Supplementary Information

Chiral discrimination of α-hydroxy acids and N-Ts-α-amino acids induced by tetraaza macrocyclic chiral solvating agents by using ¹H NMR spectroscopy

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Procedure of synthesis of TAMCSA 1d.¹

To a solution of the chiral diimine (1.2 mmol) in dried THF (60 mL) was added activated zinc powder (0.78 g, 12 mmol) and MsOH (1.15g, 12 mmol) in dried THF (20 mL) under nitrogen atmosphere at -18°C. The mixture was stirred for 24h. The reaction mixture was basified to pH = 9 with saturated NaHCO₃ solution. The precipitate formed was filtered off and washed with CHCl₃. The organic layer was separated from filtrate. The water layer was extracted with CHCl₃ (15 mL × 3). The combined organic layer was dried over anhydrous Na₂SO₄. The solvent was removed under reduce pressure and the residue was purified by column chromatography on silica gel (petroleum / ethyl acetate = 3/2) to afford TAMCSA 1d in 23% yield. Meanwhile, the chiral diamine was also obtained as known chiral compound. R_f = 0.4, mp. 176-178°C, [α]_D²⁰ -26.8(c 0.03, THF), ¹H NMR (400 MHz, CDCl₃) δ: 1.14-1.19 (m, 2H), 1.28-1.31 (m, 2H), 1.67 (d, J = 8.5Hz, 2H), 2.02 (d, J = 15.9Hz, 2H), 4.00 (d, J = 9.1Hz, 2H), 4.37 (s, 2H), 4.67(s, 2H), 5.70 (d, J = 2.1Hz,2H), 3.39 (s, 6H), 6.62-6.65 (m, 4H), 6.88 (d, J = 8.8Hz, 2H), 7.31-7.32 (m, 6H), 7.49-7.51 (s, 4H), 9.60 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ: 24.4, 31.7, 53.2, 55.7, 62.0, 69.3, 113.1, 114.3, 117.8, 126.6, 127.5, 128.3, 128.5, 138.2, 148.9, 152.5, 173.3. IR (KBr) 3307, 2934, 1664, 1496, 699 cm⁻¹. HRMS(ES⁺): calcd for C₃₈H₄₃N₄O₆ (M+H)⁺ 651.3183, found 651.3173.
Table S1. Nonequivalent chemical shifts ($\Delta\Delta\delta$, ppm) and partial $^1$H NMR spectra of (±)-6-12 in the presence of TAMCSA 1c and overlapped proton of CH$_3$ group of (±)-6-9 in the presence of TAMCSAs 1a, 1b and 1d in CDCl$_3$ at room temperature.$^a$

<table>
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<tr>
<th>TAMCSA /Guest</th>
<th>Proton /$\Delta\Delta\delta$</th>
<th>Spectra</th>
<th>TAMCSA /Guest</th>
<th>Proton /$\Delta\Delta\delta$</th>
<th>Spectra</th>
<th>TAMCSA /Guest</th>
<th>Proton /$\Delta\Delta\delta$</th>
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<td><img src="image1" alt="Spectrum" /></td>
<td>1d/(±)-7</td>
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<td>1d/(±)-9</td>
<td>PhCH$_3$</td>
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<tr>
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<td>1c/(±)-8$^b$</td>
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<td>1c/(±)-9$^b$</td>
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<td><img src="image12" alt="Spectrum" /></td>
<td>PhCH$_3$</td>
<td></td>
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</tr>
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</table>

$^a$ Nonequivalent chemical shifts and $^1$H NMR spectra of (±)-6-13 (10 $\times$ 10$^{-3}$ M) in the presence of TAMCSAs 1a-1d, respectively, H:G = 1:1.

$^b$ Nonequivalent chemical shifts and $^1$H NMR spectra of Guests (5 $\times$ 10$^{-3}$ M), CDCl$_3$/CD$_3$OD (5%), H:G = 1:1.

The guests (±)-2-13 with TAMCSAs 1a-1d were separately dissolved in CDCl₃ with a concentration of 20 mM, respectively. Subsequently, TAMCSAs 1a-1d (0.25 mL) and a guest (0.25 mL) were added to a NMR tube, respectively. For some less soluble guests and hosts, a mixing deuterated solvent of CDCl₃/CD₃OD (5%) was used. The ¹H NMR spectra of all the samples were recorded on a 400 MHz spectrometer.

Determination of enantiomeric excesses.

To examine accuracy of determination for enantiomeric excess by ¹H NMR spectroscopy, the samples were prepared containing (R)-11 with 90, 80, 65, 45, 25, 0, -25, -45, -65, -80 and -90%ee in the presence of TAMCSA 1b (1:1) in CDCl₃, respectively. Their ¹H NMR spectra were recorded on a 400 MHz spectrometer.

Determination of the stoichiometry by ¹H NMR titrations (Job plots).

The samples of mandelic acid (±)-2 with TAMCSA 1b were dissolved in CDCl₃ with a concentration of 10 mM, respectively. The solutions were distributed among the nine NMR tubes, with the molar fractions X of (±)-2 in the resulting solutions from 0.1 to 0.9, with the total concentration 10 mM of (±)-2 with TAMCSA 1b. The ¹H NMR spectra of all samples were recorded on a 400 MHz spectrometer.
NMR spectra and HRMS of TAMCSA 1d.

Figure S1. $^1$H NMR spectrum of TAMCSA 1d in CDCl$_3$ (400 MHz).

Figure S2. $^1$H NMR spectrum of TAMCSA 1d in CDCl$_3$/D$_2$O(5%) (400 MHz).
Figure S3. $^{13}$C NMR spectrum of TAMCSA 1d in CDCl$_3$ (100 MHz).

Figure S4. HRMS spectrum of TAMCSA 1d.
Figure S5. NOESY spectrum of TAMCSA 1d.

$^1$H NMR spectra of discrimination of enantiomers of (±)-2-13.

Figure S6. $^1$H NMR spectrum of (±)-2 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
**Figure S7.** $^1$H NMR spectrum of (±)-2 with TAMCSA b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

**Figure S8.** $^1$H NMR spectrum of (±)-2 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.
Figure S9. $^1$H NMR spectrum of (±)-3 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.

Figure S10. $^1$H NMR spectrum of (±)-3 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.
Figure S11. $^1$H NMR spectrum of (±)-3 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S12. $^1$H NMR spectrum of (±)-4 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S13. $^1$H NMR spectrum of (±)-4 with TAMCSA 1b in CDCl₃ (400 MHz), [1b] = 10 mM.

Figure S14. $^1$H NMR spectrum of (±)-4 with TAMCSA 1d in CDCl₃ (400 MHz), [1d] = 10 mM.
Figure S15. $^1$H NMR spectrum of (±)-5 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.

Figure S16. $^1$H NMR spectrum of (±)-5 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.
Figure S17. $^1$H NMR spectrum of (±)-5 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S18. $^1$H NMR spectrum of (±)-6 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S19. $^1$H NMR spectrum of (±)-6 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

Figure S20. $^1$H NMR spectrum of (±)-6 with TAMCSA 1c in CDCl$_3$/CD$_3$OD (5%) (400 MHz), [1c] = 5 mM.
Figure S21. $^1$H NMR spectrum of (±)-6 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S22. $^1$H NMR spectrum of (±)-7 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S23. $^1$H NMR spectrum of (±)-7 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

Figure S24. $^1$H NMR spectrum of (±)-7 with TAMCSA 1c in CDCl$_3$ / CD$_3$OD (5%) (400 MHz), [1c] = 5 mM.
Figure S25. $^1$H NMR spectrum of (±)-7 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S26. $^1$H NMR spectrum of (±)-8 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S27. $^1$H NMR spectrum of (±)-8 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

Figure S28. $^1$H NMR spectrum of (±)-8 with TAMCSA 1c in CDCl$_3$/CD$_3$OD (5%) (400 MHz), [1c] = 5 mM.
Figure S29. $^1$H NMR spectrum of (±)-8 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S30. $^1$H NMR spectrum of (±)-9 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S3.1. $^1$H NMR spectrum of (±)-9 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

Figure S3.2. $^1$H NMR spectrum of (±)-9 with TAMCSA 1c in CDCl$_3$/CD$_3$OD (5%) (400 MHz), [1c] = 5 mM.
Figure S3. $^1$H NMR spectrum of (±)-9 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S34. $^1$H NMR spectrum of (±)-10 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S3. $^1$H NMR spectrum of (±)-10 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

Figure S36. $^1$H NMR spectrum of (±)-10 with TAMCSA 1c in CDCl$_3$/CD$_2$OD (5%) (400 MHz), [1c] = 5 mM.
Figure S37. $^1$H NMR spectrum of (±)-10 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S38. $^1$H NMR spectrum of (±)-11 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
**Figure S39.** $^1$H NMR spectrum of (±)-11 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

**Figure S40.** $^1$H NMR spectrum of (±)-11 with TAMCSA 1c in CDCl$_3$/CD$_3$OD (5%) (400 MHz), [1c] = 5 mM.
Figure S4.1. $^1$H NMR spectrum of (±)-11 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S4.2. $^1$H NMR spectrum of (±)-12 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S4.1. H NMR spectrum of (±)-12 with TAMCSA 1b in CDCl₃ (400 MHz), [1b] = 10 mM.

Figure S4.2. H NMR spectrum of (±)-12 with TAMCSA 1c in CDCl₃/CD₃OD (5%) (400 MHz), [1c] = 5 mM.
Figure S45. $^1$H NMR spectrum of (±)-12 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S46. $^1$H NMR spectrum of (±)-13 with TAMCSA 1a in CDCl$_3$ (400 MHz), [1a] = 10 mM.
Figure S4. 1H NMR spectrum of (±)-13 with TAMCSA 1b in CDCl$_3$ (400 MHz), [1b] = 10 mM.

Figure S47. 1H NMR spectrum of (±)-13 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.

Figure S48. 1H NMR spectrum of (±)-13 with TAMCSA 1d in CDCl$_3$ (400 MHz), [1d] = 10 mM.
$^1$H NMR spectra of enantiomeric excesses.

Figure S49. $^1$H NMR spectrum of (R)-11 and (S)-11 (-90 % ee) with TAMCSA 1b, [1b] = 5 mM.

Figure S50. $^1$H NMR spectrum of (R)-11 and (S)-11 (-80 % ee) with TAMCSA 1b, [1b] = 5 mM.
Figure S5. $^1$H NMR spectrum of (R)-11 and (S)-11 (-65 % ee) with TAMCSA 1b, [1b] = 5 mM.

Figure S52. $^1$H NMR spectrum of (R)-11 and (S)-11 (-45 % ee) with TAMCSA 1b, [1b] = 5 mM.
Figure S53. $^1$H NMR spectrum of (R)-11 and (S)-11 (-25 % ee) with TAMCSA 1b, [1b] = 5 mM.

Figure S54. $^1$H NMR spectrum of (R)-11 and (S)-11 (0 % ee) with TAMCSA 1b, [1b] = 5 mM.
Figure S5. $^1$H NMR spectrum of (R)-11 and (S)-11 (25 % ee) with TAMCSA 1b, [1b] = 5 mM.

Figure S5. $^1$H NMR spectrum of (R)-11 and (S)-11 (45 % ee) with TAMCSA 1b, [1b] = 5 mM.
Figure S5. $^1$H NMR spectrum of (R)-11 and (S)-11 (65 % ee) with TAMCSA 1b, [1b] = 5 mM.

Figure S58. $^1$H NMR spectrum of (R)-11 and (S)-11 (80 % ee) with TAMCSA 1b, [1b] = 5 mM.
Figure S59. $^1$H NMR spectrum of (R)-11 and (S)-11 (90 % ee) with TAMCSA 1b, [1b] = 5 mM.

References