Supporting Information
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Supporting Information

Preparation of Zinc Enolate Equivalent by Zinciomethylation of Isocyanates: Catalytic Asymmetric Aldol-type Reaction

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Instrumentation and Chemicals

Nuclear magnetic resonance spectra were taken on Varian UNITY INOVA 500 (1H, 500 MHz; 13C, 125.7 MHz) spectrometer using tetramethylsilane for 1H NMR as an internal standard (δ = 0 ppm), CDCl₃ for 13C NMR as an internal standard (δ = 77.0 ppm). 1H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra were obtained with a JEOL JMS-700 spectrometer by electron ionization at 70 eV. Elemental analyses were carried out with a YANAKO MT2 CHN CORDER machine at Kyoto University Elemental Analysis Center. Infrared (IR) spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Melting points were determined using a YANAKO MP-500D. TLC analyses were performed by means of Merck Kieselgel 60 F254 (0.25 mm) Plates. Visualization was accomplished with UV light (254 nm) and an aqueous vanillin solution followed by heating. Flash column chromatography was carried out using Kanto Chemical silica gel (spherical, 40–100 μm).

Unless otherwise noted, commercially available reagents were used without purification. Tetrahydrofuran, Dehydrated stabilizer free —Super— was purchased from Kanto Chemical Co., stored under argon, and used as it is. Zinc powder was used after washing with 10% HCl according to the reported procedure.¹
Experimental Procedure

Procedure for Preparation of bis(iodozincio)methane (1)

A mixture of pure zinc dust (150 mmol), diiodomethane (1.0 mmol), and PbCl₂ (0.005 mmol) in THF (5.0 mL) was sonicated for 1 h in an ultrasonic cleaner bath under Ar. When pyrometallurgy zinc dust was used instead of pure zinc, it is not necessary to add PbCl₂. Both of pure zinc and pyrometallurgy zinc are commercially available. To the mixture, diiodomethane (50 mmol) in THF (45 mL) was added dropwise over 30 min at 0 °C with vigorous stirring. The mixture was stirred for 4 h at 25 °C. After the stirring was stopped, the reaction vessel was allowed to stand undisturbed for several hours. Excess zinc was separated by sedimentation. ¹H NMR spectra of the obtained supernatant showed a broad singlet at −1.2 ppm at 0 °C, which corresponded to the methylene proton of 1. The supernatant was used for the further reaction as a solution of 1 in THF (0.1–0.5 M). Bis(iodozincio)methane in THF can be kept unchanged at least for a month in a sealed reaction vessel.

Procedure for Preparation of 1,1-bis(iodozincio)ethane (9)

A mixture of pure zinc dust (150 mmol), 1,1-diiodoethane (1.0 mmol), and PbCl₂ (0.005 mmol) in THF (5.0 mL) was sonicated for 1 h in an ultrasonic cleaner bath under Ar. When pyrometallurgy zinc dust was used instead of pure zinc, it is not necessary to add PbCl₂. Both of pure zinc and pyrometallurgy zinc are commercially available. To the mixture, 1,1-diiodoethane (50 mmol) in THF (45 mL) was added dropwise over 30 min at 0 °C with vigorous stirring. The mixture was stirred for 4 h at 25 °C. After the stirring was stopped, the reaction vessel was allowed to stand undisturbed for several hours. Excess zinc was separated by sedimentation. ¹H NMR (300 MHz, 20°C) δ −0.08 (q, J = 7.8 Hz, 1H), 1.45 (d, J = 7.8 Hz, 3H). ¹H NMR spectra of the obtained supernatant showed a quartet at −0.08 ppm at 0 °C, which corresponded to the methyne proton of 9. The supernatant was used for the further reaction as a solution of 9 in THF (0.1–0.5 M). 1,1-bis(iodozincio)ethane in THF can be kept unchanged at least for two days in a sealed reaction vessel.

Procedure for aldol-type reaction (6aa)

To a solution of benzoyl isocyanate (2a, 29.4 mg, 0.2 mmol) in THF (4.0 mL), dizinc 1 (0.2 mmol, 0.13 M in THF) was added dropwise at −60 °C under Ar. The reaction mixture was stirred for 30 min at −60 °C. After the reaction mixture was warmed to −40 °C, benzaldehyde (5a, 20 μL, 0.2 mmol) was added to the resulting mixture. The mixture was stirred at −40 °C for 3 h, and poured into saturated NH₄Claq (10 mL). The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Purification by silica gel column chromatography (hexane / ethyl acetate) gave the title compound (6aa, 48.7 mg, 90%)
Procedure for aldol-type reaction (6ba-6da)
To a solution of isocyanate 2 (0.2 mmol) in THF or toluene (4.0 mL), the dizinc 1 (0.2 mmol, 0.13 M in THF) was added dropwise at 80 °C under Ar. The reaction mixture was stirred for 30 min at 80 °C. Then, benzaldehyde (5a, 20 μL, 0.2 mmol) was added to the resulting mixture at 80 °C. The mixture was stirred at 80 °C for 3 h, and poured into saturated NH₄Cl aq (10 mL). The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Purification by silica gel column chromatography (hexane / ethyl acetate) gave the title compound (6ba-6da).

Procedure for aldol-type reaction (6ea)
To a solution of cyclohexyl isocyanate (2e, 25.0 mg, 0.2 mmol) in THF or toluene (4.0 mL), the dizinc 1 (0.2 mmol, 0.13 M in THF) was added dropwise at 100 °C under Ar. The reaction mixture was stirred for 30 min at 100 °C. Then, benzaldehyde (5a, 20 μL, 0.2 mmol) was added to the resulting mixture at 100 °C. The mixture was stirred at 100 °C for 3 h, and poured into saturated NH₄Cl aq (10 mL). The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Purification by silica gel column chromatography (hexane / ethyl acetate) gave the title compound (6ea, 3.0 mg, 6%).

Procedure for aldol-type reaction (12aa)
To a solution of benzoyl isocyanate (2a, 29.4 mg, 0.2 mmol) in THF (4.0 mL), dizinc 9 (0.2 mmol, 0.13 M in THF) was added dropwise at –60 °C under Ar. The reaction mixture was stirred for 30 min at –60 °C. After the reaction mixture was warmed to –40 °C, benzaldehyde (5a, 20 μL, 0.2 mmol) was added to the resulting mixture. The mixture was stirred at –40 °C for 3 h, and poured into saturated NH₄Cl aq (10 mL). The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Purification by silica gel column chromatography (hexane / ethyl acetate) gave the title compound (12aa, 26.5 mg, 47%).

General procedure for asymmetric synthesis of β-hydroxy amide (6bb-6bn)
To a solution of phenyl isocyanate (2b, 23.8 mg, 0.2 mmol) in toluene (4.0 mL), dizinc 1 (0.2 mmol, 0.13 M in THF) was added dropwise at 80 °C under Ar. After being stirred for 30 min at 80 °C, the mixture was diluted with toluene (22.0 mL) at –40 °C. To the resulting mixture, we sequentially added (S)-bis(4-fluorophenyl)(1-methylpyrrolidin-2-yl)methanol (13g, 7.3 mg, 0.024 mmol) in toluene (2.0 mL) and aldehyde 5 (0.08 mmol) in toluene (2.0 mL). The resulting mixture was stirred at –40 °C for 72 h, and poured into HCl aq (1N, 10 mL). The mixture was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over Na₂SO₄. Purification by silica gel column chromatography (hexane / ethyl acetate) gave the title compound
Aminoalcohols 13 (except for 13c) were prepared by the literature procedure.3
Aminoalcohol (13c) are prepared by the literature procedure.4

Characterization Data of Products

(S)-diphenyl(pyrrolidin-2-yl)methanol (13a): CAS RN [112068-01-6].

\[
\begin{align*}
\text{White solid}. & \quad \text{1H NMR (CDCl}_3\text{)} \: \delta \: 7.58 (\text{dd}, \: J = 8.5, \: 1.0 \text{ Hz}, \: 2\text{H}), \: 7.50 (\text{dd}, \: J = 8.5, \: 1.0 \text{ Hz}, \: 2\text{H}), \: 7.29 (\text{m}, \: 4\text{H}), \: 7.17 (\text{m}, \: 2\text{H}), \: 4.26 (\text{t}, \: J = 7.5 \text{ Hz}, \: 2\text{H}), \: 3.04 (\text{m}, \: 1\text{H}), \: 2.95 (\text{m}, \: 1\text{H}), \: 1.66 (\text{m}, \: 5\text{H}). \\
\text{13C NMR (CDCl}_3\text{)} \: \delta \: 148.2, \: 145.4, \: 128.2, \: 127.9, \: 126.4, \: 126.3, \: 125.9, \: 125.5, \: 77.1, \: 64.5, \: 46.8, \: 26.3, \: 25.5.
\end{align*}
\]

(S)-ethyl 2-(hydroxydiphenylmethyl)pyrrolidine-1-carboxylate (13b): CAS RN [152326-82-4].

\[
\begin{align*}
\text{White solid}. & \quad \text{1H NMR (CDCl}_3\text{)} \: \delta \: 7.39 (\text{m}, \: 4\text{H}), \: 7.29 (\text{m}, \: 6\text{H}), \: 6.08 (\text{s}, \: 1\text{H}), \: 4.93 (\text{dd}, \: J = 9.0, \: 3.5 \text{ Hz}, \: 1\text{H}), \: 4.12 (\text{m}, \: 2\text{H}), \: 3.41 (\text{d}, \: J = 8.0 \text{ Hz}, \: 1\text{H}), \: 2.95 (\text{s}, \: 1\text{H}), \: 2.09 (\text{m}, \: 1\text{H}), \: 1.94 (\text{m}, \: 1\text{H}), \: 1.49 (\text{m}, \: 1\text{H}), \: 1.23 (\text{t}, \: J = 7.5 \text{ Hz}, \: 3\text{H}), \: 0.79 (\text{s}, \: 1\text{H}). \\
\text{13C NMR (CDCl}_3\text{)} \: \delta \: 158.4, \: 146.4, \: 143.7, \: 128.2, \: 127.9, \: 127.6, \: 127.4, \: 123.9, \: 127.2, \: 127.1, \: 81.6, \: 66.0, \: 61.9, \: 47.7, \: 29.7, \: 23.0, \: 14.6.
\end{align*}
\]

(S)-(1-benzylpyrrolidin-2-yl)diphenylmethanol (13c): CAS RN [118970-95-9].

\[
\begin{align*}
\text{White solid}. & \quad \text{1H NMR (CDCl}_3\text{)} \: \delta \: 7.73 (\text{dd}, \: J = 8.5, \: 1.0 \text{ Hz}, \: 2\text{H}), \: 7.58 (\text{dd}, \: J = 8.5, \: 1.0 \text{ Hz}, \: 2\text{H}), \: 7.23 (\text{m}, \: 8\text{H}), \: 7.10 (\text{t}, \: J = 7.5 \text{ Hz}, \: 1\text{H}), \: 7.04 (\text{d}, \: J = 7.0 \text{ Hz}, \: 2\text{H}), \: 4.94 (\text{s}, \: 1\text{H}), \: 3.98 (\text{dd}, \: J = 10.0, \: 5.0 \text{ Hz}, \: 1\text{H}), \: 3.22 (\text{d}, \: J = 12.5 \text{ Hz}, \: 1\text{H}), \: 3.03 (\text{d}, \: J = 12.5 \text{ Hz}, \: 1\text{H}), \: 2.92 (\text{m} \: 1\text{H}), \: 2.36 (\text{m}, \: 1\text{H}), \: 1.97 (\text{m}, \: 1\text{H}), \: 1.76 (\text{m}, \: 1\text{H}), \: 1.64 (\text{m}, \: 2\text{H}). \\
\text{13C NMR (CDCl}_3\text{)} \: \delta \: 148.1, \: 146.7, \: 139.7, \: 128.6, \: 128.2, \: 128.1, \: 128.1, \: 126.8, \: 126.4, \: 126.2, \: 125.6, \: 125.6, \: 77.9, \: 70.7, \: 60.6, \: 55.5, \: 29.8, \: 24.1.
\end{align*}
\]

(S)-(1-methylpyrrolidin-2-yl)diphenylmethanol (13d): CAS RN [110529-22-1].
White solid.  $^1$H NMR (CDCl$_3$) $\delta$ 7.65 (dd, $J = 8.5$, 1.0 Hz, 2H), 7.55 (dd, $J = 8.5$, 1.0 Hz, 2H), 7.28 (dt, $J = 7.0$, 3.0 Hz, 4H), 7.15 (m, 2H), 4.79 (s, 1H), 3.63 (dd, $J = 9.5$, 4.5 Hz, 1H), 3.12 (m, 1H), 2.46 (m, 1H), 1.92 (m, 1H), 1.83 (s, 3H), 1.68 (s, 3H).  $^{13}$C NMR (CDCl$_3$) $\delta$ 148.3, 146.7, 128.0, 126.1, 126.1, 125.4, 77.4, 72.0, 59.2, 43.0, 29.9, 24.0.

**S**-**bis**(4-methoxyphenyl)(1-methylpyrrolidin-2-yl)methanol (13e).

White solid.  $[^{[\alpha]}^D]_{20}$ 24.5 (c 1.02, CH$_2$Cl$_2$).  $^1$H NMR (CDCl$_3$) $\delta$ 7.64 (s, 1H), 7.50 (d, $J = 4.0$ Hz, 2H), 7.34 (t, $J = 8.0$ Hz, 2H), 7.28 (d, $J = 3.0$ Hz, 1H), 7.14 (t, $J = 8.0$ Hz, 1H), 7.03 (d, $J = 2.0$ Hz, 1H), 6.98 (t, $J = 2.5$ Hz, 1H), 5.49 (m, 1H), 3.79 (d, $J = 3.5$ Hz, 1H), 2.90 (m, 2H).  $^{13}$C NMR (CDCl$_3$) $\delta$ 169.3, 146.3, 137.2, 129.1, 126.8, 125.0, 124.7, 123.8, 120.1, 67.2, 45.8.  Mp. 81.0–81.3 °C.  TLC: R$_f$ 0.34 (chloroform/methanol = 10:1).  IR (KBr) 3367.9, 2952.2, 2905.9, 2863.5, 2811.4, 2038.9, 1605.8, 1507.4, 1456.3, 1372.4, 1296.2, 1285.6, 1243.2, 1170.8, 1139.0, 1028.1, 850.6, 823.6, 811.1, 648.2, 581.6. cm$^{-1}$.  HRMS (ESI) Calcd for C$_{20}$H$_{26}$NO$_3$: [M+H]$^+$, 328.1907. Found: m/z 328.1909.

(S)-**bis**(4-(tert-butyl)phenyl)(1-methylpyrrolidin-2-yl)methanol (13f).

White solid.  $[^{[\alpha]}^D]_{20}$ 17.9 (c 0.84, CH$_2$Cl$_2$).  $^1$H NMR (CDCl$_3$) $\delta$ 7.64 (s, 1H), 7.50 (d, $J = 4.0$ Hz, 2H), 7.34 (t, $J = 8.0$ Hz, 2H), 7.28 (d, $J = 3.0$ Hz, 1H), 7.14 (t, $J = 8.0$ Hz, 1H), 7.03 (d, $J = 2.0$ Hz, 1H), 6.98 (t, $J = 2.5$ Hz, 1H), 5.49 (m, 1H), 3.79 (d, $J = 3.5$ Hz, 1H), 2.90 (m, 2H).  $^{13}$C NMR (CDCl$_3$) $\delta$ 169.3, 146.3, 137.2, 129.1, 126.8, 125.0, 124.7, 123.8, 120.1, 67.2, 45.8.  Mp. 71.8–72.2 °C.  TLC: R$_f$ 0.45 (chloroform/methanol = 10:1).  IR (KBr) 3367.9, 2963.8, 2904.0, 2869.2, 2786.3, 2362.9, 1507.4, 1460.2, 1406.2, 1362.8, 1316.5, 1268.3, 1203.6, 1110.1, 1041.6, 823.6, 708.9, 583.5. cm$^{-1}$.  HRMS (ESI) Calcd for C$_{26}$H$_{38}$NO: [M+H]$^+$, 380.2948. Found: m/z 380.2951.

(S)-**bis**(4-fluorophenyl)(1-methylpyrrolidin-2-yl)methanol (13g): CAS RN [350236-79-2].
White solid. \(^1H\) NMR (CDCl\(_3\)) \(\delta\) 7.56 (dd, \(J = 9.0, 5.5\) Hz, 2H), 7.46 (dd, \(J = 9.0, 5.5\) Hz, 2H), 6.96 (m, 4H), 4.82 (s, 1H), 3.54 (dd, \(J = 9.0, 5.0\) Hz, 1H), 3.11 (m, 1H), 2.45 (m, 1H), 1.87 (m, 1H), 1.84 (s, 3H), 1.66 (m, 3H). \(^{13}C\) NMR (CDCl\(_3\)) \(\delta\) 162.2, 160.3, 144.0, 142.5, 127.0 (d, \(J = 8.3\) Hz), 127.0 (d, \(J = 8.3\) Hz), 114.9 (d, \(J = 4.5\) Hz), 114.8 (d, \(J = 4.0\) Hz), 76.9, 72.0, 59.1, 43.0, 29.8, 23.9.

(S)-bis(3,5-bis(trifluoromethyl)phenyl)(1-methylpyrrolidin-2-yl)methanol (13h):

CAS RN [350236-79-2].

White solid. \(^1H\) NMR (CDCl\(_3\)) \(\delta\) 8.14 (s, 2H), 7.99 (s, 2H), 7.74 (d, \(J = 7.5\) Hz, 2H), 5.30 (s, 1H), 3.72 (dd, \(J = 9.0, 6.0\) Hz, 1H), 3.19 (m, 1H), 2.56 (q, \(J = 9.0\) Hz, 1H), 1.87 (m, 4H), 1.72 (m, 2H), 1.50 (m, 1H). \(^{13}C\) NMR (CDCl\(_3\)) \(\delta\) 149.8, 147.9, 132.0 (q, \(J = 33.5\) Hz), 131.9 (q, \(J = 33.7\) Hz), 125.8, 125.5, 123.2, (q, \(J = 277.1\) Hz), 121.2, (q, \(J = 3.8\) Hz), 121.1, (q, \(J = 3.8\) Hz), 76.5, 71.7, 58.8, 42.7, 29.9, 23.6.

**General procedure for the preparation of ketoaldehyde (14)**

Ketoaldehyde (14) was prepared by the literature procedure.\(^5\) 4-hydroxybenzaldehyde (0.86 g, 7.0 mmol), 2-bromo-1-(4-methoxyphenyl)ethanone (1.60 g, 7.0 mmol), and K\(_2\)CO\(_3\) (1.94 g, 14.0 mmol) were dissolved in DMF (7.0 mL), and the solution was stirred for 1 h at 25 °C. The resulting mixture was poured into HClaq (20%, 10 mL) at 0 °C. Then, the formed white solid was separated by filtration through glass filter G3 and the residue was washed with water. The obtained white solid was purified by recrystallization from EtOH to give ketoaldehyde (14) (1.00 g, 53%) as a white solid.

(6bb), (6bd), (6be), (6bf), (6bg), (6bj), (15) were dissolved little in CDCl\(_3\). Thus, a drop of ((D\(_3\))\(_2\)S=O) was used to dissolve these compounds.

4-(2-(4-methoxyphenyl)-2-oxoethoxy)benzaldehyde (14): CAS RN [901414-44-6].
White solid. $^1$H NMR (CDCl$_3$) δ 9.88 (s, 1H), 7.98 (d, $J = 9.0$ Hz, 2H), 7.83 (d, $J = 7.0$ Hz, 2H), 7.03 (d, $J = 9.0$ Hz, 2H), 6.98 (d, $J = 9.0$ Hz, 2H), 5.33 (s, 2H), 3.89 (s, 3H). $^{13}$C NMR (CDCl$_3$) δ 191.8, 190.6, 164.3, 163.0, 131.9, 130.6, 130.5, 127.3, 115.0, 114.2, 70.4, 55.6.

$N$-acetylbenzamide (3a): CAS RN [1575-95-7].

Yellow oil. $^1$H NMR (CDCl$_3$) δ 8.55 (s, 1H), 7.84 (d, $J = 7.2$ Hz, 2H), 7.62 (t, $J = 7.2$ Hz, 1H), 7.51 (t, $J = 7.8$ Hz, 2H), 2.62 (s, 3H). $^{13}$C NMR (CDCl$_3$) δ 173.1, 165.5, 133.3, 132.7, 129.1, 127.5, 25.5.

$N^1,N^3$-dibenzoylmalonamide (4a):

$N$-phenylacetamide (3b): CAS RN [103-84-4].
White solid. $^1$H NMR (CDCl$_3$) $\delta$ 7.51 (s, 1H), 7.49 (d, $J = 8.1$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 2H), 7.09 (t, $J = 7.2$ Hz, 1H), 2.16 (s, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 168.4, 137.9, 128.9, 124.3, 119.8, 24.5.

**N-(4-methoxyphenyl)acetamide (3c):** CAS RN [51-66-1].

![MeO](image)

White solid. $^1$H NMR (CDCl$_3$) $\delta$ 7.38 (dt, $J = 9.0$, 3.5 Hz, 2H), 7.34 (s, 1H), 6.84 (dt, $J = 9.5$, 3.5 Hz, 2H), 3.78 (s, 3H), 2.13 (s, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 168.3, 156.4, 131.0, 121.9, 114.1, 114.1, 55.4, 24.3.

**N-(4-(trifluoromethyl)phenyl)acetamide (3d):** CAS RN [349-97-3].

![F3C](image)

White solid. $^1$H NMR (CDCl$_3$) $\delta$ 7.64 (d, $J = 8.5$, 2H), 7.58 (d, $J = 8.5$ Hz, 2H), 7.44 (s, 1H), 2.22 (s, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 168.5, 140.4, 126.3 (q, $J = 15.0$ Hz), 125.9, 124.0 (q, $J = 1080.0$ Hz), 119.3, 24.7. $^{19}$F NMR (CDCl$_3$) $\delta$ –62.6 ppm

**N-cyclohexylacetamide (3e):** CAS RN [1124-53-4].

![Cyclohexyl](image)

White solid. $^1$H NMR (CDCl$_3$) $\delta$ 5.45 (s, 1H), 3.73 (m, 1H), 1.94 (s, 3H), 1.89 (m, 2H), 1.64 (m, 3H), 1.33 (m, 2H), 1.12 (m, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 169.0, 48.2, 33.2, 25.5, 24.8, 23.6.

**N-(3-hydroxy-3-phenylpropanoyl)benzamide (6aa)**

![3aa](image)

Yield: 90%, white solid. $^1$H NMR (CDCl$_3$) $\delta$ 9.03 (s, 1H), 7.85 (d, $J = 7.8$ Hz, 2H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.50 (t, $J = 7.8$ Hz, 2H), 7.43 (d, $J = 7.8$ Hz, 2H), 7.37 (t, $J = 7.5$ Hz, 2H), 7.31 (d, $J = 6.9$ Hz, 1H), 5.27 (m, 1H), 3.40 (m, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 174.6, 165.5, 142.4, 133.5, 132.4, 129.0, 128.6, 127.8, 127.7, 125.8, 70.1, 46.5. Mp. 125.5–126.0 °C. TLC: R$_f$ 0.30 (hexane/EtOAc = 1:1). IR (KBr) 3475.9, 3286.8, 1700.3, 1668.5, 1510.3, 1469.8, 1375.3, 1304.9, 1248.0, 1183.4, 1032.0, 910.4, 770.6, 705.0 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{15}$NO$_3$Na: [M+Na]$^+$, 292.0944. Found: m/z 290.0937.
3-hydroxy-N,3-diphenylpropanamide (6ba): CAS RN [4198-15-6].

![Structure of 3-hydroxy-N,3-diphenylpropanamide (6ba)](image)

White solid. $^1$H NMR (CDCl$_3$) δ 9.18 (s, 1H), 7.40 (dd, $J = 8.5, 1.0$ Hz, 2H), 7.25 (d, $J = 8.5$ Hz, 2H), 7.17 (t, $J = 7.0$ Hz, 2H), 7.11 (m, 3H), 6.90 (t, $J = 7.5$ Hz, 1H), 5.08 (d, $J = 3.5$ Hz, 1H), 4.99 (m, 1H), 2.62 (dd, $J = 15.0, 9.5$ Hz, 1H), 2.53 (dd, $J = 15.0, 3.0$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ 169.9, 143.6, 138.0, 128.3, 128.0, 127.0, 125.3, 123.4, 119.6, 70.2, 45.7.

3-hydroxy-N-(4-methoxyphenyl)-3-phenylpropanamide (6ca)

![Structure of 3-hydroxy-N-(4-methoxyphenyl)-3-phenylpropanamide (6ca)](image)

White solid. $^1$H NMR (CDCl$_3$) δ 8.92 (s, 1H), 7.34 (t, $J = 9.3$ Hz, 4H), 7.25 (t, $J = 9.3$ Hz, 2H), 7.17 (t, $J = 7.5$ Hz, 1H), 6.74 (td, $J = 8.7, 3.3$ Hz, 2H), 5.04 (m, 2H), 3.69 (s, 3H), 2.64 (m, 2H). $^{13}$C NMR (CDCl$_3$) δ 169.9, 155.9, 143.6, 131.1, 128.2, 127.2, 125.4, 121.6, 113.7, 70.5, 55.2, 45.5. Mp. 140.5–141.0 ºC. TLC: Rf 0.32 (hexane/EtOAc = 1:1). IR (KBr) 3287.8, 3253.1, 1656.0, 1604.8, 1552.8, 1511.3, 1414.9, 1303.0, 1248.0, 1181.5, 1065.7, 1035.8, 967.3, 832.3, 776.4, 757.1, 698.3 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{17}$NO$_3$Na: [M+Na]$^+$, 294.1101. Found: m/z 294.1091.

3-hydroxy-3-phenyl-N-(4-(trifluoromethyl)phenyl)propanamide (6da)

![Structure of 3-hydroxy-3-phenyl-N-(4-(trifluoromethyl)phenyl)propanamide (6da)](image)

White solid. $^1$H NMR (CDCl$_3$) δ 9.56 (s, 1H), 7.44 (d, $J = 8.4$ Hz, 2H), 7.20 (d, $J = 8.1$ Hz, 2H), 7.10 (d, $J = 7.2$ Hz, 2H), 7.02 (t, $J = 7.5$ Hz, 2H), 6.93 (t, $J = 8.1$ Hz, 1H), 5.00 (d, $J = 3.9$ Hz, 1H), 4.85 (m, 1H), 2.50 (dd, $J = 15.0, 9.3$ Hz, 1H), 2.37 (dd, $J = 14.7, 3.6$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ 170.2, 143.5, 141.4, 127.9, 127.0, 125.4 (q, $J = 14.4$ Hz, 5H), 125.2, 124.4, 123.4 (q, $J = 844.8$ Hz, 5H), 119.0, 70.0, 46.0. $^{19}$F NMR (CDCl$_3$) δ −62.3 ppm. Mp. 191.2–192.0 ºC. TLC: Rf 0.50 (hexane/EtOAc = 1:1). IR (KBr) 3335.1, 1661.8, 1603.9, 1532.5, 1456.3, 1411.0, 1331.9, 1252.8, 1151.6, 1113.0, 1071.5, 1019.4, 973.1, 912.4, 888.3, 866.1, 836.2, 758.1, 702.1 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{15}$F$_3$NO$_2$: [M+H]$^+$, 310.1049. Found: m/z 310.1036.

N-cyclohexyl-3-hydroxy-3-phenylpropanamide (6ea)
Yield: 29%, white solid. $^1$H NMR (CDCl$_3$) $\delta$ 7.31 (m, 5H), 5.55 (d, $J = 7.2$ Hz, 1H), 5.09 (m, 1H), 4.31 (d, $J = 3.0$ Hz, 1H), 3.77 (m, 1H), 2.53 (m, 2H), 1.88 (m, 2H), 1.65 (m, 3H), 1.33 (m, 2H), 1.10 (m, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 170.8, 143.0, 128.5, 127.6, 125.6, 70.9, 48.2, 44.7, 33.0, 25.4, 24.8. Mp. 129.2–129.5 °C. TLC: $R_f$ 0.43 (hexane/EtOAc = 1:2). IR (KBr) 3302.3, 3087.2, 3023.6, 2933.9, 2854.8, 1638.6, 1553.7, 1450.5, 1360.8, 1207.5, 1054.1, 1020.4, 984.7, 893.1, 698.3 cm$^{-1}$. HRMS (ESI) Calcd for C$_{15}$H$_{21}$NO$_2$Na: [M+Na]$^+$, 270.1465. Found: m/z 270.1456.

(S)-N-cyclohexyl-3-hydroxy-3-(p-tolyl)propanamide (6eb)

White solid. $^1$H NMR (CDCl$_3$) $\delta$ 7.25 (d, $J = 7.2$ Hz, 2H), 7.15 (d, $J = 8.1$ Hz, 2H), 5.57 (d, $J = 6.9$ Hz, 1H), 5.06 (m, 1H), 4.17 (d, $J = 3.0$ Hz, 1H), 3.77 (m, 1H), 2.51 (m, 2H), 2.33 (s, 3H), 1.89 (m, 2H), 1.65 (m, 3H), 1.34 (m, 2H), 1.11 (m, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 170.8, 140.1, 137.3, 129.1, 125.5, 70.8, 48.2, 44.8, 33.0, 25.4, 24.8, 21.1. Mp. 137.5–137.9 °C. TLC: $R_f$ 0.27 (hexane/EtOAc = 1:1). IR (KBr) 3301.3, 3080.5, 2932.9, 2852.8, 1641.5, 1639.5, 1548.9, 1447.6, 1363.7, 1245.1, 1204.6, 1062.8, 1028.1, 983.7, 889.2, 817.9, 722.4, 686.7 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{23}$NO$_2$Na: [M+Na]$^+$, 284.1621. Found: m/z 284.1621.

$N$-propionylbenzamide (10a): CAS RN [28358-79-4].

White solid. $^1$H NMR (CDCl$_3$) $\delta$ 8.82 (s, 1H), 7.87 (dt, $J = 7.0$, 1.5 Hz, 2H), 7.61 (tt, $J = 7.5$, 1.5 Hz, 1H), 7.50 (tt, $J = 7.5$, 1.0 Hz, 2H), 3.04 (q, $J = 7.5$ Hz, 2H), 1.22 (t, $J = 7.5$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 177.1, 165.5, 133.2, 132.8, 129.0, 127.6, 31.2, 8.2.

$N$-(3-hydroxy-2-methyl-3-phenylpropanoyl)benzamide (12aa)
(including 14% diastereo mixture)
Colorless oil. $^1$H NMR (CDCl$_3$) δ 9.07 (s, 1H), 7.85 (m, 2H), 7.61 (t, $J = 7.2$ Hz, 1H), 7.50 (t, $J = 7.5$ Hz, 2H), 7.34 (m, 5H), 5.24 (s, 1H), 3.75 (m, 1H), 3.17 (d, $J = 1.5$ Hz, 1H), 1.19 (d, $J = 6.9$ Hz, 3H). $^{13}$C NMR (CDCl$_3$) δ 177.8, 165.2, 141.0, 133.3, 132.8, 129.0, 128.3, 127.7, 127.6, 126.0, 73.3, 47.2, 10.2. TLC: R$_f$ 0.50 (hexane/EtOAc = 1:2). IR (neat) 3410.3, 2981.1, 2937.7, 1730.2, 1680.1, 1601.0, 1507.4, 1484.3, 1369.5, 1264.4, 1159.3, 1121.7, 1027.1, 701.2, 665.5 cm$^{-1}$. HRMS (ESI) Calcd for C$_{17}$H$_{18}$NO$_3$: [M+H]$^+$, 284.1281. Found: m/z 284.1268.

3-hydroxy-N,3-diphenylpropanamide (6ba): CAS RN [1245719-57-6].

White solid. $^1$H NMR (CDCl$_3$) δ 9.18 (s, 1H), 7.40 (dd, $J = 8.5$, 1.0 Hz, 2H), 7.25 (d, $J = 8.5$ Hz, 2H), 7.17 (t, $J = 7.0$ Hz, 2H), 7.11 (m, 3H), 6.90 (t, $J = 7.5$ Hz, 1H), 5.08 (d, $J = 3.5$ Hz, 1H), 4.99 (m, 1H), 2.62 (dd, $J = 15.0$, 9.5 Hz, 1H), 2.53 (dd, $J = 15.0$, 3.0 Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ 169.9, 143.6, 138.0, 128.3, 128.0, 127.0, 125.3, 123.4, 119.6, 70.2, 45.7.

(S)-3-hydroxy-N-phenyl-3-(p-tolyl)propanamide (6bb)

Yield: 99%, 84% ee, white solid. $[\alpha]_D^{20} = -83.3$ (c 0.06, CH$_2$Cl$_2$). $^1$H NMR (CDCl$_3$) δ 8.86 (s, 1H), 7.50 (d, $J = 9.0$ Hz, 2H), 7.26 (m, 4H), 7.12 (d, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.5$ Hz, 1H), 5.09 (m, 1H), 4.68 (d, $J = 3.0$ Hz, 1H), 2.74 (dd, $J = 15.0$, 9.5 Hz, 1H), 2.65 (dd, $J = 15.5$, 3.0 Hz, 1H), 2.29 (s, 3H). $^{13}$C NMR (CDCl$_3$) δ 170.1, 140.5, 138.1, 137.1, 129.0, 128.7, 125.5, 123.9, 119.9, 70.5, 45.9, 21.0. Mp. 181.0–182.0 °C. TLC: R$_f$ 0.45 (hexane/EtOAc = 1:1). IR (KBr) 3330.2, 1657.9, 1540.2, 1498.8, 1442.8, 1363.7, 1064.8, 815.9, 752.3, 691.5, 502.5 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{17}$NO$_2$: [M+Cl]$^-$, 290.0942. Found: m/z 290.0956. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, $\lambda = 254$ nm, 40 °C): $t_{\text{minor}} = 17.6$ mn, $t_{\text{major}} = 20.0$ mn.
(S)-3-hydroxy-N-phenyl-3-(o-tolyl)propanamide (6bc)

Yield: 91%, 84% ee, white solid. $[^{\alpha}]_{D}^{20} -41.7$ (c 0.12, CH$_2$Cl$_2$). $^1$H NMR (CDCl$_3$) $\delta$ 7.76 (s, 1H), 7.54 (m, 3H), 7.34 (t, $J = 8.0$ Hz, 2H), 7.26 (m, 1H), 7.21 (dt, $J = 1.5, 8.5$ Hz, 1H), 7.14 (m, 2H), 5.45 (td, $J = 2.5, 10.0$ Hz, 1H), 3.31 (d, $J = 2.5$ Hz, 1H), 2.76 (dd, $J = 15.0, 10.0$ Hz, 1H), 2.65 (dd, $J = 16.0, 2.5$ Hz, 1H), 2.38 (s, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 169.8, 140.8, 137.6, 134.2, 130.6, 129.1, 127.8, 126.6, 125.1, 124.5, 120.1, 67.7, 44.9, 19.0. Mp. 161.2–162.0 °C. TLC: $R_f$ 0.53 (hexane/EtOAc = 1:1). IR (KBr) 3304.2, 1659.8, 1599.1, 1540.2, 1499.7, 1444.8, 1360.8, 1312.6, 1300.1, 1066.7, 1022.3, 756.1, 729.1, 498.6 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{17}$NO$_2$Cl: [M+Cl]$^-$, 290.0942. Found: m/z 290.0954. HPLC (Daicel Chiralcel IA, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, $\lambda$ = 254 nm, 40 °C): $t_{\text{minor}}$ = 14.0 mn, $t_{\text{major}}$ = 16.8 mn.

(S)-3-(4-fluorophenyl)-3-hydroxy-N-phenylpropanamide (6bd)

Yield: 77%, 89% ee, white solid. $[^{\alpha}]_{D}^{20} -20.8$ (c 0.24, CH$_2$Cl$_2$). $^1$H NMR (CDCl$_3$) $\delta$ 8.43 (s, 1H), 7.51 (d, $J = 8.5$ Hz, 2H), 7.38 (dt, $J = 7.0, 1.5$ Hz, 2H), 7.30 (dt, $J = 7.5, 2.0$ Hz, 2H), 7.09 (t, $J = 7.5$ Hz, 1H), 7.03 (dt, $J = 8.5, 1.5$ Hz, 2H), 5.16 (d, $J = 8.5$ Hz, 1H), 4.50 (s, 1H), 2.72 (m, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 170.0, 139.1, 137.9, 128.9, 127.3 (d, $J = 8.3$ Hz), 124.2, 120.0, 119.9, 115.3 (d, $J = 21.4$ Hz), 70.1, 45.9. $^{19}$F NMR (CDCl$_3$) $\delta$ −95.1 ppm. Mp. 169.0–170.0 °C. TLC: $R_f$ 0.32 (hexane/EtOAc = 1:1). IR (KBr) 3335.1, 1654.0, 1602.9, 1540.2, 1512.3, 1499.7, 1444.8, 1227.7, 831.4, 756.1, 691.5 cm$^{-1}$. HRMS (ESI) Calcd for C$_{15}$H$_{14}$FNO$_2$Cl: [M+Cl]$^-$, 294.0692. Found: m/z 294.0706. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, $\lambda$ = 254 nm, 40 °C): $t_{\text{minor}}$ = 19.0 mn, $t_{\text{major}}$ = 16.0 mn.

(S)-3-(4-chlorophenyl)-3-hydroxy-N-phenylpropanamide (6be)

Yield: 76%, 79% ee, white solid. $[^{\alpha}]_{D}^{20} -8.3$ (c 0.03, CH$_2$Cl$_2$). $^1$H NMR (CDCl$_3$) $\delta$ 7.50 (s, 1H), 7.49 (d, $J = 8.5$ Hz, 2H), 7.34 (m, 6H), 7.14 (t, $J = 7.0$ Hz, 1H), 5.21 (m, 1H), 3.74 (d, $J = 3.0$ Hz, 1H), 2.76 (dd, $J = 15.0, 9.0$ Hz, 1H), 2.70 (dd, $J = 15.0, 3.0$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) $\delta$ 169.9, 137.8, 128.9, 128.6, 127.0, 124.3, 120.0, 119.9, 109.7, 70.1, 45.7. Mp. 188.5–189.2 °C. TLC: $R_f$
0.46 (hexane/EtOAc = 1:1). IR (KBr) 3328.3, 1656.0, 1602.0, 1499.7, 1444.8, 1425.5, 1369.5, 1092.7, 1067.7, 1012.7, 824.6, 756.1, 744.6, 692.5, 500.6 cm$^{-1}$. HRMS (ESI) Calcd for C$_{15}$H$_{13}$ClNO$_2$: [M−H]$^-$, 274.0640. Found: m/z 274.0647. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, $\lambda = 254$ nm, 40 °C): $t_{\text{minor}} = 17.2$ mn, $t_{\text{major}} = 22.8$ mn.

(S)-3-(4-bromophenyl)-3-hydroxy-$N$-phenylpropanamide (6bf)

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\text{\begin{center}
\includegraphics[width=1cm]{structure_6bf.png}
\end{center}}
\]

Yield: 47%, 77% ee, white solid. $[\alpha]_D^{20}$ 25.0 (c 0.10, CH$_2$Cl$_2$). $^1$H NMR (CDCl$_3$) $\delta$ 9.06 (s, 1H), 7.46 (dd, $J = 8.0$, 1.0 Hz, 2H), 7.38 (d, $J = 8.0$ Hz, 2H), 7.22 (m, 4H), 7.00 (tt, $J = 7.0$, 1.0 Hz, 1H), 5.13 (d, $J = 3.5$ Hz, 1H), 5.04 (m, 1H), 2.63 (m, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 169.8, 142.7, 138.0, 131.3, 128.6, 127.3, 123.9, 121.0, 119.9, 69.9, 45.6. Mp. 186.0–186.6 °C. TLC: R$_f$ 0.44 (hexane/EtOAc = 1:1). IR (KBr) 3327.4, 1654.0, 1601.0, 1538.3, 1515.1, 1499.7, 1443.8, 1365.7, 1300.1, 1178.6, 1065.7, 1037.8, 829.5, 753.2, 692.5, 502.5 cm$^{-1}$. HRMS (ESI) Calcd for C$_{15}$H$_{14}$BrNO$_2$Cl: [M+Cl]$^-$, 353.9891. Found: m/z 353.9911. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, $\lambda = 254$ nm, 40 °C): $t_{\text{minor}} = 41.1$ mn, $t_{\text{major}} = 48.4$ mn.

(S)-3-hydroxy-3-(4-methoxyphenyl)-$N$-phenylpropanamide (6bg)

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\text{\begin{center}
\includegraphics[width=1cm]{structure_6bg.png}
\end{center}}
\]

Yield: 64%, 94% ee, white solid. $[\alpha]_D^{20}$ −35.7 (c 0.07, CH$_2$Cl$_2$). $^1$H NMR (CDCl$_3$) $\delta$ 8.96 (s, 1H), 7.49 (d, $J = 7.5$ Hz, 2H), 7.26 (m, 4H), 7.28 (d, $J = 7.5$ Hz, 1H), 6.82 (d, $J = 9.0$ Hz, 2H), 5.06 (td, $J = 3.0$, 9.5 Hz, 1H), 4.79 (d, $J = 2.5$ Hz, 1H), 3.74 (s, 3H), 2.73 (dd, $J = 15.5$, 9.5 Hz, 1H), 2.62 (dd, $J = 15.0$, 3.0 Hz 1H). $^{13}$C NMR (CDCl$_3$) $\delta$ 170.2, 158.9, 138.1, 135.7, 128.7, 126.8, 123.8, 119.9, 113.7, 70.2, 55.1, 45.9. Mp. 185.0–186.0 °C. TLC: R$_f$ 0.30 (hexane/EtOAc = 1:1). IR (KBr) 3325.4, 1658.9, 1601.0, 1538.3, 1515.1, 1499.7, 1443.8, 1365.7, 1300.1, 1178.6, 1065.7, 1037.8, 829.5, 753.2, 692.5, 502.5 cm$^{-1}$. HRMS (ESI) Calcd for C$_{16}$H$_{16}$NO$_3$: [M−H]$^-$, 270.1136. Found: m/z 270.1142. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, $\lambda = 254$ nm, 40 °C): $t_{\text{minor}} = 37.3$ mn, $t_{\text{major}} = 41.9$ mn.

(S)-3-(4-(tert-butyl)phenyl)-3-hydroxy-$N$-phenylpropanamide (6bh)
Yield: 57%, 84% ee, white solid. \([\alpha]_d^{20} = -25.0 (c 0.20, \text{CH}_2\text{Cl}_2)\). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.80 (s, 1H), 7.50 (d, \(J = 8.5\) Hz, 2H), 7.40 (d, \(J = 8.5\) Hz, 2H), 7.33 (m, 4H), 7.13 (t, \(J = 7.5\) Hz, 1H), 5.20 (m, 1H), 3.35 (d, \(J = 2.5\) Hz, 1H), 3.83 (dd, \(J = 15.5, 9.5\) Hz, 1H), 2.71 (dd, \(J = 15.0, 3.0\) Hz, 1H) 1.32 (s, 9H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 169.8, 151.0, 139.7, 137.5, 129.0, 125.6, 125.3, 124.5, 120.0, 70.9, 46.0, 34.6, 31.3. Mp. 110.0–111.0 °C. TLC: \(R_f\) 0.61 (hexane/EtOAc = 1:1). IR (KBr) 3298.4, 2961.8, 1669.5, 1603.9, 1554.7, 1499.7, 1442.8, 1312.6, 1060.9, 819.8, 754.2, 690.6, 581.6 cm\(^{-1}\). HRMS (ESI) Calcd for C\(_{19}\)H\(_{23}\)NO\(_2\)Cl: \([M+Cl]^-\), 332.1412. Found: m/z 332.1425.

HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, \(\lambda = 254\) nm, 40 °C): \(t_{\text{minor}} = 23.3\) min, \(t_{\text{major}} = 19.3\) min.

(S)-3-hydroxy-3-mesityl-N-phenylpropanamide (6bi)

Yield: 63%, 84% ee, white solid. \([\alpha]_d^{20} = -16.9 (c 0.74, \text{CH}_2\text{Cl}_2)\). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 8.05 (s, 1H), 7.53 (d, \(J = 8.5\) Hz, 2H), 7.33 (t, \(J = 8.5\) Hz, 2H), 7.12 (t, \(J = 7.0\) Hz, 1H), 6.83 (s, 2H), 5.65 (d, \(J = 10.5\) Hz, 1H), 3.14 (dd, \(J = 15.5, 5.5\) Hz, 1H), 3.10 (s, 1H), 2.49 (dd, \(J = 15.5, 2.0\) Hz, 1H), 2.43 (s, 6H) 2.26 (s, 3H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 170.0, 137.7, 137.2, 136.0, 134.8, 130.3, 129.0, 124.4, 120.0, 68.2, 42.7, 20.7, 20.7. IR (KBr) 3431.5, 3269.5, 2921.3, 1628.0, 1600.0, 1545.1, 1498.8, 1444.8, 1312.6, 1253.8, 1172.8, 1071.5, 850.6, 752.3, 690.6, 351.1 cm\(^{-1}\). Mp. 110.0–111.0 °C. TLC: \(R_f\) 0.29 (hexane/EtOAc = 3:1). HRMS (ESI) Calcd for C\(_{18}\)H\(_{20}\)NO\(_2\): \([M-H]^-\), 282.1500. Found: m/z 282.1487. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, \(\lambda = 254\) nm, 40 °C): \(t_{\text{minor}} = 15.0\) mn, \(t_{\text{major}} = 8.5\) mn.

(S)-3-hydroxy-3-(naphthalen-2-yl)-N-phenylpropanamide (6bj)

Yield: 89%, 88% ee, white solid. \([\alpha]_d^{20} = -250.0 (c 0.02, \text{CH}_2\text{Cl}_2)\). \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 8.71 (s, 1H), 8.87 (s, 1H), 7.81 (m, 3H), 7.52 (t, \(J = 8.5\) Hz, 3H), 7.45 (t, \(J = 7.5\) Hz, 2H), 7.29 (t, \(J = 7.0\) Hz, 2H), 7.07 (t, \(J = 7.5\) Hz, 1H), 5.33 (d, \(J = 9.5\) Hz, 1H), 4.79 (s, 1H), 2.85 (dd, \(J = 16.0, 8.0\) Hz, 1H), 2.78 (dd, \(J = 15.5, 3.0\) Hz, 1H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 170.1, 140.8, 133.2, 132.9, 128.8, 128.3,
127.9, 127.6, 126.1, 124.3, 124.1, 123.8, 121.1, 120.0, 70.9, 45.9. Mp. 173.0–174.0 °C. TLC: Rf 0.44 (hexane/EtOAc = 1:1). IR (KBr) 3299.4, 1664.6, 1602.0, 1549.9, 1499.7, 1488.2, 1445.7, 1363.7, 1314.5, 1068.6, 761.0, 744.6 cm⁻¹. HRMS (ESI) Calcd for C₁₉H₁₇NO₂Cl: [M+Cl]⁻, 326.0942. Found: m/z 326.0954. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, λ = 254 nm, 40 °C): tₘᵢₙᵢₙ = 39.2 mn, tₘₐⱼ舆论 = 30.7 mn.

(S)-3-hydroxy-N-phenyl-3-(thiophen-2-yl)propanamide (6bk)

Yield: 73%, 94% ee, white solid. [α]D²⁰ = 41.7 (c 0.12, CH₂Cl₂). ¹H NMR (CDCl₃) δ 7.64 (s, 1H), 7.50 (d, J = 4.0 Hz, 2H), 7.34 (t, J = 8.0 Hz, 2H), 7.28 (d, J = 3.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 7.03 (d, J = 2.0 Hz, 1H), 6.98 (t, J = 2.5 Hz, 1H), 5.49 (m, 1H), 3.79 (d, J = 3.5 Hz, 1H), 2.90 (m, 2H). ¹³C NMR (CDCl₃) δ 169.3, 146.3, 137.2, 129.1, 126.8, 125.0, 124.7, 123.8, 120.1, 67.2, 45.8. Mp. 159.5–160.2 °C. TLC: Rf 0.50 (hexane/EtOAc = 1:1). IR (KBr) 3297.5, 1679.1, 1663.7, 1607.7, 1599.1, 1554.7, 1498.8, 1444.8, 1319.4, 1254.8, 1236.4, 1086.0, 1046.4, 758.1, 744.6, 693.4, 598.0 cm⁻¹. HRMS (ESI) Calcd for C₁₃H₁₃NO₂SCl: [M+Cl]⁻, 282.0350. Found: m/z 282.0367. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, λ = 254 nm, 40 °C): tₘᵢₙᵢₙ = 18.9 mn, tₘₐⱼ舆论 = 21.4 mn.

(S)-3-(furan-2-yl)-3-hydroxy-N-phenylpropanamide (6bl)

Yield: 92%, 76% ee, white solid. [α]D²⁰ = 31.3 (c 0.24, CH₂Cl₂). ¹H NMR (CDCl₃) δ 7.71 (s, 1H), 7.50 (d, J = 8.5 Hz, 2H), 7.34 (t, J = 7.0 Hz, 2H), 7.13 (t, J = 7.5 Hz, 1H), 6.35 (m, 1H), 6.33 (d, J = 3.0 Hz, 1H), 5.24 (m, 1H), 3.62 (d, J = 4.5 Hz, 1H), 2.96 (dd, J = 16.0, 8.5 Hz, 1H), 2.87 (dd, J = 15.5, 3.5 Hz, 1H). ¹³C NMR (CDCl₃) δ 169.4, 154.6, 142.3, 137.3, 129.0, 124.7, 120.1, 110.4, 106.5, 64.7, 42.0. Mp. 133.0–134.0 °C. TLC: Rf 0.43 (hexane/EtOAc = 1:1). IR (KBr) 3284.9, 1669.5, 1608.7, 1559.5, 1491.0, 1445.7, 1314.5, 1168.0, 1060.9, 1018.5, 759.0, 744.6, 693.4, 598.0 cm⁻¹. HRMS (ESI) Calcd for C₁₃H₁₂NO₂: [M–H]⁻, 230.0823. Found: m/z 230.0812. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 20/1, flow rate = 2.0 mL/min, λ = 254 nm, 40 °C): tₘᵢₙᵢₙ = 19.6 mn, tₘₐⱼ舆论 = 22.8 mn.

(R)-3-hydroxy-N-phenylbutanamide (6bm)

Yield: 45%, 76% ee, white solid. [α]D²⁰ = 21.2 (c 0.70, CHCl₃). ¹H NMR (CDCl₃) δ 7.72 (s, 1H),
7.50 (d, J = 9.0 Hz, 2H), 7.33 (t, J = 8.0 Hz, 2H), 7.12 (t, J = 7.5 Hz, 1H), 4.32 (m, 1H), 3.17 (d, J = 3.0 Hz, 1H), 2.55 (dd, J = 3.0, 15.5 Hz, 1H), 2.48 (dd, J = 9.0, 15.5 Hz, 1H) 1.30 (d, J = 6.5 Hz, 3H).

13C NMR (CDCl3) δ 170.3, 137.5, 129.0, 124.5, 120.0, 65.0, 45.2, 23.0. Mp. 102.8–103.5 °C.

TLC: Rf 0.28 (hexane/EtOAc = 1:2). IR (KBr) 3250.2, 1662.7, 1601.0, 1553.7, 1500.7, 1445.7, 1338.7, 1319.4, 1128.4, 1064.8, 753.2, 694.4 cm⁻¹. HRMS (ESI) Calcd for C10H13NO2Cl: [M+Cl]–, 214.0629. Found: m/z 214.0643. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 33/1, flow rate = 1.0 mL/min, λ = 254 nm, 40 °C): tminor = 38.8 min, tmajor = 34.7 min.

The absolute configuration of 6l was assigned as (R) by comparing the optical rotation with the literature value. [α]D20 21.2 (c 0.70, CH2Cl2) [lit. 6 (R)-3-hydroxy-N-phenylbutanamide: [α]D20 28.6 (c 1.1, CHCl3)]. The absolute configurations of other products were assigned analogously.

(S)-3-hydroxy-4,4-dimethyl-N-phenylpentanamide (6bn)

Yield: 49%, 83% ee, yellow solid. [α]D20 27.8 (c 0.27, CH2Cl2). 1H NMR (CDCl3) δ 7.86 (s, 1H), 7.50 (d, J = 7.5 Hz, 2H), 7.32 (t, J = 7.0 Hz, 2H), 7.11 (t, J = 7.5 Hz, 1H), 3.79 (d, J = 5.0 Hz, 1H), 3.01 (s, 1H), 2.54 (dd, J = 2.0, 15.5 Hz, 1H), 2.43 (dd, J = 10.5, 15.5 Hz, 1H), 0.96 (s, 9H).
13C NMR (CDCl3) δ 177.1, 137.7, 129.0, 124.4, 120.0, 76.4, 39.2, 34.7, 25.5. Mp. 110.0–111.0 °C. TLC: Rf 0.61 (hexane/EtOAc = 1:1). IR (KBr) 3293.6, 2958.9, 1659.3, 1603.9, 1552.8, 1501.7, 1445.7, 1337.7, 1149.6, 1070.5, 754.2, 702.1, 419.5 cm⁻¹. HRMS (ESI) Calcd for C13H18NO2: [M–H]–, 220.1343. Found: m/z 220.1347. HPLC (Daicel Chiralcel AD-H, hexane/i-PrOH = 33/1, flow rate = 2.0 mL/min, λ = 254 nm, 40 °C): tminor = 13.0 mn, tmajor = 18.3 mn.

(S)-3-hydroxy-3-(4-(2-(4-methoxyphenyl)-2-oxoethoxy)phenyl)-N-phenylpropanamide (15)

Yield: 81%, 93% ee, white solid. [α]D20 10.0 (c 0.25, CH2Cl2). 1H NMR (CDCl3) δ 8.00 (d, J = 9.0 Hz, 2H), 7.73 (s, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.33 (m, 3H), 7.12 (t, J = 7.5 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 5.23 (s, 2H), 5.16 (d, J = 9.5 Hz, 1H), 3.89 (s, 3H), 3.45 (d, J = 2.5 Hz, 1H), 2.78 (dd, J = 15.5, 9.5 Hz, 1H), 2.67 (dd, J = 15.5, 3.0 Hz, 1H). 13C NMR (CDCl3) δ 193.0, 169.7, 164.1, 157.9, 137.5, 135.9, 130.6, 129.0, 127.6, 127.0, 124.5, 120.1, 115.0, 114.1, 70.8, 70.6, 55.5, 46.1. Mp. 142.5–143.0 °C. TLC: Rf 0.38
The enantiomeric excess of 15 was determined by HPLC analysis after benzylation.

**Procedure for Transformation of 15 into 16.**

To a solution of 15 (26.4 mg, 0.065 mmol) in CH₂Cl₂ (1.0 ml) was added 4-bromobenzoyl chloride (35.1 mg, 0.16 mmol), triethylamine (26.4 μL, 0.19 mmol), and DMAP (1.6 mg, 0.013 mmol) at 25 °C. After being stirred for 40 min at 25 °C, the resulting mixture was poured into sat. NaHCO₃aq and extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄. Purification by silica gel column chromatography (hexane / ethyl acetate) as an eluent gave the desired compound (16) in 50% yield.

(S)-1-(4-(2-(4-methoxyphenyl)-2-oxoethoxy)phenyl)-3-oxo-3-(phenylamino)propyl 4-bromobenzoate (16)

![Chemical structure diagram](image)

White solid. [α]D20 –250.7 (c 0.04, CH₂Cl₂). ¹H NMR (CDCl₃) δ 8.56 (m, 1H), 7.93 (dd, J = 9.0, 1.5 Hz, 2H), 7.84 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 7.44 (d, J = 7.5 Hz, 2H), 7.36 (d, J = 9.0 Hz, 2H), 7.22 (t, J = 7.5 Hz, 2H), 7.01 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 6.39 (d, J = 7.0 Hz, 1H), 5.17 (s, 2H), 3.84 (s, 3H), 3.10 (dd, J = 15.0, 9.0 Hz, 2H), 2.86 (dd, J = 15.0, 5.5 Hz, 1H). ¹³C NMR (CDCl₃) δ 192.7, 167.2, 164.6, 164.0, 158.0, 138.0, 132.5, 131.6, 131.1, 130.4, 129.0, 128.7, 128.0, 127.8, 127.4, 124.0, 119.9, 114.9, 114.0, 73.3, 70.5, 55.4, 44.3. Mp. 129.0–130.0 °C. TLC: Rf 0.43 (hexane/EtOAc = 1:1). IR (KBr) 3342.8, 2965.7, 2932.9, 2361.9, 1717.7, 1684.9, 1656.9, 1602.0, 1513.2, 1441.9, 1267.3, 1217.1, 1171.8, 1117.8, 1104.3, 1007.9, 977.0, 829.4, 757.1, 695.4, 597.0, 545.9 cm⁻¹. HRMS (ESI) Calcd for C₃₁H₂₆BrNO₆Cl: [M+Cl]⁻, 622.0650. Found: m/z 622.0627. HPLC (Daicel Chiralcel OD-H, hexane/i-PrOH = 5.7/1, flow rate = 2.0 mL/min, λ = 254 nm, 40 °C): tminor = 68.2 mn, tmajor = 79.7 mn.

NMR analysis for the enolate equivalent 7.
Phenyl isocyanate (2b, 0.07 mmol, 7.6 μL) was added to bis(iodozincio)methane (1, 0.07 mmol, 0.7 M in THF-d8) at 80 °C for 30 min. The ¹H NMR spectrum of the obtained solution indicated a broad singlet at 1.8 ppm, which may correspond to the methylene protons of 7aa, 7ab. The ¹³C NMR spectrum of the obtained solution indicated a broad singlet at 23 ppm, which corresponds to the carbon of the α-postion of the enolate equivalent 7aa, 7ab. The NMR spectra are shown on S65-70.

Benzoyl isocyanate (2b, 0.07 mmol, 7.6 μL) was added to bis(iodozincio)methane (1, 0.07 mmol, 0.7 M in THF-d8) at 80 °C for 30 min. The ¹H NMR spectrum of the obtained solution indicated a broad singlet at -1.3 ppm, which may correspond to the methylene protons of 7ba, 7bb. The ¹³C NMR spectrum of the obtained solution indicated a broad singlet at 23 ppm, which corresponds to the carbon of the α-postion of the enolate equivalent 7ba, 7bb. The NMR spectra are shown on S64-69.

References
1H NMR

\[
\text{NIR H}_1
\]

\[
N'_{\text{N,N-dibenzoylmethanamide}}(4a)
\]
$N_{1}$-dibenzoylmalonamide (4a)
N-(3-hydroxy-3-phenylpropanoyl)benzamide (6aa)
$\text{13C NMR}$

\[
\text{N-}(3\text{-hydroxy-3-phenylpropionyl)benzamide (6aa)}
\]
3-hydroxy-N-(4-methoxyphenyl)-3-phenylpropanamide (6ca)
3-hydroxy-N-(4-methoxyphenyl)-3-phenylpropanamide (6ca)

$\text{^13C NMR}$
3-hydroxy-3-phenyl-N-(4-(trifluoromethyl)phenyl)propanamide (6da)

^1H NMR
3-hydroxy-3-phenyl-N-(4-(trifluoromethyl)phenyl)propanamide (6da)
N-ε-valdoxyl-ε-Ηδρόξυ-ξ-πενληπροπαμιδε (6ea)
$\text{NMR}$

$\text{N}$-\text{cyclohexyl}-3-\text{hydroxy}-3-\text{phenypropionamide (6ea)}$
N-cyclohexyl-3-hydroxy-3-(p-tolyl)propanamide (6eb)
$\text{N-cyclohexyl-3-hydroxy-3-(p-tolyl)propanamide (6eb)}$

$\text{13C NMR}$
N-(3-hydroxy-2-methyl-3-phenylpropionyl)benzamide (12aa)
N-(3-hydroxy-2-methyl-3-phenylpropanoyl)penicillamine (12aa)
(S)-3-hydroxy-N-phenyl-3-(p-tolyl)propanamide (6bb)

$\text{H}_1$

$\text{NMR}$
(S)-3-hydroxy-N-phenyl-3-(p-tolyl)propanamide (6bb)
(S)-3-hydroxy-N-phenyl-3-(p-tolyl)propanamide (6bc)

$\text{H}_1$  

NMR
(S)-3-hydroxy-N-phenyl-3-(p-tolyl)propanamide (6aq)
(S)-3-(4-fluorophenyl)-3-hydroxy-N-phenylpropanamide (6bd)

**1H NMR**

H

(S)-

$\text{HO}$

$\text{N}$
(S)-3-(4-chlorophenyl)-3-hydroxy-N-phenylpropanamide (6b)
(S)-3-(4-chlorophenyl)-3-hydroxy-N-phenylpropanamide (6bc)
(S)-3-(4-bromophenyl)-3-hydroxy-N-phenylpropanamide (6bf)
(S)-3-(4-bromophenyl)-3-hydroxy-N-phenylpropanamide (6bf)
(S)-3-hydroxy-3-(4-methoxyphenyl)−N−phenylpropanamide (6bg)

$^1$H NMR
(S)-3-hydroxy-3-(4-methoxyphenyl)-N-phenylpropanamide (6bg)

$^{13}$C NMR
(S)-3-(4-(tert-butyl)phenyl)-3-hydroxy-N-phenylpropanamide (6bh)
(S)-3-(4-(tert-butyl)phenyl)-3-hydroxy-N-phenylpropanamide (6bh)
$\text{(S)-3-hydroxy-3-mesityl-N-phenylpropanamide (6b)}$

$\text{H NMR}$
(S)-3-hydroxy-3-mesityl-N-phenylpropamidine (669)

$^{13}$C NMR
(S)-3-hydroxy-3-(naphthalen-2-yl)-N-phenylpropanamide (6bj)

1H NMR
(S)-3-hydroxy-3-(naphthalen-2-yl)-N-phenylpropanamide (6bj)

$^{13}$C NMR
(S)-3-hydroxy-N-phenyl-3-(thiophen-2-yl)propanamide (6bk)
(S)-3-hydroxy-N-phenyl-3-(thiophen-2-yl)propanamide (6b)

$^{13}$C NMR
(S)-3-(furan-2-yl)-3-hydroxy-N-phenylpropanamide (6b)
(S)-3-(furan-2-yl)-3-hydroxy-N-phenylpropanamide (6b)

$^{13}$C NMR
(R)-3-hydroxy-N-phenylbutanamide (6bm)
(R)-3-hydroxy-N-phenylbutanamide (6bm)

$^{13}$C NMR
(S)-3-hydroxy-4,4-dimethyl-α-phenylpentanamide (6bn)

(8)-3-hydroxy-4,4-dimethyl-α-phenylpentanamide (6bn)

\[ \text{H} \]
(S)-3-hydroxy-4,4-dimethyl-N-phenylpentanamide (6bn)

$^{13}$C NMR

$^{13}$C NMR spectrum with peak assignments:
- 171.124
- 137.707
- 129.914
- 124.364
- 129.558
- 77.212
- 77.010
- 76.401
- 76.744
- 76.499
- 39.169
- 34.699
- 25.516
(S)-3-hydroxy-3-(4-(2-(4-methoxyphenyl)-2-oxoethoxy)phenyl)-N-phenylpropanamide (15)

1H NMR
(S)-1-(4-(2-(4-methoxyphenyl)-2-oxoethoxy)phenyl)-3-oxo-3-(phenylamino)propyl-4-bromobenzoate (16)

$^1$H NMR
(S)-1-(4-(2-(4-methoxyphenyl)-2-oxoethoxy)phenyl)-3-oxo-3-(phenylamino)propyl-4-bromobenzoate (16)

$^{13}$C NMR
$^1$H NMR spectrum of the enolate equivalent 7ba or 7bb
$^{13}$C NMR spectrum of the enolate equivalent $7ba$ or $7bb$
$^{13}$C NMR spectrum of the enolate equivalent Tba or 7bb (20 to 28 ppm)
$^{13}$C NMR spectrum of the enolate equivalent 7ba or 7bb (123 to 186 ppm)
$^1$H NMR spectrum of the enolate equivalent 7aa or 7ab
13C NMR spectrum of the enolate equivalent 7aa or 7ab


**HPLC Chromatogram Profiles**

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(S)-3-hydroxy-N-phenyl-3-(p-tolyl)propanamide (6bb)
(S)-3-hydroxy-N-phenyl-3-(o-tolyl)propanamide (6bc)
(S)-3-(4-fluorophenyl)-3-hydroxy-N-phenylpropanamide (6bd)
(S)-3-(4-chlorophenyl)-3-hydroxy-N-phenylpropanamide (6be)
(S)-3-(4-bromophenyl)-3-hydroxy-N-phenylpropanamide (6bf)
(S)-3-hydroxy-3-(4-methoxyphenyl)-N-phenylpropanamide (6bg)
(S)-3-(4-(tert-butyl)phenyl)-3-hydroxy-N-phenylpropanamide (6bh)
(S)-3-hydroxy-3-mesityl-N-phenylpropanamide (6bi)
(S)-3-hydroxy-3-(naphthalen-2-yl)-N-phenylpropanamide (6bj)
(S)-3-hydroxy-N-phenyl-3-(thiophen-2-yl)propanamide (6bk)
(S)-3-(furan-2-yl)-3-hydroxy-N-phenylpropanamide (6bl)
(R)-3-hydroxy-N-phenylbutanamide (6bm)
(S)-3-hydroxy-4,4-dimethyl-N-phenylpentanamide (6bn)
(S)-1-(4-(2-(4-methoxyphenyl)-2-oxoethoxy)phenyl)-3-oxo-3-(phenylamino)propyl 4-bromobenzoate (16)