

Supplementary Information:

Highly Diastereoselective Friedel-Crafts reaction of Arenes with an *N*-*tert*-Butanesulfinylimino Ester: Efficient Synthesis of Optically Active α -Arylglycines

Yi Li, Du-Ming Ji and Ming-Hua Xu*

Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, People's Republic of China.

E-Mail: xumh@mail.shcnc.ac.cn

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1. General

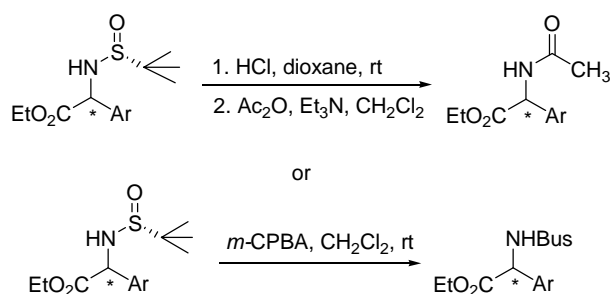
Unless otherwise specified, all reactions were carried out in flame-dried glassware with magnetic stirring under an atmosphere of nitrogen. Solvents were dried and distilled by standard procedures. NMR spectra were recorded on a Varian spectrometer (300 MHz for ^1H , and 100 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal SiMe_4 standard for ^1H NMR and chloroform-*d* (δ 77.16) for ^{13}C NMR. HPLC was performed on a JASCO 2000 instrument by using Daicel AS-H, AD-H and AD-3 column with 2-propanol/hexane as the eluent at 214 nm.

2. General Procedure for $\text{In}(\text{OTf})_3$ -catalyzed Friedel-Crafts Reaction of Arenes **1** with *N*-*tert*-Butanesulfinylimino Ester **2**.



Under nitrogen atmosphere, $\text{In}(\text{OTf})_3$ (0.075 mmol, 30 mol%) was placed into a glass reaction vessel, glyoxylate imine **2** (0.25 mmol) in 2 mL of dry CH_2Cl_2 and arene **1** (0.375 mmol) were added successively. The mixture was stirred at room temperature and monitored by TLC. When the reaction was over, a saturated aq. NH_4Cl was added and the mixture was extracted with CH_2Cl_2 (10 mL \times 3). 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 α -arylglycine product **3**.

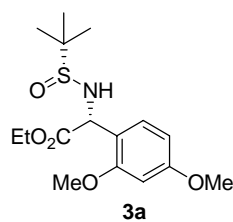
3. Determination of the Diastereoselectivity / Enantiomeric Excess.



The diastereoselectivities of the α -arylglycine products were measured as enantiomeric excess for their acetate or *N*-sulfonylate derivatives after the removal or oxidation of the sulfinyl group by chiral HPLC analysis. α -Arylglycines **3e** and **4** were converted to the corresponding *N*-sulfonylate, all others were converted to their acetate. The HPLC reference compound was a mixture of related products consisting of *R* and *S* enantiomers.

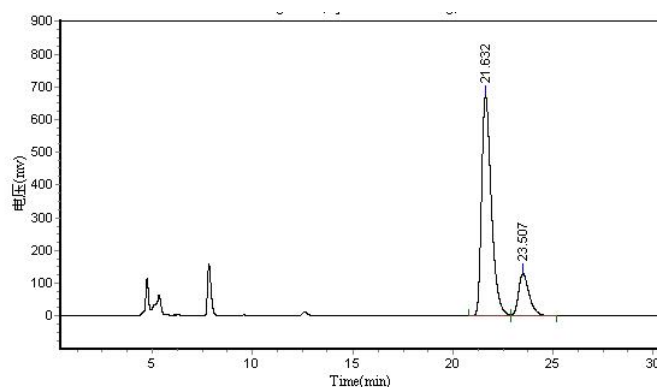
4. Characterization and HPLC of the Obtained Chiral α -Arylglycines

(*R*)-ethyl 2-(2,4-dimethoxyphenyl)-2((*R*)-1,1-dimethylethylsulfonamido)acetate (**3a**).



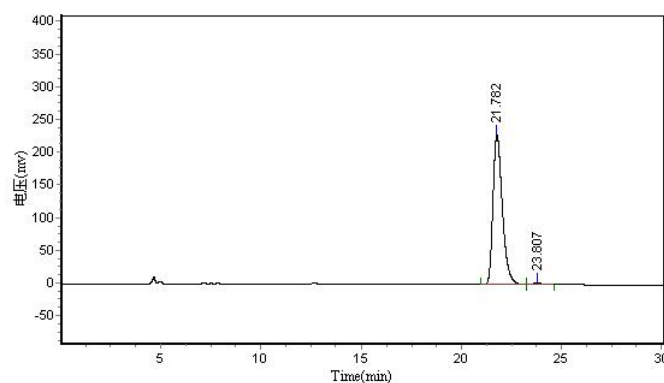
89% yield, yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 1.15 (s, 9H), 1.18 (t, 3H), 3.77 (s, 3H), 3.79 (s, 3H), 4.13-4.20 (m, 2H), 4.51 (d, $J = 4.2$ Hz, 1H), 5.19 (d, $J = 4.2$ Hz, 1H), 6.43-6.45 (m, 2H), 7.10 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.14, 22.51, 55.39, 55.55, 55.82, 56.00, 61.85, 98.94, 104.22, 118.74, 130.12, 158.21, 161.03, 172.03; ESI-MS (m/z , %) 344 $[\text{M}+\text{H}]^+$; ESI-HRMS calcd for $\text{C}_{16}\text{H}_{25}\text{NNaO}_5\text{S}$ $[\text{M}+\text{Na}^+]$ 366.1351, found 366.1351.

HPLC (acetate): 98% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 21.8 min (maj), 23.8 min.



Results

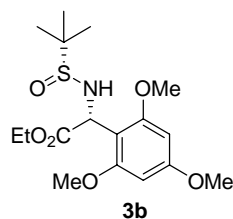
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.632	674104.563	22894638.000	82.5333
2		23.507	129262.539	4845249.500	17.4667
Total			803367.102	27739887.500	100.0000



Results

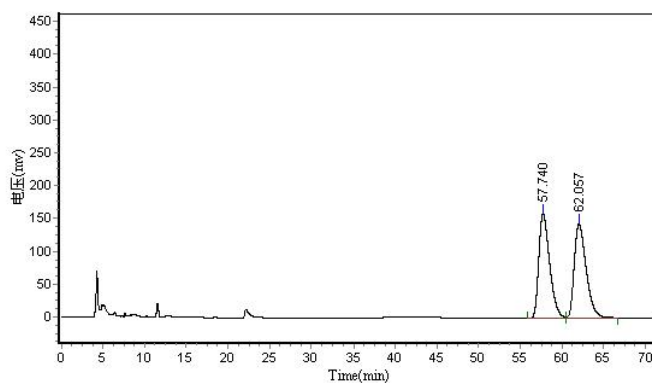
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.782	228540.984	7478351.000	99.1270
2		23.807	1939.009	65857.797	0.8730
Total			230479.993	7544208.797	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(2,4,6-trimethoxyphenyl)acetate (**3b**).



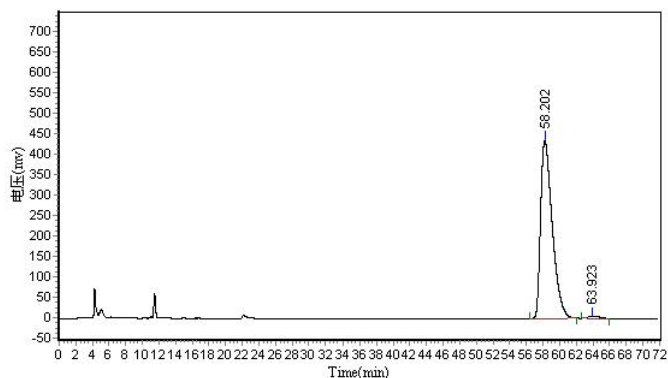
91% yield, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 1.10 (s, 9H), 1.17 (t, 3H), 3.77 (s, 6H), 3.80 (s, 3H), 4.09-4.22 (m, 2H), 4.58 (d, *J* = 5.1 Hz, 1H), 5.49 (d, *J* = 5.1 Hz, 1H), 6.09 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 14.27, 22.44, 51.35, 55.39, 55.76, 55.85, 61.59, 90.68, 107.92, 158.83, 161.38, 172.55; ESI-MS (*m/z*, %) 374 [M+H]⁺; ESI-HRMS calcd for C₁₇H₂₇NNaO₆S [M+Na]⁺ 396.1457, found 396.1454.

HPLC (acetate): 97% de. Chiracel AD-3 Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 58.2 min (maj), 63.9 min.



Results

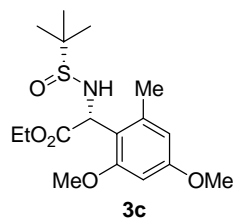
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		57.740	158619.875	14331035.000	50.0777
2		62.057	143025.125	14286591.000	49.9223
Total			301645.000	28617626.000	100.0000



Results

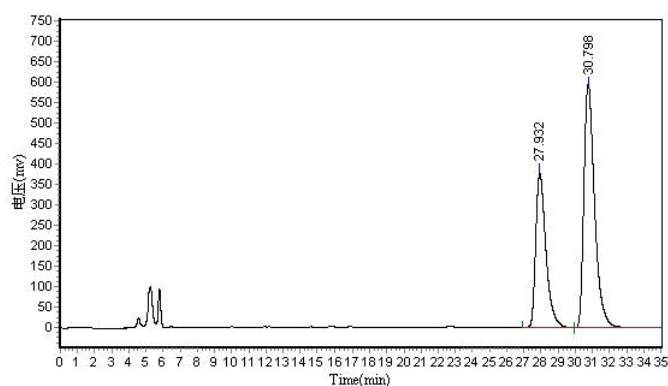
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		58.202	434911.063	42354564.000	98.6595
2		63.923	6152.331	575495.313	1.3405
Total			441063.393	42930059.313	100.0000

(*R*)-ethyl 2-(2,4-dimethoxy-6-methylphenyl)-2-((*R*)-1,1-dimethylethylsulfonamido)acetate (**3c**).

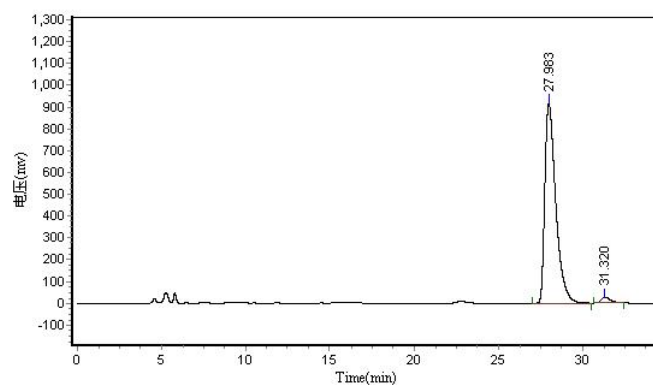


84% yield, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 1.11 (s, 9H), 1.16 (t, 3H), 2.36 (s, 3H), 3.73 (s, 3H), 3.78 (s, 3H), 4.09-4.21 (m, 2H), 4.63 (d, *J* = 3.0 Hz, 1H), 5.33 (d, *J* = 3.9 Hz, 1H), 6.29 (d, *J* = 5.7 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 14.24, 20.24, 22.50, 53.44, 55.26, 55.63, 55.71, 61.79, 96.58, 107.05, 117.52, 139.22, 158.74, 160.17, 172.34; ESI-MS (*m/z*, %) 358 [M+H]⁺; ESI-HRMS calcd for C₁₇H₂₈NO₅S [M+H]⁺ 358.1688, found 358.1697.

HPLC (**acetate**): 95% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 28.0 min (maj), 31.3 min.

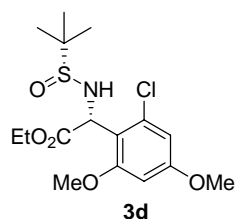


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.932	374280.063	15683889.000	37.6559
2		30.798	594641.938	25966694.000	62.3441
Total			968922.000	41650583.000	100.0000



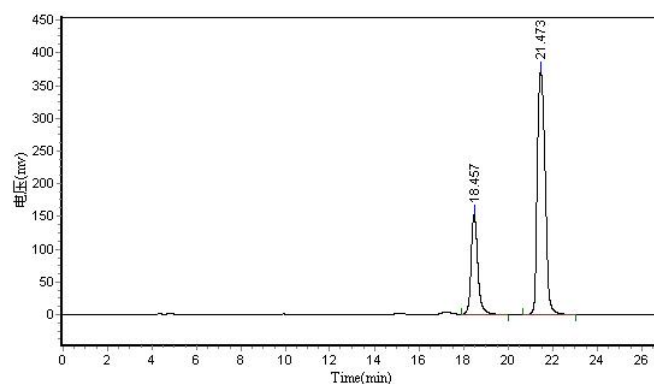
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.983	914985.313	41353624.000	97.4477
2		31.320	25893.891	1083123.125	2.5523
Total			940879.203	42436747.125	100.0000

(*R*)-ethyl 2-(2-chloro-4,6-dimethoxyphenyl)-2-((*R*)-1,1-dimethylethylsulfonamido)acetate (**3d**).

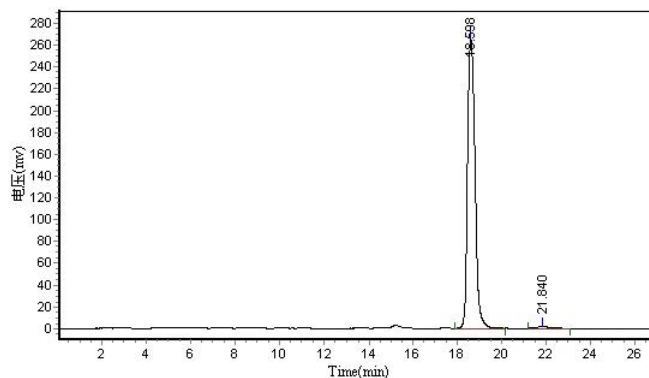


80% yield, yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 1.12 (s, 9H), 1.18 (t, 3H), 3.76 (s, 3H), 3.79 (s, 3H), 4.09-4.23 (m, 2H), 4.59 (d, *J* = 4.2 Hz, 1H), 5.60 (d, *J* = 4.2 Hz, 1H), 6.34 (d, *J* = 2.1 Hz, 1H), 6.52 (d, *J* = 2.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 14.22, 22.44, 55.65, 55.91, 56.01, 62.07, 97.93, 106.12, 117.96, 135.60, 159.09, 160.55, 171.42; ESI-MS (*m/z*, %) 378 [M+H]⁺; ESI-HRMS calcd for C₁₆H₂₄ClNNaO₅S [M+Na⁺] 400.0961, found 400.0945.

HPLC (**acetate**): 98% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 18.6 min (maj), 21.8 min.

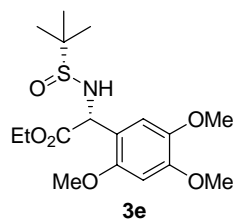


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.457	151422.688	3190979.000	25.9984
2		21.473	371378.250	9082754.000	74.0016
Total			522800.938	12273733.000	100.0000



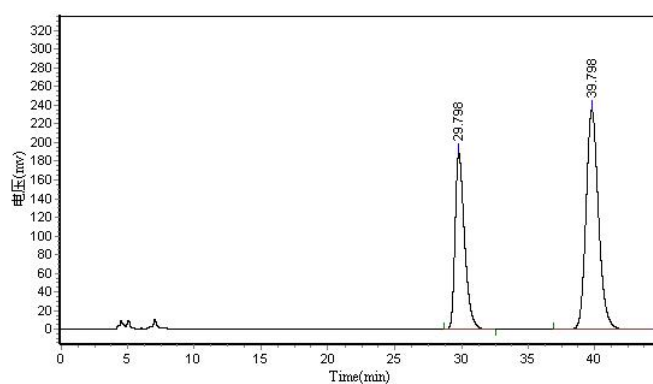
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.598	264955.781	6240307.000	98.9436
2		21.840	1725.836	66625.203	1.0564
Total			266681.617	6306932.203	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(2,4,5-trimethoxyphenyl)acetate (**3e**).

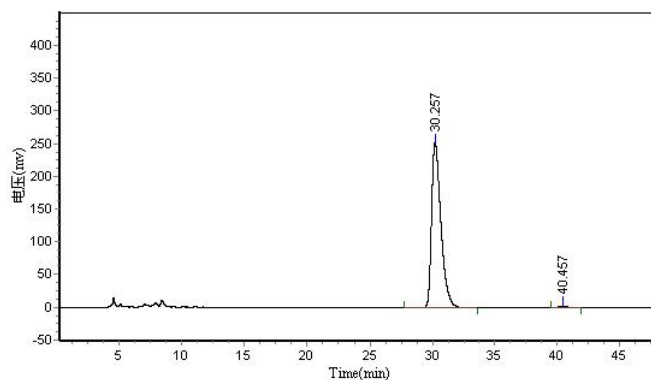


86% yield, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 1.16 (s, 9H), 1.17 (t, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 3.87 (s, 3H), 4.11-4.21 (m, 2H), 4.51 (d, *J* = 3.3 Hz, 1H), 5.30 (d, *J* = 3.9 Hz, 1H), 6.51 (s, 1H), 6.74 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 14.15, 22.56, 55.13, 55.85, 56.09, 56.57, 56.93, 61.97, 97.96, 112.45, 117.52, 143.19, 149.81, 151.89, 171.98; ESI-MS (*m/z*, %) 396 [M+Na]⁺; ESI-HRMS calcd for C₁₇H₂₇NNaO₆S [M+Na]⁺ 396.1457, found 396.1455.

HPLC (sulfonate): 98% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 30.2 min (maj), 40.4 min.

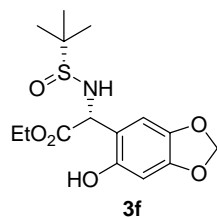


Results						
Peak No.	Peak ID	Ret Time	Height	Area	Conc.	
1		29.798	187152.141	9339194.000	37.9489	
2		39.798	234610.594	15270694.000	62.0511	
Total			421762.734	24609888.000	100.0000	



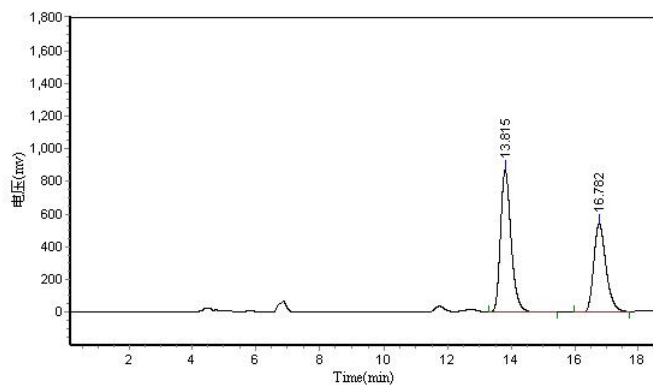
Results						
Peak No.	Peak ID	Ret Time	Height	Area	Conc.	
1		30.257	252606.844	13109203.000	99.2008	
2		40.457	1576.393	105611.766	0.7992	
Total			254183.237	13214814.766	100.0000	

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(2-hydroxy-4,5-dimethoxyphenyl)acetate (**3f**).



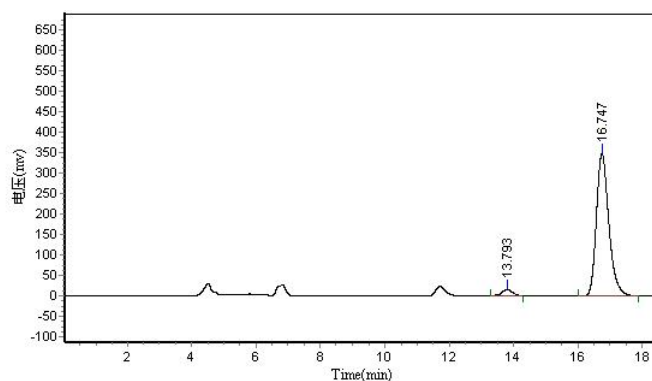
72% yield, yellow oil. $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 1.21 (t, 3H), 1.25 (s, 9H), 4.10-4.28 (m, 2H), 4.52 (d, $J = 1.5$ Hz, 1H), 5.21 (d, $J = 2.7$ Hz, 1H), 5.89 (s, 2H), 6.46 (s, 1H), 6.62 (s, 1H), 7.90 (br, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 14.16, 22.71, 55.87, 56.30, 62.49, 99.56, 101.35, 108.15, 113.68, 141.28, 148.77, 150.90, 171.63; ESI-MS (m/z , %) 344 [$\text{M}+\text{H}$] $^+$.

HPLC (**acetate**): 93% de. Chiralcel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 80 / 20; flow = 0.7 mL / min; Retention time: 13.8 min, 16.7 min (maj).



Results

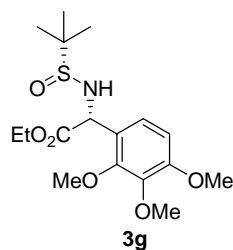
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.815	865754.625	20158124.000	57.9533
2		16.782	541351.438	14625280.000	42.0467
Total			1407106.063	34783404.000	100.0000



Results

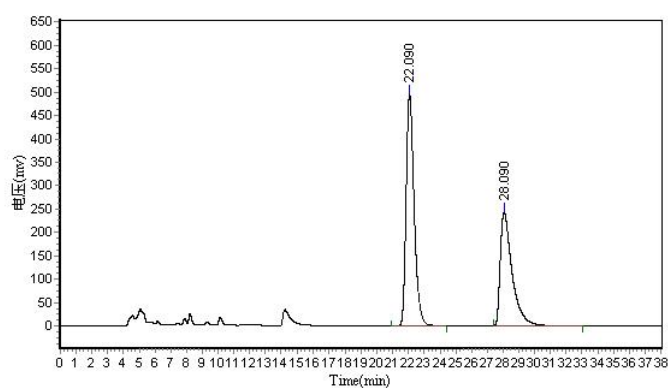
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.793	15598.970	338129.750	3.4856
2		16.747	346773.219	9362763.000	96.5144
Total			362372.188	9700892.750	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(2,3,4-trimethoxyphenyl)acetate (**3g**).

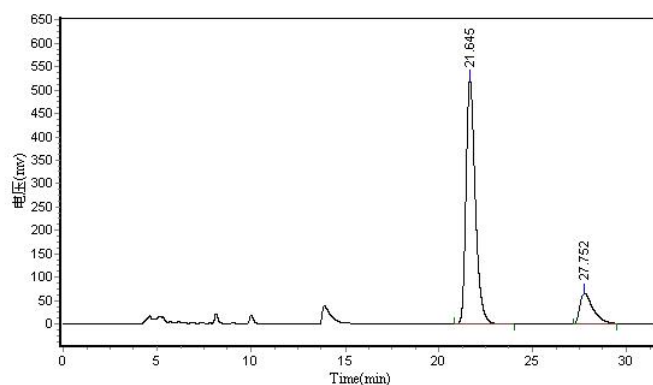


60% yield, yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 1.17 (s, 9H), 1.18 (t, 3H), 3.84 (s, 6H), 3.88 (s, 3H), 4.11-4.24 (m, 2H), 4.59 (d, $J = 3.9$ Hz, 1H), 5.18 (d, $J = 3.6$ Hz, 1H), 6.60 (d, $J = 8.4$ Hz, 1H), 6.91 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.13, 22.61, 55.75, 55.84, 55.98, 60.77, 61.14, 62.06, 106.98, 123.75, 123.90, 142.15, 151.91, 154.07, 171.84; ESI-MS (m/z , %) 374 [$\text{M}+\text{H}$] $^+$; ESI-HRMS calcd for $\text{C}_{17}\text{H}_{27}\text{NNaO}_6\text{S}$ [$\text{M}+\text{Na}^+$] 396.1457, found 396.1467.

HPLC (acetate): 70% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 21.6 min (maj), 27.8 min.

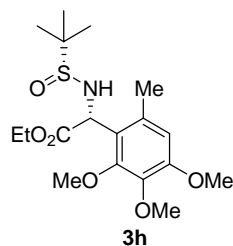


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.090	495091.188	17524566.000	58.1538
2		28.090	242659.625	12610315.000	41.8462
Total			737750.813	30134881.000	100.0000



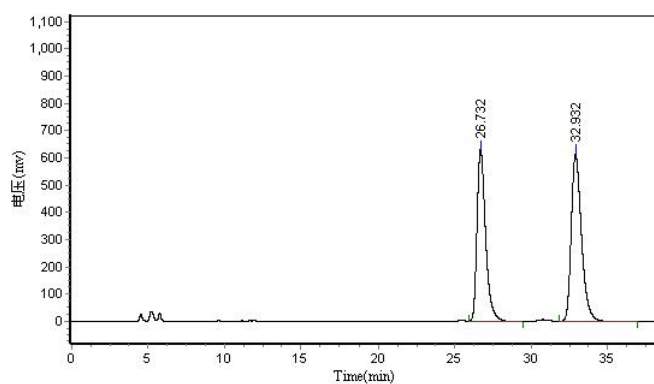
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.645	523384.250	17966410.000	84.7425
2		27.752	65641.320	3234764.000	15.2575
Total			589025.570	21201174.000	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfinamido)-2-(2,3,4-trimethoxy-6-methylphenyl)acetate (**3h**).

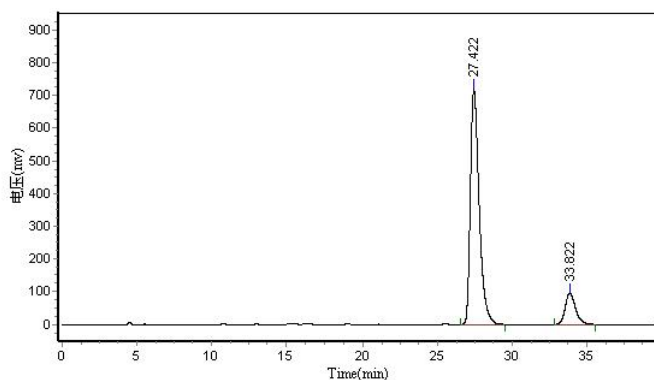


74% yield, yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 1.15 (s, 9H), 1.18 (t, 3H), 2.34 (s, 3H), 3.79 (s, 3H), 3.83 (s, 3H), 3.85 (s, 3H), 4.08-4.22 (m, 2H), 4.73 (d, $J = 1.2$ Hz, 1H), 5.29 (d, $J = 2.7$ Hz, 1H), 6.46 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.22, 19.97, 22.61, 53.61, 55.76, 55.82, 60.70, 60.98, 61.99, 109.11, 122.28, 132.79, 139.91, 152.28, 153.17, 172.08; ESI-MS (m/z , %) 388 [$\text{M}+\text{H}$] $^+$; ESI-HRMS calcd for $\text{C}_{18}\text{H}_{30}\text{NO}_6\text{S}$ [$\text{M}+\text{H}$] $^+$ 388.1794, found: 388.1791.

HPLC (acetate): 73% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 27.4 min (maj), 33.8 min.

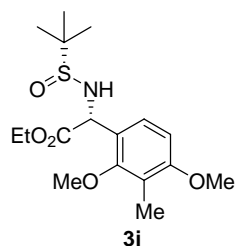


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.732	627613.938	24727806.000	46.3511
2		32.932	610408.250	28621154.000	53.6489
Total			1238022.188	53348960.000	100.0000



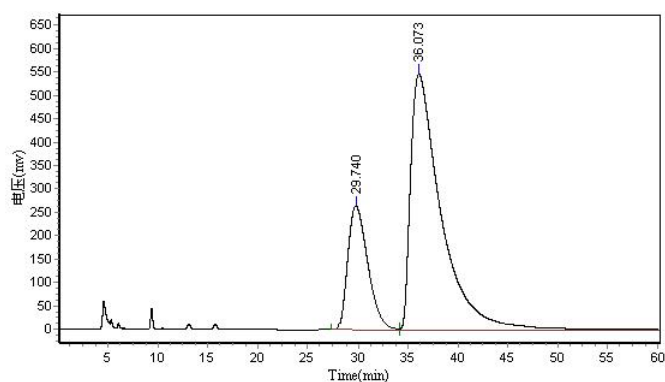
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.422	717405.188	29391672.000	86.4847
2		33.822	95841.773	4593169.000	13.5153
Total			813246.961	33984841.000	100.0000

(*R*)-ethyl 2-(2,4-dimethoxy-3-methylphenyl)-2-((*R*)-1,1-dimethylethylsulfonamido)acetate (**3i**).



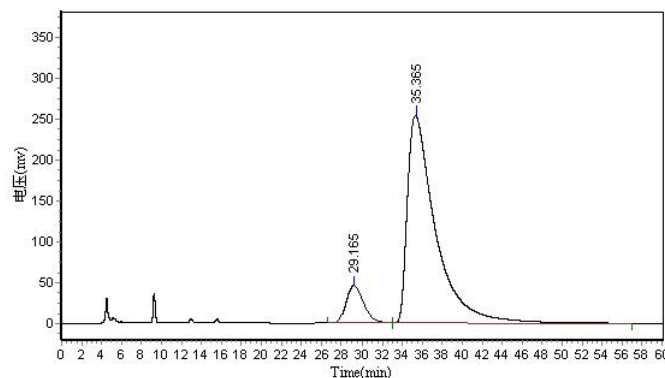
72% yield, yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 1.16-1.18 (m, 12H), 2.15 (s, 3H), 3.77 (s, 3H), 3.81 (s, 3H), 4.09-4.23 (m, 2H), 4.59 (d, *J* = 3.0 Hz, 1H), 5.27 (d, *J* = 3.9 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 9.56, 14.15, 22.67, 55.09, 55.66, 55.84, 61.55, 62.10, 106.18, 119.99, 123.10, 126.58, 157.46, 159.03, 172.15; ESI-MS (*m/z*, %) 380 [M+Na]⁺; ESI-HRMS calcd for C₁₇H₂₇NNaO₅S [M+Na]⁺ 380.1508, found 380.1506.

HPLC (**acetate**): 79% de. Chiracel AS-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 29.2 min, 35.4 min (maj).



Results

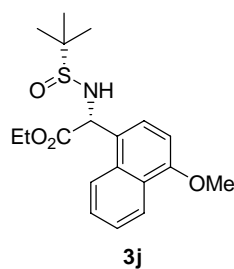
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		29.740	264567.031	37120236.000	24.1669
2		36.073	546097.250	116479080.000	75.8331
Total			810664.281	153599316.000	100.0000



Results

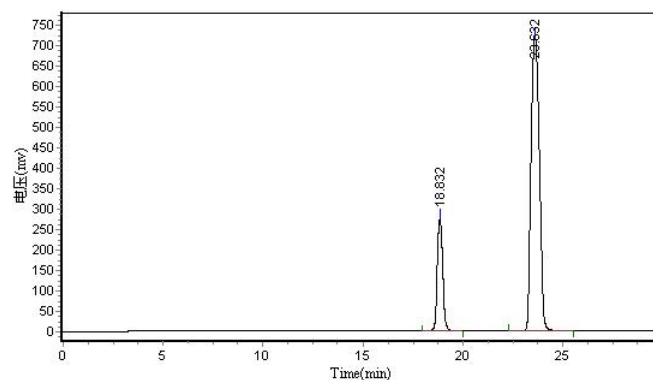
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		29.165	45889.371	5695477.000	10.2159
2		35.365	253721.891	50055768.000	89.7841
Total			299611.262	55751245.000	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(4-methoxynaphthalen-1-yl)acetate (**3j**).

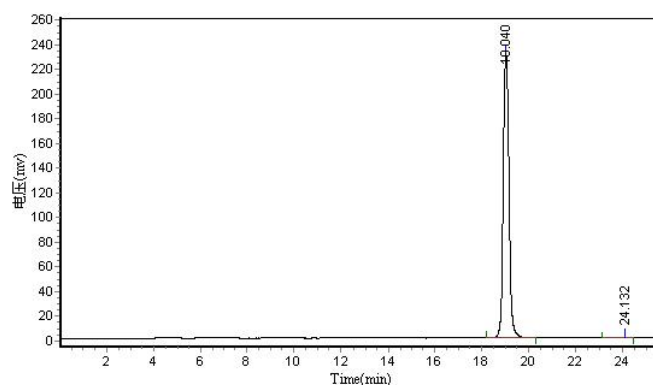


66% yield, white solid. ^1H NMR (300 MHz, CDCl_3): δ 1.10 (t, 3H), 1.13 (s, 9H), 4.01 (s, 3H), 4.08-4.21 (m, 2H), 4.66 (s, 1H), 5.50 (s, 1H), 6.76 (d, $J = 8.1$ Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.47-7.51 (m, 2H), 7.98 (d, $J = 7.8$ Hz, 1H), 8.30 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.08, 22.63, 55.63, 55.79, 59.32, 62.33, 102.97, 122.79, 123.90, 124.34, 125.33, 126.33, 126.95, 128.62, 131.90, 156.24, 172.41; ESI-MS (m/z , %) 364 $[\text{M}+\text{H}]^+$; ESI-HRMS calcd for $\text{C}_{19}\text{H}_{25}\text{NNaO}_4\text{S}$ $[\text{M}+\text{Na}^+]$ 386.1402, found 386.1411.

HPLC (acetate): >99% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 19.0 min (maj), 24.1 min.

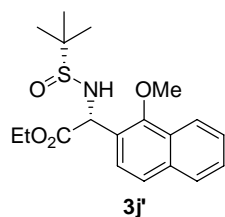


Results						
Peak No.	Peak ID	Ret Time	Height	Area	Conc.	
1		18.832	273026.938	5296722.500	20.1718	
2		23.632	720571.500	20961286.000	79.8282	
Total			993598.438	26258008.500	100.0000	



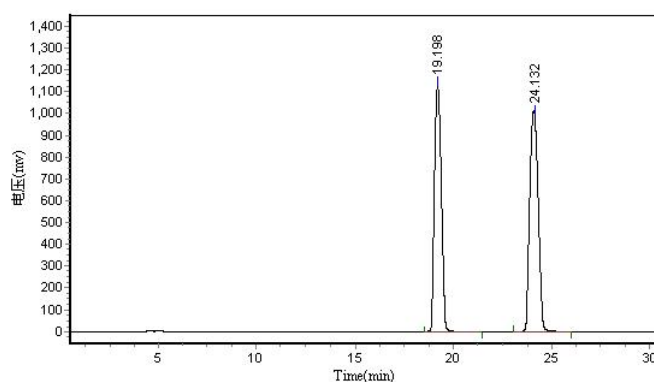
Results						
Peak No.	Peak ID	Ret Time	Height	Area	Conc.	
1		19.040	229190.500	3953454.250	99.7716	
2		24.132	148.073	6737.400	0.1700	
Total			229418.663	3962504.750	100.0000	

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(1-methoxynaphthalen-2-yl)acetate (**3j'**).

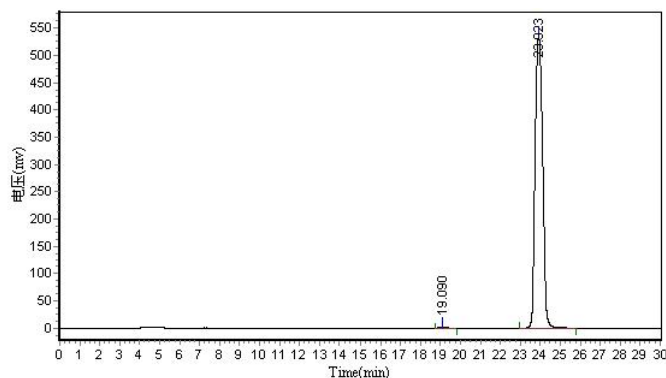


22% yield, white solid. ^1H NMR (300 MHz, CDCl_3): δ 1.13 (t, 3H), 1.21 (s, 9H), 4.00 (s, 3H), 4.07-4.21 (m, 2H), 5.73 (d, $J = 3.9$ Hz, 1H), 6.77 (d, $J = 7.8$ Hz, 1H), 7.47-7.61 (m, 3H), 8.18 (d, $J = 8.4$ Hz, 1H), 8.31 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.12, 22.65, 55.68, 56.46, 56.74, 61.88, 103.27, 122.85, 123.40, 125.06, 125.51, 126.11, 127.19, 127.46, 131.78, 156.21, 172.01; ESI-MS (m/z , %) 364 [$\text{M}+\text{H}$] $^+$; ESI-HRMS calcd for $\text{C}_{19}\text{H}_{25}\text{NNaO}_4\text{S}$ [$\text{M}+\text{Na}$] $^+$ 386.1402, found 386.1390.

HPLC (**acetate**): >99% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 19.1 min, 23.9 min (maj).

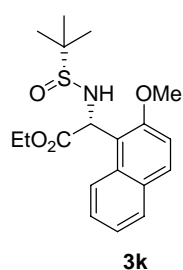


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.198	1123718.875	27573620.000	47.5011
2		24.132	1007838.500	30474742.000	52.4989
Total			2131557.375	58048362.000	100.0000



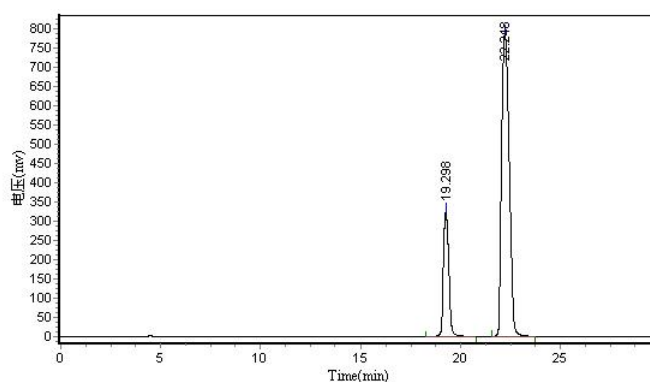
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.090	407.462	10616.800	0.0761
2		23.923	535504.375	13946546.000	99.9239
Total			535911.837	13957162.800	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(2-methoxynaphthalen-1-yl)acetate (**3k**).

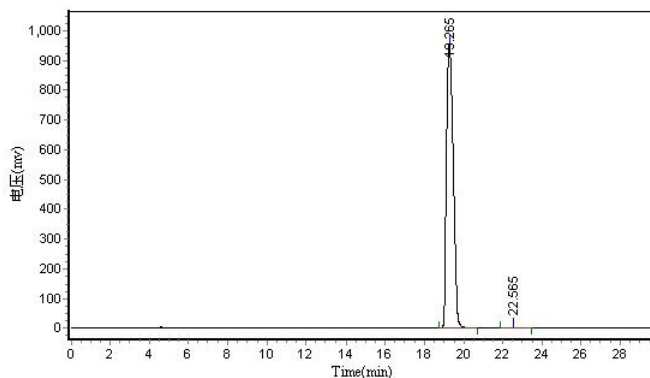


72% yield, white solid. ¹H NMR (300 MHz, CDCl₃): δ 1.06-1.10 (m, 12H), 3.98 (s, 3H), 4.11-4.18 (m, 2H), 4.76 (s, 1H), 6.10 (s, 1H), 7.28-7.36 (m, 2H), 7.46 (dd, *J* = 8.4 Hz, 7.2 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 14.14, 22.51, 52.18, 55.69, 57.17, 62.12, 113.67, 118.42, 123.34, 123.76, 127.09, 128.75, 129.47, 130.90, 132.31, 155.83, 172.77; ESI-MS (*m/z*, %) 364 [M+H]⁺; ESI-HRMS calcd for C₁₉H₂₆NO₄S [M+H]⁺ 364.1582, found: 364.1578.

HPLC (**acetate**): >99% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 19.3 min (maj), 22.6 min.

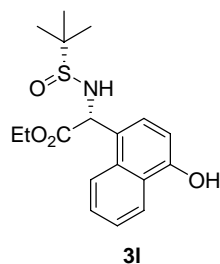


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.298	320611.969	6083979.500	22.5435
2		22.248	783896.563	20903754.000	77.4565
Total			1104508.531	26987733.500	100.0000



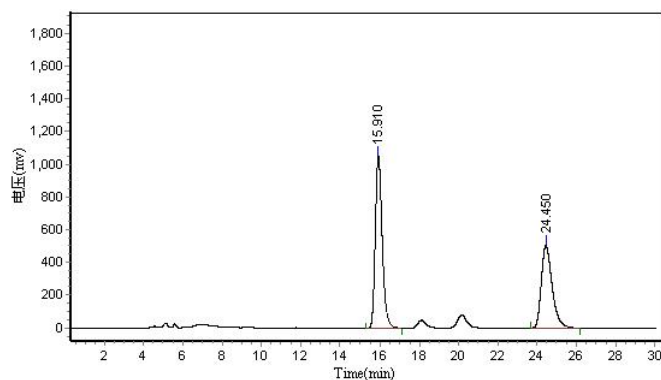
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.265	950367.125	22983524.000	99.8262
2		22.565	1149.328	40010.262	0.1738
Total			951516.453	23023534.262	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(4-hydroxynaphthalen-1-yl)acetate (**31**).



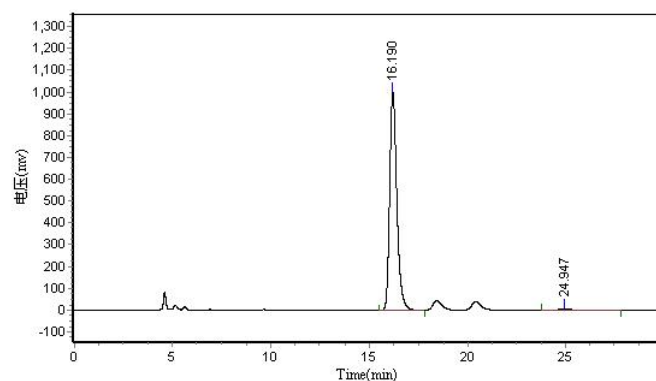
74% yield, yellow solid. ^1H NMR (300 MHz, CDCl_3): δ 1.06 (t, 3H), 1.18 (s, 9H), 4.09-4.18 (m, 2H), 4.77 (d, $J = 2.1$ Hz, 1H), 5.49 (d, $J = 2.1$ Hz, 1H), 6.78 (d, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 7.8$ Hz, 1H), 7.43-7.46 (m, 2H), 7.92-7.96 (m, 1H), 8.18 (s, 1H), 8.28-8.32 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.04, 22.74, 56.03, 59.76, 62.42, 107.83, 122.59, 123.16, 123.86, 124.93, 125.69, 126.80, 129.66, 132.14, 153.98, 172.40; ESI-MS (m/z , %) 350 $[\text{M}+\text{H}]^+$; ESI-HRMS calcd for $\text{C}_{18}\text{H}_{23}\text{NNaO}_4\text{S}$ $[\text{M}+\text{Na}^+]$ 372.1246, found 372.1244.

HPLC (acetate): 98% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 16.2 min (maj), 24.9 min.



Results

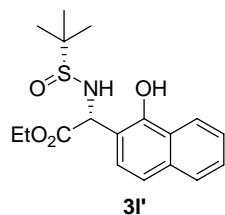
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.910	1049745.750	25747068.000	57.0066
2		24.450	503980.844	19417976.000	42.9934
Total			1553726.594	45165044.000	100.0000



Results

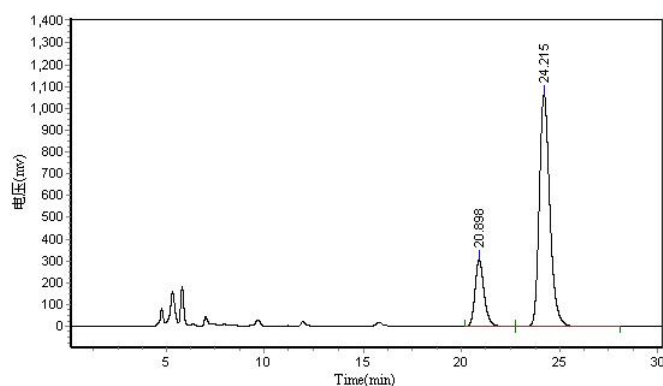
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.190	996699.875	25443638.000	98.9571
2		24.947	6078.157	268154.406	1.0429
Total			1002778.032	25711792.406	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(1-hydroxynaphthalen-2-yl)acetate (**31'**).

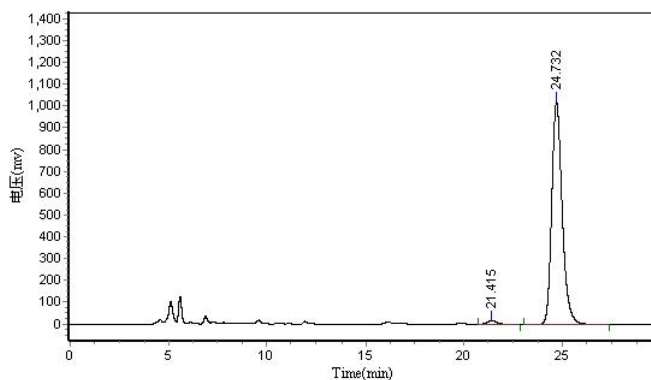


15% yield, yellow solid. ^1H NMR (300 MHz, CDCl_3): δ 1.19 (t, 3H), 1.28 (s, 9H), 4.11-4.29 (m, 2H), 4.59 (s, 1H), 5.36 (d, $J = 2.7$ Hz, 1H), 7.25 (d, $J = 8.4$ Hz, 1H), 7.39 (d, $J = 8.7$ Hz, 1H), 7.45-7.52 (m, 2H), 7.76-7.79 (m, 1H), 8.26-8.30 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.11, 22.68, 56.53, 57.25, 62.76, 114.46, 120.34, 122.67, 125.57, 126.79, 127.07, 127.51, 134.83, 151.71, 171.29; ESI-MS (m/z , %) 372 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{18}\text{H}_{23}\text{NNaO}_4\text{S}$ [$\text{M}+\text{Na}$] $^+$ 372.1246, found 372.1253.

HPLC (**acetate**): 97% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 21.4 min, 24.7 min (maj).

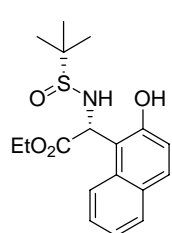


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.898	306281.656	9774731.000	19.7613
2		24.215	1063924.750	39689376.000	80.2387
Total			1370206.406	49464107.000	100.0000



Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.415	15704.157	495847.688	1.3039
2		24.732	1017129.375	37533068.000	98.6961
Total			1032833.532	38028915.688	100.0000

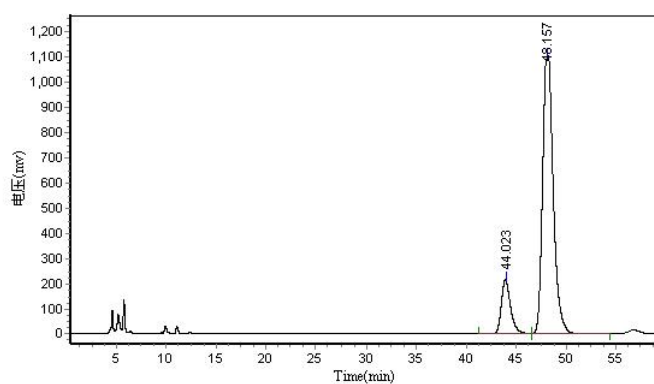
(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(2-hydroxynaphthalen-1-yl)acetate (**3m**).



3m

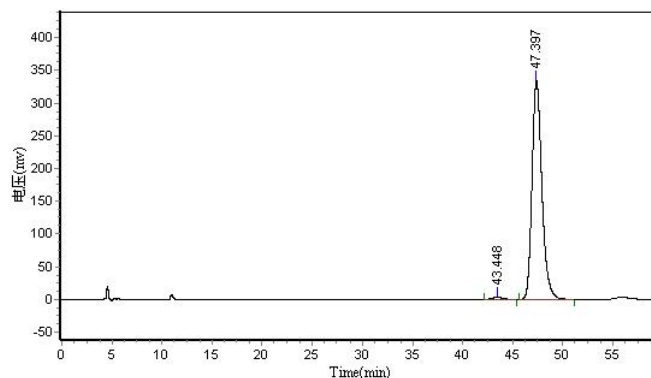
70% yield, yellow solid. ^1H NMR (300 MHz, CDCl_3): δ 1.05 (t, 3H), 1.21 (s, 9H), 4.05-4.18 (m, 2H), 4.82 (s, 1H), 6.22 (s, 1H), 7.17 (d, $J = 8.7$ Hz, 1H), 7.26 (dd, $J = 6.6$ Hz, 8.4 Hz, 1H), 7.39 (dd, $J = 8.4$ Hz, 7.2 Hz, 1H), 7.67-7.74 (dd, $J = 8.7$ Hz, 8.4 Hz, 2H), 7.80 (d, $J = 8.4$ Hz, 1H), 9.55 (br, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.07, 22.72, 52.00, 55.76, 62.32, 112.46, 118.40, 122.77, 122.90, 126.69, 128.74, 128.95, 130.81, 132.61, 155.18, 173.00; ESI-MS (m/z , %) 372 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{18}\text{H}_{23}\text{NNaO}_4\text{S}$ [$\text{M}+\text{Na}$] $^+$ 372.1246, found 372.1246.

HPLC (acetate): 98% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 43.4 min (maj), 47.4 min.



Results

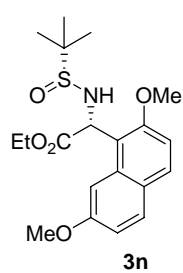
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		44.023	213212.313	13811243.000	14.4132
2		48.157	1090117.125	82012416.000	85.5868
Total			1303329.438	95823659.000	100.0000



Results

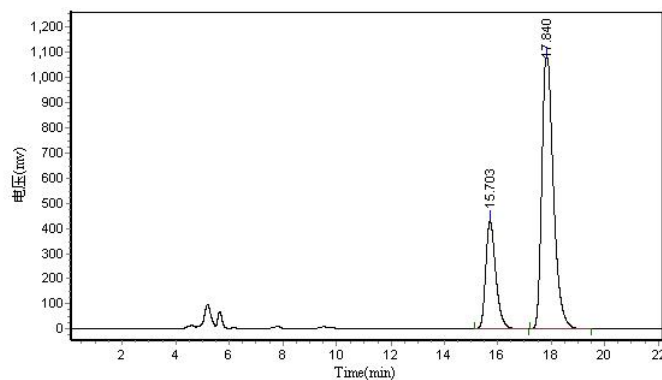
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		43.448	3228.474	208958.484	0.9039
2		47.397	334161.000	22907366.000	99.0961
Total			337389.474	23116324.484	100.0000

(*R*)-ethyl 2-(2,7-dimethoxynaphthalen-1-yl)-2-((*R*)-1,1-dimethylethylsulfonamido)acetate (**3n**).

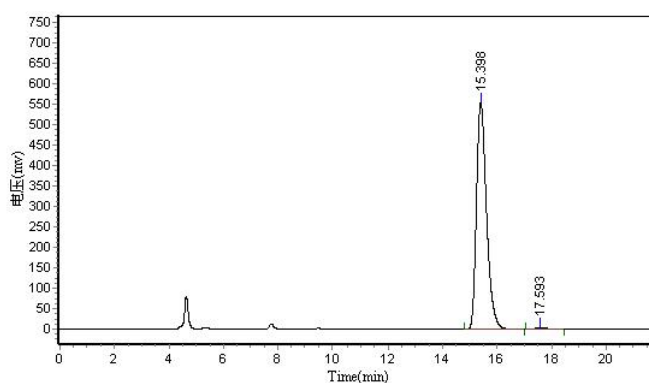


74% yield, white solid. ¹H NMR (300 MHz, CDCl₃): δ 1.05-1.24 (m, 12H), 3.86 (s, 3H), 3.95 (s, 3H), 4.10-4.17 (m, 2H), 4.71 (s, 1H), 6.06 (s, 1H), 6.96-7.00 (dd, *J* = 1.5 Hz, 8.7 Hz, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.25 (d, *J* = 1.5 Hz, 1H), 7.64 (d, *J* = 9.3 Hz, 1H), 7.738 (d, *J* = 6.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 14.16, 14.29, 22.55, 52.14, 55.33, 55.57, 57.00, 62.09, 101.66, 110.87, 116.61, 124.82, 130.20, 130.53, 133.79, 156.50, 158.59, 172.88; ESI-MS (*m/z*, %) 416 [M+Na]⁺; ESI-HRMS calcd for C₂₀H₂₇NNaO₅S [M+Na⁺] 416.1508, found 416.1516.

HPLC (**acetate**): 98% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 15.4 min (maj), 17.6 min.

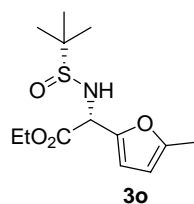


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.703	429111.094	11110039.000	25.3948
2		17.840	1077589.375	32639272.000	74.6052
Total			1506700.469	43749311.000	100.0000



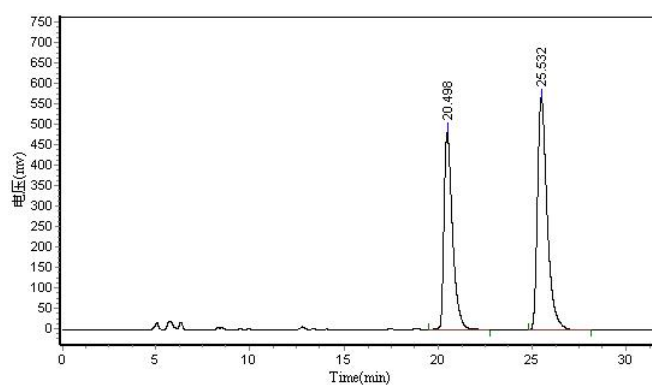
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.398	555048.375	14239966.000	99.1422
2		17.593	4385.118	123213.297	0.8578
Total			559433.493	14363179.297	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(5-methylfuran-2-yl)acetate (**3o**).

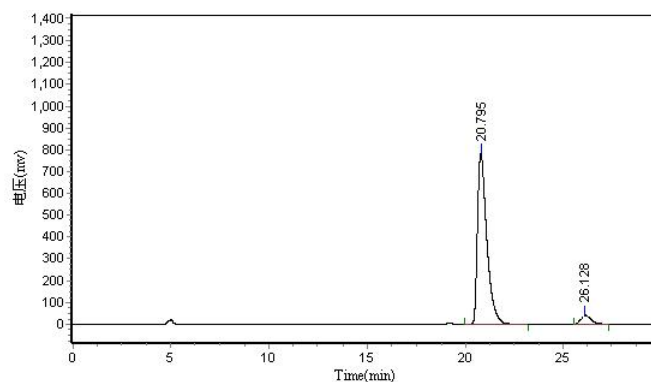


90% yield, colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 1.22 (s, 9H), 1.25 (t, 3H), 2.25 (s, 3H), 4.19-4.28 (m, 2H), 4.41 (d, $J = 4.8$ Hz, 1H), 5.03 (d, $J = 5.4$ Hz, 1H), 5.91 (s, 1H), 6.18 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 13.07, 14.13, 22.57, 55.36, 56.23, 62.52, 106.53, 109.86, 147.66, 153.04, 169.70; ESI-MS (m/z , %) 310 [$\text{M}+\text{Na}$] $^+$; ESI-HRMS calcd for $\text{C}_{13}\text{H}_{21}\text{NNaO}_4\text{S}$ [$\text{M}+\text{Na}$] $^+$ 310.1089, found 310.1094.

HPLC (acetate): 90% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 95 / 5; flow = 0.7 mL / min; Retention time: 20.8 min (maj), 26.1 min.

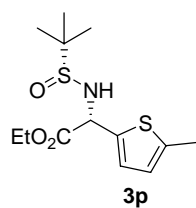


Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.498	482514.063	15349944.000	42.8937
2		25.532	567307.625	20436054.000	57.1063
Total			1050021.688	35785998.000	100.0000



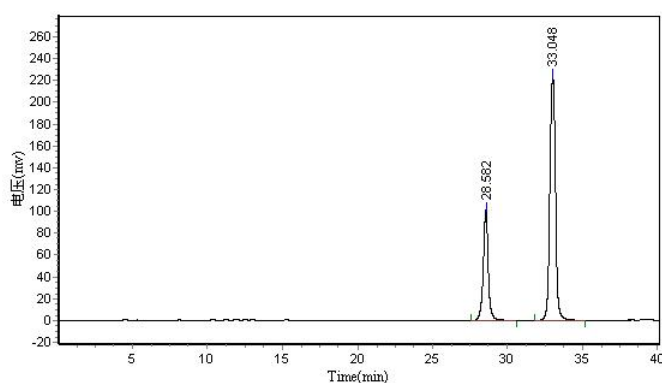
Results					
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.795	782548.563	26013320.000	94.9549
2		26.128	40046.980	1382126.250	5.0451
Total			822595.543	27395446.250	100.0000

(*R*)-ethyl 2-((*R*)-1,1-dimethylethylsulfonamido)-2-(5-methylthiophen-2-yl)acetate (**3p**).



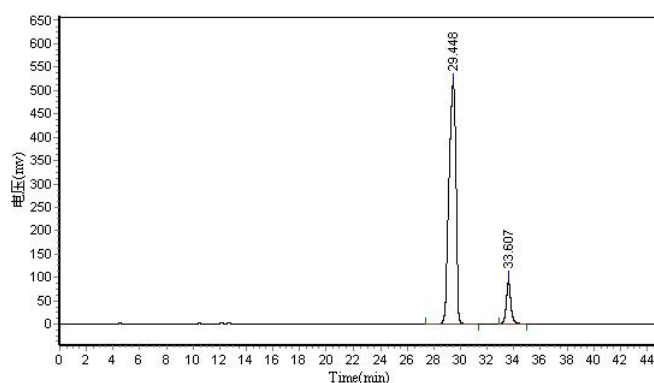
74% yield, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 1.26 (m, 12H), 2.44 (s, 3H), 4.18-4.28 (m, 2H), 4.57 (d, *J* = 4.8 Hz, 1H), 5.20 (d, *J* = 4.8 Hz, 1H), 6.60-6.61 (m, 1H), 6.84 (d, *J* = 3.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 14.14, 15.54, 22.73, 56.35, 56.95, 62.60, 125.18, 126.38, 137.78, 140.82, 170.57; ESI-MS (*m/z*, %) 326 [M+Na]⁺; ESI-HRMS calcd for C₁₃H₂₁NNaO₃S₂ [M+Na]⁺ 326.0860, found 326.0862.

HPLC (acetate): 79% de. Chiracel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 90 / 10; flow = 0.7 mL / min; Retention time: 29.4 min (maj), 33.6 min.



Results

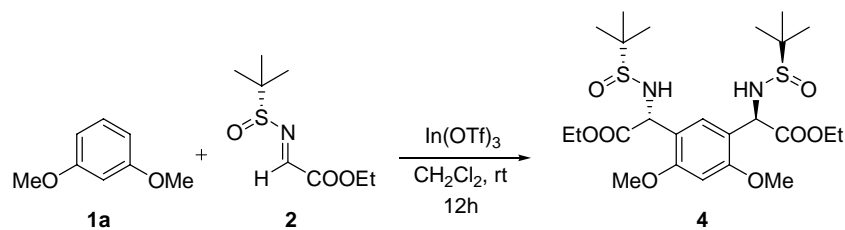
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		28.582	100177.695	2339595.750	28.4702
2		33.048	222872.891	5878101.000	71.5298
Total			323050.586	8217696.750	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		29.448	515467.469	18963830.000	89.4490
2		33.607	91384.148	2236887.750	10.5510
Total			606851.617	21200717.750	100.0000

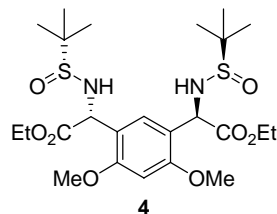
5. General procedure for the synthesis of the chiral Friedel-Crafts dialkylation product (4).



Under nitrogen atmosphere, In(OTf)₃ (0.25 mmol, 1equiv) was placed into a glass reaction vessel, glyoxylate imine **2** (0.25 mmol) in 2 mL of dry CH₂Cl₂ and arene **1** (0.125 mmol) were added successively. The mixture was stirred at room temperature and monitored by TLC. When the reaction was over, a saturated aq. NH₄Cl was added and the mixture was extracted with CH₂Cl₂ (10 mL×3). The combined organic phase was dried over Na₂SO₄, filtered, and concentrated. The residue was purified by silica gel flash chromatography to afford the corresponding product **4**.

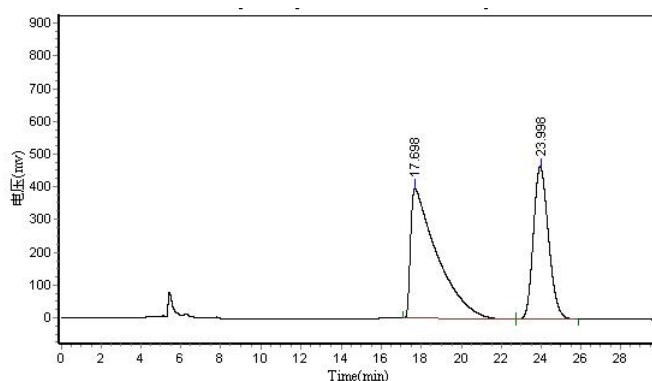
6. Characterization and HPLC of the chiral Friedel-Crafts dialkylation product (4).

(2R,2'R,26R)-diethyl-2,2'-(4,6-dimethoxy-1,3-phenylene)bis(2-((R)-1,1-dimethylethylsulfinamido)acetate) (4).



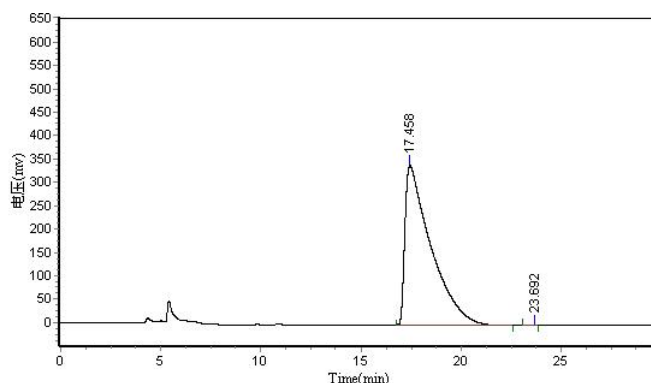
43% yield, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 1.14-1.20 (m, 24H), 3.85 (s, 6H), 4.08-4.21 (m, 4H), 4.51 (d, *J* = 4.2 Hz, 2H), 5.29 (d, *J* = 4.2 Hz, 2H), 6.44 (s, 1H), 7.07 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 14.17, 22.58, 55.00, 55.87, 55.90, 61.94, 95.56, 118.29, 129.81, 158.38, 171.73; ESI-MS (*m/z*, %) 549 [M+H]⁺; ESI-HRMS calcd for C₂₄H₄₀N₂NaO₈S₂ [M+Na]⁺ 571.2124, found 571.2133.

HPLC (sulfonate): >99% de. Chiralcel AD-H Column (250 mm); detected at 214 nm; n-hexane / i-propanol = 70 / 30; flow = 0.7 mL / min; Retention time: 17.4 min (maj), 23.7 min.



Results

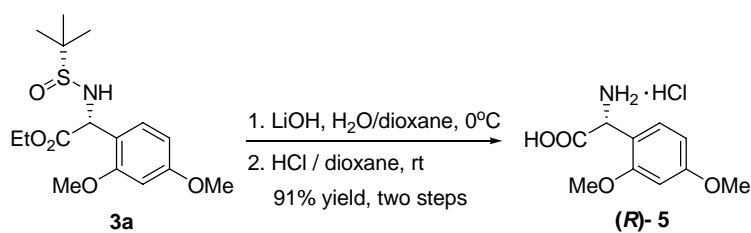
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.698	399575.188	37348212.000	60.1960
2		23.998	465545.938	24696174.000	39.8040
Total			865121.125	62044386.000	100.0000



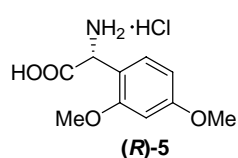
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.458	341869.594	30839148.000	99.9964
2		23.692	39.592	1116.209	0.0036
Total			341909.186	30890264.209	100.0000

7. The synthesis and HPLC of (*R*)-2-(chloroamino)-2-(2,4-dimethoxyphenyl)acetic acid (*R*)-5).



To a round bottomed flask containing LiOH (37.8 mg, 0.9mmol, 10 equiv) was added distilled H₂O (5.0 mL), and the resulting solution was cooled to 0 °C. A solution of **3a** (30.0 mg, 0.09 mmol, 1.0 equiv) in dioxane (5.0 mL) was cannulated into the reaction flask. The resulting solution was stirred at 0 °C for 3 h. The reaction mixture was then concentrated to remove the dioxane, and the remaining material was diluted with distilled H₂O (3 mL) and EtOAc (3 mL) and placed in a separatory funnel. 1 N NaHSO₄ (2 mL) was added and the aqueous layer was extracted with EtOAc (5×4 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was isolated with no further purification as a white solid. Subsequently, the crude product was treated with 5 mL solution of dry HCl in 1, 4-dioxane at room temperature for 1 h. The reaction mixture was concentrated *en vacuo*, and the amine hydrochloride was precipitated with dry diethyl ether. The precipitate was collected by filtration and washed with diethyl ether to yield the (*R*)-5 (20 mg, 91% yield) as a white solid.



91% yield, white solid. $[\alpha]_D^{20} = -111.2$ (*c* 0.5, MeOH); The absolute configuration was determined to be (*R*) according to literature [$lit^1[\alpha]_D^{22} = +106.6$ (*c* 1.0 MeOH)]. ¹H NMR (300 MHz, CD₃OD): δ 3.83 (s, 3H), 3.88 (s, 3H), 5.10 (s, 1H), 6.58-6.61 (dd, *J* = 2.4 Hz, 8.4 Hz, 1H), 6.64 (d, *J* = 2.1 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CD₃OD): δ 53.75, 56.06, 56.24, 99.73, 106.42, 114.21, 132.48, 159.90, 164.16, 171.17.

Ref 1: D. Enders, M. Seppelt, and T. Beck, *Adv. Synth. Catal.*, 2010, **352**, 1413.

8. Copies of ^1H and ^{13}C NMR Spectra of Compounds 3a-p, 4 and (R)-5.

