Diastereoselective Ritter reactions of chiral secondary benzylic alcohols
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1 Synthetic procedures and spectroscopical data

Preparation of diethyl 1-hydroxy-1-phenylpropan-2-ylphosphonate (6):

\[
\text{C}_6\text{H}_5\text{CH}_2\text{CH}_{2}\text{OH}{\text{PO(OEt)}}_2
\]

In a dry 100 mL Schlenk tube under argon, 20 mL dry tetrahydrofuran and 2.11 mL (15.0 mmol) diisopropylamine were cooled to 0 °C and 5.60 mL (14.0 mmol, 2.50 M) n-butyl lithium in hexane were added. The mixture was stirred at 0 °C for 15 minutes and subsequently cooled to −78 °C. Diethyl ethylphosphonate (2.00 g, 12.0 mmol) was added in one portion and the reaction was stirred for 1.5 hours. Benzaldehyde (1.40 g, 13.2 mmol) was added dropwise and stirring at −78 °C was continued for one hour. The reaction was warmed to room temperature over four hours and stopped by the addition of 20 mL saturated NH₄Cl-solution. The reaction was extracted with ethyl acetate (20 mL) and dichloromethane (2 × 20 mL). The combined organic extracts were dried over MgSO₄, filtered and the solvent was removed under reduced pressure. After purification by flash chromatography (pentane/ethyl acetate = 1/9 → 0/1) 2.32 g (71%, d.r. = 55/45) of 6 were obtained as a colourless solid. \( R_f = 0.37 \) (ethyl acetate); major diastereoisomer: \(^{1}\text{H-NMR} \) (360 MHz, CDCl₃): \( \delta = 1.02 \) (dd, \(^3 J_{HP} = 18.4 \text{ Hz}, ^3 J_{HH} = 7.4 \text{ Hz}, 3 \text{ H} \)), 1.36 (td, \(^3 J_{HH} = 7.1 \text{ Hz}, ^3 J_{HP} = 2.1 \text{ Hz}, 6 \text{ H} \)), 2.16-2.26 (m, 1 H), 4.04-4.25 (m, 4 H), 5.29 (dd, \(^3 J_{HH} = 9.9 \text{ Hz}, ^3 J_{HP} = 2.1 \text{ Hz}, 1 \text{ H} \)), 7.21-7.36 (m, 5 H); \(^{13}\text{C-NMR} \) (90.6 MHz, CDCl₃) \( \delta = 6.4 \) (dq, \(^2 J_{CP} = 3.2 \text{ Hz} \)), 16.6 (dq, \(^3 J_{CP} = 5.6 \text{ Hz} \)), 38.7 (dd,
$J_{CP} = 136.1$ Hz, 62.1 (dt, $^2J_{CP} = 7.0$ Hz), 62.4 (dt, $^2J_{CP} = 6.9$ Hz), 70.9 (d), 127.0 (d), 127.3 (d), 128.2 (d), 141.5 (d, $^3J_{CP} = 12.8$ Hz); minor diastereoisomer: $^1$H-NMR (360 MHz, CDCl$_3$): $\delta = 0.86$ (dd, $^3J_{HH} = 17.4$ Hz, $^3J_{HP} = 7.3$ Hz, 3 H), 1.30 (td, $^3J_{HH} = 7.0$ Hz, $^3J_{HP} = 5.3$ Hz, 1 H), 2.11-2.18 (m, 1 H), 4.04-4.25 (m, 4 H), 4.69 (dd, $^3J_{HH} = 11.0$ Hz, $^3J_{HP} = 9.4$ Hz, 1 H), 7.21-7.36 (m, 5 H); $^{13}$C-NMR (90.6 MHz, CDCl$_3$) $\delta = 11.9$ (dq, $^2J_{CP} = 5.8$ Hz), 16.5 (dq, $^3J_{CP} = 5.0$ Hz), 39.3 (dd, $^1J_{CP} = 135.4$ Hz), 62.2 (dt, $^2J_{CP} = 6.5$ Hz), 62.3 (dt, $^2J_{CP} = 7.1$ Hz), 74.9 (d, $^3J_{CP} = 3.5$ Hz), 125.9 (d), 128.0 (d), 128.4 (d), 141.7 (d, $^3J_{CP} = 13.3$ Hz); MS (EI, 70 eV), $m/z$ (%): 272 (1) [M$^+$], 227 (3), 166 (100), 139 (41), 122 (18), 111 (32), 82 (13), 45 (6); HRMS (EI) (C$_{13}$H$_{21}$O$_4$P): calc.: 272.1177; found: 272.1172.

**Preparation of 2-(ethylsulfonyl)-1-phenylpropan-1-ol (7)**

![Chemical structure](image)

In a dry 100 mL Schlenk tube under argon 30 mL dry tetrahydrofuran and 2.70 g (22.0 mmol) diethyl sulfone were cooled to $-78$ °C and 8.30 mL (20.0 mmol, 2.40 M) n-butyl lithium in hexane were added. The mixture was stirred at $-78$ °C for one hour. Benzaldehyde (2.12 g, 20.0 mmol) was added dropwise and stirring at $-78$ °C was continued for one hour. The reaction was warmed to room temperature over two hours and stopped by the addition of 30 mL saturated NH$_4$Cl-solution. The reaction was extracted with ethyl acetate (30 mL) and dichloromethane ($2 \times 30$ mL). The combined organic extracts were dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. After purification by flash chromatography (pentane/ethyl acetate = 1/1) 2.66 g (58%, d.r. = 66/34) of 7 were obtained as a colourless solid. $R_I = 0.13$ (ethyl acetate/pentane = 1/1); m.p. = 89 °C; major diastereoisomer: $^1$H-NMR (360 MHz, CDCl$_3$): $\delta = 1.30$ (d, $^3J = 7.3$ Hz, 3 H), 1.42 (t, $^3J = 7.5$ Hz, 3 H), 3.00-3.38 (m, 3 H), 5.61 (d, $^3J = 1.4$ Hz, 1 H), 7.27-7.43 (m, 5 H); $^{13}$C-NMR (90.6 MHz, CDCl$_3$) $\delta = 5.9$ (q), 6.3 (q), 45.4 (t), 63.7 (d), 69.9 (d), 125.8 (d), 128.7 (d), 129.0 (d), 140.3 (s); minor diastereoisomer: $^1$H-NMR (360 MHz, CDCl$_3$): $\delta = 1.04$ (d, $^3J = 7.3$ Hz, 3 H), 1.43 (t, $^3J = 7.5$ Hz, 3 H), 3.00-3.38 (m, 3 H), 4.94 (d, $^3J = 1.4$ Hz, 1 H), 7.27-7.43 (m, 5 H); $^{13}$C-NMR (90.6 MHz, CDCl$_3$) $\delta = 6.5$ (q), 10.9 (q), 48.7 (t), 62.4 (d), 74.7 (d), 127.1 (d), 128.1 (d), 128.9 (d), 140.6 (s); MS (EI, 70 eV), $m/z$ (%): 228 (9) [M$^+$], 134 (58), 117 (34), 107 (100), 94 (34), 79 (52), 66 (32); CHN (C$_{11}$H$_{16}$O$_3$S): calc.: C 57.87, H 7.06, S 14.04; found: C 57.93, H 7.05, S 14.09.
Preparation of 1-phenyl-2-(propylsulfonyl)butan-1-ol (15)

In a dry 100 mL Schlenk tube under argon 20 mL dry tetrahydrofuran and 2.06 mL (15.6 mmol) diisopropylamine were cooled to 0 °C and 5.60 mL (14.0 mmol, 2.50 M) n-butyllithium in hexane were added. The mixture was stirred at 0 °C for 15 minutes and subsequently cooled to −78 °C. Dipropyl sulfone (2.00 g, 13.3 mmol) was added in one portion and the reaction was stirred for two hours. Benzaldehyde (1.55 g, 14.6 mmol) was added dropwise and stirring at −78 °C was continued for one hour. The reaction was warmed to room temperature over four hours and stopped by the addition of 20 mL saturated NH₄Cl-solution. The reaction was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried with MgSO₄, filtered and the solvent was removed under reduced pressure. After purification by flash chromatography (pentane/ethyl acetate = 5/1 → 2/1) 3.09 g (91%, d.r. = 70/30) of 15 were obtained as a colourless solid. Rᵣ = 0.38 (ethyl acetate); major diastereoisomer: ¹H-NMR (360 MHz, CDCl₃): δ = 0.81 (t, ³J = 7.5 Hz, 3 H), 1.08 (t, ³J = 7.4 Hz, 3 H), 1.83-1.98 (m, 4 H), 2.89-3.04 (m, 3 H), 5.57-5.58 (m, 1 H), 7.28-7.43 (m, 5 H); ¹³C-NMR (90.6 MHz, CDCl₃) δ = 13.3 (q), 13.4 (q), 15.5 (t), 15.9 (t), 54.6 (t), 70.4 (d), 71.1 (d), 125.7 (d), 128.7 (d), 129.0 (d), 140.4 (s); minor diastereoisomer ¹H-NMR (360 MHz, CDCl₃): δ = 0.82 (t, ³J = 7.5 Hz, 3 H), 1.09 (t, ³J = 7.4 Hz, 3 H), 1.83-1.98 (m, 4 H), 2.89-3.04 (m, 3 H), 5.58-5.59 (m, 1 H), 7.28-7.43 (m, 5 H); ¹³C-NMR (90.6 MHz, CDCl₃) δ = 13.7 (q), 13.8 (q), 15.4 (t), 15.7 (t), 53.4 (t), 68.7 (d), 70.4 (d), 125.8 (d), 127.0 (d), 128.0 (d), 140.5 (s); MS (EI, 70 eV), m/z (%): 256 (4) [M⁺], 214 (2), 148 (58), 107 (43), 91 (22), 57 (19), 43 (100); HRMS (EI) (C₁₃H₂₀O₃S): calc.: 256.1133; found: 256.1128.

Preparation of methyl 3-(benzamido)-2-methyl-3-phenylpropanoate (anti-3a) – Representative Procedure for the Ritter reactions catalysed by trifluoromethanesulfonic acid:

In a typical experiment methyl 3-hydroxy-2-methyl-3-phenylpropanoate¹ (1) (48 mg, 250 μmol) and benzonitrile (103 mg, 1.0 mmol) were dissolved in dichloromethane (1 mL) and stirred at 0 °C. TfOH (28 μL, 312 μmol) was added dropwise and the solution was stirred for 1.5 h. The reaction was stopped by the addition of 5 mL saturated NaHCO₃-solution and diluted with 5 mL dichloromethane. The layers were separated, the aqueous layer was extracted with dichloromethane (2 × 10 mL), the combined organic extracts were dried over MgSO₄, filtered and the solvent was
removed under reduced pressure. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 → 3/1) to give a colourless solid (64 mg, 86%) in a diastereomeric ratio of 94/6 (anti/syn).

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{C} & \quad \text{O} \\
& \quad \text{COOMe}
\end{align*}
\]

\(R_f = 0.07\) (pentane/ethyl acetate = 10/1); \(^1\)H-NMR (360 MHz, CDCl\textsubscript{3}): \(\delta = 1.36\) (d, \(\text{J} = 7.1\) Hz, 3 H), 3.11 (qd, \(\text{J} = 7.1\) Hz, \(\text{J} = 4.7\) Hz, 1 H), 3.60 (s, 3 H), 5.38 (dd, \(\text{J} = 9.0\) Hz, \(\text{J} = 4.7\) Hz, 1 H), 7.28-7.36 (m, 5 H), 7.41-7.55 (m, 3 H), 7.87-7.90 (m, 2 H); \(^{13}\)C-NMR (90.6 MHz, CDCl\textsubscript{3}): \(\delta = 16.2\) (q), 44.8 (d), 52.1 (d), 55.6 (q), 126.3 (d), 127.2 (d), 127.6 (d), 128.7 (d), 128.8 (d), 131.8 (d), 134.4 (s), 140.7 (s), 167.0 (s), 176.4 (s); MS (EI, 70 eV), \(m/z\) (%): 297 (4) [M\(^+\)], 211 (28), 192 (28), 166 (43), 105 (100), 77 (42); HRMS (EI) (C\textsubscript{18}H\textsubscript{19}NO\textsubscript{3}): calc.: 297.1365, found: 297.1362.

The analytical data for \textit{anti}-3\textsubscript{a} are in line with the data described in the literature.\(^2\)

Methyl 3-acetamido-2-methyl-3-phenylpropanoate (\textit{anti}-3\textsubscript{b})

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{C} & \quad \text{O} \\
& \quad \text{COOMe}
\end{align*}
\]

Methyl 3-hydroxy-2-methyl-3-phenylpropanoate\(^1\) (1) (48 mg, 250 \(\mu\)mol), acetonitrile (41 mg, 1.0 mmol) and TfOH (28 \(\mu\)L, 312 \(\mu\)mol) were stirred in 1 mL dichloromethane for 1.5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 → 3/1) to give a colourless solid (52 mg, 88%) in a diastereomeric ratio of 93/7 (\textit{anti/syn}). \(R_f = 0.18\) (pentane/ethyl acetate = 1/1); \(^1\)H-NMR (360 MHz, CDCl\textsubscript{3}): \(\delta = 1.22\) (d, \(\text{J} = 7.1\) Hz, 3 H), 2.02 (s, 3 H), 2.96 (qd, \(\text{J} = 7.1\) Hz, \(\text{J} = 5.6\) Hz, 1 H), 3.56 (s, 3 H), 5.16 (dd, \(\text{J} = 9.2\) Hz, \(\text{J} = 5.6\) Hz, 1 H), 7.00 (d, \(\text{J} = 9.2\) Hz, 1 H, NH), 7.20-7.23 (m, 3 H), 7.27-7.31 (m, 2 H); \(^{13}\)C-NMR (90.6 MHz, CDCl\textsubscript{3}): \(\delta = 15.7\) (q), 23.4 (q), 44.7 (d), 51.9 (d), 55.1 (q), 126.4 (d), 127.5 (d), 128.6 (d), 140.5 (s), 169.8 (s), 175.8 (s).

The analytical data for 3\textsubscript{b} are in line with the data described in the literature.\(^3\)
Methyl 3-(isobutyramido)-2-methyl-3-phenylpropanoate (anti-3c)

\[
\begin{align*}
\text{O} & \quad \text{NH} & \quad \text{COOMe} \\
\end{align*}
\]

Methyl 3-hydroxy-2-methyl-3-phenylpropanoate\(^1\) (1) (48 mg, 250 \(\mu\)mol), isobutyronitrile (69 mg, 1.0 mmol) and TfOH (28 \(\mu\)L, 312 \(\mu\)mol) were stirred in 1 mL dichloromethane for 3 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 \(\rightarrow\) 3/1) to give a colourless solid (55 mg, 84%) in a diastereomeric ratio of 98/2 (anti/syn). \(R_f = 0.22\) (pentane/ethyl acetate = 1/1); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \(\delta = 1.18\) (d, \(\begin{align*}\text{J} = 6.9\text{ Hz}, 3\text{ H}\end{align*}\)), 1.21 (d, \(\begin{align*}\text{J} = 6.9\text{ Hz}, 3\text{ H}\end{align*}\)), 1.27 (d, \(\begin{align*}\text{J} = 7.1\text{ Hz}, 3\text{ H}\end{align*}\)), 2.47 (hept., \(\begin{align*}\text{J} = 6.9\text{ Hz}, 1\text{ H}\end{align*}\)), 2.99 (qd, \(\begin{align*}\text{J} = 7.1\text{ Hz}, \text{J} = 5.1\text{ Hz}, 1\text{ H}\end{align*}\)), 3.57 (s, 3 H), 5.17 (dd, \(\begin{align*}\text{J} = 9.1\text{ Hz}, \text{J} = 5.1\text{ Hz}, 1\text{ H}\end{align*}\)), 6.96 (d, \(\begin{align*}\text{J} = 9.1\text{ Hz}, 1\text{ H, NH}\end{align*}\)), 7.21-7.33 (m, 5 H); \(^{13}\)C-NMR (90.6 MHz, CDCl\(_3\)): \(\delta = 15.9\) (q), 19.6 (q), 19.9 (q), 36.0 (d), 44.8 (d), 51.9 (d), 54.7 (q), 126.3 (d), 127.5 (d), 128.7 (d), 140.9 (s), 176.1 (s), 176.6 (s); MS (EI, 70 eV), \(m/z\) (%): 263 (12) [M\(^+\)], 232 (5), 192 (82), 176 (24), 121 (19), 110 (100), 43 (28); HRMS (EI) (C\(_{15}\)H\(_{21}\)NO\(_3\)): calc.: 263.1521, found: 263.1522.

Methyl 3-(4-methoxybenzamido)-2-methyl-3-phenylpropanoate (anti-3d)

\[
\begin{align*}
\text{OMe} & \quad \text{NH} & \quad \text{COOMe} \\
\end{align*}
\]

Methyl 3-hydroxy-2-methyl-3-phenylpropanoate\(^1\) (1) (48 mg, 250 \(\mu\)mol), 4-methoxybenzonitrile (133 mg, 1.0 mmol) and TfOH (28 \(\mu\)L, 312 \(\mu\)mol) were stirred in 1 mL dichloromethane for 1.5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 \(\rightarrow\) 3/1) to give a colourless solid (71 mg, 87%) in a diastereomeric ratio of 92/8 (anti/syn). \(R_f = 0.17\) (pentane/ethyl acetate = 5/1); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \(\delta = 1.31\) (d, \(\begin{align*}\text{J} = 7.1\text{ Hz}, 3\text{ H}\end{align*}\)), 3.06 (qd, \(\begin{align*}\text{J} = 7.1\text{ Hz}, \text{J} = 4.7\text{ Hz}, 1\text{ H}\end{align*}\)), 3.56 (s, 3 H), 3.82 (s, 3 H), 5.33 (dd, \(\begin{align*}\text{J} = 8.9\text{ Hz}, \text{J} = 4.7\text{ Hz}, 1\text{ H}\end{align*}\)), 6.91 (d, \(\begin{align*}\text{J} = 8.8\text{ Hz}, 2\text{ H}\end{align*}\)), 7.15-7.34 (m, 5 H), 7.81 (d, \(\begin{align*}\text{J} = 8.8\text{ Hz}, 2\text{ H}\end{align*}\)); \(^{13}\)C-NMR (90.6 MHz, CDCl\(_3\)): \(\delta = 16.2\) (q), 44.8 (d), 52.1 (d), 55.3 (q), 55.6 (q), 126.3 (d), 127.2 (d), 127.6 (d), 128.7 (d), 128.8 (d), 131.8 (d), 134.4 (s), 140.7 (s), 167.0 (s), 176.4 (s); MS (EI, 70 eV), \(m/z\) (%): 327 (14)
Methyl 3-(acrylamido)-2-methyl-3-phenylpropanoate (anti-3e)

Methyl 3-hydroxy-2-methyl-3-phenylpropanoate\(^1\) (1) (48 mg, 250 \(\mu\)mol), acrylonitrile (53 mg, 1.0 mmol) and TfOH (28 \(\mu\)L, 312 \(\mu\)mol) were stirred in 1 mL dichloromethane for 3.5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 \(\rightarrow\) 3/1) to give a colourless solid (58 mg, 94%) in a diastereomeric ratio of 92/8 (anti/syn). \(R_f = 0.06\) (pentane/ethyl acetate = 3/1); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \(\delta = 1.28\) (d, \(^3J = 7.1\) Hz, 3 H), 3.03 (qd, \(^3J = 7.1\) Hz, \(^3J = 5.1\) Hz, 1 H), 3.57 (s, 3 H), 5.26 (dd, \(^3J = 9.1\) Hz, \(^3J = 5.1\) Hz, 1 H), 5.67 (dd, \(^3J = 9.9\) Hz, \(^3J = 1.8\) Hz, 1 H), 6.20 (dd, \(^3J = 17.0\) Hz, \(^3J = 9.9\) Hz, 1 H), 6.30 (dd, \(^3J = 17.0\) Hz, \(^3J = 1.8\) Hz, 1 H), 7.13 (d, \(^3J = 9.1\) Hz, 1 H, NH), 7.21-7.32 (m, 5 H); \(^{13}\)C-NMR (90.6 MHz, CDCl\(_3\)): \(\delta = 15.9\) (q), 44.6 (d), 52.0 (d), 55.2 (q), 126.4 (d), 126.9 (t), 127.6 (d), 128.7 (d), 131.0 (d), 140.4 (s), 165.3 (s), 176.0 (s); MS (EI, 70 eV), \(m/z\) (%): 247 (10) [M\(^+\)], 192 (46), 160 (47), 106 (100), 77 (9), 55 (61); HRMS (EI) (C\(_{14}\)H\(_{17}\)NO\(_3\)): calc.: 247.1208, found: 247.1209.

Methyl 3-(but-3-enamido)-2-methyl-3-phenylpropanoate (anti-3f)

Methyl 3-hydroxy-2-methyl-3-phenylpropanoate\(^1\) (1) (48 mg, 250 \(\mu\)mol), but-3-enenitrile (67 mg, 1.0 mmol) and TfOH (28 \(\mu\)L, 312 \(\mu\)mol) were stirred in 1 mL dichloromethane for 4.5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 \(\rightarrow\) 3/1) to give a colourless solid (57 mg, 87%) in a diastereomeric ratio of 91/9 (anti/syn). \(R_f = 0.77\) (pentane/ethyl acetate); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \(\delta = 1.25\) (d, \(^3J = 7.1\) Hz, 3 H), 2.98 (qd, \(^3J = 7.1\) Hz, \(^3J = 5.2\) Hz, 1 H), 3.07 (dd, \(^3J = 7.1\) Hz, \(^4J = 1.1\) Hz, 1 H), 3.56 (s, 3 H), 5.17 (dd, \(^3J = 9.2\) Hz, \(^3J = 5.2\) Hz, 1 H), 5.24-5.31 (m, 2 H), 5.93-6.05 (m, 2 H), 7.10 (d, \(^3J = 9.2\) Hz, 1 H, NH), 7.19-7.33 (m, 5 H); \(^{13}\)C-NMR (90.6 MHz, CDCl\(_3\)): \(\delta = 15.9\) (q), 41.9 (t), 44.8 (d), 51.9 (d), 55.1 (q), 120.1 (t), 126.3 (d), 127.6 (d), 131.3 (d), 140.5 (s), 170.3 (s), 175.9 (s); MS (EI, 70 eV), \(m/z\) (%): 261 (4) [M\(^+\)], 230 (2), 192 (21), 121 (20), 106 (36), 91 (100), 59 (33); HRMS (EI) (C\(_{15}\)H\(_{19}\)NO\(_3\)): calc.: 261.1365, found: 261.1360.
Methyl 3-(2-phenylacetamido)-2-methyl-3-phenylpropanoate (anti-3g)

\[
\text{Bn} \quad \text{NH} \quad \text{COOMe}
\]

Methyl 3-hydroxy-2-methyl-3-phenylpropanoate\(^1\) (I) (48 mg, 250 μmol), 2-phenylacetonitrile (117 mg, 1.0 mmol) and TfOH (28 μL, 312 μmol) were stirred in 1 mL dichloromethane for 4 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 → 3/1) to give a colourless solid (75 mg, 96%) in a diastereomeric ratio of 94/6 (anti/syn). \(R_f = 0.58\) (pentane/ethyl acetate = 1/1); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \(\delta = 1.15\) (d, \(\text{J} = 7.1\) Hz, 3 H), 2.89 (qd, \(\text{J} = 7.1\) Hz, \(\text{J} = 5.4\) Hz, 1 H), 3.44 (s, 3 H), 3.62 (d, \(\text{J} = 3.8\) Hz, 2 H), 5.13 (dd, \(\text{J} = 9.1\) Hz, \(\text{J} = 5.4\) Hz, 1 H), 6.86 (d, \(\text{J} = 9.1\) Hz, 1 H, NH), 7.05-7.10 (m, 2 H), 7.16-7.41 (m, 8 H); \(^13\)C-NMR (90.6 MHz, CDCl\(_3\)): \(\delta = 16.0\) (q), 44.4 (t), 45.2 (d), 52.1 (d), 55.4 (q), 126.5 (d), 127.8 (d), 128.9 (d), 129.4 (d), 135.3 (d), 140.7 (s), 171.0 (s), 175.6 (s); MS (EI, 70 eV), \(m/z\) (%): 311 (4) [M\(^+\)], 225 (29), 192 (13), 106 (30), 91 (100); HRMS (EI) (C\(_{19}\)H\(_{21}\)NO\(_3\)): calc.: 311.1521, found: 311.1516.

Epimerisation of anti-3a:

\[
\begin{align*}
\text{Ph} \quad \text{NH} & \quad \text{COOMe} \quad \xrightarrow{\text{KO\textsuperscript{+}Bu 65 °C (MeOH)}} \quad \text{Ph} \quad \text{NH} & \quad \text{COOMe} \\
\end{align*}
\]

Methyl 3-(benzamido)-2-methyl-3-phenylpropanoate (anti-3a) (69 mg, 232 mmol) and 56 mg K'OBU (112 mmol) were dissolved in 2 mL methanol and heated to 65 °C. After stirring for 2.5 h the reaction was stopped by the addition of 5 mL water. The aqueous phase was extracted with ethyl acetate (20 mL) and dichloromethane (2 × 20 mL). The combined organic extracts were dried with MgSO\(_4\), filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 → 3/1) to give a colourless solid (59 mg, 86%) in a diastereomeric ratio of 51/49 (anti/syn).

Spectroscopic data of syn-3a: \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \(\delta = 1.21\) (d, \(\text{J} = 7.1\) Hz, 3 H), 3.06-3.14 (m, 1 H), 3.64 (s, 3 H), 5.44 (dd, \(\text{J} = 8.7\) Hz, \(\text{J} = 6.0\) Hz, 1 H), 7.22-7.35 (m, 5 H), 7.40-7.54.
(m, 3 H), 7.80-7.82 (m, 2 H); $^{13}$C-NMR (90.6 MHz, CDCl$_3$): $\delta = 13.7$ (q), 44.7 (d), 52.0 (d), 55.7 (q), 127.1 (d), 127.1 (d), 127.8 (d), 128.7 (d), 131.7 (d), 134.5 (s), 139.3 (s), 166.6 (s), 174.6 (s).

Proof of the kinetic product formation for substrate 3a:
Methyl 3-(benzamido)-2-methyl-3-phenylpropanoate (anti-3a/syn-3a = 51/49) (48 mg, 250 $\mu$mol), benzonitrile (77 mg, 0.75 mmol) and TfOH (28 $\mu$L, 312 $\mu$mol) were stirred in 1 mL dichloromethane for 1.5 h. After aqueous work-up the $^1$H NMR spectra of the crude product showed an unchanged diastereomeric ratio of 51/49 (anti/syn) for 3a. The result rules out a thermodynamic product formation.

Methyl 3-(benzamido)-3-(4-fluorophenyl)-2-methylpropanoate

\[
\text{NH} \quad \text{O} \\
\begin{array}{c}
\text{Ph} \\
\text{COOMe}
\end{array}
\]

Methyl 3-(4-fluorophenyl)-3-hydroxy-2-methylpropanoate (48 mg, 250 $\mu$mol), benzonitrile (103 mg, 1.0 mmol) and TfOH (28 $\mu$L, 312 $\mu$mol) were stirred in 1 mL dichloromethane for 1 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1 $\rightarrow$ 3/1) to give a colourless solid (63 mg, 80%) in a diastereomeric ratio of 93/7 (anti/syn). $R_f = 0.07$ (pentane/ethyl acetate = 10/1); m.p. = 131 $^\circ$C; $^1$H-NMR (360 MHz, CDCl$_3$): $\delta = 1.35$ (d, $^3J = 7.1$ Hz, 3 H), 3.06 (qd, $^3J = 7.1$ Hz, $^3J = 4.7$ Hz, 1 H), 3.60 (s, 3 H), 5.34 (dd, $^3J = 8.8$ Hz, $^3J = 4.7$ Hz, 1 H), 6.96-7.02 (m, 2 H), 7.24-7.32 (m, 2 H), 7.38-7.54 (m, 3 H), 7.85-7.89 (m, 2 H), 7.94 (d, $^3J = 8.8$ Hz, 1 H, NH); $^{13}$C-NMR (90.6 MHz, CDCl$_3$): $\delta = 16.2$ (q), 44.8 (d), 52.1 (d), 55.0 (q), 115.6 (dd, $^2J_{CF} = 21.5$ Hz), 127.1 (d), 127.9 (dd, $^3J_{CF} = 8.2$ Hz), 128.8 (d), 131.8 (d), 134.2 (s), 136.6 (d, $^4J_{CF} = 3.2$ Hz), 162.1 (d, $^1J_{CF} = 248.8$ Hz), 167.0 (s), 176.3 (s); MS (EI, 70 eV), m/z (%): 315 (5) [M$^+$], 229 (44), 210 (30), 105 (100), 77 (34), 51 (7); HRMS (EI) (C$_{18}$H$_{18}$FNO$_3$): calc.: 315.1271, found: 315.1268.

$N$-(2-Nitro-1-phenylpropyl)benzamide (anti-9)

\[
\text{O} \\
\begin{array}{c}
\text{Ph} \\
\text{NH} \\
\text{NO}_2
\end{array}
\]
2-Nitro-1-phenylpropan-1-ol (4) (45 mg, 250 μmol), benzonitrile (103 mg, 1.0 mmol) and TfOH (28 μL, 312 μmol) were stirred in 1 mL dichloromethane for 4.5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 5/1) to give a colourless solid (60 mg, 85%) in a diastereomeric ratio of 90/10 (anti/syn). Rf = 0.22 (pentane/ethyl acetate = 5/1); 1H-NMR (360 MHz, CDCl3): δ = 1.65 (d, 3J = 6.8 Hz, 3 H), 5.14 (virt. q, 3J = 6.5 Hz, 1 H), 5.68 (dd, 3J = 9.2 Hz, 3J = 6.0 Hz, 1 H), 7.28-7.59 (m, 8 H), 7.82-7.84 (m, 2 H); 13C-NMR (90.6 MHz, CDCl3): δ = 17.5 (q), 55.7 (d), 86.8 (d), 126.5 (d), 127.2 (d), 128.7 (d), 128.9 (d), 129.3 (d), 132.2 (d), 133.7 (s), 137.1 (s), 167.2 (s); MS (EI, 70 eV), m/z (%): 238 (14), 224 (39), 147 (36), 105 (100), 77 (68), 51 (14); HRMS (EI) (C16H16NO): calc.: 238.1232, found: 238.1228.

N-(2-(1,3-Dioxoisindolin-2-yl)-1-phenylpropyl)benzamide (anti-10)

\[
\text{Ph} \quad \text{NH} \quad \text{NPht}
\]

2-(1-Hydroxy-1-phenylpropan-2-yl)isoindoline-1,3-dione (5) (70 mg, 250 μmol), benzonitrile (103 mg, 1.0 mmol) and TfOH (28 μL, 312 μmol) were stirred in 1 mL dichloromethane for 3 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 3/1 → 0/1) to give a colourless solid (75 mg, 78%) in a diastereomeric ratio of 75/25 (anti/syn). Rf = 0.27 (pentane/ethyl acetate = 3/1); 1H-NMR (360 MHz, CDCl3): δ = 1.57 (d, 3J = 7.1 Hz, 3 H), 5.01 (qd, 3J = 7.1 Hz, 3J = 6.1 Hz, 1 H), 5.75 (dd, 3J = 8.8 Hz, 3J = 6.1 Hz, 1 H), 7.13-7.29 (m, 5 H), 7.45-7.56 (m, 3 H), 7.65-7.67 (m, 2 H), 7.75-7.77 (m, 2 H), 7.98-8.01 (m, 2 H), 8.56 (d, 3J = 8.8 Hz, 1 H, NH); 13C-NMR (90.6 MHz, CDCl3): δ = 15.9 (q), 51.2 (d), 56.8 (d), 123.6 (d), 126.0 (d), 127.2 (d), 127.3 (d), 128.7 (d), 128.8 (d), 131.7 (d), 134.2 (s), 134.3 (s), 134.4 (d), 139.3 (s), 166.9 (s), 168.4 (s); MS (EI, 70 eV), m/z (%): 384 (8) [M⁺], 309 (5), 210 (78), 105 (100), 77 (26), 44 (8); HRMS (EI) (C24H20N2O3): calc.: 384.1474, found: 384.1469.

Diethyl 1-(benzamido)-1-phenylpropan-2-ylphosphonate (syn-11)

\[
\text{Ph} \quad \text{NH} \quad \text{PO(OEt)}_{2}
\]

Diethyl 1-hydroxy-1-phenylpropan-2-ylphosphonate (6) (68 mg, 250 μmol), benzonitrile (103 mg, 1.0 mmol) and TfOH (28 μL, 312 μmol) were stirred in 1 mL dichloromethane for 5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 2/1) to give a colourless
solid (84 mg, 90%) in a diastereomeric ratio of 8/92 (anti/syn). \( R_f = 0.22 \) (pentane/ethyl acetate = 1/1); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \( \delta = 1.09 \) (t, \( ^3J = 7.1\) Hz, 3 H), 1.16 (dd, \( ^3J_{HP} = 17.2\) Hz, \( ^3J_{HH} = 7.4\) Hz, 3 H), 1.29 (t, \( ^3J = 7.1\) Hz, 3 H), 2.44 (dqd, \( ^3J_{HP} = 19.9\) Hz, \( ^3J_{HH} = 7.4\) Hz, \( ^3J_{HH} = 4.5\) Hz, 1 H), 3.81-4.00 (m, 2 H), 4.03-4.14 (m, 2 H), 5.42 (dd, \( ^3J_{HP} = 27.8\) Hz, \( ^3J_{HH} = 7.8\) Hz, \( ^3J_{HH} = 4.5\) Hz, 1 H), 7.20-7.50 (m, 8 H), 7.91-7.94 (m, 2 H), 8.45 (d, \( ^3J = 7.8\) Hz, 1 H, NH); \(^13\)C-NMR (90.6 MHz, CDCl\(_3\)) \( \delta = 11.5 \) (dq, \( ^2J_{CP} = 4.6\) Hz), 16.1 (dq, \( ^3J_{CP} = 6.3\) Hz), 16.5 (dq, \( ^3J_{CP} = 5.7\) Hz), 36.8 (dd, \( ^1J_{CP} = 138.3\) Hz), 54.9 (dd, \( ^2J_{CP} = 4.3\) Hz), 61.7 (dt, \( ^2J_{CP} = 7.3\) Hz), 62.2 (dt, \( ^2J_{CP} = 6.6\) Hz), 127.2 (d), 127.4 (d), 127.5 (d), 128.2 (d), 128.6 (d), 131.5 (d), 134.3 (s), 139.0 (d, \( ^3J_{CP} = 7.5\) Hz), 166.1 (s); MS (EI, 70 eV), \( m/z \) (%): 375 (1) [M\(^+\)], 271 (1), 166 (100), 139 (36), 111 (27), 91 (6).

\textit{N-}(2-(Ethylsulfonyl)-1-phenylpropyl)benzamide (\textit{syn-12})

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{SO}_2\text{Et} & 
\end{align*}
\]

2-(Ethylsulfonyl)-1-phenylpropan-1-ol (7) (57 mg, 250 \( \mu \)mol), benzonitrile (103 mg, 1.0 mmol) and TfOH (28 \( \mu \)L, 312 \( \mu \)mol) were stirred in 1 mL dichloromethane for 3.5 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 3/1 \( \rightarrow 1/1\)) to give a colourless solid (76 mg, 92%) in a diastereomeric ratio of 4/96 (anti/syn). \( R_f = 0.05 \) (pentane/ethyl acetate = 3/1); \(^1\)H-NMR (360 MHz, CDCl\(_3\)): \( \delta = 1.36 \) (t, \( ^3J = 7.4\) Hz, 3 H), 1.45 (d, \( ^3J = 7.2\) Hz, 3 H), 2.64-2.96 (m, 2 H), 5.58 (qd, \( ^3J = 7.2\) Hz, \( ^3J = 3.9\) Hz, 1 H), 5.70 (dd, \( ^3J = 7.7\) Hz, \( ^3J = 3.9\) Hz, 1 H), 7.32-7.55 (m, 8 H), 7.81 (d, \( ^3J = 7.7\) Hz, 1 H, NH), 7.86-7.87 (m, 2 H); \(^13\)C-NMR (90.6 MHz, CDCl\(_3\)): \( \delta = 5.8\) (q), 10.4 (q), 45.6 (t), 53.6 (d), 61.0 (d), 127.2 (d), 127.2 (d), 128.3 (d), 128.8 (d), 128.9 (d), 131.9 (d), 134.0 (s), 137.3 (s), 166.8 (s); MS (EI, 70 eV), \( m/z \) (%): 309 (4), 238 (41), 210 (9), 105 (100), 77 (35); HRMS (EI) (C\(_{16}\)H\(_{16}\)NO): calc.: 238.1232, found: 238.1232.

Preparation of \textit{N-}(2-amino-1-phenylpropyl)benzamide (\textit{anti-14}) from \textit{N-}(2-nitro-1-phenylpropyl)benzamide (\textit{anti-9}):

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{NH}_2 & 
\end{align*}
\]
N-(2-Nitro-1-phenylpropyl)benzamide \((anti-9)\) (284 mg, 1.0 mmol) and 431 mg zinc (6.6 mmol) were suspended in 4 mL ethanol at ambient temperature. A mixture of water and concentrated sulphuric acid (1.6 mL/0.4 mL) was added dropwise. After stirring for 19 h the reaction mixture was concentrated under reduced pressure to remove most of the ethanol and the resulting aqueous phase was washed with diethyl ether (10 mL) to remove non-basic impurities. The aqueous layer was made strongly basic with 50% NaOH and extracted with dichloromethane \( (2 \times 20 \text{ mL}) \) and ethyl acetate (20 mL). The combined organic extracts were dried over MgSO\(_4\), filtered and the solvent was removed under reduced pressure to yield 246 mg (97%) of a colourless solid in a diastereomeric ratio of 90/10 \( (anti/syn) \).

**Preparation of N-(2-amino-1-phenylpropyl)benzamide \((anti-14)\) from N-(2-(1,3-dioxoisindolin-2-yl)-1-phenylpropyl)benzamide \((anti-10)\):**

N-(2-(1,3-Dioxoisindolin-2-yl)-1-phenylpropyl)benzamide \((anti-10)\) (84 mg, 220 \( \mu \text{mol} \)) and 33 mg hydrazine monohydrate (660 \( \mu \text{mol} \)) were dissolved in 2 mL ethanol and were refluxed for 2.5 h. The reaction mixture was concentrated under reduced pressure to remove most of the ethanol. The oily residue was diluted with dichloromethane (10 mL) and water (10 mL). The layers were separated and the aqueous layer was extracted with dichloromethane \( (3 \times 10 \text{ mL}) \). The combined extracts were washed with saturated NaHCO\(_3\)-solution, dried over Na\(_2\)SO\(_4\), filtered and the solvent was removed under reduced pressure. After purification by flash chromatography (dichloromethane/methanol/\( \text{Et}_3\)N = 100/0/1 \( \rightarrow \) 100/10/1) 43 mg (76%, d.r. = 75/25) of \(anti-14\) were obtained as a colourless solid.

\( R_t = 0.10 \) (ethyl acetate); \(anti\)-diastereoisomer: \(^1\text{H-NMR}\) (500 MHz, DMSO): \( \delta = 0.85 \) (d, \( ^3J = 6.5 \text{ Hz}, 3 \text{ H} \)), 3.22-3.27 (m, 1 H), 5.02 (\( \text{virt} \), \( ^3J = 8.1 \text{ Hz}, 1 \text{ H} \)), 5.62 (s, 2 H, NH\(_2\)), 7.22-7.55 (m, 8 H), 7.84-7.88 (m, 2 H), 8.68 (d, \( ^3J = 8.1 \text{ Hz}, 1 \text{ H, NH} \)); \(^{13}\text{C-NMR}\) (90.6 MHz, DMSO): \( \delta = 15.5 \) (q), 55.9 (d), 59.4 (d), 126.6 (d), 127.3 (d), 127.5 (d), 127.9 (d), 128.1 (d), 131.1 (d), 134.7 (s), 141.9 (s), 166.0 (s);

\(syn\)-diastereoisomer: \(^1\text{H-NMR}\) (500 MHz, DMSO): \( \delta = 0.90 \) (d, \( ^3J = 6.5 \text{ Hz}, 3 \text{ H} \)), 3.17-3.22 (m, 1 H), 4.74 (\( \text{virt} \), \( ^3J = 8.0 \text{ Hz}, 1 \text{ H} \)), 5.62 (s, 2 H, NH\(_2\)), 7.22-7.55 (m, 8 H), 7.89-7.91 (m, 2 H), 8.62 (d, \( ^3J = 8.0 \text{ Hz}, 1 \text{ H, NH} \));

MS (EI, 70 eV), \( m/z \) (%): 252 (1), 211 (100), 210 (31), 193 (16), 132 (15), 118 (35), 105 (94), 77 (42), 44 (32); HRMS (EI) (C\(_{14}\)H\(_{13}\)NO): calc.: 211.0997, found: 211.0995.
Preparation of anti-\(N,N'\)-dibenzoyl 1-methyl-2-phenylethlyendiamine

\[
\begin{align*}
\text{Preparation of } & \text{anti-}\(N,N'\)-dibenzoyl 1-methyl-2-phenylethlyendiamine} \\
N-(2\text{-amino-1-phenylpropyl})benzamide (\text{anti-14}) (50 \text{ g, 197 } \mu\text{mol}), \text{ benzoyl chloride (200 mg, 1.42 mmol), were stirred in 2 mL pyridine for 15 h. The reaction was stopped by the addition of 10 mL saturated NH}_4\text{Cl-solution. The reaction was extracted with dichloromethane (2} \times \text{20 mL) and ethyl acetate (20 mL). The combined organic extracts were dried with MgSO}_4, \text{ filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1} \rightarrow \text{0/1) to give a colourless solid.} \\
\text{The analytical data were in line with the data described in literature and therefore prove the } \text{anti-configuration of anti-14.}\]

N-(1-phenyl-2-(propylsulfonyl)butyl)benzamide (\text{anti-16})

\[
\begin{align*}
\text{1-Phenyl-2-(propylsulfonyl)butan-1-ol (15) (64 mg, 250 } \mu\text{mol), benzonitrile (103 mg, 1.0 mmol) and TfOH (28 } \mu\text{L, 312 } \mu\text{mol) were stirred in 1 mL dichloromethane for 1 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 3/1) to give a colourless solid (78 mg, 87%) in a diastereomeric ratio of 12/88 (anti/syn).} R_f = 0.20 \text{ (pentane/ethyl acetate}} = 3/1); \text{ } ^1\text{H-NMR (360 MHz, CDCl}_3\text{): } \delta = 0.93 \text{ (t, } ^3J = 7.4 \text{ Hz, 3 H), 1.23 \text{ (t, } ^3J = 7.4 \text{ Hz, 3 H), 1.72-1.83 \text{ (m, 3 H), 1.99-2.11 \text{ (m, 1 H), 2.57-2.65 \text{ (m, 1 H), 3.30-3.35 \text{ (m, 1 H), 3.45-3.54 \text{ (m, 1 H), 5.80 \text{ (dd, } ^3J = 8.7 \text{ Hz, } ^3J = 3.5 \text{ Hz, 1 H), 7.29-7.54 \text{ (m, 8 H), 7.86-7.89 \text{ (m, 2 H), 8.26 \text{ (d, } ^3J = 8.7 \text{ Hz, 1 H, NH);} \text{ } ^13\text{C-NMR (90.6 MHz, CDCl}_3\text{) } \delta = 12.5 \text{ (q), 13.2 \text{ (q), 14.6 \text{ (t), 20.1 \text{ (t), 51.8 \text{ (d), 53.0 \text{ (t), 70.0 \text{ (d), 127.2 \text{ (d), 127.8 \text{ (d), 128.5 \text{ (d), 128.8 \text{ (d), 132.0 \text{ (d), 133.9 \text{ (s), 136.5 \text{ (s), 166.2 \text{ (s); MS (EI, 70 eV), } m/z (\%): 252 \text{ (82), 210 \text{ (36), 105 \text{ (100), 84 \text{ (27), 77 \text{ (41), 57 \text{ (69); HRMS (EI) (C}_{14}\text{H}_{13}\text{NO): calc.: 252.1388, found: 252.1386.)}}}}}
\end{align*}
\]
Preparation of \(N\)-(2,3,3-trimethyl-1-phenylbutyl)benzamide (\textit{syn}-13) – Representative Procedure for the Ritter reactions catalysed by dinitrobenzenesulfonic acid (DNBSA):

In a typical experiment 2,3,3-trimethyl-1-phenylbutan-1-ol\(^8\) (8) (48 mg, 250 \(\mu\)mol) was dissolved in benzonitrile (2 mL) and DNBSA (15 mg, 51 \(\mu\)mol) was added at 65 °C. After 2 h the reaction was stopped by the addition of 5 mL saturated NaHCO\(_3\)-solution and diluted with dichloromethane. The layers were separated, the aqueous layer was extracted with dichloromethane (2 \(\times\) 20 mL), the combined organic extracts were dried over MgSO\(_4\), filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1) to give a colourless solid (51 mg, 69\%) in a diastereomeric ratio of 13/87 (\textit{anti/syn}).

\[
R_f = 0.31 \text{ (pentane/ethyl acetate = 10/1); } ^1\text{H-NMR (360 MHz, CDCl}_3\text{): } \delta = 0.94 \text{ (d, } ^3J = 7.2 \text{ Hz, 3 H), 1.07 \text{ (s, 9 H), 1.82 (qd, } ^3J = 7.2 \text{ Hz, } ^3J = 1.5 \text{ Hz, 1 H), 5.69 (dd, } ^3J = 9.1 \text{ Hz, } ^3J = 1.5 \text{ Hz, 1 H), 6.58 (dd, } ^3J = 9.1 \text{ Hz, 1 H, NH), 7.19-7.34 \text{ (m, 5 H), 7.44-7.52 \text{ (m, 3 H), 7.80-7.82 \text{ (m, 2 H); } ^13\text{C-NMR (90.6 MHz, CDCl}_3\text{): } \delta = 8.3 \text{ (q), 28.3 \text{ (q), 33.7 \text{ (s), 48.8 \text{ (d), 52.7 \text{ (d), 126.0 \text{ (d), 126.7 \text{ (d), 126.9 \text{ (d), 128.5 \text{ (d), 128.8 \text{ (d), 131.6 (d), 135.0 (s), 143.7 (s), 166.4 (s); MS (EI, 70 eV), } m/z (\%)\: 295 (1 [M^-], 238 (4), 210 (56), 166 (78), 139 (29), 105 (100), 77 (26); HRMS (EI) (C}_{20}\text{H}_{25}\text{NO): calc.: 295.1936, found: 295.1931.}}\]

\(N\)-(1-(4-chlorophenyl)-2,3,3-trimethylbutyl)benzamide (\textit{syn}-18a)

1-(4-Chlorophenyl)-2,3,3-trimethylbutan-1-ol\(^9\) (17) (57 mg, 250 \(\mu\)mol) was dissolved in benzonitrile (2 mL) and DNBSA (15 mg, 51 \(\mu\)mol) was added at 65 °C and stirred for 2 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1) to give a colourless solid (69 mg, 84\%) in a diastereomeric ratio of 8/92 (\textit{anti/syn}). \(R_f = 0.28 \text{ (pentane/ethyl acetate = 10/1); } ^1\text{H-NMR (360 MHz, CDCl}_3\text{): } \delta = 0.91 \text{ (d, } ^3J = 7.2 \text{ Hz, 3 H), 1.05 \text{ (s, 9 H), 1.75 (qd, } ^3J = 7.2 \text{ Hz, } ^3J = 1.6 \text{ Hz, 1 H), 5.60 (d, } ^3J = 8.6 \text{ Hz, 1 H), 6.53 (d, } ^3J = 8.6 \text{ Hz, 1 H, NH), 7.18 (d, } ^3J = 8.5 \text{ Hz, 2 H), 7.27 (d, } ^3J = 8.5 \text{ Hz, 2 H), 7.43-7.54 \text{ (m, 3 H), 7.76-7.80 \text{ (m, 2 H); } ^13\text{C-NMR (90.6 MHz, CDCl}_3\text{): } \delta = 8.2 \text{ (q), 28.3 \text{ (q), 33.7 \text{ (s), 48.8 \text{ (d), 52.5 \text{ (d), 126.9 \text{ (d), 127.4 \text{ (d), 128.6 \text{ (d),}}\]

\[
\text{Supplementary Material (ESI) for Chemical Communications}
\text{This journal is (c) The Royal Society of Chemistry 2009}
\]
128.9 (d), 131.8 (d), 132.4 (s), 142.4 (s), 166.4 (s); MS (EI, 70 eV), m/z (%): 329 (2) [M⁺], 272 (5), 244 (28), 105 (100), 77 (21); HRMS (EI) (C₂₀H₂₄ClNO): calc.: 329.1546, found: 329.1541.

**N-(1-(4-chlorophenyl)-2,3,3-trimethylbutyl)acetamide (syn-18b)**

![Chemical structure of N-(1-(4-chlorophenyl)-2,3,3-trimethylbutyl)acetamide (syn-18b)](image)

1-(4-Chlorophenyl)-2,3,3-trimethylbutan-1-ol⁹ (17) (57 mg, 250 μmol) was dissolved in acetonitrile (2 mL) and DNBSA (15 mg, 51 μmol) was added at 65 °C and stirred for 2 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1) to give a colourless solid (52 mg, 78%) in a diastereomeric ratio of 9/91 (anti/syn). Rᵣ = 0.16 (pentane/ethyl acetate = 10/1); ¹H-NMR (360 MHz, CDCl₃): δ = 0.78 (d, 3J = 7.2 Hz, 3 H), 0.98 (s, 9 H), 1.61 (qd, 3J = 7.2 Hz, 3J = 1.9 Hz, 1 H), 2.03 (s, 3 H), 5.40 (d, 3J = 8.8 Hz, 1 H), 5.97 (d, 3J = 8.8 Hz, 1 H, NH), 7.11 (d, 3J = 8.5 Hz, 2 H), 7.25 (d, 3J = 8.5 Hz, 2 H); ¹³C-NMR (90.6 MHz, CDCl₃): δ = 8.2 (q), 23.6 (q), 28.2 (q), 33.7 (s), 48.4 (d), 52.1 (d), 127.4 (d), 128.5 (d), 132.3 (s), 142.6 (s), 169.2 (s); MS (EI, 70 eV), m/z (%): 267 (5) [M⁺], 210 (7), 182 (81), 140 (100), 43 (34); HRMS (EI) (C₁₅H₂₂ClNO): calc.: 267.1390, found: 267.1387.

**N-(1-(4-chlorophenyl)-2,3,3-trimethylbutyl)isobutyramide (syn-18c)**

![Chemical structure of N-(1-(4-chlorophenyl)-2,3,3-trimethylbutyl)isobutyramide (syn-18c)](image)

1-(4-Chlorophenyl)-2,3,3-trimethylbutan-1-ol⁹ (17) (28 mg, 125 μmol) was dissolved in isobutyronitrile (1 mL) and DNBSA (7 mg, 25 μmol) was added at 65 °C and stirred for 26 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1) to give a colourless solid (35 mg, 95%) in a diastereomeric ratio of 12/88 (anti/syn). Rᵣ = 0.19 (pentane/ethyl acetate = 10/1); ¹H-NMR (360 MHz, CDCl₃): δ = 0.81 (d, 3J = 7.2 Hz, 3 H), 0.99 (s, 9 H), 1.18 (d, 3J = 6.9 Hz, 3 H), 1.19 (d, 3J = 6.9 Hz, 3 H), 1.64 (qd, 3J = 7.2 Hz, 3J = 1.8 Hz, 1 H), 2.43 (hept., 3J = 6.9 Hz, 1 H), 5.39 (d, 3J = 8.5 Hz, 1 H), 5.82 (d, 3J = 8.5 Hz, 1 H, NH), 7.10 (d, 3J = 8.3 Hz, 2 H), 7.27 (d, 3J = 8.3 Hz, 2 H); ¹³C-NMR (90.6 MHz, CDCl₃): δ = 8.2 (q), 19.6 (q), 19.7 (q), 28.2 (q), 33.7 (s), 36.1 (d), 48.6 (d), 51.6 (d), 127.3 (d), 128.6 (d), 132.3 (s), 142.8 (s), 175.6 (s); MS (EI, 70...
eV), $m/z$ (%): 295 (4) [M$^+$], 238 (6), 210 (52), 168 (19), 140 (100), 71 (23), 57 (14), 43 (50); HRMS (EI) (C$_{17}$H$_{26}$ClNO): calc.: 295.1703, found: 295.1701.

$N$-(1-(4-chlorophenyl)-2,3,3-trimethylbutyl)-2-phenylacetamide ($syn$-18d)

![Chemical Structure](image)

1-(4-Chlorophenyl)-2,3,3-trimethylbutan-1-ol$^9$ (17) (28 mg, 125 μmol) was dissolved in phenylacetonitrile (1 mL) and DNBSA (7 mg, 25 μmol) was added at 65 °C and stirred for 23 h. The crude product was purified by flash chromatography (pentane/ethyl acetate = 10/1) to give a colourless solid (37 mg, 86%) in a diastereomeric ratio of 12/88 (anti/$syn$). $R_f$ = 0.22 (pentane/ethyl acetate = 10/1); $^1$H-NMR (360 MHz, CDCl$_3$): $\delta$ = 0.45 (d, $^3J$ = 7.2 Hz, 3 H), 0.89 (s, 9 H), 1.50 (qd, $^3J$ = 7.2 Hz, $^3J$ = 1.7 Hz, 1 H), 3.63 (d, $^4J$ = 3.6 Hz, 2 H), 5.30 (d, $^3J$ = 8.6 Hz, 1 H), 5.72 (d, $^3J$ = 8.6 Hz, 1 H, NH), 6.92-6.95 (m, 2 H), 7.23 (d, $^3J$ = 8.5 Hz, 2 H), 7.30-7.45 (m, 5 H); $^{13}$C-NMR (90.6 MHz, CDCl$_3$): $\delta$ = 7.4 (q), 28.1 (q), 33.5 (s), 44.3 (t), 48.8 (d), 51.9 (d), 127.2 (d), 127.9 (d), 128.5 (d), 129.4 (d), 132.3 (s), 134.9 (s), 142.4 (s), 169.7 (s); MS (EI, 70 eV), $m/z$ (%): 343 (4) [M$^+$], 286 (7), 258 (67), 176 (33), 140 (100), 91 (53), 58 (61); HRMS (EI) (C$_{21}$H$_{26}$ClNO): calc.: 343.1703, found: 343.1698.

References cited in supplementary information

4 d.r. = 50/50; prepared according to ref.$^1$; analytical data: O. Chuzel, J. Deschamp, C. Chausteur and O. Riant, *Org. Lett.* 2006, 8, 5943-5946.