Supporting Information

Practical and Convenient Enzymatic Synthesis of Enantiopure α -Amino Acids and Amides

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1. Preparation of α -amino nitrile hydrochlorides **1**

Amino nitriles were synthesized through the modified Strecker reaction from the corresponding aldehydes according to the literature.¹ The resulting amino nitriles **1** were then hydrochlorided using dry HCL gas in dry ether solution.

Table S1. Yield and spectral data of the α -amino nitrile hydrochlorides **1** prepared.

nitrile 1	yield (%)	IR $\nu_{\max}$ (KBr) (cm^{-1})	^1H -NMR (ppm)
a	94	3500-2500, 1967, 1596, 1490	7.35-7.48 (m, 5H), 5.61 (s, 1H)
b	90	3300-2500, 2047, 1590, 1493	7.45 (d, $J=8.7\text{Hz}$, 2H), 7.42 (d, $J=8.7\text{ Hz}$, 2H), 5.64 (s, 1H)
c	96	3200-2500, 1992, 1600, 1555, 1406	7.55 (s, 1H), 7.37-7.49 (m, 3H), 5.68 (s, 1H)
d	84	3300-2500, 2040, 1589, 1519, 744, 593	7.38 (d, $J=8.0$, 2H), 7.26 (d, $J=8.0$, 2H) 5.59 (s, 1H), 2.25 (s, 3H)
e	67	3300-2500, 2015, 1602, 1580, 1490, 588	7.49 (d, $J=7.5$, 1H), 7.15-7.34 (m, 3H), 5.72 (s, 1H), 2.27 (s, 3H)
f	54	3300-2500, 1992, 1696, 1578, 1513, 1223, 756	7.49 (d, $J=8.7\text{Hz}$, 2H), 7.03 (d, $J=8.7\text{ Hz}$), 5.63 (s, 1H), 3.78 (s, 3H)
g	95	3200-2500, 1992, 1607, 1587, 1518, 1492, 1293, 1241, 789	7.33 (t, $J=7.9\text{Hz}$, 1H), 7.05 (d, $J=7.9\text{ Hz}$, 1H), 6.98 (d, $J=7.9\text{Hz}$, 1H), 7.01 (s, 1H), 5.57 (s, 1H), 3.69 (s, 3H)
h	78	3400-2500, 1945,	7.05 (d, $J=7.8\text{Hz}$, 1H), 7.04 (s,

		1589, 1508, 1487, 1267, 1043, 922, 817	1H), 6.91 (d, J=7.8Hz, 1H), 5.98 (s, 2H), 5.59 (s, 1H)
i	63	3500-2500, 2005	4.25 (d, J=6.2Hz, 1H), 1.88-1.52 (m, 6H), 1.17-1.00 (m, 5H)
g	89	3500-2500, 1899, 1510, 1407	4.32 (d, J=5.8Hz, 1H), 2.23-2.17 (m, 1H), 1.01, 1.03 (d, J=5.6Hz, 3H×2)
k	36	3500-2500, 2038, 1580, 1472	7.30-7.40 (m, 5H), 4.71 (d, J=8.9Hz, 1H), 3.18-3.32 (m, 2H)

2. *N*-Benzoylation of valine, cyclohexylglycine and their amides.

Amino acid or amide (20 mg) was dissolved in sodium hydrogen carbonate solution (1ml, 10%), and benzoyl chloride (40 mg) was added at room temperature while stirring. After the odor of benzoyl chloride disappeared, the resulting solution was acidified with dilute hydrochloric acid and filtered. The solid obtained was washed with a little cold ether to remove benzoic acid.

***N*-Benzoylated valine:** ¹H-NMR (CD₃OD): δ 7.83 (d, J=7.4 Hz, 2H), 7.46-7.54 (m, 3H), 4.49 (d, J=6.2Hz, 1H), 2.24 (m, 1H), 1.04 (d, J=6.8Hz, (3H×2)).

***N*-Benzoylated valine amide:** ¹H-NMR (CD₃OD): δ 7.83 (d, J=8.1Hz, 2H), 7.43-7.56 (m, 3H), 4.39 (d, J=6.2Hz, 1H), 2.16 (m, 1H), 1.02 (d, J=6.6Hz, 3H×2).

***N*-Benzoylated cyclohexylglycine:** ¹H-NMR (CD₃OD): δ 7.83 (d, J=7.4Hz, 2H),

7.43-7.58 (m, 3H), 4.49 (d, J=6.8Hz, 1H), 1.66-1.99 (m, 6H), 1.15-1.38 (m, 5H).

***N*-Benzoylated cyclohexylglycine amide:** mp 268-271; IR ν_{max} (KBr) 3370, 3297, 3191 (N-H), 1647, 1631 (C=O), $^1\text{H-NMR}$ (DMSO- d_6): δ 8.13 (d, J = 8.6 Hz, CONHPh), 7.89-7.44 (m, 6H, 5ArH and CONHH), 7.08 (s, 1H, CONHH), 4.29 (t, J = 8.1 Hz, CH), 1.79-1.63 (m, 6H), 1.15-0.99 (m, 5H); $^{13}\text{C-NMR}$ (DMSO- d_6) δ 171.9, 165.2, 133.2, 130.1, 127.1, 126.4, 56.9, 28.3, 27.5, 24.7, 24.4; MS (EI) m/z (%) 216 ([M-CONH₂]⁺, 56), 105 (PhCO⁺, 100).

3. HPLC analysis of α -amino acids **3** and amides **2**

The enantiomeric excesses of all amino acids and amides with an aromatic ring were measured with the Shmadzu LC-10AVP HPLC system using a CROWNPAK CR (+) column (150mm×4.6mm) at a flow rate of 1.0 ml/min, with H₂O-HClO₄ solution (pH=1.5-2.0) as the mobile phase. The enantioseparation of valine and its amide, cyclohexylglycine and its amide were performed through the HPLC analysis of their *N*-benzoylated derivatives using Chiralcel OD and OJ columns with hexane:2-propanol (9:1) as the mobile phase at a flow rate of 0.5/min.

Table S2. Retention times of the acids **3**.

Racemic amino acids 3	Retention Time (min)	Configuration (D or L)	Column
A	5.356	D	CROWNPAK CR (+)
	14.952	L	

b	10.340	D	CROWNPARK CR
	36.898	L	(+)
c	9.693	D	CROWNPARK CR
	22.574	L	(+)
d	7.735	D	CROWNPARK CR
	28.274	L	(+)
e	5.522	D	CROWNPARK CR
	9.537	L	(+)
f	4.757	D	CROWNPARK CR
	17.381	L	(+)
g	5.462	D	CROWNPARK CR
	13.566	L	(+)
h	4.352	D	CROWNPARK CR
	12.224	L	(+)
i^a	21.306	D	OJ
	30.658	L	
j^a	5.430	D	OJ
	7.155	L	
k	5.439	D	CROWNPARK CR
	6.893	L	(+)

^a The corresponding *N*-benzoylated acid.

Table S3. Retention times of **2**.

Racemic amide	Retention Time (min)	Configuration (D or L)	Column
2		L)	
a	2.528	D	CROWNPARK CR
	8.321	L	(+)
b	7.677	D	CROWNPARK CR
	34.142	L	(+)
c	5.680	D	CROWNPARK CR
	13.578	L	(+)
d	4.491	D	CROWNPARK CR
	14.896	L	(+)
c	6.413	D	CROWNPARK CR
	10.428	L	(+)
f	3.505	D	CROWNPARK CR
	13.418	L	(+)
g	3.829	D	CROWNPARK CR
	9.855	L	(+)
h	2.970	D	CROWNPARK CR
	7.704	L	(+)
i^a	18.374	L	OD
	20.842	D	
j^a	19.532	L	OD

	21.528	D	
k	4.028	D	CROWNPARK CR
	5.242	L	(+)

^a The corresponding *N*-benzoylated amino acid amide.

4. Results of the biotransformation of DL- α -amino amides 2.

Enzymatic hydrolysis of ($\pm$)-phenylglycine amide 2a

D-(-)-Phenylglycine amide **2a**: 2h (41%), $[\alpha]_D^{25}$ -104 (c 0.5, MeOH), ee 84% (HPLC).

L-(+)-Phenylglycine **3a**: 2h (51%), $[\alpha]_D^{25}$ +124 (c 0.5, 1NHCl), ee 85%, (HPLC).

Enzymatic hydrolysis of ($\pm$)-2-methoxyphenylglycine amide 2e

D-(-)-2-Methoxyphenylglycine amide **2e**: 9h (45%), $[\alpha]_D^{25}$ -52 (c 0.5, MeOH), ee 61%, (HPLC).

L-(+)-2-Methoxyphenylglycine **3e**: 9h (53%), $[\alpha]_D^{25}$ +104 (c 0.5, 1NHCl), ee 60%, (HPLC).

Enzymatic hydrolysis of ($\pm$)-4-methoxyphenylglycine amide 2f

D-(-)-4-Methoxyphenylglycine amide **2f**: 2h (46%), $[\alpha]_D^{25}$ -84 (c 0.5, MeOH), ee >99%, (HPLC).

L-(+)-4-Methoxyphenylglycine **3f**: 2h (53%), $[\alpha]_D^{25}$ +140 (c 0.5, 1NHCl), ee 90%,(HPLC).

Enzymatic hydrolysis of ($\pm$)-3-methoxyphenylglycine amide 2g

D-(-)-3-Methoxyphenylglycine amide **2g**: 2h (51%), $[\alpha]_D^{25}$ -48 (c 0.5, MeOH), ee 94% (HPLC).

L-(+)-3-Methoxyphenylglycine **3g**: 2h (47%), $[\alpha]_D^{25}$ +128 (c 0.5, 1NHCl), ee 95% (HPLC).

*Enzymatic hydrolysis of ($\pm$)-phenylalanine amide **2i***

D-(-)-Phenylalanine amide **2i**: 2h (43%), $[\alpha]_D^{25}$ -8 (c 1.0, MeOH), ee 87% (HPLC).

L-(-)-Phenylalanine **3i**: 2h (56%), $[\alpha]_D^{25}$ -4 (c 2.0 1NHCl), ee 60% (HPLC).

Reference

- (1) Hassan, N. A.; Bayer, E.; Jochims, J. C.; *J. Chem. Soc. Perkin Trans.1* **1998**, 3747-3757.