The ESI for *Org. Biomol. Chem.*, 2019, **17**, 1466–1470, originally published on 16th January 2019, was updated on 21st March 2019. An incorrect structure included for actinomycin D has been corrected.

Enantiomeric NMR discrimination of carboxylic acids using actinomycin D as a chiral solvating agent

Contents:

1 Genenal information

CSA **1** was purchased from Push-herb chem Biotech Inc. The compounds **2**-**15** were purchased from Aladdin biochemical technology co. Ltd (Shanghai, China), which were all used without further purification. ^{1}H NMR data were collected on a Bruker Avance 600 MHz spectrometer at 20 °C. Chemical shifts (ppm) internally referenced to $CDCl_3$ signal (δH = 7.26 ppm) or C_6D_6 (δH = 7.16 ppm) were obtained.

2 Carboxylic Acids recognized by CSA 1

(**a**) The CSA **1** and (±)-mandelic acid were dissolved in the solvent $CDCl_3$, both concentrations are 20 mM. The solutions were distributed among five NMR tubes with the mole ratio of the CSA **1** and (±)-mandelic acid increased from 0 to 1, the total concentration of host and guest in the NMR tubes (total volume of 500 µL) was 20 mM which remained unchanged.

(**b**) The CSA **1** and racemic carboxylic acids were dissolved, with their concentrations being 20 mM in $CDCl_3$. 50 µL of CSA **1** and 500 µL of each racemic carboxylic acid were mixed together, with the mole ratio being 1:10. The total concentration in the NMR tubes (total volume was 550 µL) was 20 mM.

3, Determination of enantiomeric purity of mandelic acid

To determine the enantiomeric purity of the carboxylic acids,samples with ee values of -100%, -90%, -80%, -60%, -40%, -20%, 0% were prepared by racemic mandelic acid and (*R*)-mandelic acid at the concentration of 20 mM in $CDCl_3$, expressed as % R in the data. The CAS **1** was also dissolved in $CDCl_3$ at a concentration of 20 mM. Then 50 µL of CAS **1** and 500 µL of racemic mandelic acid and (*R*)-mandelic acidmixtures with different ee's were added to the NMR tube (total concentration of 20 mM) with a molar ratio of 1:10. Then the enantiomeric purity of the carboxylic acids was determined by ^{1}H NMR method. The plotting of gravimetry ee value (y axis) versus NMR observed ee value (x axis) presented excellent linearity with R^2 = 0.9996.

4, ^{1}H NMR spectroscopy of CSA 1 and racemic carboxylic acids

Figure S1: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1**.

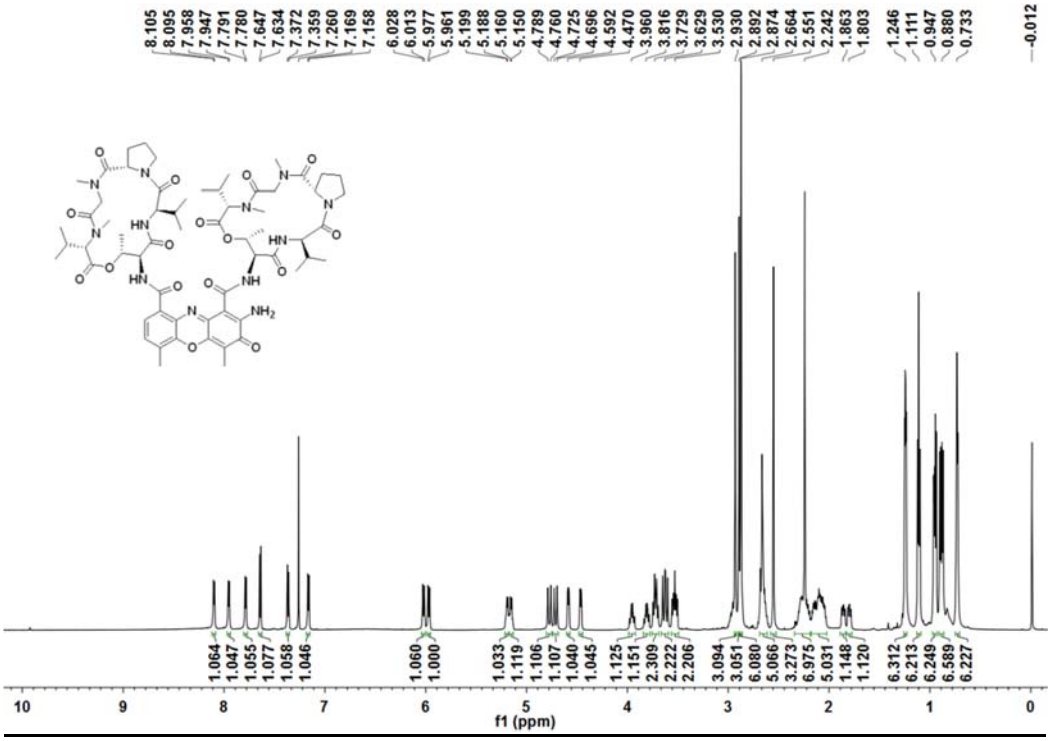


Figure S2: ^{1}H NMR (600 MHz, $CDCl_3$) of racemic mandelic acid.

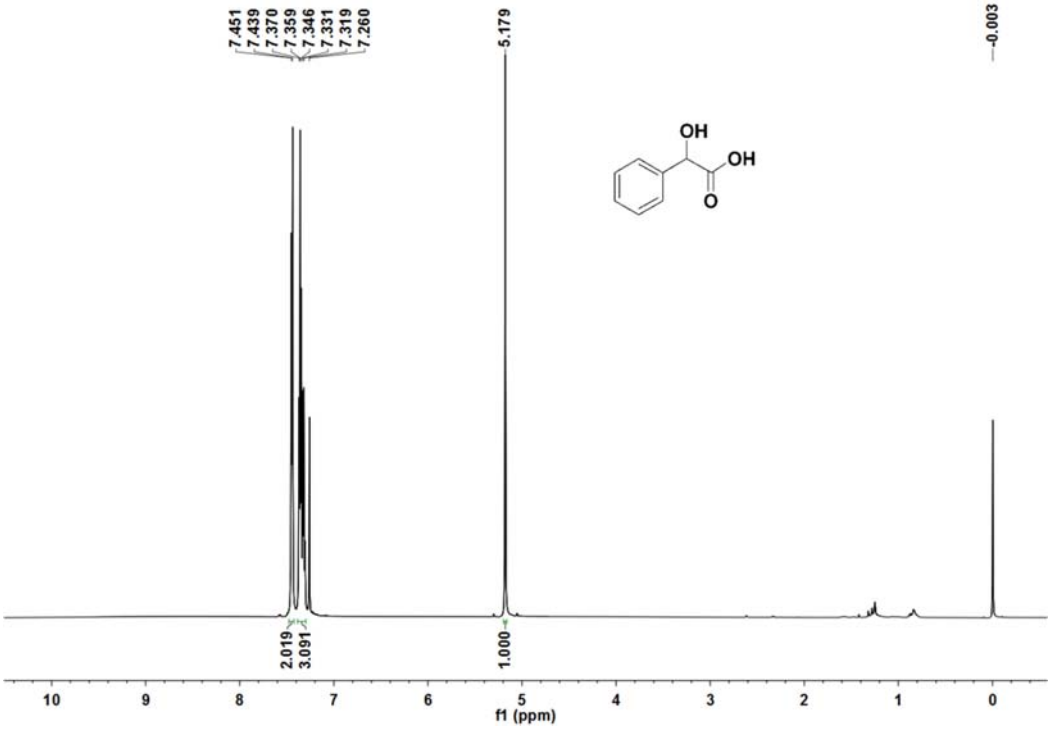


Figure S3: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic mandelic acid with the corresponding molar ratio 1:1.

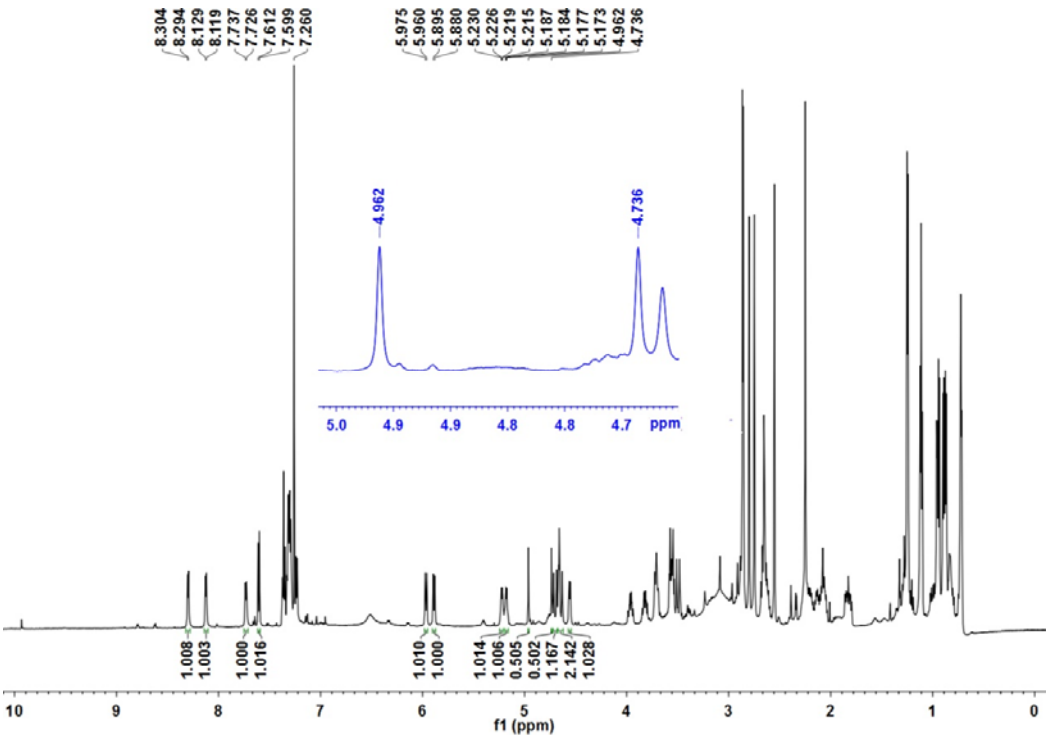


Figure S4: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic mandelic acid with the corresponding molar ratio 1:5.

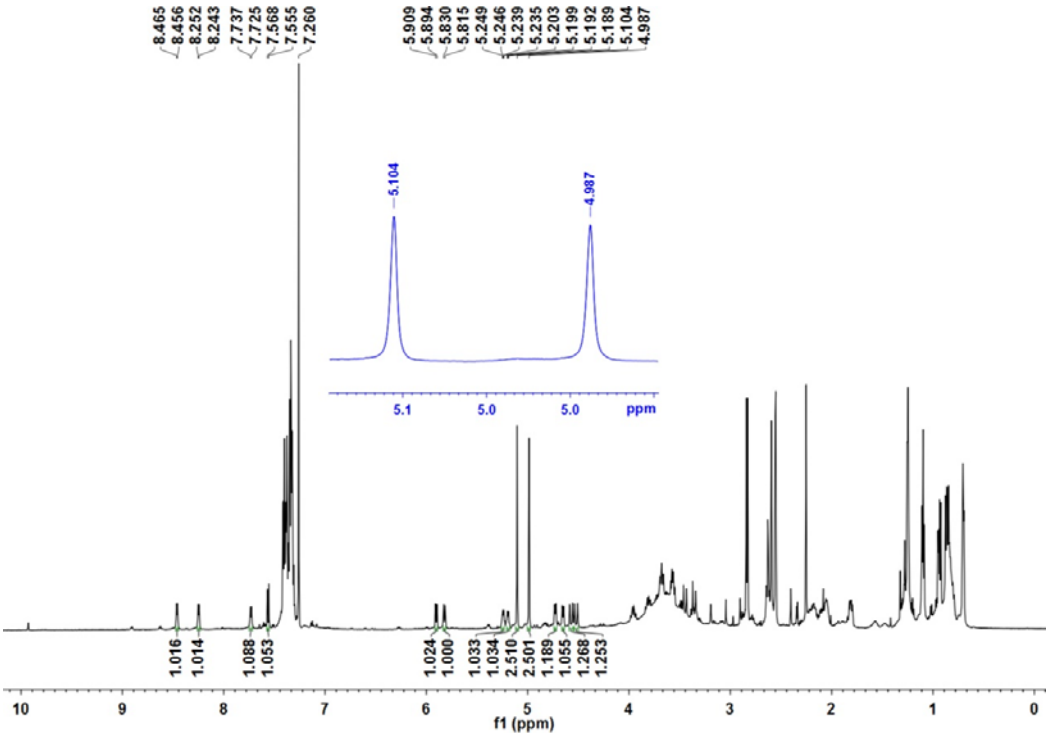


Figure S5: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic mandelic acid with the

corresponding molar ratio 1:10.

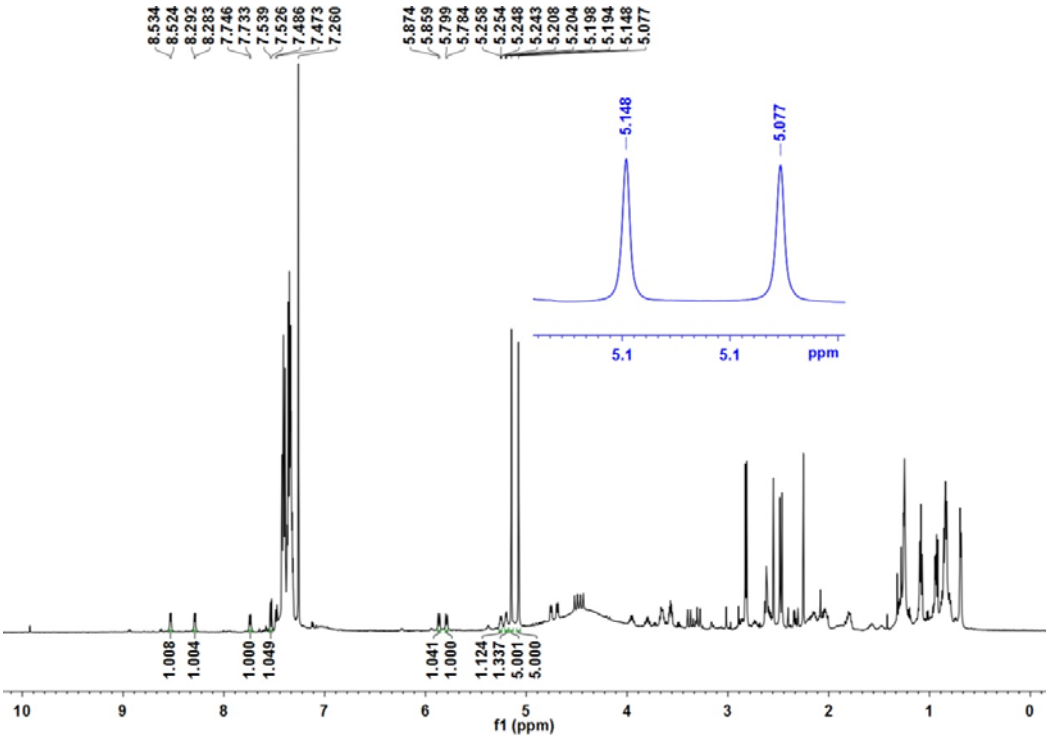


Figure S6: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic mandelic acid with the corresponding molar ratio 1:20.

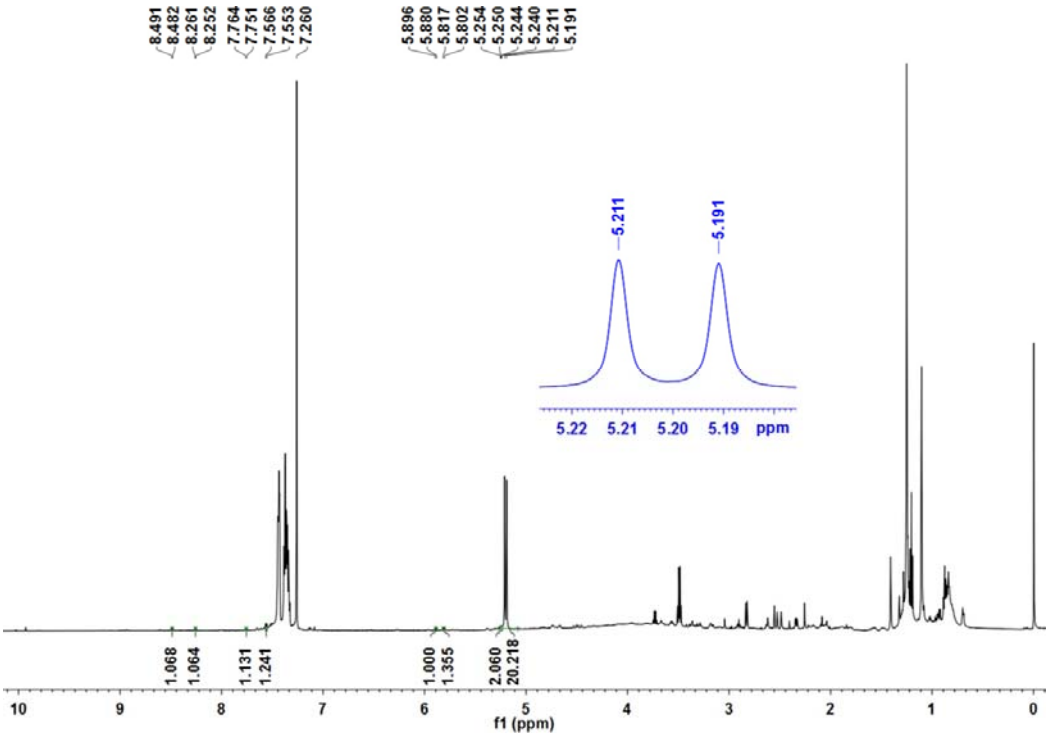


Figure S7: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-bromomandelic acid (**3**).

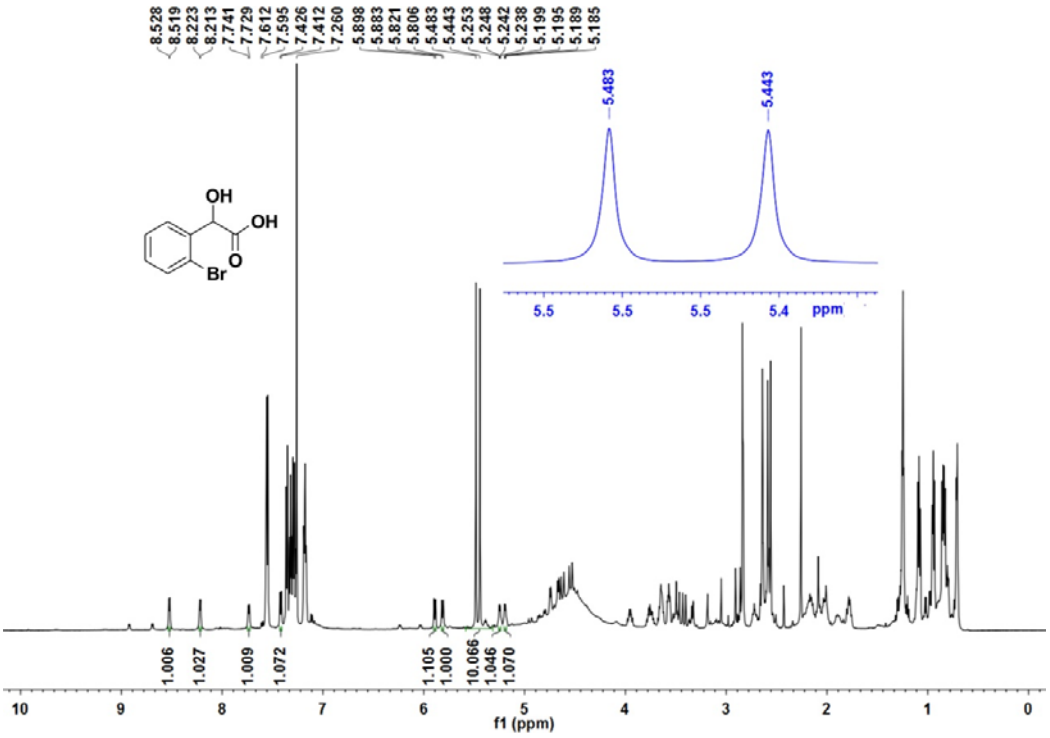


Figure S8: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-fluoromandelic acid (**4**).

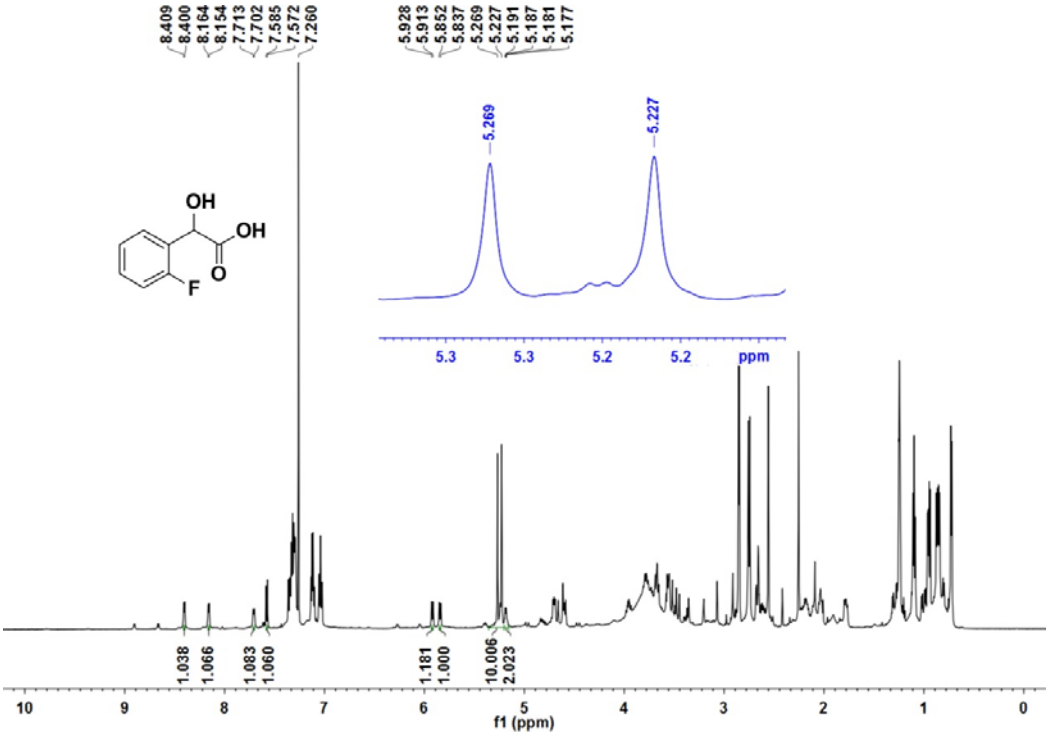


Figure S9: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 4-chloromandelic acid (**5**).

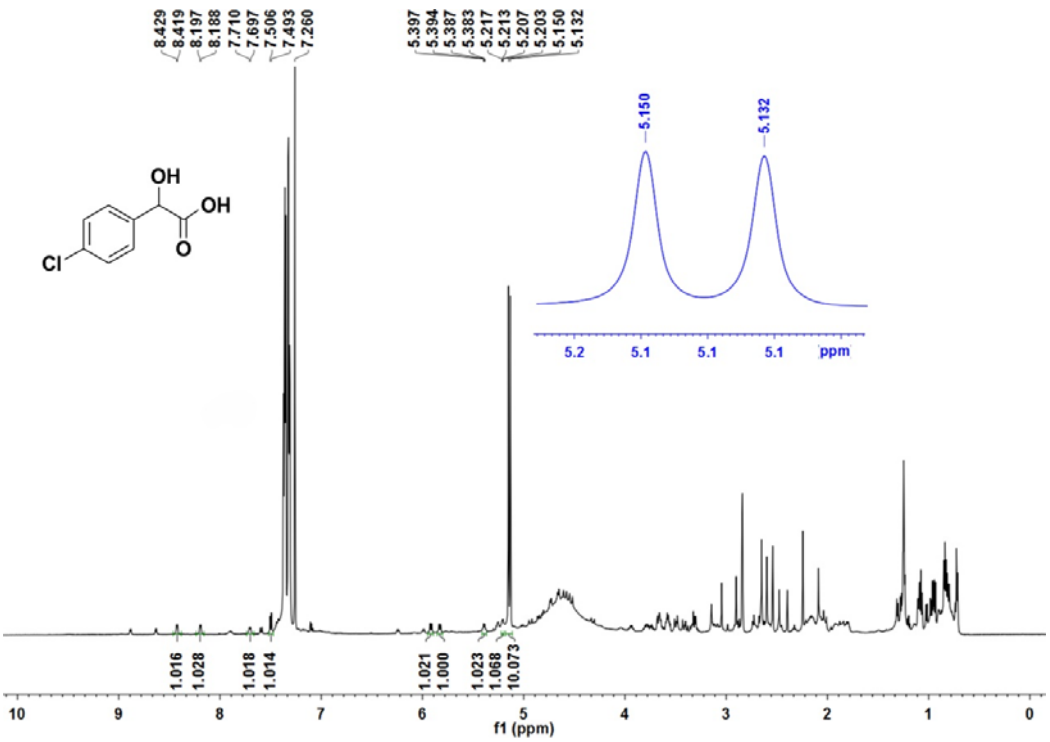


Figure S10: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 4-bromomandelic acid (**6**).

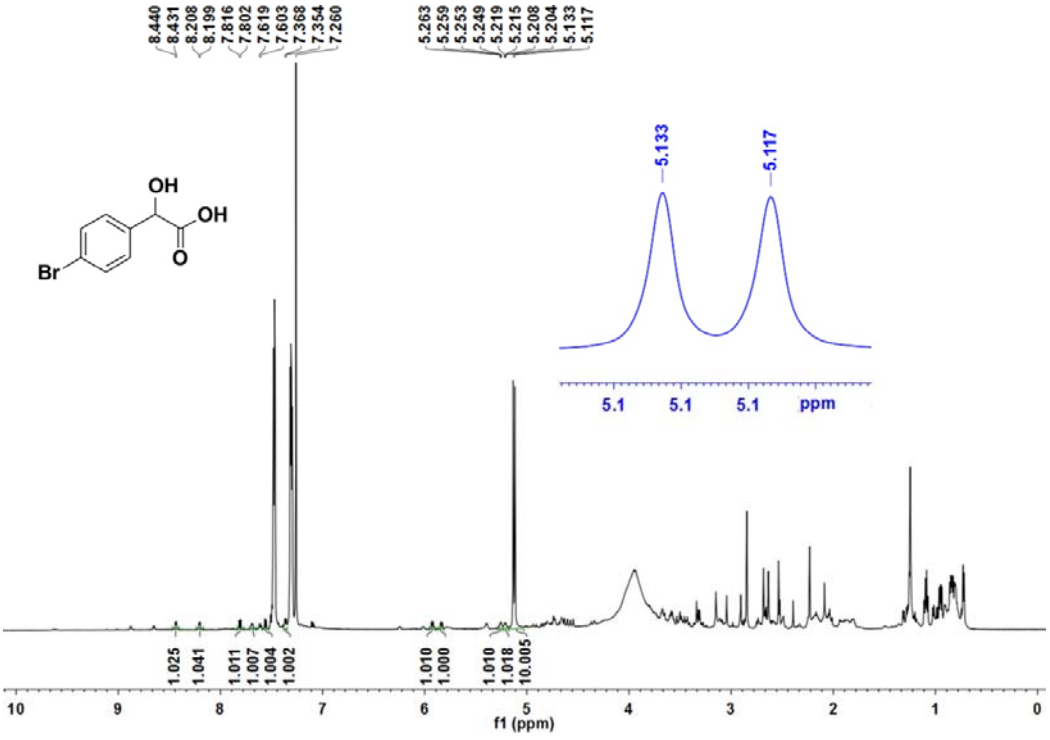


Figure S11: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 4-fluoromandelic acid (**7**).

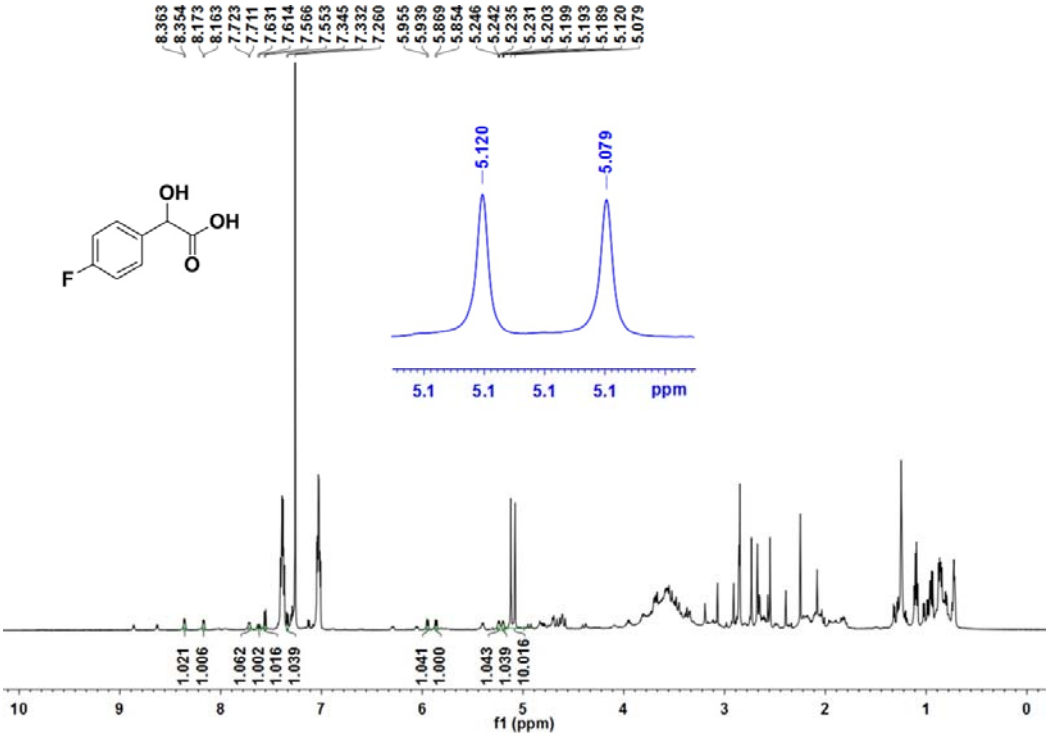


Figure S12: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 4-methoxymandelic acid (**8**).

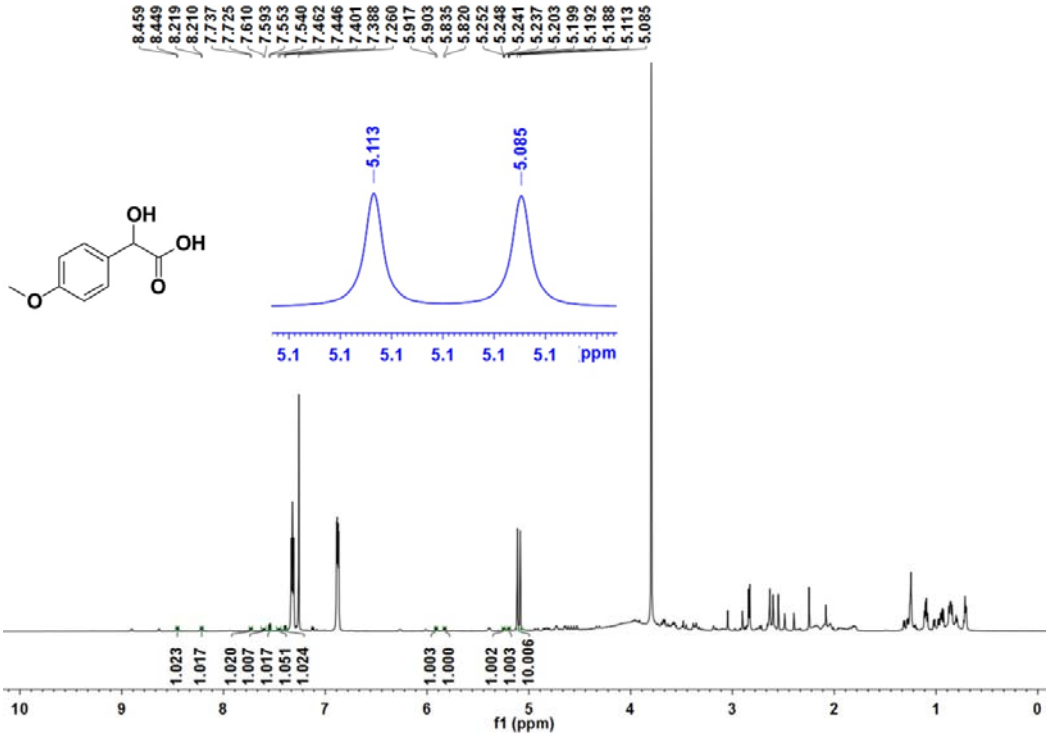


Figure S13: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 3,5-difluoromandelic acid (**9**)

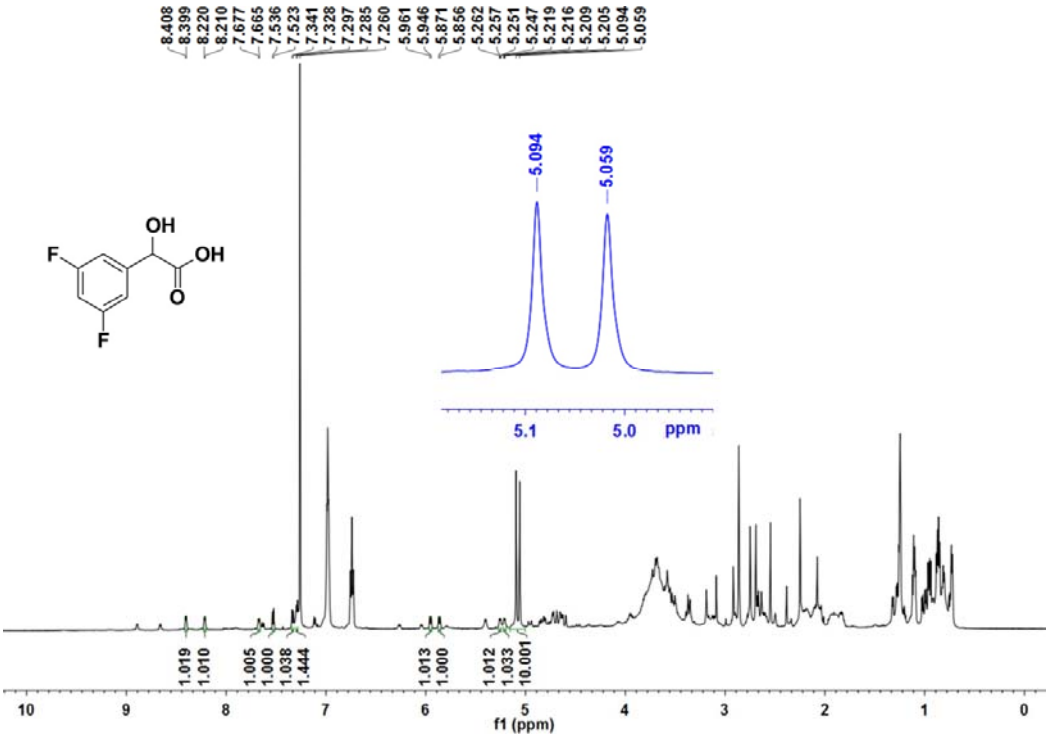


Figure S14: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic α-methoxyphenylacetic acid (**10**).

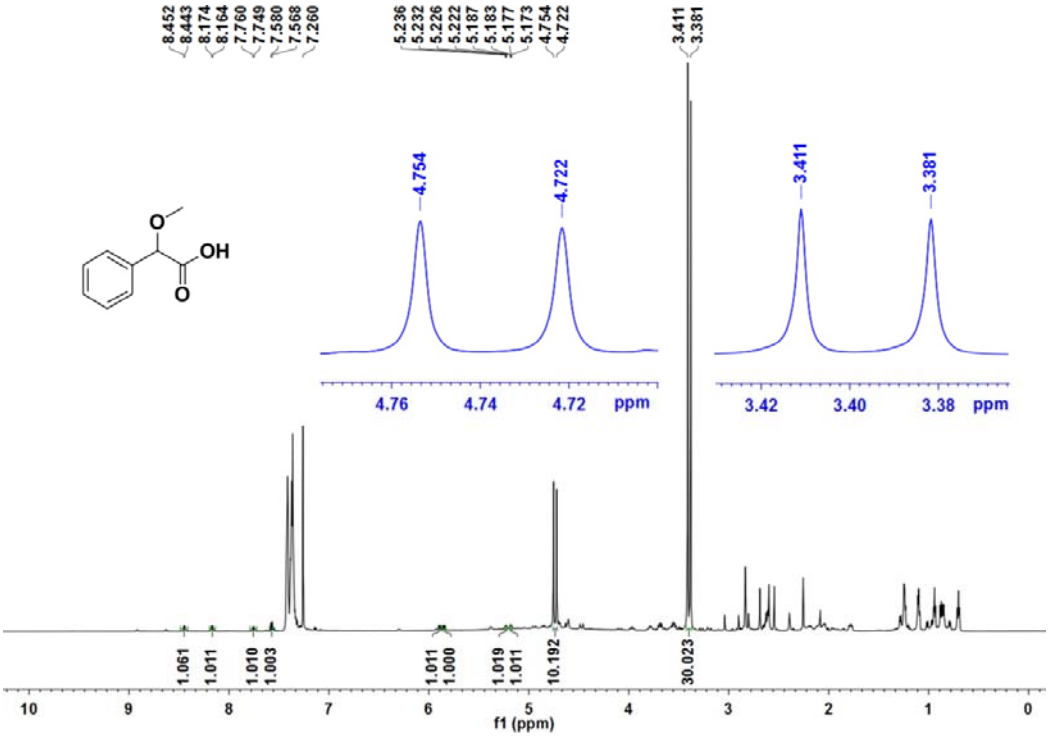


Figure S15: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-naphthaleneacetic acid (**11**).

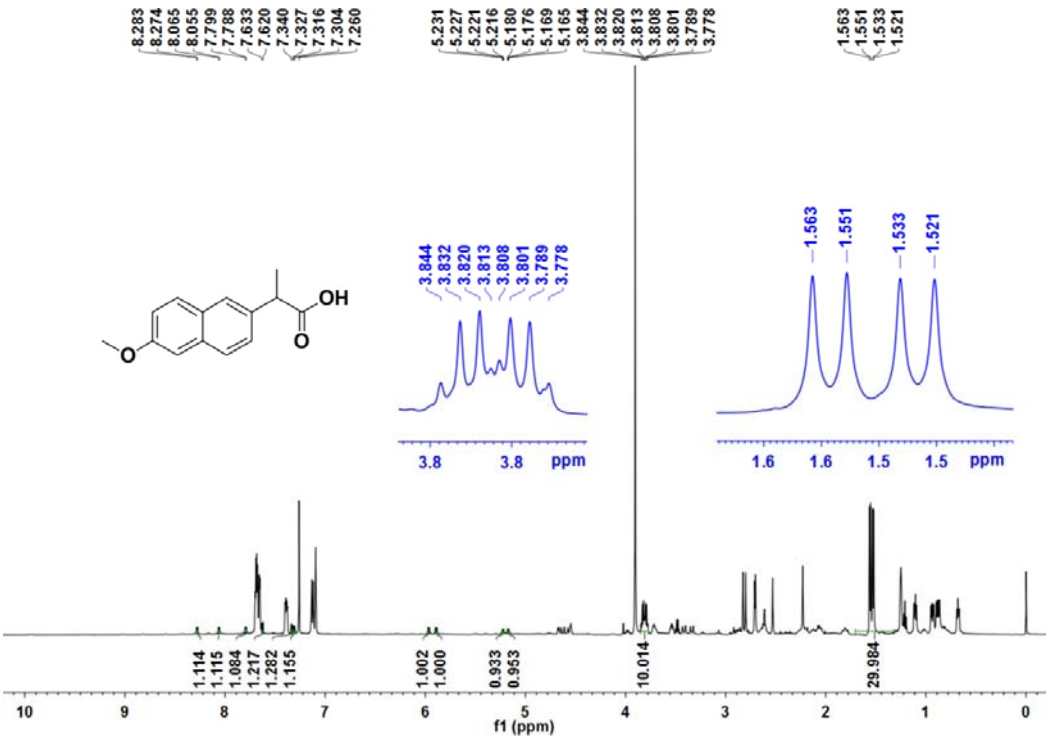


Figure S16: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-phthalimidopropionic acid (**12**).

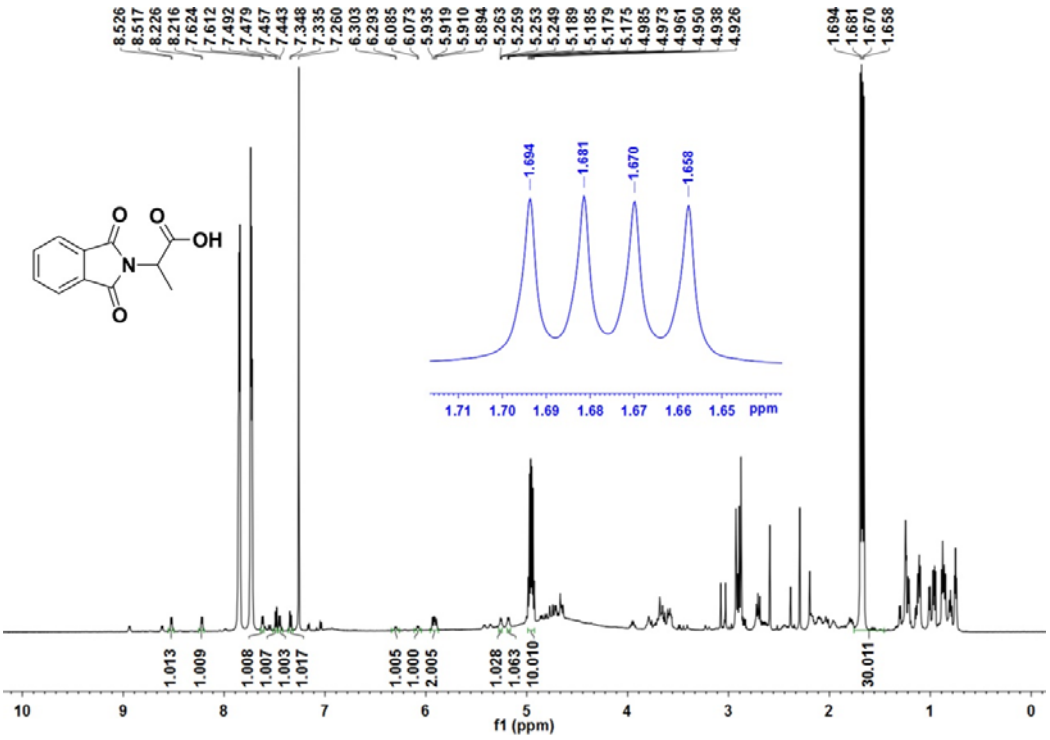


Figure S17: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic phenylsuccinic acid (**13**).

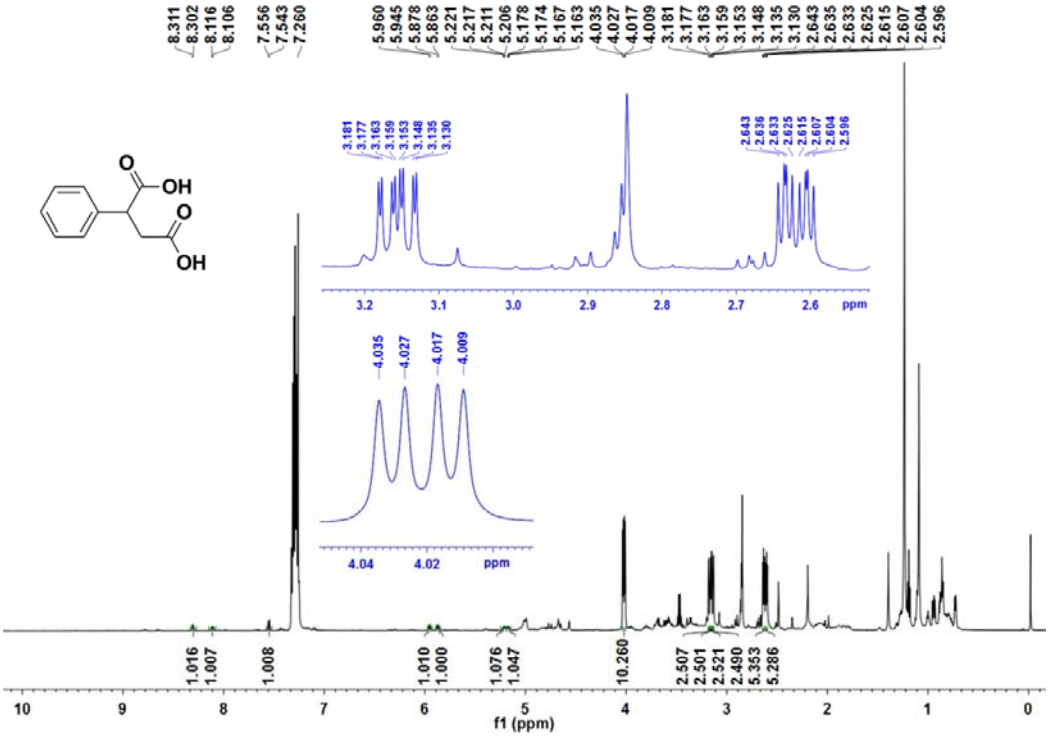


Figure S18: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-hydroxy-3-methylbutyric acid (**14**).

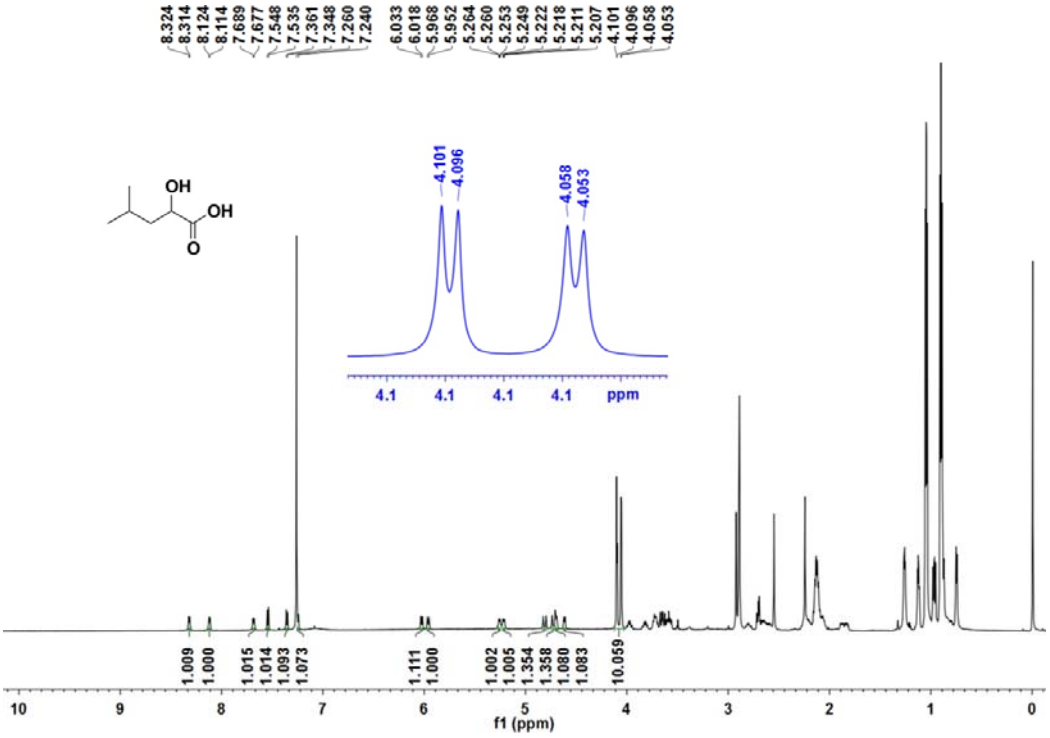
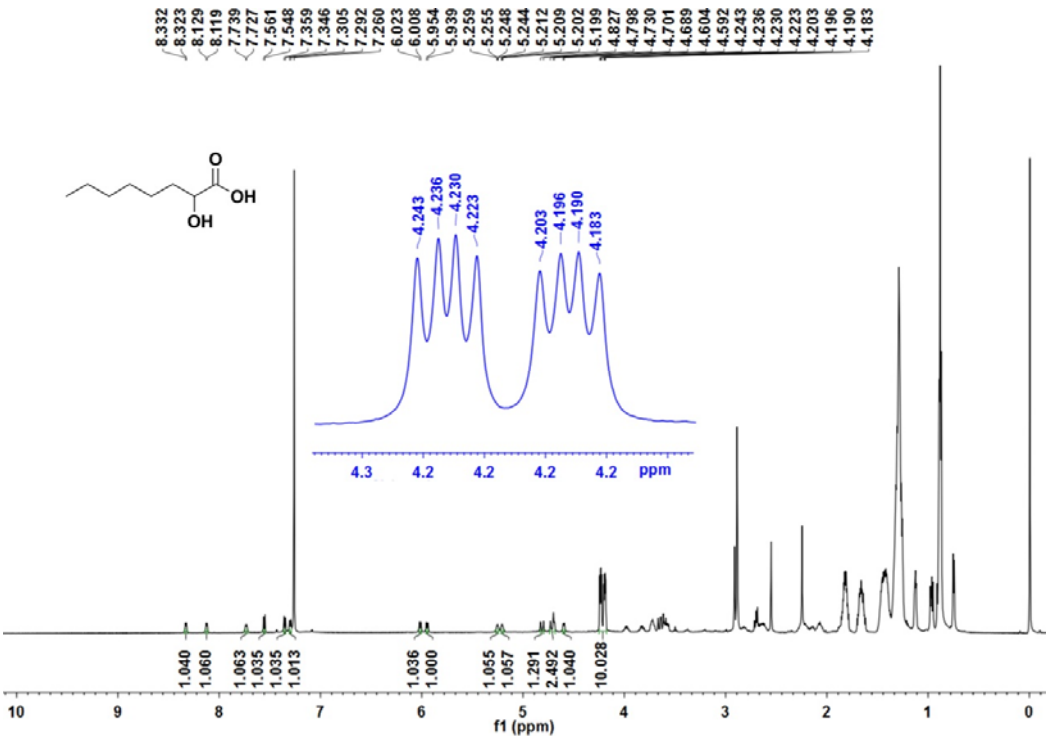
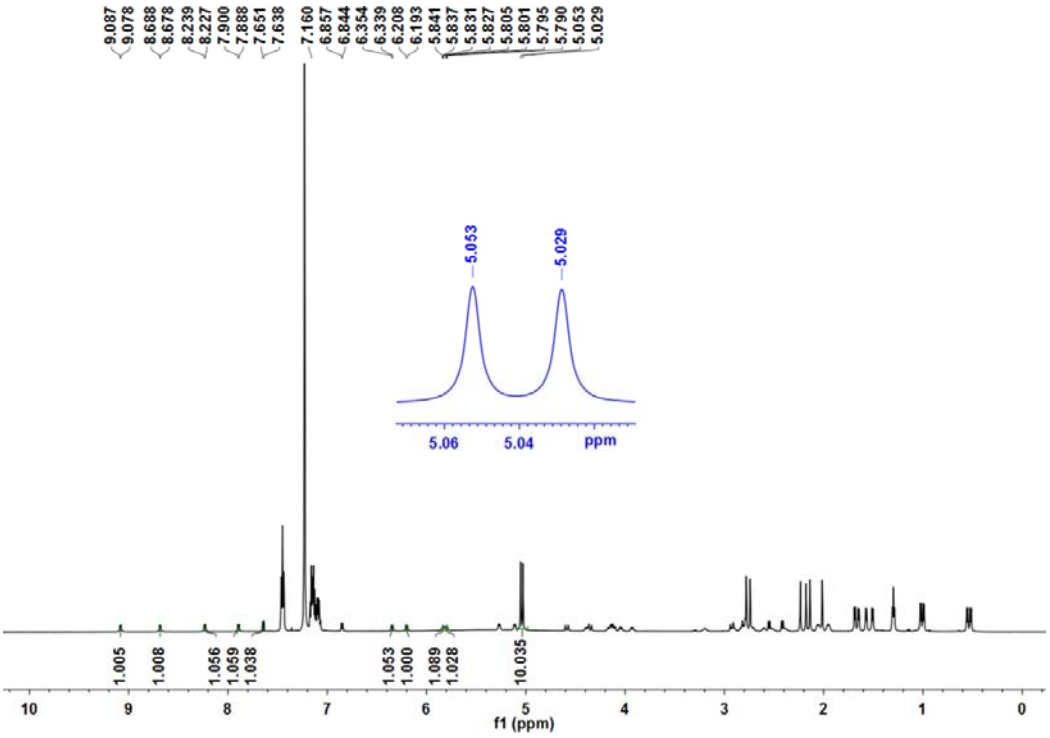


Figure S19: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-hydroxycaprylic acid (**15**).



5, ^{1}H NMR spectroscopy of CSA 1 and racemic mandelic acid in C_6D_6

Figure S20: ^{1}H NMR (600 MHz, C_6D_6) of CSA **1** and racemic mandelic acid (**2**) (The CSA **1** and racemic carboxylic acids were dissolved in C_6D_6, with their concentrations being 20 mM. 50 µL of CSA **1** and 500 µL of racemic mandelic acid were mixed, with the mole ratio being 1:10. The total concentration in the NMR tubes was 20 mM).



6, Studies of the stoichiometry of CSA 1/(R)- and (S)-4-methoxymandelic acid by ^{1}H NMR titration (Job Plots)

Figure S21: Job plot of CSA 1 with (*R*)-**8** and (*S*)-**8**. (The CSA **1**, (*R*)-**8** and (*S*)-**8** were separately dissolved in $CDCl_3$, with their concentrations being 20 mM. The solutions were distributed among 22 NMR tubes with the host-guest mole ratio increasing from 0 to 1, the total concentration of host and guest was 20mM).

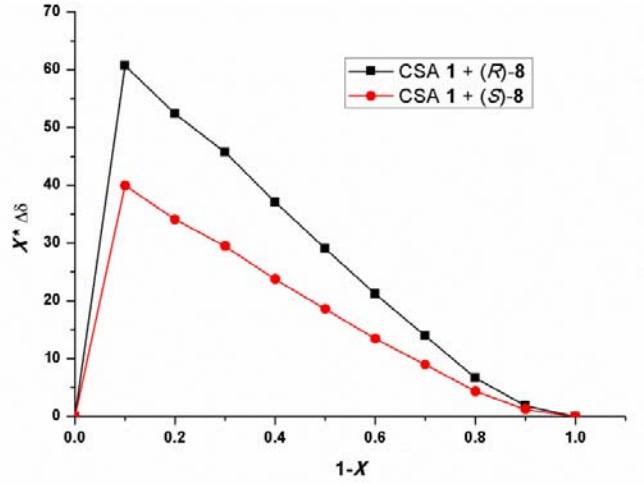


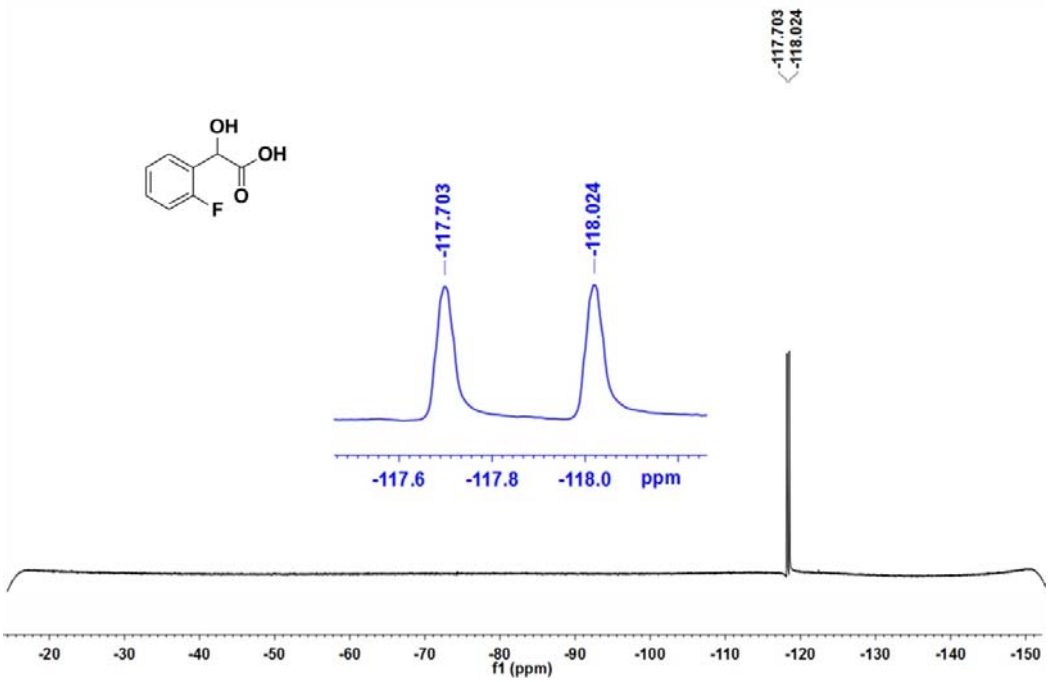
Figure S21. Job plot of CSA 1 with (*R*)-**8** and (*S*)-**8**. Δδ stands for the chemical shift change of the α-H of (*R*)-**8** and (*S*)-**8** in the presence of CSA **1**. X stands for the molar fraction of the CSA 1 (X = [CSA 1]/[CSA 1] + [**8**]). The total concentration is 20 mM in $CDCl_3$.

According to Figure S21, the α-H signal in the upfield belong to

(R)-4-methoxymandelic acid and the α-H signal in the downfield belong to (S)-4-methoxymandelic acid.

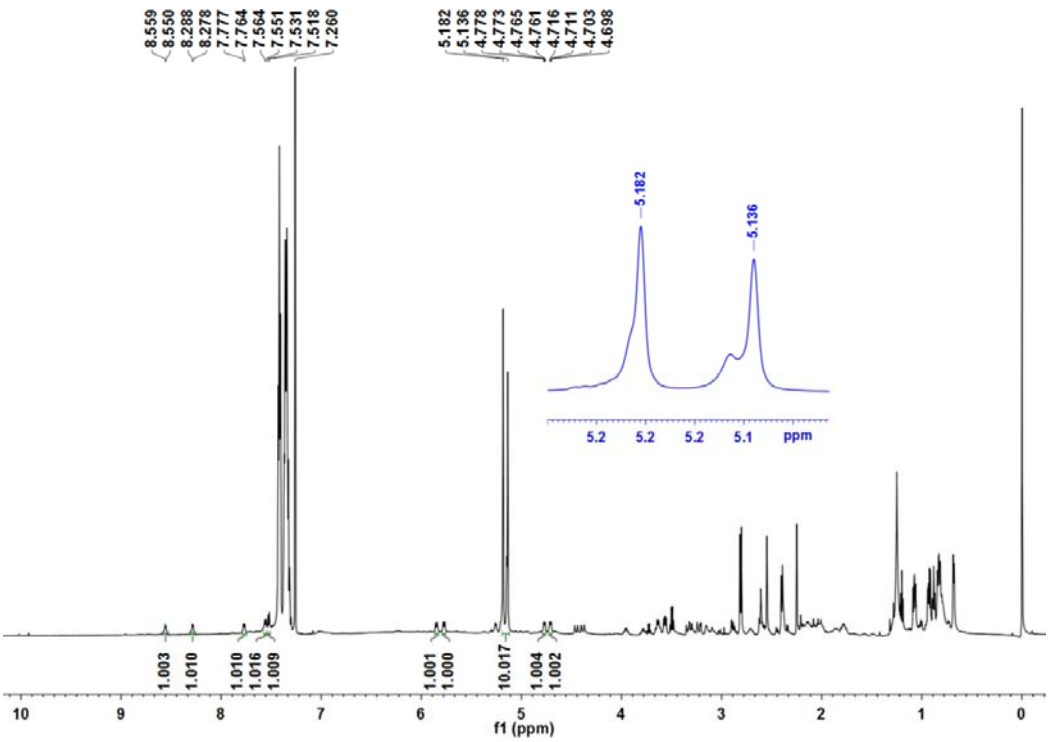
7, ^{19}F NMR spectroscopy of CSA 1 and racemic 2-fluoromandelic acid

Figure S22: ^{19}F NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-fluoromandelic acid (**4**). (The CSA **1** and racemic 2-fluoromandelic acid were dissolved in $CDCl_3$, with their concentrations being 20 mM. 50 μL of CSA **1** and 500 μL of racemic 2-fluoromandelic acid were mixed, with the mole ratio being 1:10. The total concentration in the NMR tubes was 20 mM).



8, ^{1}H NMR spectroscopy of CSA 1 and racemic mandelic acid under 10mM

Figure S23: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic mandelic acid (**2**) under the concentration of 10mM, with the molar ration being 1:10. (The sample of Act-D and mandelic acid in $CDCl_3$ (molar ratio being 1:10, the concentration was 20 mM), was diluted and the final concentration was 10 mM. The result shows that the ΔΔδ value of α-H resonance is 0.046 ppm).



9, 1H NMR spectroscopy of discrimination of a single enantiomer of racemic carboxylic acids measured in the presence of CSA 1

Equal volume of 20 mM enantiomeric pure isomer ((*R*)-(-)-mandelic acid, (*S*)-(+)-2-chloromandelic acid) and the respective racemic compounds solutions were added into NMR tubes containing 20 mM Act-D, the total molar ratio was 1:10, total concentration in the NMR tubes was 20 mM.

Figure S24: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic mandelic acid with the addition of (*R*)-(-)-mandelic acid.

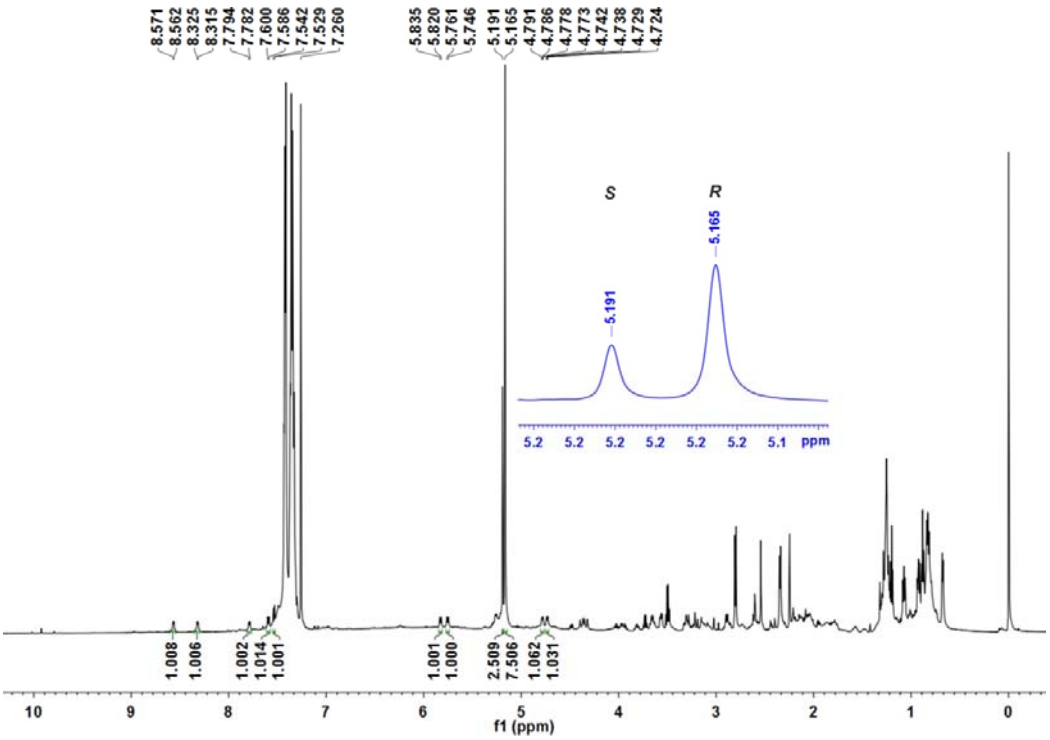


Figure S25: ^{1}H NMR (600 MHz, $CDCl_3$) of CSA **1** and racemic 2-bromomandelic acid with the addition of (*S*)-(+)-2-chloromandelic acid.