**VAPOPhosphoric Acid Catalysis: The Highly Enantioselective Addition of Imides to Imines**

_Yuxue Liang, Emily B. Rowland, Gerald B. Rowland, Jason A. Perman, and Jon C. Antilla*

**Supplementary Information**

**General Information:** All reactions were carried out in flame-dried or oven-dried screw-cap test tubes and were allowed to proceed under a dry argon atmosphere with magnetic stirring. Ether was purified by passing through a column of activated alumina under a dry argon atmosphere. (S)-VAPO and PA5 was synthesized according to the literature procedure.¹ Note: *VAPO phosphoric acid can be purchased from Aldrich or Strem chemicals.* All imines were synthesized according to the literature procedure except Schlenk filtration was required for imines of high purity to be isolated.² Phthalimide, Maleimide, 4-Methylphthalimide and 4-Bromophthalimide were purchased from commercial sources and used without further purification. 4-Flurophthalimide, 3-Methylphthalimide, 3-Flurophthalimide and 4-Chlorophthalimide were synthesized according to literature procedure.³ Substituted BINOL phosphoric acids (PA2,⁴ PA3⁵ and PA4⁶) were prepared from chiral (S)-BINOL according to the known literature procedures. Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F₂₅₄). Flash column chromatography was performed with Merck silica gel (230-400 mesh). Enantiomeric excess (ee) was determined using a Varian Prostar HPLC with a 210 binary pump and a 335 diode array detector. Optical rotations were performed on a Rudolph Research Analytical Autopol IV polarimeter (λ 589) using a 700-μL cell with a path length of 1-dm. Melting points were determined using a MEL-TEMP 3.0 instrument and are uncorrected. ¹H NMR and ¹³C NMR were recorded on a Bruker Avance DPX-250 (250 MHz) instrument with chemical shifts reported relative to tetramethylsilane (TMS). The HRMS data were measured on an Agilent 1100 LC/MS ESI/TOF mass spectrometer with electrospray ionization. Compounds described in the literature were characterized by comparing their ¹H NMR, ¹³C NMR, and melting point (mp) to the reported values.
**Racemates:** All the racemic products were prepared by using Phenylphosphinic acid (30 mol%) as a catalyst and their chiral HPLC retention time data were compared just prior to authentic samples with enantiomeric excess.

**General procedure for VAPOL-Phosphoric acid-catalyzed asymmetric addition of imides to imines:** In a typical experiment the Boc-imine (0.1 mmol), imide (0.05 mmol) and VAPOL-Phosphoric acid (5 mol%) were weighed into a dry, re-sealable test tube with septa and stir bar. Dry ether (1.0 mL) was added to the mixture via syringe and the resulting mixture was stirred at room temperature overnight. Ether was removed by rotary evaporation to give a crude solid mixture that was purified by column chromatography on silica gel to give the product.

![Chemical Structure](attachment:image)

**(-)-tert-Butyl (1,3-dioxoisindolin-2-yl)(4-methoxyphenyl)methylcarbamate, 2a**

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 18 mg, 92% yield, 96% ee, mp.: 56-59 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), t_{major} 24.03 min, t_{minor} 30.57 min. $[\alpha]^{D}_{D} = -34.1^\circ$ (c = 0.10, CHCl₃). $^1$H NMR (250 MHz, CDCl₃): $\delta$ 1.45 (s, 9H), 3.78 (s, 3H), 6.30 (s, broad, 1H), 6.86 (d, $J = 8.7$ Hz, 2H), 7.36 (d, $J = 9.0$ Hz, 2H), 7.70-7.74 (m, 2H), 7.83-7.87 (m, 2H). $^{13}$C NMR (62.5MHz, CDCl₃): $\delta$ 28.25, 28.28, 28.34, 55.31, 59.83, 80.66, 113.91, 114.09, 123.52, 123.61, 127.03, 127.39, 129.43, 131.80, 134.26, 154.31, 159.61, 167.51. MS (ESI): $m/z = 405$ ([M+Na⁺]). HRMS (ESI) Calcd for C₂₁H₂₂N₂NaO₅ ([M+Na⁺]) m/z 405.1421, Found 405.1436.
(-)-tert-Butyl (1,3-dioxoisodolin-2-yl)(phenyl)methylcarbamate, 2e

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 16 mg, 88% yield, 93% ee, mp.: 167-170 °C, HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), t_r-major 16.83 min, t_r-minor 15.69 min. [α]_D^20 = -40.1° (c = 0.25, CHCl_3). ¹H NMR (250 MHz, CDCl_3): δ 1.45 (s, 9H), 6.30 (s, broad, 1H), 7.10 (d, J =10.0 Hz, 1H), 7.32-7.45 (m, 5H), 7.71-7.74 (m, 2H), 7.84-7.87 (m, 2H). ¹³C NMR (62.5MHz, CDCl_3): δ 19.47, 28.26, 58.52, 80.62, 123.57, 126.24, 126.30, 128.70, 131.06, 131.78, 134.25, 135.48, 136.10, 167.75. MS (ESI): m/z = 375 ([M+Na]^+). HRMS (ESI) Calcd for C₂₃H₂₀N₂NaO₄ ([M+Na]^+), Found 375.1317.

(+) -tert-Butyl (1,3-dioxoisodolin-2-yl)(o-tolyl)methylcarbamate, 2f

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 94% yield, 99% ee, mp.: 154-156 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), t_r-major 13.35 min, t_r-minor 10.55 min. [α]_D^20 = 68.2° (c = 0.18, CHCl_3). ¹H NMR (250 MHz, CDCl_3): δ 1.45 (s, 9H), 2.49 (s, 3H), 6.12 (s, broad, 1H), 7.19-7.21 (m, 4H), 7.54 (d, J =7.5Hz, 1H), 7.70-7.74 (m, 2H), 7.83-7.87 (m, 2H). ¹³C NMR (62.5MHz, CDCl_3): δ 19.47, 28.26, 58.52, 80.62, 123.57, 126.24, 126.30, 128.70, 131.06, 131.78, 134.25, 135.48, 136.11, 154.10, 167.75. MS (ESI): m/z = 389 ([M+Na]^+). HRMS (ESI) Calcd for C₂₀H₂₀N₂NaO₄ ([M+Na]^+), m/z 375.1472, Found 375.1457.
(-)-tert-Butyl (1,3-dioxoisindolin-2-yl)(m-tolyl)methylcarbamate, 2g

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 16 mg, 86% yield, 90% ee, mp.: 127-129 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), $t_{\text{r-maj}}$ 12.12 min, $t_{\text{r-min}}$ 11.37 min. $[\alpha]^{20}_D = -36.1^\circ$ (c = 0.10, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ 1.45 (s, 9H), 2.33 (s, 3H), 6.28 (s, broad, 1H), 7.04-7.26 (m, 5H), 7.71-7.75 (m, 2H), 7.84-7.87 (m, 2H). $^{13}$C NMR (62.5MHz, CDCl$_3$): $\delta$ 21.50, 28.29, 60.09, 80.71, 123.05, 123.64, 126.70, 128.71, 129.29, 131.82, 134.27, 137.16, 138.59, 154.36, 167.49. MS (ESI): $m/z$ = 389 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{21}$H$_{22}$N$_2$NaO$_4$ ([M+Na]$^+$) m/z 375.1472, Found 375.1452.

(-)-tert-Butyl (1,3-dioxoisindolin-2-yl)(p-tolyl)methylcarbamate, 2h

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 90% yield, 94% ee, mp.: 132-135 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 98/2, 1.0 mL/min), $t_{\text{r-maj}}$ 11.89 min, $t_{\text{r-min}}$ 19.72 min. $[\alpha]^{20}_D = -52.3^\circ$ (c = 0.25, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ 1.47 (s, 9H), 2.34 (s, 3H), 6.32 (s, broad, 1H), 7.07-7.36 (m, 5H), 7.71-7.75 (m, 2H), 7.84-7.87 (m, 2H). $^{13}$C NMR (62.5MHz, CDCl$_3$): $\delta$ 21.10, 28.29, 60.09, 80.71, 123.61, 125.93, 129.46, 131.81, 134.26, 138.33, 154.34, 167.48. MS (ESI): $m/z$ = 389 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{21}$H$_{22}$N$_2$NaO$_4$ ([M+Na]$^+$) m/z 389.1472, Found 389.1467.
(-)-tert-Butyl (1,3-dioxoisindolin-2-yl)(2-methoxyphenyl)methylcarbamate, 2i

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 91% yield, 93% ee, mp.: 52-54 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 90/10, 1.0 mL/min), t_r-major 18.32 min, t_r-minor 14.92 min. [α]_D^20 = -32.3° (c = 0.50, CHCl₃). ¹H NMR (250 MHz, CDCl₃): δ 1.45 (s, 9H), 3.81 (s, 3H), 6.30 (s, broad, 1H), 6.85-6.96 (m, 2H), 7.27-7.33 (m, 2H), 7.52 (d, J = 7.2 Hz, 1H), 7.68-7.72 (m, 2H), 7.81-7.85 (m, 2H). ¹³C NMR (62.5MHz, CDCl₃): δ 28.24, 28.30, 55.61, 110.93, 120.26, 123.43, 125.05, 127.59, 129.90, 131.92, 134.03, 154.17, 156.67, 167.33. MS (ESI): m/z = 405 ([M+Na]+). HRMS (ESI) Caled for C₂₁H₂₂N₂O₅ ([M+Na]+) m/z 405.1421, Found 405.1412.

(R)-(−)-tert-Butyl (4-chlorophenyl)(1,3-dioxoisindolin-2-yl)methylcarbamate, 2j

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 18 mg, 93% yield, 93% ee, mp.: 170-172 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), t_r-major 18.04 min, t_r-minor 19.80 min. [α]_D^20 = -47.3° (c = 0.25, CHCl₃). The absolute configuration of this compound was determined to be R by X-ray crystallographic analysis. See X-ray data in attached file. ¹H NMR (250 MHz, CDCl₃): δ 1.45 (s, 9H), 6.28 (s, broad, 1H), 7.07 (d, J = 10.0 Hz, 1H), 7.30-7.39 (m, 4H), 7.73-7.76 (m, 2H), 7.85-7.88 (m, 2H). ¹³C NMR (62.5MHz, CDCl₃): δ 28.27, 59.46, 81.01, 123.75, 127.51, 128.96, 131.67, 134.44, 135.88, 154.25, 167.37. MS (ESI): m/z = 409 ([M+Na]+). HRMS (ESI) Caled for C₂₀H₁₉ClN₂NaO₄
Determination of Absolute Stereochemistry by Single X-Ray Crystal Analysis of (2j)

(-)-tert-butyl (4-bromophenyl)(1,3-dioxoisindolin-2-yl)methylcarbamate, 2k

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 19 mg, 87% yield, 90% ee, mp.: 158-160 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), t_r-major 18.95 min, t_r-minor 22.15 min. [α]_D^20 = -47.0° (c = 0.25, CHCl₃). ¹H NMR (250 MHz, CDCl₃): δ 1.46 (s, 9H), 6.30 (s, broad, 1H), 7.07 (d, J =10.0Hz, 1H), 7.30-7.50 (m, 4H), 7.76-7.87 (m, 4H). ¹³C NMR (62.5MHz, CDCl₃): δ 28.27, 59.48, 80.98, 122.59, 123.75, 127.83, 131.65, 131.91, 134.45, 136.42, 154.22, 167.35. MS (ESI): m/z = 453 ([M+Na]^+). HRMS (ESI) Calcd for C₂₀H₁₉BrN₂NaO₄ ([M+Na]^+) m/z 453.0420, Found 453.0421.
(-)-tert-Butyl (1,3-dioxoisocarbonyl-2-yl)(4-fluorophenyl)methylcarbamate, 2l

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 90% yield, 93% ee, mp.: 155-157 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 98/2, 1.0 mL/min), t_r-major 16.28 min, t_r-minor 21.03 min. [α]_D^20 = -48.9° (c = 0.25, CHCl₃). ¹H NMR (250 MHz, CDCl₃): δ 1.37 (s, 9H), 6.20 (s, broad, 1H), 6.92-6.99 (m, 3H), 7.32-7.34 (m, 2H), 7.65-7.68 (m, 2H), 7.77-7.80 (m, 2H). ¹³C NMR (62.5MHz, CDCl₃): δ 28.26, 59.55, 80.89, 115.53, 115.88, 123.71, 127.89, 128.03, 131.70, 133.24, 134.40, 154.24, 160.66, 164.60, 167.41. MS (ESI): m/z = 393 ([M+Na]⁺). HRMS (ESI) Calcd for C₂₀H₁₉FN₂NaO₄ ([M+Na]⁺) m/z 393.1221, Found 393.1220.

(+)-tert-Butyl (1,3-dioxoisocarbonyl-2-yl)(naphthalen-1-yl)methylcarbamate, 2m

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 86% yield, 91% ee, mp.: 182-184 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), t_r-major 19.76 min, t_r-minor 17.09 min. [α]_D^20 = 135.6° (c = 0.20, CHCl₃). ¹H NMR (250 MHz, CDCl₃): δ 1.45 (s, 9H), 6.30 (s, broad, 1H), 7.42-7.70 (m, 6H), 7.81-7.84 (m, 5H), 8.29 (d, J = 8.3 Hz, 1H). ¹³C NMR (62.5MHz, CDCl₃): δ 28.30, 58.01, 80.89, 123.29, 123.53, 123.62, 124.36, 124.89, 126.06, 127.01, 128.85, 130.37, 131.73, 132.26, 133.87, 134.30, 154.20, 167.75. MS (ESI): m/z = 425 ([M+Na]⁺). HRMS (ESI) Calcd for C₂₄H₂₂N₂NaO₄ ([M+Na]⁺) m/z 425.1472, Found 425.1469.

(-)-tert-Butyl(2,5-dioxo-2H-pyrrol-1(5H)-yl)(4-methoxyphenyl)methylcarbamate,

---

PRIVILEGED DOCUMENT FOR REVIEW PURPOSES ONLY
The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 14 mg, 82% yield, 92% ee, mp.: 128-130 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 85/15, 1.0 mL/min), $t_{\text{r-major}}$ 9.24 min, $t_{\text{r-minor}}$ 10.92 min. $[\alpha]_D^{20} = -11.5^\circ$ (c = 0.19, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ 1.45 (s, 9H), 3.78 (s, 3H), 6.15 (s, broad, 1H), 6.70-6.88 (m, 5H), 7.28 (d, $J$ = 9.0 Hz, 2H). $^{13}$C NMR (62.5MHz, CDCl$_3$): $\delta$ 28.26, 55.32, 59.77, 80.69, 114.12, 127.29, 129.20, 134.24, 154.29, 159.65, 169.89. MS (ESI): $m/z$ = 355 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{17}$H$_{20}$N$_2$O$_5$ ([M+Na]$^+$) m/z 355.1264, Found 355.1268.

(-)-tert-Butyl(4-methoxyphenyl)(4-methyl-1,3-dioxoisindolin-2-yl)methylcarbamate, 2o
The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 16 mg, 82% yield, 92% ee, mp.: 52-56 °C. HPLC analysis: Chiralcel AD-H (hexane/iPrOH = 80/20, 1.0 mL/min), $t_{\text{r-major}}$ 18.29 min, $t_{\text{r-minor}}$ 23.87 min. $[\alpha]_D^{20} = -30.63^\circ$ (c = 0.80, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ 1.45 (s, 9H), 2.68 (s, 3H), 3.77 (s, 3H), 6.31 (s, broad, 1H), 6.85 (d, $J$ = 9.0 Hz, 2H), 7.04 (d, $J$ = 10.0 Hz, 1H), 7.37 (d, $J$ = 8.5 Hz, 2H), 7.44-7.68 (m, 3H). $^{13}$C NMR(62.5MHz,CDCl$_3$):$\delta$ 17.57, 28.30, 55.29, 59.55, 80.58, 114.06, 121.20, 127.35, 128.43, 129.64, 132.19, 133.75, 136.66, 138.38, 154.35, 159.54, 167.56, 168.27. MS (ESI): $m/z$ = 419 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{22}$H$_{24}$N$_2$O$_5$ ([M+Na]$^+$) m/z 419.1577, Found 419.1562.
(-)-tert-Butyl(4-methoxyphenyl)(5-methyl-1,3-dioxoisoindolin-2-yl)methylcarbamate, 2p

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 22 mg, 90% yield, 92% ee, mp.: 47-49 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 80/20, 1.0 mL/min), $t_{\text{r-major}}$ 6.72 min, $t_{\text{r-minor}}$ 7.92 min. $[\alpha]_D^{20} = -33.8^\circ$ (c = 0.25, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): δ 1.44 (s, 9H), 2.50 (s, 3H), 3.77 (s, 3H), 6.27 (s, broad, 1H), 6.85 (d, $J = 4.5$ Hz, 2H), 7.01 (d, $J = 10.0$ Hz, 1H), 7.35 (d, $J = 9.0$ Hz, 2H), 7.49-7.73 (m, 3H). $^{13}$C NMR (62.5MHz,CDCl$_3$):δ 22.03, 28.24, 28.28, 55.29, 59.73, 80.56, 114.05, 123.51, 124.11, 127.35, 129.19, 129.57, 132.18, 134.81, 145.62, 154.33, 159.55, 167.58, 167.67. MS (ESI): $m/z$ = 419 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{22}$H$_{24}$N$_2$NaO$_5$ ([M+Na]$^+$) m/z 419.1577, Found 419.1568.

(-)-tert-Butyl(5-chloro-1,3-dioxoisoindolin-2-yl)(4-methoxyphenyl)methylcarbamate, 2q

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 19 mg, 92% yield, 93% ee, mp.: 82-85 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 90/10, 1.0 mL/min), $t_{\text{r-major}}$ 9.72 min, $t_{\text{r-minor}}$ 13.23 min. $[\alpha]_D^{20} = -24.1^\circ$ (c = 0.35, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): δ 1.36 (s, 9H), 3.71 (s, 3H), 6.14 (s, broad, 1H), 6.79 (d, $J = 8.7$ Hz, 2H), 6.93 (d, $J = 10.0$ Hz, 1H), 7.28 (d, $J = 8.5$ Hz, 2H), 7.69-7.73 (m, 3H). $^{13}$C NMR (62.5MHz,CDCl$_3$):δ 28.27, 55.33,
(-)-tert-Butyl(5-bromo-1,3-dioxoisindolin-2-yl)(4-methoxyphenyl)methylcarbamate, 2r

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 19 mg, 84% yield, 90% ee, mp.: 88-90 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 90/10, 1.0 mL/min), \( t_{\text{r-major}} \) 10.19 min, \( t_{\text{r-minor}} \) 13.03 min. \( [\alpha]_{D}^{20} = -25.1^\circ \) (c = 0.20, CHCl\(_3\)). \(^1\)H NMR (250 MHz, CDCl\(_3\)): \( \delta \) 1.44 (s, 9H), 3.78 (s, 3H), 6.21 (s, broad, 1H), 6.86 (d, \( J = 8.7 \) Hz, 2H), 7.0 (d, \( J = 10.0 \) Hz, 1H), 7.35 (d, \( J = 8.7 \) Hz, 2H), 7.69-7.97 (m, 3H). \(^{13}\)C NMR (62.5MHz, CDCl\(_3\)): \( \delta \) 28.28, 55.33, 60.14, 80.82, 114.15, 124.97, 126.95, 127.39, 129.06, 129.19, 130.32, 133.44, 137.25, 154.26, 159.70, 166.14, 166.67. MS (ESI): \( m/z = 483 \) ([M+Na\(^+\)]. HRMS (ESI) Calcd for C\(_{21}\)H\(_{21}\)BrN\(_2\)NaO\(_5\) ([M+Na\(^+\)]) \( m/z \) 483.0526, Found 483.0513.

(-)-tert-Butyl(5-fluoro-1,3-dioxoisindolin-2-yl)(4-methoxyphenyl)methylcarbamate, 2s

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 87% yield, 91% ee, mp.: 72-76 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 90/10, 1.0 mL/min), \( t_{\text{r-major}} \) 9.40 min, \( t_{\text{r-minor}} \) 15.47
min. $[\alpha]_b^{20} = -23.5^\circ$ (c = 0.20, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ 1.44 (s, 9H), 3.78 (s, 3H), 6.22 (s, broad, 1H), 6.87 (d, $J$ = 8.7 Hz, 2H), 7.00 (d, $J$ = 10.0 Hz, 1H), 7.34-7.53 (m, 4H), 7.84-7.88 (m, 1H). $^{13}$C NMR (62.5MHz, CDCl$_3$): $\delta$ 28.27, 55.31, 60.14, 80.75, 111.20, 111.60, 114.13, 121.12, 121.50, 125.93, 126.08, 127.39, 127.54, 129.15, 134.57, 134.72, 154.27, 159.69, 164.46, 166.08, 166.42, 168.55. MS (ESI): $m/z$ = 423 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{21}$H$_{21}$FN$_2$NaO$_5$ ([M+Na]$^+$) m/z 423.1327, Found 423.1332.

$(-)$-tert-Butyl(4-fluoro-1,3-dioxoisindolin-2-yl)(4-methoxyphenyl)methylcarbamate, 2t

The reaction was performed in 0.1 mmol scale for 12h using 5 mol% (S)-VAPOL-phosphoric acid. The product was obtained by flash chromatography (hexane: acetone = 3:1) as a white solid, 17 mg, 84% yield, 89% ee, mp.: 68-71 °C. HPLC analysis: Chiralcel OD-H (hexane/iPrOH = 90/10, 1.0 mL/min), $t_{\text{major}}$ 12.47 min, $t_{\text{minor}}$ 22.32 min. $[\alpha]_b^{20} = -31.7^\circ$ (c = 1.75, CHCl$_3$). $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ 1.45 (s, 9H), 3.78 (s, 3H), 6.24 (s, broad, 1H), 6.87 (d, $J$ = 8.0 Hz, 2H), 7.00 (d, $J$ = 10.0 Hz, 1H), 7.36-7.70 (m, 5H). $^{13}$C NMR (62.5MHz, CDCl$_3$): $\delta$ 28.27, 55.32, 60.14, 60.41, 60.77, 80.77, 114.13, 117.47, 117.67, 119.83, 119.88, 122.51, 122.82, 127.43, 129.08, 133.95, 136.84, 136.96, 154.24, 155.64, 159.70, 159.87, 164.29, 166.26. MS (ESI): $m/z$ = 423 ([M+Na]$^+$). HRMS (ESI) Calcd for C$_{21}$H$_{21}$FN$_2$NaO$_5$ ([M+Na]$^+$) m/z 423.1327, Found 423.1315.

References


