Supporting Information:

First Example of Organocatalytic Asymmetric Mannich Reaction between Aldimines of Glycinates and Sulphonyl Imines

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General remarks

All reactions were carried out with commercial available reagents. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plates with UV 254 indicator. Toluene, THF, EtOAc and CH_2Cl_2 was purchased as analytical pure. CH_2Cl_2 was dried with NaH under distilled condition. THF and Toluene was dried and distilled from sodium benzophenone. Melting points (m.p.) were measured on electrothermal digital melting point apparatus from Beijing Fukai Instruments Co.Ltd.

^1H NMR spectra were recorded on Bruker AMX 300 or 600 MHz with CDCl_3 or CD_3OD as solvent. Chemical shifts were reported in ppm from SiMe_4 (δ 0.0) and the signal of CDCl_3 (δ 7.26 singlet) and CD_3OD (δ 3.31 singlet). ^{13}C NMR spectra were recorded with CDCl_3 and CD_3OD as solvent. Chemical shifts were reported in ppm from SiMe_4 (δ 0.0) and the signal of CDCl_3 (δ 77.0 triplet) and CD_3OD (δ 49.0 singlet).

Enantiomeric excesses (ee) were determined by high performance liquid chromatography (HPLC) using corresponding commercial chiral column at 30 °C with Hatachidetector 254 or 210 nm. Optical rotations were reported as follows: $[\alpha]_D^{20}$ (c g/100 mL, in solvent).

^{13}C NMR spectra were collected on commercial instruments (100 or 150 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard (CDCl_3 , δ = 77.0, t). High resolution mass spectrometry (HRMS) was measured on a commercial apparatus (ESI Source micrOTOF).

The racemic products used to determine the e.e. values were obtained by using 1,1,3,3-tetramethylguanidine (TMG) as catalyst.

1. Typical preparation of glycine imine schiff base

Scheme S1. The synthesis of glycine imine schiff base

General Procedure for the Preparation of the glycine esters adlmines **4** according to previously report^[1]. To a solution of the corresponding amino acid ester chlorhydrate (30mmol, 1 equiv) in CH₂Cl₂ (45 mL) were added MgSO₄ and NEt₃ (33 mmol, 1.1 equiv). The resulting mixture was stirred at the room temperature for 30 min. Then the aldehyde (30 mmol, 1 equiv) was added, and the resulting mixture was stirred for 16 h. Then the obtained solution was filtered out and the organic layer washed with water, dried, and evaporated. The imines showed satisfactory NMR spectra. (Some of **4** were purified by base flash column chromatography).

(*E*)-ethyl 2-((2-hydroxybenzylidene)amino)acetate(**4a**)

According to the above procedure, afford **4a**, light yellow oil; 90% yield;

¹H NMR (600 MHz, CDCl₃) δ 12.91 (s, 1H), 8.37 (s, 1H), 7.38 – 7.30 (m, 1H), 7.29 – 7.26 (m, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 4.37 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H),

1.31 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 169.20, 168.43, 161.06, 132.82, 131.70, 118.71, 118.65, 117.19, 61.36, 60.00, 14.16.

ESI-HRMS: calcd for C₁₁H₁₃NO₃H⁺ ([M+H⁺]) = 208.0970, Found 208.0969.

(*E*)-ethyl 2-((2-hydroxy-4-methoxybenzylidene)amino)acetate(**4b**)

light green solid, m.p. 75-75 °C, 85% yield; ¹H NMR (600 MHz, CDCl₃) δ 13.37 (s, 1H), 8.24 (s, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 6.65 – 6.19 (m, 2H), 4.31 (s, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, DMSO-d₆) δ 169.46, 167.39, 163.90, 163.67, 132.90, 112.50, 106.62, 101.12, 61.29, 59.42, 55.37, 14.16.

ESI-HRMS: calcd for C₁₂H₁₅NO₄H⁺ ([M+H⁺]) = 238.1074, Found 238.1073.

(*E*)-tert-butyl 2-((3,5-dibromo-2-hydroxybenzylidene)amino)acetate(**4c**)

Yellow oil, m.p. 50-53 °C, yield 65%. It was purified by flash chromatography on silica gel.

¹H NMR (600 MHz, CDCl₃) δ 13.95 (s, 1H), 8.26 (s,

1H), 7.70 (t, $J = 3.9$ Hz, 1H), 7.34 (d, $J = 2.2$ Hz, 1H), 4.40 (s, 2H), 4.30 – 4.20 (m, 2H), 1.35 – 1.27 (m, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 168.41, 166.57, 157.57, 138.08, 133.05, 120.02, 112.28, 109.81, 61.68, 59.09, 14.16.

ESI-HRMS: calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_4\text{H}^+$ ($[\text{M}+\text{H}^+]$) = 365.9169, Found 365.9183

(*E*)-ethyl 2-((3,5-di-*tert*-butyl-2-hydroxybenzylidene)amino)acetate(4d)

4d

Yellow solid; m.p. 39-43 °C; yield 85%;

^1H NMR (600 MHz, CDCl_3) δ 13.33 (s, 1H), 8.39 (s, 1H), 7.42 (d, $J = 2.2$ Hz, 1H), 7.11 (d, $J = 2.3$ Hz, 1H), 4.36 (s, 2H), 4.25 (q, $J = 7.1$ Hz, 2H), 1.46 (s, 9H), 1.32 (s, 9H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.64, 169.44, 158.09, 140.19, 136.88, 127.54, 126.29, 117.76, 61.27, 59.88, 35.07, 34.13, 31.49, 29.43, 14.18.

ESI-HRMS: calcd for $\text{C}_{19}\text{H}_{29}\text{NO}_3\text{H}^+$ ($[\text{M}+\text{H}^+]$) = 320.2220, Found 320.2220.

(*E*)-ethyl 2-((4-(diethylamino)-2-hydroxybenzylidene)amino)acetate(4e)

4e

Light red solid; 90% yield; 53-55 °C; Yield=87%;

^1H NMR (600 MHz, CDCl_3) δ 13.30 (s, 1H), 8.11 (s, 1H), 7.03 (d, $J = 8.7$ Hz, 1H), 6.31 – 5.95 (m, 2H), 4.47 – 4.05 (m, 4H), 3.36 (q, $J = 7.1$ Hz, 4H), 1.23 (dt, $J = 65.6, 7.1$ Hz, 9H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 169.99, 166.69, 163.97, 151.51, 133.02, 108.42, 103.19, 97.99, 61.12, 59.36, 44.51, 14.18, 12.68.

ESI-HRMS: calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_3\text{H}^+$ ($[\text{M}+\text{H}^+]$) = 279.1703, Found 279.1711.

(*E*)-ethyl 2-((2,4-dihydroxybenzylidene)amino)acetate(4f)

4f

Yellow solid; 128-131 °C; 60% yield;

^1H NMR (600 MHz, CDCl_3) δ 8.25 (s, 1H), 7.13 (d, $J = 8.4$ Hz, 1H), 6.40 (d, $J = 2.2$ Hz, 1H), 6.36 (dd, $J = 8.4, 2.3$ Hz, 1H), 4.32 (s, 2H), 4.24 (q, $J = 7.1$ Hz, 2H), 1.30 (dd, $J = 17.2, 10.0$ Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 170.11, 168.30, 164.40, 162.50, 134.01, 111.77, 107.66, 103.01, 61.01, 58.23, 14.51.

ESI-HRMS: calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_3\text{H}^+$ ($[\text{M}+\text{H}^+]$) = 224.0917, Found 224.0925.

(*E*)-methyl 2-((3,5-di-*tert*-butyl-2-hydroxybenzylidene)amino)acetate(4g)

4g

yellow oil; 35-38 °C; yield 87%;

^1H NMR (600 MHz, CDCl_3) δ 13.28 (s, 1H), 8.39 (s, 1H), 7.42 (d, $J = 2.1$ Hz, 1H), 7.11 (d, $J = 2.2$ Hz, 1H), 4.38 (s, 1H), 3.79 (s, 1H), 1.46 (s, 1H), 1.32 (s, 1H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.87, 169.77, 158.06, 140.25, 136.90, 127.61, 126.31, 117.73, 77.24, 77.03, 76.82, 59.75, 52.24, 35.07, 34.13,

31.48, 29.43.

ESI-HRMS: calcd for $C_{15}H_{22}N_2O_3H^+$ ($[M+H]^+$) = 306.2064, Found 306.2064.

(E)-tert-butyl 2-((3,5-di-tert-butyl-2-hydroxy benzy -lidene)amino)acetate(4h)

yellow oil; 60-62 °C; yield 79%;

1H NMR (600 MHz, $CDCl_3$) δ 13.45 (s, 1H), 8.35 (s, 1H), 7.40 (d, J = 2.1 Hz, 1H), 7.09 (d, J = 2.2 Hz, 1H), 4.26 (s, 2H), 1.50 (s, 9H), 1.44 (s, 9H), 1.30 (s, 9H).

^{13}C NMR (151 MHz, MeOD) δ 169.21, 168.63, 158.15, 140.05, 136.84, 127.37, 126.19, 117.79, 81.81, 60.52, 35.05, 34.11, 31.48, 29.41, 28.08.

ESI-HRMS: calcd for $C_{15}H_{22}N_2O_3H^+$ ($[M+H]^+$) = 348.2533, Found 348.2534.

2. The preparation of sulfonyl imine^[2]

$TiCl_4$ (1.1 mL, 10 mmol, 0.5 equiv) in dry CH_2Cl_2 (10 mL) was added dropwise to a stirred, ice-cooled solution of benzaldehyde (20 mmol, 1 equiv), *p*-toluenesulfonamide (20 mmol), and Et_3N (7.1 g, 70 mmol, 7 equiv) in dry CH_2Cl_2 (40 mL). The obtained mixture was stirred for 30 min. The titanium dioxide was removed by filtration through celite and washed with dichloromethane. Evaporation of the solvent under reduced pressure afforded a white solid which was broken up by refluxing in dry diethyl ether. The residual Et_3NHCl was removed by filtration and the filtrate was concentrated to afford the crude imine. Purification by crystallization (hexane/dichloromethane) afforded **5a-5c**.

Scheme S2. The synthesis of sulfonyl imines **5a-5c**.

The method for preparation of **5d-5j** can be found in previously report^[3].

Scheme S3. The synthesis of sulfonyl imine **5d-5i**

(E)-N-benzylidene-2-methylbenzenesulfonamide (5b),

White solid; yield 72%;

1H NMR (600 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 7.3 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.0 Hz, 3H), 7.35 (dd, J = 16.4, 7.8 Hz, 2H), 7.26 (s, 1H), 2.75 (s, 3H).

(E)-N-benzylidene-4-methoxybenzenesulfonamide (5c),

5c

White solid; yield 75%;

^1H NMR (600 MHz, CDCl_3) δ 8.99 (s, 1H), 7.91 (dd, J = 12.1, 8.4 Hz, 4H), 7.59 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.00 (d, J = 8.9 Hz, 2H), 3.85 (s, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.57, 163.74, 134.80, 132.49, 131.23, 130.30, 129.63, 129.13, 114.44, 55.68.

(E)-N-benzylidenequinoline-8-sulfonamide (5d)

5d

White solid; yield 47%;

^1H NMR (600 MHz, CDCl_3) δ 9.58 (s, 1H), 8.92 (dd, J = 4.2, 1.6 Hz, 1H), 8.72 (dd, J = 7.4, 1.3 Hz, 1H), 8.20 (dd, J = 8.3, 1.6 Hz, 1H), 8.10 (dd, J = 8.2, 1.1 Hz, 1H), 8.03 – 7.95 (m, 2H), 7.71 (t, J = 7.8 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.51 – 7.38 (m, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 175.34, 151.36, 143.67, 136.50, 134.80, 134.71, 134.31, 132.75, 132.71, 131.43, 129.09, 128.88, 125.60, 122.02, 77.24, 77.03, 76.81.

3. The preparation of chiral guanidine

General procedure: The method for preparation of **6a-6h** following the above procedure can be found in previously report^[4].

Scheme S4. The synthesis route of guanidine catalyst (**6a-6h**)

The preparation of (4R,5R)-4,5-diphenylimidazolidin-2-imine **6i** according to previously literature^[5].

Scheme S5. The synthesis route of chiral guanidine **6i**

(1R,2R)-1,2-diphenylethane-1,2-diamine (1 g, 4.7 mmol) was dissolved in MeCN (5 mL). The obtained solution was cooled to 0 °C, and a 1 M solution of cyanogen bromide in MeCN (4.7 mL, 4.7 mmol) was added dropwise via syringe. The mixture was equipped a reflux condenser and heated at reflux for 48 h. The solution was concentrated and purified by column chromatography to afford white foam. The guanidinium salt was basified by dissolving in CH_2Cl_2

and adding oil-free NaH. The suspension was shaken for thirty seconds, filtered through Celite, and concentrated to provide the guanidine **6i** as a white powder in 51% yield.

^1H NMR (600 MHz, CDCl_3) δ 8.21 (s, 1H), 8.12 (s, 1H), 7.43 – 7.28 (m, 3H), 7.19 (d, J = 7.3 Hz, 2H), 4.73 (s, 1H).

^{13}C NMR (151 MHz, CDCl_3) δ 160.38, 140.57, 128.87, 128.23, 126.43, 70.31.

ESI-HRMS: calcd for $\text{C}_{15}\text{H}_{15}\text{N}_3^+$ [$\text{M}+\text{H}^+$] = 238.1301, found 238.1299.

The preparation of 1,3-bis((*S*)-1-phenylethyl)imidazolidin-2-imine **6j** can be found in previously report^[5].

Scheme S6. The synthesis route of chiral guanidine **6j**^[5].

The method for preparation of **6j-a** can be found in previously literature^[6]. **6j** was Prepared as described for **6i**.

^1H NMR (600 MHz, CDCl_3) δ 7.45 – 7.30 (m, 8H), 7.26 (t, J = 6.9 Hz, 3H), 5.15 (s, 2H), 3.13 (d, J = 5.2 Hz, 2H), 2.92 (s, 2H), 1.52 (d, J = 7.0 Hz, 6H).

The preparation of *N*-((4*R*,5*R*)-1,3-dimethyl-4,5-diphenylimidazolidin-2-ylidene)-1-phenylmethanamine **6k**^[1].

Scheme S7. The synthesis route of chiral guanidine **6k**.

The method for preparation of **6k-c** can be found in previously report^[7].

A solution of **6k-c** (3.0 g, 11.3 mmol) and oxalyl chloride (1.6 g, 12.4 mmol) in anhydrous toluene (100 ml) was refluxed for 12.5 h. After cooling, the precipitate was filtered, repeatedly washed with anhydrous toluene, and dried under reduced pressure to give **6k-d** as colorless solid. The crude solid was used for next step without further purification.

To a solution of a benzylamine (0.33 g, 3.1 mmol) and Et_3N (0.66 mg, 6.5 mmol) in CH_2Cl_2 (30 ml) was added dropwise a solution of **6k-d** (1 g) in CH_2Cl_2 (15 ml) at rt. The mixture was

stirred at RT for 1 hour and poured into dil. HCl, and extracted with dichloromethane. The organic solution was evaporated to dryness. The residue was dissolved in water and washed with toluene. The aqueous solution was made alkaline with dil. aq. NaOH and extracted with CH₂Cl₂. The obtained organic solution was dried and evaporated to yield pure guanidines **6k** as white solid.

¹H NMR (600 MHz, CDCl₃) δ 10.73 (s, 1H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.36 (dd, *J* = 15.0, 7.3 Hz, 7H), 6.96 (d, *J* = 6.6 Hz, 4H), 5.03 (s, 1H), 4.81 (d, *J* = 13.8 Hz, 1H), 4.29 (d, *J* = 52.2 Hz, 2H), 3.11 (s, 6H).

The preparation of chiral di-guanidine catalyst **6l** was found in previously literature^[8].

Scheme S8. The synthesis route of chiral guanidine **6l**

Product **6l** was obtained following the literature procedure, matching the previously published characterization data.

¹H NMR (600 MHz, CDCl₃) δ 7.08 (t, *J* = 33.6 Hz, 10H), 5.16 (s, 2H), 4.67 (s, 2H), 3.25 (d, *J* = 55.0 Hz, 2H), 2.92 (d, *J* = 32.0 Hz, 2H), 2.25 (d, *J* = 45.7 Hz, 1H), 1.95 – 1.46 (m, 14H), 1.44 – 0.81 (m, 12H).

4. The Typical Mannich-type reaction

Table S1. Examination of condition effect for Mannich-type reaction

Entry ^a	Tem.[°C]	Solvent	X[mol%]	Yield[%] ^b	dr ^c	ee[%] ^d
1	10	Toluene	20	86	1.9:1	5/3
2	0	Toluene	20	85	2:1	7/2
3	-10	Toluene	20	56	2:1	6/5

4	0	Ethyl ether	20	90	1.2:1	0/4
5	0	THF	20	58	3:1	3/0
6	0	CH ₂ Cl ₂	20	56	13:1	4/5
7	0	CHCl ₃	20	50	2.5:1	3/0
8	0	EtOH	20	92	1:1	0/0
9	0	CCl ₄	20	86	17:1	0/4
10	0	CH ₃ CN	20	75	16:1	0/0
11	0	EA	20	90	1.7:1	11/2
12	0	EA	15	87	1.7:1	11/5
13	0	EA	10	68	1.6:1	11/6

[a] Unless otherwise noted, the reaction was carried out with 0.06 mmol **4d**, 0.066 mmol **5b**, 40 mg 4 Å and catalyst in solvent (1.0 mL) for 20 h. [b] Yield of isolated product. [c] Determined by chiral HPLC. [d] Corresponding ee of anti/syn.

The Typical Mannich-type reaction.

Scheme S9. The Typical procedure of Mannich-type reaction

To a 10 mL tube with a magnetic stirring bar were sequentially added the aldimines of glycine imine schiff base **4d** (0.06 mmol, 1.0 equiv), sulfonyl imine **5** (0.066 mmol, 1.1 equiv), 40 mg 4 Å molecular sieve and 15 mol% of catalyst **6g** in 1.5 mL ice EA under dry nitrogen at 0°C for 12 h.. When the reaction completed (monitored by TLC), the obtained mixture was purified directly by flash chromatography on silica gel to afford **7** for H-NMR (confirmed the dr). The ee of the major isomer was determined by chiral HPLC analysis. (**Note:** The dr of some **7** was determined by HPLC analysis.)

(E)-ethyl 2-((3,5-dibromo-2-hydroxybenzylidene)amino)-3-(2-methylphenylsulfonamido)-3-phenylpropanoate (**7b**)

Yellow oil; 84 % yield;

¹H NMR (600 MHz, CDCl₃) δ 12.46 (s, 1H), 12.36 – 12.25 (m, 0.3H), 8.14 (s, 1H), 7.99 (s, 0.3H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.1 Hz, 0.3H), 7.32 (dt, *J* = 26.1, 8.5 Hz, 2.8H), 7.23 – 7.04 (m, 10H), 6.96 (t, *J* = 7.9 Hz, 1.4H), 6.91 – 6.84 (m, 1.3H), 5.65 (d, *J* = 8.5 Hz, 0.3H), 5.38 (d, *J* = 8.2 Hz, 1H), 4.94 (dd, *J* = 19.4, 13.8 Hz, 1.4H), 4.39 (d, *J* = 5.5 Hz, 1H), 4.19 (d, *J* = 4.7 Hz, 0.4H), 4.10 – 3.99 (m, 2H), 3.95 (d, *J* = 7.2 Hz, 0.4H), 2.54 (s, 1H), 2.42 (s, 2.8H),

1.11 (dt, $J = 14.2, 7.1$ Hz, 4H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.12, 168.85, 160.92, 137.97, 136.89, 136.21, 133.33, 132.76, 132.44, 132.26, 129.38, 128.56, 128.42, 127.31, 127.08, 126.06, 118.91, 118.39, 117.19, 75.20, 61.77, 59.66, 20.17, 13.88.

ESI-HRMS: calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}^+]$) = 465.1490, Found 465.1489

(E)-ethyl 2-((2-hydroxy-4-methoxybenzylidene)amino)-3-(2-methylphenylsulfonamido)-3-phenylpropanoate (7c)

7c

Yellow oil; 90% yield;

^1H NMR (600 MHz, CDCl_3) δ 12.90 (s, 1H), 8.01 (d, $J = 7.8$ Hz, 2H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 0.8H), 7.32 (t, $J = 7.6$ Hz, 2.6H), 7.24 – 7.15 (m, 4H), 7.12 – 7.04 (m, 4H), 6.43 (d, $J = 8.9$ Hz, 2H), 5.47 (d, $J = 8.4$ Hz,

1H), 4.92 (dd, $J = 8.2, 5.8$ Hz, 1H), 4.87 (d, $J = 36.3$ Hz, 1.6H), 4.33 (d, $J = 5.6$ Hz, 1H), 4.05 (ddd, $J = 15.4, 12.1, 10.9$ Hz, 3H), 3.82 (s, 3H), 2.69 (s, 2.4H), 2.43 (s, 3H), 1.15 – 1.06 (m, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.14, 168.08, 163.98, 163.40, 138.07, 136.92, 136.32, 133.48, 132.69, 132.41, 129.37, 128.47, 128.31, 127.33, 127.14, 126.03, 112.33, 106.82, 101.04, 74.99, 61.70, 59.67, 55.43, 20.17, 13.89.

ESI-HRMS: calcd for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}^+]$) = 495.1530, Found 495.1520

(E)-ethyl 2-((3,5-dibromo-2-hydroxybenzylidene)amino)-3-(2-methylphenyl sulfonamido)-3-phenylpropanoate (7d)

7d

Yellow oil; 78 % yield;

^1H NMR (600 MHz, CDCl_3) δ 13.37 (s, 1H), 8.04 (s, 1H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.72 (d, $J = 2.1$ Hz, 1H), 7.33 (t, $J = 7.6$ Hz, 1H), 7.22 (dd, $J = 9.1, 6.4$ Hz, 4H), 7.07 (dd, $J = 17.4, 5.7$ Hz, 3H), 5.45 (dd, $J = 14.4, 8.0$ Hz, 1H), 4.93 – 4.83 (m, 1H), 4.48 (d, $J = 5.7$ Hz, 1H), 4.10 – 4.00 (m, 2H), 2.43 (s, 3H), 1.11 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 168.38, 167.13, 156.99, 138.40, 137.76, 136.86, 135.89, 133.51, 132.87, 132.48, 129.37, 128.81, 128.67, 127.13, 126.13, 119.93, 112.05, 110.17, 74.55, 62.07, 59.77, 20.20, 13.88.

ESI-HRMS: calcd for $\text{C}_{25}\text{H}_{24}\text{Br}_2\text{N}_2\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}^+]$) = 622.9845, Found 622.9872

(E)-ethyl-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(2-methylphenylsulfonamido)-3-phenylpropanoate (7e)

7e

Yellow oil; 87% yield;

^1H NMR (600 MHz, CDCl_3) δ 12.82 (s, 1H), 12.75 – 12.60 (m, 0.4H), 8.16 (s, 1H), 8.04 (s, 0.8H), 7.90 (d, $J = 7.9$ Hz, 1H), 7.74 (d, $J = 7.9$ Hz, 0.8H), 7.42 (d, $J = 2.5$ Hz, 2H), 7.28 (d, $J = 7.6$ Hz, 2H), 7.23 – 6.99 (m, 14H),

6.94 (d, $J = 2.1$ Hz, 1H), 5.64 (d, $J = 7.8$ Hz, 0.7H), 5.44 (d, $J = 8.4$ Hz, 1H), 4.98 (dd, $J = 7.7$, 4.9 Hz, 0.8H), 4.93 (dd, $J = 8.1$, 5.5 Hz, 1H), 4.36 (d, $J = 5.3$ Hz, 1H), 4.16 (d, $J = 4.8$ Hz, 0.8H), 4.12 – 3.99 (m, 3H), 3.96 (dq, $J = 14.4$, 7.2 Hz, 0.8H), 2.58 (s, 2.5H), 2.43 (s, 3H), 1.45 (d, $J = 8.9$ Hz, 16H), 1.29 (d, $J = 16.8$ Hz, 16H).

^{13}C NMR (151 MHz, CDCl_3) δ 170.54, 170.17, 169.02, 168.97, 158.04, 140.40, 138.00, 136.91, 136.43, 132.66, 132.53, 132.43, 132.22, 129.35, 128.48, 128.32, 128.12, 127.41, 127.28, 126.83, 126.69, 126.02, 125.88, 117.50, 75.85, 75.02, 61.87, 61.67, 60.03, 59.69, 35.10, 34.15, 31.46, 31.42, 29.41, 20.28, 20.16, 13.90.

ESI-HRMS: calcd for $\text{C}_{33}\text{H}_{42}\text{N}_2\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}^+]$) = 579.2914, Found 579.2905

(E)-ethyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(4-methoxy phenyl-sulfonamido)-3-phenylpropanoate (7f)

Yellow oil; 90% yield;

^1H NMR (600 MHz, CDCl_3) δ 12.86 (s, 1H), 8.22 (s, 1H), 7.62 (d, $J = 8.8$ Hz, 2H), 7.43 (s, 1H), 7.26 (s, 1H), 7.19 (d, $J = 2.9$ Hz, 3H), 7.11 (s, 2H), 7.04 (d, $J = 2.0$ Hz, 1H), 6.73 (d, $J = 8.8$ Hz, 2H), 5.40 (d, $J = 8.2$ Hz,

1H), 4.94 (dd, $J = 8.0$, 5.3 Hz, 1H), 4.37 (d, $J = 5.2$ Hz, 1H), 4.11 – 4.04 (m, 2H), 3.75 (s, 3H), 1.45 (d, $J = 4.1$ Hz, 9H), 1.30 (s, 9H), 1.12 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 170.05, 168.97, 162.75, 158.06, 140.45, 136.90, 136.41, 131.55, 129.26, 128.42, 128.18, 128.12, 127.54, 127.39, 126.76, 117.56, 113.96, 113.85, 75.35, 61.67, 59.69, 55.48, 35.10, 34.14, 31.44, 29.39, 13.93.

ESI-HRMS: calcd for $\text{C}_{33}\text{H}_{42}\text{N}_2\text{O}_6\text{SH}^+$ ($[\text{M}+\text{H}^+]$) = 595.2836, Found 595.2854

(E)-ethyl2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-phenyl-3-(quinoline-8-sulfonamido)propanoate (7g)

Yellow oil; yield 88%;

^1H NMR (600 MHz, CDCl_3) δ 12.85 (s, 1H), 12.78 (s, 0.7H), 9.08 (d, $J = 2.7$ Hz, 0.7H), 8.69 (d, $J = 2.6$ Hz, 1H), 8.20 (d, $J = 5.0$ Hz, 2H), 8.10 (d, $J = 7.6$ Hz, 1.5H), 8.02 (d, $J = 12.4$ Hz, 2H), 7.81 (d, $J = 8.2$ Hz, 1.7H), 7.50 – 7.28 (m, 6H), 7.08 – 6.97

(m, 2H), 6.93 – 6.85 (m, 3H), 6.82 (dd, $J = 13.7$, 7.5 Hz, 4.5H), 6.73 (t, $J = 7.5$ Hz, 2H), 5.31 (dd, $J = 8.9$, 4.9 Hz, 0.7H), 5.18 (dd, $J = 9.5$, 5.6 Hz, 1H), 4.47 (d, $J = 5.6$ Hz, 1H), 4.15 (d, $J = 4.9$ Hz, 0.7H), 4.11 – 3.87 (m, 4H), 1.51 (s, 7H), 1.44 (s, 9H), 1.30 (d, $J = 26.8$ Hz, 17H).

^{13}C NMR (151 MHz, CDCl_3) δ 170.54, 170.26, 168.63, 158.05, 157.99, 151.29, 150.77, 142.99, 142.80, 140.32, 137.42, 136.92, 136.76, 136.54, 136.45, 135.29, 132.84, 132.54, 130.05, 129.52, 128.42, 128.10, 127.98, 127.72, 127.66, 127.34, 126.88, 126.78, 125.32, 121.93, 121.84, 117.49, 76.42, 75.61, 64.42, 61.67, 61.51, 60.56, 60.17, 59.55, 38.16, 35.12, 35.08, 34.14, 34.10, 31.48, 31.43, 31.24, 29.53, 29.42, 25.37, 13.93.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H

(Hexane/*i*-PrOH = 96/4, flow rate 1.0 mL/min, λ = 254 nm), t_R (major diastereomer,) = 42.9min (major enantiomer); 11.5min (minor enantiomer).

ESI-HRMS: calcd for $C_{35}H_{41}N_3O_5SH^+$ ($[M+H^+]$) = 616.2856, Found 616.2864

(E)-tert-butyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-phenyl-3-(quinoline-8-sulfonamido)propanoate (7h)

7h

Yellow oil; 87% yield;

1H NMR (600 MHz, $CDCl_3$) δ 12.99 (s, 1H), 12.91 (s, 0.4 H), 9.08 (d, J = 2.8 Hz, 0.4H), 8.67 (d, J = 2.6 Hz, 1H), 8.21 (s, 1H), 8.16 (d, J = 7.2 Hz, 1H), 8.12 – 7.94 (m, 2.4H), 7.78 (t, J = 9.4 Hz, 1.5H), 7.42 (t, J = 7.7 Hz, 3H), 7.38 – 7.28 (m, 2H), 7.00 (dd, J = 26.2, 6.0 Hz, 2H), 6.90 (d, J = 2.2 Hz, 0.5H), 6.87 – 6.74 (m, 5H), 6.70 (dt, J = 15.0, 7.6 Hz, 3H), 5.24 (dd, J = 9.4, 5.0 Hz, 0.4H), 5.13 (dd, J = 9.8, 5.7 Hz, 1H), 4.38 (d, J = 5.7 Hz, 1H), 4.08 – 3.96 (m, 8H), 1.51 (s, 4H), 1.45 (s, 9H), 1.38 (s, 4H), 1.32 (s, 9H), 1.26 (d, J = 6.1 Hz, 13H).

^{13}C NMR (151 MHz, MeOD) δ 170.16, 170.00, 167.62, 158.10, 151.19, 150.75, 142.98, 142.78, 140.24, 136.93, 136.70, 136.52, 136.40, 135.26, 132.73, 132.43, 129.95, 129.54, 128.38, 127.99, 127.84, 127.62, 127.51, 127.43, 127.16, 126.87, 126.72, 125.26, 121.80, 117.56, 82.78, 82.52, 77.22, 77.01, 76.80, 75.95, 64.41, 60.88, 60.19, 35.09, 34.14, 31.48, 31.43, 29.51, 29.43, 27.79, 27.71, 25.35, -0.03.

ESI-HRMS: calcd for $C_{37}H_{46}N_3O_5SH^+$ ($[M+H^+]$) = 644.3159, found 644.3171

5. Generality explorations of the Mannich-type reaction

(E)-ethyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(quinoline-8-sulfonamido)-3-(p-tolyl)propanoate (7j)

7j

Yellow oil; 88% yield; $[\alpha]_D^{20}$ = +0.11 (c =0.7, in CH_2Cl_2);

1H NMR (600 MHz, $CDCl_3$) δ 12.90 (s, 1H), 12.81 (s, 0.7H), 9.06 (dd, J = 4.2, 1.6 Hz, 0.7H), 8.68 (dd, J = 4.2, 1.6 Hz, 1H), 8.25 – 8.15 (m, 2.4H), 8.13 – 7.96 (m, 3.6H), 7.88 (d, J = 8.1 Hz, 0.7H), 7.82 (d, J = 8.0 Hz, 1.7H), 7.51 – 7.36 (m, 4.7H), 7.34 – 7.27 (m, 2.5H), 7.00 (d, J = 2.3 Hz, 1H), 6.92 (dd, J = 13.2, 6.0 Hz, 1.7H), 6.75 (d, J = 8.0 Hz, 1.4H), 6.68 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 7.9 Hz, 1.4H), 6.48 (d, J = 7.8 Hz, 2H), 5.25 (dd, J = 9.0, 4.9 Hz, 0.7H), 5.13 (dd, J = 9.6, 5.7 Hz, 1H), 4.46 (d, J = 5.7 Hz, 1H), 4.12 (dd, J = 13.3, 6.1 Hz, 1H), 4.05 (qd, J = 7.1, 2.9 Hz, 2H), 3.96 (dtd, J = 17.9, 10.8, 7.2 Hz, 1.4H), 2.05 (s, 2H), 2.00 (s, 3H), 1.50 (s, 6H), 1.44 (s, 9H), 1.32 (s, 9H), 1.27 (s, 6H), 1.17 – 1.10 (m, 5H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.14, 170.48, 170.24, 168.70, 158.06, 158.00, 151.25,

150.75, 143.00, 142.84, 140.28, 137.41, 137.25, 136.86, 136.74, 136.45, 136.29, 134.59, 133.94, 132.63, 132.33, 131.58, 130.14, 129.89, 129.61, 128.43, 128.23, 128.04, 127.91, 127.60, 127.27, 126.88, 126.79, 125.60, 125.31, 125.27, 121.97, 121.90, 121.79, 117.51, 76.49, 75.62, 61.64, 61.49, 60.35, 59.94, 35.12, 35.08, 34.14, 34.11, 31.48, 31.44, 29.69, 29.53, 29.43, 21.96, 21.03, 20.78, 20.73, 14.20, 13.98, 13.94.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm), t_R (major diastereomer,) = 42.9min (major enantiomer); 11.5min (minor enantiomer).

ESI-HRMS: calcd for $C_{36}H_{43}N_3O_5SH^+$ ($[M+H]^+$) = 630.2996, Found 630.3019

(E)-ethyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(4-methoxy-phenyl)-3-(quinoline-8-sulfonamido)propanoate

Yellow oil; 83% yield; $[\alpha]_D^{20} = +0.26$ ($c=0.7$, in CH_2Cl_2);

1H NMR (600 MHz, $CDCl_3$) δ 12.90 (s, 1H), 12.80 (s, 0.4H), 9.07 (s, 0.5H), 8.69 (d, $J = 2.7$ Hz, 1H), 8.23 (s, 1H), 8.20 (d, $J = 7.4$ Hz, 1H), 8.13 – 8.02 (m, 2H), 7.83 (d, $J = 7.2$ Hz, 1.6H), 7.52 – 7.38 (m, 3.4H), 7.32 (dd, $J = 8.2, 4.2$ Hz, 1H), 7.28 (d, $J = 9.1$ Hz, 0.6H), 7.02 (d, $J = 2.2$ Hz, 1H), 6.92 (d, $J = 9.7$ Hz, 1.4H), 6.77 (d, $J = 8.6$ Hz, 1H), 6.72 (d, $J = 8.6$ Hz, 2H), 6.30 (d, $J = 8.7$ Hz, 1H), 6.21 (d, $J = 8.6$ Hz, 2H), 5.23 (s, 0.6H), 5.13 (dd, $J = 9.5, 5.6$ Hz, 1H), 4.46 (d, $J = 5.5$ Hz, 1H), 4.13 (d, $J = 4.9$ Hz, 0.5H), 4.08 – 3.93 (m, 3H), 3.59 (s, 1.3H), 3.57 (s, 3H), 1.51 (s, 5H), 1.45 (s, 9H), 1.36 – 1.30 (m, 9H), 1.28 (s, 5H), 1.14 (dt, $J = 14.2, 7.2$ Hz, 5H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 170.49, 170.33, 168.69, 158.77, 158.05, 151.26, 150.77, 142.84, 140.34, 136.88, 136.74, 136.40, 132.75, 130.14, 129.66, 128.96, 128.63, 128.46, 128.09, 127.98, 127.53, 126.91, 126.80, 125.36, 121.84, 117.52, 112.95, 112.65, 76.60, 75.68, 61.67, 61.49, 60.08, 59.61, 55.04, 35.09, 34.15, 31.48, 31.43, 29.69, 29.53, 29.43, 13.99.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm), t_R (major diastereomer,) = 61.5min (major enantiomer); 15.2min (minor enantiomer).

ESI-HRMS: calcd for $C_{36}H_{43}N_3O_6SH^+$ ($[M+H]^+$) = 646.2945, Found 666.2967

(E)-ethyl 3-(4-chlorophenyl)-2-((3,5-di-tert-butyl-2-hydroxybenzylidene)-amino)-3-(quinoline-8-sulfonamido)propanoate 7l

Yellow oil; 91% yield; $[\alpha]_D^{20} = +0.19$ (c=1.2, in CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 12.76 (s, 1H), 12.66 (s, 0.3H), 9.08 (s, 0.3H), 8.68 (d, $J = 2.7$ Hz, 1H), 8.26 (s, 1H), 8.18 (d, $J = 7.2$ Hz, 1H), 8.15 (d, $J = 7.1$ Hz, 0.3H), 8.08 (dd, $J = 19.3, 11.0$ Hz, 1.5H), 7.88 (d, $J = 8.1$ Hz, 1.3H), 7.47 (dd, $J = 16.9, 9.1$ Hz, 2.9H), 7.41 – 7.33 (m, 1.4H), 7.04 (d, $J =$

2.2 Hz, 1.3H), 6.98 – 6.91 (m, 1.3H), 6.84 (d, $J = 8.5$ Hz, 0.6H), 6.79 – 6.71 (m, 2.5H), 6.65 (d, $J = 8.4$ Hz, 2H), 5.17 (dd, $J = 9.6, 5.5$ Hz, 1H), 4.46 (d, $J = 5.5$ Hz, 1H), 4.12 (d, $J = 4.8$ Hz, 0.3H), 4.09 – 4.00 (m, 2H), 4.00 – 3.92 (m, 0.6H), 1.50 (s, 3H), 1.44 (d, $J = 9.5$ Hz, 9H), 1.33 (s, 9H), 1.28 (s, 3H), 1.13 (dd, $J = 15.1, 8.0$ Hz, 4H).

^{13}C NMR (151 MHz, CDCl_3) δ 170.73, 168.37, 158.00, 150.84, 142.72, 140.56, 136.84, 136.67, 136.62, 133.92, 133.60, 132.93, 130.21, 129.66, 129.17, 128.79, 128.47, 128.25, 127.76, 127.33, 126.99, 125.41, 122.01, 117.43, 75.37, 61.85, 61.67, 59.39, 53.40, 35.10, 34.17, 31.47, 31.42, 29.69, 29.51, 29.42, 13.96.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 95/5-80/20, flow rate 1.0 mL/min, $\lambda = 254$ nm), t_R (major diastereomer,) = 60.9min (major enantiomer); 27.1min (minor enantiomer).

ESI-HRMS: calcd for $\text{C}_{36}\text{H}_{43}\text{N}_3\text{O}_6\text{SH}^+$ ($[\text{M}+\text{H}]^+$) = 649.2394, Found 649.2381

(E)-ethyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(quinoline-8-sulfonamido)-3-(o-tolyl)propanoate 7m

Yellow oil; 87% yield; $[\alpha]_D^{20} = +0.25$ (c=1.2, in CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 12.87 (s, 1H), 8.79 – 8.76 (m, 1H), 8.23 (d, $J = 7.3$ Hz, 1H), 8.05 (s, 1H), 8.01 – 7.98 (m, 1H), 7.79 (d, $J = 8.1$ Hz, 1H), 7.43 (dd, $J = 13.4, 5.5$ Hz, 1H), 7.37 (d, $J = 2.1$ Hz, 1H), 7.32 (dd, $J = 8.3, 4.2$ Hz, 1H), 6.96 (d, $J = 9.7$ Hz,

1H), 6.87 (dd, $J = 15.7, 5.0$ Hz, 2H), 6.65 – 6.53 (m, 2H), 6.43 (t, $J = 7.4$ Hz, 1H), 5.49 (dd, $J = 9.6, 7.4$ Hz, 1H), 4.39 (d, $J = 7.3$ Hz, 1H), 4.24 – 4.03 (m, 2H), 2.09 (s, 3H), 1.41 (s, 9H), 1.27 (s, 9H), 1.18 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.58, 168.99, 157.98, 151.17, 150.74, 142.74, 140.20, 136.80, 136.73, 136.42, 136.07, 134.65, 134.32, 132.90, 132.76, 131.38, 129.76, 129.69, 128.35, 127.90, 127.32, 126.70, 126.23, 125.20, 124.98, 121.82, 117.38, 77.22, 77.01, 76.80, 76.29, 61.63,

55.19, 35.04, 34.09, 31.43, 29.36, 19.25, 13.94.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm), t_R (major diastereomer,) = 42.9min (major enantiomer); 11.5min (minor enantiomer).

ESI-HRMS: calcd for $C_{36}H_{43}N_3O_5SH^+$ ($[M+H]^+$) = 630.2996, Found 630.3021

(E)-ethyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(quinoline-8-sulfonamido)-3-(thiophen-2-yl)propanoate

Yellow oil; 90% yield; $[\alpha]_D^{20} = +0.13$ ($c=1.0$, in CH_2Cl_2);

1H NMR (600 MHz, $CDCl_3$) δ 12.67 (s, 0.6H), 12.60 (s, 1H), 9.15 (d, $J = 2.6$ Hz, 0.6H), 8.71 – 8.58 (m, 1H), 8.29 (s, 1H), 8.22 (d, $J = 7.2$ Hz, 1H), 8.17 (s, 0.6H), 8.11 (dd, $J = 15.0$, 7.7 Hz, 1.2H), 8.05 (d, $J = 8.3$ Hz, 1H), 7.86 (d, $J = 8.2$ Hz, 1H), 7.82 (d, $J = 8.2$ Hz, 0.6H), 7.57 – 7.40 (m, 4.6H), 7.30 (dd, $J = 8.3$, 4.3 Hz, 1H), 7.11 – 6.95 (m, 2.7H), 6.69 (d, $J = 5.0$ Hz, 1H), 6.63 (d, $J = 5.0$ Hz, 0.6H), 6.54 (d, $J = 3.4$ Hz, 0.6H), 6.49 (d, $J = 3.4$ Hz, 1H), 6.41 – 6.26 (m, 1.6H), 5.74 – 5.65 (m, 0.6H), 5.58 (dd, $J = 9.8$, 4.6 Hz, 1H), 4.49 (d, $J = 4.6$ Hz, 1H), 4.27 – 4.16 (m, 1H), 4.12 (q, $J = 7.1$ Hz, 1.6H), 4.03 (dt, $J = 7.1$, 4.5 Hz, 2H), 1.53 (s, 5H), 1.49 (s, 9H), 1.34 (s, 9H), 1.28 (s, 5H), 1.08 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 171.82, 171.56, 168.44, 168.16, 157.99, 157.90, 151.54, 151.02, 142.79, 140.49, 138.98, 137.23, 136.86, 136.71, 136.48, 136.41, 132.84, 132.51, 129.87, 129.47, 128.39, 128.31, 128.23, 127.79, 127.29, 127.00, 125.64, 125.42, 125.27, 125.20, 125.15, 121.91, 121.87, 117.54, 75.85, 75.42, 62.05, 61.59, 60.38, 56.14, 55.74, 35.14, 34.18, 34.13, 31.49, 31.42, 29.69, 29.54, 29.50, 14.19, 14.11, 13.90.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm), t_R (major diastereomer,) = 36.8min (major enantiomer); 12.0min (minor enantiomer).

ESI-HRMS: calcd for $C_{33}H_{39}N_3O_5S_2H^+$ ($[M+H]^+$) = 622.2444, Found 622.2433

(E)-ethyl 2-((3,5-di-tert-butyl-2-hydroxybenzylidene)amino)-3-(naphthalen-1-yl)-3-

(quinoline-8-sulfonamido)propanoate (7o)

7o

Yellow oil; 82% yield; $[\alpha]_D^{20} = +0.17$ ($c=0.9$, in CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 12.83 (s, 1H), 8.59 (s, 1H), 8.14 (s, 1H), 8.05 (d, $J = 7.3$ Hz, 1H), 7.97 (d, $J = 8.5$ Hz, 1H), 7.83 (d, $J = 8.2$ Hz, 1H), 7.58 (d, $J = 8.1$ Hz, 1H), 7.50 (d, $J = 8.1$ Hz, 1H), 7.35 (dd, $J = 10.0, 5.2$ Hz, 2H), 7.29 (t, $J = 7.7$ Hz, 2H), 7.21 (s, 1H), 7.19 – 7.13 (m, 2H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.89 (s, 1H), 6.81 (t, $J = 7.7$ Hz, 1H), 6.04 (s, 1H), 4.68 (d, $J = 6.5$ Hz, 1H), 4.08 – 3.83 (m, 2H), 1.39 (s, 9H), 1.28 (s, 9H), 1.03 (d, $J = 6.6$ Hz, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.80, 168.87, 157.98, 150.50, 142.46, 140.17, 136.68, 136.30, 136.09, 133.05, 132.68, 130.16, 128.29, 128.24, 128.04, 127.89, 126.76, 126.21, 125.28, 124.93, 124.11, 122.84, 121.56, 117.36, 75.63, 61.59, 35.02, 34.09, 31.44, 29.69, 29.36, 13.80.

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 254$ nm), t_R (major diastereomer,) = 37.8min (major enantiomer); 11.1min (minor enantiomer).

ESI-HRMS: calcd for $\text{C}_{39}\text{H}_{43}\text{N}_3\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}^+]$) = 666.2996, Found 666.3014

6. Determination of absolute configuration for Mannich main adducts

Scheme S10. Determination of absolute configuration

According to the above procedure, afford **7p**, light yellow oil; 80% yield; Saturated HCl solution of AcOMe (6 ml) was added slowly to a stirred solution of **7p** (1 g, 1.5 mmol) in CH_2Cl_2 (10 ml) at 0°C. The solution was stirred for 2h at 0°C and warmed to room temperature and was stirred for another 5 h. After that, the obtained solution was dried and evaporated to afford crude product **8a** as yellow solid. Crude solid **8a** (0.40 g), benzophenone imine and 10 ml CH_2Cl_2 , were stirred at room temperature for 20 h with the exclusion of moisture (CaCl_2 tube). The reaction mixture was filtered to remove NH_4Cl and evaporated. The residue was purified by flash chromatography on silica gel to afford **9a** (140 mg, 42% yield in two steps) as white solid, matching the previously published characterization data^[9].

7p

7p, Yellow oil, 80% yield, ^1H NMR (600 MHz, CDCl_3) δ 12.78 (s, 1H), 12.59 (s, 1H), 8.20 (s, 1H), 8.00 (s,

1H), 7.57 (t, $J = 9.1$ Hz, 3H), 7.43 (s, 2H), 7.22 – 7.14 (m, 5H), 7.09 (d, $J = 7.3$ Hz, 7H), 7.03 (d, $J = 2.1$ Hz, 1H), 6.92 (d, $J = 2.1$ Hz, 1H), 5.64 (d, $J = 7.6$ Hz, 1H), 5.37 (s, 1H), 5.03 (s, 1H), 5.01 – 4.92 (m, 1H), 4.40 (d, $J = 5.2$ Hz, 1H), 4.20 (d, $J = 4.7$ Hz, 1H), 3.61 (s, 3H), 3.59 (s, 2H), 2.32 (s, 2H), 2.30 (s, 3H), 1.45 (s, 6H), 1.44 (s, 9H), 1.30 (s, 10H), 1.29 – 1.24 (m, 7H).

^{13}C NMR (151 MHz, CDCl_3) δ 170.74, 170.29, 169.39, 158.03, 157.90, 143.34, 143.16, 140.48, 137.39, 136.96, 136.34, 129.45, 129.33, 128.45, 128.39, 128.20, 127.93, 127.46, 127.26, 127.12, 126.78, 126.71, 123.07, 117.49, 75.99, 75.42, 59.90, 59.66, 52.60, 52.45, 35.09, 34.14, 31.45, 31.40, 29.43, 29.40, 21.43.

ESI-HRMS: calcd for $\text{C}_{32}\text{H}_{40}\text{N}_2\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}]^+$) = 565.2731, Found 565.2714

The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 254$ nm), t_R (major diastereomer,) = 33.8min (major enantiomer); 37.0 min (minor enantiomer). major diastereomer (ee = 29)/ minor diastereomer (ee = 42) = 1.7:1,

Product **9a** Match the previously published characterization data. The ee and dr value was determined by HPLC analysis using a Chiralpak AD-H (Hexane/ *i*-PrOH = 93/7, flow rate 1 mL/min, $\lambda = 254$ nm), $t_R = 21.5$ min (**(2R,3S)**-isomer, 35.2 min (**(2R,3R)**-isomer, 43.7 min (**(2S,3S)**-isomer, 48.0 min (**(2S,3R)**-isomer, ESI-HRMS: calcd for $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_5\text{SH}^+$ ($[\text{M}+\text{H}]^+$) = 513.1843, Found 513.1868 and $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_5\text{SNa}^+$ ($[\text{M}+\text{Na}]^+$) = 535.1662, Found 535.1684; Major diastereomer (ee = 26) / minor diastereomer (ee = 43) = 1.1:1. Therefore, the ee of major diastereomer is in accord with **9a**. Then, according to the literature of Shin-ichi Fukuzawa and co-workers^[9], compared (**(2S,3S)**)-methyl 2-((diphenylmethylene)amino)-3-(4-methylphenylsulfonamido)-3-phenylpropanoate with other isomer, the absolute configuration of this mainly Mannich product is (**(2S,3S)**) .

7. NMR spectra

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