Bio-inspired enantioselective full transamination with readily available cyclodextrin

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SUPPORTING INFORMATION

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1. General procedures

Chemicals: Solvents, inorganic salts, and organic reagents were purchased from commercial resources, and used without further purification unless otherwise mentioned. Column chromatography was performed on silica gel (200-300 mesh).

1H NMR spectra were recorded on a 400 or 600 MHz NMR spectrometer. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal (DMSO, δ=2.51). Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s=single, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constants (Hz), integration and assignment.

Enantiomeric excesses (ee) were determined by HPLC analysis using the corresponding commercial chiral column as stated in experimental procedures at 30°C with UV detector at 210 nm. CHIRAL PAK AD-H normal-phase analytical columns (4.6 mm Φ×250mm), CHIRAL PAK OD-H normal-phase analytical columns (4.6 mm Φ×250mm) and CHIRAL PAK IC normal-phase analytical columns (4.6 mm Φ×250mm) were used as solid phase.
α-Keto acids: phenylpyruvic acid, 4-hydroxy phenylpyruvic acid, benzoyl formic acid, pyruvic acid and 4-methyl-2-oxovaleric acid were purchased commercially. α-Keto acids including 2-methoxypyruvic acid, 3-methoxypyruvic acid, 4-methoxypyruvic acid, 4-methylpyruvic acid, 3,4-dimethoxypyruvic acid, 4-fluoropyruvic acid, 4-chlorophenyl pyruvic acid, 4-bromopyruvic acid, and 2-oxo-3-thien-2-ylpropanoic acid were synthesized following a modified literature method\(^1\), from the corresponding aldehydes condensed with hydantoin with ethanolamine as catalyst and then hydrolyzed under alkaline conditions. 4-Nitrophe nylpyruvic acid was prepared by following literature procedure\(^2\), from 4-nitrobenzaldehyde and N-acetyl glycine in the presence of acetic anhydride and sodium acetate, followed by ring opening under reflux, and acetamide hydrolyzed off to give the final product.

2,2-Disubstituted glycines as sacrificial amine sources including methylphenylglycine and diphenylglycine were purchased commercially, and when equimolecular suspension of diphenylglycine and bases were added to the methanol solution, removed the solvent after stirring at room temperature, alkali metal salts of diphenylglycine including lithium, sodium and potassium were prepared.

### 2. Optimization for PLP-catalyzed asymmetric transamination of phenylpyruvic acid in pure aqueous phase

Table S1. Additives and reaction time screening for PLP-catalyzed asymmetric transamination of phenylpyruvic acid\(^a\)

| Entry | Additives | Time(h) | Yield(%)\(^b\) | ee(%)\(^c\) |
|-------|-----------|---------|----------------|-------------|
| 1     | None      | 24      | 7              | 12          |
| 2     | EDTA      | 24      | 4              | 23          |
| 3     | EDTA      | 12      | 2              | 21          |
| 4     | EDTA      | 36      | 9              | 20          |
| 5     | EDTA      | 48      | 9              | 20          |
| 6     | EDTA      | 72      | 9              | 20          |
| 7     | EDTA      | 96      | 9              | 20          |
| 8     | EDTA      | 144     | 10             | 16          |

\(^a\)All reactions were carried out with phenylpyruvic acid (3a) (0.05 m mol), diphenylglycine (7a) (0.05 m mol), EDTA (0.01mmol), β-CD (0.06mmol) and PLP (0.01 m mol) in 300mM Tris buffer (4.0 mL), pH 8.0, at 50°C for certain time;
The yield was determined by chiral HPLC through standard addition method:\(^3\)-\(^4\):

The reaction liquid was divided into two parts, with the same subsequent operations except one was added 10% of the target product marked \( \text{II} \), another marked \( \text{I} \) served as blank control; results of HPLC showed that:

\[ A_\text{I} \] (the peak areas of the target product in \( \text{I} \)),
\[ A_\text{II} \] (the peak areas of the target product in \( \text{II} \)),
\[ E_\text{I} \] (the ee's of the target product in \( \text{I} \)),
\[ E_\text{II} \] (the ee's of the target product in \( \text{II} \));

\[ \text{yield} = \frac{A_\text{II}}{A_\text{I} - A_\text{II}} \times 10\% \text{ or } \text{yield} = \frac{E_\text{II}}{E_\text{I} - E_\text{II}} \times 10\% \]

The ee's were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their \( N \)-Bz derivatives, the absolute configuration of \( 4a \) was assigned as \( S \) by comparison with the standard product.

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**Fig. S1** \(^1\)H NMR contrast chart of benzophenone (top) and the reaction mixture’s \( \text{CH}_2\text{Cl}_2 \) extract fraction (bottom)\(^a\)

Reaction was carried out with phenylpyruvic acid (3a) (0.5mmol), diphenylglycine (7a) (0.5mmol), \( \beta \)-CD (0.6mmol) and PLP (0.1 mmol) in 300mM Tris buffer (40.0 mL), pH 8.0, at 50℃ for 24h. The reaction mixture was extracted with \( \text{CH}_2\text{Cl}_2 \), removed the solvent by vacuum distillation obtaining the off-white solid, compared its \(^1\)H NMR spectrum (bottom) with benzophenone (top) in \( \text{CDCl}_3 \) which proved benzophenone was produced as a byproduct.

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**Table S2. Temperature screening for PLP-catalyzed asymmetric transamination of phenylpyruvic acid\(^a\)**

| Entry | Temperature(℃) | Yield(%)\(^b\) | ee(%)\(^c\) |
|-------|---------------|----------------|-------------|
| 1     | 30            | Trace          | —           |
| 2     | 40            | 2              | 25          |
All reactions were carried out with phenylpyruvic acid (3a) (0.05 mmol), diphenylglycine (7a) (0.05 mmol), β-CD (0.06 mmol), EDTA (0.01 mmol) and PLP (0.01 mmol) in Tris buffer (4.0 mL), pH 8.0, for 36 h if not mentioned. b The yield was determined by chiral HPLC through standard addition method (Table S1†). c The ee’s were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their N-Bz derivatives, the absolute configuration of 4a was assigned as S by comparison with the standard product.

Table S3. Screening of buffers for PLP-catalyzed asymmetric transamination of phenylpyruvic acid

| Entry | Buffer                  | Concentration (mM) | pH  | Yield(%) b | ee(%) c |
|-------|-------------------------|--------------------|-----|------------|---------|
| 1     | Tris buffer             | 300                | 8.0 | 9          | 20      |
| 2     | Phosphate buffer (PB)   | 300                | 8.0 | 5          | 9       |
| 4     | Borate buffer           | 300                | 8.0 | trace nd   |         |
| 5     | Carbonic acid buffer    | 300                | 8.0 | 4          | 16      |
| 6     | EDTA buffer             | 300                | 8.0 | 6          | 12      |
| 7     | MOPS buffer             | 300                | 8.0 | 4          | 15      |
| 8     | HEPES buffer            | 300                | 8.0 | 6          | 14      |
| 9     | NaCl aqueous solution   | 300                | 8.0 | trace nd   |         |
| 10    | Tris buffer             | 150                | 8.0 | 6          | 17      |
| 11    | Tris buffer             | 600                | 8.0 | 9          | 21      |
| 12    | Tris buffer             | 300                | 6.0 | trace nd   |         |
| 13    | Tris buffer             | 300                | 6.5 | trace nd   |         |
| 14    | Tris buffer             | 300                | 7.0 | 1          | 8       |
| 15    | Tris buffer             | 300                | 7.5 | 3          | 17      |
| 16    | Tris buffer             | 300                | 8.5 | 4          | 23      |
| 17    | Tris buffer             | 300                | 9.0 | 3          | 24      |
| 18    | Tris buffer             | 300                | 10.0| 2          | 34      |

All reactions were carried out with phenylpyruvic acid (3a) (0.05 mmol), diphenylglycine (7a) (0.05 mmol), β-CD (0.06 mmol), EDTA (0.01 mmol) and PLP (0.01 mmol) in Tris buffer (4.0 mL), at 50°C for 36 h if not mentioned. b The yield was determined by chiral HPLC through standard addition method (Table S1†). c The ee’s were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their N-Bz derivatives, the absolute configuration of 4a was assigned as S by comparison with the standard product.

Table S4. Screening of catalysts for asymmetric transamination of phenylpyruvic acid

| Entry | Buffer                  | Concentration (mM) | pH  | Yield(%) b | ee(%) c |
|-------|-------------------------|--------------------|-----|------------|---------|
| 1     | Tris buffer             | 300                | 8.0 | 9          | 20      |
| 2     | Phosphate buffer (PB)   | 300                | 8.0 | 5          | 9       |
| 4     | Borate buffer           | 300                | 8.0 | trace nd   |         |
| 5     | Carbonic acid buffer    | 300                | 8.0 | 4          | 16      |
| 6     | EDTA buffer             | 300                | 8.0 | 6          | 12      |
| 7     | MOPS buffer             | 300                | 8.0 | 4          | 15      |
| 8     | HEPES buffer            | 300                | 8.0 | 6          | 14      |
| 9     | NaCl aqueous solution   | 300                | 8.0 | trace nd   |         |
| 10    | Tris buffer             | 150                | 8.0 | 6          | 17      |
| 11    | Tris buffer             | 600                | 8.0 | 9          | 21      |
| 12    | Tris buffer             | 300                | 6.0 | trace nd   |         |
| 13    | Tris buffer             | 300                | 6.5 | trace nd   |         |
| 14    | Tris buffer             | 300                | 7.0 | 1          | 8       |
| 15    | Tris buffer             | 300                | 7.5 | 3          | 17      |
| 16    | Tris buffer             | 300                | 8.5 | 4          | 23      |
| 17    | Tris buffer             | 300                | 9.0 | 3          | 24      |
| 18    | Tris buffer             | 300                | 10.0| 2          | 34      |
Table S5. Screening of CDs for PLP-catalyzed asymmetric transamination of phenylpyruvic acid

| Entry | Catalyst | Dosage (m mol) | Yield (%)<sup>b</sup> | ee (%)<sup>c</sup> |
|-------|----------|----------------|-----------------------|-------------------|
| 1     | PLP      | 0.01           | 9                     | 20                |
| 2     | PL<sup>d</sup> | 0.01           | 10                    | 0                 |
| 3     | PM       | 0.01           | 10                    | 0                 |
| 4     | PLP      | 0.005          | 5                     | 25                |
| 5     | PLP      | 0.015          | 9                     | 17                |
| 6     | PLP      | 0.025          | 11                    | 15                |
| 7     | PLP      | 0.05           | 10                    | 11                |

<sup>a</sup>All reactions were carried out with phenylpyruvic acid (3a) (0.05 mmol), diphenylglycine (7a) (0.05 mmol), β-CD (0.06 mmol), EDTA (0.01 mmol) and in Tris buffer (4.0 mL), pH 8.0, at 50°C for 36 h if not mentioned. <sup>b</sup>The yield was determined by chiral HPLC through standard addition method (Table S1). <sup>c</sup>The ee's were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their N-Bz derivatives, the absolute configuration of 4a was assigned as S by comparison with the standard product. <sup>d</sup>PL was an abbreviation for pyridoxal.

Table S6. Screening of sacrificial amine sources for PLP-catalyzed asymmetric transamination of phenylpyruvic acid

| Entry | Amine source | Dosage (m mol) | Yield (%)<sup>b</sup> | ee (%)<sup>c</sup> |
|-------|--------------|----------------|-----------------------|-------------------|
| 1     | 7a(R2:Ph, M:H) | 0.05           | 9                     | 20                |
| 2     | 7b(R2:Me, M:H) | 0.05           | 11                    | 19                |
| 3     | 7c(R2:Ph, M:Li<sup>+</sup>) | 0.05       | 23                    | 20                |

<sup>a</sup>All reactions were carried out with phenylpyruvic acid (3a) (0.05 mmol), diphenylglycine (7a) (0.05 mmol), β-CD (0.06 mmol), EDTA (0.01 mmol) and PLP (0.01 mmol) in Tris buffer (4.0 mL), pH 8.0, at 50°C for 36 h if not mentioned. <sup>b</sup>The yield was determined by chiral HPLC through standard addition method (Table S1). <sup>c</sup>The ee's were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their N-Bz derivatives, the absolute configuration of 4a was assigned as S by comparison with the standard product.
All reactions were carried out with phenylpyruvic acid (3a) (0.05 mmol), β-CD (0.06 mmol), EDTA (0.01 mmol) and in Tris buffer (4.0 mL), pH 8.0, at 50 °C for 36 h if not mentioned. The yield was determined by chiral HPLC through standard addition method (Table S1†). The ee’s were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their N-Bz derivatives, the absolute configuration of 4a was assigned as S by comparison with the standard product.

3. Synthesis of α-keto acids

A. A reaction tube was charged with 3 m mol of corresponding aldehydes, 3 m mol of hydantoin, and 0.03 m mol of ethanolamine in 7 g of permuted water, under agitation and in an inert atmosphere, heated for 2 to 4 hours with reflux until a large amount of solid was produced turn the clear solution into suspension. Thereafter, 30 mL of 6 g sodium hydroxyde or 8.5 g potassium hydroxide was introduced, continued to reflux for more than another 30 minutes until the muddy liquid turned back to clear. The obtained solution was then cooled to the ambient temperature, brought to acidity with the addition of concentrated hydrochloric acid and extracted with ethyl acetate, the organic phase was washed with iced water, dried with anhydrous Na₂SO₄, evaporated at reduced pressure to get the crude product which was purified by flash
column or recrystallization.

3b

$^1$H NMR (400 MHz, DMSO) $\delta$ 13.01 (s, 1H), 8.96 (s, 1H), 7.71 (d, $J$ = 8.8 Hz, 2H), 6.92 (d, $J$ = 8.9 Hz, 2H), 6.38 (s, 1H), 3.76 (s, 3H).

3c

$^1$H NMR (400 MHz, DMSO) $\delta$ 13.18 (s, 1H), 9.26 (s, 1H), 7.37 (s, 1H), 7.32 (d, $J$ = 7.8 Hz, 1H), 7.25 (t, $J$ = 7.9 Hz, 1H), 6.84 – 6.79 (m, 1H), 6.38 (s, 1H), 3.74 (s, 3H).

3d

$^1$H NMR (400 MHz, DMSO) $\delta$ 13.14 (s, 1H), 9.13 (s, 1H), 8.17 (dd, $J$ = 7.8, 1.6 Hz, 1H), 7.25 – 7.19 (m, 1H), 7.03 – 6.93 (m, 2H), 6.80 (s, 1H), 3.81 (s, 3H).

3e

$^1$H NMR (400 MHz, DMSO) $\delta$ 13.11 (s, 1H), 9.09 (s, 1H), 7.64 (d, $J$ = 8.1 Hz, 2H), 7.15 (d, $J$ = 8.1 Hz, 2H), 6.37 (s, 1H), 2.29 (s, 3H).

3g

$^1$H NMR (400 MHz, DMSO) $\delta$ 13.00 (s, 1H), 8.98 (s, 1H), 7.43 (d, $J$ = 1.7 Hz, 1H), 7.31 (dd, $J$ = 8.4, 1.8 Hz, 1H), 6.94 (d, $J$ = 8.5 Hz, 1H), 6.38 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H).

3i
^1^H NMR (400 MHz, DMSO) δ 13.25 (s, 1H), 9.29 (s, 1H), 7.81 (dd, J = 8.5, 5.9 Hz, 2H), 7.17 (t, J = 8.9 Hz, 2H), 6.41 (s, 1H).

![3j](image)

^1^H NMR (400 MHz, DMSO) δ 13.30 (s, 1H), 9.49 (s, 1H), 7.77 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 6.39 (s, 1H).

![3k](image)

^1^H NMR (400 MHz, DMSO) δ 13.29 (s, 1H), 9.49 (s, 1H), 7.71 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 6.37 (s, 1H).

![3l](image)

^1^H NMR (400 MHz, DMSO) δ 13.08 (s, 1H), 9.51 (s, 1H), 7.54 (d, J = 5.1 Hz, 1H), 7.26 (d, J = 3.4 Hz, 1H), 7.05 (dd, J = 5.0, 3.8 Hz, 1H), 6.78 (s, 1H).

B

A reaction tube was charged with 3 mmol of 4-nitrobenzaldehyde, 15 mmol of anhydrous sodium acetate, and 3.6 mmol of N-acetylglycine, the mixture was heated at reflux in 3ml acetic anhydride for 10 hours, this was then cooled to the ambient temperature. After standing overnight in refrigerator, the precipitate was collected on a filter, washed with cold water and ethanol, then dried in vacuo to afford 0.6 g (91%) of brown solid. Following that, 4.5 ml acetone and 3ml H₂O were added to the product obtained from the previous step, heated at reflux for 10 hours, then cooled to the ambient temperature, after removal of the solvent under reduced pressure, 15 ml of 1M HCl solution was added, kept refluxing at 120°C for 10 hours. Whereafter, the solution cooled down and crystallized out brown crystals obtaining by filtering.
and purified by recrystallization yielding 0.1g 4-nitrophenylpyruvic acid as the final product (36%).

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{COOH} \\
\text{3h}
\end{align*}
\]

\(^1\)H NMR (400 MHz, DMSO) δ 13.58 (s, 1H), 10.17 (s, 1H), 8.20 (d, \( J = 8.7 \) Hz, 2H), 7.99 (d, \( J = 8.7 \) Hz, 2H), 6.50 (s, 1H).

4. Representative procedure for asymmetric transamination of \( \alpha \)-keto acids

Table 2 Substrate screening for the asymmetric transamination of \( \alpha \)-keto acids

The general transamination reaction condition: \( \alpha \)-keto acid 3 (0.05 mmol), amine source 7d (0.05 mmol), PLP (0.01 mmol), EDTA (0.01 mmol) and \( \beta \)-CD (0.06 mmol) were added into 4mL 300mM Tris buffer, pH=8. The mixture was stirred at 50°C for
36h or 72h. Followed by N-derivatization of the amino acid as the literature procedure shown\(^5\), and the ee’s were determined by chiral HPLC analysis.

\[\text{4a} \]

\[^1\text{H NMR} (600\text{ MHz, DMSO}) \delta 12.76 (s, 1H), 8.69 (d, J = 8.1 \text{ Hz, 1H}), 7.83 – 7.76 (m, 2H), 7.52 (t, J = 7.4 \text{ Hz, 1H}), 7.44 (t, J = 7.6 \text{ Hz, 2H}), 7.32 (d, J = 7.6 \text{ Hz, 2H}), 7.26 (t, J = 7.6 \text{ Hz, 2H}), 7.18 (t, J = 7.3 \text{ Hz, 1H}), 4.63 (ddd, J = 10.8, 8.3, 4.4 \text{ Hz, 1H}), 3.20 (dd, J = 13.8, 4.3 \text{ Hz, 1H}), 3.08 (dd, J = 13.7, 10.8 \text{ Hz, 1H}).\]

\[\text{4b} \]

\[^1\text{H NMR} (400\text{ MHz, DMSO}) \delta 12.72 (s, 1H), 7.89 (d, J = 7.5 \text{ Hz, 2H}), 7.70 (d, J = 8.5 \text{ Hz, 1H}), 7.65 (t, J = 6.9 \text{ Hz, 2H}), 7.41 (t, J = 7.4 \text{ Hz, 2H}), 7.31 (dt, J = 9.9, 7.5 \text{ Hz, 2H}), 7.19 (d, J = 8.5 \text{ Hz, 2H}), 6.83 (d, J = 8.6 \text{ Hz, 2H}), 4.26 – 4.14 (m, 3H), 4.14 – 4.05 (m, 1H), 3.70 (s, 3H), 3.01 (dd, J = 13.8, 4.3 \text{ Hz, 1H}), 2.80 (dd, J = 13.7, 10.6 \text{ Hz, 1H}).\]

\[\text{4c} \]

\[^1\text{H NMR} (400\text{ MHz, DMSO}) \delta 12.78 (s, 1H), 7.88 (d, J = 7.5 \text{ Hz, 2H}), 7.74 (d, J = 8.4 \text{ Hz, 1H}), 7.64 (t, J = 6.7 \text{ Hz, 2H}), 7.40 (dd, J = 10.0, 4.5 \text{ Hz, 2H}), 7.29 (dd, J = 7.0, 4.8 \text{ Hz, 2H}), 7.18 (t, J = 7.9 \text{ Hz, 1H}), 6.93 – 6.81 (m, 2H), 6.81 – 6.71 (m, 1H), 4.28 – 4.07 (m, 4H), 3.71 (s, 3H), 3.06 (dd, J = 13.7, 4.1 \text{ Hz, 1H}), 2.85 (dd, J = 13.5, 10.8 \text{ Hz, 1H}).\]

\[\text{4d} \]

\[^1\text{H NMR} (400\text{ MHz, DMSO}) \delta 12.63 (s, 1H), 8.58 (d, J = 8.1 \text{ Hz, 1H}), 7.77 (d, J = 7.2 \text{ Hz, 2H}), 7.51 (t, J = 4.8 \text{ Hz, 1H}), 7.44 (t, J = 7.4 \text{ Hz, 2H}), 7.23 (d, J = 7.4 \text{ Hz, 1H}), 7.17 (dd, J = 11.5, 4.0 \text{ Hz, 1H}), 6.95 (d, J = 8.2 \text{ Hz, 1H}), 6.82 (t, J = 7.4 \text{ Hz, 1H}), 4.65 (dddd, J = 10.5, 8.2, 4.5 \text{ Hz, 1H}), 3.81 (s, 3H), 3.29 – 3.22 (m, 1H), 2.95 (dd, J = 13.5, 10.6 \text{ Hz, 1H}).\]
$^1$H NMR (400 MHz, DMSO) δ 8.19 (s, 1H), 7.75 (d, $J = 7.3$ Hz, 2H), 7.50 (t, $J = 7.2$ Hz, 1H), 7.43 (t, $J = 7.4$ Hz, 2H), 7.13 (d, $J = 7.7$ Hz, 2H), 7.00 (d, $J = 7.7$ Hz, 2H), 4.45 (s, 1H), 3.18 (dd, $J = 13.3$, 4.1 Hz, 1H), 3.02 (dd, $J = 13.4$, 8.7 Hz, 1H), 2.20 (s, 3H).

\[ \text{O}_2\text{N} \]
\[ \begin{array}{c}
\text{H} \\
\text{N} \\
\text{C} \\
\text{O} \\
\text{Fmoc}
\end{array} \\
\text{4f} \]

$^1$H NMR (400 MHz, DMSO) δ 9.19 (s, 1H), 7.88 (d, $J = 7.4$ Hz, 2H), 7.75 – 7.57 (m, 2H), 7.41 (td, $J = 7.1$, 3.2 Hz, 2H), 7.31 (dd, $J = 16.2$, 7.9 Hz, 2H), 7.01 (d, $J = 8.1$ Hz, 2H), 6.63 (d, $J = 8.1$ Hz, 2H), 4.25 (dd, $J = 13.2$, 8.0 Hz, 1H), 4.22 – 4.08 (m, 2H), 4.00 (dd, $J = 18.4$, 6.2 Hz, 1H), 2.98 (dd, $J = 13.8$, 3.3 Hz, 1H), 2.75 (dd, $J = 13.6$, 9.5 Hz, 1H).

\[ \text{MeO} \]
\[ \begin{array}{c}
\text{H} \\
\text{N} \\
\text{C} \\
\text{O} \\
\text{Fmoc}
\end{array} \\
\text{4g} \]

$^1$H NMR (400 MHz, DMSO) δ 12.70 (s, 1H), 7.88 (d, $J = 7.5$ Hz, 2H), 7.67 (d, $J = 21.3$, 7.8 Hz, 3H), 7.41 (t, $J = 7.2$ Hz, 2H), 7.36 – 7.17 (m, 2H), 6.92 (s, 1H), 6.80 (dd, $J = 21.1$, 8.1 Hz, 2H), 4.34 – 4.00 (m, 4H), 3.70 (d, $J = 8.9$ Hz, 6H), 3.01 (dd, $J = 13.6$, 4.1 Hz, 1H), 2.79 (dd, $J = 13.7$, 10.8 Hz, 1H).

\[ \text{OH} \]
\[ \begin{array}{c}
\text{H} \\
\text{N} \\
\text{C} \\
\text{O} \\
\text{Fmoc}
\end{array} \\
\text{4h} \]

$^1$H NMR (600 MHz, DMSO) δ 8.13 (d, $J = 8.3$ Hz, 2H), 7.86 (d, $J = 7.4$ Hz, 2H), 7.76 (d, $J = 8.5$ Hz, 1H), 7.67 – 7.57 (m, 2H), 7.54 (d, $J = 8.3$ Hz, 2H), 7.39 (t, $J = 7.4$ Hz, 2H), 7.28 (dd, $J = 16.2$, 7.8 Hz, 2H), 4.30 – 4.24 (m, 1H), 4.21 (dd, $J = 12.2$, 9.2 Hz, 2H), 4.15 (t, $J = 6.7$ Hz, 1H), 3.25 – 3.22 (m, 1H), 3.05 – 2.96 (m, 1H).

\[ \text{F} \]
\[ \begin{array}{c}
\text{H} \\
\text{N} \\
\text{C} \\
\text{O} \\
\text{Ph}
\end{array} \\
\text{4i} \]

$^1$H NMR (400 MHz, DMSO) δ 12.79 (s, 1H), 8.72 (d, $J = 8.2$ Hz, 1H), 7.79 (d, $J = 7.2$ Hz, 2H), 7.52 (t, $J = 7.3$ Hz, 1H), 7.45 (t, $J = 7.4$ Hz, 2H), 7.35 (dd, $J = 8.4$, 5.7 Hz, 2H), 7.09 (t, $J = 8.8$ Hz, 2H), 4.60 (ddd, $J = 10.9$, 8.3, 4.4 Hz, 1H), 3.18 (dd, $J = 13.8$, 4.3 Hz, 1H), 3.05 (dd, $J = 13.6$, 11.0 Hz, 1H).

\[ \text{Cl} \]
\[ \begin{array}{c}
\text{H} \\
\text{N} \\
\text{C} \\
\text{O} \\
\text{Fmoc}
\end{array} \\
\text{4j} \]
$^1$H NMR (400 MHz, DMSO) δ 12.87 (s, 1H), 7.88 (d, $J = 7.5$ Hz, 2H), 7.75 (d, $J = 8.5$ Hz, 1H), 7.69 – 7.56 (m, 2H), 7.41 (t, $J = 7.3$ Hz, 2H), 7.35 – 7.25 (m, 6H), 4.17 (dt, $J = 12.5$, 4.9 Hz, 4H), 3.08 (dd, $J = 13.7$, 4.1 Hz, 1H), 2.86 (dd, $J = 13.4$, 11.1 Hz, 1H).

$^1$H NMR (400 MHz, DMSO) δ 8.74 (d, $J = 8.1$ Hz, 1H), 7.79 (d, $J = 7.6$ Hz, 2H), 7.52 (t, $J = 7.3$ Hz, 1H), 7.45 (dd, $J = 7.7$, 6.1 Hz, 4H), 7.28 (d, $J = 8.2$ Hz, 2H), 4.66 – 4.55 (m, 1H), 3.17 (dd, $J = 13.8$, 4.3 Hz, 1H), 3.08 – 2.96 (dd, $J = 13.8$, 8.9 Hz, 1H).

$^1$H NMR (400 MHz, DMSO) δ 12.85 (s, 1H), 8.76 (d, $J = 16.2$ Hz, 1H), 7.85 (d, $J = 7.3$ Hz, 2H), 7.51 (dt, $J = 27.5$, 7.2 Hz, 3H), 7.32 (d, $J = 4.8$ Hz, 1H), 6.93 (dd, $J = 11.8$, 7.0 Hz, 2H), 4.69 – 4.47 (m, 1H), 3.48 – 3.29 (m, 2H).

$^1$H NMR (400 MHz, DMSO) δ 12.87 (s, 1H), 7.88 (d, $J = 7.5$ Hz, 2H), 7.75 (d, $J = 8.5$ Hz, 1H), 7.69 – 7.57 (m, 2H), 7.41 (t, $J = 7.3$ Hz, 2H), 7.33 – 7.26 (m, 5H), 4.17 (dt, $J = 12.5$, 4.9 Hz, 4H), 3.08 (dd, $J = 13.7$, 4.1 Hz, 1H), 2.86 (dd, $J = 13.4$, 11.1 Hz, 1H).

$^1$H NMR (400 MHz, DMSO) δ 12.52 (s, 1H), 8.65 (d, $J = 7.1$ Hz, 1H), 7.88 (d, $J = 7.2$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.47 (t, $J = 7.4$ Hz, 2H), 4.42 (p, $J = 7.4$ Hz, 1H), 1.39 (d, $J = 7.3$ Hz, 3H).

$^1$H NMR (400 MHz, DMSO) δ 12.53 (s, 1H), 8.57 (d, $J = 7.9$ Hz, 1H), 7.89 (d, $J = 7.3$ Hz, 2H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.47 (t, $J = 7.3$ Hz, 2H), 4.59 – 4.33 (m, 1H), 1.91 – 1.63 (m, 2H), 1.59 (dd, $J = 12.7$, 8.8, 4.2 Hz, 1H), 0.90 (dd, $J = 17.1$, 6.3 Hz, 6H).
5. Table S7. Control experiments for PLP-catalyzed asymmetric transamination of 4-fluorophenylpyruvic acid

| entry | condition | Yield(%)<sup>b</sup> | ee(%)<sup>c</sup> |
|-------|-----------|----------------------|------------------|
| 1     | one-pot method<sup>a</sup> | 37                   | 35               |
| 2     | 3i+β-CD<sup>d</sup> | 39                   | 44               |
| 3     | 7d+β-CD<sup>e</sup> | 36                   | 35               |
| 4     | 3i+β-CD(2.4eq)<sup>f</sup> | 38                   | 50               |

<sup>a</sup> All reactions were carried out with 4-fluorophenylpyruvic acid (3i) (0.05 m mol), β-CD (0.06 m mol), EDTA (0.01 m mol) and in Tris buffer (4.0 m L), pH 8.0, at 50°C for 48 h if not mentioned. <sup>b</sup> The yield was determined by chiral HPLC through standard addition method(Table S1†). <sup>c</sup>The ee’s were determined by chiral HPLC (Chiralpak AD-H column) after the amines were converted into their N-Bz derivatives, the absolute configuration of 4i was assigned as S by comparison with the standard product. <sup>d</sup>3i, β-CD, EDTA and Tris buffer solution were stirred overnight at 50 °C to get the resulting mixture, then added 7d and PLP keeping on stirring for another 48h. <sup>e</sup>7d, β-CD, EDTA and Tris buffer solution were stirred overnight at 50 °C to get the resulting mixture, then added 3i and PLP keeping on stirring for another 48h. <sup>f</sup>The same as <sup>d</sup> except dosage of β-CD was 2.4 eq.(0.12mmol).

6. Characterization data

**1H NMR of the α-keto acids and derivatives of amino acids**

**1H NMR of the α-keto acids**
$^1$H NMR of the $\alpha$-amino acid derivatives
HPLC for the determination of enantiomeric excesses

Table 3, compound 4a

![Chemical Structure of Compound 3a](image)

**HPLC Conditions:** Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(14/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

**Racemic**

| Peak# | RT(min) | Area  | Aera% |
|-------|---------|-------|-------|
| 1     | 19.470  | 47234600 | 49.025 |
| 2     | 22.490  | 49113239 | 50.975 |

**The Reaction Result**

| Peak# | RT(min) | Area  | Aera% |
|-------|---------|-------|-------|
| 1     | 19.180  | 34667956 | 60.861 |
| 2     | 22.655  | 22294653 | 39.139 |
Table 2, compound 4b

\[
\begin{array}{c}
\text{4b} \\
\text{MeO} \\
\text{H} \\
\text{NH} \\
\text{Fmoc}
\end{array}
\]

**HPLC Conditions:** Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(10:1)containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

**Racemic**

| Peak# | RT(min) | Area     | Area%  |
|-------|---------|----------|--------|
| 1     | 24.052  | 32654064 | 49.814 |
| 2     | 25.940  | 3289368  | 50.186 |

**The Reaction Result**

| Peak# | RT(min) | Area     | Area%  |
|-------|---------|----------|--------|
| 1     | 23.875  | 6560276  | 30.889 |
| 2     | 26.035  | 14677691 | 69.111 |
Table 2, compound 4c

![Chemical Structure](image)

**HPLC Conditions:** Column: Chiraleel OD-H, Daicel Chemical Industries, Ltd.,
Eluent: Hexanes / IPA (14/1) containing 0.3% TFA; Flow rate: 1.0 mL/min; Detection:
UV 210 nm

**Racemic**

| Peak# | RT(min) | Area    | Aera% |
|-------|---------|---------|-------|
| 1     | 46.767  | 63690881| 49.722|
| 2     | 63.597  | 64403855| 50.278|

**The Reaction Result**

| Peak# | RT(min) | Area    | Aera% |
|-------|---------|---------|-------|
| 1     | 47.378  | 27909618| 35.787|
| 2     | 63.822  | 50078348| 64.213|
Table 2, compound 4d

\[
\begin{align*}
\text{O} & \\
\text{HN} & \\
\text{OMe} & \\
\text{Bz} & \\
\end{align*}
\]

4d

**HPLC Conditions:** Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA (8/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

**Racemic**

| Peak# | RT(min) | Area   | Area%  |
|-------|---------|--------|--------|
| 1     | 19.020  | 3750251| 48.362 |
| 2     | 24.248  | 3859756| 49.775 |

Table 2, compound 4e

\[
\begin{align*}
\text{O} & \\
\text{HN} & \\
\text{Bz} & \\
\end{align*}
\]

4e

**HPLC Conditions:** Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(10:1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm
Racemic

| Peak# | RT(min) | Area       | Aera% |
|-------|---------|------------|-------|
| 1     | 19.390  | 29771168   | 49.811|
| 2     | 22.212  | 29996595   | 50.189|

The Reaction Result

| Peak# | RT(min) | Area       | Aera% |
|-------|---------|------------|-------|
| 1     | 20.228  | 12598767   | 72.052|
| 2     | 22.650  | 4886826    | 27.948|

Table 2, compound 4f

![4f](attachment:image_url)

**HPLC Conditions:** *Column:* Chiralcel AD-H, Daicel Chemical Industries, Ltd.,
Eluent: Hexanes / IPA(14/1)containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection:
UV 210 nm
Table 2, compound 4g

| Peak# | RT(min) | Area     | Aera% |
|-------|---------|----------|-------|
| 1     | 60.205  | 95597538 | 50.084|
| 2     | 68.530  | 95276723 | 49.916|

**HPLC Conditions:** Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd.,
Eluent: Hexanes / IPA(14/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

**Racemic**

| Peak# | RT(min) | Area     | Aera% |
|-------|---------|----------|-------|
| 1     | 53.343  | 50882363 | 49.896|
| 2     | 65.230  | 51094863 | 50.104|
Table 2, compound 4h

HPLC Conditions: Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(7/3) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

Racemic

| Peak# | RT(min) | Area   | Aera% |
|-------|---------|--------|-------|
| 1     | 6.570   | 3672084| 48.432|
| 2     | 7.805   | 3704707| 48.862|

The Reaction Result

| Peak# | RT(min) | Area   | Aera% |
|-------|---------|--------|-------|
| 1     | 6.500   | 2304690| 42.022|
| 2     | 7.722   | 3179808| 57.978|
Table 2, compound 4i

HPLC Conditions: Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(5.4/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

Racemic

| Peak# | RT(min) | Area   | Area% |
|-------|---------|--------|-------|
| 1     | 8.048   | 21053054 | 49.609 |
| 2     | 9.430   | 21385147 | 50.391 |

The Reaction Result

| Peak# | RT(min) | Area   | Area% |
|-------|---------|--------|-------|
| 1     | 8.538   | 6493229 | 71.988 |
| 2     | 10.082  | 2526666 | 28.012 |
### Table 2, compound 4j

![Structure of compound 4j](image)

**HPLC Conditions:**
- **Column:** Chiralcel IC, Daicel Chemical Industries, Ltd.
- **Eluent:** Hexanes / IPA(14/1) containing 0.1% TFA
- **Flow rate:** 0.8 mL/min
- **Detection:** UV 210 nm

#### Racemic

| Peak# | RT(min) | Area    | Area% |
|-------|--------|---------|-------|
| 1     | 19.743 | 30332380| 50.175|
| 2     | 24.612 | 30120286| 49.825|

#### The Reaction Result

| Peak# | RT(min) | Area    | Area% |
|-------|--------|---------|-------|
| 1     | 19.677 | 12624137| 65.249|
| 2     | 24.122 | 6723489 | 34.751|
Table 2, compound 4k

HPLC Conditions: Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(5.4/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

Racemic

| Peak# | RT(min) | Area     | Aera%  |
|-------|---------|----------|--------|
| 1     | 8.823   | 17498240 | 50.098 |
| 2     | 10.940  | 17429685 | 49.902 |

The Reaction Result

| Peak# | RT(min) | Area     | Aera%  |
|-------|---------|----------|--------|
| 1     | 8.827   | 7777919  | 73.019 |
| 2     | 11.072  | 2874055  | 26.981 |
Table 2, compound 4l

HPLC Conditions: Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(10/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

Racemic

| Peak# | RT(min) | Area   | Aera% |
|-------|---------|--------|-------|
| 1     | 14.440  | 6668761| 50.228|
| 2     | 16.833  | 6608261| 49.772|

The Reaction Result

| Peak# | RT(min) | Area   | Aera% |
|-------|---------|--------|-------|
| 1     | 15.003  | 1564163| 56.912|
| 2     | 17.357  | 1184238| 43.088|
Table 2, compound 4m

HPLC Conditions: Column: Chiralcel AD-H, Daicel Chemical Industries, Ltd., Eluent: Hexanes / IPA(14/1) containing 0.1% TFA; Flow rate: 1.0 mL/min; Detection: UV 210 nm

Racemic

| Peak# | RT(min) | Area  | Aera% |
|-------|---------|-------|-------|
| 1     | 35.765  | 32183825 | 49.742 |
| 2     | 51.192  | 32517685 | 50.258 |

The Reaction Result

| Peak# | RT(min) | Area  | Aera% |
|-------|---------|-------|-------|
| 1     | 4318863  | 3827439 | 52.460 |
| 2     | 3468480  | 3468480 | 47.540 |
**Table 2, compound 4n**

![Structural formula of compound 4n](image)

**HPLC Conditions:**
- **Column:** Chiralcel AD-H, Daicel Chemical Industries, Ltd.
- **Eluent:** Hexanes / IPA(25/1) containing 0.1% TFA
- **Flow rate:** 1.0 mL/min
- **Detection:** UV 210 nm
- **Racemic**

| Peak# | RT(min) | Area     | Area%  |
|-------|---------|----------|--------|
| 1     | 28.797  | 50278778 | 49.668 |
| 2     | 31.920  | 50950890 | 50.332 |

**Table 2, compound 4o**

![Structural formula of compound 4o](image)

**HPLC Conditions:**
- **Column:** Chiralcel AD-H, Daicel Chemical Industries, Ltd.
- **Eluent:** Hexanes / IPA(10/1) containing 0.1% TFA
- **Flow rate:** 1.0 mL/min
- **Detection:** UV 210 nm
### Racemic

![Graph of racemic compounds](image)

| Peak# | RT(min) | Area     | Aera% |
|-------|---------|----------|-------|
| 1     | 10.782  | 11696299 | 49.761|
| 2     | 12.208  | 11808811 | 50.239|

### The Reaction Result

![Graph of reaction results](image)

| Peak# | RT(min) | Area     | Aera% |
|-------|---------|----------|-------|
| 1     | 10.975  | 1903220  | 53.015|
| 2     | 12.278  | 1686733  | 46.985|

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