Supporting Information

Highly Enantioselective Ir/f-amphox-Catalyzed Hydrogenation of Ketoamides: Efficient Access to Chiral Hydroxy Amides

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1. General remarks

All reactions and manipulations which are sensitive to moisture or air were performed in an argon-filled glovebox or using standard Schlenk techniques. Hydrogen gas (99.999%) was purchased from Shanghai Regulator Factory Co., Ltd. Anhydrous *i*-PrOH, EtOH, MeOH, DCM, EtOAc, toluene and CHCl₃ were purchased from J&K. Anhydrous THF, 1,4-dioxane was distilled from sodium benzophenone ketyl. Anhydrous ClCH₂CH₂Cl were freshly distilled from calcium hydride. K₂CO₃, Cs₂CO₃, KOH, MeOK, t-BuONa and t-BuOK were purchased from J&K. [Ir(COD)Cl]₂ was prepared according to the literature.¹⁻² ¹H, ¹³C and ³¹P NMR spectra were recorded with a Bruker ADVANCE III (400 MHz) spectrometer with CDCl₃ as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in parts per million (ppm, δ scale) downfield from TMS at 0.00 ppm and referenced to the CDCl₃ at 7.26 ppm (for ¹H NMR) or 77.0 ppm (for ¹³C NMR). Data are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz) and signal area integration in natural numbers. ¹³C NMR and ³¹P NMR analyses were run with decoupling. Optical rotations $[\alpha]_D$ were determined using a PERKIN ELMER polarimeter 343 instrument. HPLC analyses were performed using Daicel chiral column. A single crystal of (R)-2i was grown from its solution in ethyl acetate, which is suitable for X-ray diffraction analysis. The structure showed that the absolute configuration of 2i is (R). The absolute configuration of other hydrogenation products were assigned by analogy. The absolute configuration of products 2m and 2n were assigned by the comparison of optical rotation datas according to literature.³⁻⁴

2. General procedure for the preparation of substrate compounds



Scheme S1. General procedure for the preparation of substrates route 1. 5-6

Step 1:

Under a nitrogen atmosphere, a mixture of anhydrous aluminum chloride (8.0 g, 60 mmol) in anhydrous dichloromethane (50 mL) was stirred and cooled to -10 °C. A solution of glutaric anhydride (4.8 g, 42 mmol) and substituted benzene (**SM-1**, 40 mmol) was added dropwise to the cooled mixture with stirring. After 5h at -10 °C, the reaction mixture was poured into ice-cooled 3.5 M HCl (100 mL), and the product was extracted into dichloromethane. The extract was washed with cold saturated aqueous sodium carbonate, and the aqueous layers were acidified and extracted with dichloromethane. The extract was washed with brine, dried over anhydrous sodium sulfate and evaporated in vacuo without further purification to give **SM-2** as white crystal.

Step 2:

SM-2 (20 mmol) and aniline (1.95 g, 21 mmol) were resolved in 100 mL dry dichloromethane and cooled in ice-water bath protected by N₂ flushed, then 1-ethy-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC HCl) (4.01 g, 21 mmol) and 4-dimethylaminopyridine (4-DMAP) (0.244 g, 2 mmol) were added; Ice-water bath was removed after adding. The mixture was stirred overnight. Wash the mixture with 1% HCl aqueous solution (x 3), saturated brine (x 1), 1 M NaHCO₃ (x 3) and saturated brine (x 1) respectively. The crude product was chromatographed on silica gel by 0-10% Ethyl acetate (EA) in DCM as eluent.

5-oxo-N,5-diphenylpentanamide (1a)



¹H NMR (400 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 7.5 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 3H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 3.18 (t, *J* = 6.7 Hz, 2H), 2.53 (t, *J* = 7.1 Hz, 2H), 2.25-2.20 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 200.26, 170.99, 137.99, 136.63, 133.33, 129.01, 128.70, 128.14, 124.22, 119.84, 37.31, 36.49, 20.13.

5-oxo-N-phenyl-5-(p-tolyl)pentanamide (1d)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, J = 8.2 Hz, 2H), 7.58 (s, 1H), 7.53 (d, J = 7.8 Hz, 2H), 7.32 (t, J = 7.9 Hz, 2H), 7.27-7.25 (m, 2H), 7.10 (t, J = 7.4 Hz, 1H), 3.10 (t, J = 6.7 Hz, 2H), 2.47 (t, J = 7.1 Hz, 2H), 2.41 (s, 3H), 2.21-2.14 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 199.94, 170.92, 144.18, 137.96, 134.17, 129.38, 129.01, 128.28, 124.20, 119.76, 37.11, 36.60, 21.70, 20.28.

5-(4-methoxyphenyl)-5-oxo-N-phenylpentanamide (1g)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, J = 8.9 Hz, 2H), 7.62 (s, 1H), 7.54 (d, J = 7.8 Hz, 2H), 7.32 (t, J = 7.9 Hz, 2H), 7.10 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H), 3.08 (t, J = 6.7 Hz, 2H), 2.47 (t, J = 7.1 Hz, 2H), 2.20-2.13 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 198.89, 170.98, 163.65, 138.00, 130.48, 129.72, 129.01, 124.18, 119.76, 113.82, 55.53, 36.86, 36.62, 20.45.

5-(4-fluorophenyl)-5-oxo-N-phenylpentanamide (1h)

¹H NMR (400 MHz, Chloroform-*d*) δ 8.09-7.91 (m, 2H), 7.56-7.52 (m, 3H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.13 (t, *J* = 8.7 Hz, 3H), 3.10 (t, *J* = 6.8 Hz, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.20-2.13 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 198.57, 170.87, 165.85 (d, *J* = 255.1 Hz), 137.91, 133.07 (d, *J* = 3.0 Hz), 130.80 (d, *J* = 9.4 Hz), 129.03, 124.29, 119.82, 115.79 (d, *J* = 21.9 Hz), 37.24, 36.38, 20.06.

5-(4-chlorophenyl)-5-oxo-N-phenylpentanamide (1i)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 8.6 Hz, 2H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 3H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 1H),

3.11 (t, J = 6.8 Hz, 2H), 2.49 (t, J = 7.0 Hz, 2H), 2.20-2.14 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 198.90, 170.75, 139.74, 137.86, 134.95, 129.56, 129.04, 129.01, 124.30, 119.78, 37.28, 36.35, 19.97.

5-oxo-N-phenyl-5-(thiophen-2-yl)pentanamide (1k)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 3.2 Hz, 1H), 7.65 (d, *J* = 4.9 Hz, 1H), 7.58 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.16-7.08 (m, 3H), 3.07 (t, *J* = 6.8 Hz, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.22-2.15 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 193.35, 170.91, 143.99, 138.01, 134.02, 132.46, 128.99, 128.33, 124.21, 119.86, 37.93, 36.32, 20.55.

4-oxo-N,4-diphenylbutanamide (10)



¹H NMR (400 MHz, Chloroform-*d*) δ 8.00 (d, J = 7.2 Hz, 2H), 7.84 (s, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.52 (d, J = 7.9 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.9 Hz, 2H), 7.08 (t, J = 7.4 Hz, 1H), 3.46 (t, J = 6.4 Hz, 2H), 2.82 (t, J = 6.4 Hz, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 199.34, 170.52, 138.02, 136.36, 133.51, 128.96, 128.71, 128.16, 124.14, 119.78, 34.12, 31.40.

Scheme S2. General procedure for the preparation of substrates route 2. 6-7



Step 1:

1) A three-necked round bottom flask equipped with condenser was flame dried and cooled to room temperature. Into this flask was placed (1.46 g, 60 mmol) magnesium turnings, anhydrous THF (40 mL) and a chip of iodine. The mixture was heated to 70 $^{\circ}$ C, then started to add the anhydrous THF solution of substituted bromophenyl (**SM-3**, 20 mmol) dropwise. When the solution in the flask started to bubble and the colour of iodine started to fade, the flask was moved out of the oil bath and kept dropping. The mixture was heated to 70 $\,^{\circ}$ C and kept 2h. The solution was then cooled to room temperature and used directly.

2) To the solution of glutaric anhydride (2.4 g, 21 mmol) in THF under a N₂ atmosphere **SM-4** was added dropwise the corresponding Grignard reagent at 0 °C. The solution was warmed to room temperature and stirred for a further 3 hours. The reaction was quenched with 10% HCl, and THF was removed under vacuum. The resulting aqueous solution was extracted with DCM. The combined organic layers were washed with brine, dried (Na₂SO₄) and evaporated under vacuum to give a white solid as a crude product **SM-4**.

Step 2:

SM-4 (20 mmol) and aniline (1.95 g, 21 mmol) were resolved in 100 mL dry dichloromethane and cooled in ice-water bath protected by N₂ flushed, then 1-ethy-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC HCl) (4.01 g, 21 mmol) and 4-dimethylaminopyridine (4-DMAP) (0.244 g, 2 mmol) were added; Ice-water bath was removed after adding. The mixture was stirred overnight. Wash the mixture with 1% HCl aqueous solution (x 3), saturated brine (x 1), 1 M NaHCO₃ (x 3) and saturated brine (x 1) respectively. The crude product was chromatographed on silica gel by 0-10% Ethyl acetate (EA) in DCM as eluent.

5-oxo-N-phenyl-5-(o-tolyl)pentanamide (1b)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 7.5 Hz, 1H), 7.64 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.25 (t, *J* = 6.9 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.04 (t, *J* = 6.8 Hz, 2H), 2.50 (s, 3H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.18-2.11 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 204.20, 170.91, 138.19, 137.94, 137.55, 132.08, 131.55, 129.02, 128.70, 125.83, 124.24, 119.81, 40.11, 36.59, 21.50, 20.28.

5-oxo-N-phenyl-5-(m-tolyl)pentanamide (1c)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.78 (s, 1H), 7.76 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 3H), 7.41-7.29 (m, 4H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.12 (t, *J* = 6.7 Hz, 2H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 2.21-2.14 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 200.49, 170.92, 138.51, 137.96, 136.68, 134.10, 129.02, 128.66, 128.58, 125.37, 124.21, 119.77, 37.28, 36.55, 21.39, 20.19.

5-(2-methoxyphenyl)-5-oxo-N-phenylpentanamide (1e)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, J = 7.7 Hz, 1H), 7.54 (d, J = 7.8 Hz, 2H), 7.47 (t, J = 7.8 Hz, 1H), 7.31 (t, J = 7.9 Hz, 2H), 7.09 (t, J = 7.4 Hz, 1H), 7.00 (dd, J = 11.0, 4.0 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 3.12 (t, J = 6.7 Hz, 2H), 2.45 (t, J = 7.3 Hz, 2H), 2.17-2.10 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 202.66, 171.22, 158.69, 138.09, 133.76, 130.27, 128.98, 128.00, 124.09, 120.68, 119.72, 111.61, 55.53, 42.38, 36.88, 20.40.

5-(3-methoxyphenyl)-5-oxo-N-phenylpentanamide (1f)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.57-7.48 (m, 5H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.14 – 7.08 (m, 2H), 3.85 (s, 3H), 3.12 (t, *J* = 6.7 Hz, 2H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.21-2.14 (m, *J* = 6.9 Hz, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 200.07, 170.94, 159.86, 138.00, 137.98, 129.71, 129.01, 124.22, 120.83, 119.81, 119.78, 112.26, 55.46, 37.42, 36.47, 20.19.

5-(naphthalen-2-yl)-5-oxo-N-phenylpentanamide (1j)



¹H NMR (400 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 8.04 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.88 (t, *J* = 8.2 Hz, 2H), 7.61 (t, *J* = 6.9 Hz, 1H), 7.55 (t, *J* = 6.9

Hz, 4H), 7.32 (t, J = 7.9 Hz, 2H), 7.10 (t, J = 7.4 Hz, 1H), 3.28 (q, J = 6.7 Hz, 2H), 2.53 (t, J = 7.1 Hz, 2H), 2.28-2.21 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 200.17, 170.89, 137.94, 135.67, 133.97, 132.52, 130.00, 129.65, 129.04, 128.61, 128.57, 127.80, 126.87, 124.25, 123.75, 119.76, 37.28, 36.57, 20.30

5-cyclohexyl-5-hydroxy-N-phenylpentanamide (11)



¹H NMR (400 MHz, Chloroform-*d*) δ 7.58 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 2.59 (t, *J* = 6.8 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 2.03-1.95 (m, 2H), 1.87-1.74 (m, 5H), 1.44-1.11 (m, 6H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 214.43, 170.91, 137.95, 129.01, 124.19, 119.73, 50.89, 39.21, 36.58, 33.97, 28.50, 25.81, 25.63, 24.96, 19.61.





Step 1:

A mixture of acetophenone **SM-5** (4.8 g, 40 mmol) and selenium dioxide (6.7 g, 60 mmol) in dry pyridine (20 mL) was stirred at 100 °C under nitrogen atmosphere for 15 h and then cooled in an ice bath. After the disappearance of acetophenone **SM-5** detected by TLC, the mixture was filtrated and removing the organic solvent by evaporation. Then 2 M sodium hydroxide solution was added to the residue and some ethyl acetate followed. Subsequently 36–38% concentrated hydrochloric acid was put into the mixture dropwise and α -keto acid **SM-6** was separated out as a pale yellow oil in 78% yield.

Step 2:

SM-6 (20 mmol) and aniline (1.94 g, 21 mmol) were resolved in 100 mL dry dichloromethane and cooled in ice-water bath protected by N_2 flushed, then 1-ethy-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC HCl) (4.01 g, 21 mmol)

and 4-dimethylaminopyridine (4-DMAP) (0.244 g, 2 mmol) were added; Ice-water bath was removed after adding. The mixture was stirred overnight. Wash the mixture with 1% HCl aqueous solution (x 3), saturated brine (x 1), 1 M NaHCO₃ (x 3) and saturated brine (x 1) respectively. The crude product was chromatographed on silica gel by 0-10% Ethyl acetate (EA) in DCM as eluent.

2-oxo-N,2-diphenylacetamide (1m)

O H O N

¹H NMR (400 MHz, Chloroform-*d*) δ 8.95 (s, 1H), 8.42 (d, *J* = 7.2 Hz, 2H), 7.71 (d, *J* = 7.7 Hz, 2H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 187.46, 158.88, 136.64, 134.70, 133.08, 131.51, 129.28, 128.61, 125.35, 119.95.

Scheme S4. General procedure for the preparation of substrates route 4. 6,9



Step 1:

A 250 mL round-bottom flask was equipped with a magnetic stir bar and charged with ethyl 3-oxo-3-phenylpropanoate **SM-7** (80 mmol, 14 mL) and 80 mL NaOH (1 M) solution. After stirring overnight, the solution was poured into a separatory funnel and washed four times with 10 mL of DCM each. The aqueous layer was cooled in an ice bath and a 3 M solution of HCl was added until the solution was around pH \approx 1. The 3-oxo-3-phenylpropanoic acid **SM-8** was obtained, which was used immediately without further purification. White solid, 62% yield (8.0 g).

Step 2:

SM-8 (20 mmol) and aniline (1.94 g, 21 mmol) were resolved in 100 mL dry dichloromethane and cooled in ice-water bath protected by N_2 flushed, then 1-ethy-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC HCl) (4.01 g, 21 mmol) and 4-dimethylaminopyridine (4-DMAP) (0.244 g, 2 mmol) were added; Ice-water bath was removed after adding. The mixture was stirred overnight. Wash the mixture

with 1% HCl aqueous solution (x 3), saturated brine (x 1), 1 M NaHCO₃ (x 3) and saturated brine (x 1) respectively. The crude product was chromatographed on silica gel by 0-10% Ethyl acetate (EA) in DCM as eluent.

3-oxo-N,3-diphenylpropanamide (1n)



¹H NMR (400 MHz, Chloroform-*d*) δ 9.32 (s, 1H), 8.05 (d, *J* = 7.3 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.9 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 4.13 (s, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 196.49, 163.90, 137.57, 136.02, 134.42, 129.03, 129.01, 128.64, 124.61, 120.22, 45.55.

3. Asymmetric hydrogenation of ketoamides

$$R \xrightarrow{O}_{H} N \xrightarrow{Ph}_{H} Ph \xrightarrow{[Ir(COD)CI]_2/f-amphox L5}_{H_2 (40 atm), KOH (4 mol%)} OH O$$

$$R \xrightarrow{O}_{H} N \xrightarrow{Ph}_{H} Ph$$

$$R \xrightarrow{O}_{H} N \xrightarrow{Ph}_{H} Ph$$

$$R \xrightarrow{O}_{H} N \xrightarrow{Ph}_{H} Ph$$

General procedure (S/C = 10 000): To a 4.0 mL vial was added the catalyst precursor [Ir(COD)Cl]₂ (1.4 mg, 2.0×10^{-3} mmol), ligand L5 (2.4 mg, 4.2×10^{-3} mmol) and anhydrous ^{*i*}PrOH (2.0 mL) in the argon-filled glovebox. The mixture was stirred for 2.0 h at room temperature giving orange red solution. And then 0.2 mmol ketoamides, KOH (4 mol%) were added into a 5 mL hydrogenation vessel. 1.0 mL anhydrous ^{*i*}PrOH was added as solvent and a solution of Ir/f-amphox L5 in anhydrous ^{*i*}PrOH (10.0 µL) was added via an injection port. Then the vessel was placed in an autoclave, closed it and moved it out from golvebox. The autoclave quickly purged with hydrogen gas for three times, then pressurized to 40 atm H₂. The reaction solution was stirred at room temperature was purified by a flash chromatography on a silical gel with ethyl acetate and the solvent was removed under reduced pressure. The ee value was determined by chiral HPLC analysis of the chiral amino alcohol directly.

Asymmetric hydrogenation of 5-(4-fluorophenyl)-5-oxo-N-phenylpentanamide (1h) at S/C = 50 000:



To a 4.0 mL vial was added the catalyst precursor [Ir(COD)Cl]₂ (1.4 mg, 2.0×10^{-3} mmol), ligand f-amphox **L5** (2.4 mg, 4.2×10^{-3} mmol) and anhydrous ¹PrOH (2.0 mL) in the argon-filled glovebox. The mixture was stirred for 2.0 h at 25 °C giving orange red solution. 5-(4-fluorophenyl)-5-oxo-N-phenylpentanamide (**1h**) (1 mmol, 286 mg) and KOH (0.02 mmol, 1.1 mg) were added into a 5 mL hydrogenation vessel. 1.0 mL anhydrous ¹PrOH was added as solvent and a solution of Ir/f-amphox **L5** in anhydrous ¹PrOH (10 µL, 2.0×10^{-3} mol/L) was added via an injection port. Then the vessel was placed in an autoclave, closed it and moved it out from golvebox. The autoclave was quickly purged with hydrogen gas for three times, then pressurized to 80 atm H₂. The reaction solution was stirred at room temperature (25 °C-30 °C) until for 36 h, then released pressure carefully. The solvent of the reaction mixture was removed under reduced pressure and the residue was purified by a flash chromatography on a silical gel with ethyl acetate as eluent to afford the chiral (*R*)-5-(4-fluorophenyl)-5-hydroxy-N-phenylpentanamide (**2h**), >99% conversion, >99% ee.

(*R*)-5-hydroxy-N,5-diphenylpentanamide (2a)



White solid, $[\alpha]_D^{20} = 25.7$ (c = 1.0, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 85:15; flow 1.0 mL/min; t_R (major) = 13.9 min, t_R (minor) = 12.3 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.53 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.33 (d, *J* = 4.4 Hz, 4H), 7.32-7.26 (m, 3H), 7.09 (t, *J* = 7.4 Hz, 1H), 4.72 (s, 1H), 2.55 (d, *J* = 2.2 Hz, 1H), 2.39 (t, *J* = 6.7 Hz, 2H), 1.91-1.75 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.31, 144.52, 137.88, 129.02, 128.56, 127.66, 125.80, 124.25, 119.79, 74.33, 38.14, 37.26, 21.91.

(R)-5-hydroxy-N-phenyl-5-(o-tolyl)pentanamide (2b)



White solid, $[\alpha]_D^{20} = 39.4$ (c = 1.0, CHCl₃), >99% conversion, 95% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 90:10; flow 1.0 mL/min; t_R (major) = 21.2 min, t_R (minor) = 22.5 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.52-7.46 (m, 4H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.17 (t, *J* = 6.6 Hz, 1H), 7.14-7.08 (m, 2H), 5.00 (s, 1H), 2.46-2.42 (m, 2H), 2.33 (s, 3H), 2.24 (s, 1H), 2.00-1.76 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.28, 142.68, 137.89, 134.27, 130.47, 129.03, 127.31, 126.38, 125.06, 124.25, 119.77, 70.60, 37.30, 36.94, 22.21, 19.10.

(*R*)-5-hydroxy-N-phenyl-5-(m-tolyl)pentanamide (2c)



White solid, $[\alpha]_D^{20} = 16.3$ (c = 1.0, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 85:15; flow 1.0 mL/min; t_R (major) = 13.8 min, t_R (minor) = 10.7 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.52 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.17-7.05 (m, 4H), 4.69 (s, 1H), 2.46 (s, 1H), 2.40 (t, *J* = 6.8 Hz, 2H), 2.34 (s, 3H), 1.87-1.75 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.39, 144.47, 138.17, 137.89, 128.96, 128.40, 128.34, 126.46, 124.19, 122.81, 119.78, 74.29, 38.09, 37.22, 21.96, 21.46.

(R)-5-hydroxy-N-phenyl-5-(p-tolyl)pentanamide (2d)

White solid, $[\alpha]_D^{20} = 19.9$ (c = 1.0, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AS-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 90:10; flow 1.0 mL/min; t_R (major) = 20.1 min, t_R (minor) = 22.4 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.53 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.22 (t, *J* = 7.9 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 7.01 (t, *J* = 7.4 Hz, 1H), 4.61 (t, *J* = 5.8 Hz, 1H), 2.47 (s, 1H), 2.31 (t, *J* = 6.5 Hz, 2H), 2.26 (s,

3H), 1.85-1.61 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.42, 141.49, 137.88, 137.25, 129.15, 128.92, 125.70, 124.15, 119.78, 74.09, 38.02, 37.19, 21.95, 21.08.

(R)-5-hydroxy-5-(2-methoxyphenyl)-N-phenylpentanamide (2e)

White solid, $[\alpha]_D^{20} = 17.9$ (c = 2.5, CHCl₃), >99% conversion, 88% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20°C, *n*-hexane: *i*-PrOH = 90:10; flow 1.0 mL/min; t_R (minor) = 44.2 min, t_R (major) = 56.1 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.64 (s, 1H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.36-7.27 (m, 3H), 7.24-7.22 (m, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 4.95 (d, *J* = 4.9 Hz, 1H), 3.82 (s, 3H), 2.92 (d, *J* = 5.5 Hz, 1H), 2.44-2.40 (m, 2H), 1.92-1.80 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.56, 156.36, 138.05, 132.21, 128.97, 128.43, 126.76, 124.13, 120.84, 119.81, 110.51, 70.40, 55.31, 37.38, 36.15, 22.36.

(R)-5-hydroxy-5-(3-methoxyphenyl)-N-phenylpentanamide(2f)



White solid, $[\alpha]_D^{20} = 20.1$ (c = 1.0, CHCl₃), >99% conversion, 98% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 90:10; flow 1.0 mL/min; t_R (major) = 43.4 min, t_R (minor) = 35.1 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.29 (t, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.95-6.85 (m, 2H), 6.81-6.79 (m, 1H), 4.69 (s, 1H), 3.78 (s, 3H), 2.70 (s, 1H), 2.38 (t, *J* = 6.7 Hz, 2H), 1.88-1.75 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.47, 159.75, 146.32, 137.91, 129.56, 129.00, 124.24, 119.84, 118.13, 112.97, 111.29, 74.15, 55.25, 38.11, 37.20, 21.91.

(R)-5-hydroxy-5-(4-methoxyphenyl)-N-phenylpentanamide (2g)



White solid, $[\alpha]_D^{20} = 76.0$ (c = 0.2, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AS-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 90:10; flow 1.0 mL/min; t_R (major) = 40.2 min, t_R (minor) = 60.6 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.06 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.28-7.16 (m, 4H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.87-6.75 (m, 2H), 4.58 (t, *J* = 5.8 Hz, 1H), 3.74 (s, 3H), 3.20 (s, 1H), 2.33-2.30 (m, 2H), 1.86-1.60 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.92, 158.92, 138.07, 136.75, 128.93, 127.11, 124.19, 120.00, 113.81, 73.71, 55.30, 38.12, 37.10, 22.06.

(R)-5-(4-fluorophenyl)-5-hydroxy-N-phenylpentanamide (2h)



White solid, $[\alpha]_D^{20} = 25.1$ (c = 1.0, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 85:15; flow 0.5 mL/min; t_R (major) = 21.8 min, t_R (minor) = 20.3 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.68 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.32-7.27 (m, 3H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 8.7 Hz, 2H), 4.68 (t, *J* = 5.6 Hz, 1H), 2.96 (s, 1H), 2.38 (t, *J* = 6.5 Hz, 2H), 1.90-1.70 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.52, 162.12 (d, *J* = 245.3 Hz), 140.34 (d, *J* = 3.1 Hz), 137.86, 129.01, 127.43 (d, *J* = 8.0 Hz), 124.33, 119.89, 115.27 (d, *J* = 21.3 Hz), 73.48, 38.31, 37.06, 21.78.

(R)-5-(4-chlorophenyl)-5-hydroxy-N-phenylpentanamide (2i)



White solid, $[\alpha]_D^{20} = 46.4$ (c = 0.25, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AS-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 95:5; flow 1.0 mL/min; t_R (major) = 72.5 min, t_R (minor) = 80.9 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 7.8 Hz, 2H), 7.37 (s, 1H), 7.30-7.20 (m, 6H), 7.03 (t, *J* = 7.4 Hz, 1H), 4.64 (t, *J* = 5.7 Hz, 1H), 2.61 (s, 1H), 2.34 (t, *J* = 6.6 Hz, 2H), 1.83-1.65 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.22,

142.98, 137.73, 133.10, 128.99, 128.57, 127.14, 124.30, 119.76, 73.42, 38.19, 37.01, 21.56.

(R)-5-hydroxy-5-(naphthalen-2-yl)-N-phenylpentanamide (2j)



White solid, $[\alpha]_D^{20} = 24.4$ (c = 0.8, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AS-H column, 220 nm, 20°C, *n*-hexane: *i*-PrOH = 95:5; flow 1.0 mL/min; t_R (major) = 29.4 min, t_R (minor) = 34.3 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.85-7.76 (m, 4H), 7.52-7.42 (m, 5H), 7.39 (s, 1H), 7.29 (t, *J* = 7.9 Hz, 4H), 7.09 (t, *J* = 7.4 Hz, 1H), 4.92-4.86 (m, 1H), 2.56 (s, 1H), 2.41 (t, *J* = 6.7 Hz, 2H), 1.97-1.80 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.27, 141.87, 137.85, 133.26, 132.98, 129.02, 128.40, 127.97, 127.71, 126.23, 125.90, 124.51, 124.26, 123.97, 119.78, 74.41, 38.02, 37.25, 21.87.

(R)-5-hydroxy-N-phenyl-5-(thiophen-2-yl)pentanamide (2k)



White solid, $[\alpha]_D^{20} = 12.6$ (c = 0.9, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel OD-H column, 254 nm, 20°C, *n*-hexane: *i*-PrOH = 90:10; flow 1.0 mL/min; t_R (major) = 37.7 min, t_R (minor) = 34.8 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 7.8 Hz, 2H), 7.34 (s, 1H), 7.33-7.29 (m, 2H), 7.26-7.24 (m, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.98-6.95 (m, 2H), 5.03-4.95 (m, 1H), 2.54 (d, *J* = 3.8 Hz, 1H), 2.44 (t, *J* = 6.9 Hz, 2H), 2.04-1.77 (m, 4H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.23, 148.49, 137.83, 129.03, 126.73, 124.60, 124.31, 123.74, 119.84, 70.03, 38.40, 37.06, 21.72.

(R)-5-cyclohexyl-5-hydroxy-N-phenylpentanamide (2l)



White solid, $[\alpha]_D^{20} = 1.4$ (c = 1.6, CHCl₃), >99% conversion, 77% ee. The enantiomeric excess was determined by HPLC on Chiracel OD-H column, 254 nm, 20

°C, *n*-hexane: *i*-PrOH = 95:5; flow 0.7 mL/min; t_R (major) = 42.4 min, t_R (minor) = 47.1 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.58-7.49 (m, 3H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.41 (s, 1H), 2.45-2.41 (m, 2H), 1.94-1.80 (m, 3H), 1.80-1.73 (m, 3H), 1.67-1.50 (m, 3H), 1.38-0.96 (m, 7H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.61, 138.02, 128.99, 124.16, 119.80, 76.05, 43.79, 37.41, 32.96, 29.17, 27.86, 26.50, 26.30, 26.15, 22.15.

(S)-2-hydroxy-N,2-diphenylacetamide (2m)

White solid, $[\alpha]_D^{20} = 17.8$ (c = 0.9, acetone), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel OJ-H column, 220 nm, 20°C, *n*-hexane: *i*-PrOH = 85:15; flow 1.0 mL/min; t_R (major) = 16.0 min, t_R (minor) = 14.1 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.43 – 7.35 (m, 3H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 5.17 (d, *J* = 2.9 Hz, 1H), 3.50 (d, *J* = 3.2 Hz, 1H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 170.04, 139.00, 137.05, 129.09, 129.00, 128.91, 126.90, 124.75, 119.82, 74.67.

(R)-3-hydroxy-N,3-diphenylpropanamide (2n)



White solid, $[\alpha]_D^{20} = 8.8$ (c = 0.5, MeOH), 23% conversion, 90% ee. The enantiomeric excess was determined by HPLC on Chiracel OD-H column, 254 nm, 20 °C, *n*-hexane: *i*-PrOH = 95:5; flow 0.5 mL/min; t_R (major) = 85.9 min, t_R (minor) = 82.5 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.40-7.34 (m, 7H), 7.13 (t, *J* = 7.4 Hz, 1H), 5.22 (d, *J* = 9.4 Hz, 1H), 3.58 (d, *J* = 2.8 Hz, 1H), 2.84-2.69 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 169.80, 142.72, 137.42, 129.05, 128.71, 127.99, 125.58, 124.60, 120.09, 71.04, 46.02.

(R)-4-hydroxy-N,4-diphenylbutanamide (20)



White solid, $[\alpha]_D^{20} = 61.5$ (c = 1.0, CHCl₃), >99% conversion, >99% ee. The enantiomeric excess was determined by HPLC on Chiracel AD-H column, 220 nm, 20 °C, *n*-hexane: *i*-PrOH = 90:10; flow 0.5 mL/min; t_R (major) = 33.7 min, t_R (minor) = 30.0 min. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.01 (s, 1H), 7.46 (d, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 4.4 Hz, 4H), 7.29-7.22 (m, 3H), 7.08 (t, *J* = 7.4 Hz, 1H), 4.76 (s, 1H), 3.81 (s, 1H), 2.47-2.43 (m, 2H), 2.10-2.04 (m, 2H). ¹³C NMR (100 MHz, Chloroform-*d*) δ 171.90, 144.17, 137.80, 129.02, 128.53, 127.60, 125.75, 124.41, 120.00, 73.60, 34.20, 33.96.

4. NMR spectra of substrate compounds

5-oxo-N,5-diphenylpentanamide (1a)



210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 f1 (ppm)



19

5-oxo-N-phenyl-5-(m-tolyl)pentanamide (1c)



20

5-oxo-N-phenyl-5-(p-tolyl)pentanamide (1d)



5-(2-methoxyphenyl)-5-oxo-N-phenylpentanamide (1e)







5-(4-methoxyphenyl)-5-oxo-N-phenylpentanamide (1g)



5-(4-fluorophenyl)-5-oxo-N-phenylpentanamide (1h)





210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 f1 (ppm)

5-(4-chlorophenyl)-5-oxo-N-phenylpentanamide (1i)







210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 f1 (ppm)

5-oxo-N-phenyl-5-(thiophen-2-yl)pentanamide (1k)



, | | , O ∥ O ∐ ∖_Ph H 0.83 2.01^A 2.04^A 0.994 2.00H 2.34± 2.06H 4.58H 6.27-5.0 4.5 f1 (ppm) 8.5 10.0 9.5 9.0 8.0 7.5 7.0 6.5 6.0 5.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ~ 129.01 - 124.19 - 119.73 - 214.43 - 137.95 - 170.91 ₹ 77.37 77.06 76.74 39.21 36.58 33.97 28.50 28.50 25.63 25.63 19.61 - 50.89 0 I 0 ∖_Ph N H 210 200 190 180 170 160 150 140 130 120 110 100 90 f1 (ppm) 80 70 60 50 40 30 20 10 0 -10

5-cyclohexyl-5-hydroxy-N-phenylpentanamide (11)

2-oxo-N,2-diphenylacetamide (1m)





210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 f1 (ppm) 3-oxo-N,3-diphenylpropanamide (1n)





210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 f1 (ppm) 4-oxo-N,4-diphenylbutanamide (10)





5. NMR spectra of products

(R)-5-hydroxy-N,5-diphenylpentanamide (2a)





(R)-5-hydroxy-N-phenyl-5-(o-tolyl)pentanamide (2b)

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 f1 (ppm)








(R)-5-hydroxy-5-(3-methoxyphenyl)-N-phenylpentanamide (2f)



(R)-5-hydroxy-5-(4-methoxyphenyl)-N-phenylpentanamide (2g)





(R)-5-(4-fluorophenyl)-5-hydroxy-N-phenylpentanamide (2h)



(R)-5-(4-chlorophenyl)-5-hydroxy-N-phenylpentanamide (2i)



(R)-5-hydroxy-5-(naphthalen-2-yl)-N-phenylpentanamide (2j)





(R)-5-hydroxy-N-phenyl-5-(thiophen-2-yl)pentanamide (2k)



(R)-5-cyclohexyl-5-hydroxy-N-phenylpentanamide (2l)

7,75





(S)-2-hydroxy-N,2-diphenylacetamide (2m)



(R)-3-hydroxy-N,3-diphenylpropanamide (2n)



(R)-4-hydroxy-N,4-diphenylbutanamide (20)



6. HPLC spectra

(R)-5-hydroxy-N,5-diphenylpentanamide (2a)

Data File E:\DATA\YXG\HY-2017-9-6\LWD-2-179-KOH 2017-09-06 15-18-34\001-0201.D Sample Name: RAC



1260HPLC-VWD 3/8/2018 10:09:25 AM SYSTEM

Data File E:\DATA\YXG\HY-2017-9-6\LWD-2-179-K0H 2017-09-06 15-18-34\006-0701.D Sample Name: iPrOH _____ Acq. Operator : SYSTEM Acq. Instrument : 1260HPLC-VWD Seq. Line : 7 Location : Vial 6 Injection Date : 9/6/2017 5:40:47 PM Inj: 1 Inj Volume : 1.000 µl Acq. Method : E:\DATA\YXG\HY-2017-9-6\LWD-2-179-KOH 2017-09-06 15-18-34\VWD-AD(1-2)-85 -15-1.0-5UL-220NM-60MIN.M Last changed : 9/6/2017 4:44:52 PM by SYSTEM Analysis Method : E:\DATA\YXG\HY-2017-9-6\LWD-2-179-K0H 2017-09-06 15-18-34\VWD-AD(1-2)-85 -15-1.0-5UL-220NM-60MIN.M (Sequence Method) Last changed : 3/4/2018 11:16:07 AM by SYSTEM (modified after loading) Additional Info : Peak(s) manually integrated VWD1A,Wavelength=220 nm (E:\DATAYYXG\HY:2017-9-6\LWD-2-179-KOH 2017-09-06 15-18-344006-0701.D) mAU 600 OH `ŃPh H 13.760 500 400 300 200 100 0 10 12 14 min _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area [mAU] \$ # [min] [min] [mAU*s] 1 13.760 BB 0.3813 1.18646e4 468.67468 100.0000 Totals : 1.18646e4 468.67468 *** End of Report ***

1260HPLC-VWD 3/4/2018 11:16:17 AM SYSTEM

(R)-5-hydroxy-N-phenyl-5-(o-tolyl)pentanamide (2b)

Data File E:\DATA\YXG\HY-4-OME\HY-4-OME 2018-03-21 08-47-13\003-0201.D Sample Name: 2-me-rac



50

Data File E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\041-0201.D Sample Name: HY-2-Me _____ Acq. Operator : SYSTEM Acq. Instrument : 1260HPLC-VWD Seq. Line : 2 Location : Vial 41 Injection Date : 3/6/2018 8:42:49 AM Inj: 1 Inj Volume : 3.000 µl Acq. Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AD(1-2)-90-10-1ML-3UL-210NM-40MIN.M Last changed : 3/6/2018 8:31:13 AM by SYSTEM Analysis Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AD(1-2)-90-10-1ML-3UL-210NM-40MIN.M (Sequence Method) : 3/8/2018 10:42:43 AM by SYSTEM Last changed (modified after loading) Additional Info : Peak(s) manually integrated VWD1A, Wavelength=220 nm (E:\DATA\YXG\HY:20180306\HY:20180306 2018-03-06 08-31-130041-0201.D) mAU OH 800 `ŃPh H 600 400 200 . 982.10¹ 82 St. Sala 0 14 16 18 ź 28 28 24 min _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area [min] [mAU*s] [mAU] * # [min] ------11 21.288 MF 0.6874 3.51288e4 851.66882 97.3342 2 22.625 FM 0.6569 962.10657 24.40915 2.6658 Totals : 3.60909e4 876.07797 _____ *** End of Report *** Page 1 of 1 1260HPLC-VWD 3/8/2018 10:42:53 AM SYSTEM

(*R*)-5-hydroxy-N-phenyl-5-(m-tolyl)pentanamide (2c)

Data File E:\DATA\HY\HY-2017-12-06\HY-2017-12-06 2017-12-06 22-26-24\001-0201.D Sample Name: HY-2017-12-06-3Me-RAC

_____ Acq. Operator : SYSTEM Seq. Line : 2 Acq. Instrument : 1260HPLC-VWD Location : Vial 1 Injection Date : 12/6/2017 10:48:07 PM Inj : 1 Inj Volume : 1.000 μ1 : E:\DATA\HY\HY-2017-12-06\HY-2017-12-06 2017-12-06 22-26-24\VWD-AD(1-2)-Acq. Method 85-15-1.0-1UL-220NM-40MIN.M : 12/6/2017 10:26:25 PM by SYSTEM Last changed Analysis Method : E:\DATA\HY\HY-2017-12-06\HY-2017-12-06 2017-12-06 22-26-24\VWD-AD(1-2)-85-15-1.0-1UL-220NM-40MIN.M (Sequence Method) Last changed : 3/4/2018 11:30:18 AM by SYSTEM (modified after loading) Additional Info : Peak(s) manually integrated VWD1A, Wavelength=220 nm (E:\DATAWHYNHY-2017-12-06/HY-2017-12-06 2017-12-06 22-26-24001-0201.D) mAU 140 OH 120 Ph 10.754 100 13.807 80 60 40 20 0 12 14 16 6 ŝ 10 min _____ Area Percent Report Sorted Bv : Signal Multiplier 1.0000 : 1.0000 Dilution : Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] ÷ ------- 1 ------|----|-----| ---1 1 10.754 BB 0.2921 1834.05481 95.48607 50.0238 0.3945 1832.30615 70.90994 49.9762 2 13.807 BB 3666.36096 166.39601 Totals : *** End of Report *** Page 1 of 1 1260HPLC-VWD 3/4/2018 11:30:26 AM SYSTEM



1260HPLC-VWD 3/4/2018 11:32:10 AM SYSTEM

(*R*)-5-hydroxy-N-phenyl-5-(p-tolyl)pentanamide (2d)

Data File E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 11-02-48\032-0101.D Sample Name: HY-4-Me-RACE

_____ Acq. Operator : SYSTEM Seq. Line : 1 Acq. Instrument : 1260HPLC-VWD Location : Vial 32 Injection Date : 3/5/2018 11:03:34 AM Inj : 1 Inj Volume : 3.000 μ1 : E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 11-02-48\DAD-AS Acq. Method (1-6)-90-10-1ML-3UL-220NM-60MIN.M Last changed : 3/5/2018 11:26:15 AM by SYSTEM (modified after loading) Analysis Method : E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 11-02-48\DAD-AS (1-6)-90-10-1ML-3UL-220NM-60MIN.M (Sequence Method) : 3/19/2018 8:41:28 PM by SYSTEM Last changed (modified after loading) Additional Info : Peak (s) manually integrated VWD1 A, W avelength=220 nm (E:\DATAYXG\HY:20180305-RACE\HY:20180305-RACE 2018-03-05 11-02-481032-0101.D) mAU 8 OH O `ŃPh H ŝ 卷 200 ล้ 150 100 50 o 20 24 14 16 18 26 min Area Percent Report Sorted By Signal Multiplier 1.0000 : Dilution 1.0000 : Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] * -|----|----|-----|------|-----!-----!-------1 20.050 BV 0.9438 1.39227e4 225.03658 49.3087 2 22.403 VB 1.1303 1.43130e4 191.87627 50.6913 Totals : 2.82357e4 416.91284 ------

1260HPLC-VWD 3/19/2018 8:41:36 PM SYSTEM

Data File E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\042-0301.D Sample Name: HY-4-Me _____ Acq. Operator : SYSTEM Acq. Instrument : 1260HPLC-VWD Seq. Line : 3 Location : Vial 42 Injection Date : 3/6/2018 9:23:38 AM Inj: 1 Inj Volume : 5.000 µl Acq. Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AS(1-6)-90-10-1ML-3UL-220NM-40MIN.M Last changed : 3/6/2018 8:31:13 AM by SYSTEM Analysis Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AS(1-6)-90-10-1ML-3UL-220NM-40MIN.M (Sequence Method) : 3/8/2018 10:45:45 AM by SYSTEM Last changed (modified after loading) Additional Info : Peak(s) manually integrated VWD1A,Wavelength=220 nm (E:\DATA\YXG\HY:20180306\HY:20180306 2018-03-06 08-31-13042-0301.D) mAU . OH \cap `ŃPh H 250 200 150 100 50 0 12.5 15 17.5 20 225 25 27.5 min _____ Area Percent Report Sorted Bv : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [mAU*s] [mAU] * -----|-----| 1 19.845 BB 0.9927 2.02177e4 309.24850 100.0000 2.02177e4 309.24850 Totals : *** End of Report ***

1260HPLC-VWD 3/8/2018 10:45:54 AM SYSTEM

(R)-5-hydroxy-5-(2-methoxyphenyl)-N-phenylpentanamide (2e)

Data File E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\034-0201.D Sample Name: HY-2-OMe RACE

_____ Acq. Operator : SYSTEM Seq. Line : 2 Acq. Instrument : 1260HPLC-VWD Location : Vial 34 Injection Date : 3/5/2018 1:38:28 PM Inj : 1 Inj Volume : 5.000 μ1 : E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\VWD-AD Acq. Method (1-2)-90-10-1.0ML-3UL-220NM-60MIN.M Last changed : 3/5/2018 2:37:01 PM by SYSTEM (modified after loading) Analysis Method : E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\VWD-AD (1-2)-90-10-1.0ML-3UL-220NM-60MIN.M (Sequence Method) : 3/8/2018 10:00:17 AM by SYSTEM Last changed (modified after loading) Additional Info : Peak (s) manually integrated \VWD1 A, W avelength=220 nm (E:\DATAYXG\HY:20180305-RACE\HY:20180305-RACE 2018-03:05 12-01-44/034-0201.D) mAU OH \cap 200 , 1881^{1,0} N^{Ph} H 175 150 125 100 75 50 25 o 4ò 45 ல் 55 εÒ. min Area Percent Report Sorted By : Signal 1.0000 Multiplier : 1.0000 Dilution : Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] * - 1 1 43.653 BB 1.1906 1.65428e4 211.93987 49.8962 2 54.960 MM 1.6947 1.66116e4 163.36815 50.1038 Totals : 3.31544e4 375.30801 _____

1260HPLC-VWD 3/8/2018 10:00:30 AM SYSTEM



$(R) \hbox{-} 5 \hbox{-} hydroxy \hbox{-} 5 \hbox{-} (3 \hbox{-} methoxy phenyl) \hbox{-} N \hbox{-} phenyl pentanamide} \ (2f)$

Data File E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\035-0301.D Sample Name: HY-3-0Me-RACE

Acq. Operator	: SYSTEM Seg. Line : 3
Acq. Instrument	: 1260HPLC-VWD Location : Vial 35
Injection Date	: 3/5/2018 2:44:16 PM Inj : 1
	Inj Volume : 5.000 µl
Acq. Method	: E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\VWD-AD
Lost showrod	(1-2)-90-10-1.0ML-30L-220NM-60MIN.M
Last changed	(modified after loading)
Analvsis Method	: E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\VWD-AD
	(1-2)-90-10-1.0ML-3UL-220NM-60MIN.M (Sequence Method)
Last changed	: 3/8/2018 9:57:50 AM by SYSTEM
	(modified after loading)
Additional Info	: Peak(s) manually integrated
VWD1A, Wa	welength=220 nm (E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-444035-0301.D)
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1	
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1	
32	
	Area Dercent Deport
Sorted By	: Signal
Multiplier	: 1.0000
Dilution	: 1.0000
Do not use Multi	plier & Dilution Factor with ISTDs
Simpll VUD1	Were longth - 220 nm
Signai I. YWDI #	r, wavelengun-220 nm
Peak RetTime Tvr)e Width Area Height Area
# [min]	[min] [mAU*s] [mAU] 💲
1 34.630 BB	0.9675 4264.64502 67.01236 50.0685
2 42.505 BB	1.2125 4252.97168 53.26817 49.9315
Totale .	8517 61670 120 28053
iocais :	0317.01070 120.20033

1260HPLC-VWD 3/8/2018 9:58:03 AM SYSTEM

Data File E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\045-0601.D Sample Name: HY-3-0Me

_____ Acq. Operator : SYSTEM Acq. Instrument : 1260HPLC-VWD Seq. Line : 6 Location : Vial 45 Injection Date : 3/6/2018 1:01:11 PM Inj: 1 Inj Volume : 5.000 µl Acq. Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AD(1-2)-90-10-1ML-5UL-220NM-60MIN.M Last changed : 3/6/2018 8:31:13 AM by SYSTEM Analysis Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AD(1-2)-90-10-1ML-5UL-220NM-60MIN.M (Sequence Method) : 3/15/2018 3:30:54 PM by SYSTEM Last changed (modified after loading) Additional Info : Peak (s) manually integrated VWD1 A, Wavelength=220 nm (E:\DATA\YX:G\HY:20180306\HY:20180306 2018-03-06 08-31-130045-0601.D) mAU OH `N^{∠Ph} H 400 300 200 100 80.98 o 40 45 35 42.5 47.5 32.5 37.5 min Area Percent Report Sorted By : Signal Multiplier 1.0000 : Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Height Area Area [mAU*s] [mAU] # [min] [min] * - - - - 1 _ _ _ _ _ _ 1 35.090 BB 0.9146 343.49542 5.28935 0.8160 2 43.451 BB 1.2260 4.17513e4 492.03580 99.1840 Totals : 4.20948e4 497.32515 ------*** End of Report *** Page 1 of 1 1260HPLC-VWD 3/15/2018 3:32:34 PM SYSTEM

(R)-5-hydroxy-5-(4-methoxyphenyl)-N-phenylpentanamide (2g)

Data File E:\DATA\SC...21-4-0ME\HY-20180321-4-0ME 2018-03-21 12-14-05\HY-20180321-4-0Me1.D Sample Name: HY-20180321-4-0Me-RAC



1260 3/21/2018 3:20:12 PM SYSTEM

Data File E:\DATA\SC...21-4-0Me\HY-20180321-4-0Me 2018-03-21 12-14-05\HY-20180321-4-0Me2.D Sample Name: HY-20180321-4-0Me-0PT

```
_____
Acq. Operator : SYSTEM
                                       Seq. Line : 3
Acq. Instrument : 1260
                                                  24
1
                                        Location :
Injection Date : 3/21/2018 2:03:46 PM
                                            Inj :
                                       Inj Volume : 5.000 µl
            : E:\DATA\SC\ZHANG-HY-20180321-4-0Me\HY-20180321-4-0Me 2018-03-21 12-14-05\SC
Acq. Method
              -1-ASH-90-10-DAD--90MIN-1ML.M
           : 3/21/2018 12:14:05 PM by SYSTEM
Last changed
Analysis Method : E:\DATA\SC\ZHANG-HY-20180321-4-0Me\HY-20180321-4-0Me 2018-03-21 12-14-05\SC
              -1-ASH-90-10-DAD--90MIN-1ML.M (Sequence Method)
Last changed
             : 3/21/2018 3:34:48 PM by SYSTEM
               (modified after loading)
      DAD1 B, Sig=254,4 Ref=360,100 (E:/DATA\SC...e\HY-20180321-4-OMe 2018-03-21 12-14-05/HY-20180321-4-OMe2.D)
   mAU 🗍
                              83
                                                       OH
   175 -
                                                                      Ph
   150 -
   125 -
   100 -
   75 -
   50 -
   25
    D -
              20
                       30
                                40
                                         50
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                                                                    80
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                        -----
                   Area Percent Report
Sorted By
                       Sional
                 :
Multiplier
                 :
                       1.0000
Dilution
                       1.0000
                 :
Do not use Multiplier & Dilution Factor with ISTDs
Signal 1: DAD1 B, Sig=254,4 Ref=360,100
Peak RetTime Type Width
                               Height
                       Area
                                        Area
                                         *
 # [min]
               [min] [mAU*s]
                               [mAU]
----|-----|-----|-----|-----|-----|
  1 38.057 BB 1.8393 2.68096e4 180.97954 100.0000
                     2.68096e4 180.97954
Totals :
-----
```

1260 3/21/2018 3:35:02 PM SYSTEM

(R)-5-(4-fluorophenyl)-5-hydroxy-N-phenylpentanamide (2h)

Data File E:\DATA\YXG\HY-2017-9-25\HY-2017-9-25 2017-09-25 18-54-05\003-0201.D Sample Name: HY-2017-9-25-4-F-RAC-3

```
------
Acq. Operator : SYSTEM
                                         Seq. Line :
                                                     2
Acq. Instrument : 1260HPLC-VWD
                                          Location : Vial 3
Injection Date : 9/25/2017 7:05:33 PM
                                               Inj :
                                                      1
                                         Inj Volume : 1.000 µl
             : E:\DATA\YXG\HY-2017-9-25\HY-2017-9-25 2017-09-25 18-54-05\VWD-AD(1-6)-85
Acg. Method
               -15-0.5-1UL-220NM-60MIN.M
Last changed
             : 9/25/2017 7:51:08 PM by SYSTEM
               (modified after loading)
Analysis Method : E:\DATA\YXG\HY-2017-9-25\HY-2017-9-25 2017-09-25 18-54-05\VWD-AD(1-6)-85
               -15-0.5-1UL-220NM-60MIN.M (Sequence Method)
Last changed
             : 3/4/2018 11:36:18 AM by SYSTEM
               (modified after loading)
Additional Info : Peak(s) manually integrated
VWD1A, Wavelength=220 nm (E:\DATA\YXG\HY:2017-9-25\HY:2017-9-25 2017-09-25 18-54-05003-0201.D)
   mAU
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                    OH
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                                `Ņ´<sup>₽h</sup>
                                                       2
   200
   150
   100
    50
     o
             16
                           18
                                          20
                                                        22
                                                                       24
                                                                             min
_____
                     Area Percent Report
------
Sorted By
                        Signal
                   :
                        1.0000
Multiplier
                  :
Dilution
                        1.0000
                  :
Do not use Multiplier & Dilution Factor with ISTDs
Signal 1: VWD1 A, Wavelength=220 nm
Peak RetTime Type Width
                        Area
                                 Height
                                          Area
    [min]
                [min]
                      [mAU*s]
                                 [mAU]
                                            *
 #
----!-----!----!-----!-----!-----!
  1 20.294 BV
                0.4576 7041.72607 232.35959 49.6944
  2 21.823 VB
                0.4910 7128.32568 219.42799 50.3056
Totals :
                      1.41701e4 451.78758
```

1260HPLC-VWD 3/4/2018 11:36:28 AM SYSTEM



1260HPLC-VWD 3/4/2018 11:33:44 AM SYSTEM

(R)-5-(4-chlorophenyl)-5-hydroxy-N-phenylpentanamide (2i)

Data File E:\DATA\YXG\HY-20180305-RACE\HY-20180305-RACE 2018-03-05 12-01-44\033-0101.D Sample Name: HY-4-C1-RACE

Acq. Operator : SYSTEM Seq. Line : 1
Acq. Instrument : 1260HPLC-VWD Location : Vial 33
Injection Date : 3/5/2018 12:02:33 PM Inj : 1
ing Voltame : د. ۱۵ مالی ایس ایس ایس ایس ایس ایس ایس ایس ایس ای
(1-6)-95-5-IML-6UL-220MM-60MIN.M
Last changed : 3/5/2018 1:27:26 PM by SYSTEM
(modified after loading)
Analysis Method : E:\DATA\YXGHY-20180305-RACE HY-20180305-RACE 2018-03-05 12-01-44\DAD-AS
(1-6)-35-3-INF-601-220WR-60WNW.N (Sequence Mechod)
(modified after loading)
Additional Info : Peak(s) manually integrated
VWD1 A, Wavelength=220 nm (E:\DATA\YX.6\HY:20180306-RACE\Y:20180306-RACE 2018-03-05 12-01-44033-0101.D)
A A A A A A A A A A A A A A A A A A A
OH Q / v ⁴ ä _k s ^a
$\downarrow $ ^{®1} $\land \downarrow \land \downarrow \land$
60 65 70 75 80 85 m
Area Percent Report
Sorted By : Signal
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs
Signal 1: VWD1 A, Wavelength=220 nm
Deab DetTime Tyme Width Area Height Area
[min] [min] [mAU*s] [mAU] %
1 72.654 MF 3.8065 2.22891e4 97.59178 49.8239
2 80.959 FM 4.4414 2.24466e4 84.23253 50.1761
Totals · / /7357e/ 181 82/31
100415 . 4.4/33/04 101.02431

1260HPLC-VWD 3/8/2018 10:02:24 AM SYSTEM

Data File E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\043-0401.D Sample Name: HY-4-Cl _____ Acq. Operator : SYSTEM Seq. Line : 4 Location : Vial 43 Acq. Instrument : 1260HPLC-VWD Injection Date : 3/6/2018 10:04:32 AM Inj: 1 Inj Volume : 5.000 µl Acq. Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AS(1-6)-95-5 -1ML-5UL-220NM-100MIN.M Last changed : 3/6/2018 8:31:13 AM by SYSTEM Analysis Method : E:\DATA\YXG\HY-20180306\HY-20180306 2018-03-06 08-31-13\VWD-AS(1-6)-95-5 -1ML-5UL-220NM-100MIN.M (Sequence Method) : 3/8/2018 10:48:06 AM by SYSTEM Last changed (modified after loading) Additional Info : Peak(s) manually integrated VWD1A,Wavelength=220 nm (E:\DATA\YXG\HY:20180306\HY:20180306 2018-03-06 08-31-13043-0401.D) mAU 175 ΟН 150 Ph 125 100 75 50 25 0 ல் 55 ல் es 70 75 ဆ် es β 45 min _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [mAU*s] [mAU] * -----|-----| 1 72.344 BB 3.1905 4.47401e4 170.10446 100.0000 Totals : 4.47401e4 170.10446 *** End of Report ***

1260HPLC-VWD 3/8/2018 10:48:17 AM SYSTEM

(R)-5-hydroxy-5-(naphthalen-2-yl)-N-phenylpentanamide (2j)

Data File E:\DATA\YXG\HY-20180226RACE\HY-20180226-RACE 2018-02-26 13-44-52\001-0201.D Sample Name: HY-NAI-RACE



66

Data File E:\DATA\YXG\HY-20180226RACE\HY-20180226-RACE 2018-02-26 15-00-53\011-0201.D Sample Name: HY-NAI _____ Acq. Operator : SYSTEM Acq. Instrument : 1260HPLC-VWD Seq. Line : 2 Location : Vial 11 Injection Date : 2/26/2018 4:03:18 PM Inj: 1 Inj Volume : 5.000 µl Acq. Method : E:\DATA\YXG\HY-20180226RACE\HY-20180226-RACE 2018-02-26 15-00-53\VWD-AS(1-6)-95-5-1.0ML-3UL-210NM-60MIN.M Last changed : 2/26/2018 3:00:53 PM by SYSTEM Analysis Method : E:\DATA\YXG\HY-20180226RACE\HY-20180226-RACE 2018-02-26 15-00-53\VWD-AS(1-6)-95-5-1.0ML-3UL-210NM-60MIN.M (Sequence Method) Last changed : 3/4/2018 10:59:10 AM by SYSTEM (modified after loading) Additional Info : Peak(s) manually integrated VWD1A,Wavelength=220 nm (E:\DATAYXG\HY-20180228RACE\HY-20180226RACE 2018-02-28 15-00-530011-0201.D) mAU 29.396 2000 OH Ph 1500 1000 500 34,302 0 -10 15 25 зò 40 45 min 20 э́5 _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % # [min] 1 29.396 VB 1.5956 2.15094e5 2049.17432 99.6990 2 34.302 BB 1.1069 649.41217 8.38173 0.3010 2.15743e5 2057.55604 Totals : _____ *** End of Report *** Page 1 of 1

1260HPLC-DAD 3/4/2018 10:59:20 AM SYSTEM

(R)-5-hydroxy-N-phenyl-5-(thiophen-2-yl)pentanamide (2k)

Data File E:\DATA\HYI\HYI-2-154-0.5ML\HYI-2-153-154 2017-12-20 14-43-53\001-0201.D Sample Name: HY-SAIFEN-RAC

Acq. Operator : SYSTEM Seq. Line : 2 Acq. Instrument : 1260HPLC-DAD Location : Vial 1 Injection Date : 12/20/2017 2:56:55 PM Inj : 1 Inj Volume : 1.000 µl Acq. Method : E:\DATA\HYI\HYI-2-154-0.5ML\HYI-2-153-154 2017-12-20 14-43-53\DAD-0D(1-2))-90-10-1ML-1UL-ALL-1H.M			
Last changed : 12/20/2017 3:36:51 FM by SYSTEM (modified after loading) Analysis Method : E:\DATA\HYI\HYI-2-154-0.5ML\HYI-2-153-154 2017-12-20 14-43-53\DAD-0D(1-2			
)-90-10-1ML-1UL-ALL-1H.M (Sequence Method) Last changed : 3/8/2018 10:18:08 AM by SYSTEM (modified after loading)			
Additional Info : Peak(s) manually integrated DAD1 B, Sig=254,4 Re⊨off (EADATAWYNWY)-2-154-0.5MLNY)-2-153-154-2017-12-20 1443-53001-0201.D) 			
$ \begin{array}{c} & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ $			
Area Percent Report			
Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs			
Signal 1: DAD1 B, Sig=254,4 Ref=off			
Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 34.789 MF 1.7133 8077.33350 78.57515 49.5213 2 38.595 FM 1.9492 8233.48340 70.40156 50.4787			
Totals : 1.63108e4 148.97671			

1260HPLC-VWD 3/8/2018 10:18:39 AM SYSTEM

Data File E:\DATA\YXG\YXG-894-2\HY-BUSHUJU20180208 2018-02-08 13-18-12\022-0301.D Sample Name: HY-saifen _____ Acq. Operator : SYSTEM Seq. Line : 3 Location : Vial 22 Acq. Instrument : 1260HPLC-DAD Injection Date : 2/8/2018 2:51:07 PM Inj: 1 Inj Volume : 3.000 µl Acq. Method : E:\DATA\YXG\YXG-894-2\HY-BUSHUJU20180208 2018-02-08 13-18-12\DAD-0D(1-2) -90-10--1ML-210-230NM-60MIN.M Last changed : 2/8/2018 1:18:12 PM by SYSTEM Analysis Method : E:\DATA\YXG\YXG-894-2\HY-BUSHUJU20180208 2018-02-08 13-18-12\DAD-0D(1-2) -90-10--1ML-210-230NM-60MIN.M (Sequence Method) : 3/4/2018 12:37:40 PM by SYSTEM Last changed (modified after loading) Additional Info : Peak(s) manually integrated DAD1 B, Sig=254.4 Re⊨off (EADATANYXGYXG-894-2HY-BU SHUJU20180208 2018-02-08 13-18-12022-0301.D) mAU 8 250 200 OH `ŃPh H 150 100 k^r⁰ 50 888 0 15 20 зο зŚ 40 46 25 min _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: DAD1 B, Sig=254,4 Ref=off Peak RetTime Type Width Area Height Area # [min] - 1 2 37.743 BB 1.7114 3.17273e4 270.70624 99.9827 Totals : 3.17328e4 270.86835 _____ *** End of Report *** Page 1 of 1 1260HPLC-VWD 3/4/2018 12:37:48 PM SYSTEM

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(R)-5-cyclohexyl-5-hydroxy-N-phenylpentanamide (2l)

Data File E:\DATA\YXG\HY-HUANJIJI-RACE\HY-HUANJIJI-RACE 2018-02-27 15-51-59\032-0201.D Sample Name: HY-HUANJIJI-RACE

Acq. Operator : SYSTEM Seq. Line : 2
Acq. Instrument : 1260HPLC-DAD Location : Vial 32
Injection Date : 2/27/2018 4:04:00 PM Inj : 1
Inj Volume : 5.000 µl
ACQ. MECHON : E: ()ARAYIXOYAT-ROAMUJUI-KALE/ATT-ROAMUJUI-KALE/2010-02-2/ 13-31-39/DAD-0D (12).051-07000 (12).023000-60000 W
Last changed : 2/27/2018 4:56:09 PM by SYSTEM
(modified after loading)
Analysis Method : E:\DATA\YXG\HY-HUANJIJI-RACE\HY-HUANJIJI-RACE 2018-02-27 15-51-59\DAD-0D
(1-2)-95-5-0.7ML-210-230NM-60MIN.M (Sequence Method)
Last changed : 3/8/2018 10:23:23 AM by SYSTEM
(modified after loading)
Additional finite : Peak(s) manuality integrated DAD18.Sim2544 Refeot(EXDATAYXGHY-HUANJULRACEHY-HUANJULRACE 2018-02-27 15-51-59032-0201 D)
mAU mAU
\square
40-1
Area Percent Report
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs
Circuit In DADI D. Circuit 4 Diff. 46
Signai I: DADI B, Sig=254,4 REI=OII
Peak RetTime Type Width Area Height Area
[min] [mAU*s] [mAU] %
!!!!!!
1 41.873 MF 1.9117 1.22385e4 106.70069 48.8931
2 45.730 FM 2.1120 1.27926e4 100.95264 51.1069
Totals · 2 50312e4 207 65333
100115 . 2.3031254 207.03333

1260HPLC-VWD 3/8/2018 10:23:31 AM SYSTEM

Data File E:\DATA\YXG\HY-HUANJIJI-RACE\HY-HUANJIJI-RACE 2018-02-27 15-51-59\033-0301.D Sample Name: HY-HUANJIJI _____ Acq. Operator : SYSTEM Seq. Line : 3 Location : Vial 33 Acq. Instrument : 1260HPLC-DAD Injection Date : 2/27/2018 5:04:56 PM Inj: 1 Inj Volume : 5.000 µl Acq. Method : E:\DATA\YXG\HY-HUANJIJI-RACE\HY-HUANJIJI-RACE 2018-02-27 15-51-59\DAD-OD (1-2)-95-5-0.7ML-210-230NM-60MIN.M Last changed : 2/27/2018 4:56:09 PM by SYSTEM Analysis Method : E:\DATA\YXG\HY-HUANJIJI-RACE\HY-HUANJIJI-RACE 2018-02-27 15-51-59\DAD-0D (1-2)-95-5-0.7ML-210-230NM-60MIN.M (Sequence Method) : 3/8/2018 10:26:20 AM by SYSTEM Last changed (modified after loading) Additional Info : Peak(s) manually integrated DAD1 B, Sig=254.4 Re⊨o#(E:DATAYYXG\HY-HUANJUI-RACE\HY-HUANJUI-RACE 2018-02-27 15-51-59033-0301.D) mAU 54 566 554 5. 1 350 300 OH ∠Ph 250 200 150 100 ARANA 136 ₩.S. 50 0 зò 35 4o 46 50 55 min _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: DAD1 B, Sig=254,4 Ref=off Peak RetTime Type Width Area Height Area [min] [mAU*s] [mAU] * # [min] _____ ------1 42.413 MF 1.9221 3.55451e4 308.21945 88.2708 2 47.135 FM 2.0490 4723.13672 38.41894 11.7292 Totals : 4.02683e4 346.63839 _____ *** End of Report *** Page 1 of 1 1260HPLC-VWD 3/8/2018 10:26:30 AM SYSTEM

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(S)-2-hydroxy-N,2-diphenylacetamide (2m)

Data File E:\DATA\HY\HY-2017-9-27\SUB-20170926 2017-09-27 09-42-12\005-0701.D Sample Name: HY-AERFA-RAC

Acq. Operator	: SYSTEM Seq. Line : 7
Acq. Instrument	: 1260HPLC-VWD Location : Vial 5
Injection Date	: 9/27/2017 12:50:58 PM Inj: 1 Tri Volume : 1 000 ul
Acg. Method	: E:\DATA\HY\HY-2017-9-27\SUB-20170926 2017-09-27 09-42-12\VWD-0J(1-6)-85-
	15-1ML-1UL-220MM-40MIN.M
Last changed	: 9/27/2017 1:23:09 PM by SYSTEM
	(modified after loading)
Analysis Method	: E:\DATA\HY\HY-2017-9-27\SUB-20170926 2017-09-27 09-42-12\VWD-0J(1-6)-85-
Lest showed	15-IML-IUL-22UNM-4UMIN.M (Sequence Method)
rast cuanded	(modified after loading)
Additional Info	: Peak(s) manually integrated
VWD1 A, Wa	velength=220 nm (E:\DATA\H'\HY-2017-9-27\SUB-20170926 2017-09-27 09-42-12\005-0701.D)
mAU]	× 4
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120-	
100 -	
80-	
1 ~ 1	
40-	
20-	
1 1	
14	16 18 20 22 24 min
	Area Percent Report
Sorted Bu	. Simel
Multiplier	: 1.0000
Dilution	: 1.0000
Do not use Multi	plier & Dilution Factor with ISTDs
Signal 1: VWD1 A	, Wavelength=220 nm
Doob DotTime T-	a Width dree Height dree
feak Reclime Typ # [min]	'e widdh Afea heighd Afea [min] [màllts] [màll] %
	·
1 15.677 BB	0.4301 3683.54932 127.85548 49.4296
2 17.473 BB	0.4279 3768.55908 132.85428 50.5704
Totals :	7452.10840 260.70976

1260HPLC-VWD 3/4/2018 11:41:13 AM SYSTEM
Data File E:\DATA\YXG\YXG-894-2\HY-BUSHUJU20180208 2018-02-08 13-18-12\023-0401.D Sample Name: HY-a-chanwu Acq. Operator : SYSTEM Seq. Line : 4 Acq. Instrument : 1260HPLC-VWD Location : Vial 23 Injection Date : 2/8/2018 3:52:08 PM Inj: 1 Inj Volume : 1.000 µl Acq. Method : E:\DATA\YXG\YXG-894-2\HY-BUSHUJU20180208 2018-02-08 13-18-12\VWD-0J(1-6) -85-15-1ML-1UL-220NM-40MIN.M Last changed : 2/8/2018 1:18:12 PM by SYSTEM Analysis Method : E:\DATA\YXG\YXG-894-2\HY-BUSHUJU20180208 2018-02-08 13-18-12\VWD-0J(1-6) -85-15-1ML-1UL-220NM-40MIN.M (Sequence Method) : 3/4/2018 12:55:04 PM by SYSTEM Last changed (modified after loading) Additional Info : Peak (s) manually integrated [VWD1A, Wavelength=220 nm (EADATANXGNXG-894 2NHY-BU SHUJU20180208 2018-02-08 13-18-12023-0401.D) mAU . 800 16.004 700 OH н 600 500 400 300 200 100 14,114 n. 25 15 20 10 min Area Percent Report Sorted By Signal : Multiplier 1.0000 : 1.0000 Dilution : Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] * 1 14.114 BB 0.4061 123.46416 4.26015 0.4575 2 16.004 BB 0.6175 2.68627e4 664.73956 99.5425 Totals : 2.69861e4 668.99971 *** End of Report *** Page 1 of 1 1260HPLC-VWD 3/4/2018 12:55:12 PM SYSTEM

73

$(R) \textbf{-3-hydroxy-N,3-diphenylpropanamide} \ (2n)$

Data File E:\DATA\YCC\YCC-2018-01-17\YCC-222 2018-03-20 12-34-29\031-2201.D Sample Name: BEITA-RAC

Acq. Operator : SYSTEM	Seq. Line : 22
Acq. Instrument : 1260HPLC-DAD Injection Date : 3/20/2018 10:03:42 PM	Location : Vial 31
Injection Date . 3/20/2010 10.03.42 FM	Inj Volume : 10.000 ul
Acq. Method : E:\DATA\YCC\YCC-2018-01-17\YCC	-222 2018-03-20 12-34-29\DAD-0D(1-2)-95-5-
0.5ML-10UL-100MIN.M	
Last changed : 3/20/2018 8:14:42 PM by SYSTEM	
0.5ML-10UL-100MIN.M (Sequence Method)	
Last changed : 3/21/2018 3:47:55 PM by SYSTEM	
(modified after loading)	
Add tribinal finite : Feak (5) manuality integrated DAD18, Sig=2544, Refeot (EXDATA)/CC/VCC-2018-01-170/CC-222 2018-03-20 12-34-29/031-2201,D)	
mAU]	
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OH O	8 Alto
	ere and a second
150 -	
50 -	
0	
	75 90 95 00 05
	<u>,, a a s s min</u>
Area Percent Report	
Sorted By : Signal	
Dilution : 1.0000	
Do not use Multiplier & Dilution Factor with IST	Ds
Signal 1. DNDI B. Sig-254 4 Def-off	
Signal I. DADI D, Sig-234,4 Kel-Oll	
Peak RetTime Type Width Area Height	Area
# [min] [mAU*s] [mAU]	\$
1 80 723 MF 3 0053 4 27600e4 237 13538	 //8_0272
2 86.393 FM 3.7267 4.62729e4 206.94102	51.9728
Totals: 8.90329e4 444.07640	
*** End of Report ***	

1260HPLC-DAD 3/21/2018 3:48:15 PM SYSTEM

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(R)-4-hydroxy-N,4-diphenylbutanamide (20)

Data File E:\DATA\WSW\LWD-2-197-11-12\LWD-2-197-11-12 2017-09-25 11-25-46\003-0201.D Sample Name: HY-2017-9-25-JIAMA-RAC



1260HPLC-VWD 3/4/2018 11:48:56 AM SYSTEM

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Data File E:\DATA\WSW\LWD-2-197-11-12\LWD-2-197-11-12 2017-09-25 11-25-46\004-0301.D Sample Name: HY-2017-9-25-JIAMA-EE _____ Acq. Operator : SYSTEM Seq. Line : 3 Location : Vial 4 Acq. Instrument : 1260HPLC-VWD Injection Date : 9/25/2017 12:24:58 PM Inj: l Inj Volume : 1.000 µl Acq. Method : E:\DATA\WSW\LWD-2-197-11-12\LWD-2-197-11-12 2017-09-25 11-25-46\VWD-AD(1 -6)-90-10-0.5-220NM-40MIN.M Last changed : 9/25/2017 11:25:46 AM by SYSTEM Analysis Method : E:\DATA\WSW\LWD-2-197-11-12\LWD-2-197-11-12 2017-09-25 11-25-46\VWD-AD(1 -6)-90-10-0.5-220NM-40MIN.M (Sequence Method) : 3/4/2018 11:51:19 AM by SYSTEM Last changed (modified after loading) Additional Info : Peak(s) manually integrated VWD1A,Wavelength=220 nm (E:\DATAW/SW\LWD-2-197-11-12\LWD-2-197-11-12 2017-09-25 11-25-460004 0301.D) mAU 175 33.238 OH 150 Ph 125 റ 100 75 50 25 0 28 зò 32 34 36 38 28 min _____ Area Percent Report Sorted By : Signal Multiplier : 1.0000 Dilution : 1.0000 Do not use Multiplier & Dilution Factor with ISTDs Signal 1: VWD1 A, Wavelength=220 nm Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 33.238 BB 0.7485 7760.06836 155.95757 100.0000 7760.06836 155.95757 Totals : *** End of Report ***

1260HPLC-VWD 3/4/2018 11:51:31 AM SYSTEM

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7. References

- (1) C. Joyanta, P. Susmita, R. Sujit, J. Am. Chem. Soc., 2005, 127, 6162;
- (2) D. Yang, Y. Long, H. Wang, Z. Zhang, Org. Lett., 2008, 10, 4723;
- (3) N. C. Mamillapalli, G. Sekar, Chem. Eur. J., 2015, 21, 18584;
- (4) N. A. Cortez, G. Aguirre, M. Parra-Hake, R. Somanathan, *Tetrahedron: Asymmetric*, 2013, **24**, 1297;
- (5) C. David; B. Juan; K. Donnald, WO2006017257, 2006;
- (6) C. Liu, Y. Li, C. Li, W. Li, C. Zhou, H. Liu, Z. Bo and Y. Li, J. Phy. Chem. C, 2009, 113, 21970;
- (7) M. Zhao, B. Lu, G. Ding, K. Ren, X. Xie and Z. Zhang, Org. & Biomol. Chem., 2016, 14, 2723;
- (8) J. Zhuang, C. Wang, F. Xie and W. Zhang, Tetrahedron, 2009, 65, 9797;
- (9) M. Wasa, R. Y. Liu, S. P. Roche and E. N. Jacobsen, J. Am. Chem. Soc., 2014, 136, 12872.