Electronic Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Highly Enantioselective Organocatalytic Cascade Reactions of β, γ–Unsaturated α–Keto Esters and 1, 2-Diones

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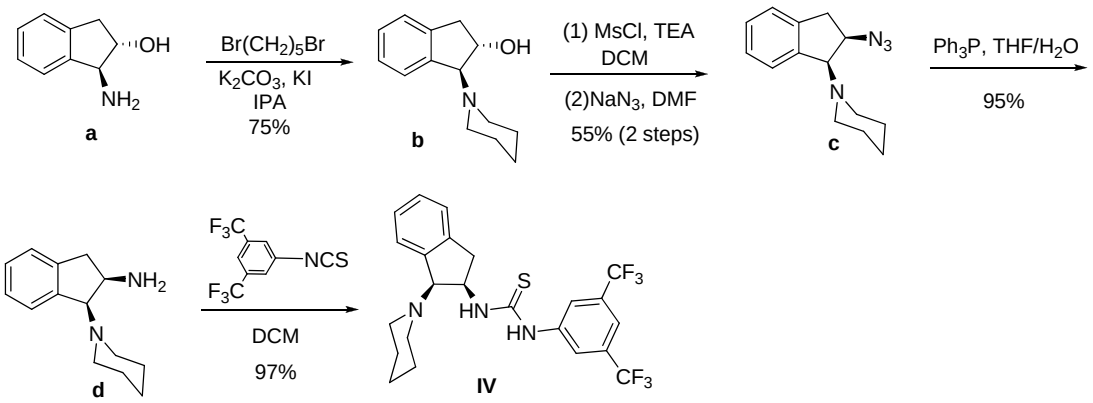
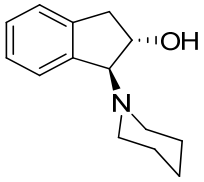
1. General Information

Chemicals and solvents were purchased from commercial suppliers and used as received. ^{1}H and ^{13}C NMR spectra were recorded on a AMX500 (500 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0) or tetramethylsilane (TMS δ 0.00) was used as a reference. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), bs (broad singlet). Coupling constants were reported in Hertz (Hz). Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode, and a Finnigan/MAT 95XL-T mass spectrometer in EI mode. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, or ninhydrin followed by heating using a heat gun. Flash chromatography separations were performed on Merck 60 (0.040-0.063 mm) mesh silica gel. The enantiomeric excesses of products were determined by chiral phase HPLC analysis. Optical rotations were recorded on Jasco DIP-1000 polarimeter.

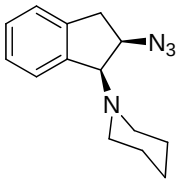
2. Preparation of Catalysts



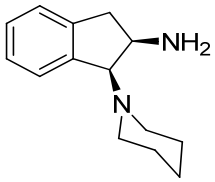
Scheme 1, Synthetic route for catalyst V



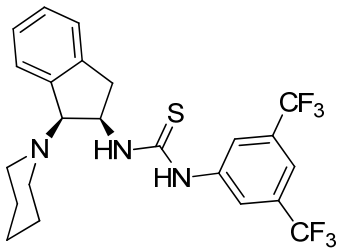
(1*S*,2*S*)-1-(Piperidin-1-yl)-2,3-dihydro-1*H*-inden-2-ol (b)[1]. Compound **a** (0.75 g, 5.0 mmol), 1,5-dibromopentane (1.38 g, 6.0 mmol), potassium carbonate (1.80 g, 13 mmol), potassium iodide (0.17 g, 1.0 mmol) and 10 mL iso-propanol were added into a sealed tube. The mixture was heated at 80 °C for 48hrs and then allowed to cool to room temperature. The mixture was filtered and washing with DCM, the filtrate was concentrated and the resulting residue was purified by silica gel chromatography (eluting with 1:5 EtOAc-hexane then 1:10 methanol-DCM) to obtain the product **b** (0.82 g, 75% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.33 (m, 1H), 7.12-7.16 (m, 3H), 4.66 (dd, *J* = 12.3, 5.3 Hz, 1H), 4.08 (d, *J* = 4.8 Hz, 1H), 3.25 (dd, *J* = 16.2, 7.1 Hz, 1H), 2.80 (dd, *J* = 16.2, 5.5 Hz, 1H), 2.62-2.61 (m, 4H), 1.58-1.54 (m, 4H), 1.46 (d, *J* = 5.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.62, 140.33, 127.66, 126.41, 125.82, 124.90, 78.49, 73.54, 50.79, 40.06, 26.51, 24.66; HRMS (ESI) calcd for $C_{14}H_{20}NO$ ($M + H^+$) 218.1545, found 218.1545.



1-((1*S*,2*R*)-2-Azido-2,3-dihydro-1*H*-inden-1-yl)piperidine (c)[2]. To a stirred solution of compound **b** (0.78 g, 3.6 mmol) and triethylamine (1.1 g, 10.8 mmol) in dry DCM (10 mL) at 0°C under nitrogen was added dropwise methanesulfonyl chloride (0.62 g, 5.4 mmol). The mixture was stirred for another 20 min at room temperature, and the solvent was evaporated under reduced pressure. The residue was extracted with DCM, washed successively with water, and brine, and dried over $MgSO_4$. The organic layer was concentrated to afford crude mesylate intermediate. Then the crude mesylate intermediate was redissolve d in DMF (10 mL), followed by adding NaN_3 (1.87 g, 28.8 mmol). The mixture was heated under nitrogen at 70°C for 6 hrs. After the mixture was cooled, the solvent was evaporated under reduced pressure and the residue was extracted with EtOAc (25 mL x 3) and dried over $MgSO_4$. The organic layer was removed under reduced pressure, and the crude product was purified by silica gel chromatography (eluting with 1:10 EtOAc-hexane) to afford product **c** (0.48 g, 55% yield, two step). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26-7.10 (m, 4H), 4.63 (d, *J* = 6.9 Hz, 1H), 3.17 (td, *J* = 8.0 Hz, 6.8, 1H), 3.03 (dd, *J* = 15.8, 7.9 Hz, 1H), 2.81 (dd, *J* = 15.8, 7.9 Hz, 1H), 2.48 (ddt, *J* = 38.5, 10.7, 5.2 Hz, 4H), 1.53 (dt, *J* = 11.3, 5.7 Hz, 4H), 1.39 (dd, *J* = 11.7, 6.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.43, 139.14, 128.56, 126.94, 124.71, 124.15, 72.82, 66.85, 51.91, 33.83, 25.94, 24.30; HRMS (ESI) calcd for $C_{14}H_{19}N_4$ ($M + H^+$) 243.1610, found 243.1612.



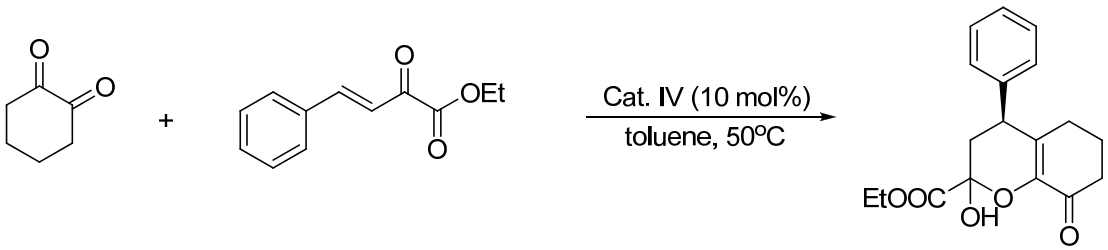
(1*S*,2*R*)-1-(Piperidin-1-yl)-2,3-dihydro-1*H*-inden-2-amine (d)[5]. To a solution of compound **c** (0.46 g, 1.9 mmol) in 10 mL THF was added triphenylphosphane (1.5 g, 5.7 mmol). The mixture was stirred at room temperature for 3h, then added 3 mL water, heated at 60 ^{o}C for 4 hrs. The solvent was removed by reduced pressure, and the resulting residue was purified by a very short silica gel column (eluting with 1:10 to 1: 5 methanol-DCM) to afford compound **d** (0.39 g, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (t, *J* = 5.8 Hz, 1H), 7.19-7.11 (m, 3H), 4.31 (d, *J* = 6.9 Hz, 1H), 2.99-2.83 (m, 3H), 2.60-2.58(m, 4H), 2.45 (s, 2H), 1.64-1.59 (m, 4H), 1.45 (dt, *J* = 11.7, 5.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.92, 139.73, 127.18, 126.54, 124.36, 123.34, 77.45, 58.16, 51.84, 31.67, 25.82, 24.29; HRMS (ESI) calcd for $C_{14}H_{21}N_2$ ($M + H^+$) 217.1705, found 217.1708.



1-(3,5-Bis(trifluoromethyl)phenyl)-3-((1*S*,2*R*)-1-(piperidin-1-yl)-2,3-dihydro-1*H*-inden-2-yl)thiourea (IV). To a solution of compound **d** (0.39 g, 1.81 mmol) in 10 mL DCM was added 1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (0.52 g, 1.90 mmol) dropwise. The mixture was stirred at room temperature for 30min, reaction completed. The solvent was removed by rotary evaporation and pure product **IV** (0.90 g, 97% yield) was obtained by silica gel chromatography (eluting with 1:10 EtOAc-hexane then 1: 10 methanol-DCM). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.14

(s, 1H), 7.98 (s, 2H), 7.61 (s, 1H), 7.27 (ddd, J = 20.9, 12.6, 4.3 Hz, 4H), 6.68 (s, 1H), 5.22 (m, 1H), 3.63 (dd, J = 6.2, 8.3 Hz, 1H), 3.13 (dd, J = 16.1, 8.6 Hz, 1H), 2.92 (dd, J = 16.2, 8.9 Hz, 1H), 2.68-2.60 (m, 4H), 1.56-1.44 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 183.34, 141.50, 140.33, 137.67, 132.31, 131.87, 131.42, 130.98, 129.36, 127.78, 125.76, 125.53, 124.93, 123.58, 121.31, 118.75, 75.21, 62.01, 50.56, 26.29, 25.90, 23.78; HRMS (ESI) calcd for $C_{23}H_{24}F_6N_3S$ ($M + H^+$) 488.1595, found 488.1587.

3. Procedure for Michael–Enolation-Cyclization Reaction

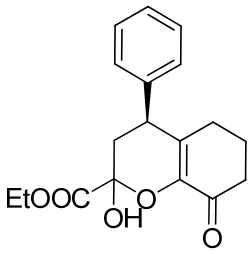


1 **2a** **3a**

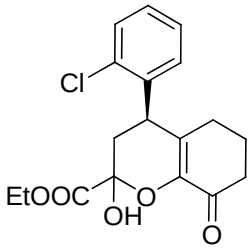
Typical procedure for the cascade reaction:

To a solution of (*E*)-ethyl 2-oxo-4-phenylbut-3-enoate **2a** (20.4 mg, 0.1 mmol) and cyclohexane-1,2-dione **1** (16.8 mg, 0.15 mmol) in 0.2 ml toluene, catalyst V (4.9 mg, 0.01 mmol) was added. The reaction mixture was stirred at 50 °C for 8h. The crude product was purified by column chromatography on silica gel, eluted by hexane/EtOAc = 5:1 then 3:1 to afford 30.0 mg (94% yield) of the desired product **3a** as colorless oil.

4. Analytical Data of Michael–Enolation-Cyclization Products

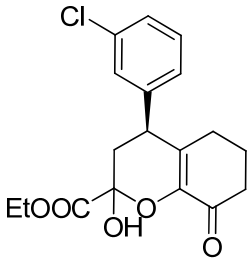


(2*R*,4*S*)-Ethyl 2-hydroxy-8-oxo-4-phenyl-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3a) (Table 3 , entry 1). 94% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 7.4 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.24 (d, *J* = 7.2 Hz, 2H), 4.50 (br, 1H), 4.38–4.23 (m, 2H), 3.81 (dd, *J* = 12.5, 6.5 Hz, 1H), 2.55–2.41 (m, 2H), 2.34 (t, *J* = 13.1 Hz, 1H), 2.23 (dd, *J* = 13.6, 6.5 Hz, 1H), 2.09–2.01 (m, 2H), 1.96–1.84 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.83, 169.13, 142.88, 140.83, 134.12, 128.94, 128.53, 127.31, 93.67, 63.01, 40.09, 38.29, 36.86, 27.81, 22.11, 13.93; HRMS (EI) calcd for $C_{18}H_{20}O_5$ 316.1311, found 316.1307; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 9.6 min, t_R (minor) = 11.9 min, *ee* = 95%; $[\alpha]^{25}_D$ = +113.0 (*c* = 1.11 in $CHCl_3$).

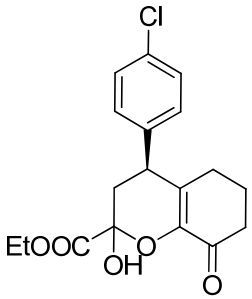


(2*R*,4*R*)-Ethyl 4-(2-chlorophenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3b) (Table 3 , entry 2). 92% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 (dd, *J* = 11.8, 4.7 Hz, 1H), 7.32–7.17 (m, 3H), 4.54 (br, 1H), 4.38–4.23 (m, 2H), 2.59–2.43 (m, 2H), 2.35–2.03 (m, 4H), 2.00–1.93 (m, 2H), 1.32 (td, *J* = 7.1, 3.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.77, 168.96, 144.26, 138.11, 134.14, 133.59, 131.86, 129.83, 129.72, 128.50, 128.35, 127.49, 126.86, 94.51,

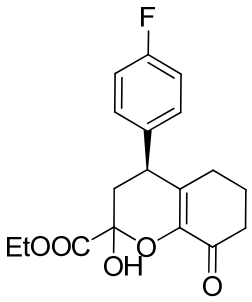
93.66, 63.04, 62.79, 38.41, 38.26, 35.55, 34.09, 34.04, 28.06, 27.59, 22.25, 22.10, 13.96, 13.92; HRMS (EI) calcd for $C_{18}H_{19}O_5Cl$ 350.0921, found 350.0916; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 9.8 min, t_R (minor) = 11.9 min, *ee* = 96%; $[\alpha]^{25}_D$ = +75.3 (*c* = 0.98 in $CHCl_3$).



(2*R*,4*S*)-Ethyl 4-(3-chlorophenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3c) (Table 3 , entry 3). 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.22 (m, 3H), 7.13 (dt, *J* = 7.0, 1.5 Hz, 1H), 4.71 (br, 1H), 4.38–4.24 (m, 2H), 3.81 (dd, *J* = 12.3, 6.7 Hz, 1H), 2.57–2.41 (m, 2H), 2.34–2.26 (m, 1H), 2.23 (dd, *J* = 13.6, 6.7 Hz, 1H), 2.14–1.99 (m, 2H), 1.94–1.89 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.80, 168.93, 142.95, 142.90, 134.75, 132.98, 130.21, 128.59, 127.57, 126.72, 93.57, 63.04, 39.86, 38.18, 36.66, 27.69, 22.05, 13.90; HRMS (EI) calcd for $C_{18}H_{19}O_5Cl$ 350.0921, found 350.0918; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 9.0 min, t_R (minor) = 11.4 min, *ee* = 92%; $[\alpha]^{25}_D$ = +104.2 (*c* = 0.96 in $CHCl_3$).

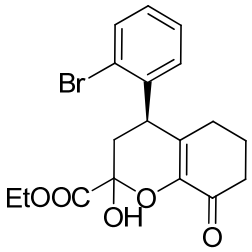


(2*R*,4*S*)-Ethyl 4-(4-chlorophenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3d) (Table 3 , entry 4). 90% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 4.54 (br, 1H), 4.38–4.21 (m, 2H), 3.80 (dd, *J* = 12.4, 6.6 Hz, 1H), 2.56–2.41 (m, 2H), 2.29 (t, *J* = 13.0 Hz, 1H), 2.21 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.09–1.98 (m, 2H), 1.96–1.85 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.70, 168.96, 153.86, 142.97, 139.32, 133.19, 129.85, 129.16, 93.58, 63.08, 39.53, 38.24, 36.77, 27.75, 22.08, 13.92; HRMS (EI) calcd for $C_{18}H_{19}O_5Cl$ 350.0921, found 350.0910; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 11.1 min, t_R (minor) = 14.0 min, *ee* = 96%; $[\alpha]^{25}_D$ = +120.9 (*c* = 1.09 in $CHCl_3$).

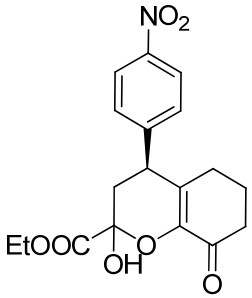


(2*R*,4*S*)-Ethyl 4-(4-fluorophenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3e) (Table 3 , entry 5). 91% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20 (dd, *J* = 8.6, 5.3 Hz, 2H), 7.05 (t, *J* = 8.6 Hz, 2H), 4.50 (br, 1H), 4.36–4.27 (m, 2H), 3.81 (dd, *J* = 12.5, 6.6 Hz, 1H), 2.54–2.46 (m, 2H), 2.30 (t, *J* = 13.1 Hz, 1H), 2.21 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.08–2.02 (m, 2H), 1.93–1.88 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.83, 169.01, 162.96, 161.00, 142.88, 136.45, 136.42, 133.68, 130.03, 129.96, 115.94, 115.78, 93.62, 63.10, 39.34, 38.24, 36.88, 27.77, 22.08, 13.93; HRMS (EI) calcd for $C_{18}H_{19}O_5F$ 334.1217, found 334.1216; HPLC

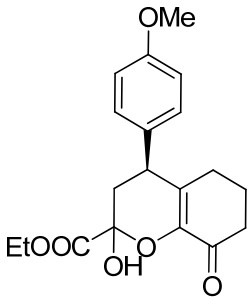
(Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 10.7 min, t_R (minor) = 13.5 min, *ee* = 95%; $[\alpha]^{25}_D$ = +102.4 (*c* = 1.15 in $CHCl_3$).



(2*R*,4*R*)-Ethyl 4-(2-bromophenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3f) (Table 3 , entry 6). 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 (dd, *J* = 12.7, 4.6 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.21–7.13 (m, 2H), 4.63 (br, 1H), 4.51 (dd, *J* = 11.2, 6.3 Hz, 1H), 4.38–4.22 (m, 2H), 2.59–2.43 (m, 2H), 2.32 (dd, *J* = 13.2, 6.5 Hz, 1H), 2.24–2.02 (m, 3H), 2.01–1.88 (m, 2H), 1.32 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.75, 168.89, 143.36, 140.17, 133.57, 133.07, 132.94, 129.12, 128.70, 128.61, 128.14, 127.50, 125.24, 93.63, 62.98, 62.72, 38.98, 38.34, 38.24, 35.73, 34.40, 27.61, 22.21, 22.07, 13.95, 13.88; HRMS (EI) calcd for $C_{18}H_{19}O_5Br$ 394.0416, found 394.0400; HPLC (Chiralpak IA, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 17.8 min, t_R (minor) = 21.6 min, *ee* = 97%; $[\alpha]^{25}_D$ = +63.3 (*c* = 0.98 in $CHCl_3$).

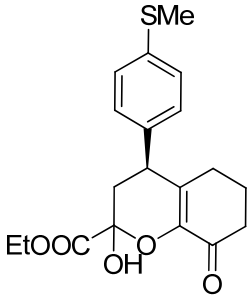


(2*R*,4*S*)-Ethyl 2-hydroxy-4-(4-nitrophenyl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3g) (Table 3 , entry 7). 84% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.7 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 4.50 (br, 1H), 4.37–4.28 (m, 2H), 3.97 (dd, *J* = 12.4, 6.6 Hz, 1H), 2.61–2.43 (m, 2H), 2.31 (dd, *J* = 20.1, 7.7 Hz, 1H), 2.24 (dd, *J* = 13.5, 6.6 Hz, 1H), 2.07–1.87 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.48, 168.68, 148.57, 147.38, 143.28, 131.47, 129.46, 124.29, 93.40, 63.29, 40.09, 38.25, 36.63, 27.80, 22.11, 13.94; HRMS (EI) calcd for $C_{18}H_{19}O_7N$ 361.1162, found 361.1160; HPLC (Chiralcel OD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 17.8 min, t_R (minor) = 29.3 min, *ee* = 93%; $[\alpha]^{25}_D$ = +127.2 (*c* = 1.00 in $CHCl_3$).

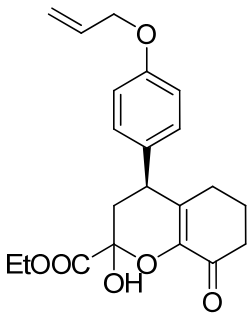


(2*R*,4*S*)-Ethyl 2-hydroxy-4-(4-methoxyphenyl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3h) (Table 3 , entry 8). 82% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.15 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.52 (br, 1H), 4.39–4.22 (m, 2H), 3.81 (s, 3H), 3.77 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.55–2.41 (m, 2H), 2.31 (t, *J* = 13.1 Hz, 1H), 2.20 (dd, *J* = 13.6, 6.5 Hz, 1H), 2.12–2.01 (m, 2H), 1.95–1.83 (m, 2H), 1.32 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.76, 169.16, 158.88, 142.77, 134.53, 132.69, 129.48, 114.39, 93.74, 62.94, 55.28, 39.22, 38.28, 36.90, 27.80, 22.11, 13.91; HRMS (EI) calcd for $C_{19}H_{22}O_6$ 346.1416, found 346.1413; HPLC (Chiralpak IA, *i*-propanol/hexane =

10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 12.8 min, t_R (minor) = 16.9 min, *ee* = 95%; $[\alpha]^{25}_D$ = +142.6 (*c* = 0.95 in $CHCl_3$).

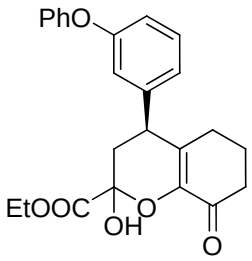


(2*R*,4*S*)-Ethyl 2-hydroxy-4-(4-(methylthio)phenyl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3i) (Table 3 , entry 9). 82% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 4.50 (br, 1H), 4.39–4.22 (m, 2H), 3.77 (dd, *J* = 12.5, 6.5 Hz, 1H), 2.56–2.41 (m, 5H), 2.31 (t, *J* = 13.0 Hz, 1H), 2.20 (dd, *J* = 13.6, 6.5 Hz, 1H), 2.13–2.01 (m, 2H), 1.97–1.83 (m, 2H), 1.32 (t, *J* =7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.85, 169.07, 142.86, 137.57, 137.51, 133.98, 128.98, 127.07, 93.62, 63.05, 39.53, 38.26, 36.74, 27.79, 22.08, 15.80, 13.92; HRMS (EI) calcd for $C_{19}H_{22}O_5S$ 362.1188, found 362.1180; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 12.6 min, t_R (minor) = 17.2 min, *ee* = 95%; $[\alpha]^{25}_D$ = +140.8 (*c* = 0.97 in $CHCl_3$).



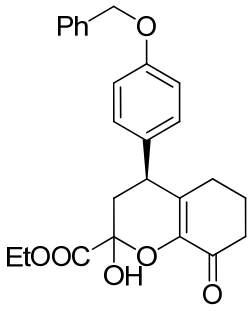
(2*R*,4*S*)-Ethyl 4-(4-(allyloxy)phenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-

carboxylate (3j) (Table 3 , entry 10). 87% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.16– 7.11(m, 2H), 6.93–6.88 (m, 2H), 6.12–5.98 (m, 1H), 5.42 (ddd, *J* = 17.3, 3.1, 1.6 Hz, 1H), 5.30 (ddd, *J* = 10.5, 2.7, 1.3 Hz, 1H), 4.55–4.53 (m, 3H), 4.39–4.22 (m, 2H), 3.76 (dd, *J* = 12.5, 6.6 Hz, 1H), 2.56–2.41 (m, 2H), 2.36–2.27 (m, 1H), 2.20 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.13–1.98 (m, 2H), 1.97–1.83 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.02, 169.19, 157.85, 142.71, 134.73, 133.18, 132.77, 129.48, 117.71, 115.14, 93.71, 68.87, 63.01, 39.20, 38.25, 36.84, 27.80, 22.08, 13.93; HRMS (EI) calcd for $C_{21}H_{24}O_6$ 372.1573, found 372.1561; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 11.7 min, t_R (minor) = 15.0 min, *ee* = 94%; $[\alpha]^{25}_D$ = +144.6 (*c* = 0.83 in $CHCl_3$).

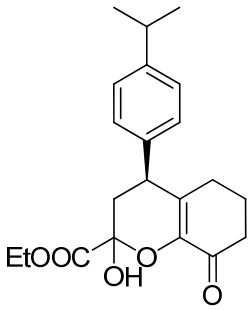


(2*R*,4*S*)-ethyl 2-hydroxy-8-oxo-4-(3-phenoxyphenyl)-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3k) (Table 3 , entry 11). 94% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37-7.29 (m, 3H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.05–6.99 (m, 2H), 6.97 (d, *J* = 7.7 Hz, 1H), 6.94–6.88 (m, 2H), 4.52 (br, 1H), 4.38–4.23 (m, 2H), 3.78 (dd, *J* = 12.4, 6.6 Hz, 1H), 2.56–2.40 (m, 2H), 2.31 (t, *J* = 13.0 Hz, 1H), 2.23 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.18–2.02 (m, 2H), 1.98–1.85 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.82, 169.02, 157.82, 156.82, 142.85, 142.83, 133.60, 130.19, 129.80, 123.56, 123.21, 118.95, 118.85, 117.44, 93.58, 63.04, 39.94, 38.24, 36.64, 27.71, 22.08, 13.92; HRMS (EI) calcd for $C_{24}H_{24}O_6$ 408.1573, found 408.1559; HPLC (Chiralpak IA, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 17.5 min, t_R (minor) = 21.9 min, *ee* = 96%; $[\alpha]^{25}_D$ =

+95.0 (c = 1.05 in $CHCl_3$).

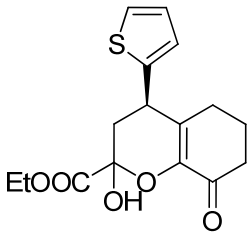


(2*R*,4*S*)-Ethyl 4-(4-(benzyloxy)phenyl)-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3l) (Table 3 , entry 12). 86% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.30 (m, 5H), 7.17–7.12 (m, 2H), 6.99–6.94 (m, 2H), 5.06 (s, 2H), 4.51 (br, 1H), 4.37–4.23 (m, 2H), 3.76 (dd, J = 12.5, 6.5 Hz, 1H), 2.56–2.40 (m, 2H), 2.35–2.27 (m, 1H), 2.20 (dd, J = 13.6, 6.5 Hz, 1H), 2.12–1.97 (m, 2H), 1.96–1.83 (m, 2H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.91, 169.17, 158.08, 142.75, 136.89, 134.60, 132.94, 129.53, 128.59, 128.00, 127.43, 115.28, 93.71, 70.12, 63.00, 39.22, 38.26, 36.87, 27.82, 22.09, 13.92; HRMS (EI) calcd for $C_{25}H_{26}O_6$ 422.1729, found 422.1709; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 17.5 min, t_R (minor) = 22.4 min, *ee* = 93%; $[\alpha]^{25}_D$ = +104.5 (c = 1.11 in $CHCl_3$).

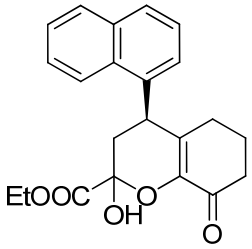


(2*R*,4*S*)-Ethyl 2-hydroxy-4-(4-isopropylphenyl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3m) (Table 3 , entry 13). 91% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 (d, J = 8.1 Hz,

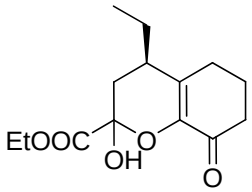
2H), 7.16–7.12 (m, 2H), 4.53 (br, 1H), 4.38–4.22 (m, 2H), 3.78 (dd, J = 12.5, 6.5 Hz, 1H), 2.91 (dt, J = 13.9, 6.9 Hz, 1H), 2.56–2.41 (m, 2H), 2.33 (t, J = 13.1 Hz, 1H), 2.21 (dd, J = 13.6, 6.6 Hz, 1H), 2.15–1.99 (m, 2H), 1.96–1.83 (m, 2H), 1.31 (t, J = 7.3 Hz, 3H), 1.26 (d, J = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.01, 169.21, 147.95, 142.76, 137.97, 134.69, 128.41, 126.93, 93.69, 62.99, 39.65, 38.27, 36.89, 33.70, 27.85, 23.92, 22.07, 13.92; HRMS (EI) calcd for $C_{21}H_{26}O_5$ 358.1780, found 358.1764; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 7.0 min, t_R (minor) = 9.8 min, *ee* = 95%; $[\alpha]^{25}_D$ = +121.1 (c = 0.95 in $CHCl_3$).



(2*R*,4*R*)-Ethyl 2-hydroxy-8-oxo-4-(thiophen-2-yl)-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3n) (Table 3 , entry 14). 84% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25 (dd, J = 5.0, 0.6 Hz, 1H), 7.00–6.94 (m, 2H), 4.60 (br, 1H), 4.41–4.24 (m, 2H), 4.19 (dd, J = 12.5, 6.3 Hz, 1H), 2.51–2.40 (m, 3H), 2.33 (dd, J = 13.5, 6.4 Hz, 1H), 2.21–2.11 (m, 2H), 1.91 (dd, J = 10.2, 4.2 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$): δ = 193.04, 168.90, 143.29, 142.01, 133.44, 126.84, 126.43, 124.65, 93.60, 63.10, 38.12, 37.04, 35.00, 27.24, 21.98, 13.91; HRMS (EI) calcd for $C_{16}H_{18}O_5S$ 322.0875, found 322.0870; HPLC (Chiralpak IA, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 17.4 min, t_R (minor) = 20.8 min, *ee* = 93%; $[\alpha]^{25}_D$ = +82.9 (c = 1.02 in $CHCl_3$).

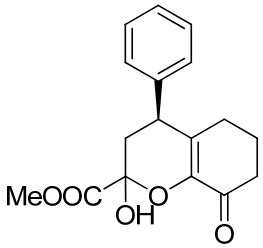


(2*R*,4*S*)-Ethyl 2-hydroxy-4-(naphthalen-1-yl)-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3o) (Table 3 , entry 15). 91% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24–7.98 (m, 1H), 7.94–7.87 (m, 1H), 7.86–7.75 (m, 1H), 7.61–7.32 (m, 4H), 4.86–4.63 (m, 1H), 4.38–4.21 (m, 2H), 2.89 (t, *J* = 13.3 Hz, 0.4H), 2.65–2.45 (m, 2H), 2.39 (d, *J* = 8.5, 1H), 2.29 (dd, *J* = 14.9, 7.9 Hz, 0.8H), 2.20 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.05–1.79 (m, 4H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.93, 169.13, 143.80, 141.98, 137.31, 136.05, 135.50, 134.95, 134.50, 133.95, 132.03, 131.04, 129.45, 129.33, 129.13, 128.70, 127.61, 126.60, 126.42, 125.91, 125.75, 125.66, 125.60, 125.48, 125.42, 123.57, 122.32, 93.93, 93.83, 63.02, 41.71, 38.38, 38.21, 37.12, 34.30, 34.08, 29.65, 27.74, 27.25, 22.23, 22.05, 14.01, 13.90; HRMS (EI) calcd for $C_{22}H_{22}O_5$ 366.1467, found 366.1481; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 9.2 min, t_R (minor) = 11.1 min, *ee* = 95%; $[\alpha]^{25}_{D}$ = +84.8 (*c* = 1.01 in $CHCl_3$).



(2*R*,4*R*)-Ethyl 4-ethyl-2-hydroxy-8-oxo-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3p) (Table 3 , entry 16). 72% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.40–4.19 (m, 2H), 2.63–2.22 (m, 4H), 2.11–1.78 (m, 4H), 1.45–1.16 (m, 6H), 0.96 (t, *J* = 7.5, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.96, 169.51, 142.24, 135.43, 93.72, 62.97, 37.98, 33.10, 32.36, 29.69, 26.78, 23.74, 22.02, 13.96, 10.71; HRMS (EI) calcd for $C_{14}H_{20}O_5$ 268.1311, found 268.1310; HPLC (Chiralpak AD-H,

i-propanol/hexane = 2/98, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 34.5 min, t_R (minor) = 37.3 min, *ee* = 96%; $[\alpha]^{25}_D$ = +13.3 (*c* = 0.15 in $CHCl_3$).



(2*R*,4*S*)-Methyl 2-hydroxy-8-oxo-4-phenyl-3,4,5,6,7,8-hexahydro-2*H*-chromene-2-carboxylate (3q)

(Table 3 , entry 17). 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (t, *J* = 7.4 Hz, 2H), 7.31–7.27 (m, 1H), 7.23 (dd, *J* = 5.2, 3.1 Hz, 2H), 4.48 (br, 1H), 3.85 (s, 3H), 3.81 (dd, *J* = 12.6, 6.6 Hz, 1H), 2.56–2.41 (m, 2H), 2.39–2.30 (m, 1H), 2.24 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.13–2.00 (m, 2H), 1.96–1.84 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.90, 169.56, 142.74, 140.67, 134.26, 128.94, 128.49, 127.33, 93.74, 53.54, 39.97, 38.22, 36.82, 27.78, 22.06; HRMS (EI) calcd for $C_{17}H_{18}O_5$ 302.1154, found 302.1151; HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 10.4 min, t_R (minor) = 13.1 min, *ee* = 96%; $[\alpha]^{25}_D$ = +124.0 (*c* = 1.05 in $CHCl_3$).

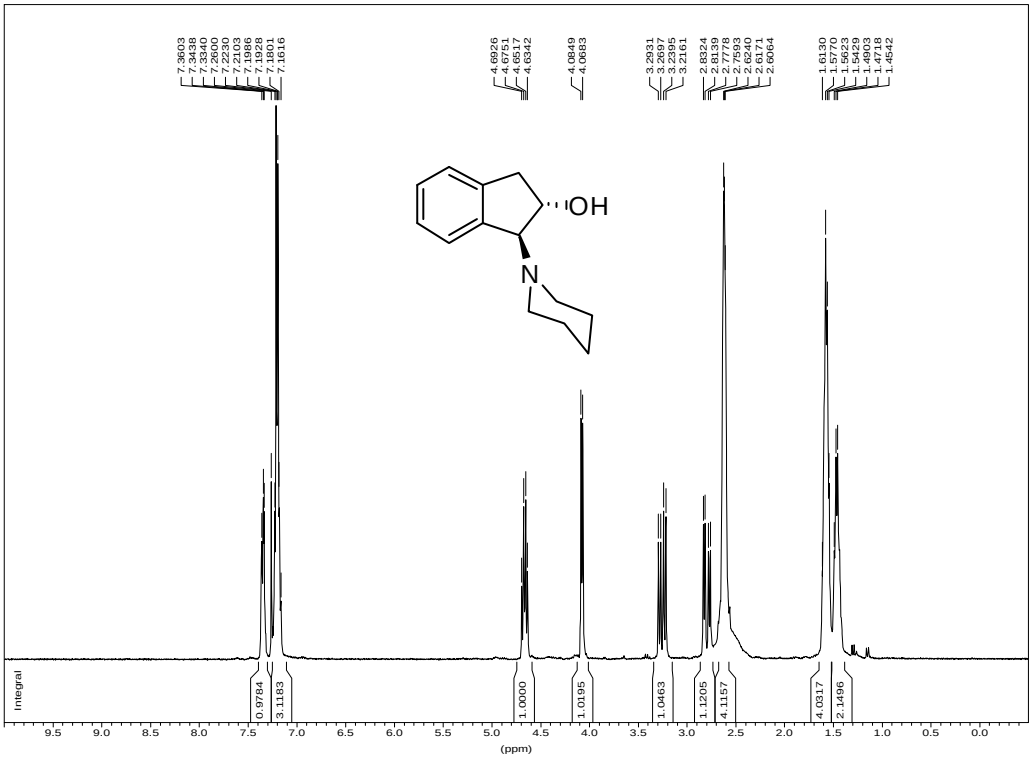
Reference:

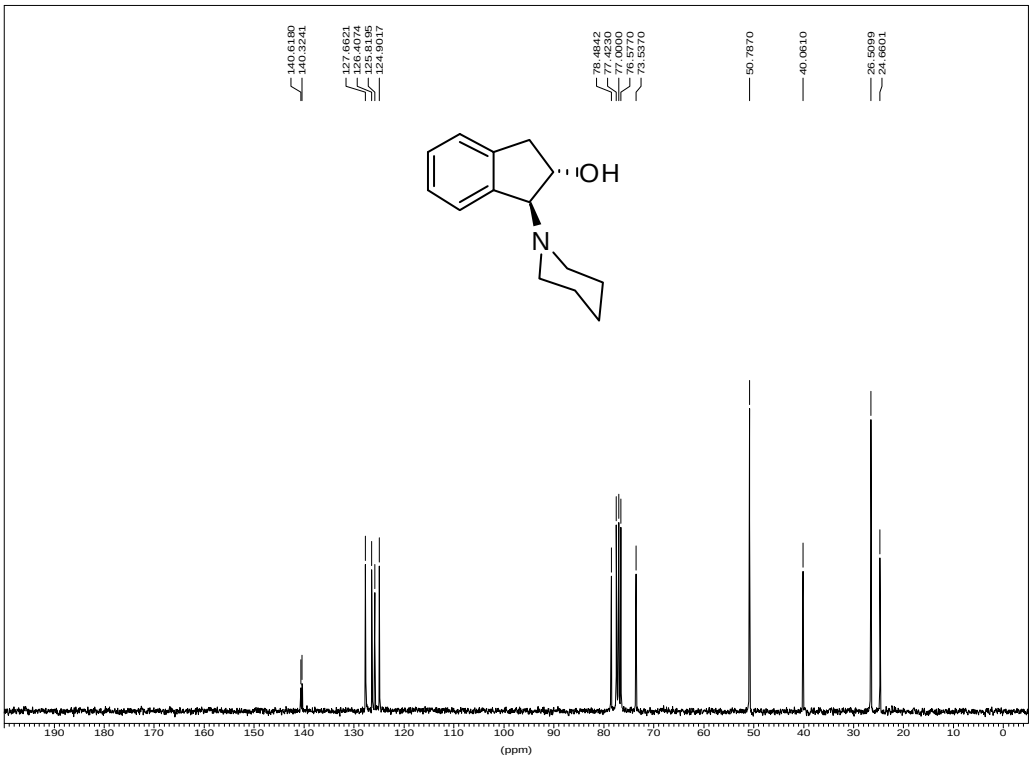
1. Soh, J. Y.-T.; Tan, C.-H. *J. Am. Chem. Soc.* **2009**, *131*, 6904-6905.

2. Govindaraju, T.; Kumar, V. A.; Ganesh, K. N. *J. Org. Chem.* **2004**, *69*, 5725-5734.

5. HPLC Chromatogram Profile and NMR Spectra of the Catalysts and Products

Compound **b**


7.3603
7.3438
7.3340
7.2800
7.2230
7.2103
7.1986
7.1928
7.1801
7.1616
4.6926
4.6751
4.6517
4.6342
4.0849
4.0683
3.2931
3.2697
3.2395
3.2161
2.8324
2.8139
2.7778
2.7593
2.6240
2.6071
2.6064
1.6130
1.5770
1.5623
1.5429
1.4903
1.4718
1.4542
OH
N
Integral
0.9784
3.1183
1.0000
1.0195
1.0463
1.1205
4.1157
4.0317
2.1496
(ppm)


140.6180
140.3241
127.6621
126.4074
125.8195
124.9017
78.4842
77.4230
77.0000
76.5770
73.5370
50.7870
40.0610
26.5099
24.6601
OH
N
(ppm)

Compound **c**


7.2568
7.2454
7.2344
7.1660
7.1622
7.1559
7.1483
7.1446
7.1118
7.1067
7.0954
4.6395
4.6269
3.1934
3.1770
3.1632
3.1480
3.0685
3.0421
3.0257
3.0106
2.8341
2.8177
2.8006
2.7762
2.5328
2.5215
2.5114
2.5013
2.4672
2.4572
2.4458
2.4345
2.4244
1.5570
1.5457
1.5230
1.5116
1.4070
1.3944
1.3830
1.3717
1.3603
N3
N
Integral
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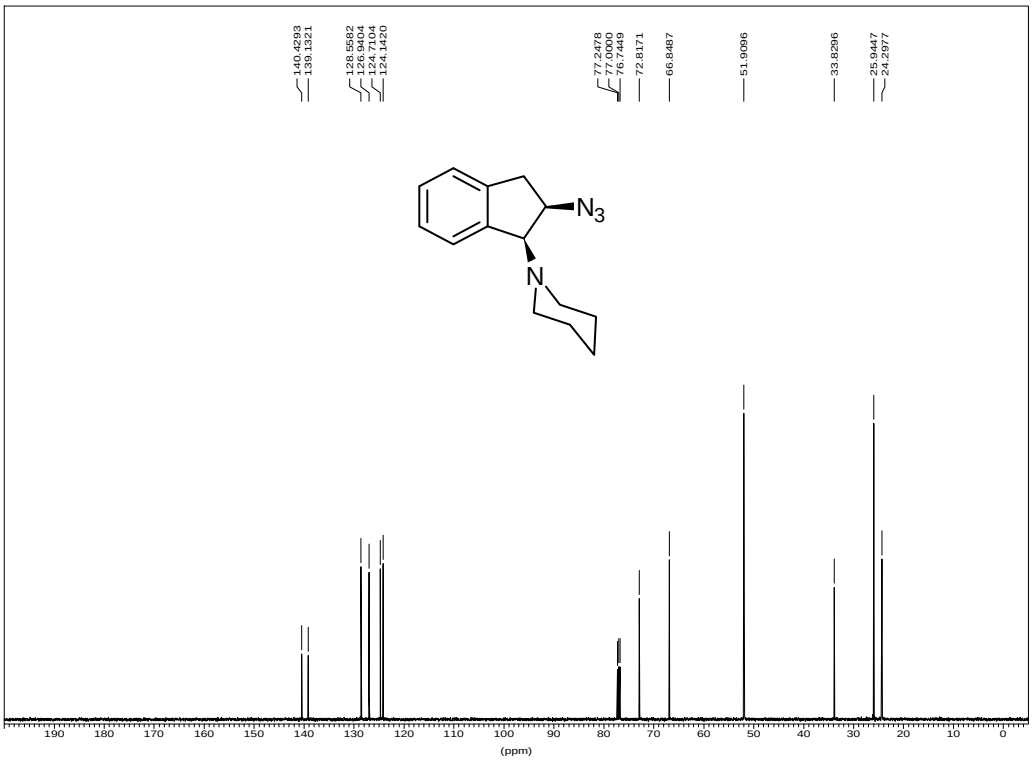
0.9410
1.0000
1.0378
1.0261
4.1220
4.1275
2.1250
(ppm)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139.1321
128.5582
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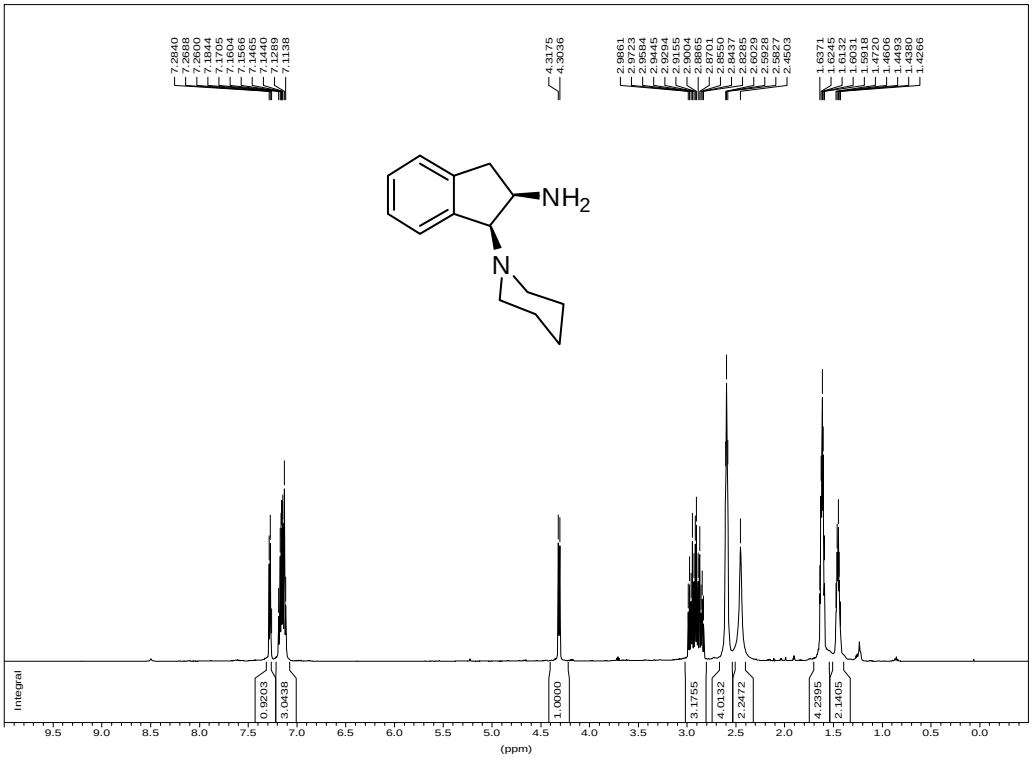
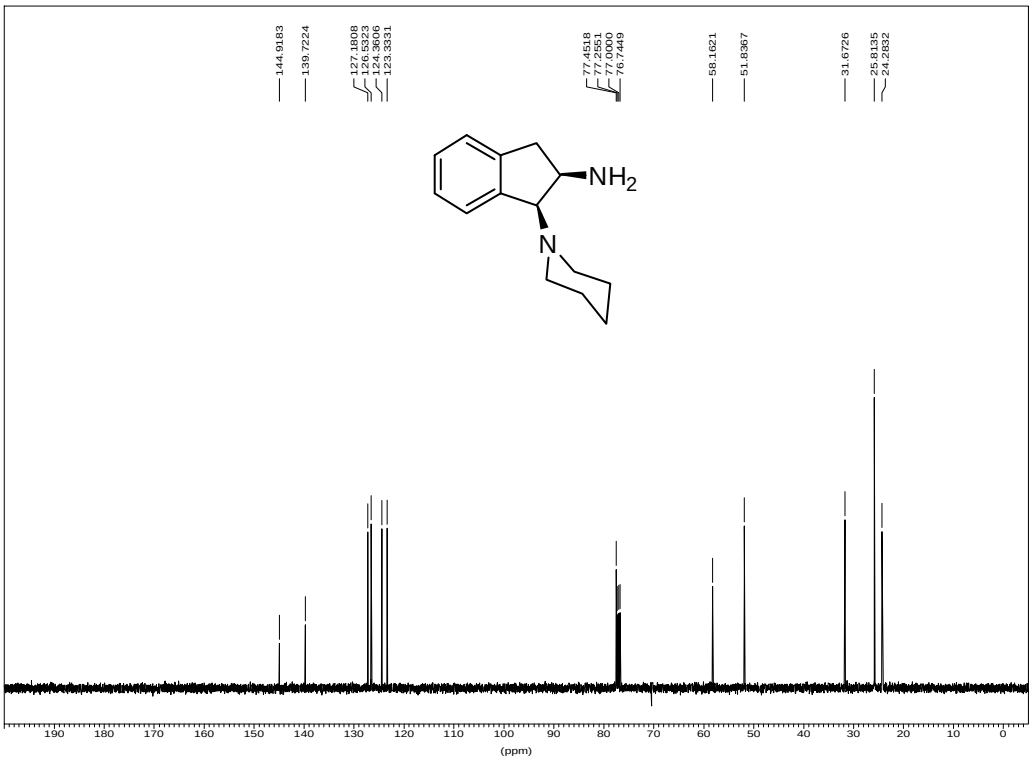
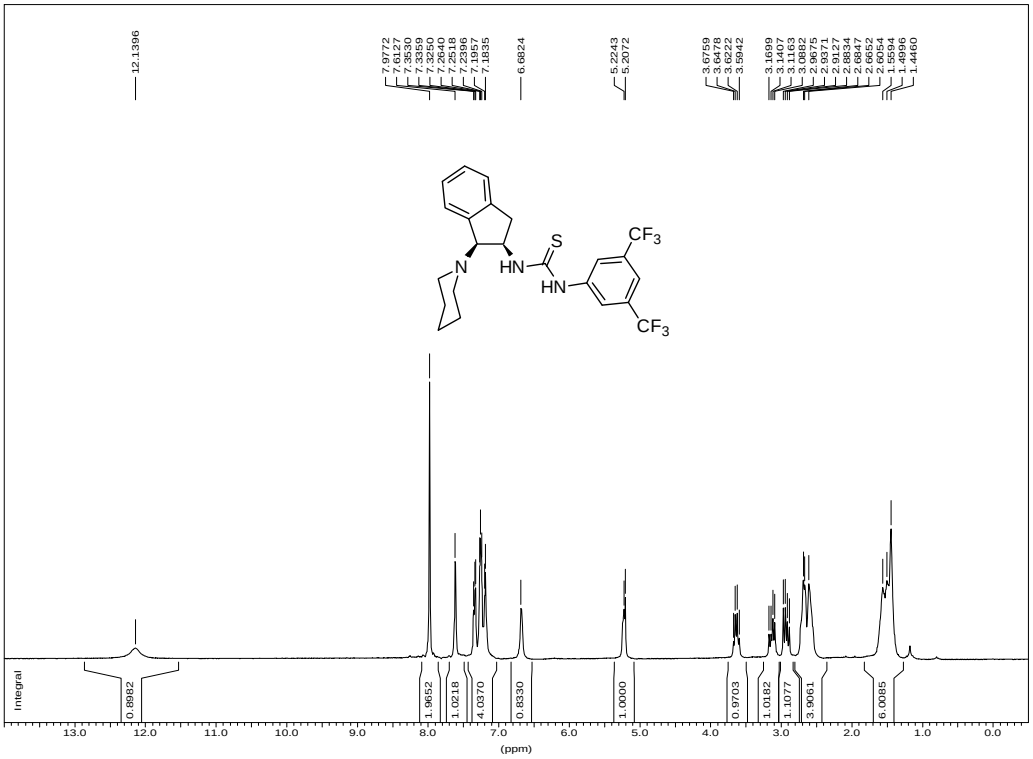
124.7104
124.1420
77.2478
77.0000
76.7449
72.8171
66.8487
51.9096
33.8296
25.9447
24.2977
N3
N
(ppm)

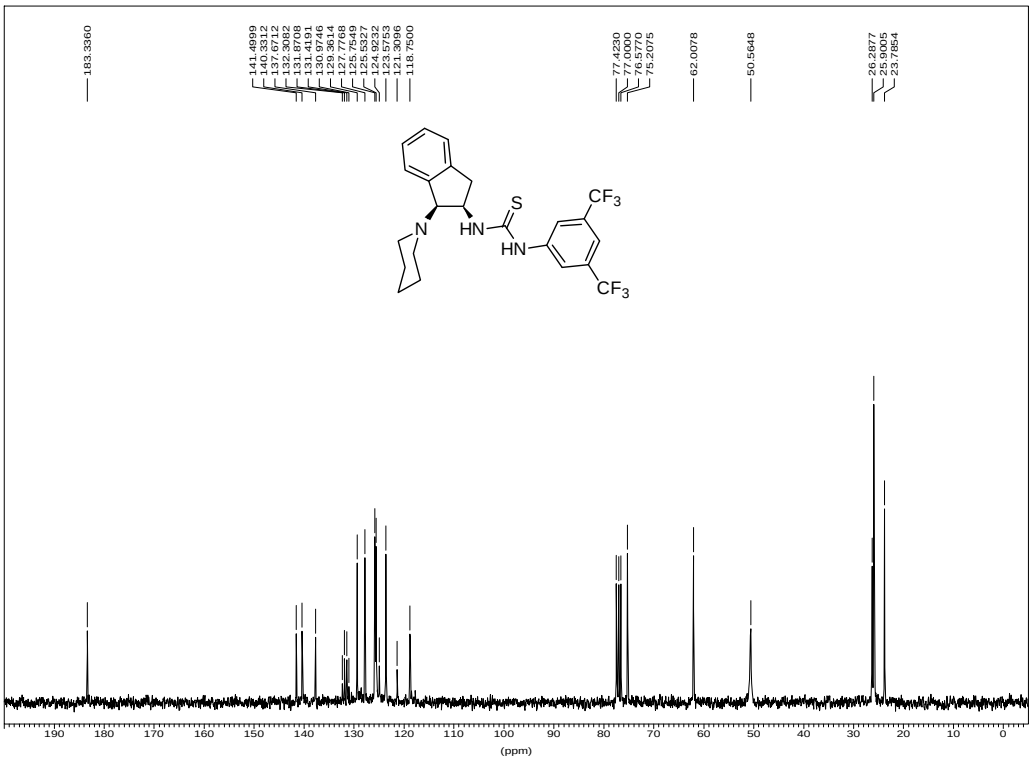
Compound **d**


NH2
N
Integral
0.9203
3.0438
1.0000
3.1755
4.0132
2.2472
4.2395
2.1405
(ppm)

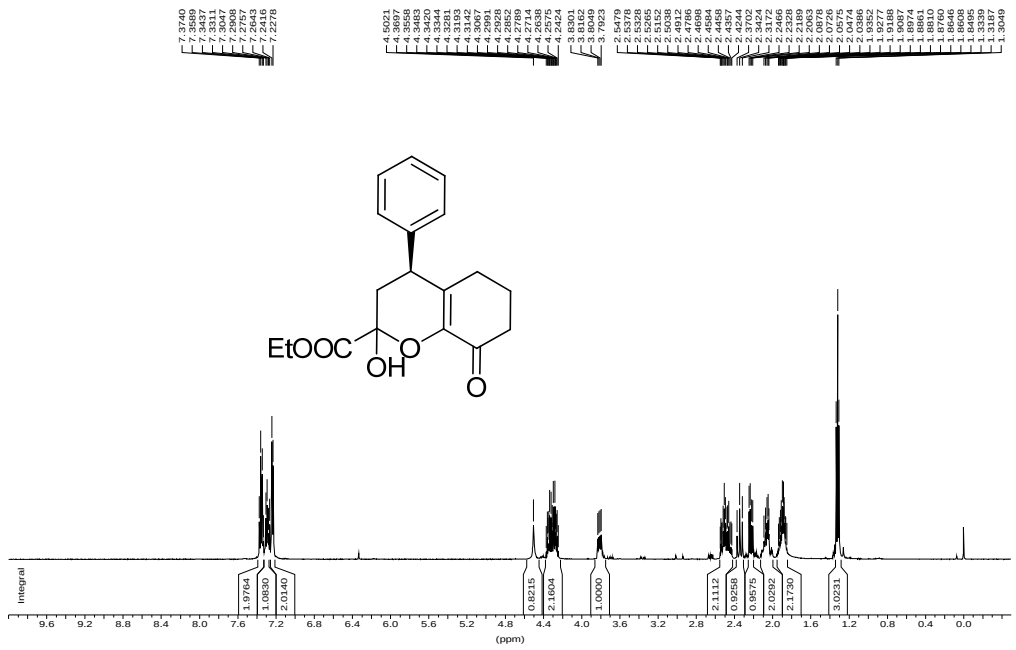

144.9183
139.7224
127.1808
126.5323
124.3606
123.3331
77.4518
77.2551
77.0000
76.7449
58.1621
51.8367
31.6726
25.8135
24.2832
NH2
N
(ppm)

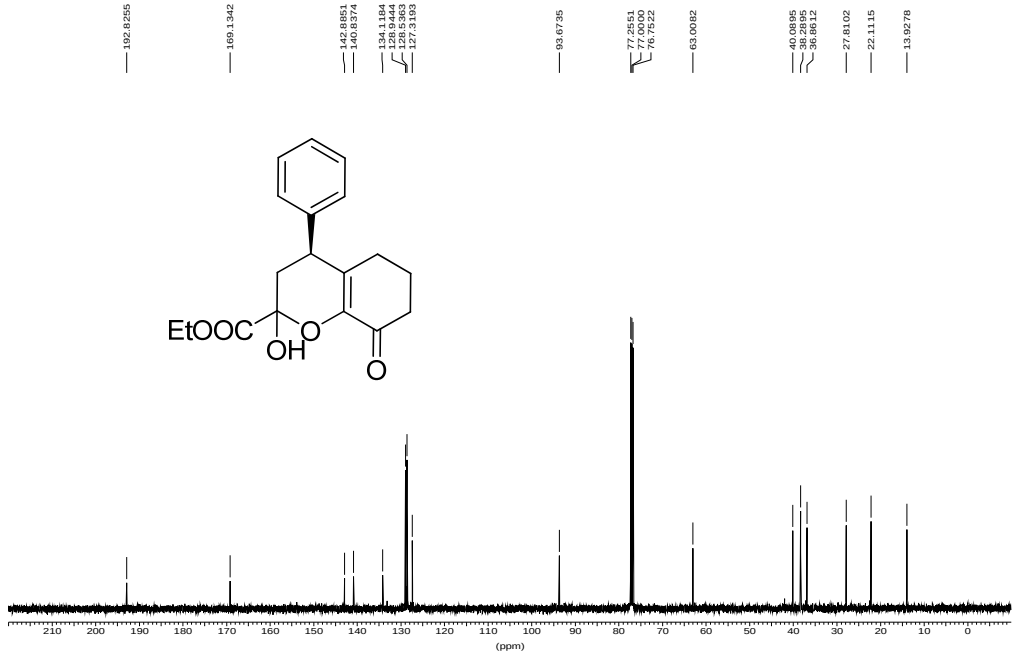
Catalyst **V**


12.1396
7.9772
7.6127
7.3580
7.3359
7.3250
7.2640
7.2518
7.2396
7.1957
7.1835
6.6824
5.2243
5.2072
3.6759
3.6478
3.6222
3.5942
3.1699
3.1407
3.1163
3.0892
3.0665
2.9371
2.9127
2.8834
2.8647
2.6852
2.6054
1.5594
1.4996
1.4460
CF3
S
HN
N
HN
CF3
Integral
0.8992
1.9652
1.0218
4.0370
0.8330
1.0000
0.9703
1.0182
1.1077
3.9061
6.0085
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

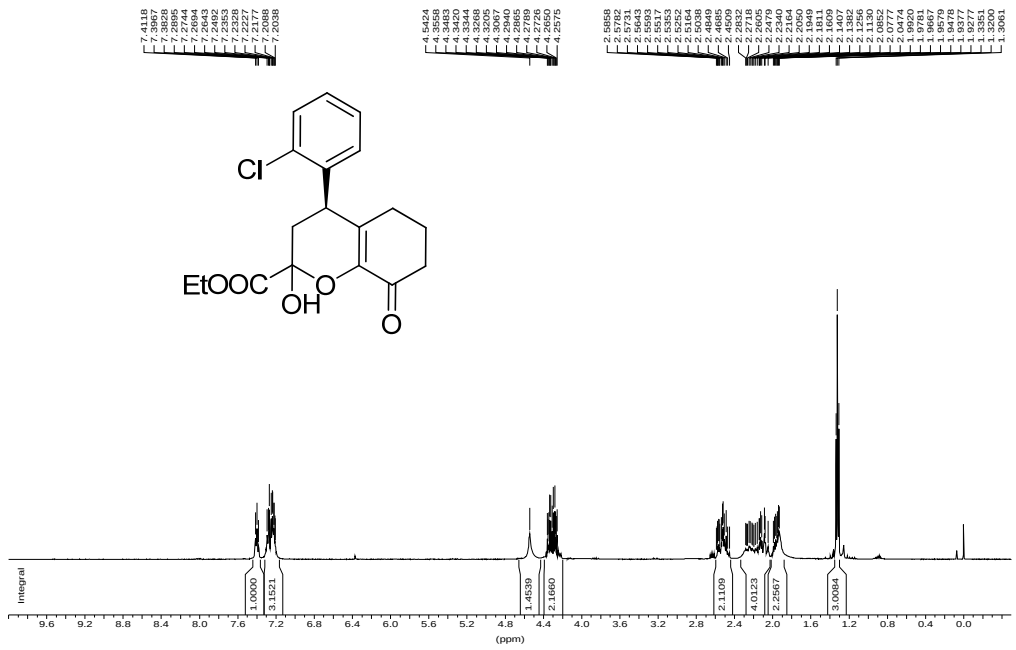

183.3360
141.4999
140.3312
137.6712
132.3082
131.5708
131.4191
130.9746
129.3614
127.7768
125.7549
125.5327
124.9232
123.5753
121.3096
118.7500
77.4230
77.0000
76.5770
75.2075
62.0078
50.5648
26.2877
25.5005
23.7854
CF3
S
HN
N
HN
CF3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

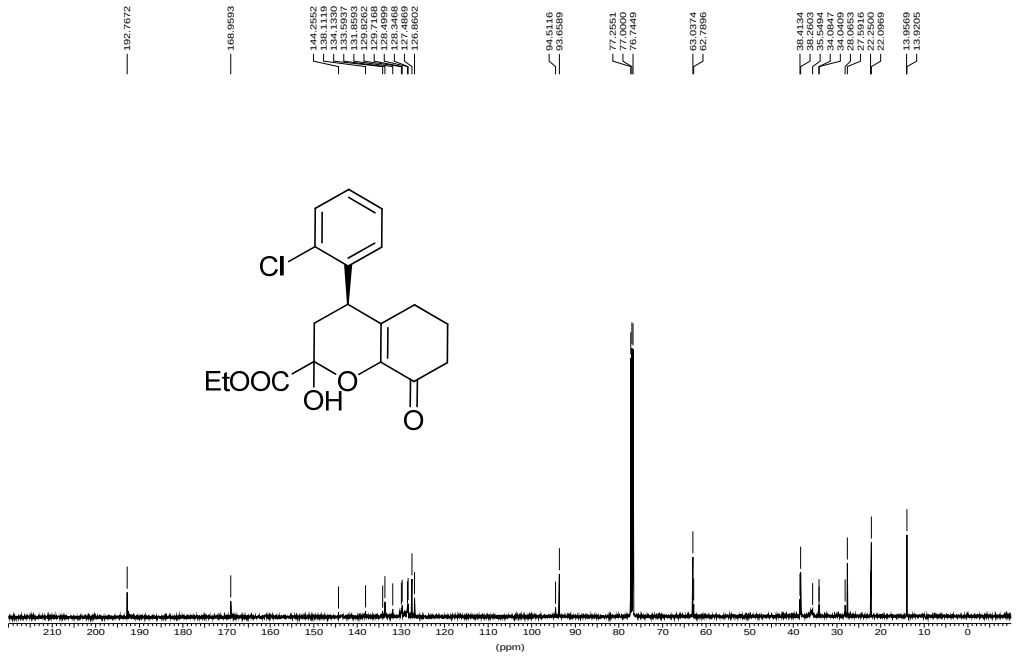
Compound **3a**


EtOOC
OH
O
integral
1.9764
1.0830
2.0140
0.8215
2.1604
1.0000
2.1112
0.9258
0.9575
2.0292
2.1730
3.0231
(ppm)

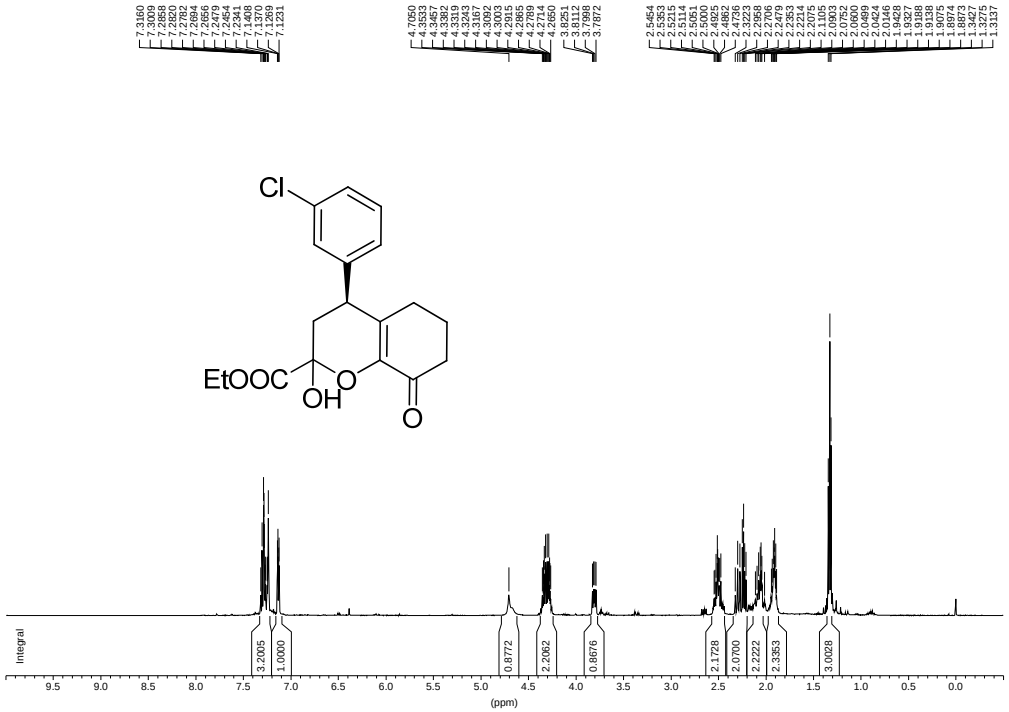

192.8255
169.1342
142.8851
140.8374
134.1184
128.9444
128.3563
127.3193
93.6735
77.2551
77.0000
76.7522
63.0082
40.0895
38.2895
36.8612
27.8102
22.1115
13.9278
EtOOC
OH
O
(ppm)

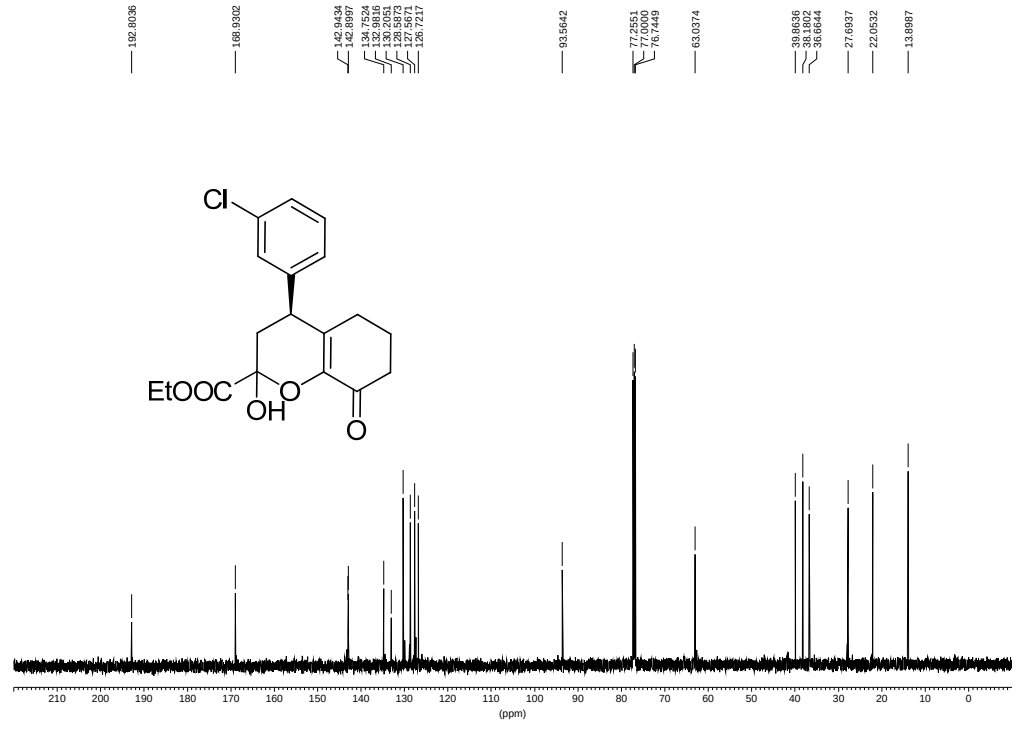
Compound **3b**


Cl
EtOOC
OH
O
O
integral
1.0000
3.1521
1.4539
2.1660
2.1109
4.0123
2.2567
3.0084
(ppm)

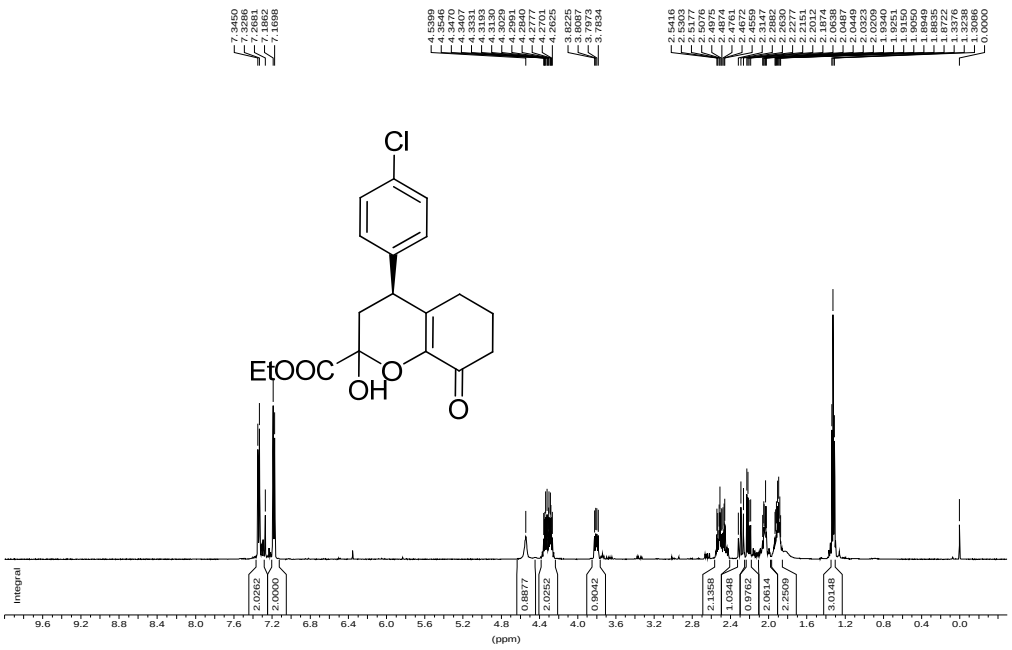

Cl
EtOOC
OH
O
O
(ppm)

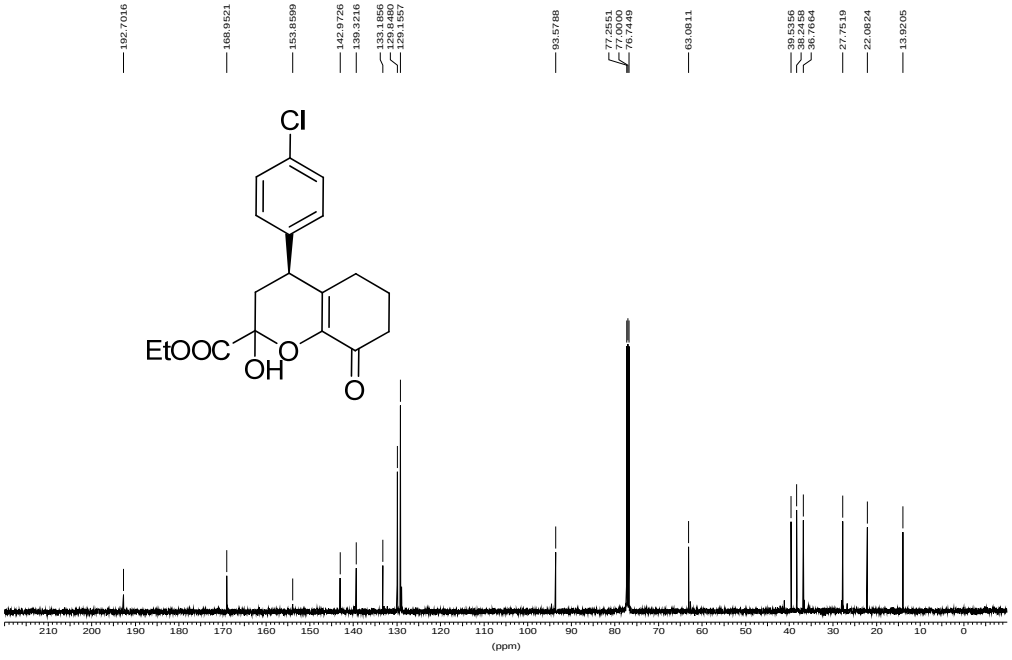
Compound **3c**


Cl
EtOOC
OH
O
Integral
3.2005
1.0000
0.8772
2.2062
0.8676
2.1728
2.0700
2.2222
2.3353
3.0028
(ppm)


192.8036
168.9302
142.9434
142.6997
134.7524
132.9815
130.2051
128.5873
127.5671
126.7217
93.5642
77.2551
77.0000
76.7449
63.0374
39.8636
38.1802
36.6644
27.6937
22.0532
13.8987
Cl
EtOOC
OH
O
(ppm)

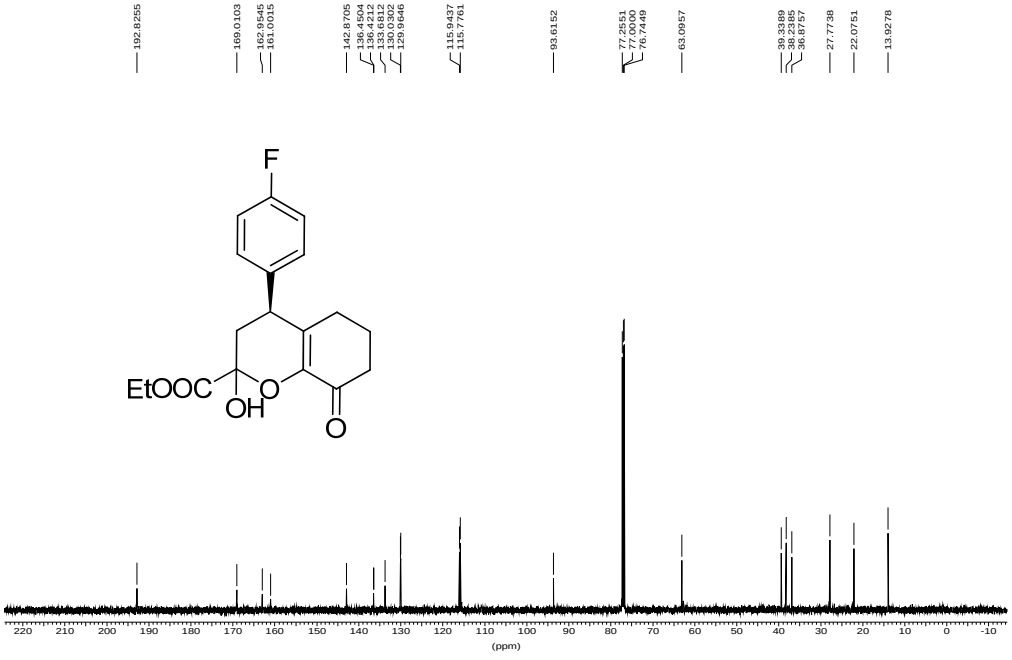
Compound **3d**


Cl
EtOOC
OH
O
O
integral
2.0262
2.0000
0.8877
2.0252
0.9042
2.1358
1.0348
0.9762
2.0614
2.2509
3.0148
(ppm)

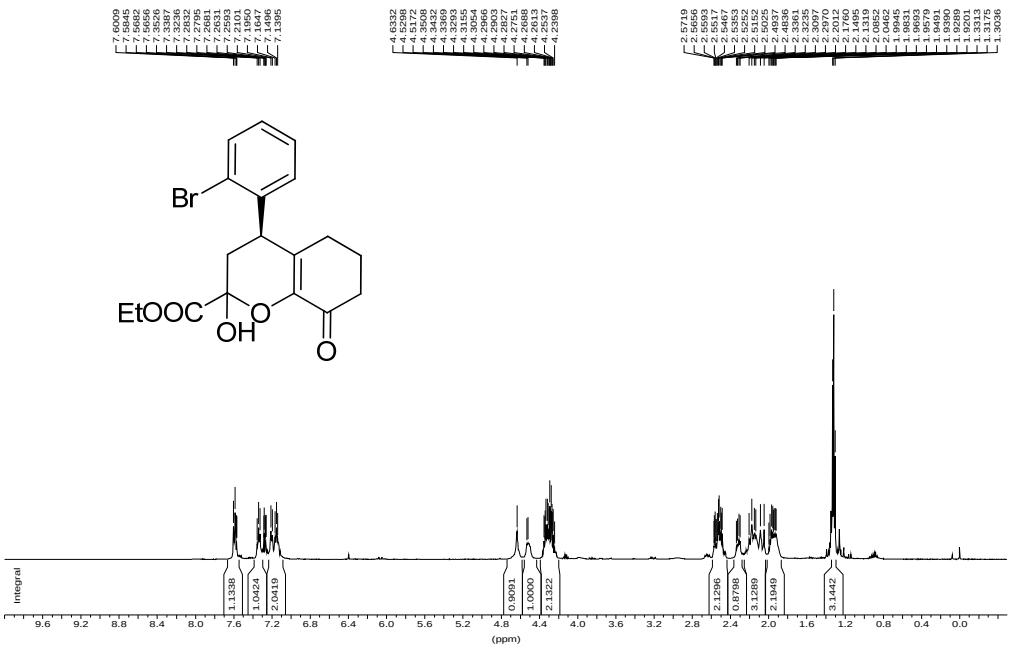

192.7016
168.9521
153.8599
142.9726
139.3216
133.1856
129.8480
129.1557
93.5788
77.2551
77.0000
76.7449
63.0811
39.5356
38.2458
36.7664
27.7519
22.0824
13.9205
Cl
EtOOC
OH
O
O
(ppm)

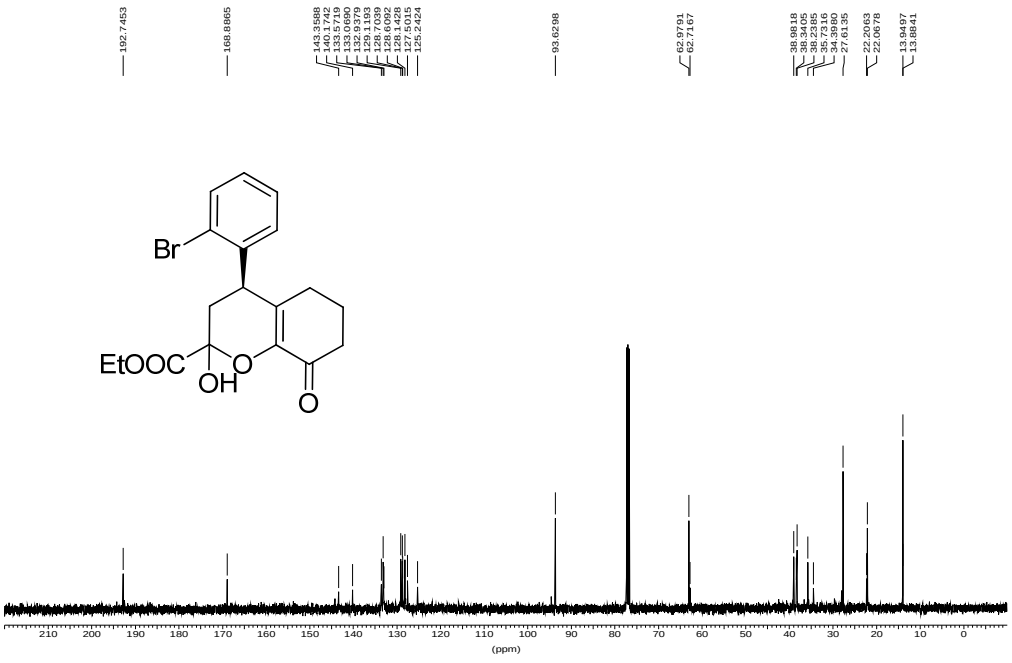
Compound **3e**


F
EtOOC
O
OH
O
integral
2.0966
2.0174
0.9154
2.1856
1.0000
2.0895
1.1242
1.1382
2.1226
2.1467
3.0614
(ppm)

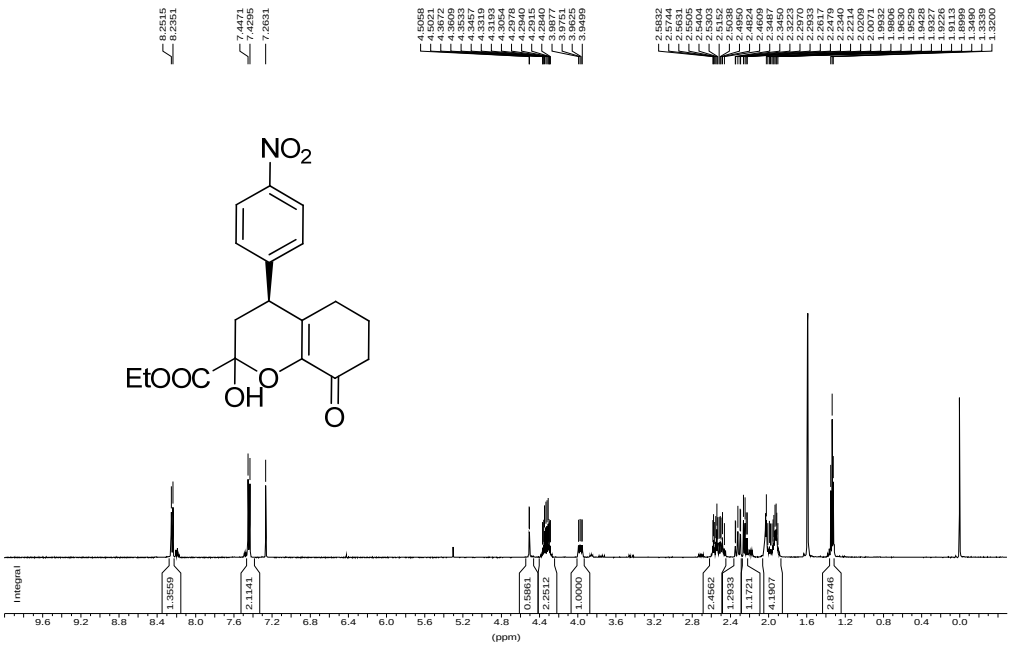

192.8255
169.0103
162.9545
161.0015
142.8705
136.4504
136.2212
133.6812
130.0302
129.9646
115.9437
115.7761
93.6152
77.2551
77.0000
76.7449
63.0957
39.3389
39.2981
38.8757
27.7738
22.0751
13.9278
F
EtOOC
O
OH
O
(ppm)

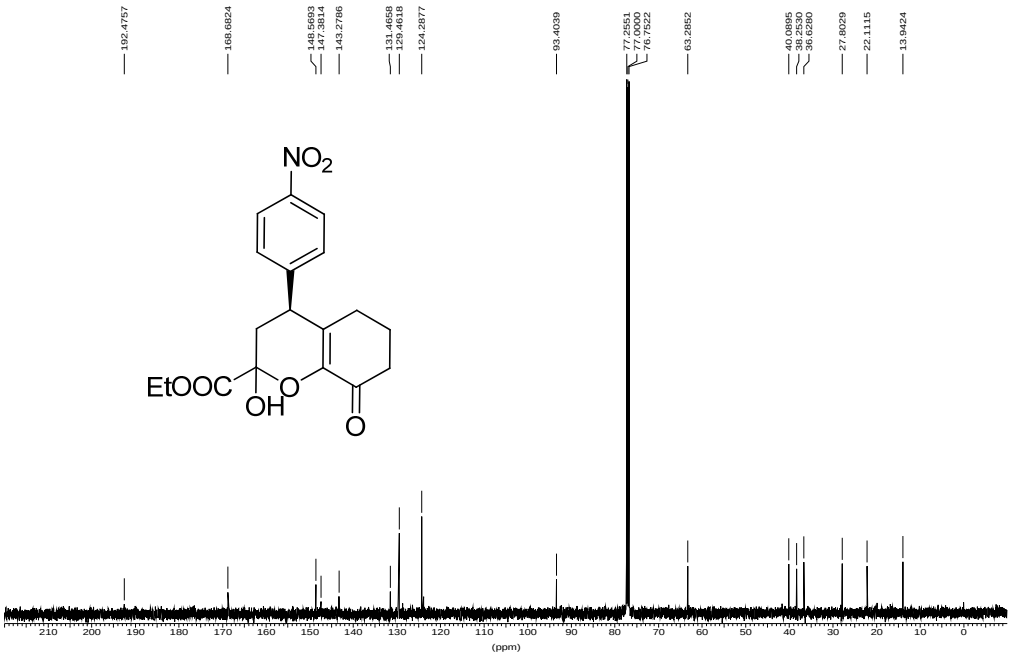
Compound **3f**


Br
EtOOC
O
OH
O
integral
1.1338
1.0424
2.0419
0.9091
1.0000
2.1322
2.1296
0.8798
3.1289
2.1949
3.1442
(ppm)

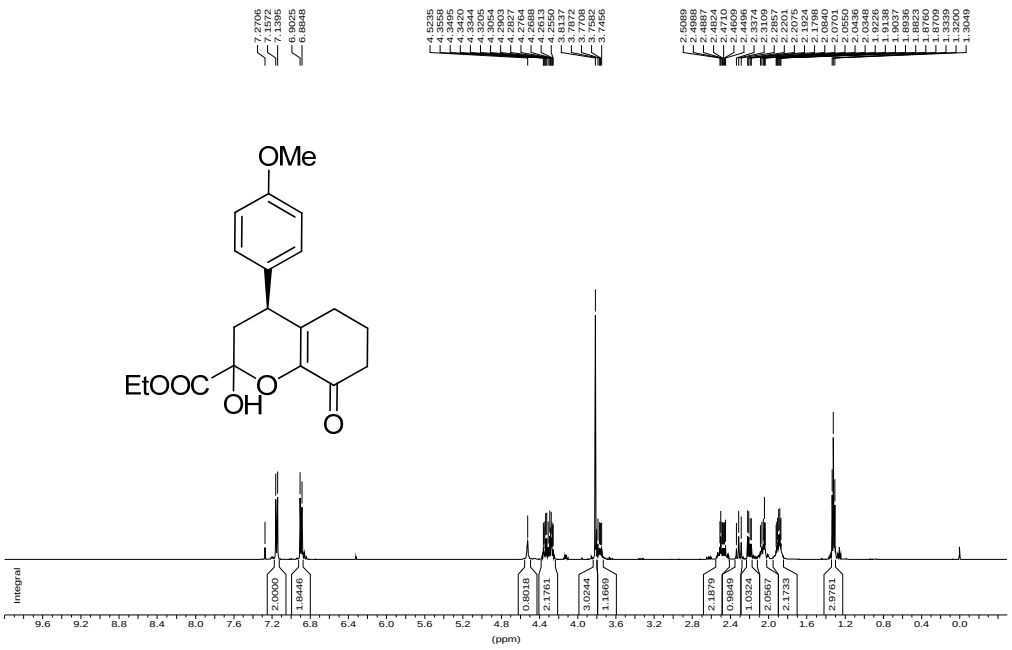

Br
EtOOC
O
OH
O
(ppm)

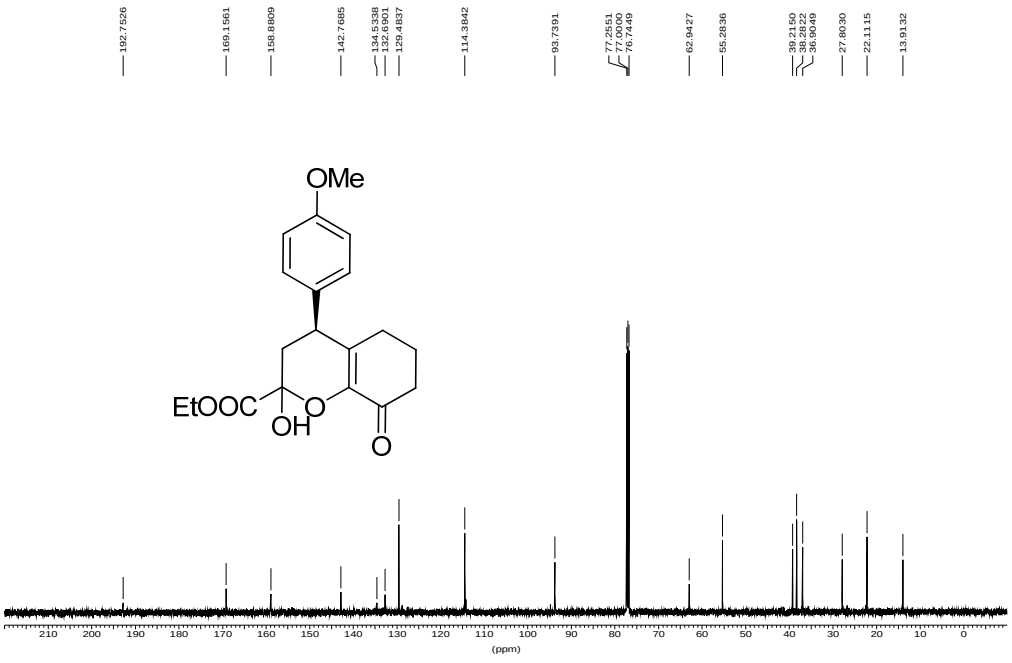
Compound **3g**



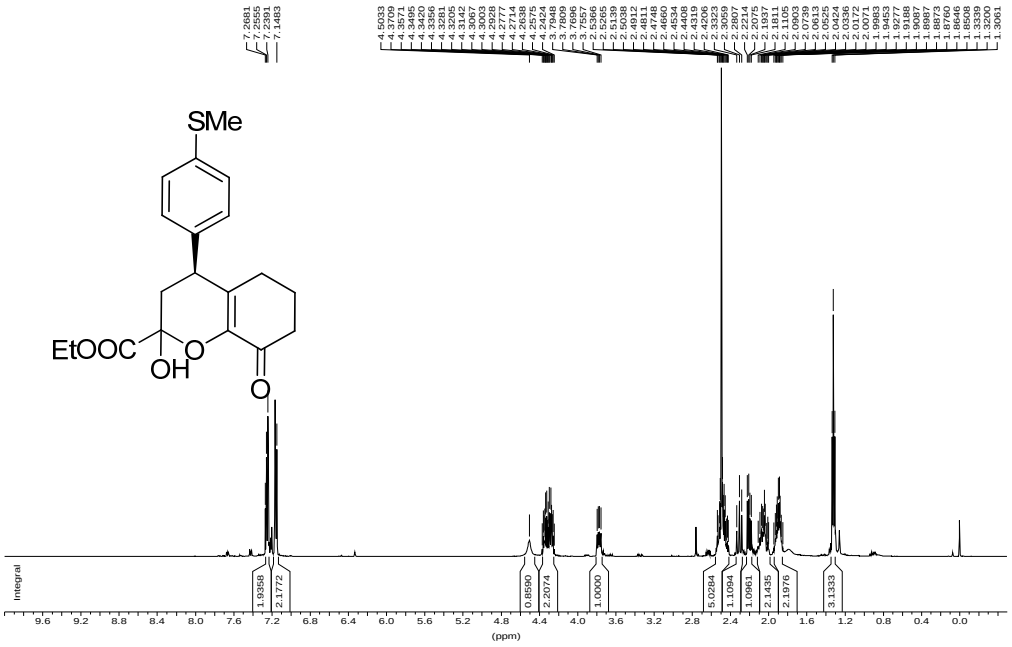


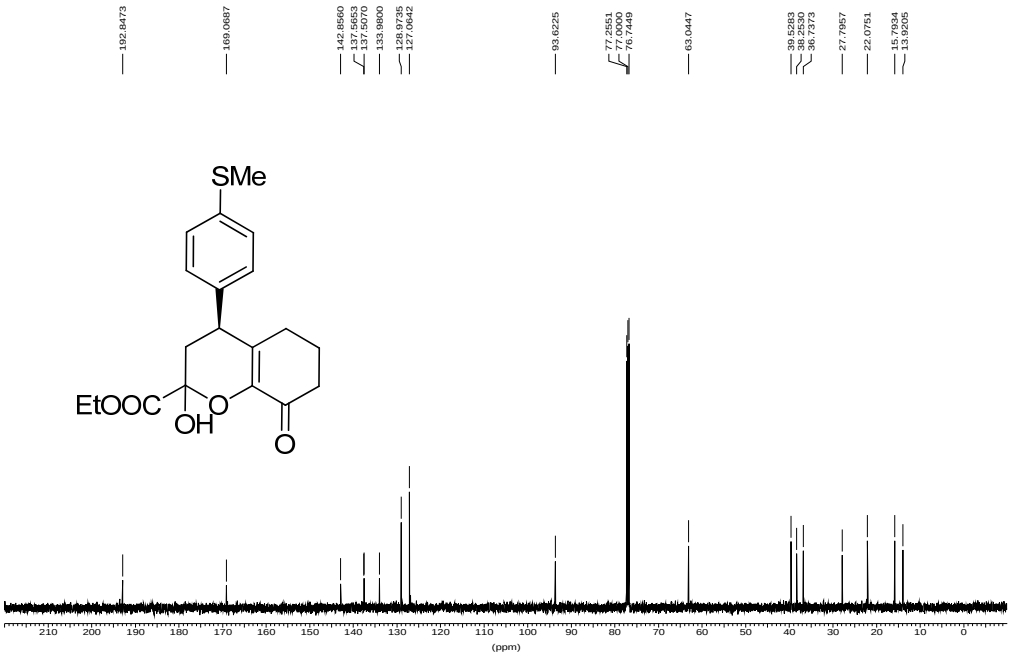
Compound **3h**


OMe
EtOOC
O
OH
O
integral
2.0000
1.8446
0.8018
2.1761
3.0244
1.1669
2.1879
0.9849
1.0324
2.0567
2.1733
2.9761
(ppm)

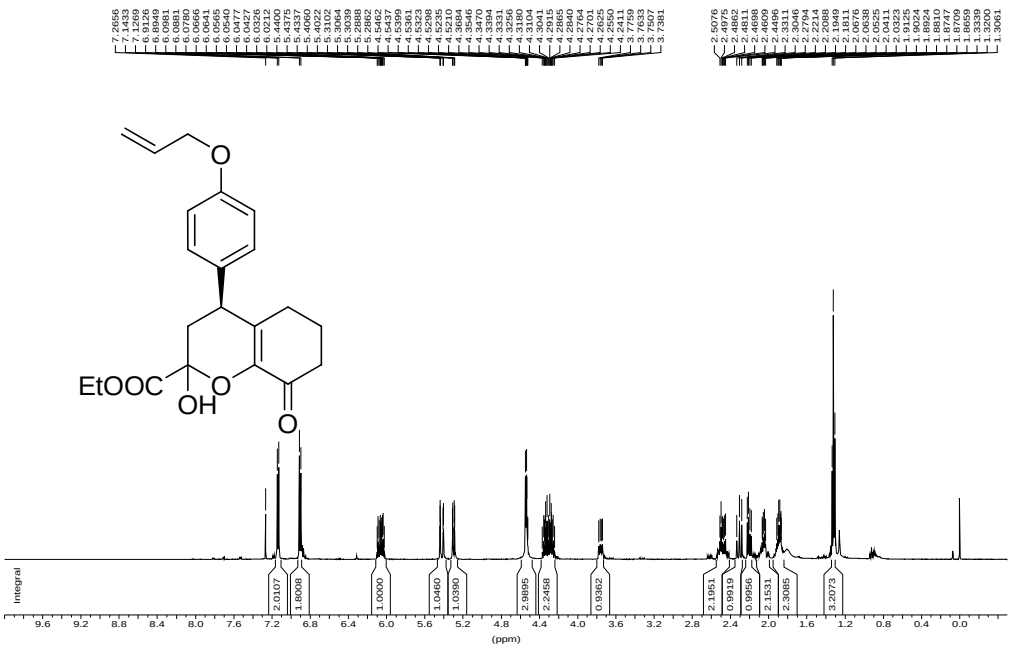

OMe
EtOOC
O
OH
O
(ppm)

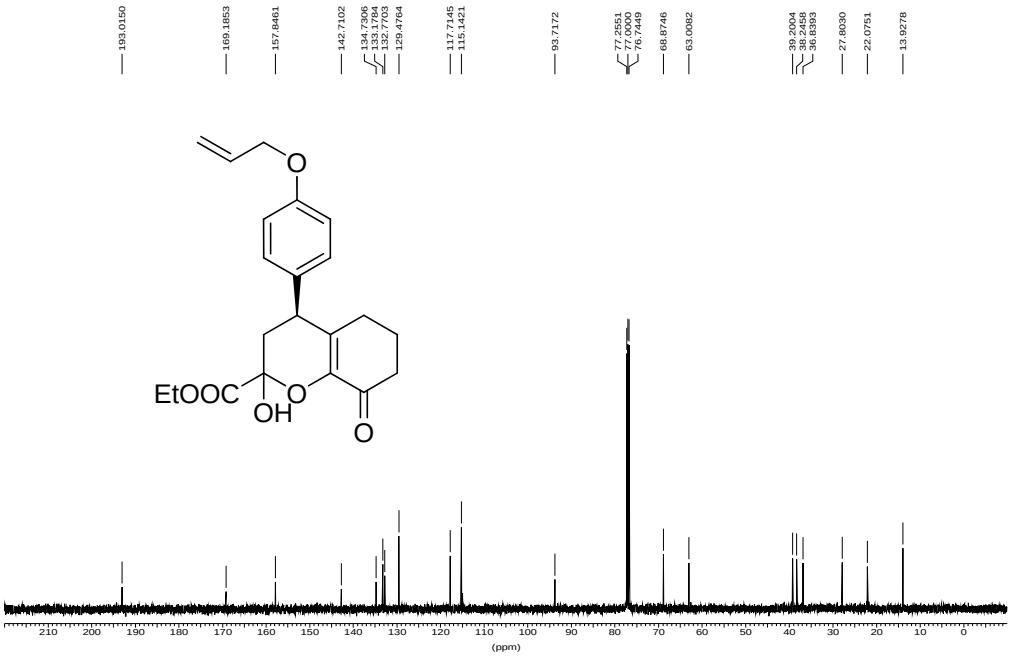
Compound **3i**


SMe
EtOOC
O
OH
O
integral
1.9398
2.1772
0.8590
2.2074
1.0000
5.0284
1.1094
1.0961
2.1435
2.1976
3.1333
(ppm)

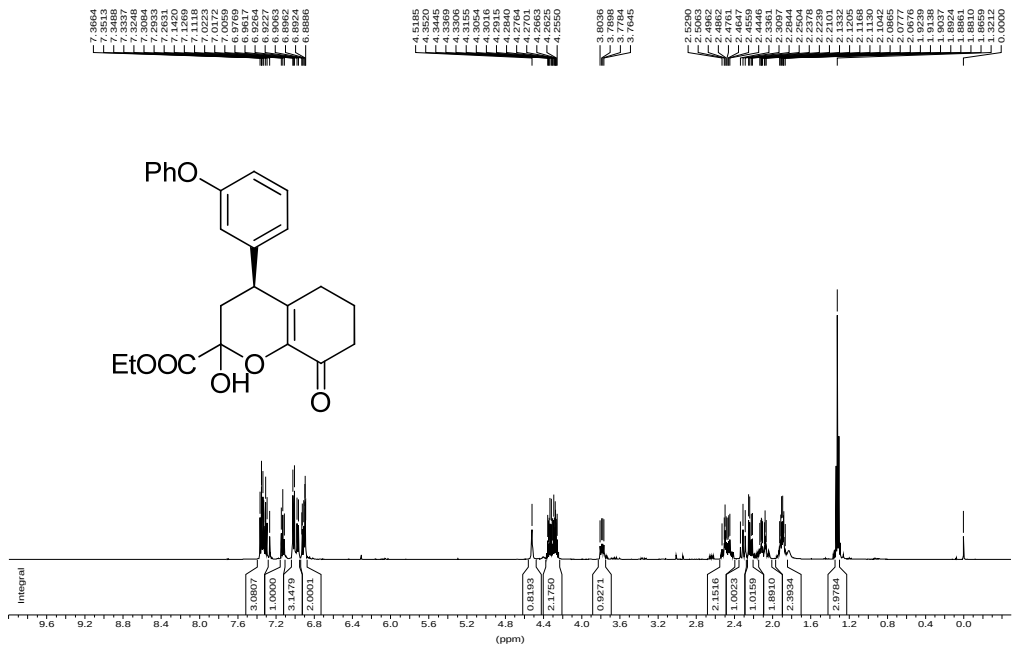

SMe
EtOOC
O
OH
O
(ppm)

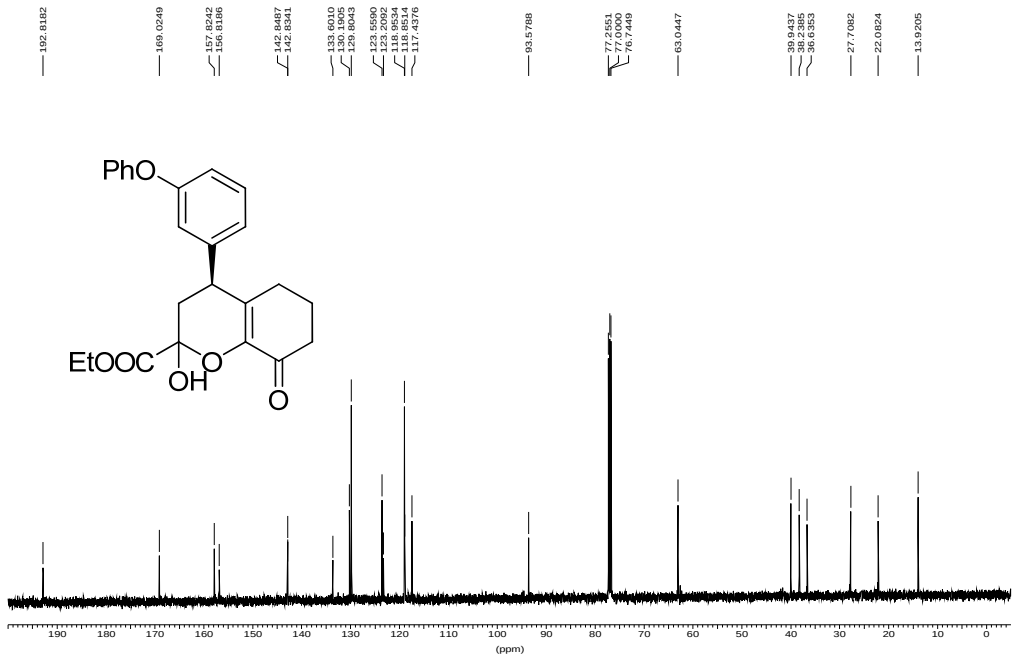
Compound **3j**


EtOOC
OH
O
integral
2.0107
1.8008
1.0000
1.0460
1.0390
2.9895
2.2458
0.9362
2.1951
0.9919
0.9956
2.1531
2.3085
3.2073
(ppm)

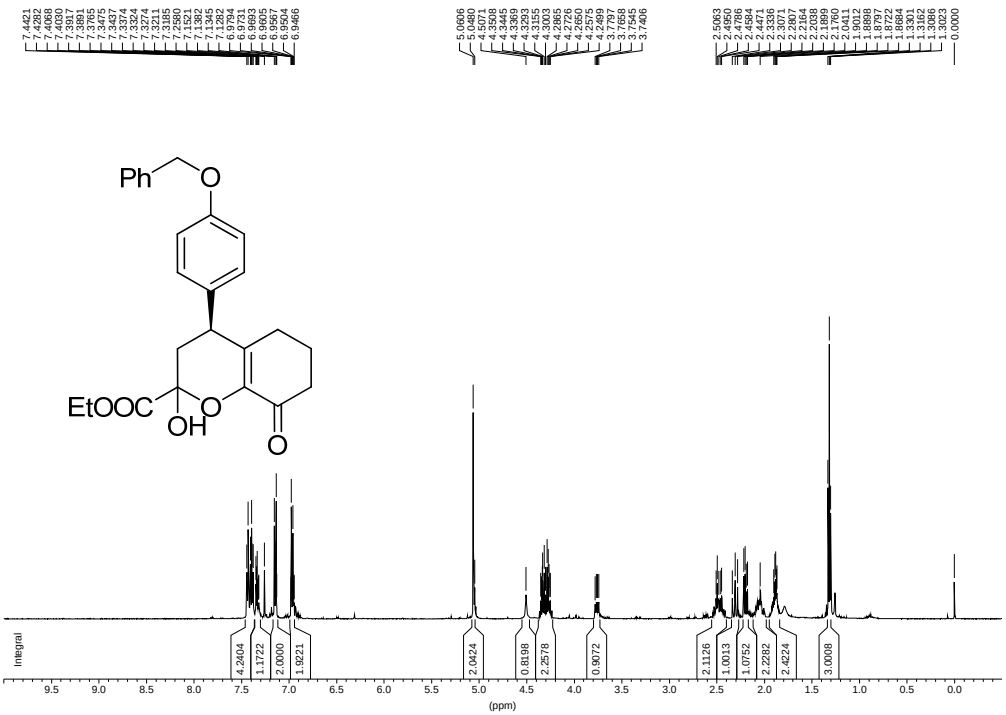

EtOOC
OH
O
(ppm)

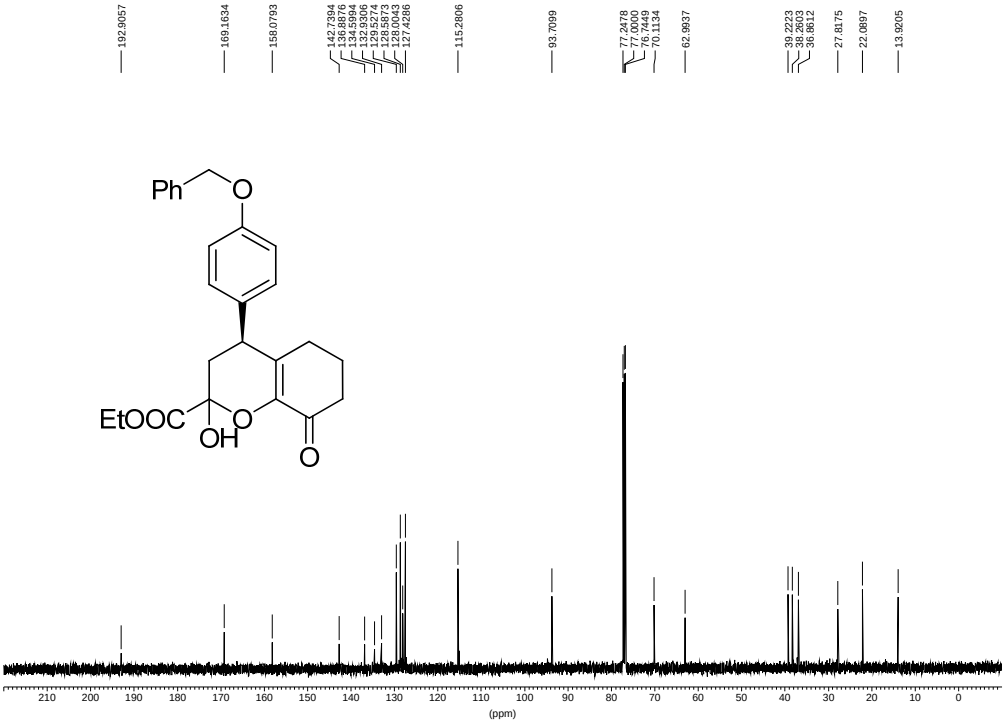
Compound **3k**


PhO
EtOOC
OH
O
integral
3.0807
1.0000
3.1479
2.0001
0.8193
2.1750
0.9271
2.1516
1.0023
1.0159
1.8910
2.3934
2.9784
(ppm)

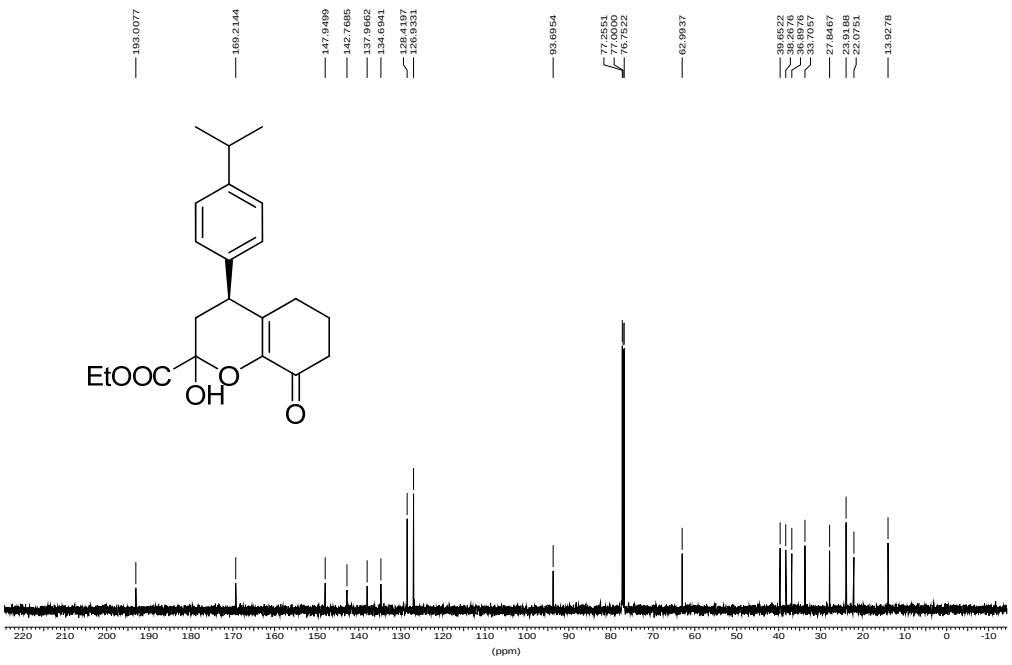

PhO
EtOOC
OH
O
(ppm)

Compound **3l**


Ph
O
EtOOC
O
OH
O
Integral
4.2404
1.1722
2.0000
1.9221
2.0424
0.8198
2.2578
0.9072
2.1126
1.0013
1.0752
2.2282
2.4224
3.0008
(ppm)

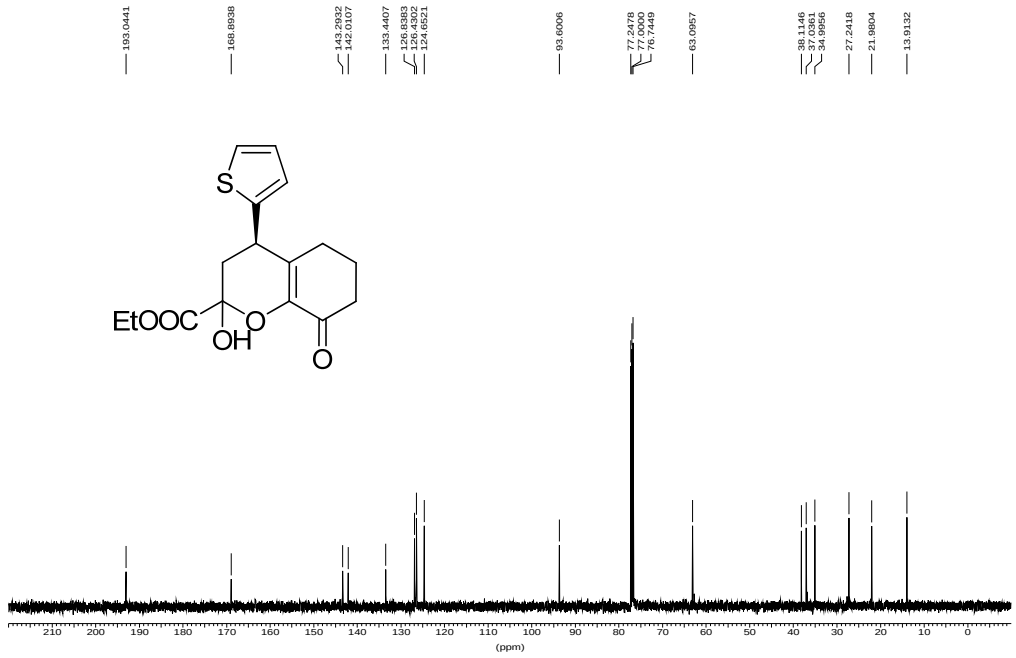

192.9057
169.1634
158.0793
142.7394
136.8876
134.5964
132.9306
129.5274
128.5873
128.1043
127.4286
115.2806
93.7099
77.2478
77.0000
76.7449
70.1134
62.9937
39.2223
38.2603
36.8612
27.8175
22.0897
13.9205
Ph
O
EtOOC
O
OH
O
(ppm)

Compound **3m**



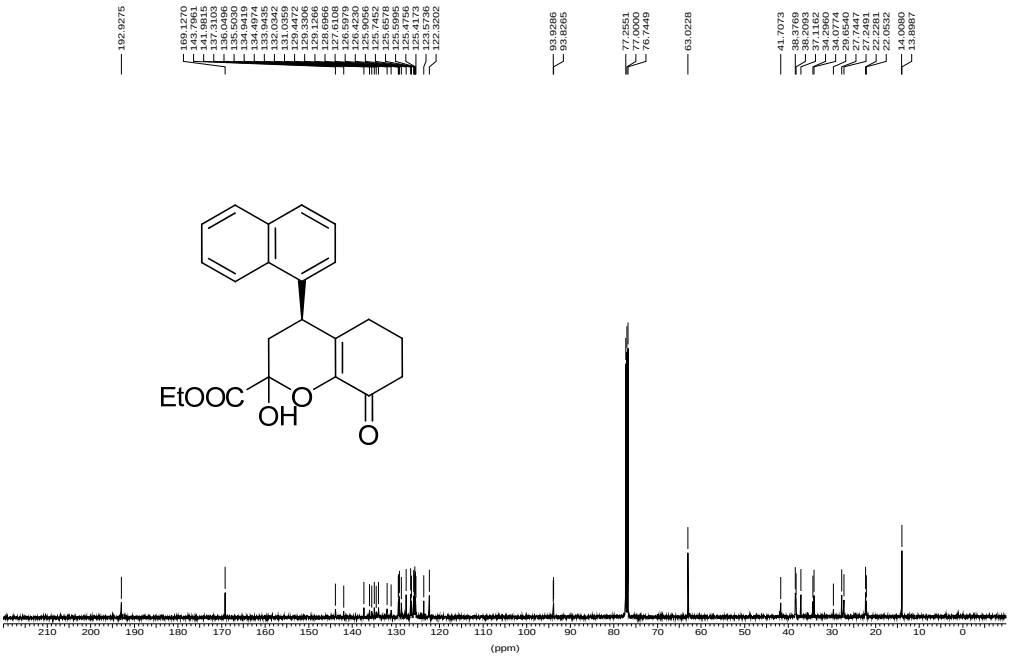
Compound **3n**


7.2681
7.2530
7.2429
6.9911
6.9794
6.9718
6.9630
6.9565
6.9554
4.6017
4.3946
4.3871
4.3508
4.3432
4.3356
4.3293
4.3256
4.3205
4.3142
4.3104
4.3067
4.2999
4.2928
4.2852
4.2777
4.2701
4.2562
4.2058
4.1932
4.1892
4.1680
2.5051
2.4937
2.4824
2.4672
2.4622
2.4483
2.4206
2.3954
2.3487
2.3361
2.3223
2.3097
2.1760
2.1647
2.1553
2.1508
1.9239
1.9188
1.8956
1.8949
1.3490
1.3351
S
EtOOC
OH
O
O
integral
0.8206
2.0578
0.8518
2.2720
1.0000
3.2795
1.1452
2.0202
2.2065
2.9907
9.6 9.2 8.8 8.4 8.0 7.6 7.2 6.8 6.4 6.0 5.6 5.2 4.8 4.4 4.0 3.6 3.2 2.8 2.4 2.0 1.6 1.2 0.8 0.4 0.0
(ppm)

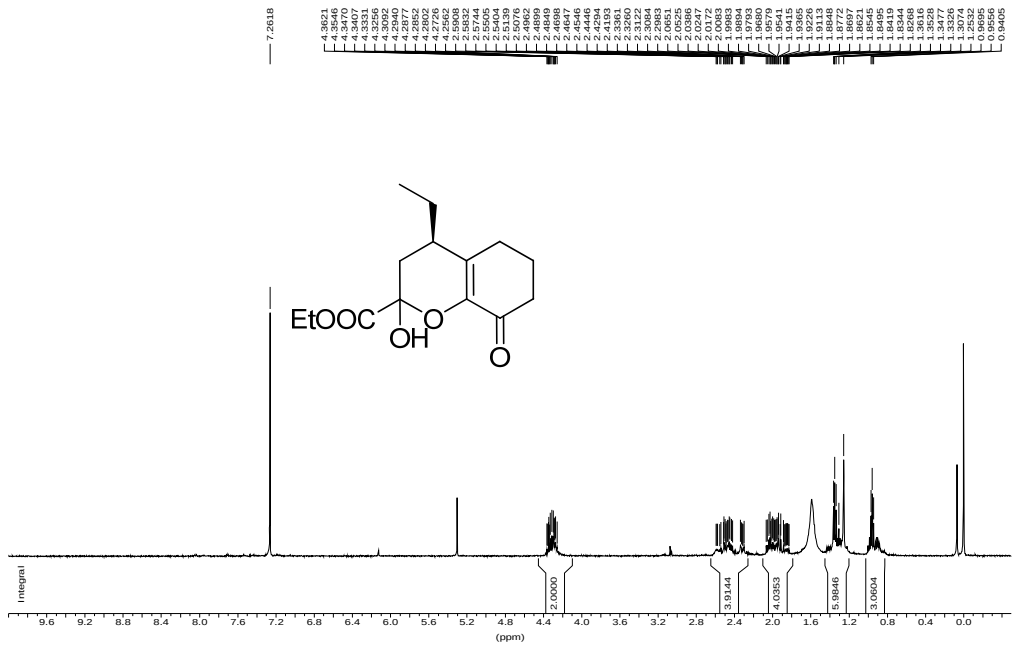

193.0441
168.8938
143.2932
142.0107
133.4407
126.9383
126.4302
124.6521
93.6006
77.2478
77.0000
76.7449
63.0957
38.1146
37.0361
34.9856
27.2418
21.9804
13.9132
S
EtOOC
OH
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

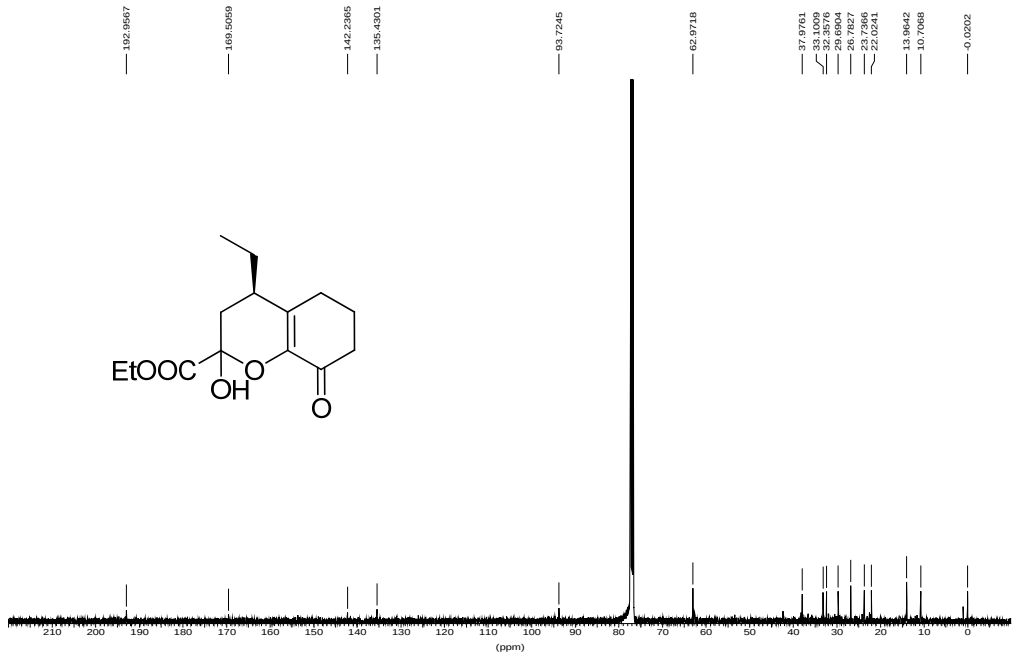
Compound **3o**


EtOOC
OH
O
integral
1.0000
0.8113
0.8687
3.8511
1.0890
2.1586
0.4284
2.1383
1.0924
0.6745
0.9766
4.1151
3.0476
(ppm)

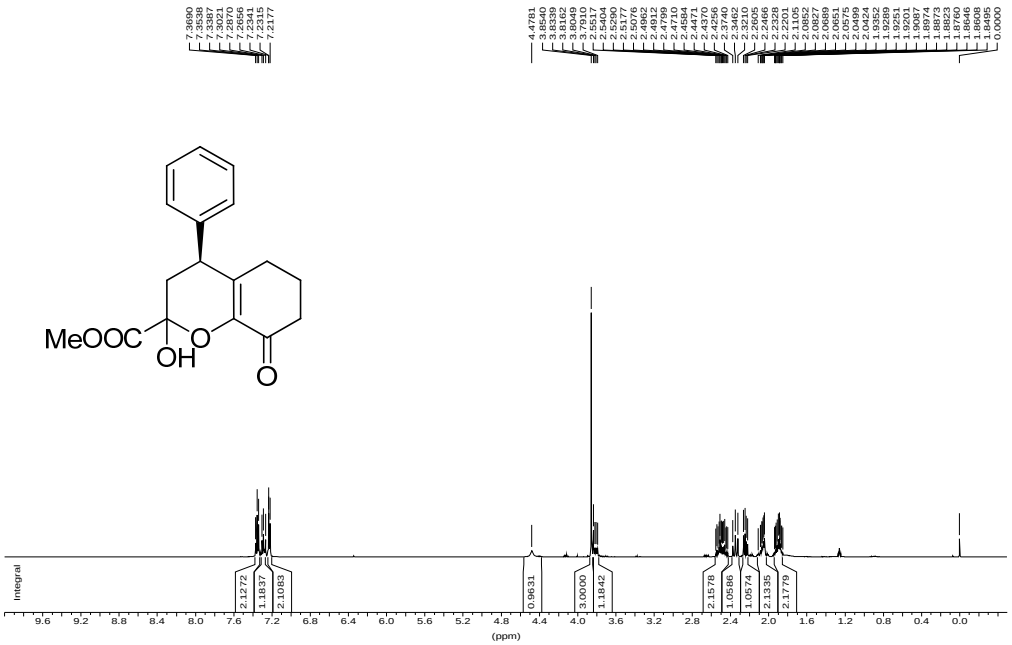

EtOOC
OH
O
(ppm)

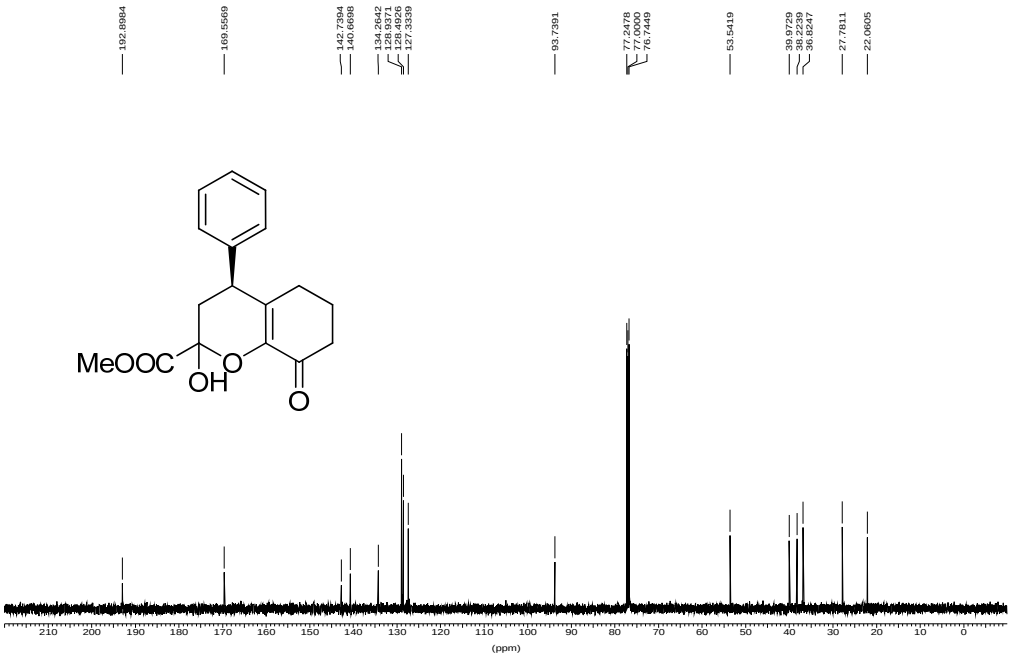
Compound **3p**


7.2618
EtOOC
OH
O
Integral
2.0000
3.9144
4.0353
5.9846
3.0604
(ppm)


192.9567
169.5059
142.2365
135.4301
93.7245
62.9718
37.9761
33.1009
32.3576
29.6804
28.7927
23.7367
22.0241
13.9642
10.7068
-0.0202
EtOOC
OH
O
(ppm)

Compound **3q**

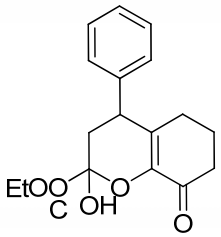

MeOOC
OH
O
O
Integral
2.1272
1.1837
2.1083
0.9631
3.0000
1.1842
2.1578
1.0586
1.0574
2.1335
2.1779
(ppm)


192.8984
169.5569
142.7394
140.6698
134.2642
128.9371
128.4456
127.3339
93.7391
77.2478
77.0000
76.7449
53.5419
39.9729
38.2239
36.8247
27.7811
22.0605
MeOOC
OH
O
(ppm)

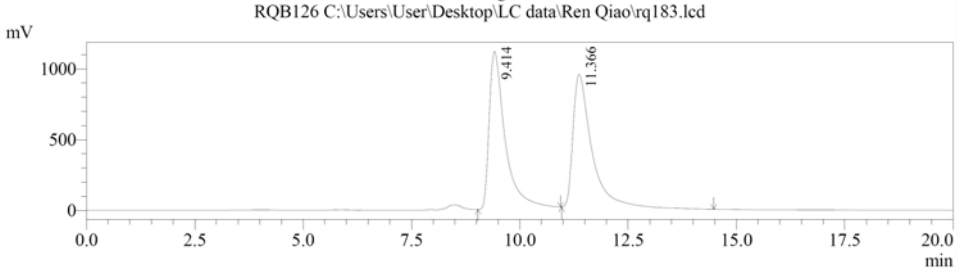
Racemic **3a**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq183.lcd
Acquired by : Admin
Sample Name : RQB126
Sample ID : RQ
Data File Name : rq183.lcd
Method File Name : 10%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB126 C:\Users\User\Desktop\LC data\Ren Qiao\rq183.lcd



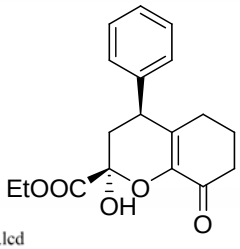
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.414	28364108	1114114	50.000	54.272
2	11.366	28363719	938716	50.000	45.728
Total		56727827	2052829	100.000	100.000

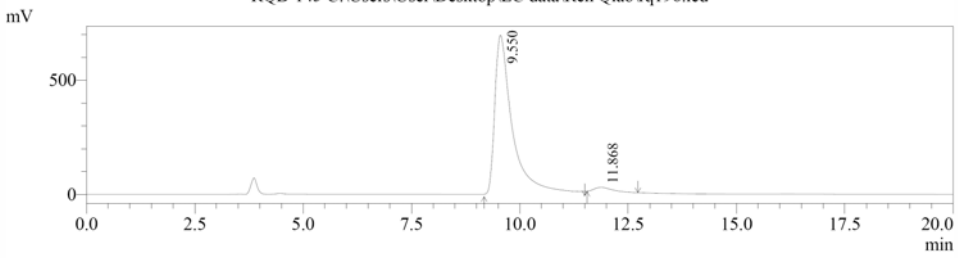
Enantiomeric enriched **3a**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq198.lcd
Acquired by : Admin
Sample Name : RQB-145
Sample ID : RQ
Data File Name : rq198.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB-145 C:\Users\User\Desktop\LC data\Ren Qiao\rq198.lcd



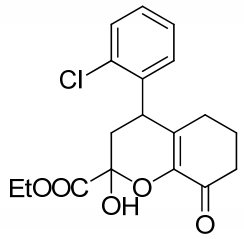
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.550	21093179	705947	97.425	97.334
2	11.868	557402	19333	2.575	2.666
Total		21650582	725280	100.000	100.000

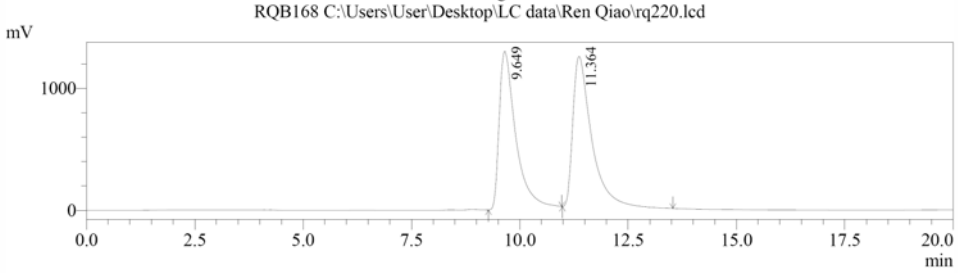
Racemic **3b**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq220.lcd
Acquired by : Admin
Sample Name : RQB168
Sample ID : RQ
Data File Name : rq220.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB168 C:\Users\User\Desktop\LC data\Ren Qiao\rq220.lcd



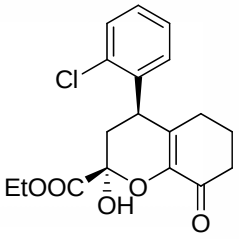
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.649	33985043	1293737	47.849	51.226
2	11.364	37040415	1231819	52.151	48.774
Total		71025458	2525556	100.000	100.000

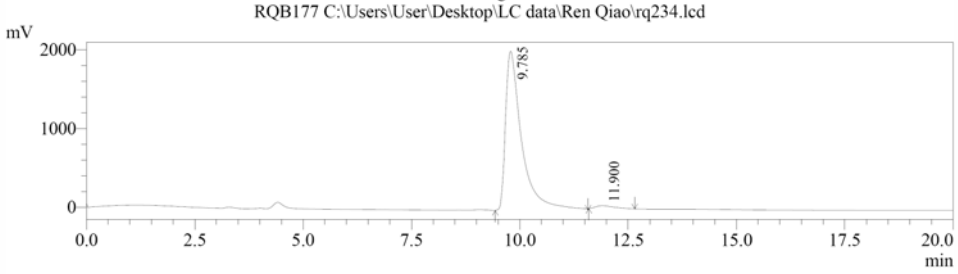
Enantiomeric enriched **3b**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq234.lcd
Acquired by : Admin
Sample Name : RQB177
Sample ID : RQ
Data File Name : rq234.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB177 C:\Users\User\Desktop\LC data\Ren Qiao\rq234.lcd



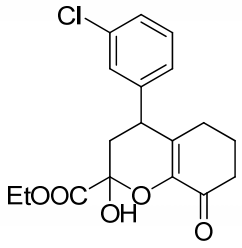
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.785	52794407	2022766	97.998	98.178
2	11.900	1078279	37539	2.002	1.822
Total		53872686	2060305	100.000	100.000

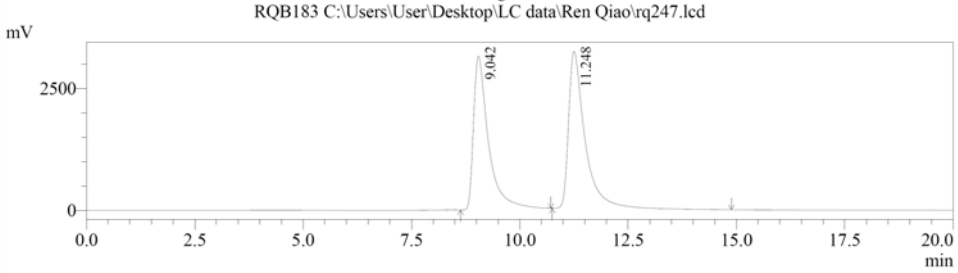
Racemic **3c**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq247.lcd
Acquired by : Admin
Sample Name : RQB183
Sample ID : RQ
Data File Name : rq247.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB183 C:\Users\User\Desktop\LC data\Ren Qiao\rq247.lcd



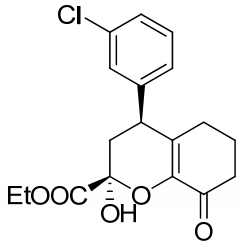
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.042	75601606	3152978	46.942	49.401
2	11.248	85451918	3229414	53.058	50.599
Total		161053525	6382391	100.000	100.000

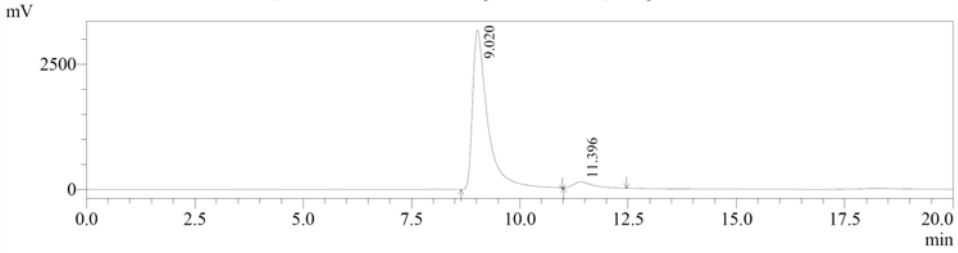
Enantiomeric enriched **3c**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq251.lcd
Acquired by : Admin
Sample Name : RQB185
Sample ID : RQ
Data File Name : rq251.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



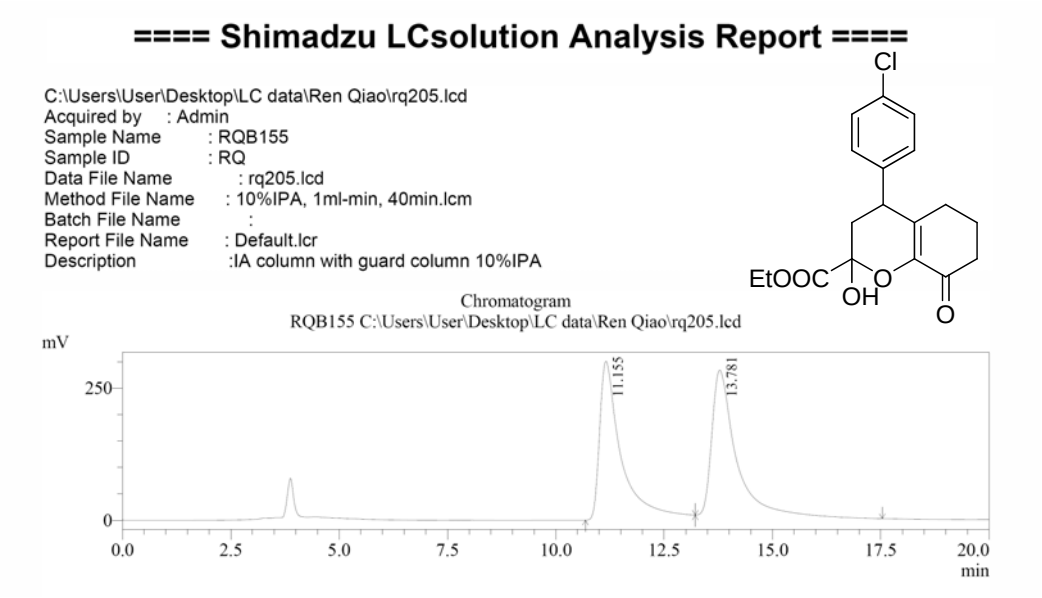
Chromatogram
RQB185 C:\Users\User\Desktop\LC data\Ren Qiao\rq251.lcd



PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.020	79615338	3185852	95.790	96.425
2	11.396	3499458	118107	4.210	3.575
Total		83114796	3303958	100.000	100.000

Racemic **3d**

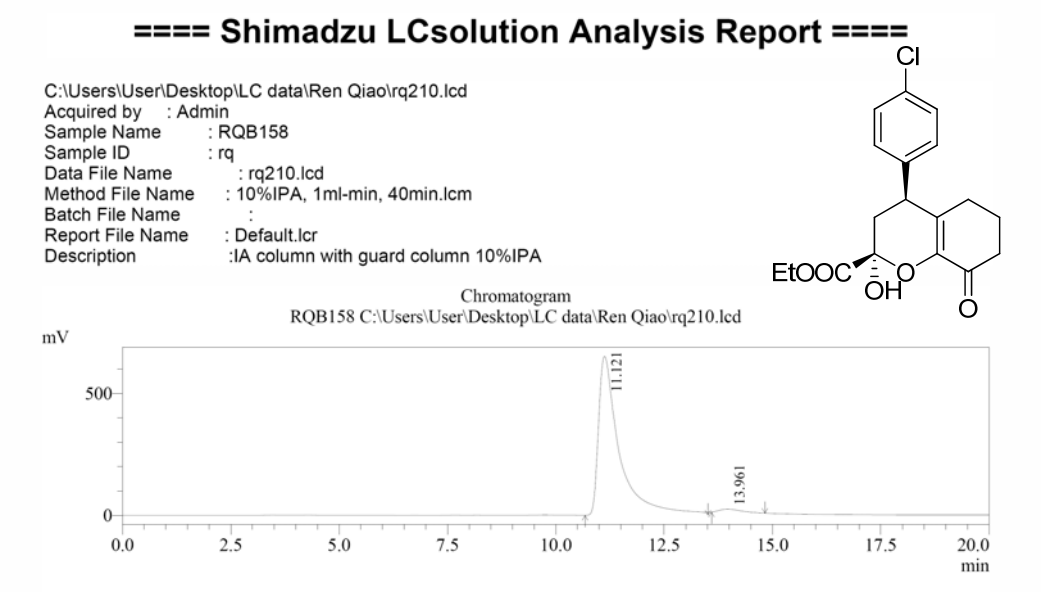


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.155	9930224	298967	48.256	52.071
2	13.781	10648016	275188	51.744	47.929
Total		20578240	574155	100.000	100.000

Enantiomeric enriched **3d**

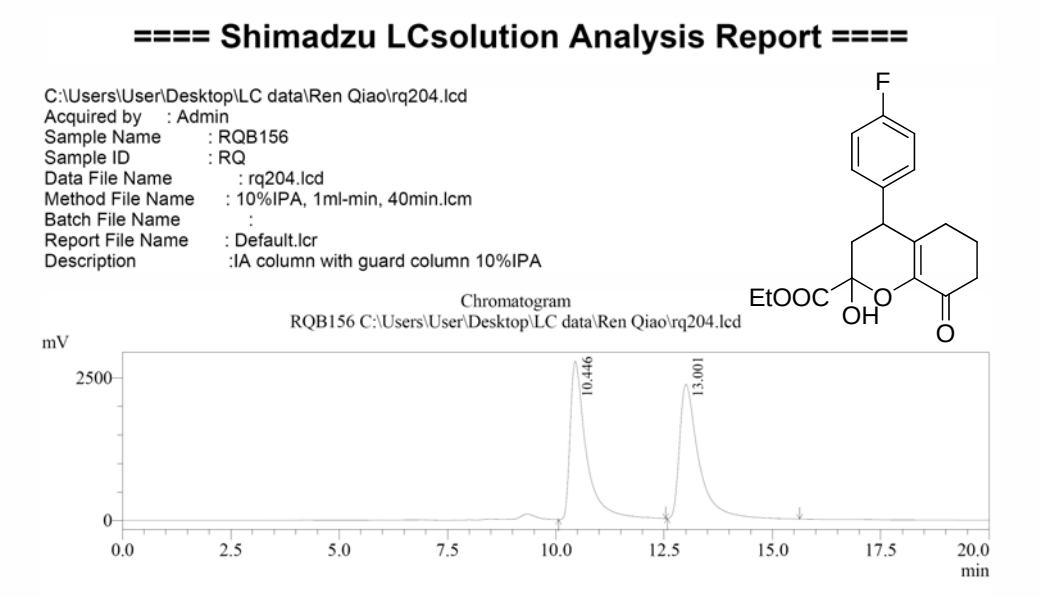


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.121	22099768	652662	97.990	97.999
2	13.961	453293	13328	2.010	2.001
Total		22553061	665990	100.000	100.000

Racemic **3e**

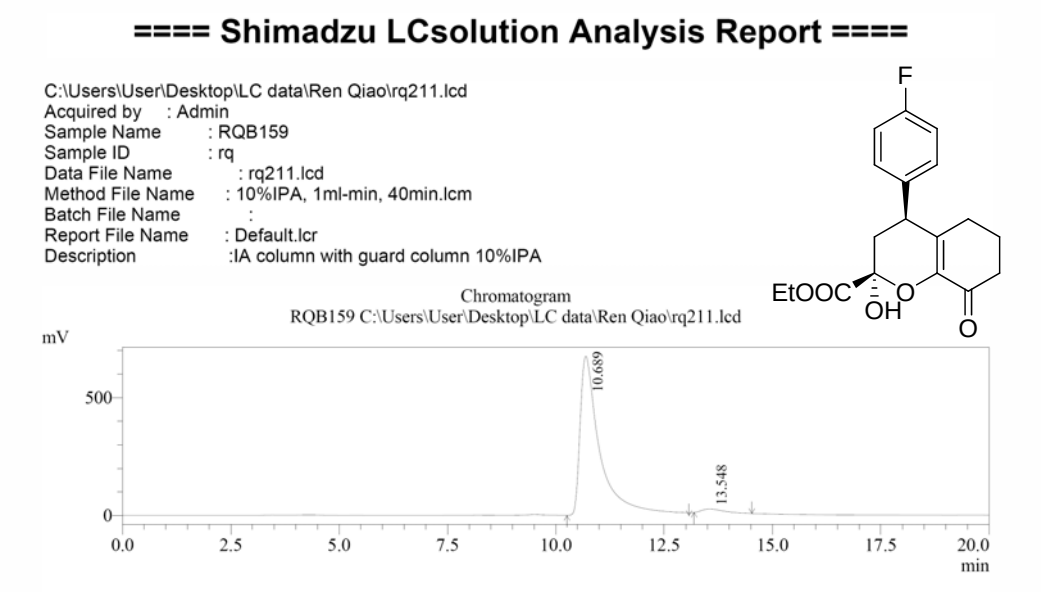


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.446	71622262	2776480	49.642	54.110
2	13.001	72654282	2354691	50.358	45.890
Total		144276544	5131170	100.000	100.000

Enantiomeric enriched **3e**



PeakTable

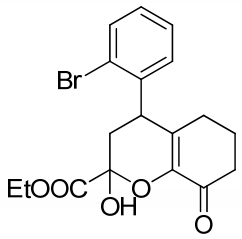
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.689	22007263	675926	97.567	97.689
2	13.548	548692	15988	2.433	2.311
Total		22555955	691914	100.000	100.000

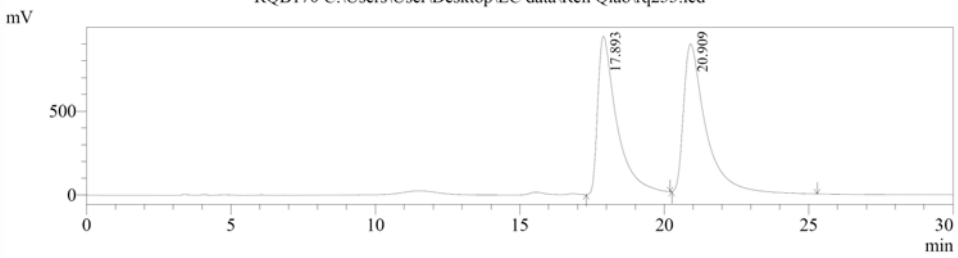
Racemic **3f**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq233.lcd
Acquired by : Admin
Sample Name : RQB170
Sample ID : RQ
Data File Name : rq233.lcd
Method File Name : 5%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 5%IPA



Chromatogram
RQB170 C:\Users\User\Desktop\LC data\Ren Qiao\rq233.lcd



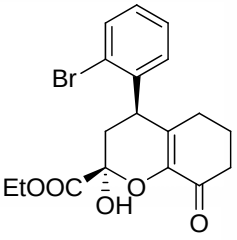
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.893	42679416	939831	47.969	51.606
2	20.909	46292676	881347	52.031	48.394
Total		88972092	1821179	100.000	100.000

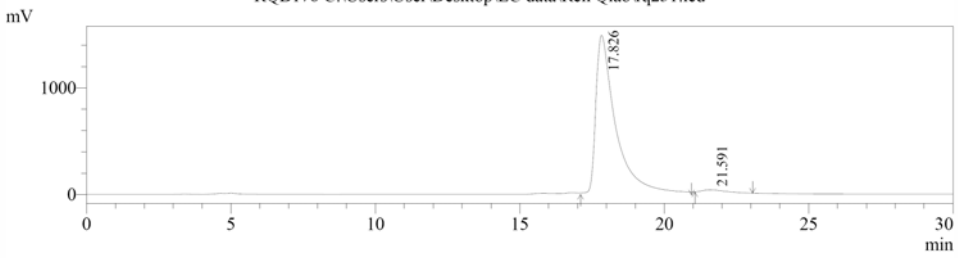
Enantiomeric enriched **3f**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq231.lcd
Acquired by : Admin
Sample Name : RQB178
Sample ID : RQ
Data File Name : rq231.lcd
Method File Name : 5%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 5%IPA



Chromatogram
RQB178 C:\Users\User\Desktop\LC data\Ren Qiao\rq231.lcd



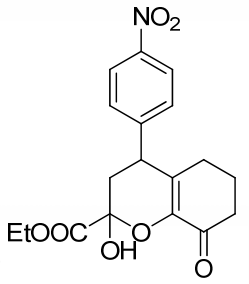
PeakTable
SPD-20A Ch1 254nm

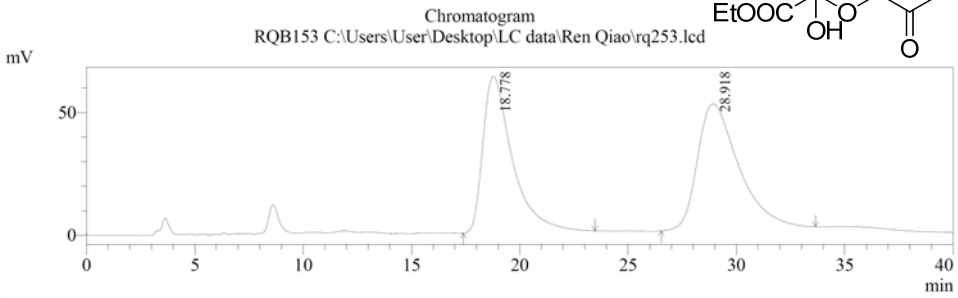
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.826	73219892	1495769	98.445	98.531
2	21.591	1156385	22293	1.555	1.469
Total		74376277	1518062	100.000	100.000

Racemic **3g**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq253.lcd
Acquired by : Admin
Sample Name : RQB153
Sample ID : RQ
Data File Name : rq253.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :OD-H column with guard column 10%IPA





PeakTable

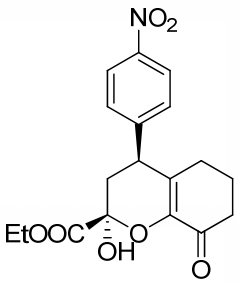
SPD-20A Ch1 254nm

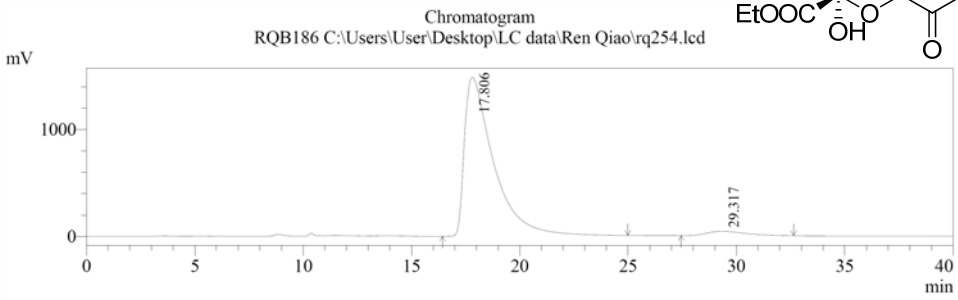
Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.778	6009780	63782	46.878	55.405
2	28.918	6810358	51337	53.122	44.595
Total		12820138	115120	100.000	100.000

Enantiomeric enriched **3g**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq254.lcd
Acquired by : Admin
Sample Name : RQB186
Sample ID : RQ
Data File Name : rq254.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :OD-H column with guard column 10%IPA



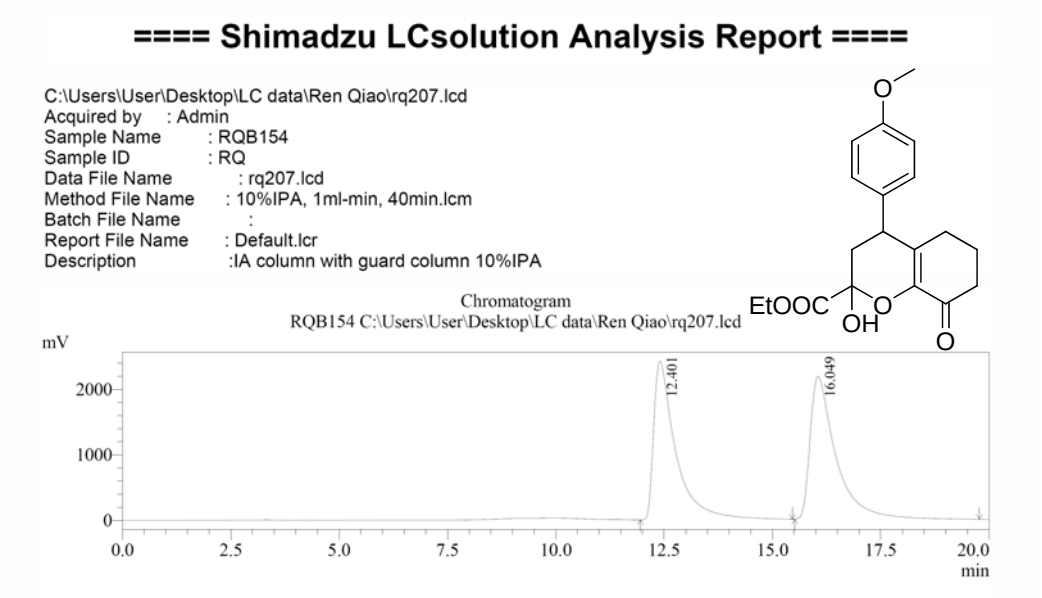


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.806	138967707	1486366	96.437	97.305
2	29.317	5134627	41173	3.563	2.695
Total		144102333	1527538	100.000	100.000

Racemic **3h**

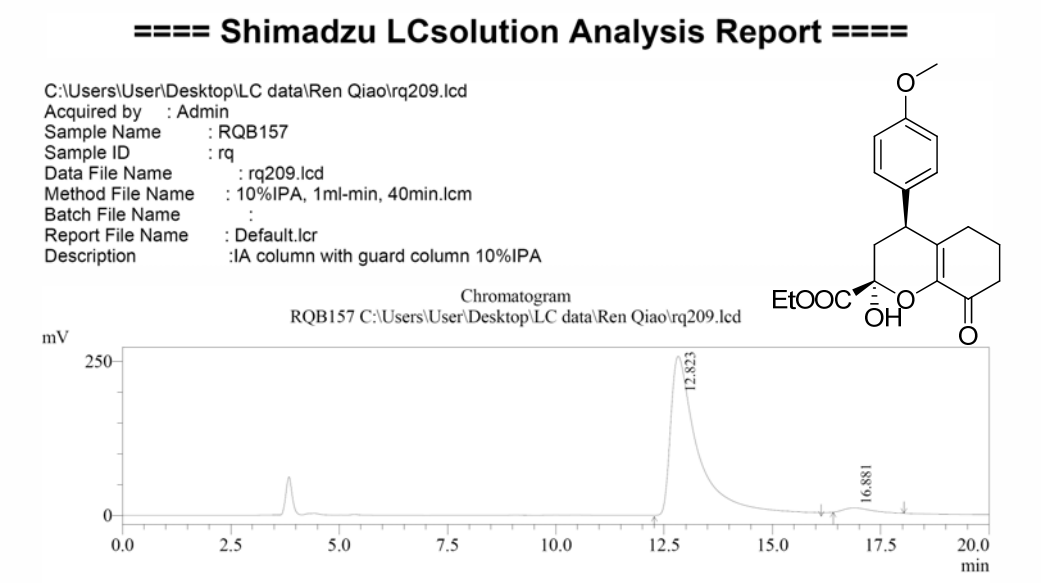


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.401	85664877	2421868	48.676	52.624
2	16.049	90323893	2180311	51.324	47.376
Total		175988770	4602179	100.000	100.000

Enantiomeric enriched **3h**

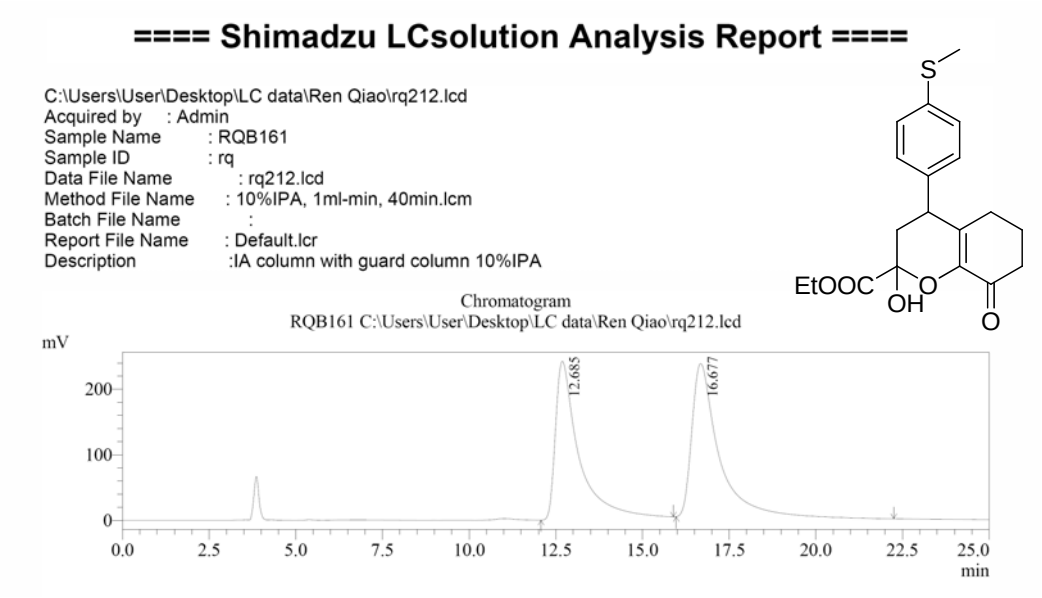


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.823	12035111	260376	97.341	97.166
2	16.881	328771	7594	2.659	2.834
Total		12363882	267970	100.000	100.000

Racemic **3i**

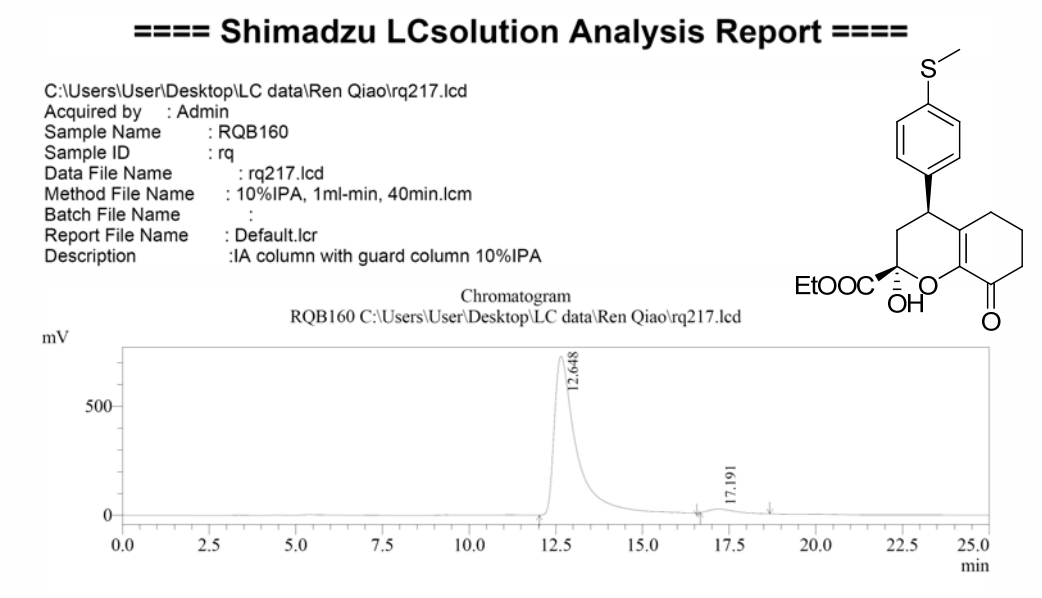


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.685	11268500	241475	46.935	50.794
2	16.677	12740241	233923	53.065	49.206
Total		24008741	475398	100.000	100.000

Enantiomeric enriched **3h**

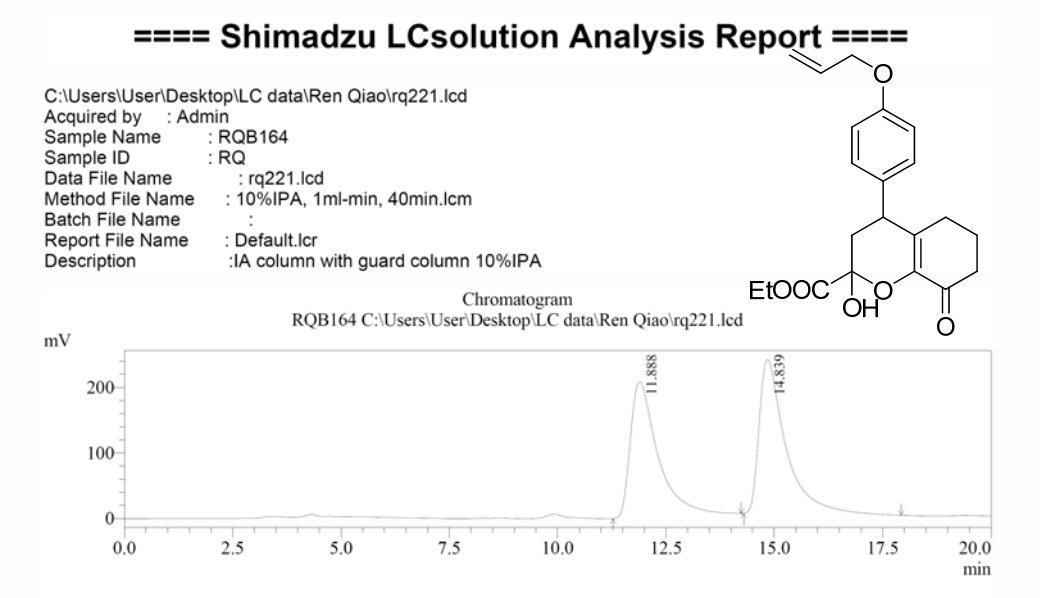


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.648	34324313	729164	97.536	97.632
2	17.191	867072	17688	2.464	2.368
Total		35191385	746852	100.000	100.000

Racemic **3j**

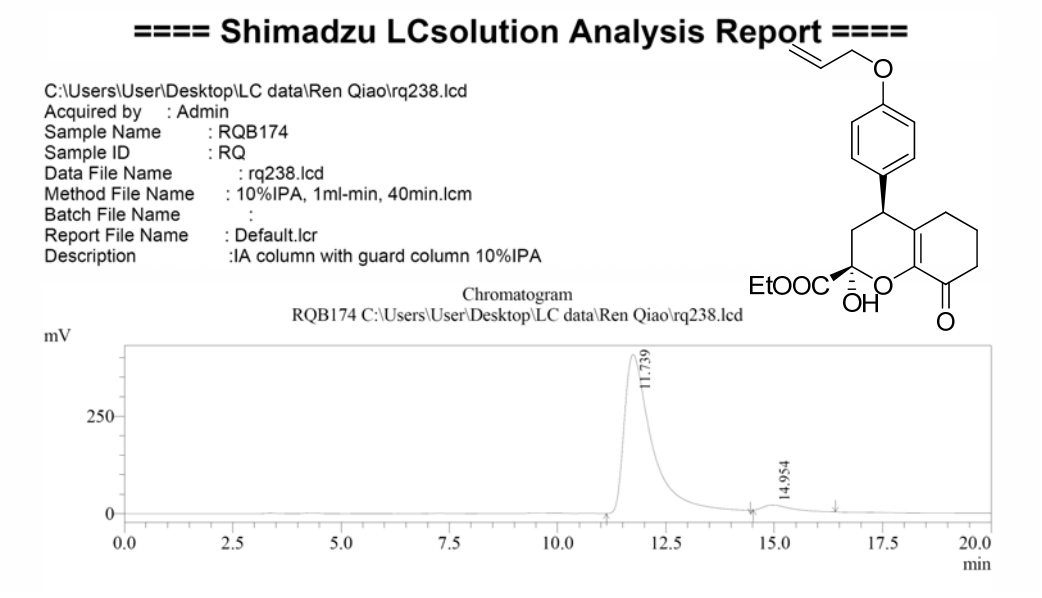


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.888	9183632	207466	47.511	46.865
2	14.839	10145782	235225	52.489	53.135
Total		19329414	442691	100.000	100.000

Enantiomeric enriched **3j**



PeakTable

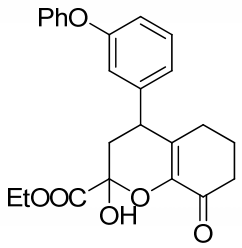
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.739	18845313	408742	96.989	96.655
2	14.954	585022	14147	3.011	3.345
Total		19430336	422888	100.000	100.000

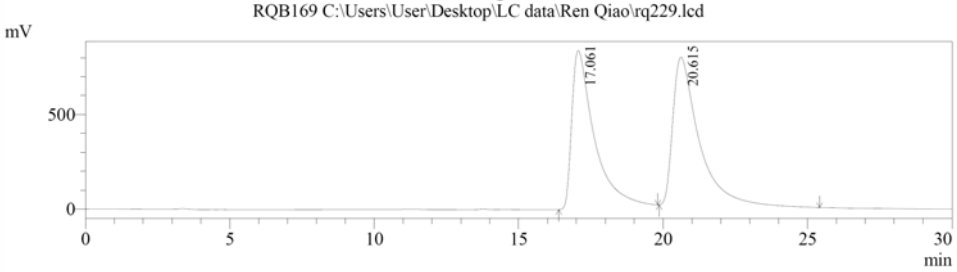
Racemic **3k**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq229.lcd
Acquired by : Admin
Sample Name : RQB169
Sample ID : RQ
Data File Name : rq229.lcd
Method File Name : 5%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 5%IPA



Chromatogram
RQB169 C:\Users\User\Desktop\LC data\Ren Qiao\rq229.lcd



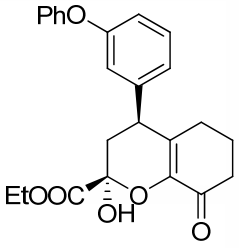
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.061	44948865	835928	47.700	51.680
2	20.615	49283028	781566	52.300	48.320
Total		94231894	1617495	100.000	100.000

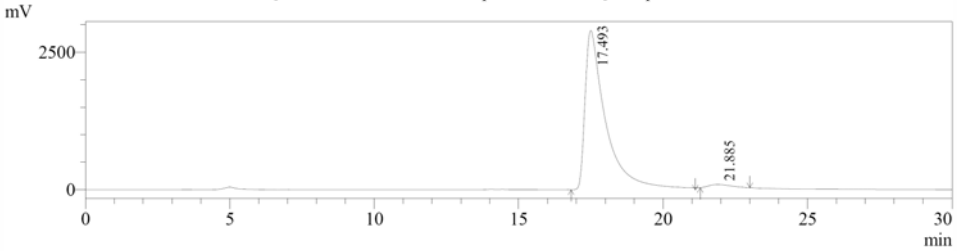
Enantiomeric enriched **3k**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq242.lcd
Acquired by : Admin
Sample Name : RQB181
Sample ID : RQ
Data File Name : rq242.lcd
Method File Name : 5%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 5%IPA



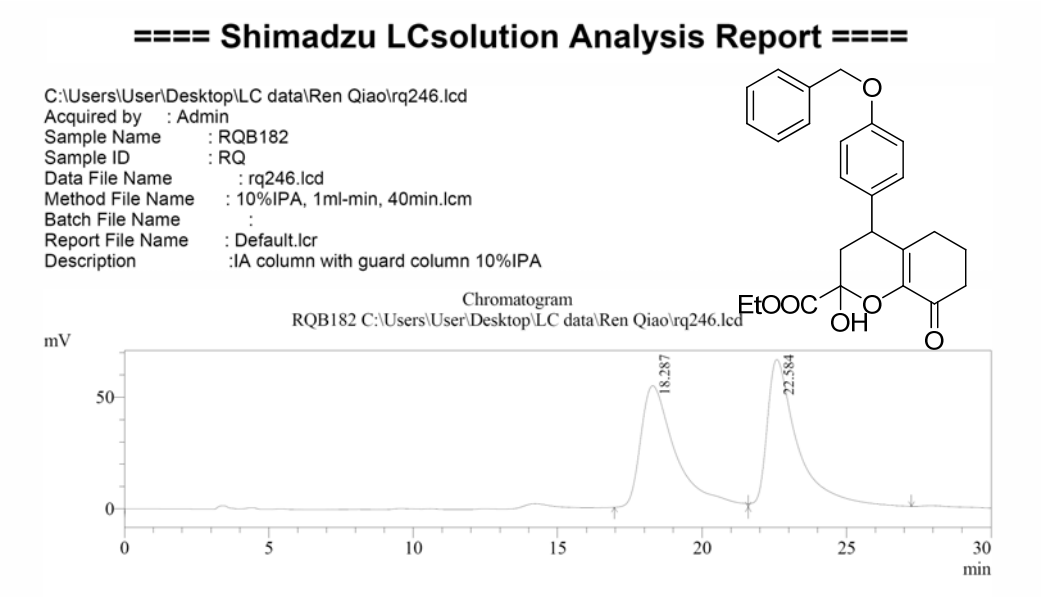
Chromatogram
RQB181 C:\Users\User\Desktop\LC data\Ren Qiao\rq242.lcd



PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.493	145416243	2896162	97.936	98.011
2	21.885	3064012	58777	2.064	1.989
Total		148480255	2954940	100.000	100.000

Racemic **3l**

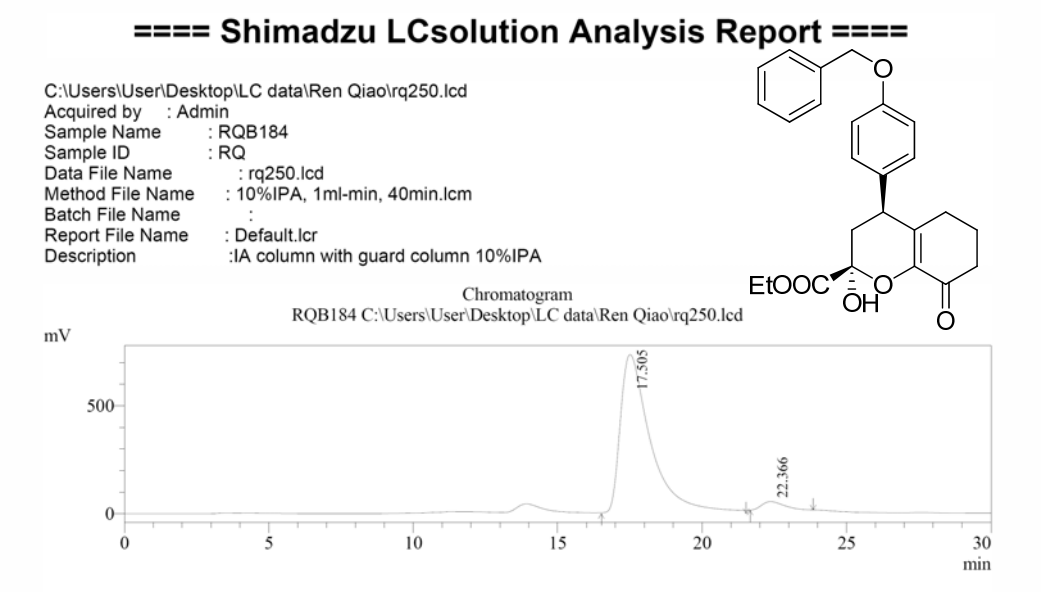


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.287	4585255	54453	48.573	45.196
2	22.584	4854721	66030	51.427	54.804
Total		9439976	120484	100.000	100.000

Enantiomeric enriched **3l**

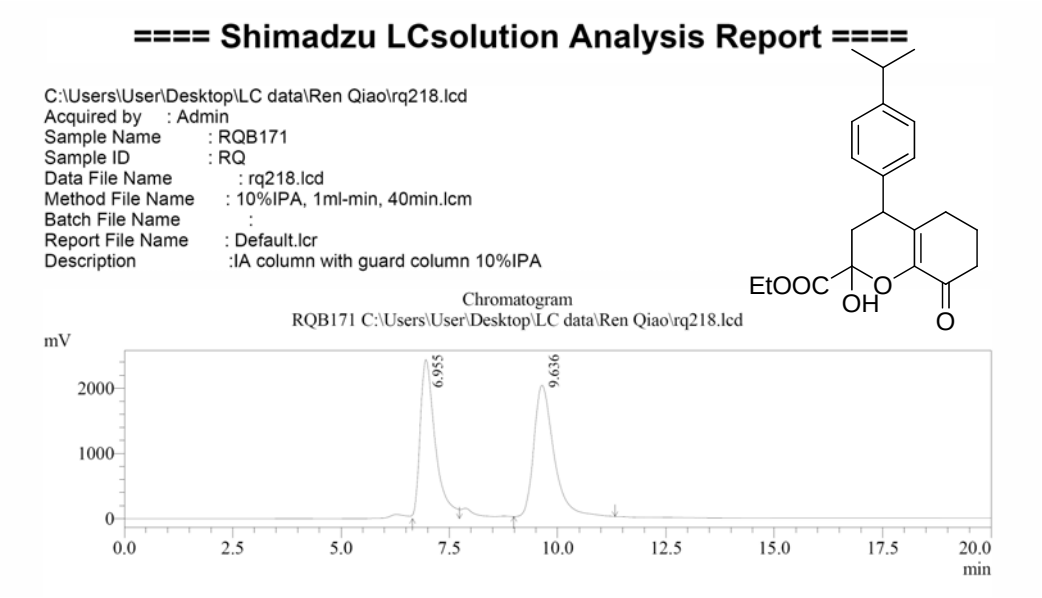


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.505	54788859	738426	96.275	94.940
2	22.366	2120122	39353	3.725	5.060
Total		56908981	777779	100.000	100.000

Racemic **3m**

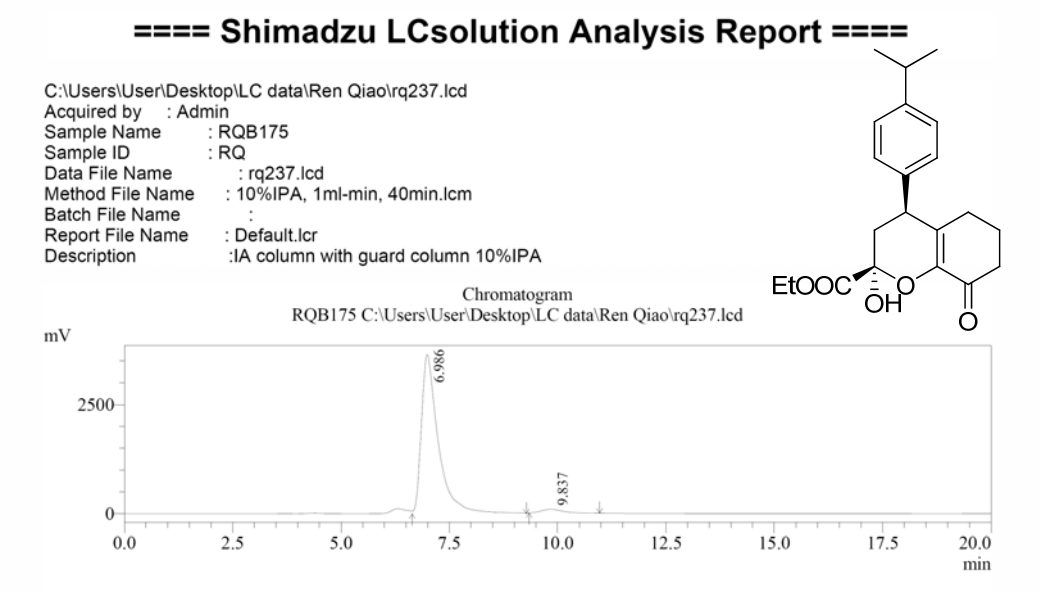


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.955	59587655	2440258	47.958	54.777
2	9.636	64662141	2014645	52.042	45.223
Total		124249796	4454902	100.000	100.000

Enantiomeric enriched **3m**



PeakTable

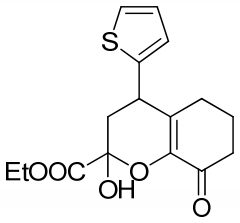
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.986	100118599	3650585	97.267	97.731
2	9.837	2813427	84762	2.733	2.269
Total		102932026	3735347	100.000	100.000

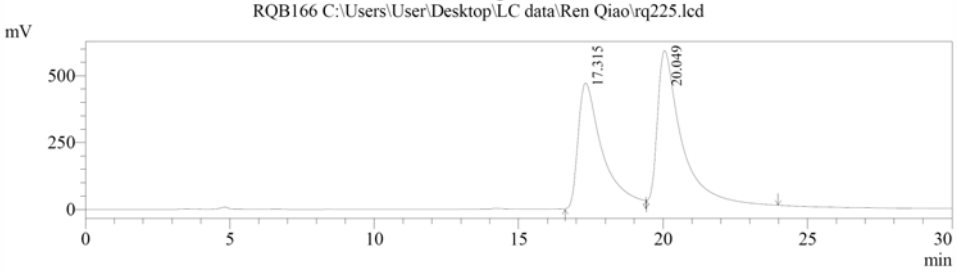
Racemic **3n**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq225.lcd
Acquired by : Admin
Sample Name : RQB166
Sample ID : RQ
Data File Name : rq225.lcd
Method File Name : 5%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 5%IPA



Chromatogram
RQB166 C:\Users\User\Desktop\LC data\Ren Qiao\rq225.lcd



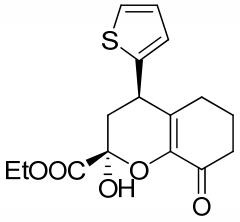
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.315	28364780	472312	47.762	45.643
2	20.049	31023426	562489	52.238	54.357
Total		59388206	1034801	100.000	100.000

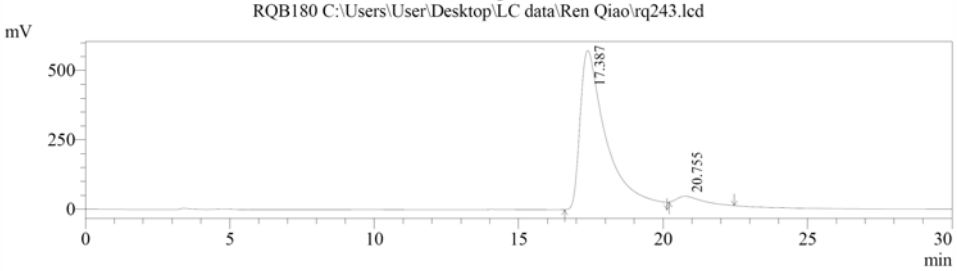
Enantiomeric enriched **3n**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq243.lcd
Acquired by : Admin
Sample Name : RQB180
Sample ID : RQ
Data File Name : rq243.lcd
Method File Name : 5%IPA, 1ml-min, 60min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 5%IPA



Chromatogram
RQB180 C:\Users\User\Desktop\LC data\Ren Qiao\rq243.lcd



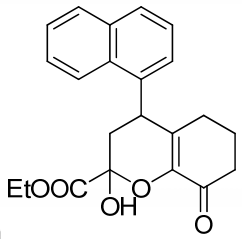
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.387	37240417	575369	96.502	95.958
2	20.755	1349926	24233	3.498	4.042
Total		38590343	599602	100.000	100.000

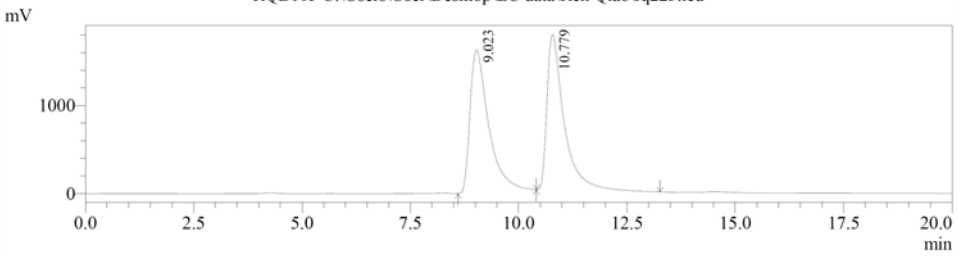
Racemic **3o**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq223.lcd
Acquired by : Admin
Sample Name : RQB165
Sample ID : RQ
Data File Name : rq223.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB165 C:\Users\User\Desktop\LC data\Ren Qiao\rq223.lcd



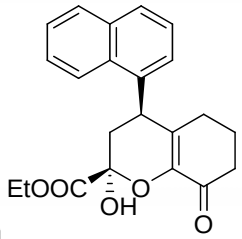
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.023	48152170	1617821	49.813	47.843
2	10.779	48513528	1763726	50.187	52.157
Total		96665698	3381546	100.000	100.000

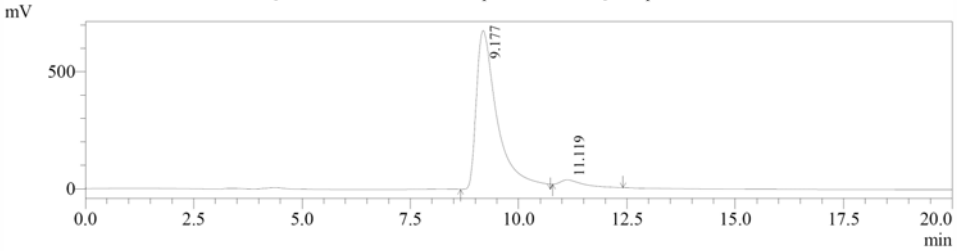
Enantiomeric enriched **3o**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq245.lcd
Acquired by : Admin
Sample Name : RQB179
Sample ID : RQ
Data File Name : rq245.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB179 C:\Users\User\Desktop\LC data\Ren Qiao\rq245.lcd



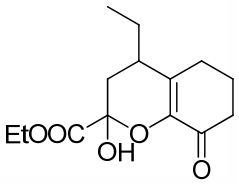
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.177	23166417	679669	97.421	96.901
2	11.119	613183	21736	2.579	3.099
Total		23779600	701405	100.000	100.000

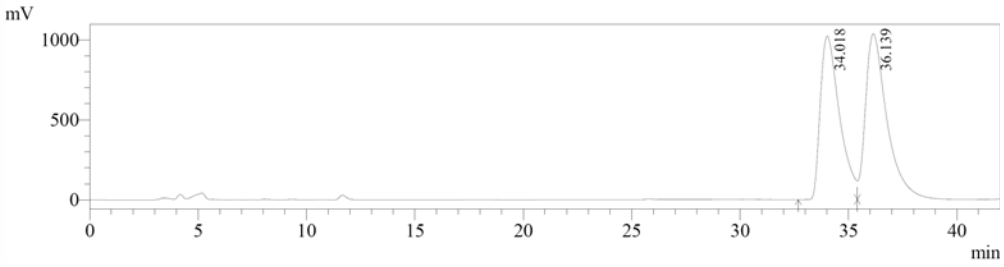
Racemic **3p**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq260.lcd
Acquired by : Admin
Sample Name : RQB172
Sample ID : RQ
Data File Name : rq260.lcd
Method File Name : 2%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :AD-H column with guard column 2%IPA



Chromatogram
RQB172 C:\Users\User\Desktop\LC data\Ren Qiao\rq260.lcd



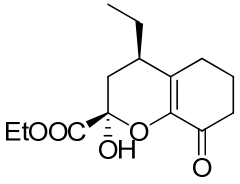
PeakTable
SPD-20A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.018	62966379	1021379	47.247	49.653
2	36.139	70302878	1035669	52.753	50.347
Total		133269257	2057048	100.000	100.000

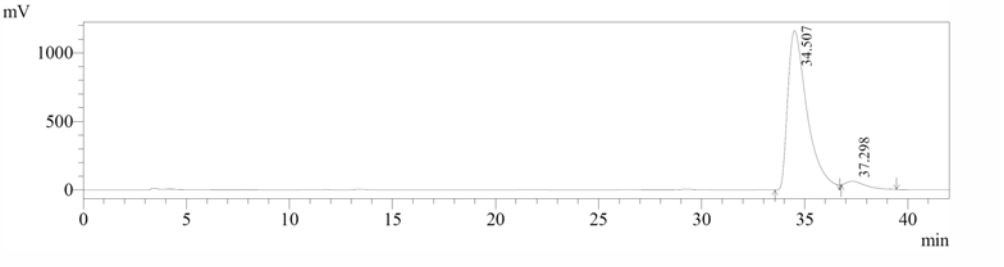
Enantiomeric enriched **3p**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq264.lcd
Acquired by : Admin
Sample Name : RQB187
Sample ID : RQ
Data File Name : rq264.lcd
Method File Name : 2%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :AD-H column with guard column2%IPA



Chromatogram
RQB187 C:\Users\User\Desktop\LC data\Ren Qiao\rq264.lcd



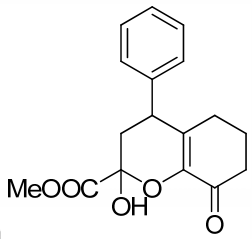
PeakTable
SPD-20A Ch2 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.507	76475401	1162023	98.052	97.240
2	37.298	1519686	32977	1.948	2.760
Total		77995087	1195000	100.000	100.000

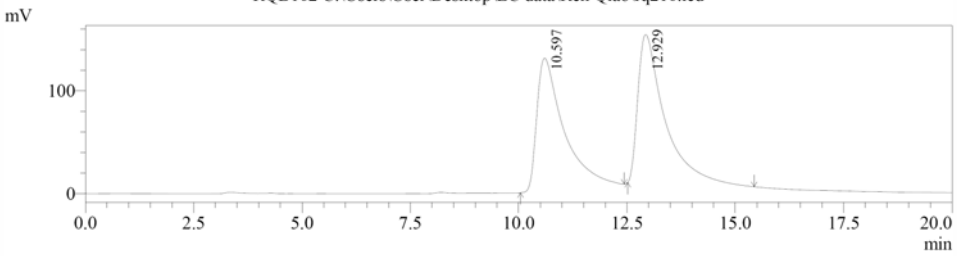
Racemic **3q**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq216.lcd
Acquired by : Admin
Sample Name : RQB162
Sample ID : rq
Data File Name : rq216.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB162 C:\Users\User\Desktop\LC data\Ren Qiao\rq216.lcd



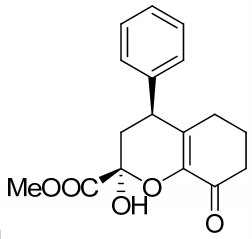
PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.597	5536205	128863	46.958	47.172
2	12.929	6253525	144312	53.042	52.828
Total		11789730	273175	100.000	100.000

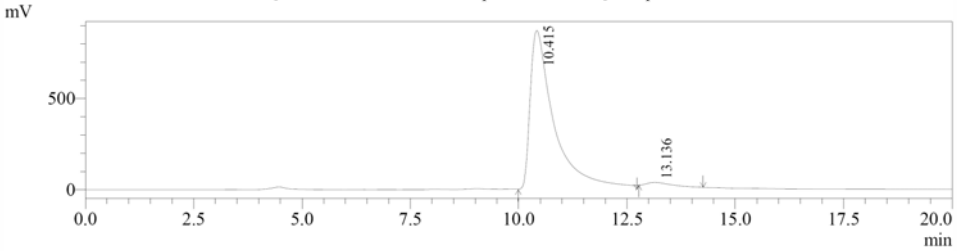
Enantiomeric enriched **3p**

==== Shimadzu LCsolution Analysis Report ====

C:\Users\User\Desktop\LC data\Ren Qiao\rq215.lcd
Acquired by : Admin
Sample Name : RQB163
Sample ID : rq
Data File Name : rq215.lcd
Method File Name : 10%IPA, 1ml-min, 40min.lcm
Batch File Name :
Report File Name : Default.lcr
Description :IA column with guard column 10%IPA



Chromatogram
RQB163 C:\Users\User\Desktop\LC data\Ren Qiao\rq215.lcd



PeakTable
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.415	33993741	872586	98.029	97.902
2	13.136	683467	18697	1.971	2.098
Total		34677208	891283	100.000	100.000