Supporting Information

Application of Bis(oxazoline) in Asymmetric β-Amination of Chalcones

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1. General

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. \(^1\)H NMR spectra were recorded at 500 MHz using CDCl\(_3\) as solvent. Elemental analysis was performed on a Vario EL III recorder. Mass spectra were obtained with an automated Fininigan TSQ Advantage mass spectrometer. Most of the products were known compounds and were identified by comparison of their physical and spectra data with those of authentic samples. The enantiomeric excess of the \(\beta\)-imidoketones was determined by HPLC on Ultron ES-OVM column.

2. General procedure

2.1 Synthesis of chalcones (1a as an example)

A mixture of acetophenone (10 mmol) and benzaldehyde (1.1 equiv) in anhydrous EtOH (15 mL) was stirred at room temperature for 5 min. Then, NaOH (3 equiv) was added. The reaction mixture was stirred at room temperature overnight until aldehyde consumption. After that, HCl (10%) was added until neutrality. Then dichloromethane was added to dilute the reaction mixture. The organic layer was dried over anhydrous Na\(_2\)SO\(_4\) and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography to give 1a.

2.2 Typical procedure for the \(\beta\)-amination of chalcones

General procedure for the preparation of 2 (2a as an example): A mixture of chalcone 1a (208 mg, 1.0 mmol), L3 (30.6 mg, 0.1 mmol), and DBU (0.18 mL, 1.2 mmol) in MeCN (2.0 mL) was stirred at room temperature. To the mixture were then added NBS (213 mg, 1.2 mmol). After the starting material 1a was consumed as indicated by TLC, the reaction mixture was poured into water and then extracted with CH\(_2\)Cl\(_2\) (3 \times 10\,\text{mL}). The combined organic phase was washed with water (3 \times 10 \,\text{mL}), dried over anhydrous MgSO\(_4\), filtered and concentrated under reduced pressure. The
crude product was purified by flash chromatography.

3. $^1$H, $^{13}$C NMR spectras and HPLC chromatograms

3.1 1-(3-Oxo-1,3-diphenylpropyl)pyrrolidine-2,5-dione (2a)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (76% yield); m.p. 118-120ºC; $^1$H NMR (500 MHz, CDCl₃): $\delta$: 7.99-7.97 (m, 2H), 7.59-7.57 (m, 3H), 7.47 (d, $J = 7.5$ Hz, 2H), 7.38-7.31 (m, 3H), 5.91-5.88 (m, 1H), 4.64-4.58 (m, 1H), 3.71-3.66 (m, 1H), 2.66-2.63 (m, 4H). $^{13}$C NMR (125 MHz, CDCl₃): $\delta$: 28.0, 40.0, 51.2, 127.8, 128.6, 128.9, 129.2, 129.8, 134.6, 137.7, 141.2, 177.5, 198.2. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH₂PO₄ (0.02 mol/L), flow rate = 1.8 ml/min, UV = 254 nm, major enantiomer $t_1 = 1.87$ min, minor enantiomer $t_2 = 0.72$ min; 90% ee.
3.2 1-(1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl)pyrrolidine-2,5-dione (2b)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (83% yield); m.p. 142-144°C. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$: 7.97 (d, J = 7.6 Hz, 2H), 7.61-7.58 (m, 2H), 7.54-7.46 (m, 4H), 7.34-7.28 (d, J = 8.3 Hz, 2H), 5.89-5.86 (m, 1H), 4.52-4.47 (m, 2H), 3.75-3.67 (m, 2H), 2.68-2.64 (m, 4H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$: 28.3, 39.2, 49.9, 127.4, 128.0, 128.7, 129.2, 133.5, 134.1, 136.6, 137.1, 176.5, 196.1. HPLC analysis: Ultron ES-OVM column, 32:68 alcohol/KH$_2$PO$_4$ (0.02 mol/L), flow rate = 1.5 ml/min, UV = 273nm, major enantiomer $t_1$ = 3.49 min, minor enantiomer $t_2$ = 2.34 min; 94% ee.
This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 7 : 1) to give a white solid (73% yield); m.p. 120-122°C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 8.03-7.92 (m, 2H), 7.59 (t, $J = 7.4$ Hz, 1H), 7.53-7.42 (m, 4H), 7.17 (d, $J = 7.9$ Hz, 2H), 5.88-5.85 (m, 1H), 3.3 1-(3-Oxo-3-phenyl-1-(p-tolyl)propyl)pyrrolidine-2,5-dione(2c)
4.61-4.55 (m, 1H), 3.70-3.65 (m, 1H), 2.66-2.62 (m, 4H), 2.35 (s, 3H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$: 20.1, 27.0, 38.2, 50.0, 127.0, 127.1, 127.7, 128.4, 132.4, 135.0, 135.5, 137.1, 176.3, 196.1. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH$_2$PO$_4$ (0.02 mol/L), flow rate = 1.8 ml/min, UV = 254 nm, major enantiomer $t_1 = 1.84$ min, minor enantiomer $t_2 = 0.71$ min; 80% ee.
3.4 1-(1-(4-(Dimethylamino)phenyl)-3-oxo-3-phenylpropyl)pyrrolidine-2,5-dione (2d)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 8 : 1) to give a white solid (62% yield); m.p. 147-149°C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 8.17-8.08 (m, 2H), 7.77 (d, $J$ = 5.0 Hz, 1H), 7.58-7.56 (m, 3H), 6.76 (d, $J$ = 2.5 Hz, 2H), 6.66 (d, $J$ = 5.0 Hz, 1H), 5.80-5.72 (m, 1H), 4.61-4.56 (m, 1H), 3.53-3.48 (m, 1H), 2.96 (s, 6H), 2.80-2.78 (m, 4H). $^{13}$C NMR (125MHz, CDCl$_3$) δ: 27.8, 38.8, 40.5, 50.9, 111.9, 127.5, 128.5, 128.9, 129.2, 132.1, 138.9, 148.3, 177.5, 197.8. ESI-MS (m/z): 351 ([M+H]$^+$).

Anal. calcd. for C$_{21}$H$_{22}$N$_2$O$_3$: C, 71.98; H, 6.33; N, 7.99. Found: C, 71.77; H, 6.43; N, 8.11. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH$_2$PO$_4$ (0.02 mol/L), flow rate = 1.8 ml/min, UV = 254 nm, major enantiomer $t_1$ = 0.65 min, minor enantiomer $t_2$ = 1.82 min; 40% ee.
3.5 1-(3-oxo-3-phenyl-1-(pyridin-4-yl)propyl)pyrrolidine-2,5-dione (2e)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a yellow solid (67% yield); m.p. 140-142ºC. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.57 (d, $J = 4.5$ Hz, 2H), 7.95-7.93 (m, 2H), 7.59-7.56 (m, 1H), 7.47-7.44 (m, 2H), 7.40 (d, $J = 6.0$ Hz, 2H), 5.87-
5.84 (m, 1H), 4.44-4.38 (m, 1H), 3.77-3.72 (m, 1H), 2.69-2.65 (m, 4H). $^{13}$C NMR (125MHz, CDCl$_3$) δ: 28.1, 38.7, 50.1, 122.8, 128.7, 128.9, 133.8, 136.2, 147.2, 150.5, 177.1, 196.3. ESI-MS (m/z): 309 ([M+H]$^+$). Anal. calcd. for C$_{18}$H$_{16}$N$_2$O$_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.31; H, 5.15; N, 9.23. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH$_2$PO$_4$ (0.02 mol/L), flow rate = 1.5 ml/min, UV = 280 nm, major enantiomer $t_1 = 5.78$ min, minor enantiomer $t_2 = 4.40$ min; 64% $ee$. 
3.6 1-(3-(4-Methoxyphenyl)-3-oxo-1-phenylpropyl)pyrrolidin-2,5-dione (2f)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (52% yield); m.p. 127-129°C. 1H NMR (500 MHz, CDCl₃) δ: 7.98 (d, J = 7.4 Hz, 2H), 7.65-7.37 (m, 5H), 6.88 (d, J = 8.7 Hz, 2H), 5.87-5.84 (m, 1H), 4.58-4.53 (m, 1H), 3.81 (s, 3H), 3.71-3.61 (m, 1H), 2.69-2.62 (m, 4H). 13C NMR (125MHz, CDCl₃) δ: 27.0, 38.3, 49.7, 54.3, 113.0, 127.1, 127.7, 128.4, 130.1, 132.4, 135.5, 158.4, 176.3, 196.0. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH₂PO₄ (0.02 mol/L), flow rate = 2.0 ml/min, UV = 254 nm, major enantiomer t₁ = 1.86 min, minor enantiomer t₂ = 0.71 min; 80% ee.
3.7 1-(3-(4-Methylphenyl)-3-oxo-1-phenylpropyl)pyrrolidine-2,5-dione (2g)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (71% yield); m.p. 131-133°C. $^1$H NMR (500 MHz, CDCl$_3$) δ:7.87 (d, J = 7.8 Hz, 2H),
7.56 (d, J = 7.9 Hz, 2H), 7.36-7.30 (m, 3H), 7.26 (d, J = 7.9 Hz, 2H), 5.89-5.86 (m, 1H), 4.55-4.52 (m, 1H), 3.67-3.63 (m, 1H), 2.65-2.61 (m, 4H), 2.41 (s, 3H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$: 20.7, 27.0, 38.0, 50.3, 127.1, 127.2, 127.8, 128.4, 133.0, 138.0, 143.3, 176.4, 195.6. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH$_2$PO$_4$ (0.025 mol/L), flow rate = 1.2 ml/min, UV = 273 nm, major enantiomer $t_1$ = 2.71 min, minor enantiomer $t_2$ = 1.52 min; 76% ee.
3.8 1-(3-(4-(Trifluoromethyl)-3-oxo-1-phenylpropyl) pyrrolidine-2,5-dione(2h)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 8 : 1) to give a white solid (60% yield); m.p. 144-146°C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.96 (d, J = 7.5 Hz, 2H), 7.60-7.57 (m, 1H), 7.52-7.47 (m, 4H), 7.32 (d, J = 8.4 Hz, 2H), 5.88-5.85 (m, 1H), 4.51-4.46 (m, 1H), 3.74-3.69 (m, 1H), 2.67-2.63 (m, 4H). $^{13}$C NMR (125MHz, CDCl$_3$) δ: 26.1, 38.2, 48.8, 123.9, 127.2, 127.9, 128.5, 129.9, 133.8, 134.6, 136.9, 138.2, 179.3, 198.3. $^{19}$F NMR (500 MHz, CDCl$_3$) δ: -63.18. ESI-MS (m/z): 376 ([M+H$^+$]). Anal. calcd. for C$_{20}$H$_{16}$F$_3$NO$_3$: C, 64.00; H, 4.30; N, 3.73. Found: C, 64.18; H, 4.22; N, 3.67. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH$_2$PO$_4$ (0.025 mol/L), flow rate = 1.5 ml/min, UV = 254 nm, major enantiomer $t_1$ = 2.46 min, minor enantiomer $t_2$ = 1.26min; 66% ee.
3.9 1-(3-(4-Bromophenyl)-3-oxo-1-phenylpropyl)pyrrolidine-2,5-dione(2i)

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 7 : 1) to give a white solid (72% yield); m.p. 149-151°C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 7.81(d, J = 10 Hz, 2H), 7.60-7.52 (m, 4H), 7.35-7.29 (m, 3H), 5.85-5.82 (m, 1H), 4.56-4.51 (m, 1H), 3.63-3.59 (m, 1H), 2.65-2.60 (m, 4H). $^{13}$C NMR (125MHz, CDCl$_3$) δ: 27.0, 38.1, 49.6, 127.1, 127.8, 128.0, 132.6, 133.2, 135.3, 136.3, 176.2, 195.6. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH$_2$PO$_4$ (0.02 mol/L), flow rate = 1.2 ml/min, UV = 230 nm, major enantiomer $t_1$ = 3.00 min, minor enantiomer $t_2$ = 1.64min; 92% ee.
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