Supporting Information

Highly Enantioselective Synthesis of Functionalized Azepino[1,2-*a*]indoles *via* NHC-Catalyzed [3+4] Annulation

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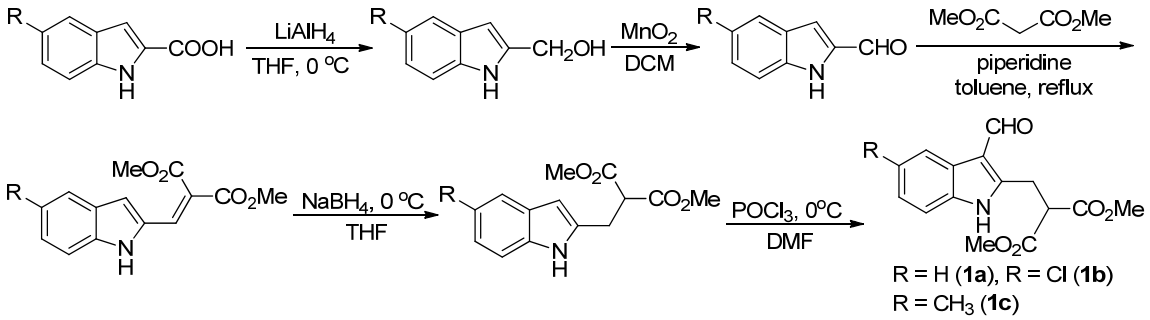
Contents

1. General information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE III 400 spectrometer using tetramethylsilane as internal reference, and chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. The HRMS analysis was obtained on a Bruker Apex II FT-ICR mass spectrometer with ESI ionization method. Optical rotation was measured by the Perkin Elmer 341 polarimeter. The *ee* value determination was carried out using HPLC with chiral Chirapak column on Agilent 1260 with a UV-detector. Melting points were taken on an X–4 melting point apparatus and were uncorrected. Dichloromethane, trichloromethane and 1,2-dichloroethane were freshly distilled from phosphorous pentoxide. Toluene and THF were freshly distilled from a deep-blue solution of sodium-benzophenone under nitrogen. DABCO, DMAP, Cs_2CO_3 and DIPEA were purchased from commercial suppliers and used directly. Triethylamine was dried by calcium hydride and freshly distilled under nitrogen atmosphere. All syntheses and manipulations were carried out under a dry nitrogen atmosphere. Flash column chromatography was carried out utilizing 200–300 mesh silica gel.

2. General procedure for preparation of substrates **1a**–**1c**



The substituted 2-indolecarboxylic acid (20 mmol) was dissolved in dry THF (60 mL) and the reaction was cooled to 0 °C. Then $LiAlH_4$ (40 mmol, 1.52 g) was added slowly with stirring. After this, the reaction was kept for 10 min, and then warmed to room temperature and reacted for 6 h. The reaction was monitored by TLC. After completion, HCl solution (5.0 M) was added dropwise. The mixture was extracted with EtOAc (20 mL×3) and washed with saturated brine. The organic phase was combined and purified by column chromatography to give the substituted 2-indole methanol as a white solid.

The substituted 2-indole methanol (10 mmol) was dissolved in dry DCM (30 mL) and then added MnO_2 (50 mmol, 4.35 g) in portions. The reaction was carried out at room temperature and TLC monitored until substituted 2-indole methanol was consumed completely. Then, the remaining MnO_2 was removed by filtration through celite. The filtrate was concentrated and purified by column chromatography (PE / EA = 10:1) to give the substituted 2-indole formaldehyde as a white solid.

The substituted 2-indole formaldehyde (7.5 mmol) was dissolved in toluene (30 mL). Diethyl malonate (9 mmol, 1.03 mL) and piperidine (0.3 mL) were added with syringe to the solution. Then, the reaction was refluxed for 4 h at 120 °C. After the reaction was completed, the mixture was cooled to room temperature

and the toluene was evaporated under reduced pressure. The residue was purified by column chromatography (PE / EA = 5:1) to afford pale yellow solid.

The pale yellow solid (5 mmol) was dissolved in dry THF (30 mL) and the reaction was cooled to 0 °C. Sodium borohydride (5.5 mmol, 0.21 g) was added in portions. The reaction was stirred for 3 h at 0 °C. After the material was consumed completely, an aqueous solution of hydrogen chloride (5.0 M) was added dropwise until no bubbles are formed. The mixture was extracted with dichloromethane (20 mL×3) and the organic phase was combined, washed with water and saturated brine successively. The solution was dried, filtered and concentrated. The residue was purified by column chromatography (PE / EA = 5:1) and the product was obtained as a pale yellow solid.

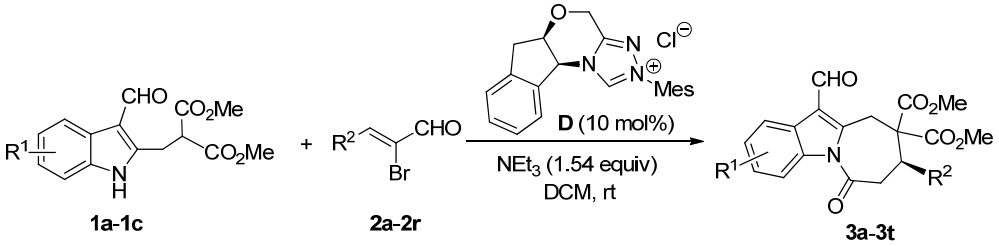
The product (4 mmol) was dissolved in dry DCM (10 mL) and DMF (0.8 mL) and was cooled to 0 °C. A solution of $POCl_3$ (8 mmol, 0.75 mL) in DCM (3 mL) was added slowly. The reaction was stirred for 5 min, and then warm to room temperature. After the reaction was completed, concentrated HCl (1.5 mL) was added and then saturated potassium carbonate solution was added dropwise at 0 °C to adjust the pH to 7–8. The aqueous phase was extracted with dichloromethane (10 mL×3) and the organic phase was combined. The solution was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated. The residue was purified by column chromatography (PE / EA = 2:1) to give the desired products **1** as a pale yellow solid.

dimethyl 2-((3-formyl-1*H*-indol-2-yl)methyl)malonate (**1a**). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 9.40 (br s, 1H), 8.20 – 8.18 (m, 1H), 7.41 – 7.36 (m, 1H), 7.30 – 7.27 (m, 2H), 3.92 (t, J = 6.4 Hz, 1H), 3.76 (s, 6H), 3.69 (d, J = 6.8 Hz, 2H).

dimethyl 2-((5-chloro-3-formyl-1*H*-indol-2-yl)methyl)malonate (**1b**). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 9.41 (br s, 1H), 8.18 – 8.16 (m, 1H), 7.42 – 7.37 (m, 1H), 7.28 – 7.27 (m, 1H), 3.92 (t, J = 6.4 Hz, 1H), 3.76 (s, 6H), 3.68 (d, J = 6.8 Hz, 2H).

dimethyl 2-((3-formyl-5-methyl-1*H*-indol-2-yl)methyl)malonate (**1c**). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 9.40 (br s, 1H), 8.02 – 7.98 (m, 1H), 7.41 – 7.38 (m, 1H), 7.30 – 7.27 (m, 1H), 3.92 (t, J = 6.4 Hz, 1H), 3.75 (s, 6H), 3.69 (d, J = 6.8 Hz, 2H), 2.45 (s, 3H).

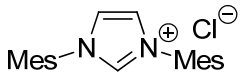
3. General procedure for the enantioselective synthesis of products 3a–3t.



To a solution of dimethyl 2-((3-formyl-1*H*-indol-2-yl)methyl)malonate (**1**) (0.10 mmol), substituted (*Z*)-2-bromo-3-phenylacrylaldehyde (**2**) (0.14 mmol, 1.4 equiv) and *N*-heterocyclic carbene catalyst **D** (10

mol %, 0.01 mmol, 3.7 mg) in DCM (1 mL), NEt_3 (0.154 mmol, 21 μL, 1.54 equiv) was added at room temperature under nitrogen atmosphere. The reaction was stirred at room temperature (monitored by TLC). When the substrate **1** was disappeared, the reaction was quenched by water (2 mL). The mixture was extracted with ethyl acetate (10 mL×3) and the combined organic layer was dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography on silica gel using petroleum ether/EtOAc (5:1–3:1) to afford the product **3**.

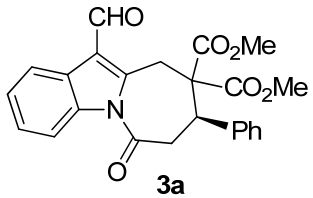
Racemic samples **3a**–**3t** for the chiral HPLC spectra were prepared by the reaction of **1** (0.1 mmol) with **2** (0.14 mmol, 1.4 equiv) using racemic NHC precursor **E (**20 mol %) in the presence of Cs_2CO_3 (0.11 mmol, 1.1 equiv).



cat. **E**

4. Characterization of compounds 3a–3t and 4

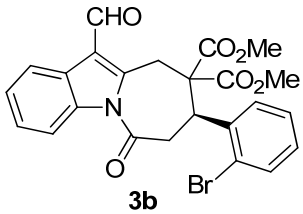
dimethyl (*R*)-11-formyl-6-oxo-8-phenyl-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3a)



3a

White solid, mp 186 – 188 °C, $[\alpha]_D^{20}$ –176 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.40 – 8.28 (m, 2H), 7.45 – 7.39 (m, 2H), 7.32 – 7.23 (m, 6H), 4.37 (d, J = 15.6 Hz, 1H), 4.16 (d, J = 12.0 Hz, 1H), 4.00 (d, J = 15.6 Hz, 1H), 3.91 (dd, J = 12.0, 17.2 Hz, 1H), 3.70 (s, 3H), 3.28 – 3.23 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.42, 171.28, 169.79, 169.18, 142.37, 139.69, 135.67, 128.39, 128.35, 127.77, 126.50, 125.96, 125.59, 121.15, 119.71, 115.90, 61.26, 53.25, 52.74, 42.11, 41.88, 29.37. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{22}NO_6$ $(M+H)^+$: 420.1442, Found: 420.1444. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{minor} = 15.050 min, t_{major} = 16.957 min, 98% ee).

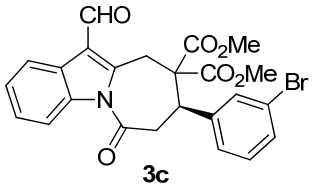
dimethyl (*S*)-8-(2-bromophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3b)



3b

White solid, mp 158 – 160 °C, $[\alpha]_D^{20}$ –132 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.44 (s, 1H), 8.43 – 8.41 (m, 1H), 8.33 – 8.31 (m, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.42 – 7.40 (m, 2H), 7.25 – 7.21 (m, 1H), 7.12 (t, J = 7.2 Hz, 2H), 5.12 (d, J = 9.6 Hz, 1H), 4.56 (d, J = 16.4 Hz, 1H), 3.99 (d, J = 16.4 Hz, 1H), 3.59 (d, J = 14.8 Hz, 1H), 3.52 (s, 3H), 3.28 (s, 3H), 3.17 (dd, J = 2.4, 15.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.36, 185.32, 170.84, 169.59, 169.04, 142.01, 141.82, 135.73, 131.51, 131.43, 130.95, 129.90, 127.31, 126.63, 126.05, 125.69, 122.33, 121.15, 119.89, 115.90, 61.23, 53.31, 52.90, 41.76, 41.67, 29.44. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}BrNO_6$ $(M+H)^+$: 498.0547, Found: 498.0548. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, retention time: t_{minor} = 42.992 min, t_{major} = 50.924 min, 98% ee).

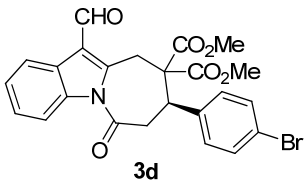
dimethyl (*R*)-8-(3-bromophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3c)



3c

White solid, mp 187 – 189 °C, $[\alpha]_D^{20}$ –117 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.38 – 8.36 (m, 1H), 8.30 – 8.27 (m, 1H), 7.45 – 7.39 (m, 4H), 7.22 – 7.15 (m, 2H), 4.39 (d, J = 15.6 Hz, 1H), 4.10 (d, J = 12.0 Hz, 1H), 4.00 (d, J = 15.6 Hz, 1H), 3.90 (dd, J = 12.0, 17.6 Hz, 1H), 3.72 (s, 3H), 3.36 (s, 3H), 3.21 (d, J = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.35, 185.31, 170.83, 169.58, 169.03, 142.00, 141.81, 135.72, 131.50, 131.42, 130.94, 129.89, 127.30, 126.62, 126.04, 125.69, 122.32, 121.14, 119.89, 115.89, 61.22, 53.30, 52.89, 42.75, 41.66, 29.43. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}BrNO_6$ $(M+H)^+$: 498.0547, Found: 498.0551. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 25.550 min, t_{minor} = 26.910 min, 91% ee).

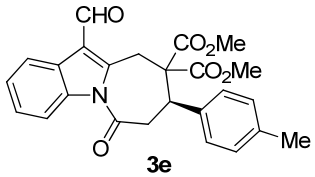
dimethyl (*R*)-8-(4-bromophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3d)



3d

White solid, mp 171 – 173 °C, $[\alpha]_D^{20}$ –171 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.38 – 8.35 (m, 1H), 8.29 – 8.27 (m, 1H), 7.44 – 7.41 (m, 4H), 7.13 (d, J = 8.8 Hz, 2H), 4.37 (d, J = 16.0 Hz, 1H), 4.09 (d, J = 12.0 Hz, 1H), 3.98 (d, J = 15.6 Hz, 1H), 3.89 (dd, J = 12.4, 17.2 Hz, 1H), 3.71 (s, 3H), 3.33 (s, 3H), 3.19 (d, J = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.33, 170.94, 169.68, 169.06, 141.88, 138.73, 135.68, 131.46, 130.20, 126.59, 126.00, 125.66, 121.85, 121.14, 119.81, 115.87, 61.09, 53.31, 52.88, 41.86, 41.47, 29.39. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}BrNO_6$ $(M+H)^+$: 498.0547, Found: 498.0553. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{minor} = 25.161 min, t_{major} = 29.280 min, 96% ee).

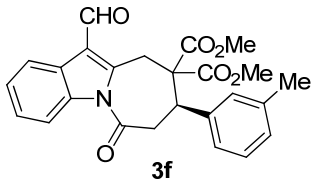
dimethyl (*R*)-11-formyl-6-oxo-8-(*p*-tolyl)-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3e)



3e

White solid, mp 175 – 177 °C, $[\alpha]_D^{20}$ –139 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.39 – 8.37 (m, 1H), 8.30 – 8.28 (m, 1H), 7.41 (t, J = 4.0 Hz, 2H), 7.11 (brs, 4H), 4.37 (d, J = 15.6 Hz, 1H), 4.12 (d, J = 11.6 Hz, 1H), 4.12 (d, J = 11.6 Hz, 1H), 3.99 (d, J = 15.6 Hz, 1H), 3.88 (dd, J = 12.4, 17.2 Hz, 1H), 3.68 (s, 3H), 3.29 (s, 3H), 3.22 (d, J = 17.2 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.46, 185.42, 171.36, 169.85, 169.26, 142.45, 137.47, 136.61, 135.70, 129.01, 128.26, 126.47, 125.99, 125.57, 121.14, 119.70, 115.91, 61.23, 53.14, 52.71, 42.27, 41.66, 29.37, 20.97. HRMS (ESI): Exact Mass Calcd. for $C_{25}H_{24}NO_6$ $(M+H)^+$: 434.1598, Found: 434.1601. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 20.014 min, t_{major} = 25.775 min, 97% ee).

dimethyl (*R*)-11-formyl-6-oxo-8-(*m*-tolyl)-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3f)

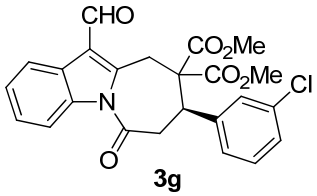


3f

White solid, mp 175 – 177 °C, $[\alpha]_D^{20}$ –139 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 8.40 – 8.38 (m, 1H), 8.31 – 8.29 (m, 1H), 7.43 – 7.40 (m, 2H), 7.18 (t, J = 8.4 Hz, 1H), 7.08 – 7.02 (m, 3H), 4.39 (d, J = 15.6 Hz, 1H), 4.13 (d, J = 12.0 Hz, 1H), 4.02 (d, J = 16.0 Hz, 1H), 3.92 – 3.88 (m, 1H), 3.69 (s, 3H), 3.28 – 3.22 (m, 4H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.45, 171.31, 169.81, 169.26, 142.42, 139.64, 137.99, 135.73, 129.09, 128.48, 128.25, 126.51, 126.02, 125.59, 125.44, 121.14, 119.76,

115.95, 61.25, 53.22, 52.66, 42.27, 41.95, 29.44, 21.41. HRMS (ESI): Exact Mass Calcd. for $C_{25}H_{24}NO_6$ $(M+H)^+$: 434.1598, Found: 434.1599. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 16.726 min, t_{major} = 18.910 min, 96% ee).

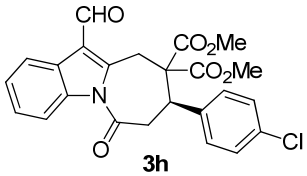
dimethyl (*R*)-8-(3-chlorophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3g)



3g

White solid, mp 157 – 159 °C, $[\alpha]_D^{20}$ –151 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.38 – 8.28 (m, 2H), 7.42 (d, *J* = 2.8 Hz, 2H), 7.25 – 7.16 (m, 4H), 4.39 (d, *J* = 16.0 Hz, 1H), 4.11 (d, *J* = 12.0 Hz, 1H), 4.01 (d, *J* = 15.6 Hz, 1H), 3.91 (dd, *J* = 12.8, 16.8 Hz, 1H), 3.73 (s, 3H), 3.35 (s, 3H), 3.22 (d, *J* = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.29, 170.63, 169.54, 168.97, 141.49, 139.92, 135.71, 132.47, 132.06, 130.55, 130.24, 128.03, 126.68, 126.05, 125.73, 121.14, 119.93, 115.86, 61.09, 53.41, 52.98, 41.67, 41.32, 29.43. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}ClNO_6$ $(M+H)^+$: 454.1052, Found: 454.1055. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 24.826 min, t_{major} = 28.925 min, 96% ee).

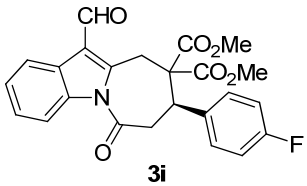
dimethyl (*R*)-8-(4-chlorophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3h)



3h

White solid, mp 170 – 172 °C, $[\alpha]_D^{20}$ –162 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.37 – 8.35 (m, 1H), 8.29 – 8.27 (m, 1H), 7.43 – 7.40 (m, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 4.37 (d, *J* = 15.6 Hz, 1H), 4.11 (d, *J* = 12.0 Hz, 1H), 3.97 (d, *J* = 15.6 Hz, 1H), 3.89 (dd, *J* = 12.4, 17.6 Hz, 1H), 3.71 (s, 3H), 3.33 (s, 3H), 3.19 (d, *J* = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.34, 185.30, 170.95, 169.69, 169.07, 141.89, 138.23, 135.69, 133.72, 129.88, 128.49, 126.58, 126.02, 125.66, 121.14, 119.81, 115.88, 61.16, 53.34, 52.83, 41.98, 41.38, 29.39. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}ClNO_6$ $(M+H)^+$: 454.1052, Found: 454.1058. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 19.954 min, t_{major} = 22.269 min, 96% ee).

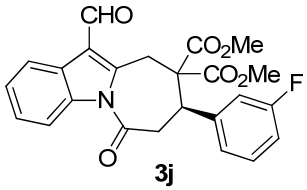
dimethyl (*R*)-8-(4-fluorophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3i)



3i

White solid, mp 168 – 170 °C, $[\alpha]_D^{20}$ –157 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.39 – 8.37 (m, 1H), 8.30 – 8.28 (m, 1H), 7.42 (t, J = 3.6 Hz, 2H), 7.26 – 7.23 (m, 2H), 6.99 (t, J = 8.4 Hz, 2H), 4.38 (d, J = 15.6 Hz, 1H), 4.13 (d, J = 12.0 Hz, 1H), 4.00 (d, J = 15.6 Hz, 1H), 3.91 (dd, J = 12.0, 17.2 Hz, 1H), 3.72 (s, 3H), 3.32 (s, 3H), 3.22 (d, J = 17.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.36, 171.06, 169.77, 169.17, 163.34, 160.88, 142.00, 135.73, 135.55, 135.51, 130.23, 130.15, 126.59, 126.05, 125.66, 121.16, 119.83, 115.92, 115.36, 115.14, 61.25, 53.29, 52.83, 42.20, 41.28, 29.42. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}FNO_6$ $(M+H)^+$: 438.1347, Found: 438.1351. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 23.726 min, t_{major} = 25.900 min, 97% ee).

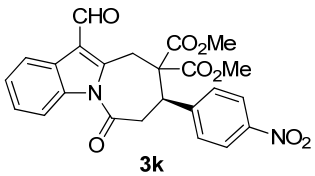
dimethyl (*R*)-8-(3-fluorophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3j)



3j

White solid, mp 179 – 181 °C, $[\alpha]_D^{20}$ –109 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.38 – 8.36 (m, 1H), 8.29 – 8.27 (m, 1H), 7.43 – 7.41 (m, 2H), 7.30 – 7.28 (m, 1H), 7.02 – 6.95 (m, 3H), 4.38 (d, J = 15.6 Hz, 1H), 4.14 (d, J = 12.0 Hz, 1H), 3.99 (d, J = 16.0 Hz, 1H), 3.89 (dd, J = 12.4, 17.6 Hz, 1H), 3.72 (s, 3H), 3.32 (s, 3H), 3.23 (d, J = 17.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.32, 170.89, 169.65, 169.03, 163.69, 161.23, 142.24, 142.17, 141.87, 135.73, 129.88, 129.80, 126.59, 126.06, 125.66, 124.04, 121.14, 119.86, 115.91, 115.70, 114.86, 114.65, 61.24, 53.32, 52.81, 41.86, 41.64, 29.45. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}FNO_6$ $(M+H)^+$: 438.1347, Found: 438.1348. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 93/7, flow rate = 1.0 mL/min, retention time: t_{minor} = 31.490 min, t_{major} = 34.618 min, 96% ee).

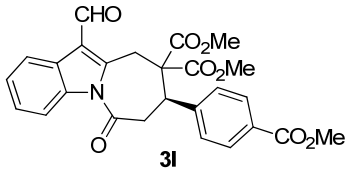
dimethyl (*R*)-11-formyl-8-(4-nitrophenyl)-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3k)



3k

White solid, mp 196 – 198 °C, $[\alpha]_D^{20}$ –119 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 8.38 – 8.36 (m, 1H), 8.30 – 8.28 (m, 1H), 8.17 (d, J = 8.8 Hz, 2H), 7.47 – 7.43 (m, 4H), 4.43 (d, J = 16.0 Hz, 1H), 4.23 (d, J = 12.0 Hz, 1H), 4.05 – 3.94 (m, 2H), 3.75 (s, 3H), 3.33 (s, 3H), 3.21 (d, J = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.26, 170.43, 169.50, 168.81, 147.32, 147.09, 141.21, 135.72, 129.70, 126.76, 126.07, 125.80, 123.43, 121.14, 120.02, 115.88, 61.16, 53.51, 52.98, 41.82, 41.53, 29.50. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}N_2O_8$ $(M+H)^+$: 465.1292, Found: 465.1294. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 32.450 min, t_{major} = 37.718 min, 98% ee).

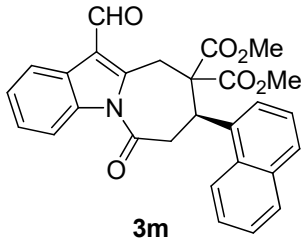
dimethyl (*R*)-11-formyl-8-(4-(methoxycarbonyl)phenyl)-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3l)



3l

White solid, mp 107 – 109 °C, $[\alpha]_D^{20}$ –183 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.39 – 8.36 (m, 1H), 8.30 – 8.28 (m, 1H), 7.97 (d, J = 8.4 Hz, 2H), 7.44 – 7.41 (m, 2H), 7.33 (d, J = 8.0 Hz, 2H), 4.40 (d, J = 16.0 Hz, 1H), 4.20 (d, J = 12.0 Hz, 1H), 4.02 (d, J = 16.0 Hz, 1H), 3.98 – 3.93 (m, 1H), 3.91 (s, 3H), 3.72 (s, 3H), 3.27 (s, 3H), 3.23 (d, J = 17.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.34, 170.87, 169.63, 168.98, 166.53, 144.86, 141.81, 135.73, 129.59, 129.57, 128.61, 126.62, 126.05, 125.68, 121.14, 119.89, 115.91, 61.20, 53.34, 52.83, 52.19, 41.94, 41.79, 29.74. HRMS (ESI): Exact Mass Calcd. for $C_{26}H_{24}NO_8$ $(M+H)^+$: 478.1496, Found: 478.1499. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 39.198 min, t_{major} = 53.570 min, 99% ee).

dimethyl (*R*)-11-formyl-8-(naphthalen-1-yl)-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3m)

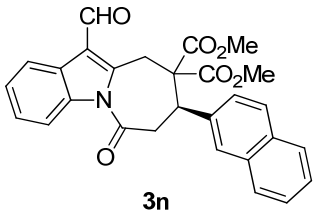


3m

White solid, mp 209 – 211 °C, $[\alpha]_D^{20}$ –192 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.40 (d, J = 5.6 Hz, 1H), 8.31 (d, J = 5.2 Hz, 1H), 7.79 – 7.77 (m, 3H), 7.72 (s, 1H), 7.48 – 7.42 (m, 4H), 7.34 (d, J = 8.0 Hz, 1H), 4.43 (d, J = 16.0 Hz, 1H), 4.33 (d, J = 12.0 Hz, 1H), 4.11 – 4.00 (m, 2H), 3.71 (s, 3H), 3.35 (d, J = 17.2 Hz, 1H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.41, 171.24, 169.83, 168.28, 142.27, 137.08, 135.75, 133.03, 132.58, 127.95, 127.90, 127.71, 127.52, 126.53, 126.38, 126.29, 126.05,

125.61, 121.14, 119.81, 115.92, 61.30, 53.25, 52.73, 42.27, 42.18, 29.52. HRMS (ESI): Exact Mass Calcd. for $C_{28}H_{24}NO_6$ $(M+H)^+$: 470.1598, Found: 470.1602. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 19.690 min, t_{major} = 25.953 min, 98% ee).

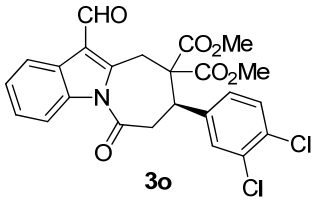
dimethyl (*R*)-11-formyl-8-(naphthalen-2-yl)-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3n)



3n

White solid, mp 217 – 219 °C, $[\alpha]_D^{20}$ –188 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.40 (d, *J* = 5.6 Hz, 1H), 8.32 (d, *J* = 4.8 Hz, 1H), 7.79 – 7.77 (m, 3H), 7.72 (s, 1H), 7.48 – 7.42 (m, 4H), 7.35 (d, *J* = 8.0 Hz, 1H), 4.43 (d, *J* = 15.6 Hz, 1H), 4.33 (d, *J* = 16.0 Hz, 1H), 4.11 – 4.00 (m, 2H), 3.71 (s, 3H), 3.35 (d, *J* = 17.6 Hz, 1H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.65, 170.30, 170.10, 169.25, 142.79, 136.58, 135.73, 133.81, 131.35, 128.75, 128.65, 126.54, 126.48, 126.02, 125.97, 125.66, 124.92, 124.60, 123.76, 121.05, 119.83, 116.47, 61.07, 53.40, 52.10, 43.79, 35.79, 25.34. HRMS (ESI): Exact Mass Calcd. for $C_{28}H_{24}NO_6$ $(M+H)^+$: 470.1598, Found: 470.1600. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{major} = 32.008 min, >99% ee).

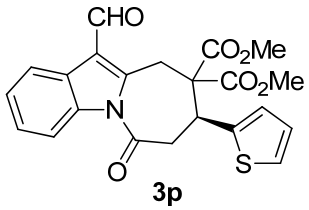
dimethyl (*R*)-8-(3,4-dichlorophenyl)-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3o)



3o

White solid, mp 152 – 154 °C, $[\alpha]_D^{20}$ –132 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.37 – 8.35 (m, 1H), 8.29 – 8.27 (m, 1H), 7.44 – 7.41 (m, 2H), 7.39 – 7.35 (m, 2H), 7.11 (dd, *J* = 2.4, 8.4 Hz, 1H), 4.39 (d, *J* = 16.0 Hz, 1H), 4.06 (d, *J* = 12.0 Hz, 1H), 3.98 (d, *J* = 15.6 Hz, 1H), 3.90 (dd, *J* = 12.0, 17.2 Hz, 1H), 3.73 (s, 3H), 3.40 (s, 3H), 3.17 (d, *J* = 17.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.28, 170.62, 169.53, 168.97, 141.48, 139.91, 135.71, 132.46, 132.05, 130.54, 130.23, 128.03, 126.68, 126.04, 125.72, 119.93, 115.85, 61.08, 53.41, 52.97, 41.67, 41.31, 29.43. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{20}Cl_2NO_6$ $(M+H)^+$: 488.0662, Found: 488.0669. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 38.943 min, t_{major} = 53.120 min, 98% ee).

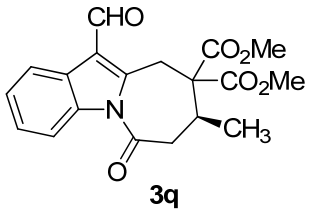
dimethyl (*S*)-11-formyl-6-oxo-8-(thiophen-2-yl)-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3p)



3p

White solid, mp 189 – 191 °C, $[\alpha]_D^{20}$ –93 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 8.36 – 8.33 (m, 1H), 8.30 – 8.27 (m, 1H), 7.42 – 7.40 (m, 2H), 7.20 (d, J = 5.2 Hz, 1H), 6.92 (t, J = 8.8 Hz, 1H), 6.87 (d, J = 3.2 Hz, 1H), 4.43 (d, J = 11.2 Hz, 1H), 4.37 (d, J = 15.6 Hz, 1H), 3.97 (d, J = 15.6 Hz, 1H), 3.90 (dd, J = 12.0, 17.2 Hz, 1H), 3.72 (s, 3H), 3.46 (d, J = 14.8 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.47, 170.53, 169.71, 168.95, 141.92, 141.43, 135.69, 126.55, 126.46, 126.43, 125.98, 125.62, 125.24, 121.18, 119.79, 115.80, 61.31, 53.34, 53.08, 42.75, 38.06, 29.01. HRMS (ESI): Exact Mass Calcd. for $C_{22}H_{20}NO_6S$ $(M+H)^+$: 426.1006, Found: 426.1009. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 30.133 min, t_{major} = 37.459 min, 76% ee).

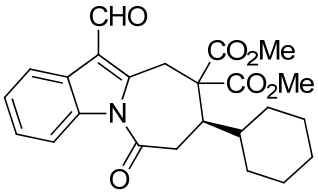
dimethyl (*S*)-11-formyl-8-methyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3q)



3q

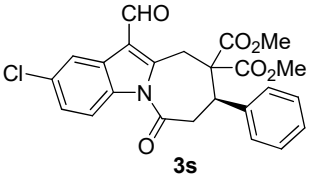
White solid, mp 101 – 103 °C, $[\alpha]_D^{20}$ –147 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.34 – 8.32 (m, 1H), 8.30 – 8.28 (m, 1H), 7.43 – 7.36 (m, 2H), 4.26 (d, J = 15.6 Hz, 1H), 3.83 (s, 3H), 3.80 (d, J = 15.6 Hz, 1H), 3.76 (s, 3H), 3.42 (dd, J = 10.8, 18.0 Hz, 1H), 2.87 – 2.76 (m, 2H), 1.13 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.90, 172.00, 170.01, 169.79, 142.50, 135.66, 135.66, 126.42, 125.95, 125.46, 121.26, 119.67, 115.62, 59.42, 53.18, 52.93, 42.36, 32.51, 29.22, 18.52. HRMS (ESI): Exact Mass Calcd. for $C_{19}H_{20}NO_6$ $(M+H)^+$: 358.1285, Found: 358.1286. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{minor} = 17.240 min, t_{major} = 20.795 min, 93% ee).

dimethyl (*R*)-8-cyclohexyl-11-formyl-6-oxo-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3r)



White solid, mp 165 – 168 °C, $[\alpha]_D^{20}$ –185 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.16 (s, 1H), 8.34 – 8.31 (m, 1H), 8.27 – 8.24 (m, 1H), 7.42 – 7.35 (m, 2H), 4.24 (d, J = 15.6 Hz, 1H), 4.13 (d, J = 12.0 Hz, 1H), 3.82 – 3.78 (m, 4H), 3.74 (s, 3H), 3.13 (dd, J = 11.6, 18.4 Hz, 1H), 2.97 (d, J = 15.6 Hz, 1H), 2.44 (d, J = 11.2 Hz, 1H), 1.85 (t, J = 10.8 Hz, 1H), 1.75 – 1.72 (m, 2H), 1.65 – 1.59 (m, 2H), 1.27 – 1.21 (m, 3H), 1.12 – 1.07 (m, 2H), 0.97 – 0.90 (m, 1H). HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{28}NO_6$ $(M+H)^+$: 426.1911, Found: 426.1915. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 90/10, flow rate = 1.0 mL/min, retention time: t_{minor} = 23.333 min, t_{major} = 26.554 min, 93% ee).

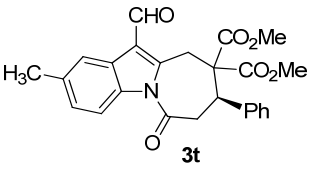
dimethyl (*R*)-2-chloro-11-formyl-6-oxo-8-phenyl-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3s)



3s

White solid, mp 178 – 180 °C, $[\alpha]_D^{20}$ –165 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.31 – 8.29 (m, 2H), 7.36 (dd, J = 2.0, 8.8 Hz, 1H), 7.33 – 7.23 (m, 5H), 4.36 (d, J = 16.0 Hz, 1H), 4.17 (d, J = 12.0 Hz, 1H), 4.02 (d, J = 16.0 Hz, 1H), 3.89 (dd, J = 12.0, 17.2 Hz, 1H), 3.69 (s, 3H), 3.28 – 3.24 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.98, 170.97, 169.73, 169.05, 143.37, 139.50, 133.98, 131.38, 128.41, 128.36, 127.87, 127.09, 126.71, 120.94, 119.01, 117.00, 61.18, 53.32, 52.79, 42.09, 41.85, 29.38. HRMS (ESI): Exact Mass Calcd. for $C_{24}H_{21}ClNO_6$ $(M+H)^+$: 454.1052, Found: 454.1056. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 93/7, flow rate = 1.0 mL/min, retention time: t_{minor} = 24.806 min, t_{major} = 32.109 min, 98% ee).

dimethyl (*R*)-11-formyl-2-methyl-6-oxo-8-phenyl-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (3t)



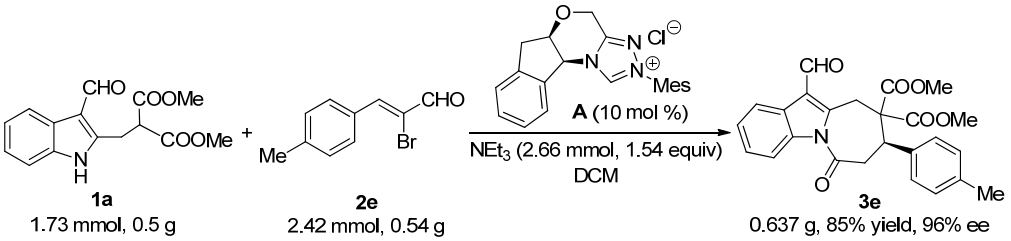
3t

White solid, mp 131 – 134 °C; $[\alpha]_D^{20}$ –116 (c 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.39 – 8.37 (m, 1H), 8.30 – 8.28 (m, 1H), 7.43 – 7.40 (m, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.08 – 7.02 (m, 3H),

4.37 (d, J = 15.6 Hz, 1H), 4.13 (d, J = 12.0 Hz, 1H), 4.01 (d, J = 15.6 Hz, 1H), 3.88 (dd, J = 12.4, 17.6 Hz, 1H), 3.69 (s, 3H), 3.28 (s, 3H), 3.24 (d, J = 15.6 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.44, 171.31, 169.79, 169.23, 142.44, 139.62, 137.96, 135.69, 129.07, 128.46, 128.22, 126.47, 125.98, 125.56, 125.42, 121.13, 119.71, 115.92, 61.22, 53.21, 52.65, 42.22, 41.91, 29.93, 21.40. HRMS (ESI): Exact Mass Calcd. for $C_{25}H_{23}NO_6Na$ $(M+Na)^+$: 456.1418, Found: 456.1411. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 95/5, flow rate = 1.0 mL/min, retention time: t_{major} = 33.451 min, t_{minor} = 36.741 min, 88% ee).

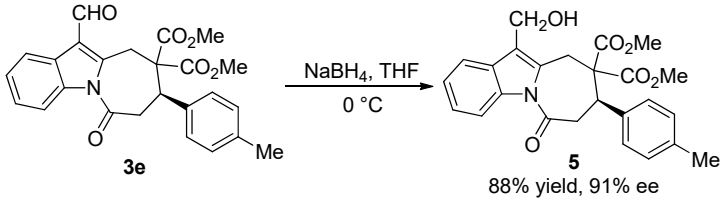
5. A Scale-up Synthesis of compound 3e

To a solution of dimethyl 2-((3-formyl-1*H*-indol-2-yl)methyl)malonate (**1a**) (1.73 mmol, 0.50 g), (*Z*)-2-bromo-3-(*p*-tolyl)acrylaldehyde (**2a**) (2.42 mmol, 0.54 g) and *N*-heterocyclic carbene precatalyst **A** (0.173 mmol, 63.66 mg) in DCM (15 mL), NEt_3 (2.66 mmol, 0.37 mL) was added at room temperature under nitrogen atmosphere. The reaction was stirred at room temperature (monitored by TLC), and then was quenched by water (5 mL). The mixture was extracted with ethyl acetate (10 mL×3) and dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography on silica gel using petroleum ether/EtOAc (5:1) to afford the product **3e** as a white solid (0.637 g, 85% yield, 96% ee).



6. The reduction of product 3e

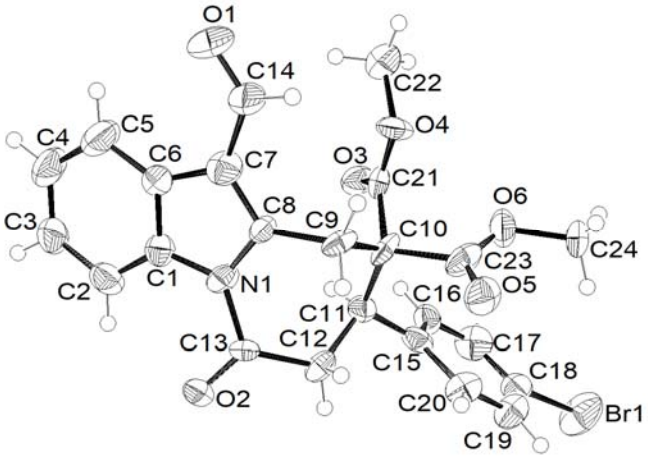
To a solution of **3e** (0.1 mmol, 43.3 mg) in THF (1 mL) was added $NaBH_4$ (0.11 mmol, 4.2 mg) at 0 °C, and the reaction mixture was stirred at 0 °C for 8 h. After completion of the reaction (monitored by TLC), and then was quenched by saturated NH_4Cl. The mixture was extracted with ethyl acetate (5 mL×3) and the solvents were removed *in vacuo*. The crude product was purified by flash column chromatograph (petroleum ether/EtOAc = 3/1) to afford the product **5** (38.3 mg, 88%).



dimethyl (*R*)-11-(hydroxymethyl)-6-oxo-8-(*p*-tolyl)-7,8-dihydro-6*H*-azepino[1,2-*a*]indole-9,9(10*H*)-dicarboxylate (5)

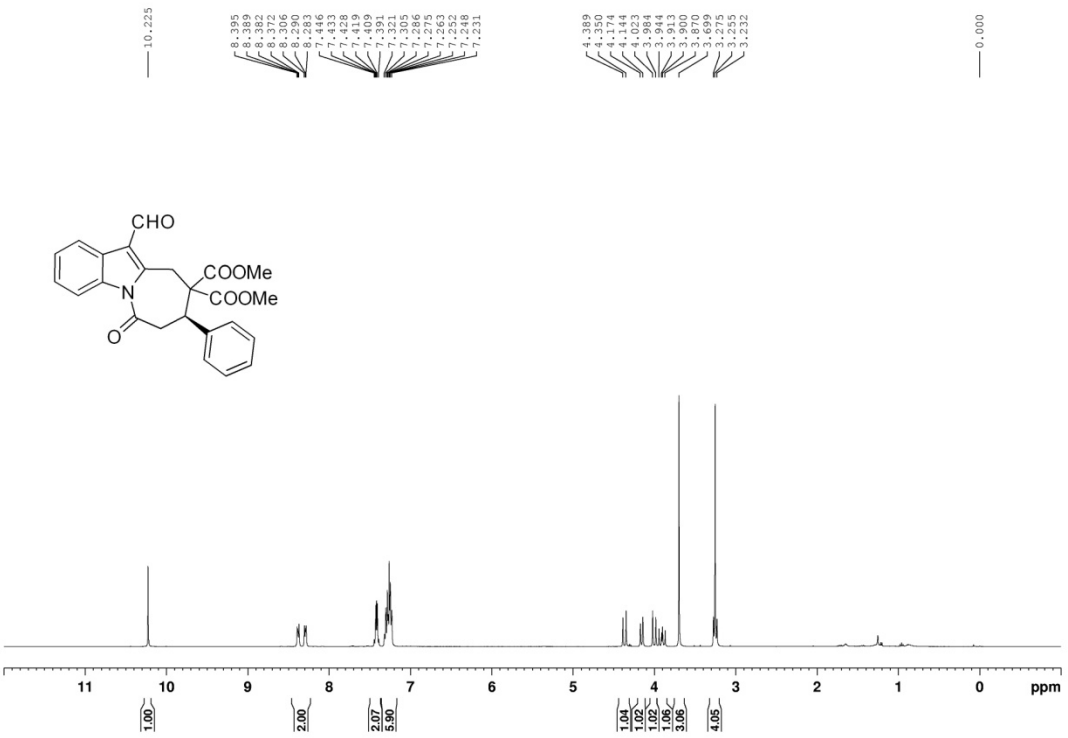
White solid, mp 199 – 201 °C, $[\alpha]_D^{20}$ –99 (c 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, *J*= 1.6, 7.2 Hz, 1H), 7.68 – 7.66 (m, 1H), 7.39 – 7.31 (m, 2H), 7.07 (s, 4H), 4.82 – 4.73 (m, 2H), 4.06 (dd, *J* = 1.2, 11.6 Hz, 1H), 3.90 – 3.80 (m, 3H), 3.70 (s, 3H), 3.30 (s, 3H), 3.13 (dd, *J* = 1.20, 17.2 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.27, 170.93, 169.84, 137.31, 137.17, 135.95, 130.36, 128.91, 125.52, 124.10, 120.89, 118.63, 116.36, 61.51, 54.99, 53.10, 52.51, 42.35, 42.25, 29.98, 21.01. HRMS (ESI): Exact Mass Calcd. for $C_{25}H_{26}NO_6$ $(M+H)^+$: 435.1676, Found: 435.1677. HPLC (Chiralpak AD–H column, *n*-hexane/*i*-PrOH = 70/30, flow rate = 1.0 mL/min, retention time: t_{minor} = 10.644 min, t_{major} = 21.661 min, 92% ee).

7. X-Ray crystal structure of compound 3d

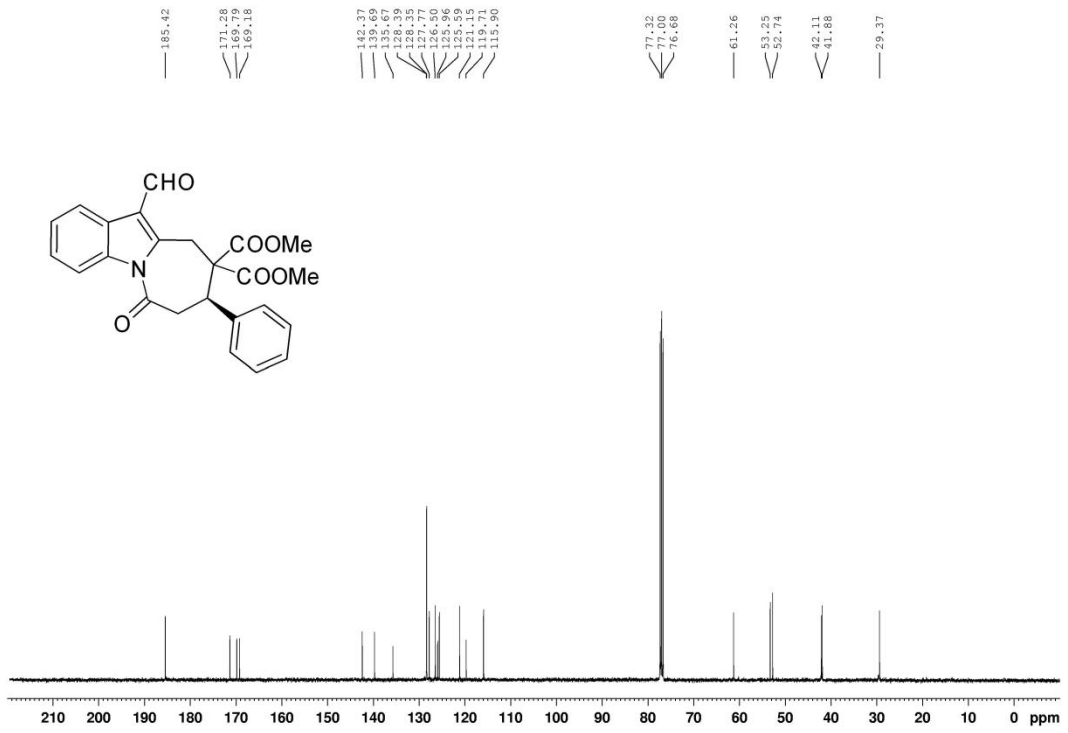


8. NMR spectra of compounds 3a–3t and 5

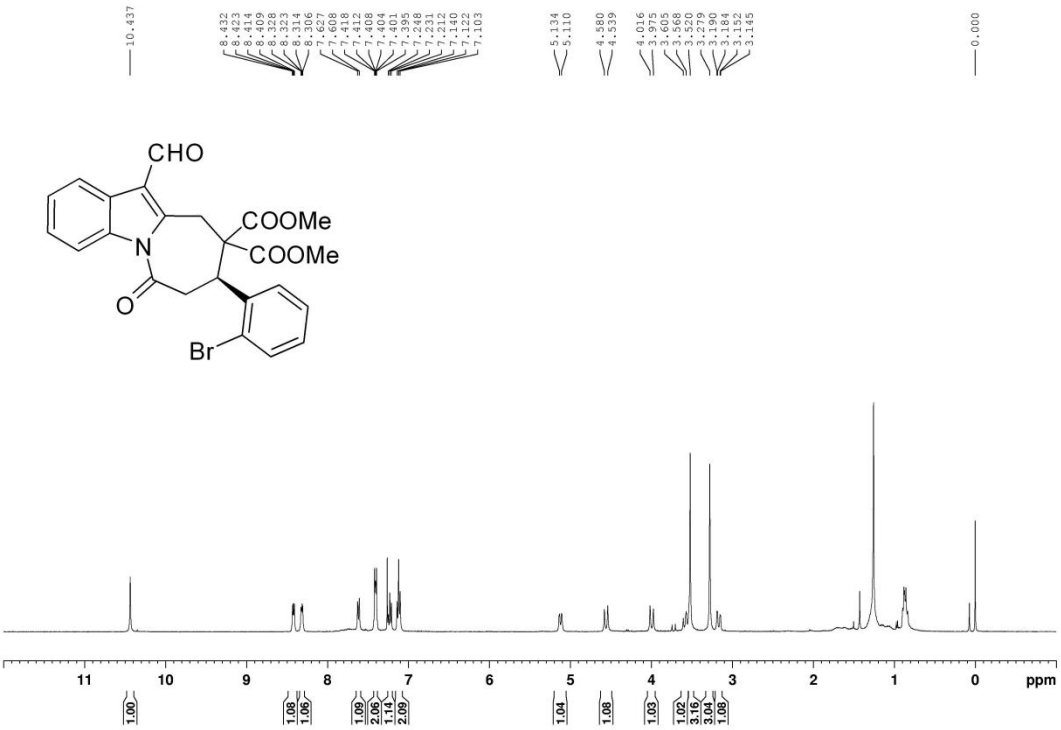
^{1}H NMR spectrum of compound **3a** ($CDCl_3$, 400 MHz)



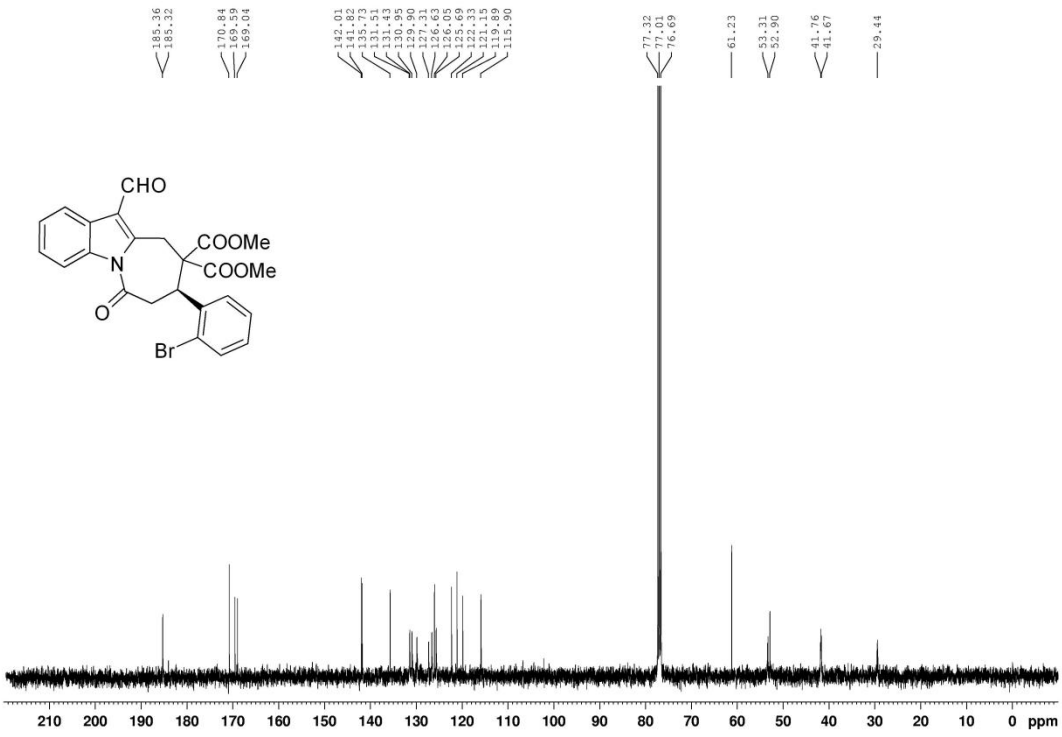
^{13}C NMR spectrum of compound **3a** ($CDCl_3$, 100 MHz)



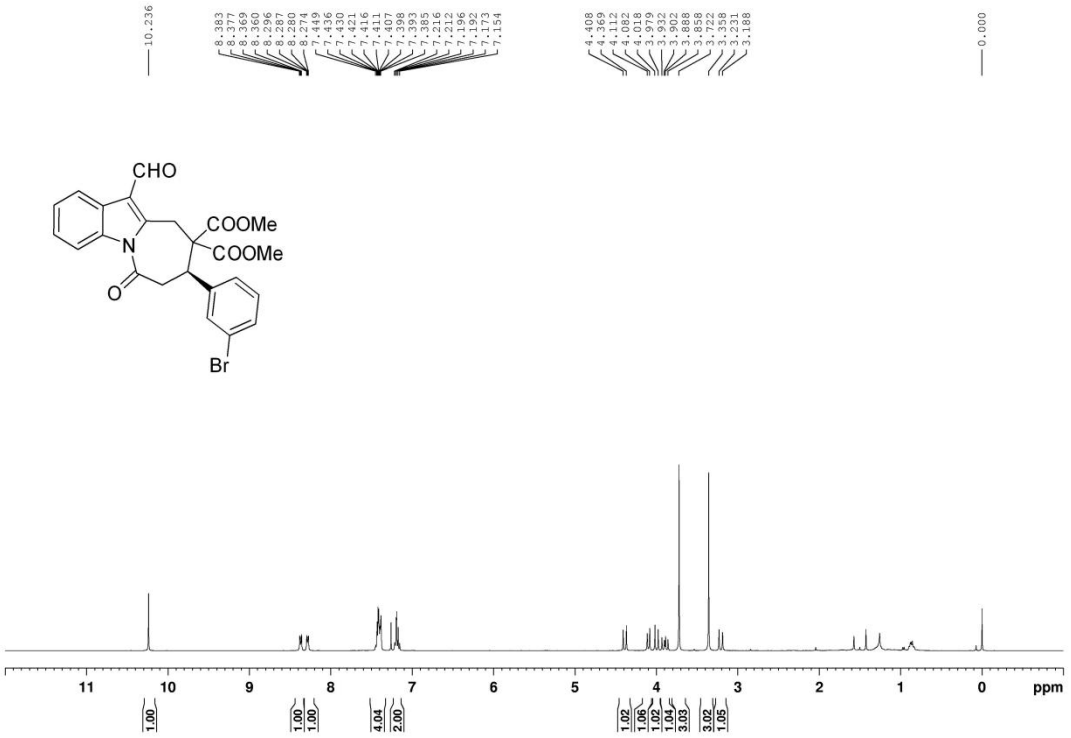
^{1}H NMR spectrum of compound **3b** ($CDCl_3$, 400 MHz)



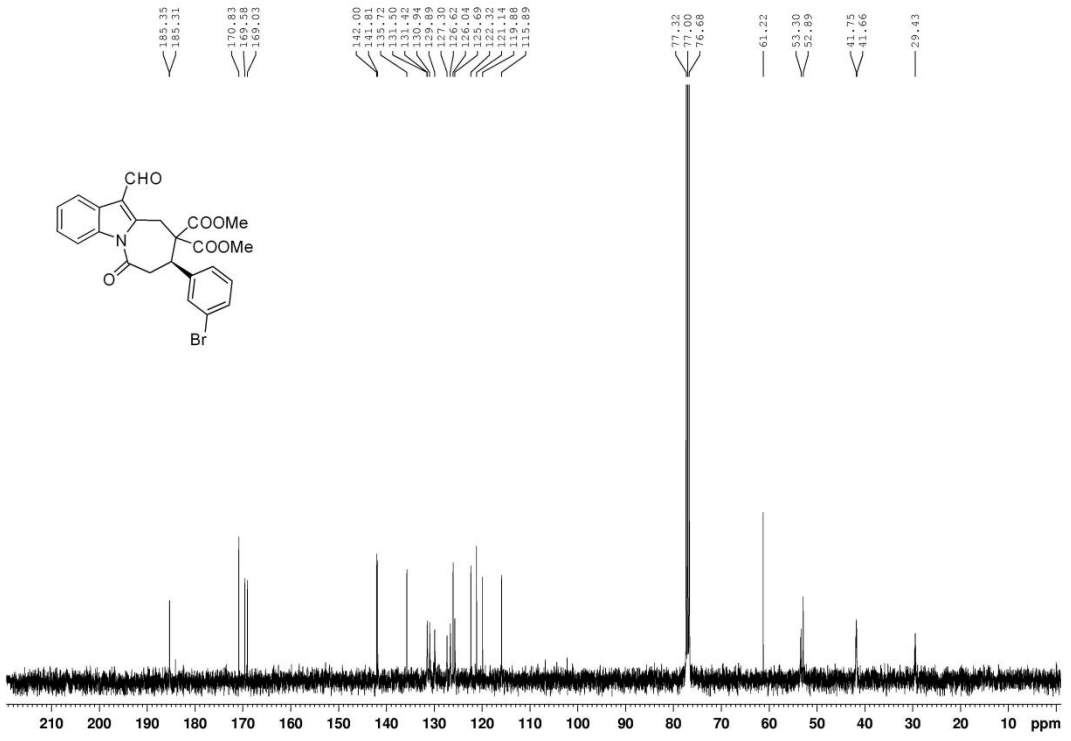
^{13}C NMR spectrum of compound **3b** ($CDCl_3$, 100 MHz)



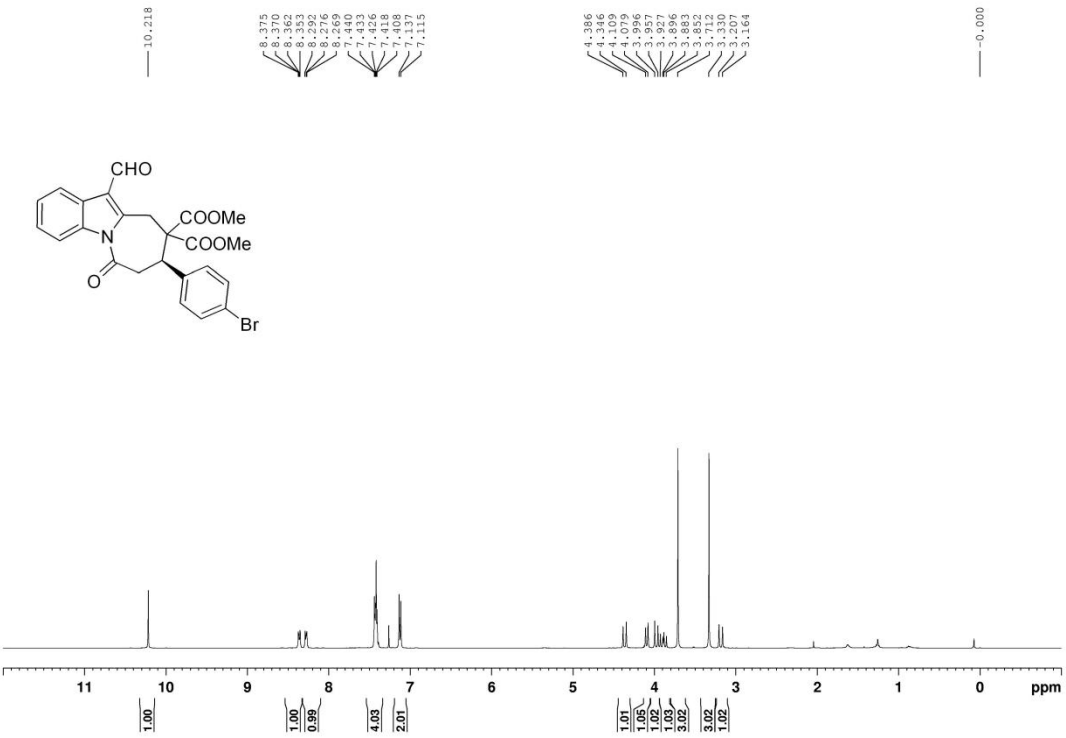
^{1}H NMR spectrum of compound **3c** ($CDCl_3$, 400 MHz)



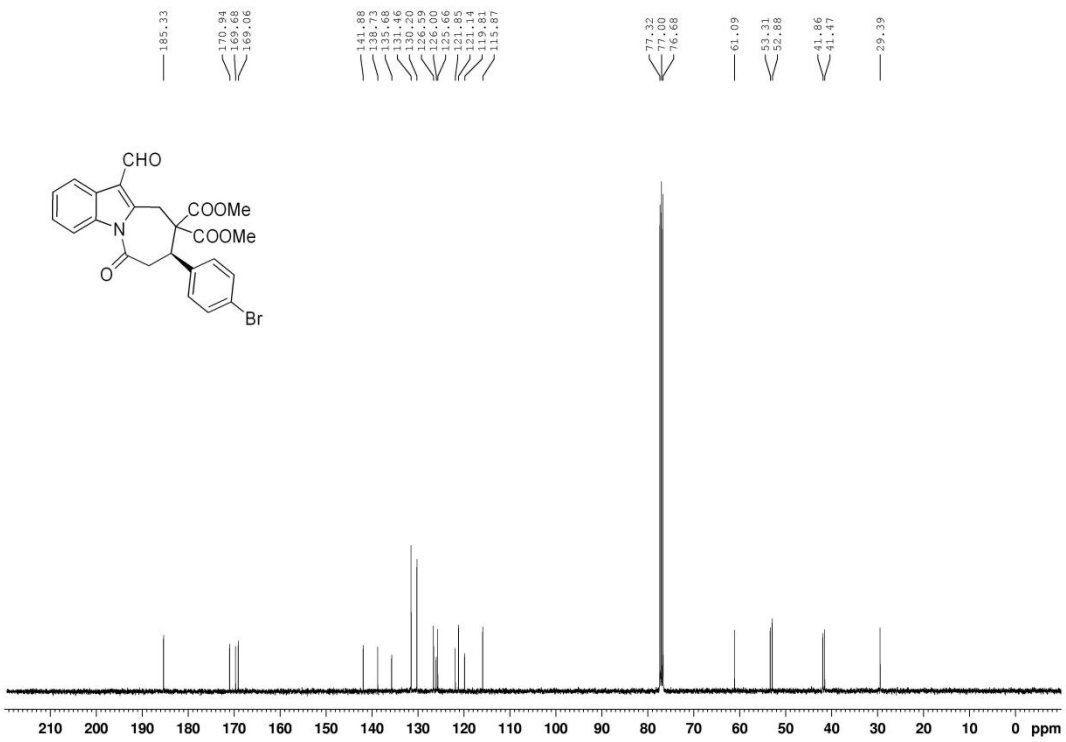
^{13}C NMR spectrum of compound **3c** ($CDCl_3$, 100 MHz)



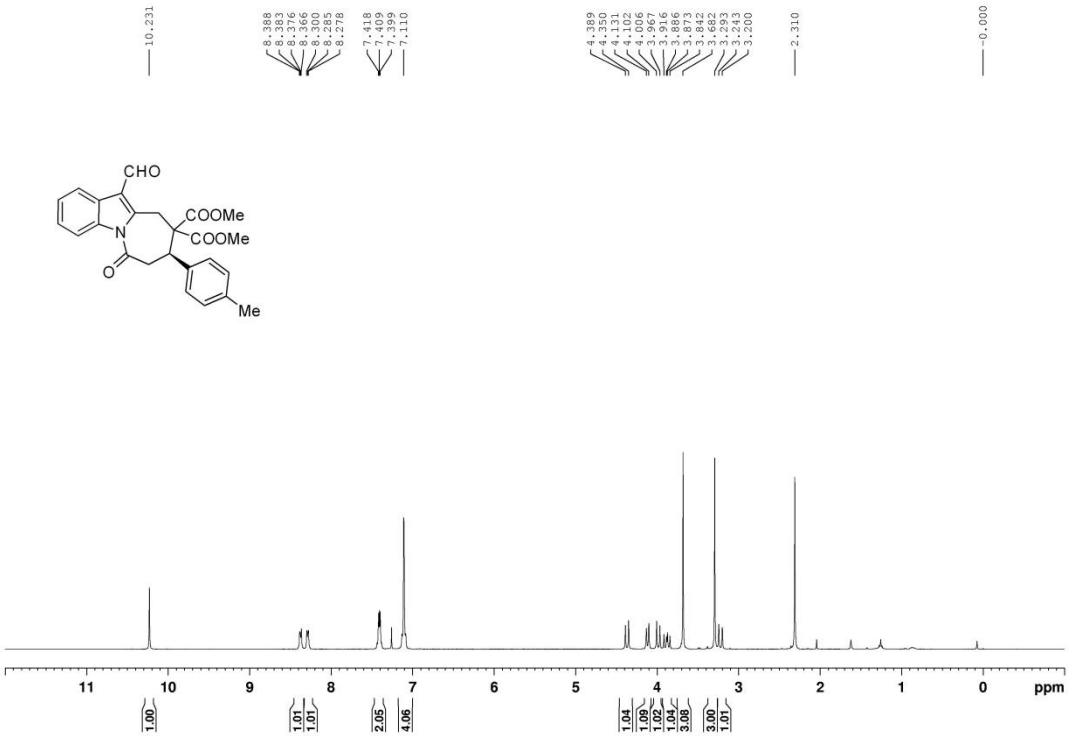
^{1}H NMR spectrum of compound **3d** ($CDCl_3$, 400 MHz)



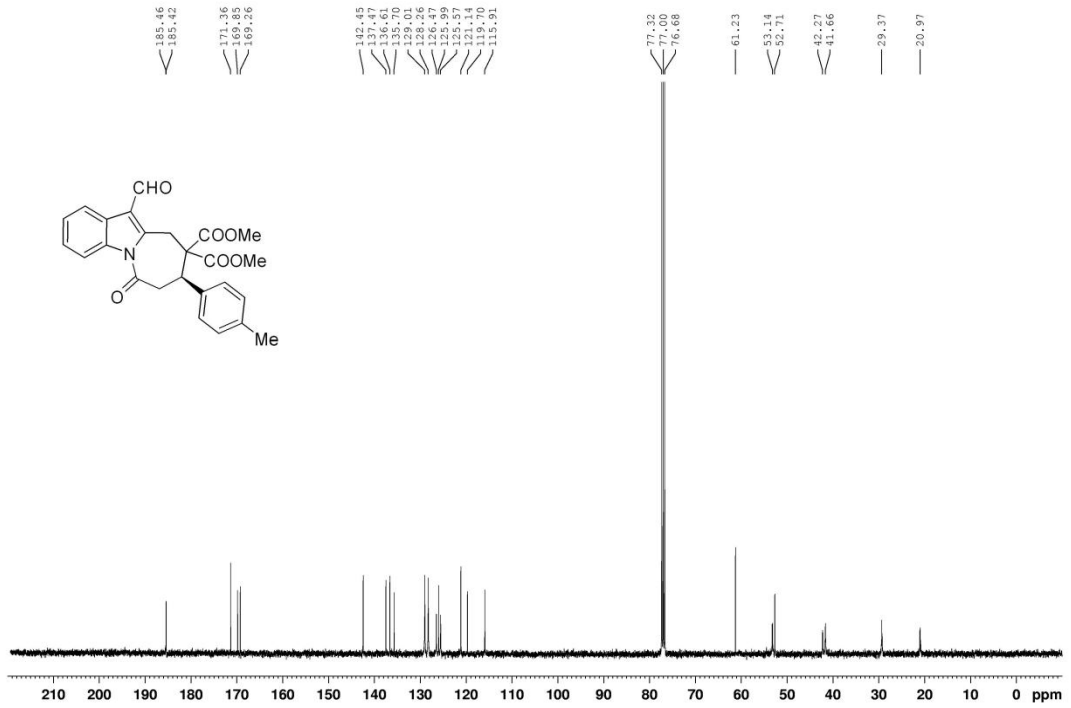
^{13}C NMR spectrum of compound **3d** ($CDCl_3$, 100 MHz)



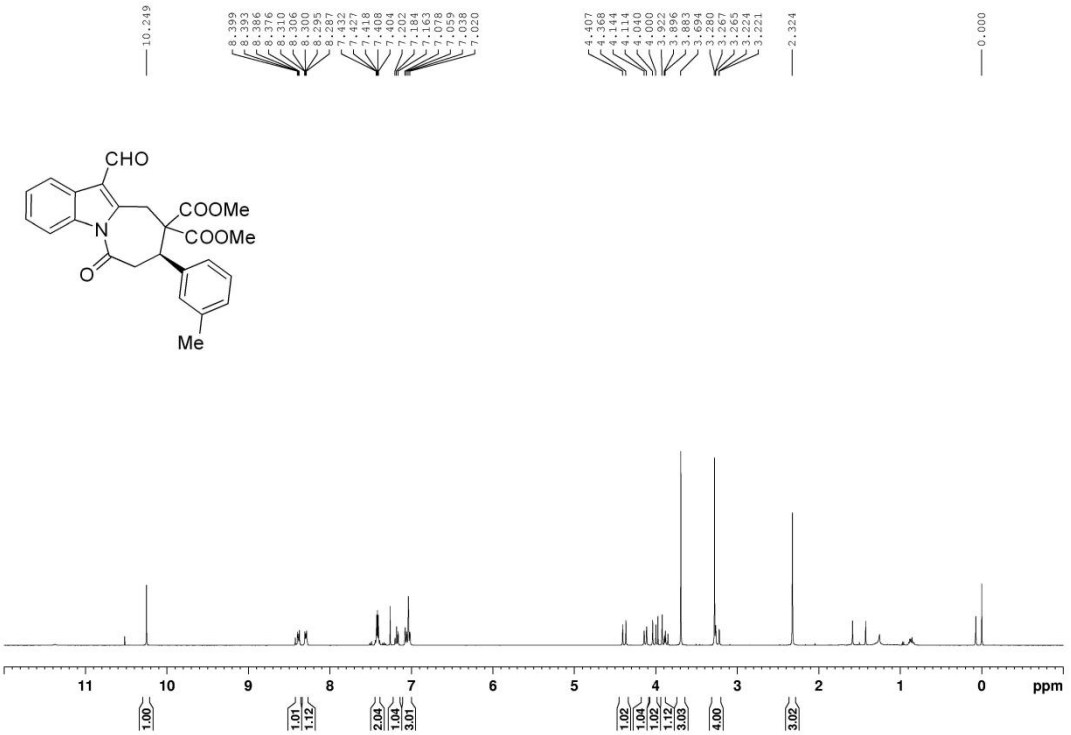
^{1}H NMR spectrum of compound **3e** ($CDCl_3$, 400 MHz)



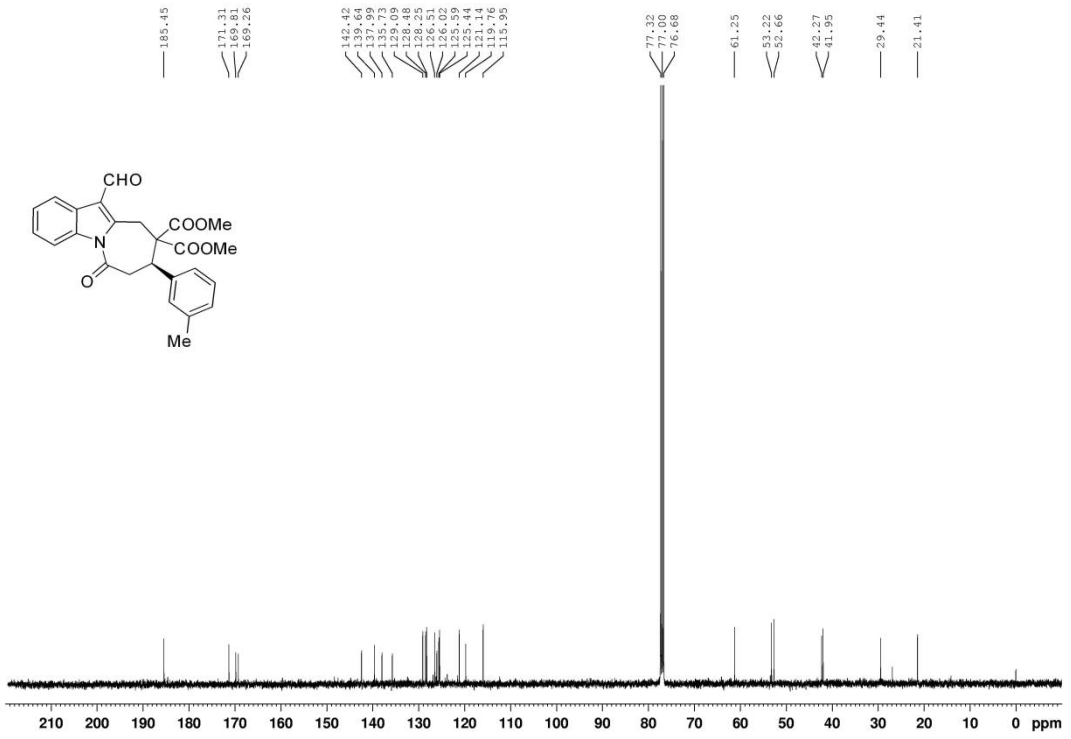
^{13}C NMR spectrum of compound **3e** ($CDCl_3$, 100 MHz)



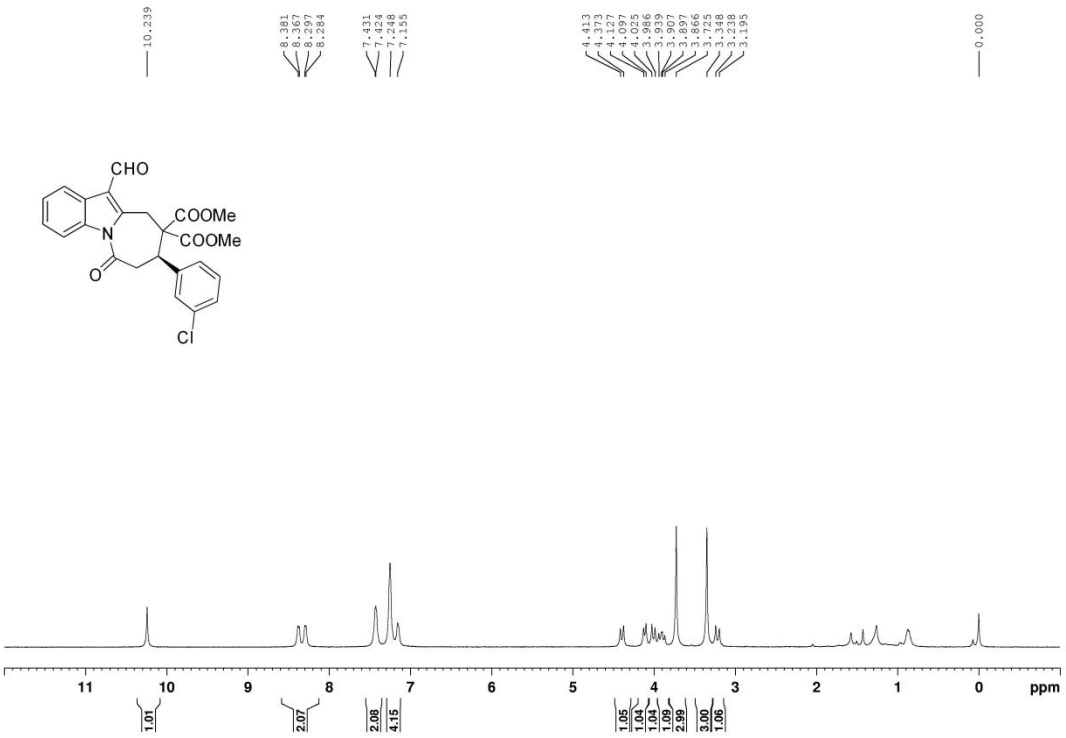
^{1}H NMR spectrum of compound **3f** ($CDCl_3$, 400 MHz)



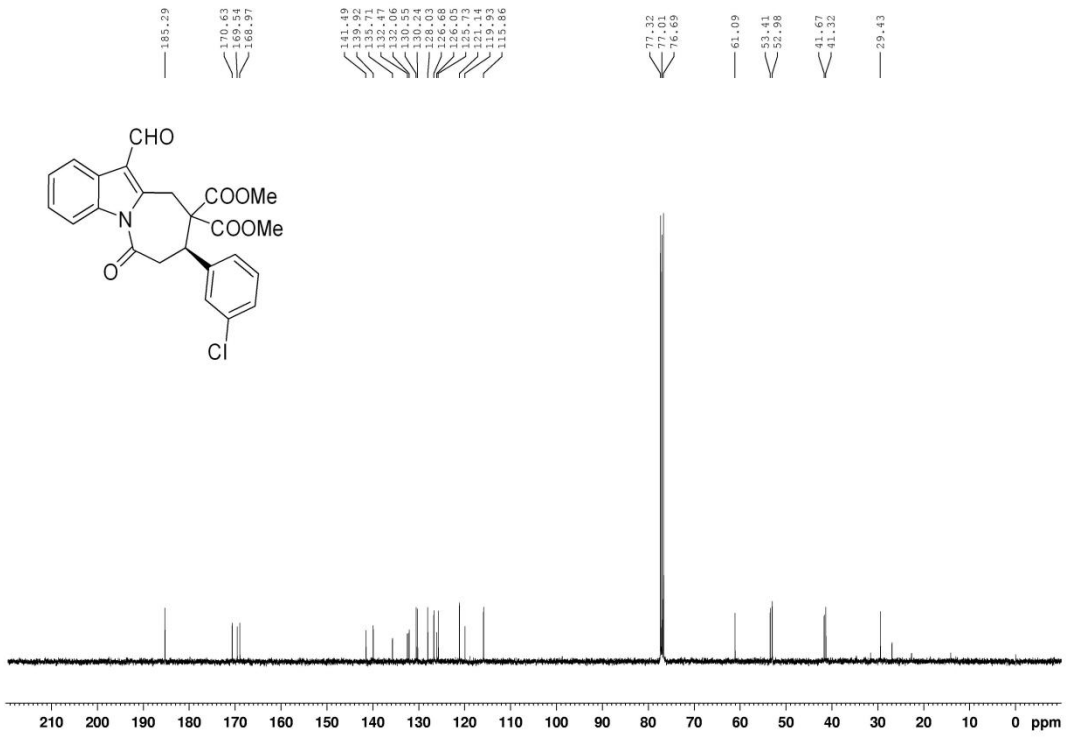
^{13}C NMR spectrum of compound **3f** ($CDCl_3$, 100 MHz)



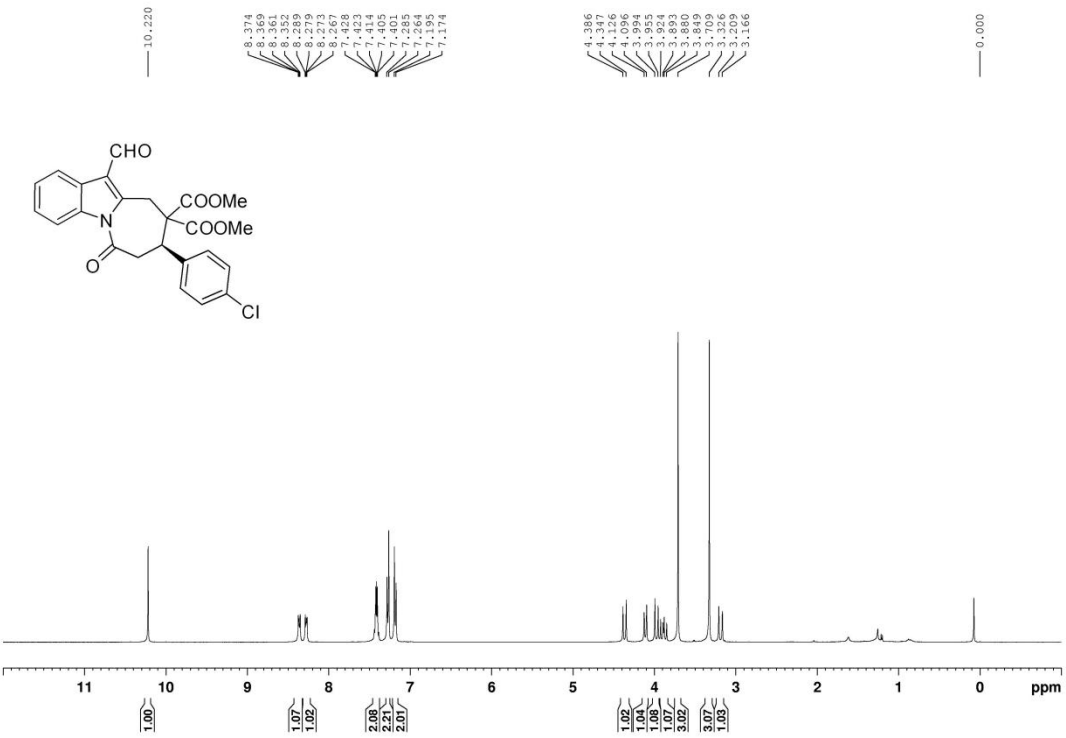
^{1}H NMR spectrum of compound **3g** ($CDCl_3$, 400 MHz)



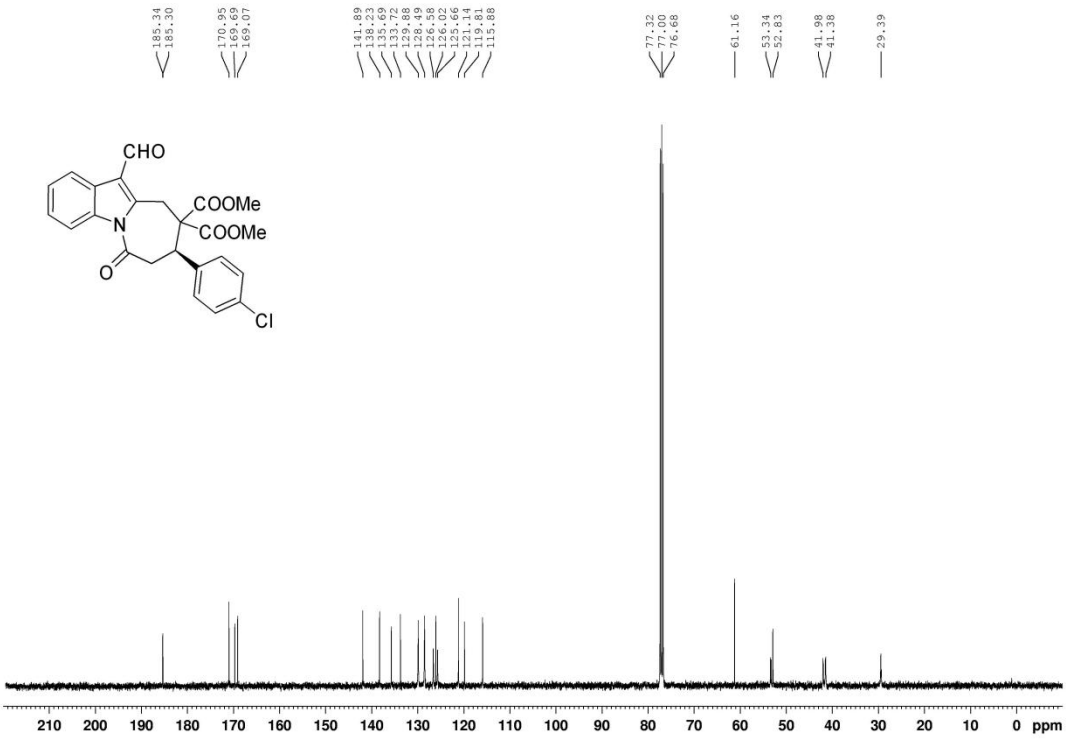
^{13}C NMR spectrum of compound **3g** ($CDCl_3$, 100 MHz)



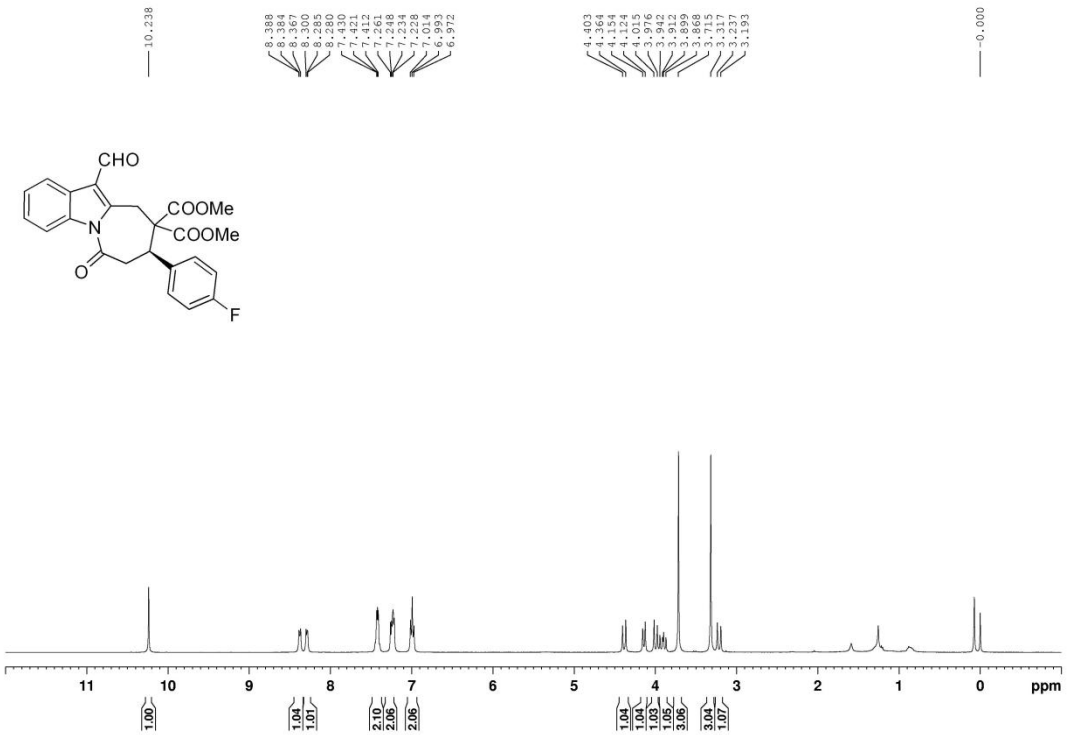
^{1}H NMR spectrum of compound **3h** ($CDCl_3$, 400 MHz)



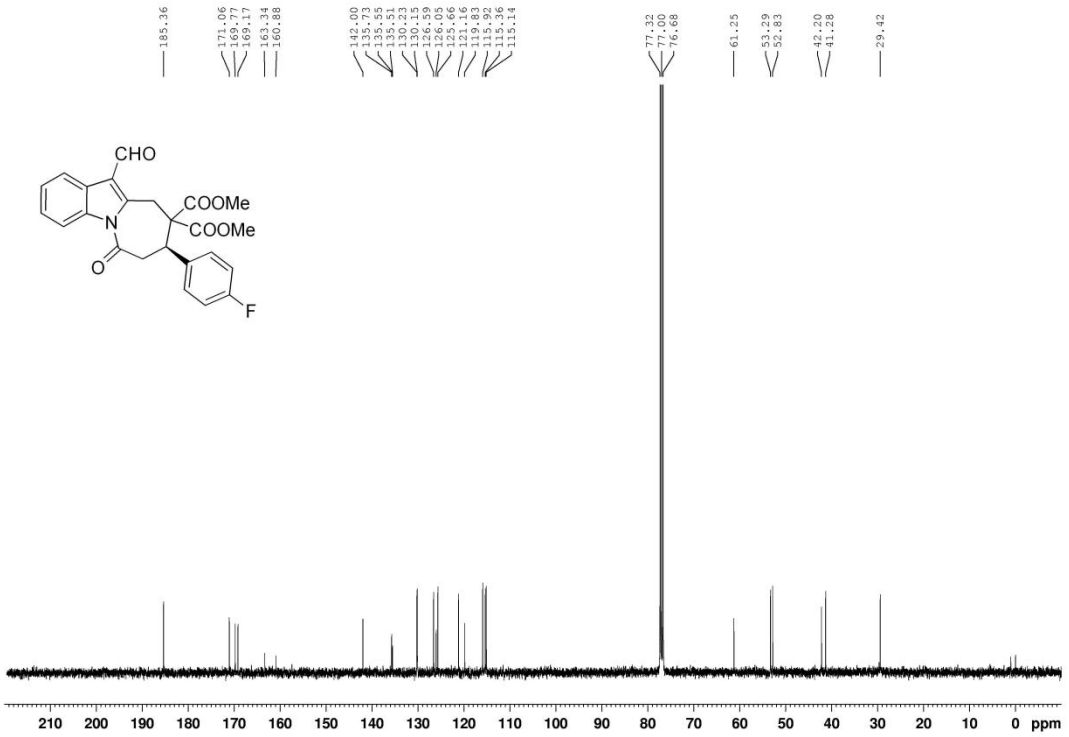
^{13}C NMR spectrum of compound **3h** ($CDCl_3$, 100 MHz)



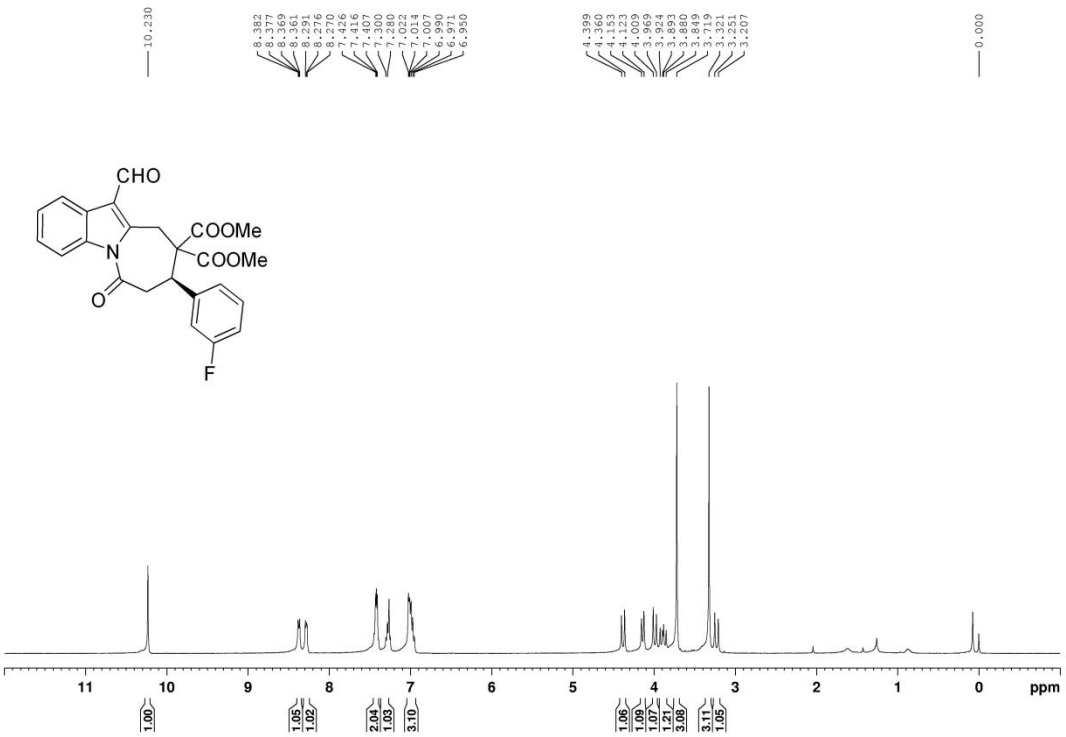
^{1}H NMR spectrum of compound **3i** ($CDCl_3$, 400 MHz)



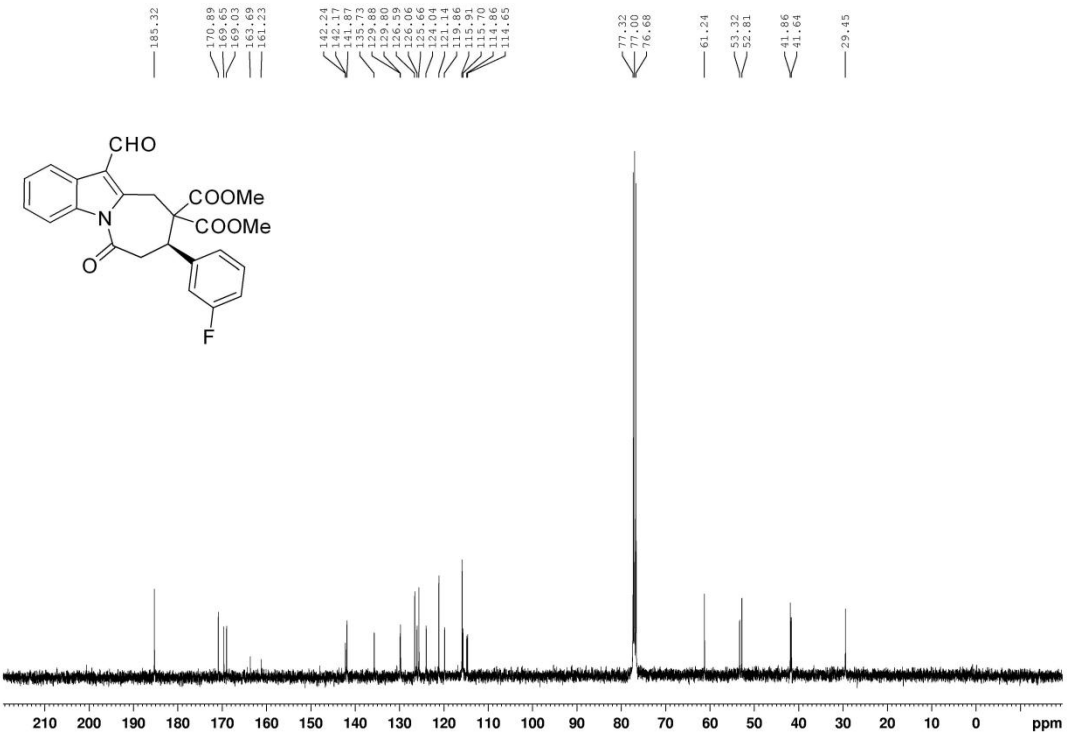
^{13}C NMR spectrum of compound **3i** ($CDCl_3$, 100 MHz)



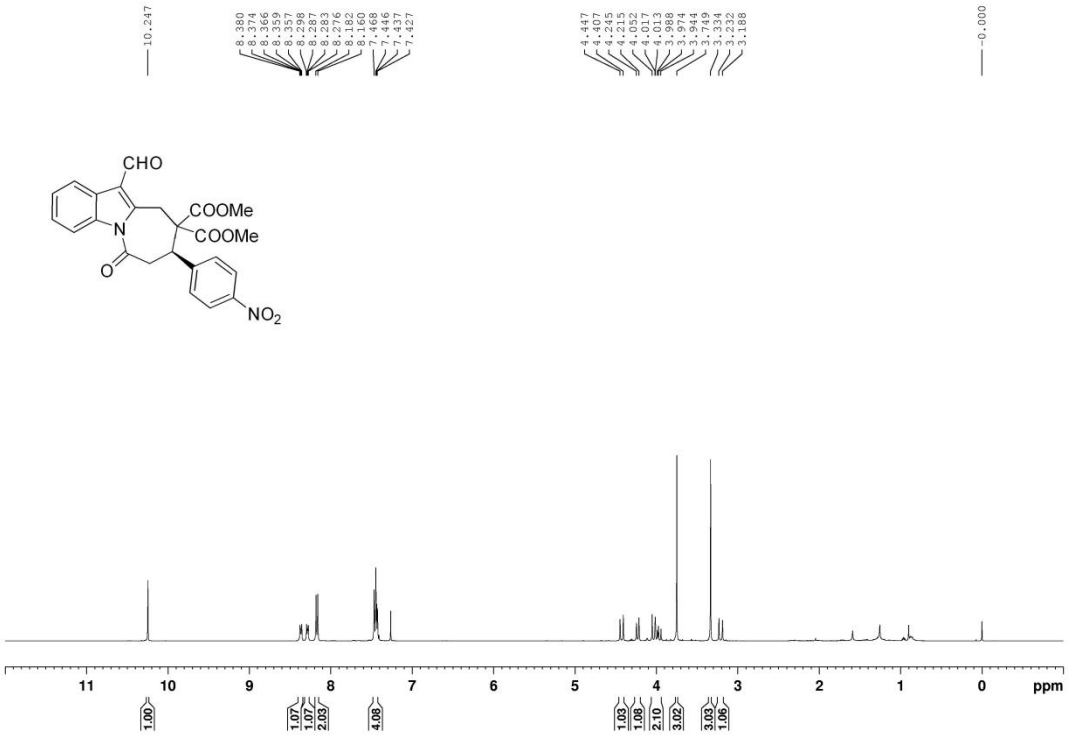
^{1}H NMR spectrum of compound **3j** ($CDCl_3$, 400 MHz)



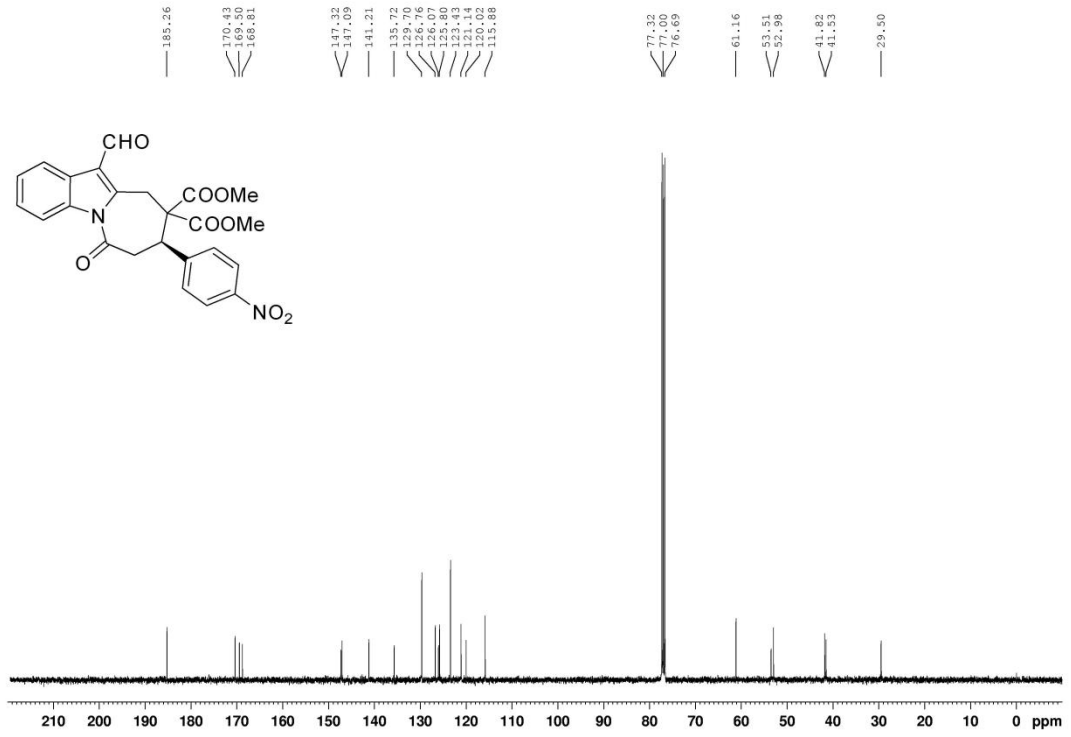
^{13}C NMR spectrum of compound **3j** ($CDCl_3$, 100 MHz)



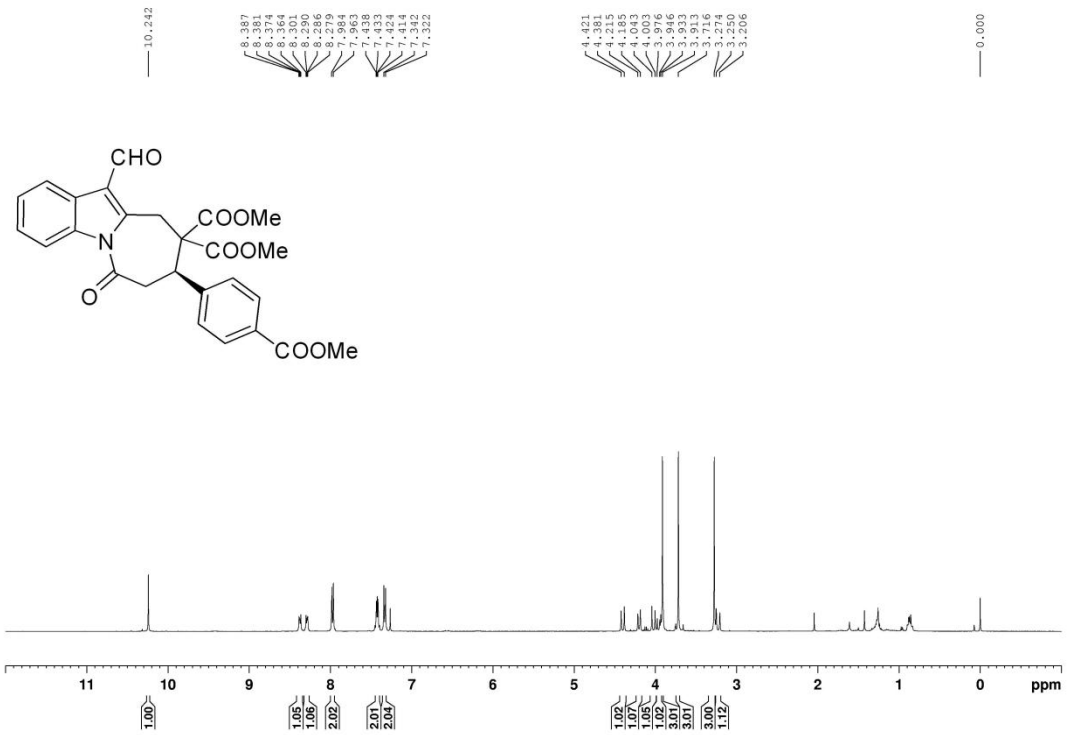
^{1}H NMR spectrum of compound **3k** ($CDCl_3$, 400 MHz)



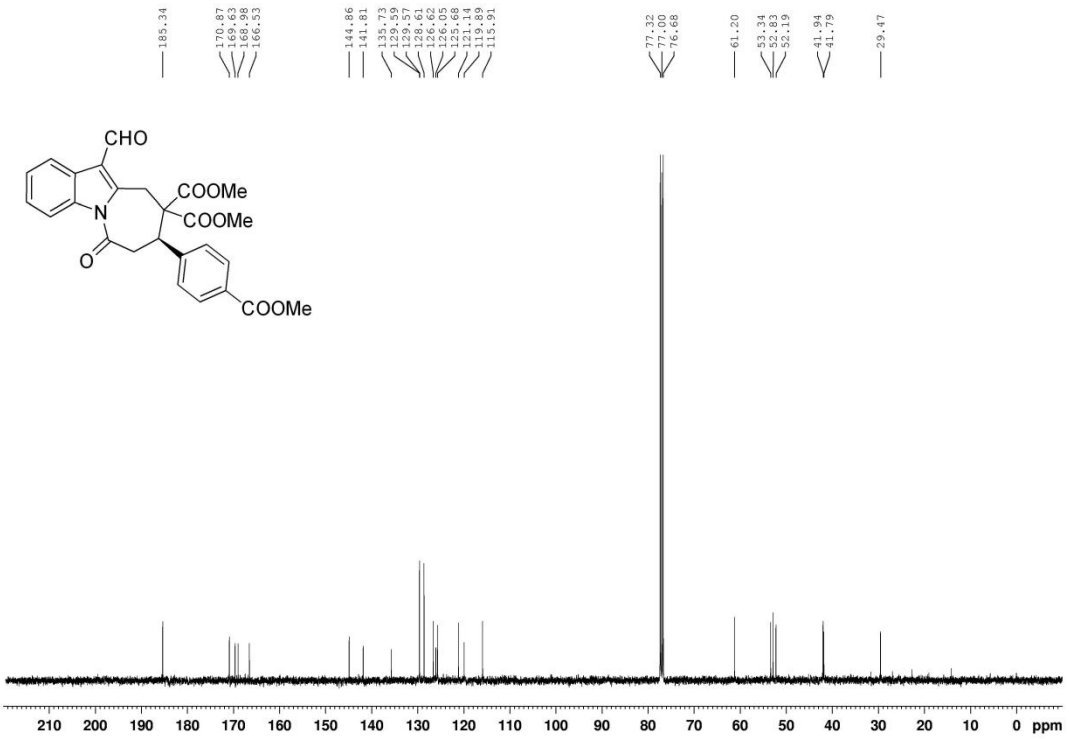
^{13}C NMR spectrum of compound **3k** ($CDCl_3$, 100 MHz)



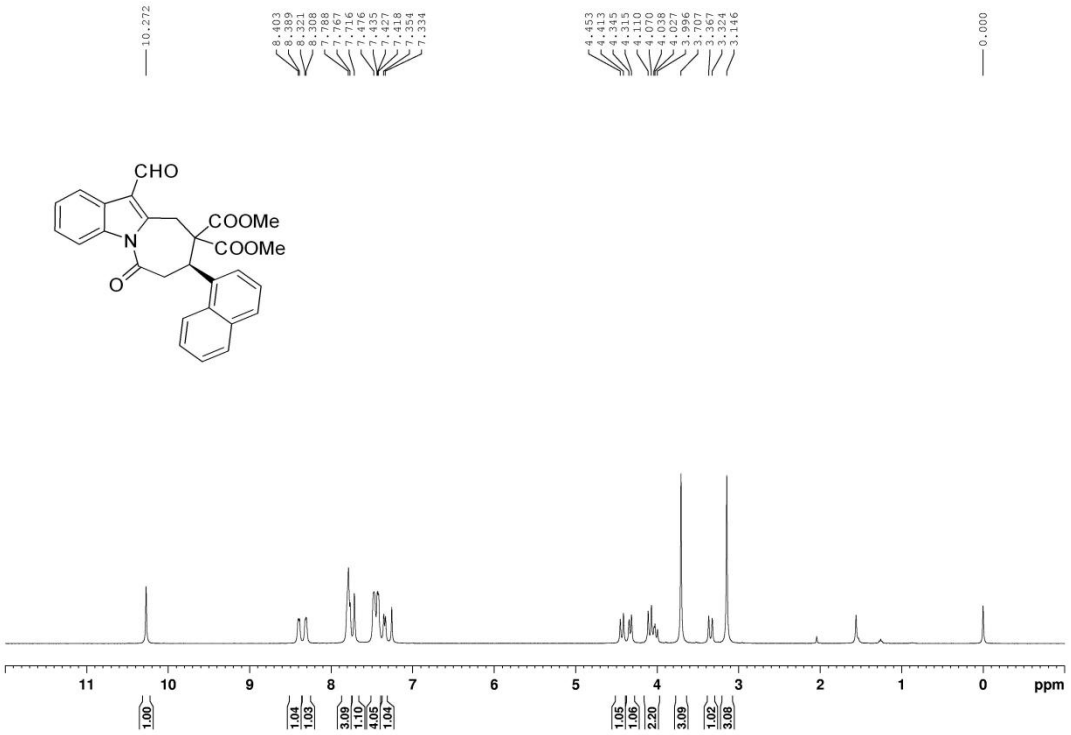
^{1}H NMR spectrum of compound **3l** ($CDCl_3$, 400 MHz)



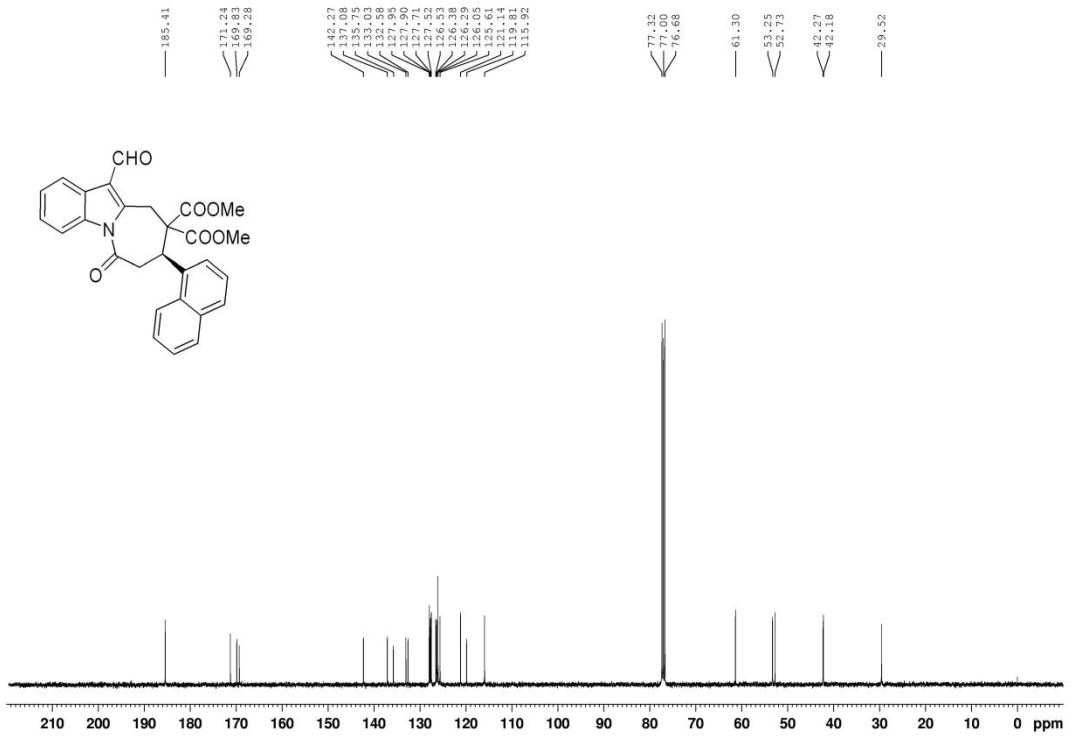
^{13}C NMR spectrum of compound **3l** ($CDCl_3$, 100 MHz)



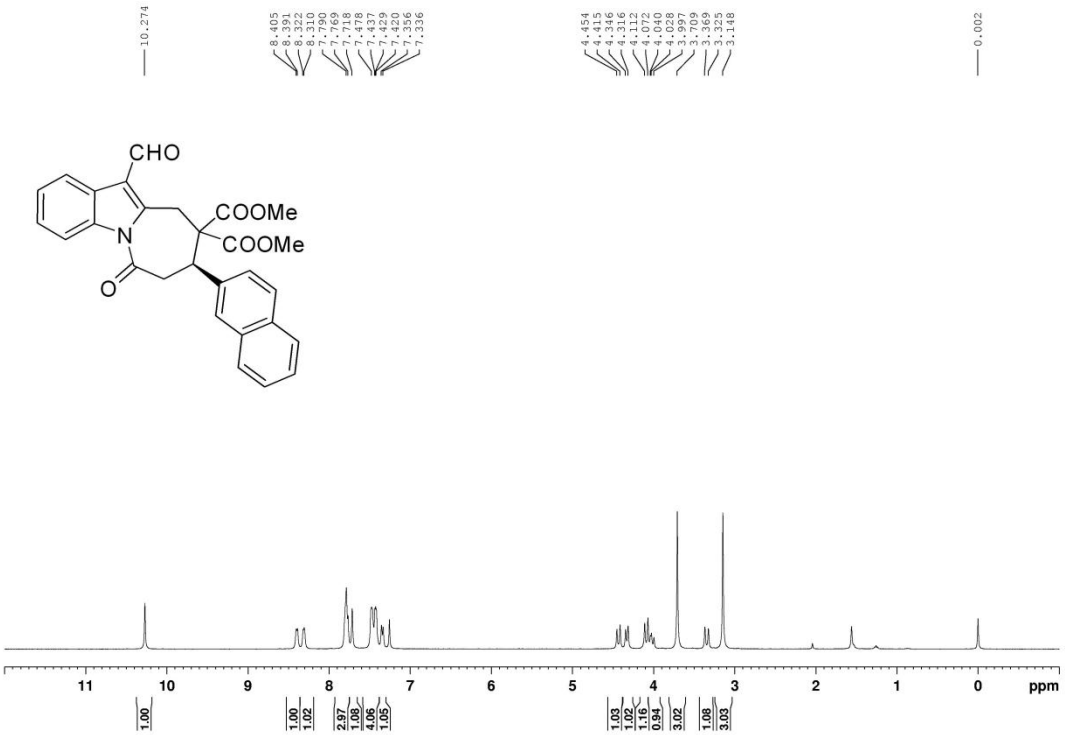
^{1}H NMR spectrum of compound **3m** ($CDCl_3$, 400 MHz)



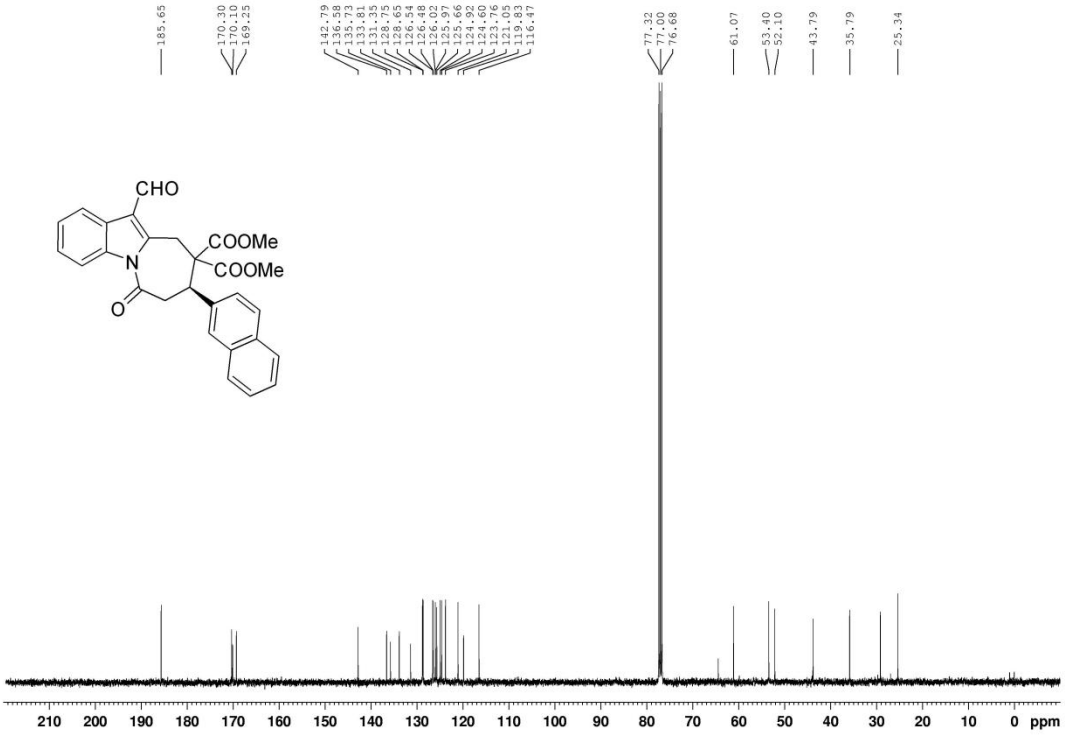
^{13}C NMR spectrum of compound **3m** ($CDCl_3$, 100 MHz)



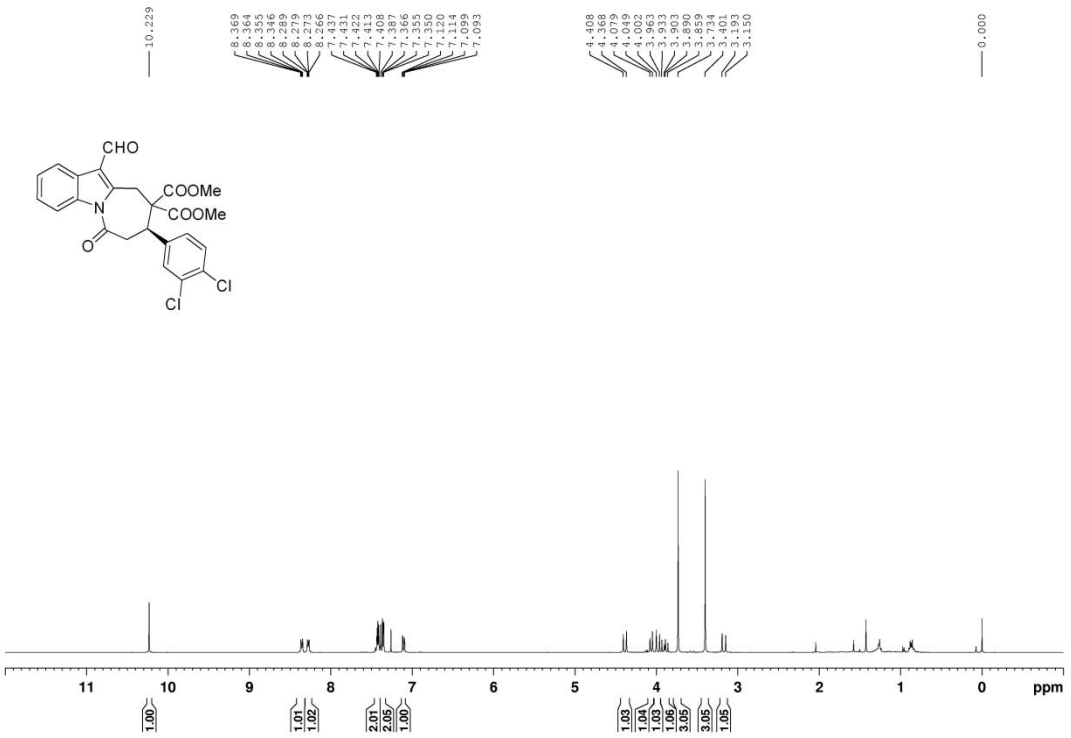
^{1}H NMR spectrum of compound **3n** ($CDCl_3$, 400 MHz)



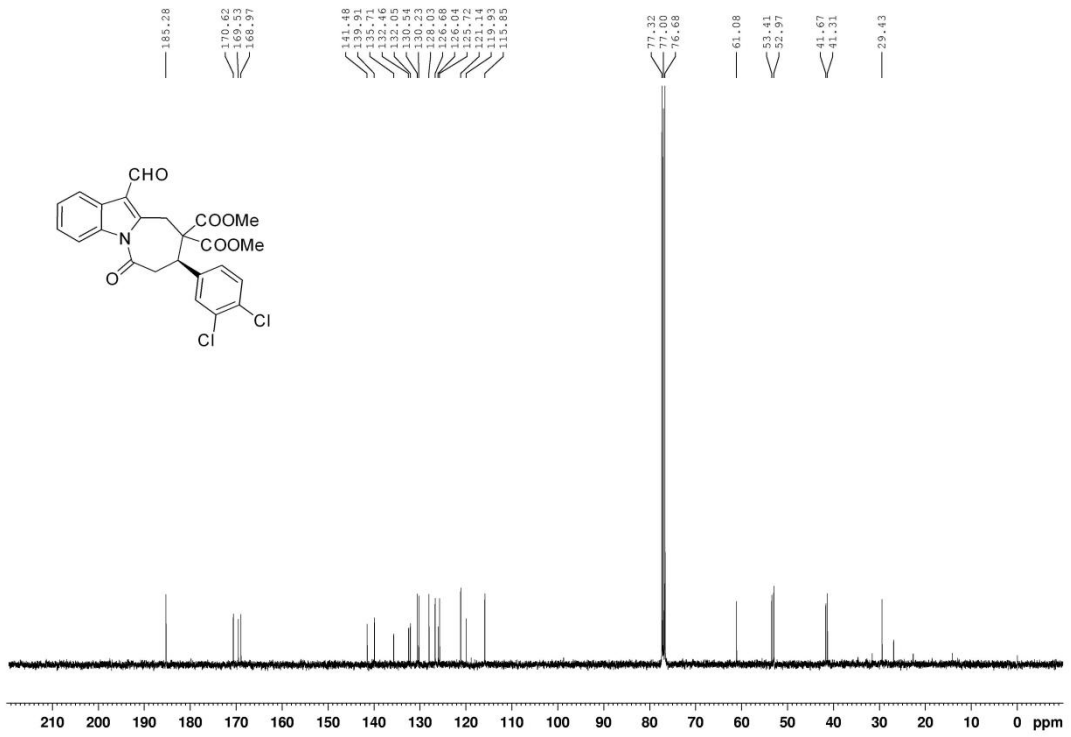
^{13}C NMR spectrum of compound **3n** ($CDCl_3$, 100 MHz)



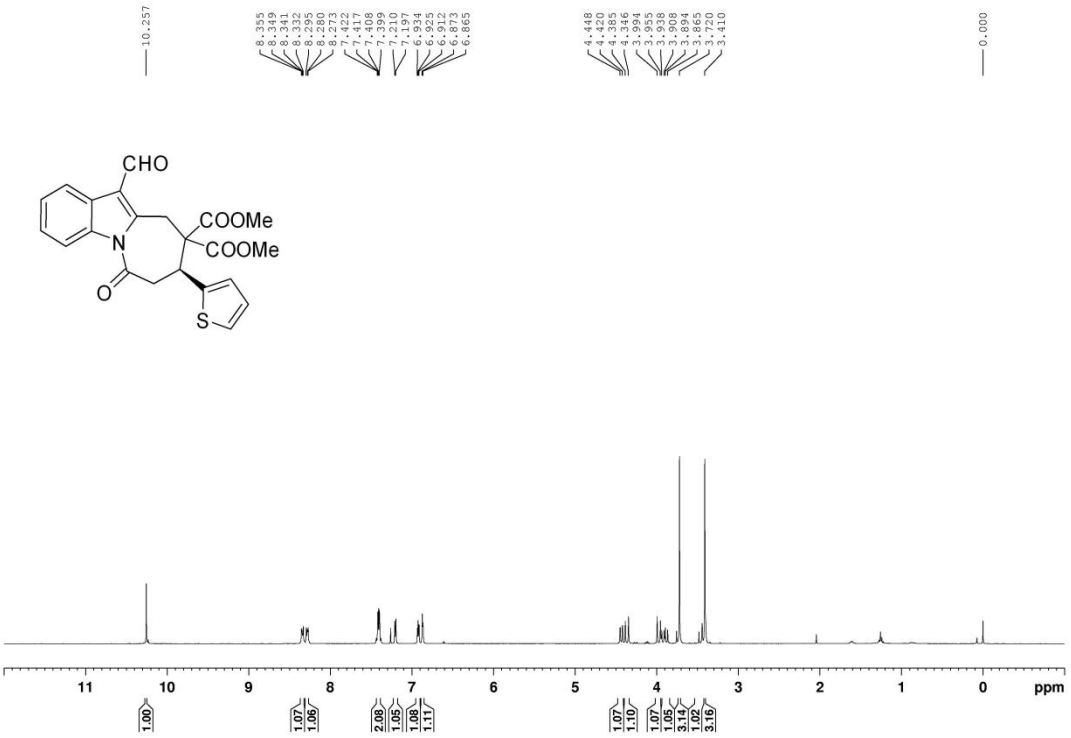
^{1}H NMR spectrum of compound **3o** ($CDCl_3$, 400 MHz)



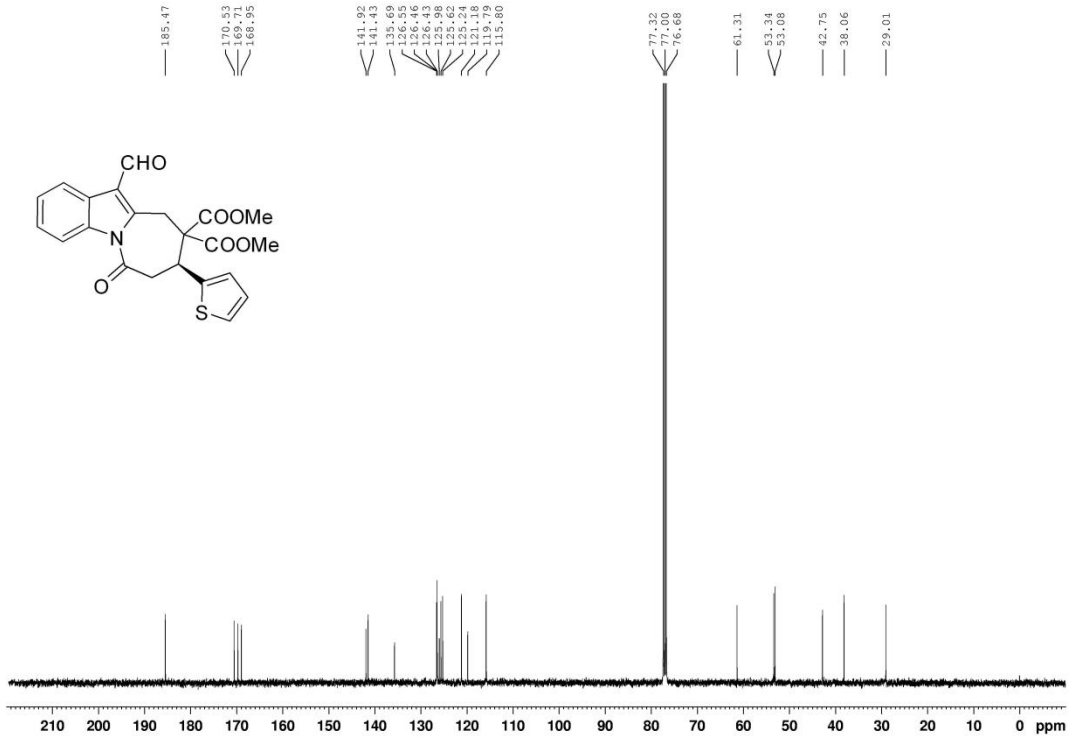
^{13}C NMR spectrum of compound **3o** ($CDCl_3$, 100 MHz)



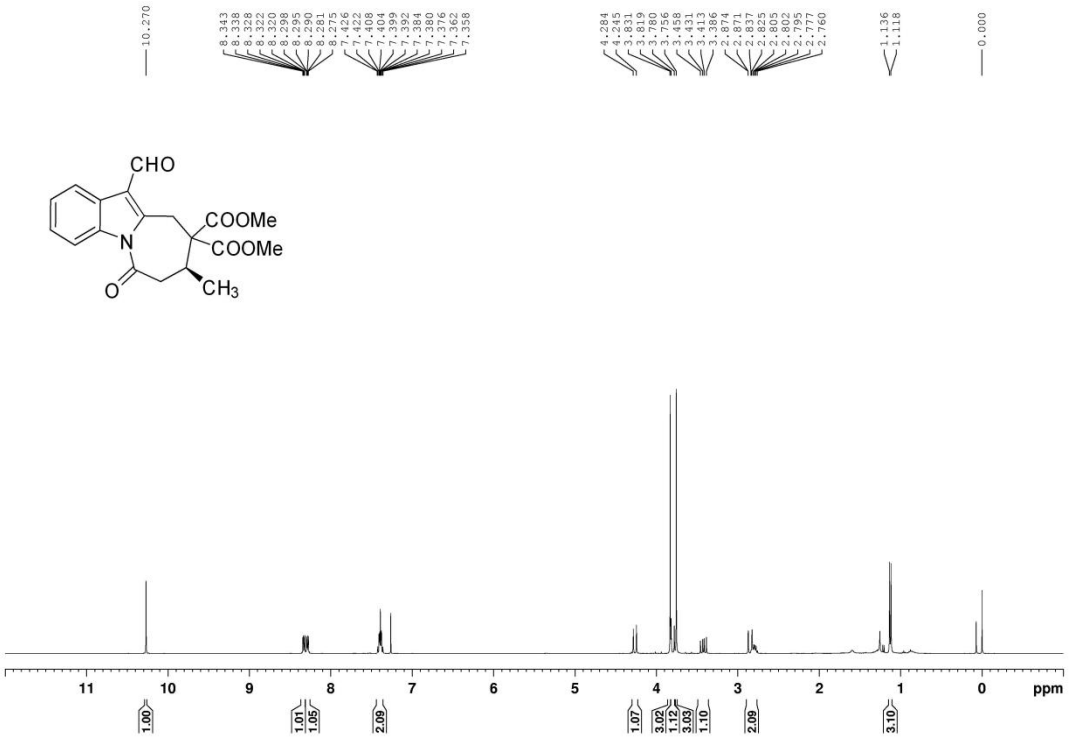
^{1}H NMR spectrum of compound **3p** ($CDCl_3$, 400 MHz)



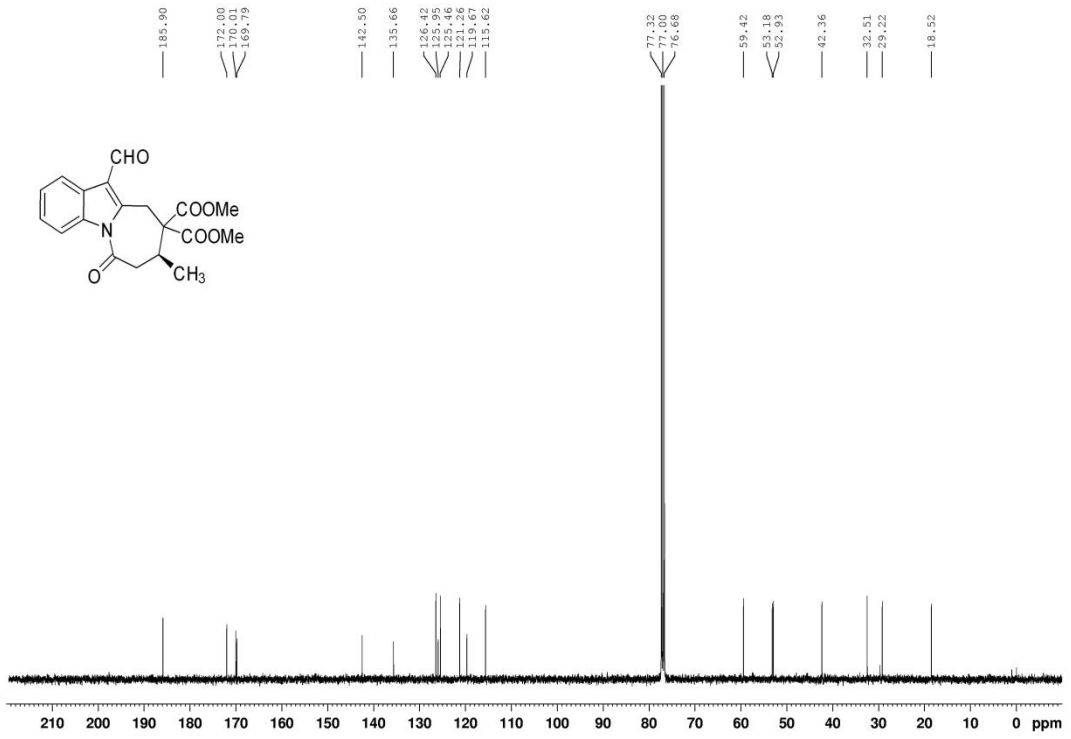
^{13}C NMR spectrum of compound **3p** ($CDCl_3$, 100 MHz)



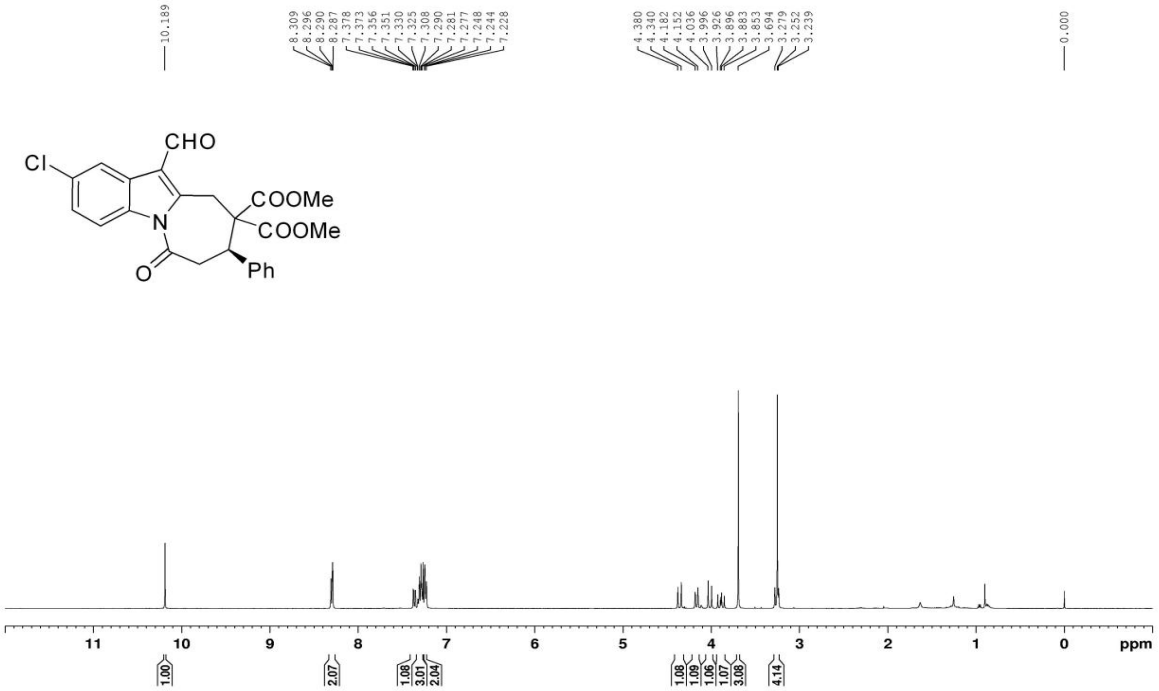
^{1}H NMR spectrum of compound **3q** ($CDCl_3$, 400 MHz)



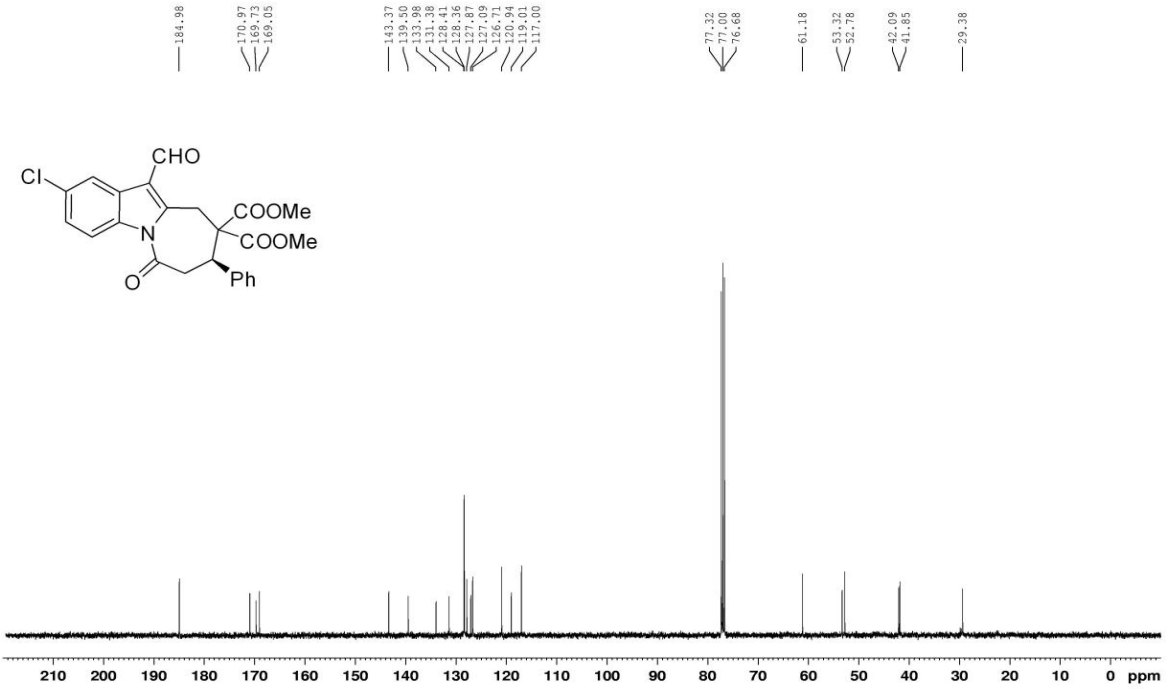
^{13}C NMR spectrum of compound **3q** ($CDCl_3$, 100 MHz)



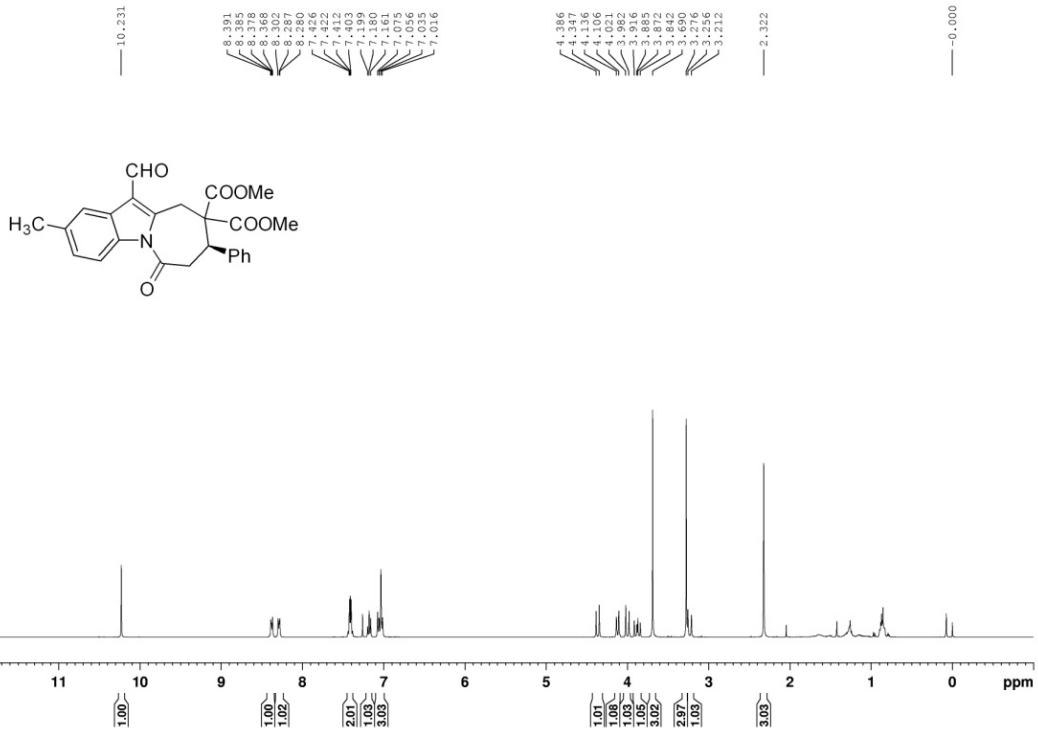
^{1}H NMR spectrum of compound **3s** ($CDCl_3$, 400 MHz)



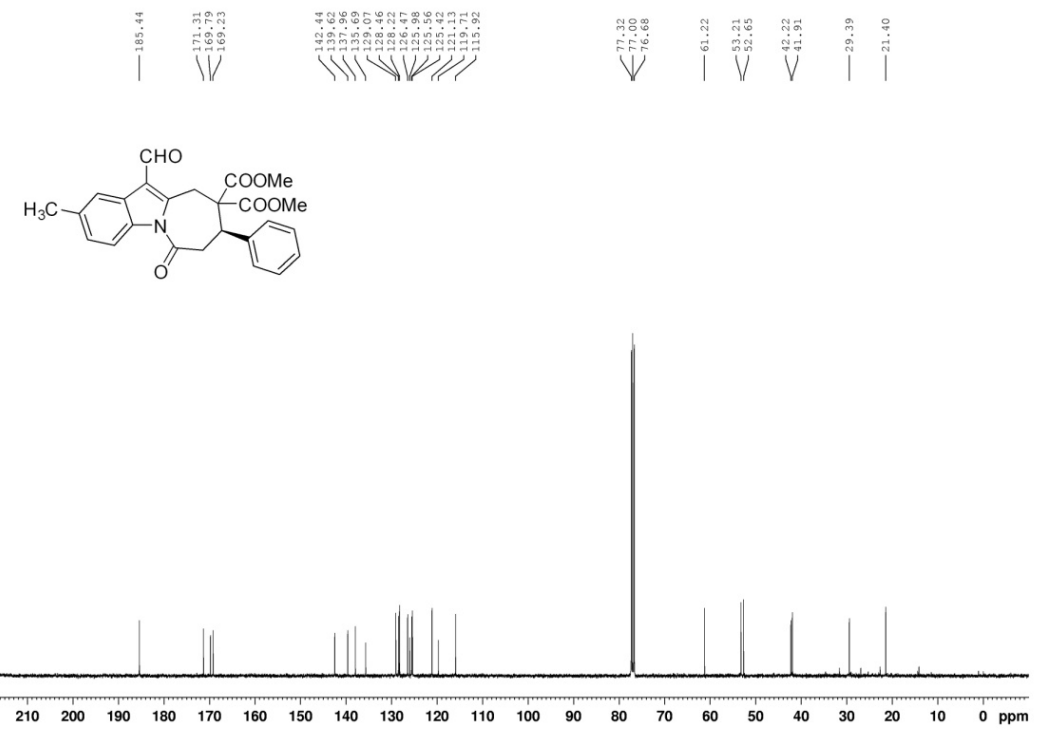
^{13}C NMR spectrum of compound **3s** ($CDCl_3$, 100 MHz)



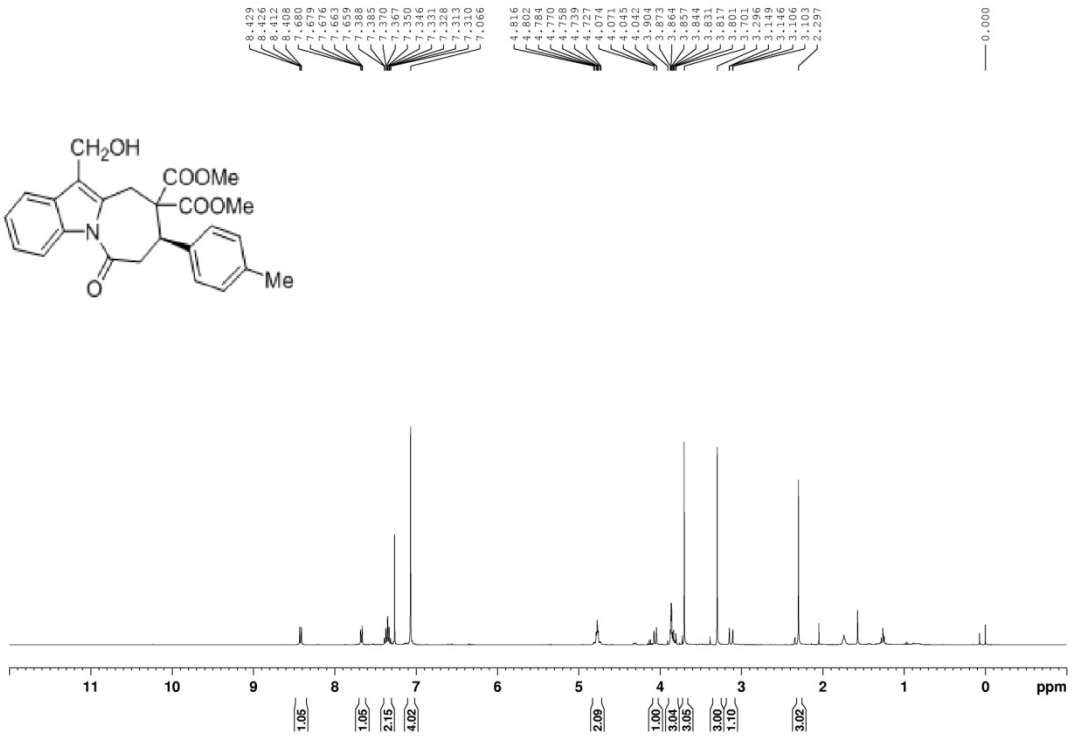
^{1}H NMR spectrum of compound **3t** ($CDCl_3$, 400 MHz)



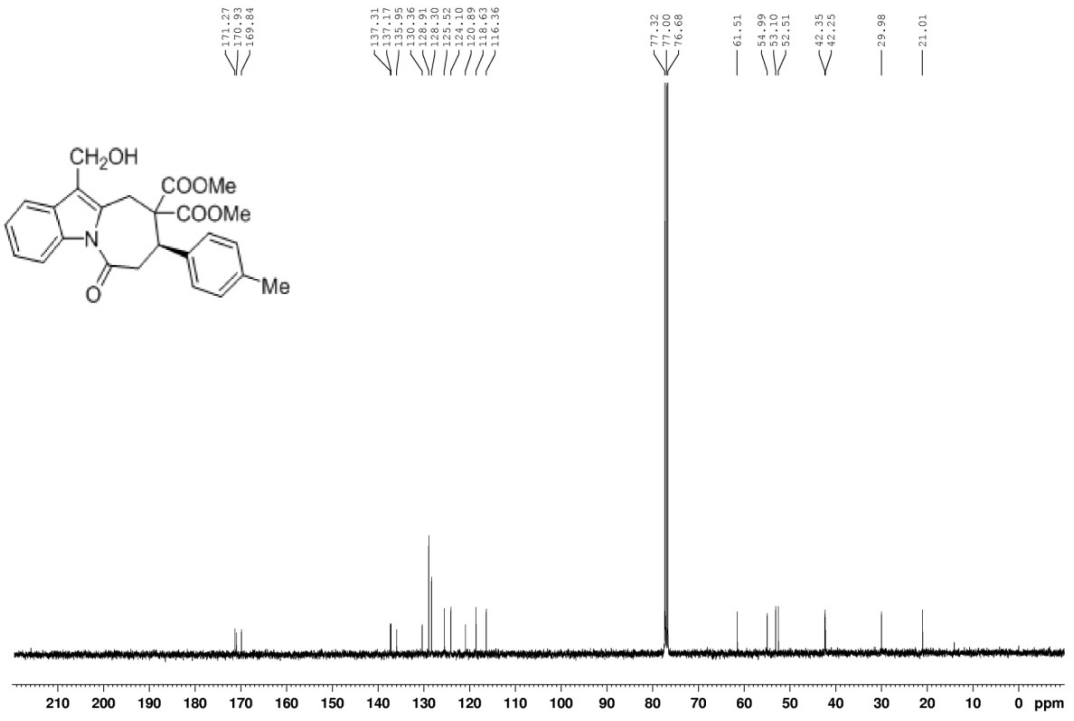
^{13}C NMR spectrum of compound **3t** ($CDCl_3$, 100 MHz)



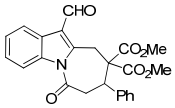
^{1}H NMR spectrum of compound **5** ($CDCl_3$, 400 MHz)



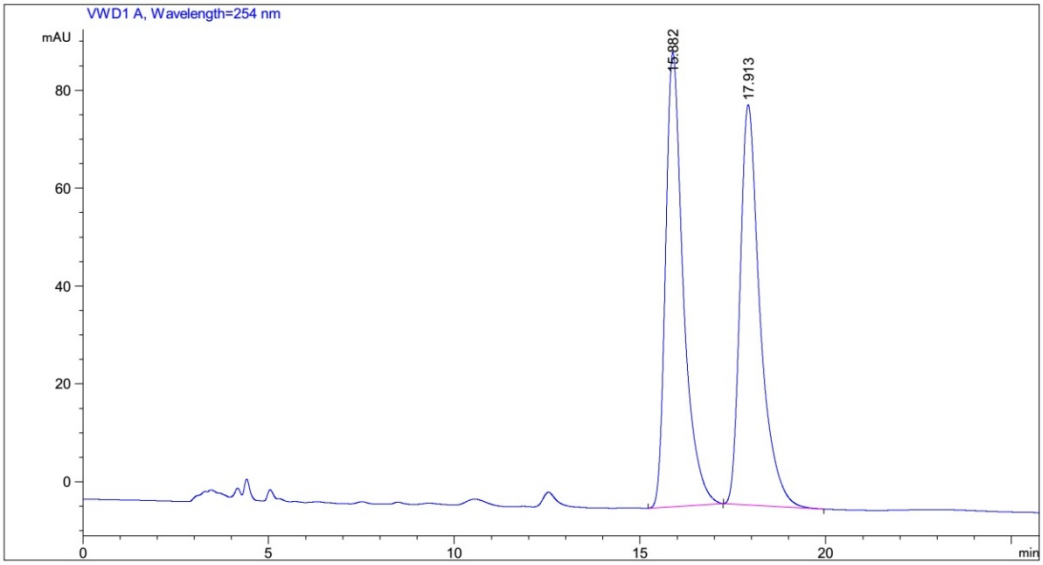
^{13}C NMR spectrum of compound **5** ($CDCl_3$, 100 MHz)



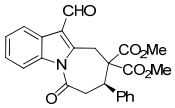
9. HPLC spectra for compounds 3a–3t and 5



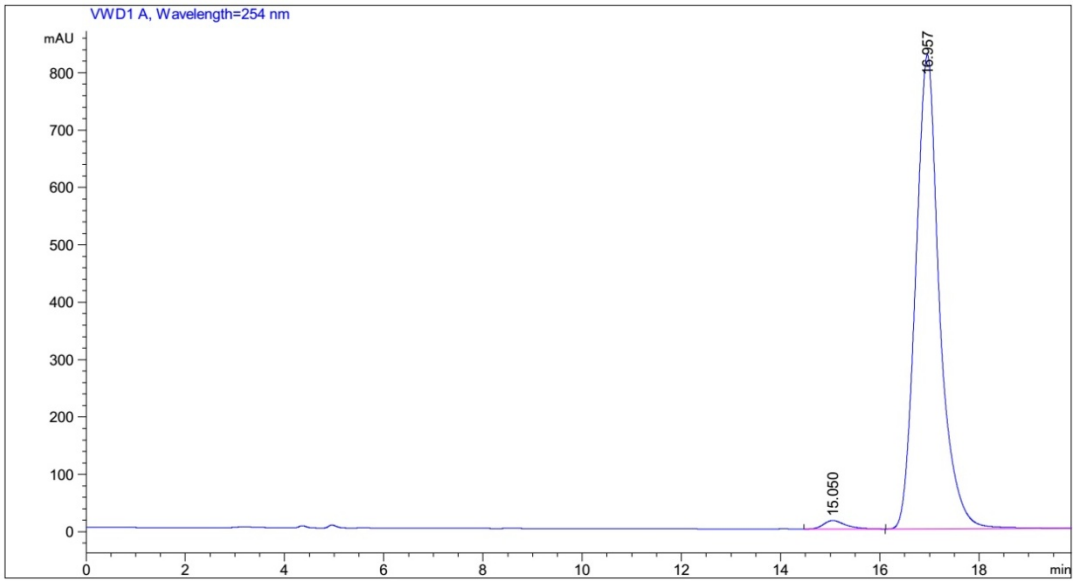
rac **3a**



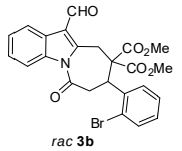
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	15.882	3079.31323	92.88444	50.20
2	PDA 254 nm	17.913	3054.67798	81.81023	49.80



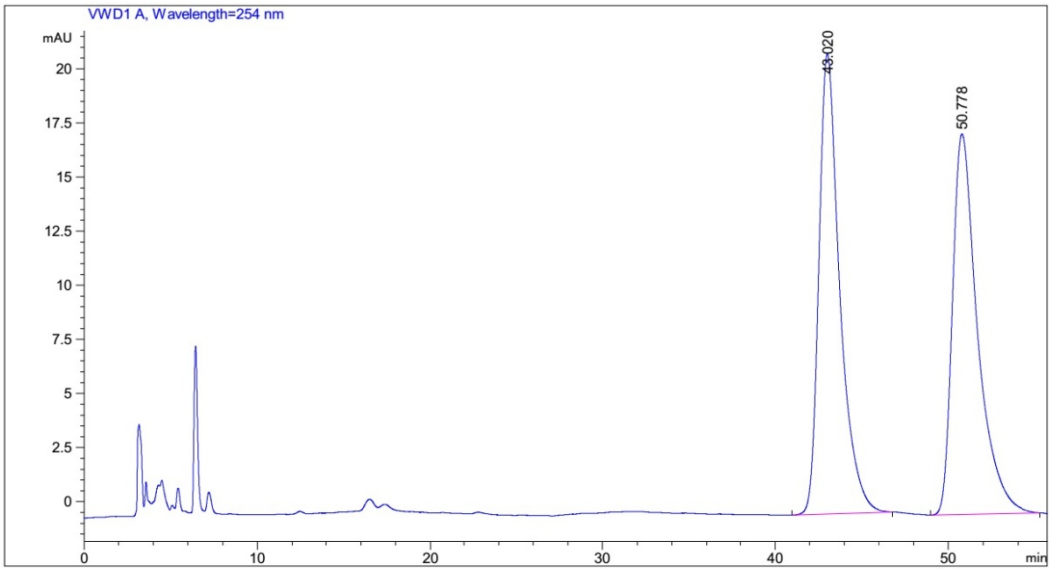
3a



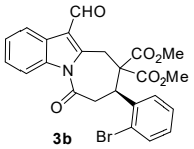
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	15.050	444.27975	14.66463	0.87
2	PDA 254 nm	16.957	2.75429e4	826.58057	99.13



rac **3b**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	43.020	1780.43250	21.27642	50.30
2	PDA 254 nm	50.778	1759.50159	17.59102	49.70



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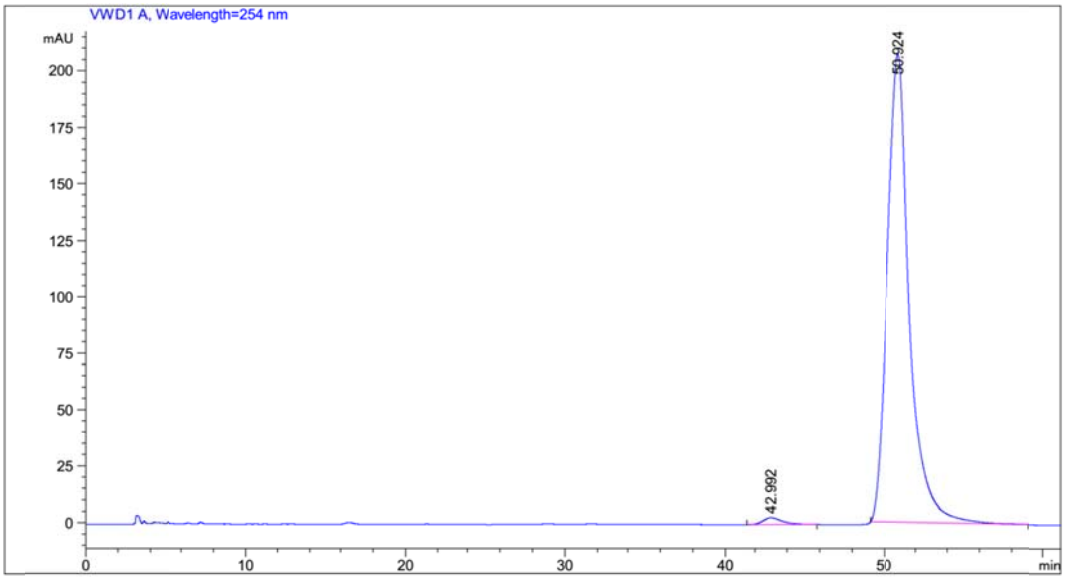
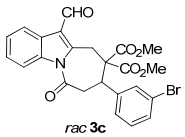
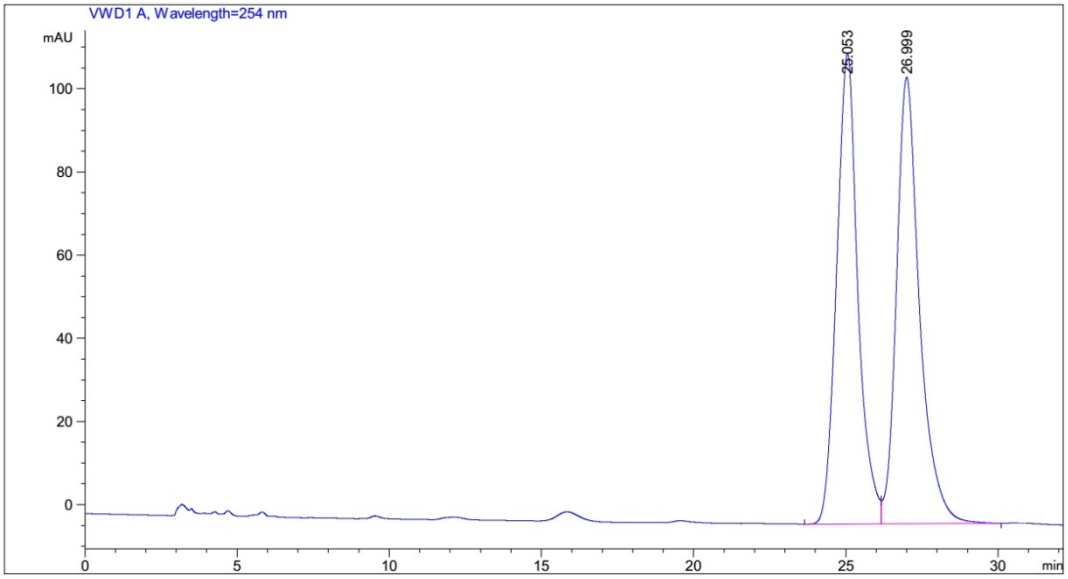


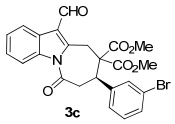
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	42.992	247.31979	3.00852	1.21
2	PDA 254 nm	50.924	2.01428e4	206.97060	98.79



rac **3c**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	25.053	5498.93164	113.13150	49.21
2	PDA 254 nm	26.999	5675.34619	107.40786	50.79



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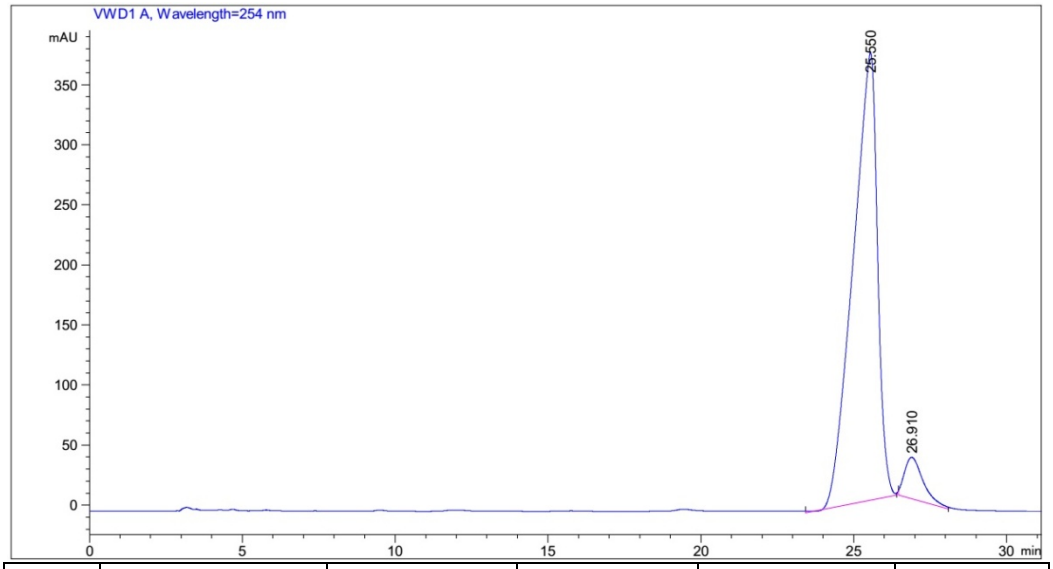
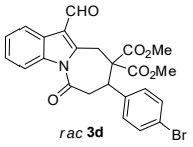
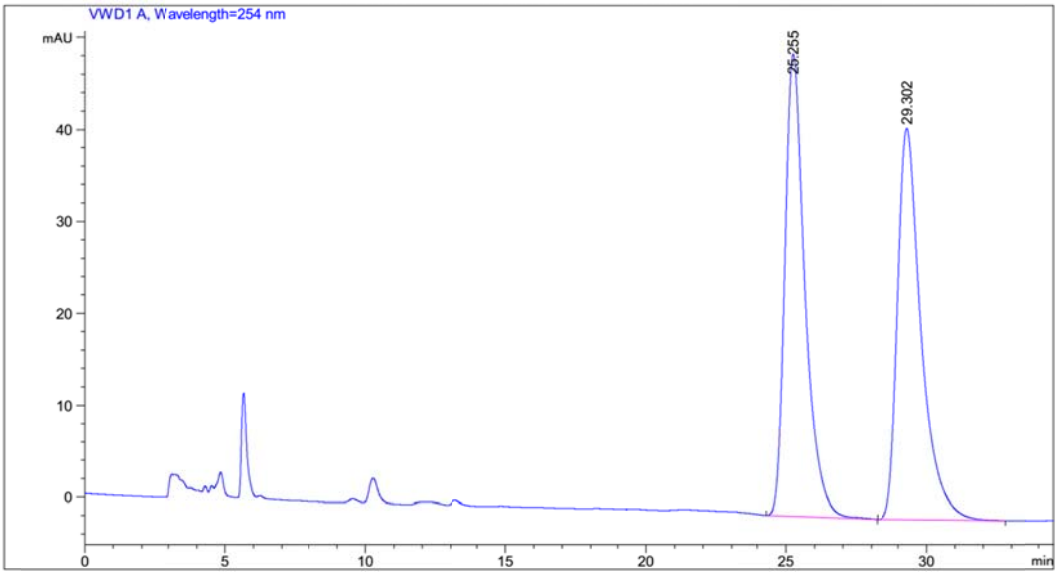


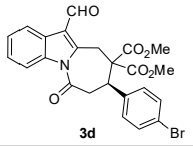
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	25.550	2.06855e4	372.51086	95.31
2	PDA 254 nm	26.910	1469.78088	34.62076	4.69



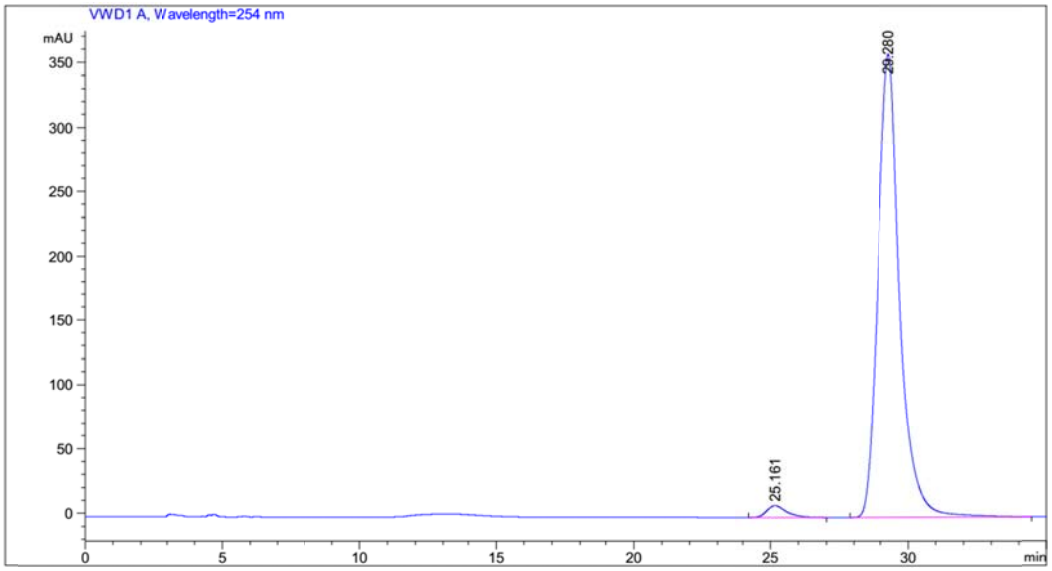
rac **3d**



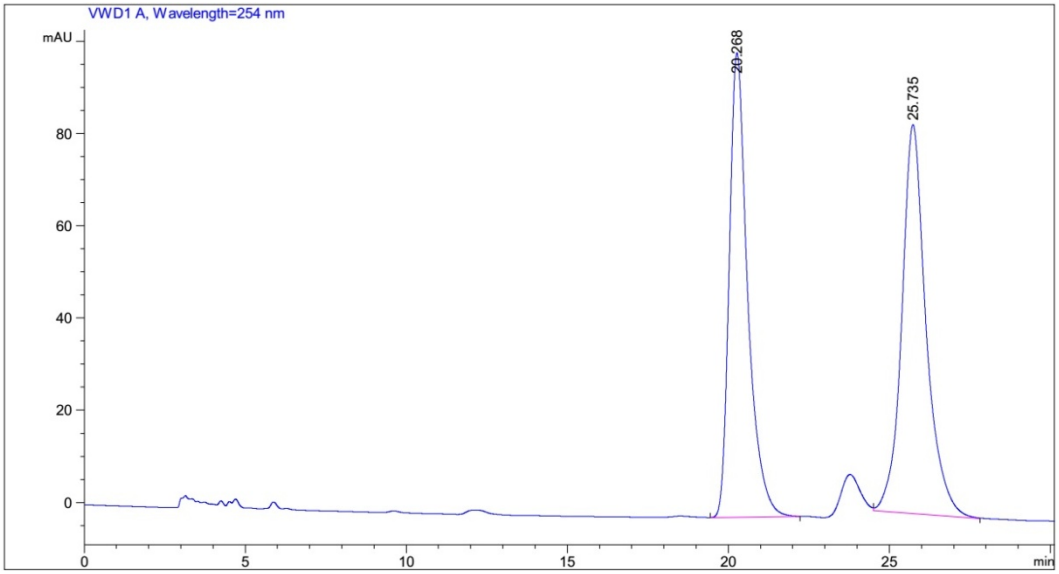
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	25.255	2462.05151	50.26923	49.88
2	PDA 254 nm	29.302	2474.18115	42.59083	50.12



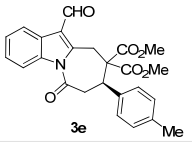
3d

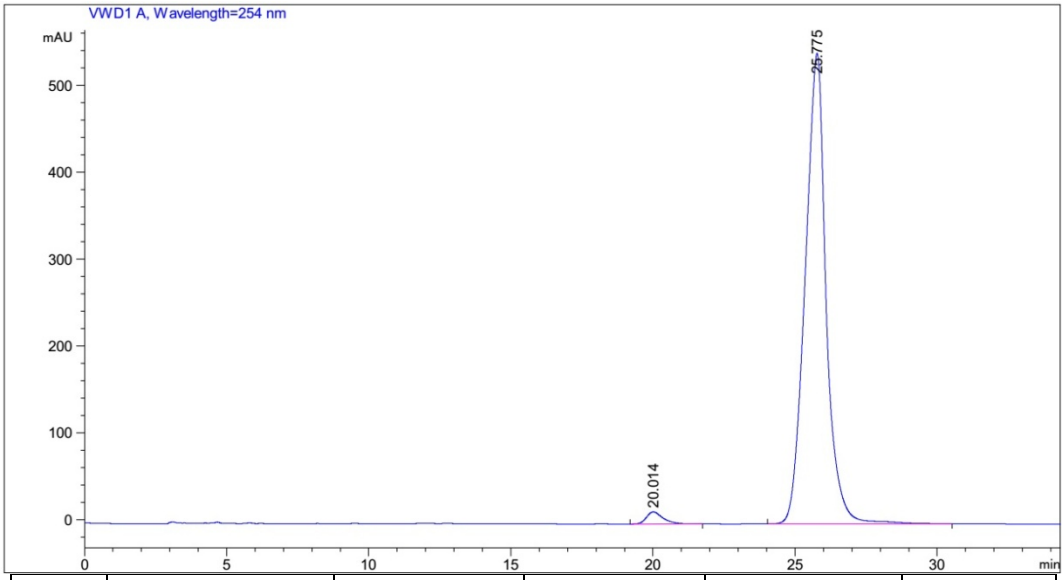


Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	25.161	444.90439	9.11667	2.14
2	PDA 254 nm	29.280	2.02676e4	359.26944	97.86

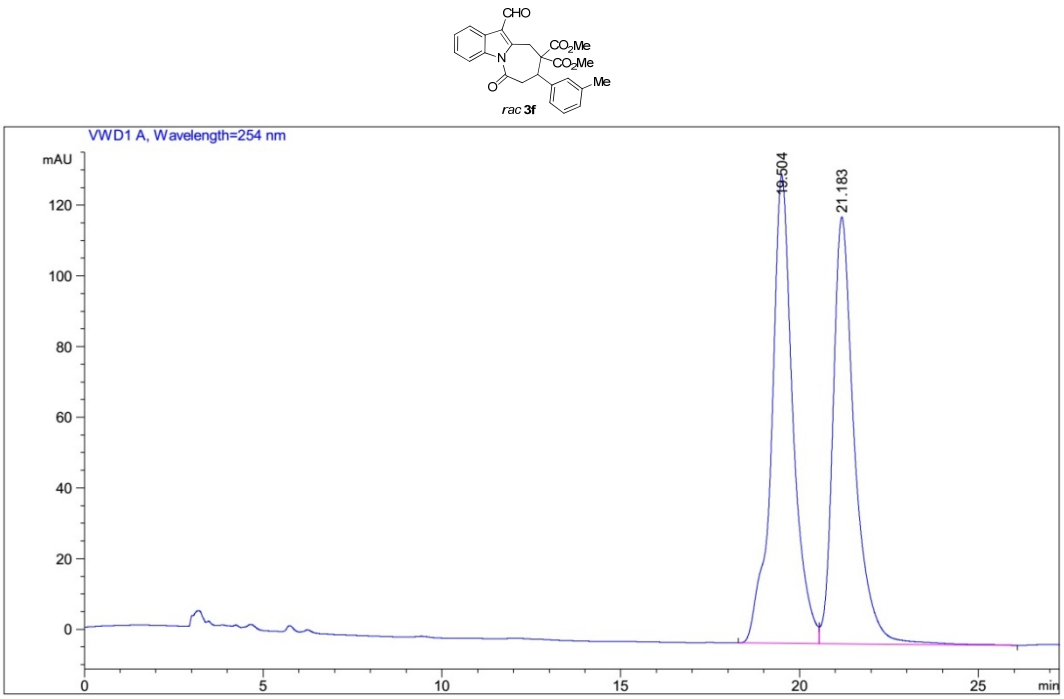


Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	20.268	3995.37817	100.64333	47.44
2	PDA 254 nm	25.735	4425.96680	84.38345	52.56

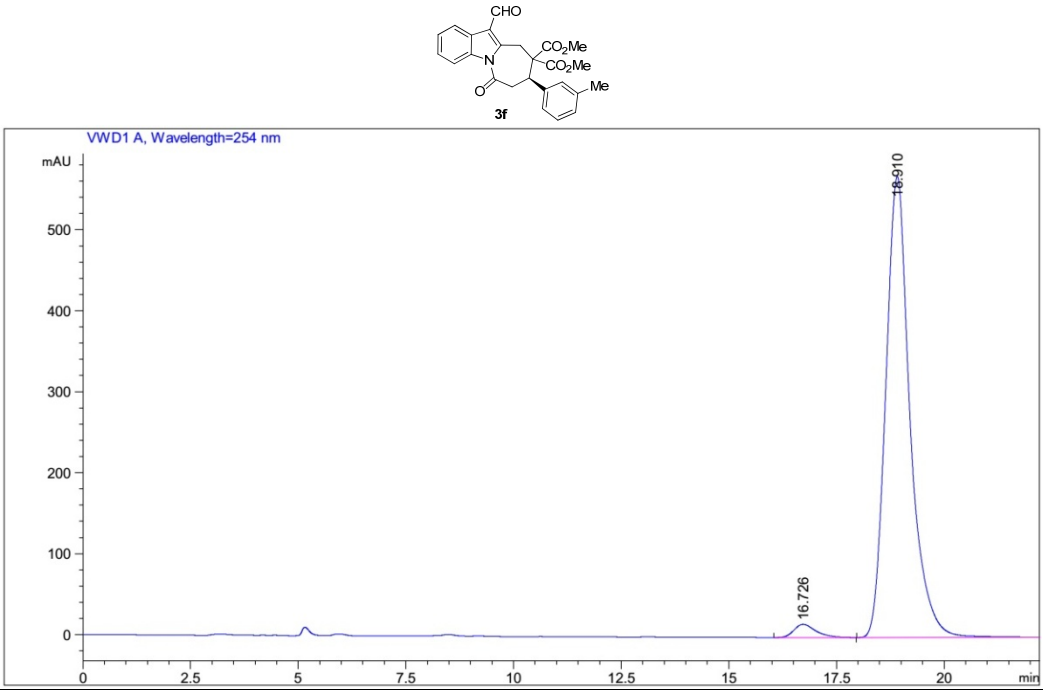




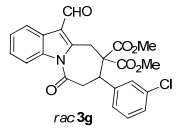
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	20.014	564.96466	13.92814	1.44
2	PDA 254 nm	25.775	2.77108e4	541.39917	98.56



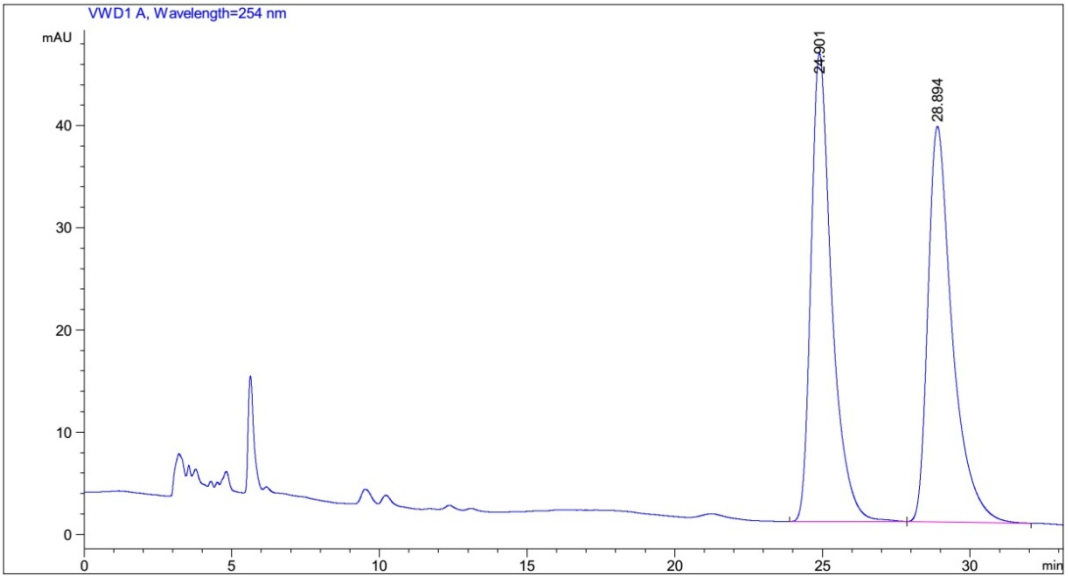
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	19.504	5508.10547	132.38724	52.04
2	PDA 254 nm	21.183	5075.58203	120.76781	47.96



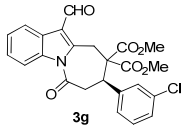
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	16.726	579.63678	16.30833	2.04
2	PDA 254 nm	18.910	2.22229e4	569.15881	97.96



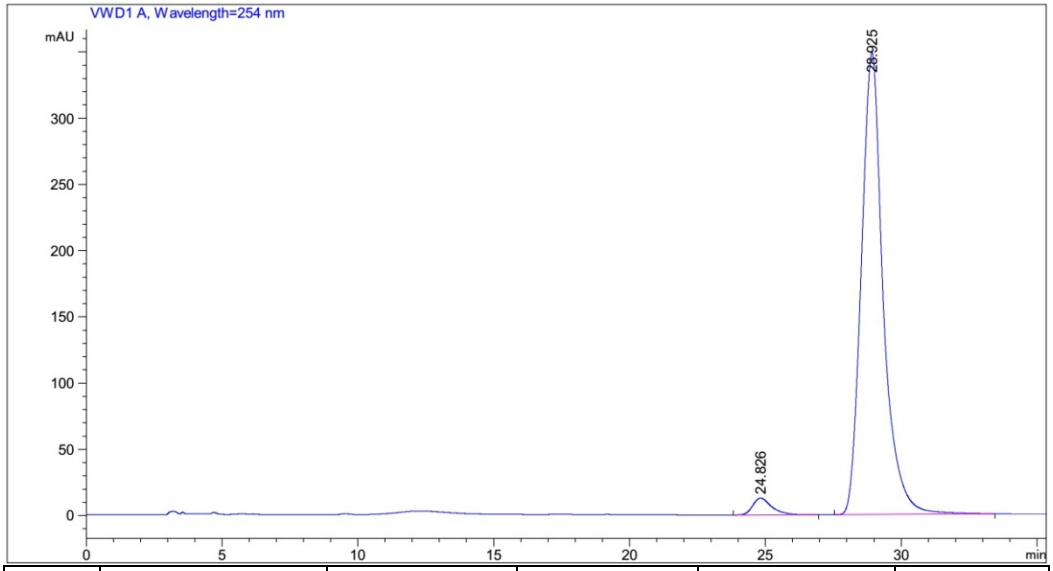
rac **3g**



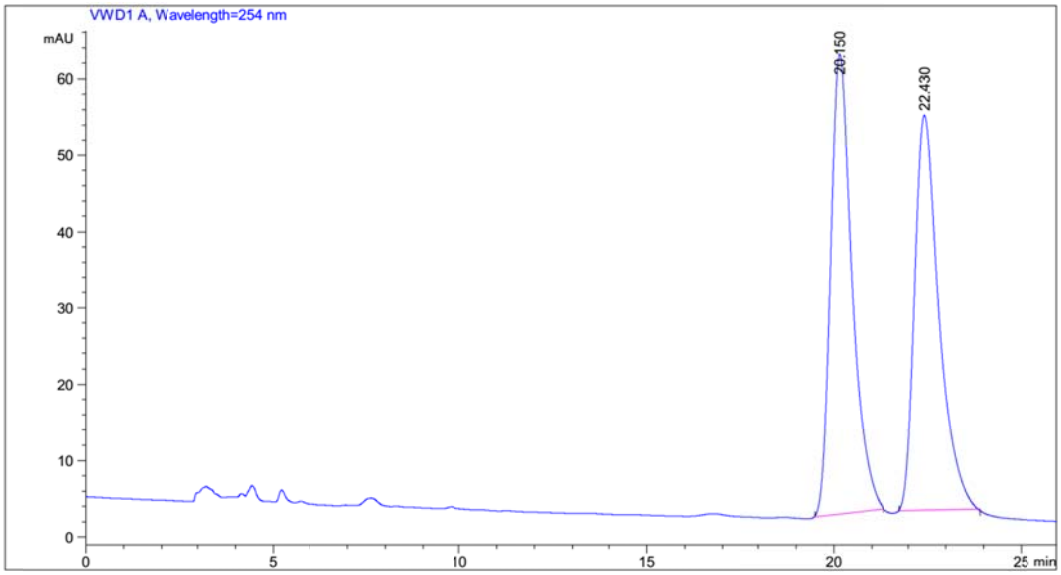
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	24.901	2239.90234	45.81277	50.13
2	PDA 254 nm	28.894	2228.58105	38.72662	49.87



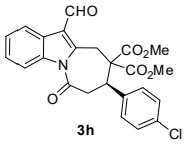
3g



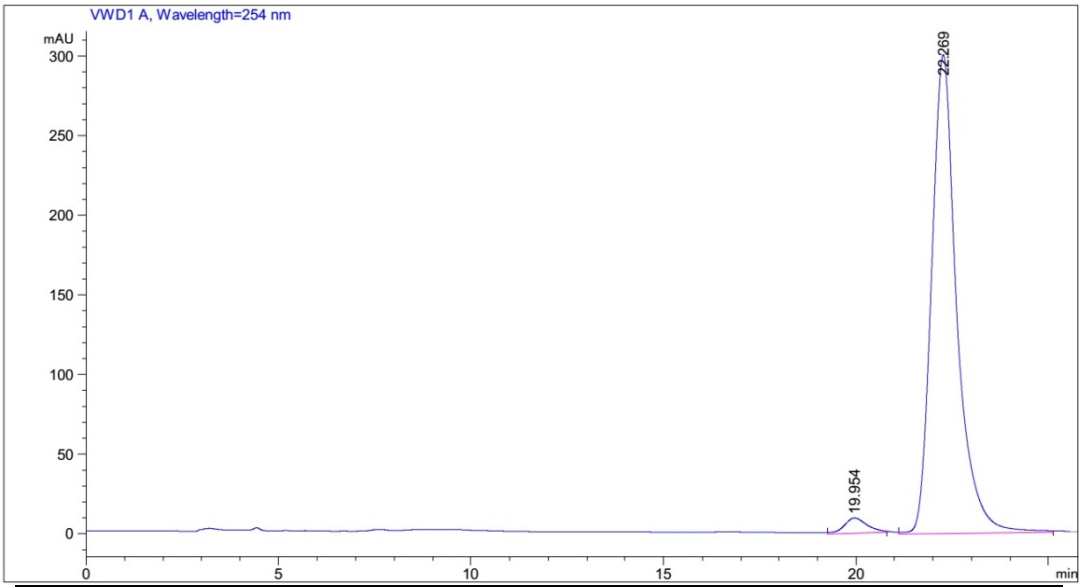
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	24.826	613.99811	12.67376	2.06
2	PDA 254 nm	28.925	1.94936e4	348.95114	97.94



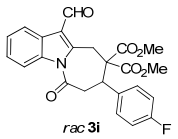
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	20.150	2346.76123	60.17454	50.24
2	PDA 254 nm	22.430	2352.74219	51.75787	49.76



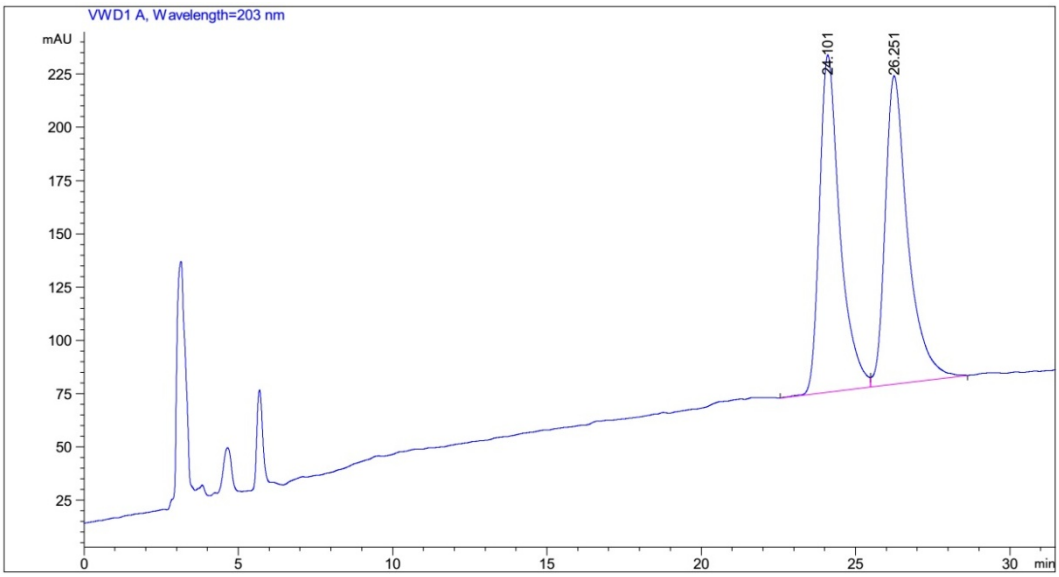
3h



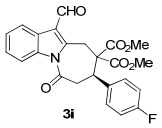
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	19.954	395.56198	9.58714	2.16
2	PDA 254 nm	22.269	1.35730e4	300.62967	97.84



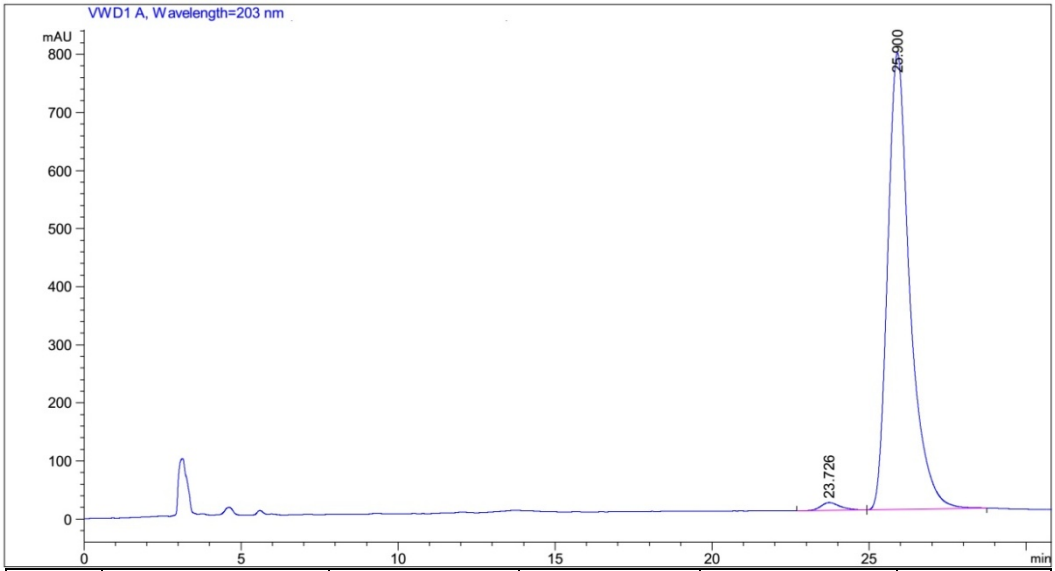
rac **3i**



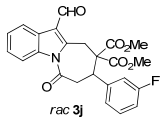
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	24.101	7289.02051	158.31729	49.57
2	PDA 254 nm	26.251	7416.65381	144.73343	50.43



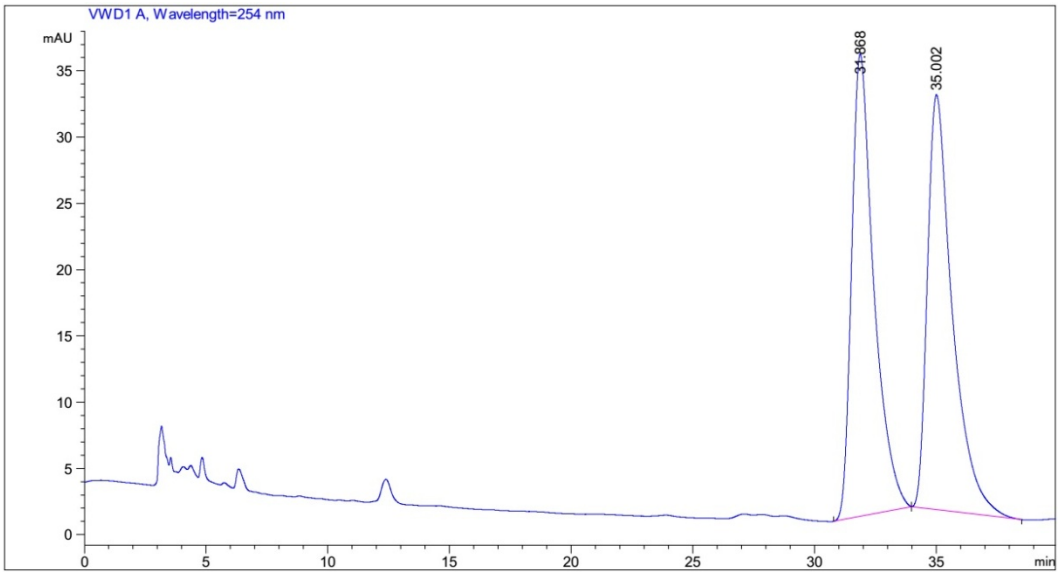
3i



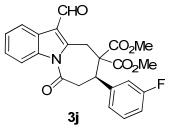
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	23.726	577.18036	13.49769	1.47
2	PDA 254 nm	25.900	3.85929e4	786.30078	98.53



rac **3j**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	31.868	2213.85840	34.88191	49.79
2	PDA 254 nm	35.002	2232.61011	31.30276	50.21



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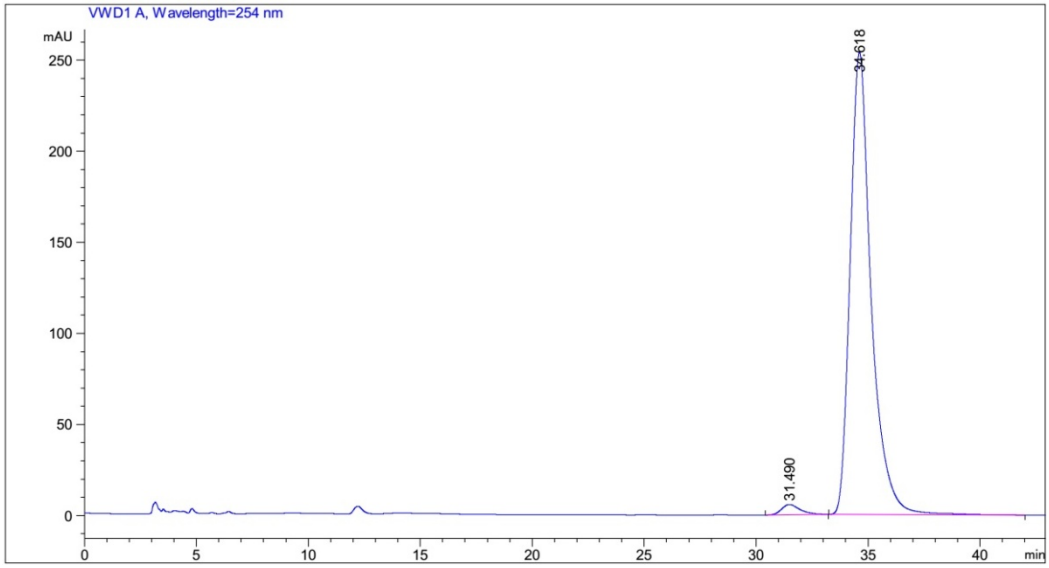
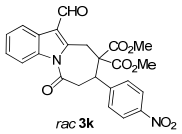
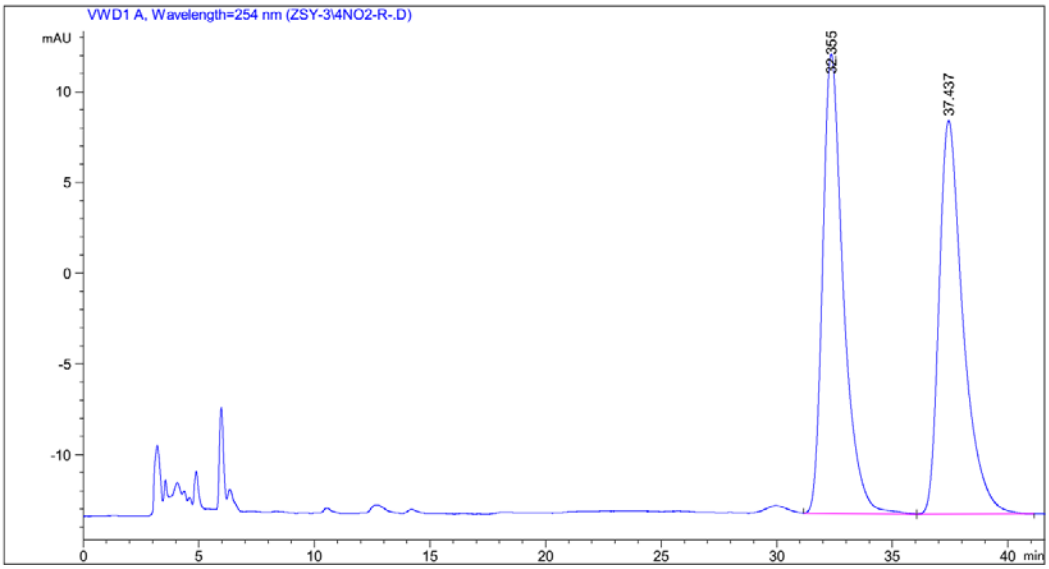


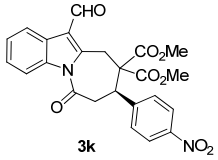
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	31.490	321.31934	5.59857	1.90
2	PDA 254 nm	34.618	1.65543e4	253.69046	98.10



rac **3k**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	32.355	1571.88513	25.31546	50.10
2	PDA 254 nm	37.437	1565.37329	21.69898	49.87



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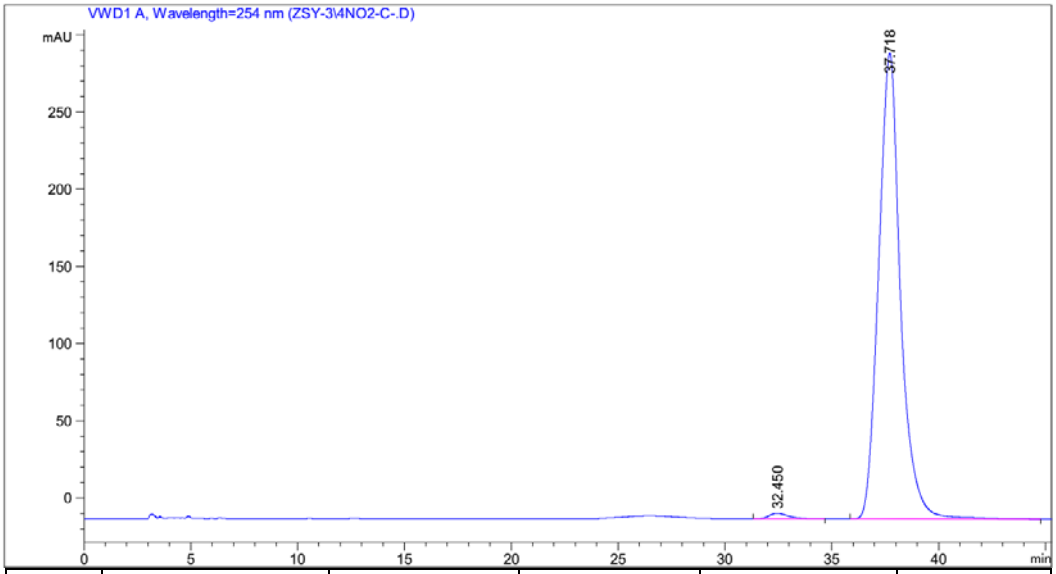
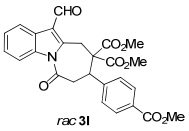
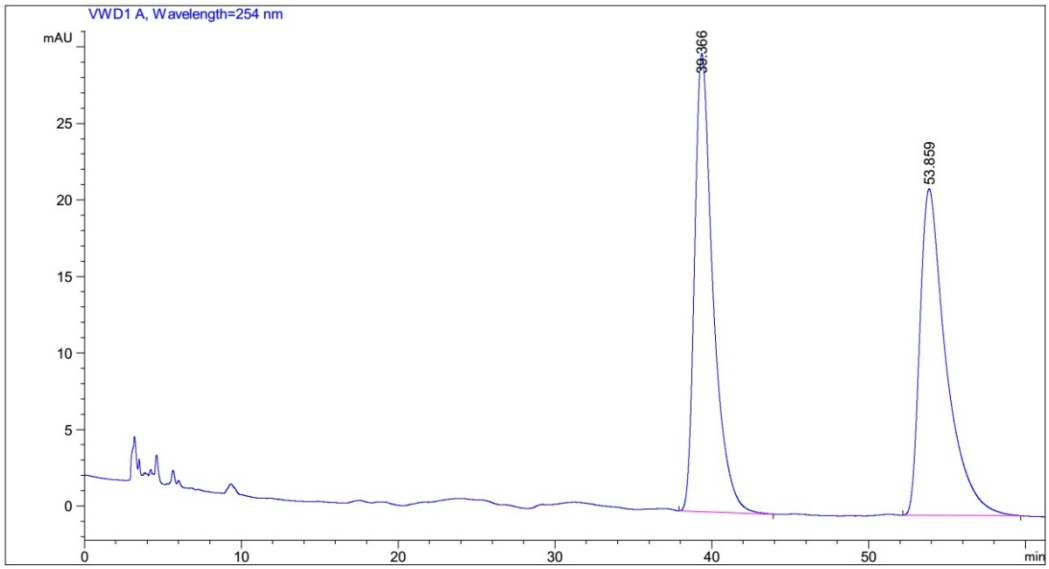


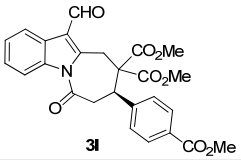
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	32.450	225.65536	3.63144	1.04
2	PDA 254 nm	37.718	2.14416e4	301.75464	98.96



rac **3l**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	39.366	2449.46362	29.93681	49.75
2	PDA 254 nm	53.859	2474.37280	21.33892	50.25



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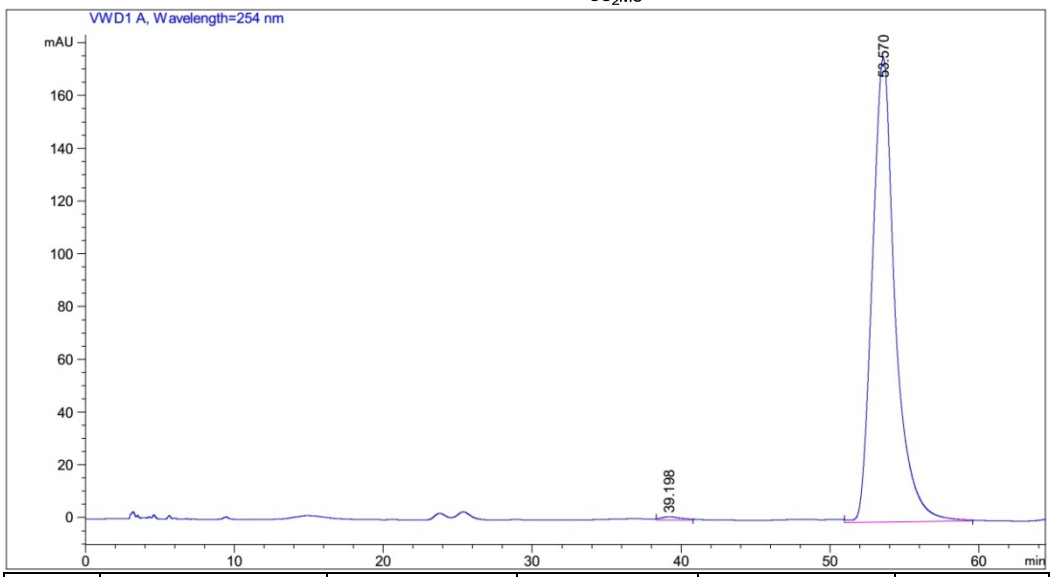
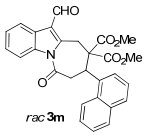
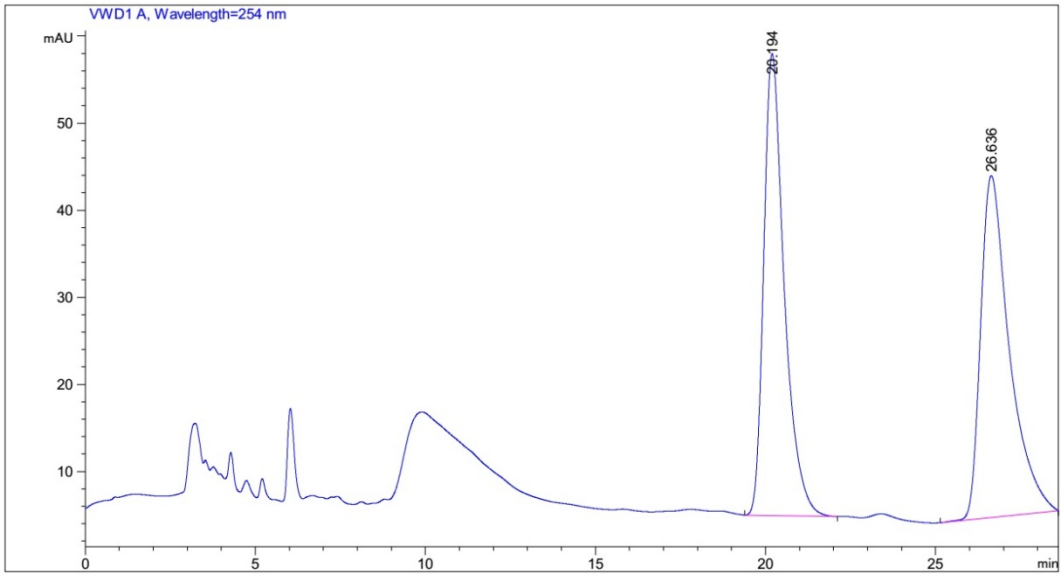
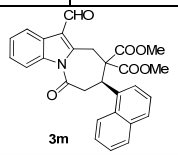


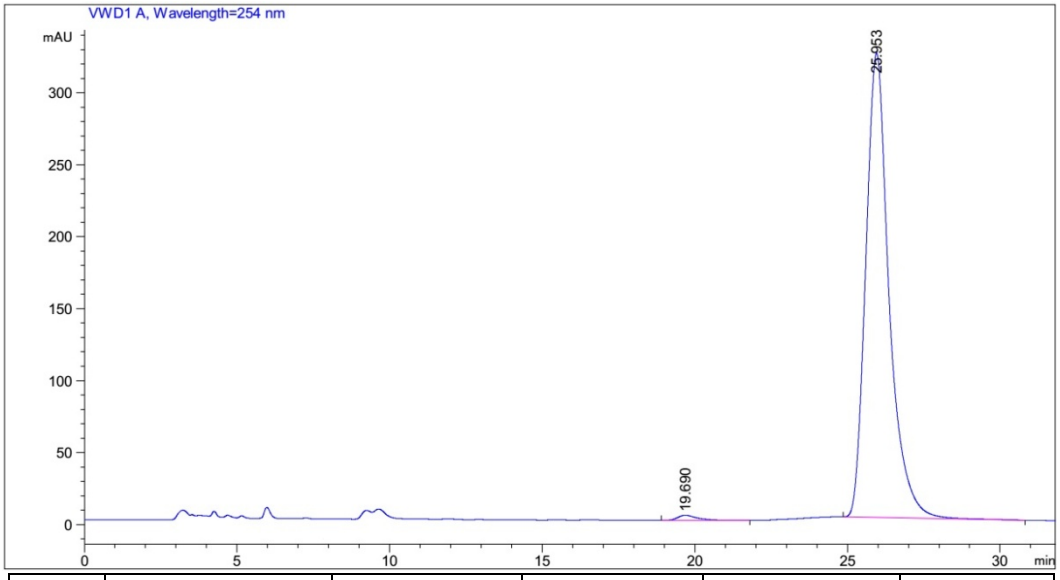
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	39.198	107.69574	1.19247	0.42
2	PDA 254 nm	53.570	1.87283e4	176.03407	99.58



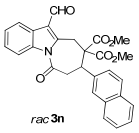


Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	20.194	2226.10034	53.03053	49.16
2	PDA 254 nm	26.636	2302.19238	39.28353	50.84

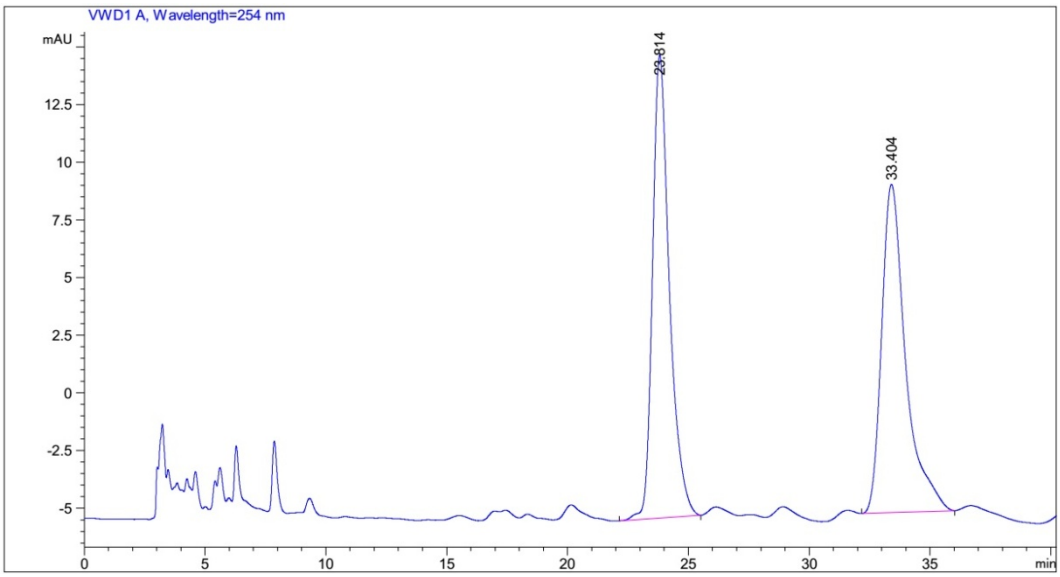




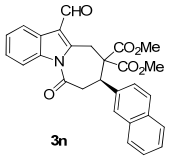
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	19.690	162.69215	3.56492	0.94
2	PDA 254 nm	25.953	1.70973e4	322.83136	99.06



rac **3n**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	23.814	976.73474	20.06803	49.96
2	PDA 254 nm	33.404	978.22925	14.22949	50.04



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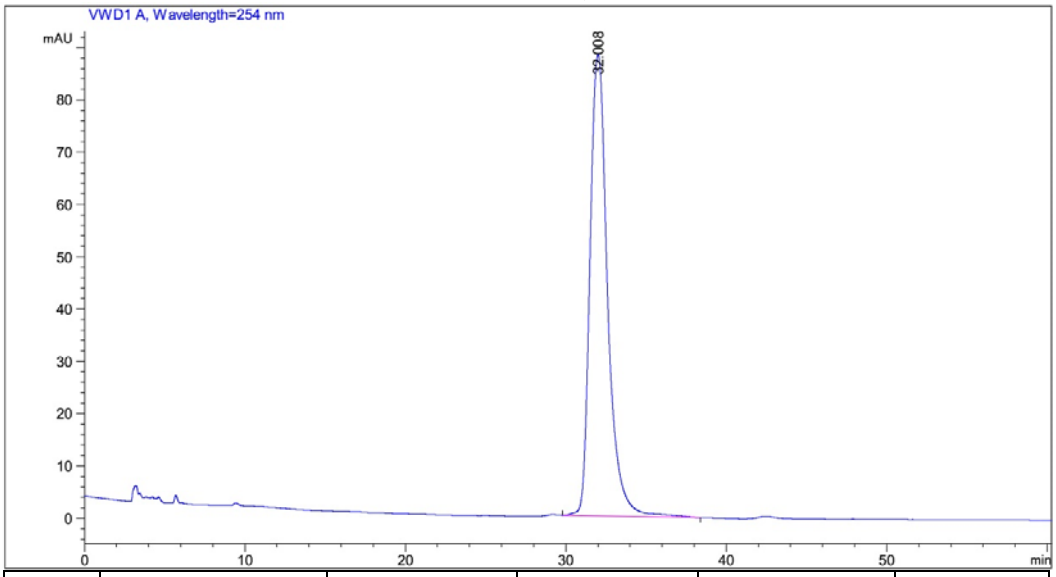
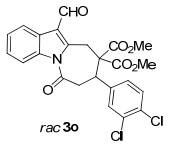
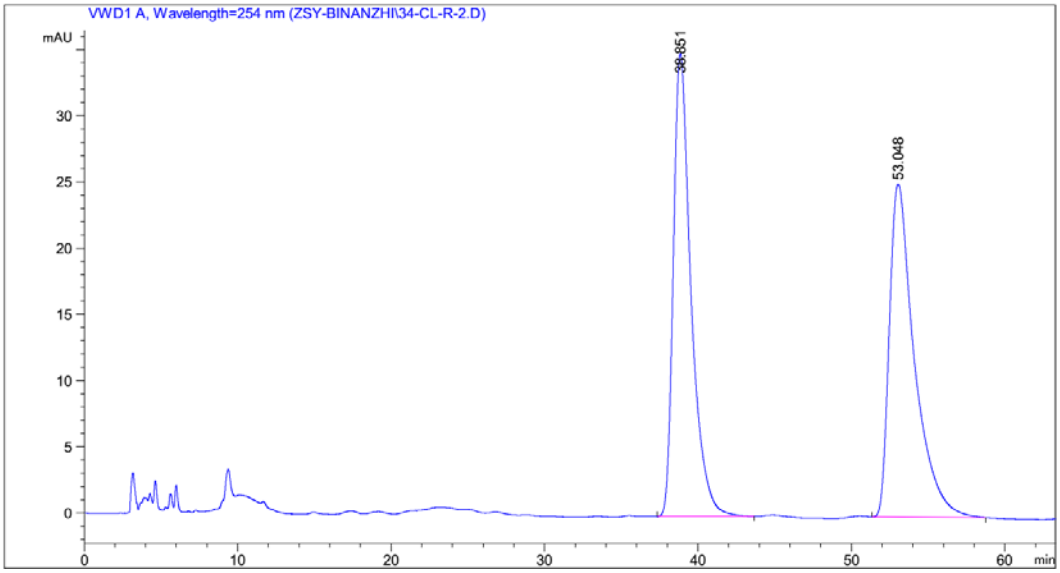


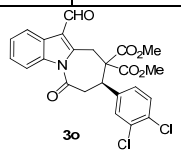
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	32.008	6735.25391	88.27187	100.00



rac **3o**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	38.851	2804.87915	35.01058	49.54
2	PDA 254 nm	53.048	2856.76245	25.16640	50.46



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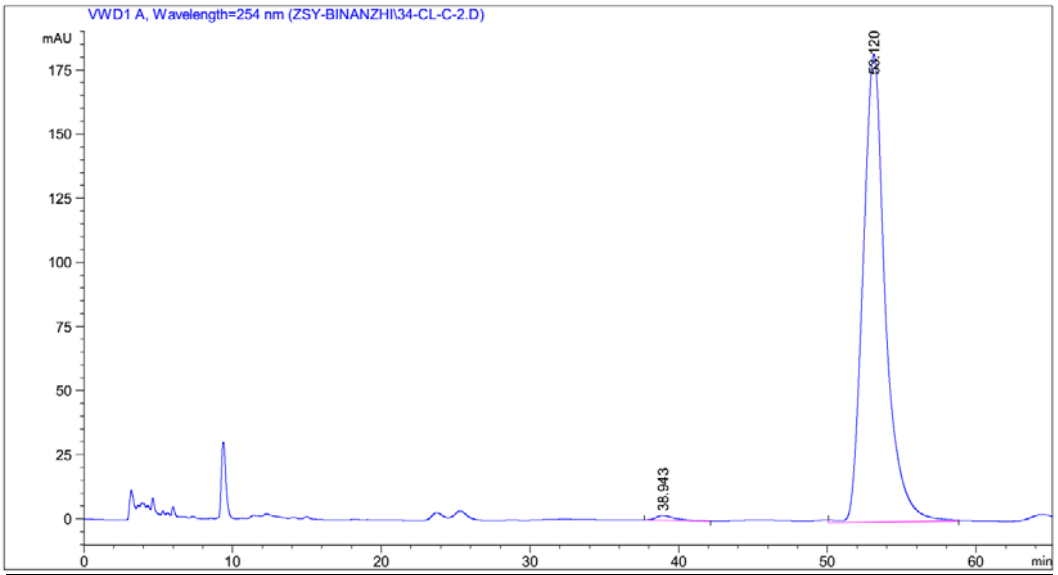
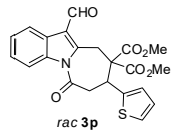
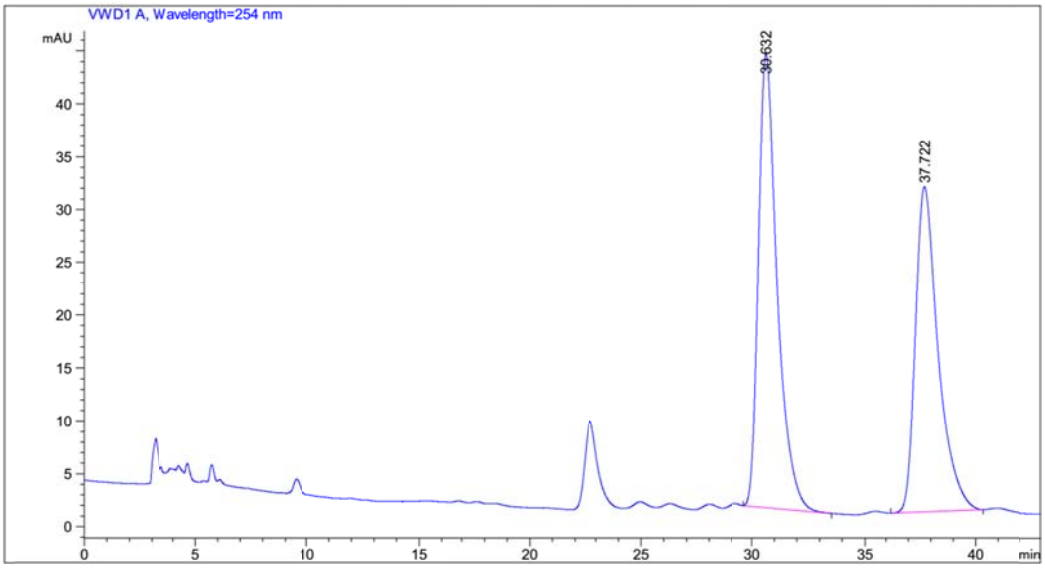


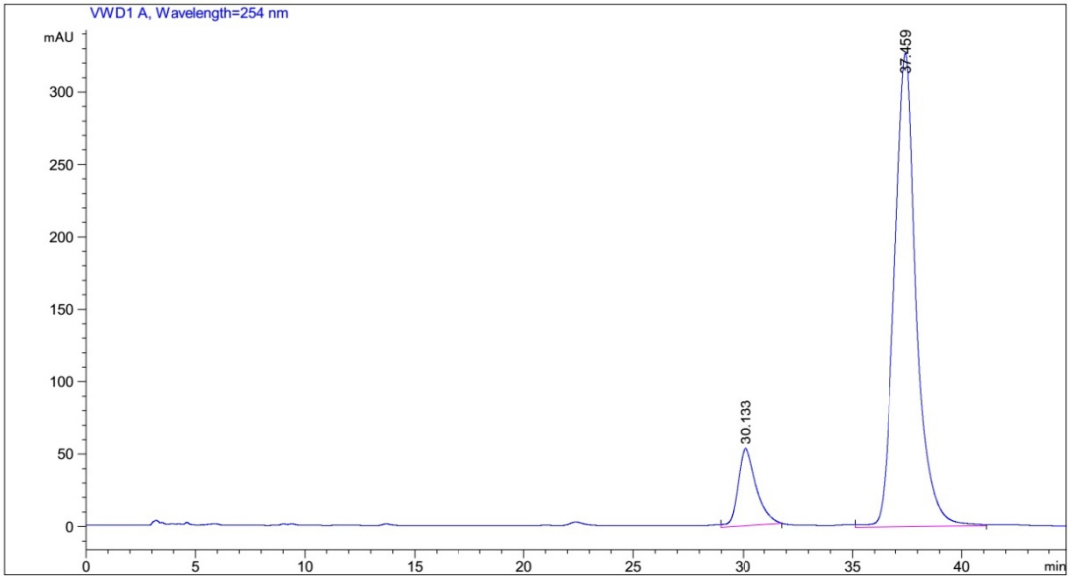
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	38.943	154.92036	1.87085	0.81
2	PDA 254 nm	53.120	1.90304e4	182.34341	99.19



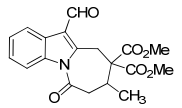
rac **3p**



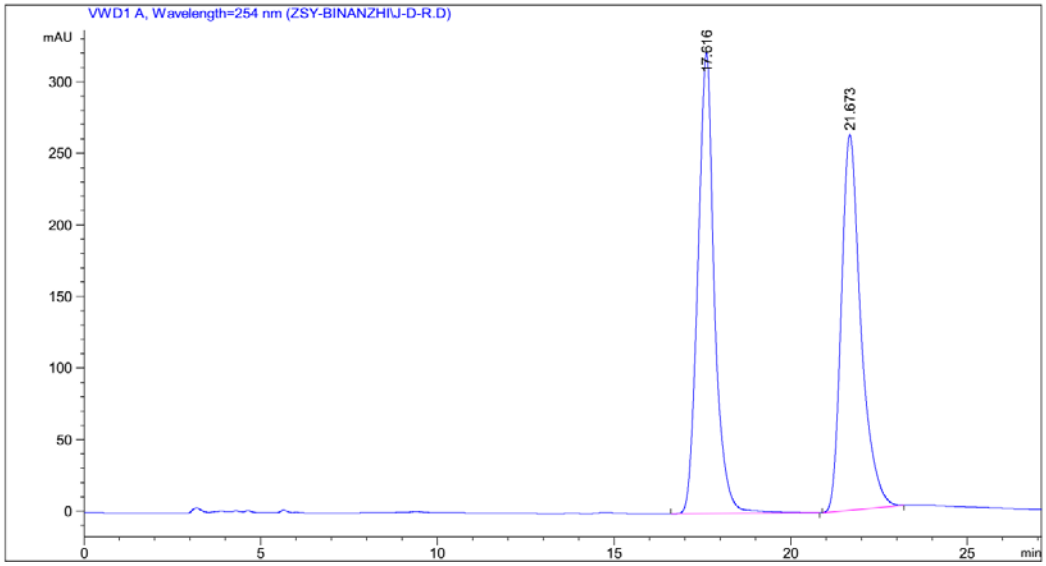
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	30.632	2473.70239	42.91519	52.32
2	PDA 254 nm	37.722	2165.68555	30.77025	47.68



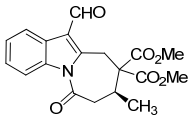
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	30.133	3229.32373	53.63680	12.09
2	PDA 254 nm	37.459	2.27867e4	326.81662	87.91



rac **3q**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	17.616	1.04763e4	321.77036	50.85
2	PDA 254 nm	21.673	1.01247e4	262.41068	49.15



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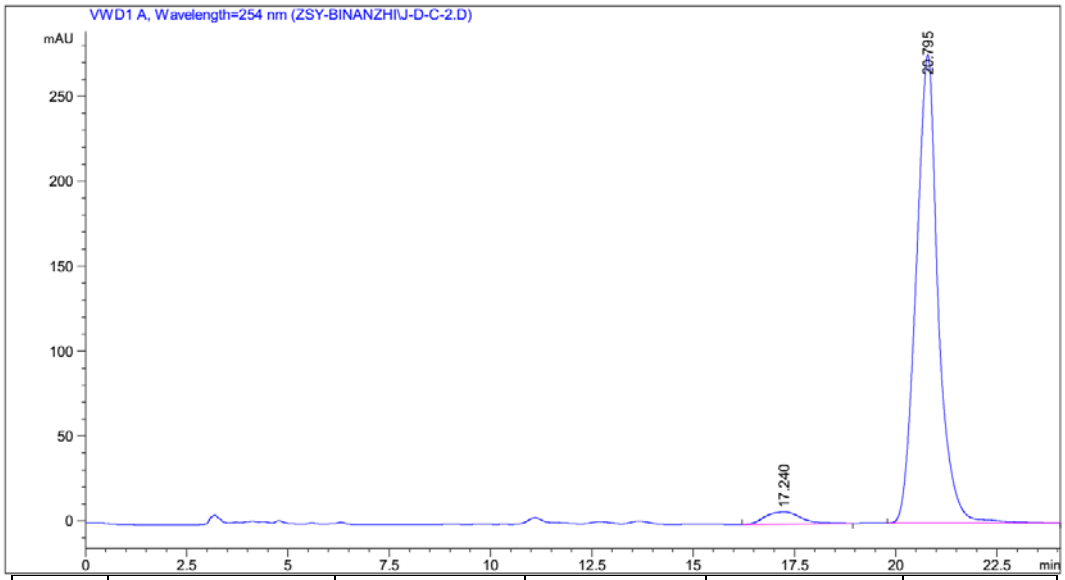
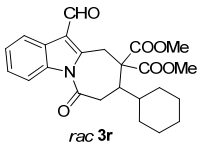
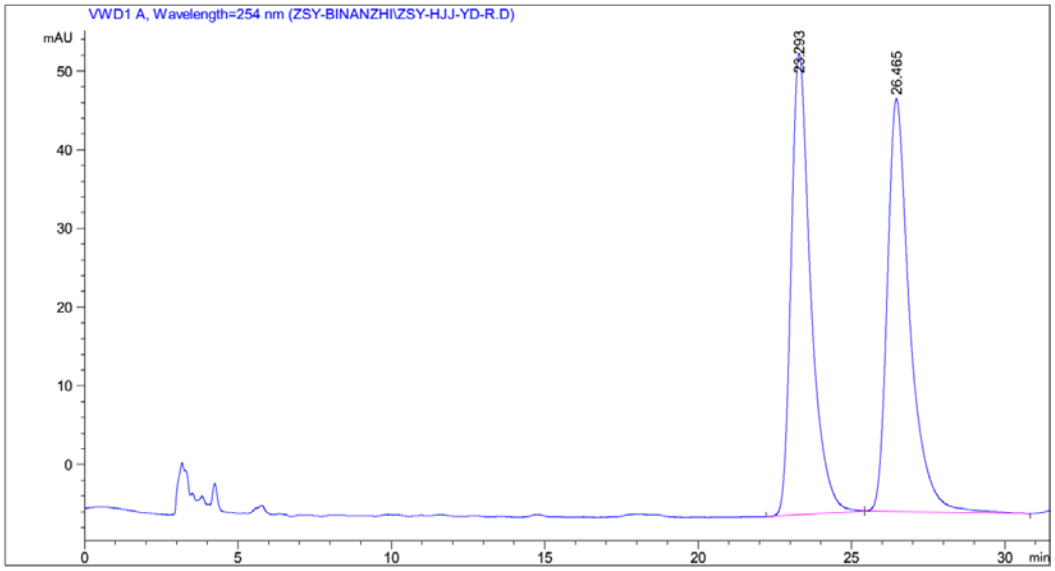


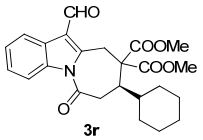
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	17.240	431.82895	7.08924	3.48
2	PDA 254 nm	20.795	1.04263e4	275.85303	96.52



rac **3r**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	23.293	2600.33691	58.64137	49.28
2	PDA 254 nm	26.465	2676.17456	52.43189	50.72



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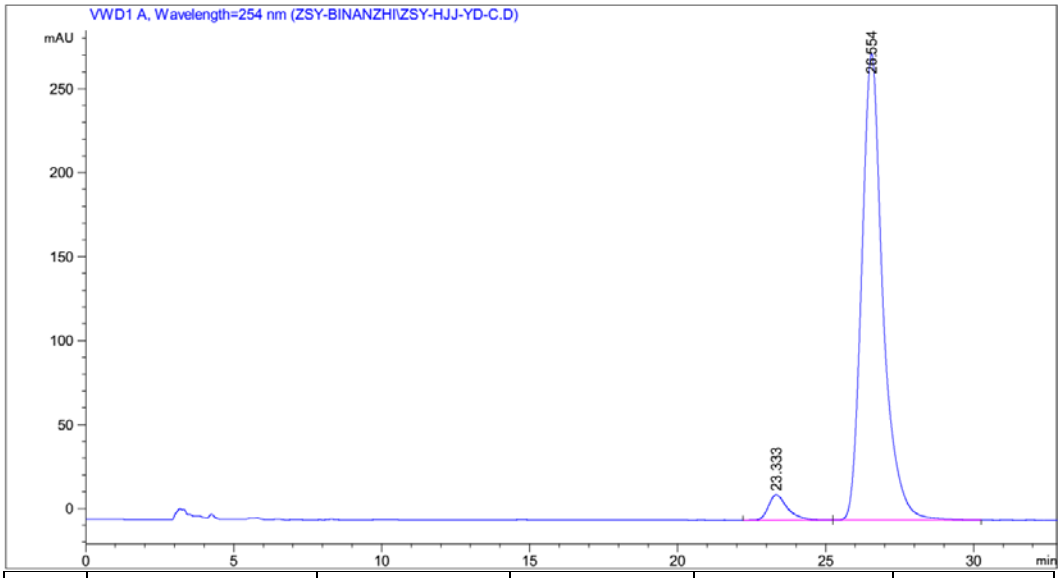
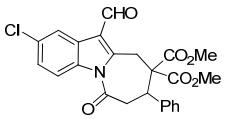
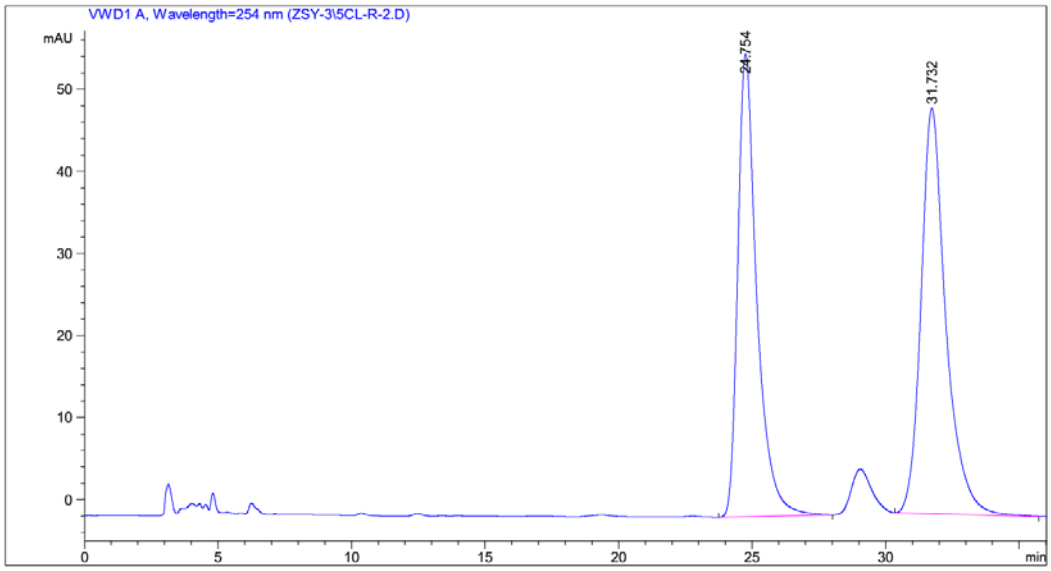


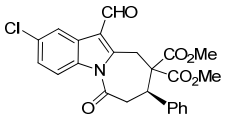
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	23.333	674.79163	15.11364	96.33
2	PDA 254 nm	26.554	1.38005e4	277.93979	3.67



rac **3s**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	24.754	2807.59204	56.41724	48.77
2	PDA 254 nm	31.732	3195.31055	49.44144	51.23



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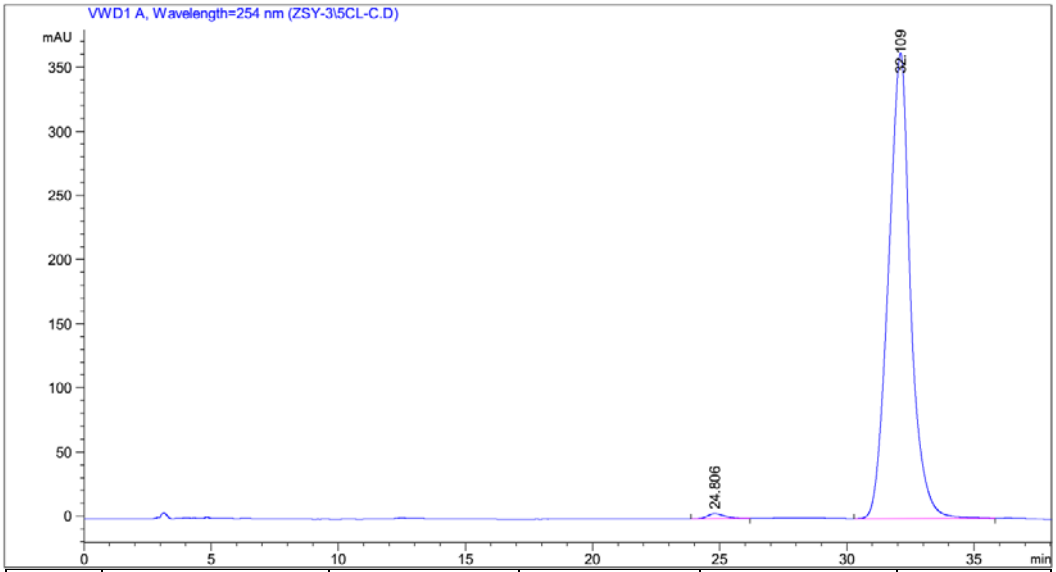
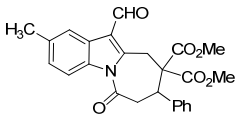
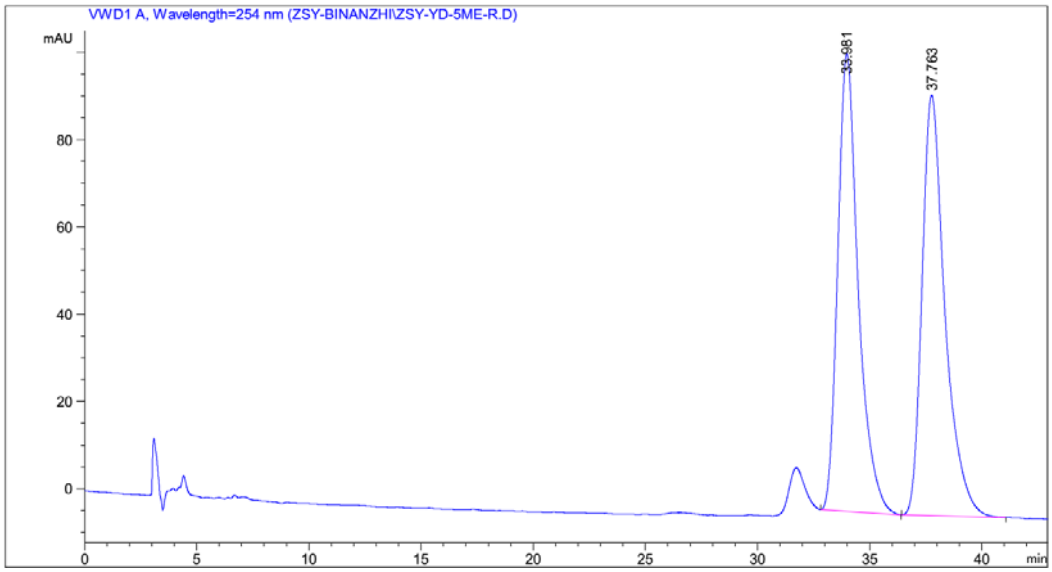


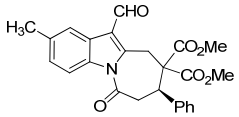
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	24.806	187.44237	3.99209	0.85
2	PDA 254 nm	32.109	2.19065e4	362.75488	99.15



rac **3t**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	33.981	6661.94238	104.78264	49.32
2	PDA 254 nm	37.763	6846.77539	96.36919	50.68



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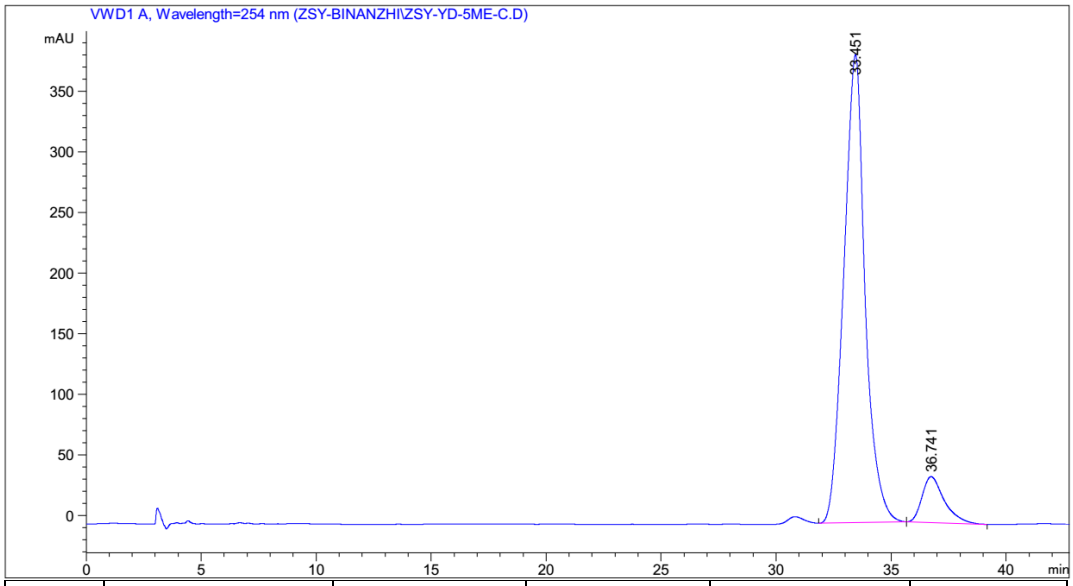
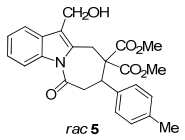
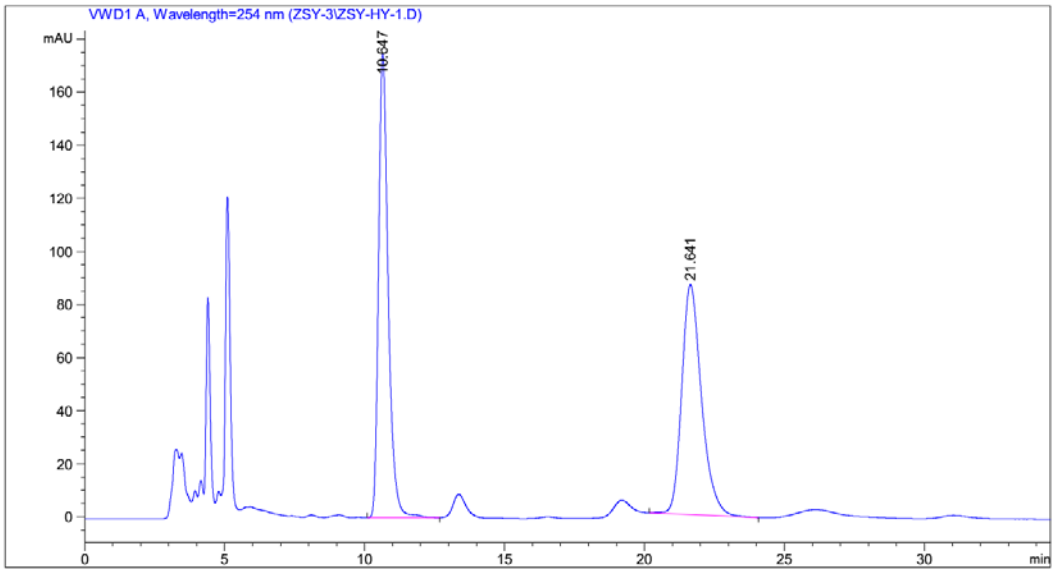


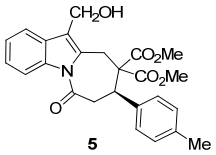
Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	33.451	2.48209e4	386.35223	94.16
2	PDA 254 nm	36.741	2546.06543	37.93715	5.84



rac **5**



Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	10.647	4192.97266	174.80443	49.68
2	PDA 254 nm	21.641	4246.17334	86.62885	50.32



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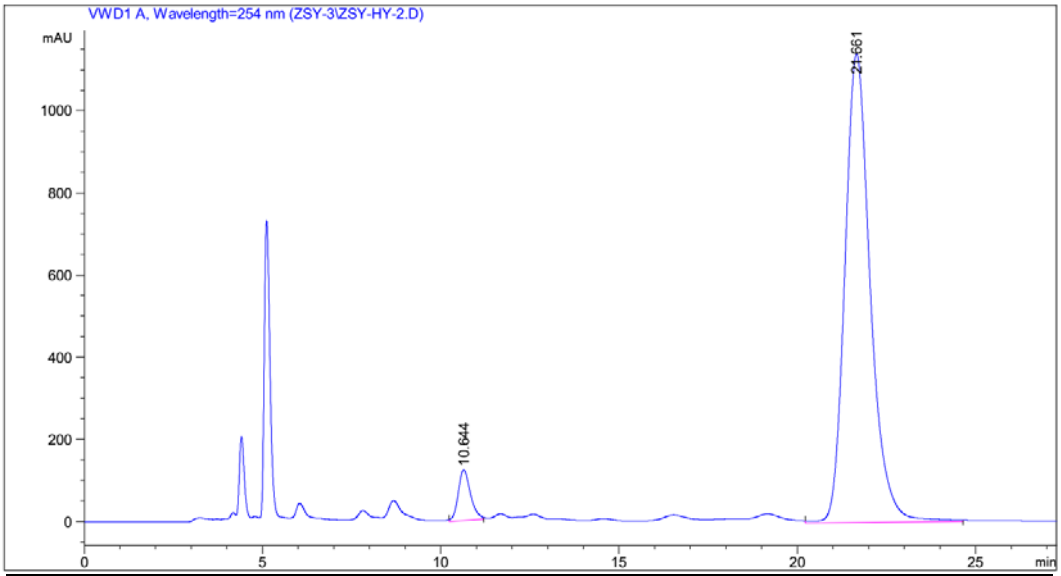

Peak	Processed channel	Retention time (min)	Peak area (mAU*s)	Peak height (mAU)	Peak area (%)
1	PDA 254 nm	10.644	2955.58569	123.65279	4.14
2	PDA 254 nm	21.661	5.66555e4	1142.22803	95.86