

Supplementary Information:

A New Versatile Approach to Enantioenriched 3-Hydroxyoxindoles, 1, 3-Dihydroisobenzofuran and 3-Isochromanone Derivatives by Rhodium-Catalyzed Asymmetric Arylation/Cyclization Sequence

Yi Li, Dong-Xing Zhu and Ming-Hua Xu*

Shanghai Institute of Materia Medica, Chinese Academy of Sciences

555 Zuchongzhi Road, Shanghai 201203

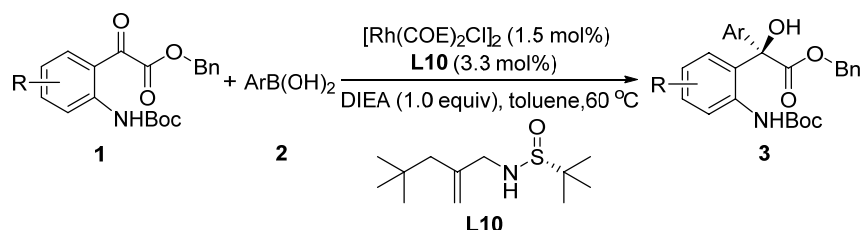
E-mail: xumh@simm.ac.cn

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1. General

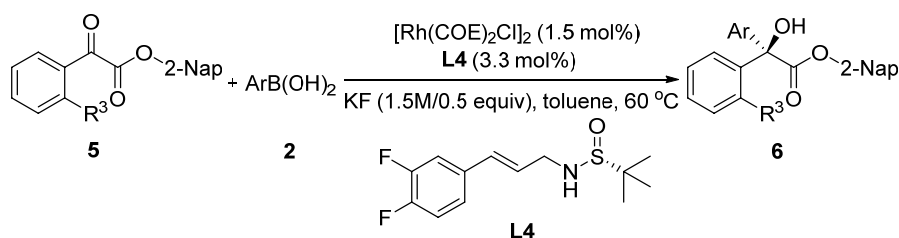
Unless otherwise specified, all reactions were carried out in flame-dried glassware with magnetic stirring. Solvents were dried and distilled by standard procedures. NMR spectra were recorded on a Varian spectrometer (300 MHz for ^1H , and 100 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal SiMe_4 standard for ^1H NMR and CDCl_3 (δ 77.16) or $(\text{CD}_3)_2\text{CO}$ (δ 29.84, 206.26) for ^{13}C NMR. Chiral HPLC was performed on a JASCO 2000 instrument by using Daicel columns with 2-propanol/hexane as the eluent at 254 nm.

2. General procedure for Rh-catalyzed 1, 2-addition of *ortho*-NHBoc-substituted aryl α -ketoester **1** with arylboronic acid **2**.



Under Ar atmosphere, a solution of *ortho*-NHBoc-substituted aryl α -ketoesters **1** (0.25 mmol), $[\text{Rh}(\text{COE})_2\text{Cl}]_2$ (2.7 mg, 0.0075 mmol of Rh), ligand **L10** (1.9 mg, 0.00825 mmol), and arylboronic acid **2** (0.5 mmol) in 1.0 mL of toluene was stirred at 60 °C for 30 min. To this mixture was added DIEA (41.0 μL , 0.25 mmol). After being stirred at 60 °C for 12h, a saturated aq. NH_4Cl was added and the mixture was extracted with EtOAc. The combined organic phase was dried over Na_2SO_4 , filtered, and concentrated. The residue was purified by silica gel flash chromatography to afford the corresponding product **3**.

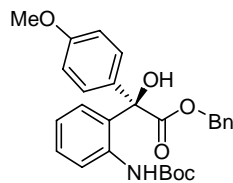
3. General procedure for Rh-catalyzed 1, 2-addition of *ortho*- $\text{CH}_3/\text{CH}_2\text{OMOM}$ -substituted aryl α -ketoester **5** with arylboronic acid **2**.



Under Ar atmosphere, a solution of *ortho*- $\text{CH}_3/\text{CH}_2\text{OMOM}$ -substituted aryl α -ketoesters **5** (0.25 mmol), $[\text{Rh}(\text{COE})_2\text{Cl}]_2$ (2.7 mg, 0.0075 mmol of Rh), ligand **L4** (2.3 mg, 0.00825 mmol), and arylboronic acid **2** (0.5 mmol) in 1.0 mL of toluene was stirred at 60 °C for 30 min. To this mixture was added KF (84.0 μL , 1.5M, 0.125 mmol). After being stirred at 60 °C for 6h, a saturated aq. NH_4Cl was added and the mixture was extracted with EtOAc. The combined organic phase was dried over Na_2SO_4 , filtered, and concentrated. The residue was purified by silica gel flash chromatography to afford the corresponding product **6**.

4. Characterization data and HPLC chromatogram of addition products 3b-s and 6a-k.

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl) amino)phenyl)-2-hydroxy-2-(4-methoxyphenyl)acetate **3b**.



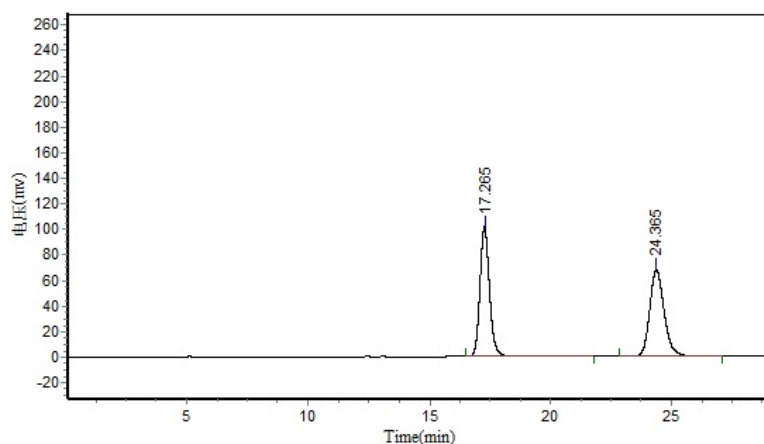
3b

73% yield, colorless oil, 93% ee.

^1H NMR (300 MHz, CDCl_3): δ 1.38 (s, 9H), 3.80 (s, 3H), 4.24 (s, 1H), 5.26 (q, $J = 12.0$ Hz, 2H), 6.81-6.85 (m, 3H), 6.92 (dd, $J = 1.2$ Hz, 8.1 Hz, 1H), 7.19-7.22 (m, 2H), 7.30-7.38 (m, 6H), 7.51 (s, 1H), 7.76 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 55.4, 68.5, 80.1, 81.0, 113.7, 123.2, 124.3, 127.1, 128.0, 128.1, 128.4, 128.6, 128.7, 129.3, 132.1, 134.7, 137.5, 153.2, 159.6, 174.2; ESI-MS (m/z , %) 486 [$\text{M}+\text{Na}$] $^+$;

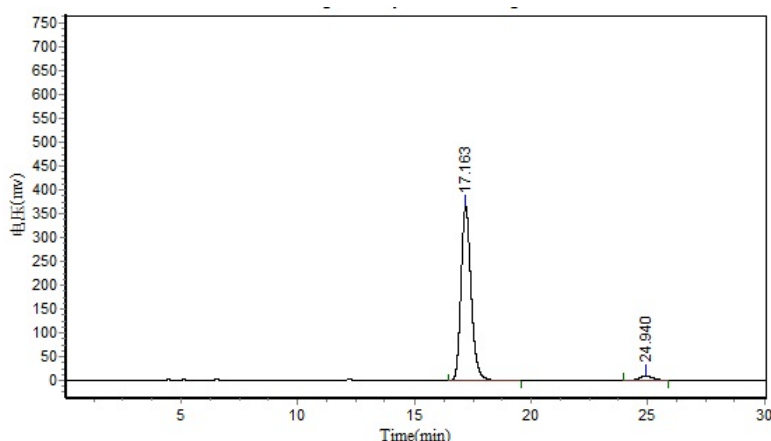
ESI-HRMS calcd for $\text{C}_{27}\text{H}_{29}\text{NNaO}_6$ [$\text{M}+\text{Na}$] $^+$ 486.1893, found 486.1892.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 17.2 min (maj), 24.9 min.



Results

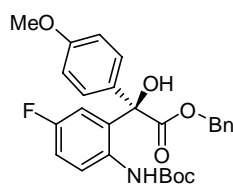
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.265	101382.359	2750522.500	49.6694
2		24.365	67552.063	2787137.500	50.3306
Total			168934.422	5537660.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.163	365193.469	11001478.000	96.5429
2		24.940	9273.073	393946.969	3.4571
Total			374466.542	11395424.969	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl) amino)-5-fluorophenyl)-2-hydroxy-2-(4-methoxyphenyl) acetate **3c**.

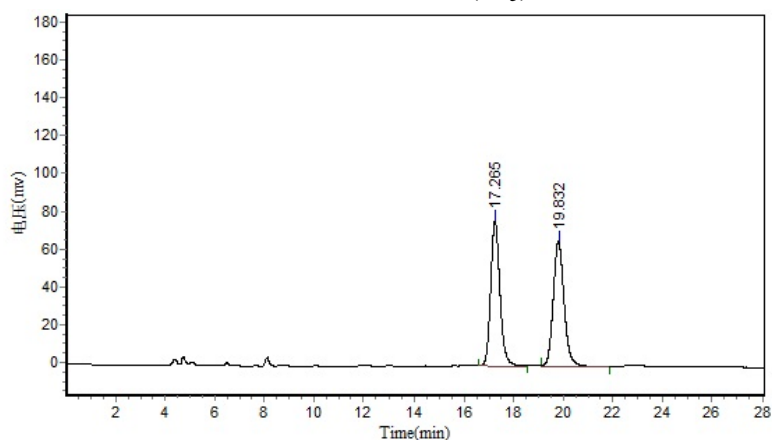


3c

77% yield, colorless oil, 87% ee.

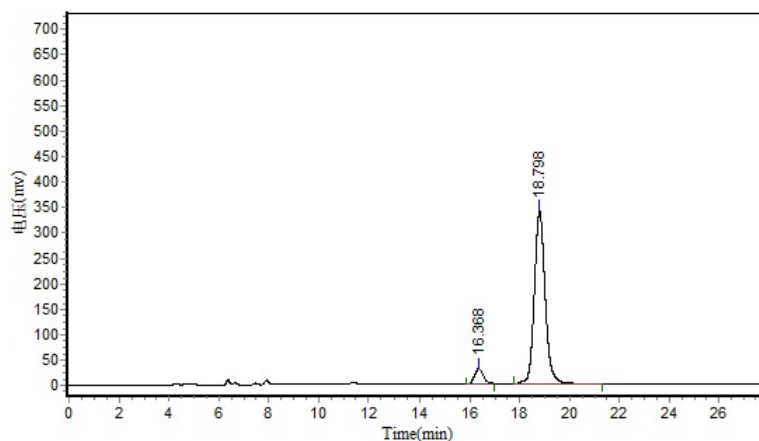
^1H NMR (300 MHz, CDCl_3): δ 1.39 (s, 9H), 3.80 (s, 3H), 4.25 (s, 1H), 5.25 (q, $J = 11.7$ Hz, 2H), 6.54-6.58 (m, 1H), 6.84 (d, $J = 6.9$ Hz, 2H), 7.01 (dt, $J = 2.7$ Hz, 7.8 Hz, 1H), 7.21-7.34 (m, 6H), 7.67 (dd, $J = 5.4$ Hz, 8.1 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 55.4, 68.8, 80.3, 80.4, 113.9, 115.5 (d, $J_{\text{CF}} = 25.0$ Hz), 115.7 (d, $J_{\text{CF}} = 21.0$ Hz), 126.1, 127.1, 128.0, 128.6, 128.8, 128.9, 131.4, 133.3, 133.4, 134.5, 153.3, 158.5 (d, $J_{\text{CF}} = 241.3$ Hz), 173.9; ESI-MS (m/z , %) 504 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{27}\text{H}_{28}\text{NNaO}_6\text{F}$ $[\text{M}+\text{Na}]^+$ 504.1798, found 504.1793.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 16.4 min, 18.8 min (maj).



Results

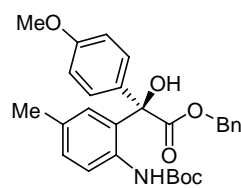
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.265	76413.719	1999923.625	49.9475
2		19.832	65634.195	2004129.625	50.0525
Total			142047.914	4004053.250	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.368	30170.873	728092.250	6.5921
2		18.798	338912.531	10316795.000	93.4079
Total			369083.404	11044887.250	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl) amino)-5-methylphenyl)-2-hydroxy-2-(4-methoxyphenyl) acetate **3d**.



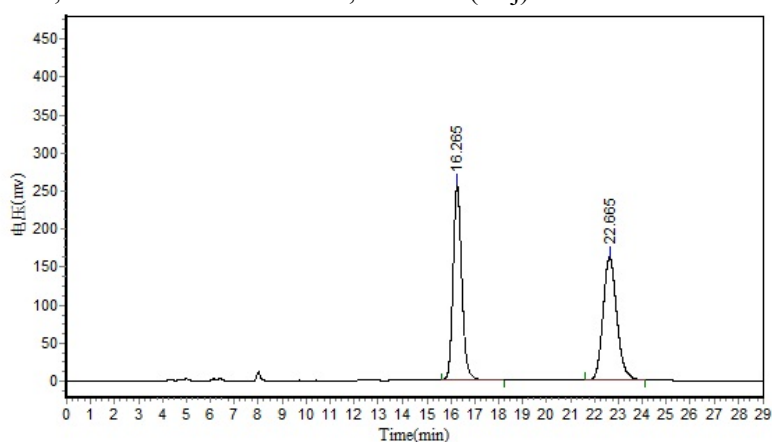
3d

75% yield, colorless oil, 90% ee.

¹H NMR (300 MHz, CDCl₃): δ 1.35 (s, 9H), 2.12 (s, 3H), 3.80 (s, 3H), 4.23 (s, 1H), 5.26 (s, 2H), 6.59 (s, 1H), 6.83 (d, *J* = 9.0 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.24-7.35 (m, 8H), 7.58 (d, *J* = 7.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 21.0, 28.3, 55.4, 68.5, 79.8, 80.8, 113.7, 124.6, 128.1, 128.5, 128.7, 128.8, 129.8, 132.2, 132.5, 132.8, 134.7, 134.8, 153.4, 159.5,

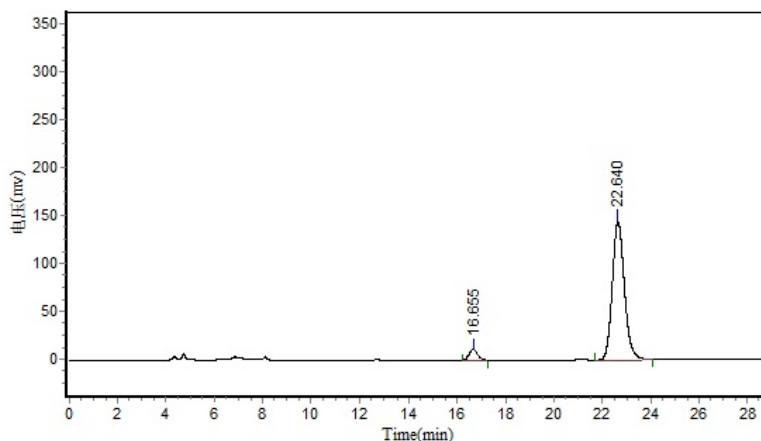
174.3; ESI-MS (*m/z*, %) 500 [M+Na]⁺; ESI-HRMS calcd for C₂₈H₃₁NNaO₆ [M+Na]⁺ 500.2049, found 500.2051.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 16.7 min, 22.6 min (maj).



Results

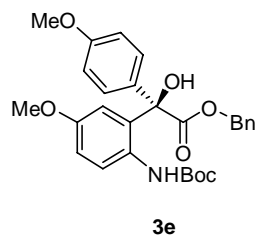
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.265	255872.719	6657808.500	50.1313
2		22.665	162132.141	6622922.000	49.8687
Total			418004.859	13280730.500	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.655	11449.926	275068.156	5.1969
2		22.640	144111.672	5017873.500	94.8031
Total			155561.598	5292941.656	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl) amino)-5-methoxyphenyl)-2-hydroxy-2-(4-methoxyphenyl) acetate **3e**.

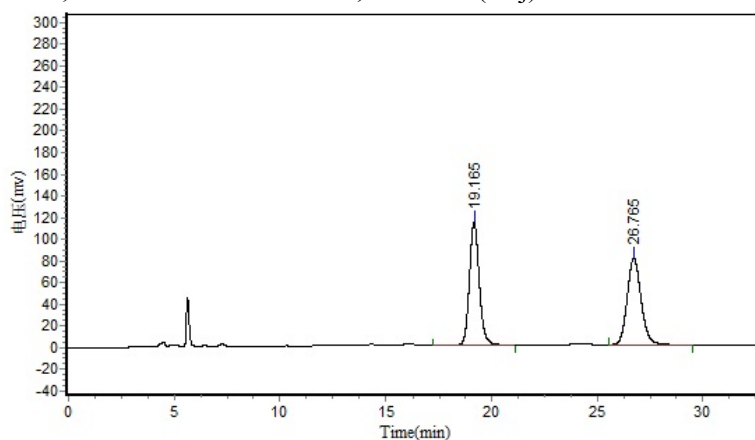


81% yield, white solid, 88% ee.

¹H NMR (300 MHz, CDCl₃): δ 1.38 (s, 9H), 3.60 (s, 3H), 3.79 (s, 3H), 4.29 (s, 1H), 5.25 (q, *J* = 12.0 Hz, 2H), 6.43 (d, *J* = 3.0 Hz, 1H), 6.81-6.86 (m, 3H), 7.13 (s, 1H), 7.21-7.25 (m, 2H), 7.30-7.38 (m, 5H), 7.56 (d, *J* = 8.7 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.4, 55.4, 55.5, 68.6, 80.0, 80.7, 113.5, 113.7, 114.9, 126.4, 127.1, 128.1, 128.6, 128.7, 128.8, 130.1, 131.9, 134.8, 153.7, 155.7, 159.6, 174.2; ESI-MS (*m/z*, %) 516 [M+Na]⁺;

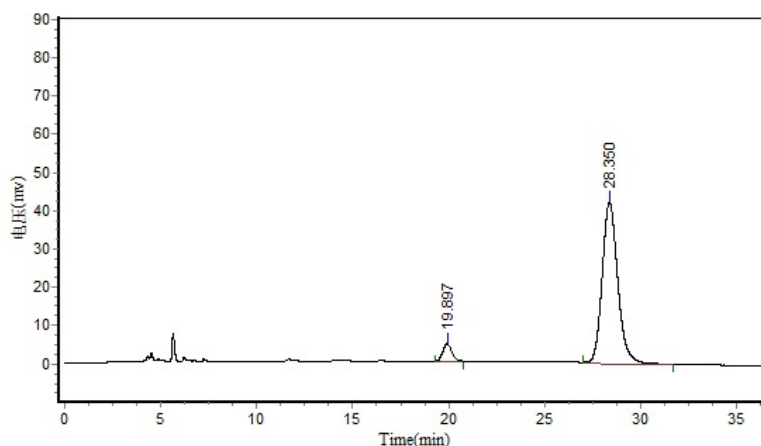
ESI-HRMS calcd for C₂₈H₃₁NNaO₇ [M+Na]⁺ 516.1998, found 516.2004.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 19.9 min, 28.4 min (maj).



Results

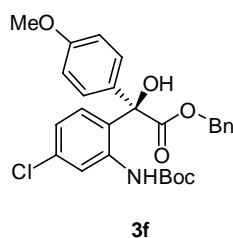
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.165	113175.625	3698059.500	50.1923
2		26.765	79914.531	3669719.250	49.8077
Total			193090.156	7367778.750	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.897	4611.024	151355.203	6.0655
2		28.350	42012.738	2343993.250	93.9345
Total			46623.763	2495348.453	100.0000

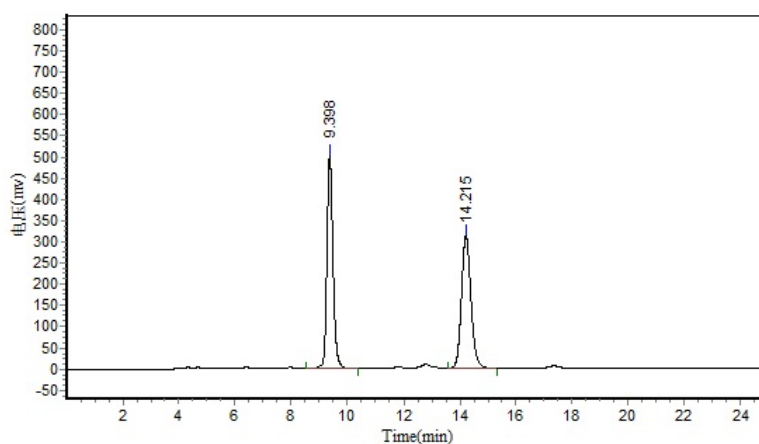
Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl) amino)-4-chlorophenyl)-2-hydroxy-2-(4-methoxyphenyl) acetate **3f**.



68% yield, colorless oil, 90% ee.

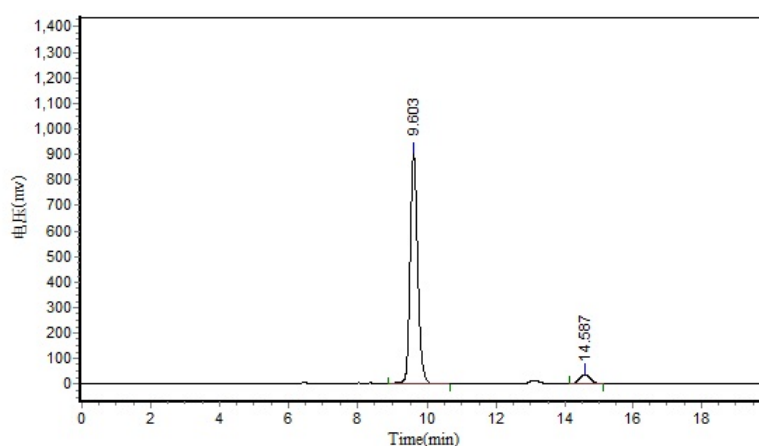
^1H NMR (300 MHz, CDCl_3): δ 1.39 (s, 9H), 3.80 (s, 3H), 4.20 (s, 1H), 5.26 (q, $J = 12.0$ Hz, 2H), 6.72 (d, $J = 8.4$ Hz, 1H), 6.83-6.88 (m, 3H), 7.20-7.23 (m, 2H), 7.29-7.38 (m, 5H), 7.66 (s, 1H), 7.89 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 55.4, 68.8, 80.5, 80.7, 113.9, 122.9, 123.4, 128.1, 128.5, 128.8, 128.9, 129.2, 131.7, 134.5, 135.1, 138.7, 152.7, 159.8, 173.9; ESI-MS (m/z , %) 520 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{27}\text{H}_{28}\text{NNaO}_6\text{Cl}$ [$\text{M}+\text{Na}$] $^+$ 520.1503, found 520.1499.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 9.6 min (maj), 14.6 min.



Results

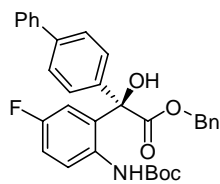
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.398	500307.000	7656206.500	50.3651
2		14.215	313428.188	7545205.000	49.6349
Total			813735.188	15201411.500	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.603	899993.500	14011612.000	94.8099
2		14.587	34310.766	767030.188	5.1901
Total			934304.266	14778642.188	100.0000

Benzyl (*R*)-2-([1,1'-biphenyl]-4-yl)-2-(2-((*tert*-butoxycarbonyl)amino)-5-fluorophenyl)-2-hydroxy acetate **3g**.

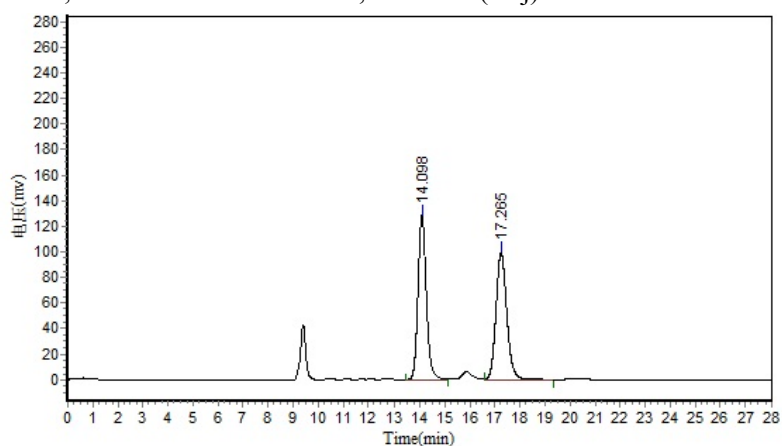


3g

53% yield, white solid, 92% ee.

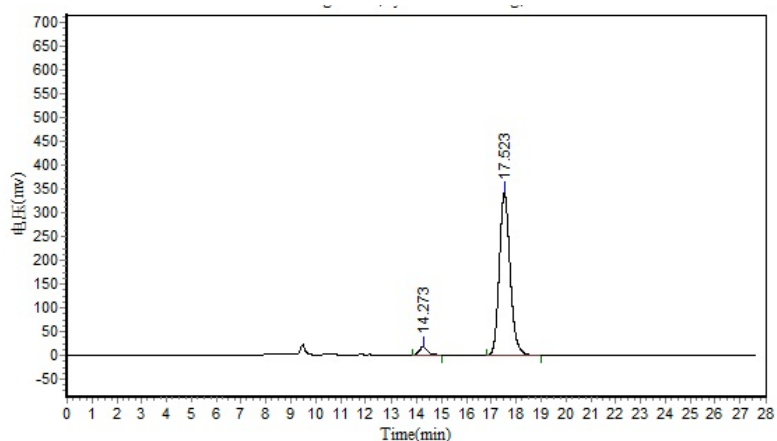
^1H NMR (300 MHz, CDCl_3): δ 1.35 (s, 9H), 4.40 (s, 1H), 5.30 (q, $J = 12.0$ Hz, 2H), 6.65 (dd, $J = 3.0$ Hz, 10.2 Hz, 1H), 7.01-7.07 (m, 1H), 7.22-7.24 (m, 2H), 7.31-7.41 (m, 5H), 7.45-7.50 (m, 4H), 7.54-7.59 (m, 4H), 7.66-7.72 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 69.0, 80.3, 80.6, 115.4 (d, $J_{\text{CF}} = 25.0$ Hz), 115.9 (d, $J_{\text{CF}} = 22.0$ Hz), 126.4, 127.1, 127.2, 127.3, 127.7, 128.6, 128.8, 128.9, 129.0, 133.3 (d, $J_{\text{CF}} = 3.0$ Hz), 134.4, 138.4, 140.5, 141.6, 153.3, 158.6 (d, $J_{\text{CF}} = 242.0$ Hz), 173.6; ESI-MS (m/z , %) 550 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{32}\text{H}_{30}\text{NNaO}_5\text{F}$ $[\text{M}+\text{Na}]^+$ 550.2006, found 550.2014.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 14.3 min, 17.5 min (maj).



Results

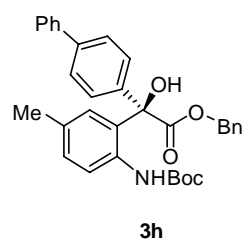
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.098	128352.453	3009115.750	50.1266
2		17.265	99190.945	2993920.500	49.8734
Total			227543.398	6003036.250	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.273	18288.936	431064.719	3.9953
2		17.523	341490.219	10358160.000	96.0047
Total			359779.154	10789224.719	100.0000

Benzyl(*R*)-2-([1,1'-biphenyl]-4-yl)-2-(2-((*tert*-butoxycarbonyl)amino)-5-methylphenyl)-2-hydroxy acetate **3h**.

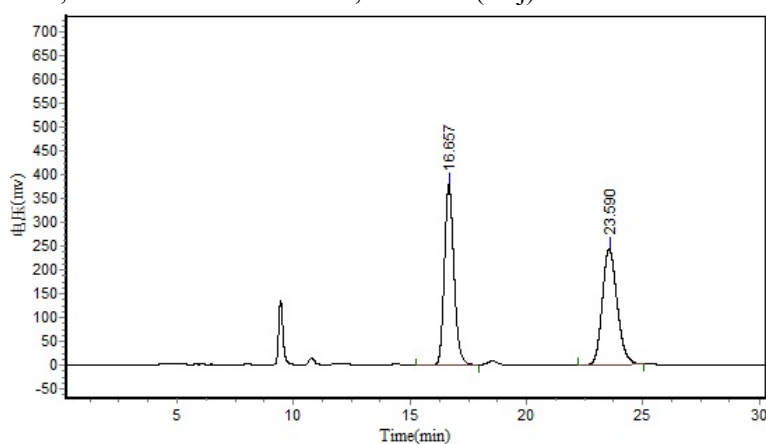


54% yield, white solid, 92% ee.

^1H NMR (300 MHz, CDCl_3): δ 1.31 (s, 9H), 2.14 (s, 3H), 4.36 (s, 1H), 5.31 (q, $J = 12.3$ Hz, 2H), 6.66 (d, $J = 1.5$ Hz, 1H), 7.41 (dd, $J = 2.1$ Hz, 8.1 Hz, 1H), 7.25-7.29 (m, 2H), 7.32-7.38 (m, 5H), 7.42-7.50 (m, 6H), 7.53-7.60 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.1, 28.3, 68.7, 79.9, 81.0, 124.9, 127.0, 127.2, 127.3, 127.6, 128.4, 128.6, 128.7, 128.8, 128.9, 129.9, 132.4, 133.0, 134.7, 134.8, 139.3, 140.7, 141.1, 153.3, 174.0;

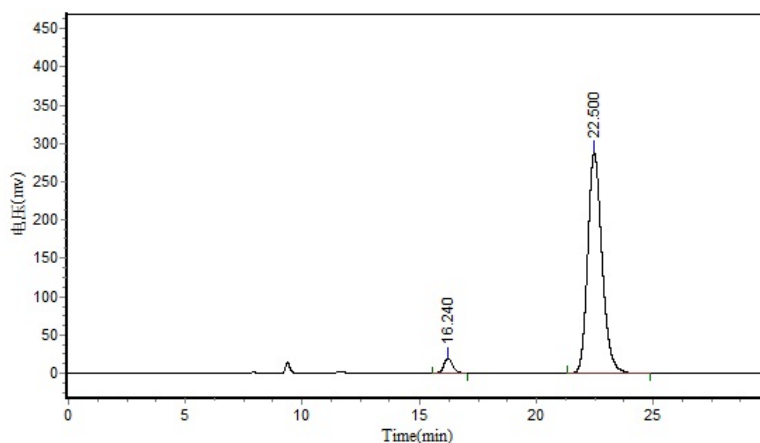
ESI-MS (m/z , %) 546 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{33}\text{H}_{33}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$ 546.2256, found 546.2251.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 16.2 min, 22.5 min (maj).



Results

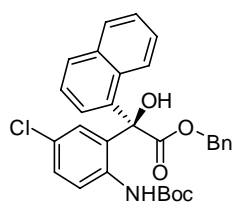
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.657	377795.031	10940012.000	49.9673
2		23.590	244525.172	10954331.000	50.0327
Total			622320.203	21894343.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.240	19175.686	507490.406	3.9804
2		22.500	288028.594	12242214.000	96.0196
Total			307204.279	12749704.406	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl) amino)-5-chlorophenyl)-2-hydroxy-2-(naphthalen-1-yl) acetate **3i**.



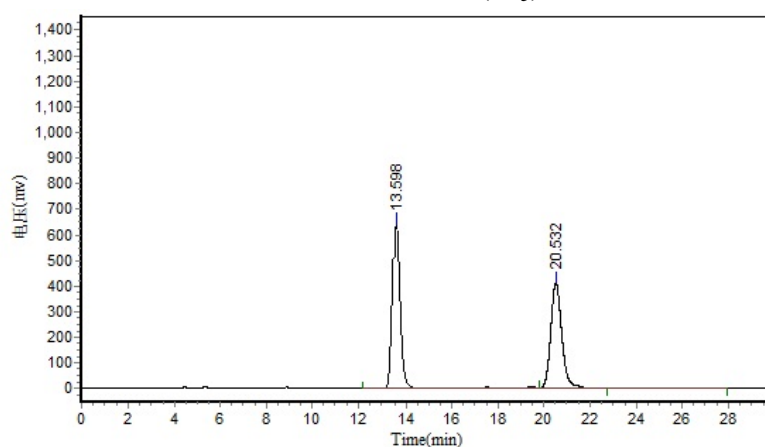
3i

75% yield, white solid, 97% ee.

¹H NMR (300 MHz, CDCl₃): δ 1.35 (s, 9H), 4.39 (s, 1H), 5.32 (s, 2H), 6.91 (s, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 7.13-7.16 (m, 2H), 7.27-7.37 (m, 6H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.87 (dd, *J* = 5.1 Hz, 7.8 Hz, 2H), 7.96 (d, *J* = 8.7 Hz, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 8.13 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.3, 69.2, 80.4, 83.2, 124.2, 124.7, 126.0, 126.2, 126.3, 126.6,

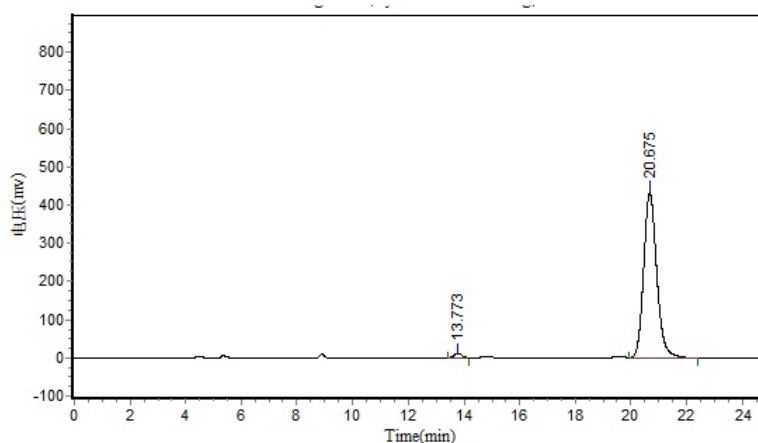
128.1, 128.5, 128.8, 128.9, 129.0, 129.3, 130.5, 131.1, 131.2, 134.2, 134.6, 134.9, 136.7, 153.0, 174.2; ESI-MS (*m/z*, %) 540 [M+Na]⁺; ESI-HRMS calcd for C₃₀H₂₈NNaO₅Cl [M+Na]⁺ 540.1554, found 540.1556.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 13.7 min, 20.7 min (maj).



Results

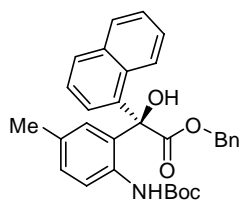
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.598	639095.063	14048495.000	50.4442
2		20.532	411877.688	13801064.000	49.5558
Total			1050972.750	27849559.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.773	12079.235	239536.344	1.6623
2		20.675	432744.031	14170561.000	98.3377
Total			444823.267	14410097.344	100.0000

Benzyl (R)-2-(2-((*tert*-butoxycarbonyl)amino)-5-methylphenyl)-2-hydroxy-2-(naphthalen-1-yl)acetate **3j**.



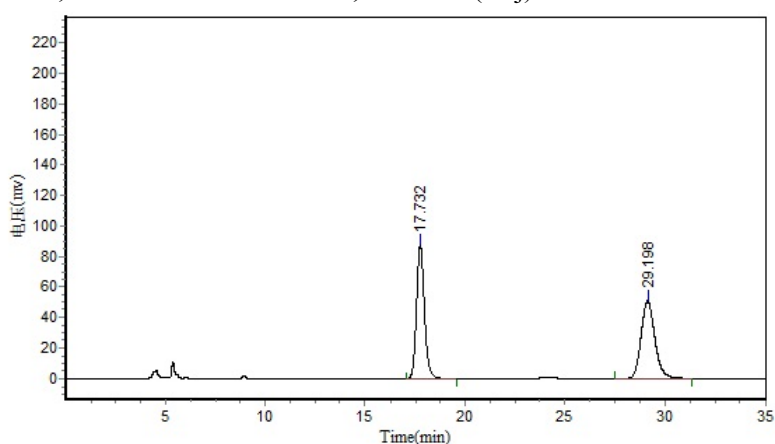
3j

68% yield, colorless oil, 97% ee.

¹H NMR (300 MHz, CDCl₃): δ 1.30 (s, 9H), 2.08 (s, 3H), 4.34 (s, 1H), 5.28 (q, *J* = 12.3 Hz, 2H), 6.68 (d, *J* = 1.2 Hz, 1H), 7.08-7.17 (m, 4H), 7.23-7.37 (m, 5H), 7.42-7.48 (m, 1H), 7.79-7.91 (m, 4H), 8.11 (d, *J* = 8.1 Hz, 1H); 21.0, 28.3, 68.7, 79.8, 83.4, 123.7, 124.8, 125.7, 126.1, 126.5, 126.6, 128.6, 128.7, 128.8, 128.9, 129.9, 130.0, 130.1, 131.4, 132.6, 134.6, 134.8, 135.1, 135.5, 153.3, 174.9; ESI-MS (*m/z*, %) 520 [M+Na]⁺;

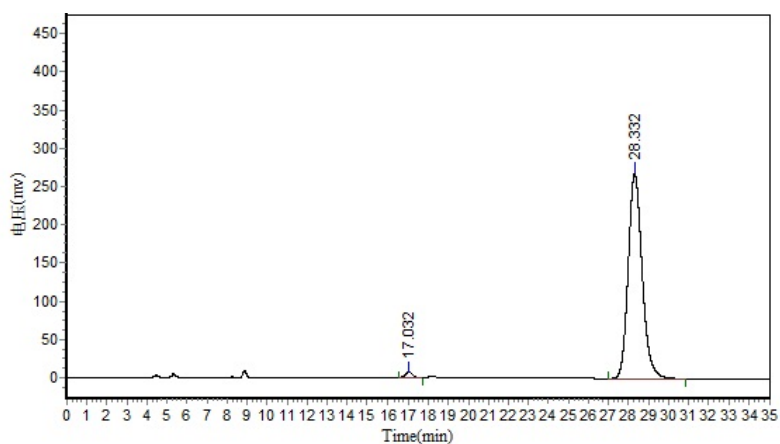
ESI-HRMS calcd for C₃₁H₃₁NNaO₅ [M+Na]⁺ 520.2100, found 520.2110.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 17.0 min, 28.3 min (maj).



Results

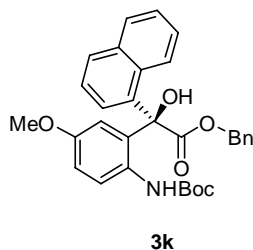
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.732	87209.602	2469526.250	50.0532
2		29.198	50694.574	2464276.500	49.9468
Total			137904.176	4933802.750	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.032	7883.643	211658.563	1.6061
2		28.332	267845.719	12966429.000	98.3939
Total			275729.362	13178087.563	100.0000

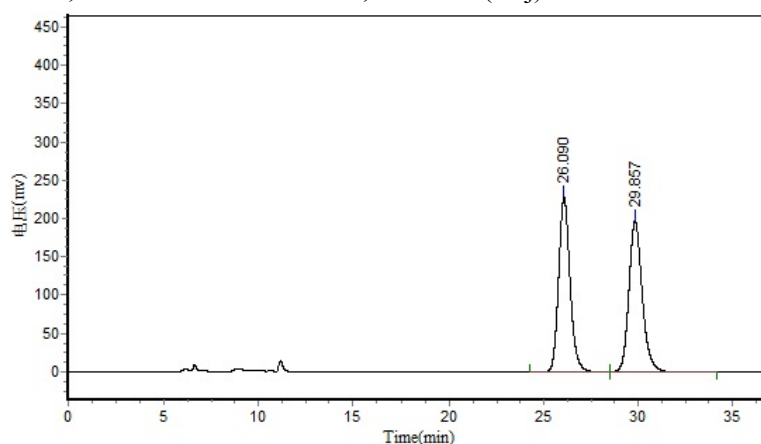
Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)-5-methoxyphenyl)-2-hydroxy-2-(naphthalen-1-yl)acetate **3k**.



70% yield, yellow oil, 98% ee.

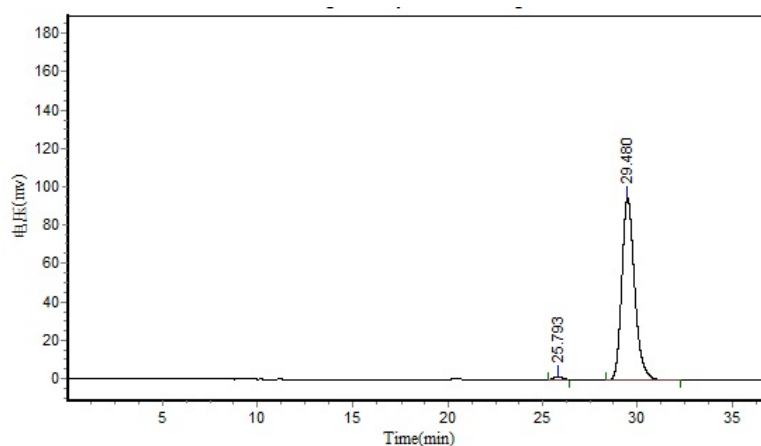
¹H NMR (300 MHz, CDCl₃): δ 1.33 (s, 9H), 3.57 (s, 3H), 4.40 (s, 1H), 5.30 (q, *J* = 12.0 Hz, 2H), 6.56 (d, *J* = 2.1 Hz, 1H), 6.90 (dd, *J* = 2.7 Hz, 8.7 Hz, 1H), 7.11-7.13 (m, 3H), 7.24-7.38 (m, 5H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.73-7.86 (m, 4H), 8.09 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.3, 55.4, 68.7, 79.8, 83.3, 113.7, 114.9, 124.7, 125.8, 126.0, 126.3, 126.8, 127.1, 127.8, 128.5, 128.7, 128.9, 130.1, 130.9, 131.3, 134.5, 134.8, 135.2, 153.6, 155.5, 174.7; ESI-MS (*m/z*, %) 536 [M+Na]⁺; ESI-HRMS calcd for C₃₁H₃₁NNaO₆ [M+Na]⁺ 536.2049, found 536.2053.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 25.6 min, 29.5 min (maj).



Results

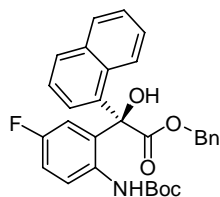
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.090	227919.906	9648403.000	49.7467
2		29.857	197366.188	9746647.000	50.2533
Total			425286.094	19395050.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.793	1548.934	52352.898	1.1533
2		29.480	95363.813	4487151.000	98.8467
Total			96912.747	4539503.898	100.0000

Benzyl (R)-2-(2-((*tert*-butoxycarbonyl)amino)-5-fluorophenyl)-2-hydroxy-2-(naphthalen-1-yl)acetate **3l**.

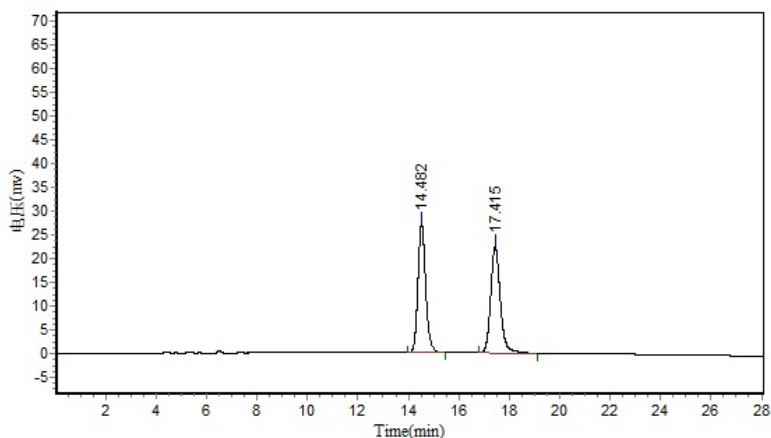


3l

77% yield, colorless oil, 97% ee.

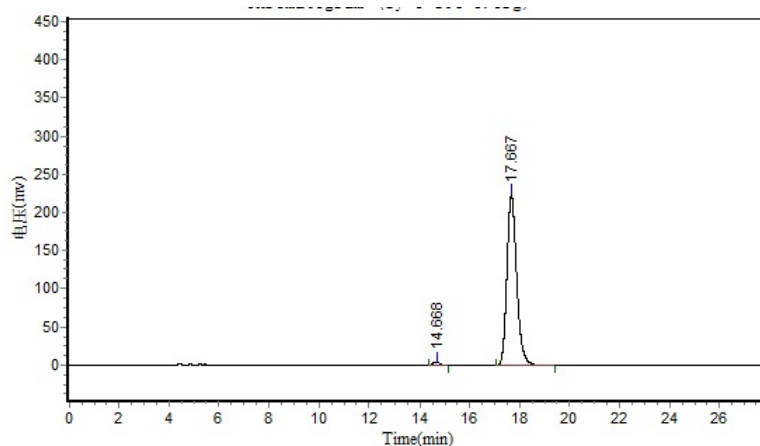
^1H NMR (300 MHz, CDCl_3): δ 1.36 (s, 9H), 4.38 (s, 1H), 5.30 (q, $J = 12.0$ Hz, 2H), 6.62 (dd, $J = 2.4$ Hz, 9.9 Hz, 1H), 7.00-7.08 (m, 2H), 7.12-7.15 (m, 2H), 7.25-7.35 (m, 5H), 7.42-7.48 (m, 1H), 7.83-7.90 (m, 3H), 7.98 (s, 1H), 8.04 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 69.0, 80.2, 83.2, 115.8 (d, $J_{\text{CF}} = 21.0$ Hz), 116.0 (d, $J_{\text{CF}} = 26.0$ Hz), 124.7, 125.0, 125.9, 126.0, 126.2, 126.8, 128.5, 128.8, 128.9, 129.0, 130.5, 131.1, 131.9, 133.9 (d, $J_{\text{CF}} = 2.0$ Hz), 134.3, 134.8, 134.9, 153.3, 158.4 (d, $J_{\text{CF}} = 241.0$ Hz), 174.3; ESI-MS (m/z , %) 524 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{30}\text{H}_{28}\text{NNaO}_5\text{F}$ $[\text{M}+\text{Na}]^+$ 524.1849, found 524.1851.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 14.7 min, 17.7 min (maj).



Results

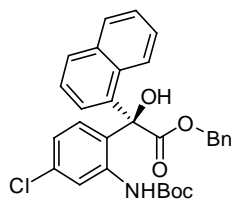
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.482	27132.400	585561.813	49.7266
2		17.415	22376.285	592000.875	50.2734
Total			49508.686	1177562.688	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.668	4649.988	97418.797	1.5840
2		17.667	223154.375	6052662.500	98.4160
Total			227804.363	6150081.297	100.0000

Benzyl (R)-2-(2-((tert-butoxycarbonyl)amino)-4-chlorophenyl)-2-hydroxy-2-(naphthalen-1-yl)acetate **3m**.

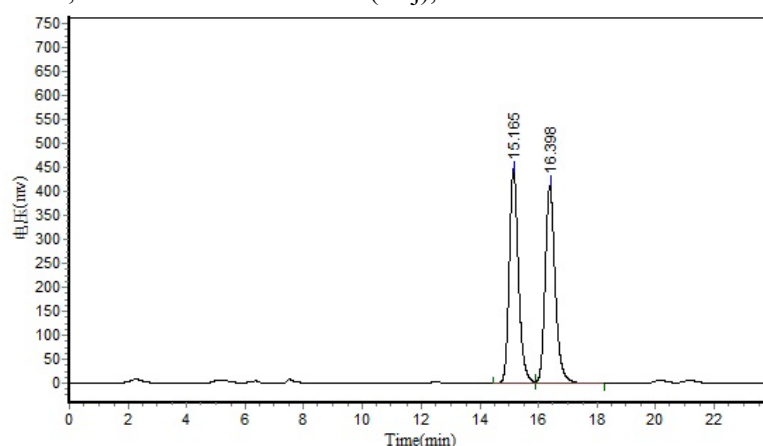


3m

72% yield, colorless oil, 98% ee.

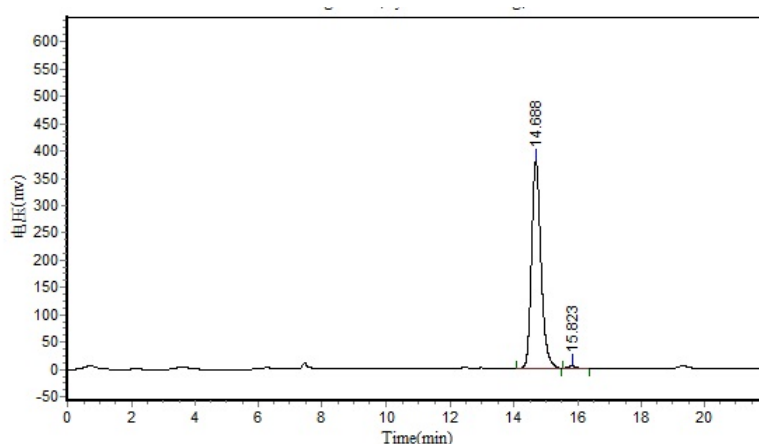
^1H NMR (300 MHz, CDCl_3): δ 1.41 (s, 9H), 4.36 (s, 1H), 5.32 (q, $J = 12.0$ Hz, 2H), 6.71-6.82 (m, 2H), 7.06 (d, $J = 9.0$ Hz, 1H), 7.08-7.16 (m, 2H), 7.26-7.36 (m, 5H), 7.44-7.49 (m, 1H), 7.85-7.89 (m, 2H), 8.06 (d, $J = 8.4$ Hz, 1H), 8.16 (s, 1H), 8.42 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 68.9, 80.6, 83.6, 122.1, 122.6, 124.6, 125.9, 126.0, 126.2, 127.0, 128.4, 128.7, 128.8, 129.0, 130.2, 130.5, 131.2, 134.3, 134.9, 135.1, 135.2, 139.3, 152.8, 174.3; ESI-MS (m/z , %) 540 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{30}\text{H}_{28}\text{NNaO}_5\text{Cl}$ $[\text{M}+\text{Na}]^+$ 540.1554, found 540.1548.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 14.7 min (maj), 15.8 min.



Results

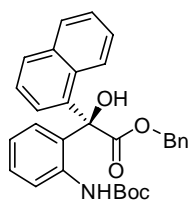
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.165	445179.219	9806962.000	50.0173
2		16.398	410782.500	9800160.000	49.9827
Total			855961.719	19607122.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.688	382040.344	7904547.000	98.9580
2		15.823	4247.661	83233.508	1.0420
Total			386288.004	7987780.508	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-hydroxy-2-(naphthalen-1-yl)acetate **3n**.

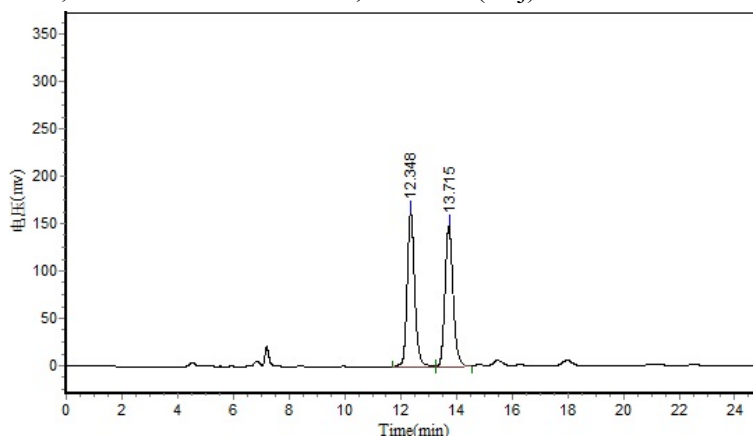


3n

65% yield, colorless oil, 98% ee.

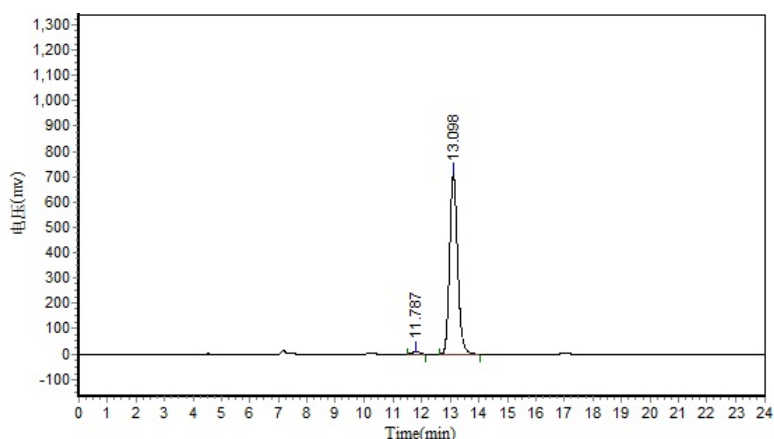
¹H NMR (300 MHz, CDCl₃): δ 1.36 (s, 9H), 4.36 (s, 1H), 5.30 (q, *J* = 12.6 Hz, 2H), 6.86-6.87 (m, 2H), 7.07-7.11 (m, 3H), 7.22-7.37 (m, 6H), 7.44 (t, *J* = 10.2 Hz, 1H), 7.82-7.87 (m, 2H), 7.99 (d, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 9.0 Hz, 1H), 8.19 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.4, 68.7, 80.0, 83.7, 123.0, 123.2, 124.7, 125.8, 126.0, 126.3, 127.0, 128.4, 128.7, 128.8, 128.9, 129.4, 129.6, 130.2, 131.4, 134.5, 134.8, 135.3, 138.1, 153.2, 174.8; ESI-MS (*m/z*, %) 506 [M+Na]⁺; ESI-HRMS calcd for C₃₀H₂₉NNaO₅ [M+Na]⁺ 506.1943, found 506.1941.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 85 / 15; flow = 0.7 mL / min; Retention time: 11.8 min, 13.1 min (maj).



Results

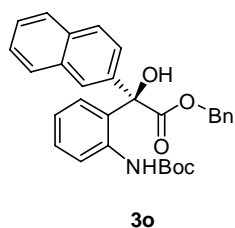
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		12.348	163533.828	3109795.750	50.4795
2		13.715	148305.875	3050715.250	49.5205
Total			311839.703	6160511.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		11.787	10766.391	173713.547	1.2298
2		13.098	709879.250	13951077.000	98.7701
Total			720645.641	14124790.547	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-hydroxy-2-(naphthalen-2-yl)acetate **3o**.

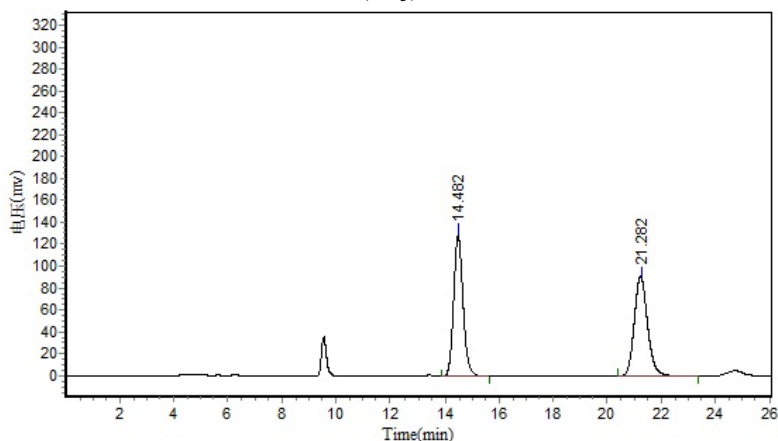


46% yield, yellow oil, 88% ee.

^1H NMR (300 MHz, CDCl_3): δ 1.18 (s, 9H), 4.42 (s, 1H), 5.30 (q, $J = 11.7$ Hz, 2H), 6.87-6.97 (m, 2H), 7.23-7.37 (m, 6H), 7.43-7.50 (m, 4H), 7.74-7.83 (m, 4H), 7.97 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.1, 68.7, 80.0, 81.3, 123.4, 124.6, 125.1, 125.6, 126.4, 126.6, 127.6, 128.1, 128.6, 128.7, 128.8, 129.5, 132.2, 133.0, 133.2, 134.7, 137.5, 137.6, 153.1, 174.0;

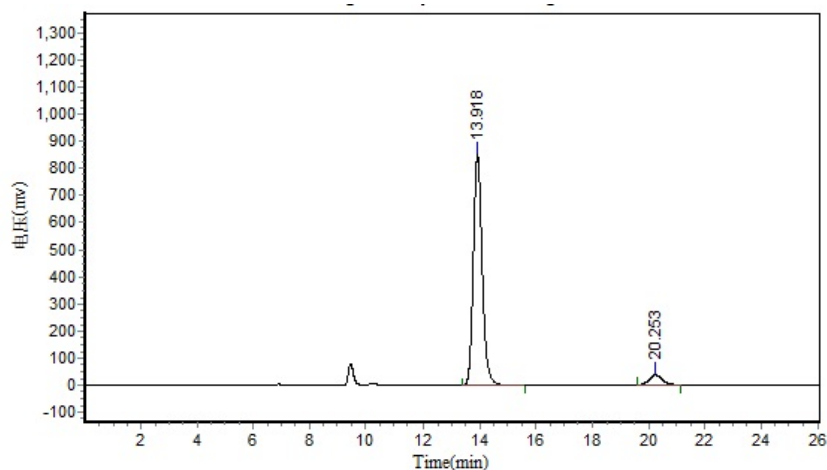
ESI-MS (m/z , %) 506 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{30}\text{H}_{29}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$ 506.1943, found 506.1943.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 13.9 min (maj), 20.3 min.



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.482	128500.750	3146278.000	50.0006
2		21.282	91033.117	3146200.500	49.9994
Total			219533.867	6292478.500	100.0000

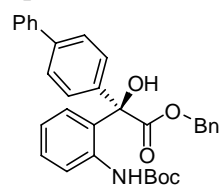


Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.918	847825.250	18519880.000	93.9505
2		20.253	36257.457	1192492.000	6.0495
Total			884082.707	19712372.000	100.0000

Benzyl (R)-2-([1,1'-biphenyl]-4-yl)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-hydroxyacetate

3p.

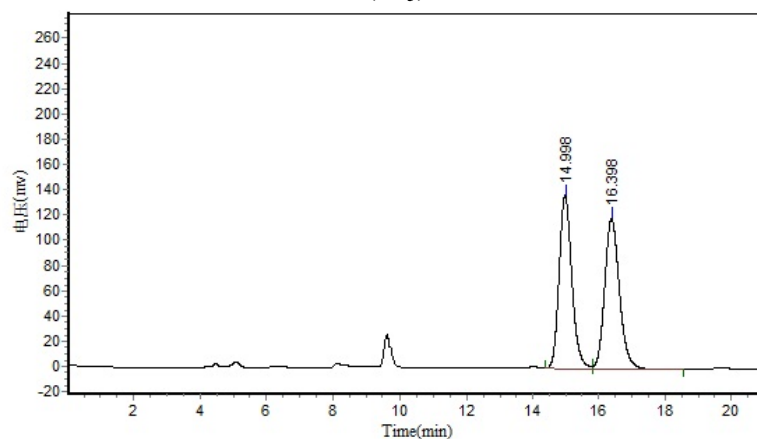


50% yield, white solid, 93% ee.

¹H NMR (300 MHz, CDCl₃): δ 1.34 (s, 9H), 4.36 (s, 1H), 5.30 (q, *J* = 12.3 Hz, 2H), 6.89-6.99 (m, 2H), 7.19-7.22 (m, 2H), 7.29-7.38 (m, 5H), 7.42-7.59 (m, 9H), 7.77 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.3, 68.7, 80.1, 81.2, 123.3, 124.5, 127.1, 127.2, 127.3, 127.6, 128.0, 128.4, 128.7, 129.0, 129.5, 132.1, 134.6, 137.5, 139.2, 140.6, 141.3, 153.2, 174.0; ESI-MS

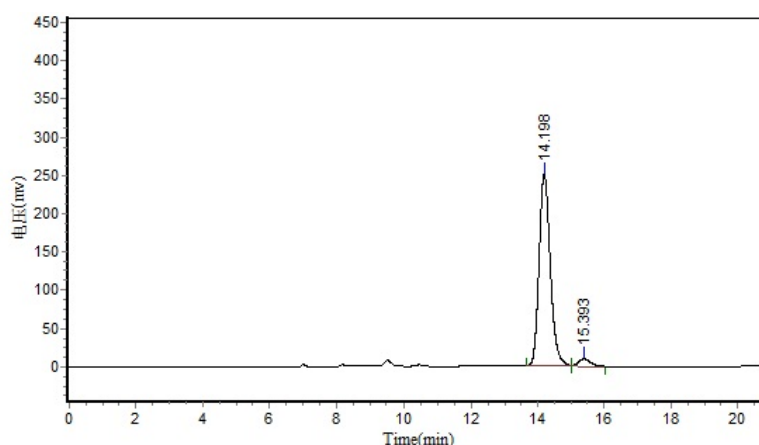
(*m/z*, %) 532 [M+Na]⁺; ESI-HRMS calcd for C₃₂H₃₁NNaO₅ [M+Na]⁺ 532.2100, found 532.2103.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 14.2 min (maj), 15.4 min.



Results

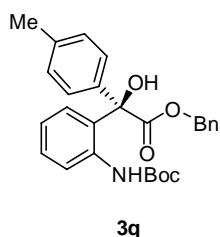
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.998	137234.156	3684705.500	50.0138
2		16.398	119048.859	3682669.750	49.9862
Total			256283.016	7367375.250	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.198	250375.766	5823746.500	96.6869
2		15.393	8669.356	199556.719	3.3131
Total			259045.122	6023303.219	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-hydroxy-2-(*p*-tolyl)acetate **3q**.

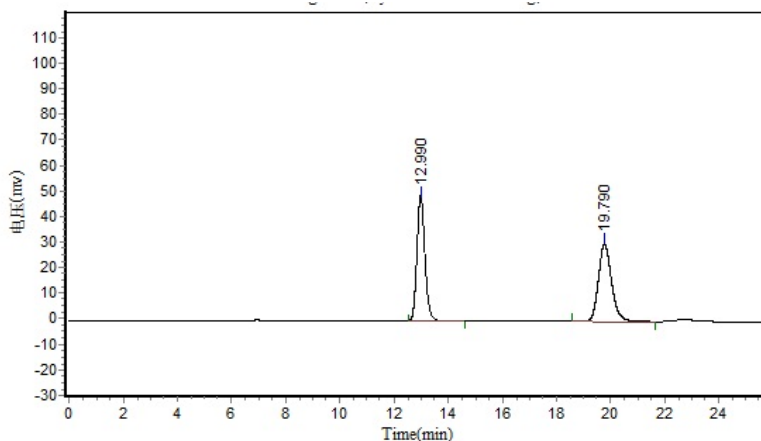


65% yield, white solid, 92% ee.

^1H NMR (300 MHz, CDCl_3): δ 1.37 (s, 9H), 2.34 (s, 3H), 4.23 (s, 1H), 5.26 (q, $J = 12.3$ Hz, 2H), 6.80-6.83 (m, 1H), 6.91 (dt, $J = 1.2$ Hz, 7.8 Hz, 1H), 7.12 (d, $J = 8.4$ Hz, 2H), 7.19-7.22 (m, 2H), 7.30-7.34 (m, 6H), 7.51 (s, 1H), 7.75 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.2, 28.3, 68.6, 80.0, 81.2, 123.2, 124.2, 126.7, 128.1, 128.4, 128.6, 128.7, 129.1, 129.3, 132.2, 134.7, 137.1, 137.5, 138.2, 153.2, 174.2; ESI-MS (m/z , %) 470

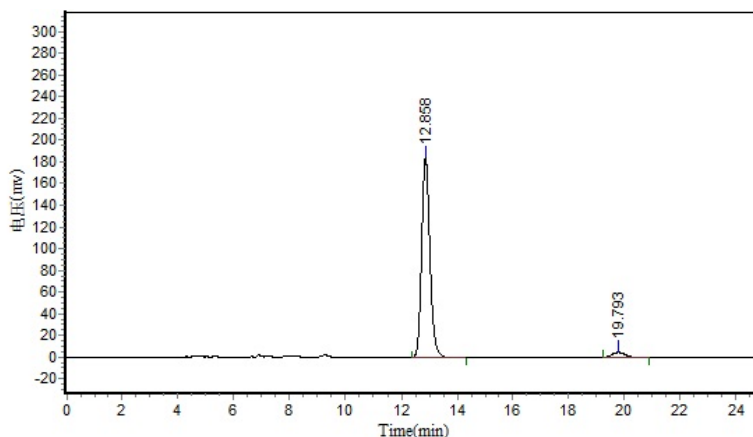
$[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{27}\text{H}_{29}\text{NNaO}_5$ $[\text{M}+\text{Na}]^+$ 470.1943, found 470.1943.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 12.9 min (maj), 19.8 min.



Results

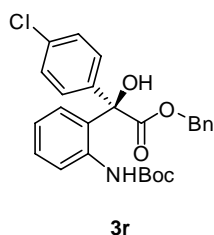
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		12.990	48929.879	1032301.250	50.2946
2		19.790	30325.648	1020206.500	49.7054
Total			79255.527	2052507.750	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		12.858	184407.063	3820726.000	95.8406
2		19.793	4956.256	165816.297	4.1594
Total			189363.319	3986542.297	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-(4-chlorophenyl)-2-hydroxyacetate **3r**.

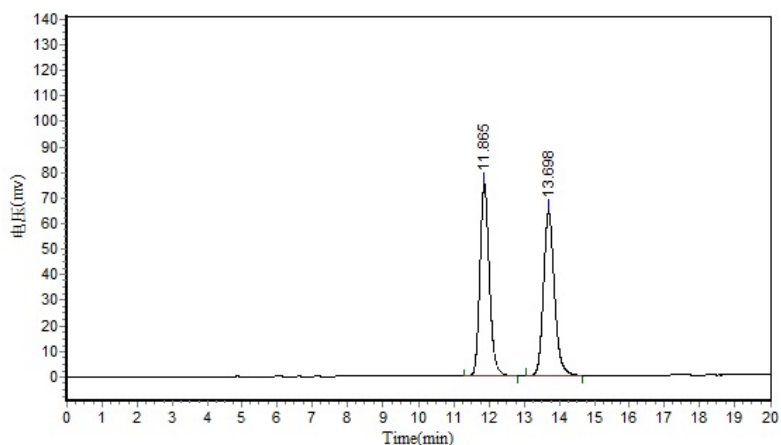


44% yield, colorless oil, 90% ee.

¹H NMR (300 MHz, CDCl₃): δ 1.35 (s, 9H), 4.38 (s, 1H), 5.27 (q, *J* = 12.0 Hz, 2H), 6.83-6.86 (m, 1H), 6.95 (t, *J* = 7.8 Hz, 1H), 7.18-7.21 (m, 2H), 7.25-7.36 (m, 9H), 7.72 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 28.1, 68.7, 80.2, 80.7, 123.4, 124.9, 127.5, 128.2, 128.3, 128.4, 128.7, 128.8, 129.5, 132.0, 134.2, 134.3, 137.2, 138.7, 153.0, 173.5; ESI-MS (*m/z*, %) 490

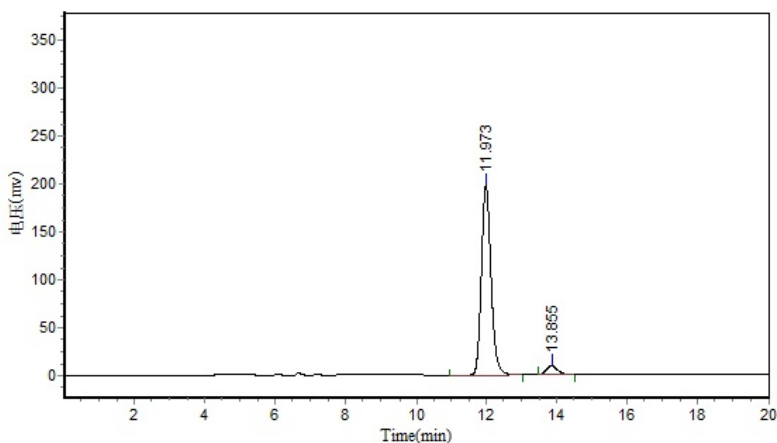
[*M*+Na]⁺; ESI-HRMS calcd for C₂₆H₂₆NNaO₅Cl [*M*+Na]⁺ 490.1397, found 490.1396.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 12.0 min (maj), 13.9 min.



Results

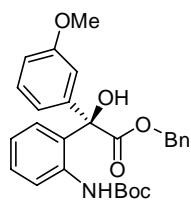
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		11.865	74799.469	1402243.750	50.1888
2		13.698	64148.395	1391696.250	49.8112
Total			138947.863	2793940.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		11.973	197773.141	3770406.500	94.9731
2		13.855	9243.227	199567.797	5.0269
Total			207016.367	3969974.297	100.0000

Benzyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-hydroxy-2-(3-methoxyphenyl)acetate **3s**.

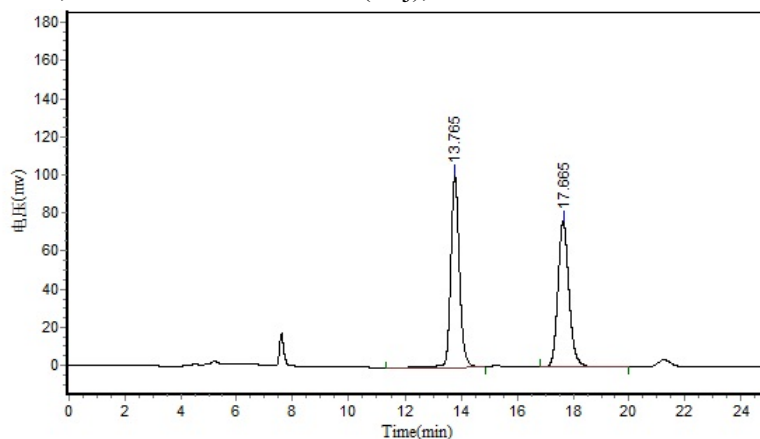


3s

40% yield, colorless oil, 91% ee.

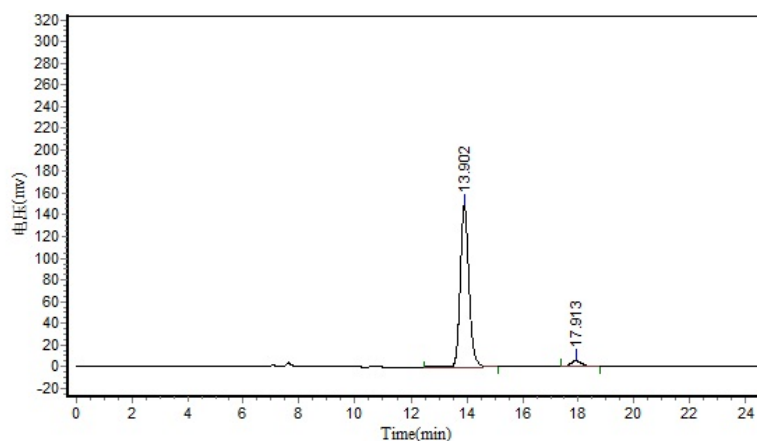
^1H NMR (300 MHz, CDCl_3): δ 1.39 (s, 9H), 3.67 (s, 3H), 4.29 (s, 1H), 5.27 (q, J = 12.0 Hz, 2H), 6.81-7.03 (m, 5H), 7.19-7.35 (m, 7H), 7.48 (s, 1H), 7.75 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 28.3, 55.3, 68.6, 80.1, 81.1, 111.9, 114.5, 119.3, 123.3, 124.4, 128.1, 128.5, 128.7, 129.4, 129.5, 132.1, 134.7, 137.5, 141.5, 153.2, 159.7, 174.1; ESI-MS (m/z , %) 486 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{27}\text{H}_{29}\text{NNaO}_6$ $[\text{M}+\text{Na}]^+$ 486.1893, found 486.1898.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 13.9 min (maj), 17.9 min.



Results

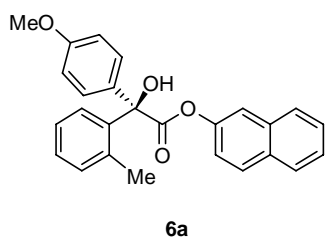
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.765	99647.016	2176944.750	50.7679
2		17.665	76633.602	2111086.500	49.2321
Total			176280.617	4288031.250	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.902	148764.625	3242318.750	95.5494
2		17.913	5448.087	151024.359	4.4506
Total			154212.712	3393343.109	100.0000

Naphthalen-2-yl (*R*)-2-hydroxy-2-(4-methoxyphenyl)-2-(*o*-tolyl)acetate **6a**.



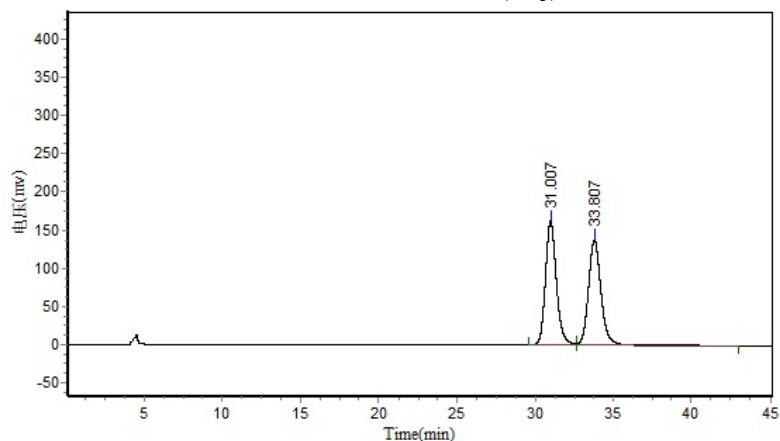
6a

90% yield, white solid, 90% ee.

^1H NMR (300 MHz, CDCl_3): δ 2.44 (s, 3H), 3.88 (s, 3H), 4.04 (s, 1H), 7.00 (d, $J = 9.0$ Hz, 2H), 7.08-7.19 (m, 3H), 7.28-7.29 (m, 2H), 7.47-7.55 (m, 3H), 7.67 (d, $J = 9.0$ Hz, 2H), 7.78-7.86 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 20.9, 55.5, 81.8, 113.8, 118.2, 120.3, 125.6, 126.2, 126.9, 127.8, 128.0, 128.5, 128.7, 128.8, 129.8, 131.8, 132.5, 132.8, 133.7, 138.3, 140.0, 148.3, 160.0, 174.2; ESI-MS

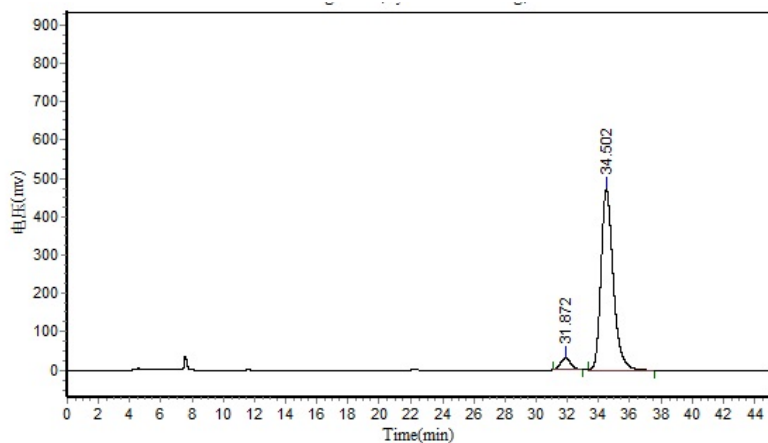
(m/z , %) 421 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{26}\text{H}_{22}\text{NaO}_4$ [$\text{M}+\text{Na}$] $^+$ 421.1416, found 421.1417.

HPLC: Chiralcel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 31.9 min, 34.5 min (maj).



Results

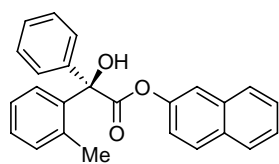
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.007	160927.391	7825855.000	50.7296
2		33.807	136849.172	7600740.000	49.2704
Total			297776.563	15426595.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.872	30362.699	1399554.500	5.1680
2		34.502	471175.531	25681550.000	94.8320
Total			501538.230	27081104.500	100.0000

Naphthalen-2-yl (*R*)-2-hydroxy-2-phenyl-2-(*o*-tolyl)acetate **6b**.



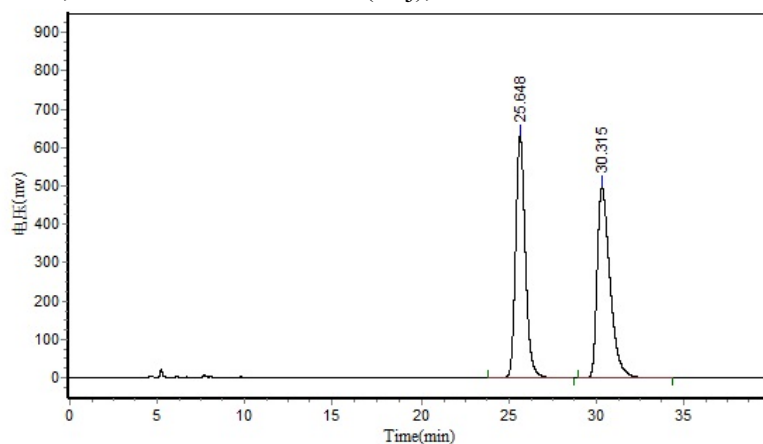
6b

83% yield, white solid, 86% ee.

^1H NMR (300 MHz, CDCl_3): δ 2.43 (s, 3H), 4.09 (s, 1H), 7.08-7.20 (m, 3H), 7.29-7.31 (m, 2H), 7.42-7.56 (m, 6H), 7.47-7.86 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.0, 82.2, 118.2, 120.3, 125.6, 126.2, 127.0, 127.3, 127.8, 128.0, 128.4, 128.5, 128.7, 128.8, 129.8, 131.8, 132.5, 133.7, 138.4, 139.8, 140.9, 148.3, 174.1; ESI-MS (m/z , %) 391

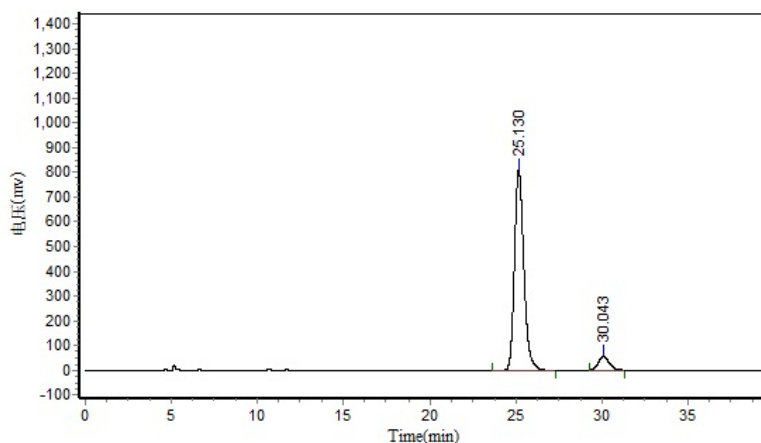
$[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{25}\text{H}_{20}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 391.1310, found 391.1316.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 25.1 min (maj), 30.0 min.



Results

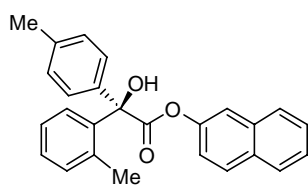
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.648	628404.500	24146402.000	49.0014
2		30.315	494313.250	25130550.000	50.9986
Total			1122717.750	49276952.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.130	810632.938	30620236.000	92.8445
2		30.043	53733.867	2359907.500	7.1555
Total			864366.805	32980143.500	100.0000

Naphthalen-2-yl (R)-2-hydroxy-2-(*o*-tolyl)-2-(*p*-tolyl)acetate **6c**.



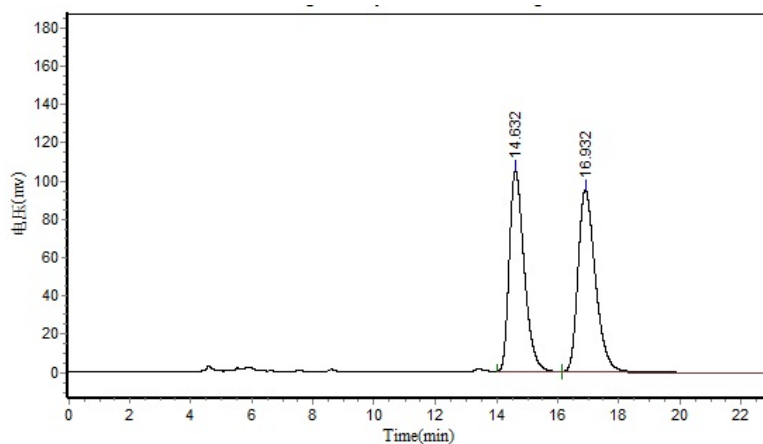
6c

86% yield, white solid, 87% ee.

^1H NMR (300 MHz, CDCl_3): δ 2.43 (s, 3H), 2.45 (s, 3H), 4.03 (s, 1H), 7.07-7.20 (m, 3H), 7.26-7.29 (m, 4H), 7.47-7.56 (m, 3H), 7.64 (d, $J = 8.1$ Hz, 2H), 7.79-7.86 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.0, 21.3, 82.0, 118.2, 120.3, 125.5, 126.2, 126.9, 127.2, 127.8, 127.9, 128.7, 129.3, 129.8, 131.8, 132.4, 133.7, 137.8, 138.2, 138.3, 139.9, 148.3, 174.2; ESI-MS (m/z , %) 405 $[\text{M}+\text{Na}]^+$; ESI-HRMS

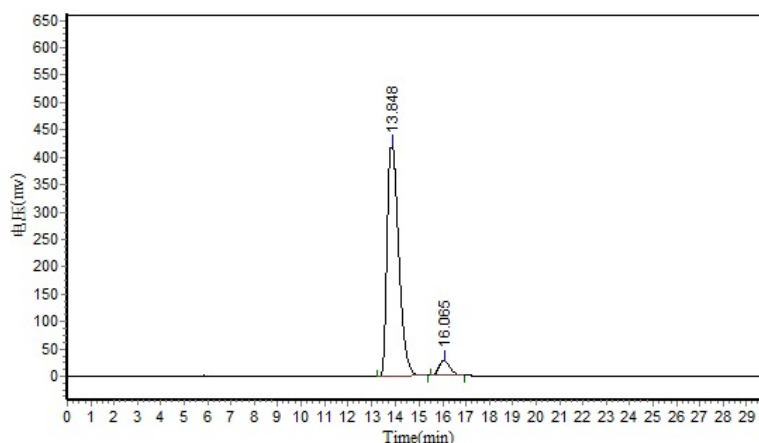
calcd for $\text{C}_{26}\text{H}_{22}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 405.1467, found 405.1465.

HPLC: Chiralcel OD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 13.8 min (maj), 16.0 min.



Results

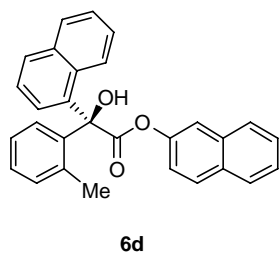
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.632	105421.508	3617367.500	48.6767
2		16.932	95247.820	3814049.250	51.3233
Total			200669.328	7431416.750	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.848	419663.844	13138141.000	93.4093
2		16.065	27836.000	926996.313	6.5907
Total			447499.844	14065137.313	100.0000

Naphthalen-2-yl (*S*)-2-hydroxy-2-(naphthalen-1-yl)-2-(*o*-tolyl)acetate **6d**.

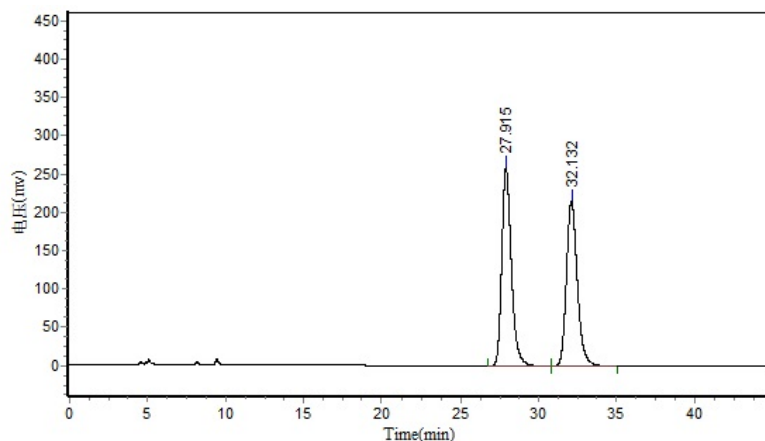


77% yield, colorless oil, 96% ee.

^1H NMR (300 MHz, CDCl_3): δ 2.42 (s, 3H), 4.17 (s, 1H), 7.11-7.21 (m, 2H), 7.31-7.33 (m, 3H), 7.41-7.52 (m, 7H), 7.78-7.84 (m, 3H), 7.91 (d, $J = 8.1$ Hz, 2H), 8.33 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 22.1, 84.3, 118.2, 120.4, 124.8, 125.9, 126.1, 126.2, 126.3, 126.9, 127.3, 127.8, 127.9, 128.6, 128.7, 129.0, 129.8, 130.1, 131.6, 131.8, 132.8, 133.7, 134.9, 136.9, 138.5, 139.2, 148.3, 174.6; ESI-MS (m/z , %)

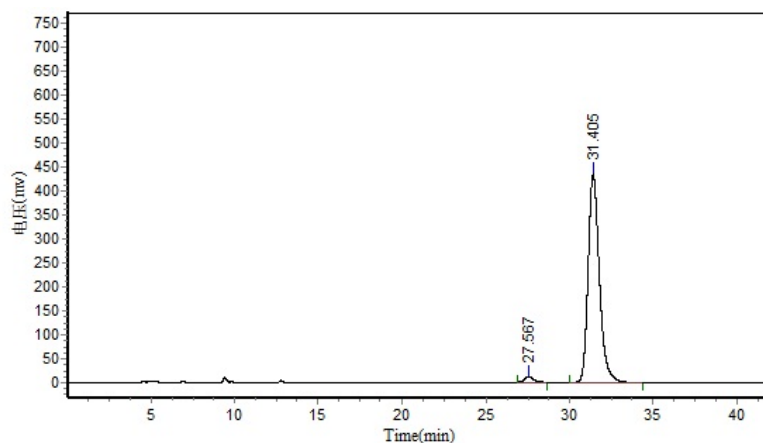
441 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{29}\text{H}_{22}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 441.1467, found 441.1470.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 27.6 min, 31.4 min (maj).



Results

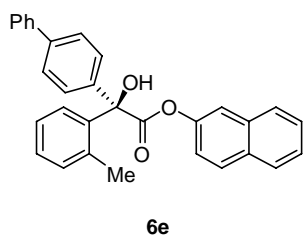
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.915	258137.219	10988206.000	51.2590
2		32.132	215546.156	10448413.000	48.7410
Total			473683.375	21436619.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.567	11293.260	434513.813	2.1042
2		31.405	433723.250	20214830.000	97.8958
Total			445016.510	20649343.813	100.0000

Naphthalen-2-yl (*R*)-2-([1,1'-biphenyl]-4-yl)-2-hydroxy-2-(*o*-tolyl)acetate **6e**.

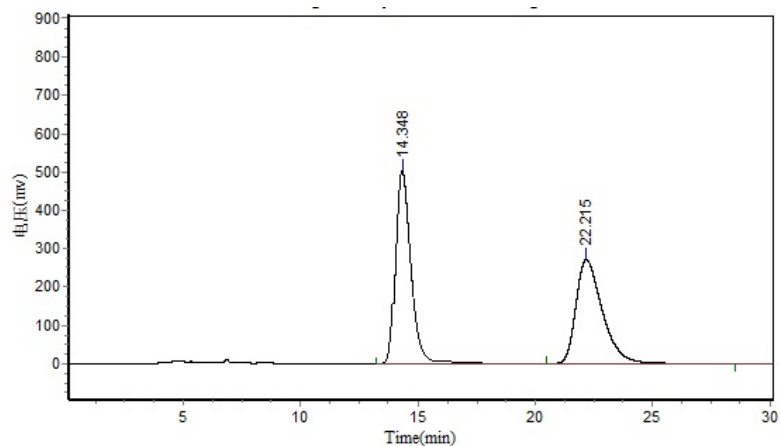


81% yield, white solid, 87% ee.

¹H NMR (300 MHz, CDCl₃): δ 2.47 (s, 3H), 4.13 (s, 1H), 7.17-7.23 (m, 3H), 7.31-7.42 (m, 3H), 7.46-7.54 (m, 4H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.68-7.73 (m, 5H), 7.80-7.87 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 21.0, 82.1, 118.2, 120.3, 125.6, 126.2, 127.0, 127.2, 127.3, 127.7, 127.8, 127.9, 128.0, 128.7, 128.9, 129.0, 129.9, 131.8, 132.5, 133.7, 138.3, 139.7, 139.8, 140.6, 141.2, 148.3, 174.0; ESI-MS (*m/z*, %)

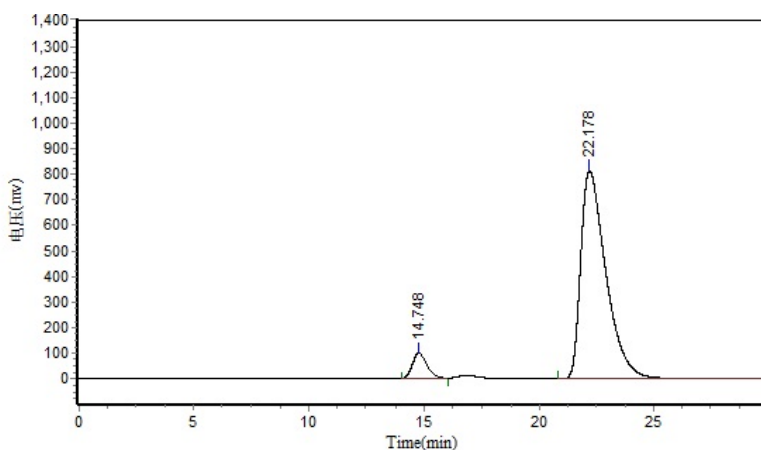
467 [M+Na]⁺; ESI-HRMS calcd for C₃₁H₂₄NaO₃ [M+Na]⁺ 467.1623, found 467.1620.

HPLC: Chiracel OD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 14.7 min, 22.2 min (maj).



Results

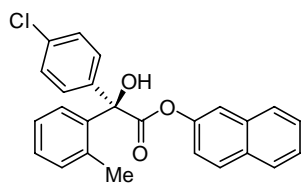
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.348	503164.656	22649578.000	51.5982
2		22.215	271376.750	21246508.000	48.4018
Total			774541.406	43896086.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.748	99840.461	4467566.500	6.7063
2		22.178	814645.688	62149644.000	93.2937
Total			914486.148	66617210.500	100.0000

Naphthalen-2-yl (*R*)-2-(4-chlorophenyl)-2-hydroxy-2-(*o*-tolyl)acetate **6f**.

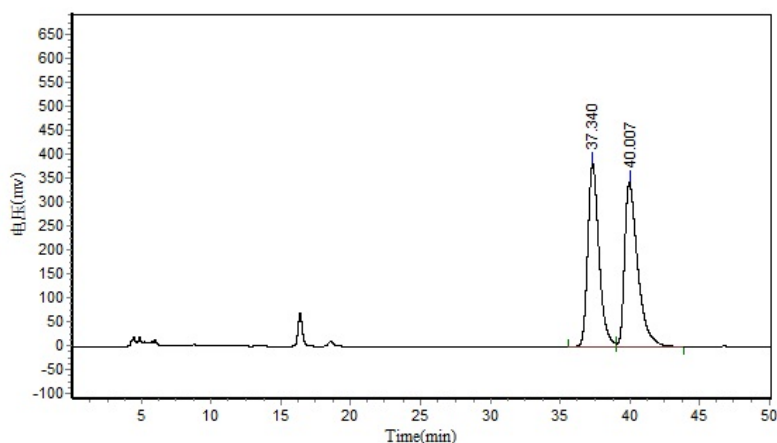


6f

55% yield, white solid, 91% ee.

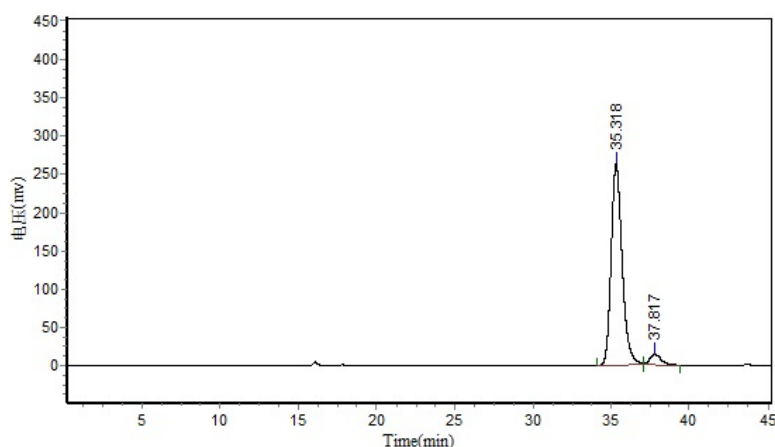
^1H NMR (300 MHz, CDCl_3): δ 2.37 (s, 3H), 4.13 (s, 1H), 7.11-7.22 (m, 3H), 7.27-7.34 (m, 2H), 7.44 (d, $J = 9.0$ Hz, 2H), 7.48-7.56 (m, 3H), 7.69 (d, $J = 9.0$ Hz, 2H), 7.82-7.88 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.0, 81.9, 118.1, 120.1, 125.7, 126.3, 127.1, 127.8, 128.0, 128.3, 128.7, 128.8, 129.0, 129.9, 131.8, 132.7, 133.7, 134.4, 138.3, 139.4, 148.2, 173.7; ESI-MS (m/z , %) 425 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{25}\text{H}_{19}\text{NaO}_3\text{Cl}$ [$\text{M}+\text{Na}$] $^+$ 425.0920, found 425.0921.

HPLC: Chiralcel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 35.3 min (maj), 37.8 min.



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		37.340	381792.969	21319232.000	48.7768
2		40.007	342721.531	22388476.000	51.2232
Total			724514.500	43707708.000	100.0000

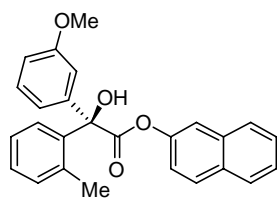


Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		35.318	260969.516	12695871.000	95.6509
2		37.817	12360.717	577263.813	4.3491
Total			273330.232	13273134.813	100.0000

Naphthalen-2-yl (*R*)-2-hydroxy-2-(3-methoxyphenyl)-2-(*o*-tolyl)acetate **6g**.

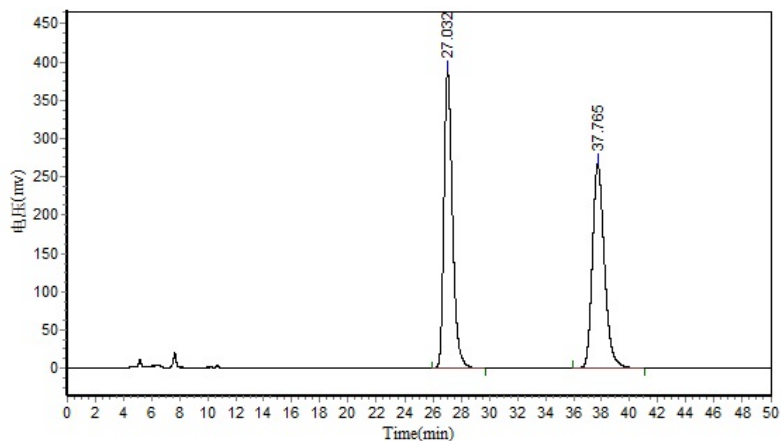
71% yield, colorless oil, 88% ee.



6g

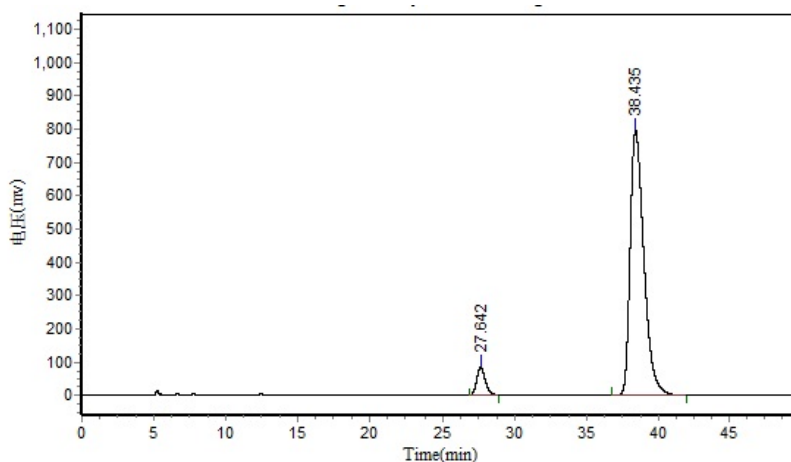
^1H NMR (300 MHz, CDCl_3): δ 2.46 (s, 3H), 3.84 (s, 3H), 4.08 (s, 1H), 6.95-6.99 (m, 1H), 7.06-7.21 (m, 3H), 7.28-7.41 (m, 5H), 7.48-7.56 (m, 3H), 7.79-7.87 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 20.9, 55.5, 82.1, 112.9, 114.0, 118.2, 119.8, 120.3, 125.6, 126.2, 127.0, 127.8, 128.0, 128.7, 128.8, 129.5, 129.8, 131.8, 132.4, 133.7, 138.3, 139.6, 142.5, 148.3, 159.9, 174.0; ESI-MS (m/z , %) 421 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{26}\text{H}_{22}\text{NaO}_4$ [$\text{M}+\text{Na}$] $^+$ 421.1416, found 421.1413.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 27.6 min, 38.4 min (maj).



Results

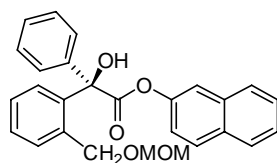
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.032	387062.469	16439376.000	50.9510
2		37.765	265551.281	15825676.000	49.0490
Total			652613.750	32265052.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.642	83091.008	3493688.250	6.2146
2		38.435	794739.875	52723840.000	93.7854
Total			877830.883	56217528.250	100.0000

Naphthalen-2-yl (*R*)-2-hydroxy-2-((methoxymethoxy)methyl)phenyl)-2-phenylacetate **6h**.



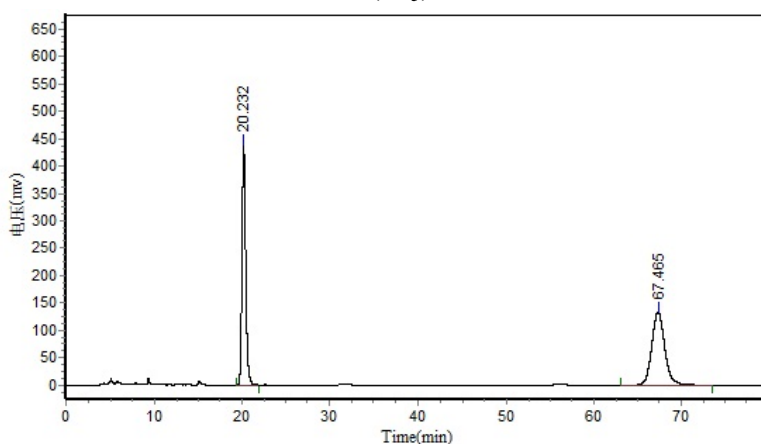
6h

50% yield, white solid, 86% ee.

^1H NMR (300 MHz, CDCl_3): δ 3.37 (s, 3H), 4.65 (q, $J = 6.3$ Hz, 2H), 4.65 (q, $J = 6.3$ Hz, 2H), 4.72 (q, $J = 12.3$ Hz, 2H), 4.89 (s, 1H), 7.18-7.21 (m, 2H), 7.30 (dt, $J = 1.5$ Hz, 7.8 Hz, 1H), 7.39-7.54 (m, 6H), 7.58-7.61 (m, 2H), 7.71-7.75 (m, 2H), 7.78-7.86 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.8, 68.2, 82.3, 96.1, 118.3, 120.5, 126.1, 126.9,

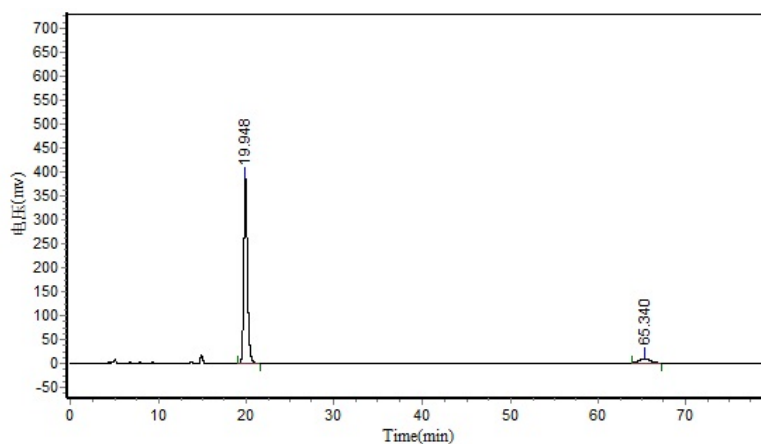
127.3, 127.8, 127.9, 128.5, 128.8, 128.9, 129.7, 131.1, 131.7, 133.8, 137.0, 140.7, 141.0, 148.4, 173.1; ESI-MS (m/z , %) 451 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{27}\text{H}_{24}\text{NaO}_5$ $[\text{M}+\text{Na}]^+$ 451.1521, found 451.1519.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 19.9 min (maj), 65.3 min.



Results

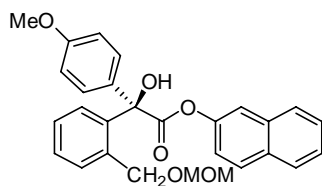
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.232	436048.781	12891297.000	48.6707
2		67.465	132571.906	13595480.000	51.3293
Total			568620.688	26486777.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.948	385145.844	11115067.000	92.9507
2		65.340	9525.766	842955.625	7.0493
Total			394671.609	11958022.625	100.0000

Naphthalen-2-yl (*R*)-2-hydroxy-2-(2-((methoxymethoxy)methyl) phenyl)-2-(4-methoxyphenyl) acetate **6i**.

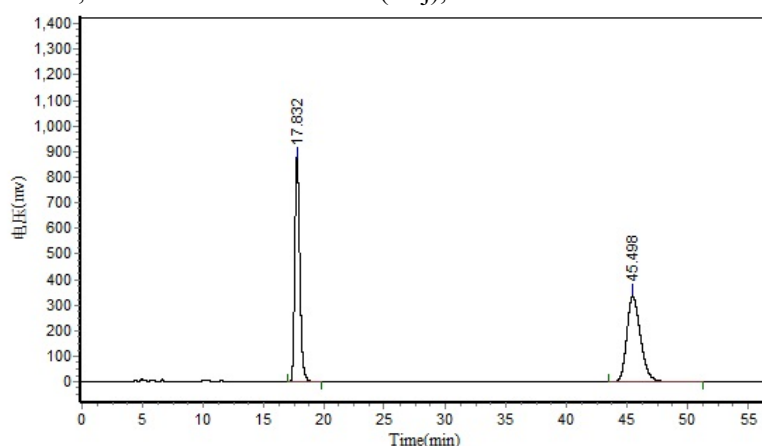


6i

75% yield, colorless oil, 88% ee.

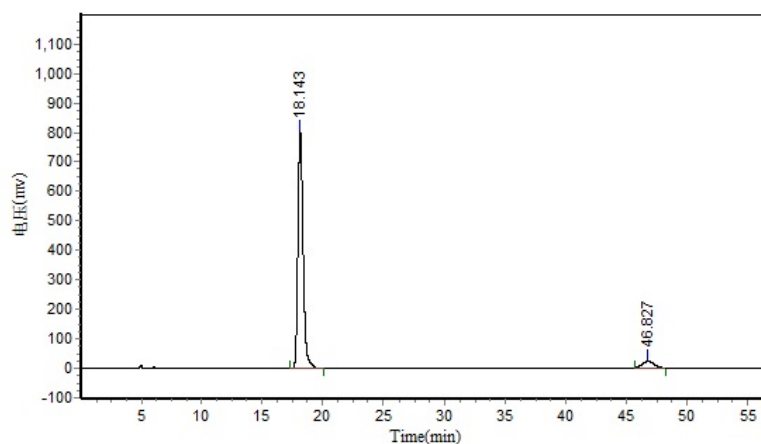
^1H NMR (300 MHz, CDCl_3): δ 3.37 (s, 3H), 3.86 (s, 3H), 4.66 (q, J = 5.7 Hz, 2H), 4.73 (q, J = 12.6 Hz, 2H), 4.84 (s, 1H), 6.98 (d, J = 9.0 Hz, 2H), 7.17-7.20 (m, 2H), 7.28-7.31 (m, 1H), 7.39 (dt, J = 1.2 Hz, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.5, 55.8, 68.2, 81.9, 96.1, 113.9, 118.3, 120.5, 126.1, 126.9, 127.8, 127.9, 128.0, 128.6, 128.8, 128.9, 129.7, 131.1, 131.7, 133.0, 133.8, 136.9, 140.9, 148.4, 159.7, 173.3; ESI-MS (m/z , %) 481 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{28}\text{H}_{26}\text{NaO}_6$ [$\text{M}+\text{Na}$] $^+$ 481.1627, found 481.1630.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 60 / 40; flow = 0.7 mL / min; Retention time: 18.1 min (maj), 46.8 min.



Results

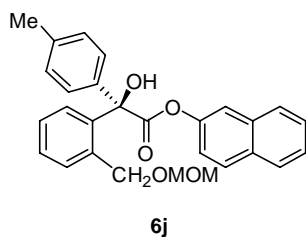
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.832	878200.500	25341780.000	48.9732
2		45.498	334456.281	26404442.000	51.0268
Total			1212656.781	51746222.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.143	802812.813	23861316.000	94.1110
2		46.827	21347.330	1493111.375	5.8890
Total			824160.143	25354427.375	100.0000

Naphthalen-2-yl (*R*)-2-hydroxy-2-(2-((methoxymethoxy)methyl)phenyl)-2-(*p*-tolyl)acetate **6j**.

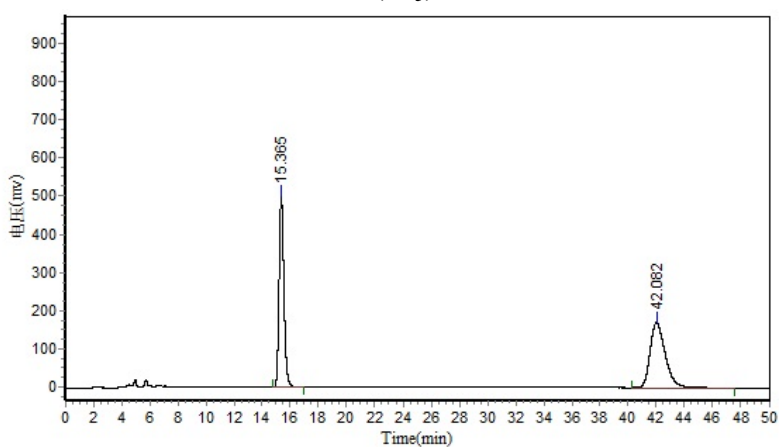


66% yield, colorless oil, 86% ee.

^1H NMR (300 MHz, CDCl_3): δ 2.42 (s, 3H), 3.37 (s, 3H), 4.65 (q, J = 6.9 Hz, 2H), 4.73 (q, J = 12.3 Hz, 2H), 4.83 (s, 1H), 7.17-7.21 (m, 2H), 7.25-7.30 (m, 3H), 7.37-7.42 (m, 1H), 7.46-7.52 (m, 2H), 7.58-7.61 (m, 4H), 7.78-7.85 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 55.8, 68.2, 82.2, 96.1, 118.3, 120.5, 126.1, 126.8, 127.2, 127.8, 127.9, 128.8, 129.0, 129.3, 129.7, 131.1, 131.7, 133.8, 137.0,

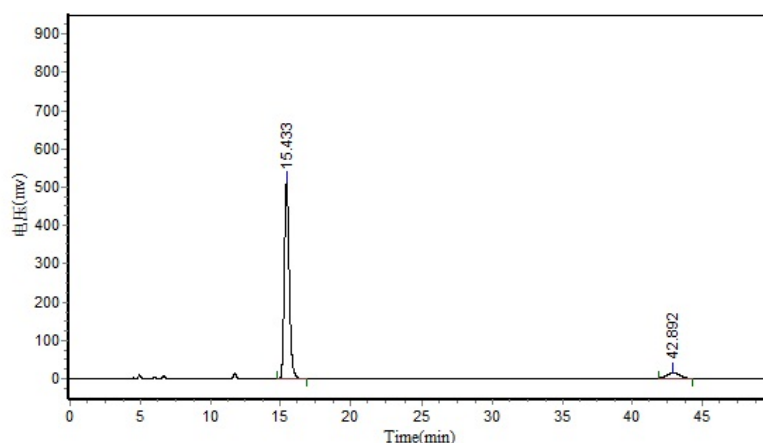
138.0, 138.3, 140.8, 148.5, 173.3; ESI-MS (m/z , %) 465 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{28}\text{H}_{26}\text{NaO}_5$ [$\text{M}+\text{Na}$] $^+$ 465.1678, found 465.1676.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 60 / 40; flow = 0.7 mL / min; Retention time: 15.4 min (maj), 42.9 min.



Results

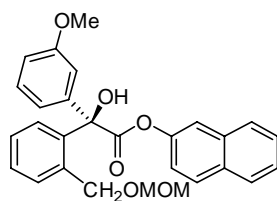
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.365	496142.344	12022131.000	48.7046
2		42.082	168891.391	12661621.000	51.2954
Total			665033.734	24683752.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.433	510049.875	12468271.000	92.9146
2		42.892	14617.654	950794.750	7.0854
Total			524667.529	13419065.750	100.0000

Naphthalen-2-yl (R)-2-hydroxy-2-(2-((methoxymethoxy)methyl)phenyl)-2-(3-methoxyphenyl) acetate **6k**.

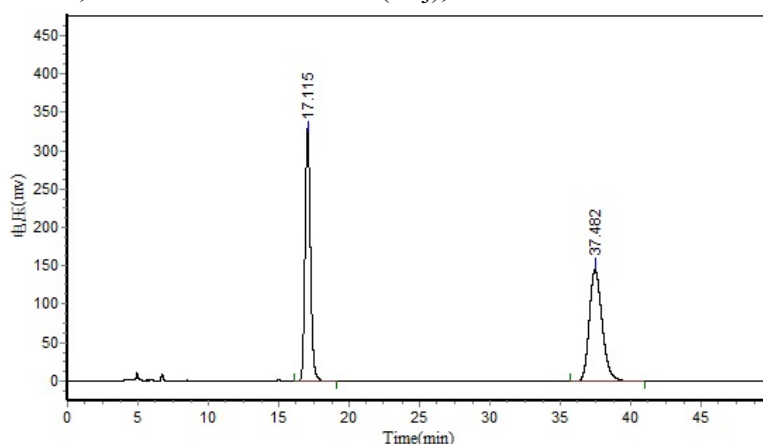


6k

42% yield, colorless oil, 88% ee.

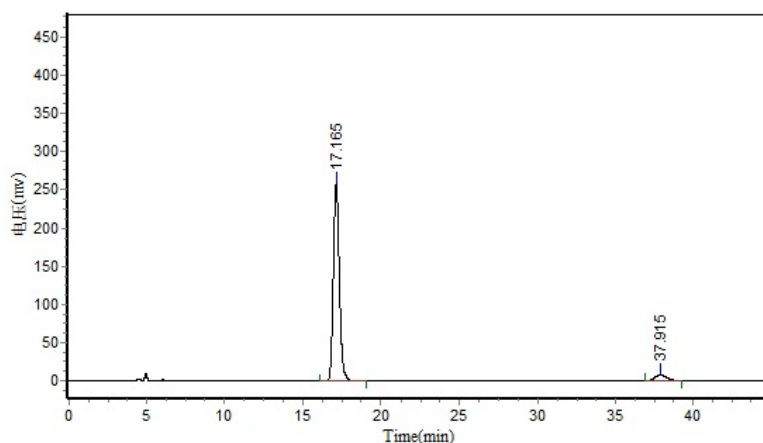
^1H NMR (300 MHz, CDCl_3): δ 3.37 (s, 3H), 3.83 (s, 3H), 4.66 (q, J = 3.3 Hz, 2H), 4.74 (q, J = 12.6 Hz, 2H), 4.89 (s, 1H), 6.96 (dd, J = 2.1 Hz, 8.1 Hz, 1H), 7.16-7.22 (m, 2H), 7.26-7.42 (m, 5H), 7.46-7.50 (m, 2H), 7.56-7.58 (m, 2H), 7.78-7.85 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.5, 55.8, 68.2, 82.2, 96.1, 112.9, 114.2, 118.3, 119.8, 120.5, 126.1, 126.9, 127.8, 127.9, 128.0, 128.9, 129.1, 129.5, 129.7, 131.1, 131.7, 133.8, 136.9, 140.6, 142.6, 148.4, 159.9, 173.1; ESI-MS (m/z , %) 481 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{28}\text{H}_{26}\text{NaO}_6$ $[\text{M}+\text{Na}]^+$ 481.1627, found 481.1628.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 60 / 40; flow = 0.7 mL / min; Retention time: 17.1 min (maj), 37.9 min.



Results

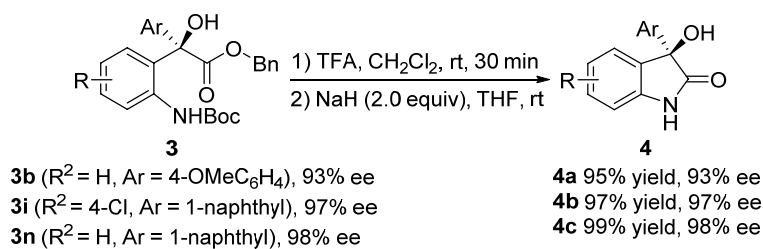
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.115	326760.781	8860883.000	48.8414
2		37.482	145321.672	9281264.000	51.1586
Total			472082.453	18142147.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.165	257156.250	6941720.500	93.9110
2		37.915	7723.188	450085.188	6.0890
Total			264879.438	7391805.688	100.0000

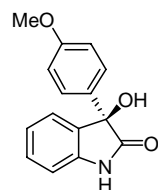
5. General procedure for the synthesis of 3-aryl-3-hydroxyoxindole 4a-c.



Trifluoroacetic acid (0.2 mL) was added to a solution of the compound **3b**, **3i** or **3n** (0.1 mmol, 1.0 equiv) in CH₂Cl₂ (1.0 mL), then the mixture was stirred at ambient temperature for 30 min, and later quenched by aq. NaHCO₃. The mixture was extracted with EtOAc and washed with aq. brine, dried over Na₂SO₄, and concentrated under reduced pressure. Subsequently, the residue was dissolved in dry THF (2.0 mL), and NaH (0.2 mmol, 2.0 equiv) was added slowly. The mixture was stirred at room temperature for another 30 min and monitored by TLC. When the reaction was over, a saturated aq. NaCl was added and the mixture was extracted with EtOAc. The combined organic phase was dried over Na₂SO₄, filtered, and concentrated. The residue was purified by silica gel flash chromatography to afford the corresponding products **4a-c**.

6. Characterization data and HPLC chromatogram of compounds 4a-c.

(*R*)-3-hydroxy-3-(4-methoxyphenyl)indolin-2-one **4a**.



4a

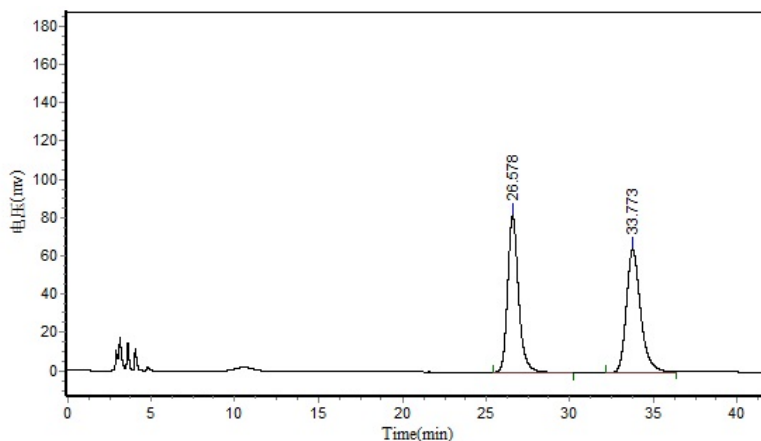
95% yield, white solid, 93% ee.

$^1\text{H NMR}$ (300 MHz, $(\text{CD}_3)_2\text{CO}$): δ 3.77 (s, 3H), 5.43 (s, 1H), 6.87 (d, $J = 9.3$ Hz, 2H), 6.96-7.04 (m, 2H), 7.19-7.29 (m, 2H), 7.34 (d, $J = 9.0$ Hz, 2H), 9.32 (s, 1H).

The absolute configuration of known compound **4a** was unambiguously determined to be *R* by comparison of its HPLC chromatogram with the literature data.^{ref}

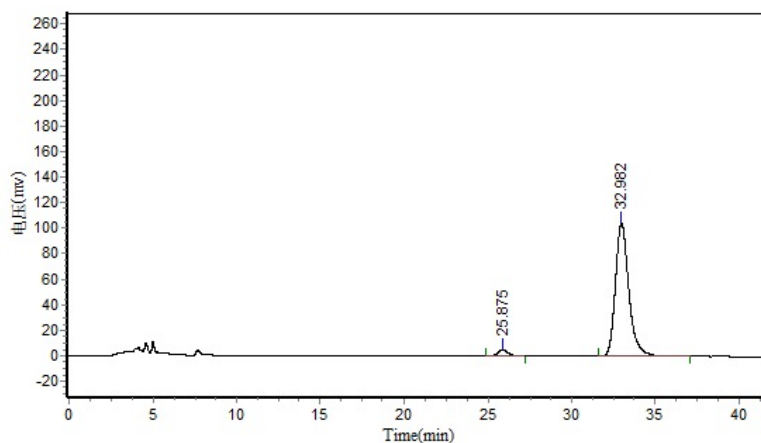
Reference: L. Yin, M. Kanai, M. Shibasaki, *Angew. Chem. Int. Ed.* 2011, 50, 7620.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 1.0 mL / min; Retention time: 25.9 min, 33.0 min (maj).



Results

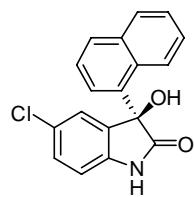
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.578	81896.398	3691888.500	49.2034
2		33.773	64255.988	3811435.750	50.7966
Total			146152.387	7503324.250	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.875	5105.101	211345.250	3.4958
2		32.982	104283.258	5834273.500	96.5042
Total			109388.358	6045618.750	100.0000

(*R*)-5-chloro-3-hydroxy-3-(naphthalen-1-yl)indolin-2-one **4b**.

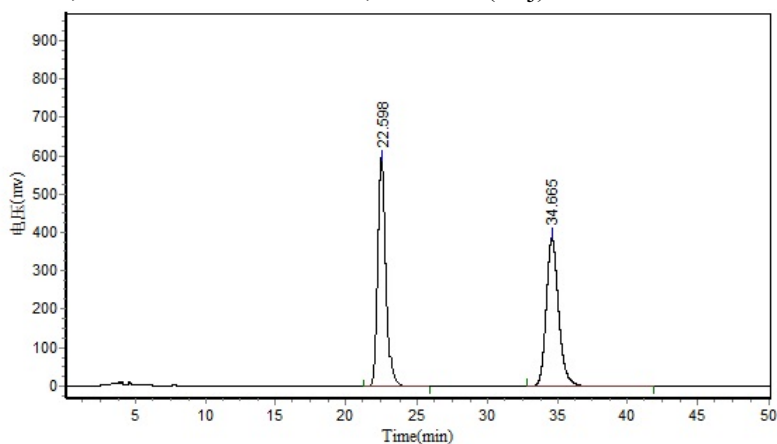


4b

97% yield, white solid, 97% ee.

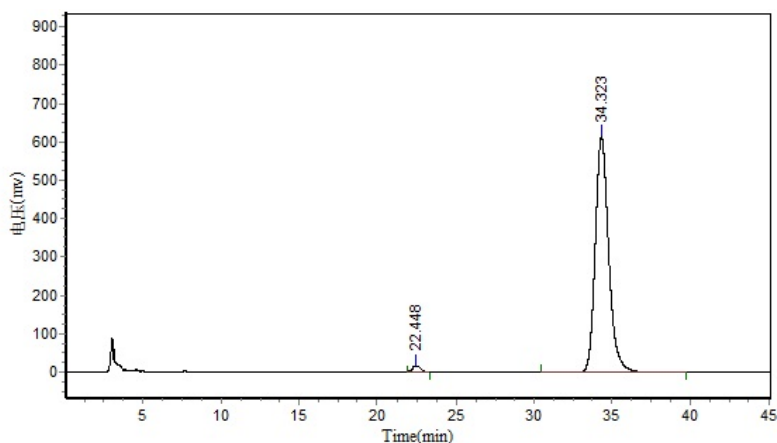
^1H NMR (300 MHz, $(\text{CD}_3)_2\text{CO}$): δ 5.99 (s, 1H), 7.02 (s, 1H), 7.12 (d, $J = 8.4$ Hz, 1H), 7.31-7.44 (m, 2H), 7.46 (t, $J = 5.7$ Hz, 1H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.84-7.94 (m, 3H), 8.12 (d, $J = 6.9$ Hz, 1H), 9.86 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 78.8, 112.7, 125.3, 125.7, 125.9, 126.0, 126.3, 126.9, 127.8, 129.9, 130.1, 130.5, 131.1, 135.2, 136.3, 136.5, 141.8, 178.3; ESI-MS (m/z , %) 332 $[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{18}\text{H}_{12}\text{NNaO}_2\text{Cl}$ $[\text{M}+\text{Na}]^+$ 332.0454, found 332.0451.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 1.0 mL / min; Retention time: 22.4 min, 34.3 min (maj).



Results

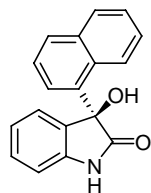
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.598	591887.875	23644852.000	49.8765
2		34.665	386544.125	23761956.000	50.1235
Total			978432.000	47406808.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.448	15942.583	568529.250	1.5311
2		34.323	612951.250	36563084.000	98.4689
Total			628893.833	37131613.250	100.0000

(*R*)-3-hydroxy-3-(naphthalen-1-yl)indolin-2-one **4c**.



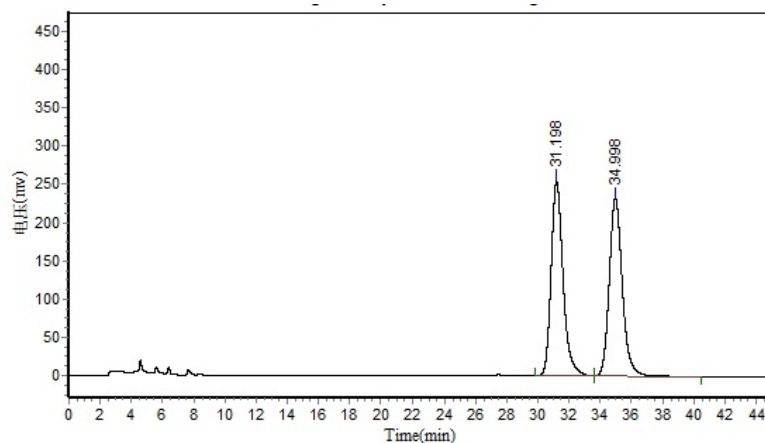
4c

99% yield, white solid, 98% ee.

^1H NMR (300 MHz, $(\text{CD}_3)_2\text{CO}$): δ 5.76 (s, 1H), 6.90 (t, $J = 7.5$ Hz, 1H), 7.01-7.10 (m, 2H), 7.26-7.34 (m, 2H), 7.42 (t, $J = 6.9$ Hz, 1H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.88-7.91 (m, 3H), 8.12 (d, $J = 7.2$ Hz, 1H), 9.71 (s, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 78.8, 111.1, 123.1, 125.5, 125.6, 125.8, 125.9, 126.1, 126.6, 129.7, 129.8, 130.5, 131.3, 134.5, 135.2, 137.3, 142.9, 178.8; ESI-MS (m/z , %) 298

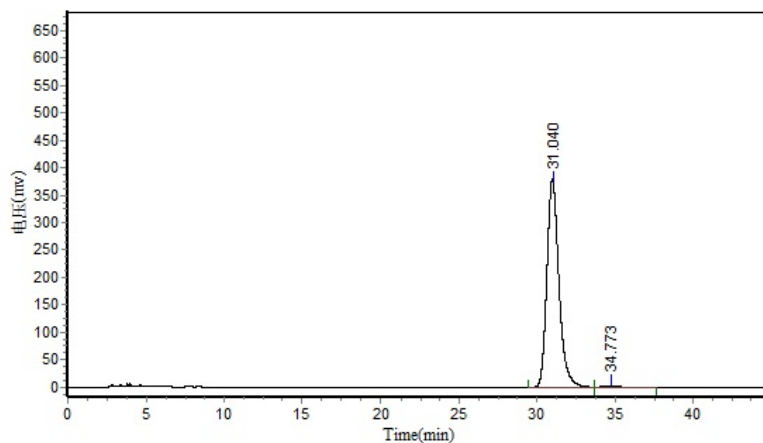
$[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{18}\text{H}_{13}\text{NNaO}_2$ $[\text{M}+\text{Na}]^+$ 298.0844, found 298.0837.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 90 / 10; flow = 1.0 mL / min; Retention time: 31.0 min (maj), 34.8 min.



Results

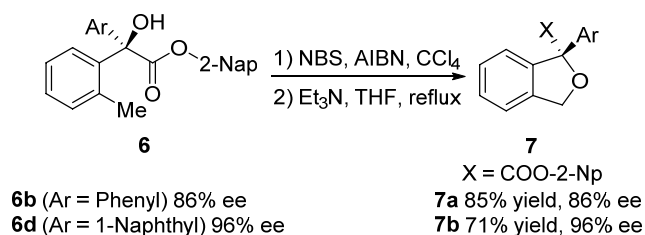
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.198	253179.703	13569195.000	50.1879
2		34.998	231671.953	13467576.000	49.8121
Total			484851.656	27036771.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.040	377554.406	20370726.000	99.0610
2		34.773	2961.273	193096.219	0.9390
Total			380515.680	20563822.219	100.0000

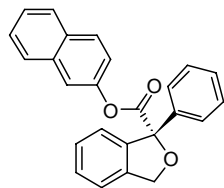
7. General procedure for the synthesis of 1,3-dihydroisobenzofuran derivatives **7a-b**.



Under nitrogen atmosphere, compound **6b** or **6d** (0.5 mmol, 1.0 equiv), NBS (0.55 mmol, 98 mg, 1.1 equiv), and a trace amount of AIBN was dissolved in 5.0 mL of CCl₄ and heated to reflux. The reaction was monitored by TLC, and later quenched by aq. Na₂SO₃. The mixture was extracted with EtOAc and washed with aq. NaHCO₃ and brine, dried over Na₂SO₄, and concentrated under reduced pressure. Subsequently, the residue was dissolved in dry THF (3.0 mL), and Et₃N (1.5 mmol, 0.2 mL, 3.0 equiv) was added. This mixture was heated to reflux for 1 h and monitored by TLC. When the reaction was over, a saturated aq. NaCl was added and the mixture was extracted with EtOAc. The combined organic phase was dried over Na₂SO₄, filtered, and concentrated. The residue was purified by silica gel flash chromatography to afford the corresponding products **7a-b**.

8. Characterization data and HPLC chromatogram of compounds 7a-b.

Naphthalen-2-yl (*R*)-1-phenyl-1,3-dihydroisobenzofuran-1-carboxylate **7a**.



7a

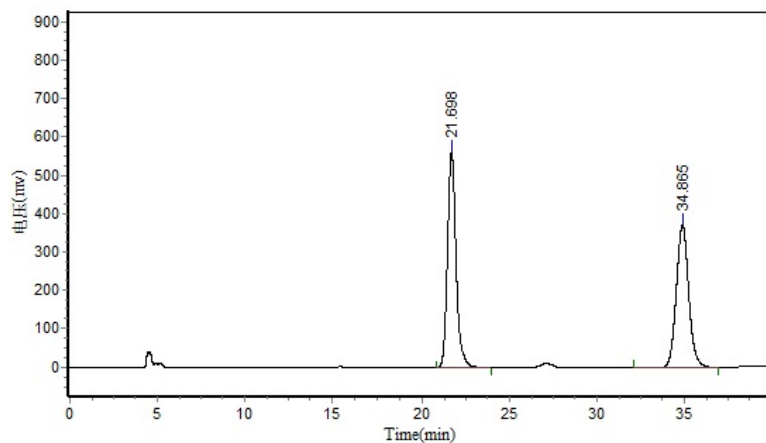
85% yield, colorless oil, 86% ee.

^1H NMR (300 MHz, CDCl_3): δ 5.39 (q, $J = 12.3$ Hz, 2H), 7.09-7.16 (m, 1H), 7.33-7.50 (m, 9H), 7.64-7.67 (m, 2H), 7.74-7.79 (m, 4H); ESI-MS (m/z , %) 389 $[\text{M}+\text{Na}]^+$.

The absolute configuration of known compound **7a** was unambiguously determined to be *R* by comparison of its HPLC chromatogram with the literature data.^{ref}

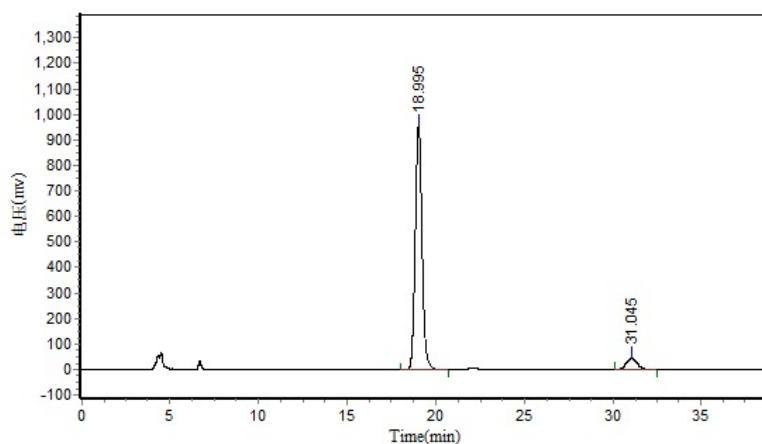
Reference: T.-S. Zhu, S.-S. Jin and M.-H. Xu, *Angew. Chem. Int. Ed.* **2012**, *51*, 780.

HPLC: Chiralcel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 19.0 min (maj), 31.0 min.



Results

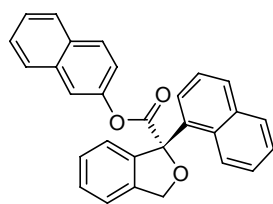
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.698	559534.438	19216434.000	51.1869
2		34.865	370824.250	18325246.000	48.8131
Total			930358.688	37541680.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.995	955391.125	25566966.000	93.0264
2		31.045	43883.160	1916605.375	6.9736
Total			999274.285	27483571.375	100.0000

Naphthalen-2-yl (*R*)-1-(naphthalen-1-yl)-1,3-dihydroisobenzofuran-1-carboxylate **7b**.



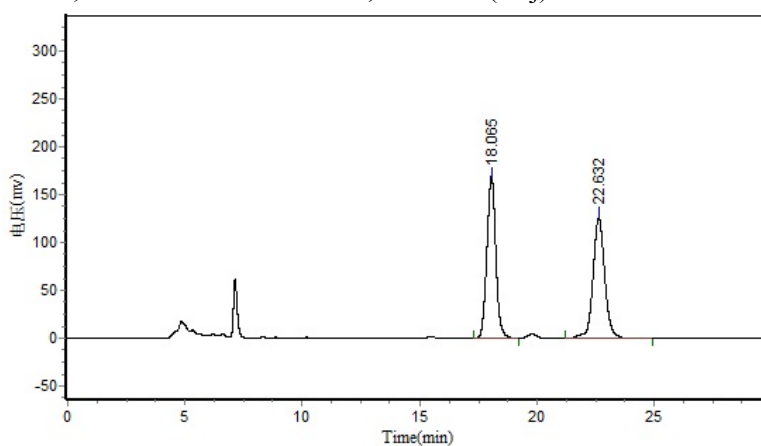
7b

71% yield, white solid, 96% ee.

^1H NMR (300 MHz, CDCl_3): δ 5.35 (q, $J = 12.0$ Hz, 2H), 6.92 (dd, $J = 2.4$ Hz, 8.7 Hz, 1H), 7.27 (s, 1H), 7.28-7.47 (m, 5H), 7.52-7.62 (m, 3H), 7.66-7.79 (m, 4H), 7.86-7.96 (m, 3H), 8.59 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 74.0, 92.8, 118.4, 120.7, 122.1, 124.8, 125.1, 125.4, 125.5, 125.9, 126.2, 126.7, 127.1, 127.7, 127.9, 129.1, 129.5, 129.7, 130.0, 131.6, 131.7, 133.7, 134.7, 135.7, 137.8, 141.1,

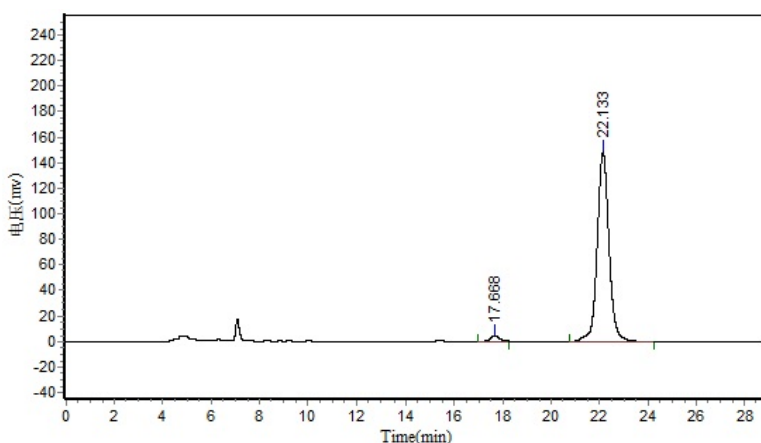
148.4, 172.3; ESI-MS (m/z , %) 439 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{29}\text{H}_{20}\text{NaO}_3$ [$\text{M}+\text{Na}$] $^+$ 439.1310, found 439.1313.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 17.7 min, 22.1 min (maj).



Results

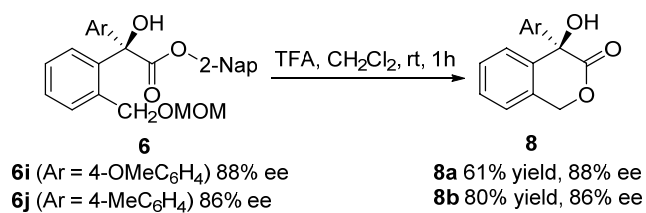
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.065	169075.063	4541467.500	50.4916
2		22.632	126097.086	4453024.000	49.5083
Total			295172.148	8994491.500	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.668	4100.503	101425.352	1.9909
2		22.133	148030.188	4993055.000	98.0091
Total			152130.691	5094480.352	100.0000

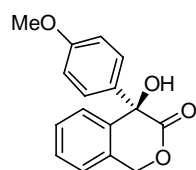
9. General procedure for the synthesis of 3-isochromanone derivatives **8a-b**.



Trifluoroacetic acid (0.3 mL) was added to a solution of the compound **6i** or **6j** (0.1 mmol, 1.0 equiv) in CH₂Cl₂ (1.0 mL), then the mixture was stirred at ambient temperature for 1h, and later quenched by aq. NaHCO₃. The mixture was extracted with EtOAc and washed with aq. brine. The combined organic phase was dried over Na₂SO₄, filtered, and concentrated. The residue was purified by silica gel flash chromatography to afford the corresponding products **8a-b**.

10. Characterization data and HPLC chromatogram of compounds 8a-b.

(*R*)-4-hydroxy-4-(4-methoxyphenyl)isochroman-3-one **8a**.



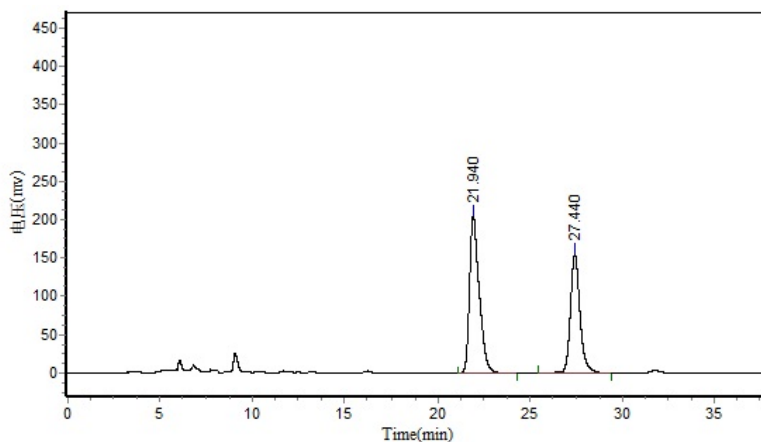
8a

61% yield, colorless oil, 88% ee.

^1H NMR (300 MHz, CDCl_3): δ 3.77 (s, 3H), 4.27 (s, 1H), 5.02 (q, $J = 13.8$ Hz, 2H), 6.81 (d, $J = 9.0$ Hz, 2H), 7.06 (d, $J = 8.7$ Hz, 2H), 7.21 (d, $J = 7.8$ Hz, 1H), 7.42 (t, $J = 7.8$ Hz, 1H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.91 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.5, 69.9, 75.8, 114.4, 124.6, 125.6, 128.3, 128.4, 129.4, 129.9, 130.7, 136.7, 160.2, 174.6; ESI-MS (m/z , %) 293 [$\text{M}+\text{Na}$] $^+$;

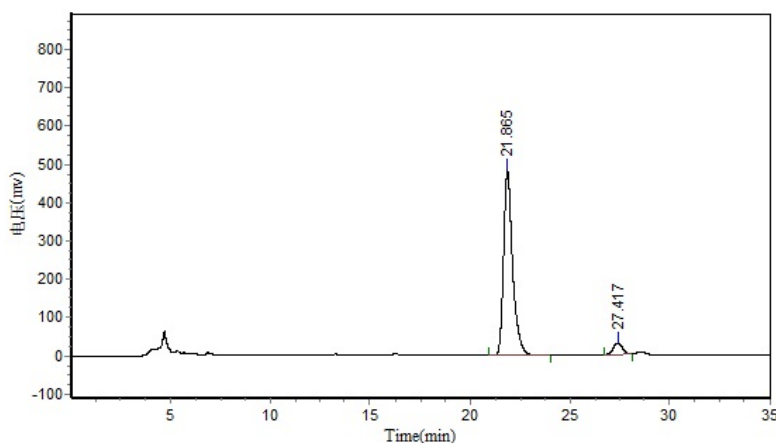
ESI-HRMS calcd for $\text{C}_{16}\text{H}_{14}\text{NaO}_4$ [$\text{M}+\text{Na}$] $^+$ 293.0790 found 293.0796.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 21.9 min (maj), 27.4 min.



Results

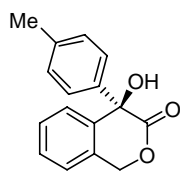
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.940	205692.313	7519873.000	57.1192
2		27.440	155264.922	5645352.500	42.8808
Total			360957.234	13165225.500	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.865	482370.594	15314426.000	94.2210
2		27.417	29384.098	939302.375	5.7790
Total			511754.691	16253728.375	100.0000

(*R*)-4-hydroxy-4-(*p*-tolyl)isochroman-3-one **8b**.



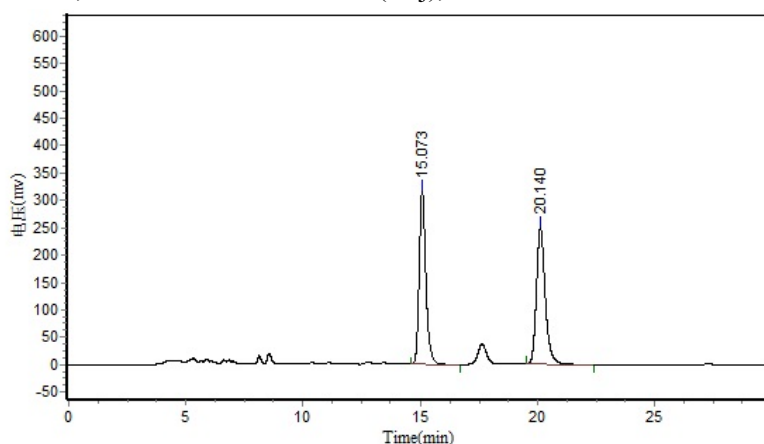
8b

80% yield, colorless oil, 85% ee.

^1H NMR (300 MHz, CDCl_3): δ 2.31 (s, 3H), 4.28 (s, 1H), 5.02 (q, $J = 13.8$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 7.12 (d, $J = 8.1$ Hz, 2H), 7.21 (d, $J = 7.2$ Hz, 1H), 7.42 (dt, $J = 1.2$ Hz, 7.5 Hz, 1H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.91 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.2, 69.9, 76.0, 124.6, 125.7, 126.8, 128.4, 129.4, 129.8, 130.7, 135.0, 136.6, 139.3, 174.6; ESI-MS (m/z , %) 277

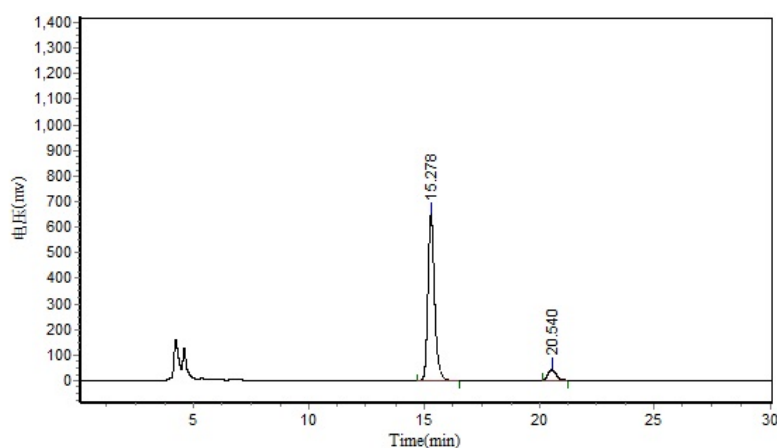
$[\text{M}+\text{Na}]^+$; ESI-HRMS calcd for $\text{C}_{16}\text{H}_{14}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 277.0841, found 277.0845.

HPLC: Chiracel AD-H Column (250 mm); detected at 254 nm; *n*-hexane / *i*-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 15.3 min (maj), 20.5 min.



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.073	316138.531	6361604.500	48.9229
2		20.140	249497.438	6641712.000	51.0771
Total			565635.969	13003316.500	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.278	649831.750	13158241.000	92.6333
2		20.540	41619.535	1046420.563	7.3667
Total			691451.285	14204661.563	100.0000

11. Copies of ^1H and ^{13}C NMR Spectra of Compounds 3b-s, 6a-k, 4a-c, 7a-b and 8a-b.

