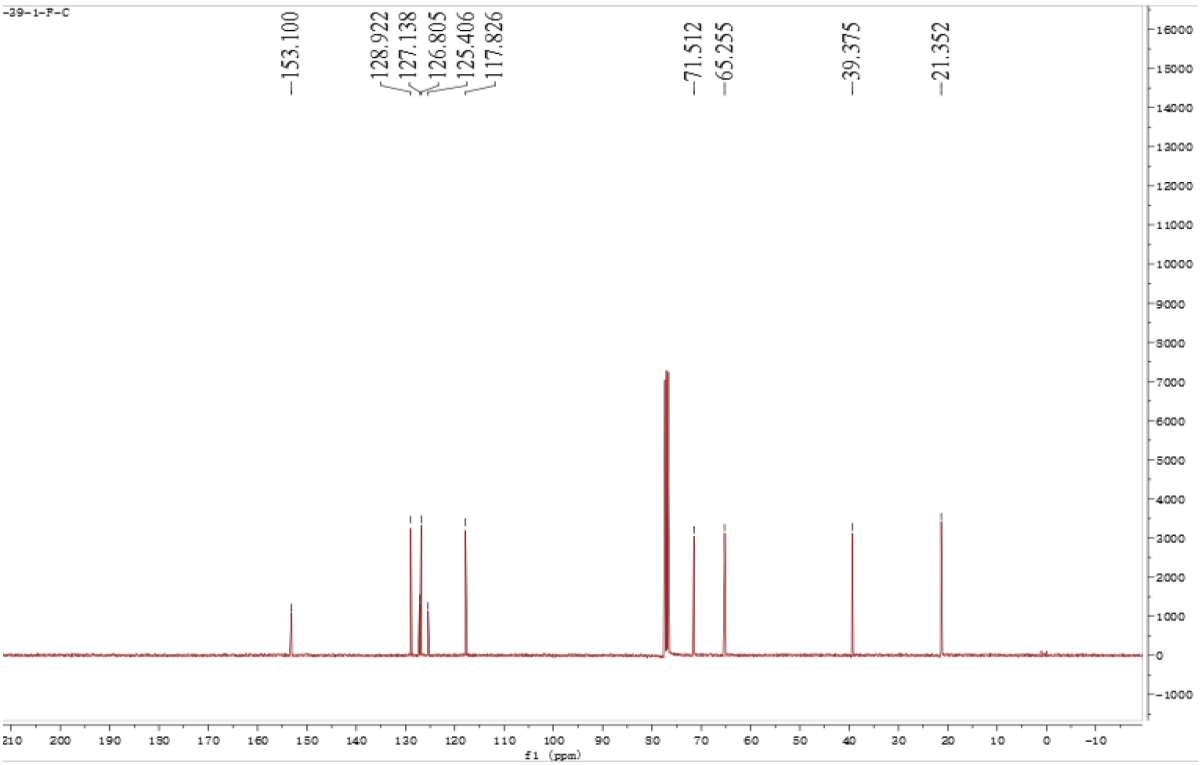

7.331
7.316
7.301
7.283
7.262
7.247
7.236
7.221
7.034
6.813
6.796
4.914
4.911
4.908
4.088
4.079
4.067
3.793
2.924
2.907
2.897
2.889
2.878
2.860
2.844
2.828
2.817
2.327
2.315
2.302
2.290
2.135
2.125
2.108
2.097
1.944
1.930
1.833
1.811
1.787
1.764
5.36
1.09
1.85
1.00
1.15
3.10
2.33
1.16
1.26
1.26
2.12
f1 (ppm)

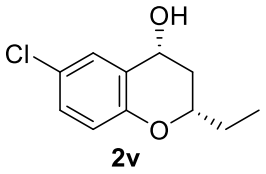

153.716
148.505
141.611
128.545
128.443
126.316
125.941
117.299
115.611
111.123
73.710
65.771
55.808
38.236
37.178
31.342
f1 (ppm)


OH
Cl
O

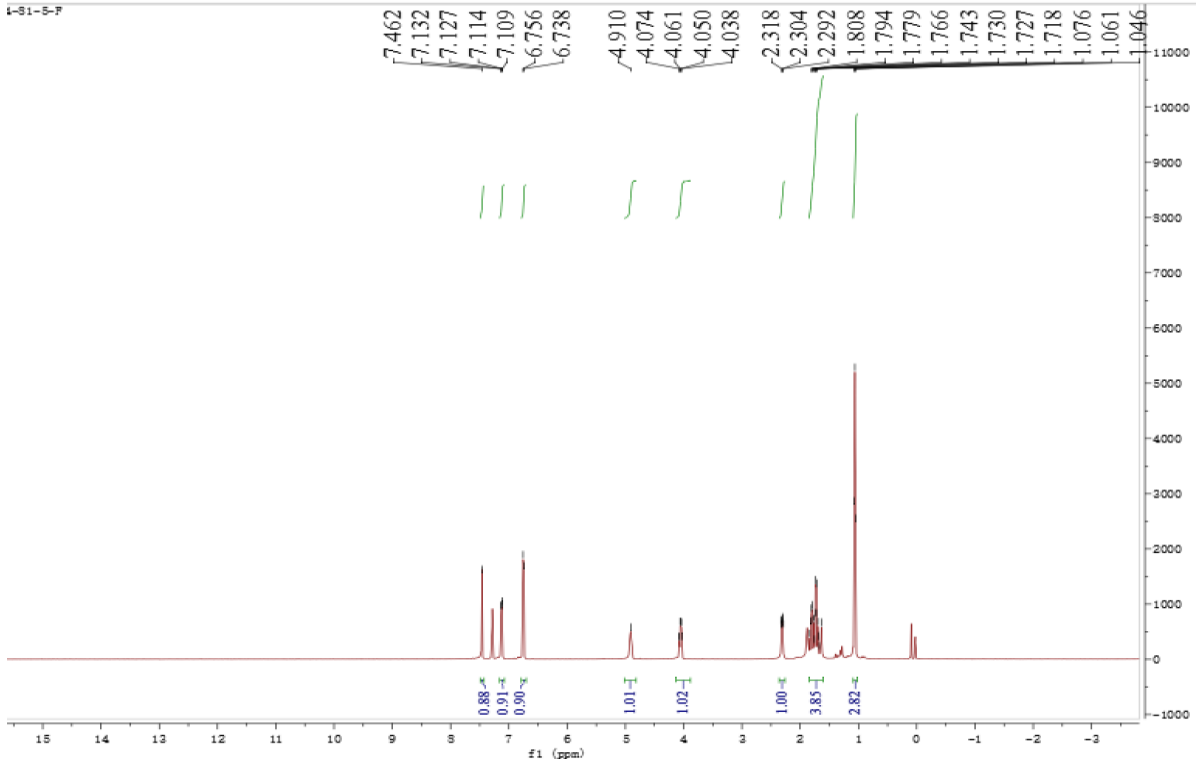
2u

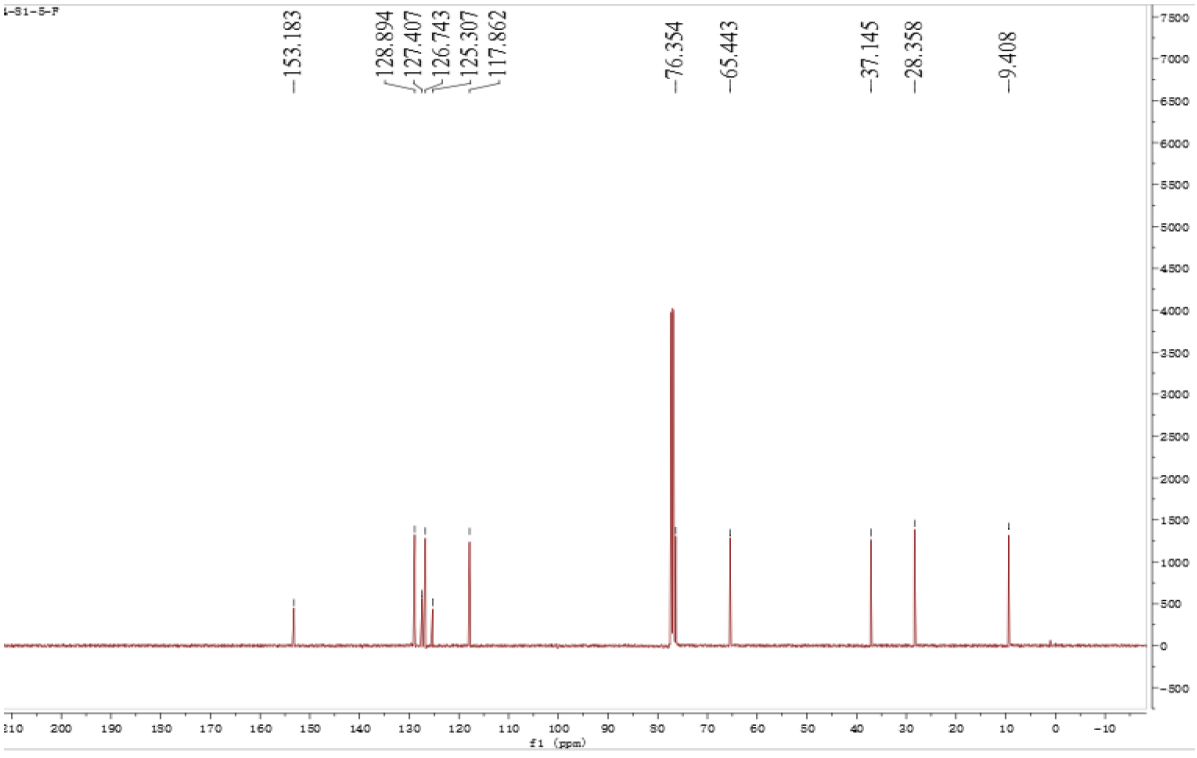

7.404
7.402
7.119
7.117
7.088
7.084
6.727
6.721
6.717
6.705
6.700
6.695
4.892
4.889
4.887
4.883
4.877
4.875
4.250
4.239
4.235
4.226
4.222
2.297
2.293
2.281
2.277
2.265
2.261
2.249
1.726
1.722
1.699
1.694
1.649
1.647
1.425
1.415
1.404
1.399
0.92
0.92
0.94
1.04
1.04
1.24
1.76
3.20
f1 (ppm)

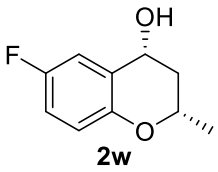

-39-1-F-C
153.100
128.922
127.138
126.805
125.406
117.826
71.512
65.255
39.375
21.352
f1 (ppm)


OH
Cl
O

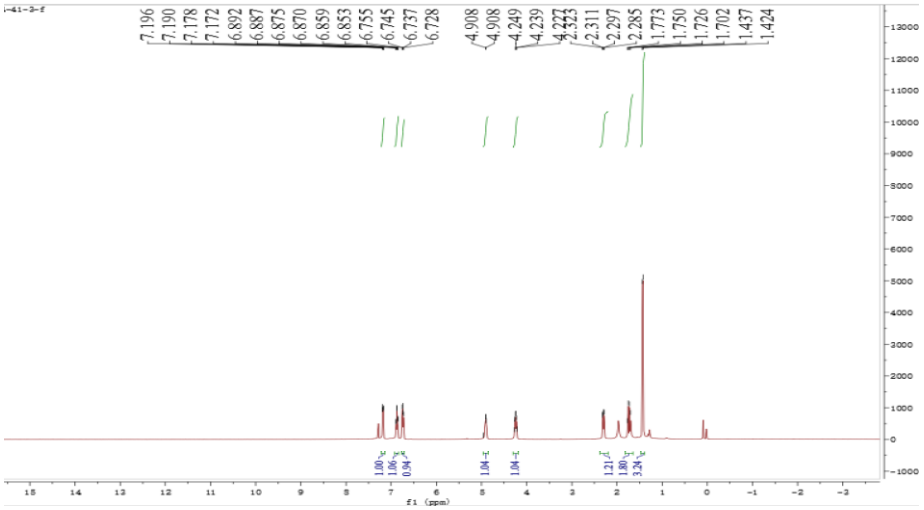
2v

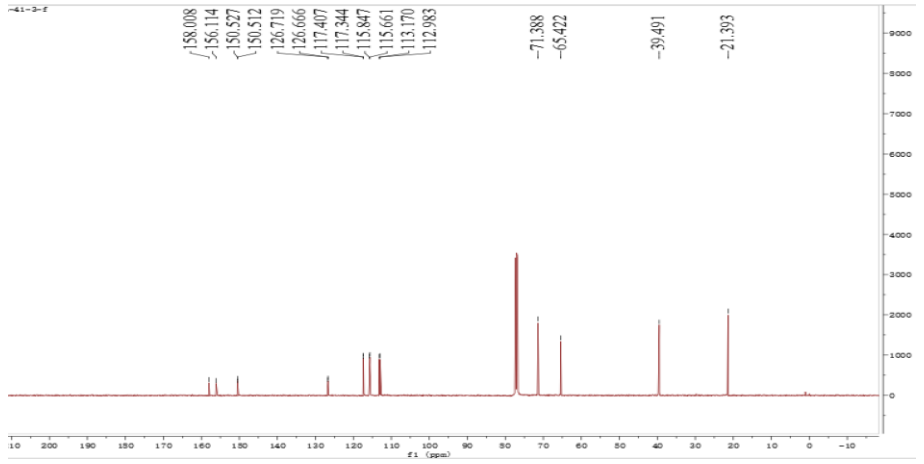

4-S1-5-F
7.462
7.132
7.127
7.114
7.109
6.756
6.738
4.910
4.074
4.061
4.050
4.038
2.318
2.304
2.292
1.808
1.794
1.779
1.766
1.743
1.730
1.727
1.718
1.076
1.061
1.046
0.88
0.91
0.90
1.01
1.02
1.00
3.85
2.82
f1 (ppm)

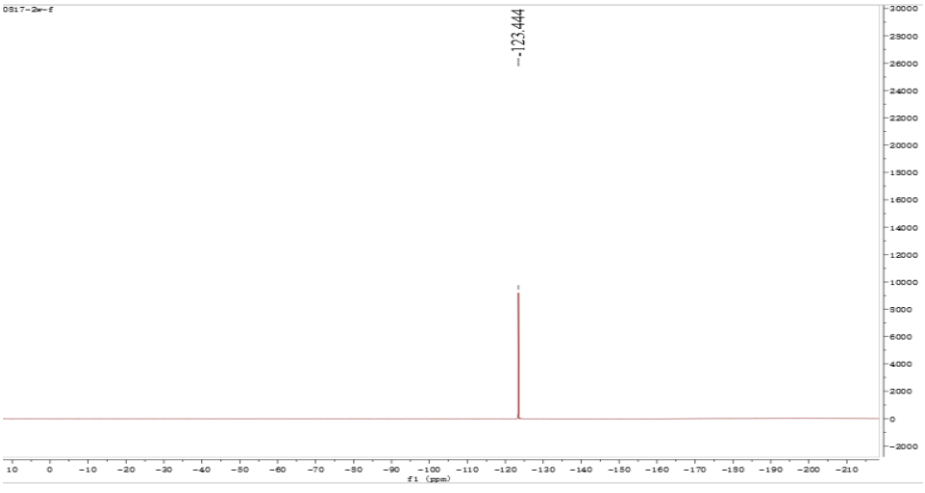

4-S1-5-F
153.183
128.894
127.407
126.743
125.307
117.862
76.354
65.443
37.145
28.358
9.408
f1 (ppm)

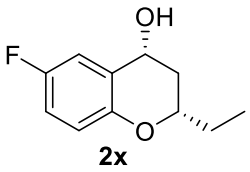

OH
F
O

2w

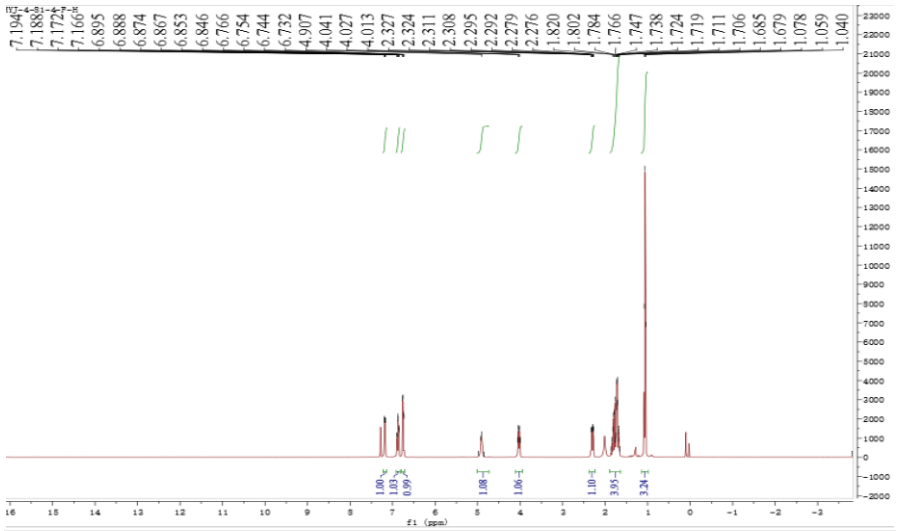

7.196
7.190
7.178
7.172
6.892
6.887
6.875
6.870
6.859
6.853
6.755
6.745
6.737
6.728
4.908
4.908
4.249
4.239
4.227
4.223
2.311
2.297
2.285
1.773
1.750
1.726
1.702
1.437
1.424
f1 (ppm)

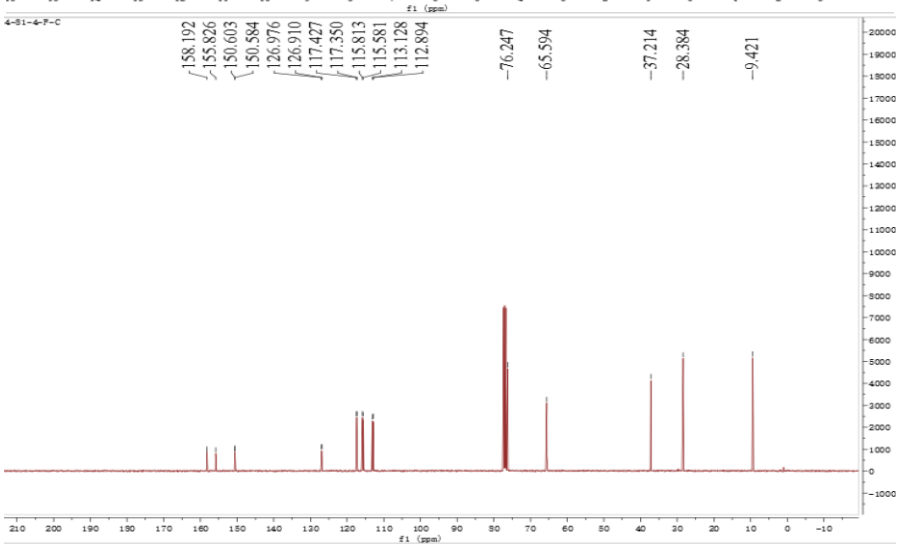

158.008
156.114
150.527
150.512
126.719
126.666
117.407
117.344
115.847
115.661
113.170
112.983
71.388
65.422
39.491
21.393
f1 (ppm)

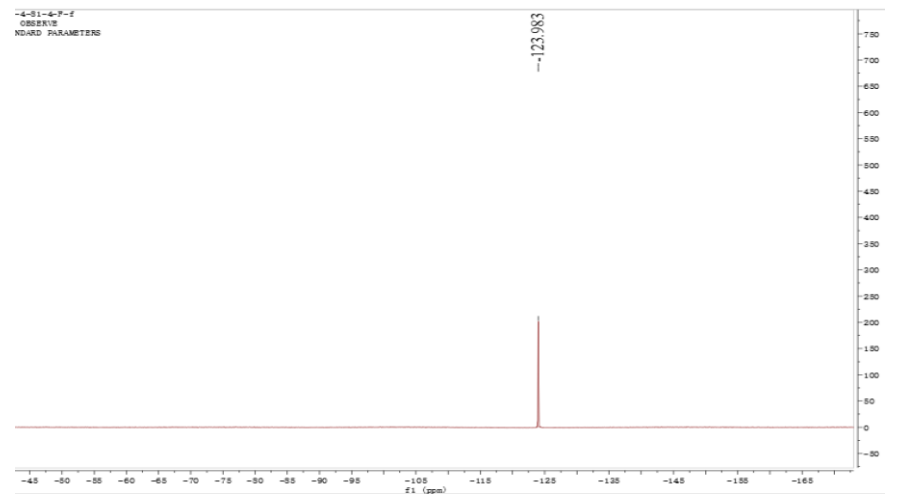

-123.444
f1 (ppm)

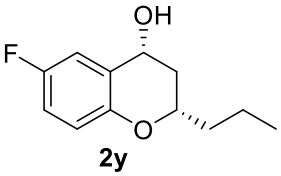

OH
F
O

2x

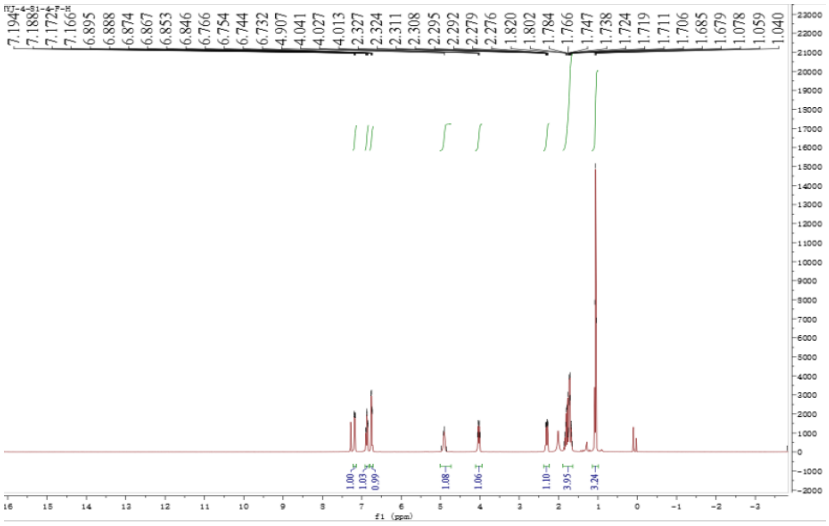

7.194
7.188
7.172
7.166
6.895
6.888
6.874
6.867
6.853
6.846
6.766
6.754
6.744
6.732
4.907
4.041
4.027
4.013
2.327
2.324
2.311
2.308
2.295
2.292
2.279
2.276
1.820
1.802
1.784
1.766
1.747
1.738
1.724
1.719
1.711
1.706
1.685
1.679
1.078
1.059
1.040
f1 (ppm)

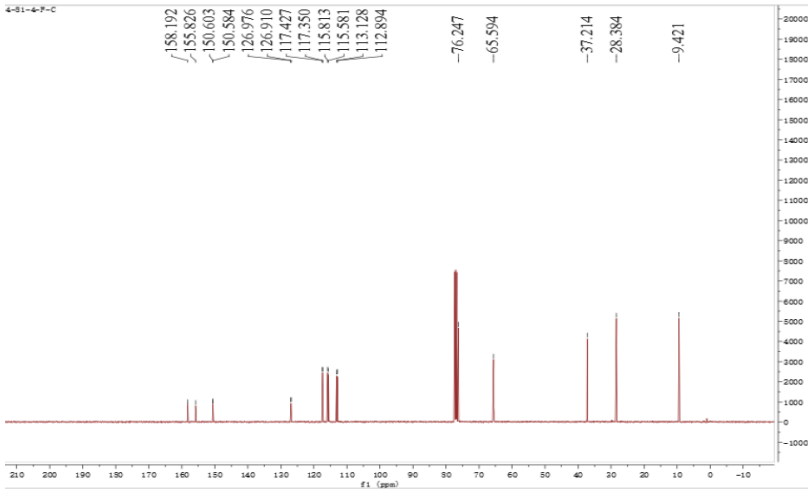

158.192
155.826
150.603
150.584
126.976
126.910
117.427
117.350
115.813
115.581
113.128
112.894
76.247
65.594
37.214
28.384
9.421
f1 (ppm)

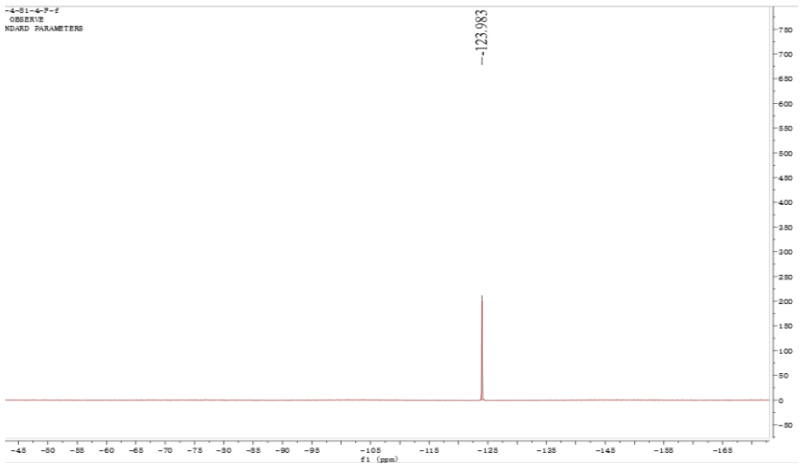

123.983
f1 (ppm)

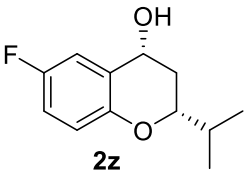

OH
F
O

2y

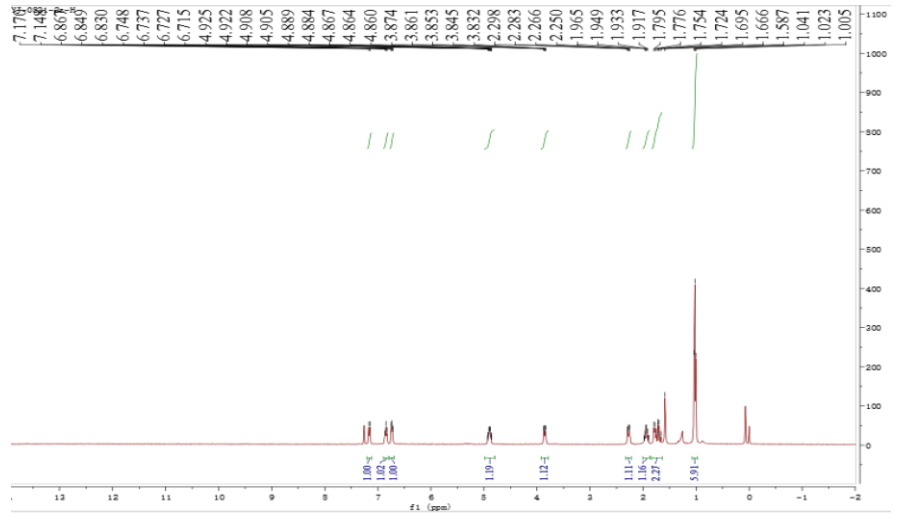

7.194
7.188
7.172
7.166
6.895
6.888
6.874
6.867
6.853
6.846
6.766
6.754
6.744
6.732
4.907
4.041
4.027
4.013
2.327
2.324
2.311
2.308
2.295
2.292
2.279
2.276
1.820
1.802
1.784
1.766
1.747
1.738
1.724
1.719
1.711
1.706
1.685
1.679
1.078
1.059
1.040
1.00
1.03
0.99
1.08
1.06
1.10
3.95
3.24
f1 (ppm)

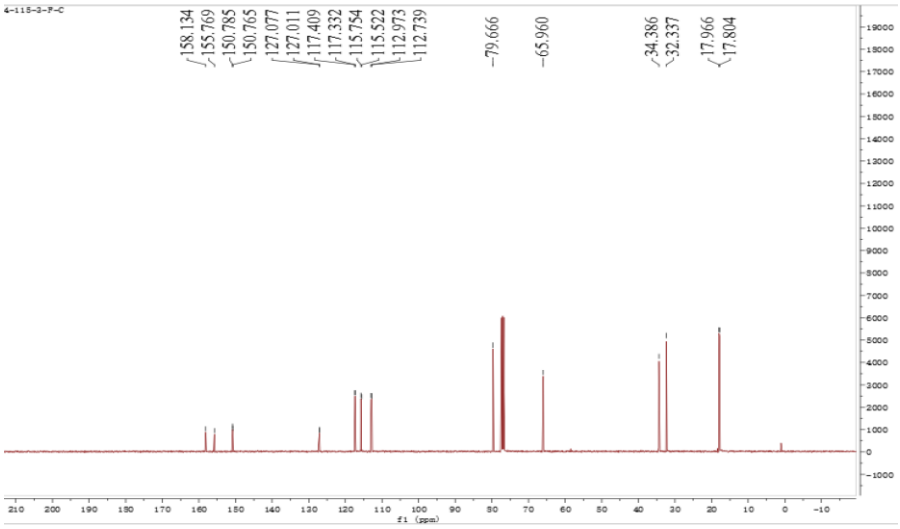

4-S1-4-F-C
158.192
155.826
150.603
150.584
126.976
126.910
117.427
117.350
115.813
115.581
113.128
112.894
76.247
65.594
37.214
28.384
9.421
f1 (ppm)

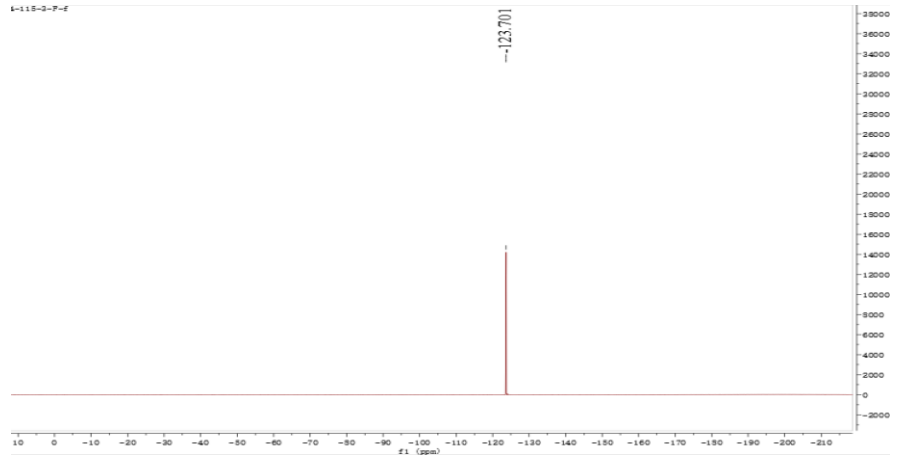

4-S1-4-F-f
OBSERVE
NDARD PARAMETERS
-123.983
f1 (ppm)

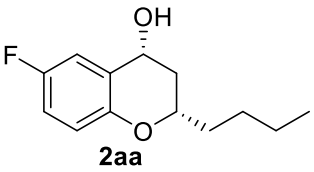

OH
F
O

2z

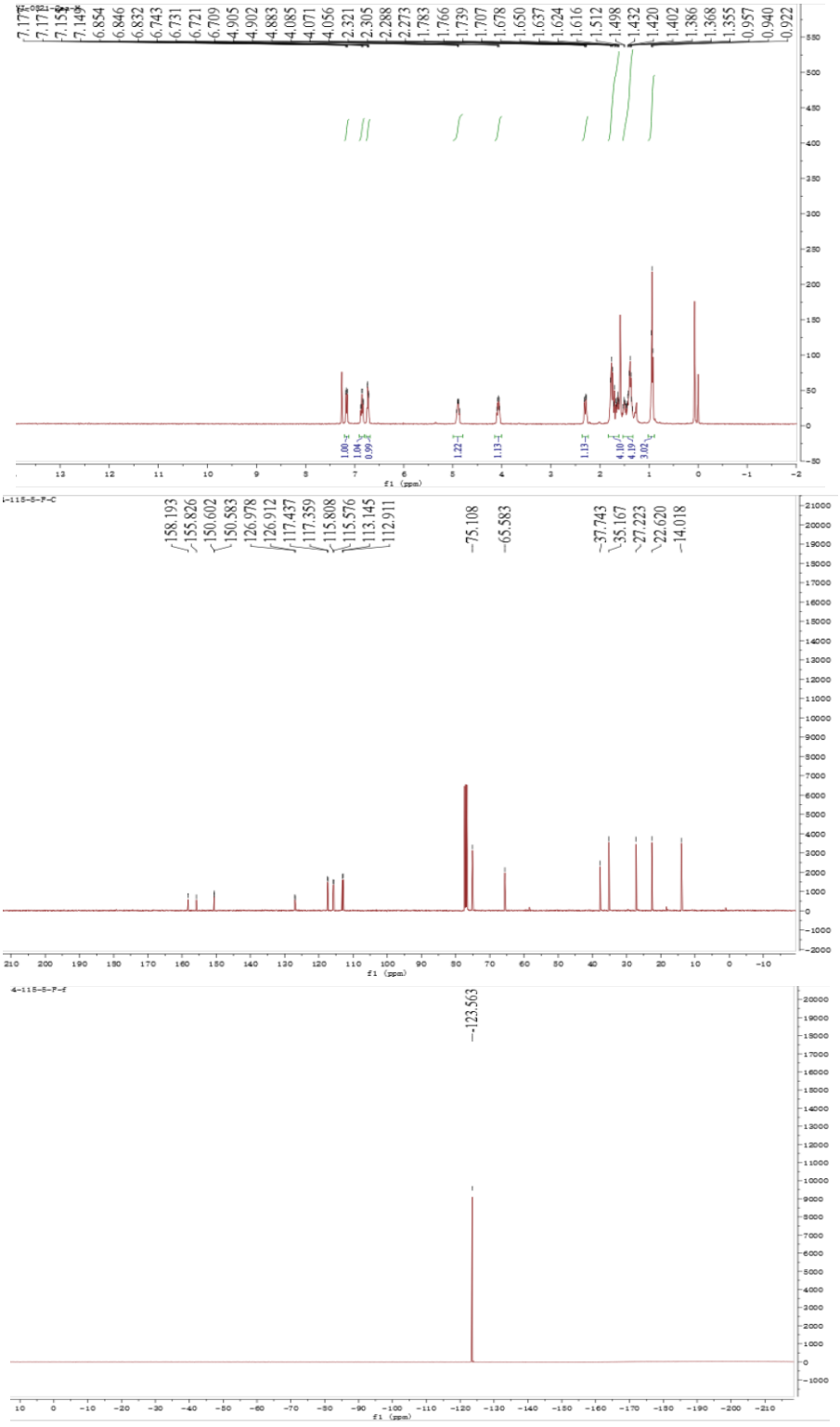

7.176
7.148
6.867
6.849
6.830
6.748
6.737
6.727
6.715
4.925
4.922
4.908
4.905
4.889
4.884
4.867
4.864
4.860
3.874
3.861
3.853
3.845
3.832
2.298
2.283
2.266
2.250
1.965
1.949
1.933
1.917
1.795
1.776
1.754
1.724
1.695
1.666
1.587
1.041
1.023
1.005
1.00
1.02
1.00
1.19
1.12
1.11
1.16
2.27
5.91
f1 (ppm)

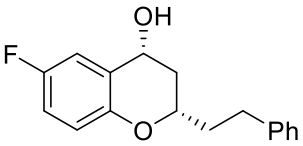

158.134
155.769
150.785
150.765
127.077
127.011
117.409
117.332
115.754
115.522
112.973
112.739
79.666
65.960
34.386
32.337
17.966
17.804
f1 (ppm)


123.701
f1 (ppm)

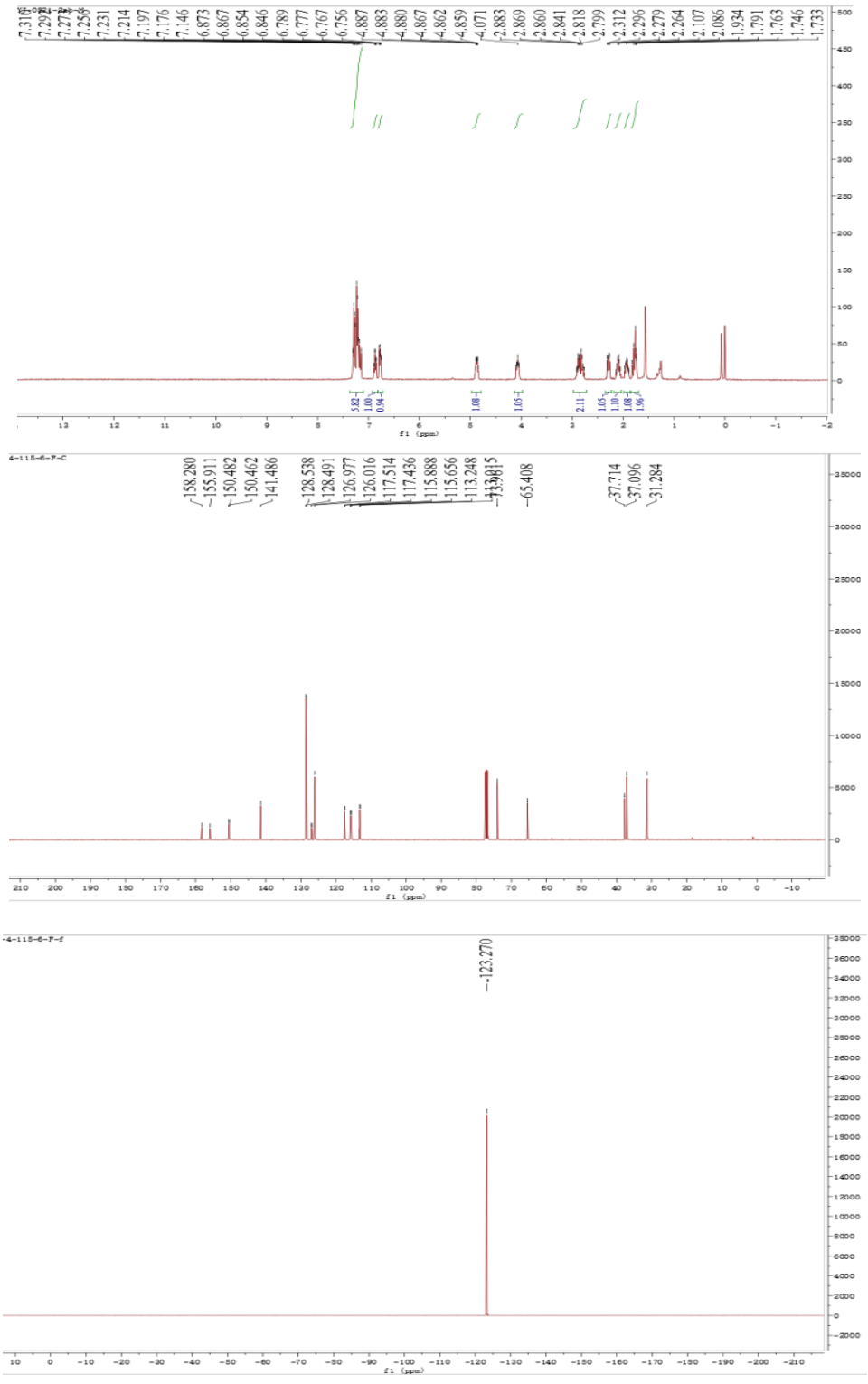

OH
F
O

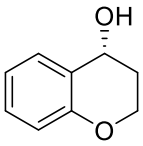
2aa


7.177
7.171
7.152
7.149
6.854
6.846
6.832
6.743
6.731
6.721
6.709
4.905
4.902
4.883
4.085
4.071
4.056
2.321
2.305
2.288
2.273
1.783
1.766
1.739
1.707
1.678
1.650
1.637
1.624
1.616
1.512
1.498
1.432
1.420
1.402
1.386
1.368
1.355
0.957
0.940
0.922
1.00
1.04
0.99
1.22
1.13
1.13
4.10
4.19
3.02
f1 (ppm)
158.193
155.826
150.602
150.583
126.978
126.912
117.437
117.359
115.808
115.576
113.145
112.911
75.108
65.583
37.743
35.167
27.223
22.620
14.018
f1 (ppm)
123.563
f1 (ppm)

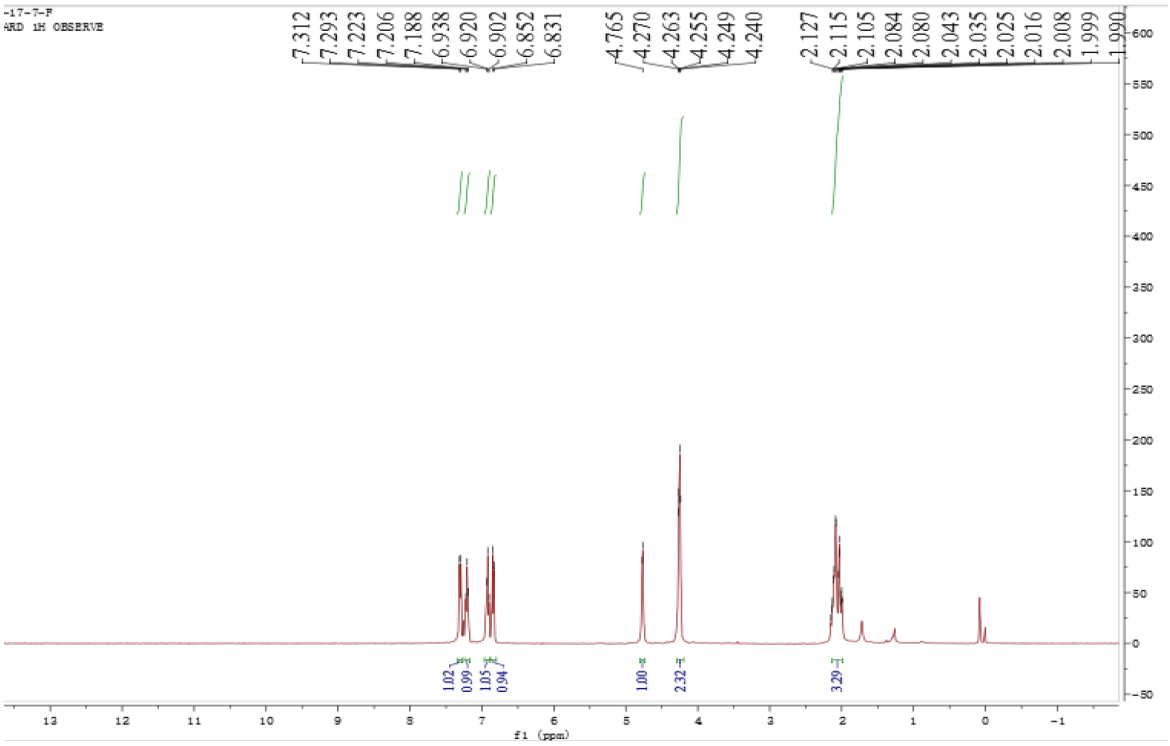


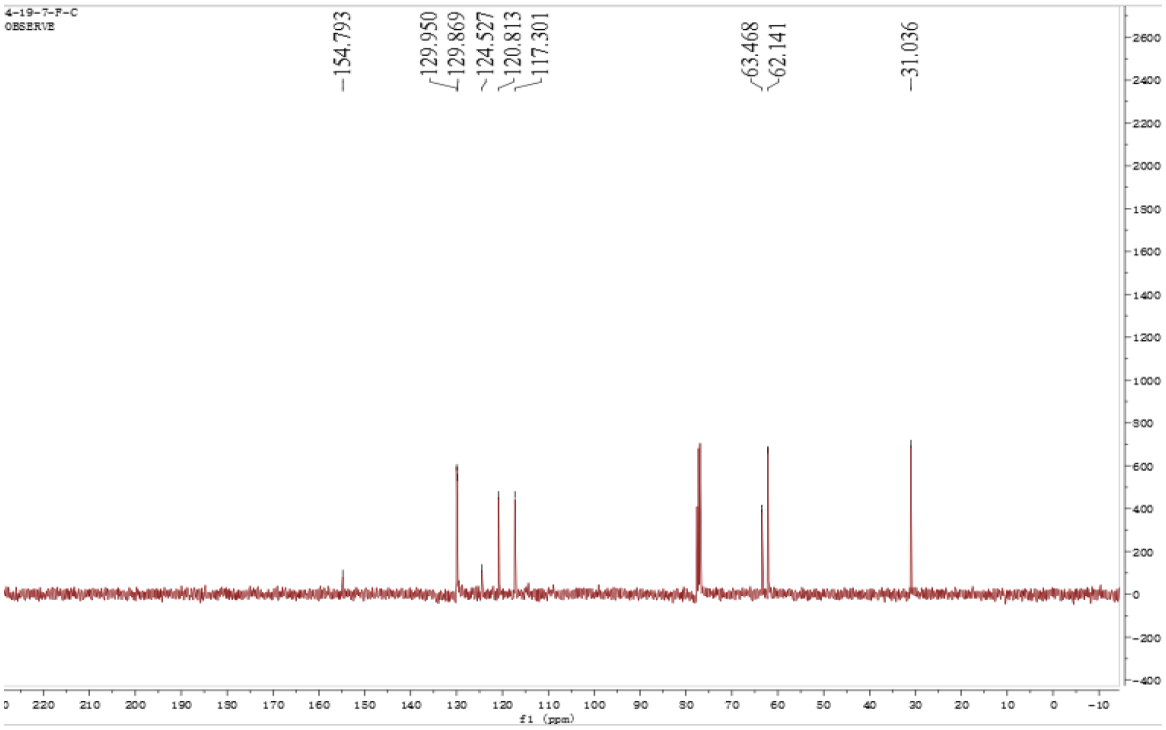
2ab

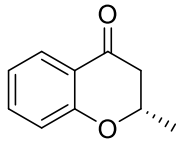



OH
O

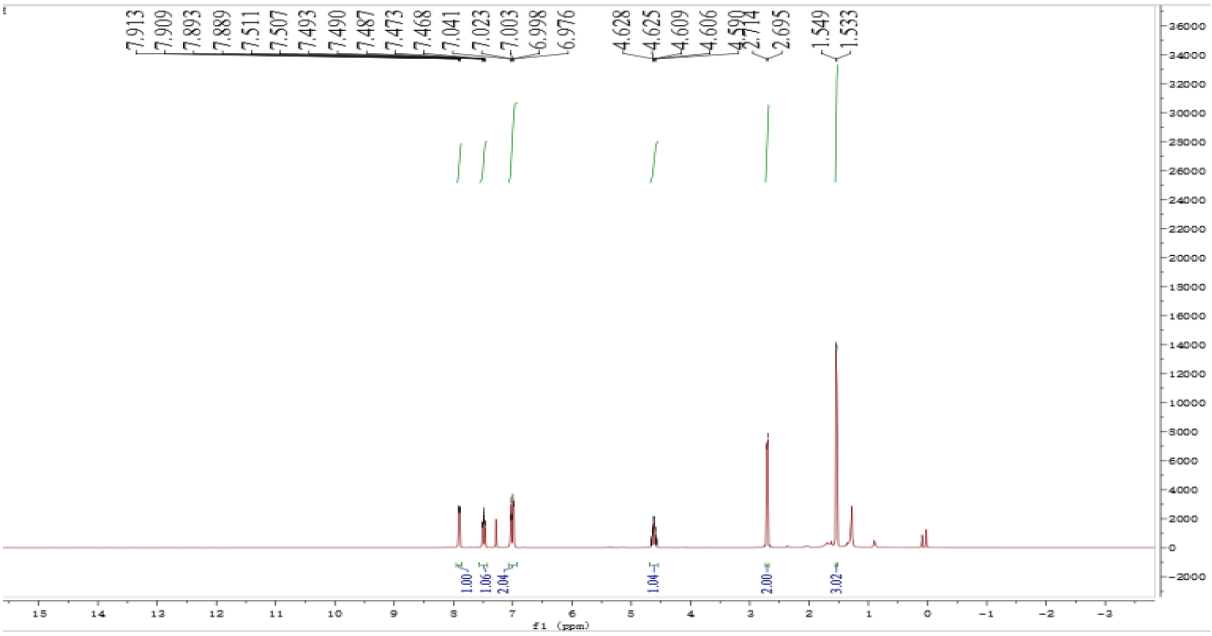
2ac

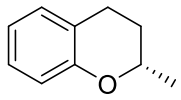

-17-7-F
ARD 1H OBSERVE
7.312
7.293
7.223
7.206
7.188
6.938
6.920
6.902
6.852
6.831
4.765
4.270
4.263
4.255
4.249
4.240
2.127
2.115
2.105
2.084
2.080
2.043
2.035
2.025
2.016
2.008
1.999
1.990
1.02
0.99
1.05
0.94
1.00
2.32
3.29
f1 (ppm)


4-19-7-F-C
OBSERVE
154.793
129.950
129.869
124.527
120.813
117.301
63.468
62.141
31.036
f1 (ppm)

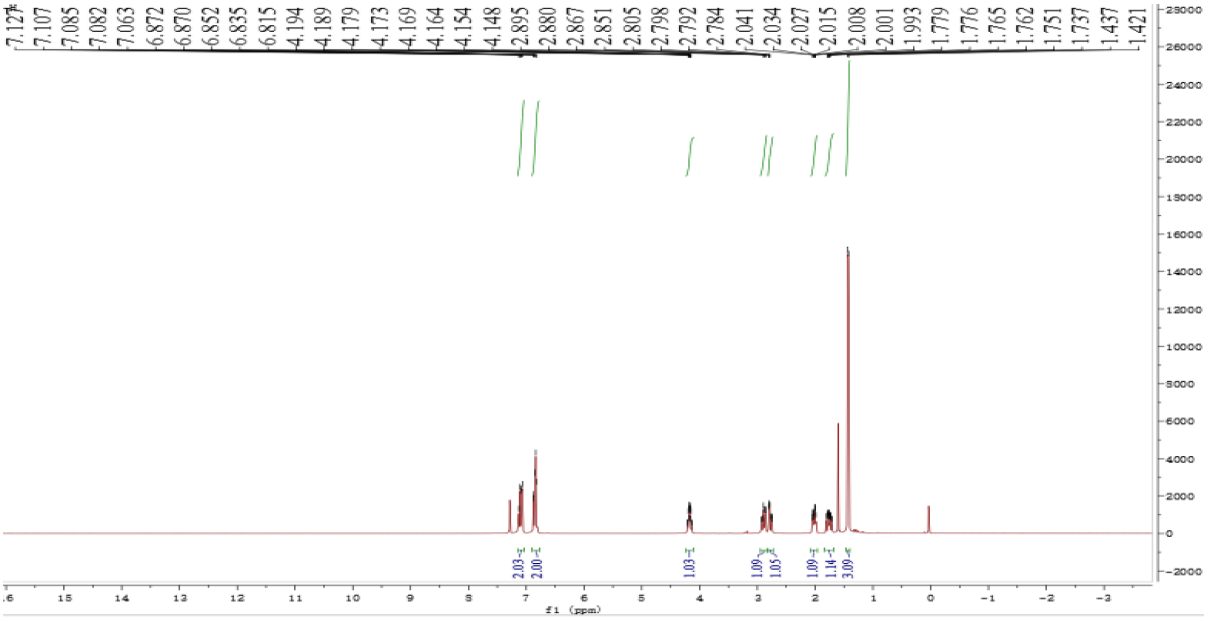


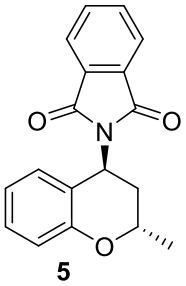
3


7.913
7.909
7.893
7.889
7.511
7.507
7.493
7.490
7.487
7.473
7.468
7.041
7.023
7.003
6.998
6.976
4.628
4.625
4.609
4.606
4.590
2.714
2.695
1.549
1.533
f1 (ppm)

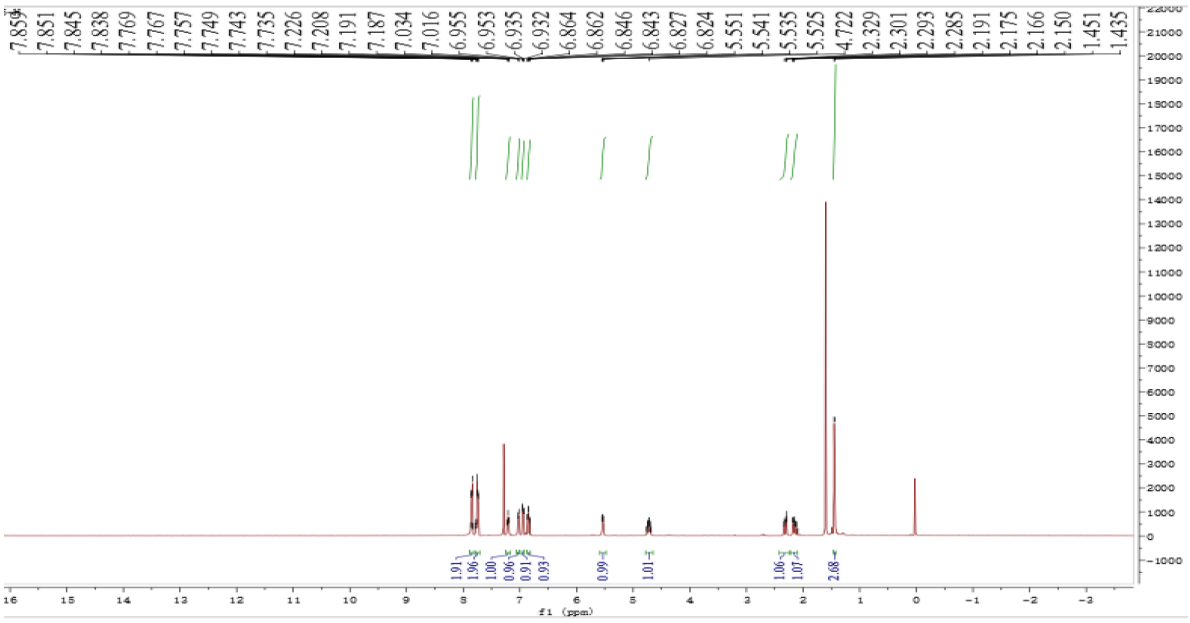


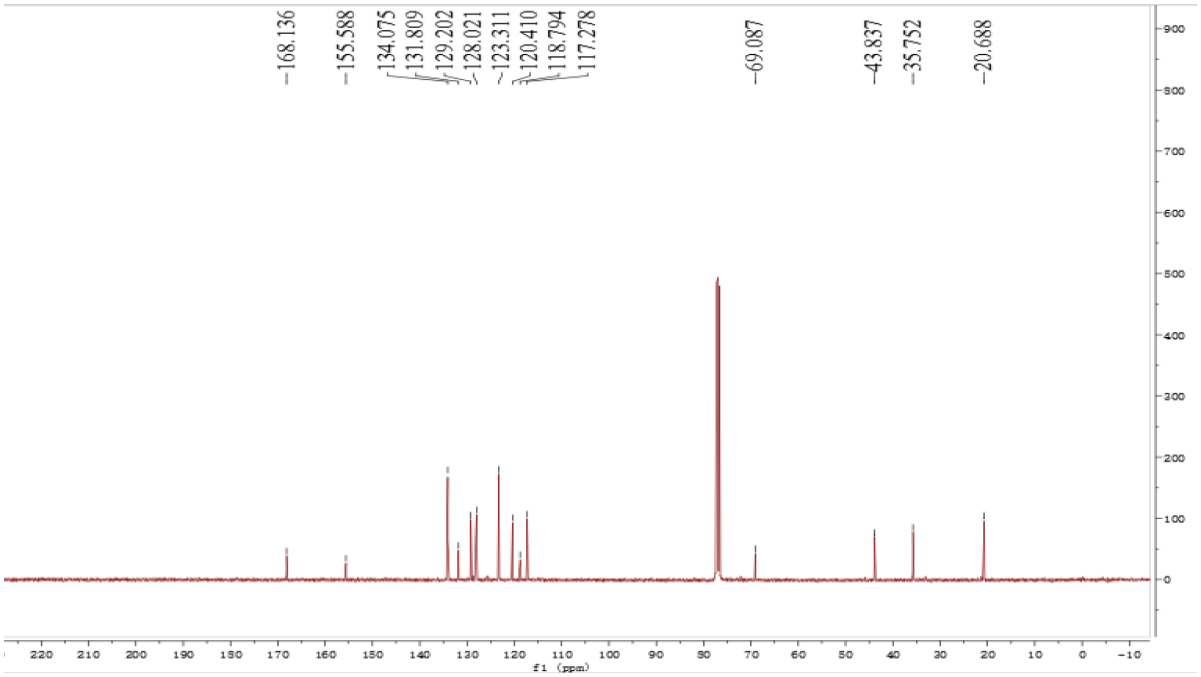
4

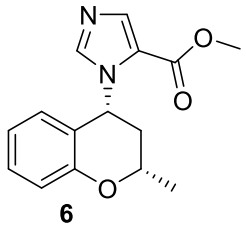

7.127
7.107
7.085
7.082
7.063
6.872
6.870
6.852
6.835
6.815
4.194
4.189
4.179
4.173
4.169
4.164
4.154
4.148
2.895
2.880
2.867
2.851
2.805
2.798
2.792
2.784
2.041
2.034
2.027
2.015
2.008
2.001
1.993
1.779
1.776
1.765
1.762
1.751
1.737
1.437
1.421
f1 (ppm)



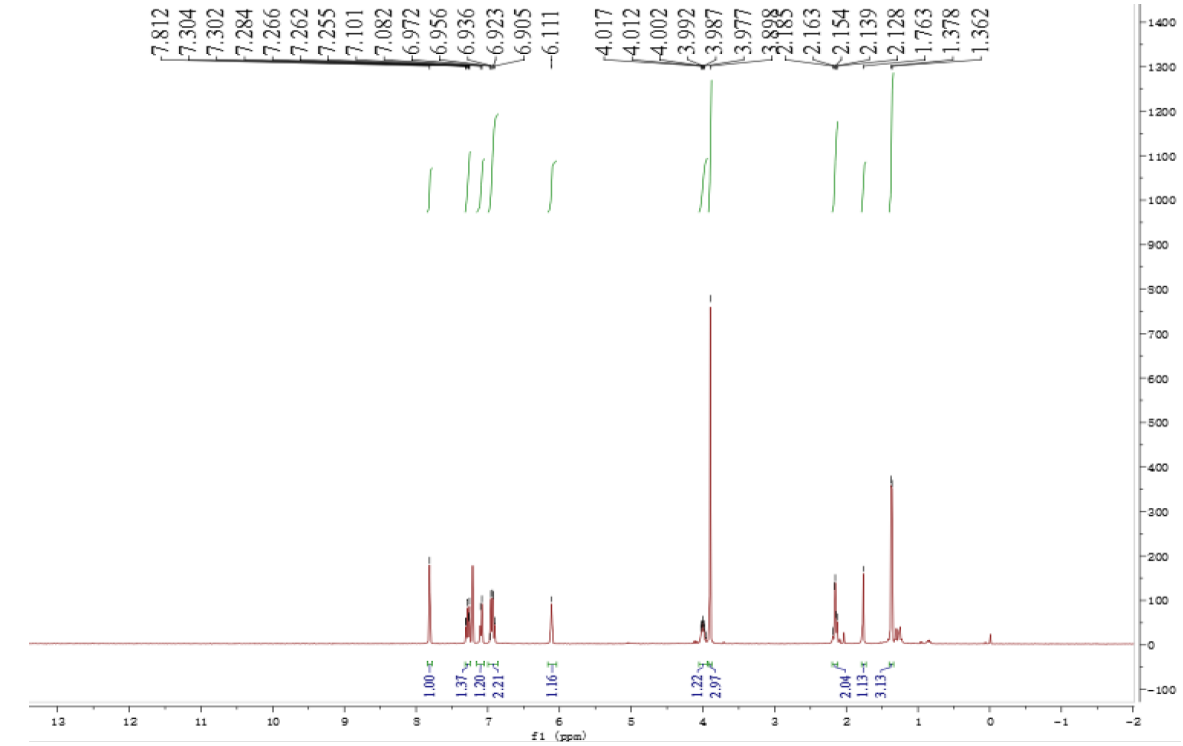
5

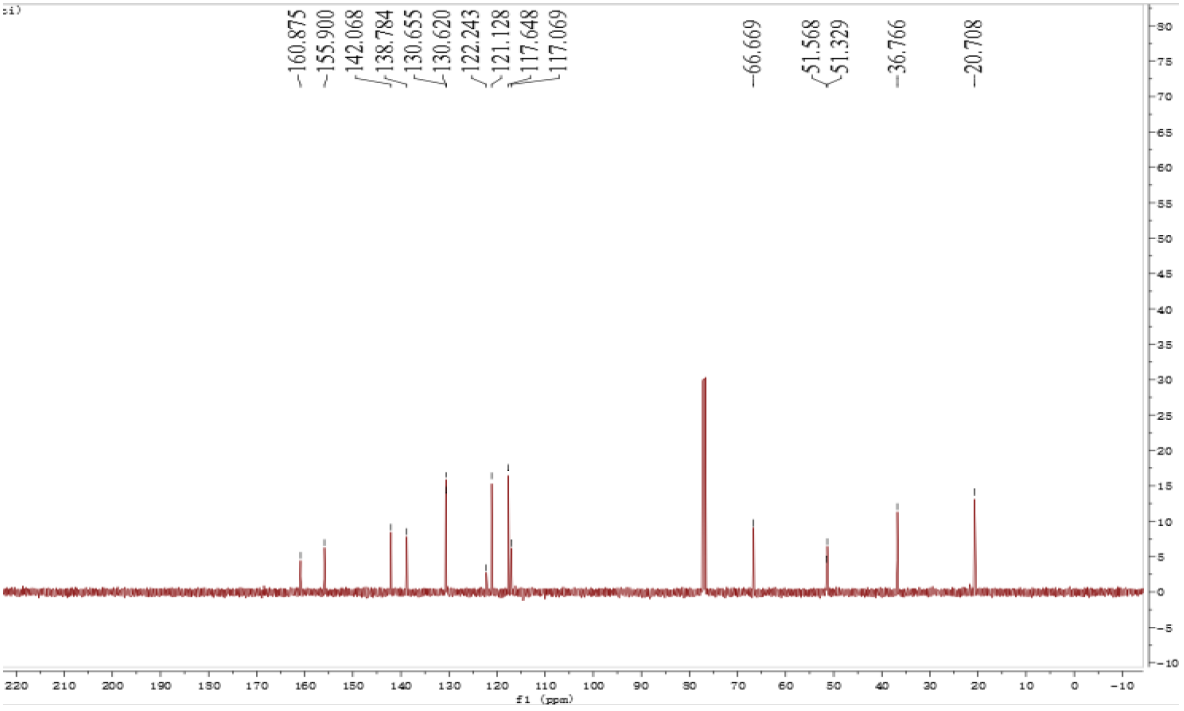

7.859
7.851
7.845
7.838
7.769
7.767
7.757
7.749
7.743
7.735
7.226
7.208
7.191
7.187
7.034
7.016
6.955
6.953
6.935
6.932
6.864
6.862
6.846
6.843
6.827
6.824
5.551
5.541
5.535
5.525
4.722
2.329
2.301
2.293
2.285
2.191
2.175
2.166
2.150
1.451
1.435
1.91
1.96
1.00
0.96
0.91
0.93
0.99
1.01
1.06
1.07
2.08
f1 (ppm)

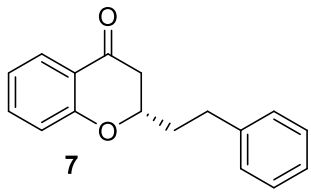

168.136
155.588
134.075
131.809
129.202
128.021
123.311
120.410
118.794
117.278
69.087
43.837
35.752
20.688
f1 (ppm)


N
N
O
O
O

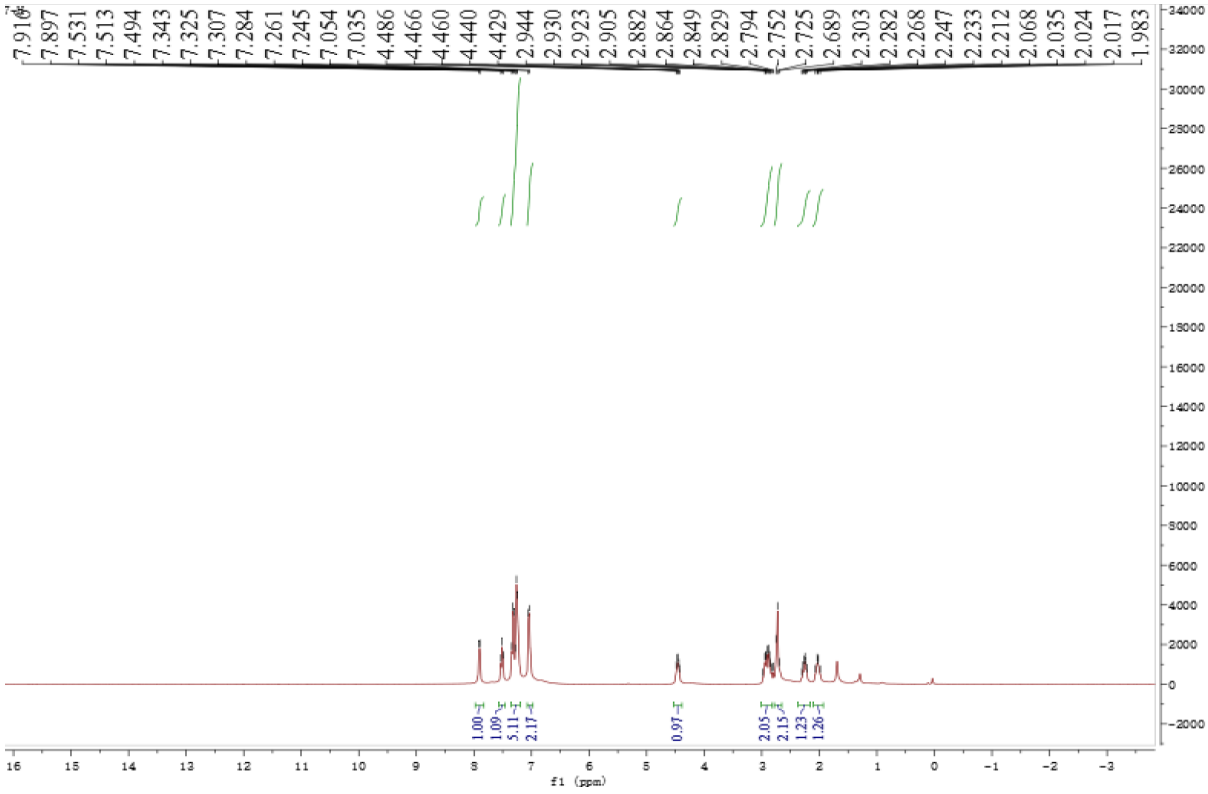
6


7.812
7.304
7.302
7.284
7.266
7.262
7.255
7.101
7.082
6.972
6.956
6.936
6.923
6.905
6.111
4.017
4.012
4.002
3.992
3.987
3.977
3.898
2.185
2.163
2.154
2.139
2.128
1.763
1.378
1.362
1.00
1.37
1.20
2.21
1.16
1.22
2.97
2.04
1.13
3.13
f1 (ppm)

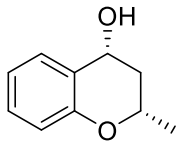

160.875
155.900
142.068
138.784
130.655
130.620
122.243
121.128
117.648
117.069
66.669
51.568
51.329
36.766
20.708
f1 (ppm)


O
O

7

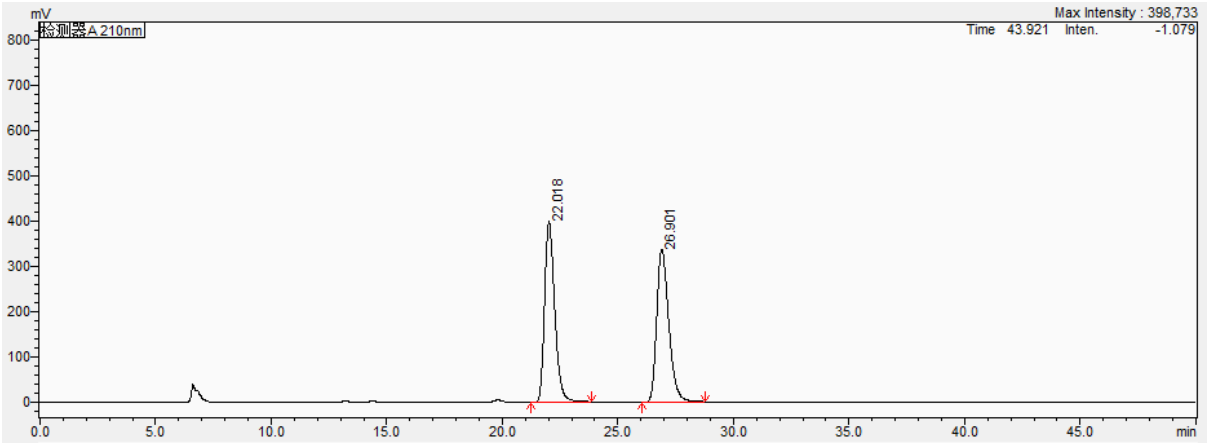

7.918
7.897
7.531
7.513
7.494
7.343
7.325
7.307
7.284
7.261
7.245
7.054
7.035
4.486
4.466
4.460
4.440
4.429
2.944
2.930
2.923
2.905
2.882
2.864
2.849
2.829
2.794
2.752
2.725
2.689
2.303
2.282
2.268
2.247
2.233
2.212
2.068
2.035
2.024
2.017
1.983
1.00
1.09
5.11
2.17
0.97
2.05
2.15
1.23
1.26
f1 (ppm)

8. HPLC data

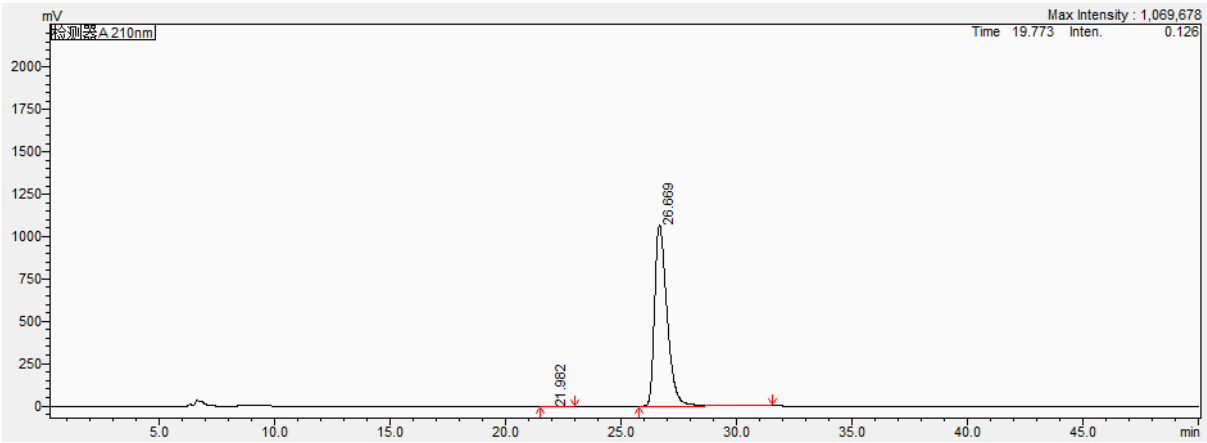


2a

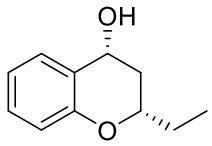
Racemate



Chiral

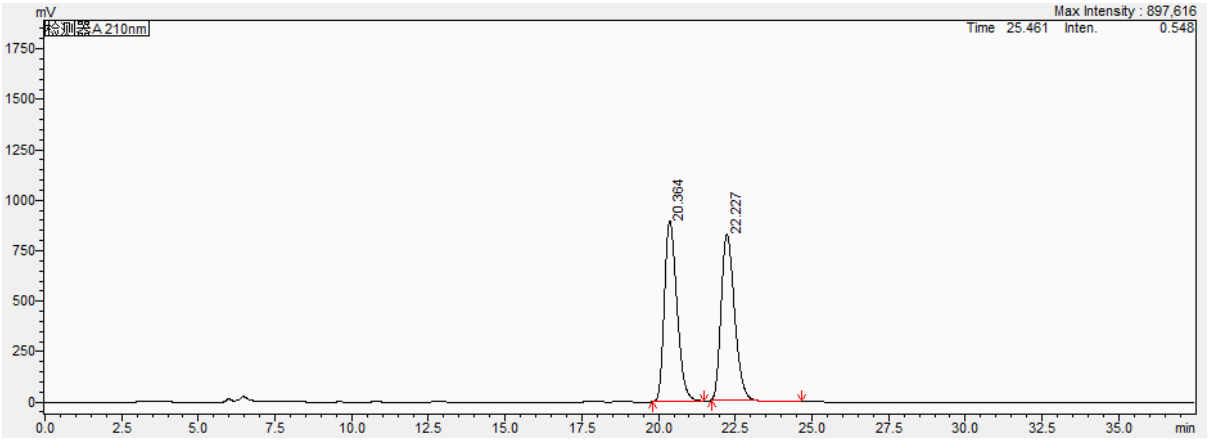


	Retention Time (min)	Area (%)	
Peak 1	21.982	0.054	**99.9% ee**
Peak 2	26.669	99.946	

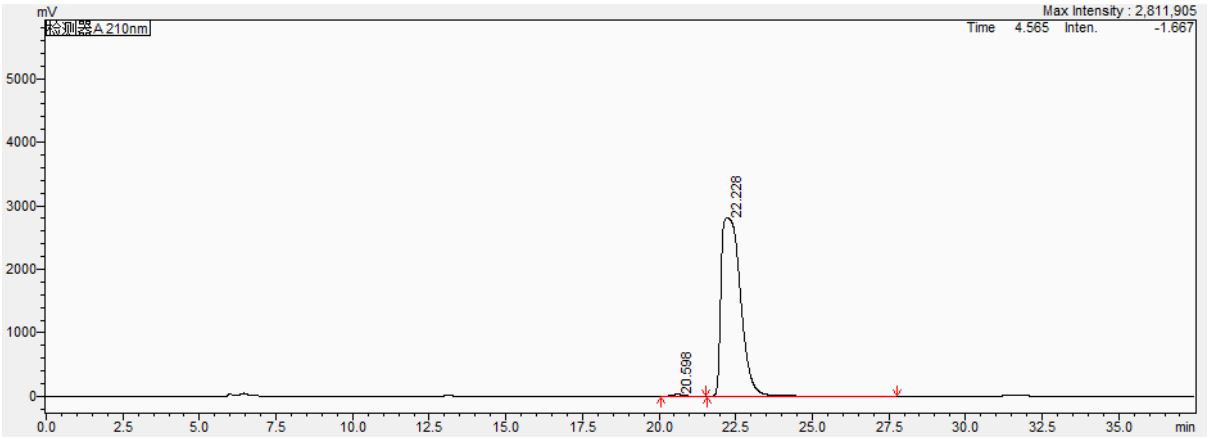


2b

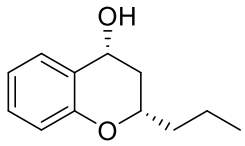
Racemate



Chiral

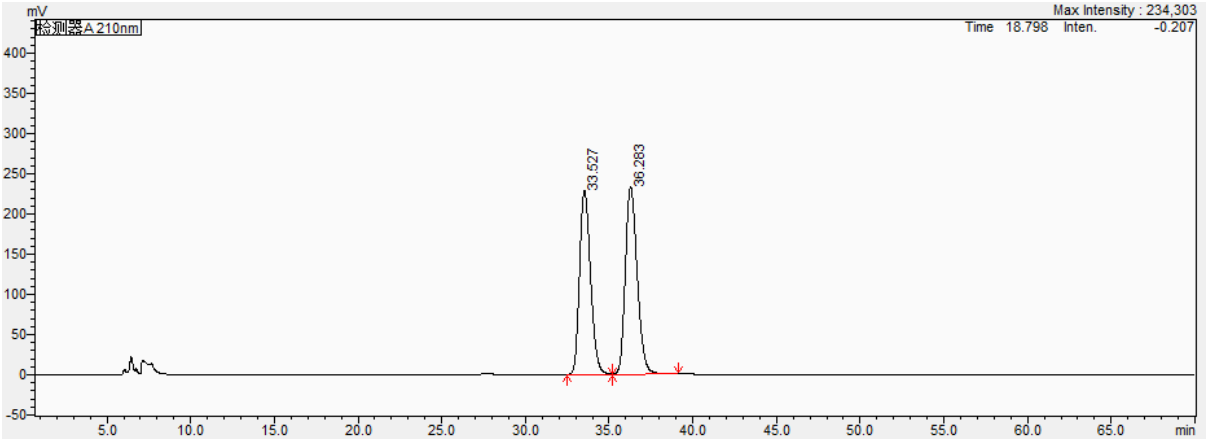


	Retention Time (min)	Area (%)	
Peak 1	20.598	0.679	**99% ee**
Peak 2	22.228	99.321	

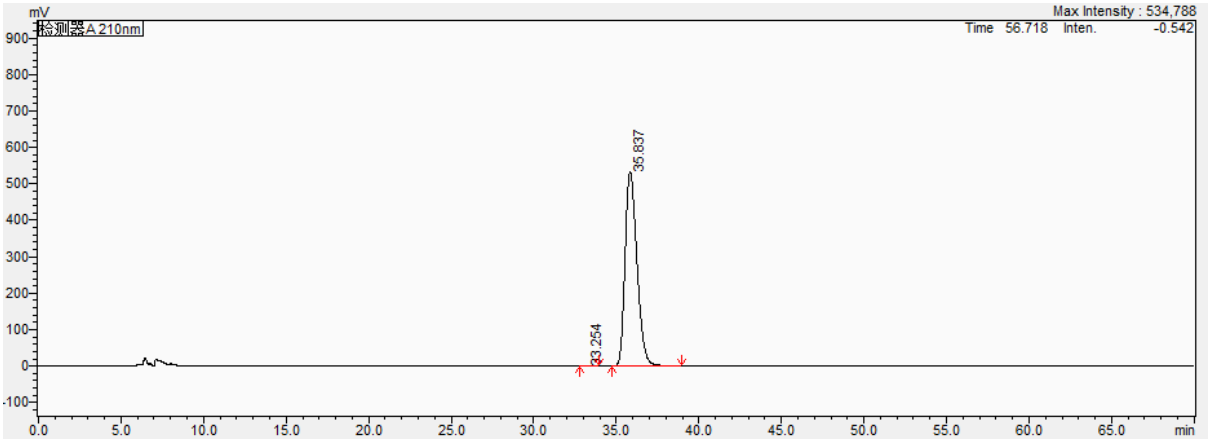


2c

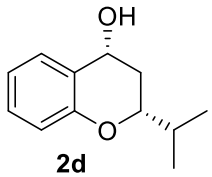
Racemate



Chiral

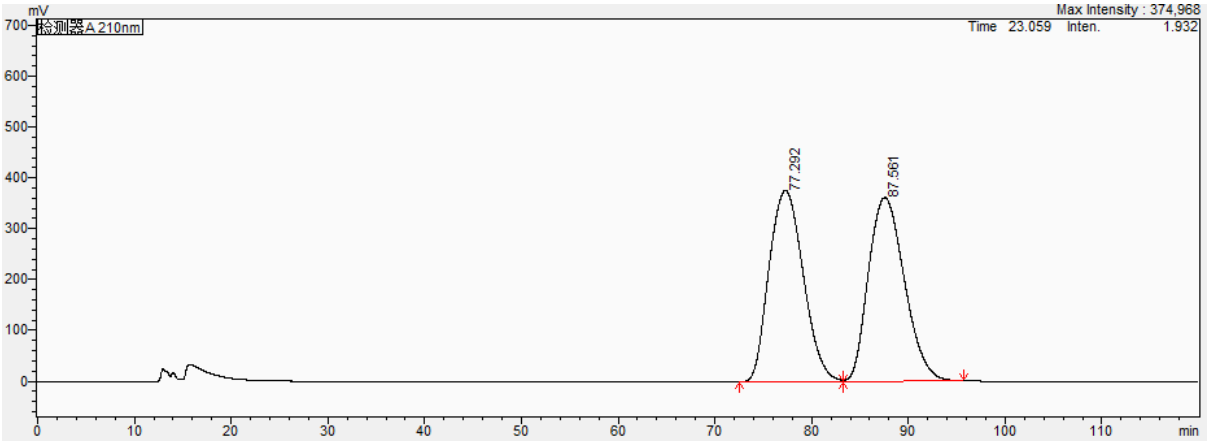


	Retention Time (min)	Area (%)	
Peak 1	33.254	0.134	**99.7% ee**
Peak 2	35.837	99.866	

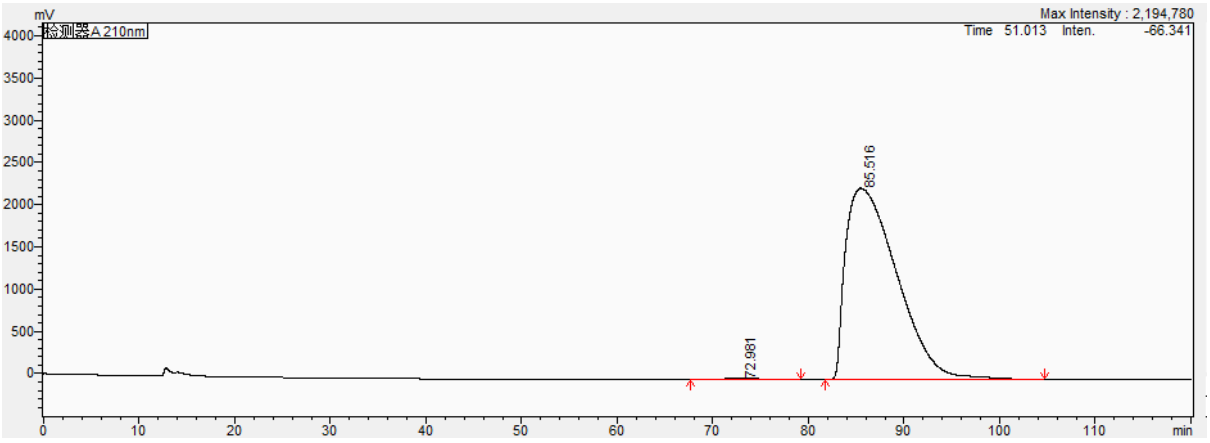


2d

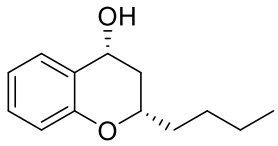
Racemate



Chiral

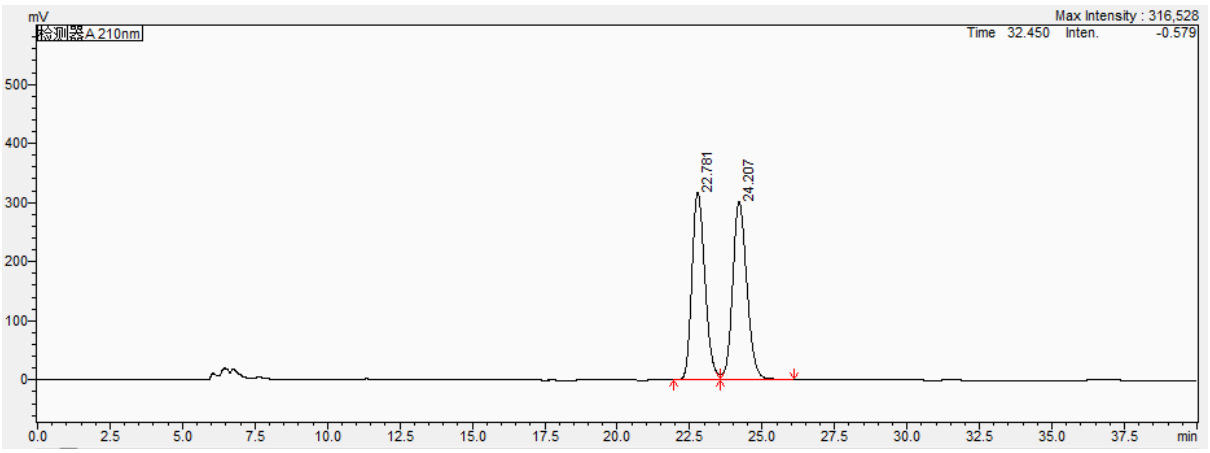


	Retention Time (min)	Area (%)	
Peak 1	72.981	0.433	**99.1% ee**
Peak 2	85.516	99.567	

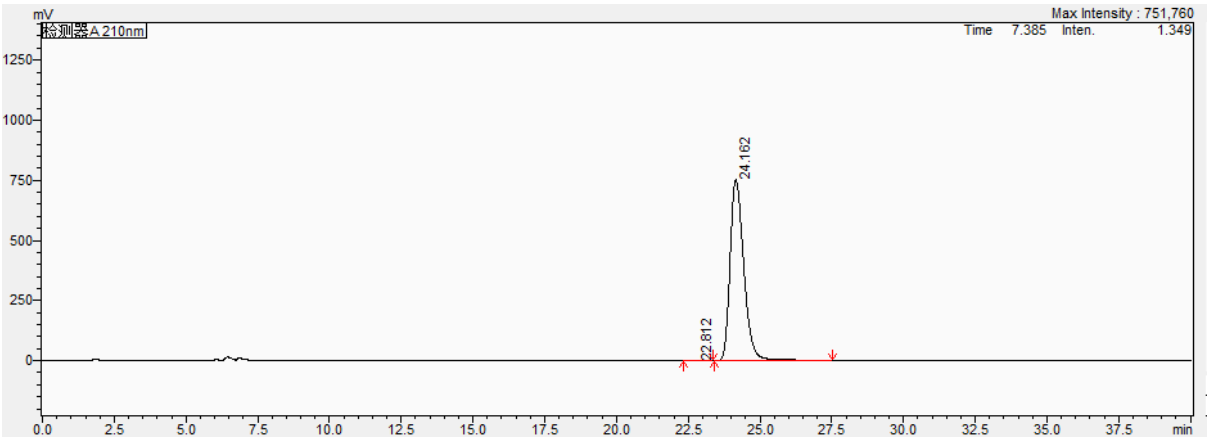


2e

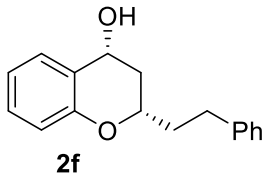
Racemate



Chiral

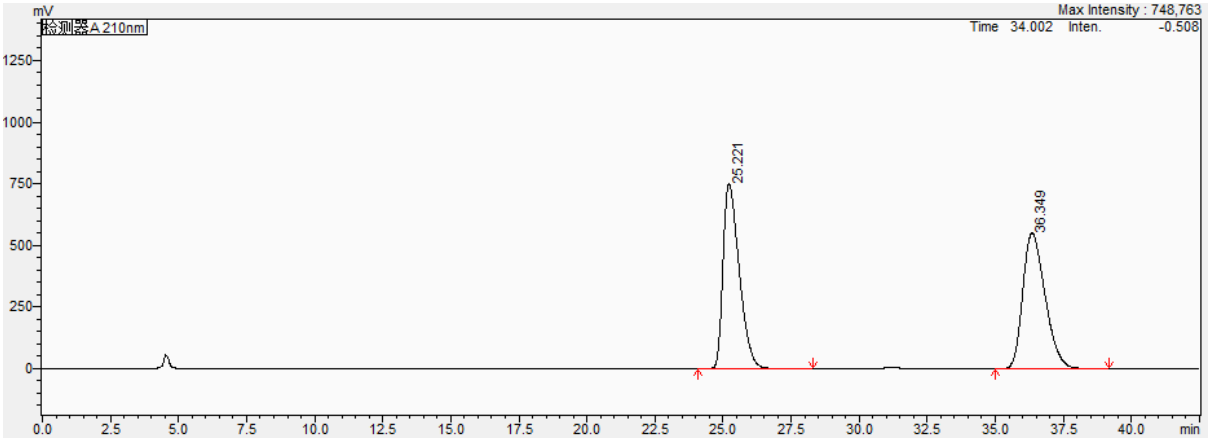


	Retention Time (min)	Area (%)	
Peak 1	22.812	0.204	**99.6 % ee**
Peak 2	24.162	99.796	

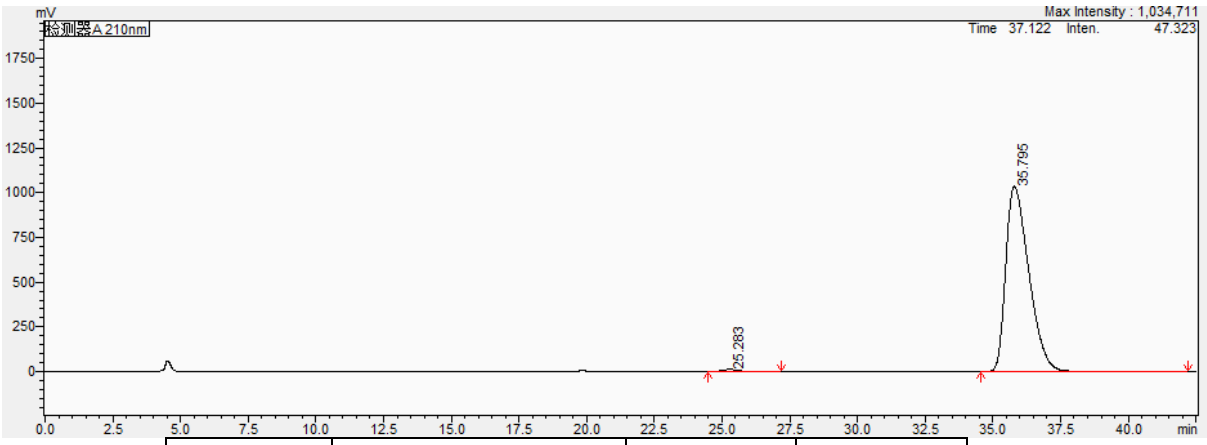


2f

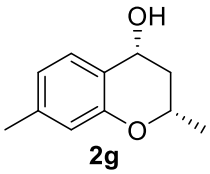
Racemate



Chiral

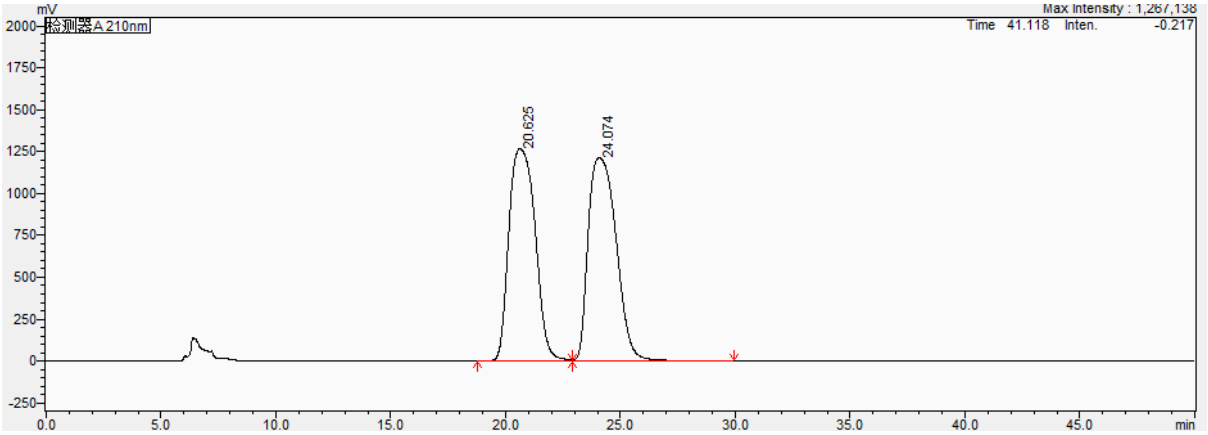


	Retention Time (min)	Area (%)	
Peak 1	25.283	0.786	**98% ee**
Peak 2	35.795	99.214	

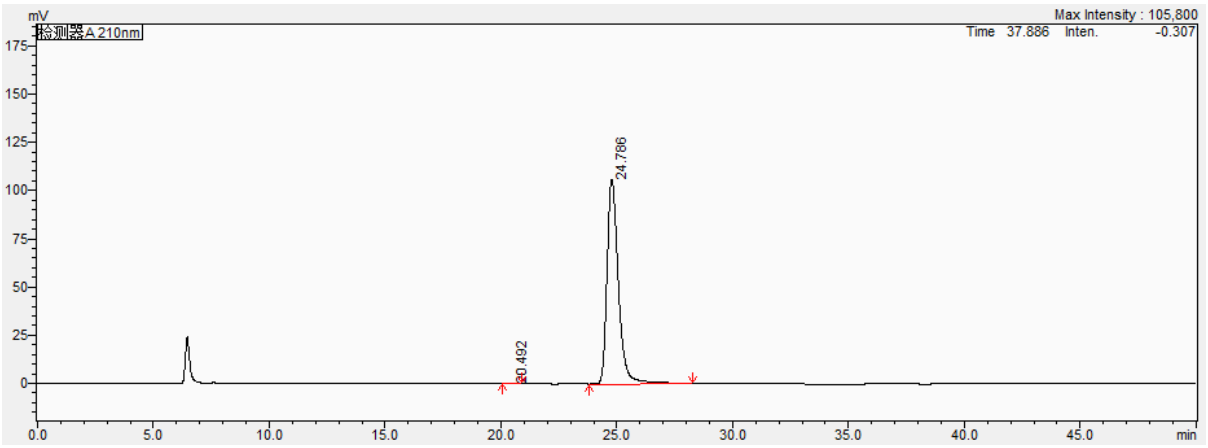


2g

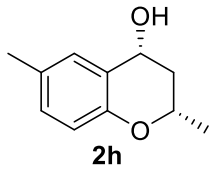
Racemate



Chiral

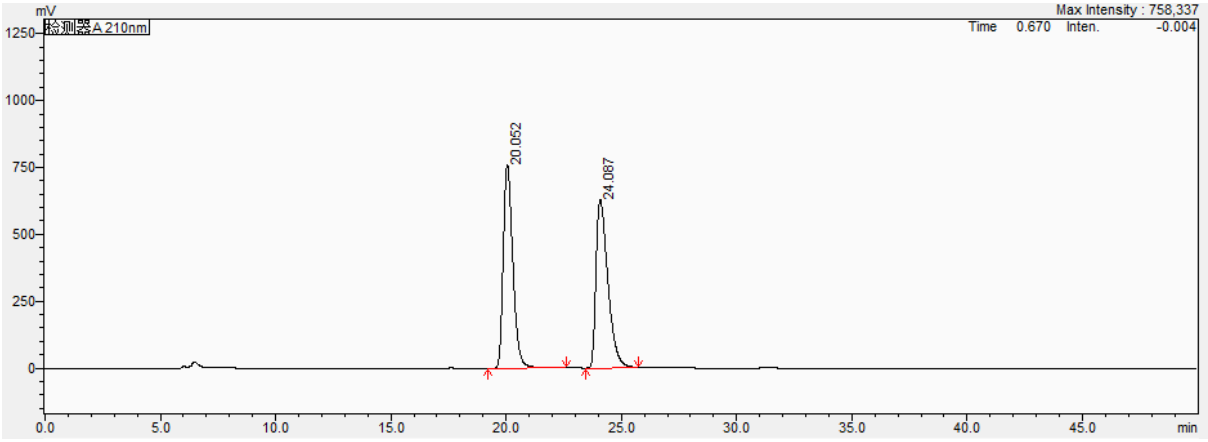


	Retention Time (min)	Area (%)	
Peak 1	20.492	0.168	**99.7% ee**
Peak 2	24.786	99.832	

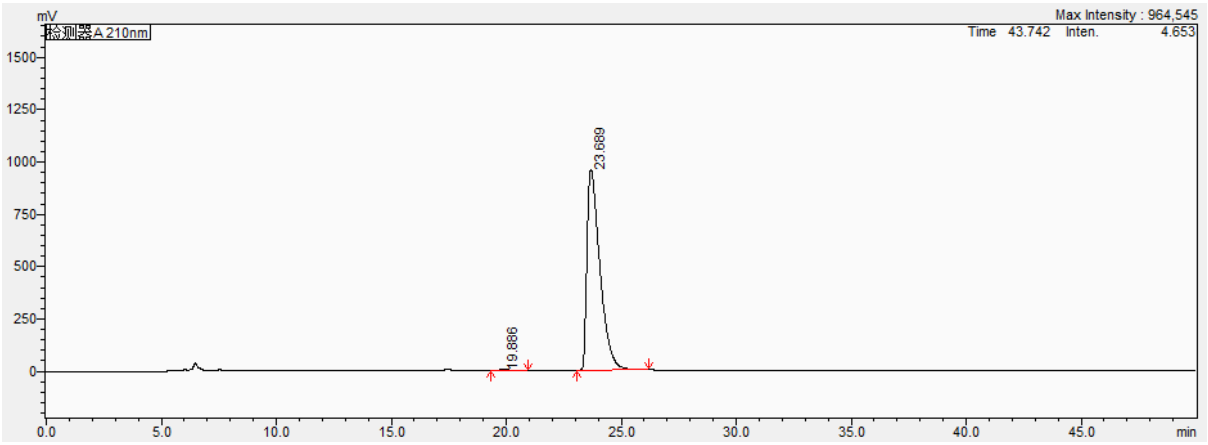


2h

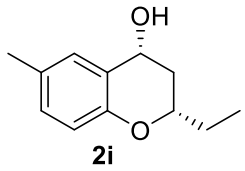
Racemate



Chiral

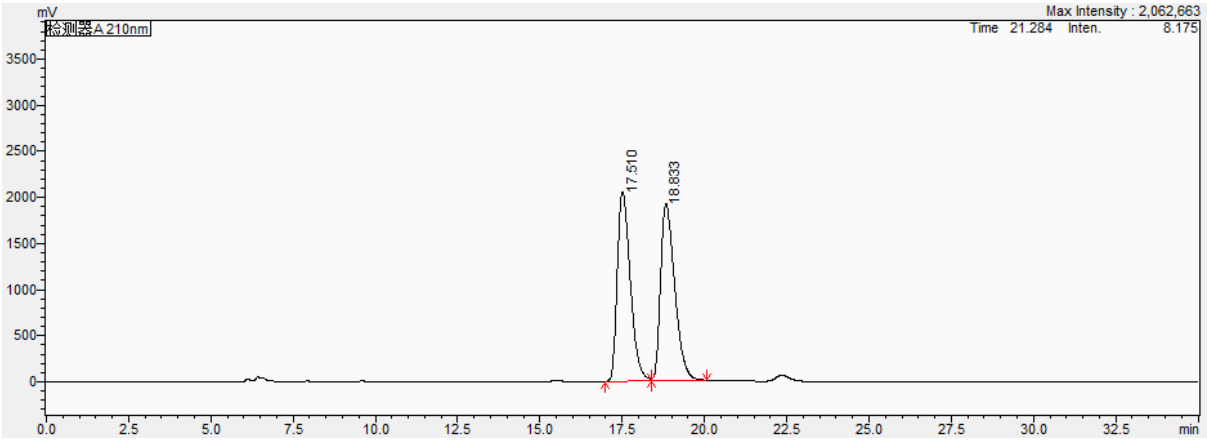


	Retention Time (min)	Area (%)	
Peak 1	19.886	0.323	**99.3% ee**
Peak 2	23.689	99.677	

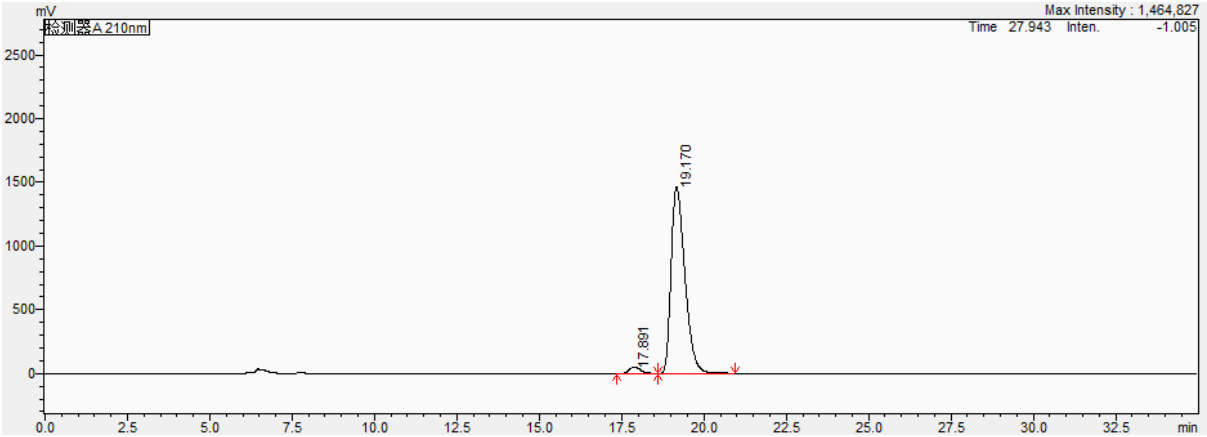


2i

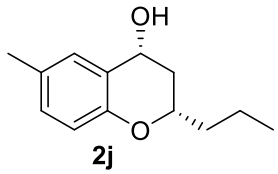
Racemate



Chiral

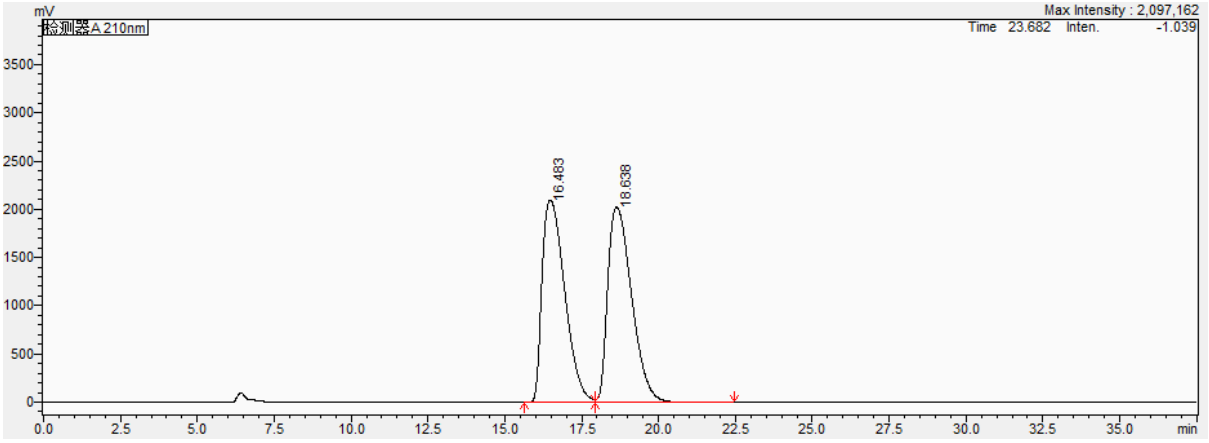


	Retention Time (min)	Area (%)	
Peak 1	17.891	2.867	**94% ee**
Peak 2	19.170	97.133	

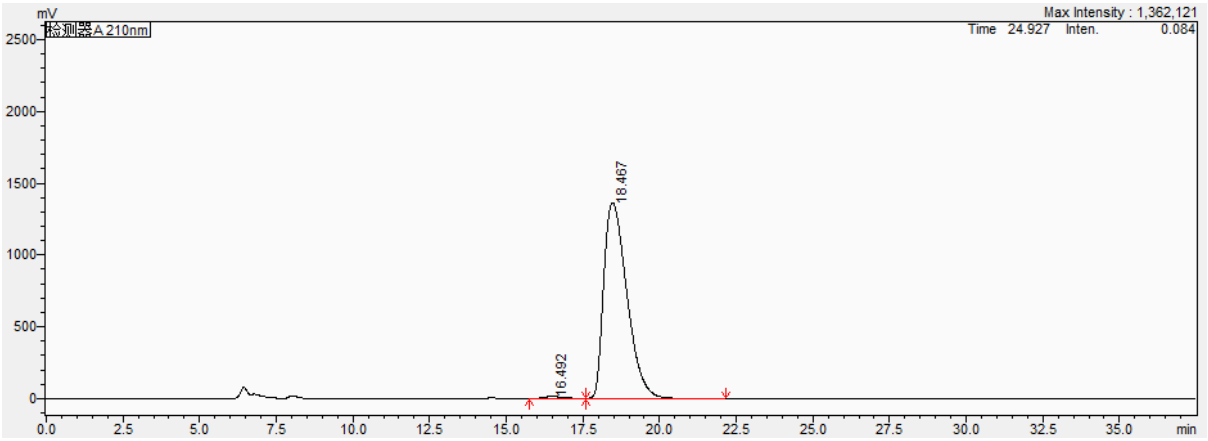


2j

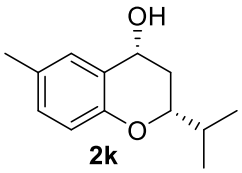
Racemate



Chiral

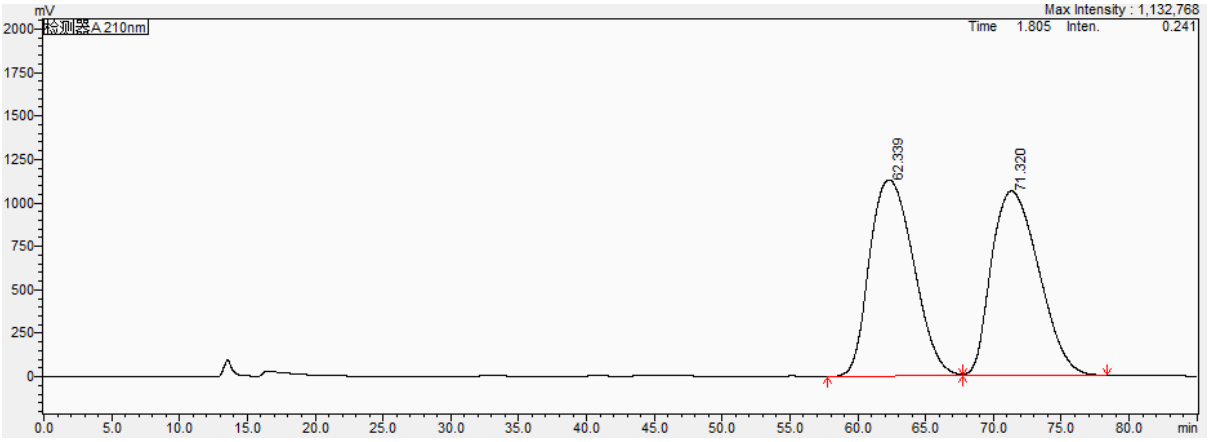


	Retention Time (min)	Area (%)	
Peak 1	16.492	0.857	**98% ee**
Peak 2	18.467	99.143	

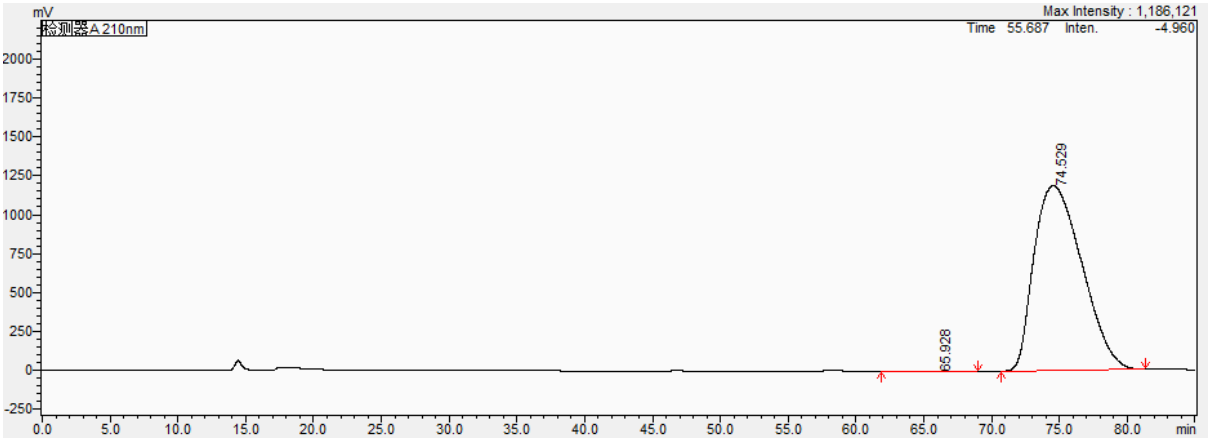


2k

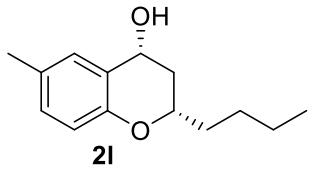
Racemate



Chiral

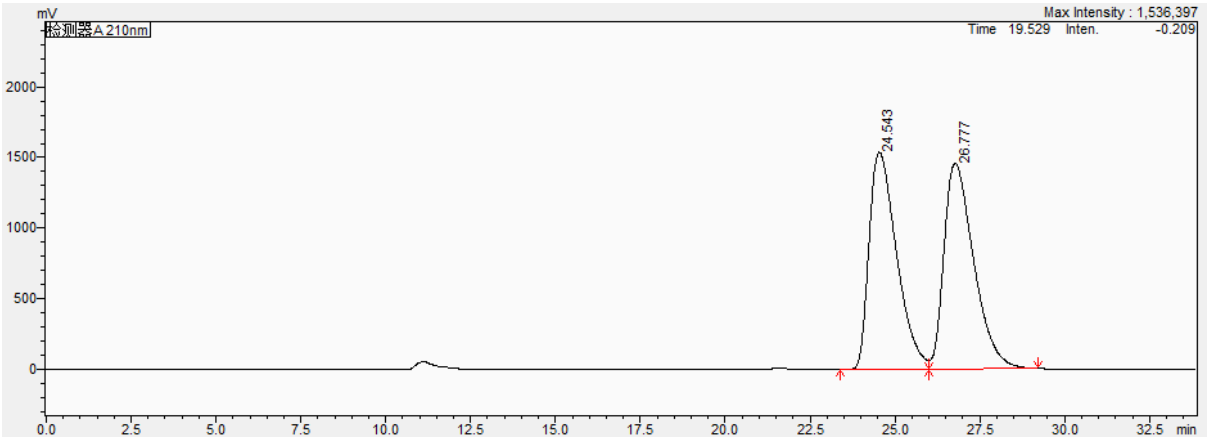


	Retention Time (min)	Area (%)	
Peak 1	65.928	0.099	**99.8% ee**
Peak 2	74.529	99.901	

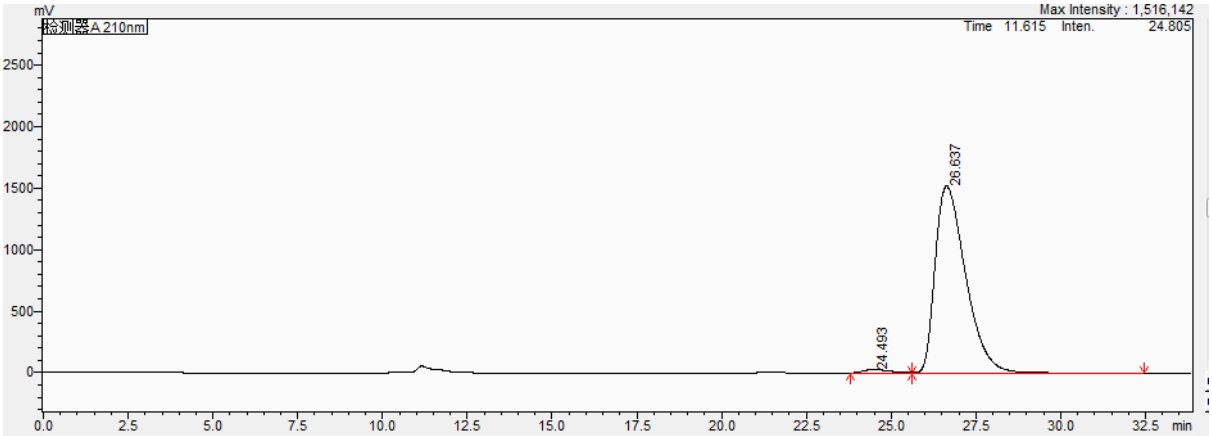


2l

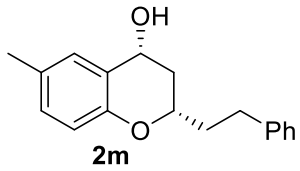
Racemate



Chiral

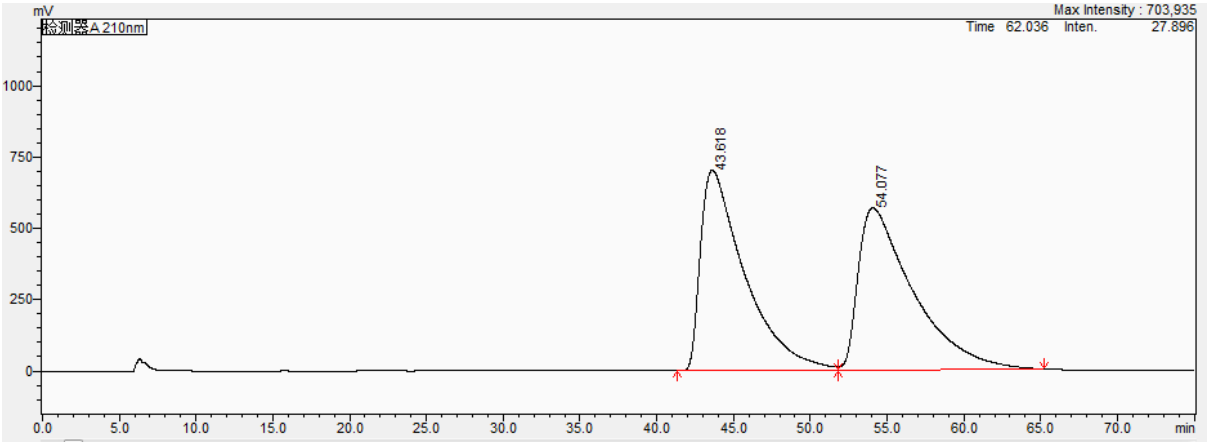


	Retention Time (min)	Area (%)	
Peak 1	24.493	1.523	**97% ee**
Peak 2	26.637	98.477	

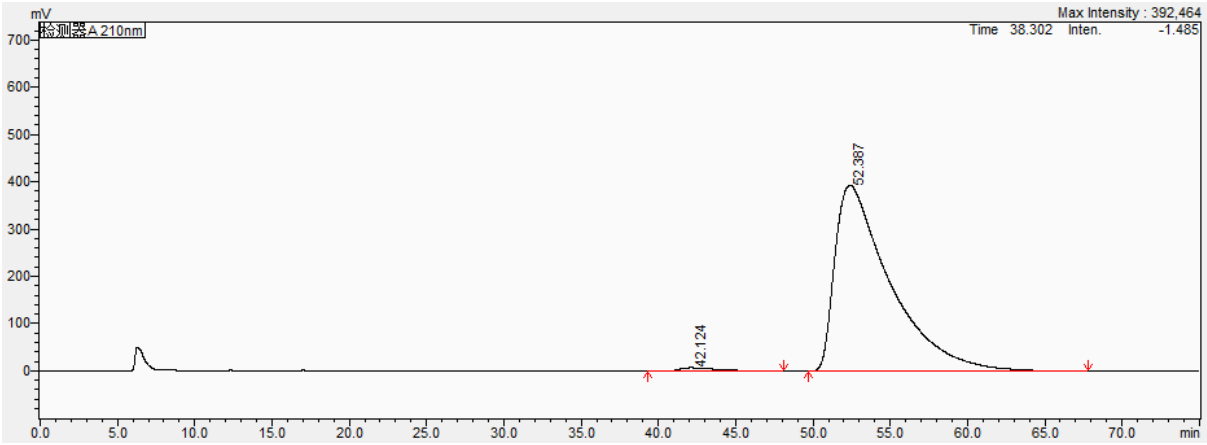


2m

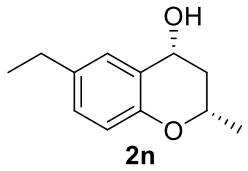
Racemate



Chiral

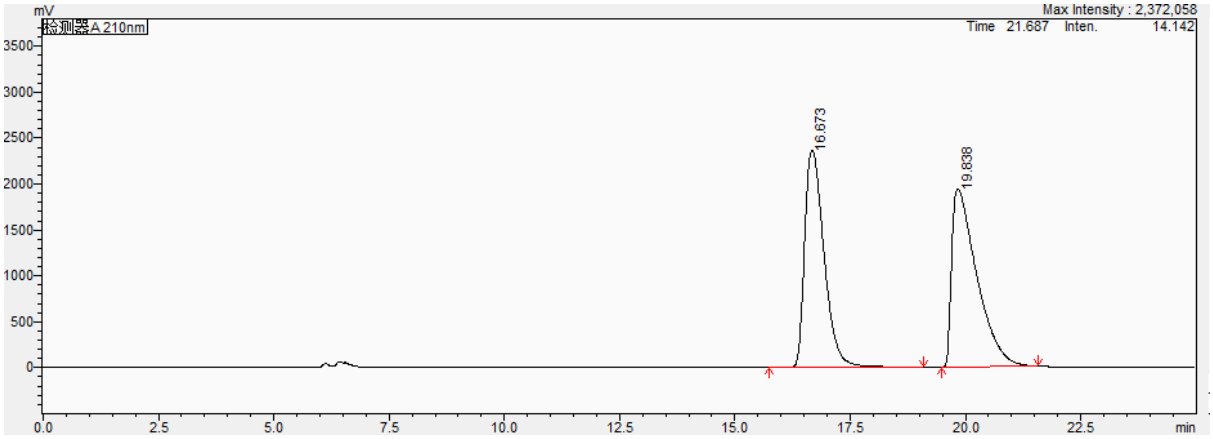


	Retention Time (min)	Area (%)	
Peak 1	42.124	1.434	**97% ee**
Peak 2	52.387	98.566	

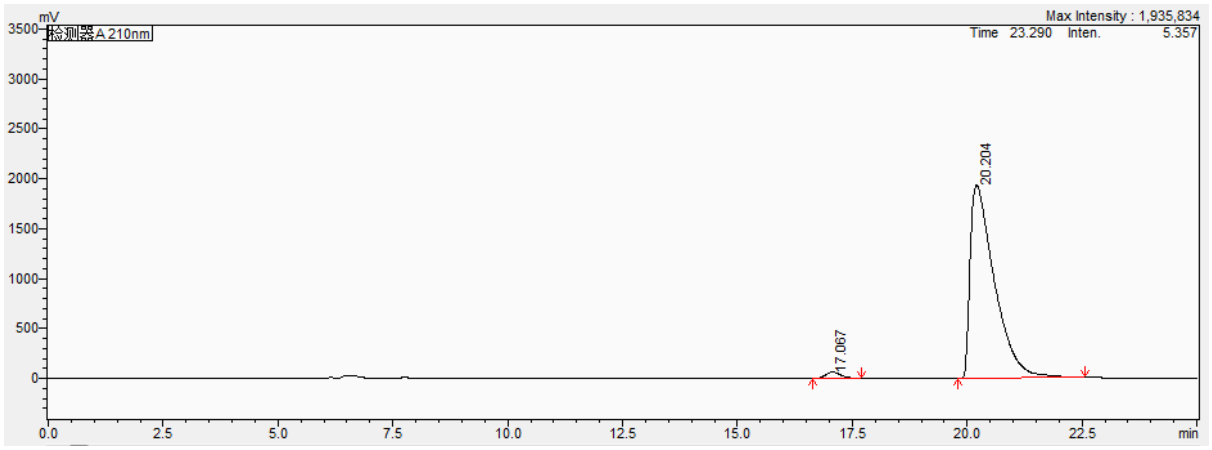


2n

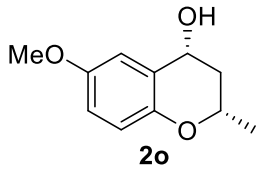
Racemate



Chiral

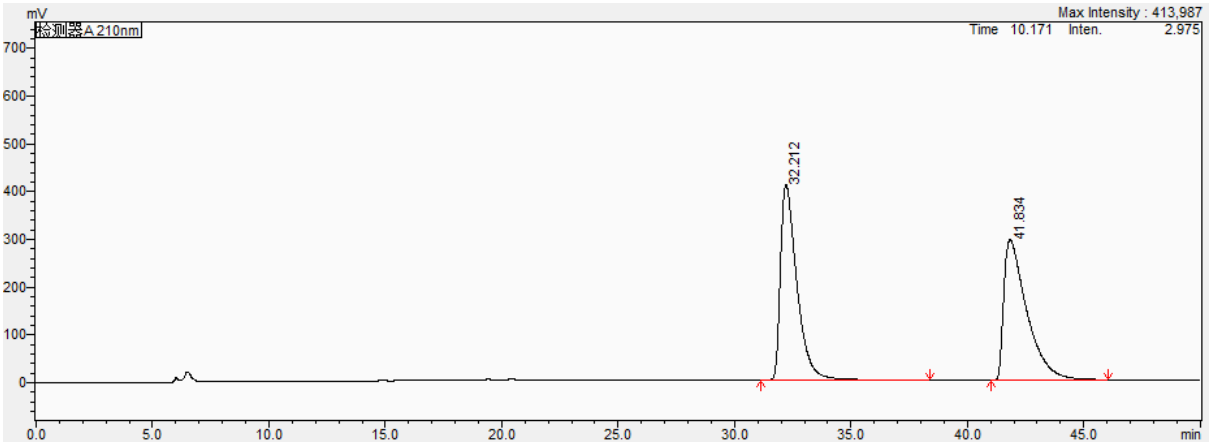


	Retention Time (min)	Area (%)	
Peak 1	17.067	1.914	**96% ee**
Peak 2	20.204	98.086	

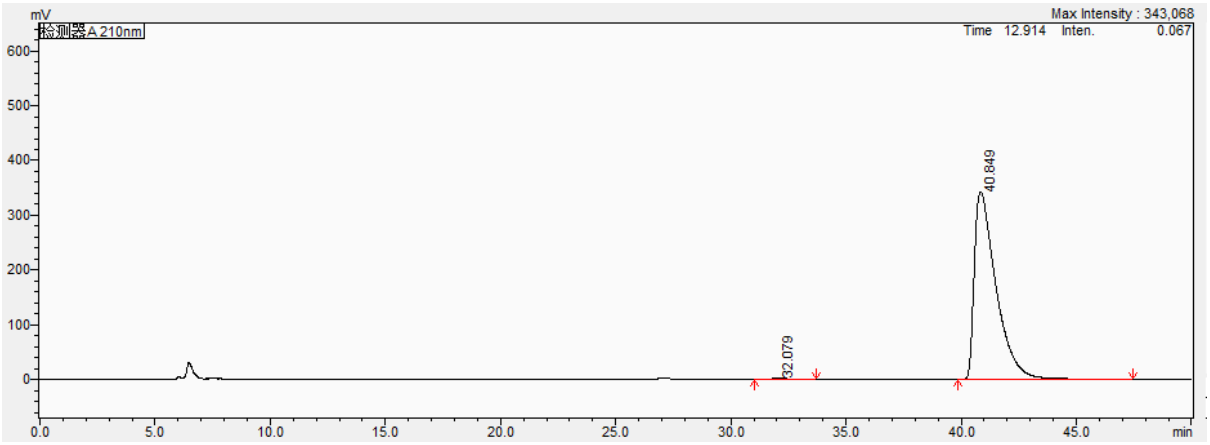


2o

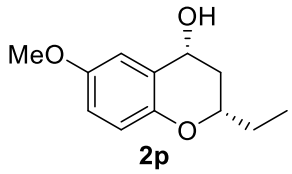
Racemate



Chiral

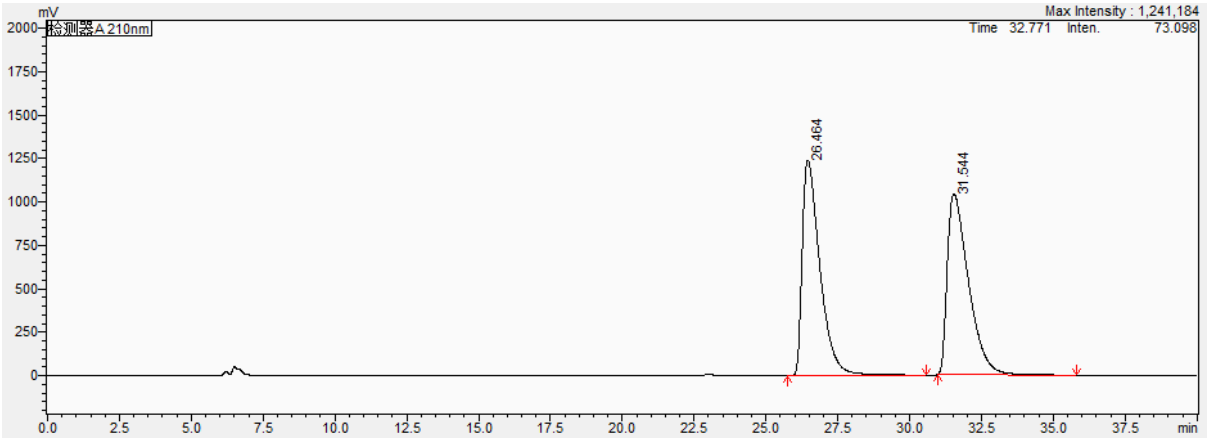


	Retention Time (min)	Area (%)	
Peak 1	32.079	0.437	**99.1% ee**
Peak 2	40.849	99.563	

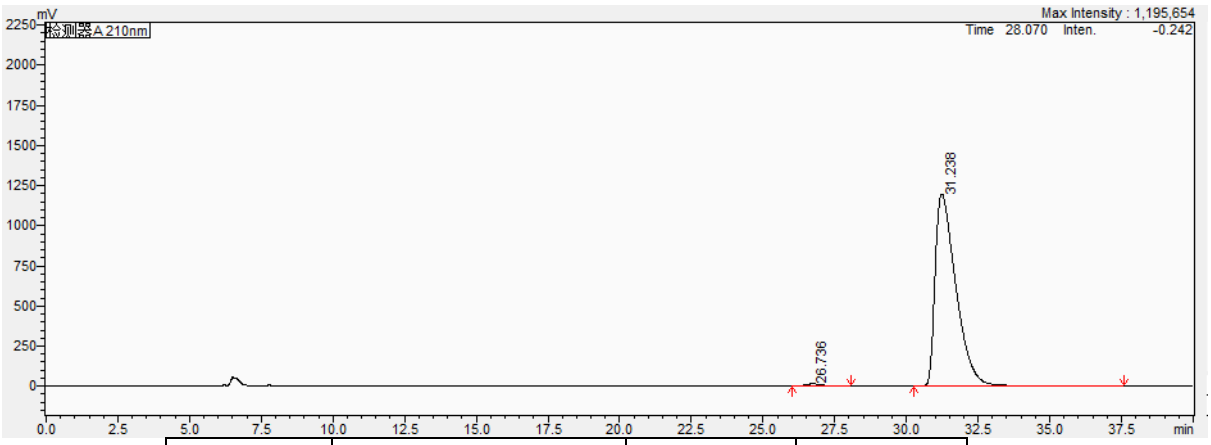


2p

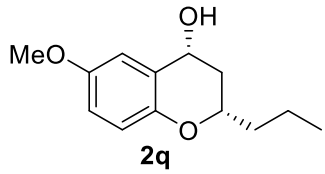
Racemate



Chiral

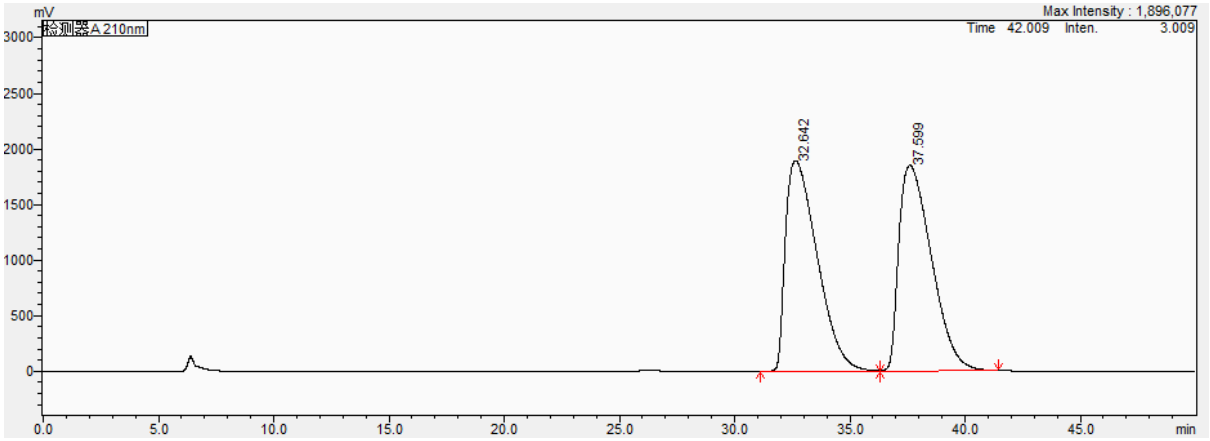


	Retention Time (min)	Area (%)	
Peak 1	26.736	0.942	**98% ee**
Peak 2	31.238	99.058	

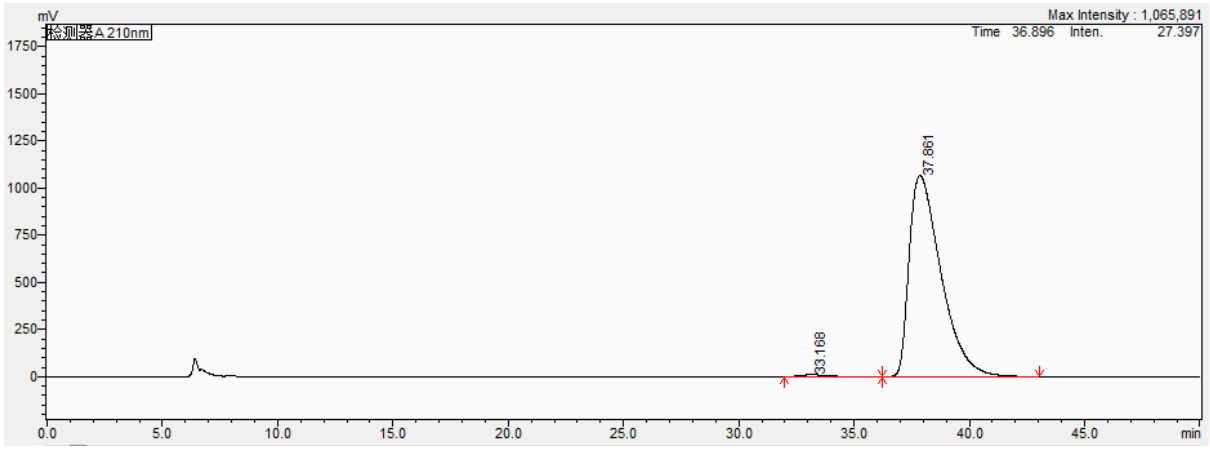


2q

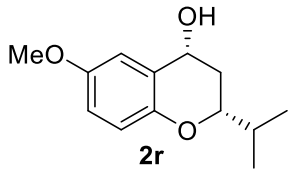
Racemate



Chiral

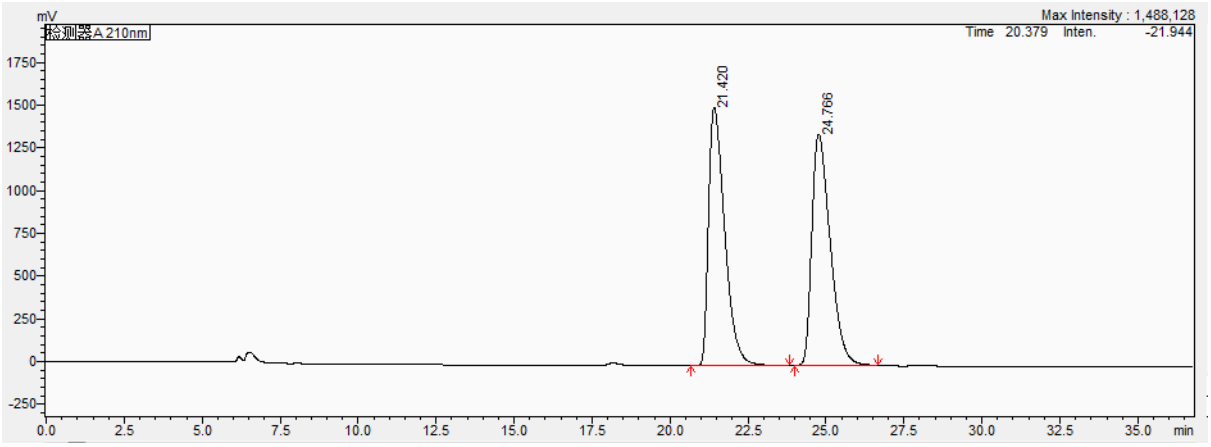


	Retention Time (min)	Area (%)	
Peak 1	33.168	0.856	**98% ee**
Peak 2	37.861	99.144	

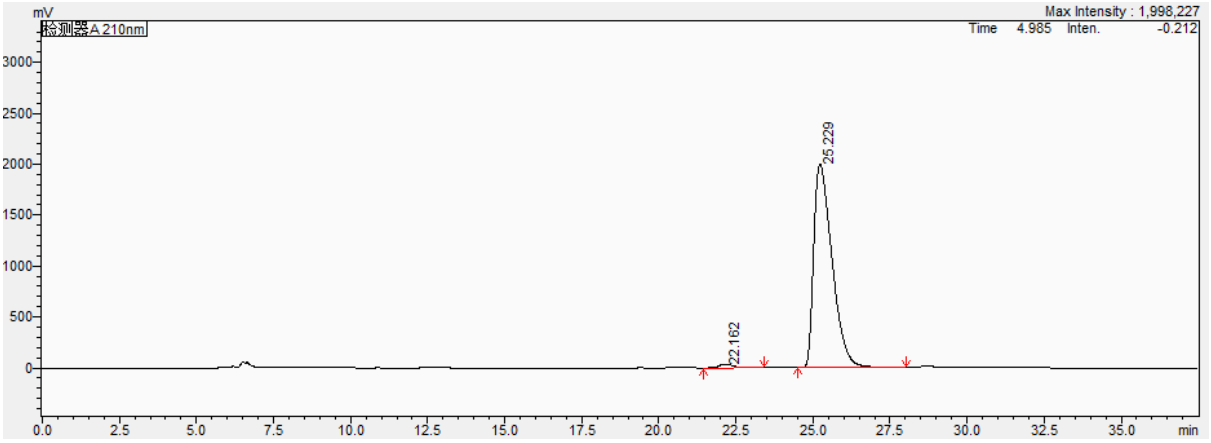


2r

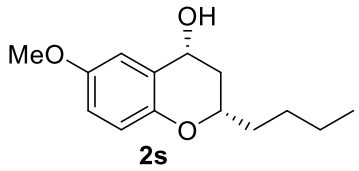
Racemate



Chiral

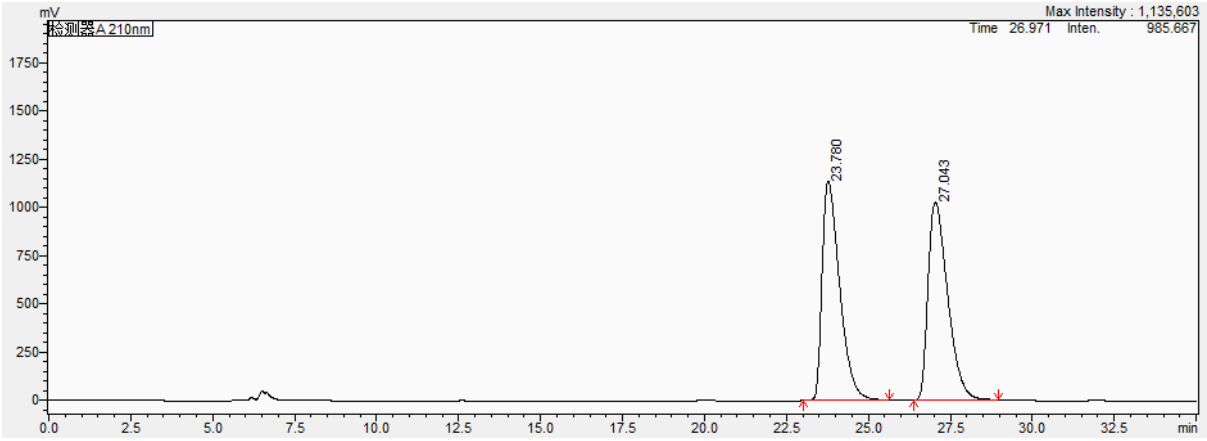


	Retention Time (min)	Area (%)	
Peak 1	22.162	1.344	**97% ee**
Peak 2	25.229	98.656	

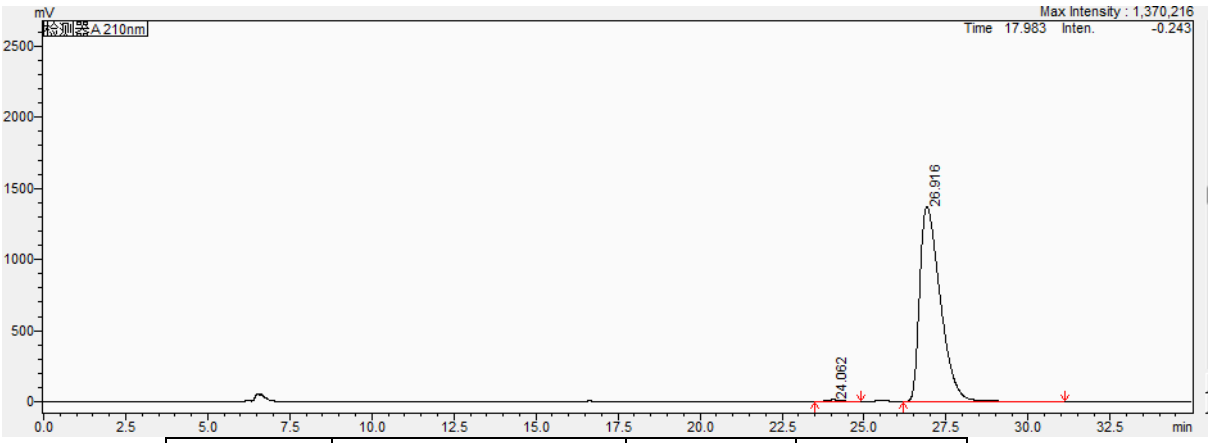


2s

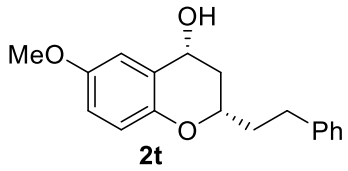
Racemate



Chiral

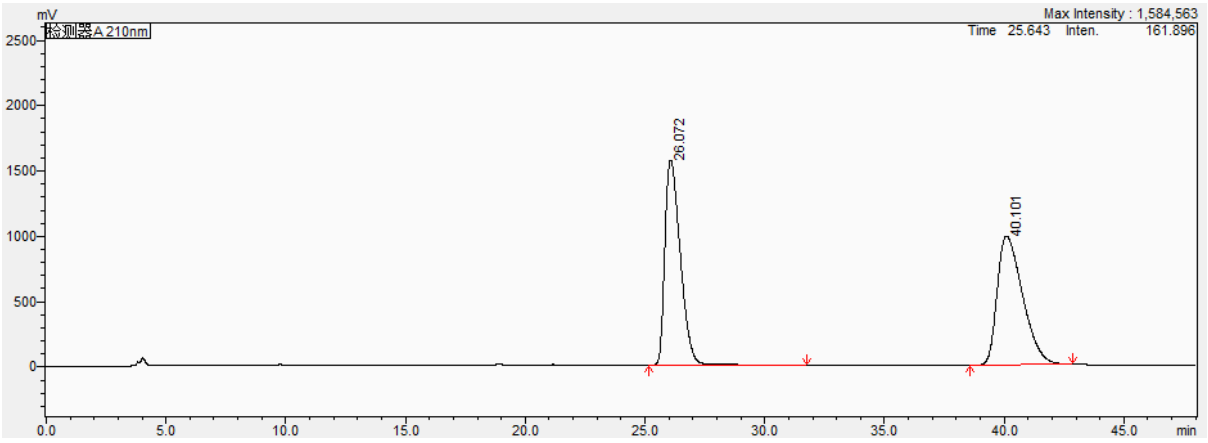


	Retention Time (min)	Area (%)	
Peak 1	24.062	0.710	**99% ee**
Peak 2	26.916	99.290	

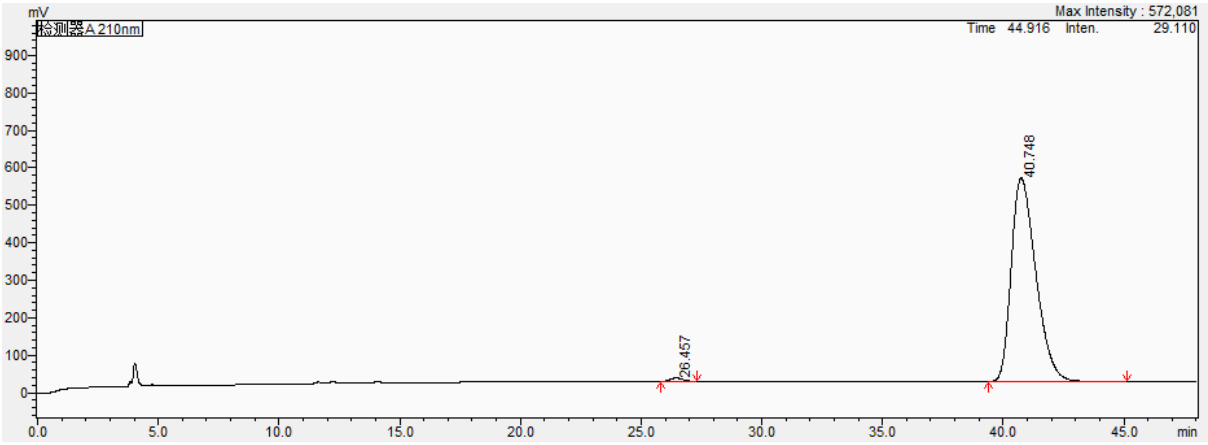


2t

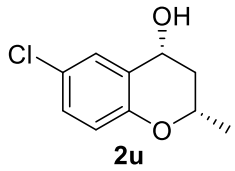
Racemate



Chiral

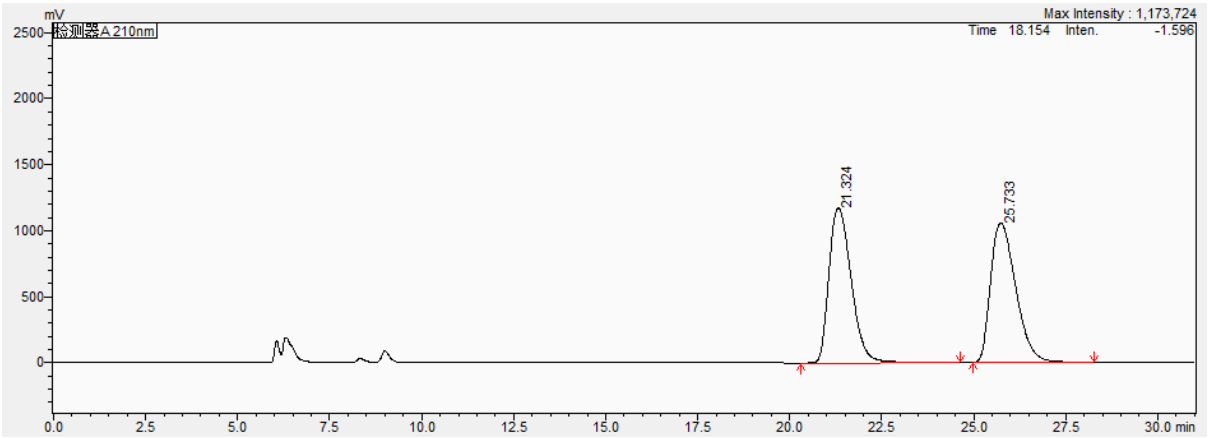


	Retention Time (min)	Area (%)	
Peak 1	26.457	1.023	**98% ee**
Peak 2	40.748	98.977	

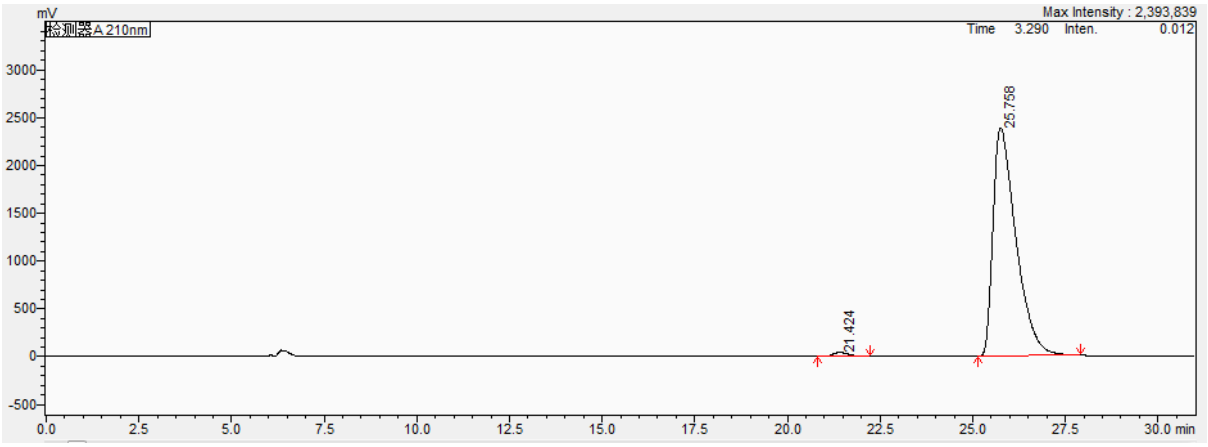


2u

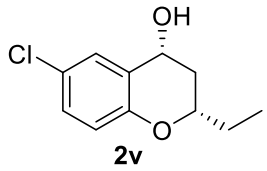
Racemate



Chiral

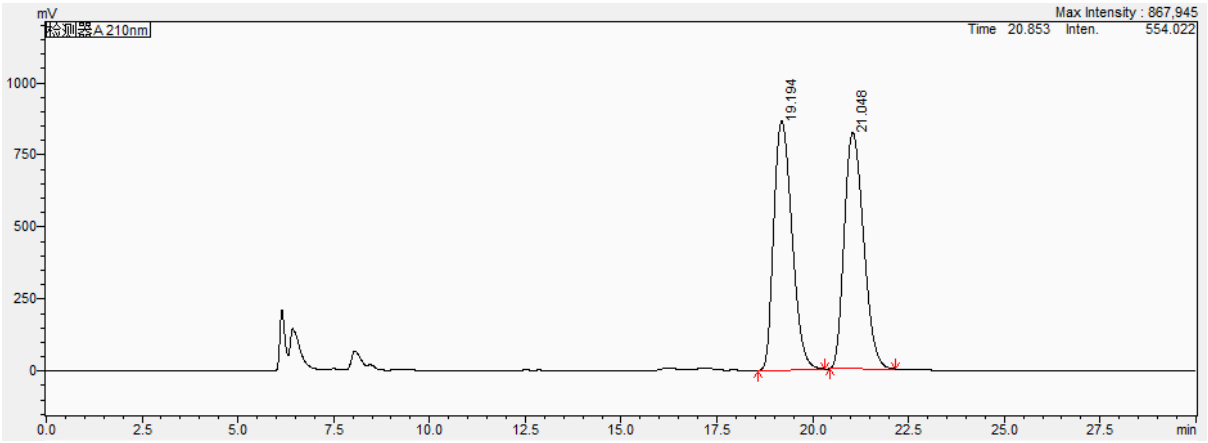


	Retention Time (min)	Area (%)	
Peak 1	21.424	1.230	**98% ee**
Peak 2	25.758	98.770	

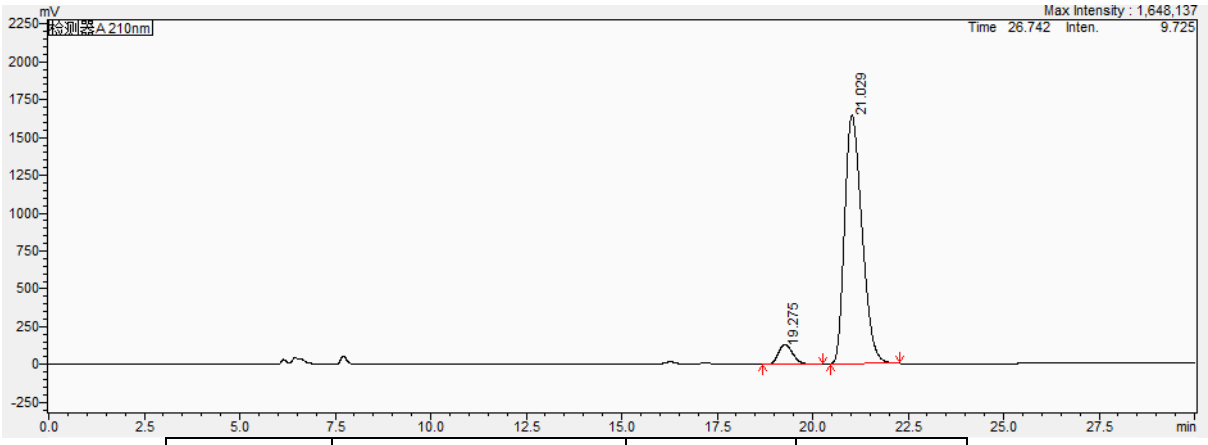


2v

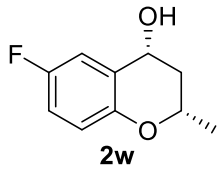
Racemate



Chiral

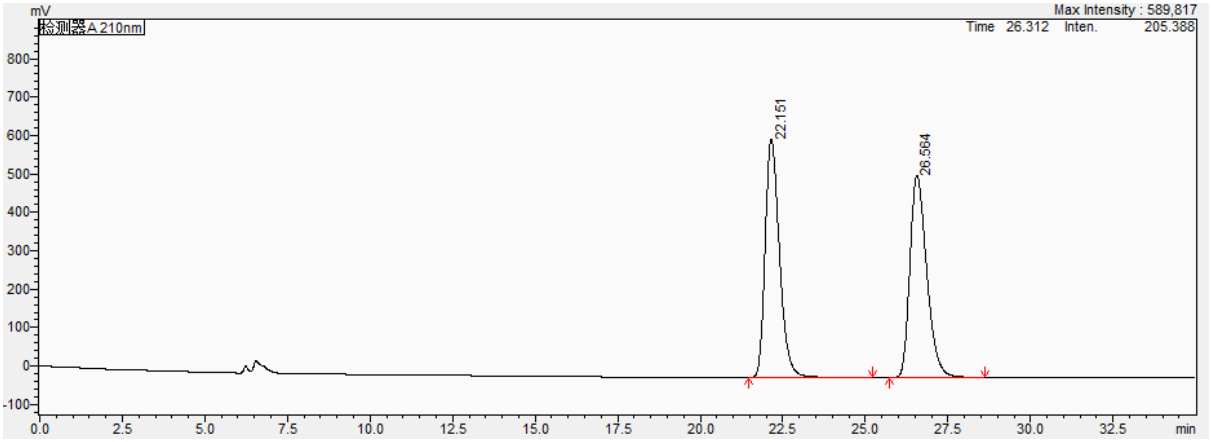


	Retention Time (min)	Area (%)	
Peak 1	19.275	6.311	**87% ee**
Peak 2	21.029	93.689	

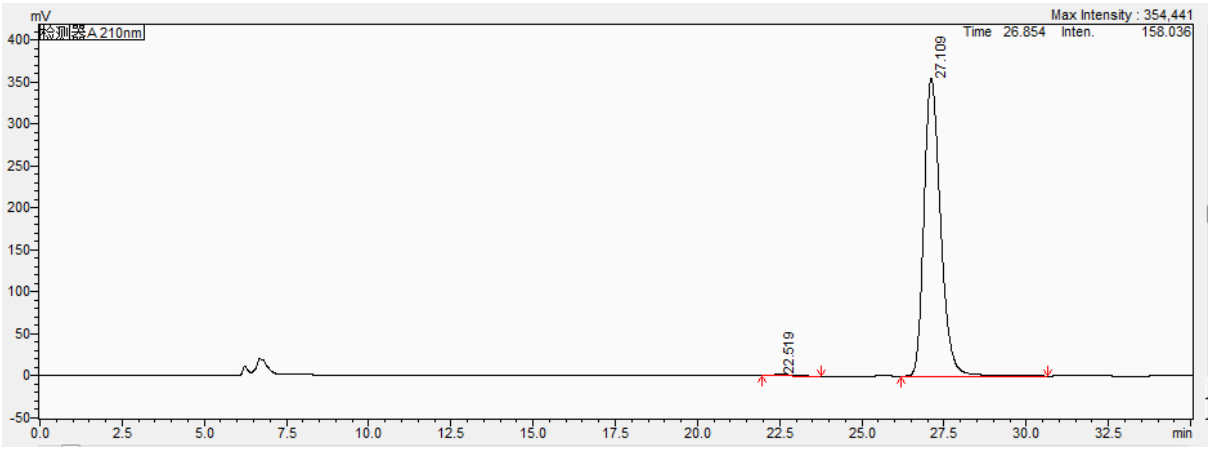


2w

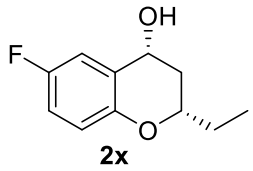
Racemate



Chiral

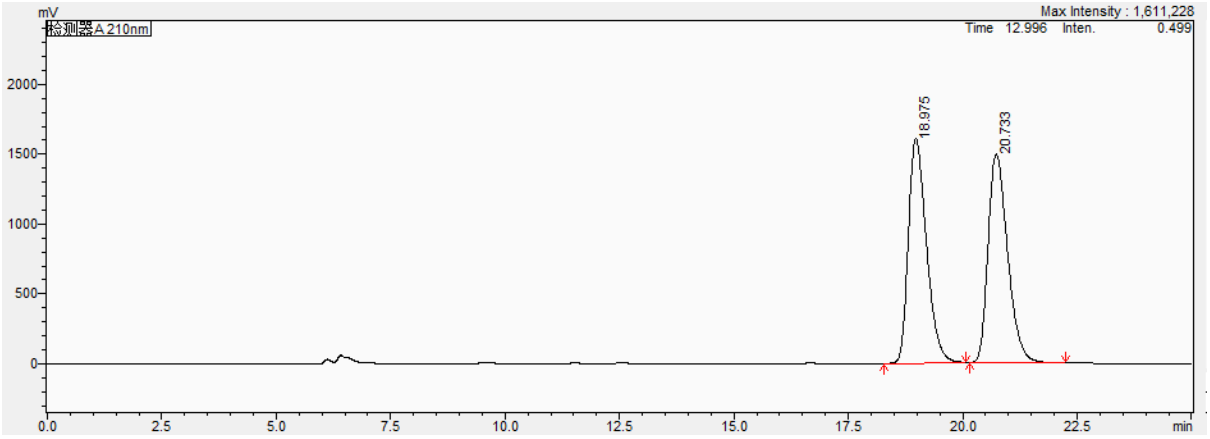


	Retention Time (min)	Area (%)	
Peak 1	22.519	0.683	**99% ee**
Peak 2	27.109	99.317	

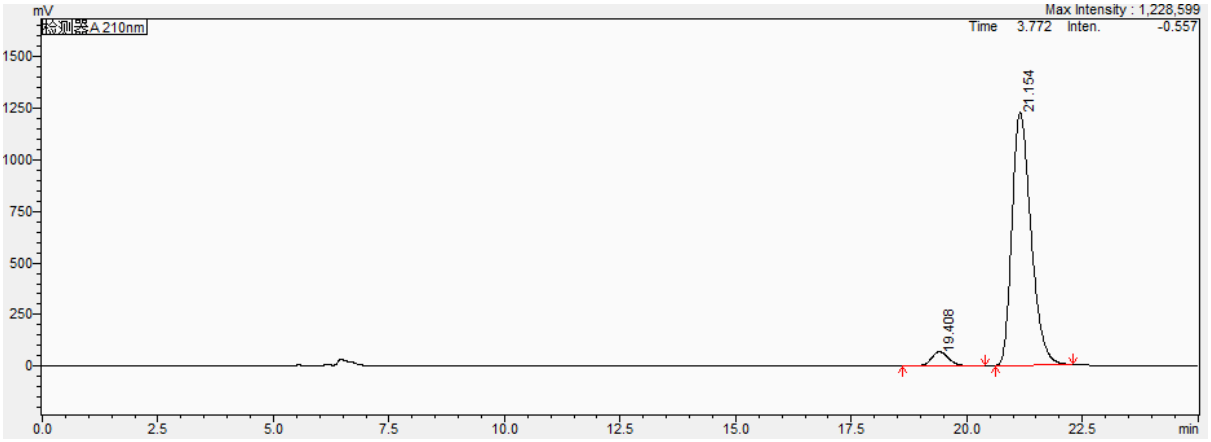


2x

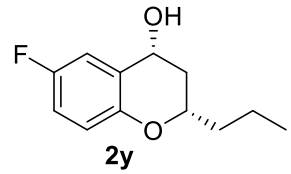
Racemate



Chiral

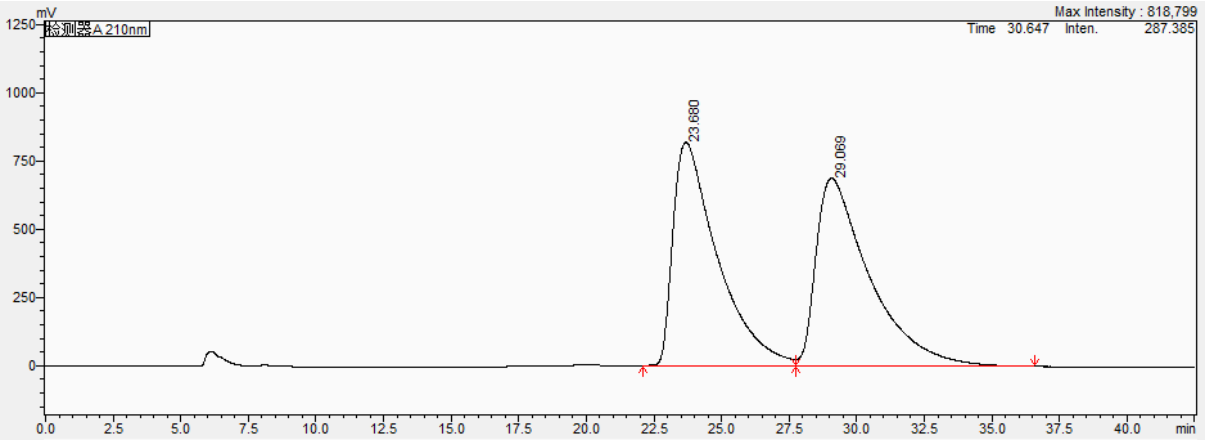


	Retention Time (min)	Area (%)	
Peak 1	19.408	4.853	**90% ee**
Peak 2	21.154	95.147	

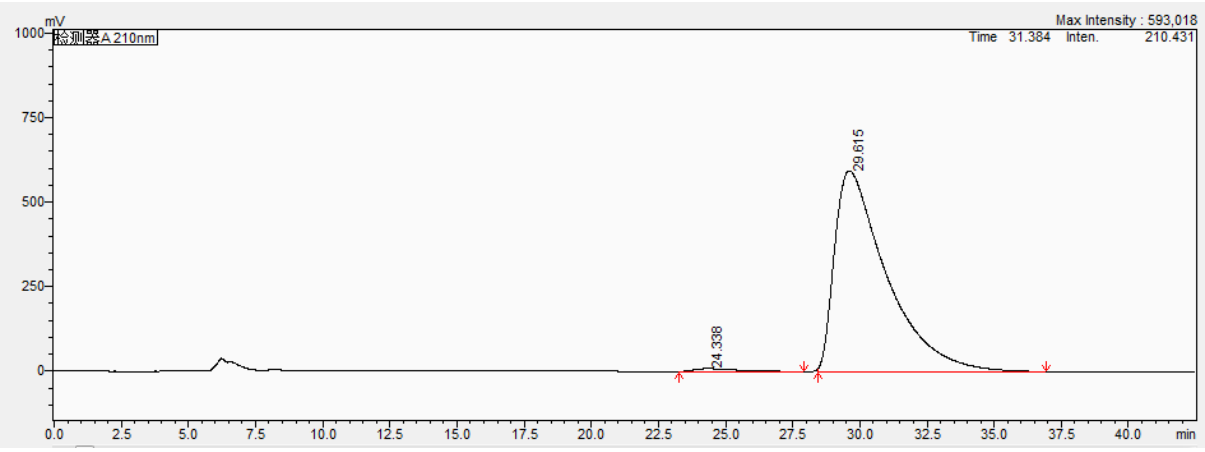


2y

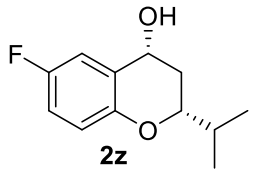
Racemate



Chiral

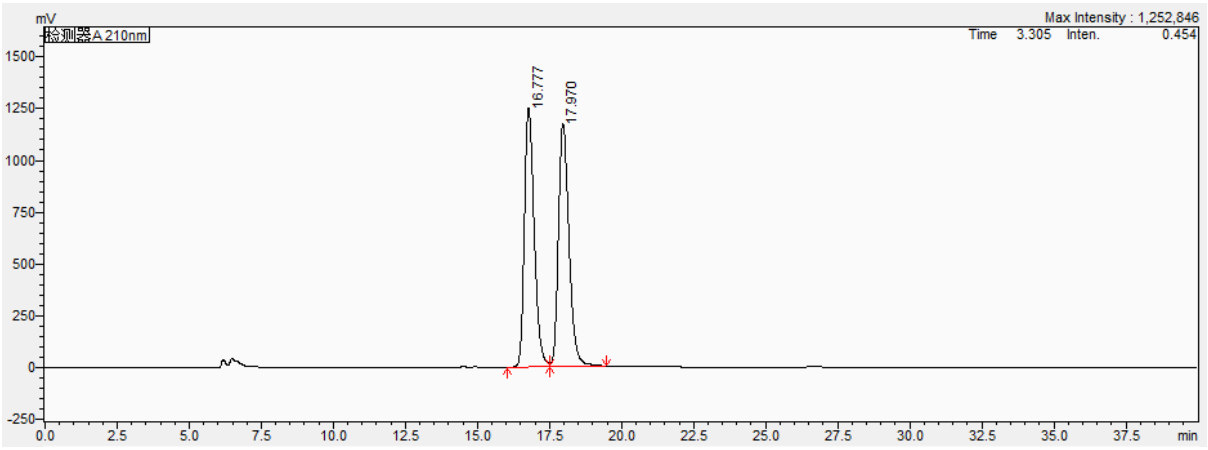


	Retention Time (min)	Area (%)	
Peak 1	24.338	1.179	**98% ee**
Peak 2	29.615	98.821	

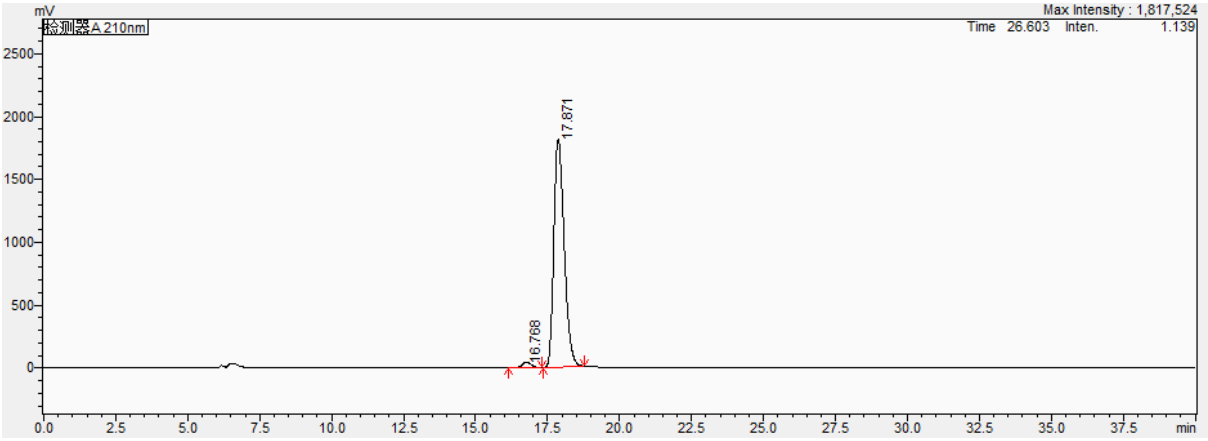


2z

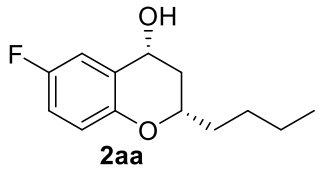
Racemate



Chiral

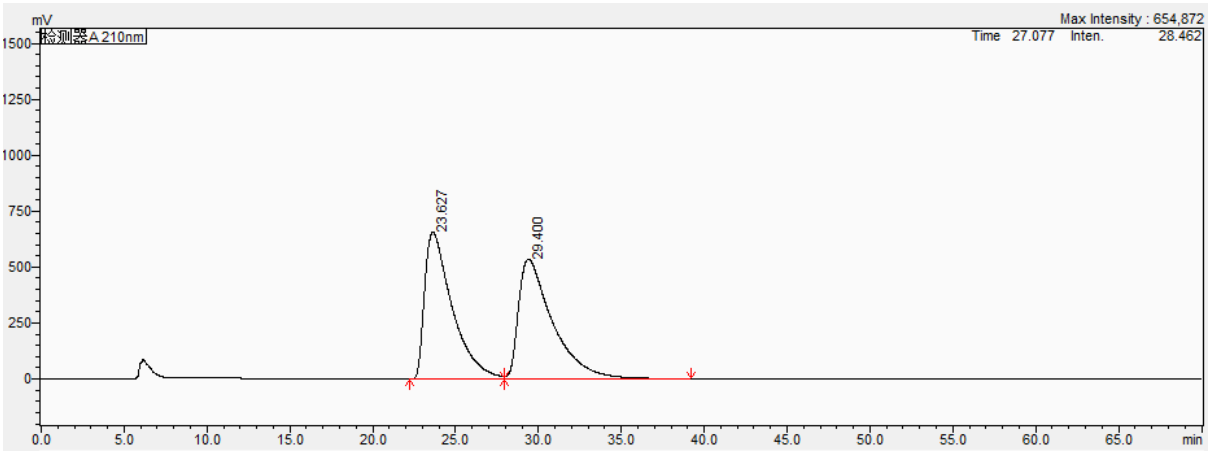


	Retention Time (min)	Area (%)	
Peak 1	16.768	2.065	**96% ee**
Peak 2	17.871	97.935	

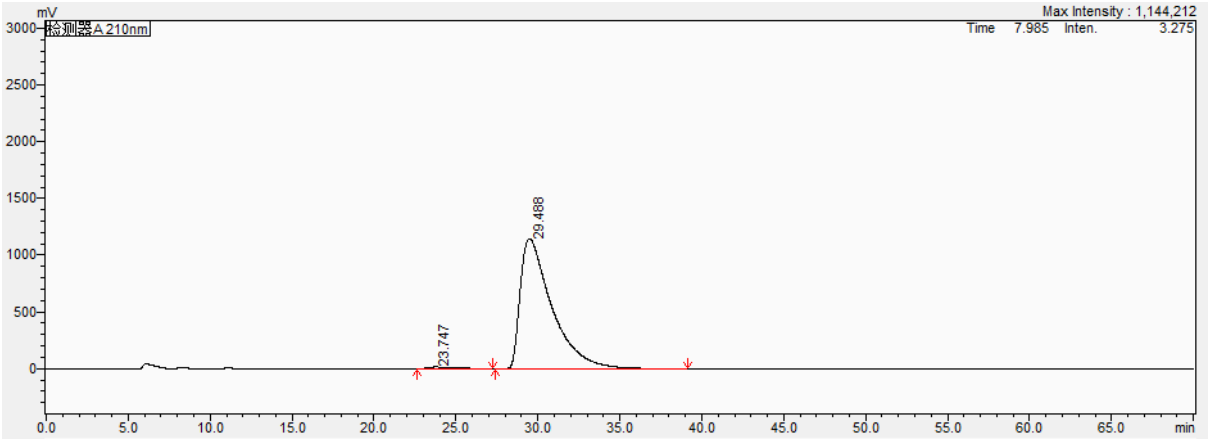


2aa

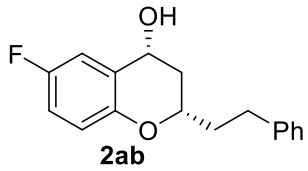
Racemate



Chiral

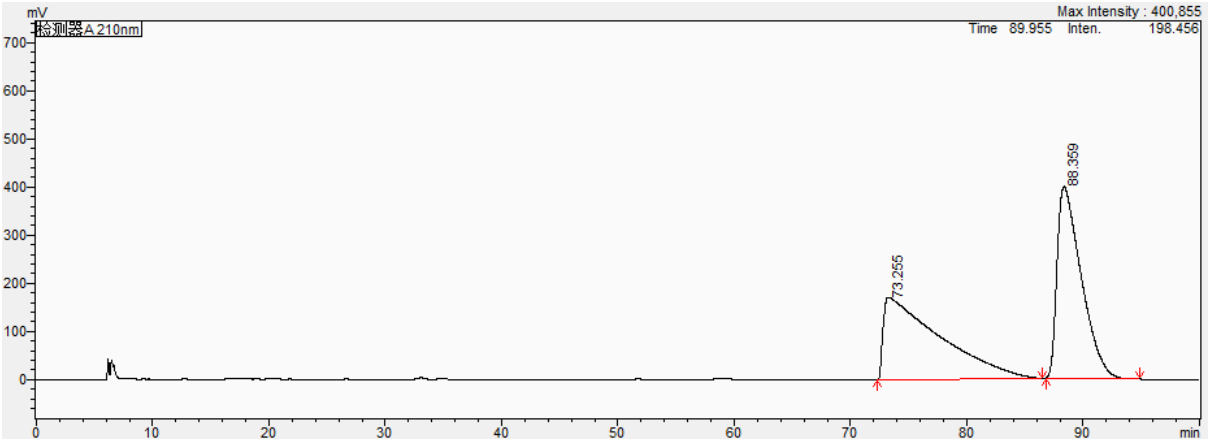


	Retention Time (min)	Area (%)	
Peak 1	23.747	0.875	**98% ee**
Peak 2	29.488	99.125	

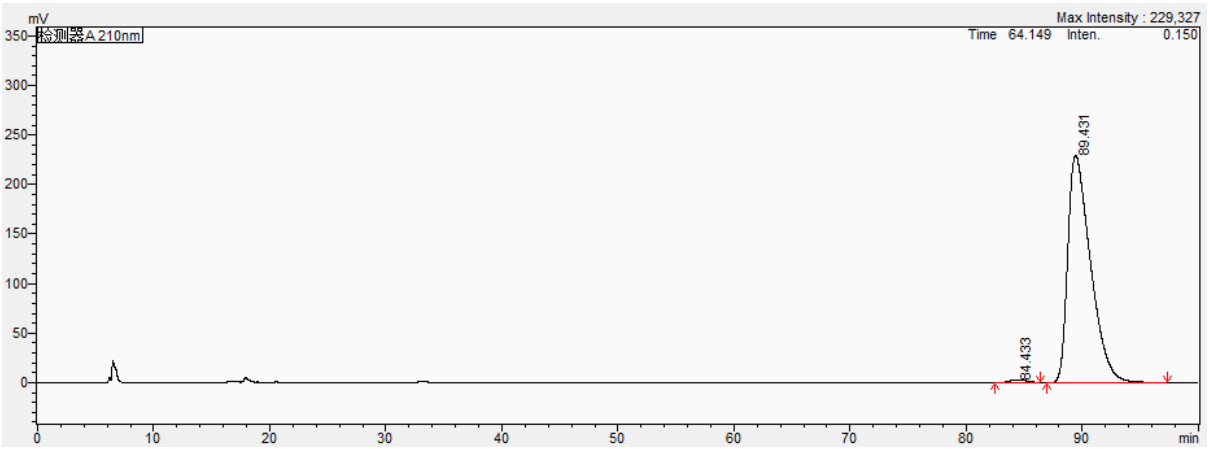


2ab

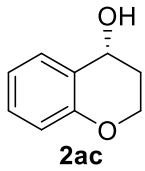
Racemate



Chiral

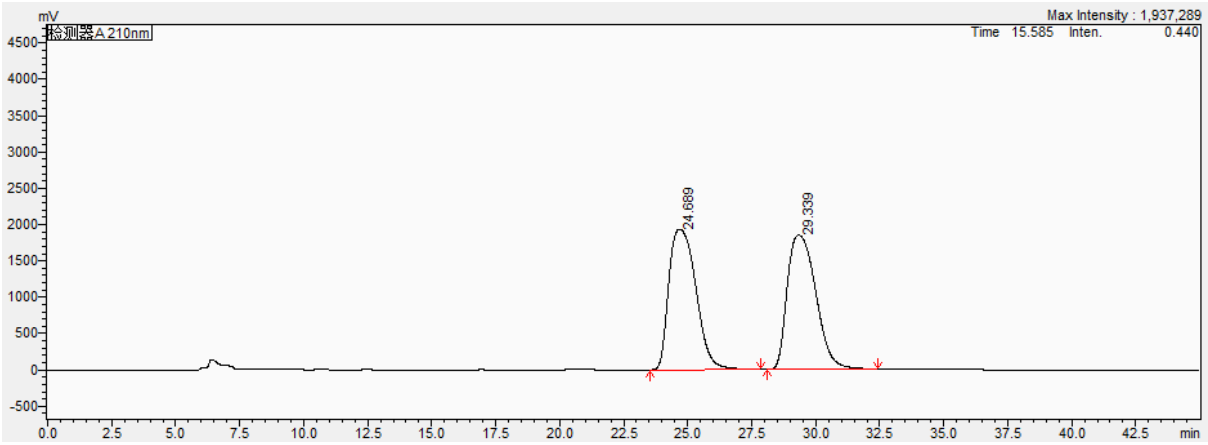


	Retention Time (min)	Area (%)	
Peak 1	84.433	0.783	**98% ee**
Peak 2	89.431	99.217	

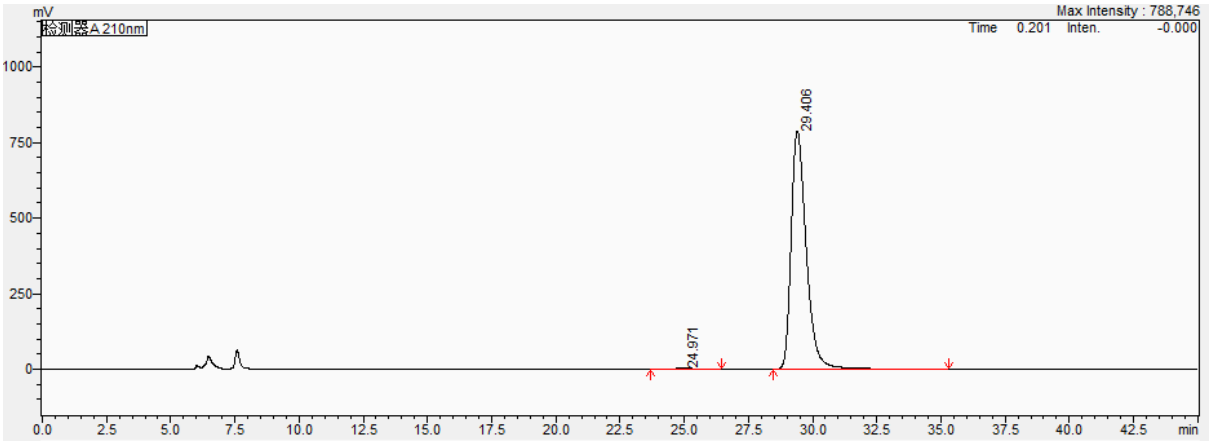


2ac

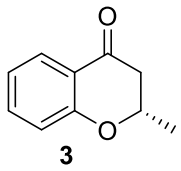
Racemate



Chiral

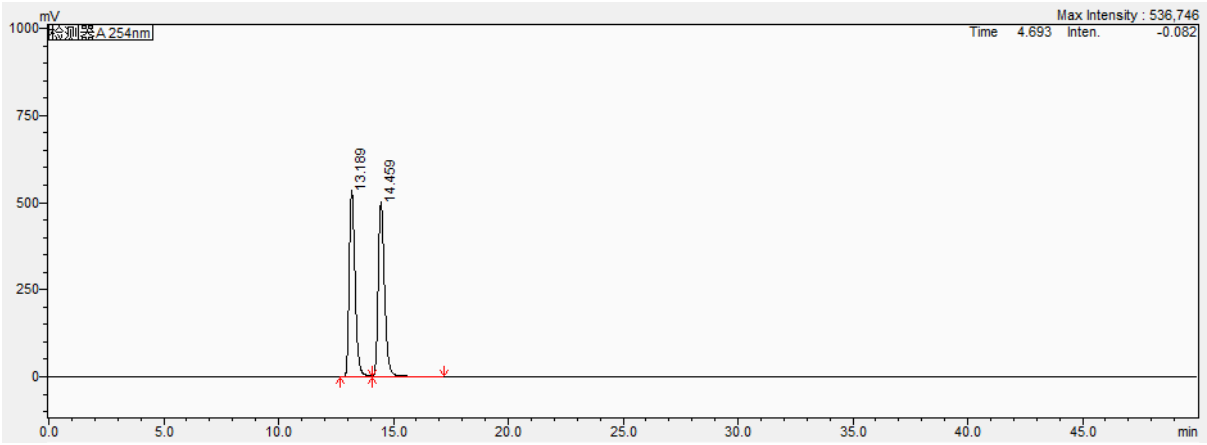


	Retention Time (min)	Area (%)	
Peak 1	24.971	0.690	**99% ee**
Peak 2	29.406	99.310	

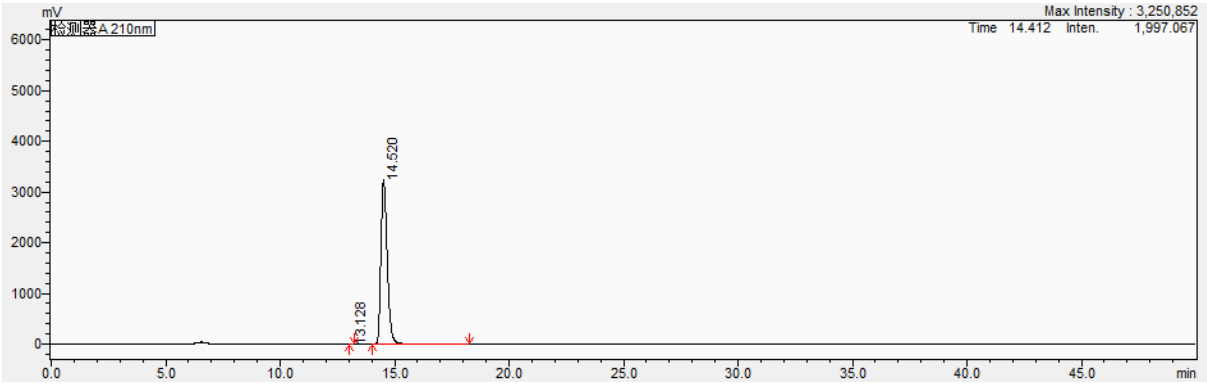


3

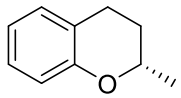
Racemate



Chiral

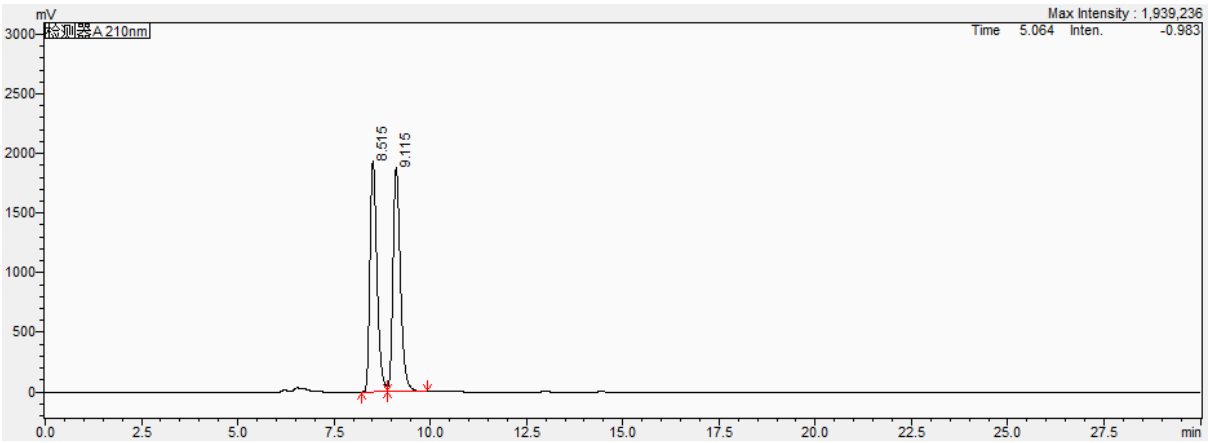


	Retention Time (min)	Area (%)	
Peak 1	13.128	0.065	**99.9% ee**
Peak 2	14.520	99.935	

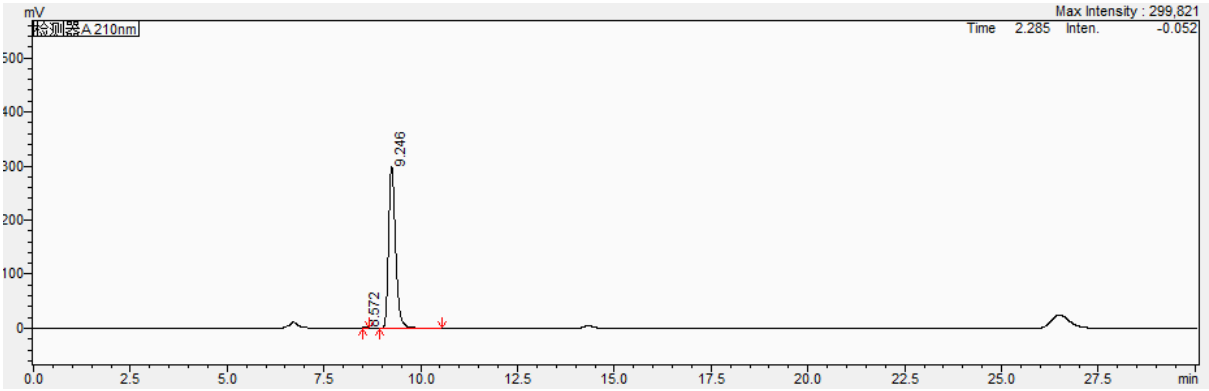


4

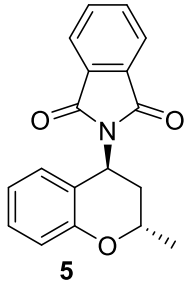
Racemate



Chiral

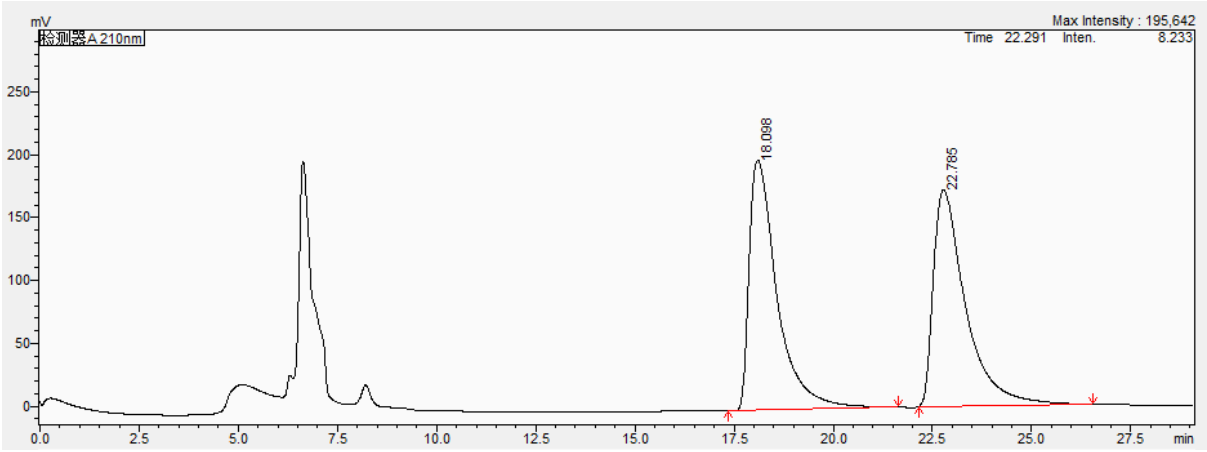


	Retention Time (min)	Area (%)	
Peak 1	8.572	0.121	**99.8% ee**
Peak 2	9.246	99.879	

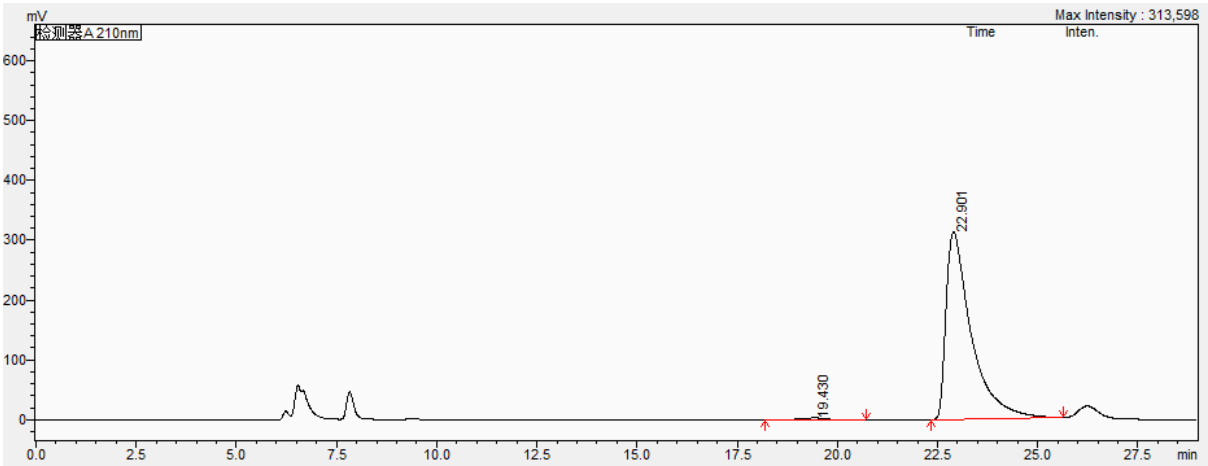


5

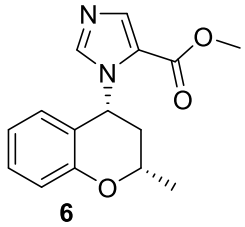
Racemate



Chiral

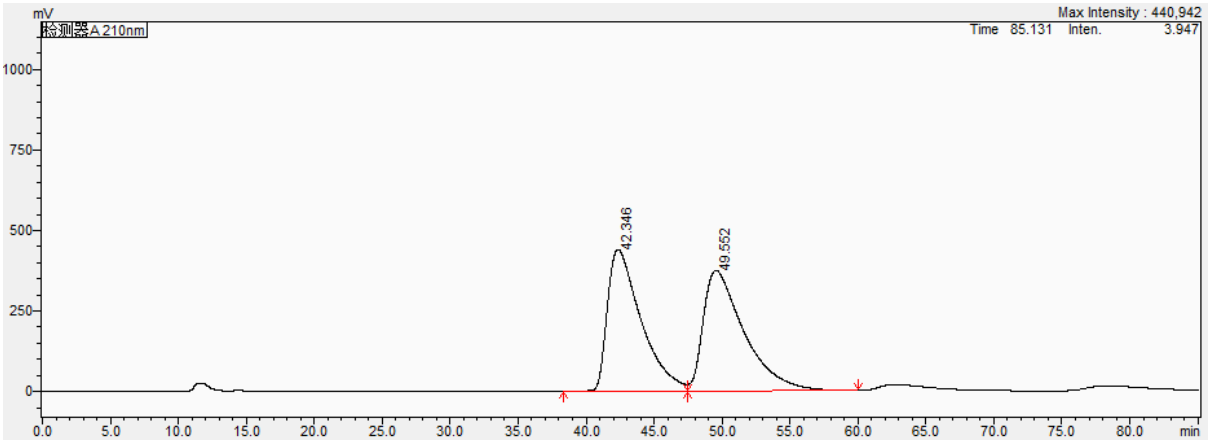


	Retention Time (min)	Area (%)	
Peak 1	19.430	1.172	**98% ee**
Peak 2	22.901	98.828	

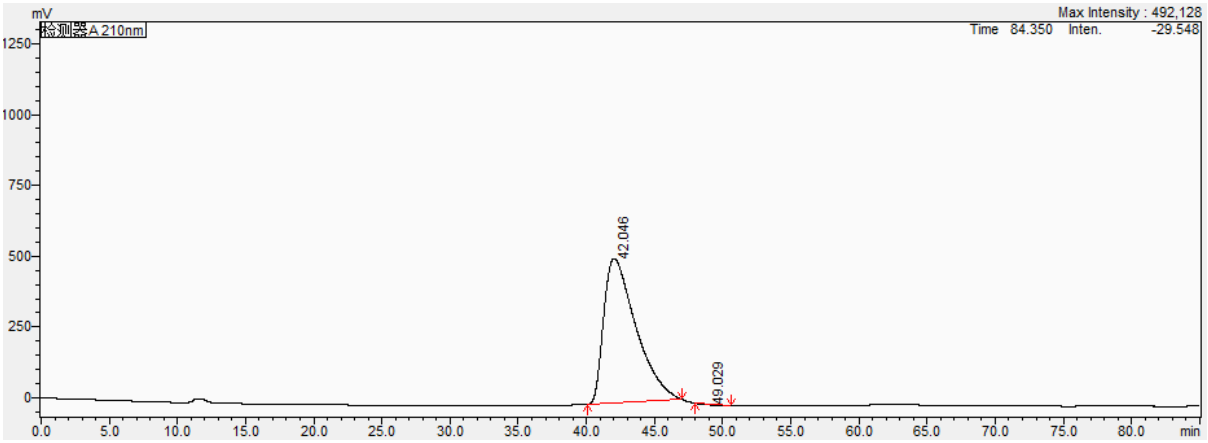


6

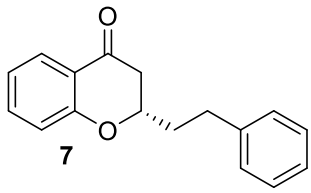
Racemate



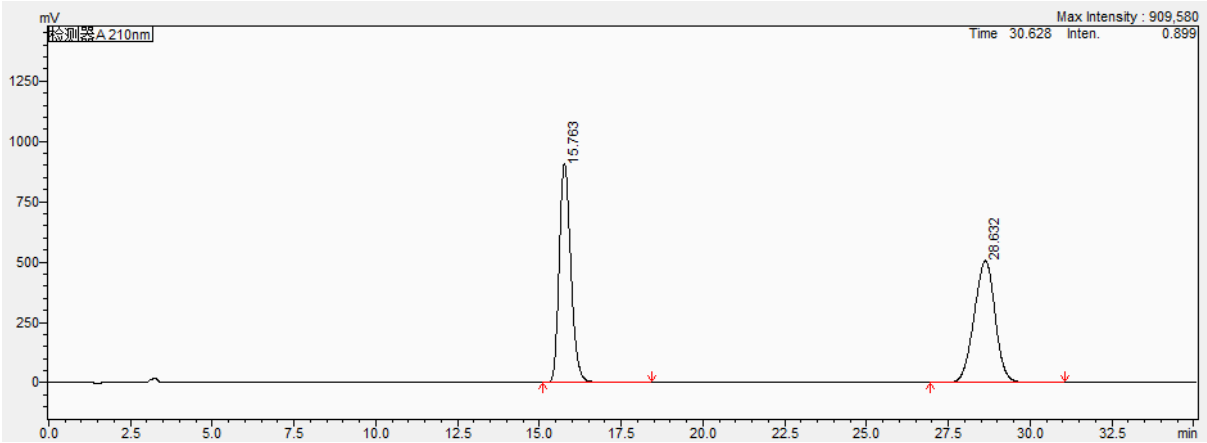
Chiral



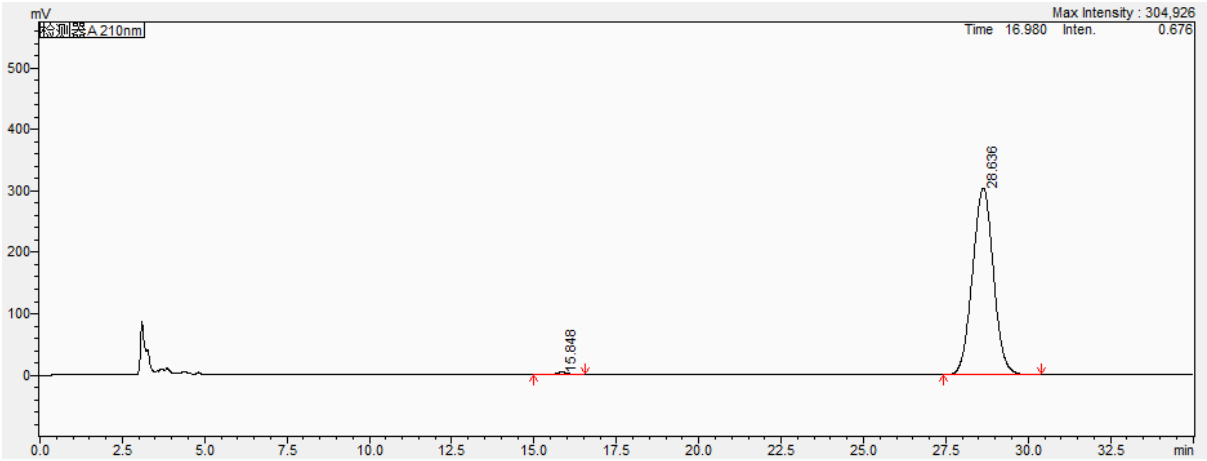
	Retention Time (min)	Area (%)	
Peak 1	42.046	99.972	**99.9% ee**
Peak 2	49.029	0.028	



Racemate



Chiral



	Retention Time (min)	Area (%)	
Peak 1	15.848	0.815	**98% ee**
Peak 2	28.636	99.185	