

**Controllable Enantioselective Friedel-Crafts Reaction between Indoles and Alkylidene Malonates Catalyzed by Pseudo-C<sub>3</sub>-Symmetric Trisoxazoline Copper (II) Complexes**

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**SUPPORTING INFORMATION**

**Table of Contents**

<b>1. General Information</b>	<b>S2</b>
<b>2. Ligand Preparation</b>	<b>S2-S4</b>
<b>3. General Information for Asymmetric Friedel-Crafts Reaction</b>	<b>S4-S5</b>
<b>4. Data for Alkylation Products and Derivatives</b>	<b>S6-S15</b>
<b>5. IR Spectrum Data</b>	<b>S16-S17</b>
<b>6. References</b>	<b>S17</b>
<b>7. Chiral HPLC Data for All Indole Alkylation Products.</b>	<b>S18-S43</b>

### General Information

Cu(OTf)<sub>2</sub> was purchased from TCI, Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O from Fluka, KOTf from Acros, Indole and substituted indoles from TCI or Acros. Alcohols were purchased from Aldrich and used without purification. Isopropyl-pybox was purchased from Fluka and used without further purification. Alkyl halides were purchased from Shanghai Reagents Company of Chinese Medical Corporation. Purification of reaction products was carried out by flash chromatography on silica gel. Ether was dried by distillation over sodium-benzophenone ketyl prior to use. Acetonitrile, carbon tetrachloride were distilled over P<sub>2</sub>O<sub>5</sub> then over calcium hydride under nitrogen, and stored over MS 4Å; Triethylamine was distilled over calcium hydride under nitrogen, and stored over MS 4Å. Acetone was first distilled over anhydrous CaSO<sub>4</sub> and stored over MS 4Å.

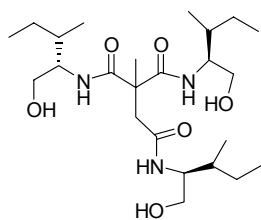
1,1,2,2-tetrachloroethane (TTCE) was purified as follows: TTCE (200 mL) was stirred with conc. H<sub>2</sub>SO<sub>4</sub> at 80°C for about 10 minutes. Then the yellow acid layer was removed. This operation was repeated for several times until that conc. H<sub>2</sub>SO<sub>4</sub> no longer turned yellow. The organic layer was washed successively by water, saturated NaHCO<sub>3</sub> and saturated NaCl solution. The resulting white emulsion was dried over Na<sub>2</sub>SO<sub>4</sub>, distilled under reduced pressure over P<sub>2</sub>O<sub>5</sub>, then over CaH<sub>2</sub>, and stored under N<sub>2</sub> for use.

*It should be noted that oil temperature should keep below 80°C during the course of distillation, to avoid the decomposition of 1,1,2,2-tetrachloroethane.*

### Ligand preparation:

Ligand **1c**<sup>1</sup> and **2a**<sup>2</sup> have been synthesized according to literature methods.

#### (S)-N, N, N-Tris[1 – (hydroxymethyl)–2–methylpropyl]–1, 2, 2–propane tricarboxamide **9b**

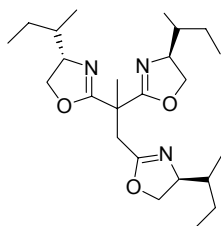


To trimethyl 1,2,2 –propanetricarboxylate **8** (2.45 g, 11.2 mmol) was added L-isoleucinol (5.2 g, 45.0 mmol). And the resulting mixture was stirred at 70°C for 10 hours. Then the generated methanol was removed under reduced pressure at 30°C. Repeat the same operation for six times (total reaction time: 70 hours). The mixture was cooled to room temperature and was purified by

chromatography on silica gel (pure ethyl acetate) to give **9b** as highly hydroscopic white solid (2.26 g, 44% based on compound **8**).  $[\alpha]_D^{20} = +27.9$  (19.3 mg/2 mL CHCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 0.83-0.92 (m, 18H), 1.09-1.21 (m, 3H), 1.41-1.60 (m, 9H), 2.48 (ABd, *J* = 14.1 Hz, 1H), 3.19 (ABd, *J* = 14.4 Hz, 1H), 3.31-3.38 (m, 1H), 3.45 –3.57 (m, 2H), 3.63-3.70 (m, 3H), 3.74-3.96 (m, 6H), 6.98 (d, *J* = 9.9 Hz, 1H), 8.12 (d, *J* = 9.0 Hz, 1H), 8.75 (d, *J* = 8.7 Hz, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 174.39, 173.53, 173.20, 63.10, 62.69, 62.57, 56.40, 56.00, 55.87, 53.91, 42.61, 35.92, 35.80, 35.74, 28.12, 25.58, 25.51, 25.35, 15.60, 15.56, 15.50, 11.30, 11.13; IR (KBr): 3321, 2965, 2936, 2879, 1699,

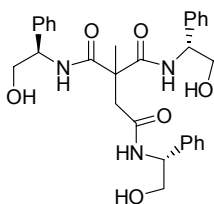
1655, 1541, 1463, 1383, 1236, 1074, 1033, 756, 666; MS (EI): 474 [(M+1)<sup>+</sup>, 2], 357 (100), 313 (67), 295 (48), 69 (40), 41 (34), 55 (26), 196 (24), 339 (24). HRMS (ESI): Exact mass calcd for C<sub>24</sub>H<sub>47</sub>O<sub>6</sub>N<sub>3</sub> [M+Na]<sup>+</sup> 496.3356450, Found: 496.3357073.

**(S)-1,2,2-Tris[2-[4-s-butyl-1,3-oxazoliny]] propane 2b.**



To a solution of compound **9b** (750 mg, 1.6 mmol) and triphenylphosphine (2.54 g, 9.6 mmol) in a mixture of carbon tetrachloride (7.5 mL) and CH<sub>3</sub>CN (18 mL) was added 7.5 mL of triethylamine at 25 °C under N<sub>2</sub>. After 24 hours, the mixture was diluted with ethyl acetate (10 mL) and washed with saturated aqueous NaHCO<sub>3</sub> (3 mL). The organic layer was separated. And the aqueous layer was extracted with ethyl acetate (5×3 mL). The combined organic layer was washed with saturated aqueous NaCl (5×2 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (acetone/petroleum ether, 1/4, v/v) to afford crude **2b** as pale yellow oil. The pure product was obtained by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1/1, v/v then ethyl acetate), Yield: 476 mg (72%). [α]<sub>D</sub><sup>20</sup> = -110.5 (20.6 mg/2ml CHCl<sub>3</sub>) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 0.78 (t, *J* = 7.8 Hz, 9H), 0.91 (t, *J* = 7.8 Hz, 9H), 1.11-1.20 (m, 3H), 1.39-1.69 (m, 6H), 1.74 (s, 3H), 2.94 (ABd, *J* = 14.7 Hz, 1H), 3.07 (ABd, *J* = 14.7 Hz, 1H), 3.87 (t, *J* = 7.8 Hz, 1H), 3.82–4.34 (m, 8H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 166.84, 166.82, 163.52, 70.62, 70.43, 70.04, 69.70, 69.35, 69.29, 40.76, 38.75, 38.59, 38.40, 34.89, 26.09, 26.02, 26.00, 21.20, 14.26, 13.94, 13.55, 11.70, 11.62, 11.44. IR (KBr): 2963, 2878, 1663, 1463, 1380, 1354, 1235, 1180, 1095, 981, 927, 776cm<sup>-1</sup>. MS (EI): 419 (M<sup>+</sup>, 4.7), 362 (100), 225 (37), 363 (18), 235 (19), 262 (15), 155 (13), 55 (12), 223 (11). Anal. calcd. for C<sub>24</sub>H<sub>41</sub>O<sub>3</sub>N<sub>3</sub>: C, 68.70; H, 9.85; N, 10.01. Found: C, 68.72; H, 9.75; N, 9.75.

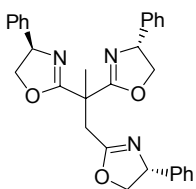
**(S)-N, N, N-Tris[1-(hydroxymethyl)-2-methylpropyl]-1, 2, 2-propane tricarboxamide 9c**



To trimethyl 1,2,2 –propanetricarboxylate **8** (1.33 g, 6.1 mmol) was added D-phenylglycinol (3.72 g, 27.0 mmol). And the resulting mixture was stirred at 70°C for 10 hours. Then the generated methanol was removed under reduced pressure at 30°C. Repeat the same operation for eight times (total reaction time: 90 hours). The mixture was cooled to room temperature and was purified by chromatography on silica gel (pure ethyl acetate) to give **9c** as highly hydroscopic white solid (1.06 g, 33% based on compound **8**). [α]<sub>D</sub><sup>20</sup> = -102.3 (c = 1.14, HCCl<sub>3</sub>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 1.54 (s, 3H); 1.63 (brs, 3H), 2.63 (ABd, *J* = 14.4 Hz, 1H), 3.20 (AB, *J* = 14.4 Hz, 1H), 3.66-4.15 (m, 6H), 5.10-5.28 (m, 3H), 7.28 (m, 15H), 7.47 (d, *J* = 9.5 Hz, 1H),

8.63 (d,  $J = 8.1$  Hz, 1H), 9.45 (d,  $J = 8.3$  Hz, 1H),  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 173.59, 173.14, 172.72, 138.60, 138.35, 128.73, 128.67, 127.65, 127.58, 126.73, 126.71, 126.43, 66.43, 65.66, 65.51, 56.05, 55.60, 53.38, 42.71, 25.74; IR: 3324, 3062, 3030, 2937, 1651, 1537, 1495, 1453, 1372, 1239, 1068, 1039, 756, 700, 637; MS ( $m/z$ ): 534  $[(M+1)^+]$ , 47], 106 (100), 397 (89), 365 (73), 103 (51), 516 (42), 104(42), 77(41). Anal. calcd. for  $\text{C}_{30}\text{H}_{35}\text{O}_6\text{N}_3$ : C, 67.53; H, 6.61; N, 7.87. Found: C, 67.12; H, 6.50; N, 7.43.

### (R)-1,2,2-Tris[2-[4-phenyl-1,3-oxazoliny]] propane 2c.



To a solution of compound **9c** (452 mg, 0.85 mmol) and triphenylphosphine (1.34 g, 5.1 mmol) in a mixture of carbon tetrachloride (3.6 mL) and  $\text{CH}_3\text{CN}$  (10 mL) was added 3.6 mL of triethylamine at  $25^\circ\text{C}$  under  $\text{N}_2$ . After 24 hours, the mixture was diluted with ethyl acetate (10 mL) and washed with saturated aqueous  $\text{NaHCO}_3$  (3 mL). The organic layer was separated. And the aqueous layer was extracted with ethyl acetate ( $5 \times 3$  mL). The combined organic layer was washed with saturated aqueous  $\text{NaCl}$  ( $5 \times 2$  mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (THF/petroleum ether, 1/4, v/v) to afford crude **2c** as yellow oil. The pure product was obtained by flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1/1, v/v). Yield: 276 mg (68%).  $[\alpha]_D^{20} = +149.7$  (13.2 mg/2mL  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.86 (s, 3H), 3.25 (ABd,  $J = 14.1$  Hz, 1H), 3.31 (ABd,  $J = 14.1$  Hz, 1H), 4.03–4.19 (m, 3H), 4.67–4.70 (m, 3H), 5.10–5.32 (m, 3H), 7.23–7.31 (m, 15H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 168.29, 168.25, 164.61, 142.01, 142.00, 141.98, 128.38, 128.32, 127.24, 127.20, 126.59, 126.42, 75.31, 74.22, 69.40, 69.41, 69.28, 41.05, 34.90, 30.10, 21.52; IR(KBr): 3063, 3030, 2960, 2901, 1736, 1658, 1604, 1494, 1455, 1355, 1171, 1099, 982, 919, 761,  $700\text{cm}^{-1}$ ; MS (EI): 479 ( $M^+$ , 10), 480  $[(M+1)^+]$ , 14], 205 (100), 265 (48), 220 (35), 104 (30), 201 (30); HRMS (EI): Exact mass calcd for  $\text{C}_{30}\text{H}_{29}\text{O}_3\text{N}_3$   $[M]^+$ : 479.22090. Found: 479.21840.

## 2. Catalytic Asymmetric Friedel-Crafts Reaction:

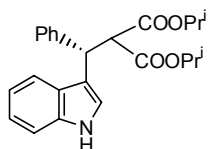
**General Procedure (A) for the preparation of (+)-enantiomer using trisoxazoline / $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  as the chiral catalyst.** To a Schlenk tube was added  $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  (0.10 eq), followed by (*S*)-isopropyl-trisoxazoline **2a** (0.12 eq) in a mixed solvent of acetone-ether (1:3, v/v) under  $\text{N}_2$  atmosphere. The solution was stirred at room temperature for two hours and a mixture of malonate **6** (1.0 eq) and HFIP (2.0 eq) was added. The concentration of  $\text{Cu}^{2+}$  was maintained about 0.015 mol/mL. The resulting

mixture was kept stirring for 15 minutes, then cooled to  $-20\text{ }^{\circ}\text{C}$  and stirred for another 15 minutes before the indoles (1.2 eq) was added. After the reaction was complete (monitored by TLC), the solution was concentrated. The residue was purified by flash column chromatography on silica gel [eluted with  $\text{CH}_2\text{Cl}_2$ /petroleum ether (1/1, v/v) then pure  $\text{CH}_2\text{Cl}_2$ ] to afford the desired product.

**General Procedures for using trisoxazoline/ $\text{Cu}(\text{OTf})_2$  as the chiral catalyst.** It should be noted that keeping the ratios of ligand **2a** and  $\text{Cu}(\text{OTf})_2$  as indicated is crucial to reproduce the high ee. To obtain (+)-enantiomer, the ratio of ligand **2a** and  $\text{Cu}(\text{OTf})_2$  could vary from 1.1:1.0 to 1.2:1.0, but to obtain (-)-enantiomer, the ratio of ligand **2a** and  $\text{Cu}(\text{OTf})_2$  must be strictly kept at 1:0:1.5, and any deviation from this ratio will lead to a loss of enantioselectivity.

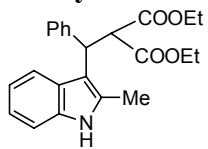
**General Procedure B for the preparation of (+)-enantiomer in isobutanol.** Under air atmosphere, to a Schlenk tube was added  $\text{Cu}(\text{OTf})_2$  (0.10 eq), followed by (*S*)-isopropyl-trisoxazoline **2a**. Then *t*-BuOH was added, and the concentration of  $\text{Cu}^{2+}$  was maintained about 0.005 mol/mL. The resulting blue-green solution was stirred at room temperature ( $10\text{-}25^{\circ}\text{C}$ ) for two hours before alkylidene malonate (1.0 eq) was added into the mixture. The resulting mixture was kept stirring at room temperature for 15 minutes, then cooled to  $-25\text{ }^{\circ}\text{C}$  and stirred for another 15 minutes before the indoles (1.2 eq) was added. After the reaction was complete (monitored by TLC), the reaction mixture was concentrated under reduced pressure at room temperature, and the residue was purified by flash column chromatography on silica gel [eluted with  $\text{CH}_2\text{Cl}_2$ /petroleum ether (1/1, v/v) then pure  $\text{CH}_2\text{Cl}_2$ ] to afford the desired product.

**General Procedure C for the preparation of (-)-enantiomer in TTCE.** Under  $\text{N}_2$  atmosphere, to a Schlenk tube was added  $\text{Cu}(\text{OTf})_2$  (0.10 eq), followed by (*S*)-isopropyl-trisoxazoline **2a** (0.067 eq). Then 1,1,2,2-tetrachloroethane was added. The concentration of  $\text{Cu}^{2+}$  was maintained about 0.01 mol/mL. The resulting blue cloudy solution, (if catalyst solution is green, TTCE needs to be repurified), was stirred at  $20^{\circ}\text{C}$  for 2 hours before alkylidene malonate (1.0 eq) was added into the mixture. The resulting mixture was kept stirring at  $20^{\circ}\text{C}$  for 30 minutes until the mixture was clear. Then the reaction system was cooled to  $0^{\circ}\text{C}$  and stirred for another 15 min before the indoles (1.2 eq) was added. The reaction mixture was quenched by silica when the reaction was complete (monitored by TLC). Purification by flash column chromatography on silica gel [eluted with  $\text{CH}_2\text{Cl}_2$ /petroleum ether (1/1, v/v), then pure  $\text{CH}_2\text{Cl}_2$ ] afforded the desired product.

**Isopropyl-2-isopropoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate 7d (entry 3,**

**Table 8)** Prepared according to general procedure B from indole (35 mg) and diisopropyl benzylidene malonate (83 mg) at  $-25\text{ }^{\circ}\text{C}$  for 120 hours to provide the pure product as a white solid. Yield: 28 mg (26%). HPLC analysis (Chiralcel OD-H, 20%  $^i\text{PrOH}$ /hexanes, 0.55 mL/min, 254 nm;  $t_r$  (minor) = 10.32 min,  $t_r$  (major) = 11.94 min) gave the

isomeric composition of the product: 90.7% ee.  $[\alpha]_D^{20} = +46.6$  (13.0 mg/2 mL  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.92-1.00 (m, 9H), 1.09 (d,  $J = 6.6$  Hz, 3H), 4.26 (d,  $J = 11.7$  Hz, 1H), 4.82-4.87 (m, 2H), 5.05 (d,  $J = 11.7$  Hz, 1H), 7.01-7.07 (m, 1H), 7.10-7.30 (m, 6H), 7.39 (m, 2H), 7.59 (d,  $J = 8.1$  Hz, 1H), 8.06 (brs, 1H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 167.58, 167.38, 141.47, 136.06, 128.22, 128.19, 126.64, 126.58, 122.06, 120.78, 119.36, 119.32, 117.02, 110.92, 68.86, 68.84, 58.55, 42.68, 21.36, 21.24, 21.21, 21.17; IR (film) 3414, 3134, 3028, 2980, 2933, 1745, 1718, 1495, 1490, 1421, 1360, 1421, 1367, 1325, 1274, 1188, 1162, 1105, 1012, 908, 742,  $591\text{cm}^{-1}$ ; MS (EI,  $m/z$ ): 393 ( $\text{M}^+$ , 19), 206 (100), 205 (21), 204 (35), 246 (29), 245 (16), 43 (14), 203 (12); Anal. Calcd for  $\text{C}_{24}\text{H}_{27}\text{NO}_4$ : C, 73.26; H, 6.92; N, 3.56. Found: C, 73.43, H, 6.99, N, 3.31. mp  $145^{\circ}\text{C}$ .

**Methyl-2-methoxycarbonyl-3-[3-(2-methylindolyl)]-3-phenyl propanoate 7e (entry**

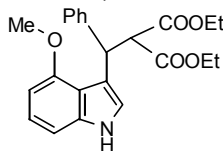
**1, Table 9) (-)-enantiomer:** Prepared according to general procedure A from 2-methylindole (42 mg) and diethyl benzylidene malonate (66 mg) at  $-20\text{ }^{\circ}\text{C}$  for 80 hours to provide the pure product as a white solid. Yield: 98 mg (99%). HPLC analysis (Chiralcel OD-H, 15%

$^i\text{PrOH}$ /hexanes, 0.90 mL/min, 254 nm;  $t_r$  (major) = 9.65 min,  $t_r$  (minor) = 18.4 min) gave the isomeric composition of the product: 73.0% ee.  $[\alpha]_D^{20} = -24.7$  (86.1 mg/2 mL  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.84 (t,  $J = 7.2$  Hz, 3H), 1.18 (t,  $J = 7.2$  Hz, 3H), 2.44 (s, 3H), 3.86-3.92 (m, 2H), 4.17 (q,  $J = 6.9$  Hz, 2H), 4.80 (d,  $J = 11.7$  Hz, 1H), 5.14 (d,  $J = 12.0$  Hz, 1H), 7.10-7.12 (m, 2H), 7.19-7.24 (m, 2H), 7.27-7.32 (m, 2H) 7.46 (d,  $J = 6.9$  Hz, 2H), 7.75 (m, 1H), 8.00 (brs, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ) 168.29, 168.03, 141.74, 135.10, 132.09, 128.24, 127.45, 127.13, 126.26, 120.60, 119.14, 118.93, 111.01, 110.29, 61.44, 61.43, 61.11, 55.70, 55.69, 42.38, 13.80, 13.33, 12.11; IR (film) 3393, 3052, 2984, 1727, 1622, 1581, 1562, 1494, 1462, 1391, 1370, 1336, 1302, 1269, 1233, 1219, 1174, 1157, 1095, 1037,  $1020\text{cm}^{-1}$ ; MS (EI,  $m/z$ ): 379 ( $\text{M}^+$ , 8), 220 (100), 221 (18), 218 (15), 217 (11), 304 (6), 219 (5), 130 (5); Anal. Calcd for  $\text{C}_{23}\text{H}_{25}\text{NO}_4$ : C, 72.80; H, 6.64; N, 3.69. Found: C, 72.61, H, 6.77, N, 3.35. mp  $126\text{-}129^{\circ}\text{C}$ .

**(+)-enantiomer:** Prepared according to general procedure C:  $\text{Cu}(\text{OTf})_2$  (15.8 mg), (*S*)-isopropyl-trisoxazoline **2a** (11.0 mg), 1,1,2,2-tetrachloroethane (5.0 mL), 2-methyl indole (63 mg) and diethyl benzylidene malonate (108 mg) at  $0\text{ }^{\circ}\text{C}$  for 23 hours to provide the pure product as a white solid. Yield: 148 mg (90%). HPLC analysis (Chiralcel OD-H, 15%  $^i\text{PrOH}$ /hexanes, 0.70 mL/min, 254 nm;  $t_r$  (major) = 16.19 min,  $t_r$

(minor) = 19.62 min) gave the isomeric composition of the product: 65.5% ee.  $[\alpha]_D^{20} = +18.2$  (20.7 mg/2 mL CHCl<sub>3</sub>).

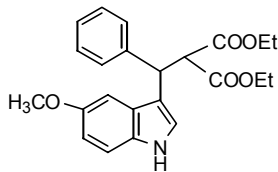
**Ethyl 2-ethoxycarbonyl-3-[3-(4-methoxyindolyl)]-3-phenylpropanoate 7f (entry 2, Table 9)**<sup>2</sup>



**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (12.3 mg), (*S*)-isopropyl-trisoxazoline **2a** (13.7 mg), *t*BuOH (7.5 mL), 4-methoxyindole (55 mg) and diethyl benzylidene malonate (84 mg) at -25°C for 50 hours to provide the pure product as a white solid. Yield: 131 mg (98%). HPLC analysis (Chiralcel OD-H, 6% <sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub>(minor) = 23.16 min, *t*<sub>r</sub>(major) = 26.97 min.) gave the isomeric composition of the product: 97.7% ee. Analytical data for:  $[\alpha]_D^{20} = +63.1$  (34.3 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.98-1.00 (m, 6H), 3.82 (s, 3H), 3.9-4.01 (m, 4H), 4.28 (d, *J* = 12.3 Hz, 1H), 5.49 (d, *J* = 12.3 Hz, 1H), 6.39 (d, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.98-7.11 (m, 3H), 7.19 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.8 Hz, 2H), 8.08 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (13.6 mg), (*S*)-isopropyl-trisoxazoline **2a** (9.5 mg), 1,1,2,2-tetrachloroethane (3.6 mL), 4-methoxyindole (58 mg) and diethyl benzylidene malonate (92 mg) at 0°C for 24 hours, and 15°C for 36 hours to provide the pure product as a white solid. Yield: 20 mg (14%), and 79 mg (86 %) of malonate was recovered. HPLC analysis (Chiralcel OD-H, 6% <sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub>(major) = 27.63 min, *t*<sub>r</sub>(minor) = 33.14min.) gave the isomeric composition of the product: 61.1% ee.  $[\alpha]_D^{20} = -34.5$  (20.0 mg/2 mL CHCl<sub>3</sub>).

**(S)-Ethyl 2-ethoxycarbonyl-3-[3-(5-methoxyindolyl)]-3-phenylpropanoate 7g (entry 3, Table 9)**<sup>2,3</sup>

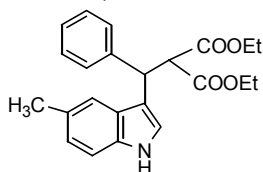


**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (11.9 mg), (*S*)-isopropyl-trisoxazoline **2a** (13.5 mg), *t*BuOH (6.5 mL), 5-methoxyindole (58 mg) and diethyl benzylidene malonate (82 mg) at -25°C for 60 hours to provide the pure product as a white solid. Yield: 103 mg (79%). HPLC analysis (Chiralcel OD-H, 10% <sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub>(minor) = 19.99 min, *t*<sub>r</sub>(major) = 25.50 min.) gave the isomeric composition of the product: 94.2% ee.  $[\alpha]_D^{20} = +11.1$  (15.9 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.97-1.02 (m, 6H), 3.77 (s, 3H), 3.94-4.05 (m, 4H), 4.26 (d, *J* = 11.7 Hz, 1H), 5.02 (d, *J* = 11.7 Hz, 1H), 6.78 (dd, *J* = 2.4, 5.7 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 7.11-7.17 (m, 3H), 7.20-7.25 (m, 2H), 7.37-7.38 (m, 2H), 7.99 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (13.6 mg), (*S*)-isopropyl-trisoxazoline **2a** (9.3 mg), 1,1,2,2-tetrachloroethane (3.5 mL), 5-methoxy-

indole (60 mg) and diethyl benzylidene malonate (92 mg) at 0°C for 22 hours to provide the pure product as a white solid. Yield: 98 mg (67%). HPLC analysis (Chiralcel OD-H, 15% <sup>i</sup>PrOH/hexanes, 0.70 mL/min, 254 nm;  $t_r$  (major) = 14.88 min,  $t_r$  (minor) = 19.09 min.) gave the isomeric composition of the product: 59.5% ee.  $[\alpha]_D^{20} = -7.2$  (16.5 mg/2 mL CHCl<sub>3</sub>).

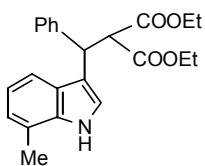
**Ethyl 2-ethoxycarbonyl-3-[3-(5-methylindolyl)]-3-phenylpropanoate 7h (entry 4, Table 9)**<sup>2</sup>



**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (8.3 mg), (*S*)-isopropyl-trisoxazoline **2a** (9.4 mg), <sup>i</sup>BuOH (5.0 mL), 5-methylindole (36 mg) and diethyl benzylidene malonate (57 mg) at -25°C for 52 hours to provide the pure product as a white solid. Yield: 77 mg (89%). HPLC analysis (Chiralcel OD-H, 10% <sup>i</sup>PrOH/hexanes, 0.80 mL/min, 254 nm;  $t_r$  (minor) = 13.33 min,  $t_r$  (major) = 16.9 min.) gave the isomeric composition of the product: 95.1% ee.  $[\alpha]_D^{20} = +38.2$  (18.2 mg/2 mL CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  1.00 (m, 6H), 2.38 (s, 3H), 3.98 (m, 4H), 4.27 (d,  $J = 12.3$  Hz, 1H), 5.04 (d,  $J = 11.7$  Hz, 1H), 6.95 (m, 1H), 7.11-7.25 (m, 5H), 7.33-7.38 (m, 3H), 7.96 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (12.4 mg), (*S*)-isopropyl-trisoxazoline **2a** (8.6 mg), TTCE (3.5 mL), 5-methylindole (53 mg) and diethyl benzylidene malonate (85 mg) at 0°C for 28 hours to provide the pure product as a white solid. Yield: 97 mg (75%), and 17 mg of malonate (20 %) was recovered. HPLC analysis (Chiralcel OD-H, 15% <sup>i</sup>PrOH/hexanes, 0.70 mL/min, 254 nm;  $t_r$  (major) = 13.16 min,  $t_r$  (minor) = 16.35 min.) gave the isomeric composition of the product: 73.4% ee.  $[\alpha]_D^{20} = -32.0$  (14.5 mg/2 mL CH<sub>2</sub>Cl<sub>2</sub>).

**Ethyl 2-ethoxycarbonyl-3-[3-(7-methylindolyl)]-3-(phenyl) propanoate 7i (entry 5, Table 9)**



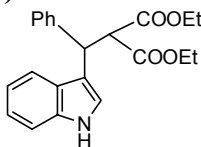
**(+)-enantiomer:** Prepared according to general procedure **B** from 7-methylindole (25 mg) and diethyl benzylidene malonate (40 mg) at -25°C for 40 hours to provide the pure product as a white solid. Yield: 50 mg (82%). HPLC analysis (Chiralpak OD-H, 20% <sup>i</sup>PrOH/hexanes, 0.60 mL/min, 254 nm;  $t_r$  (minor) = 11.47 min,  $t_r$  (major) = 13.98 min) determined the product in 89.1% ee.  $[\alpha]_D^{20} = +74.5$  (17.0 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>),  $\delta$  0.97-1.03 (m, 6H), 2.40 (s, 3H), 3.93-4.04 (m, 4H), 4.29 (d,  $J = 12.0$  Hz, 1H), 5.06 (d,  $J = 11.7$  Hz, 1H), 6.94 (d,  $J = 6.9$  Hz, 2H), 7.11-7.24 (m, 4H), 7.34-7.40 (m, 3H) 8.10 (d,  $J = 8.7$  Hz, 2H), 8.02 (brs, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 168.03, 167.84, 141.34, 135.71, 128.24, 128.11, 126.62, 126.11, 122.63, 120.49, 120.47, 120.10, 119.59, 117.27, 117.00, 61.46, 61.37, 58.30, 42.95, 16.45, 13.71; IR (film) 3471,

2982, 1744, 1716, 1371, 1326, 1307, 1265, 1150, 1025, 777, 748, 701, 447 $\text{cm}^{-1}$ ; MS (EI,  $m/z$ ): 379 ( $M^+$ , 12), 220 (100), 221 (18), 204 (9), 43 (7), 217 (7), 260 (6); Anal. Calcd for  $\text{C}_{23}\text{H}_{25}\text{NO}_4$ : C, 72.80; H, 6.64; N, 3.69. Found: C, 72.49, H, 6.96, N, 3.31. mp 116-118 $^\circ\text{C}$ .

**(-)-enantiomer:** Prepared according to general procedure C:  $\text{Cu}(\text{OTf})_2$  (8.4 mg), (*S*)-isopropyl-trisoxazoline **2a** (5.9 mg), 1,1,2,2-tetrachloroethane (2.5 mL), 7-methyl indole (32 mg) and diethyl benzylidene malonate (57 mg) at 0  $^\circ\text{C}$  for 23 hours to provide the pure product as a white solid. Yield: 73 mg (90%). HPLC analysis (Chiralcel OD-H, 20%  $^i\text{PrOH}$ /hexanes, 0.60 mL/min, 254 nm;  $t_r$ (major) = 9.67 min,  $t_r$ (minor) = 11.14 min) gave the isomeric composition of the product: 55.7% ee.  $[\alpha]_D^{20} = -43.6$  (22.0 mg/2 mL  $\text{CHCl}_3$ ).

**Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate 7a (entry 1, Table 10)**<sup>3</sup>

**(S)-enantiomer:** Prepared according to general procedure B:  $\text{Cu}(\text{OTf})_2$  (7.2 mg), (*S*)-isopropyl-trisoxazoline **2a** (8.4 mg),  $^i\text{BuOH}$  (4.5 mL), indole (28 mg) and diethyl benzylidene malonate (50 mg) at -25 $^\circ\text{C}$  for 45 hours to provide the pure product as a white solid. Yield: 71 mg (99%). HPLC analysis (Chiralcel OD-H, 10%  $^i\text{PrOH}$ /hexanes, 0.80 mL/min,

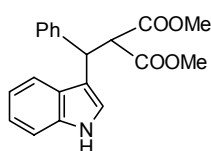


254 nm;  $t_r$ (minor) = 16.11 min,  $t_r$ (major) = 19.51 min.) gave the isomeric composition of the product: 94.3% ee.  $[\alpha]_D^{20} = +60.9$  (22.0 mg/2 mL  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.00 (m, 6H), 3.99 (m, 4H), 4.29 (d,  $J = 11.4$  Hz, 1H), 5.08 (d,  $J = 11.7$  Hz, 1H), 7.03-7.06 (m, 1H), 7.10-7.30 (m, 6H), 7.36 (d,  $J = 6.9$  Hz, 2H), 7.55 (d,  $J = 7.8$  Hz, 1H), 8.06 (brs, 1H).

**(R)-enantiomer:** Prepared according to general procedure C:  $\text{Cu}(\text{OTf})_2$  (9.0 mg), (*S*)-isopropyl-trisoxazoline **2a** (6.3 mg), 1,1,2,2-tetrachloroethane (2.5 mL), indole (35 mg) and diethyl benzylidene malonate (62 mg) at 0 $^\circ\text{C}$  for 22 hours to provide the pure product as a white solid. Yield: 78 mg (86%). HPLC analysis (Chiralcel OD-H, 10%  $^i\text{PrOH}$ /hexanes, 0.80 mL/min, 254 nm;  $t_r$ (major) = 15.45 min,  $t_r$ (minor) = 19.28 min.) gave the isomeric composition of the product: 79.9% ee.  $[\alpha]_D^{20} = -55.2$  (17.0 mg/2 mL  $\text{CHCl}_3$ ).

**Methyl 2-methoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate 7b (entry 2, Table 10)**<sup>2,3</sup>

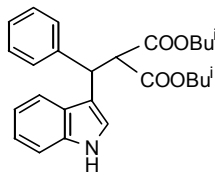
**(+)-enantiomer:** Prepared according to general procedure B:  $\text{Cu}(\text{OTf})_2$  (13.7 mg), (*S*)-isopropyl-trisoxazoline **2a** (16.0 mg),  $^i\text{BuOH}$  (8.0 mL), indole (53 mg) and dimethyl benzylidene malonate (83 mg) at -25  $^\circ\text{C}$  for 45 hours to provide the pure product as a white solid. Yield: 118 mg (93%). HPLC analysis (Chiralcel OD-H, 10%  $^i\text{PrOH}$ /hexanes, 0.80 mL/min, 254 nm;  $t_r$ (minor) = 23.42 min,  $t_r$ (major) = 27.48 min) gave the isomeric composition of the product: 90.5% ee.  $[\alpha]_D^{20} = +63.9$



(18.7 mg/2 mL CHCl<sub>3</sub>) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 3.52 (s, 3H), 3.56 (s, 3H), 4.31 (d, *J* = 11.7 Hz, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 7.11-7.17 (m, 3H), 7.21-7.36 (m, 5H), 7.51 (d, *J* = 7.8 Hz, 1H), 8.06 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure C: Cu(OTf)<sub>2</sub> (8.1 mg), (*S*)-isopropyl-trisoxazoline **2a** (5.6 mg), 1,1,2,2-tetrachloroethane (2.3 mL), indole (35 mg) and dimethyl benzylidene malonate (55 mg) at 0 °C for 23 hours to provide the pure product as a white solid. Yield: 63 mg (83%). HPLC analysis (Chiralcel OD-H, 15% <sup>i</sup>PrOH/hexanes, 0.70 mL/min, 254 nm; *t*<sub>r</sub> (major) = 16.19 min, *t*<sub>r</sub> (minor) = 19.62 min) gave the isomeric composition of the product: 65.5% ee. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -47.5 (20.9 mg/2 mL CHCl<sub>3</sub>).

**(S)-Ethyl 2-isobutoxycarbonyl-3-[3-(5-methoxyindolyl)]-3-phenylpropanoate 7c (entry 3, Table 10)**

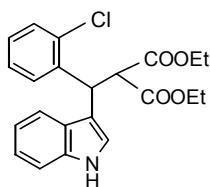


**(+)-enantiomer:** Prepared according to general procedure B: Cu(OTf)<sub>2</sub> (10.4 mg), (*S*)-isopropyl-trisoxazoline **2a** (11.5 mg), <sup>i</sup>BuOH (6.5 mL), indole (40 mg) and diisobutyl benzylidene malonate (87 mg) at -25°C for 60 hours to provide the pure product as a white solid.

Yield: 121 mg (99%). HPLC analysis (Chiralcel OD-H, 10% <sup>i</sup>PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub> (minor) = 15.66 min, *t*<sub>r</sub> (major) = 19.52 min.) gave the isomeric composition of the product: 97.1% ee. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = + 49.2 (28.1 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): 0.71-0.78 (m, 12H), 1.70-1.76 (m, 2H), 3.71-3.75 (m, 4H), 4.32 (d, *J* = 12.0 Hz, 1H), 5.10 (d, *J* = 12.0 Hz, 1H), 7.01-7.07 (m, 1H), 7.11-7.16 (m, 2H), 7.19-7.31 (m, 4H), 7.37-7.40 (m, 2H), 7.56 (d, *J* = 7.8 Hz, 1H), 8.05 (s, br, 1H).  $\delta$  <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 168.44, 168.22, 141.66, 136.46, 128.62, 128.34, 126.96, 126.82, 122.43, 121.06, 119.71, 119.57, 117.18, 111.24, 71.79, 71.76, 58.66, 43.05, 43.02, 27.73, 19.11, 19.08, 18.98, 18.92. IR (KBr): 3431, 2961, 2874, 1749, 1720, 1493, 1460, 1378, 1139, 746, 593, 424cm<sup>-1</sup>. MS (EI): 421 (M<sup>+</sup>, 22), 206 (100), 246 (33), 363 (18), 207 (23), 205 (19), 218 (10), 247 (8), 219 (6). Anal. calcd. for C<sub>26</sub>H<sub>31</sub> N O<sub>4</sub>: C, 74.08; H, 7.41; N, 3.32. Found: C, 74.22; H, 7.52; N, 3.25.

**(-)-enantiomer:** Prepared according to general procedure C: Cu(OTf)<sub>2</sub> (14.3 mg), (*S*)-isopropyl-trisoxazoline **2a** (10.0 mg), 1,1,2,2-tetrachloroethane (4.0mL), indole (37 mg) and diisobutyl benzylidene malonate (80 mg) at 0°C for 36 hours to provide the pure product as a white solid. Yield: 71 mg (73%). HPLC analysis (Chiralcel OD-H, 15% <sup>i</sup>PrOH/hexanes, 0.70 mL/min, 254 nm; *t*<sub>r</sub> (major) = 10.94 min, *t*<sub>r</sub> (minor) = 13.58 min.) gave the isomeric composition of the product: 74.9% ee. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -39.5 (18.0 mg/2 mL CHCl<sub>3</sub>).

**Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(o-chlorophenyl) propanoate 7j (entry 4, Table 10)**<sup>2,3</sup>

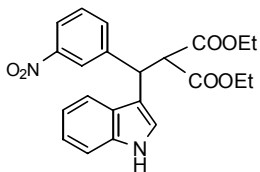


**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (13.7 mg), (*S*)-isopropyl-trisoxazoline **2a** (15.4 mg), *t*BuOH (8.0 mL), indole (53 mg) and diethyl *o*-chlorobenzylidene malonate (107 mg) at -25 °C for 75 hours to provide the pure product as a white solid. Yield: 141 mg (93%). HPLC analysis (Chiralcel OD-H, 10% <sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub>(minor) = 15.01 min, *t*<sub>r</sub>(major) = 21.68 min.)

gave the isomeric composition of the product: 97.0% ee. [α]<sub>D</sub><sup>20</sup> = +46.3 (24.8 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.92 (t, *J* = 6.9, 7.2 Hz, 3H), 1.00 (t, *J* = 6.9, 7.2 Hz, 3H), 3.94 (q, *J* = 6.9, 7.2 Hz, 2H), 4.00 (q, *J* = 6.9, 7.2 Hz, 2H), 4.41 (d, *J* = 11.7 Hz, 1H), 5.67 (d, *J* = 11.7 Hz, 1H), 7.01-7.12 (m, 5H), 7.20 (m, 1H), 7.30 (dd, *J* = 0.9, 7.5 Hz, 1H), 7.38 (dd, *J* = 1.2, 7.5 Hz, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 8.27 (brs, 1H).

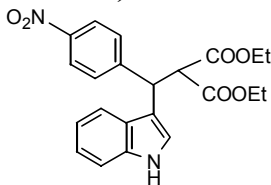
**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (13.0 mg), (*S*)-isopropyl-trisoxazoline **2a** (9.0 mg), 1,1,2,2-tetrachloroethane (4.0 mL), indole (50 mg) and diethyl *o*-chlorobenzylidene malonate (109 mg) at 0 °C for 24 hours to provide the pure product as a white solid. Yield: 143 mg (99%). HPLC analysis (Chiralcel OD-H, 10% <sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub>(major) = 15.42 min, *t*<sub>r</sub>(minor) = 23.88 min.) gave the isomeric composition of the product: 85.3% ee. [α]<sub>D</sub><sup>20</sup> = -40.6 (38.9 mg/2 mL CHCl<sub>3</sub>).

**Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(*m*-nitrophenyl) propanoate 7k (entry 5, Table 10)<sup>2</sup>**



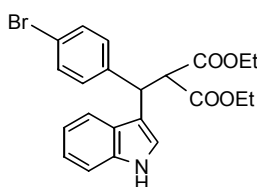
**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (7.2 mg), (*S*)-isopropyl-trisoxazoline **2a** (8.4 mg), *t*BuOH (4.5 mL), indole (30 mg) and diethyl *m*-nitrobenzylidene malonate (60 mg) at 0 °C for 18 hours to provide the pure product as a pale yellow solid. Yield: 87 mg (99%). HPLC analysis (Chiralpak AS, 8% <sup>1</sup>PrOH/hexanes, 1.00 mL/min, 254 nm; *t*<sub>r</sub>(major) = 39.23 min, *t*<sub>r</sub>(minor) = 46.35 min.) gave the isomeric composition of the product: 83.1% ee. [α]<sub>D</sub><sup>20</sup> = +32.3 (31 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.04 (m, 6H), 4.04 (m, 4H), 4.34 (d, *J* = 11.4 Hz, 1H), 5.21 (d, *J* = 11.7 Hz, 1H), 7.04-7.07 (m, 1H), 7.12-7.19 (m, 2H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.39 (t, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 8.23 (s, 1H), 8.36 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (12.5 mg), (*S*)-isopropyl-trisoxazoline **2a** (8.7 mg), 1,1,2,2-tetrachloroethane (3.5 mL), indole (48 mg) and diethyl *m*-nitrobenzylidene malonate (101 mg) at 0 °C for 24 hours to provide the pure product as a pale yellow solid. Yield: 136 mg (96%). HPLC analysis (Chiralpak AS, 8% <sup>1</sup>PrOH/hexanes, 1.00 mL/min, 254 nm; *t*<sub>r</sub>(minor) = 38.28 min, *t*<sub>r</sub>(major) = 43.18 min.) gave the isomeric composition of the product: 88.5% ee. [α]<sub>D</sub><sup>20</sup> = -34.5 (34.5 mg/2 mL CHCl<sub>3</sub>).

**Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-nitrophenyl) propanoate 7l (entry 6, Table 10)**<sup>2</sup>

**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (6.9 mg), (*S*)-isopropyl-trisoxazoline **2a** (7.9 mg), *i*BuOH (4.0 mL), indole (26 mg) and diethyl *p*-nitrobenzylidene malonate (56 mg) at 0°C for 19 hours to provide the pure product as a pale yellow solid. Yield: 77 mg (99%). HPLC analysis (Chiralpak AS, 10% *i*PrOH/hexanes, 1.00 mL/min, 254 nm; *t*<sub>r</sub> (major) = 28.51 min, *t*<sub>r</sub> (minor) = 37.95 min) gave the isomeric composition of the product: 91.1% ee.  $[\alpha]_{\text{D}}^{20} = +4.3$  (16.3 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>), δ 1.00 (t, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H), 4.03 (q, *J* = 7.2 Hz, 4H), 4.32 (d, *J* = 11.7 Hz, 1H), 5.20 (d, *J* = 11.7 Hz, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 7.16-7.22 (m, 2H), 7.30-7.33 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 8.10 (d, *J* = 8.7 Hz, 2H), 8.20 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (7.5 mg), (*S*)-isopropyl-trisoxazoline **2a** (5.3 mg), 1,1,2,2-tetrachloroethane (2.2mL), indole (28 mg) and diethyl *p*-nitrobenzylidene malonate (61 mg) at 0°C for 15 hours to provide the pure product as a pale yellow solid. Yield: 98 mg (99%). HPLC analysis (Chiralpak AS, 10% *i*PrOH/hexanes, 1.00 mL/min, 254 nm; *t*<sub>r</sub> (minor) = 32.17 min, *t*<sub>r</sub> (major) = 38.62 min) gave the isomeric composition of the product: 81.1% ee.  $[\alpha]_{\text{D}}^{20} = -3.4$  (20.0 mg/2 mL CHCl<sub>3</sub>).

**Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-bromophenyl) propanoate 7m (entry 7, Table 10)**<sup>2,3</sup>

**(+)-enantiomer:** Prepared according to general procedure **B**: Cu(OTf)<sub>2</sub> (11.4 mg), (*S*)-isopropyl-trisoxazoline **2a** (12.8 mg), *i*BuOH (8.0 mL), indole (44 mg) and diethyl *p*-bromobenzylidene malonate (103 mg) at -25°C for 45 hours to provide the pure product as a white solid. Yield: 118 mg (85%). HPLC analysis (Chiralcel OD-H, 4% *i*PrOH/hexanes, 0.80 mL/min, 254 nm; *t*<sub>r</sub> (minor) = 45.96 min, *t*<sub>r</sub> (major) = 50.61 min.) gave the isomeric composition of the product: 93.5% ee.  $[\alpha]_{\text{D}}^{20} = +21.5$  (18.4 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 0.97 (t, *J* = 7.2 Hz, 3H), 1.04 (t, *J* = 7.2 Hz, 3H), 3.95-4.04 (m, 4H), 4.25 (d, *J* = 11.7 Hz, 1H), 5.04 (d, *J* = 11.7 Hz, 1H), 7.02-7.05 (m, 1H), 7.05-7.12 (m, 2H), 7.21-7.27 (m, 3H), 7.32-7.35 (m, 2H), 7.48 (d, *J* = 7.5Hz, 1H), 8.22 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure **C**: Cu(OTf)<sub>2</sub> (10.1 mg), (*S*)-isopropyl-trisoxazoline **2a** (7.1 mg), 1,1,2,2-tetrachloroethane (3.0mL), indole (39 mg) and diethyl *p*-bromobenzylidene malonate (92 mg) at 0°C for 24 hours to provide the pure product as a white solid. Yield: 115 mg (93%). HPLC analysis (Chiralcel OD-H, 4%

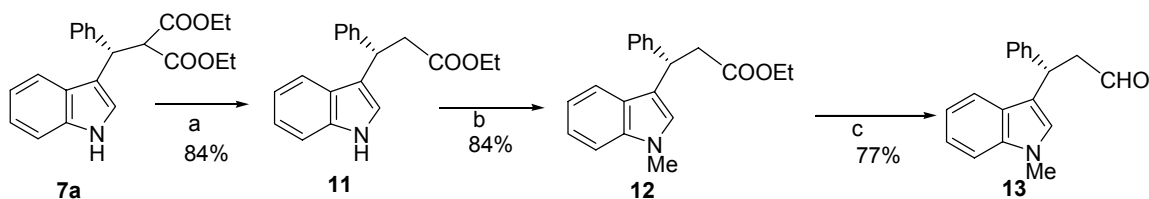
<sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm;  $t_r$ (major) = 48.33 min,  $t_r$ (minor) = 56.80 min.) gave the isomeric composition of the product: 70.6% ee.  $[\alpha]_D^{20} = -19.1$  (32.5 mg/2 mL CHCl<sub>3</sub>).

**(R)-Ethyl 2-ethoxycarboxy-3-(3-indolyl)-3-methylpropanoate 7n (entry 8, Table 10)**

**(+)-enantiomer:** Prepared according to general procedure A from indole (84 mg) and diethyl ethylidene malonate (107 mg) at  $-78^\circ\text{C}$  for 40 hours to provide the pure product as colorless oil. Yield: 142 mg (78%). HPLC analysis (Chiralcel OD-H, 10% <sup>1</sup>PrOH/hexanes, 0.70 mL/min, 254 nm;  $t_r$ (major) = 10.74 min,  $t_r$ (minor) = 12.6 min.) gave the isomeric composition of the product: 85.1% ee.  $[\alpha]_D^{20} = +1.3$  (54.1 mg/2 mL CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  0.91 (t,  $J = 6.9$  Hz, 3H), 1.26 (t,  $J = 6.9$  Hz, 3H), 1.45 (d,  $J = 6.6$  Hz, 3H), 3.81 (d,  $J = 6.9$  Hz, 1H), 3.86-3.93 (m, 3H), 4.22 (q,  $J = 6.9$  Hz, 1H), 7.00 (d,  $J = 2.7$  Hz, 1H), 7.10-7.18 (m, 2H), 7.31 (d,  $J = 7.5$  Hz, 1H), 7.67 (d,  $J = 7.5$  Hz, 1H), 8.18 (brs, 1H).

**(-)-enantiomer:** Prepared according to general procedure C : Cu(OTf)<sub>2</sub> (9.3 mg), (*S*)-isopropyl-trisoxazoline **2a** (6.5 mg), 1,1,2,2-tetrachloroethane (2.5 mL), indole (36 mg) and ethylidene malonate (46 mg) at  $-35^\circ\text{C}$  for 40 hours to provide the pure product as a colorless oil. Yield: 54 mg (60%). HPLC analysis (Chiralcel OD-H, 10% <sup>1</sup>PrOH/hexanes, 0.70 mL/min, 254 nm;  $t_r$ (major) = 9.67 min,  $t_r$ (minor) = 11.14 min) gave the isomeric composition of the product: 55.7% ee.  $[\alpha]_D^{20} = -1.3$  (18.0 mg/2 mL CHCl<sub>3</sub>).

**3. Determination of the absolute configuration:** The absolute configuration of **7a** was determined by an independent synthesis. Compound **7a** was transformed into compound **13**, whose optical rotation was compared to a known compound **13**.<sup>5</sup>



**a: Decarboxylation of compound 7a<sup>6</sup>:** To a suspension of NaCl (60 mg, 1 mmol) and malonate **7a** (160 mg, 0.5 mmol, 86% ee) in anhydrous DMSO (3 mL) was added H<sub>2</sub>O (40  $\mu$ L). The resulting mixture was stirred at  $160^\circ\text{C}$  for 18 hours and then  $80^\circ\text{C}$  for 11 hours. After cooling to room temperature, to the reaction mixture was added 40 mL of distilled water and extracted with dichloromethane (4 $\times$ 25 mL). The combined organic extracts were washed with brine, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered through cotton and concentrated *in vacuo*. Purification by flash chromatography (1:1

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## S14

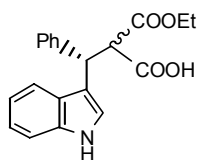
CH<sub>2</sub>Cl<sub>2</sub>/petroleum ether) gave 122 mg **11**<sup>3</sup> as white solid (84%).  $[\alpha]_D^{20} = + 25.5$  (25.9 mg/2 mL, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.12 (m, 3H), 3.01 (dd, *J* = 8.4, 15.3 Hz, 1H), 3.16 (dd, *J* = 7.5, 15.3 Hz, 1H), 4.04 (m, 2H), 4.81 (t, *J* = 7.6 Hz, 1H), 6.99-7.06 (m, 2H), 7.12-7.20 (m, 2H), 7.24-7.34 (m, 5H), 7.42 (d, *J* = 7.8 Hz, 1H), 8.01 (brs, 1H).

**b: N-methylation of 11 :** To a Schlenk tube containing NaH (30 mg, 0.62 mmol, 60% in mineral oil) was added compound **11** (120 mg, 0.41 mmol) in 2 mL of THF at 0°C. The resulting pale-yellow suspension was stirred for 15 minutes and CH<sub>3</sub>I (80 μL, 1.28 mmol) in 1 mL of THF was added. After 30 minutes at 0°C, the mixture was stirred at room temperature overnight. The resulting solution was passed through a short silica gel column, which was eluted with ether and dichloromethane. And the solvent was removed, and the pure product **12** was obtained as pale-yellow oil in 84% yield after purification by flash chromatography (1:15 Ethyl acetate/petroleum ether).  $[\alpha]_D^{20} = + 26.3$  (31.0 mg/2 mL, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 1.10 (t, *J* = 7.5 Hz, 3H), 3.00 (dd, *J* = 15.3, 8.4 Hz, 1H), 3.14 (dd, *J* = 15.0, 7.5 Hz, 1H), 3.73 (s, 3H), 4.03 (m, 2H), 4.79 (t, *J* = 7.8 Hz, 1H), 6.86 (s, 1H), 6.87-7.03 (m, 1H), 7.16-7.20 (m, 2H), 7.24-7.41 (m, 5H), 7.418-7.44 (m, 1H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 172.38, 144.07, 128.82, 128.65, 128.01, 127.97, 126.64, 126.23, 121.94, 119.78, 119.09, 109.40, 60.63, 41.82, 39.49, 32.97, 14.35; IR(KBr): 3110, 3059, 2976, 2902, 1723, 1612, 1550, 1485, 1474, 1367, 1330, 1265, 1253, 1033, 739, 697, 517 cm<sup>-1</sup>. MS (EI): 307 (M<sup>+</sup>, 26), 220 (100), 221 (19), 218 (9), 308 (6), 204 (6), 42 (4), 234 (4); HRMS (EI): Exact mass calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>2</sub> [M]<sup>+</sup>: 307.15723. Found: 307.15808.

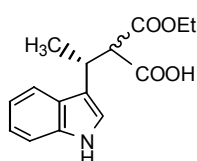
**c: Reduction of 12:** To a solution of compound **12** (72 mg, 0.23 mmol) in 1 mL of dichloromethane was added DIBAL-H (0.35 mL, 1.0 M in toluene) dropwise at -100 to -90 °C. The resulting mixture was stirred for 30 minutes and then 1 mL of anhydrous methanol was added. After stirring at -78 °C for 30 minutes, the mixture was warmed to room temperature, washed with HCl (0.5 N, 1 mL) and was extracted with dichloromethane (3 × 15 mL). The combined extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the removal of solvent, the residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1/10, v/v) to give aldehyde **13**<sup>5</sup> as colorless oil. Yield: 47.4 mg (77%).  $[\alpha]_D^{20} = + 29.9$  (47.4 mg/2 mL, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 3.08 (ddd, *J* = 1.8, 7.5, 15 Hz, 1H), 3.20 (ddd, *J* = 2.4, 8.1, 16.5 Hz, 1H), 3.74 (s, 3H), 4.86 (t, *J* = 7.8 Hz, 1H), 6.85 (s, 1H), 6.99-7.04 (dt, *J* = 1.2, 7.5 Hz, 1H), 7.16-7.22 (m, 2H), 7.24-7.38 (m, 5H), 7.38-7.41 (m, 1H), 9.74 (dd, *J* = 2.1, 2.7 Hz, 1H).

### Hydrolysis of alkylation adduct **7**<sup>7</sup>

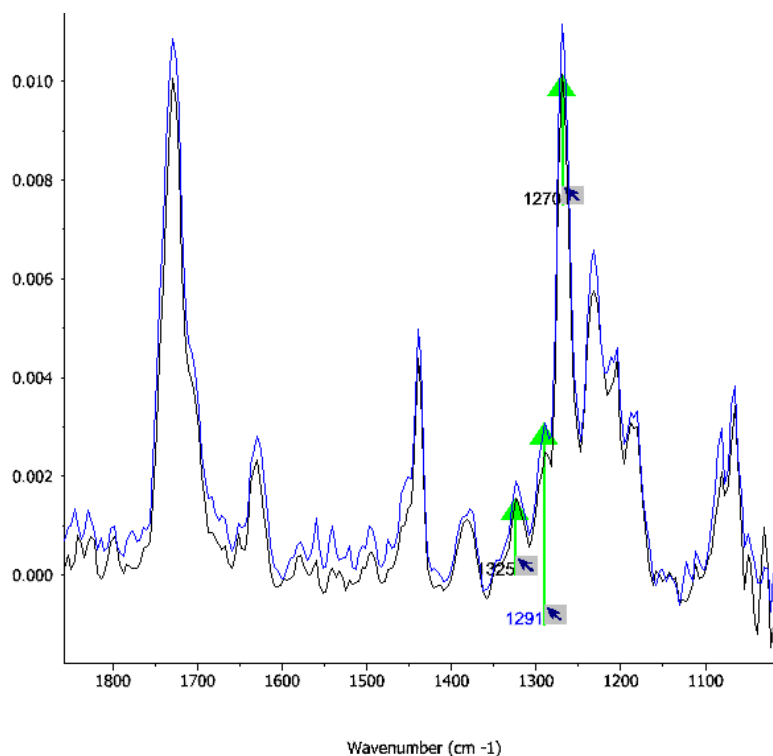
## S15



To a solution of compound **7a** (R-enantiomer, >99.0%ee, 109 mg, 0.30 mmol) in 3 mL of mixed solvent of THF and ethanol (1/1, v/v), was added KOH (20 mg, 0.36 mmol). The resulting solution was stirred at room temperature. After the reaction was complete (monitored by TLC), the mixture was concentrated under reduced pressure. Then 5 mL of water was added to the mixture, followed by a solution of HCl (0.5 N) in dropwise till PH = 1. The resulting white suspension was extracted with ethyl acetate (5 × 10 mL). The combined extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the removal of solvent, the residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1/1, v/v) to give **14a** as pale yellow solid (mixtures of diastereomers, about 1:1). Yield: 79 mg (81%). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>COCD<sub>3</sub>): δ 0.94-0.99 (m, 3H), 3.89-3.97 (m, 2H), 4.39-4.47 (m, 1H), 5.02-5.08 (m, 1H), 6.94-6.97 (m, 1H), 6.99-7.15 (m, 2H), 7.21-7.25 (m, 2H), 7.32-7.35 (m, 1H), 7.45-7.59 (m, 4H), 10.15 (brs, 1H).

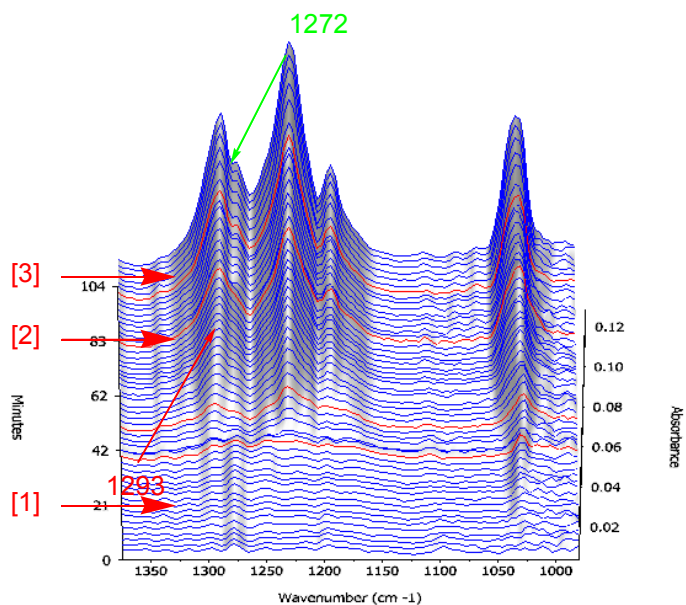


To a solution of compound **7n** (90 mg, 0.30 mmol) in 3 mL of mixed solvent of THF and ethanol (1/1, v/v), was added KOH (28 mg, 0.45 mmol). The resulting solution was stirred at room temperature. After the reaction was complete (monitored by TLC), the mixture was concentrated under reduced pressure. Then 5 mL of water was added to the mixture, followed by a solution of HCl (0.5 N) in dropwise till PH = 1. The resulting white suspension was extracted with ethyl acetate (5 × 10 mL). The combined extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After the removal of solvent, the residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1/1, v/v) to give **14n** as viscous oil (mixtures of diastereomers, about 2:1). Yield: 81 mg (92 %). <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>COCD<sub>3</sub>): δ 0.86 (t, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 1H), 1.43 (m, 3H), 3.84 (m, 3.4H), 4.18 (q, *J* = 7.2 Hz, 0.7H), 6.99-7.11 (m, 2H), 7.21-7.24 (m, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 10.1 (brs, 1H).

**The IR spectrum of malonate 6b in TTCE.**

**The in situ IR spectrum of trisoxazoline 2a/Cu(OTf)<sub>2</sub> and malonate 6b in TTCE.** Background: TTCE. Cu(OTf)<sub>2</sub> (1 equiv) was added to a solution of trisoxazoline **2a** (1 equiv) in six equal aliquots under N<sub>2</sub> at time intervals of about eight minutes. Only frequency at 1293 cm<sup>-1</sup> were observed with the addition of Cu(OTf)<sub>2</sub>. After the addition of Cu(OTf)<sub>2</sub>, the resulting cloudy solution was stirred for another 30 minutes. Then one equivalent of malonate **6b** was added, and a small peak at 1272 cm<sup>-1</sup> was observed, which might be the vibrational frequency of C-O bond. Although a sharp peak at 1293 cm<sup>-1</sup> was still observed, we could not draw any conclusion that the triflate anion coordinated to copper center after the addition of malonate **6b**, due to the disturbance of the vibrational frequency of C-O bond. To be simplicity, the absorption changes which could be attributed to CF<sub>3</sub> and SO<sub>3</sub> vibrational frequencies are not discussed.

S17

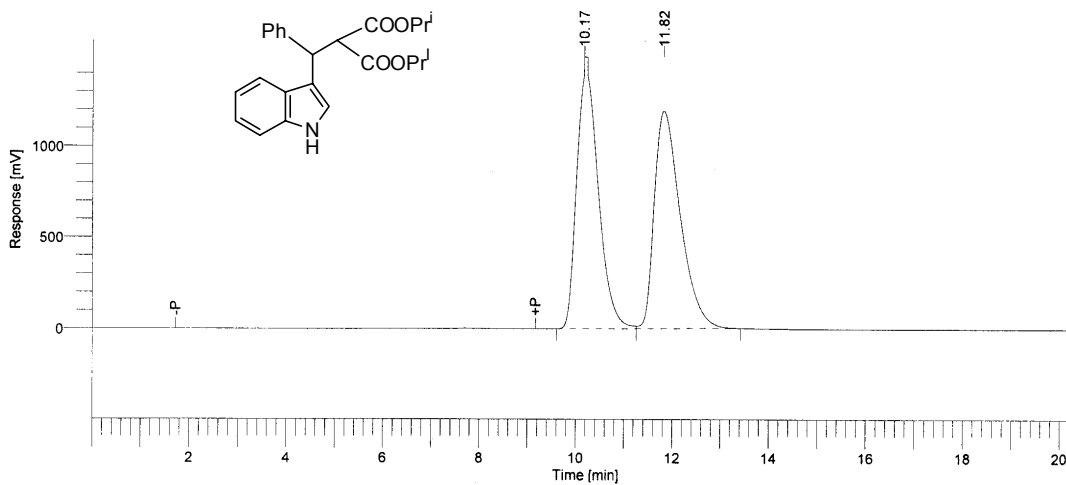


[1]: Cu(OTf)<sub>2</sub> was added. [2] 1.0 equivalent of Cu(OTf)<sub>2</sub> was fully added. [3] 1 equivalent of malonate **6b** was added.

**References:**

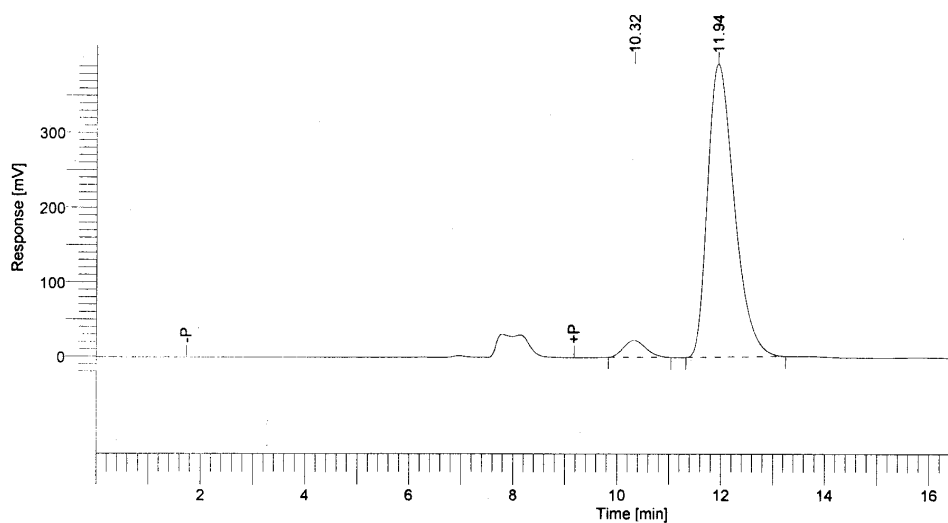
- (1) (a) Evans, D. A.; Peterson, G. S.; Johnson, J. S.; Barnes, D. M.; Campos, K. R.; Woerper, K. A. *J. Org. Chem.*, **1998**, 63, 4541; (b) Muller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta.* **1991**, 74, 232.
- (2) Zhou, J.; Tang, Y. *J. Am. Chem. Soc.* **2002**, 124, 9030.
- (3) Zhuang, W.; Hansen, T.; Jørgensen, K. A. *Chem. Commun.* **2001**, 347.
- (4) Albright, J. D.; Snyder, H. R. *J. Am. Chem. Soc.* **1959**, 81, 223.
- (5) Austin, J. F.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, 124, 1172.
- (6) Krapcho, A. P. *Synthesis* **1982**, 805.
- (7) Jeannin, L.; Nagy, T.; Vassileva, E.; Sapi, J.; Laronze, J. Y. *Tetrahedron Lett.* **1995**, 36, 2057.

**(+)-Isopropyl-2-isopropoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 3, table 8) Chiralcel OD-H, 20% iPrOH/n-hexane, 0.55 mL/min, 254nm).



### report

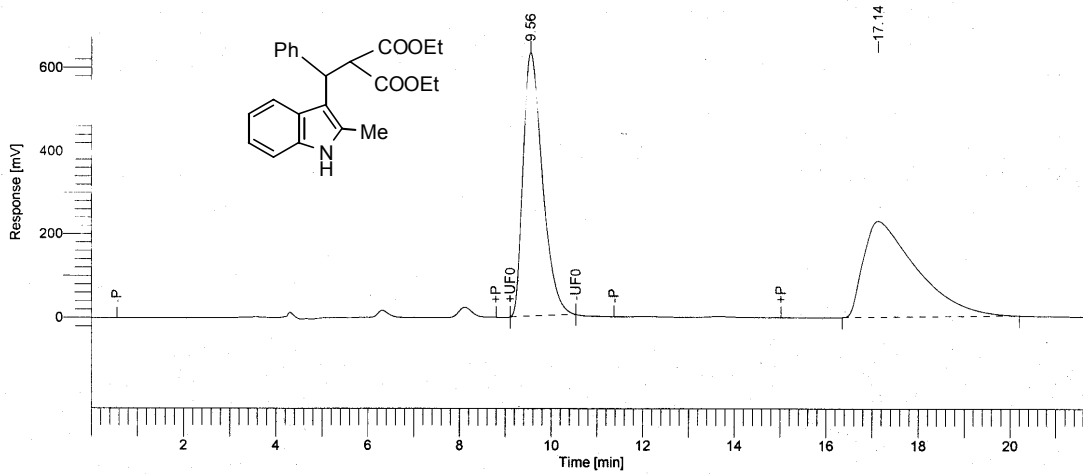
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		10.170	87730789.60	2.90e+06	50.17
2		11.823	87134160.43	2.32e+06	49.83
			1.75e+08	5.22e+06	100.00



### report

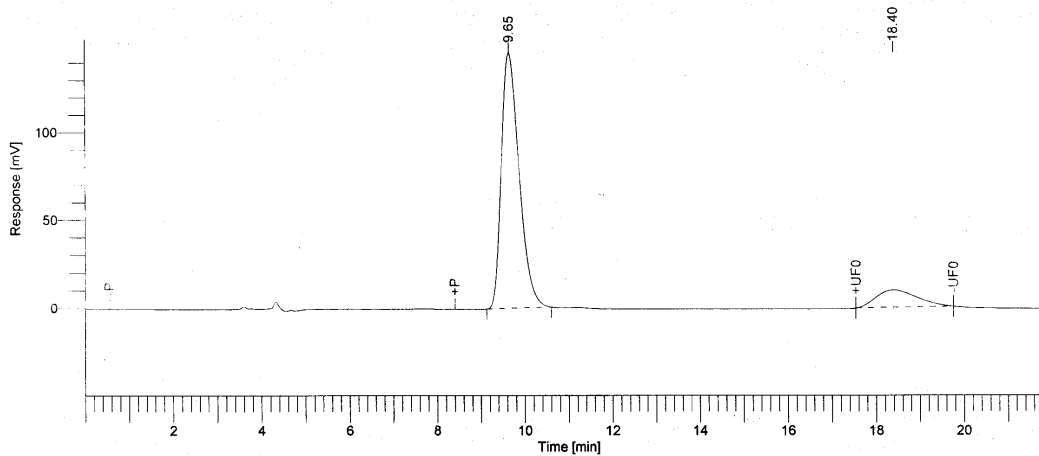
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		10.325	1338207.72	44806.72	4.64
2		11.938	27480044.38	768186.67	95.36
			28818252.10	812993.38	100.00

**(-)-Ethyl 2-ethoxycarbonyl-3-[3-(2-methylindolyl)]-3-phenylpropanoate (entry 1, Table 9).** Chiralcel OD-H, 15% iPrOH/n-hexane, 0.90 mL/min, 254nm.



## report

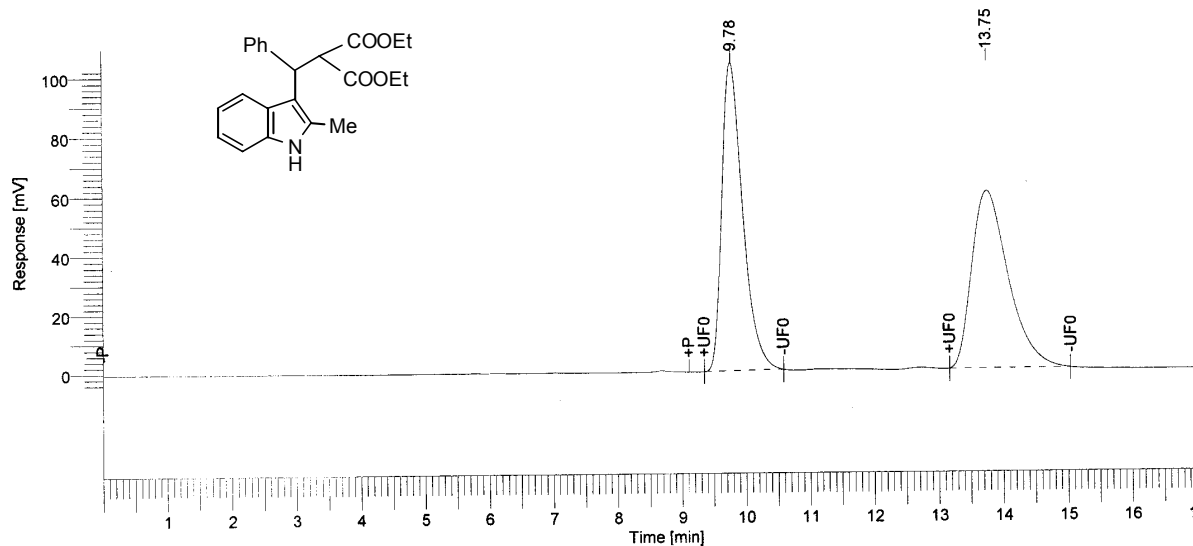
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		9.557	35986957.30	1.23e+06	50.27
2		17.136	35601120.46	446068.98	49.73
			71588077.77	1.67e+06	100.00



## report

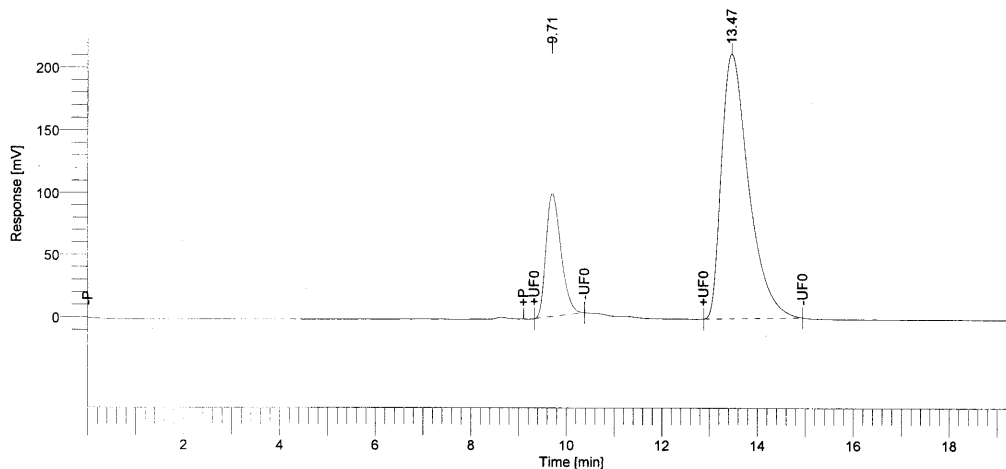
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		9.645	7922378.79	282998.92	86.50
2		18.395	1236955.85	19215.59	13.50
			9159334.64	302214.51	100.00

**(+)-Ethyl 2-ethoxycarbonyl-3-[3-(2-methylindolyl)]-3-phenylpropanoate (entry 1, Table 9).** Chiralcel OD-H, 15% iPrOH/n-hexane, 0.70 mL / min, 254nm.



## report

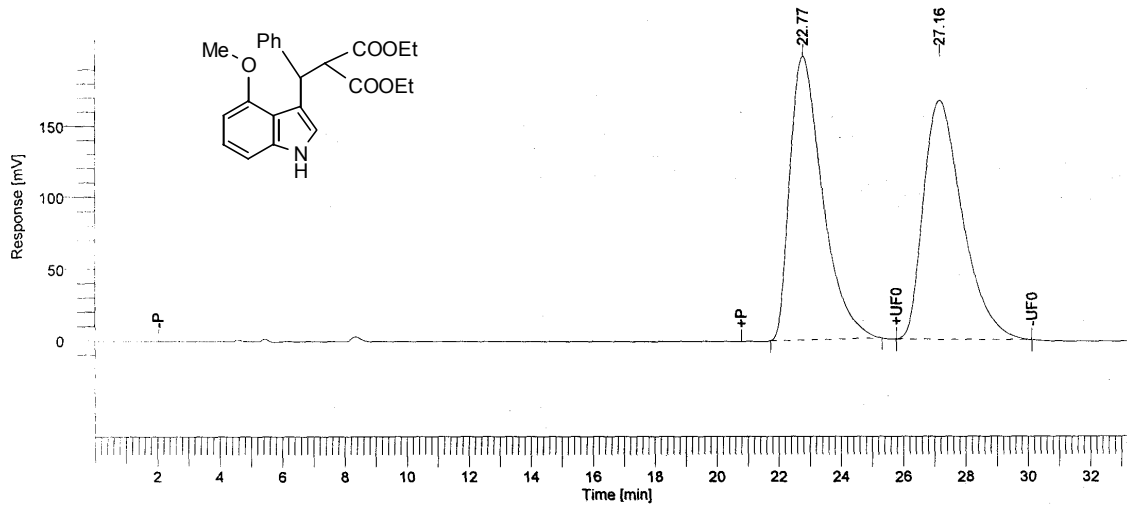
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		9.775	4581420.55	202547.55	49.97
2		13.748	4586418.04	117041.09	50.03
			9167838.59	319588.63	100.00



## report

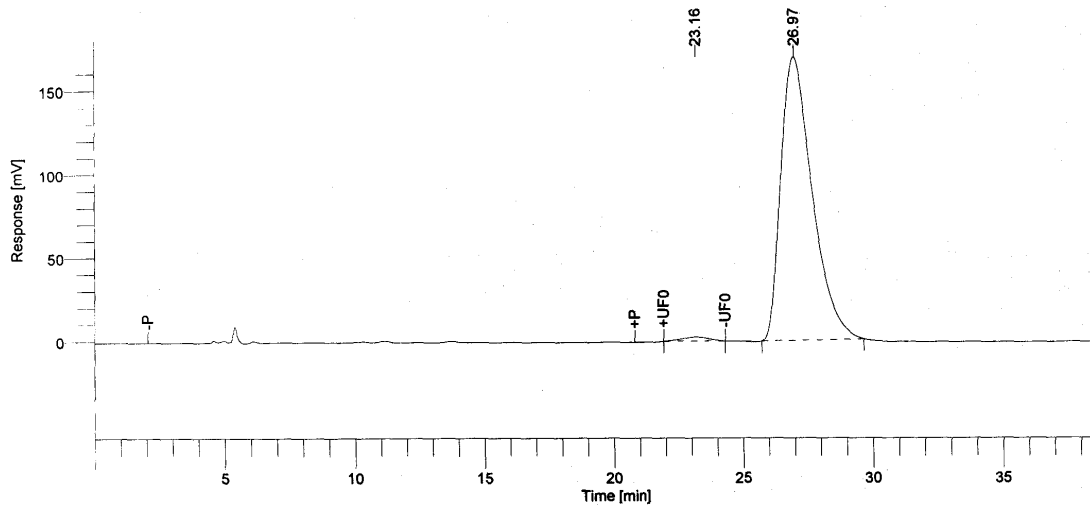
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		9.707	4156524.82	192074.82	20.32
2		13.473	16301130.39	411805.99	79.68
			20457655.22	603880.82	100.00

**(+)-Ethyl 2-ethoxycarbonyl-3-[3-(4-methoxyindolyl)]-3-phenylpropanoate (entry 2, Table 9).** Chiralcel OD-H, 6% iPrOH/n-hexane, 0.80 mL/min, 254nm



## report

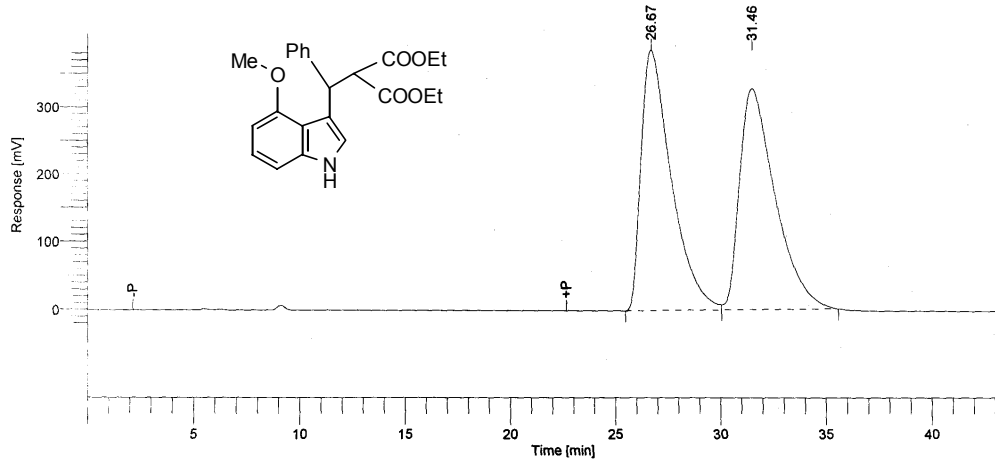
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		22.775	28252433.94	387686.54	50.04
2		27.160	28206041.18	325961.15	49.96
			56458475.12	713647.69	100.00



## report

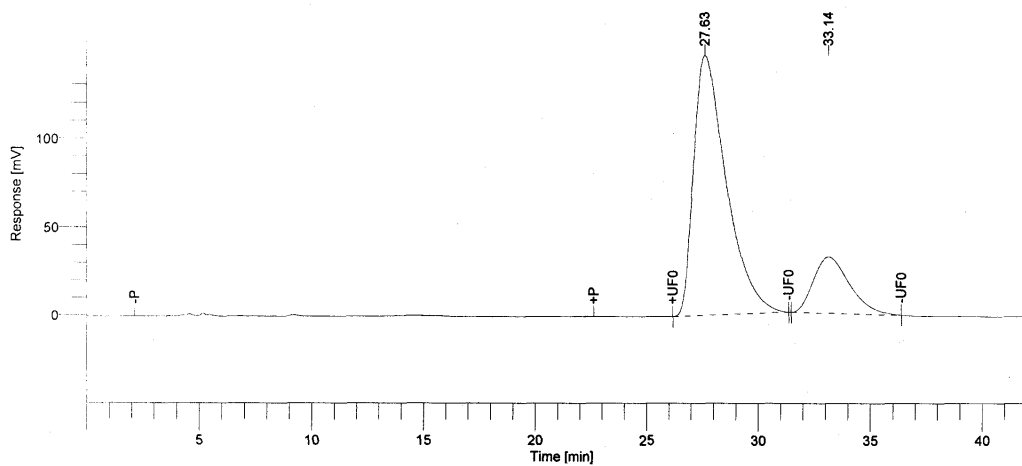
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		23.162	328044.98	4799.01	1.17
2		26.967	27610756.12	327964.41	98.83
			27938801.10	332763.42	100.00

**(-)-Ethyl 2-ethoxycarbonyl-3-[3-(4-methoxyindolyl)]-3-phenylpropanoate (entry 2, Table 9).** Chiralcel OD-H, 6% iPrOH/n-hexane, 0.80 mL / min, 254nm



## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		26.670	75304862.72	755847.84	50.15
2		31.461	74839488.44	641635.00	49.85
			1.50e+08	1.40e+06	100.00

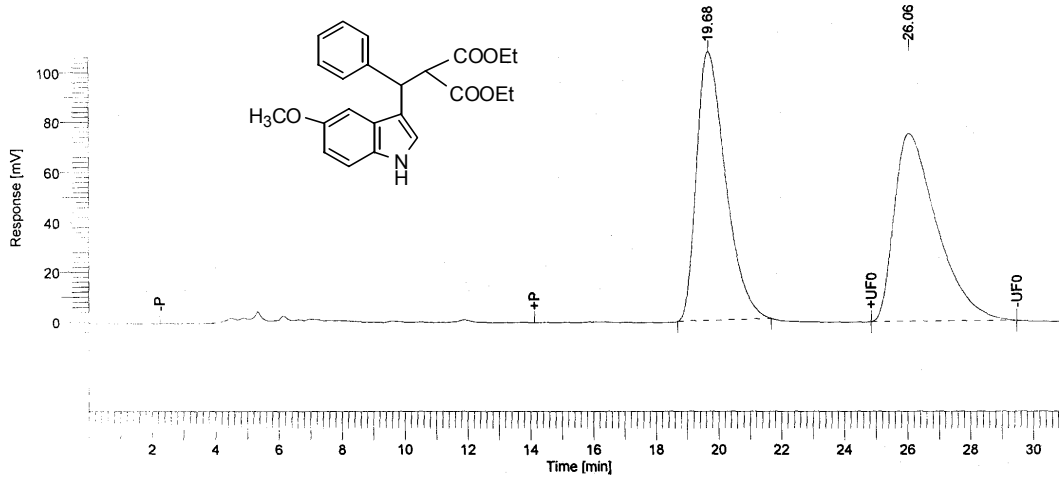


## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		27.627	29099997.55	284254.36	80.56
2		33.143	7023022.53	62673.29	19.44
			36123020.08	346927.65	100.00

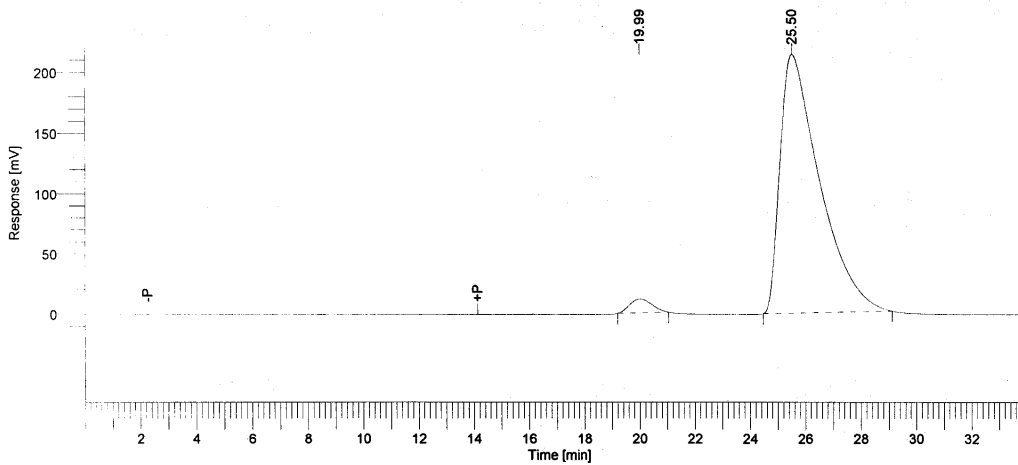
S23

(+)-Ethyl 2-ethoxycarbonyl-3-[3-(5-methoxyindolyl)]-3-phenylpropanoate (entry 3, Table 9). Chiralcel OD-H, 10% iPrOH / n-hexane, 0.80 mL min, 254nm



report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		19.678	13373495.38	207228.82	49.75
2		26.058	13506250.70	143540.25	50.25
			26879746.08	350769.07	100.00

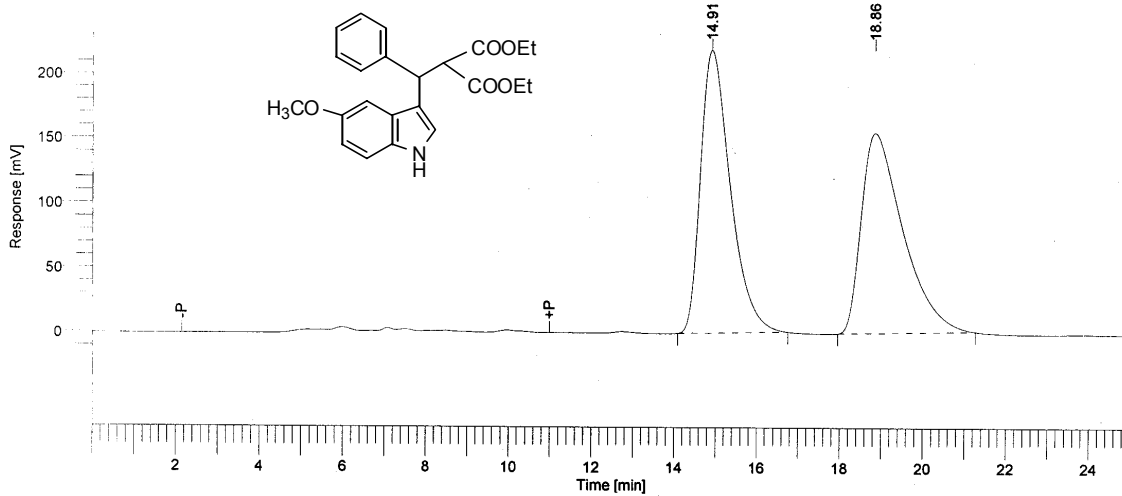


report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		19.987	1238231.42	22235.81	2.90
2		25.497	41405078.27	415051.50	97.10
			42643309.69	437287.31	100.00

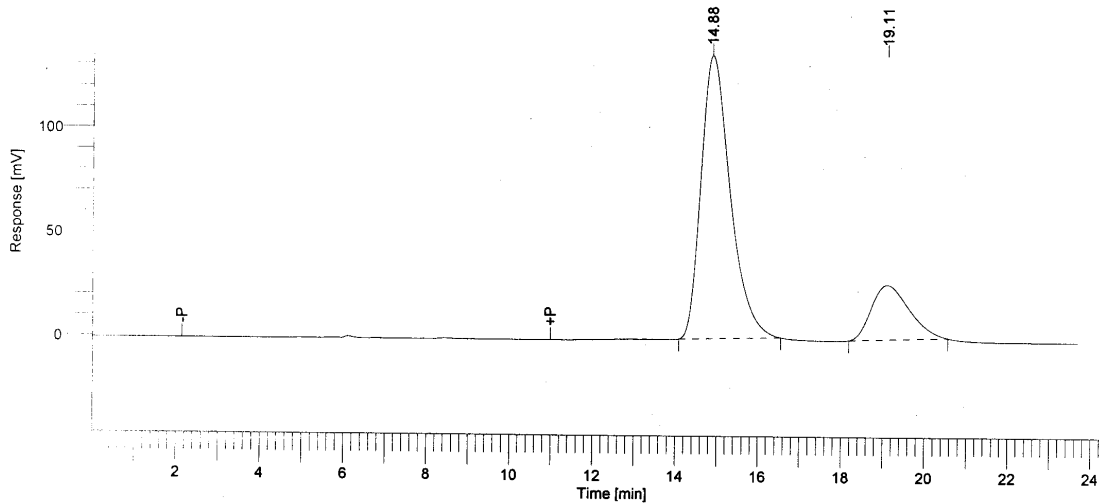
S24

**(-)-Ethyl 2-ethoxycarbonyl-3-[3-(5-methoxyindolyl)]-3-phenylpropanoate (entry 2, Table 9).** Chiralcel OD-H, 15% iPrOH / n-hexane, 0.70 mL / min, 254nm



report

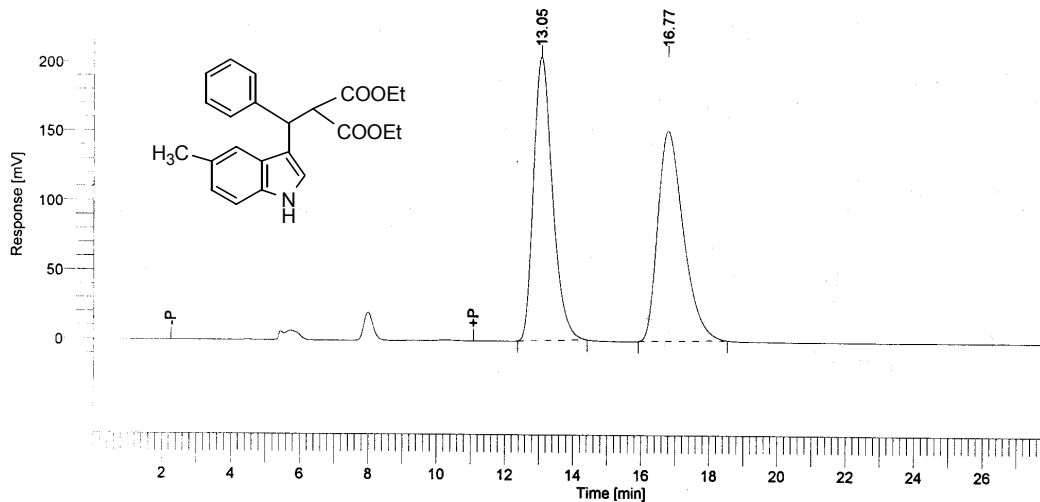
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		14.912	21333757.32	424810.80	50.39
2		18.855	21003968.58	299659.67	49.61
			42337725.90	724470.47	100.00



report

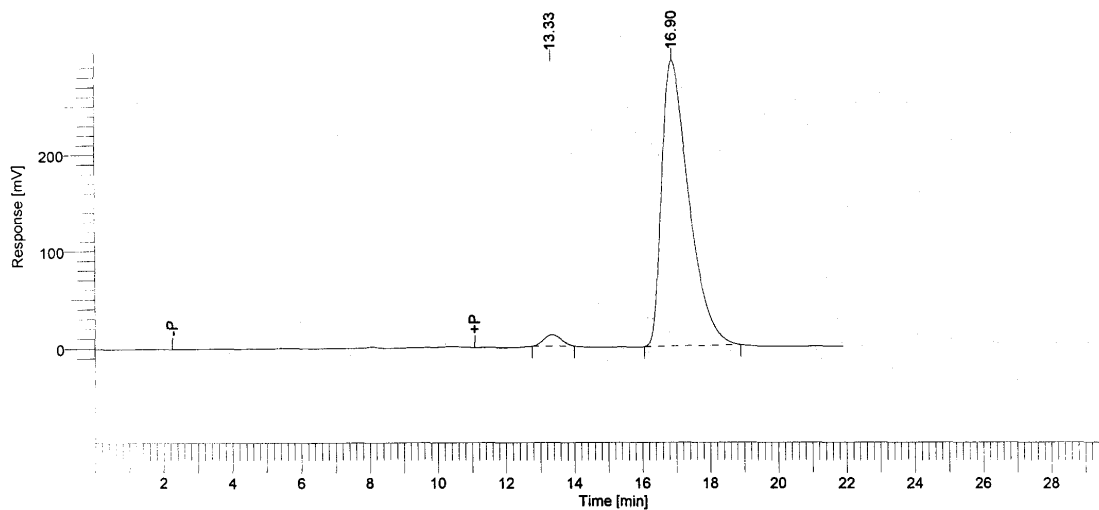
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		14.877	12945230.64	262556.75	80.23
2		19.105	3189240.58	50675.51	19.77
			16134471.22	313232.26	100.00

**(+)-Ethyl 2-ethoxycarbonyl-3-[3-(5-methylindolyl)]-3-phenylpropanoate (entry 4, Table 9).** Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm



## report

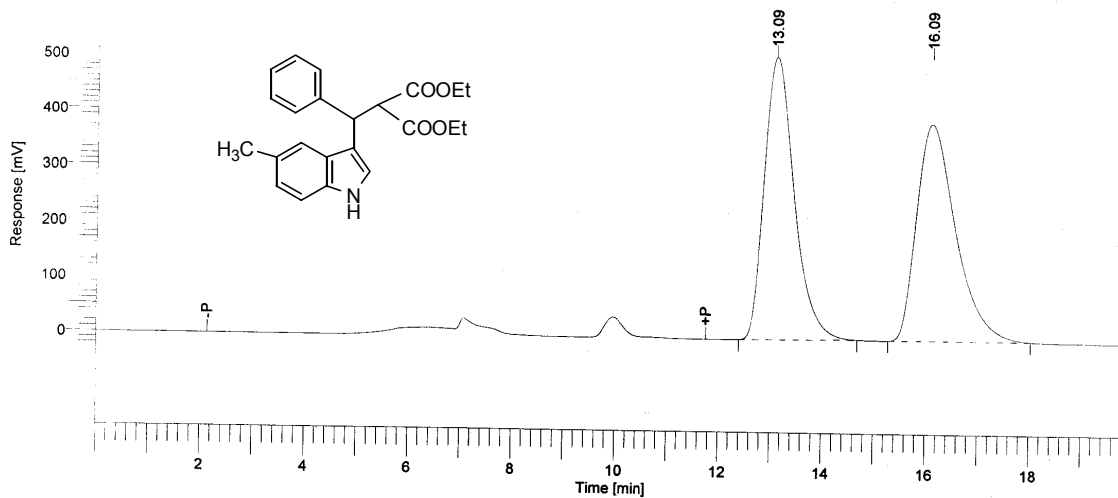
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		13.051	15354696.69	398336.09	49.98
2		16.771	15368801.70	294151.57	50.02
			30723498.39	692487.66	100.00



## report

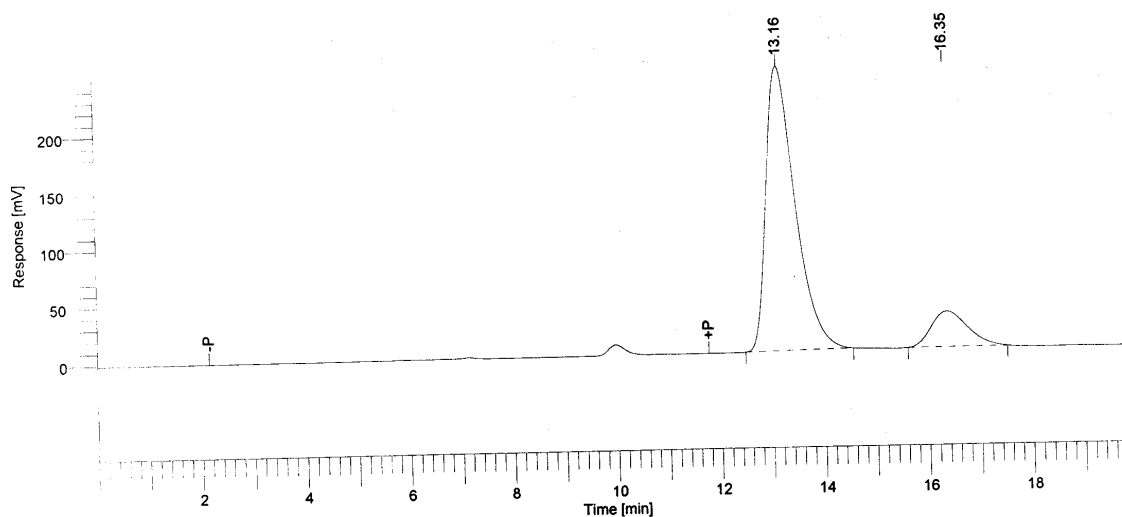
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		13.334	783559.86	22102.74	2.44
2		16.895	31383779.73	566915.20	97.56
			32167339.59	589017.94	100.00

(-)-Ethyl 2-ethoxycarbonyl-3-[3-(5-methylindolyl)]-3-phenylpropanoate (entry 4, Table 9). Chiralcel OD-H, 15% iPrOH/n-hexane, 0.70 mL/min, 254nm



## report

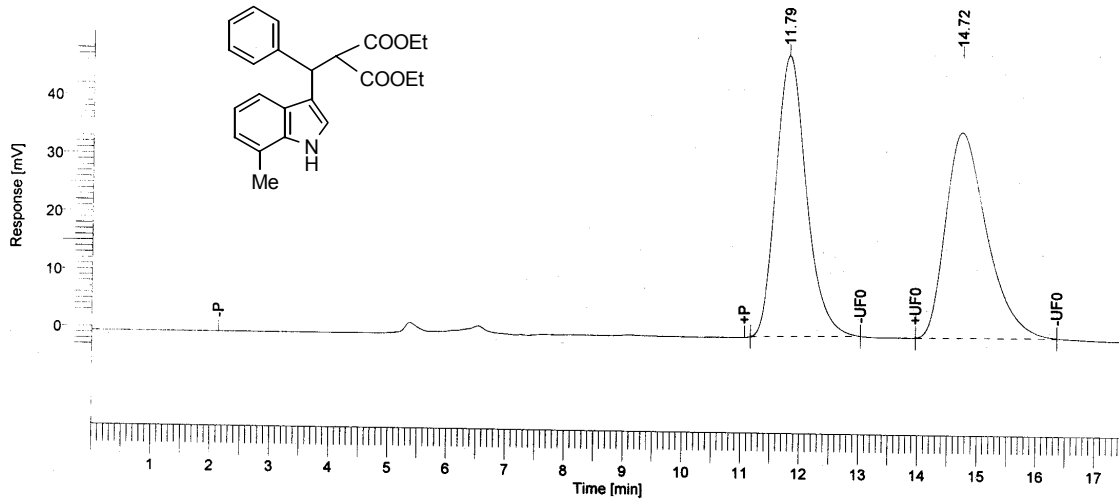
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		13.089	39922668.03	994676.33	50.05
2		16.090	39843607.25	761066.04	49.95
			79766275.28	1.76e+06	100.00



## report

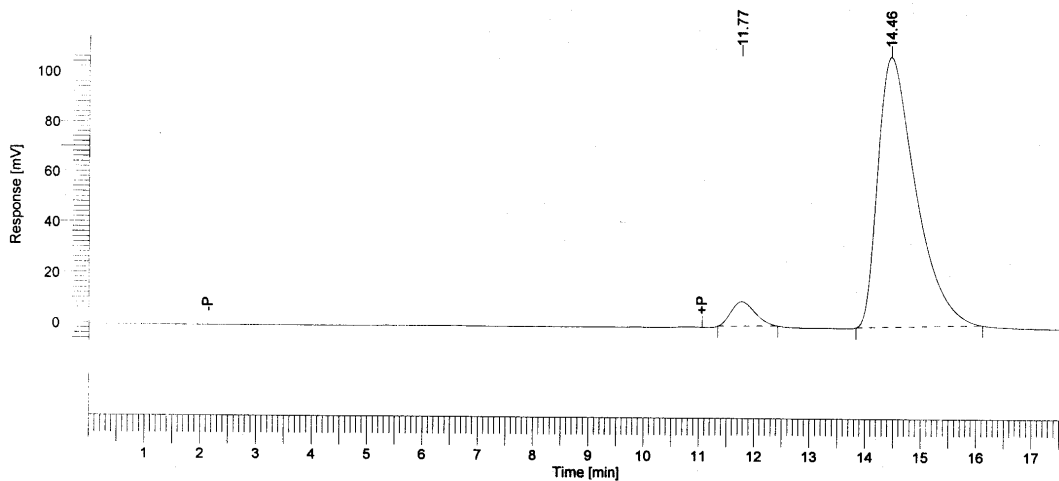
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		13.158	18717106.07	480653.04	86.70
2		16.355	2871738.57	59628.85	13.30
			21588844.64	540281.89	100.00

**(+)-Ethyl 2-ethoxycarbonyl-3-[3-(7-methylindolyl)]-3-phenylpropanoate (entry 5, Table 9).** Chiralcel OD-H, 20% iPrOH/n-hexane, 0.6 mL/min, 254nm.



## report

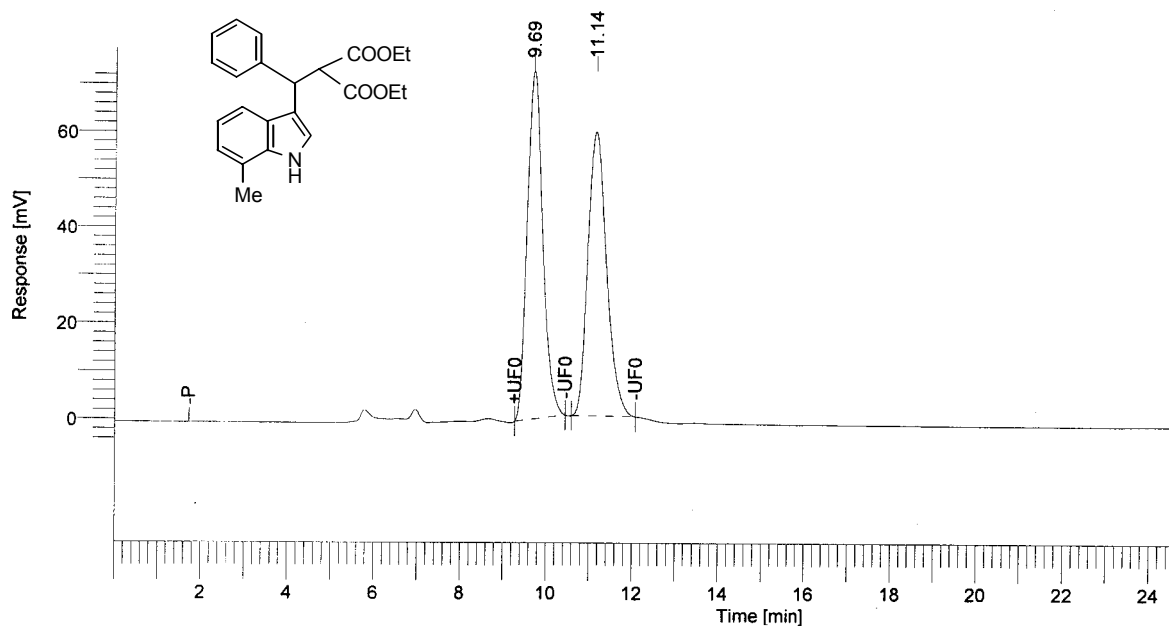
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		11.792	3378514.81	93920.72	50.24
2		14.720	3346239.37	69065.38	49.76
			6724754.18	162986.10	100.00



## report

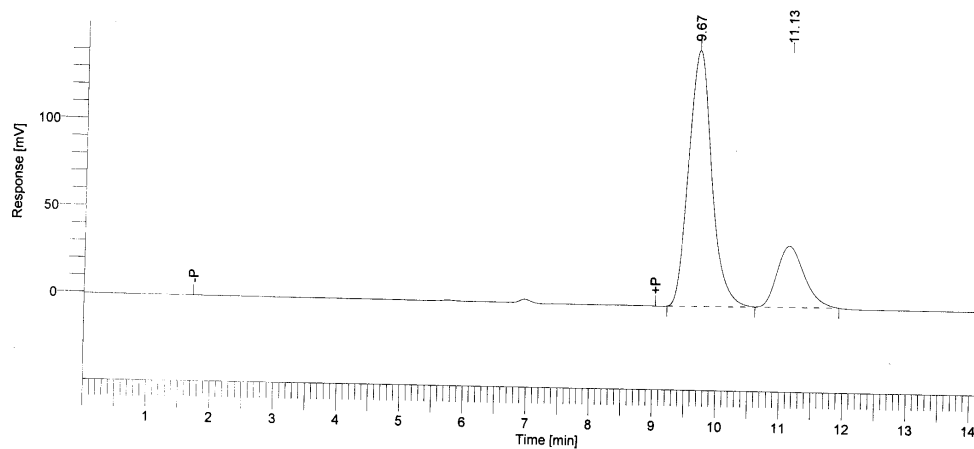
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		11.774	572304.69	18912.23	5.48
2		14.459	9868032.23	209481.75	94.52
			10440336.91	228393.98	100.00

**(-)-Ethyl 2-ethoxycarbonyl-3-[3-(5-methylindolyl)]-3-phenylpropanoate (entry 5, Table 9).** Chiralcel OD-H, 20% iPrOH / n-hexane, 0.60 mL / min, 254nm.



### report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		9.693	3560405.27	141591.33	50.45
2		11.143	3497539.26	115566.69	49.55
			7057944.53	257158.02	100.00

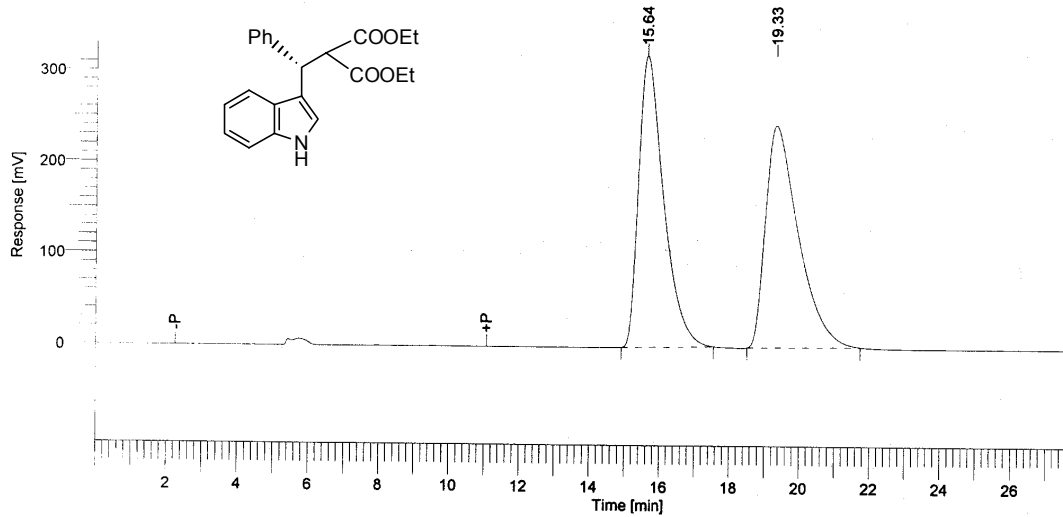


### report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		9.670	7352979.31	288724.73	77.83
2		11.132	2094127.48	69988.41	22.17
			9447106.79	358713.14	100.00

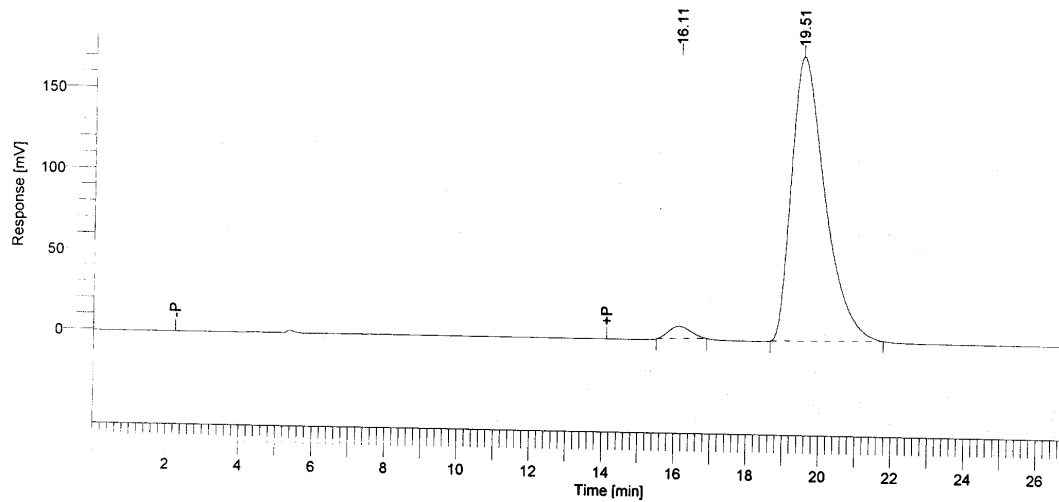
**(S)-Ethyl-2-ethoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 1, table 10)

Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm



## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.638	30931125.92	619085.93	50.06
2		19.335	30862237.19	471385.52	49.94
			61793363.11	1.09e+06	100.00



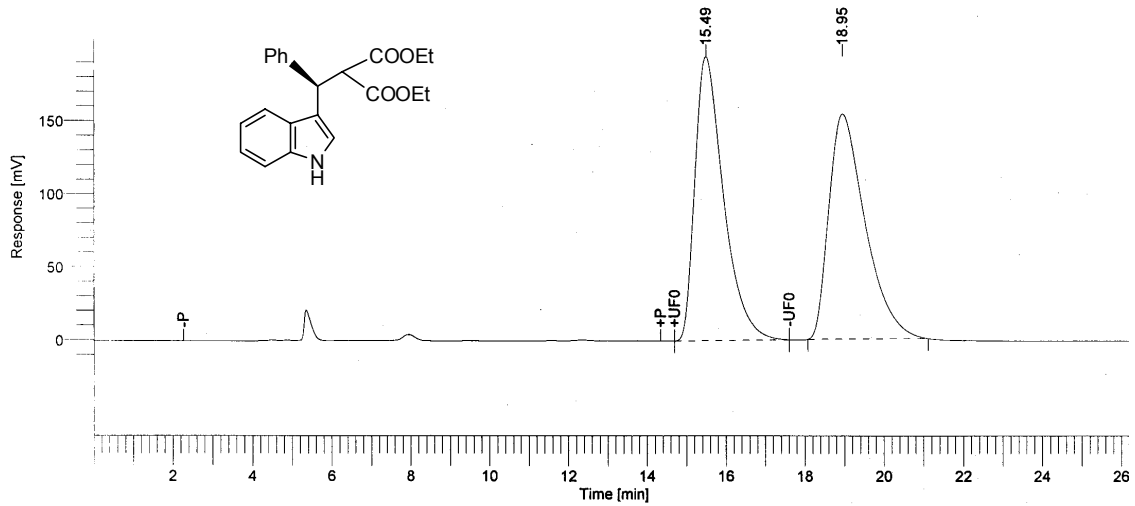
## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		16.110	639606.79	15134.85	2.84
2		19.511	21847045.90	340752.72	97.16
			22486652.69	355887.56	100.00

S30

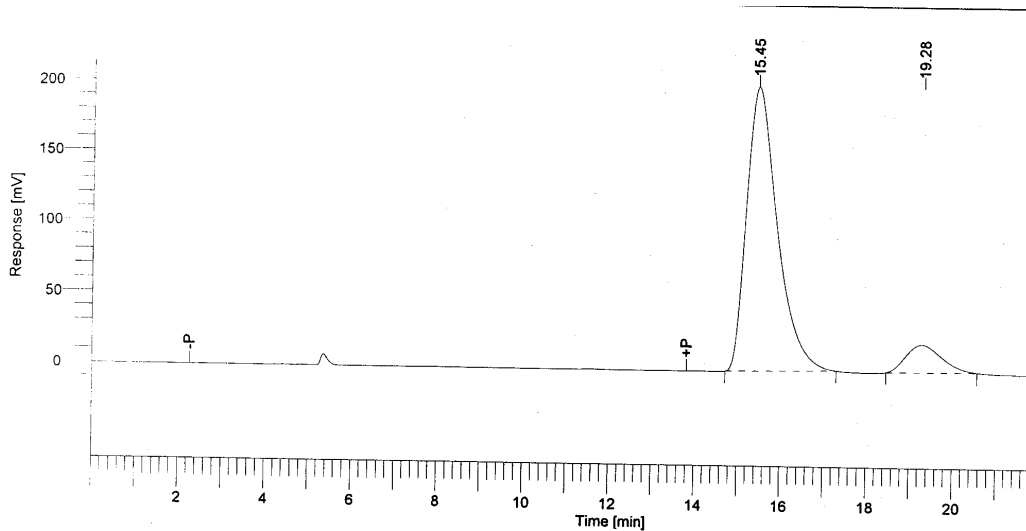
**(R)-Ethyl-2-ethoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 1, table 10)

Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm



report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.488	19081807.18	376950.61	49.98
2		18.949	19098492.93	298769.66	50.02
			38180300.11	675720.27	100.00



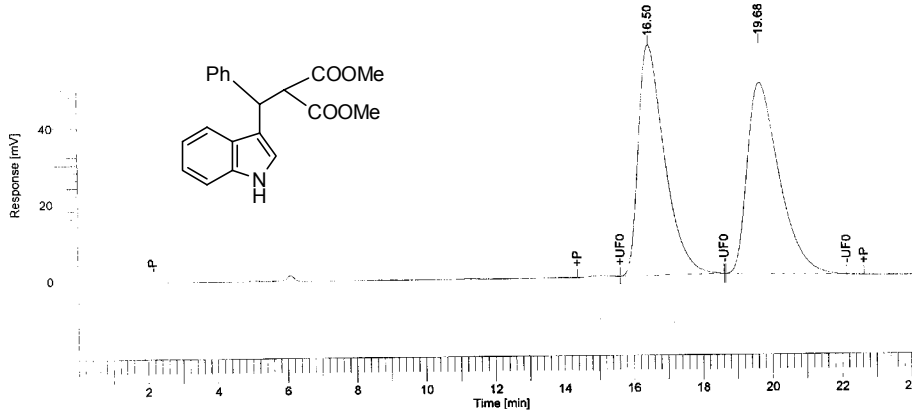
report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.447	19573268.61	391563.50	89.92
2		19.282	2193875.52	38153.17	10.08
			21767144.13	429716.67	100.00

S31

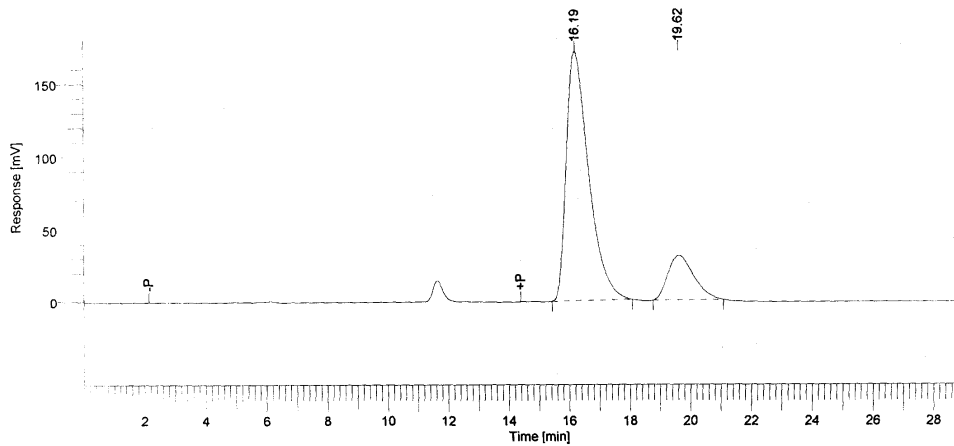
**(-)-Methyl-2-methoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 2, table 10)

Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm



report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		16.495	6142089.59	117005.98	50.00
2		19.683	6143304.19	97044.36	50.00
			12285393.78	214050.33	100.00

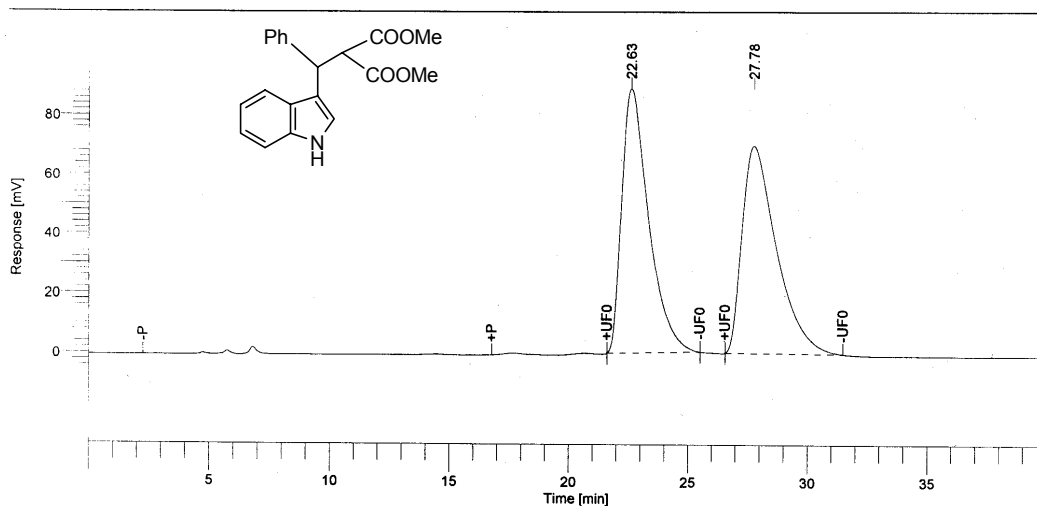


report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		16.195	17001929.86	330172.83	82.77
2		19.619	3539044.98	59568.20	17.23
			20540974.84	389741.04	100.00

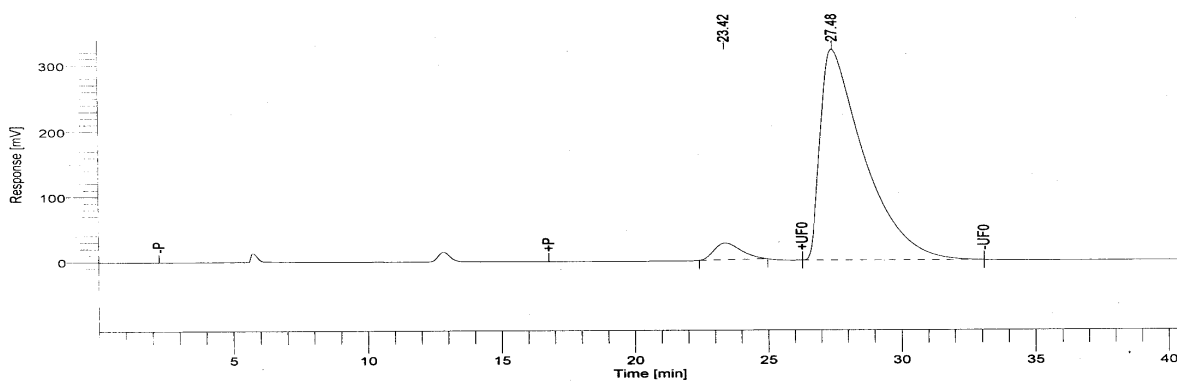
S32

**(+)-Methyl-2-methoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 2, table 10)  
 Chiralcel OD-H, 15% iPrOH/n-hexane, 0.70 mL/min, 254nm



report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		22.630	13511866.65	172635.56	50.02
2		27.782	13502856.98	135731.98	49.98
			27014723.64	308367.54	100.00

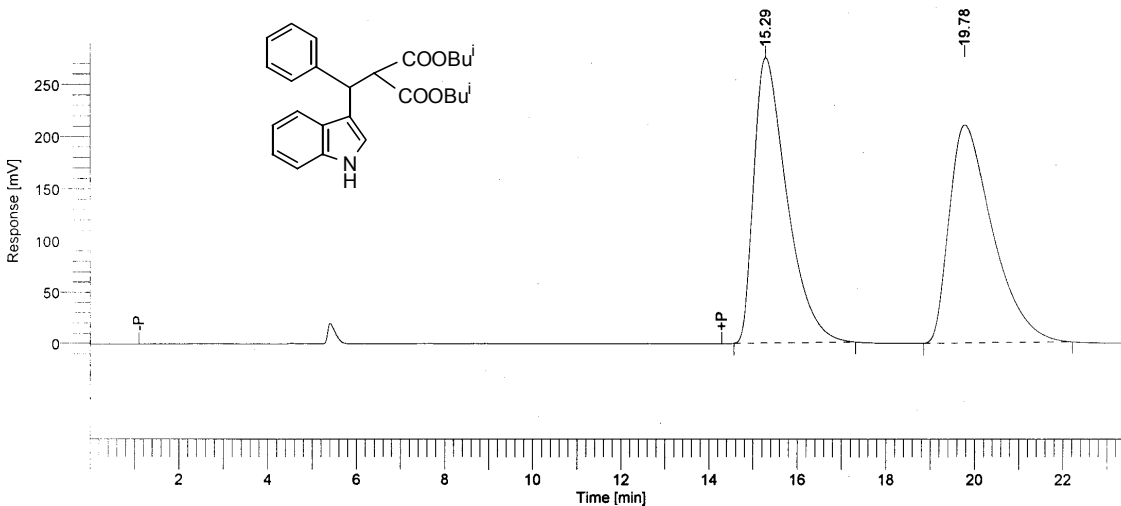


report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		23.416	3539138.47	50511.44	4.73
2		27.475	71320288.93	623468.57	95.27
			74859427.40	673980.02	100.00

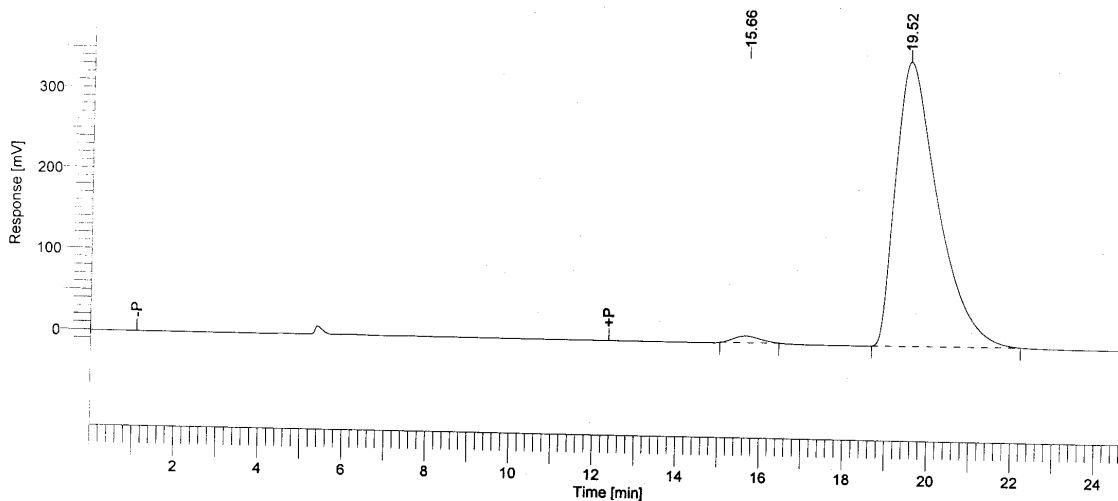
S33

**(+)-iso-Butyl-2-isobutoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 3, table 10) Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm



report

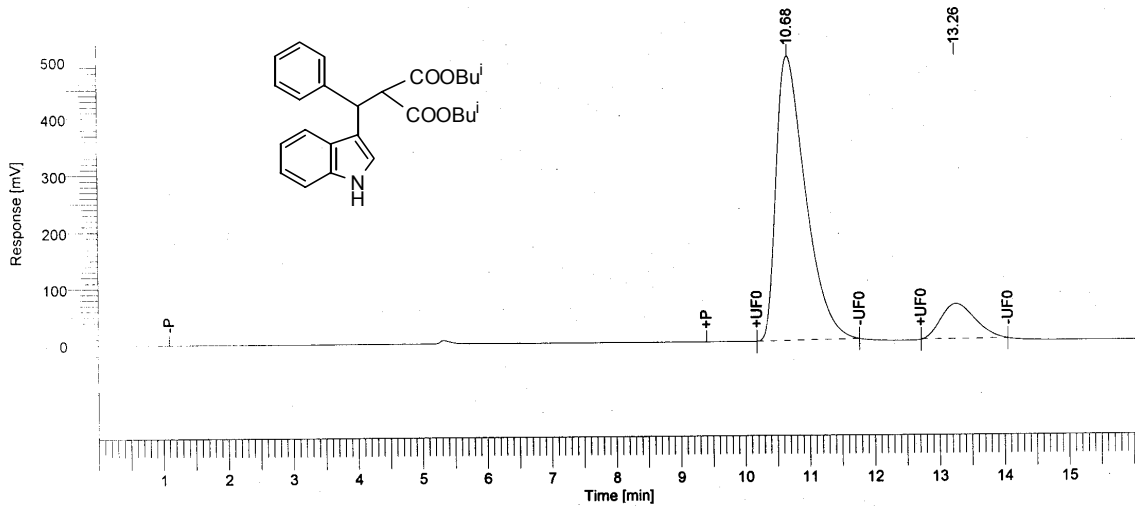
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.292	27869879.37	532157.98	50.03
2		19.782	27838883.27	406800.79	49.97
			55708762.64	938958.76	100.00



report

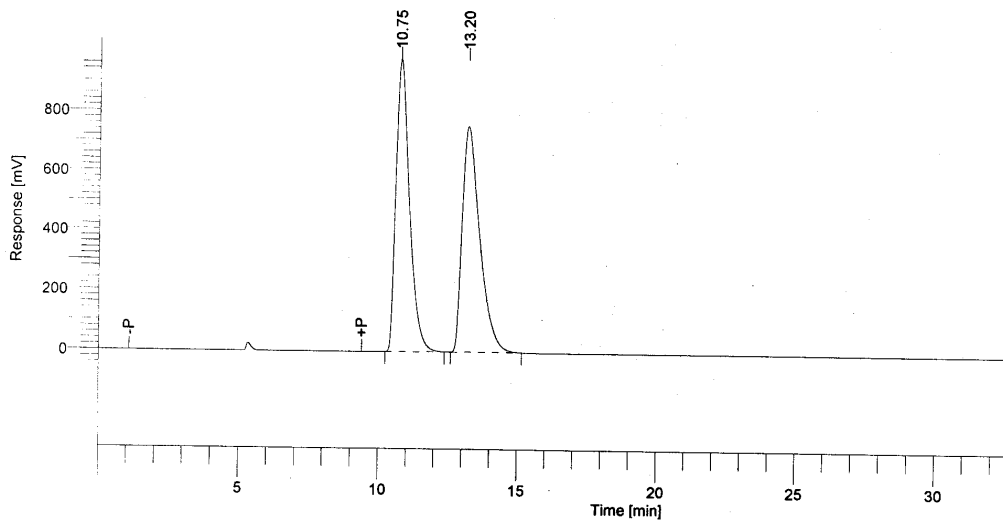
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.655	704745.95	16166.84	1.46
2		19.516	47695225.90	685096.65	98.54
			48399971.85	701263.49	100.00

**(-)-iso-Butyl-2-isobutoxycarbonyl-3-(3-indolyl)-3-phenyl propanoate** (entry 3, table 10) Chiralcel OD-H, 15% iPrOH/n-hexane, 0.70 mL/min, 254nm



## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		10.678	30779170.87	971345.96	87.43
2		13.257	4425837.29	121454.22	12.57
			35205008.16	1.09e+06	100.00

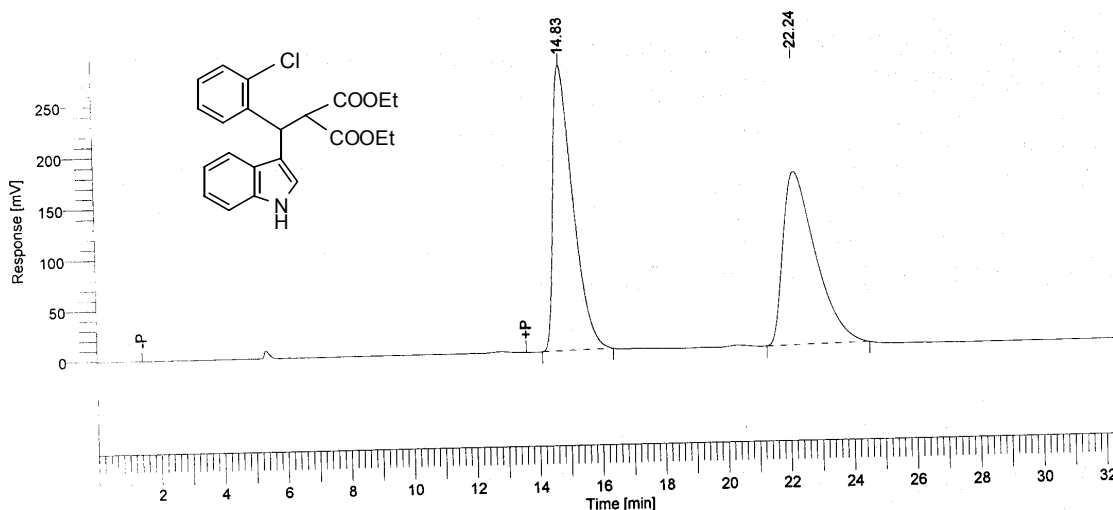


## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		10.749	64281990.18	1.90e+06	50.02
2		13.195	64218679.06	1.47e+06	49.98
			1.29e+08	3.37e+06	100.00

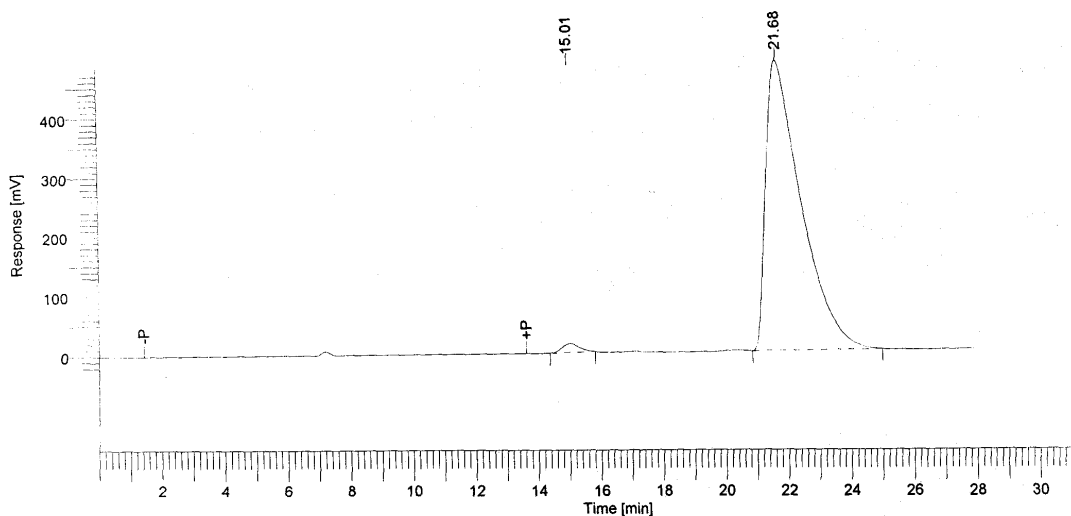
S35

**(+)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(o-chlorophenyl) propanoate (entry 4, Table 10)** Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm



report

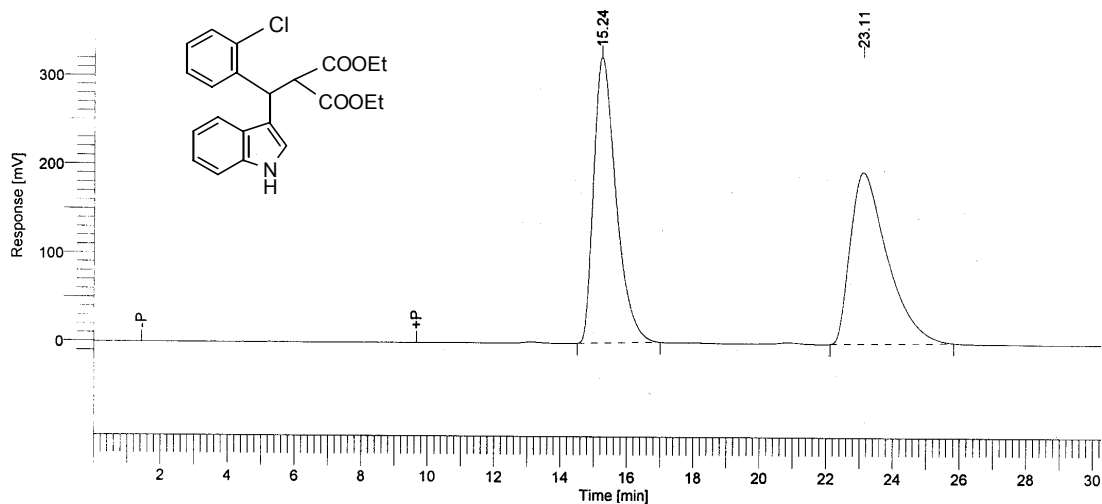
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		14.833	23807169.40	540742.84	50.37
2		22.241	23454227.80	327456.32	49.63
			47261397.20	868199.17	100.00



report

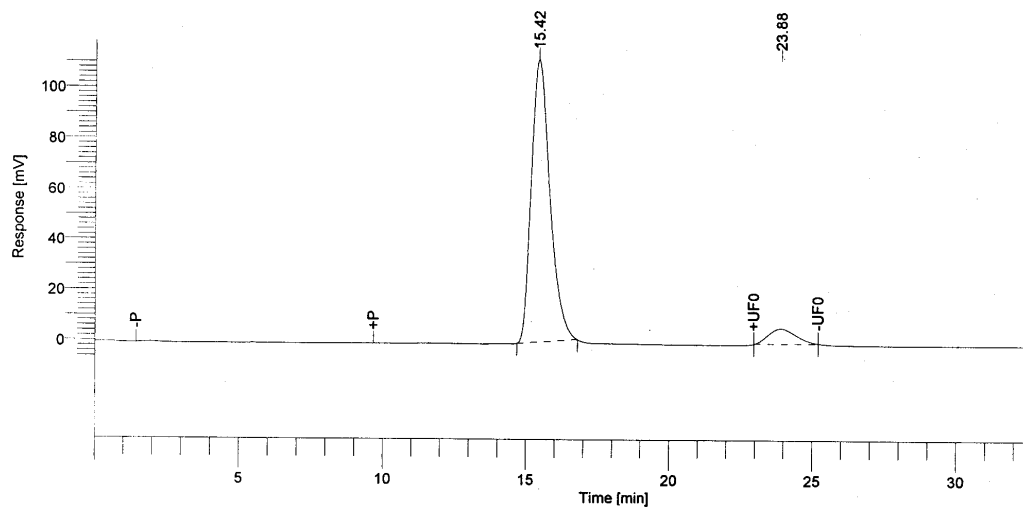
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.006	1105140.17	28103.70	1.52
2		21.681	71609175.95	923268.14	98.48
			72714316.12	951371.84	100.00

**(-)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(o-chlorophenyl) propanoate (entry 4, Table 10)** Chiralcel OD-H, 10% iPrOH/n-hexane, 0.80 mL/min, 254nm.



## report

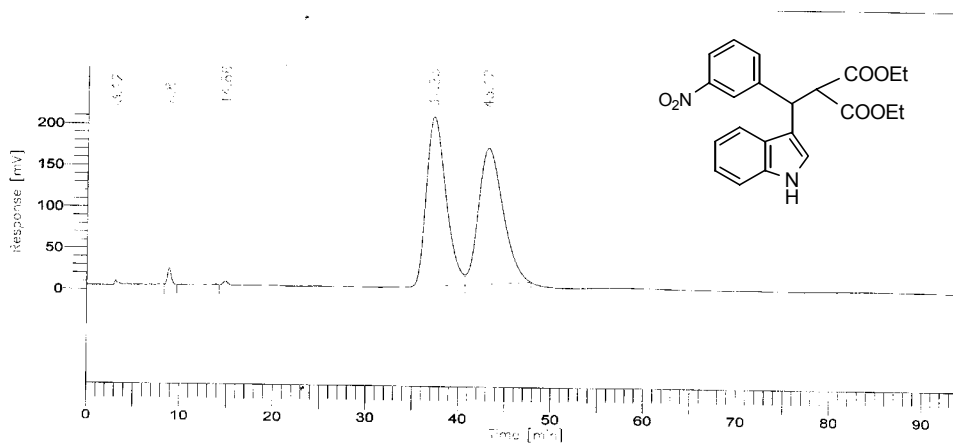
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.236	29313534.44	626891.11	50.21
2		23.110	29062869.08	375171.98	49.79
			58376403.52	1.00e+06	100.00



## report

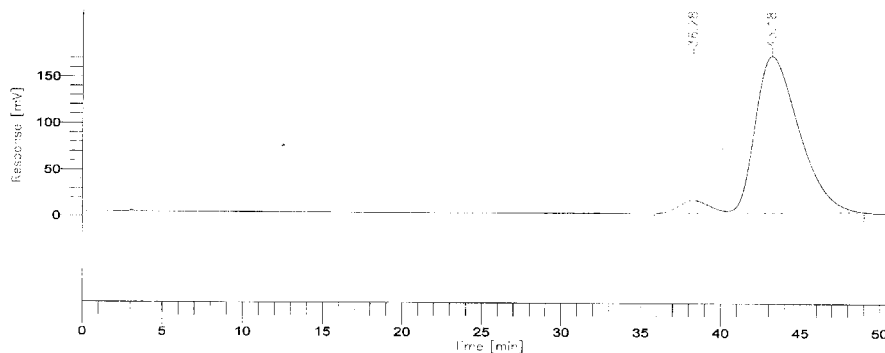
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		15.425	9832857.31	217180.13	92.66
2		23.883	779396.71	11796.22	7.34
			10612254.01	228976.34	100.00

**(-)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(m-nitrophenyl) propanoate (entry 5, Table 10)** Chiralpak AS, 8% iPrOH/hexanes, 1.0 mL/min, 254 nm.



## REPORT

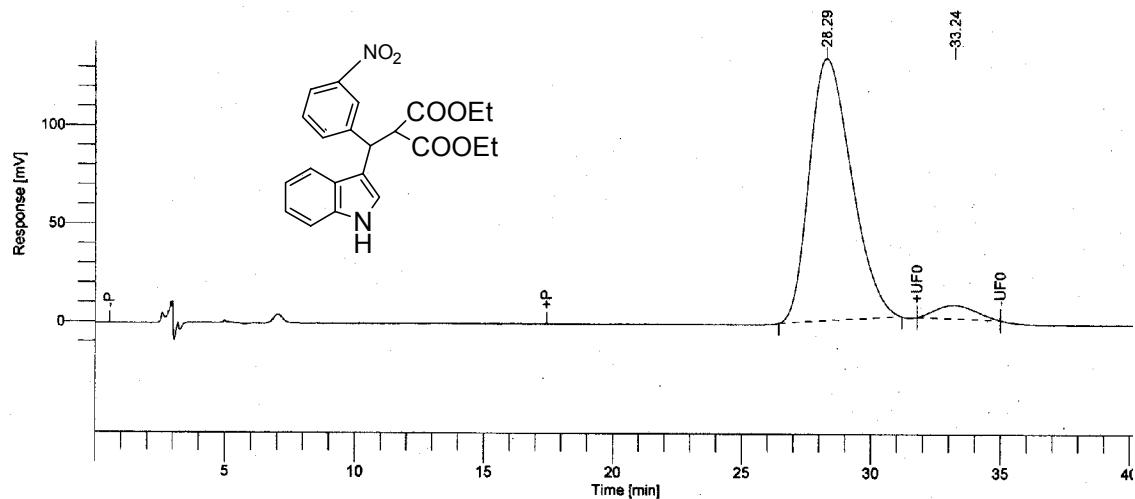
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Area BL	Area/Height [sec]
1	3.124	116373.25	5002.25	0.19	0.00	BB	23.2642
2	8.871	553925.50	19943.31	0.90	0.00	BB	27.7750
3	14.857	147742.50	4468.64	0.24	0.00	BB	33.0621
4	37.228	30328147.03	204620.16	49.34	0.00	BV	148.2168
5	43.115	30315772.97	164192.86	49.32	0.00	VB	184.6352



## REPORT

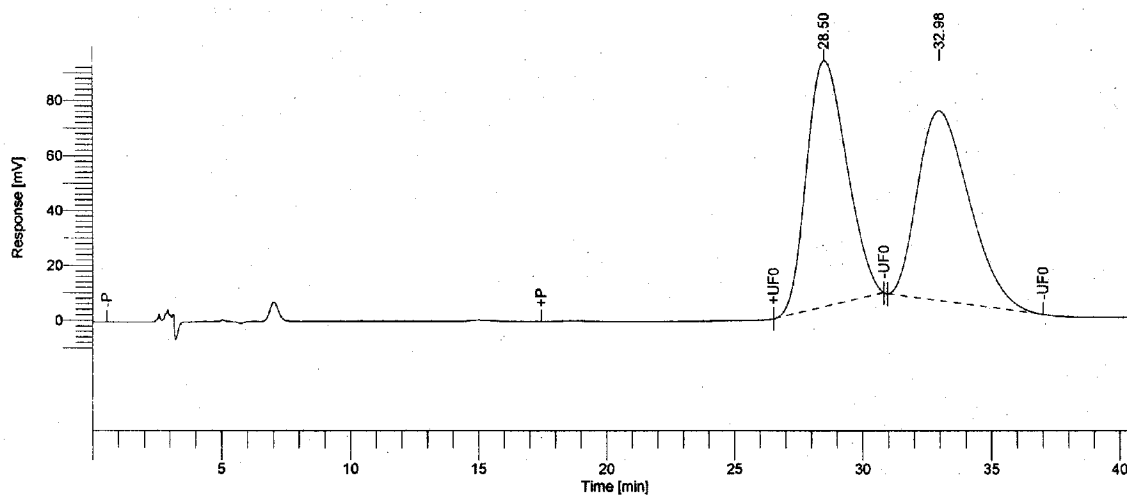
Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Area BL	Area/Height [sec]
1	38.277	1972128.71	14488.82	5.73	0.00	BV	136.1138
2	43.181	32429995.79	169627.50	94.27	0.00	VB	191.1836
		34402124.50	184116.32	100.00	0.00		

**(+)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(m-nitrophenyl) propanoate (entry 5, Table 10)** Chiralpack AS; 92:8 n-hexane/iPrOH;  $\lambda = 254 \text{ nm}$ ;  $v = 1.4 \text{ ml}\cdot\text{min}^{-1}$



## report

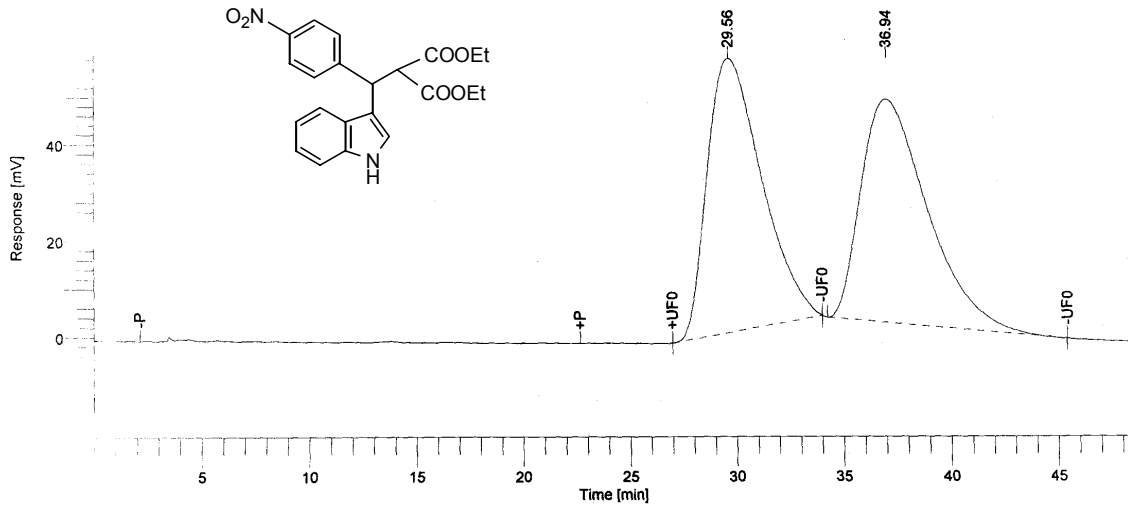
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		28.294	29344291.42	259692.11	95.28
2		33.245	1453349.56	13658.22	4.72
			30797640.98	273350.34	100.00



## report

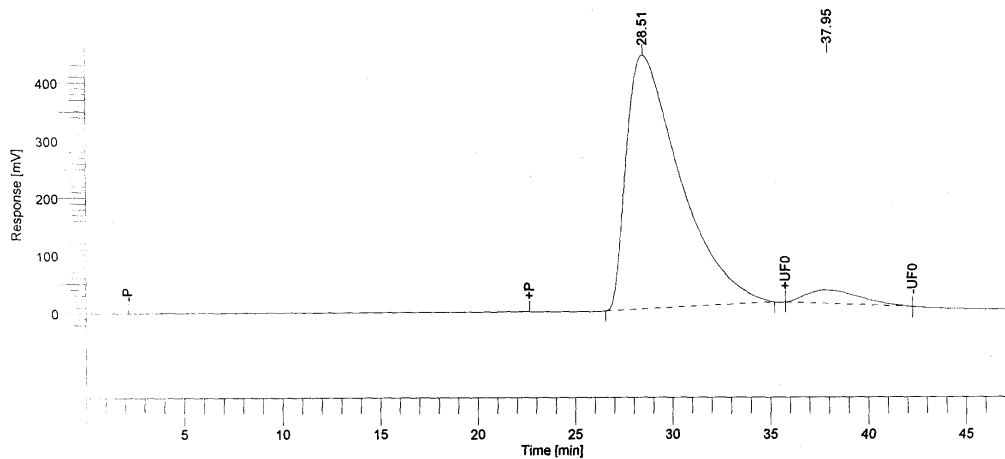
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		28.503	18799288.81	173204.62	50.27
2		32.985	18598822.57	133595.62	49.73
			37398111.38	306800.24	100.00

(+)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-nitrophenyl) propanoate (entry 6, Table 10) Chiralpak AS, 10% iPrOH/hexanes, 1.0 mL/min, 254 nm



## report

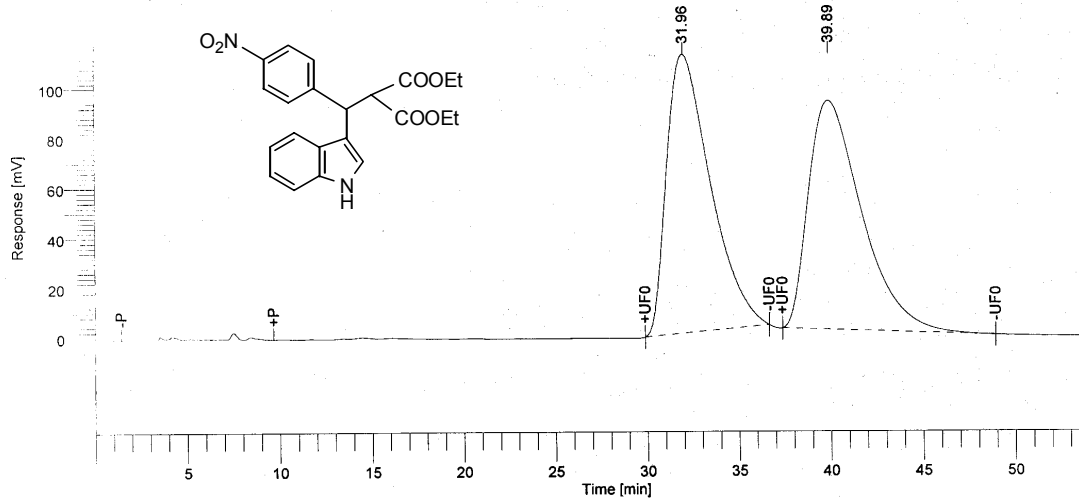
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		29.563	19789397.09	111889.11	50.33
2		36.942	19529887.27	90661.53	49.67
			39319284.36	202550.64	100.00



## report

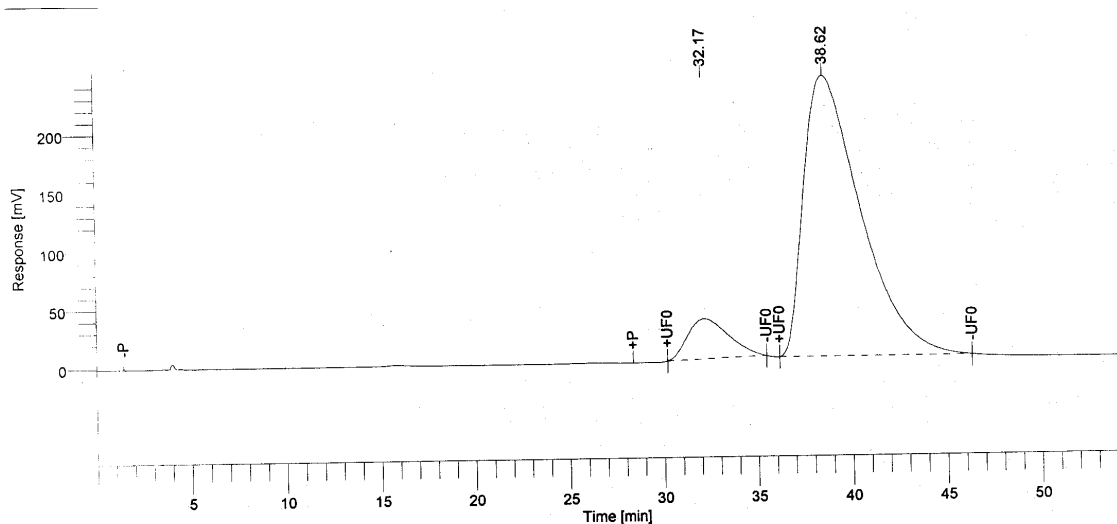
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		28.507	1.64e+08	846795.42	95.05
2		37.952	8523843.91	44846.54	4.95
			1.72e+08	891641.96	100.00

(-)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-nitrophenyl) propanoate (entry 6, Table 10) Chiralpak AS, 10% iPrOH/hexanes, 1.0 mL/min, 254 nm.



## report

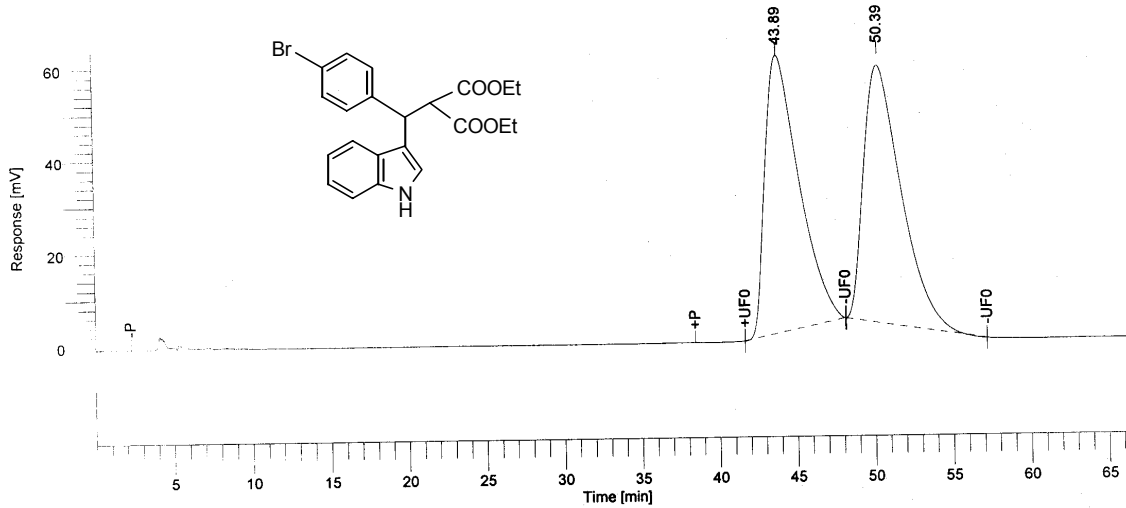
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		31.960	36079324.13	217740.69	50.21
2		39.890	35771815.28	178106.00	49.79
			71851139.40	395846.68	100.00



## report

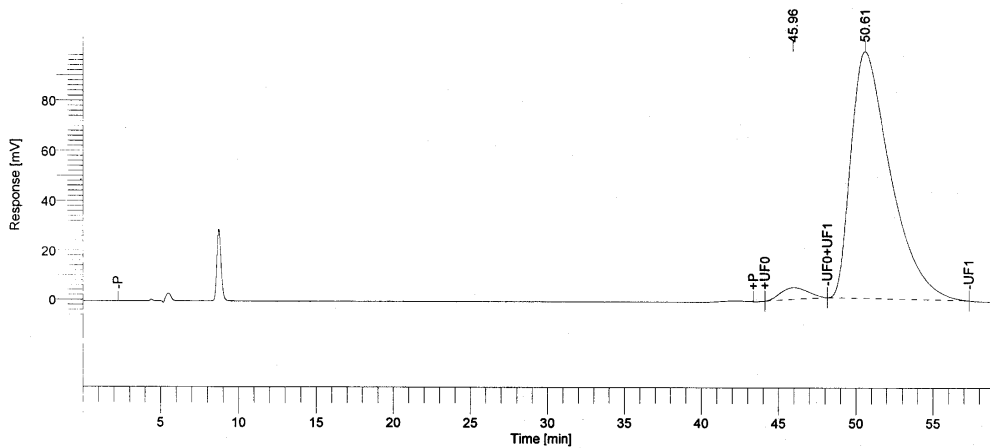
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		32.168	10170235.40	67154.87	9.48
2		38.623	97124437.30	463312.67	90.52
			1.07e+08	530467.55	100.00

(+)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-bromophenyl) propanoate (entry 7, Table 10) Chiralcel OD-H, 4% <sup>1</sup>PrOH/hexanes, 0.80 mL/min, 254 nm;



## report

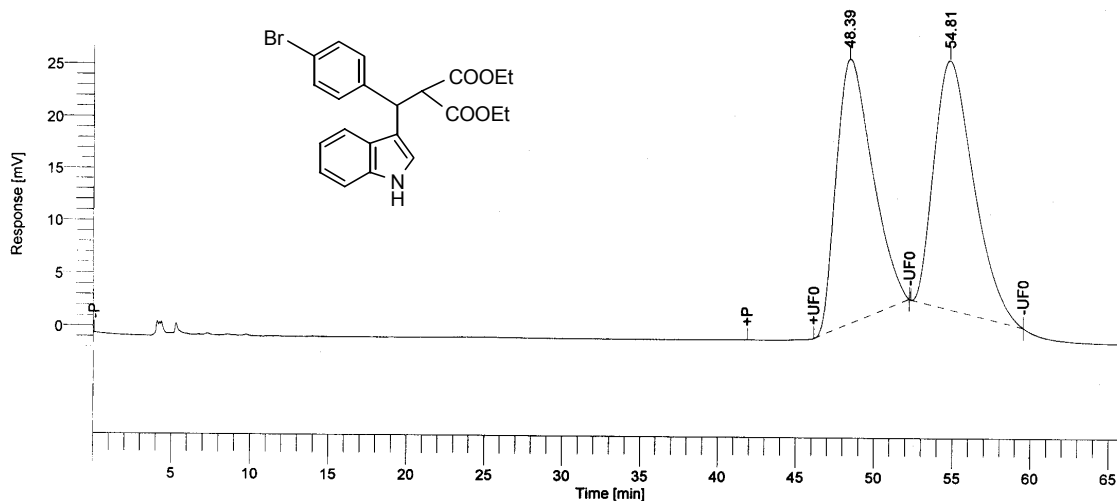
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		43.892	17625048.87	115779.24	49.61
2		50.385	17902235.37	107148.42	50.39
			35527284.24	222927.66	100.00



## report

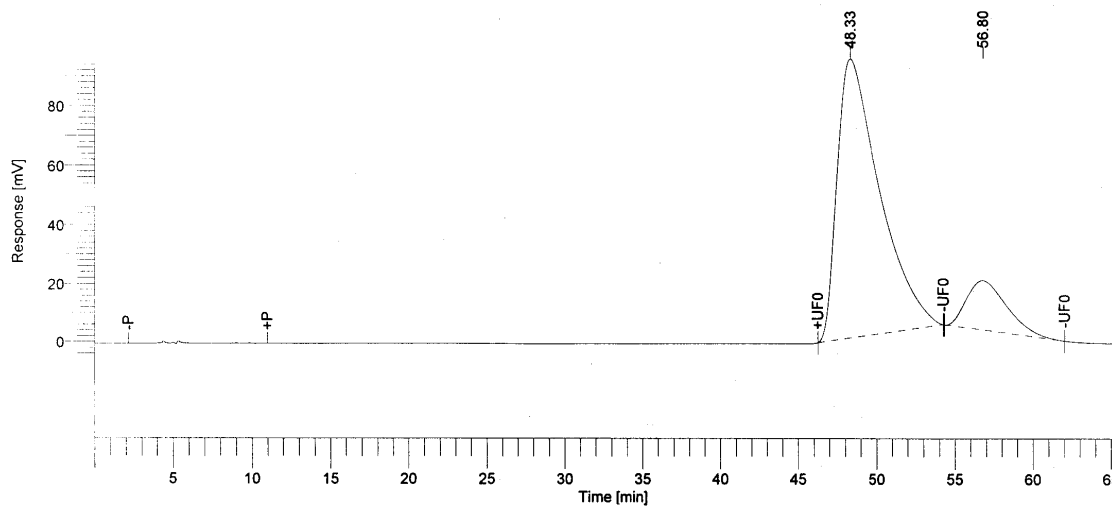
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		45.955	1154075.09	9457.62	3.26
2		50.610	34300550.52	191732.49	96.74
			35454625.61	201190.11	100.00

(-)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-(p-bromophenyl) propanoate (entry 7, Table 10) Chiralcel OD-H, 4% <sup>i</sup>PrOH/hexanes, 0.80 mL/min, 254 nm;



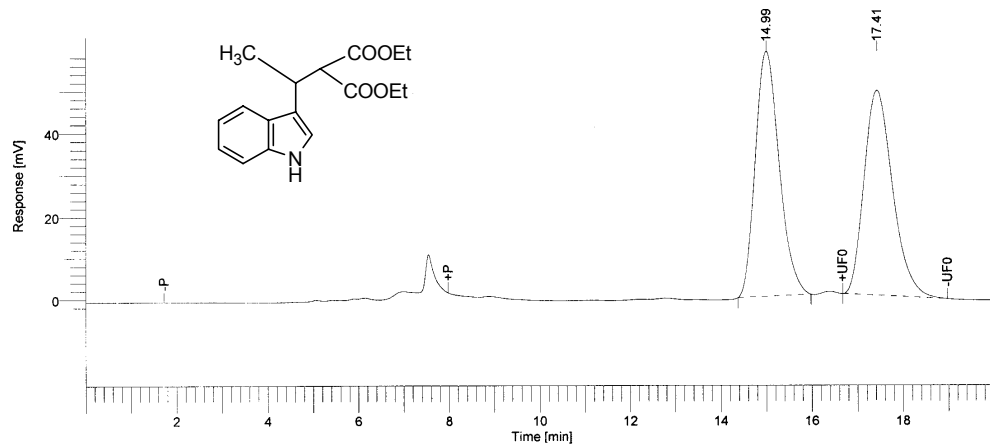
## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		48.388	7831662.83	48979.07	49.22
2		54.807	8079214.07	46098.73	50.78
			15910876.90	95077.80	100.00

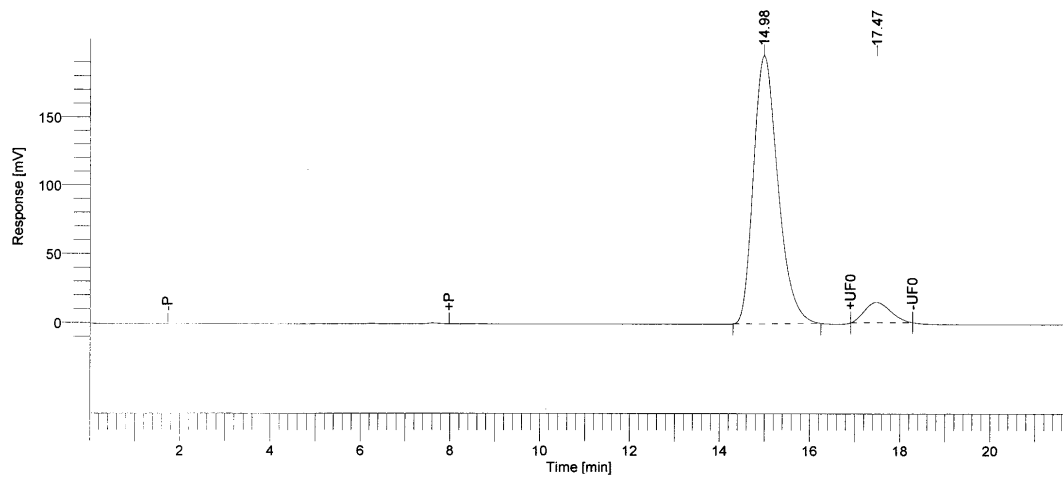


## report

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		48.330	34742144.30	182822.41	85.30
2		56.795	5987031.34	32975.09	14.70
			40729175.64	215797.49	100.00

**(+)-Ethyl 2-ethoxycarbonyl-3-(3-indolyl)-3-methylpropanoate (entry 8, Table 10)**Chiralcel OD-H, 10% <sup>i</sup>PrOH/hexanes, 0.70 mL/min, 254 nm.**report**

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		14.986	4202510.34	114288.15	50.02
2		17.412	4198844.72	95647.85	49.98
			8401355.06	209936.00	100.00

**report**

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]
1		14.978	14338964.56	381061.06	92.54
2		17.473	1156151.51	28981.05	7.46
			15495116.07	410042.11	100.00