Electronic Supplementary Material (ESI) for Chemical Communications

Highly enantioselective Friedel-Crafts alkylation reaction catalyzed by rosin derived tertiary amine-thiourea: synthesis of modified chromanes with anticancer potency

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Supporting information

Contents

1.0. General Methods for Procedure of the Synthesis: All reactions were carried out under an argon atmosphere condition unless otherwise noted and solvents were dried according to established procedures. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel GF254. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Brucker 300 MHz spectrometer in $CDCl_3$ unless otherwise noted and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Brucker 300 MHz spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard unless otherwise noted. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, cm = complex multiplet) and coupling constant in Hertz (Hz). Infrared (IR) spectra were recorded on a FT-IR spectrometer. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HR-MS was measured with an APEX II 47e mass spectrometer. Melting points were measured on an XT-4 melting point apparatus and were uncorrected. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiracel AD-H, OD-H column on Waters with a 2996 UV-detector and the dr values determined by 300 Hz 1H NMR.

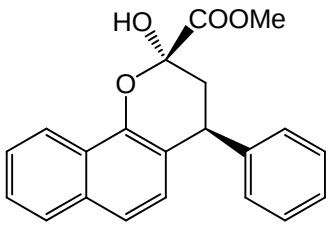
Synthesis of *β,γ*-unsaturated *α*-ketoesters according to literatures [1, 2]

2.0. General Procedure for the Asymmetric Synthesis:

To a stirred solution of L (0.01 mmol, 10.0 mol %) and *β,γ*-unsaturated *α*-ketoesters (0.10 mmol) in dry diethyl ether (1.0 mL), The solution was stirred at room temperature for 0.5 h, then the naphthols (0.20 mmol) was added and stired for 36 h. After the reaction was completed (monitored by TLC), the resulting mixture was concentrated under reduced pressure and the residue was purified through column chromatography on silica gel (eluent, EtOAc / PE 1:15) to give the optical pure product. The enantiomeric purity of the product was determined by using HPLC and the dr values determined by 300 Hz ^{1}H NMR.

3.0. Characterization of Products:

(*2R,4S*)-methyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4a)

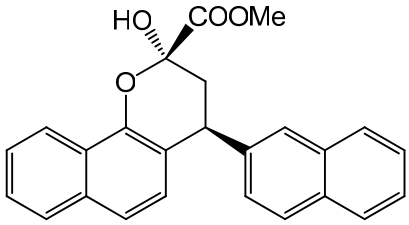


White solid, mp 142 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.70-7.75(m, 1 H), 7.44-7.48(m, 2 H), 7.25-7.36(m, 6 H), 6.85-6.88(d, *J* = 8.4 Hz, 1 H), 4.46-4.52(m, 2 H), 3.95(s, 3 H), 2.53-2.62(m, 1 H), 2.38-2.44(dd, *J* = 5.7 Hz, 13.2 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.4, 146.2, 143.5, 133.3, 130.9, 128.9, 128.8, 128.8, 127.4, 127.0, 126.7, 126.1, 125.5, 124.8, 121.5, 120.9, 119.1, 94.4, 53.6, 37.9, 36.9. **IR**: 3421.90, 3054.37, 2956.55, 2924.75, 2854.40, 2727.48, 2668.86, 1747.88, 1648.66, 1601.46, 1574.39, 1539.79, 1461.50, 1377.55, 1289.58, 1260.13, 1240.92, 1188.35, 1140.65, 1096.07, 1074.64, 1047.34, 975.79, 905.57, 873.79, 809.77, 764,54, 749.93, 722.90, 703.14, 662.20cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{18}O_4$+NH_4^+: 352.1543; found: 352.1549, 1.7ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 236 nm.) Retention time: t_{major} =9.03 min, t_{minor} =11.58 min, ee = 93%.

(*2R,4S*)-methyl 2-hydroxy-4-(naphthalen-2-yl)-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4b)



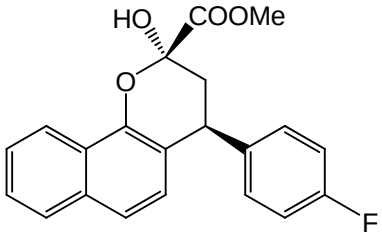
White solid, mp 75 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.18-8.23(m, 1 H), 7.81-7.87(m, 4 H), 7.73-7.76(m, 1 H), 7.46-7.52(m, 4 H), 7.29-7.33(dd, *J* = 2.1 Hz, 5.4 Hz, 2 H), 6.86-6.89(d, *J* = 8.7 Hz, 1 H), 4.64-4.70(q, *J* = 6.0 Hz, 1 H), 4.49(d, *J* = 2.1 Hz, 1 H), 3.97(s, 3 H), 2.64-2.74(m, 1 H), 2.44-2.50(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.4, 146.3, 140.8, 133.5, 133.4, 132.6, 128.6, 128.0, 127.7, 127.6, 127.5, 126.7, 126.6, 126.2, 126.1, 125.8, 125.6, 124.8, 121.6, 120.9, 119.0, 94.4, 53.7, 38.1, 36.7. **IR**: 3427.26, 3054.44, 3018.12, 2957.00, 1926.40, 2855.93, 1915.29, 1747.14, 1711.34, 1633.30, 1600.27, 1572.72, 1506.11, 1438.86, 1378.58, 1289.43, 1263.32, 1240.87, 1216.49, 1138.83, 1096.11, 1075.93, 1049.08, 981.42, 955.96, 902.71, 861.79, 808.82, 750.08, 707.53, 656.16,cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{25}H_{20}O_4$+NH_4^+: 402.1700; found: 402.1707, 1.7ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 10/90, 1.0 mL/min, 239 nm.) Retention time: t_{major} =13.78 min, t_{minor} =18.69 min, ee = 82%.

(*2R,4S*)-methyl 4-(4-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy

late (4c)

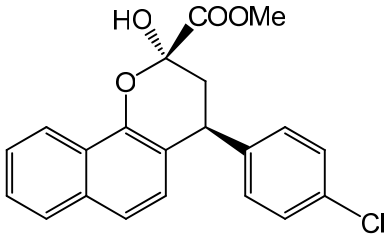


White solid, mp 145 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.15-8.18(m, 1 H), 7.72-7.76(m, 1 H), 7.45-7.50(m, 2 H), 7.31-7.34(d, *J* = 8.7 Hz, 1 H), 7.21-7.26(m, 2 H), 7.01-7.07(m, 2 H), 6.82-6.85(d, *J* = 8.7 Hz, 1 H), 4.45-4.51(m, 2 H), 3.96(s, 3 H), 2.48-2.57(m, 1 H), 2.36-2.42(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.2, 146.2, 139.2, 139.2, 133.4, 130.4, 130.3, 127.4, 126.4, 126.2, 125.6, 124.8, 121.5, 121.0, 118.9, 115.8, 115.5, 94.3, 53.6, 37.2, 37.0. **IR**: 3408.22, 3054.23, 2958.81, 2924.64, 2850.08, 1742.96, 1656.91, 1601.22, 1572.71, 1506.37, 1437.92, 1378.22, 1293.86, 1223.65, 1188.32, 1139.28, 1095.22, 1074.64, 1047.00, 974.85, 905.81, 874.46, 840.24, 808.47, 778.01, 750.32, 659.55 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{17}FO_4$+NH_4^+: 370.1449; found: 370.1445, 1.6ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 235 nm.) Retention time: t_{major} =10.27 min, t_{minor} =14.85 min, ee = 93%.

(*2R,4S*)-methyl 4-(4-chlorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4d)

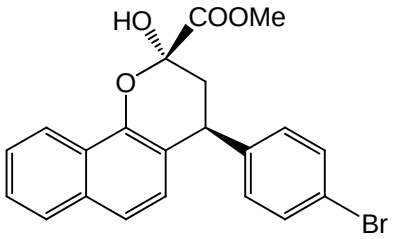


White solid, mp 178 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.15-8.18(m, 1 H), 7.72-7.77(m, 1 H), 7.46-7.49(m, 2 H), 7.32-7.34(d, J = 8.4 Hz, 3 H), 7.20-7.23(d, *J* = 8.4 Hz, 2 H), 6.81-6.84(d, *J* = 8.4 Hz, 1 H), 4.45-4.51(m, 2 H), 3.96(s, 3 H), 2.47-2.57(m, 1 H), 2.35-2.42(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.2, 146.3, 142.1, 133.4, 132.7, 130.3, 129.0, 127.5, 126.4, 126.2, 125.7, 124.8, 121.5, 121.0, 118.5, 94.3, 53.7, 37.4, 36.8. **IR**: 3429.42, 3056.51, 2952.94, 2889.62, 1897.73, 1745.77, 1704.74, 1574.19, 1490.60, 1438.44, 1379.72, 1295.31, 1238.45, 1188.68, 1140.40, 1094.82, 1048.22, 1017.99, 976.41, 907.10, 874.40, 835.39, 810.15, 785.93, 752.16, 729.40, 649.66cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{17}ClO_4$+NH_4^+: 386.1154; found: 386.1161, 1.8ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 234 nm.) Retention time: t_{major} =10.95 min, t_{minor} =17.82 min, ee = 91%.

(*2R,4S*)-methyl 4-(4-bromophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4e)

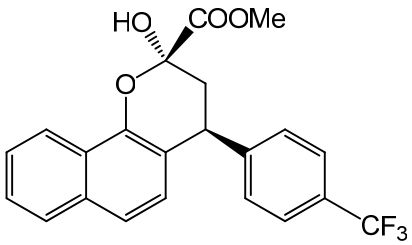


White solid, mp 178 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.15-8.18(m, 1 H), 7.73-7.76(m, 1 H), 7.46-7.50(m, 4 H), 7.32-7.34(d, *J* = 8.4 Hz, 1 H), 7.14-7.17(d, *J* = 8.4 Hz, 2 H), 6.81-6.84(d, *J* = 8.4 Hz, 1 H), 4.43-4.45(m, 2 H), 3.96(s, 3 H), 2.47-2.56(m, 1 H), 2.36-2.42(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.2, 146.3, 142.6, 133.4, 131.9, 130.6, 127.4, 126.3, 126.2, 125.7, 124.8, 121.5, 121.0, 120.8, 118.4, 94.2, 53.7, 37.5, 36.8. **IR**: 3312.23, 3053.65, 3014.51, 2954.19, 2925.06, 2853.57, 1937.32, 1913.42, 1889.48, 1822.58, 1734.38, 1636.33, 1597.40, 1573.25, 1508.95, 1460.02, 1375.46, 1298.97, 1257.63, 1185.23, 1132.08, 1096.73, 1068.61, 1023.63, 905.92, 871.75, 802.00, 731.03, 705.15, 663.15, cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{17}BrO_4$+NH_4^+:430.0648; found: 430.0653, 1.2ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 236 nm.) Retention time: t_{major} =12.14 min, t_{minor} =20.56 min, ee = 94%.

(*2R,4S*)-methyl 2-hydroxy-4-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-benzo[h]chromene -2-carboxylate (4f)



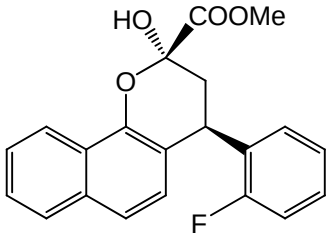
White solid, mp 172 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.74-7.77(m, 1 H), 7.60-7.63(d, *J* = 8.1 Hz, 2 H), 7.47-7.50(m, 2 H), 7.39-7.42(d, *J* = 8.1 Hz, 2 H), 7.33-7.35 (d, *J* = 8.7 Hz, 1 H), 6.78-6.81(d, *J* = 8.7 Hz, 1 H), 4.54-4.61(q, *J* = 6.0 Hz, 1 H) (m, 1 H), 4.49(s, 1 H), 3.96(s, 3 H), 2.50-2.59(m, 1 H), 2.38-2.44(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz,

CDC_3): δ 170.1, 147.8, 146.4, 133.5, 129.6, 129.3, 129.1,127.5, 126.3, 126.3, 125.8, 125.8, 124.8, 121.5, 121.1, 118.0, 94.2, 53.7, 37.9, 36.8. **IR**: 3431.38, 3054.64, 3010.89, 2956.15, 2896.21, 2853.56, 2644.61, 1923.50, 1748.90, 1709.56, 1618.45, 1574.73, 1540.44, 1506.69, 1438.78, 1418.48, 1380.52, 1326.60, 1306.34, 1241.70, 1189.14, 1162.06, 1125.93, 1069.96, 1047.57, 1020.76, 976.50, 908.50, 846.71, 810.06, 752.06, 726.99, 705.72, 663.48,642.18, 598.94cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{22}H_{17}F_3O_4+NH_4^+$: 420.1417; found: 420.1422, 1.2ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 234 nm.) Retention time: t_{major} =9.02 min, t_{minor} =13.29 min, ee = 95%.

(*2R,4R*)-methyl 4-(2-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4g)

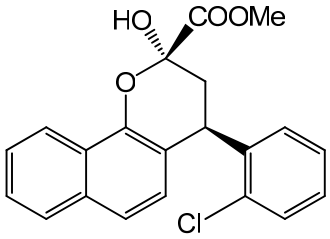


White solid, mp 151 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.73-7.76(m, 1 H), 7.44-7.50(m, 2 H), 7.33-7.36(d, *J* = 8.7 Hz, 1 H),7.27-7.30(m, 1 H), 7.18-7.23(m, 1 H), 7.08-7.14(m, 1 H),6.87-6.90(d, *J* = 8.4 Hz, 1 H), 4.83-4.89(dd, *J* = 5.7 Hz, 12.6 Hz, 1 H), 4.44-4.45(d, *J* = 2.1 Hz, 1 H), 3.96(s, 3 H), 2.59-2.68(m, 1 H), 2.39-2.45(dd, *J* = 6.0 Hz, 13.2 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.2, 146.3, 133.4, 128.7, 128.6, 127.4, 126.1, 126.0, 125.6, 124.9, 124.5, 124.5, 121.5, 121.0, 118.1, 115.9, 115.6, 94.3, 53.6, 34.9. **IR**: 3454.00, 3057.58, 3010.51, 2956.24, 2926.21, 2854.20, 2253.24, 1951.55, 1914.15, 1746.25, 1663.00, 1635.13, 1578.85, 1490.87, 1452.42, 1379.85, 1350.18, 1295.30, 1258.05, 1226.24, 1189.32, 1141.86, 1098.40, 1076.10, 1048.27, 977.48, 910.30, 872.99, 811.68, 757.27, 733.17, 703.76, 656.19, 614.77, 572.30, 526.35cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{17}FO_4+NH_4^+$: 370.1449; found: 370.1441, 2.2ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 238 nm.) Retention time: t_{major} =9.17 min, t_{minor} =12.79 min, ee = 92%.

(*2R,4R*)-methyl 4-(2-chlorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4h)

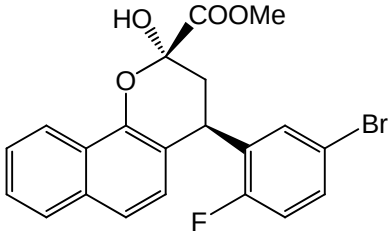


White solid, mp 161 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.74-7.77(m, 1 H), 7.44-7.49(m, 3 H), 7.34-7.37(d, *J* = 8.4 Hz, 1 H), 7.12-7.23(m, 3 H), 6.86-6.89(d, *J* = 8.7 Hz, 1 H), 5.15(s, 1 H), 4.44-4.45(d, *J* = 1.5 Hz, 1 H), 3.95(s, 3 H), 2.49(s, 2 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.2, 133.4, 129.6, 128.1, 127.4, 127.3, 126.4, 126.2, 125.6, 125.0, 121.5, 121.0, 118.1, 94.4, 53.6. **IR**: 3455.33, 3057.95, 3013.42, 2957.27, 2929.16, 2854.57, 2252.84, 1955.62, 1922.20, 1745.33, 1598.77, 1574.53, 1506.53, 1471.76, 1439.75, 1380.27, 1293.41, 1261.43, 1240.84, 1189.86, 1143.19, 1097.65, 1076.19, 1037.08, 977.62, 908.53, 872.19, 811.26, 791.76, 755.36, 732.85, 696.71, 655.48, 614.63, 570.61 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{17}ClO_4$+NH_4^+: 386.1154; found: 386.1153, 0.3ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 2/98, 1.0 mL/min, 234 nm.) Retention time: t_{minor} =9.03 min, t_{major} =11.58 min, ee = 93%.

(*2R,4R*)-methyl 4-(5-bromo-2-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4i)

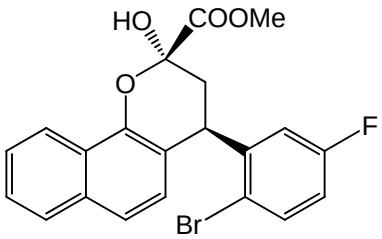


White solid, mp 72 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.15-8.23(m, 1 H), 7.73-7.82(m, 1 H), 7.46-7.49(m, 2 H), 7.31-7.38(m, 3 H), 6.98-7.04(m, 1 H), 6.85-6.87(d, *J* = 8.4 Hz, 1 H), 4.74-4.86(m, 1 H), 4.56(*syn*: s, 0.8 H), 4.26(*anti*: s, 0.2 H), 3.96(*syn*: s, 2.6 H), 3.89(*anti*: s, 0.4 H), 2.54-2.62(t, *J* = 12.9 Hz, 1 H), 2.37-2.44(m, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.0, 146.4, 133.5, 133.1, 132.4, 131.7, 131.5, 127.5, 126.3, 125.7, 124.9, 121.5, 121.3, 117.8, 117.5, 117.2, 117.0, 94.2, 53.7, 34.9. **IR**: 3432.87, 3057.81, 3014.83, 2954.71, 2924.35, 2854.67, 1747.60, 1659.41, 1602.06, 1575.16, 1507.17, 1482.07, 1440.21, 1280.61, 1292.99, 1239.33, 1188.75, 1142.95, 1097.59, 1047.09, 979.29, 919.37, 881.11, 812.25, 754.39, 661.74cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{18}O_4$+NH_4^+: 448.0554; found: 448.0560, 1.3ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 1/99, 1.0 mL/min, 227 nm.) Retention time: t_{minor} =36.71 min, t_{major} =46.36 min, ee = 93%.

(*2R,4R*)-methyl 4-(2-bromo-5-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene -2-carboxylate (4j)

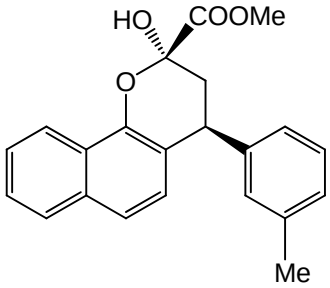


White solid, mp 65 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.72-7.75(m, 1 H), 7.43-7.59(m, 3 H), 7.34-7.37(*syn*: d, *J* = 8.4 Hz, 0.8 H), 6.93-6.96(*anti*: d, *J* = 8.4 Hz, 0.2 H), 6.83-6.90(m, 3 H), 5.06-5.12(*syn*: br, 0.8 H), 4.82-4.86(*anti*: br, 0.2 H), 4.62-4.63(*syn*: d, *J* = 1.8 Hz, 0.8 H), 4.38(*anti*: d, *J* = 1.8 Hz, 0.2 H), 3.91(*syn*: s, 2.5 H), 3.87(*anti*: s, 0.5 H), 2.30-2.56(m, 2 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.0, 163.8, 160.0, 147.4, 146.7, 145.3, 133.7, 133.4, 127.4, 127.1, 126.5, 126.3, 126.1, 125.8, 125.7, 125.0, 121.7, 121.5, 121.2, 117.3, 116.0, 115.8, 115.7, 95.0, 94.3, 53.6, 53.4, 38.3, 37.4, 35.3, 33.7. **IR**: 3437.03, 3057.38, 3008.24, 2955.22, 2924.76, 2853.47, 1748.73, 1661.30, 1603.24, 1576.37, 1506.30, 1465.92, 1402.22, 1380.27, 1276.39, 1242.53, 1221.45, 1190.42, 1141.83, 1107.24, 1076.33, 1050.90, 1027.40, 988.54, 957.92, 877.46, 809.41, 754.31, 662.08cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{18}O_4$+NH_4^+: 448.0554; found: 448.0557, 0.7ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 10/90, 1.0 mL/min, 234 nm.) Retention time: t_{minor} =7.80 min, t_{major} =9.41 min, ee = 93%.

(*2R,4S*)-methyl 2-hydroxy-4-m-tolyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4k)



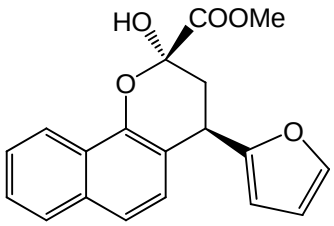
White solid, mp 155 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.72-7.77(m, 1 H), 7.45-7.47(m, 2 H), 7.31-7.33(d, *J* = 6.8 Hz, 1 H), 7.22-7.27(m, 1 H), 7.07-7.12(m, 1 H), 6.86-6.89(d, *J* = 8.4 Hz, 1 H), 4.42-4.48(dd, *J* = 5.7 Hz, 12.9 Hz, 2 H), 3.95(s, 3 H), 2.53-2.61(t, *J*

= 13.2 Hz, 1 H), 2.36-2.43(dd, *J* = 5.7 Hz, 13.2 Hz, 1 H), 2.33(s, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.4, 146.2, 143.5, 138.4, 133.3, 129.6, 128.6, 127.7, 127.4, 126.7, 126.0, 125.5, 124.8, 121.4, 120.8, 119.3, 94.4, 53.6, 37.8, 36.8, 21.4. **IR**: 3458.90, 3054.20, 3018.43, 2957.58, 2923.88, 2854.34, 2733.15, 2251.06, 1945.02, 1745.37, 1634.59, 1604.25, 1574.01, 1505.38, 1488.30, 1439.69, 1379.15, 1347.22, 1291.15, 1259.36, 1236.47, 1187.32, 1138.47, 1096.53, 1048.88, 1026.52, 977.76, 937.32, 909.72, 875.72, 808.99, 733.69, 698.57, 657.19, 623.36, 569.56cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{22}H_{20}O_4$+NH_4^+: 366.1700; found: 366.1698, 0.5ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 2/98, 1.0 mL/min, 236 nm.) Retention time: t_{minor} =23.72 min, t_{major} =29.46 min, ee = 90%.

(*2R,4R*)-methyl 4-(furan-2-yl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4l)

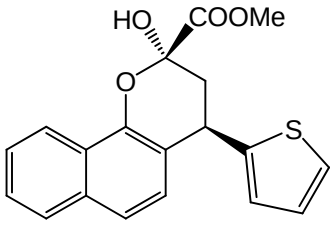


White solid, mp 128 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.13-8.16(m, 1 H), 7.73-7.76(m, 1 H), 7.44-7.47(m, 2 H), 7.36-7.39(m, 2 H), 6.99-7.02(d, *J* = 5.4 Hz, 1 H), 6.39-6.40(dd, *J* = 1.8 Hz, 3.0Hz, 1 H), 6.32-6.33(d, *J* = 3.0 Hz, 1 H), 4.61-4.67(dd, *J* = 5.4 Hz, 12.9 Hz, 1 H), 4.45-4.46(d, *J* = 2.1 Hz, 1 H), 3.96(s, 3 H), 2.72-2.82(m, 1 H), 2.37-2.43(dd, *J* = 5.4 Hz, 13.2 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.2, 155.0, 145.8, 142.1, 133.5, 127.4, 126.1, 125.5, 125.4, 124.8, 121.5, 121.0, 116.7, 110.2, 107.7, 94.3, 53.6, 33.1, 31.4. **IR**: 3435.90, 3055.73, 2955.18, 2923.60, 2854.31, 1744.85, 1599.56, 1575.22, 1505.20, 1460.58, 1444.12, 1379.22, 1291.22, 1263.34, 1231.34, 1208.86, 1141.13, 1096.15, 1049.90, 1013.88, 977.04, 949.28, 890.39, 808.73, 778.65, 744.66, 652.37cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{19}H_{16}O_5$+Na^+: 347.0890; found: 347.0879, 3.2ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 10/90, 1.0 mL/min, 238 nm.) Retention time: t_{major} =11.12 min, t_{minor} =12.53 min, ee = 86%.

(*2R,4R*)-methyl 2-hydroxy-4-(thiophen-2-yl)-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4m)

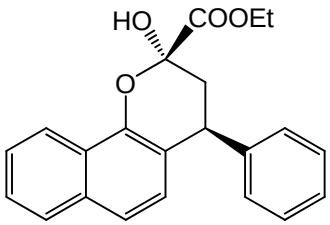


White solid, mp 83 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.14-8.19(m, 1 H), 7.72-7.76(m, 1 H), 7.45-7.48(m, 2 H), 7.35-7.38(d, *J* = 8.4 Hz, 1 H), 7.26(m, 1 H), 7.01-7.08(m, 3 H), 4.82-4.89(q, *J* = 6.0 Hz, 1 H), 4.45-4.46(d, *J* = 1.8 Hz, 1 H), 3.97(s, 3 H), 2.61-2.70(m, 1 H), 2.49-2.55(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.1, 146.4, 145.6, 133.5, 127.4, 126.7, 126.4, 126.2, 126.0, 125.6, 124.7, 124.5, 121.6, 120.9, 118.8, 94.3, 53.6, 37.3, 33.2. **IR**: 3443.76, 3109.25, 3057.61, 2973.00, 2955.04, 2892.91, 2293.69, 2251.77, 1908.92, 1749.21, 1706.16, 1634.06, 1598.62, 1574.52, 1535.34, 1506.03, 1437.97, 1379.11, 1299.11, 1263.12, 1234.75, 1190.72, 1141.66, 1095.55, 1047.02, 972.22, 884.60, 850.82, 808.37, 778.38, 752.28, 702.30, 654.54, 624.16, 595.57, 571.54 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{19}H_{16}O_4S+NH_4^+$: 358.1108; found: 358.1100, 2.2ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 5/95, 1.0 mL/min, 239 nm.) Retention time: t_{minor} = 18.18 min, t_{major} = 22.49 min, ee = 91%.

(*2R,4S*)-ethyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4n)

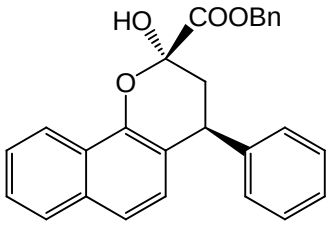


Wax solid. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.16-8.19(m, 1 H), 7.71-7.76(m, 1 H), 7.45-7.48(m, 2 H), 7.28--7.37(m, 6 H), 6.85-6.88(d, *J* = 8.4 Hz, 1 H), 4.46-4.53(m, 2 H), 4.37-4.44(q, *J* = 6.9 Hz, 2 H), 2.53-2.61(t, *J* = 13.2 Hz, 1 H), 2.37-2.44(dd, *J* = 6.0 Hz, 13.5 Hz, 1 H), 1.36-1.41(t, *J*=7.2 Hz, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 169.9, 146.3, 143.6, 133.4, 129.0, 128.8, 127.4, 127.0, 126.7, 126.1, 125.8, 125.5, 124.8, 121.5, 120.8, 119.1, 94.3, 63.0, 37.9, 36.9, 14.1. **IR**: 3440.13, 3058.61, 3028.22, 2977.55, 2961.92, 2935.92, 2873.89, 1953.01, 1742.98, 1709.69, 1600.39, 1574.80, 1451.72, 1380,21, 1289.71, 1239.57, 1188.43, 1140.87, 1096.55, 1073.85, 1048.13, 972.00, 906.78. 863.37, 837.29, 811.61, 786.60, 763.25, 752.98, 704.27, 659.54, 616.78, 570.40, 530.02cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{18}O_4$+NH_4^+: 366.1700; found: 366.1709, 2.5ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 236 nm.) Retention time: t_{major} =8.77 min, t_{minor} =10.55 min, ee = 82%.

(*2R,4S*)-benzyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4o)

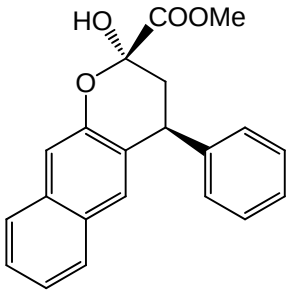


Wax solid.**^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.13-8.16(m, 1 H), 7.71-7.74(m, 1 H), 7.44-7.47(m, 2 H), 7.23-7.42(m, 11 H), 6.83-6.86(d, *J* = 8.7 Hz, 1 H), 5.36(s, 2 H), 4.45-4.53(m, 2 H), 2.53-2.62(m, 1 H), 2.38-2.45(dd, *J* = 5.7 Hz, 13.5 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 169.7, 146.2, 143.5, 134.7, 133.3, 129.0, 128.7, 128.7, 128.7, 128.2, 127.8, 127.4, 127.0, 126.6, 126.1, 125.5, 124.8, 121.5, 120.8, 119.2, 94.2, 68.3, 37.9, 36.7. **IR**: 3444.69, 3060.19, 3031.08, 2969.77, 2891.78, 1952.79, 1901.87, 1809.84, 1746.55, 1600.90, 1574.56, 1499.41, 1453.80, 1435.88, 1380.04, 1351.75, 1285.85, 1259.06, 1237.91, 1187.83, 1139.46, 1097.22, 1048.10, 973.08, 907.18, 881.75, 810.27, 784.95, 750.64, 701.17, 659.63, 600.75, 569.71,cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{27}H_{22}O_4$+NH_4^+: 428.1856; found: 428.1846, 2.3ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel AD-H, *i*-PrOH/ Hexane = 20/80, 1.0 mL/min, 236 nm.) Retention time: t_{major} =11.01 min, t_{minor} =17.31 min, ee = 87%.

(*2R,4S*)-methyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[g]chromene-2-carboxylate (5a)



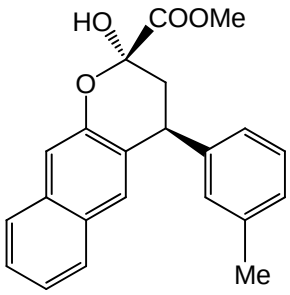
White solid, mp 142 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.71-7.81(m, 2 H), 7.28-7.45(m, 2 H), 7.09-7.22(m, 6 H), 4.72-4.82(m, 1 H), 4.21(*syn*: s, 0.6 H), 4.00(*anti*: s, 0.4 H), 3.87(*anti*: s, 1.1 H), 3.81(*syn*: s, 1.9 H), 2.86-2.93(*anti*: q, *J* = 7.2 Hz, 0.4 H), 2.48-2.66(*syn*: m, 1.6 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.1, 170.1, 150.2, 149.9, 145.8, 143.8, 132.4, 132.1, 130.3, 129.8, 129.3,

129.3, 128.8, 128.4, 128.3, 128.3, 128.2, 127.6, 126.5, 126.3, 125.7, 123.7, 123.6, 123.4, 119.0, 118.9, 116.0, 113.9, 94.6, 93.8, 53.4, 39.9, 36.6, 35.6, 34.9. **IR**: 3432.26, 3060.25,3025.42, 3004.42, 2954.35, 2929.80, 2877.36, 2855.07, 1894.14, 1750.76, 1707.58, 1622.91, 1599.76, 1397.75, 1361.79,725.54, 701.98 cm^{-1}.

HRMS-ESI (*m/z*): calcd for $C_{21}H_{18}O_4+NH_4^+$: 352.1543; found: 352.1549, 1.1ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 10/90, 1.0 mL/min, 232 nm.) Retention time: t_{major} =12.34 min, t_{minor} =26.54 min, ee = 91%.

(*2R,4S*)-methyl 2-hydroxy-4-m-tolyl-3,4-dihydro-2H-benzo[g]chromene-2-carboxylate (5b)

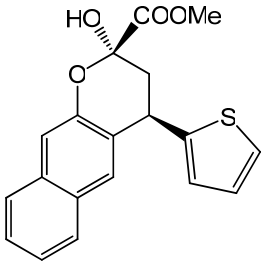


White solid, mp 154 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.17-8.20(m, 1 H), 7.73-7.78(m, 1 H), 7.44-7.50(m, 2 H), 7.08-7.13(m, 1 H), 6.87-6.90(d, *J* = 8.7 Hz, 1 H), 4.47-4.49(d, *J* = 5.7 Hz, 1 H), 4.43-4.44(d, *J* = 5.7 Hz, 1 H), 3.96(s, 3 H), 2.54-2.62(t, *J*=13.2 Hz, 1 H), 2.37-2.44(dd, *J* = 5.7 Hz, 13.2 Hz, 1 H), 2.34(s, 3 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 170.4, 146.2, 143.5, 138.4, 133.3, 129.6, 128.6, 127.7, 127.4, 126.7, 126.0, 125.5, 124.8, 121.5, 120.8, 119.3, 94.4, 53.6, 37.8, 36.8, 21.4. **IR**: 3445.43, 3103.79, 3056.49, 3014.04, 2953.15, 2922.71, 2876.44, 2251.57, 1748.93, 1707.41, 1623.34, 1602.09, 1463.60, 1437.74, 1398.64, 1227.59, 1142.14, 1097.68, 1066.04, 1048.18, 942.33, 912.37, 814.97, 783.76, 732.63, 703.73 cm^{-1}

HRMS-ESI (*m/z*): calcd for $C_{22}H_{20}O_4+NH_4^+$: 366.1700; found: 366.1704, 1.1ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 10/90, 1.0 mL/min, 229 nm.) Retention time: t_{major} =10.40 min, t_{minor} =20.14 min, ee = 91%.

(*2R,4R*)-methyl 2-hydroxy-4-(thiophen-2-yl)-3,4-dihydro-2H-benzo[g]chromene-2-carboxy late (5c)



White solid, mp 122 °C. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.72-7.79(m, 2 H), 7.57-7.64(m, 1 H), 7.24-7.39(m, 2 H), 7.14-7.18(m, 1 H), 7.10-7.12(m, 1 H), 6.84-6.87(*syn*: dd, *J* = 3.3 Hz, 5.1 Hz, 0.7 H), 6.79-6.82(*anti*: dd, *J* =3.6 Hz, 5.1 Hz, 0.3 H), 6.70-6.71(*syn*: d, *J* = 3.3 Hz, 0.7 H), 6.54-6.55(*anti*: d, *J* = 3.6 Hz, 0.3 H), 5.03-5.09(dd, *J* = 7.5 Hz, 9.6 Hz, 1 H), 4.17(*syn*: d, *J* = 1.5 Hz, 0.7 H), 4.12(*anti*: d, *J* = 1.2 Hz, 0.3 H), 3.89(*anti*: s, 0.9 H), 3.79(*syn*: s, 2.1 H), 2.83-2.90(*anti*: m, 0.3 H), 2.68-2.78(*syn*: m, 0.7 H), 2.60-2.67(dd, *J* = 7.5 Hz, 13.8 Hz, 1 H); **^{13}C NMR** (75MHz, $CDCl_3$): δ 169.9, 149.8, 149.0, 132.1, 130.2, 129.7, 128.4, 126.7, 126.6, 126.0, 125.7, 125.0, 124.5, 124.1, 123.8, 123.6, 123.3, 118.9, 115.7, 94.4, 93.8, 53.5, 40.1, 31.9, 30.4, 29.7. **IR**: 3404.58, 3056.96, 2955.74, 2921.86, 2852.18, 1743.31, 1650.93, 1599.18, 1574.56, 1505.74, 1458.97, 1438.38, 1378.42, 1289.32, 1263.24, 1235.51, 1189.68, 1127.73, 1093.93, 1074.31, 1046.37, 1026.80, 970.79, 892.11, 848.66, 807.01, 778.49, 749.54, 701.14, cm^{-1}

HRMS-ESI (*m/z*): calcd for $C_{19}H_{16}FO_4S+Na^+$: 363.0662; found: 363.0655, 1.9ppm.

Major diastereomer: ee was determined by HPLC analysis (Chiralcel OD-H, *i*-PrOH/ Hexane = 10/90, 1.0 mL/min, 229 nm.) Retention time: t_{major} =10.40 min, t_{minor} =20.14 min, ee = 86%.

4.0. Supplementary references

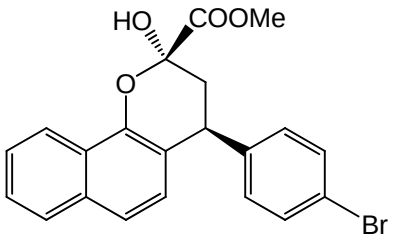
1. E. D. Stecher and H. F. Ryder, *J. Am. Chem. Soc*, 1952, **74**, 4392.

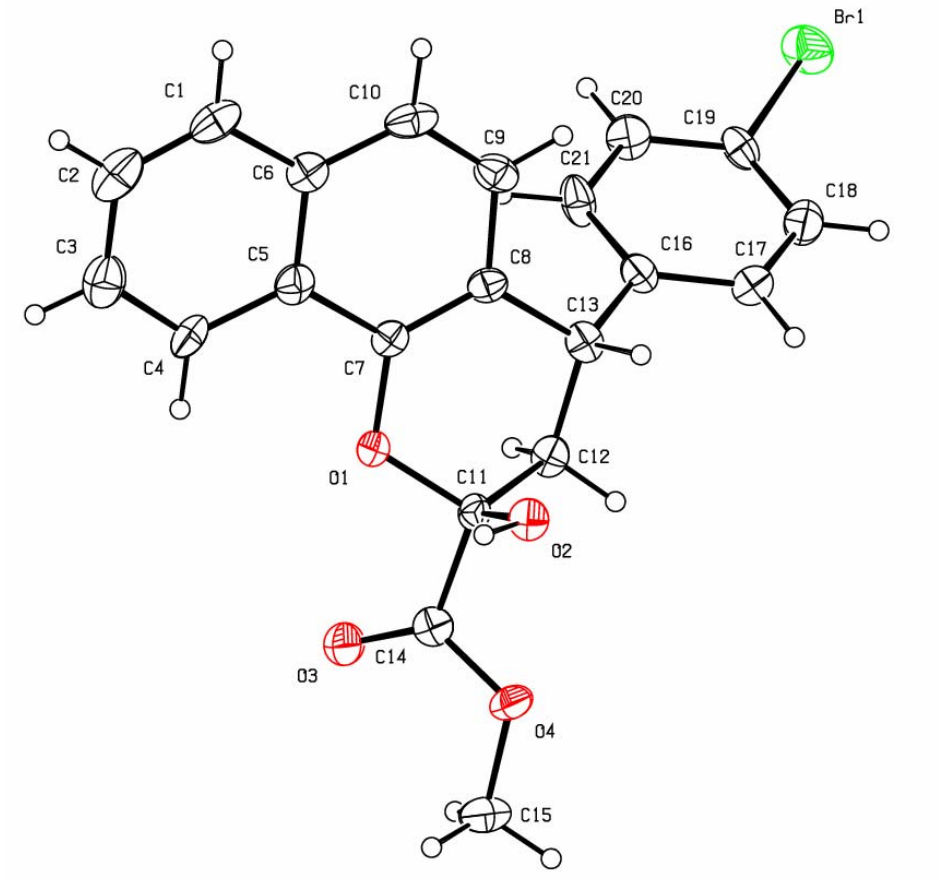
2. H. Audrain, J. Thorhauge, R. G. Hazell and K. A. Joergensen, *J. Org. Chem*, 2000, **65**, 4487.

3. Selected examples of *β*,*γ*-unsaturated *α*-ketoesters in Friedel-Craft-type reactions, see: (*a*) J. Lv, X. Li, L. Zhong, S. Z. Luo and J.-P. Cheng, *Org. Lett*., 2010, **12**, 1096; (*b*) G. Faita, M. Mella, M. Toscanini and G. Desimoni, *Tetrahedron,* 2010, **66**, 3024; (*c*) X. S. Wang, C. W. Zheng, S. L. Zhao, Z. Chai, G. Zhao and G. S. Yang, *Tetrahedron: Asymmetry,* 2008, **19**, 2699; (*d*) G. Desimoni, G. Faita, M. Toscanini and M. Boiocchi, *Chem. Eur. J.,* 2008, **14**, 3630; (*e*) Hester L. van Lingen, Wei Zhuang, Tore Hansen, Floris P. J. T. Rutjes and K. A. Jørgensen, *Org. Biomol. Chem*., 2003, **1**, 1953; (*f*) K. B. Jacob, J. Thorhauge, R. G. Hazell and K. A. Jørgensen, *Angew. Chem. Int. Ed*., 2001, **40**, 160.

5.0. X-Ray Structure of 4e

(*2R,4S*)-methyl 4-(4-bromophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4e) (CCDC: 834600)





6.0. Supplementary Methods for Biological Studies

6.1 Chemicals

All compounds used in this study were synthesized in our laboratory, all of them were dissolved in deionized water with 5% DMSO (dimethyl sulphoxide) and further diluted with deionized water. Control trials were performed in the presence of corresponding concentration of DMSO to rule out any possible nonspecific action of this solvent. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were purchased from Sigma (St. Louis, Mo.). RPMI 1640, Dulbecco's Modified Eagle Medium (DMEM) and Fetal Bovine Serum (FBS) were purchased from Gibco.

6.2 Cell culture

Human breast cancer cell line (MDA-MB-231), human cervical cancer cell line (HeLa), human T-cell leukemia cell line (Jurkat),human neuroglia cancer cell line (U251), human liver cancer cell line (HepG-2), and human prostate cancer cell line (PC-3) were obtained from ATCC. PC-3 and Jurkat cells were cultured in RPMI 1640 (Gibco–BRL, USA) supplemented with 10% fetal bovine serum (Gibco–BRL, USA) at 37 ºC in a humidified atmosphere containing 5% CO_2. MDA-MB-231, Hela, HepG-2, U251 cells were maintained in DMEM (Gibco–BRL, USA) supplemented with 10% fetal bovine serum (Gibco–BRL, USA) at 37 ºC in a humidified atmosphere containing 5% CO_2. Media were supplemented with penicillin (50 U/ml) and Streptomycin (50 U/ml).

6.3 Cytotoxic activity assays (method)

Cytotoxic activity was assessed by standard MTT assay. A suspension of cells (5 000/well in 90 uL) were seeded in 96-well plates and cultured for 24 h. 7 different concentrations of drugs ranging from 5×10^{-6} to 3.2×10^{-4} M were added to the corresponding plates with 100.0 μL/well, and the plates were incubated for 72 h. Then, 20uL of MTT (Sigma, USA) solution (5.0 mg/mL) was added to each well. After 4 h of incubation at 37 ºC, the optical density was determined with ELISA plate reader (Biorad model 680) following removal of the medium and dissolution of the dye crystals in DMSO (Sigma, USA). The result was expressed as IC_{50} value, which was a measure of the effectiveness of a compound in inhibiting biological or biochemical function. This quantitative measure indicates how much of a particular drug is needed to inhibit a given biological process by half. In other words, it is the half maximal (50%) inhibitory concentration

(IC) of a substance.

Supplementary Table 1. *In vitro* anticancer activity of **(*2R,4S*)-4a**, **4d**, **4e**, **4i** and **4j** [a]

Compounds	IC_{50}(μM±error) [a]				
	4a	**4d**	**4e**	**4i**	**4j**
HELA	60.233±3.562	53.256±2.569	43.422±3.254	40.352±0.968	38.128±1.255
HepG-2	56.250±5.241	41.589±3.241	37.569±2.012	43.024±2.033	40.056±3.520
U251	50.023±0.966	48.052±3.230	35.041±2.563	26.782±2.122	30.032±2.695
MDA-MB-231	52.231±4.334	48.013±0.962	36.230±2.102	35.563±0.892	30.125±3.201
PC-3	49.026±2.304	42.105±4.236	30.125±1.253	26.120±3.012	19.103±2.030
Jurkat	46.852±3.014	40.029±1.564	26.257±2.034	24.756±3.012	18.389±2.306

[a] IC_{50} is 50% inhibitory concentration. Values are means of three experiments each done in duplicate. IC_{50} values are expressed in μM/L.

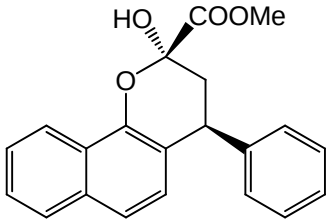
Supplementary Table 2. *In vitro* anticancer activity of **(*2S,4R*)-4a**, **4d**, **4e** and **4j** [a]

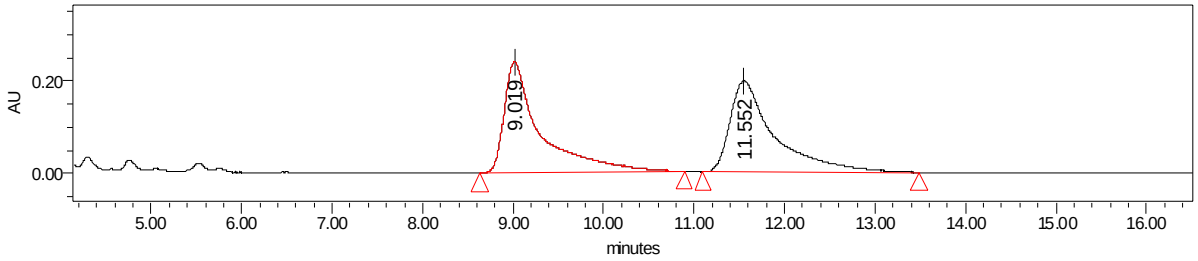
Comp.	IC50(μM) [a]			
	4a	**4d**	**4e**	**4j**
HELA	19.274	33.783	22.123	40.983
HepG-2	20.733	43.859	23.809	42.373
U251	28.162	71.428	37.313	38.461
MDA-MB-231	40.702	78.047	56.818	65.789
PC-3	34.833	45.454	43.103	39.483
Jurkat	18.013	53.191	22.523	29.411

[a] IC50 (uM/L) is 50% inhibitory concentration, and values are means of three experiments each done in duplicate.

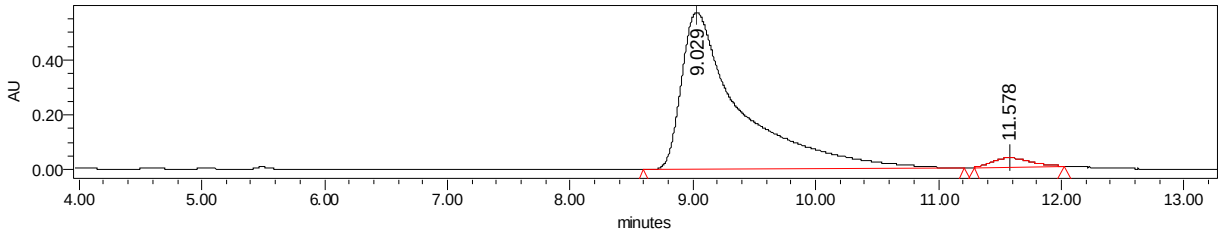
7.0. Copies of HPLC Spectra of Racemic /Chiral Products

(*2R,4S*)-methyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4a)



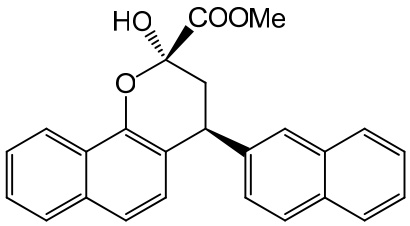


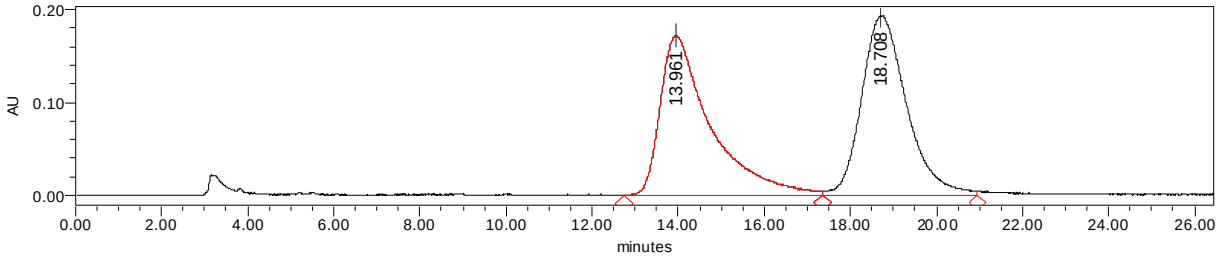
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	9.019	6687973	50.06	239711	bb	Unknown
2	11.552	6671050	49.94	196890	bb	Unknown



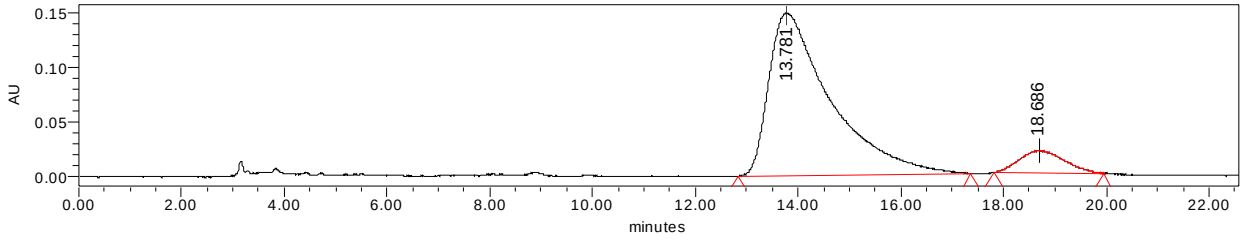
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	9.029	19194277	96.44	573634	bb	Unknown
2	11.578	709341	3.56	33635	bb	Unknown

(*2R,4S*)-methyl 2-hydroxy-4-(naphthalen-2-yl)-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4b)



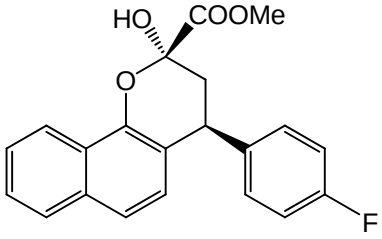


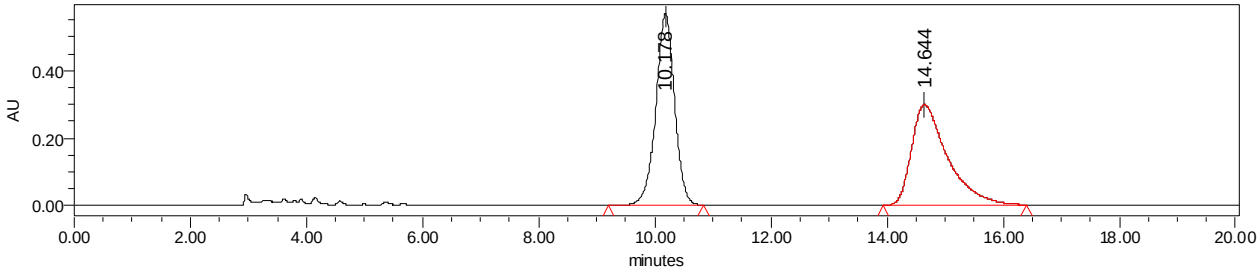
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	13.961	13858191	49.85	171881	bb	Unknown
2	18.708	13939760	50.15	192915	bb	Unknown



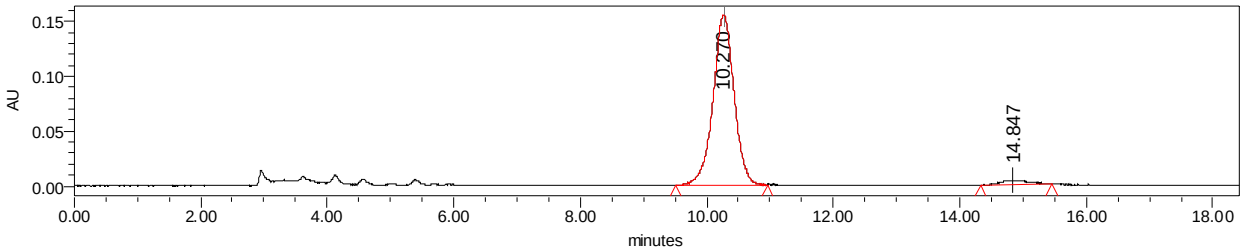
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	13.781	12408040	90.99	148659	bb	Unknown
2	18.686	1228625	9.01	20238	bb	Unknown

(*2R,4S*)-methyl 4-(4-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4c)



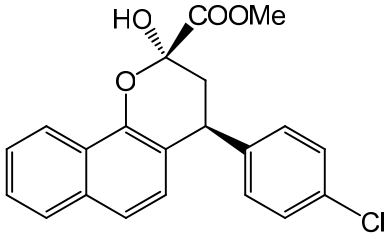


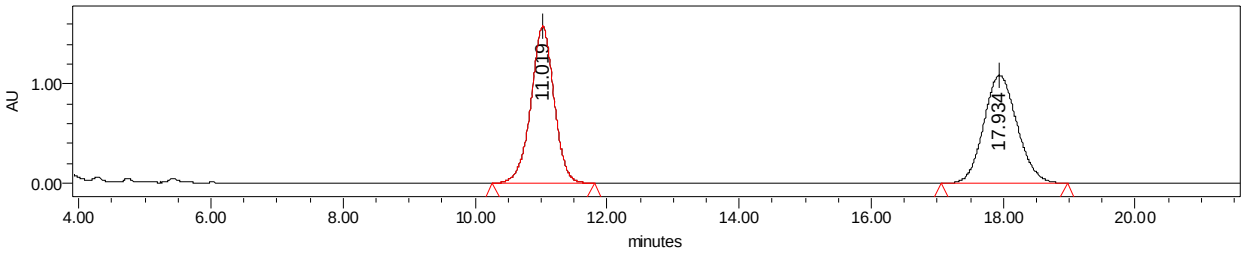
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	10.178	12732291	49.69	565793	bb	Unknown
2	14.644	12891040	50.31	299157	bb	Unknown



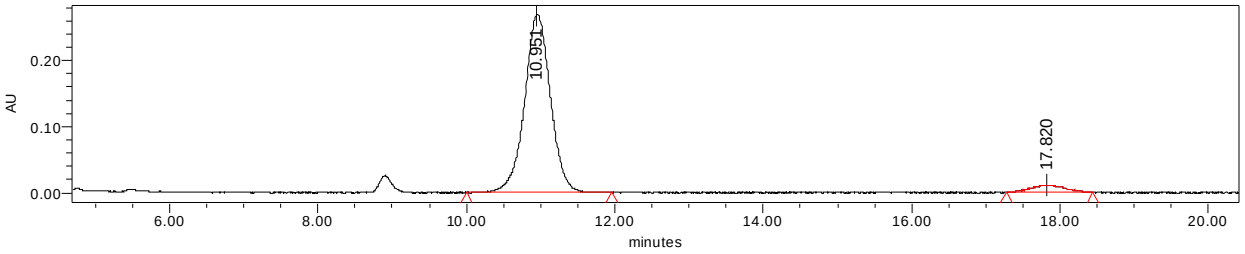
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	10.270	3571832	96.63	155128	bb	Unknown
2	14.847	124662	3.37	4027	bb	Unknown

(*2R,4S*)-methyl 4-(4-chlorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4d)



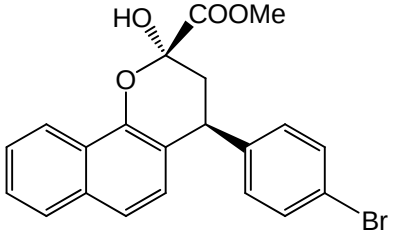


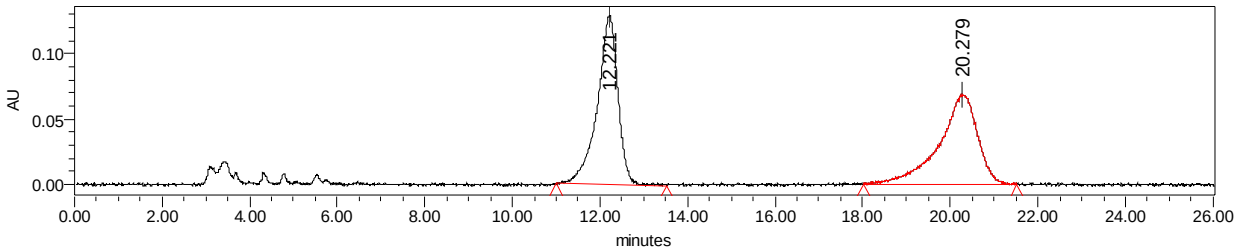
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	11.019	38334204	50.05	1580594	bb	Unknown
2	17.934	38254350	49.95	1087542	bb	Unknown



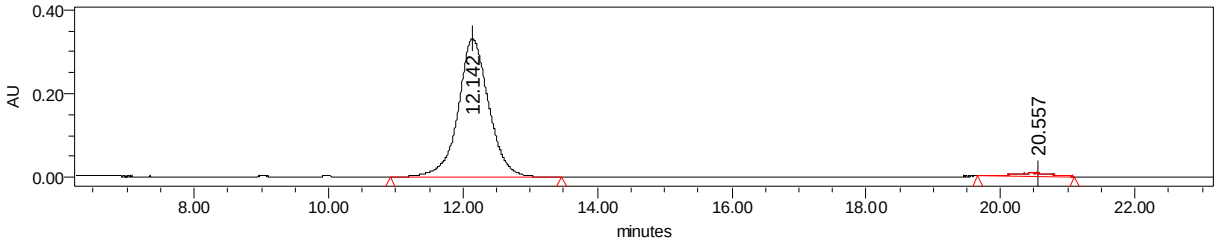
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	10.951	6528326	95.30	269010	bb	Unknown
2	17.820	321861	4.70	10682	bb	Unknown

(*2R,4S*)-methyl 4-(4-bromophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4e)



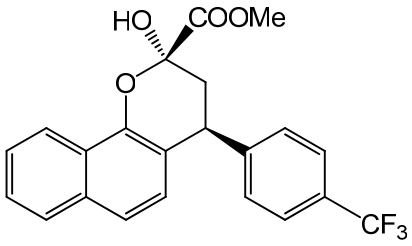


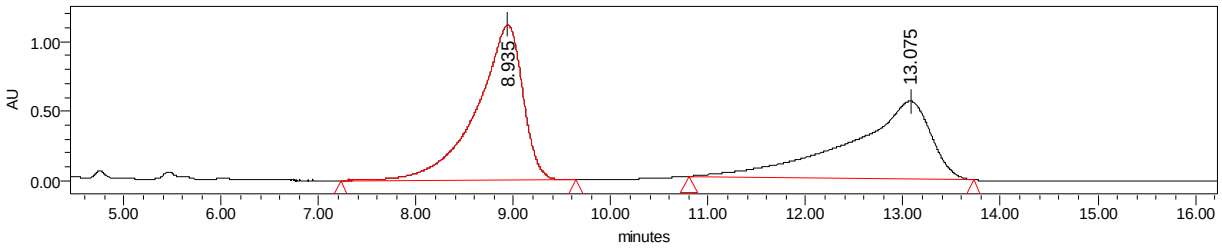
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	12.221	4216193	50.20	129530	bb	Unknown
2	20.279	4182560	49.80	68662	bb	Unknown



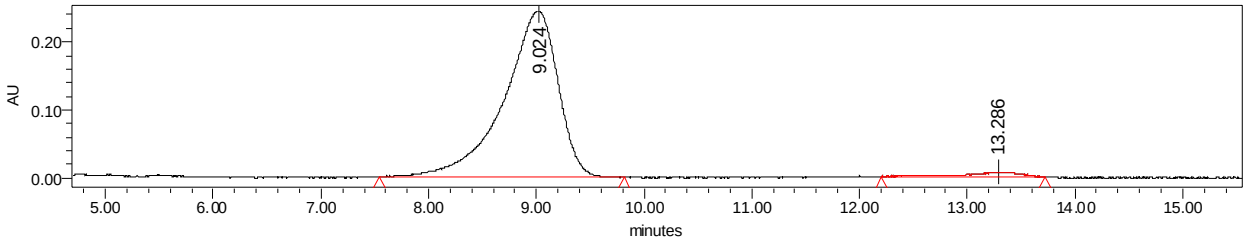
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	12.142	10413726	97.12	330002	bb	Unknown
2	20.557	308333	2.88	7346	bb	Unknown

(*2R,4S*)-methyl 2-hydroxy-4-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-benzo[h]chromene -2-carboxylate (4f)



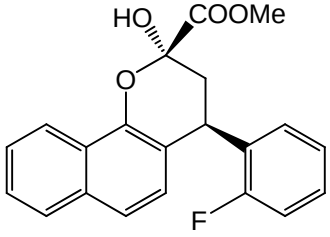


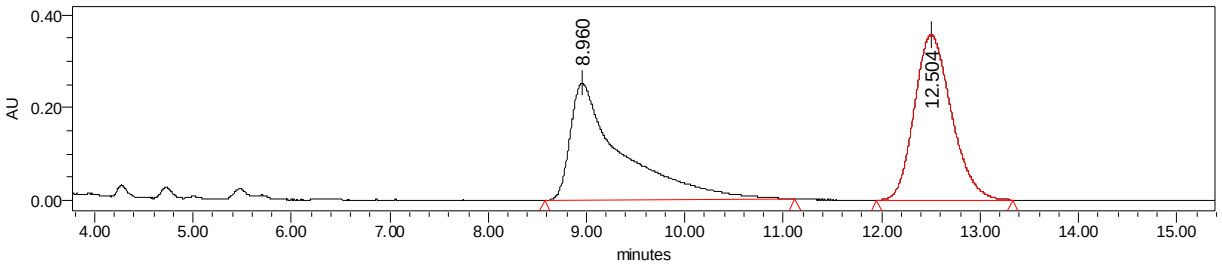
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.935	36550201	53.01	1117949	bb	Unknown
2	13.075	32400373	46.99	557452	bb	Unknown



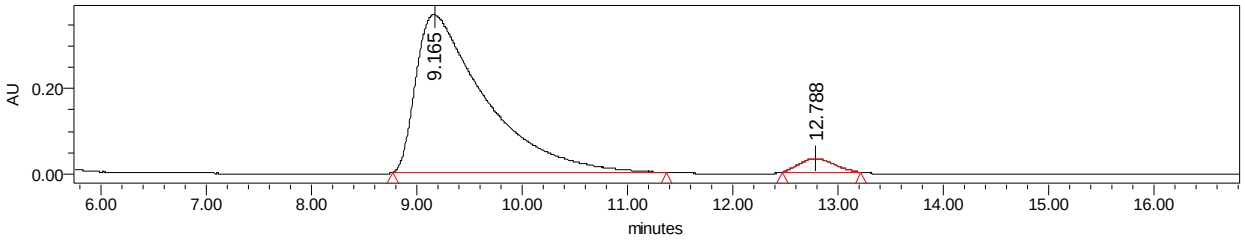
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	9.024	8511266	97.39	245071	bb	Unknown
2	13.286	227684	2.61	7162	bb	Unknown

(*2R,4R*)-methyl 4-(2-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4g)





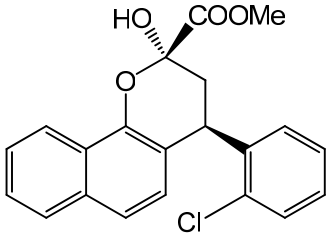
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.960	9155503	49.58	251553	bb	Unknown
2	12.504	9309858	50.42	356125	bb	Unknown

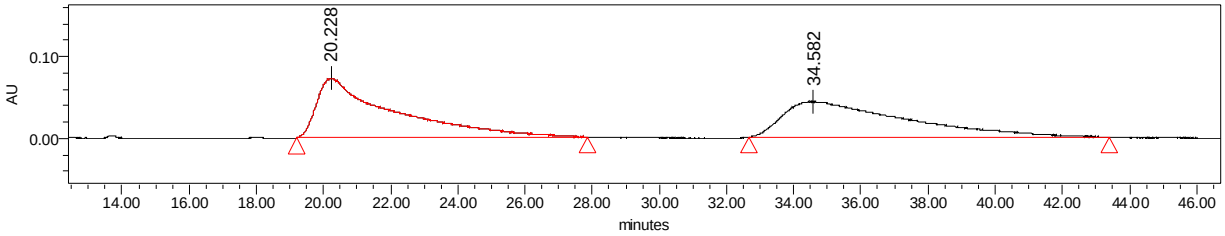


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	9.165	16853923	95.81	368055	bb	Unknown
2	12.788	736242	4.19	31903	bb	Unknown

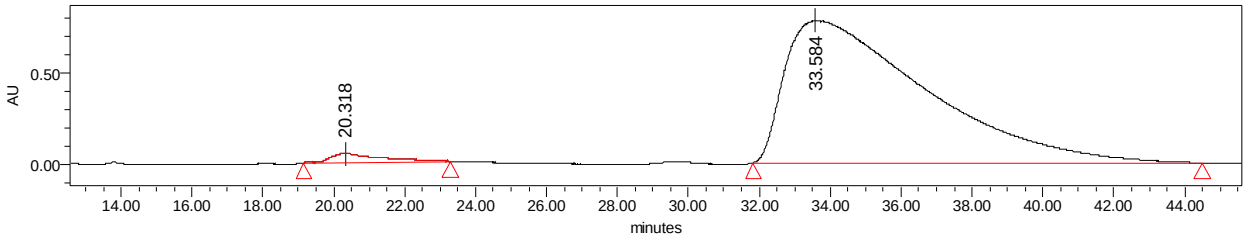
(*2R,4R*)-methyl 4-(2-chlorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxy

late (4h)



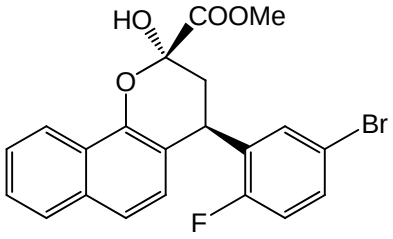


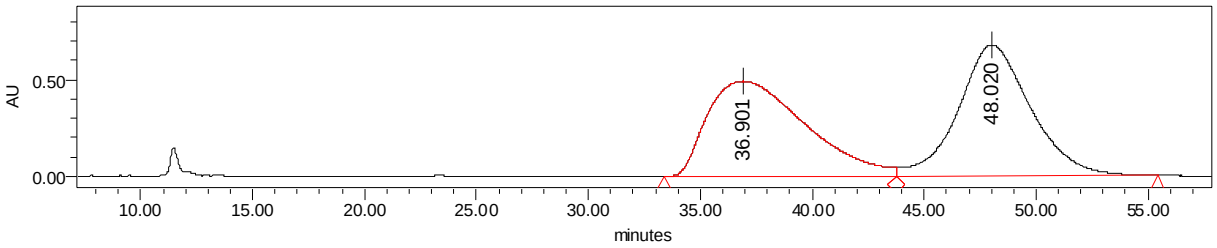
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	20.228	11413253	51.00	72666	bb	Unknown
2	34.582	10966396	49.00	43490	bb	Unknown



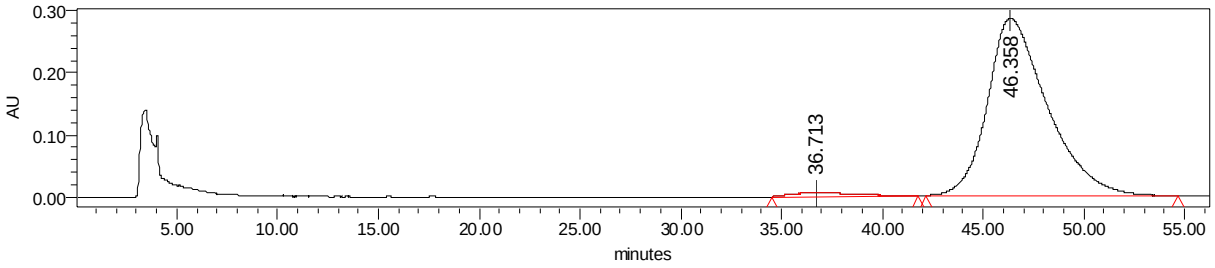
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	20.318	4415089	2.03	46685	bb	Unknown
2	33.584	213554708	97.97	43490	bb	Unknown

(*2R,4R*)-methyl 4-(5-bromo-2-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4i)



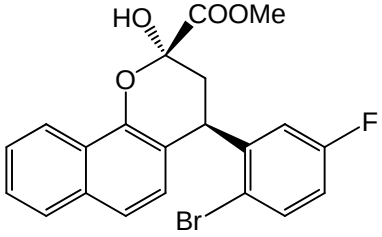


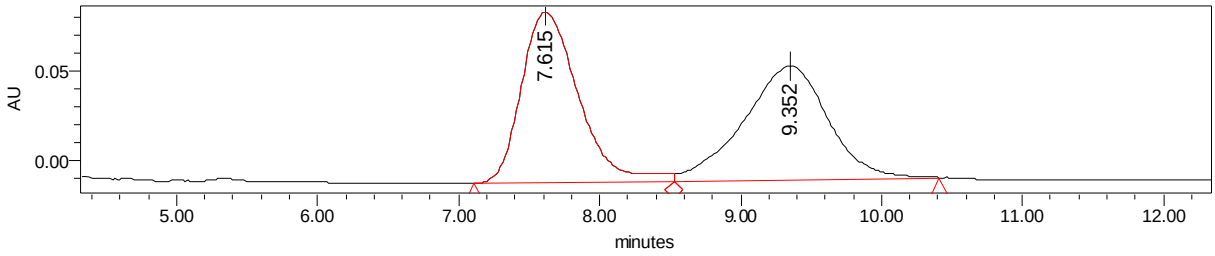
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	36.901	149690733	49.66	491988	BV	Unknown
2	48.020	151736174	50.34	675303	VB	Unknown



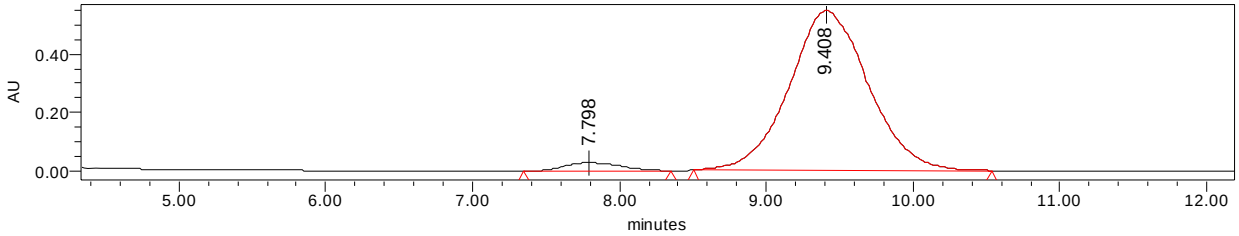
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	36.713	1237597	2.05	5550	BV	Unknown
2	46.358	59029002	97.95	285965	VB	Unknown

(*2R,4R*)-methyl 4-(2-bromo-5-fluorophenyl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene -2-carboxylate (4j)



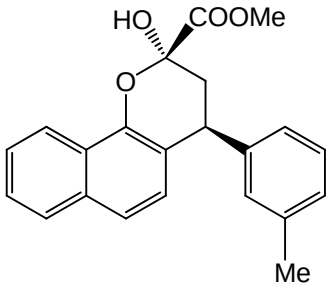


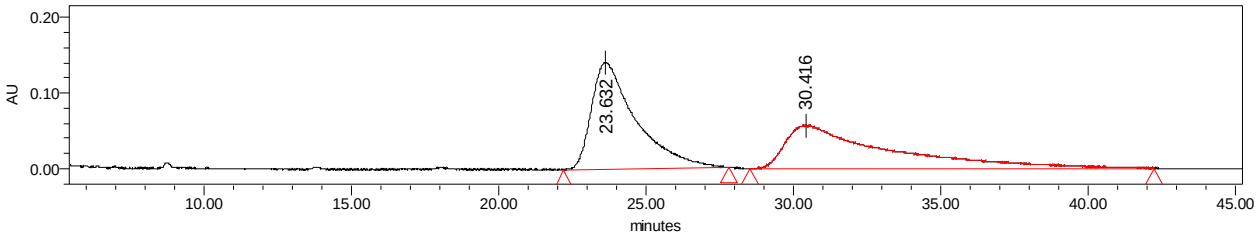
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.615	2680506	50.48	95707	BV	Unknown
2	9.352	2629231	49.52	63620	VB	Unknown



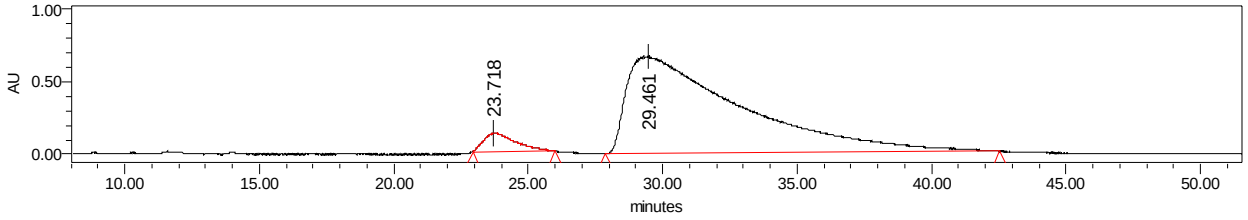
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	7.798	754388	3.54	28306	bb	Unknown
2	9.408	20543070	96.46	547803	bb	Unknown

(*2R,4S*)-methyl 2-hydroxy-4-m-tolyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4k)





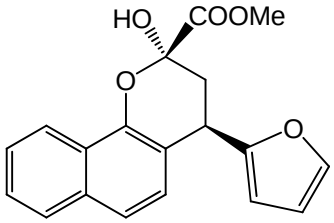
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	23.632	14709785	51.70	141467	bb	Unknown
2	30.416	13743949	48.30	57010	bb	Unknown

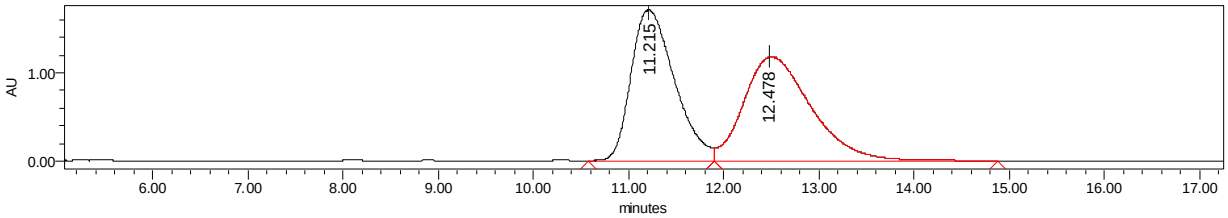


Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	23.718	10486349	5.06	126721	bb	Unknown
2	29.461	196745976	94.94	665528	bb	Unknown

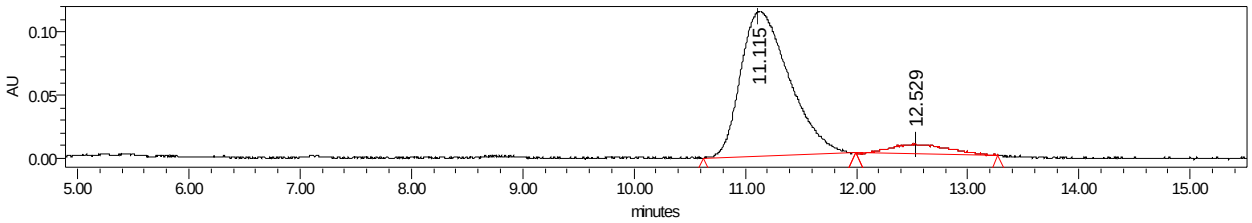
(*2R,4R*)-methyl 4-(furan-2-yl)-2-hydroxy-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate

(4l)



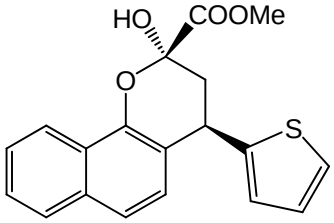


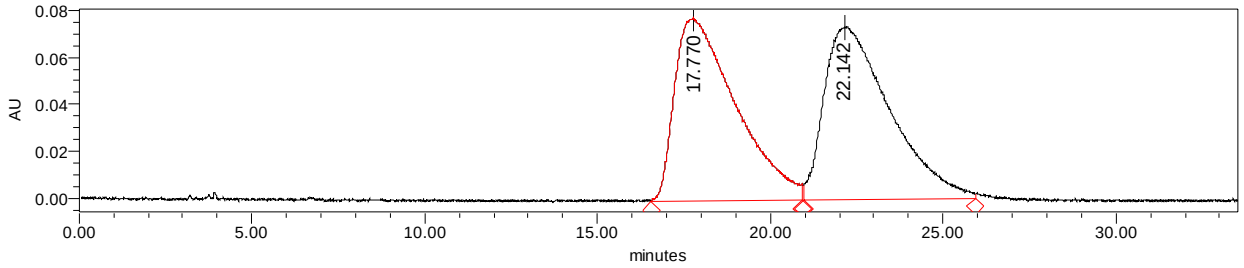
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	11.215	54400447	48.47	1719428	bb	Unknown
2	12.478	57845150	51.53	1180136	bb	Unknown



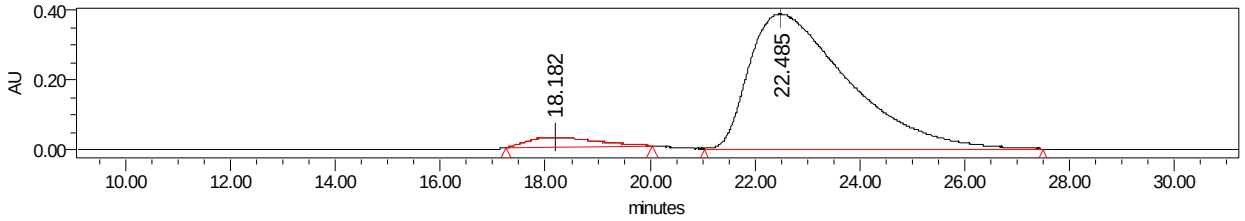
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	11.115	3480671	92.92	115024	bb	Unknown
2	12.529	265367	7.08	7803	bb	Unknown

(*2R,4R*)-methyl 2-hydroxy-4-(thiophen-2-yl)-3,4-dihydro-2H-benzo[h]chromene-2-carboxy late (4m)



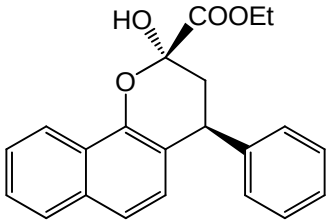


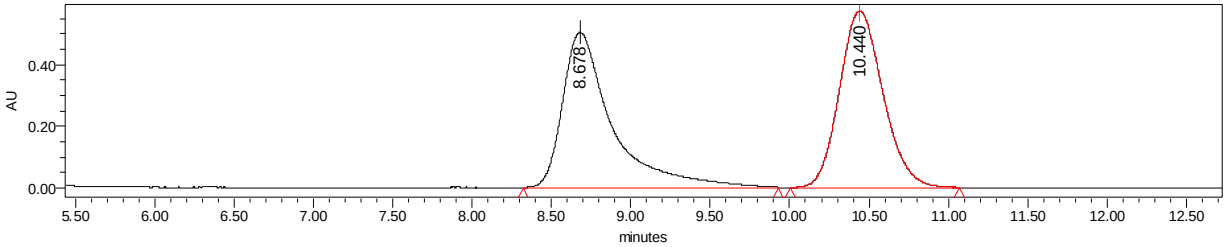
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	17.770	9622149	49.71	78100	bb	Unknown
2	22.142	9732799	50.29	73649	bb	Unknown



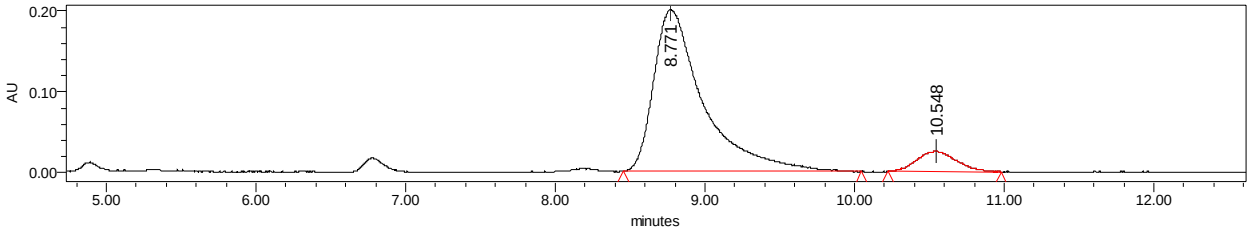
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	18.182	2457279	4.67	28018	bb	Unknown
2	22.485	50178044	95.33	385109	bb	Unknown

(*2R,4S*)-ethyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4n)



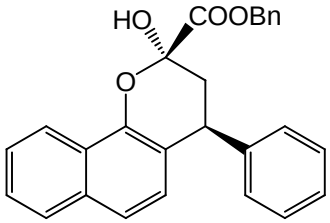


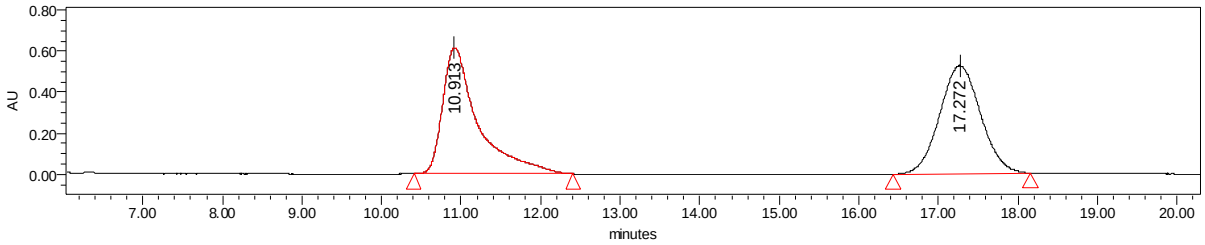
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.678	10849601	49.87	504287	bb	Unknown
2	10.440	10905974	50.13	573735	bb	Unknown



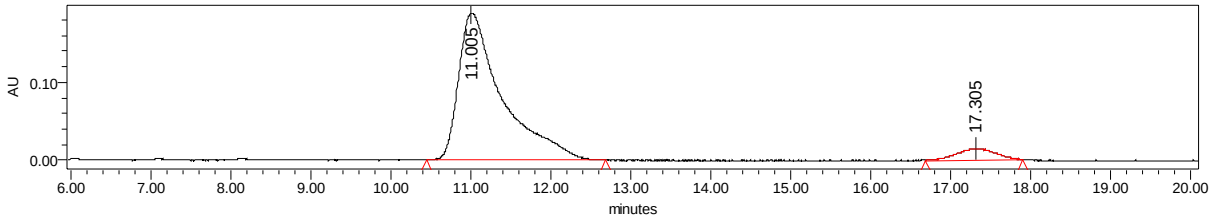
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	8.771	4620312	90.79	200571	bb	Unknown
2	10.548	468689	9.21	25617	bb	Unknown

(*2R,4S*)-benzyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[h]chromene-2-carboxylate (4o)



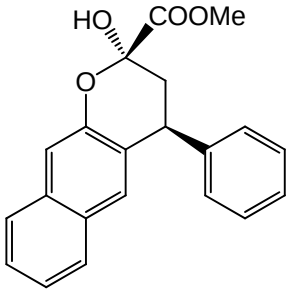


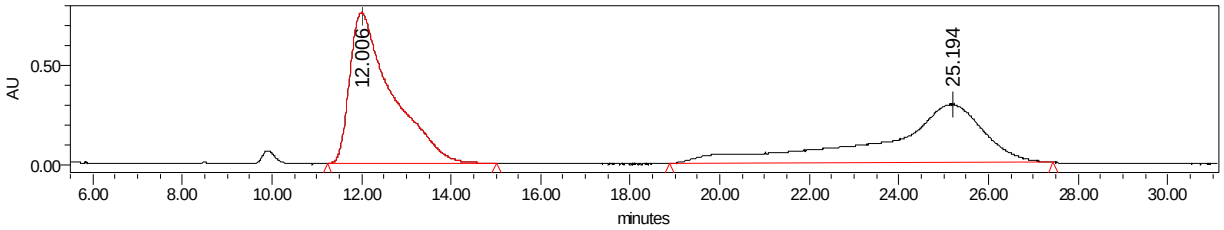
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	10.913	18856522	50.14	613563	bb	Unknown
2	17.272	18751534	49.86	525260	bb	Unknown



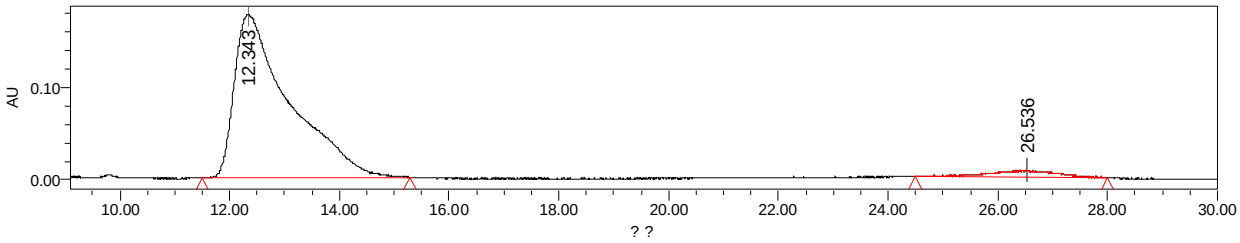
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	11.005	7106075	93.34	188656	bb	Unknown
2	17.305	507213	6.66	14587	bb	Unknown

(*2R,4S*)-methyl 2-hydroxy-4-phenyl-3,4-dihydro-2H-benzo[g]chromene-2-carboxylate (5a)



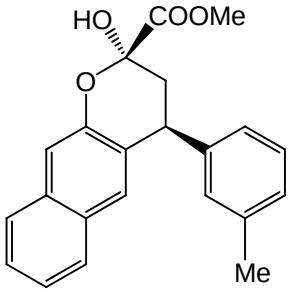


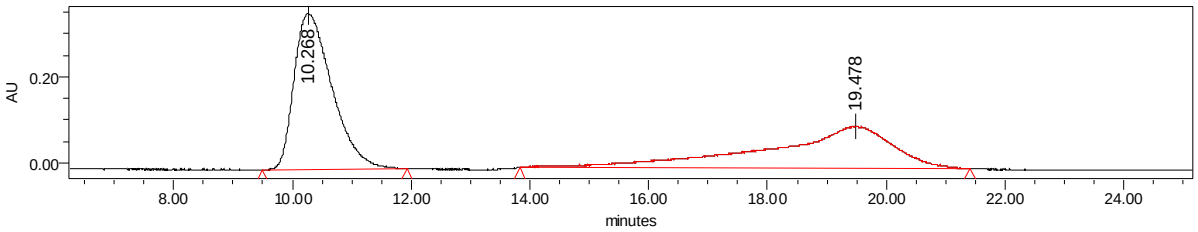
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	12.006	49656986	50.66	762123	bb	Unknown
2	25.194	48372207	49.34	297607	bb	Unknown



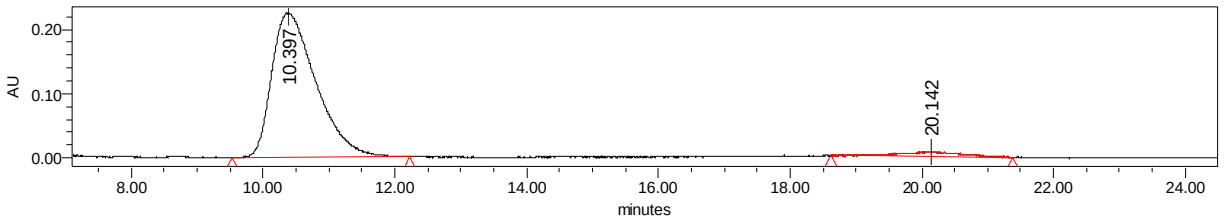
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	12.343	12228267	95.34	175938	bb	Unknown
2	26.536	597538	4.66	7267	bb	Unknown

(*2R,4S*)-methyl 2-hydroxy-4-m-tolyl-3,4-dihydro-2H-benzo[g]chromene-2-carboxylate (5b)



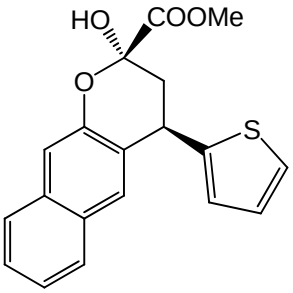


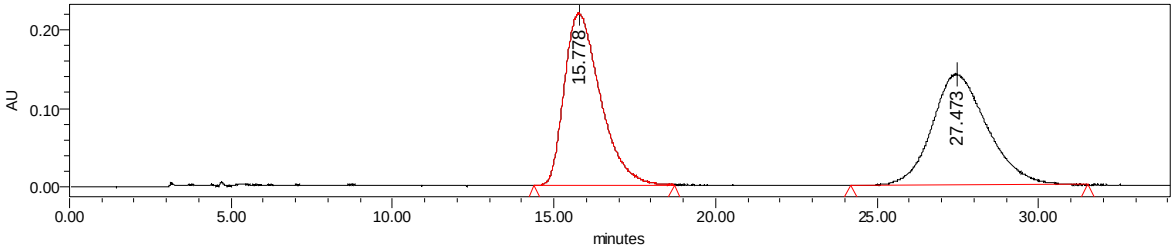
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	10.268	16026213	52.95	362602	bb	Unknown
2	19.478	14243139	47.05	97045	bb	Unknown



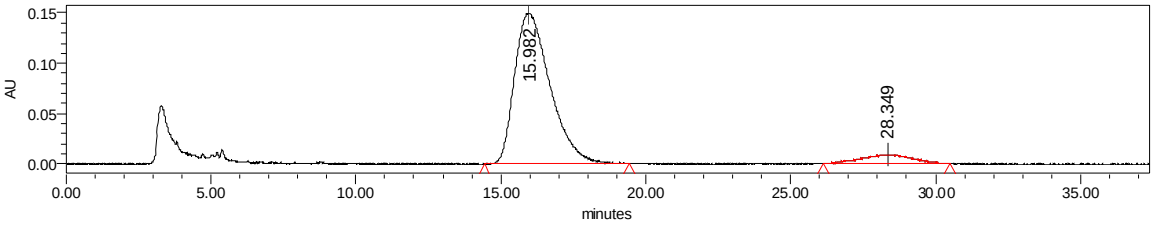
Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	10.397	10426191	95.56	224721	bb	Unknown
2	20.142	484391	4.44	7339	bb	Unknown

(*2R,4R*)-methyl 2-hydroxy-4-(thiophen-2-yl)-3,4-dihydro-2H-benzo[g]chromene-2-carboxy late (5c)





Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	15.778	17093891	50.40	220474	bb	Unknown
2	27.473	16825245	49.60	142270	bb	Unknown



Entry	Retention Time	Area	Area (%)	Height	Int Type	Peak Type
1	15.982	12743273	92.92	149912	bb	Unknown
2	28.349	970462	7.08	8549	bb	Unknown