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Supporting Information

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Large Non-Linear Effect Between Enantiomeric Excess (*ee*) of Proline Solution and *Ee* of Proline Solid

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1) L-proline and D-proline, purchased from Watanabe Chem. Ind., Ltd. and TCI, respectively, were recrystallized from dry EtOH under an Ar atmosphere. The crystals were filtered under an Ar atmosphere and ground by mortar, also under an Ar atmosphere.
2) Chloroform, which was purchased from Aldrich (No. 472476 containing amylenes and free from EtOH), was distilled from CaH_2 just before to use.

Typical experimental procedure using 10% ee proline (Table S1, Entry 1)

To a mixture of 550 mg of L-proline and 450 mg of D-proline (combined *ee* 10%, L-isomer rich) was added a solution of $CHCl_3$ (20 mL) and EtOH (0.2 mL) at 0 °C, and the suspension was stirred for 24 h at the same temperature under an Ar atmosphere. After filtration of the suspension using filter paper removing particles over 1 μ, the volatile solvent was removed from the filtrate (18 mL) under reduced pressure to afford solid proline (61.4 mg). The *ee* of proline in solution was determined by chiral HPLC analysis after conversion to its *N*-carbobenzyloxyproline methyl ester. This experiment was performed several times and the results are summarized in Table S1.

The determination of ee was performed as follows:

To the above proline was added sat. $NaHCO_3$ solution (2 mL), THF (1 mL) and ZCl (50 μL) at room temperature, and the reaction mixture was stirred for 6 h at that temperature. The reaction mixture was diluted with Et_2O, and the aqueous layer was acidified by the addition of HCl solution (2 M) to pH 1. The organic materials were extracted with Et_2O, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure after filtration to give crude Z-proline, which was used directly in the next reaction without purification.

To the crude Z-proline was added a Et_2O solution of trimethylsilyl diazomethane (2 M, 0.1 mL) at room temperature. After stirring for 10 minutes, the solvent was removed in vacuo. Purification by preparative thin layer chromatography (ethyl acetate:hexane=1:3) gave Z-proline methylester.

Enantiomeric excess was determined to be >99%ee by HPLC analysis with a Chiralpak AD-H column (10:1 hexane:2-propanol), 1.0 mL/min; major enantiomer tr = 17.8 min, minor enantiomer tr =16.3 min.

Table S1. The relationship between the solubility and ee of the solution of 10% ee proline

entry	weight of proline in the filtrate [mg]	Solubility [g/L]	ee of proline in solution [%]
1[a]	61.4	3.1	94 (L)
2[a]	66.6	3.3	85 (L)
3[a]	46.1	2.3	85 (L)
4[a]	67.6	3.4	97 (L)
5[a]	43.7	2.2	98 (L)
6[a]	95.6	4.8	98 (L)
7[a]	64.5	3.2	88 (L)
8[a]	64.6	3.2	96 (L)
9[a]	39.2	3.9	99 (L)
10[a]	42.4	4.5	99 (D)
11[b]	44.6	2.2	91 (D)
12[b]	53.7	2.7	87 (D)
13[b]	45.9	2.3	92 (D)
14[b]	47.1	2.4	85 (D)
15[b]	47.5	2.4	93 (D)
16[b]	54.8	2.7	85 (D)
17[b]	54.4	2.7	85 (D)
18[b]	45.1	2.3	94 (D)

[a] L-proline (550 mg) and D-proline (450 mg) were employed. [b] L-proline (450 mg) and D-proline (550 mg) were employed.

Typical experimental procedure using 1% ee proline (Table S2, Entry 1)

To a mixture of 505 mg of L-proline and 495 mg of D-proline (combined *ee* 1.0%, L-isomer rich) was added a solution of $CHCl_3$ (20 mL) and EtOH (0.2 mL) at 0 °C, and the suspension was stirred for 24 h at the same temperature under an Ar atmosphere. After filtration of the suspension using filter paper removing particles over 1 μ, the volatile solvent was removed from the filtrate (18 mL) under reduced pressure, to afford solid proline (31.4 mg). The *ee* of proline in solution was determined by chiral HPLC analysis after conversion to its *N*-carbobenzyloxyproline methyl ester. This experiment was performed several times and the results are summarized in Table S2.

Table S2. The relationship between the solubility and ee of the solution of 1.0% ee proline[a]

entry	weight of proline in the filtrate [mg]	Solubility [g/L]	ee of proline in solution [%]
1	31.4	1.6	99 (L)
2	23.0	1.2	97 (L)
3	30.9	1.5	97 (L)
4	34.7	1.7	99 (L)
5	28.0	1.4	99 (L)
6	32.9	1.6	98 (L)
7	23.1	1.2	99 (L)
8	30.8	1.5	99 (L)

[a] L-proline (505 mg) and D-proline (495 mg) were employed. $CHCl_3$ (20 mL) and EtOH (0.2 mL) were used as solvent.

Typical experimental procedure using nearly racemic proline (<0.4% ee) (Table S3)

To a mixture of 250 ±1.0 mg of L-proline and 250±1 mg of D-proline (combined *ee* <0.4%) was added a solution of $CHCl_3$ (10 mL) and EtOH (0.1 mL) at 0 °C, and the suspension was stirred for 24 h at the same temperature under an Ar atmosphere. After filtration of the suspension using filter paper removing particles over 1 μ, the volatile solvent was removed from the filtrate under reduced pressure to afford solid proline. The *ee* of proline in solution was determined by chiral HPLC analysis after conversion to its *N*-carbobenzyloxyproline methyl ester. This experiment was performed several times and the results are summarized in Table S3.

Table S3. The relationship between the solubility and ee of the solution of proline (<0.4% ee)[a]

entry	weight of proline in the filtrate [mg]	Ee of proline in solution [%]
1	18.2	99 (L)
2	7.9	96 (L)
3	8.8	98 (L)
4	2.0	96 (L)
5	1.6	97 (L)
6	12.6	98 (L)
7	8.6	96 (L)
8	10.8	98 (L)
9	11.8	99(L)
10	12.4	99(L)
11	8.4	98(L)
12	4.8	96(L)
13	31.8	>99(D)
14	3.8	92(D)
15	12.7	97(L)
16	12.8	97(L)
17	3.0	95(L)
18	4.0	87(D)
19	4.2	96(D)
20	18.0	>99(D)
21	7.1	>99(D)
22	7.4	>99(D)
23	17.2	>99(D)
24	6.8	>99(D)
25	6.0	>99(D)
26	6.3	>99(D)
27	7.0	>99(D)
28	5.1	>99(D)
29	3.3	96(L)
30	17.6	>99(D)
31	2.3	91(D)
32	7.8	>99(D)
33	2.0	98(D)
34	12.1	>99(D)
35	57.8	>99(D)
36	7.2	>99(D)
37	21.3	99(D)
38	14.8	>99(L)

[a] L-proline (250.0±1.0 mg) and D-proline (250.0±1.0 mg) were employed. $CHCl_3$ (10 mL) and EtOH (0.1 mL) were used as solvent.

α-Aminoxylation of propanal using proline solution prepared from 10% ee.

A proline solution was prepared by the procedure described above by the filtration of the suspension prepared from L-proline (550 mg), D-proline (450 mg) in 20 mL of

$CHCl_3$ and EtOH 0.2 mL. A portion of this filtrate (5 mL) was transferred to the reaction flask and nitrosobenzene (428.4 mg, 4 mmol) and propanal (0.87 mL, 12 mmol) were added at 0 °C. After the reaction mixture had been stirred for 4 h at this temperature, MeOH (1 mL) and $NaBH_4$ (756.6 mg, 20 mmol) were added and the reaction mixture was stirred for 30 minutes at 0 °C. The reaction was quenched with pH 7.0 phosphate buffer solution and the organic materials were extracted with ethyl acetate three times and the combined organic extracts were dried over anhydrous Na_2SO_4, and concentrated in vacuo after filtration. Purification by silica gel column chromatography (ethyl acetate:hexane=1:10 ~ 1:3) gave (*R*)-2-anilinoxypropanol (648.8 mg, 3.88 mmol) 97% yield. The enaniomeric excess of the product was 96% as determined by chiral HPLC analysis. CHIRALPAK AD-H, iPrOH/hexane 1/10, 1.0 mL/min; major enantiomer tr = 19.4 min, minor enantiomer tr =17.6 min.

α-Aminoxylation of propanal using proline solid (10% ee).

To a $CHCl_3$ (5 mL) and EtOH (0.05 mL) suspension of L-proline (30.7 mg), D-proline (25.4 mg) and nitrosobenzene (428.4 mg, 4 mmol) was added propanal (0.87 mL, 12 mmol) at 0 °C. After stirring the reaction mixture for 4 h at this temperature, MeOH (1 mL) and $NaBH_4$ (756.6 mg, 20 mmol) were added and the reaction mixture was stirred for 30 minutes at 0 °C. The reaction was quenched with pH 7.0 phosphate buffer solution and the organic materials were extracted with ethyl acetate three times and the combined organic extracts were dried over anhydrous Na_2SO_4, and concentrated in vacuo after filtration. Purification by silica gel column chromatography (ethyl acetate:hexane=1:10 ~ 1:3) gave (*R*)-2-anilinoxypropanol (601.8 mg, 3.60 mmol) 90% yield. The enaniomeric excess of the product was 19% as determined by chiral HPLC analysis. CHIRALPAK AD-H, iPrOH/hexane 1/10, 1.0 mL/min; major enantiomer tr = 19.4 min, minor enantiomer tr =17.6 min.

XRD study (Table 1)

To a mixture of L-proline (2,265 mg) and D-proline (2,749 mg) were added $CHCl_3$ (100 mL) and EtOH (1 mL) at 0 °C and the reaction mixture was stirred at this temperature. After 10 minutes, 1 h, 6 h, and 12 h, 10 mL of the suspension was removed from the reaction mixture by syringe and this aliquot was filtered to give a solid. After drying the solid under reduced pressure, its DL-proline content was analyzed by power X-ray diffractometer (Rigaku RINT 2500).

XRD study (Table 2)

To L-proline (2,258 mg) were added $CHCl_3$ (100 mL) and EtOH (1 mL) at 0 °C and the reaction mixture was stirred for 6 h at this temperature. To this mixture was added D-proline (2,751 mg) in one portion. After 10 minutes, 1 h, 6 h, and 12 h, 10 mL of the suspension was removed from the reaction mixture by syringe and this aliquot was filtered to give a solid. After drying the solid under reduced pressure, its DL-proline content was analyzed by power X-ray diffractometer (Rigaku RINT 2500)..

DL-Proline was recrystallized from EtOH. A CIF file for DL-proline was deposited to the Cambridge Crystallographic Data Centre with the deposition number, CCDC 254728. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: +44(1223)336033; or deposit@ccdccam.ac.uk.