Supplementary Information

Highly Sensitive Determination of Enantiomer Composition of Chiral Acids Based on Aggregation-Induced Emission

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Materials and Methods

Materials. All reagents and solvents were chemical pure (CP) grade or analytical reagent (AR) grade and were used as received otherwise indicated.

Measurements. ^{1}H NMR and ^{13}C NMR spectra were measured on a 400 MHz spectrometer at 298 K in $CDCl_3$. Absorption spectra were recorded on a UV–Vis spectrophotometer. Mass spectrum was measured on a FTMS instrument. Field emission scanning electron microscopy (FE-SEM) images were taken on an electron microscope operating at 5 kV or 10 kV. The suspension or solution of sample was dropped onto a slide and air-dried.

Fluorescent emission spectra were collected on a fluorophotometer at 298 K. The fluorescence spectrum was measured after the aggregation appeared and stood for 4 h. For measuring change of fluorescence intensity ratio with concentration, all samples in chloroform were standing for 24 h before their fluorescence was measured, but the samples in a mixed solvent of chloroform and hexane were standing for 4 h before measurement.

^{1}H NMR titration was carried out by addition of concentrated solution of one enatiomer of chiral acid **3** into the solution of (*1S,2R*)-**2** in $CDCl_3$. To keep constant concentration of (*1S,2R*)-**2** and account for dilution effects during titration, the solution of chiral acid was prepared with the solution of (*1S,2R*)-**2** at its initial concentration as a solvent. The association constants were calculated by nonlinearly curve fitting in Origin 6.1 using following equation (*Chem Eur J*. 1998, 4, 845):

$$\delta_{obs} = \delta_{\mathbf{H}} + \frac{([\mathbf{H}] + [\mathbf{G}] + 1/K_a) - \sqrt{([\mathbf{H}] + [\mathbf{G}] + 1/K_a)^2 - 4[\mathbf{H}][\mathbf{G}]}}{2[\mathbf{H}]} \cdot (\delta_{com} - \delta_{\mathbf{H}})$$

δ_{obs}: chemical shift of the methylene group connected to nitrogen in (*1S,2R*)-**2** after acid **3** was gradually added;

δ_{H}: chemical shift of the methylene group connected to nitrogen in (*1S,2R*)-**2** without addition of acid;

δ_{com}: chemical shift of the methylene group connected to nitrogen in (*1S,2R*)-**2** in (*1S,2R*)-**2**-**3** complex;

[H]: molar concentration of (*1S,2R*)-**2**;

[G]: molar concentration of acid added during titration.

Synthesis of (*1S,2R*)-2. To a flask was added **1** (230 mg, 0.40 mmol), (*1S,2R*)-2-amino-1,2-diphenylethanol (341 mg, 1.60 mmol), K_2CO_3 (111 mg, 0.80 mmol) and dry acetonitril (10 mL). The mixture was refluxed for about 7 h until **1** disappeared (monitored by TLC, ethylacetate/petroleum 1:5). After acetonitrile was removed by evaporation under reduced pressure, to the residue was added dichloromethane. The organic phase was washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness under reduced pressure. The crude product was purified by flash column chromatography (silica gel, dichloromethane/methanol 100:1) to give light yellow solid (*1S,2R*)-**2** (240 mg, 71%). Mp 217–219 ^{o}C; $[\alpha]^{20}_{D}$ +59 (*c* 1.3, THF); IR (KBr) ν 3456, 3318, 3079, 2924, 2854, 1603, 1508, 1424, 1237, 1048, 1059 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.25 (m, 6H), 7.23 – 7.21 (m, 6H), 7.18 – 7.15 (m, 4H), 7.13 – 7.07 (m, 10H), 7.03 – 7.00 (m, 4H), 6.90 (d, J = 8.8 Hz, 4H), 6.52 (d, J = 8.4 Hz, 4H), 4.85 (d, J = 5.6 Hz, 2H), 3.92 (d, J = 5.6 Hz, 2H), 3.89 – 3.87 (m, 4H), 2.85 – 2.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 144.2, 140.4, 140.0, 139.4, 138.8, 136.6, 132.5, 131.4, 128.4, 128.2, 128.1, 127.7, 127.6, 126.8,

126.1, 113.6, 68.6, 66.8, 46.2; ESI-MS *m/z* calcd for $C_{58}H_{54}N_2O_4$ 842 [M], Found 843 $[(M+1)]^+$. Anal. Calcd for $C_{58}H_{54}N_2O_4$: C, 82.63; H, 6.46; N, 3.32. Found: C, 82.60; H, 6.47; N, 3.36.

Synthesis of (*1R,2S*)-2. (*1R,2S*)-**2** was prepared in the same procedure as that for (*1S,2R*)-**2**. Mp 216−218 °C; $[\alpha]^{20}_D$ −58 (*c* 1.0, THF); IR (KBr) ν 3447, 3319, 3060, 2926, 2858, 1604, 1508, 1424, 1239, 1048, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 12H), 7.18 – 7.16 (m, 4H), 7.14 – 7.09 (m, 10H), 7.03 – 7.01 (m, 4H), 6.90 (d, J = 8.8 Hz, 4H), 6.52 (d, J = 8.4 Hz, 4H), 4.82 (d, J = 5.6 Hz, 2H), 3.92 (d, J = 5.6 Hz, 2H), 3.88 – 3.83 (m, 4H), 2.87 – 2.74 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 144.2, 140.4, 140.0, 139.3 139.1, 136.6, 132.5, 131.4, 128.3, 128.2, 128.1, 127.8, 127.7, 126.8, 126.1, 113.6, 68.6, 66.9, 46.3; ESI-MS *m/z* calcd for $C_{58}H_{54}N_2O_4$ 842 [M], Found 843 $[(M+1)]^+$. Anal. Calcd for $C_{58}H_{54}N_2O_4$: C, 82.63; H, 6.46; N, 3.32. Found: C, 82.69; H, 6.49; N, 3.35.

Supporting Figures

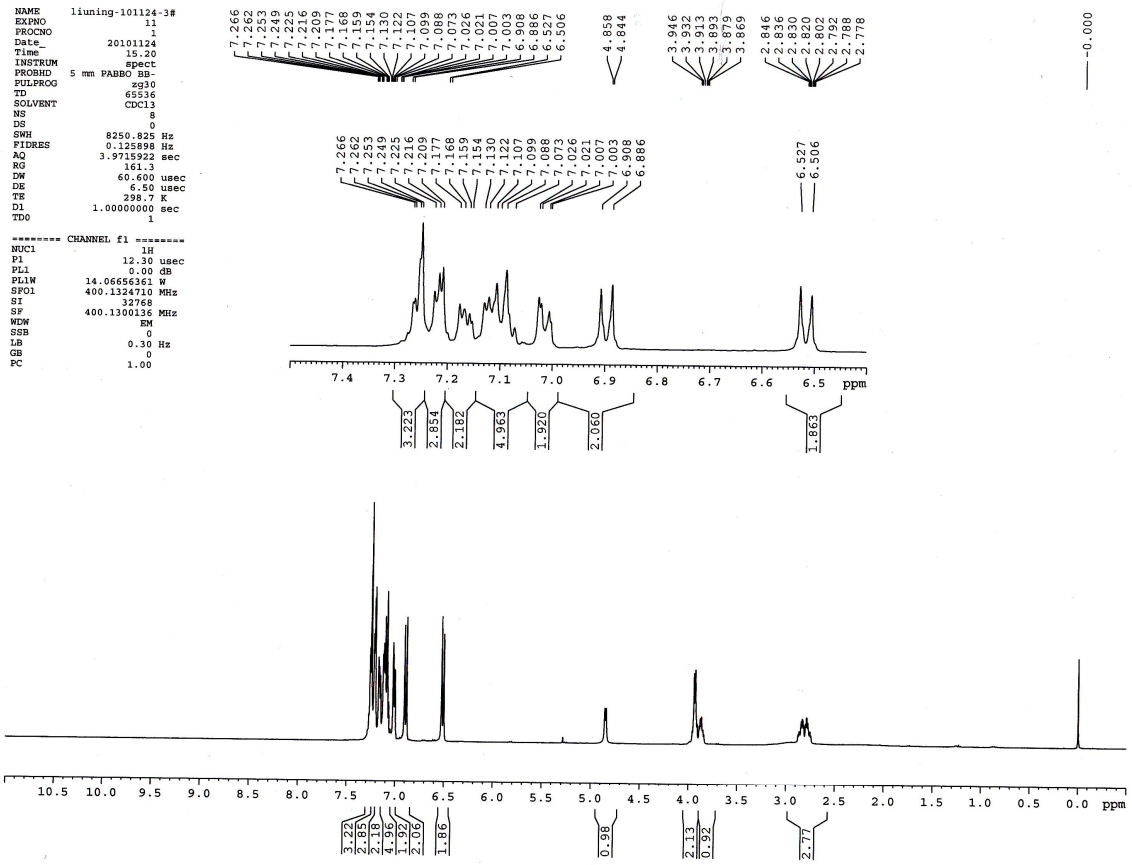

Figure S1. ^{1}H NMR of (*1S,2R*)-**2** in $CDCl_3$.

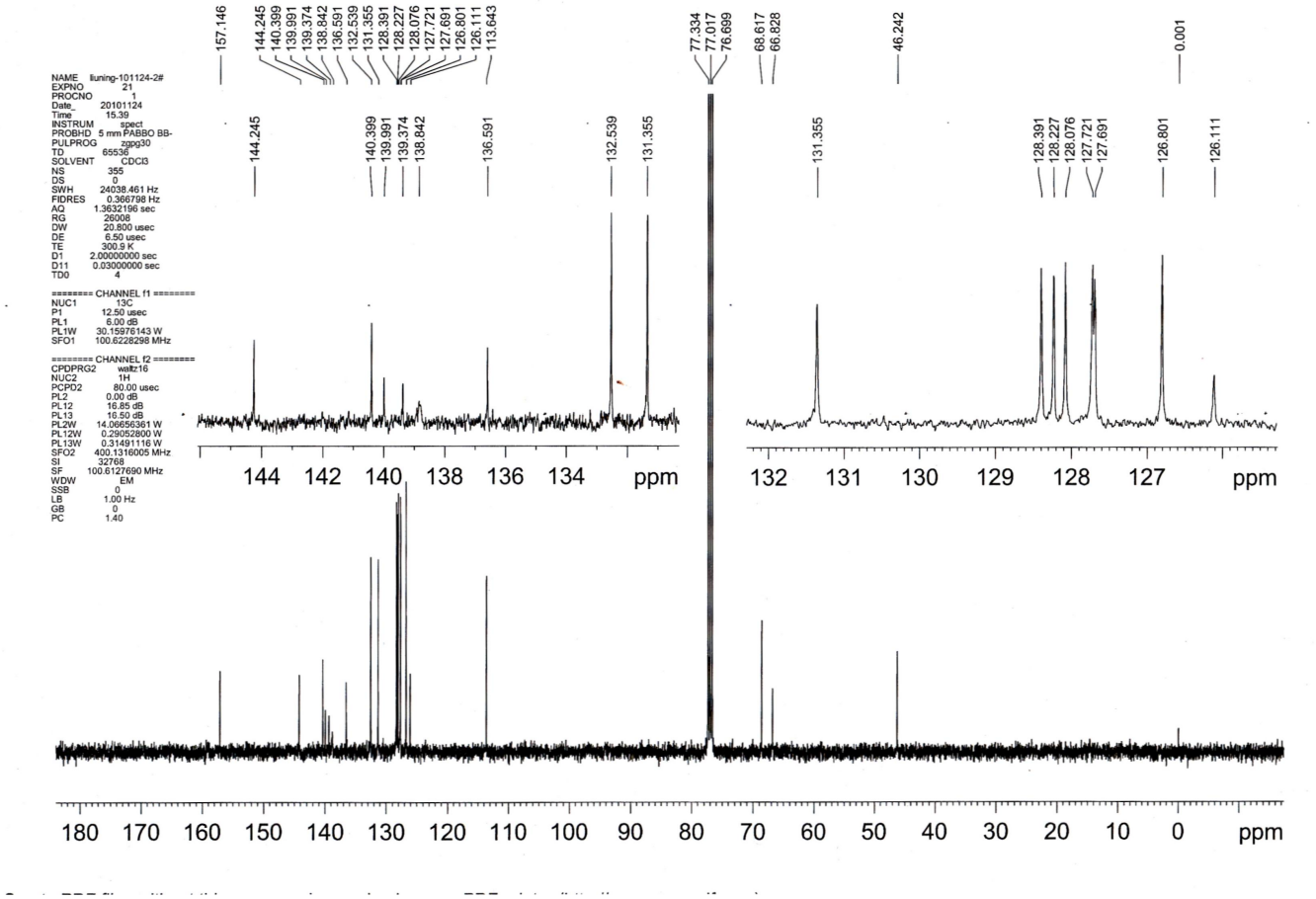

Figure S2. ^{13}C NMR of (*1S,2R*)-**2** in $CDCl_3$.

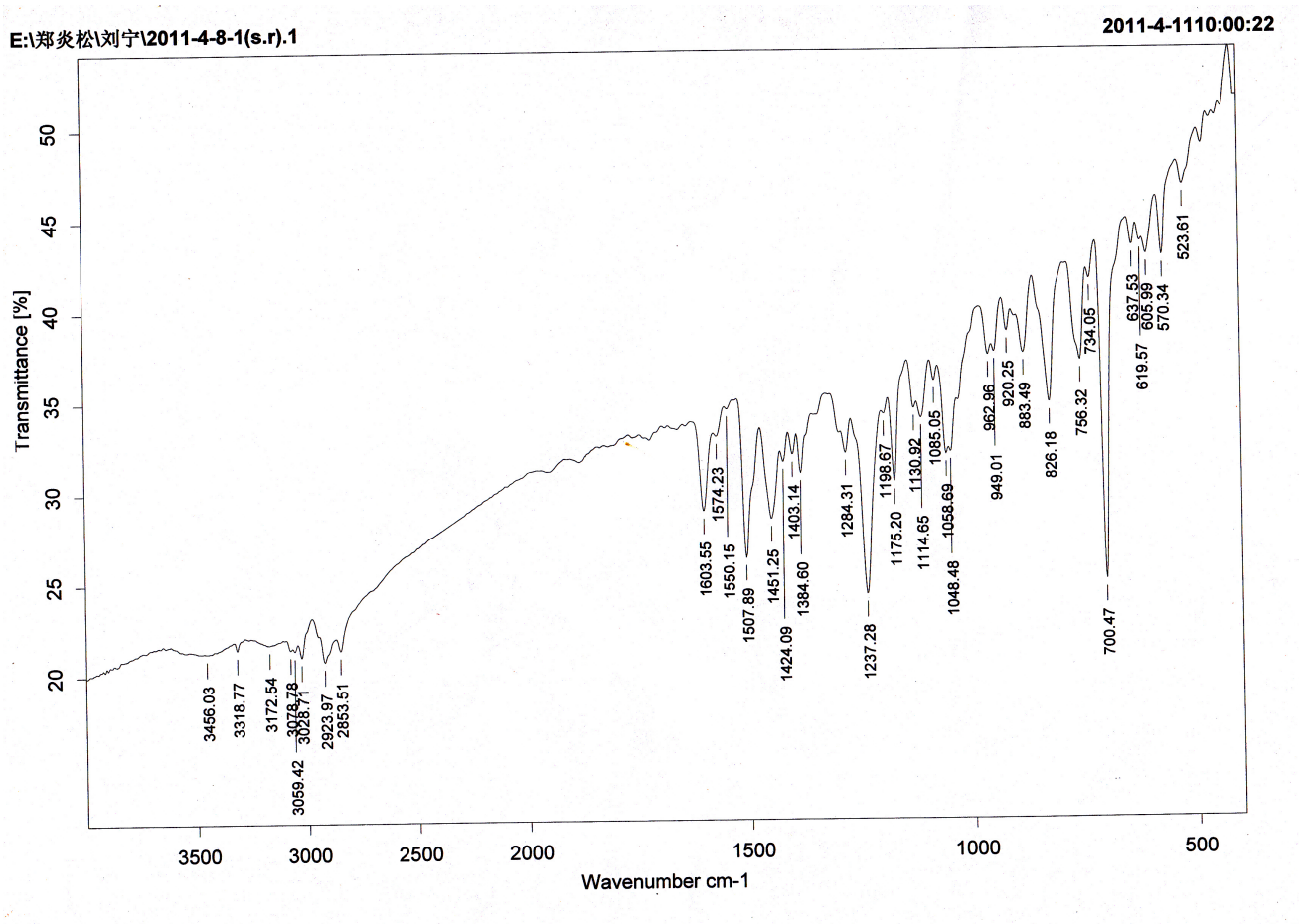

Figure S3. IR spectrum of (*1S,2R*)-**2**.

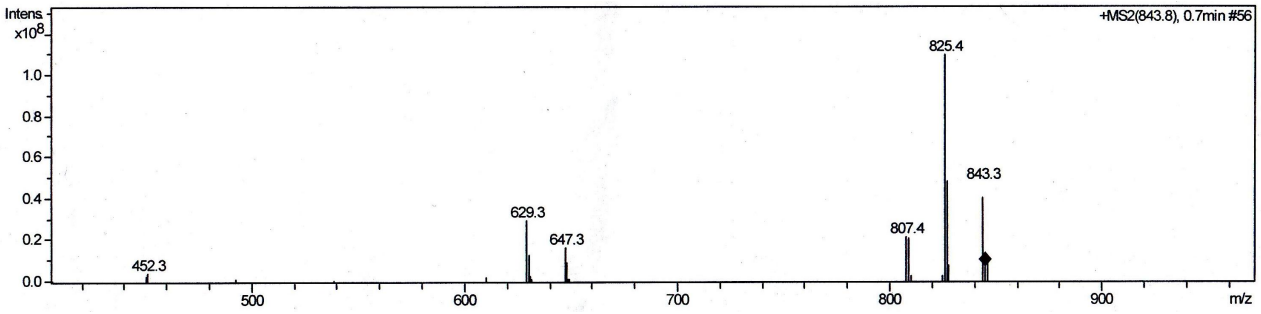

Figure S4. MS spectrum of (*1S,2R*)-**2**.

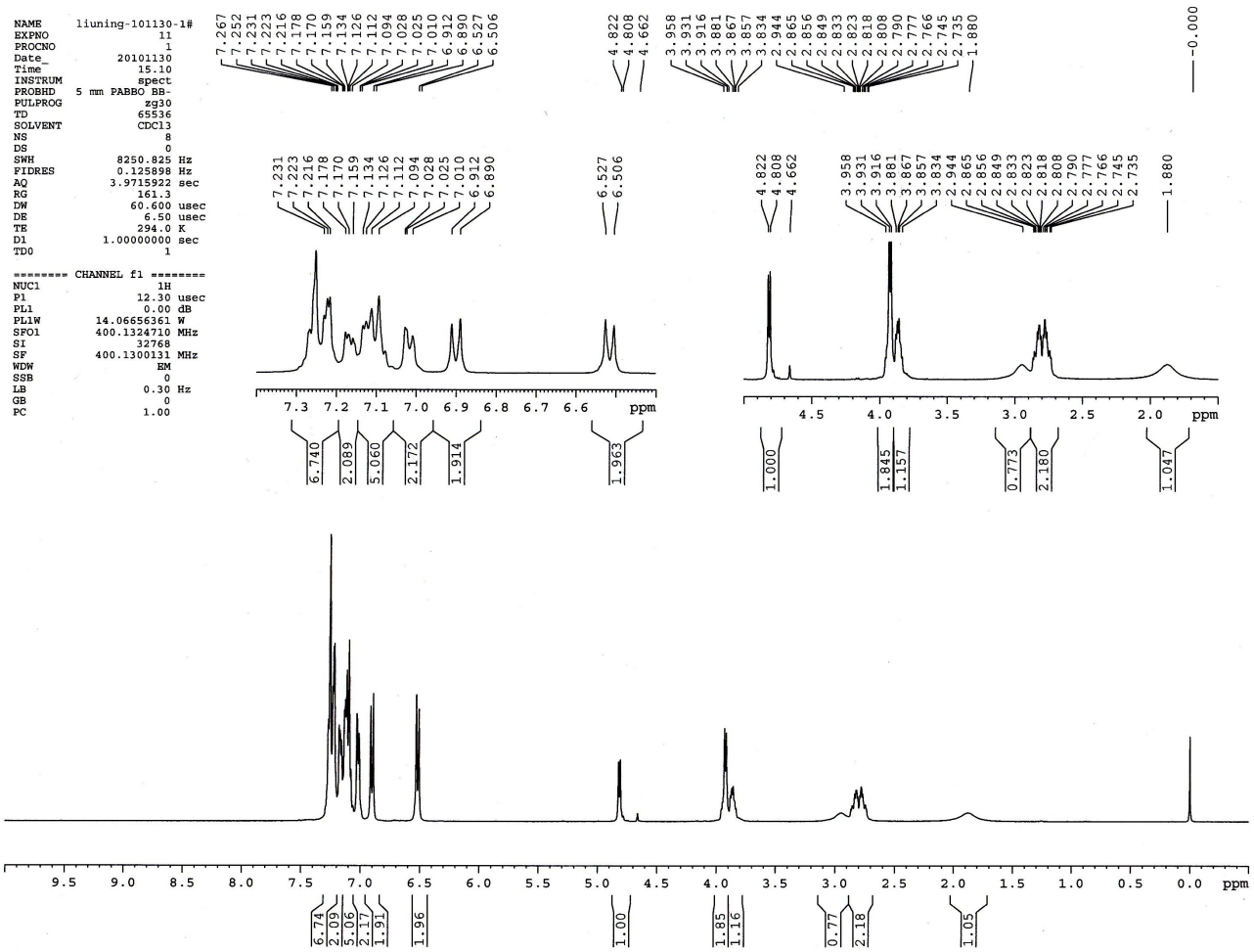

Figure S5. ^{1}H NMR of (*1R,2S*)-**2** in $CDCl_3$.

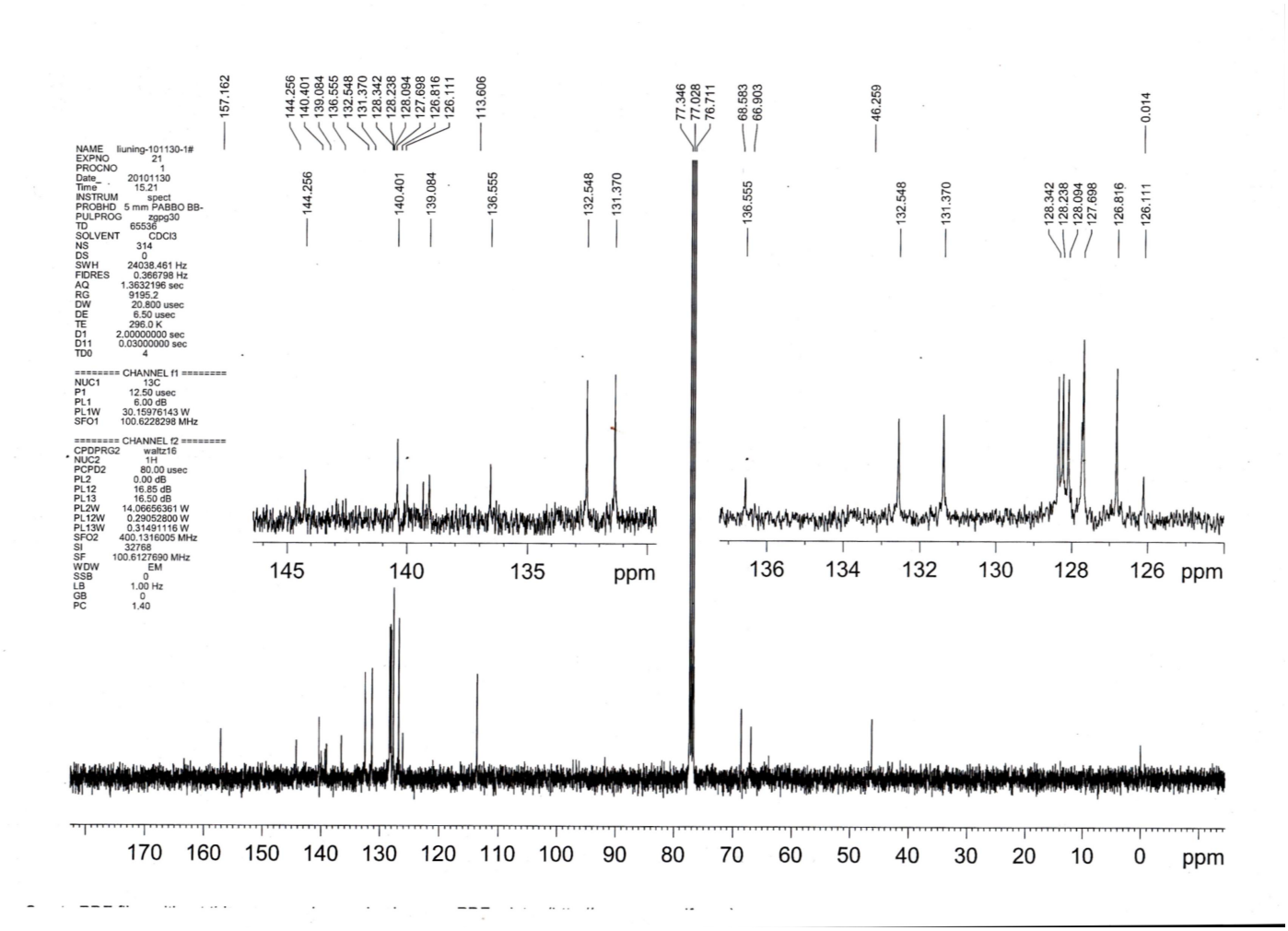

Figure S6. ^{13}C NMR of (*1R,2S*)-**2** in $CDCl_3$.

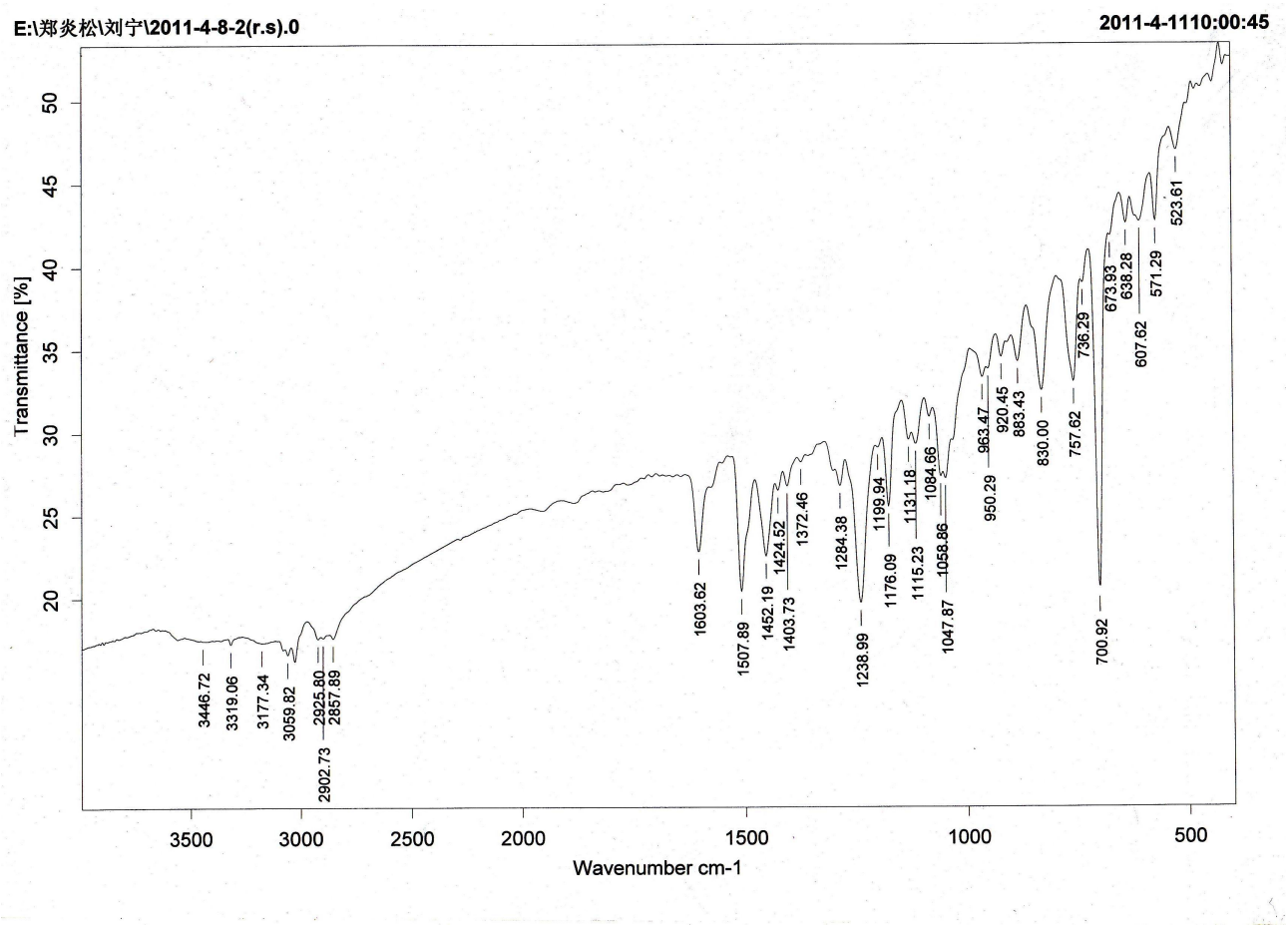

Figure S7. IR spectrum of (*1R,2S*)-**2**.

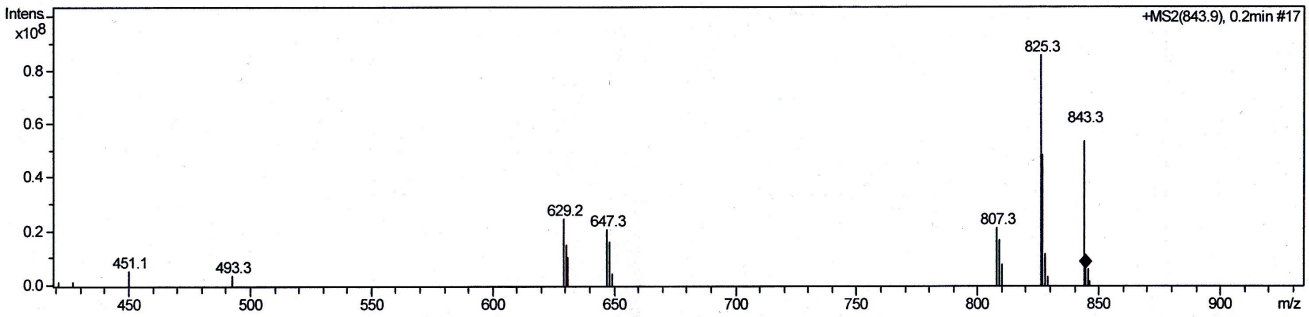

Figure S8. MS spectrum of (*1R,2S*)-**2**.

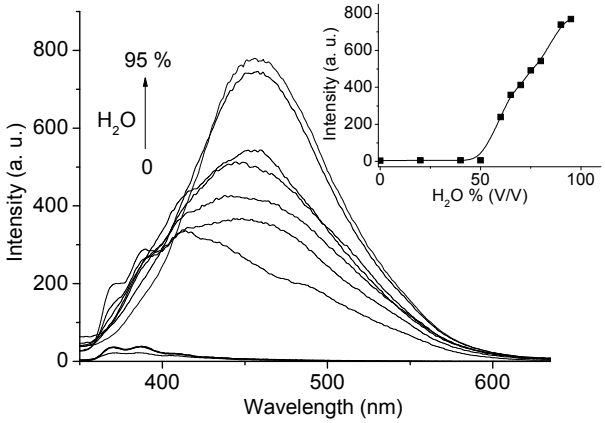

Figure S9. Change of fluorescence spectra of (*1S,2R*)-**2** (1.0×10^{-4} M) with content of H_2O in THF. λ_{ex} = 323 nm, ex/em slits = 5/3 nm. Inset, curve of fluorescence intensity at λ_{max} = 460 nm vs percentage of H_2O.

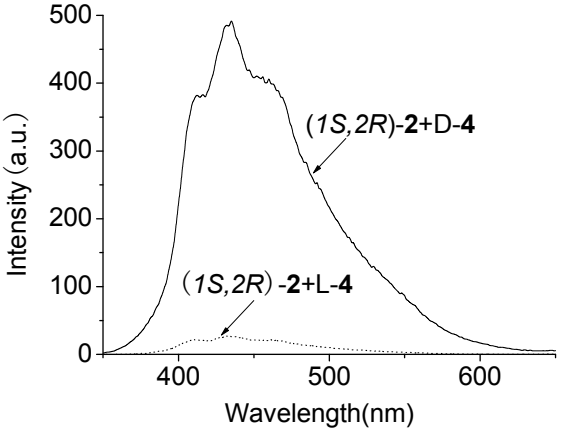

Figure S10. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of 2,3-dibenzoyltartaric acid **4** in chloroform. [(*1S,2R*)-**2**] = [**4**] = 5.0×10^{-4} M, λ_{ex} = 323 nm, ex/em slits = 10/10 nm.

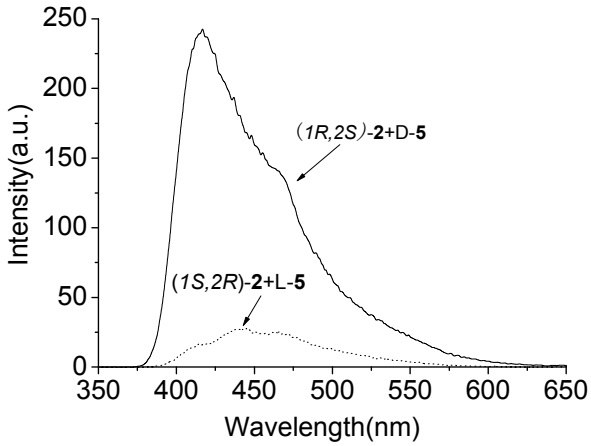

Figure S11. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of malic acid **5** in water and THF (volume ratio 2 : 1). [(*1S,2R*)-**2**] = [**5**] = 4×10^{-3} M, λ_{ex} = 323 nm, ex/em slits = 10/10 nm.

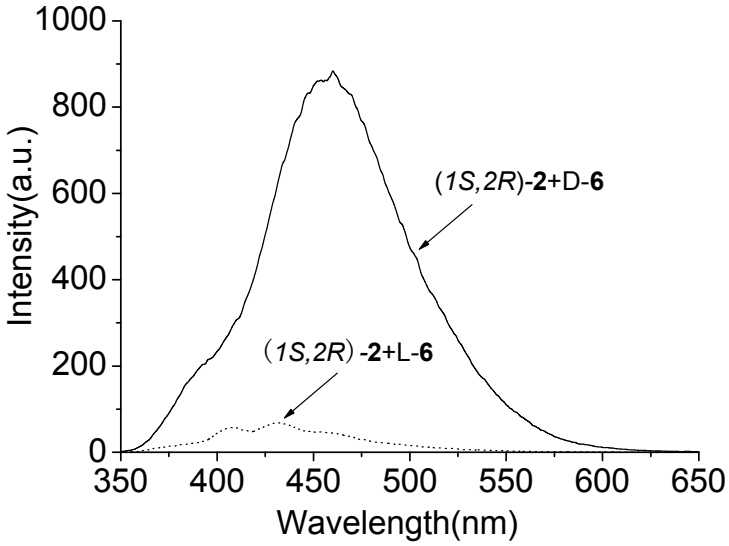

Figure S12. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of N-Boc-glumatic acid **6** in water and THF (volume ratio 7 : 13). [(*1S,2R*)-**2**] = [**6**] = 2.5×10^{-4} M, λ_{ex} = 323 nm, ex/em slits = 10/10 nm.

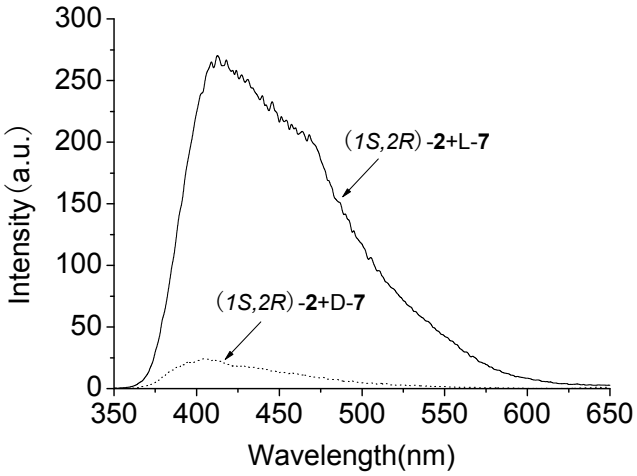

Figure S13. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of N-Cbz-aspartic acid **7** in water and THF (volume ratio 4 : 5). [(*1S,2R*)-**2**] = [**7**] = 1.6×10^{-3} M, λ_{ex} = 323 nm, ex/em slits = 10/10 nm.

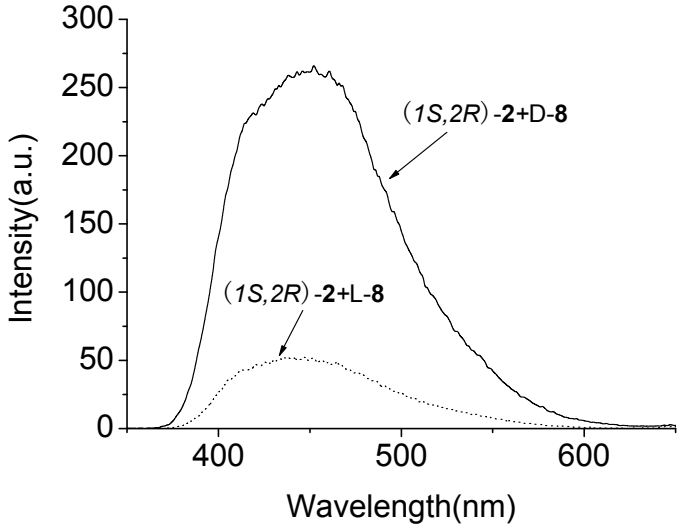

Figure S14. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of N-Boc-serine **8** in 1,2-dichloroethane. [(*1S,2R*)-**2**] = [**8**] = 2.5×10^{-3} M, λ_{ex} = 323 nm, ex/em slits = 15/15 nm.

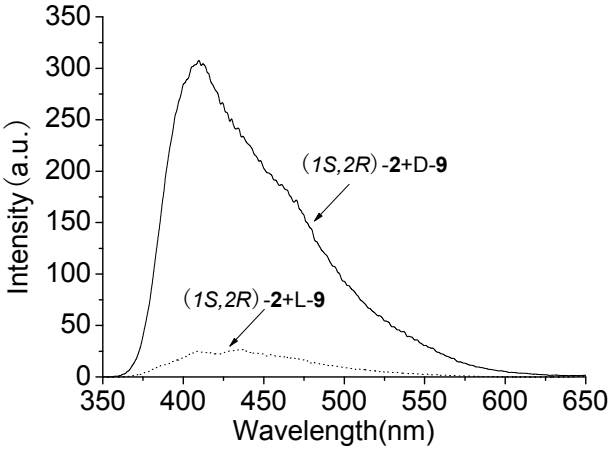

Figure S15. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of pyroglumatic acid **9** in water and THF (volume ratio 1 : 1). 2× [(*1S,2R*)-**2**] = [**9**] = 2.5×10^{-3} M, λ_{ex} = 323 nm, ex/em slits = 10/10 nm.

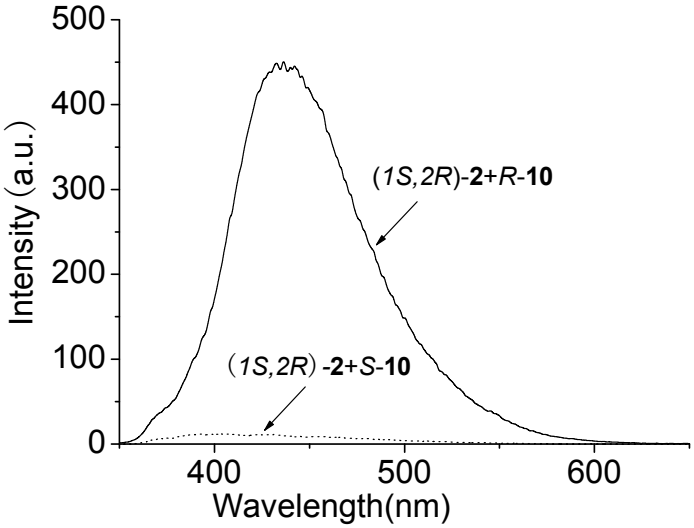

Figure S16. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of mandelic acid **10** in 1,2-dichloroethane and hexane (volume ratio 1 : 1). [(*1S,2R*)-**2**] = [**10**] = 2.5×10^{-4} M, λ_{ex} = 323 nm, ex/em slits = 10/5 nm.

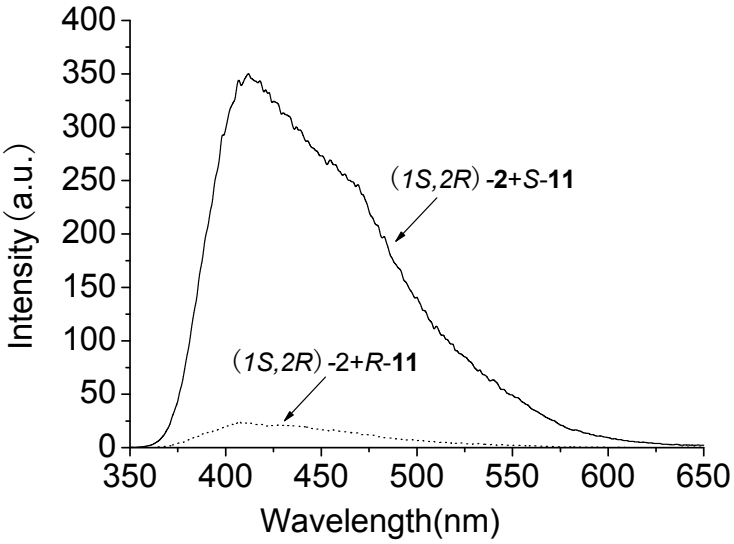

Figure S17. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of 2-chloromandelic acid **11** in water and THF (volume ratio 1 : 1). [(*1S,2R*)-**2**] = [**11**] = 1.25×10^{-3} M, λ_{ex} = 323 nm, ex/em slits = 10/15 nm.

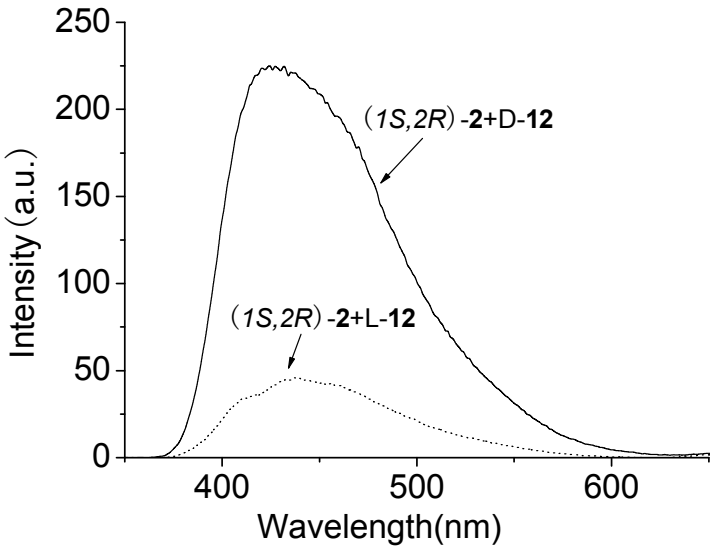

Figure S18. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of camphorsulfonic acid **12** in 1,2-dichloroethane. [(*1S,2R*)-**2**] = [**12**] = 2.5×10^{-3} M, λ_{ex} = 323 nm, ex/em slits = 15/15 nm.

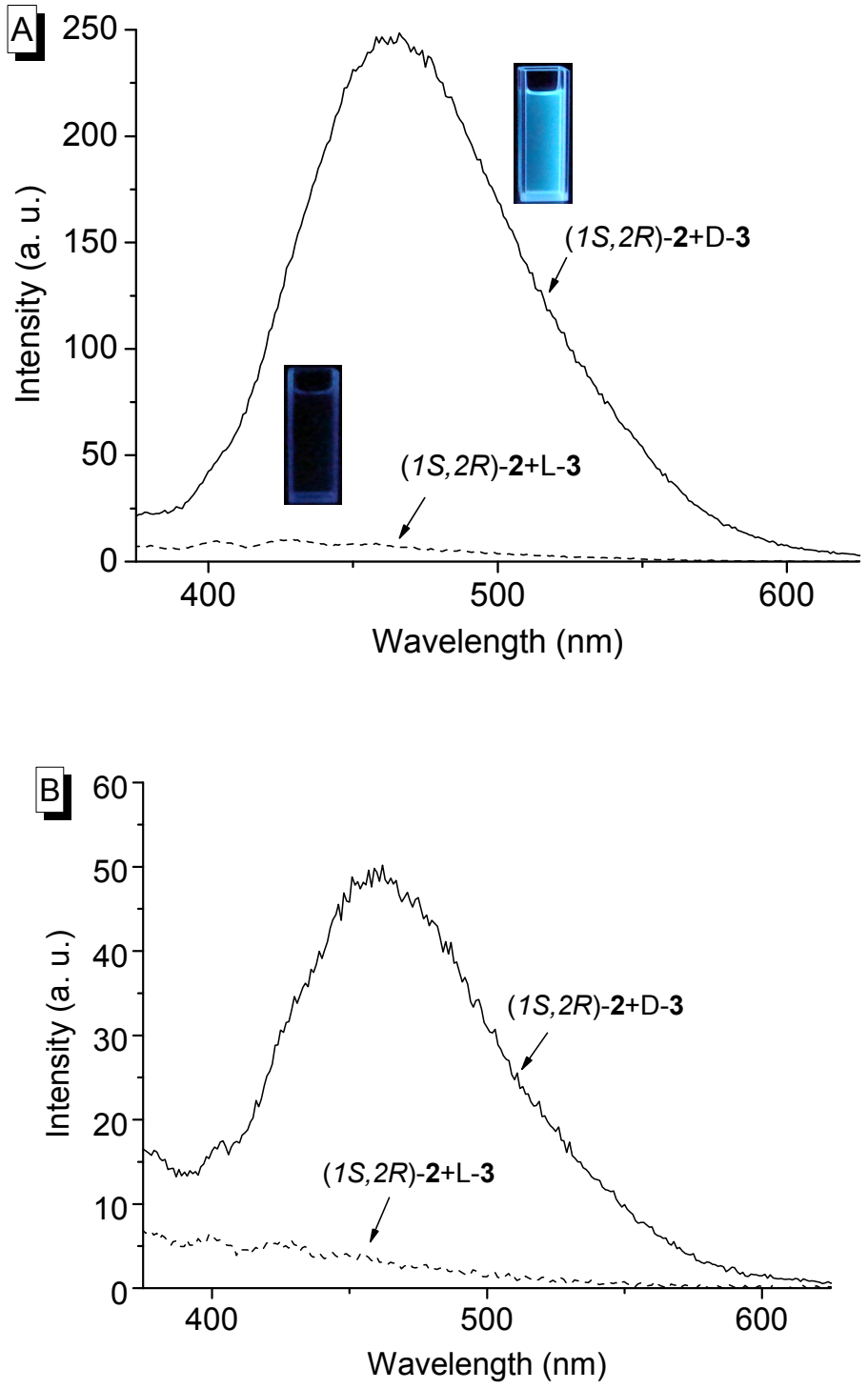

Figure S19. Fluorescence spectra of a mixture of (*1S,2R*)-**2** and enantiomers of 2,3-di(*p*-toluoyl)tartaric acid **3** (A) in chloroform/hexane 1:2 ([(*1S,2R*)-**2**] = [**3**] = 3.0×10^{-5} M; inset: fluorescence photos) and (B) in chloroform/hexane 1:4 ([(*1S,2R*)-**2**] = [**3**] = 3.0×10^{-6} M). λ_{ex} = 323 nm, ex/em slits = 5/3 nm

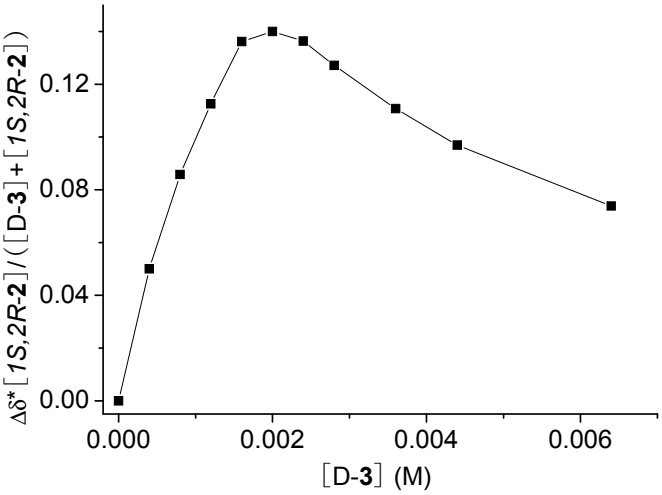

Figure S20. Job plot for ^{1}H NMR titration of (*1S,2R*)-**2** (0.002 M) with D-**3** in $CDCl_3$.

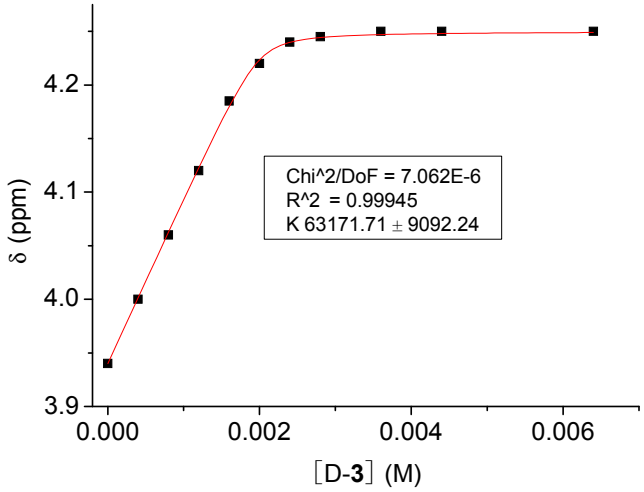

Figure S21. Chemical shift of (*1S,2R*)-**2** (0.002 M) with concentration of D-**3** added. The red curve is the result by fitting.

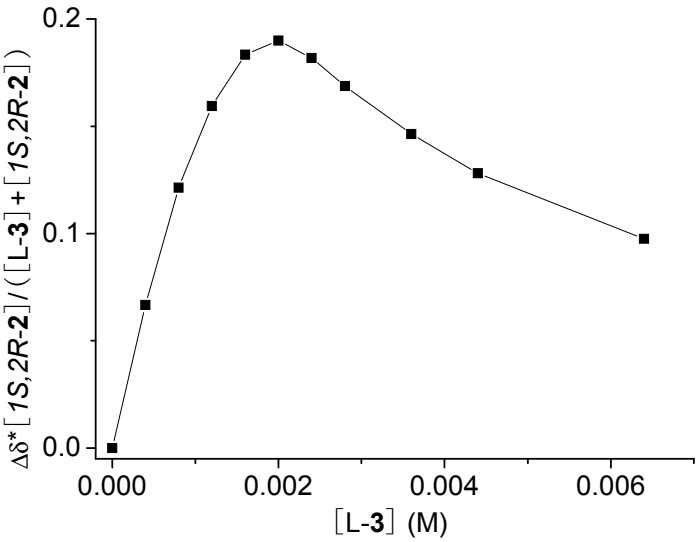

Figure S22. Job plot for ^{1}H NMR titration of (*1S,2R*)-**2** (0.002 M) with L-**3** in $CDCl_3$.

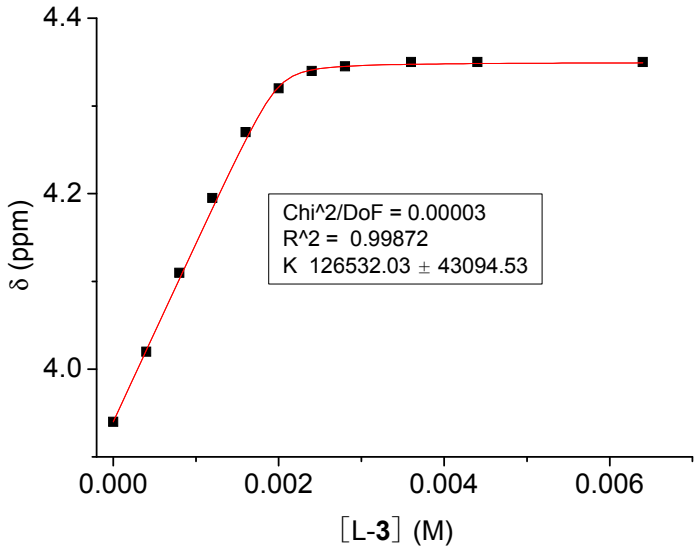

Figure S23. Chemical shift of (*1S,2R*)-**2** (0.002 M) with concentration of L-**3** added. The red curve is the result by fitting.

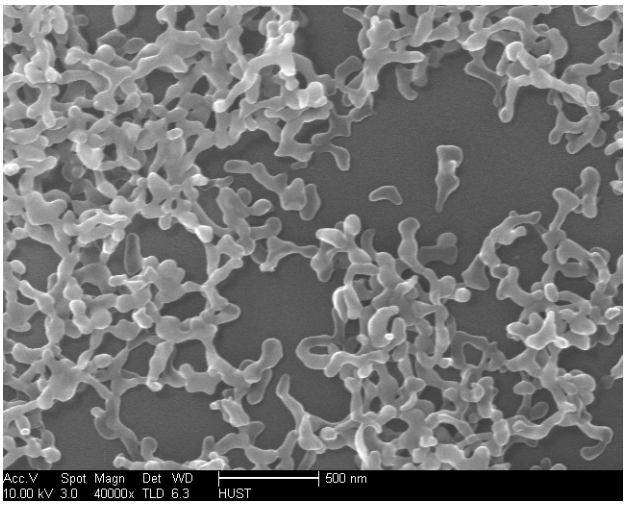

Figure S24. FE-SEM image of suspension of (*1S,2R*)-**2** and D-**3** in chloroform/hexane 1:2 V/V ([(*1S,2R*)-**2**] = [D-**3**] = 3.3×10^{-5}M).

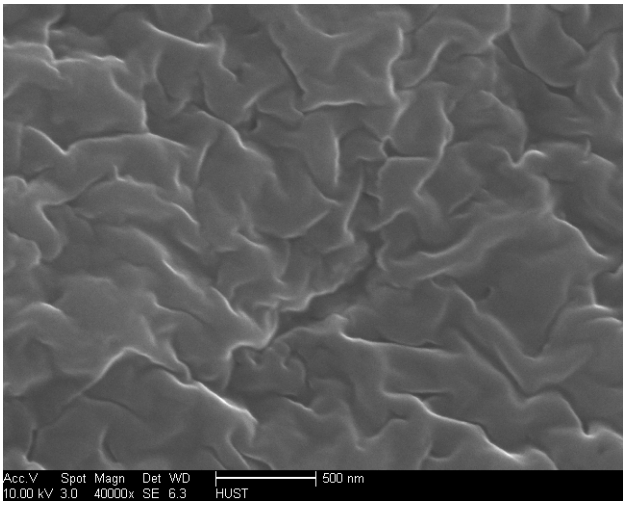

Figure S25. FE-SEM image of solution of (*1S,2R*)-**2** and L-**3** in chloroform/hexane 1:2 V/V ([(*1S,2R*)-**2**] = [L-**3**] = 3.3×10^{-5}M).

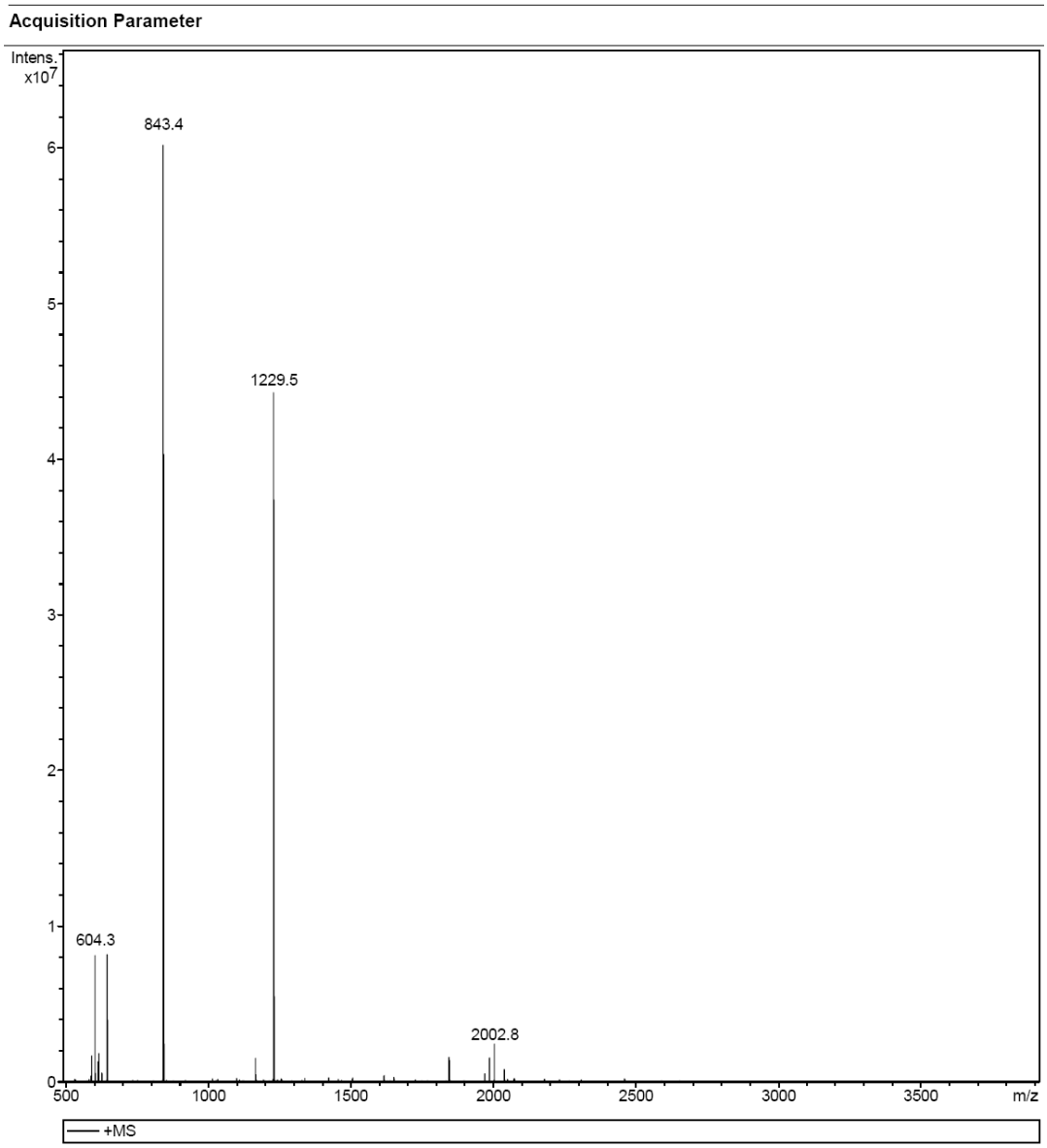

Figure S26. Mass spectrum of mixture of (*1S,2R*)-**2**.and L-**3** in chloroform. Measured on a Bruker APEXIII 7.0T FTMS instrument under the ESI positive scan mode from 500 – 4000.

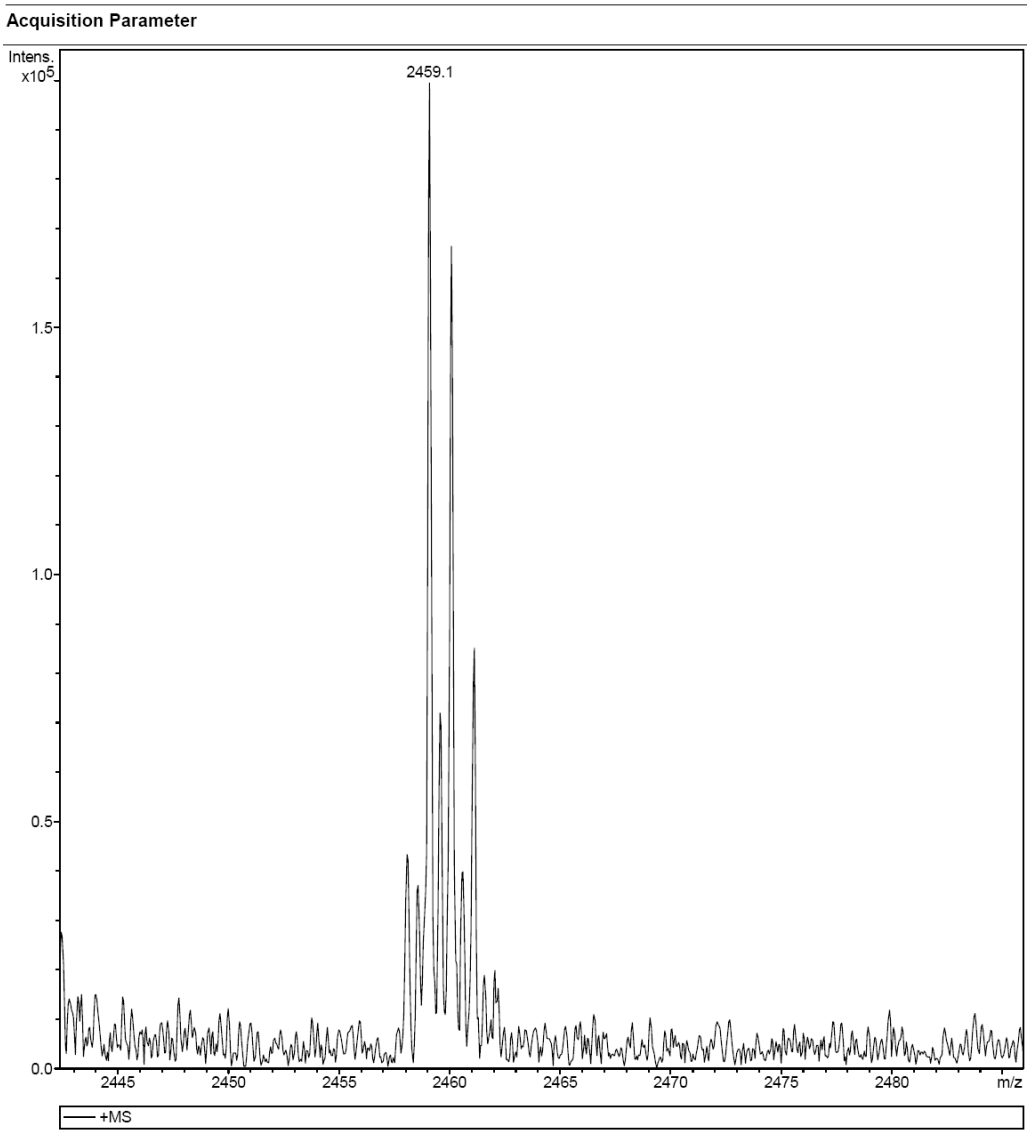

Figure S27. Mass spectrum of mixture of (*1S,2R*)-**2**.and L-**3** in chloroform. Measured on a Bruker APEXIII 7.0T FTMS instrument under the ESI positive scan mode from 500 – 4000.

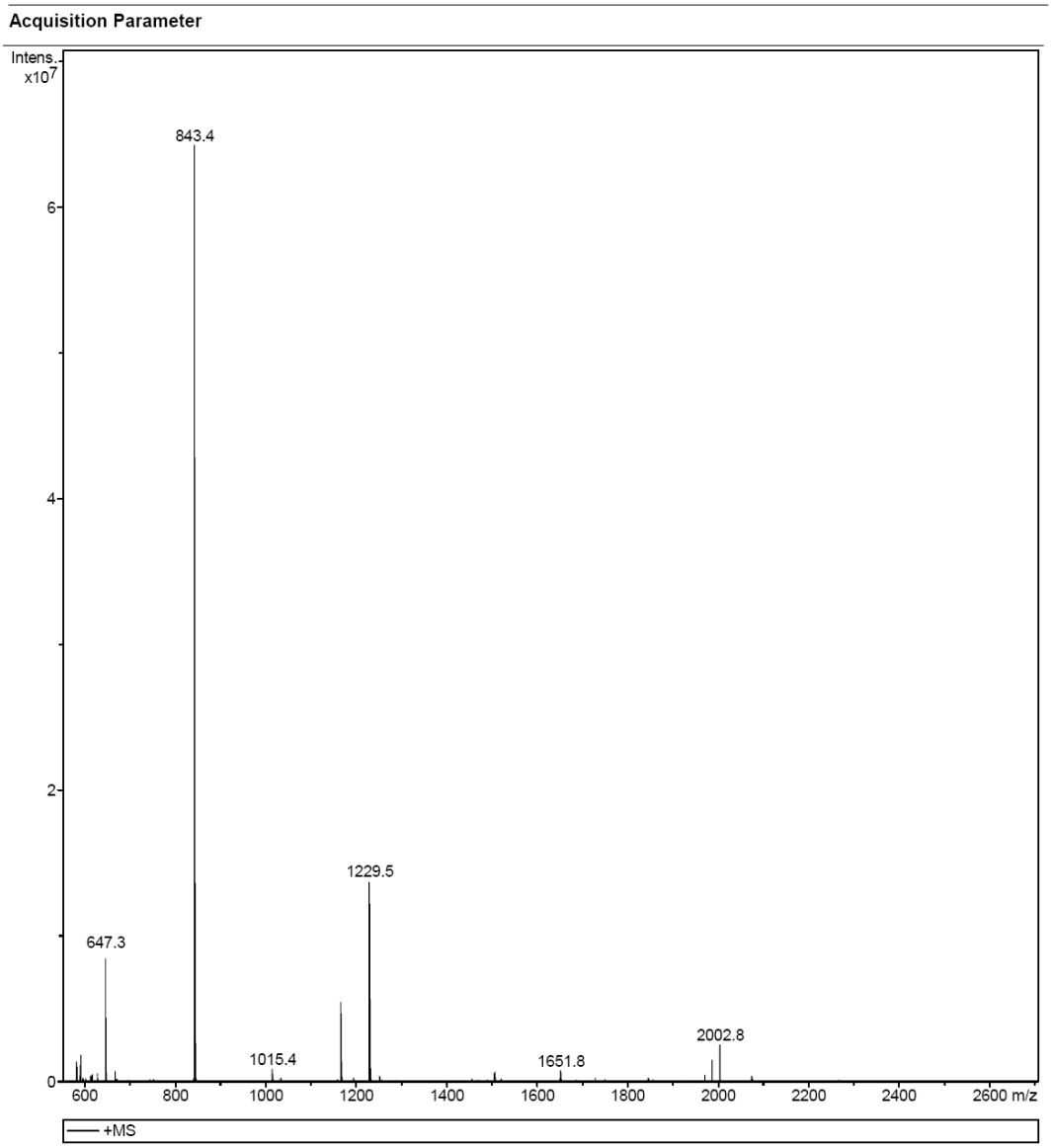

Figure S28. Mass spectrum of mixture of (*1S,2R*)-**2**.and D-**3** in chloroform. Measured on a Bruker APEXIII 7.0T FTMS instrument under the ESI positive scan mode from 500 – 4000.

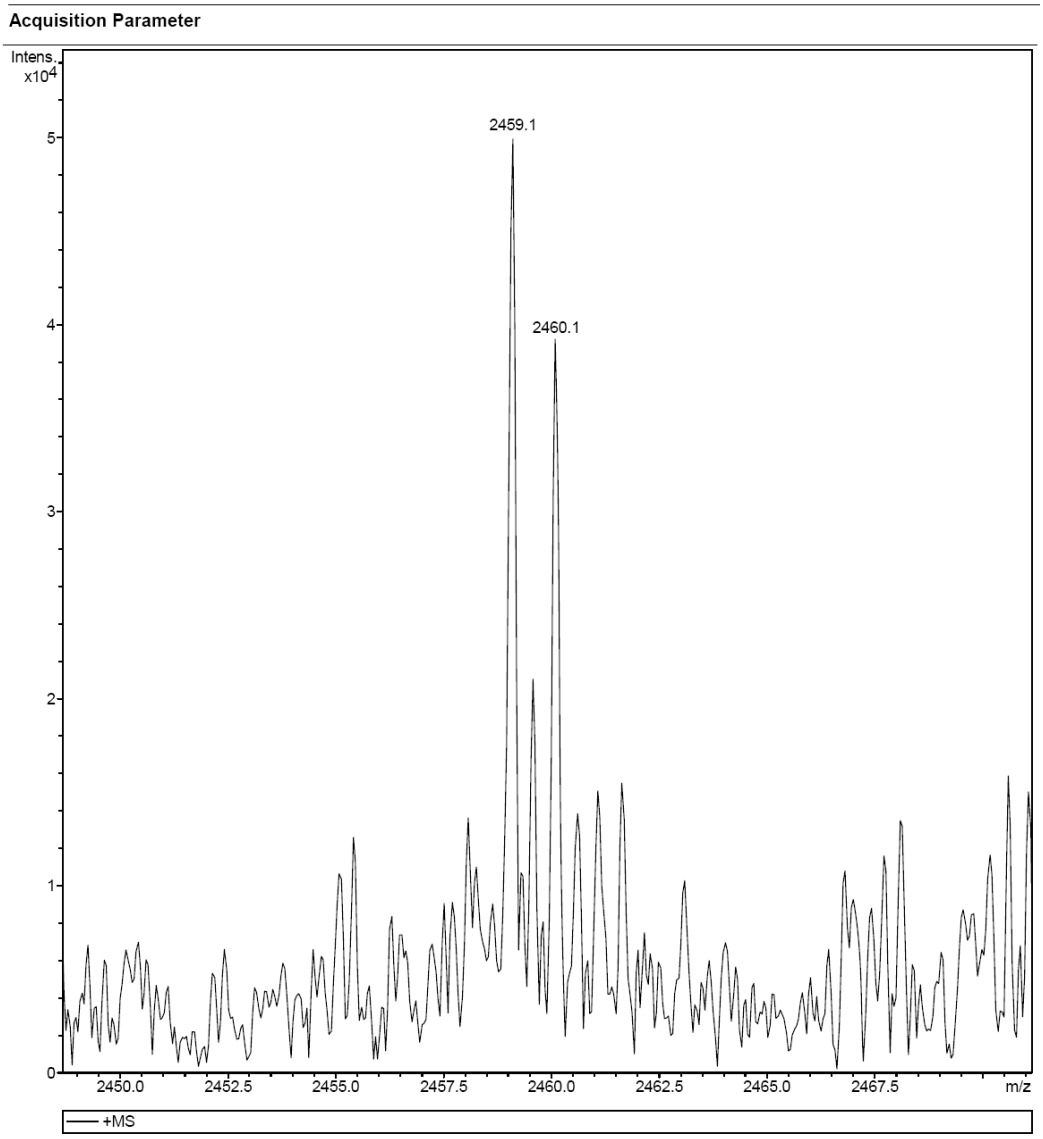

Figure S29. Mass spectrum of mixture of (*1S,2R*)-**2**.and D-**3** in chloroform. Measured on a Bruker APEXIII 7.0T FTMS instrument under the ESI positive scan mode from 500 – 4000.

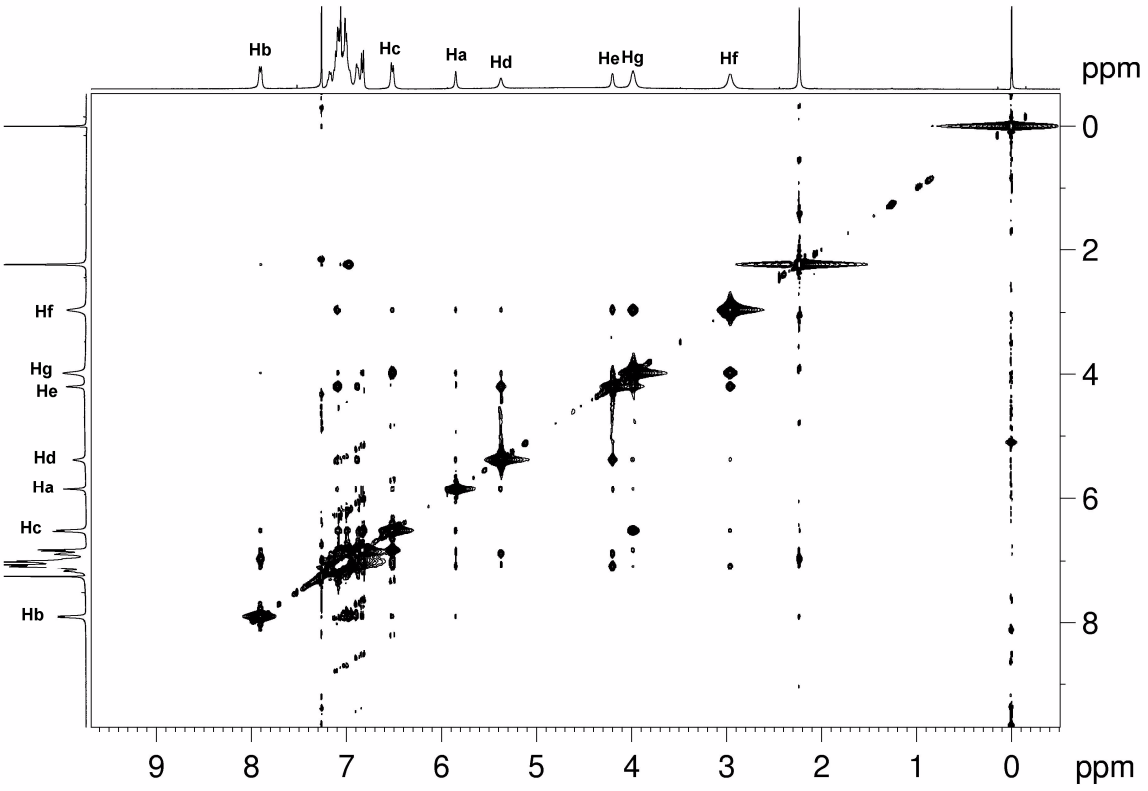

Figure S30. 2D NOESY spectrum of a 1:1 mixture of mixture of (*1S,2R*)-**2** and D-**3** (measured by a 400 MHz instrument over 12 h, 5 mM in $CDCl_3$ at 25°C).

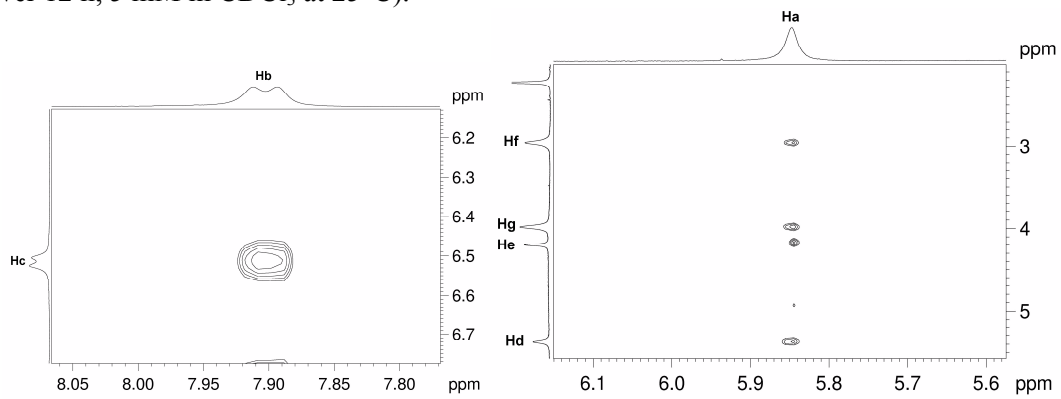

Figure S31. Portions of 2D NOESY spectrum of a 1:1 mixture of mixture of (*1S,2R*)-**2** and D-**3** (measured by a 400 MHz instrument over 12 h, 5 mM in $CDCl_3$ at 25°C).

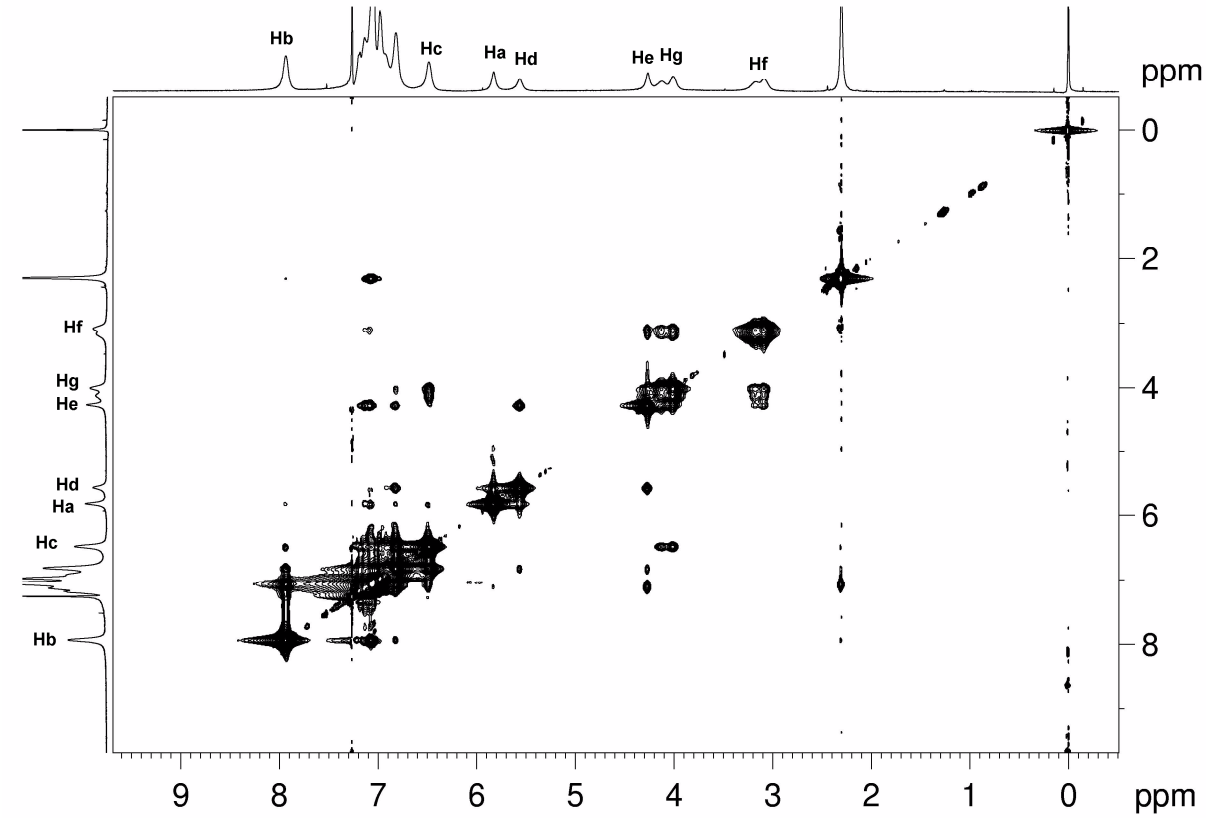

Figure S32. 2D NOESY spectrum of a 1:1 mixture of mixture of (*1S,2R*)-**2** and L-**3** (measured by a 400 MHz instrument over 12 h, 5 mM in $CDCl_3$ at 25°C).

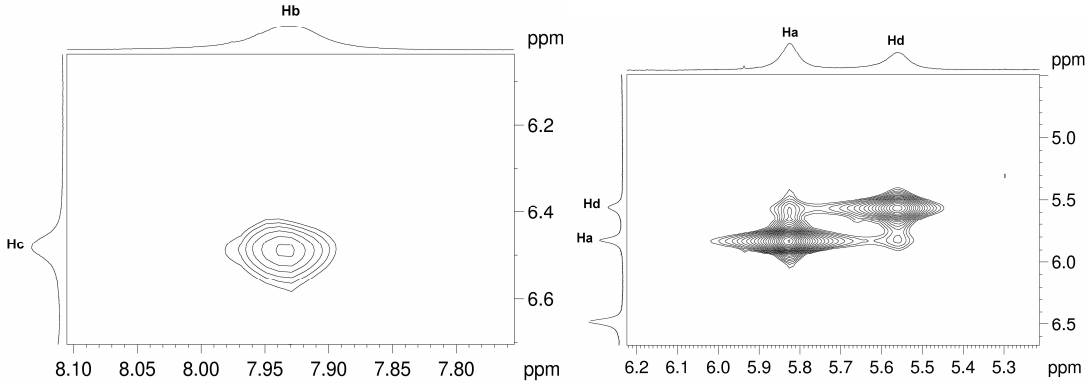

Figure S33. Portions of 2D NOESY spectrum of a 1:1 mixture of mixture of (*1S,2R*)-**2** and L-**3** (measured by a 400 MHz instrument over 12 h, 5 mM in $CDCl_3$ at 25°C).

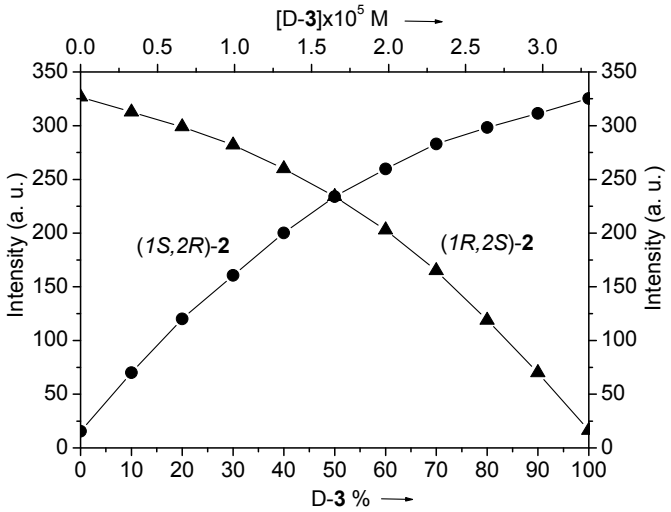

Figure S34. Change of fluorescence intensity of (*1S,2R*)-**2** (●) and (*1R,2S*)-**2** (▲) with enantiomeric content of D-**3** in two enantiomers of **3**. [(*1S,2R*)-**2**] = [(*1R,2S*)-**2**] = [D-**3**] + [L-**3**] = 3.3×10^{-5} M in $CHCl_3$/hexane 1:2 (V/V).