Supporting Information

A Novel Chiral Surfactant-Type Metallomicellar Catalyst for Asymmetric Michael

Addition in Water

Xinping Liang^a, Yang Gui^a, Kuiliang Li^a, Jindong Li^a, Zhenggen Zha^a, Lei Shi^{b*} and Zhiyong Wang^{a*}

^[a]Hefei National Laboratory for Physical Sciences at Microscale, CAS Key Laboratory of Soft Matter Chemistry & Center for Excellence in Molecular Synthesis of Chinese Academy of Sciences, Collaborative Innovation Center of Suzhou Nano Science and Technology & School of Chemistry and Materials Science in University of Science and Technology of China, Hefei, Anhui 230026, P. R. China, Fax: (+86)551-63603185, E-mail: zwang3@ustc.edu.cn

^(b)Hefei National Laboratory for Physical Sciences at the Microscale University of Science and Technology of China, Hefei, 230026, P. R. China. E-mail: leishi@ustc.edu.cn

Table of Contents

1.	General Information	S-2
2.	General procedure for the preparation of L	S-2
3.	General procedure for the reaction	S-6
4.	Mechanism study	S-6
5.	Experimental data of the reaction	S-11
6.	Copies of ¹ H NMR, ¹⁹ F NMR and ¹³ C NMR Spectra	S-25
7.	Copies of HPLC Traces	. S-93

1. General Information

¹H NMR and ¹³C NMR were recorded on a 400MHz Nuclear Magnetic Resonance Spectrometer (¹H NMR: 400MHz, ¹³C NMR: 100MHz) using TMS as internal reference. The chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. UV-Vis Spectrophotometry was carried out on infrared spectrometer. HPLC analysis was carried out on HPLC with a multiple wavelength detector by commercial chiral columns. Optical rotations were measured on a Polarimeter. HRMS (ESI) were recorded on a Q-TOF Premier. Commercially available compounds were used without further purification. Solvents were purified according to the standard procedures unless otherwise noted.

L2 and L3 were synthetized according to literature as show in S24¹. Substrates of **2** were synthetized according to literature as show in S24².

2. General procedure for the preparation of L

a) Preparation for ligand L1, L4, L5

4-bromo-2-(trifluoromethyl)phenol (60 mmol) was added to a oven dried Schlenck flask under nitrogen. Then anhydrous THF (100 mL) and DMF (10 mL) was added as solvent. The solution was cooled to 0°C and NaH (90 mmol) was added, the resulting solution was kept at this temperature for 1 h, then benzyl bromide was (65 mmol) was added slowly, the cooling bath was removed, allowing the reaction mixture to warm up to room temperature overnight. Finally, the reaction mixture was quenched with water (10 mL) and extracted with Et₂O (3 × 50 mL), the organic layers were combined and dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product **G-1** was obtained as a colorless oil and used for the next step without purification.

To a round bottom flask was added magnesium strips (70.0 mmol), one small crystal of iodine, and 1-(benzyloxy)-4-bromo-2-(trifluoromethyl)benzene (G-1) (5 mmol) in dry THF (15 mL). The reaction mixture was stirred at reflux to start the reaction. A solution of 1-(benzyloxy)-4-bromo-2-(trifluoromethyl)benzene (G-1) (55 mmol) in dry THF (50 ml) was added dropwise over 30 min. After addition, the reaction mixture was continued to stirring at reflux for 1.0 hours and cooled to room temperature. Then a solution of long-chain aldehyde (55 mmol) in dry THF (30 ml) was added dropwise to the Grignard reagent at room temperature over 30 min. The resulting mixture was further stirred overnight and was then quenched with saturated aqueous solution of NH₄Cl. The product was extracted with ethyl acetate and the combined organic phase was dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product G-2 was used for next step without purification.



The alcohol product **G-2** obtained was dissolved in toluene (100 mL), and *p*-toluenesulfonic acid (catalytic amount) was added and the solution was heated to 90-100°C until the alcohol disappeared from TLC analysis. The reaction was then cooled to room temperature and quenched by saturated ammonium chloride solution, extracted by ether (100 mL \times 3), dried over MgSO₄. Then, the reaction was filtered, concentrated in vacuo to give the alkene crude product **G-3**.

The crude alkene product was dissolved in ethyl alcohol (80 mL), Pd/C (5%) was added, and the solution was then purged with hydrogen balloon for 15 minutes and then went overnight under hydrogen balloon. Then, the reaction was filtered over a short path of celite, concentrated in vacuo, and the crude mixture was purified by flash column chromatography (hexane) to afford product **G-4**.

Sodium hydride (2.80 g of a 60% dispersion in mineral oil, 70 mmol) was washed with hexane and transferred to a 2-neck 250 mL round bottom flask under an atmosphere of N₂. After addition of anhydrous THF (50 mL) the slurry was cooled with stirring to 0°C. To the resulting grey suspension

was added dropwise a solution of G-4 in anhydrous THF (25 mL) at such a rate that the evolution of hydrogen did not become too vigorous. After complete addition the ice bath was removed and the brown reaction mixture stirred for 1 hour. Chloromethylmethyl ether (5.5 mL, 70 mmol) was added dropwise and the resulting white suspension stirred overnight. Ice/water (100 mL) was added cautiously and the mixture extracted with Et₂O (3 \times 100 mL). The combined Et₂O extracts were washed with NaOH (2M, 50 mL), HCl (2M, 50 mL), and brine (50 mL). The solution was dried over MgSO₄ and the solvent was removed in vacuo to yield a colourless liquid. To a solution of the colourless liquid in anhydrous THF (100 mL) at -78°C under an atmosphere of N2 was added nbutyllithium (24.0 mL of a 2.5 M solution, 60 mmol) dropwise with stirring. After an additional hour stirring at this temperature, a solution of anhydrous DMF (5.5 mL, 70 mmol) in anhydrous THF (10 mL) was added to the mixture and the resulting solution was allowed to warm to room temperature and stirred overnight. The yellow solution was hydrolysed by the addition of water (150 mL) and the mixture extracted with Et₂O (3×150 mL). The combined Et₂O extracts were then washed with 2M HCl (100 mL) and brine (100 mL), dried over MgSO₄ and the solvent was removed in vacuo to yield the corresponding aldehyde. Corresponding aldehyde was dissolved in THF (100 mL) and concentrated HCl (10 mL) was added. The mixture was heated to 50°C for 4 hours, at which stage TLC analysis (silica, CH₂Cl₂) indicated the complete disappearance of starting material. The mixture extracted with Et₂O (3×50 mL). The combined Et₂O extracts were then washed with brine (100 mL), dried over MgSO₄ and the solvent was removed in vacuo to yield the crude salicylaldehyde derivative **G-5**.

To a solution of chiral amino alcohol (2 mmol) in methanol (10 mL) was added corresponding salicylaldehyde derivative (2 mmol). The solution was stirred for 2 h at room temperature then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (CH₂Cl₂/MeOH = 5/1 as eluent) to give the corresponding Schiff base ligand L1, L4, L5.

b) Preparation for ligand L2

To a round bottom flask was added magnesium strips (0.36 g, 15 mmol), one small crystal of iodine, and 4-bromo-*N*, *N*-dimethylbenzylamine in dry THF (25 mL). The reaction mixture was stirred at reflux to start the reaction. A solution of 4-bromo-*N*, *N*-dimethylbenzylamine (3.20 g, 15 mmol) in dry THF (5 ml) was added dropwise over 30 min. After addition, the reaction mixture was continued to stirring at reflux for 2 hours and cooled to room temperature. Then a solution of methyl (*tert*-butoxycarbonyl)-*L*-phenylalaninate (1.40 g, 5 mmol) in dry THF (5 ml) was added dropwise to the Grignard reagent at room temperature over 30 min. The resulting mixture was further stirred overnight and was then quenched with saturated aqueous solution of NH₄Cl. The product was extracted with

ethyl acetate and the combined organic phase was dried over Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product was used for next step without purification.

The crude product in CH_2Cl_2 (15 mL) was added 2,2,2-Trifluoroacetic acid (10 mL), then the reaction mixture was stirred at room temperature for 5h and concentrated under reduced pressure. To the residue was added aqueous HCl (2 M, 5.0 mL) and the mixture was extracted with ethyl acetate (3 x 5 mL). The aqueous layer was basified with aqueous buffer solution of NH₃ (1 M)/NH₄Cl (1 M) and extracted with dichloromethane (3 x 10 mL). The combined organic phases were dried over anhydrous sodium sulfate and concentrated under reduced pressure, the crude product was purified by column chromatography (CH₂Cl₂/MeOH/NEt₃ = 100:10:1) to give product

To a solution of chiral amino alcohol (2 mmol) in methanol (10 mL) was added salicylaldehyde derivative (2 mmol). The solution was stirred for 2 h at room temperature then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography ($CH_2Cl_2/MeOH = 5/1$ as eluent) to give the corresponding Schiff base ligand L2 quantitatively as yellow foam.

c) Preparation for ligand L3

To a round bottom flask was added magnesium strips (0.36 g, 15 mmol), one small crystal of iodine, and 2-(4-bromophenyl)-N, N-dimethylethan-1-amine in dry THF (25 mL). The reaction mixture was stirred at reflux to start the reaction. A solution of 2-(4-bromophenyl)-N, N-dimethylethan-1-amine (3.41 g, 15 mmol) in dry THF (5 ml) was added dropwise over 30 min. After addition, the reaction mixture was continued to stirring at reflux for 2 hours and cooled to room temperature. Then a solution of methyl (tert-butoxycarbonyl)-L-phenylalaninate (1.40 g, 5 mmol) in dry THF (5 ml) was added dropwise to the Grignard reagent at room temperature over 30 min. The resulting mixture was further stirred overnight and was then quenched with saturated aqueous solution of NH₄Cl. The product was extracted with ethyl acetate and the combined organic phase was dried over Na_2SO_4 . The solvent was evaporated under reduced pressure and the crude product was purified by silica gel column chromatography $(CH_2Cl_2/MeOH/NEt_3 = 100:10:1)$ to give tert-butyl (1, 1-bis(4-(2-(dimethylamino)ethyl)phenyl)-1-hydroxy-3-phenylpropan-2-yl)carbamate as a colorless oil (2.37g, 87% yield). The product in CH₂Cl₂ (15 mL) was added 2,2,2-Trifluoroacetic acid (10 mL), then the reaction mixture was stirred at room temperature for 5 h and concentrated under reduced pressure. To the residue was added aqueous HCl (2 M, 5.0 mL) and the mixture was extracted with ethyl acetate (3 x 5 mL). The aqueous layer was basified with aqueous buffer solution of NH₃ (1 M)/NH₄Cl (1 M) and extracted with dichloromethane (3 x 10 mL). The combined organic phases were dried over anhydrous sodium sulfate and concentrated under reduced pressure, the crude product was used for next step without purification.

To a solution of chiral amino alcohol (2 mmol) in methanol (10 mL) was added salicylaldehyde derivative (2 mmol). The solution was stirred for 2 h at room temperature then the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (CH₂Cl₂/MeOH = 5/1 as eluent) to give the corresponding Schiff base ligand L3 quantitatively as yellow foam.

3. General procedure for the reaction

A mixture of L4 (0.02 mmol, 14.6 mg), $Zn(NO_3)_2$ (0.02 mmol, 3.7 mg) in water (1.0 mL) was stirred for 1 h at ambient atmosphere. CHCl₃ (50 µL) as the oil phase of emulsion was then added to generate the emulsified system. 2-Enoylpyridine 1-oxides and indoles were added to the emulsion and kept at 25 °C for 24 h and the organic phase was separated after demulsification by adding a small amount of dilute hydrochloric acid (1 M, 0.4 mL), the resulting solution was concentrated under reduced pressure, the residue was purified by column chromatograph to afford Michael adducts.

4. Mechanism study

(1) TEM and SEM analyses

1) Preparation of samples

Catalyst: L4 (7.2 mg, 0.01 mmol) and Zn(NO₃)₂ (3.6 mg 0.01 mmol) were dissolved in 1 mL of H₂O. The mixture was stirred at 25°C for 1 h. CHCl₃ (50 μ L) as the oil phase of emulsion was then added to generate the emulsified system. The mixture was stirred at 25°C for 1 h.

Reaction mixture: After preparing the catalyst, indole (11.7 mg 0.1 mmol) and 2-Enoylpyridine 1-oxide (22.5 mg 0.1 mmol) were added to the solution. Then the solution was stirred at 25°C for 1 h.

A drop of the colloidal aqueous suspensions was deposited on a carbon-coated copper grid. Then the excess solution was immediately removed with the help of filter paper. The grid was dried in air and then observed by TEM and SEM.

2) SEM analyses (Fig S1)



Fig S1a. Metallomicelles of precatalyst (Zn-L4); Fig S1b. Metallomicelles of reaction mixture

3). TEM analyses (Fig S2)



Fig S2. Metallomicelles of reaction mixture

(2) XPS analyses

a) Preparation of samples

Sample 1: Zn (NO₃)₂.

Sample 2: the pre-catalyst was prepared by mixing L4 (0.02 mmol) and Zn (NO₃)₂ (0.02 mmol) in water only and stirred for two hours at ambient atmosphere, then evaporated in vacuum.

Sample 3: the pre-catalyst was prepared by mixing L4 (0.02 mmol) and Zn (NO₃)₂ (0.02 mmol) in water (1 ml) and stirred for one hour at ambient atmosphere. CHCl₃ (50 μ L) as the oil phase of emulsion was then added to generate the emulsified system. The water of the metallomicellar catalytic system was removed by anhydrous MgSO₄. The oil phase was separated, evaporated in vacuum to obtain the precatalyst.

Sample 4: the pre-catalyst was prepared by mixing L4 (0.02 mmol) and Zn (NO₃)₂ (0.02 mmol) in CHCl₃ only and stirred for two hours at ambient atmosphere, then evaporated in vacuum.

The spectra of the XPS was as showed in Fig S3. The results showed that the binding energy of the Zn 2P of the precatalyst was decreased compared to that of $Zn(NO_3)_2$, which indicated that electronic density of the Zn^{2+} was increased. This increasement should come from the coordination with the oxygen of the L4.

b) Spectra of XPS (Fig S3).



Fig S3 Analyses of XPS

(3) The detection of ¹H NMR to confirm the formation of two ammonium salts

The micellar catalytic system was prepared by mixing ligand 4 (0.02 mmol) and $Zn(NO_3)_2$ (0.02 mmol) in water (1 mL) and stirred for one hour at ambient atmosphere. $CDCl_3$ (50 µL) as the oil phase of emulsion was then added to generate the emulsified system. The water of the metallomicellar catalytic system was removed by anhydrous MgSO₄. The oil phase was separated, evaporated in vacuum to obtain the precatalyst, which was characterized by ¹H NMR.

¹H NMR response of the precatalyst and ligand **4** was listed in Fig S4. It was found that chemical shifts of the methyl groups attached to the N presented in lower field compared to that of **L4**, which can be ascribed to the electron-withdrawing effect of the generated ammonium salts.



Fig S4 ¹H NMR of the precatalyst (**Zn-L4**)

(4) The detection of IR to confirm the formation of the ammonium salts

The test of IR to confirm the formation of ammonium salts was shown in Fig S5. The infra-red absorption peak of ammonium salt group could be observed at 1250-1450 cm⁻¹ through comparative analyses of the difference between tertiary amine **G-6** and the corresponding nitrate **G-7**. As to the test of a similar catalytic system ($L2+Zn(NO_3)_2$), a strong absorption peak was found at the same wavelength range, that directly revealed the formation of ammonium salts.





Fig S5 IR test of the formation of two ammonium salts

(5) The pH detection

1. General procedure for the pH analyse

(a) Zinc salt (0.01 mmol) was dissolved in 1 mL of H₂O, and the obtained aqueous solution was directly tested by Portable pH meter (Model: S2-Meter, Manufacturer: Mettler-Toledo).

(b) Zinc salt (0.01 mmol) and L4 (0.01 mmol) was dissolved in 1 mL of H_2O . The mixture was stirred at 25°C for 1 h and the obtained aqueous solution was directly tested by Portable pH meter (Model: S2-Meter, Manufacturer: Mettler-Toledo).

(c) Zinc salt (0.01 mmol) and L4 (0.01 mmol) was dissolved in 1 mL of H_2O . The mixture was stirred at 25°C for 1 h. CHCl₃ (50 µL) as the oil phase of emulsion was then added to generate the emulsified system. The mixture was stirred at 25°C for 1 h and the obtained emulsion was directly tested by Portable pH meter (Model: S2-Meter, Manufacturer: Mettler-Toledo).

Zinc salt pH	(a)	(b)	(c)
$Zn(NO_3)_2$	5.45	6.10	5.43
ZnF ₂	5.68	6.32	5.51
ZnCl ₂	5.69	6.14	5.54
ZnBr ₂	5.40	6.15	5.64
ZnSO ₄	5.56	6.13	5.62

2.	Results	of	the	pН	test
----	---------	----	-----	----	------

5. Experimental data of the reaction



4-octyl-2-(trifluoromethyl) phenol

87% yield over four steps. ¹H NMR (400 MHz, CDCl₃) δ 7.29 (s, 1H), 7.23-7.19 (d, *J* = 8.4 Hz, 1H), 6.91-6.83 (d, *J* = 8.4 Hz, 1H), 5.43 (s, 1H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.70-1.51(m, 2H), 1.40-1.15 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 151.4, 135.3, 133.4, 128.4-120.2 (q, *J* = 270.5 Hz), 126.3, 117.6, 116.5-115.6 (q, *J* = 29.7 Hz), 34.9, 31.9, 31.5, 29.4, 29.24, 29.16, 22.7, 14.1; ¹⁹F NMR (376 MHz, CDCl₃) δ -60.7; HRMS (ESI) m/z calcd for C₁₅H₂₂F₃O [M+H]⁺ 275.1623, found 275.1628.



4-dodecyl-2-(trifluoromethyl) phenol

85% yield over four steps. ¹H NMR (400 MHz, CDCl₃) δ 7.29 (s, 1H), 7.24-7.18 (d, J = 8.4 Hz, 1H), 6.90-6.83 (d, J = 8.4 Hz, 1H), 5.31 (s, 1H), 2.56 (t, J = 7.6 Hz, 2H), 1.70-1.51(m, 2H), 1.40-1.20 (m, 18H), 0.88 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 151.3, 135.4, 133.4, 128.4-120.2 (q, J = 270.5 Hz), 126.3, 117.6, 116.5-115.6 (q, J = 29.7 Hz), 34.9, 31.9, 31.5, 29.68, 29.66, 29.6, 29.5, 29.4, 29.2, 22.7, 14.1; ¹⁹F NMR (376 MHz, CDCl₃) δ -60.6; HRMS (ESI) m/z calcd for C₁₉H₃₀F₃O [M+H]⁺ 331.2249, found 331.2235.



(S, E)-2-(((1,1-bis(4-((dimethylamino)methyl)phenyl)-1-hydroxy-3-phenylpropan-2-yl)imino)

methyl)-4-dodecyl-6-(trifluoromethyl)phenol (L1)

¹H NMR (400 MHz, CDCl₃): δ 13.55 (br, 1H), 7.61-7.30 (m, 8H), 7.20-7.10 (m, 5H), 7.00-6.94 (m, 2H), 6.80-6.70 (m, 1H), 4.35-4.29 (m, 1H), 3.50-3.24 (m, 4H), 3.04-2.80 (m, 3H), 2.46-2.41 (m, 2H),

2.27 (s, 6H), 2.11 (s, 6H), 1.53-1.46 (m, 2H), 1.26 (s, 18H), 0.88 (t, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.9, 157.4, 144.1, 142.8, 138.8, 137.7, 137.4, 134.5, 132.0, 129.7, 129.3, 129.2, 128.4, 127.7, 126.4, 126.0, 125.9, 125.0-122.3 (q, J = 270.9 Hz), 118.8, 117.6-117.0 (q, J = 30.3 Hz), 79.7, 78.9, 63.9, 63.8, 45.4, 45.2, 37.3, 34.6, 31.9, 31.4, 29.7, 29.65, 29.57, 29.44, 29.36, 29.1, 22.7, 14.1; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.4; $[\alpha]_D^{25}$ -66.8 (c 1.0, CHCl₃); HRMS (ESI) m/z calcd for C₄₇H₆₃F₃N₃O₂ [M+H]⁺ 758.4872, found 758.4878.



(*S*,*E*)-2-(((1,1-bis(4-((dimethylamino)methyl)phenyl)-1-hydroxy-3-phenylpropan-2-yl)imino)methyl)-6-(trifluoromethyl)phenol (L2)

¹H NMR (400 MHz, CDCl₃): δ 13.91 (br, 1 H), 7.64-7.30 (m, 8 H), 7.20-7.11 (m, 5 H), 7.00-6.94 (m, 3 H), 6.80-6.70 (m, 1 H), 4.35-4.31 (m, 1 H), 3.51-3.22 (m, 4 H), 3.10-3.01 (m, 2 H), 2.91-2.79 (m, 1 H), 2.24 (s, 6 H), 2.11 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃): δ 165.8, 160.0, 144.0, 142.7, 138.7, 137.7, 137.4, 135.1, 129.9, 129.7, 129.3, 129.2, 128.5, 126.5, 126.0, 125.9, 124.9-122.2 (q, *J* = 270.0 Hz), 118.8, 118.4-117.5 (q, *J* = 30.0 Hz), 117.3, 79.6, 78.7, 63.9, 63.7, 45.4, 45.2, 37.2; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.6.



(*S*,*E*)-2-(((1,1-bis(4-(2-(dimethylamino)ethyl)phenyl)-1-hydroxy-3-phenylpropan-2-yl)imino)methyl)-6-(trifluoromethyl)phenol (L3)

¹H NMR (400 MHz, CDCl₃): δ 7.54-7.50 (m, 4 H), 7.40-7.31 (m, 2 H), 7.25-7.00 (m, 8 H), 7.05-6.91 (m, 3 H), 6.81-6.70 (m, 1 H), 4.31 (d, *J* = 8.9 Hz, 1 H), 3.38 (br, 1 H), 3.08-3.01 (d, *J* = 13.0 Hz, 1 H), 2.88-2.72 (m, 4 H), 2.71-2.64 (m, 2 H), 2.62-2.51 (m, 2 H), 2.50-2.41 (m, 2 H), 2.30 (s, 6 H), 2.23 (s,

6 H); ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 160.5, 142.9, 141.8, 139.0, 138.9, 138.7, 135.2, 130.0, 129.7, 128.8, 128.6, 128.4, 126.5, 126.3, 126.1, 125.0-122.3 (q, *J* = 270.9 Hz), 118.8, 118.2-117.9 (q, *J* = 30.4 Hz), 117.1, 79.4, 78.5, 61.2, 61.1, 45.3, 45.2, 37.3, 33.7, 33.5; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.6.



(*S*, *E*)-2-(((1,1-bis(4-(2-(dimethylamino)ethyl)phenyl)-1-hydroxy-3-phenylpropan-2-yl)imino) methyl)-4-octyl-6-(trifluoromethyl)phenol (L4)

¹H NMR (400 MHz, CDCl₃): δ 13.63 (br, 1 H), 7.53-7.33 (m, 6 H), 7.25-7.00 (m, 7 H), 7.00-6.90 (m, 2 H), 6.80-6.78 (m, 1 H), 4.35-4.27 (m, 1 H), 3.27-3.00 (m, 2 H), 2.90-2.70 (m, 3 H), 2.69-2.63 (m, 2 H), 2.55-2.40 (m, 6 H), 2.29 (s, 6 H), 2.22 (s, 6 H), 1.52-1.46 (m, 2 H), 1.26 (s, 10 H), 0.88 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.7, 157.7, 143.0, 141.9, 139.1, 139.0, 138.9, 134.6, 131.9, 129.7, 129.0, 128.7, 128.6, 128.4, 126.4, 126.3, 126.1, 125.1-122.4 (q, *J* = 271.0 Hz), 118.8, 117.9-117.3 (q, *J* = 30.0 Hz), 79.5, 78.8, 61.4, 61.2, 45.42, 45.36, 37.4, 34.7, 33.8, 33.7, 31.9, 31.4, 29.4, 29.2, 29.1, 22.7, 14.1; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.3; [α]_D²⁵ -88.6 (c 1.0, CHCl₃); HRMS (ESI) m/z calcd for C₄₅H₅₉F₃N₃O₂ [M+H]⁺ 730.4559, found 730.4551.



(S, E) - 2 - (((1, 1-bis(4 - (2 - (dimethylamino)ethyl)phenyl) - 1 - hydroxy - 3 - phenylpropan - 2 - yl)imino)

methyl)-4-dodecyl-6-(trifluoromethyl)phenol (L5)

¹H NMR (400 MHz, CDCl₃): δ 13.59 (br, 1 H), 7.53-7.30 (m, 6 H), 7.23-7.00 (m, 7 H), 6.98-6.90 (m, 2 H), 6.80-6.78 (m, 1 H), 4.35-4.27 (m, 1 H), 3.10-2.90 (m, 2 H), 2.86-2.70 (m, 3 H), 2.69-2.65 (m, 2 H), 2.55-2.40 (m, 6 H), 2.30 (s, 6 H), 2.23 (s, 6 H), 1.52-1.47 (m, 2 H), 1.26 (s, 18 H), 0.88 (t, J = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.8, 157.5, 143.0, 141.8, 139.1, 139.0, 138.9, 134.5, 132.0, 129.7, 128.7, 128.6, 128.4, 126.4, 126.2, 126.0, 125.0-122.3 (q, J = 270.9 Hz), 118.8, 117.9-117.3 (q, J = 30.6 Hz), 79.5, 78.8, 61.3, 61.2, 45.42, 45.36, 37.4, 34.6, 33.8, 33.7, 31.9, 31.4, 29.66, 29.65, 29.58, 29.43, 29.35, 29.1, 22.7, 14.1; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.4; [α]_D²⁵ -73.8 (c 1.0, CHCl₃); HRMS (ESI) m/z calcd for C₄₉H₆₇F₃N₃O₂ [M+H]⁺ 786.5185, found 786.5192.



(*S*, *E*)-4-dodecyl-2-(((1-hydroxy-1,1,3-triphenylpropan-2-yl)imino)methyl)-6-(trifluoromethyl) phenol (L6)

¹H NMR (400 MHz, CDCl₃): δ 13.53 (br, 1 H), 7.65-7.32 (m, 8 H), 7.30-7.09 (m, 6 H), 6.97-6.94 (m, 2 H), 6.79 (s, 1 H), 4.37-4.32 (m, 1 H), 3.04-3.00 (m, 1 H), 2.90-2.82 (m, 2 H), 2.48-2.42 (m, 2 H), 1.50 (s, 2 H), 1.26 (s, 18 H), 0.88 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 166.0, 157.4, 145.3, 144.0, 138.8, 134.6, 132.1, 129.8, 128.6, 128.4, 127.2, 127.1, 126.4, 126.1, 126.0, 125.0, 122.3, 118.7, 117.6, 117.3 79.7, 78.7, 37.3, 34.6, 32.0, 31.4, 29.7, 29.67, 29.6, 29.5, 29.4, 29.1, 22.7, 14.2; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.4; [α]_D²⁵ -116.6 (c 1.0, CHCl₃); HRMS (ESI) m/z calcd for C₄₁H₄₈F₃NO₂ [M+H]⁺ 644.3715, found 644.3701.



(*S*, *E*)-2-(((1,1-bis(4-(2-(dimethylamino)ethyl)phenyl)-3-phenyl-1-((trimethylsilyl)oxy)propan-2-yl)imino)methyl)-4-octyl-6-(trifluoromethyl)phenol (L7)

¹H NMR (400 MHz, CDCl₃) δ 13.59 (br, 1 H), 7.72 (s, 1H), 7.54-7.52 (2H), 7.47-7.11 (m, 10H), 6.99-6.96 (2H), 6.91 (s, 1H), 4.23- 4.19 (d, 1H), 3.38-3.33 (2H), 2.93-2.83 (m, 4H), 2.71-2.66 (m, 4H), 2.66-2.52 (t, 2H), 2.40-2.38 (12H), 1.52 (2H), 1.27 (10 H), 0.90-0.86 (3H), -0.18 (9H). ¹³C NMR (100 MHz, CDCl₃) δ 164.8, 140.4, 140.2, 139.1, 139.0, 134.4, 131.4, 130.8, 129.5, 129.3, 129.1, 128.2, 127.8, 126.1, 118.8, 82.4, 61.0, 60.9, 45.1, 44.9, 37.8, 34.5, 33.4, 33.3, 31.7, 31.3, 29.3, 29.1, 29.0, 22.5, 13.9, 1.7; ¹⁹F NMR (376 MHz, CDCl₃) δ -62.3; HRMS (ESI) m/z calcd for C₄₈H₆₆F₃N₃O₂Si [M+H]⁺ 802.4955, found 802.4961.



(R)-2-(3-(1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4a)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 90% yield. $[\alpha]_D^{25} = 19.2$ (c = 1.0, THF, 94% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min,254 nm; t_R = 26.50 min (major) and 31.25 min (minor); ¹H NMR(400 MHz, CDCl₃) δ 8.29-8.01 (m, 2H), 7.50-7.35 (m, 1H), 7.32-7.18 (m, 6H), 7.15-6.90 (m, 6H), 4.93 (t, J = 7.6 Hz, 1H), 4.11-4.05 (dd, J = 16.8, 7.2 Hz, 1H), 3.99-3.93 (dd, J = 16.4, 7.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 197.1, 147.1, 143.9, 140.1, 136.5, 128.4, 127.9, 127.5, 126.7, 126.5, 126.4, 125.7, 122.1, 121.6, 119.5, 119.4, 118.7, 111.1, 49.1, 38.6.



(R)-2-(3-(4-fluorophenyl)-3-(1H-indol-3-yl)propanoyl)pyridine 1-oxide (4b)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 95% yield. $[\alpha]_D^{25} = 11.7$ (c = 1.0, in THF, 91% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 25.15 min (major) and 32.66 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.29-8.08 (m, 2H), 7.41-7.32 (m, 1H), 7.30-7.18 (m, 5H), 7.15-7.01 (m, 3H), 7.01-6.90 (m, 1H), 6.90-6.80 (m, 2H), 4.93 (t, J = 7.6 Hz, 1H), 4.09-4.03 (dd, J = 16.8, 7.6 Hz, 1H), 3.99-3.92 (dd, J = 16.8, 8.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 196.7, 162.6-160.2 (d, J = 242.7 Hz), 146.9, 140.2, 139.7-139.6 (d, J = 3.2 Hz), 136.6, 129.4-129.3 (d, J = 7.9Hz), 127.7, 126.7, 126.5, 125.7, 122.2, 121.6, 119.44-119.37 (d, J = 6.2 Hz), 118.6, 115.2, 115.0, 111.1, 49.2, 37.7; ¹⁹F NMR (376 MHz, CDCl₃) δ -113.7.



(*R*)-2-(3-(4-chlorophenyl)-3-(1H-indol-3-yl)propanoyl)pyridine 1-oxide (4c)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 94% yield. $[\alpha]_D^{25} = 17.9$ (c=1.0, THF, 97% ee). HPLC on Daicel Chiralpak AD-H column, n-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 26.97 min (major) and 36.95 min(minor); ¹H NMR (400 MHz, CDCl₃) δ 8.21-8.11 (m, 2H), 7.32-7.18 (m, 1H), 7.22-6.95 (m, 10 H), 6.95-6.80 (m, 1H), 4.85 (t, *J* = 7.6 Hz, 1H), 4.02-3.96 (dd, *J* = 16.8, 7.6 Hz, 1H), 3.92-3.85 (dd, *J* = 16.4, 8.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 195.5, 145.8, 141.5, 139.2, 135.5, 130.9, 128.3, 127.4, 126.7, 125.7, 125.4, 124.7, 121.2, 120.6, 118.4, 118.3, 117.2, 110.1, 47.9, 36.7.



(R)-2-(3-(4-bromophenyl)-3-(1H-indol-3-yl)propanoyl)pyridine 1-oxide (4d)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 95% yield. $[\alpha]_D^{25} = 16.1$ (c = 1.0, THF, 97% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 30.13 min (major) and 41.18 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.20-8.11 (m, 2H), 7.42-6.93 (m, 12 H), 4.92 (t, J = 7.6 Hz, 1H), 4.10-4.04 (dd, J = 16.8, 7.6 Hz, 1H), 4.00-3.93 (dd, J = 16.4, 8.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 196.4, 146.8, 143.0, 140.3, 136.5, 131.4, 129.7, 127.8, 126.8, 126.5, 125.6, 122.3, 121.6, 120.1, 119.5, 119.3, 118.2, 111.0, 48.9, 37.8.



(R)-2-(3-(1H-indol-3-yl)-3-(4-(trifluoromethyl)phenyl)propanoyl)pyridine 1-oxide (4e)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 93% yield. $[\alpha]_D^{25} = 10.5$ (c = 1.0, THF, 95% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 18.65 min (major) and 23.85 min (minor);¹H NMR (400 MHz, DMSO- d_6) δ 10.95 (s, 1H), 8.33-8.31 (d, J = 6.4 Hz, 1H), 7.61-7.50 (m, 5H), 7.39-7.27 (m, 5 H), 7.03 (t, J = 7.5 Hz, 1H), 6.89 (t, J = 7.8 Hz, 1H), 4.95-4.90 (m, 1H), 4.09-4.07 (m, 1H), 4.03-3.88 (m, 1H); ¹³C NMR (100 MHz, DMSO- d_6) δ 197.3, 150.0, 146.6, 140.6, 136.9, 129.0, 128.9-120.8 (q, J = 270.0 Hz), 127.6-126.7 (q, J = 30.0 Hz), 126.6, 126.4, 126.3, 125.54, 125.50, 122.8, 121.6, 118.9, 117.0, 111.9, 79.6, 48.1, 37.9. ¹⁹F NMR (376 MHz, DMSO- d_6) δ -60.7; HRMS (ESI) m/z calcd for C₂₃H₁₇F₃N₂NaO₂ [M+Na]⁺ 433.1140, found 433.1136.



(R)-2-(3-(1H-indol-3-yl)-3-(p-tolyl)propanoyl)pyridine 1-oxide (4f)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 95% yield. $[\alpha]_D^{25} = 7.3$ (c = 1.0, THF, 93% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 25.29 min (major) and 32.69 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.16-8.14 (d, J = 5.6 Hz, 1H), 8.01 (s, 1 H), 7.45-7.42 (d, J = 7.6 Hz, 1H), 7.32-6.90 (m, 11H), 4.89 (t, J = 6.8 Hz, 1H), 4.11-4.04 (dd, J = 16.0, 7.2 Hz, 1H), 3.97-3.91 (dd, J = 16.0, 8.0 Hz, 1H), 2.26(s, 3H) ;¹³C NMR (100 MHz, CDCl₃) δ 197.2, 140.8, 136.5, 135.8, 129.1, 127.7, 127.5, 126.7, 126.6, 125.6, 122.1, 121.5, 119.5, 119.4, 119.1, 111.0, 49.1, 38.1, 21.0.



(R)-2-(3-(1H-indol-3-yl)-3-(4-methoxyphenyl)propanoyl)pyridine 1-oxide (4g)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 92% yield. $[\alpha]_D^{25} = 17.0$ (c = 1.0, THF, 87% ee). HPLC on Daicel Chiralpak AD-H column, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 40.92 min (major) and 47.16 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.20-8.09 (m, 2H), 7.45-7.39 (m, 1 H), 7.30-6.95 (m, 9H), 6.80-6.69 (m, 2H), 4.88 (t, J = 8.0 Hz, 1H), 4.08-4.03 (dd, J = 16.0, 7.2 Hz, 1H), 3.96-3.90 (dd, J = 16.0, 8.0 Hz, 1H), 3.72 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 197.3, 158.0, 147.2, 140.1, 136.6, 136.0, 128.9, 127.5, 126.7, 126.5, 125.6, 122.0, 121.5, 119.5, 119.3, 119.1, 114.4, 113.7, 111.1, 55.2, 49.2, 37.8.



(S)-2-(3-(2-fluorophenyl)-3-(1H-indol-3-yl)propanoyl)pyridine 1-oxide (4h)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 89% yield. $[\alpha]_D^{25} = -13.3$ (c = 1.0, THF, 93% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 25.86 min (major) and 35.89 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.22 (s, 1H), 8.06-8.05 (d, J = 6.4 Hz, 1H), 7.44-7.42 (d, J = 7.9 Hz, 1H), 7.20-7.13 (m, 4H), 7.05-7.01 (m, 4H), 6.95-6.85 (m, 3H), 5.19 (t, J = 7.6 Hz, 1H), 4.17-4.10 (dd, J = 17.0, 7.6 Hz, 1H), 3.89-3.83 (dd, J = 17.0, 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 196.4, 161.7-159.3 (d, J = 244.1 Hz), 146.8, 140.2, 136.4, 130.8-130.6 (d, J = 13.9 Hz), 129.5-129.4 (d, J = 4.2 Hz), 128.0-127.9 (d, J = 7.6 Hz), 127.7, 126.6, 125.8, 124.2-124.1 (d, J = 3.3 Hz), 122.1, 121.9, 119.4, 119.2, 117.6, 115.5, 115.3, 111.2, 47.7, 31.2; ¹⁹F NMR (376 MHz, CDCl₃) δ -118.6.



(S)-2-(3-(2-chlorophenyl)-3-(1H-indol-3-yl)propanoyl)pyridine 1-oxide (4i)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 90% yield. $[\alpha]_D^{25} = -73.7$ (c = 1.0, THF, 90% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 23.73 min (major) and 30.57 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.27 (s, 1H), 8.15-8.12 (m, 1H), 7.49-7.47 (d, J = 7.9 Hz, 1H), 7.35-7.16 (m, 5H), 7.15-6.95 (m, 6H), 5.46 (t, J = 7.6 Hz, 1H), 4.27-4.21 (dd, J = 17.0, 8.3 Hz, 1H), 3.83-3.77 (dd, J = 17.0, 6.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 196.3, 146.9, 141.1, 140.2, 136.5, 133.5, 129.5, 129.3, 127.7, 127.6, 127.0, 126.7, 126.6, 125.9, 122.3, 122.1, 119.5, 117.6, 111.2, 47.8, 34.6.



(S)-2-(3-(2-bromophenyl)-3-(1H-indol-3-yl)propanoyl)pyridine 1-oxide (4j)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 94% yield. $[\alpha]_D^{25} = -49.6$ (*c* = 1.0, THF, 92%

ee). HPLC on Chiralpak OD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 24.74 min (major) and 31.36 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.40 (s, 1H), 8.12-8.11 (d, J = 4.2 Hz, 1H), 7.51-7.47 (m, 2H), 7.25-6.94 (m, 10H), 5.43 (t, J = 7.0 Hz, 1H), 4.26-4.20 (dd, J = 16.8, 8.4 Hz, 1H), 3.79-3.73 (dd, J = 16.6, 6.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 196.2, 142.8, 136.6, 132.9, 129.5, 128.0, 127.6 126.7, 126.5, 124.4, 122.4, 122.1, 119.6, 119.4, 117.5, 111.2, 48.0, 37.5.



(S)-2-(3-(1H-indol-3-yl)-3-(2-methoxyphenyl)propanoyl)pyridine 1-oxide (4k)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 91% yield. $[\alpha]_D^{25} = 16.6$ (c = 1.0, THF, 84% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 27.7 min (minor) and 38.5 min (major); ¹H NMR (400 MHz, CDCl₃) δ 8.30 (s, 1H), 8.10-8.09 (d, J = 6.4, 1H), 7.51-7.49 (d, J = 7.9 Hz, 1H), 7.25-6.94 (m, 9H), 6.80-6.72 (m, 2H), 5.35 (t, J = 7.7 Hz, 1H), 4.18-4.12 (dd, J = 8.3, 16.4 Hz, 1H), 3.85-3.70 (dd, J = 7.3, 16.4 Hz, 1H), 3.76 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 197.5, 156.7, 147.3, 140.0, 136.5, 131.9, 128.6, 127.4, 127.3, 127.0, 126.3, 125.6, 122.1, 121.9, 120.6, 119.6, 119.2, 118.4, 111.0, 110.5, 55.4, 47.7, 31.4; HRMS (ESI) m/z calcd for C₂₃H₂₀N₂NaO₃ [M+Na]⁺ 395.1372, found 395.1366.



(R)-2-(3-(1H-indol-3-yl)-3-(2-(trifluoromethyl)phenyl)propanoyl)pyridine 1-oxide (41)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 93% yield. $[\alpha]_D^{25} = 17.3$ (c = 1.0, THF, 90% ee). HPLC on Chiralpak OD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 21.11 min (major) and 29.88 min (minor);¹H NMR (400 MHz, CDCl₃) δ 8.28 (s, 1H), 8.16-8.14 (d, J = 6.4 Hz, 1H), 7.65-7.62 (d, J = 7.6 Hz, 1H), 7.41-6.94 (m, 11 H), 5.46-5.42 (dd, J = 4.4, 9.9 Hz, 1H), 4.45-4.38 (dd, J = 10, 17.8 Hz, 1H), 3.55-3.48 (dd, J = 4.5, 17.8 Hz, 1H);¹³C NMR (100 MHz, CDCl₃)

δ 195.5, 146.8, 143.1, 140.3, 136.7, 132.0, 129.9, 128.9-120.7 (q, J = 272.4 Hz), 127.9-127.1 (q, J = 26.7 Hz), 127.8, 126.7, 126.6, 126.4, 126.0, 125.9-125.8 (q, J = 6.0 Hz), 122.6, 122.1, 119.5, 119.4, 117.7, 111.1, 49.1, 33.6; ¹⁹F NMR (376 MHz, CDCl₃) δ -125.2; HRMS (ESI) m/z calcd for C₂₃H₁₇F₃N₂NaO₂ [M+Na]⁺ 433.1140, found 433.1138.



(R)-2-(3-(1H-indol-3-yl)-3-(3-methoxyphenyl)propanoyl)pyridine 1-oxide (4m)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 92% yield. $[\alpha]_D^{25} = 13.4$ (c = 1.0, THF, 90% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 30.98 min (major) and 33.44 min (minor);¹H NMR (400 MHz, CDCl₃) δ 8.17 (s, 1H), 8.15-8.12 (d, J = 6.4, 1H), 7.47-7.44 (d, J = 7.9 Hz, 1H), 7.29-6.85 (m, 10H), 6.69-6.65 (dd, J = 2.0, 8.1 Hz, 1H), 4.91 (t, J = 7.7 Hz, 1H), 4.11-4.04 (dd, J = 7.6, 16.6 Hz, 1H), 3.98-3.91 (dd, J = 8.0 Hz, 16.6, 1H), 3.70 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 197.1, 159.6, 147.1, 145.5, 140.1, 136.5, 129.3, 127.5, 126.7, 126.6, 125.6, 122.1, 121.6, 120.4, 119.43, 119.38, 118.6, 113.8, 111.6, 111.1, 55.1, 49.0, 38.6; HRMS (ESI) m/z calcd for C₂₃H₂₀N₂NaO₃ [M+Na]⁺ 395.1372, found 395.1367.



(R)-2-(3-(1H-indol-3-yl)-3-(naphthalen-2-yl)propanoyl)pyridine 1-oxide (4n)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 95% yield. $[\alpha]_D^{25} = -36.4$ (c = 1.0, THF, 97% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 40.64 min (minor) and 46.06 min (major); ¹H NMR (400 MHz, CDCl₃) δ 8.21-8.01 (m, 2H), 7.80-7.61 (m, 4H), 7.48-7.31 (m, 4H), 7.30-7.19 (m, 2H), 7.12-6.88 (m, 5H), 5.10 (t, J = 7.7 Hz, 1H), 4.20-3.89 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 197.0, 147.0, 141.3,140.1, 136.5, 133.4, 132.3, 128.1, 127.8, 127.5, 126.7, 126.62, 126.57, 126.1, 125.9, 125.6, 125.4, 122.1, 121.7, 119.5, 119.4, 118.7, 111.0, 48.9, 38.7.



(S)-2-(3-(1H-indol-3-yl)-3-(thiophen-2-yl)propanoyl)pyridine 1-oxide (40)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 88% yield. $[\alpha]_D^{25} = 19.3$ (c = 1.0, THF, 92% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 29.11 min (major) and 31.26 min (minor);¹H NMR (400 MHz, CDCl₃) δ 8.20 (s, 1H), 8.06-8.04 (d, J = 6.2, 1H), 7.47-7.44 (d, J = 7.9 Hz, 1H), 7.22-6.75 (m, 10H), 5.17 (t, J = 7.5, 1H), 4.10-4.03 (dd, J = 7.3, 16.6 Hz, 1H), 3.99-3.92 (dd, J = 7.9, 16.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 196.5, 148.4, 146.9, 140.1, 136.4, 127.7, 126.6,126.5, 126.3, 125.7, 124.3, 123.6, 122.2, 121.8, 119.5, 119.3, 118.5, 111.2, 50.0, 33.9; HRMS (ESI) m/z calcd for C₂₀H₁₆N₂NaO₂S [M+Na]⁺ 371.0830, found 371.0827.



(R)-2-(3-(5-fluoro-1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4p)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 95% yield. $[\alpha]_D^{25} = 20.1$ (c = 1.0, THF, 96% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 20.78 min (major) and 23.09 min (minor); ¹H NMR (400 MHz, DMSO- d_6) δ 10.98(s, 1H), 8.33-8.31 (d, J = 6.4 Hz, 1H), 7.55-7.50 (m, 1 H), 7.38-7.00 (m, 10H), 6.89-6.83 (m, 1H), 4.76-4.71 (t, J = 7.8 Hz, 1H), 4.05-3.98 (dd, J = 8.0, 16.8 Hz, 1H), 3.81-3.74 (dd, J = 7.4, 16.9 Hz, 1H); ¹³C NMR (100 MHz, DMSO- d_6) δ 197.6, 158.1-155.8 (d, J = 229.7 Hz), 146.8, 144.7, 140.5, 133.5, 128.9, 128.7, 128.1, 126.95-126.85 (d, J = 9.6 Hz), 126.5, 126.30, 126.25, 124.7, 118.1-118.0 (d, J = 4.9 Hz), 112.8-112.7 (d, J = 9.8 Hz), 109.7-109.4 (d, J = 26.1 Hz), 103.8-103.6 (d, J = 23.0 Hz), 48.4, 38.0; ¹⁹F NMR (376 MHz, DMSO- d_6) δ -124.4.



(R)-2-(3-(5-chloro-1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4q)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 92% yield. $[\alpha]_D^{25}$ = 40.0 (*c* = 1.0, THF, 98% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 19.15 min (major) and 22.02 min (minor); ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.09 (s, 1H), 8.33-8.31 (d, *J* = 6.4 Hz, 1H), 7.55-7.50 (m, 1 H), 7.42-6.95 (m, 11H), 4.76-4.71 (t, *J* = 7.8 Hz, 1H), 4.04-3.98 (dd, *J* = 8.4, 17.0 Hz, 1H), 3.79-3.73 (dd, *J* = 7.2, 16.8 Hz, 1H); ¹³C NMR (400 MHz, DMSO-*d*₆) δ 197.6, 146.7, 144.7, 140.6, 135.3, 128.9, 128.7, 128.1, 127.9, 126.6, 126.34, 126.29, 124.5, 123.4, 121.4, 118.2, 117.7, 113.4, 48.5, 37.8.



(R)-2-(3-(5-bromo-1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4r)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 93% yield. $[\alpha]_D^{25} = 55.4$ (c = 1.0, THF, 98% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 19.25 min (major) and 22.64 min (minor); ¹H NMR (400 MHz, DMSO- d_6) δ 11.1 (s, 1H), 8.34-8.32 (d, J = 6.4 Hz, 1H), 7.60-7.08 (m, 12H), 4.79-4.75 (t, J = 7.6 Hz, 1H), 4.04-3.98 (dd, J = 8.2, 17.0 Hz, 1H), 3.79-3.73 (dd, J = 7.2, 16.9 Hz, 1H); ¹³C NMR (100 MHz, DMSO- d_6) δ 197.5, 146.8, 144.7, 140.6, 135.5, 128.9, 128.7, 128.6, 128.1, 126.6, 126.4, 126.3, 124.4, 124.0, 121.2, 117.6, 113.9, 111.4, 48.5, 37.8.



(R)-2-(3-(5-methoxy-1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4s)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 90% yield. $[\alpha]_D^{25} = 36.4$ (c = 1.0, THF, 90% ee). HPLC on Daicel Chiralpak AD-H column, n-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 27.49 min (major) and 33.57 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.16-8.11 (m, 2H), 7.35-6.98 (m, 10H), 6.85-6.84 (d, J = 2.4 Hz, 1H), 6.77-6.74 (m, 1H), 4.87 (t, J = 7.8 Hz, 1H), 4.11-4.05 (dd, J = 7.6, 16.4 Hz, 1H), 3.96-3.90 (dd, J = 8.0, 16.4 Hz, 1H), 3.72 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 197.2, 153.7, 147.1, 143.8, 140.0, 131.7, 128.4, 127.9, 127.6, 127.1, 126.5, 126.4, 125.7, 122.4, 118.3, 122.2, 111.8, 101.3, 55.8, 49.0, 38.6.



(R)-2-(3-(5-acetyl-1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4t)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 90% yield. $[\alpha]_D^{25} = 33.1$ (c = 1.0, THF, 83% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R = 22.27 min (major) and 25.50 min (minor); ¹H NMR (400 MHz, CDCl₃) δ 8.72 (s, 1H), 8.12 (s, 1H), 8.09-8.07 (d, J = 4.8 Hz, 1H), 7.74-7.71 (dd, J = 1.4, 8.6 Hz, 1H), 7.24-7.01 (m, 10H), 4.91 (t, J = 7.6 Hz, 1H), 4.03-3.96 (dd, J = 7.6, 16.9 Hz, 1H), 3.94-3.87 (dd, J = 7.8, 16.6 Hz, 1H), 3.79 (s, 3H);¹³C NMR (100 MHz, CDCl₃) δ 196.6, 168.2, 146.9, 143.5, 140.2, 139.1, 128.5, 127.8, 127.7, 126.6, 126.5, 126.3, 125.9, 123.5, 123.0, 122.2, 121.4, 120.1, 110.9, 51.9, 49.2, 38.1; HRMS (ESI) m/z calcd for C₂₄H₂₀NaN₂O₄ [M+Na]⁺ 423.1321, found 423.1315.



(R)-2-(3-(6-chloro-1H-indol-3-yl)-3-phenylpropanoyl)pyridine 1-oxide (4u)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid in 93% yield. $[\alpha]_D^{25} = 36.5$ (c = 1.0, THF, 96% ee). HPLC on Chiralpak AD-H column, hexane/2-propanol = 80:20, flow rate 1.0 mL/min, 254 nm; t_R

= 26.41 min (major) and 30.16 min (minor);¹H NMR (400 MHz, CDCl₃) δ 8.22 (s, 1H), 8.17-8.15 (d, J = 6.4 Hz, 1H), 7.31-7.08 (m, 11 H), 6.95-6.92 (dd, J = 1.8, 8.5 Hz, 1H), 4.90 (t, J = 7.7 Hz, 1H), 4.12-4.05 (dd, J = 7.6, 16.9 Hz, 1H), 3.95-3.88 (dd, J = 7.8, 16.6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 196.8, 147.0, 143.5, 140.2, 136.9, 128.5, 128.0, 127.8, 127.7, 126.6, 126.5, 125.8, 125.3, 122.2, 120.4, 120.1, 119.0, 111.0, 49.0, 38.3; HRMS (ESI) m/z calcd for C₂₂H₁₇ClN₂NaO₂ [M+Na]⁺ 399.0876, found 399.0873.

References

1. Y. Gui, Y. Li, J. Sun, Z. Zha, Z. Wang, J. Org. Chem. 2018, 83, 7491-7499.

2. P. Singh, V. Singh, Org. Lett. 2008, 10, 4121-4124.

6. Copies of ¹H NMR, ¹⁹F NMR and ¹³C NMR Spectra


































--62.337


















































































































7. Copies of HPLC Traces



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
		-				
1	26.668	BB	0.7982	2.17536e4	427.09064	50.0074
2	31.390	BB	0.9614	2.17472e4	355.64304	49.9926
Totals :			4.35008e4	782.73367		

Results obtained with enhanced integrator!





Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] 8 1 25.116 VV 0.6698 9516.56641 216.06914 50.9274 2 32.720 BP 0.8954 9169.95801 155.63040 49.0726 Totals : 1.86865e4 371.69954

Results obtained with enhanced integrator!

Signal 4: DAD1 D, Sig=240,16 Ref=360,100





Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Results obtained with enhanced integrator!





Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 ----|-----|----|-----|-----|-----| 1 29.684 VB 0.9463 4513.34863 72.89516 50.9745 2 40.427 PV 1.2149 4340.78711 51.31431 49.0255 8854.13574 124.20947 Totals :

Results obtained with enhanced integrator!



Totals :



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

Peak RetTime Type Width Area Height Area [mAU*s] 8 # [min] [min] [mAU] ----|-----|-----|-----| -----| _____ 1 18.690 VB 0.4918 3175.78882 94.55867 50.5529 2 23.841 VV 0.6271 3106.32153 75.02407 49.4471 Totals : 6282.11035 169.58274

Results obtained with enhanced integrator!



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Туре	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.654	VB	0.2396	4.76252e4	2729.20068	97.7478
2	23.849	vv	0.6324	1097.33411	22.60127	2.2522

Totals :

4.87226e4 2751.80196



Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 1 25.174 VB 0.7935 4322.22266 81.13294 50.6807 2 32.673 BP 1.0141 4206.12500 60.27697 49.3193 8528.34766 141.40992 Totals :

Results obtained with enhanced integrator!

Signal 4: DAD1 D, Sig=240,16 Ref=360,100



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
		-				
1	25.291	vv	0.5732	1.04703e5	2900.22632	96.7215
2	32.691	vv	1.3906	3549.05542	32.38370	3.2785
2000220 302				1.1 1010101010101		

Totals: 1.08252e5 2932.61002



 Peak RetTime Type
 Width
 Area
 Height
 Area

 # [min]
 [min]
 [mAU*s]
 [mAU]
 %

 ----|-----|

 -----|
 -----|

 1
 40.994 VB
 1.1918
 7220.98193
 89.64089
 50.6599

 2
 47.638 VB
 1.1816
 7032.86084
 76.42580
 49.3401

 Totals :
 1.42538e4
 166.06670

Results obtained with enhanced integrator!



#	[min]	-,	[min]	[mAU*s]	[mAU]	8
	40.924	 VB	0.9231	1.46090e5	2383.41162	93.3621
2	47.159	BBA	1.2820	1.03867e4	118.10255	6.6379
Totals :				1.56477e5	2501.51417	



Signal 4: DAD1 D, Sig=240,16 Ref=360,100 Peak RetTime Type Width Height Area Area [min] [mAU*s] [mAU] 8 # [min] -----| 1 25.826 BP 0.6474 1489.26562 34.51617 50.8356 0.7999 1440.30945 24.14571 49.1644 2 36.105 BB 2929.57507 Totals : 58.66189

Results obtained with enhanced integrator!





Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 1 23.390 VV 0.7556 4343.30322 86.23058 50.4732 0.9955 4261.86523 2 30.065 VP 63.14269 49.5268 8605.16846 149.37327 Totals :

Results obtained with enhanced integrator!




Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 ----|-----|----|-----|-----| -----| -----1 24.689 VV 0.5066 2.67934e4 732.81940 53.4324 2 31.627 VV 0.8860 2.33510e4 399.48334 46.5676 5.01444e4 1132.30273 Totals :

Results obtained with enhanced integrator!





Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 -----| 1 27.100 MM 0.9671 3296.28906 56.80935 49.4226 1.1055 3373.31226 37.49756 50.5774 2 38.517 VP Totals : 6669.60132 94.30691

Results obtained with enhanced integrator!

Signal 4: DAD1 D, Sig=240,16 Ref=360,100



1

reak #	[min]	туре	Width [min]	Area [mAU*s]	[mAU]	area %
1	27.728	MM	0.9871	1.15092e4	194.32687	8.0239
2	38.474	BB	0.8921	1.31928e5	1840.94043	91.9761
Total	.s :			1.43437e5	2035.26730	



Peak RetTime Type Width Height Area Area 8 # [min] [min] [mAU*s] [mAU] -----| 1 21.115 BB 0.5038 1.81073e4 533.78015 52.6108 2 29.885 BB 0.8671 1.63102e4 286.97375 47.3892 3.44175e4 Totals : 820.75391

Results obtained with enhanced integrator!





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
1 2	30.050	BV VB	0.9771 1.0235	3651.51489 3461.09302	50.50610	51.3386 48.6614
Total	ls :			7112.60791	105.61329	

Results obtained with enhanced integrator!





Peak RetTime Type Width Height Area Area [min] [mAU*s] [mAU] 8 [min] # ----|-----|-----|-----|------|-----------| ____ 49.8741 1 40.570 MM 1.3343 2062.33643 25.75996 1.5440 2072.74536 22.37351 50.1259 2 46.161 MM 4135.08179 Totals : 48.13347

Results obtained with enhanced integrator!



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
		-				
1	40.636	BV	1.0591	2482.18506	29.94384	1.6698
2	46.066	VB	0.9077	1.46171e5	2030.90881	98.3302
Total	ls :			1.48654e5	2060.85265	

Results obtained with enhanced integrator!

S-113



Peak	RetTime Type	Width	Area	Heiqht	Area
#	[min]	[min]	[mAU*s]	[mAU]	%
1	28.664 VV	0.6615	2857.62573	59.16293	49.8885
2	30.854 VB	0.7244	2870.40332	54.68626	50.1115
Total	ls :		5728.02905	113.84919	

Results obtained with enhanced integrator!



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
		-				
1	29.113	MM	0.5242	4.72320e4	1501.66919	95.7669
2	31.256	MM	0.6523	2087.77319	53.34237	4.2331
Total	ls :			4.93198e4	1555.01156	



Area

Signal 4: DAD1 D, Sig=240,16 Ref=360,100 Peak RetTime Type Width Area Height

#	[min]	[min]	[mAU*s]	[mAU]	8
· 1 2	 21.270 VV 22 712 VB	0.5715	4935.80664	132.23991	 50.3572 40.6428
2 Total:	23.713 VD 3 :	0.0379	9801.59668	249.07352	19.0120

Results obtained with enhanced integrator!



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak RetTime Type # [min]	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
1 20.783 VV	0.4184	6.58387e4	2507.28467	97.7939
2 23.087 VV	0.6880	1485.22034	32.82004	2.2061

Totals :

6.73239e4 2540.10471



Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 _____ ----| 65.83404 1 19.237 VB 0.5307 2294.94604 50.9639 0.6088 2208.13745 55.42449 2 22.209 VB 49.0361 4503.08350 121.25853 Totals :

Results obtained with enhanced integrator!



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
1	19.150	vv	0.6211	1.21045e5	3353.40576	98.8826
2	22.022	vv	0.6662	1367.77979	29.00519	1.1174
	0.000			1 00440 5		

Totals :

1.22413e5 3382.41095



Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] ÷ ----|-----|---- | ------ | ------- | --------| ----| 1 19.245 VV 0.5384 4591.45605 130.53687 50.7190 2 22.679 VP 0.6191 4461.27441 110.47253 49.2810 9052.73047 241.00940 Totals :

Results obtained with enhanced integrator!



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	8
		-				
1	19.253	VV	0.5248	9.76993e4	3124.35278	98.8646
2	22.641	vv	0.6252	1121.99121	27.20411	1.1354

Totals :

9.88213e4 3151.55690



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Heiqht [mAU]	Area %
1	27.486	vv	0.7495	4844.80615	97.20631	51.0472
2	33.570	VP	0.9514	4646.02295	75.76279	48.9528
Total	ls :			9490.82910	172.96911	



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Туре	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.725	vv	0.6525	1.15605e5	2830.39673	95.2864
2	33.635	vv	0.9784	5718.66406	86.59795	4.7136
Total	ls :			1.21323e5	2916.99467	

Results obtained with enhanced integrator!

S-118



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 1 22.651 VV 0.7808 3.53936e4 51.8832 638.42169 2 25.788 VV 0.8907 3.28242e4 537.35980 48.1168 6.82179e4 1175.78149 Totals :

Results obtained with enhanced integrator!





Peak RetTime Type Width Height Area Area # [min] [min] [mAU*s] [mAU] 8 ----|-----|----|-----|-----| -----| 19.79937 1 26.329 MM 1.1371 1350.81702 49.9801 2 29.956 MM 1.3453 1351.89160 16.74867 50.0199 2702.70862 36.54804 Totals :

Results obtained with enhanced integrator!

