Supplementary Information

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

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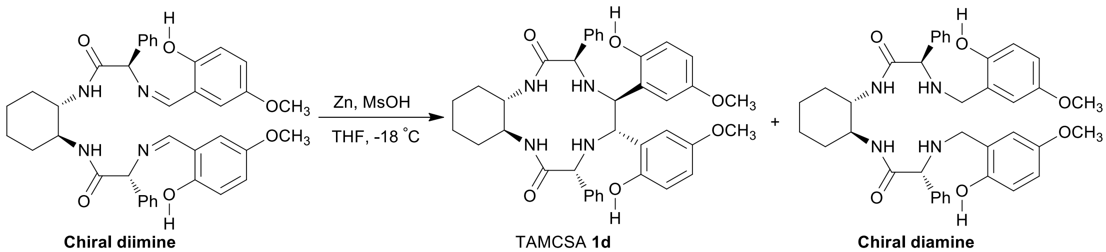
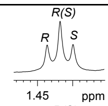
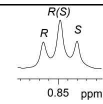
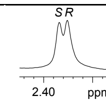
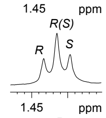
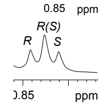
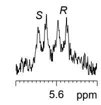
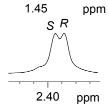
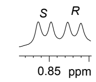
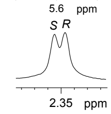
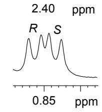
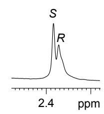
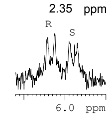
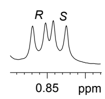
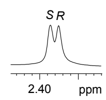
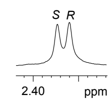
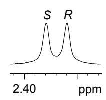
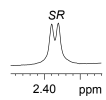
Procedure of synthesis of TAMCSA 1d.[1]



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 $NaHCO_3$ solution. The precipitate formed was filtered off and washed with $CHCl_3$. The organic layer was separated from filtrate. The water layer was extracted with $CHCl_3$ (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4. 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℃, $[\alpha]_D^{20}$ -26.8(*c* 0.03, THF), ^{1}H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{38}H_{43}N_4O_6$ $(M+H)^+$ 651.3183, found 651.3173.

Table S1. Nonequivalent chemical shifts (ΔΔδ, 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]

TAMCSA /Guest	Proton /ΔΔδ	Spectra	TAMCSA /Guest	Proton /ΔΔδ	Spectra	TAMCSA /Guest	Proton /ΔΔδ	Spectra
1a/(±)-**6**	CH_3 0.018		**1d**/(±)-**7**	CH_3 0.018		**1d**/(±)-**9**	Ph*CH*$_3$ 0.008	
1b/(±)-**6**	CH_3 0.018		**1c**/(±)-**8**[b]	CH_3 0.016		**1c**/(±)-**10**[b]	Ts*NH* 0.049	
1c/(±)-**6**[b]	Ph*CH*$_3$ 0.006		**1d**/(±)-**8**	CH_3 0.037		**1c**/(±)-**11**[b]	Ph*CH*$_3$ 0.008	
1a/(±)-**7**	CH_3 0.028		**1a**/(±)-**9**	Ph*CH*$_3$ 0.012			Ts*NH* 0.052	
1b/(±)-**7**	CH_3 0.027		**1b**/(±)-**9**	Ph*CH*$_3$ 0.011		**1c**/(±)-**12**[b]	Ph*CH*$_3$ 0.013	
1c/(±)-**7**[b]	Ph*CH*$_3$ 0.020		**1c**/(±)-**9**[b]	Ph*CH*$_3$ 0.009				

[a] Nonequivalent chemical shifts and ^{1}H NMR spectra of (±)-**6**-**13** (10×10^{-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 (5×10^{-3} M), $CDCl_3$/CD_3OD (5%), H:G = 1:1

Discrimination of enantiomers of (±)-**2-13**.

The guests (±)-**2-13** with TAMCSAs **1a-1d** were separately dissolved in $CDCl_3$ 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 $CDCl_3/CD_3OD$ (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 $CDCl_3$, 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 $CDCl_3$ 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.

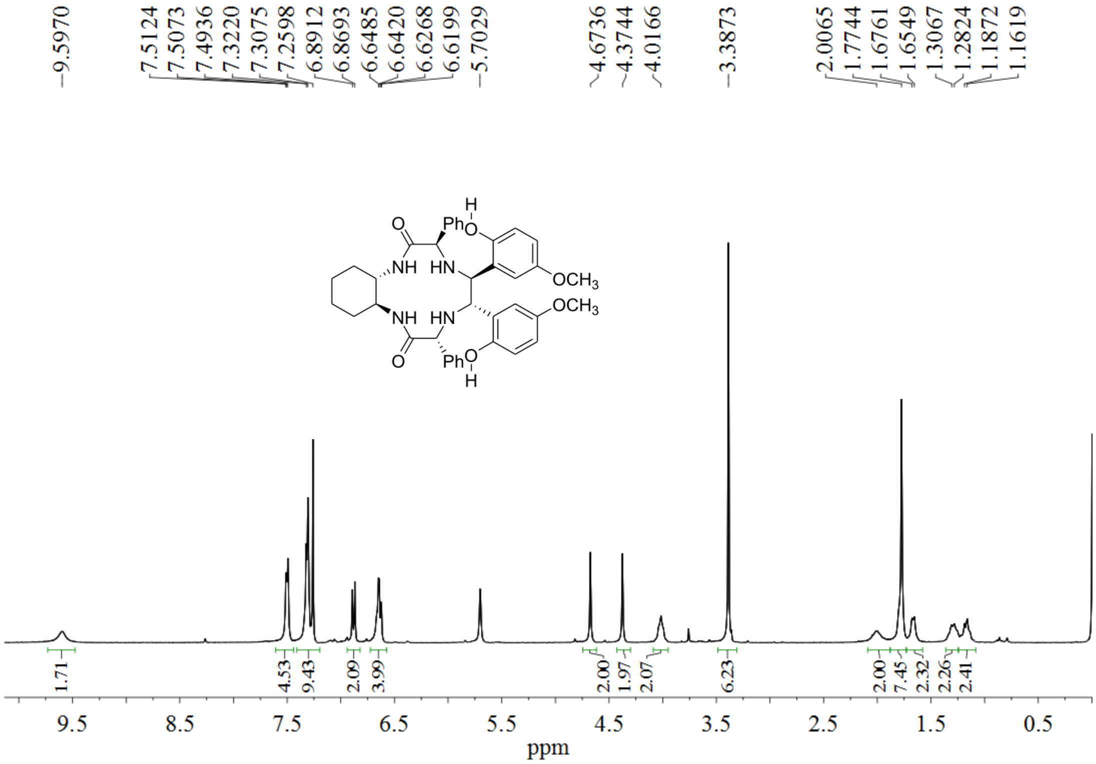


Figure S1. ^{1}H NMR spectrum of TAMCSA **1d** in $CDCl_3$ (400 MHz).

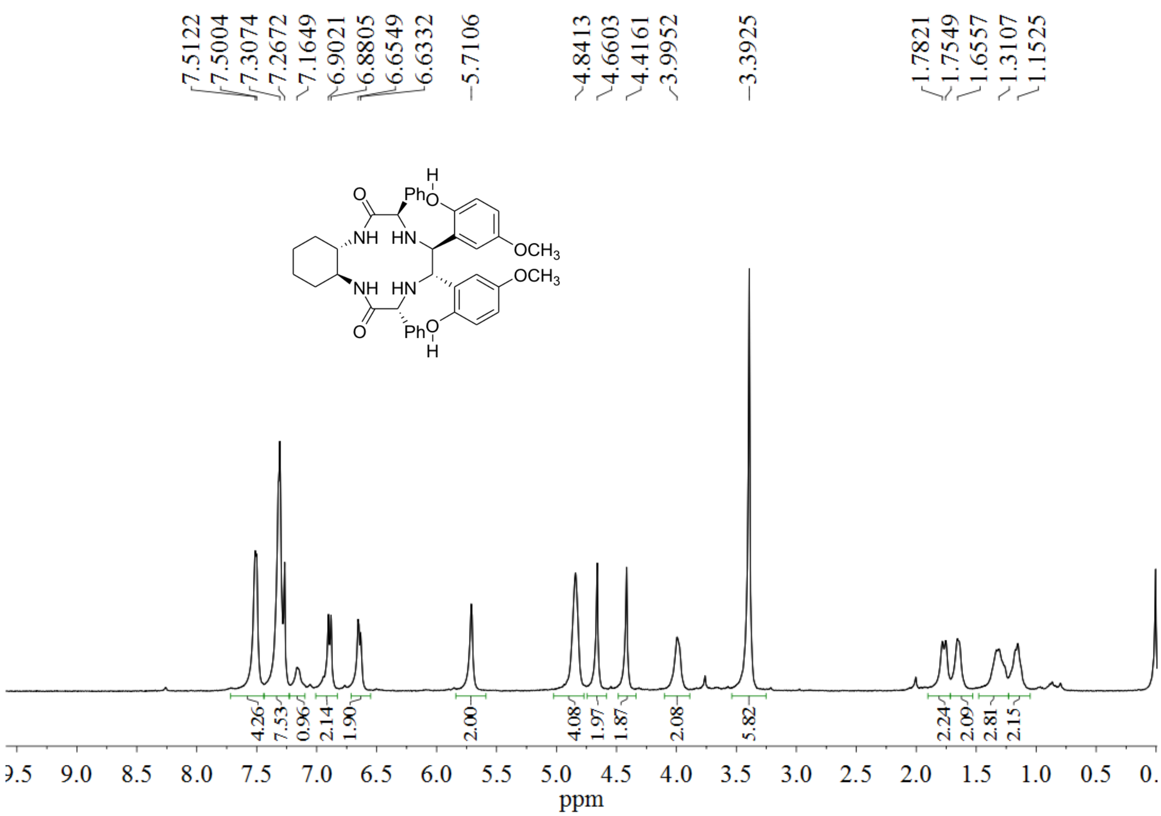


Figure S2. ^{1}H NMR spectrum of TAMCSA **1d** in $CDCl_3/D_2O$(5%) (400 MHz).

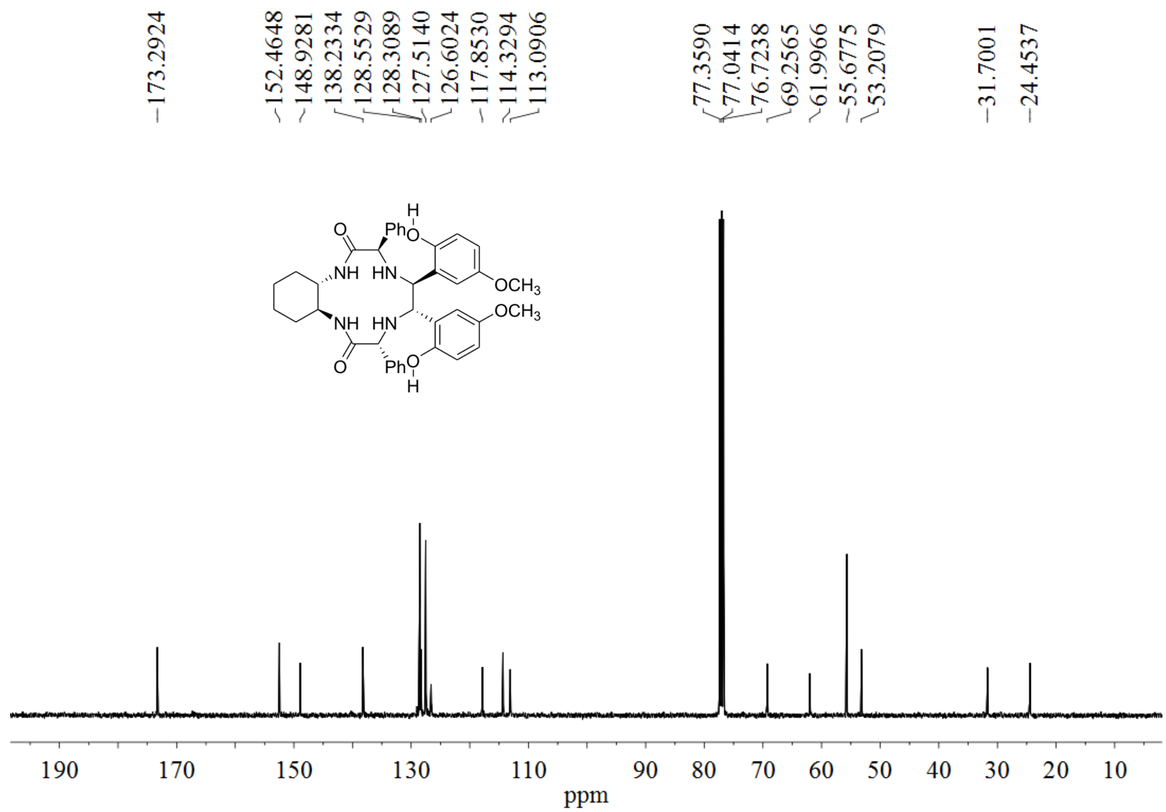


Figure S3. ^{13}C NMR spectrum of TAMCSA **1d** in $CDCl_3$ (100 MHz).

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 2.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1175 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-40 H: 0-45 N: 0-10 O: 0-10 Br: 0-2

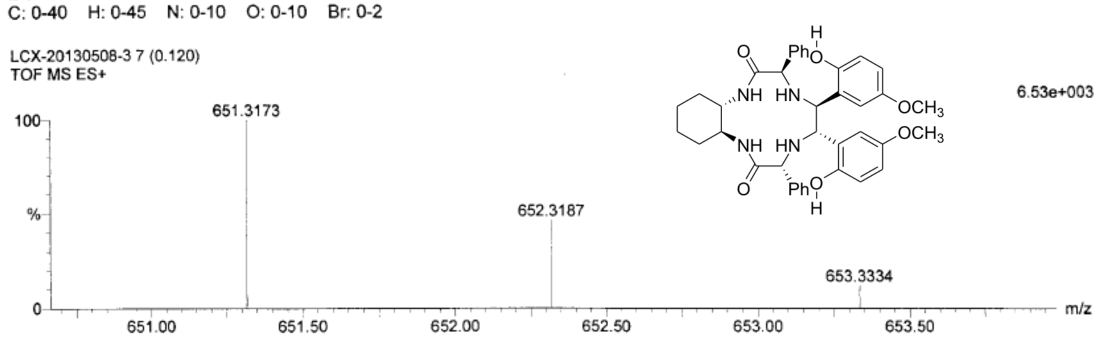


Figure S4. HRMS specutrum of TAMCSA **1d**.

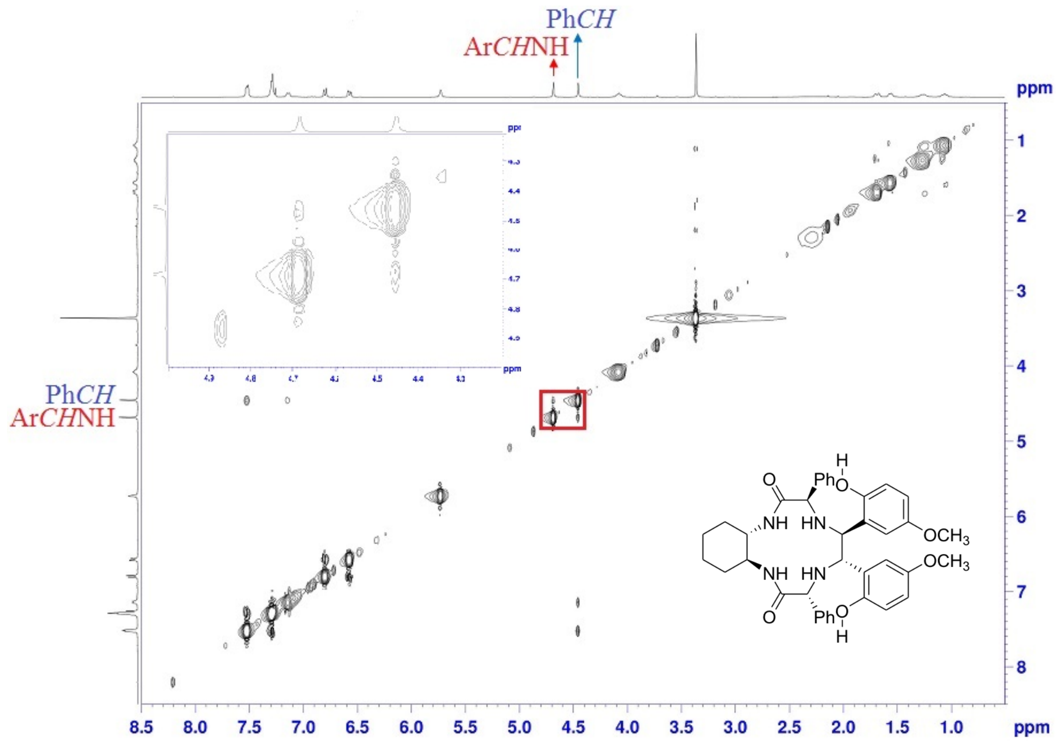


Figure S5. NOESY specutrum of TAMCSA **1d**.

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

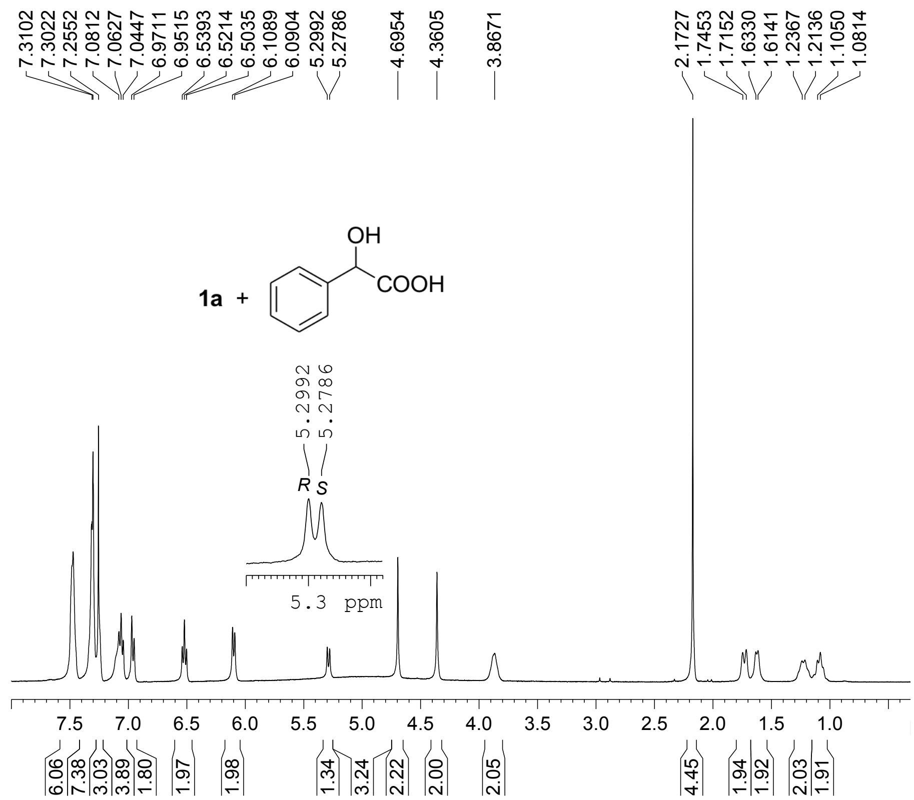


Figure S6. ^{1}H NMR spectrum of (±)-**2** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

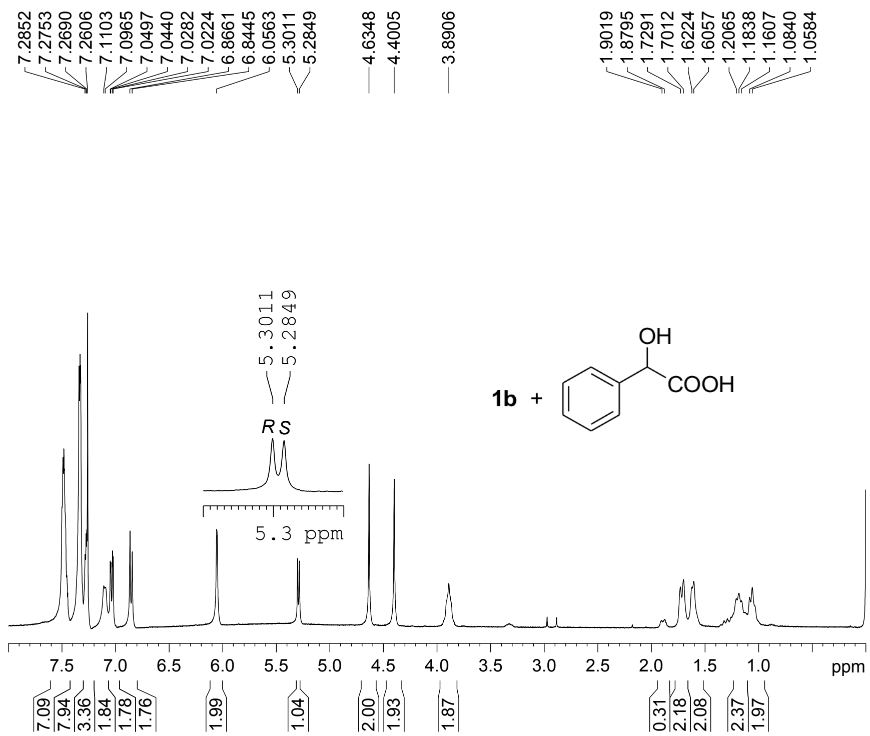


Figure S7. [1]H NMR spectrum of (±)-**2** with TAMCSA **b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

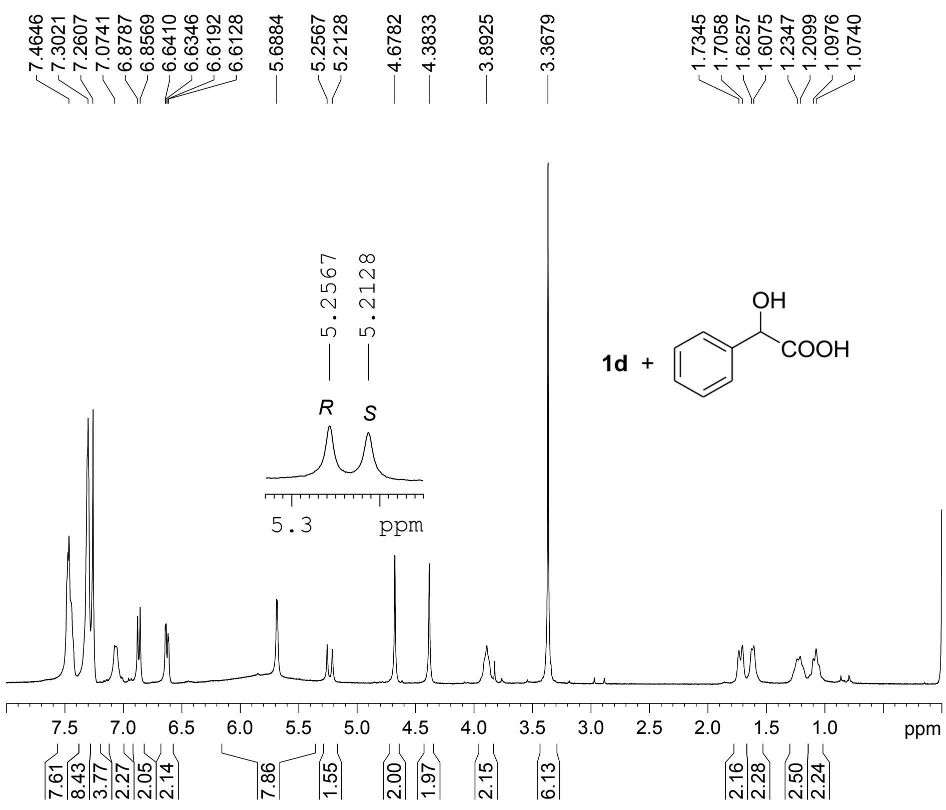


Figure S8. [1]H NMR spectrum of (±)-**2** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

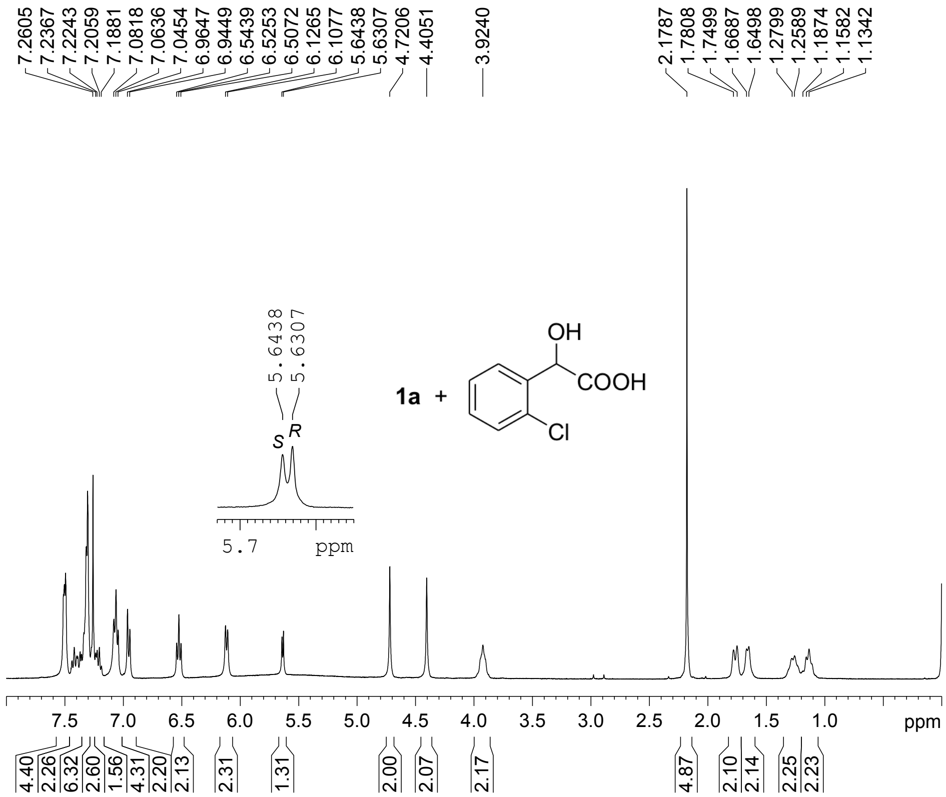


Figure S9. [1]H NMR spectrum of (±)-**3** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

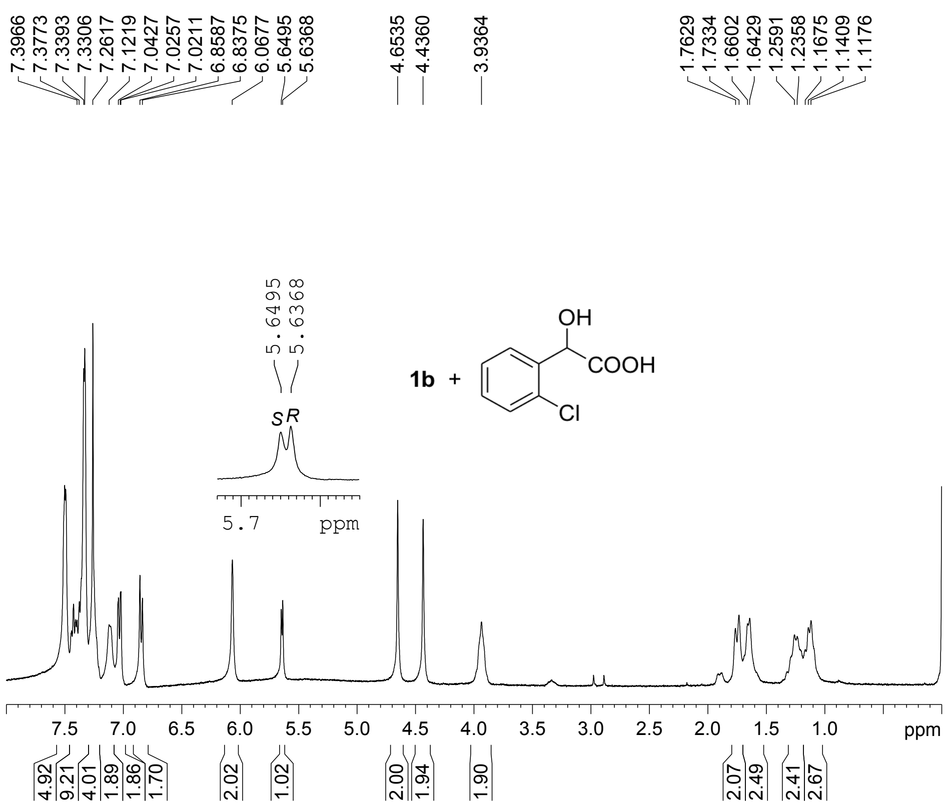


Figure S10. [1]H NMR spectrum of (±)-**3** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

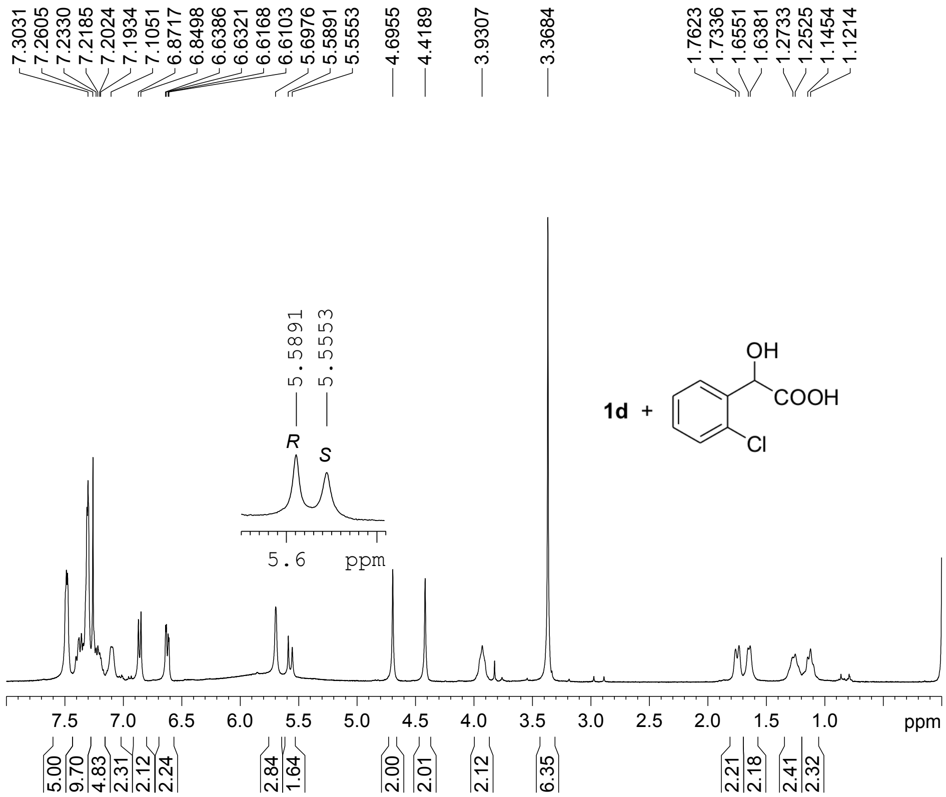


Figure S11. [1]H NMR spectrum of (±)-**3** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

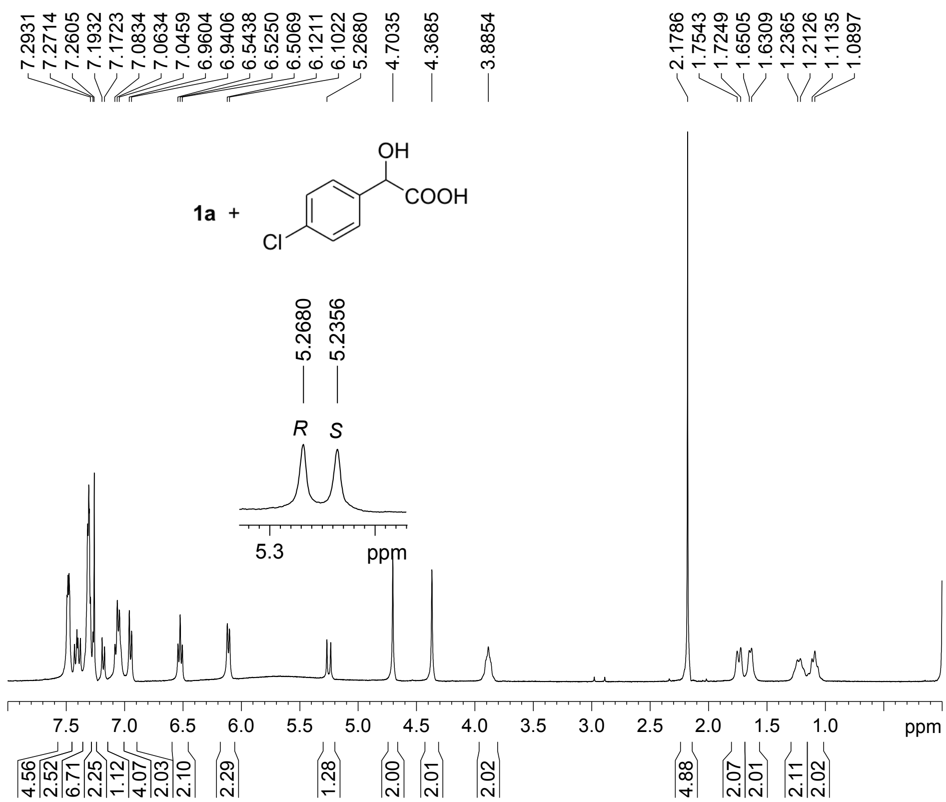


Figure S12. [1]H NMR spectrum of (±)-**4** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

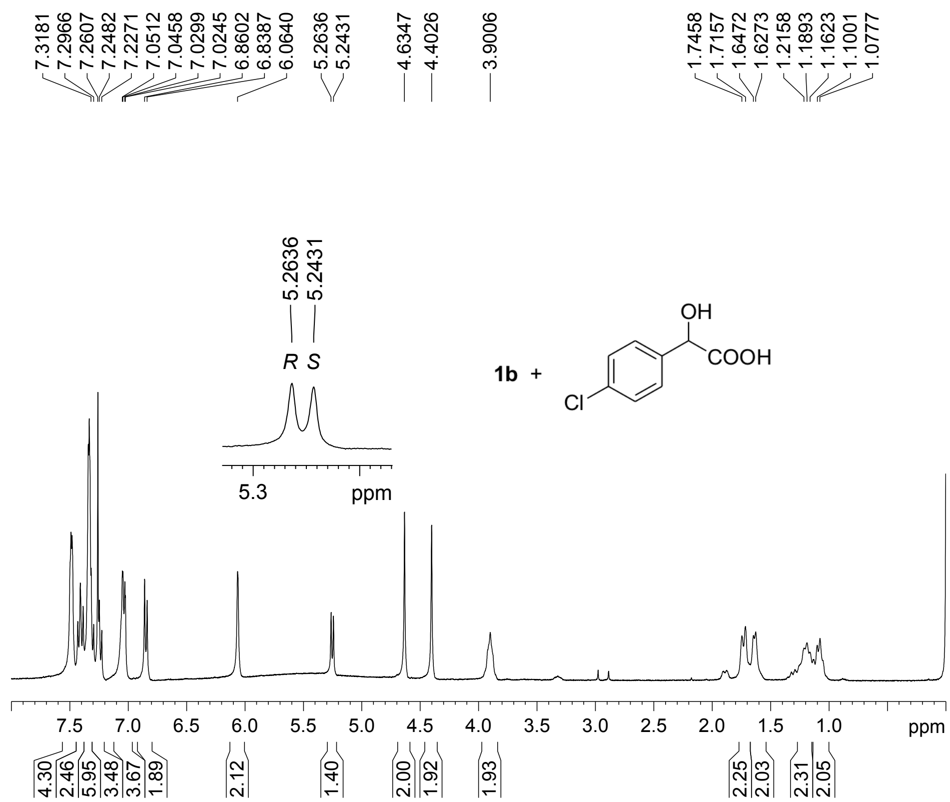


Figure S13. ^{1}H NMR spectrum of (±)-**4** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

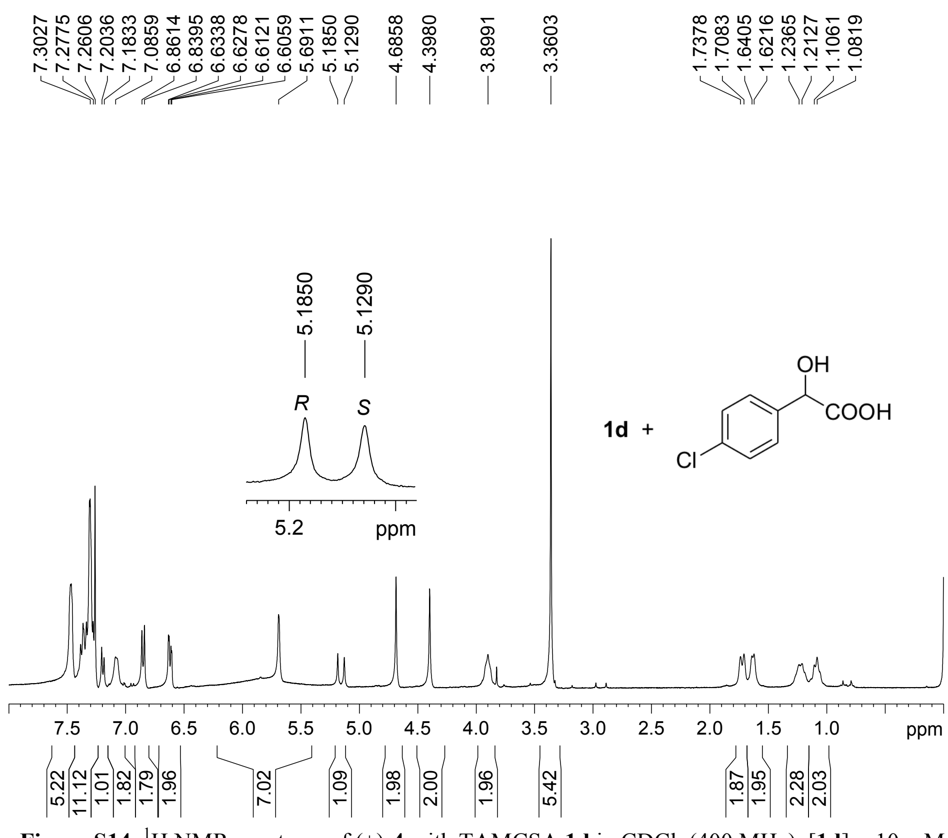


Figure S14. ^{1}H NMR spectrum of (±)-**4** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

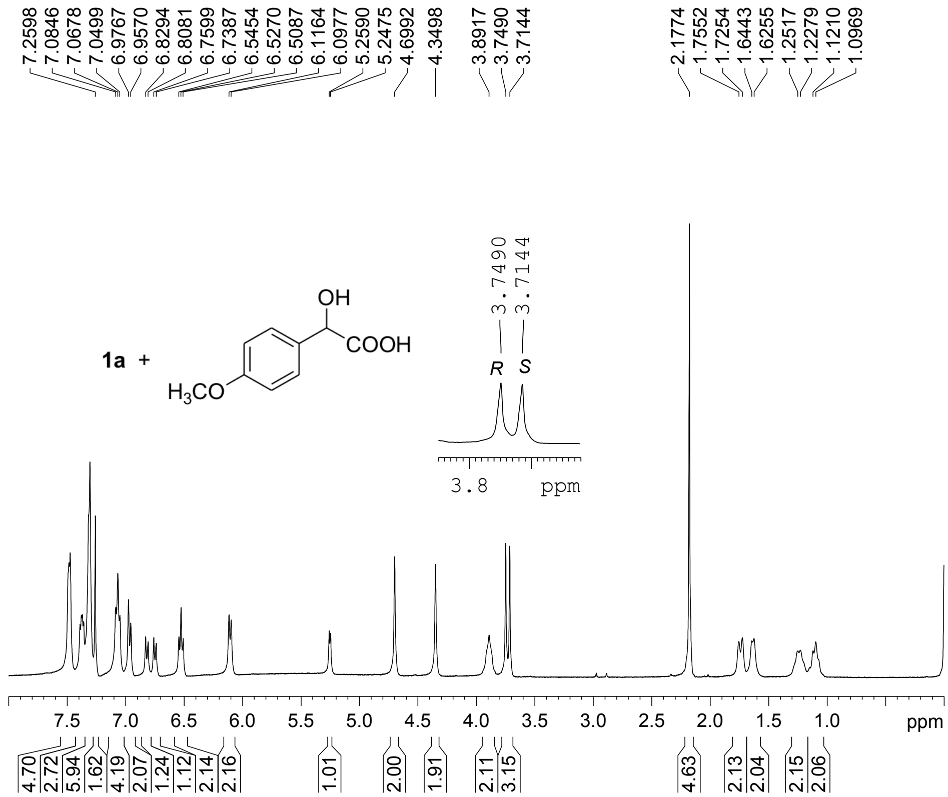


Figure S15. [1]H NMR spectrum of (±)-**5** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

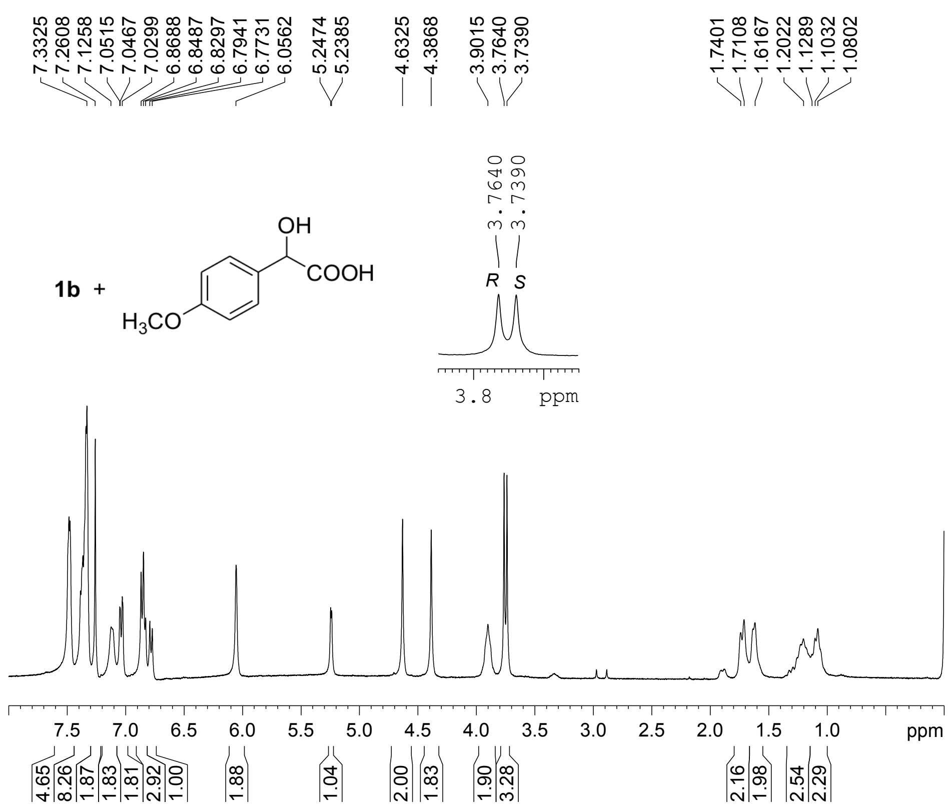


Figure S16. [1]H NMR spectrum of (±)-**5** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

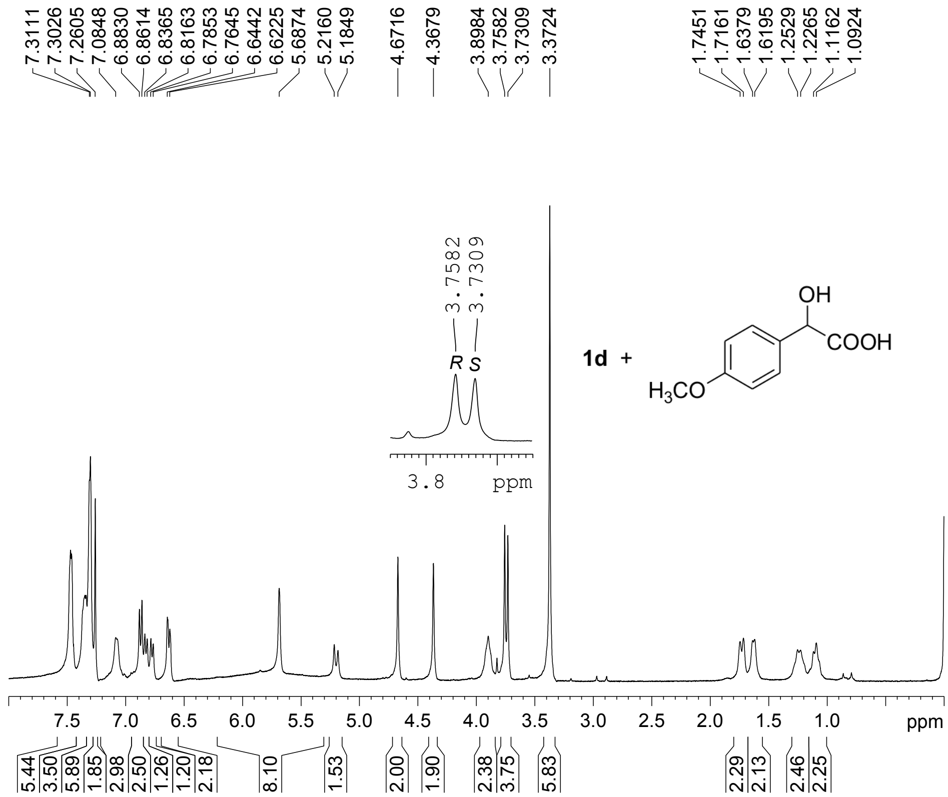


Figure S17. ^{1}H NMR spectrum of (±)-**5** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

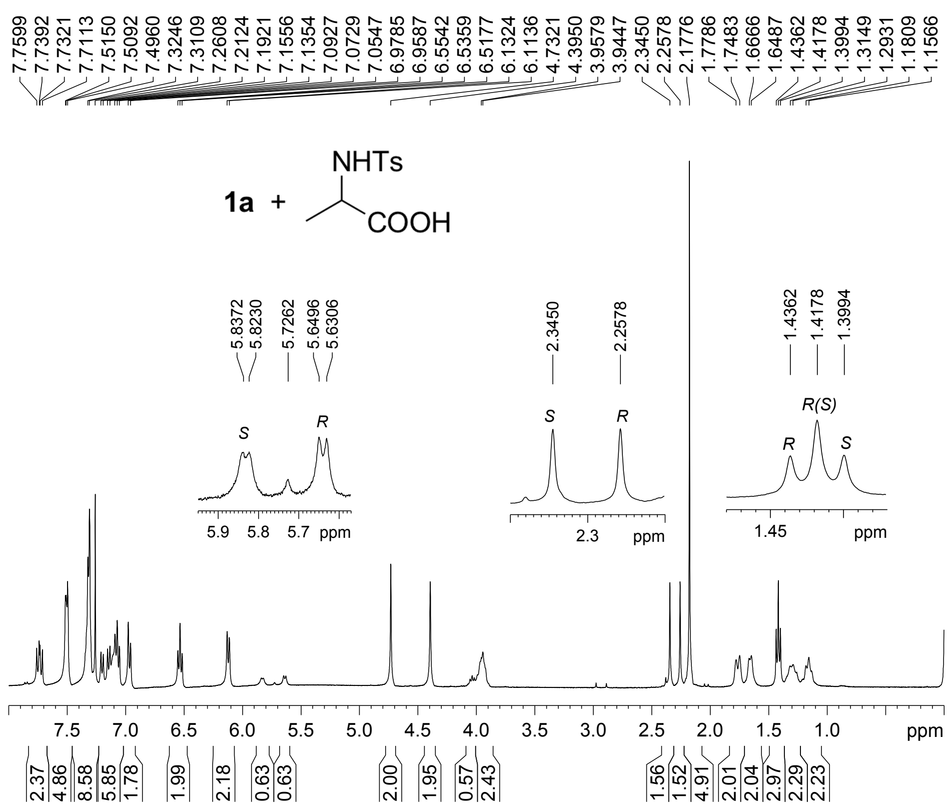


Figure S18. ^{1}H NMR spectrum of (±)-**6** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

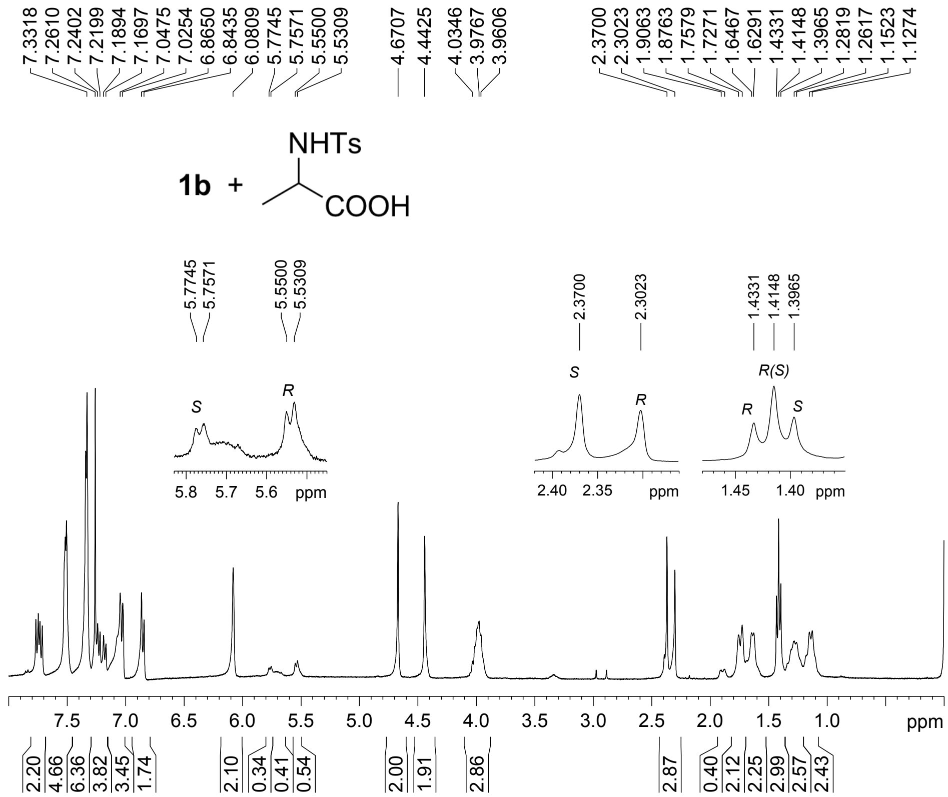


Figure S19. ^{1}H NMR spectrum of (±)-**6** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

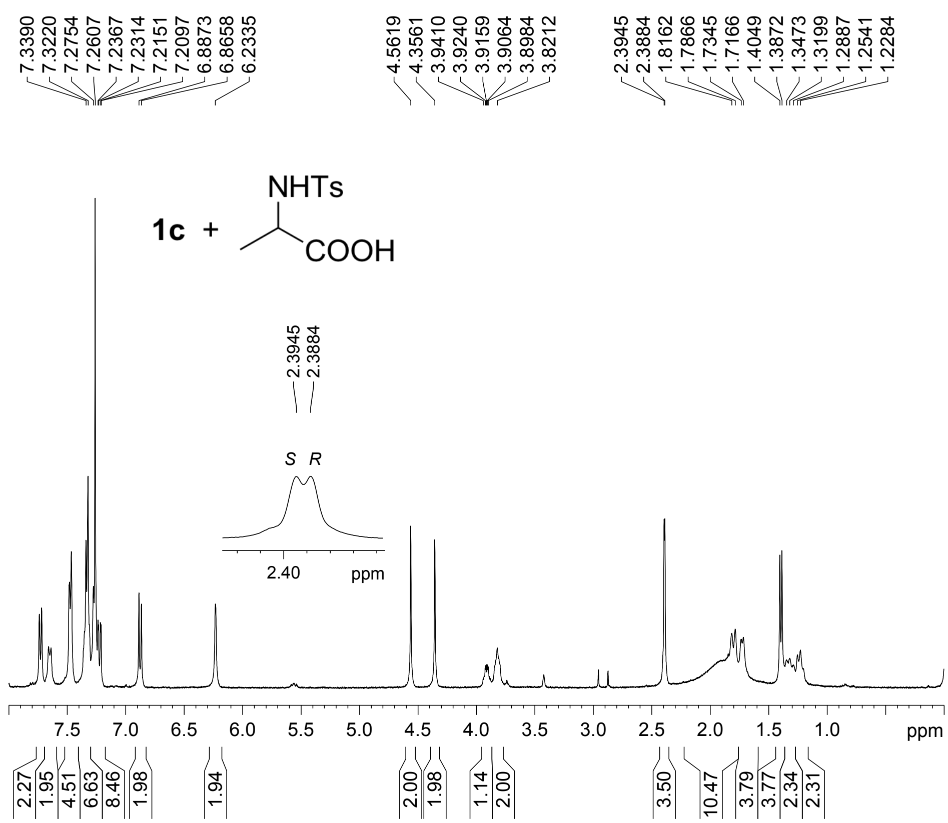


Figure S20. ^{1}H NMR spectrum of (±)-**6** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

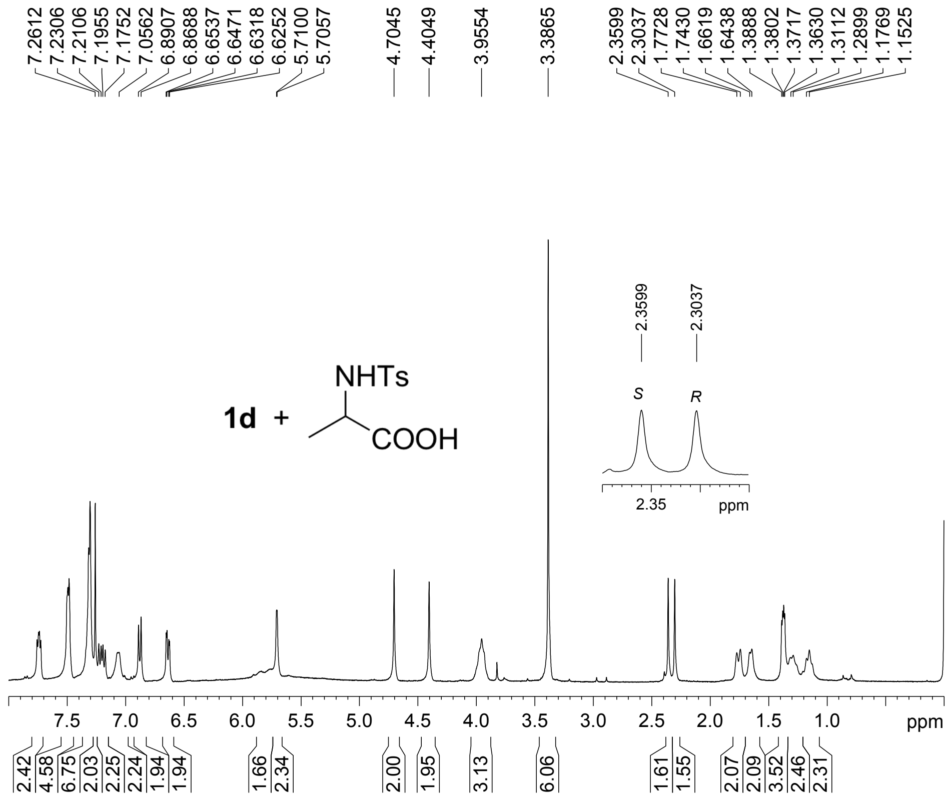


Figure S21. ^{1}H NMR spectrum of (±)-**6** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

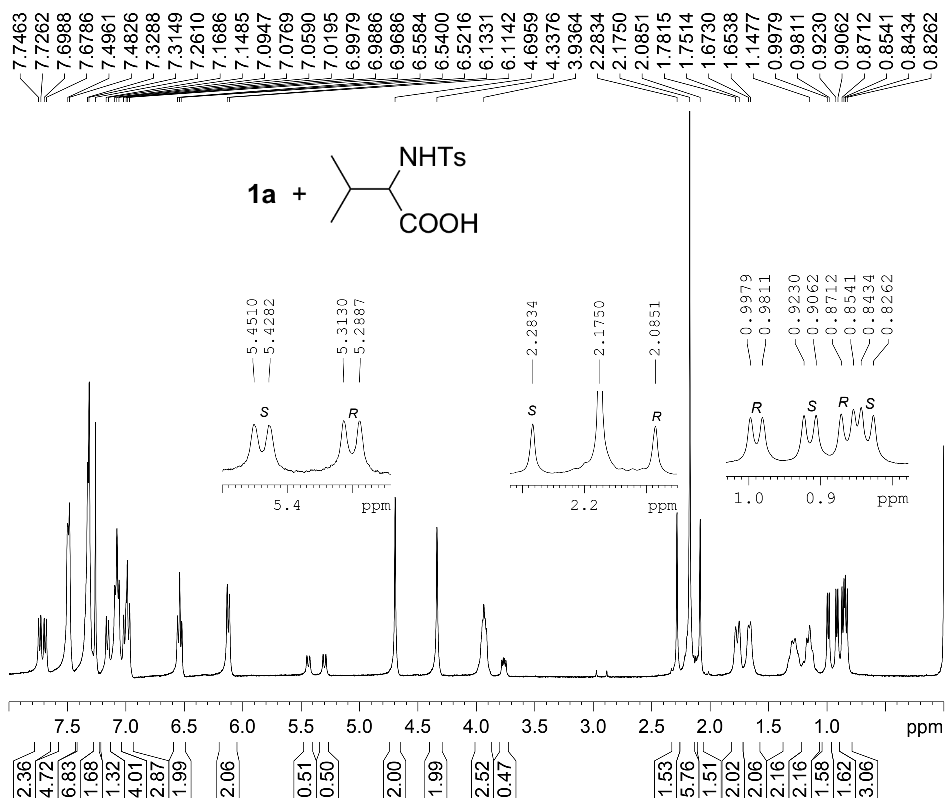


Figure S22. ^{1}H NMR spectrum of (±)-**7** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

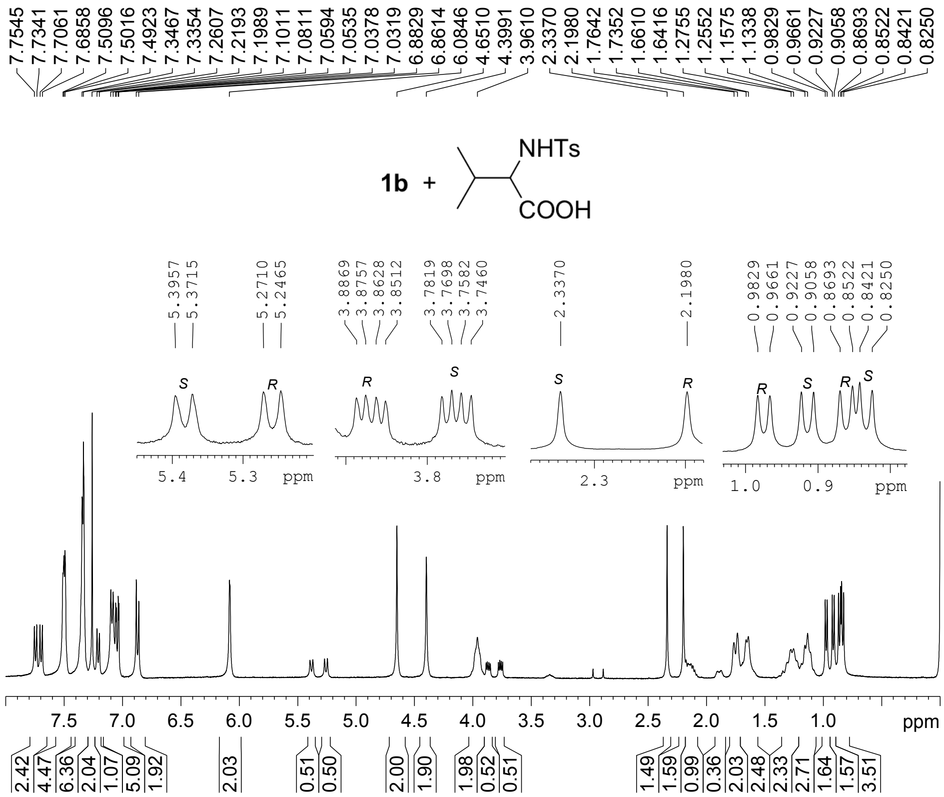


Figure S23. [1]H NMR spectrum of (±)-**7** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

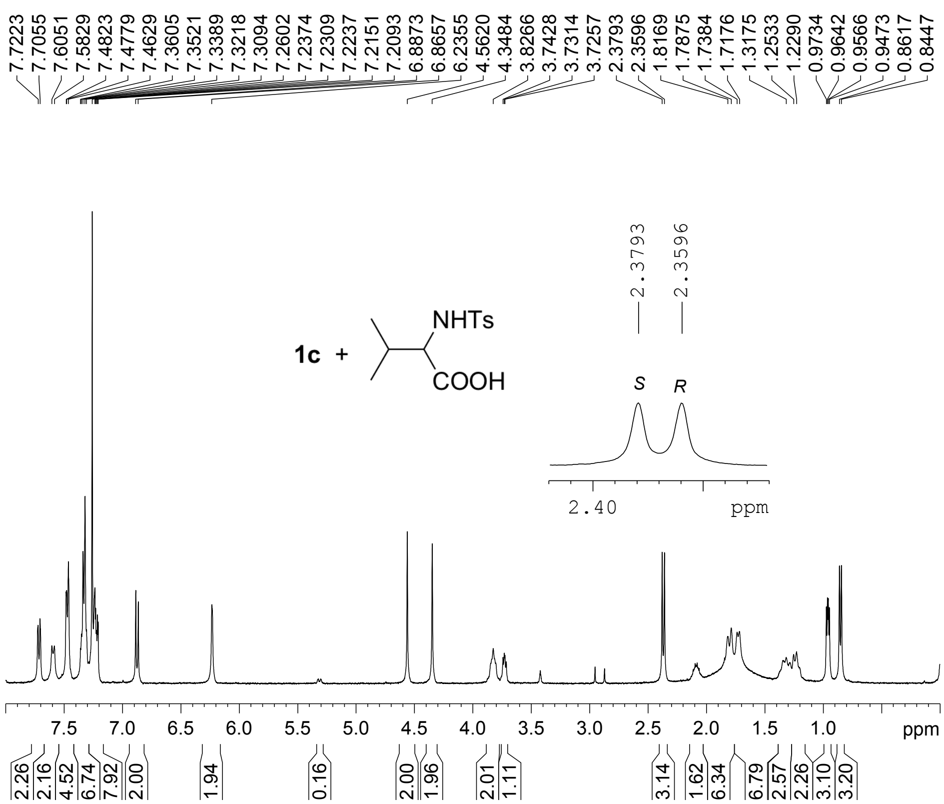


Figure S24. [1]H NMR spectrum of (±)-**7** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

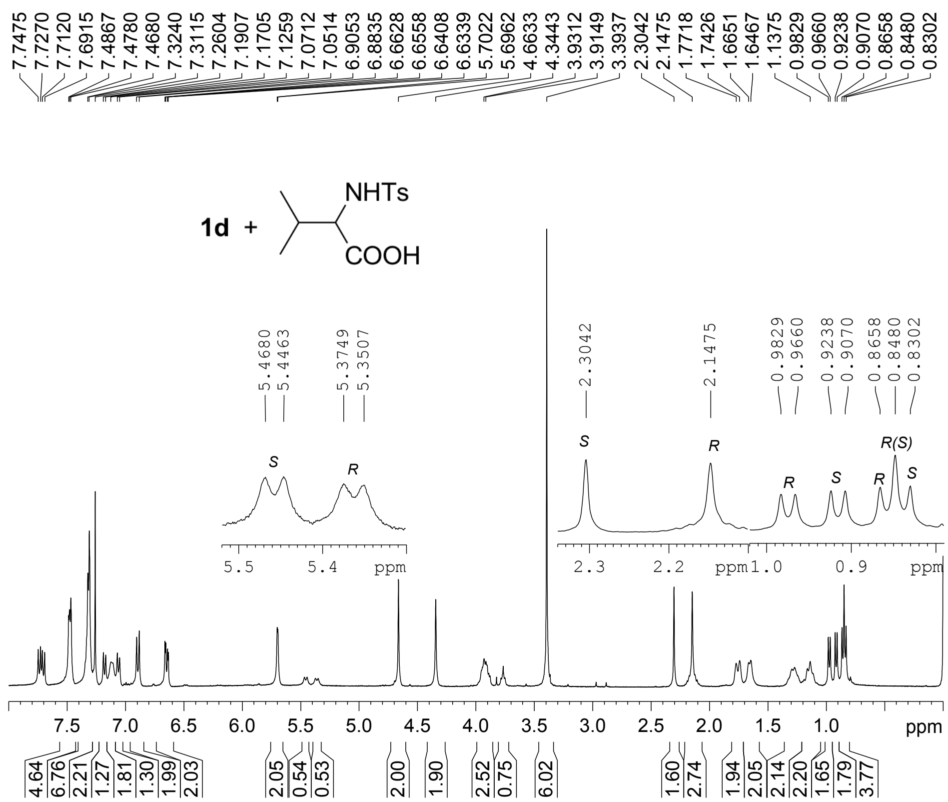


Figure S25. ^{1}H NMR spectrum of (±)-**7** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

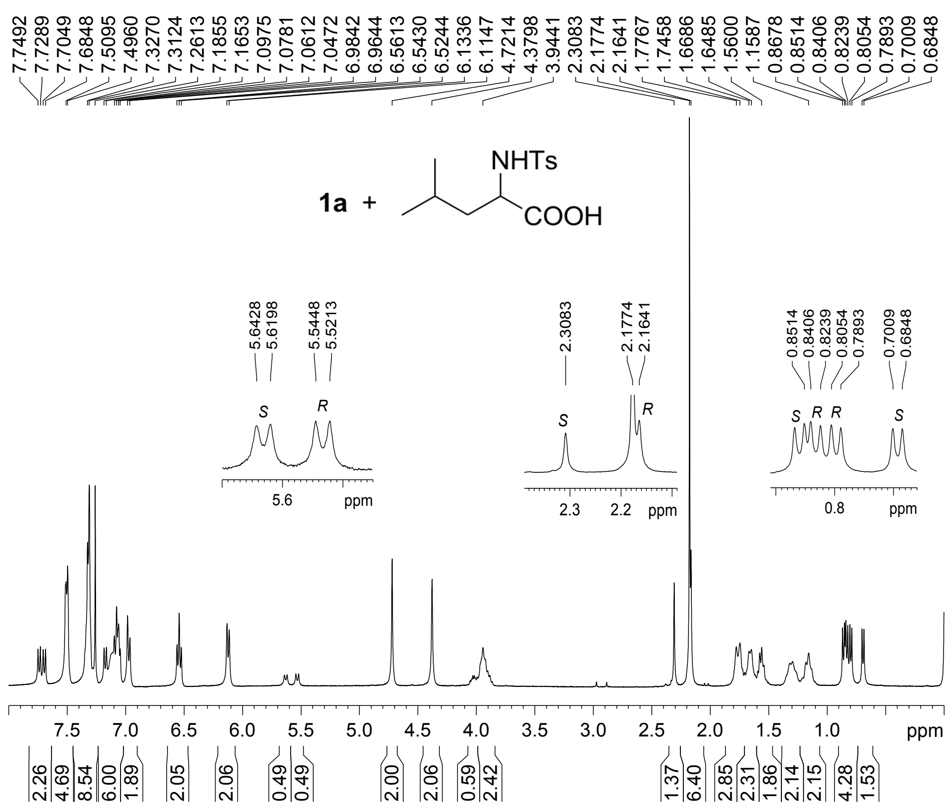


Figure S26. ^{1}H NMR spectrum of (±)-**8** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

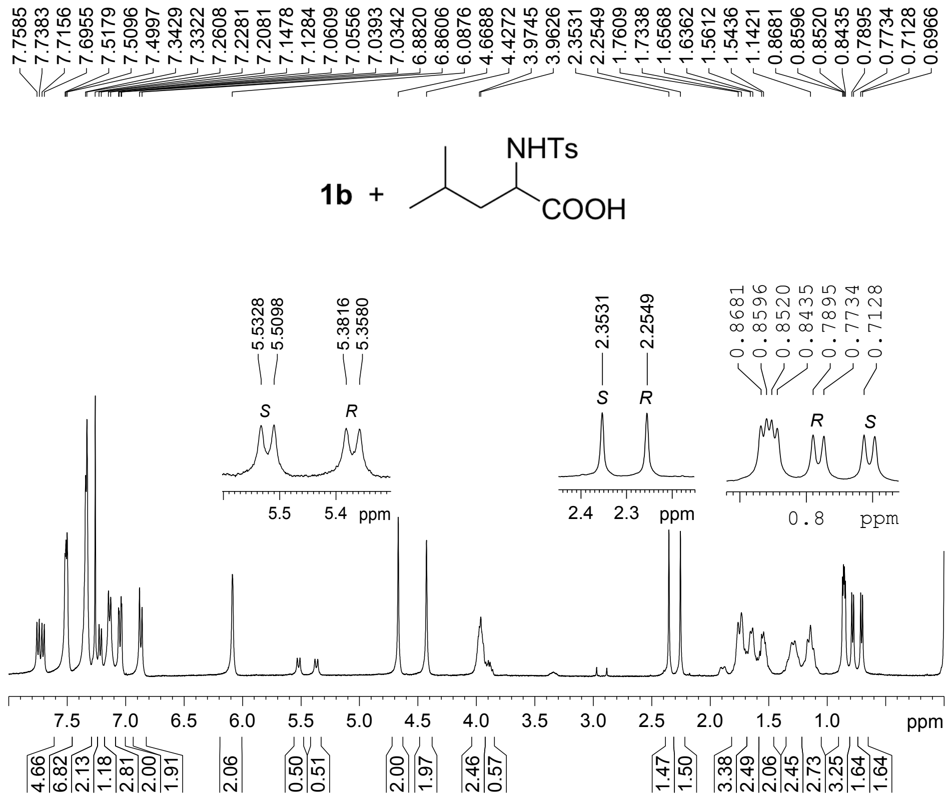


Figure S27. [1]H NMR spectrum of (±)-**8** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

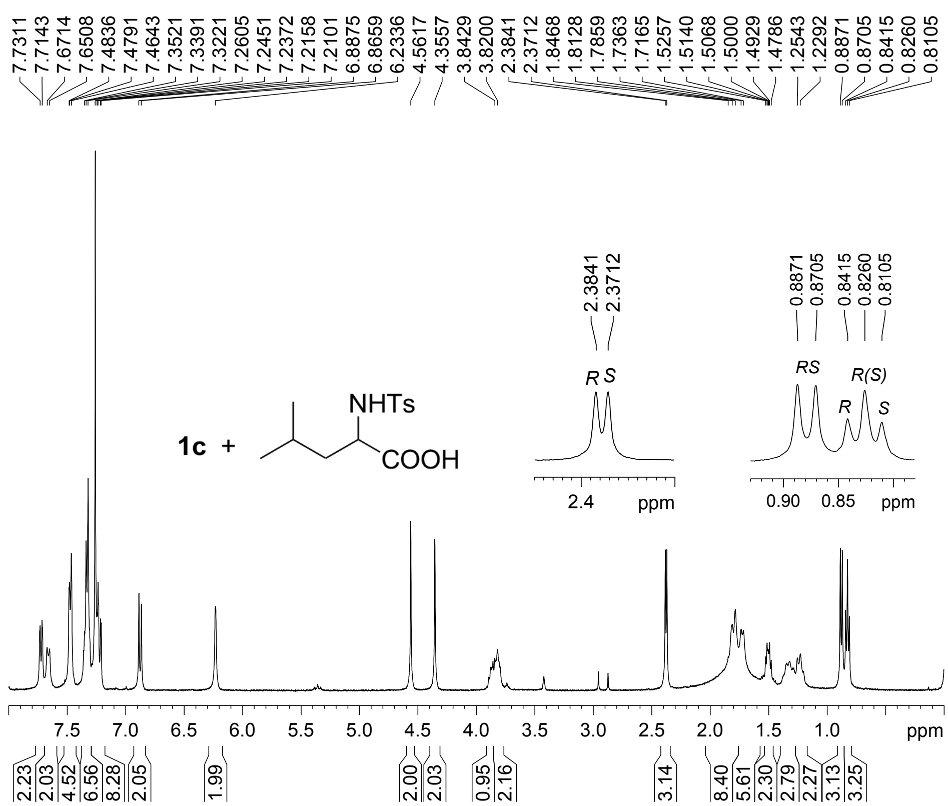


Figure S28. [1]H NMR spectrum of (±)-**8** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

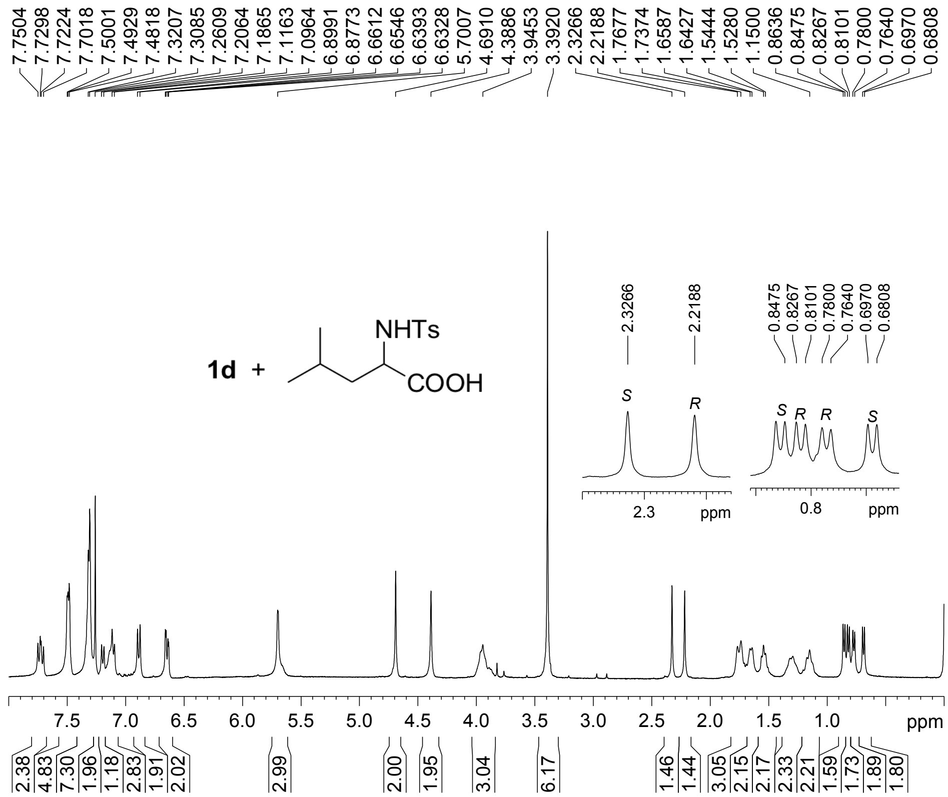


Figure S29. [1]H NMR spectrum of (±)-**8** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

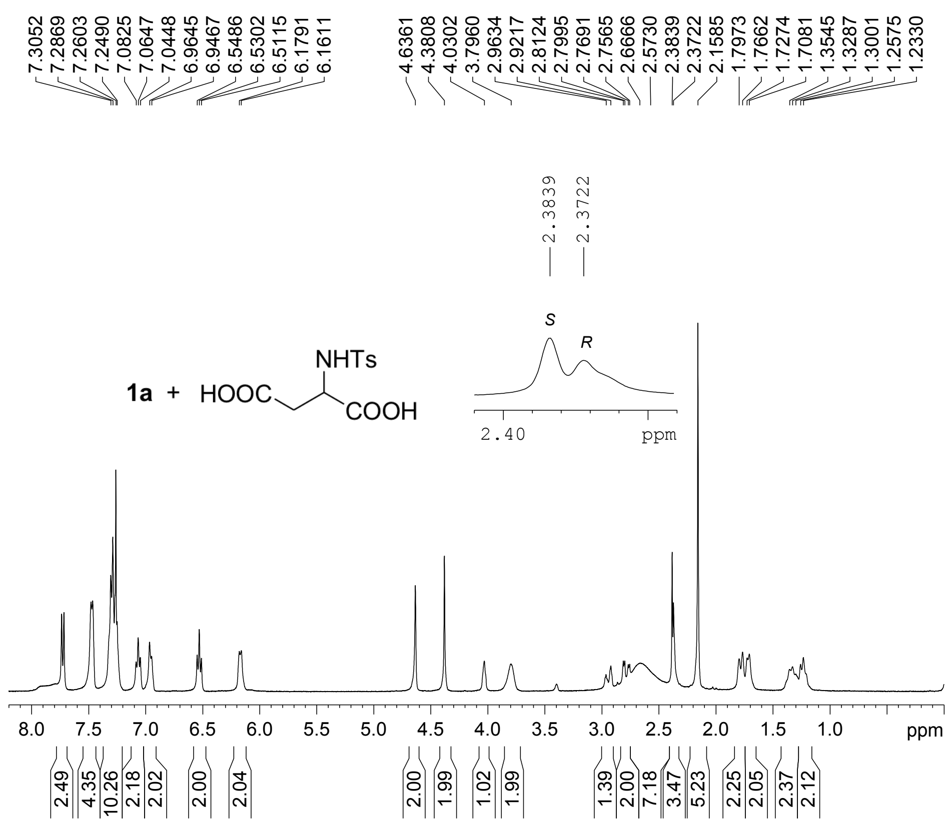


Figure S30. [1]H NMR spectrum of (±)-**9** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

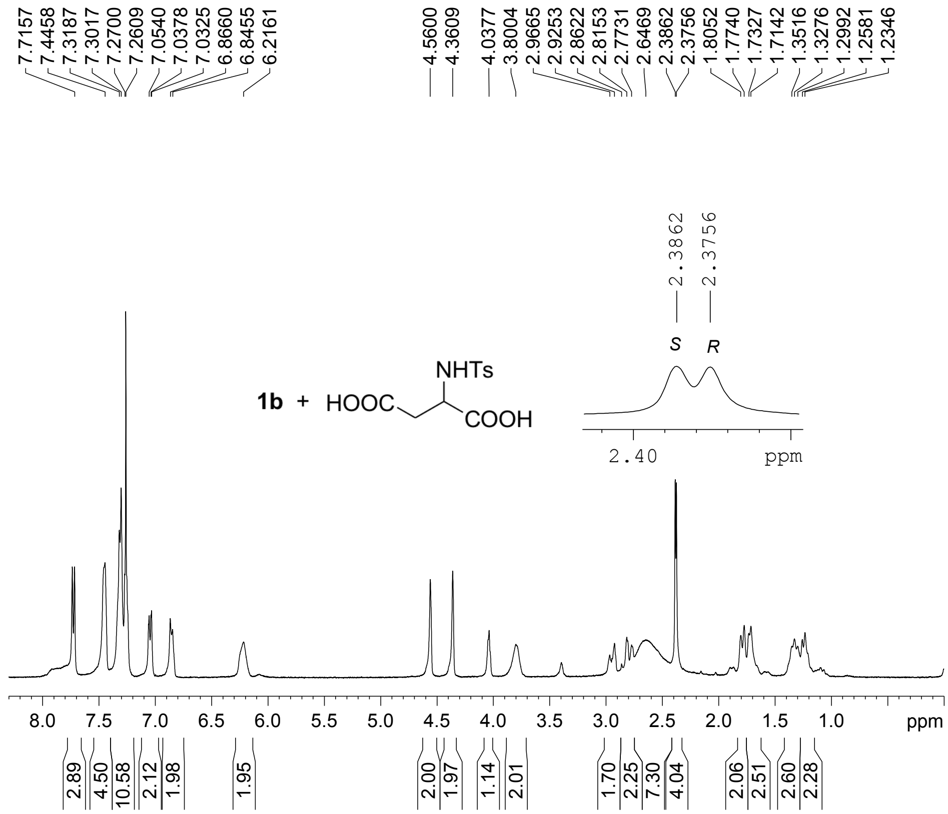


Figure S31. ^{1}H NMR spectrum of (±)-**9** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

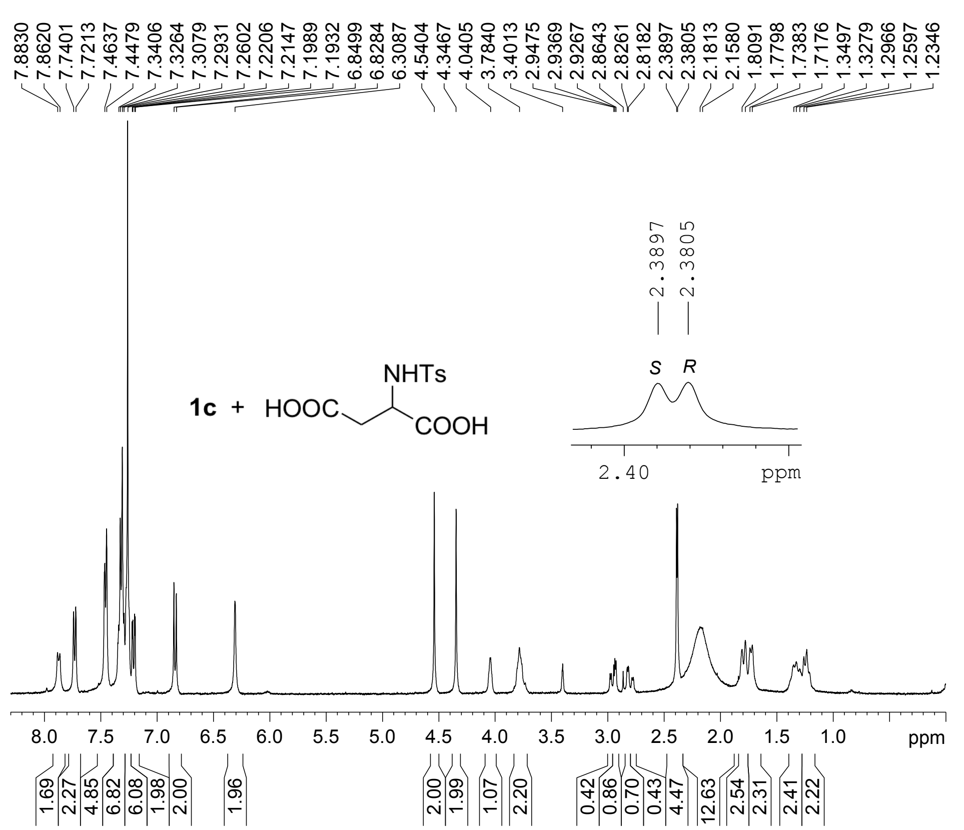


Figure S32. ^{1}H NMR spectrum of (±)-**9** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

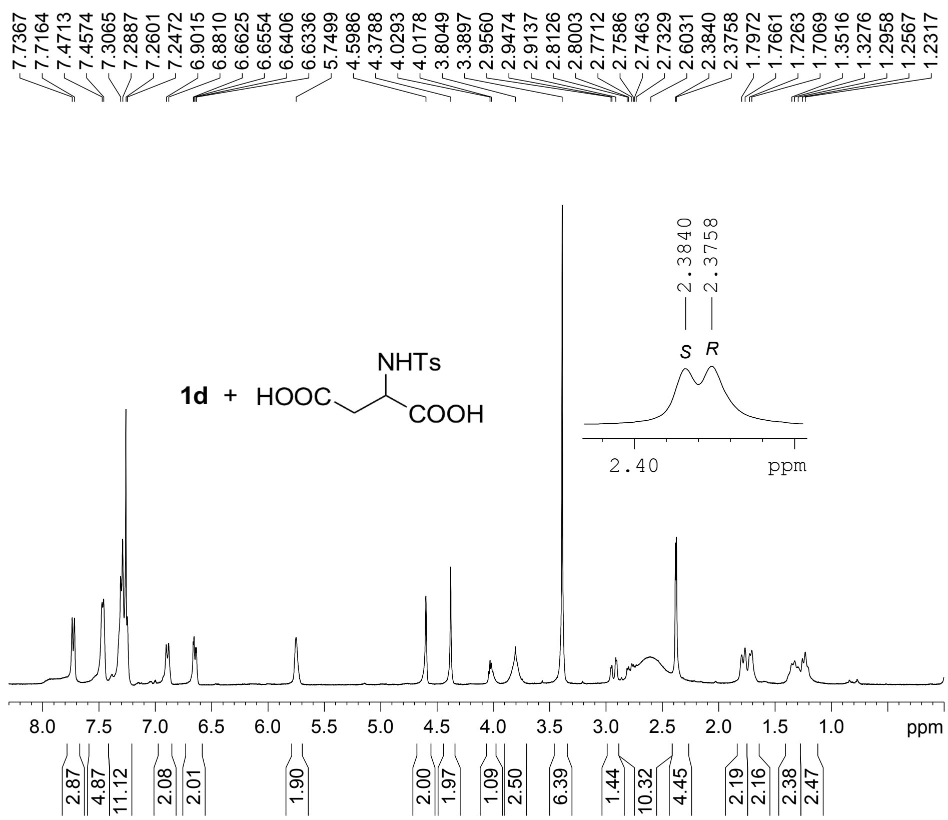


Figure S33. [1]H NMR spectrum of (±)-**9** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

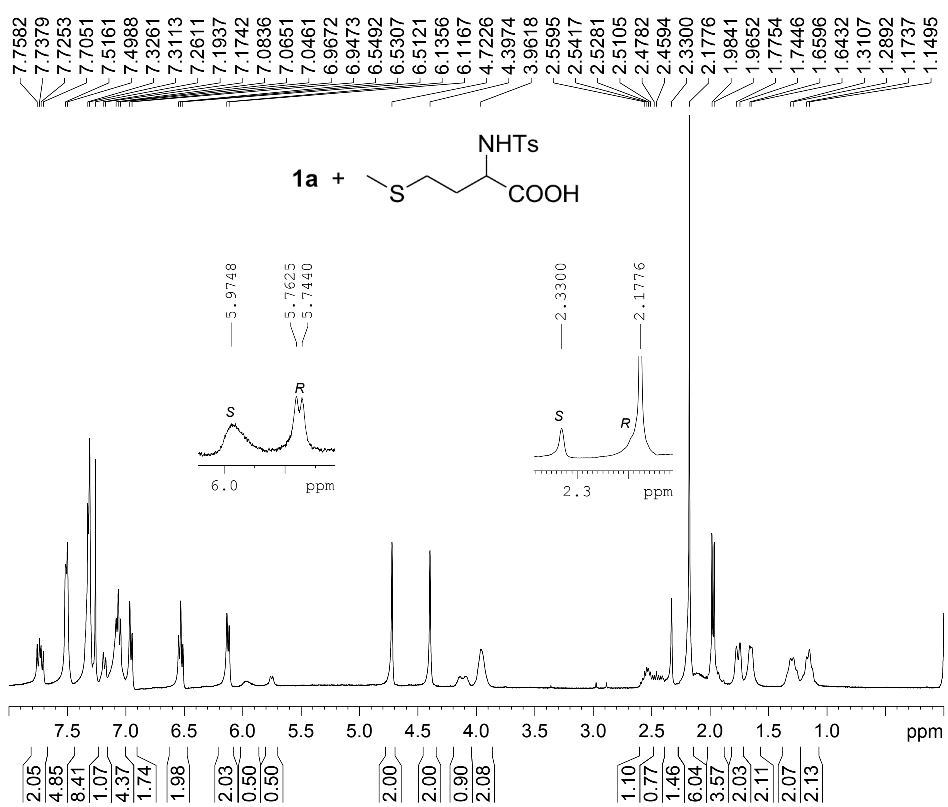


Figure S34. [1]H NMR spectrum of (±)-**10** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

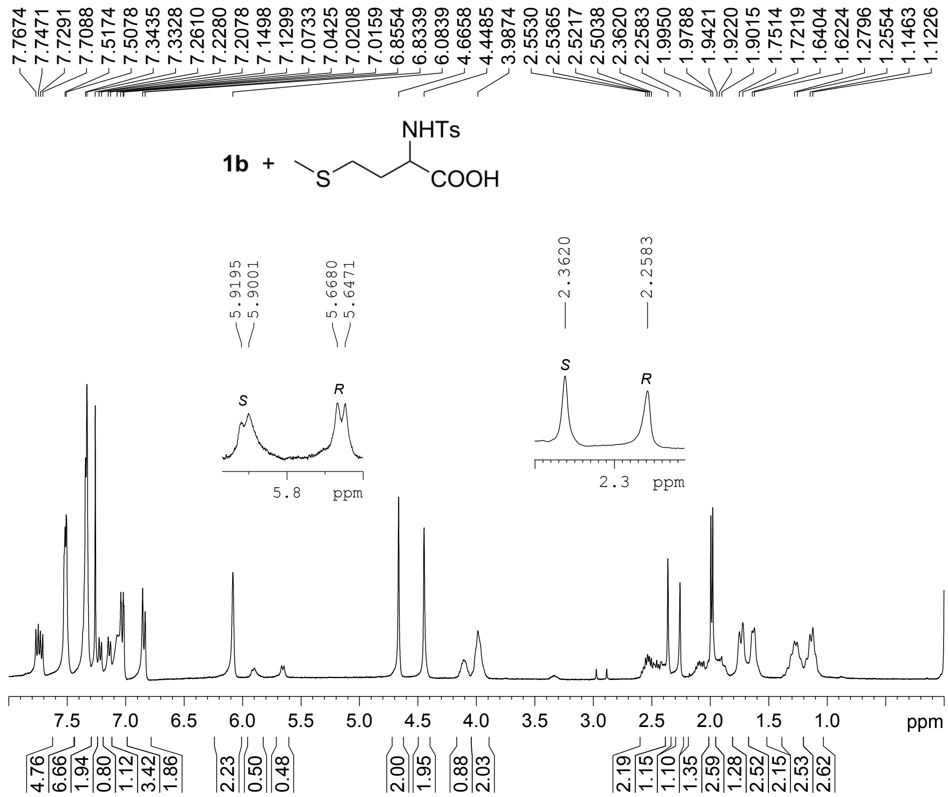


Figure S35. ^{1}H NMR spectrum of (±)-**10** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

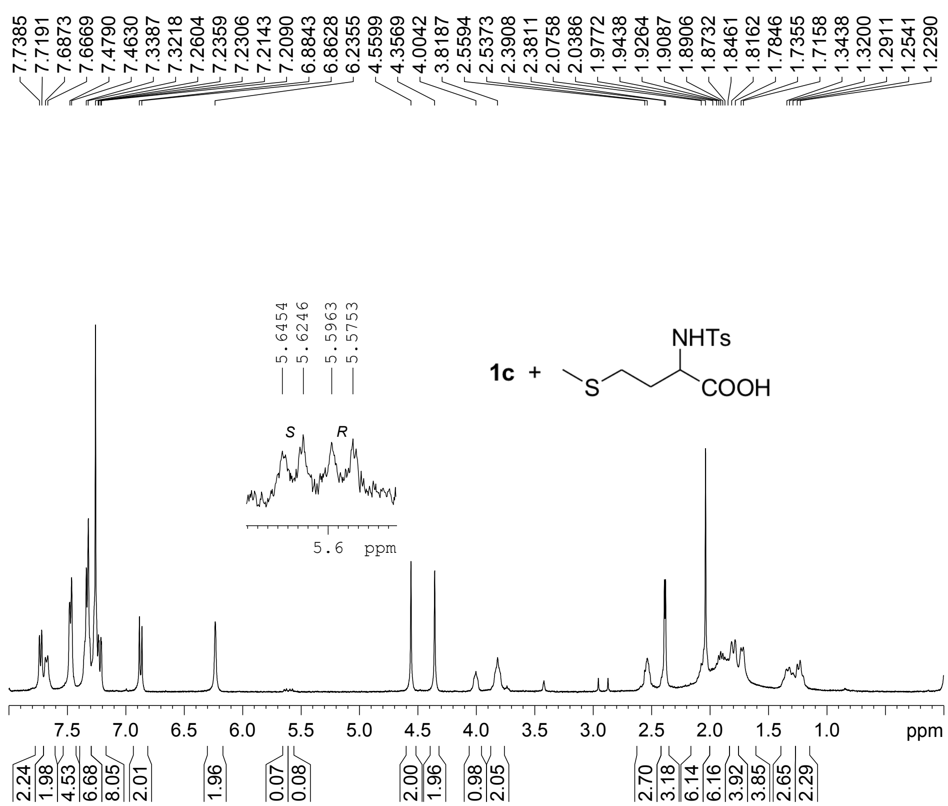


Figure S36. ^{1}H NMR spectrum of (±)-**10** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

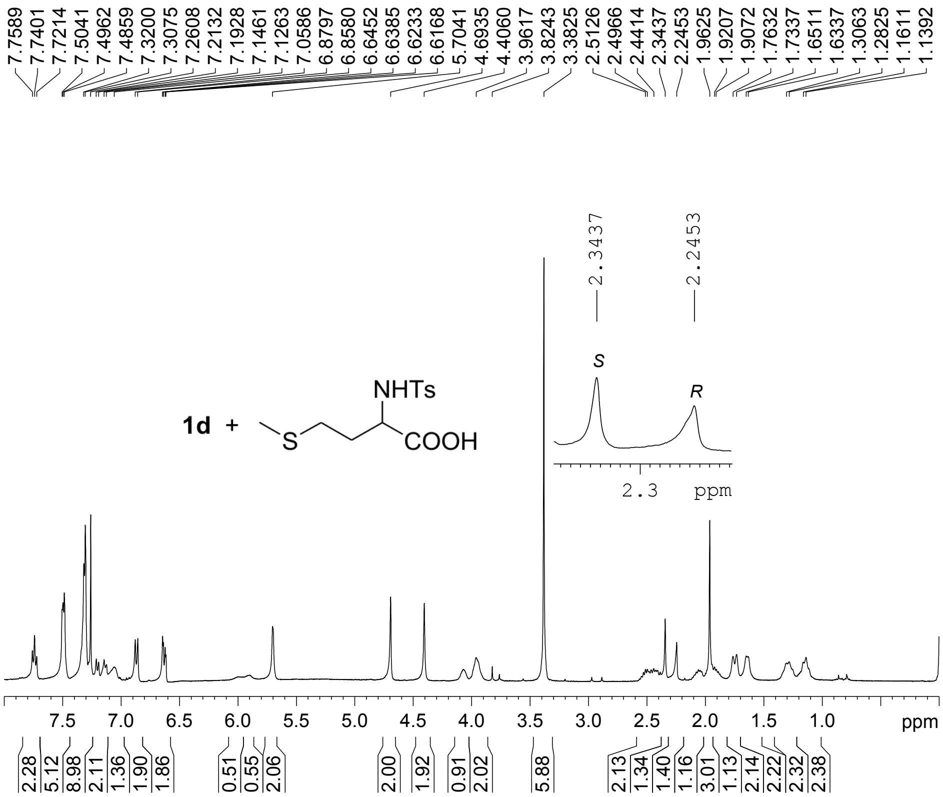


Figure S37. ^{1}H NMR spectrum of (±)-**10** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

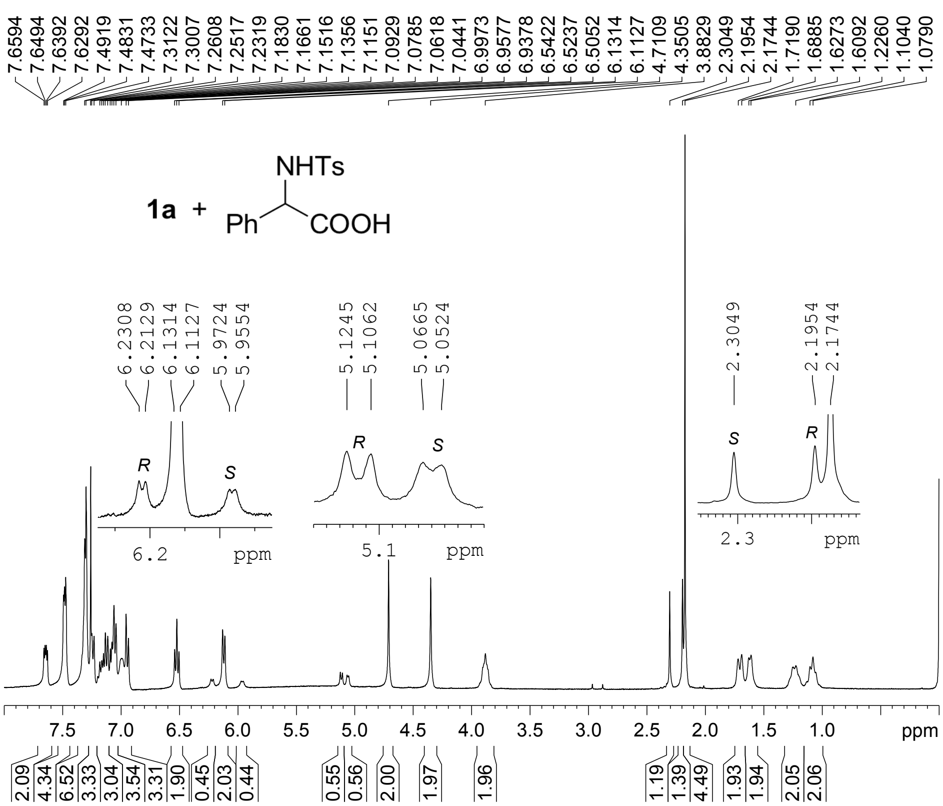


Figure S38. ^{1}H NMR spectrum of (±)-**11** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

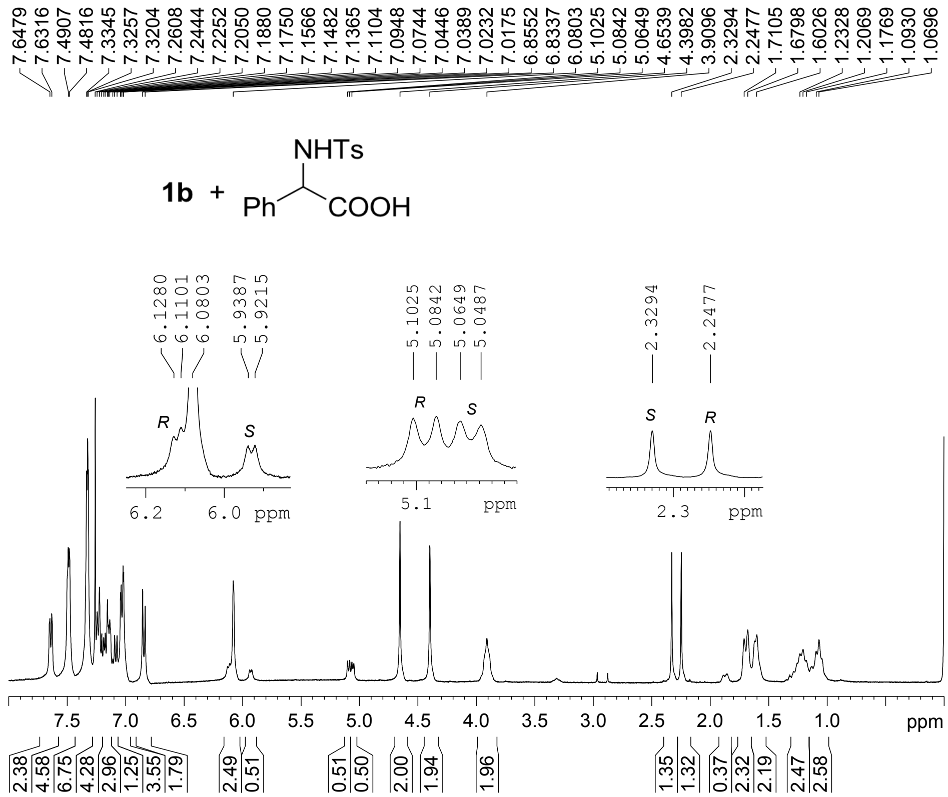


Figure S39. [1]H NMR spectrum of (±)-**11** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

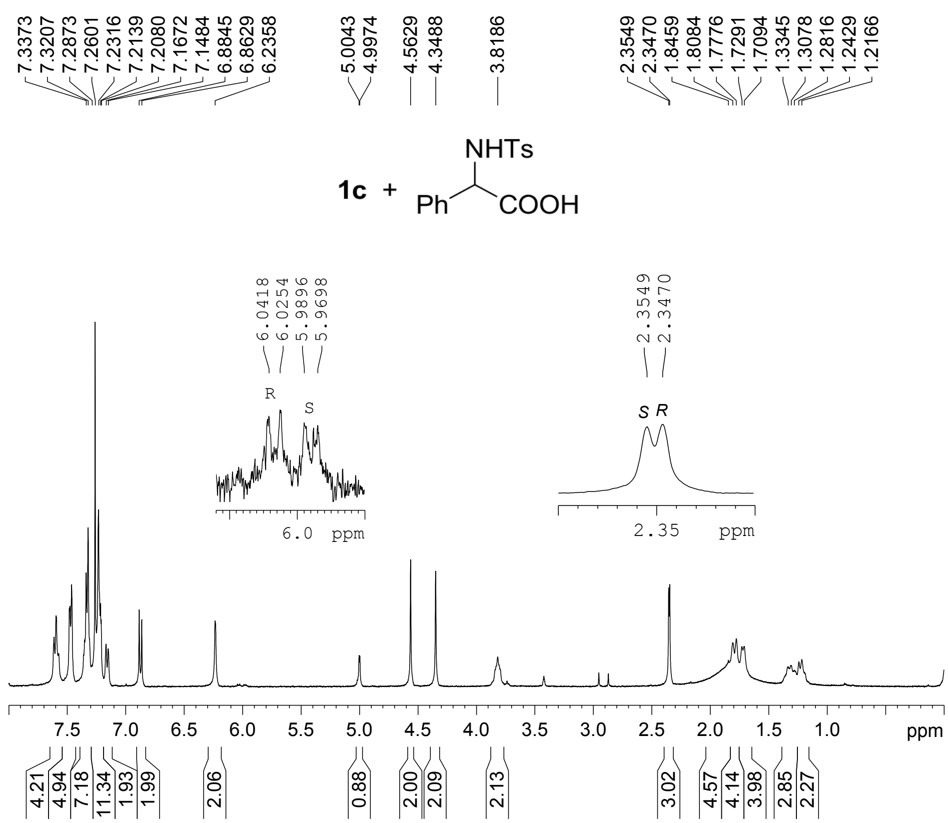


Figure S40. [1]H NMR spectrum of (±)-**11** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

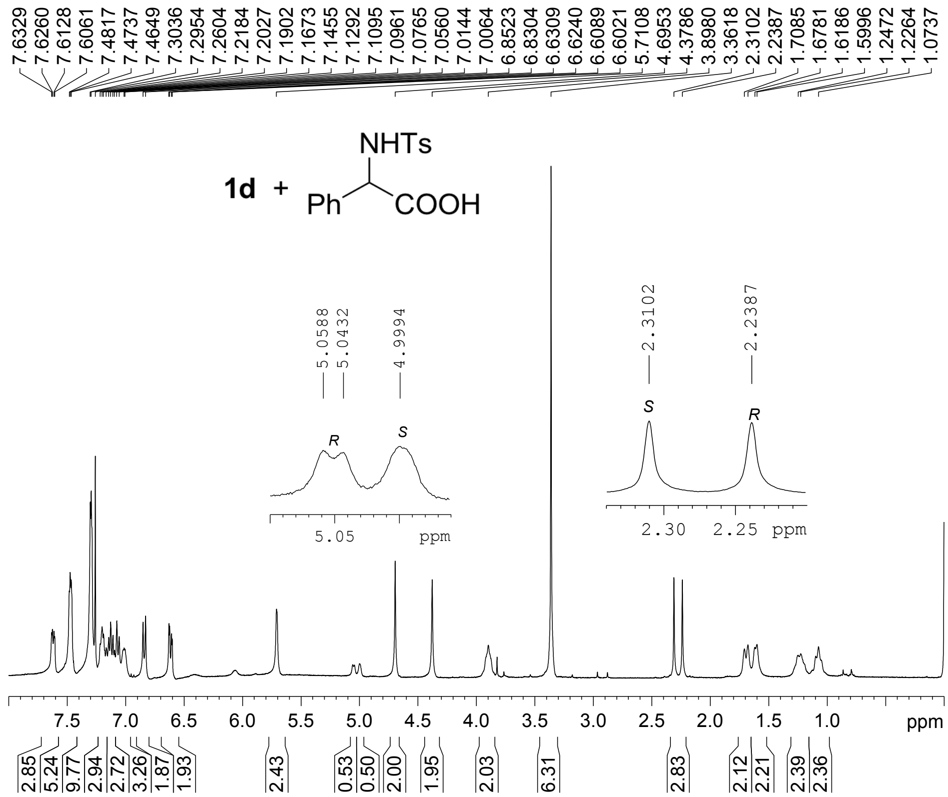


Figure S41. ^{1}H NMR spectrum of (±)-**11** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

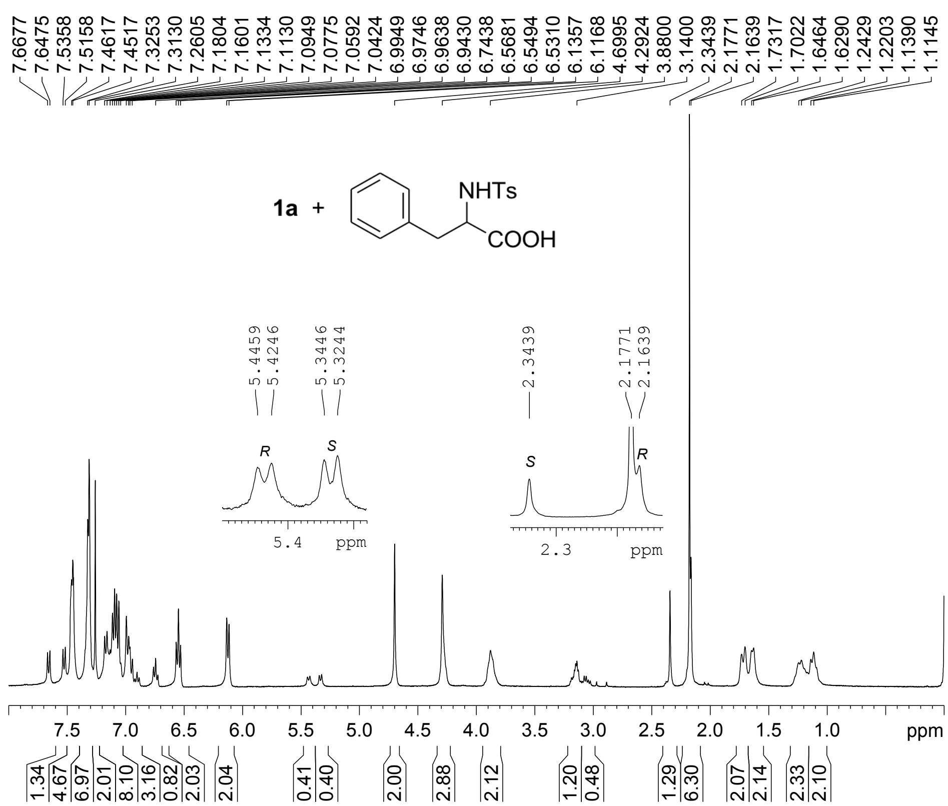


Figure S42. ^{1}H NMR spectrum of (±)-**12** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

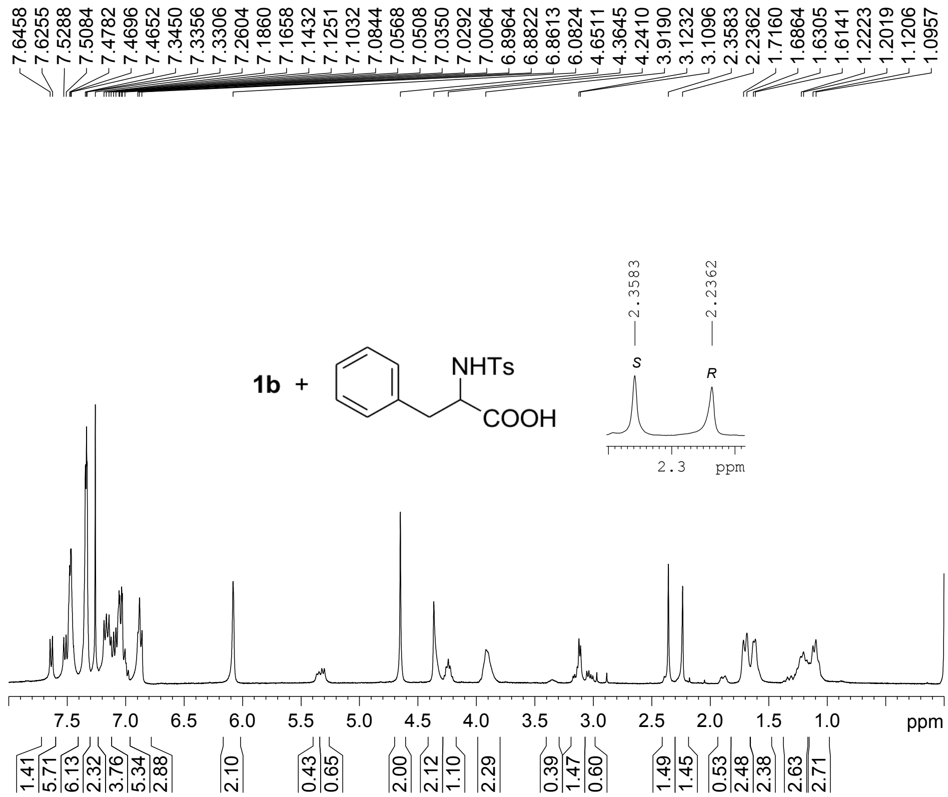


Figure S43. [1]H NMR spectrum of (±)-**12** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

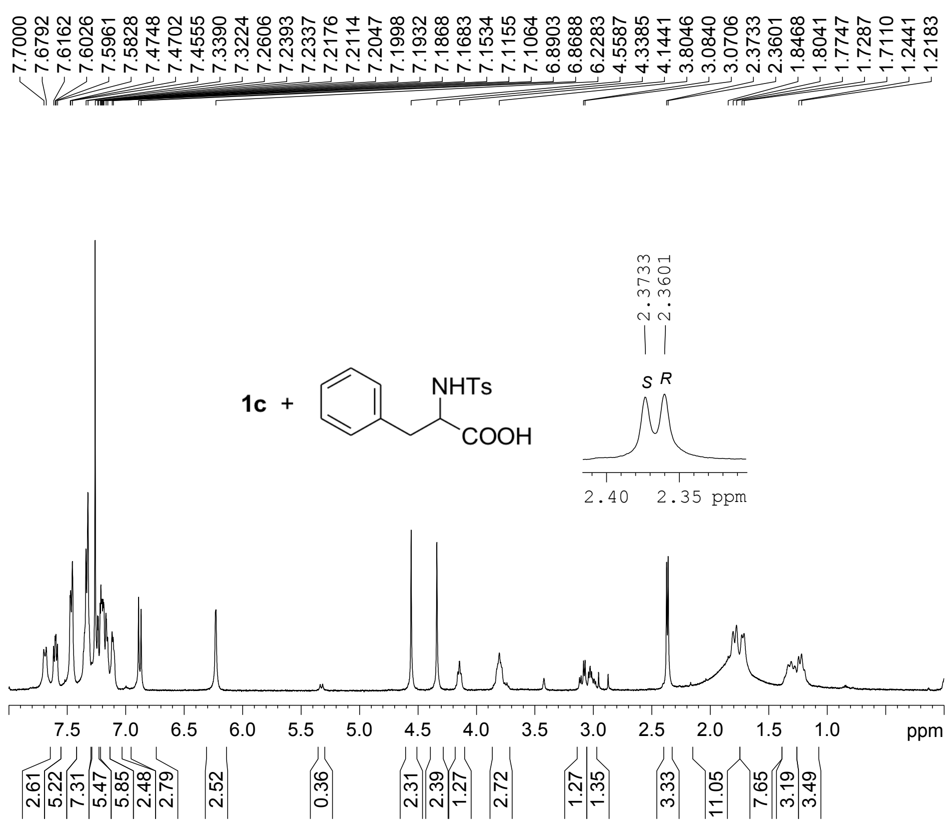


Figure S44. [1]H NMR spectrum of (±)-**12** with TAMCSA **1c** in $CDCl_3$ /CD_3OD (5%) (400 MHz), [**1c**] = 5 mM.

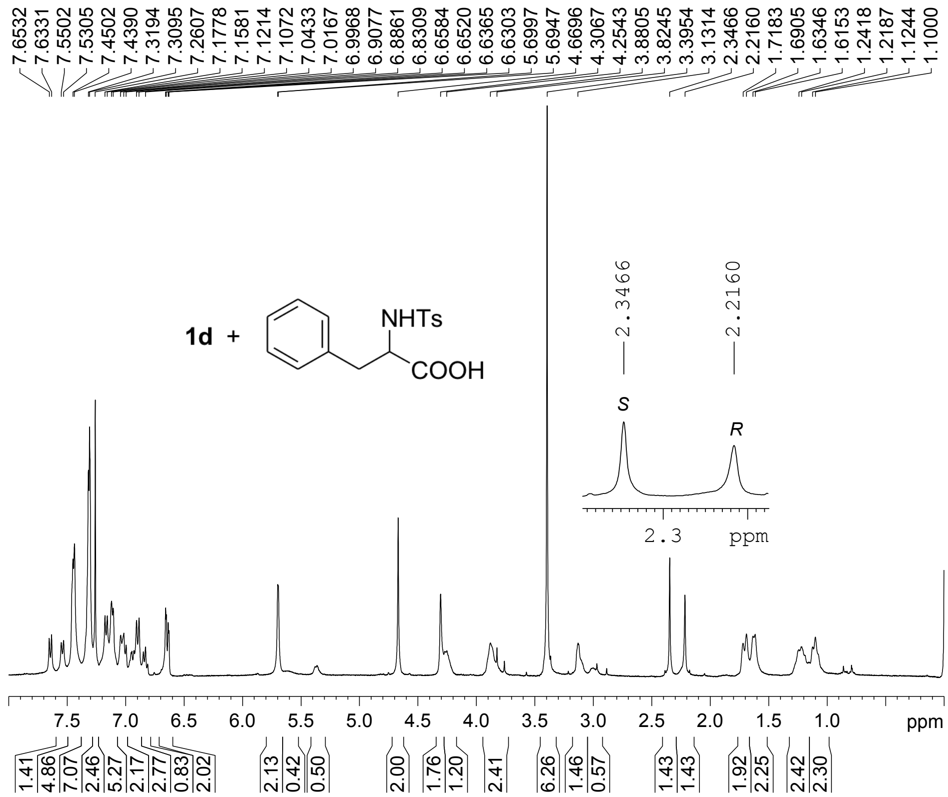


Figure S45. [1]H NMR spectrum of (±)-**12** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

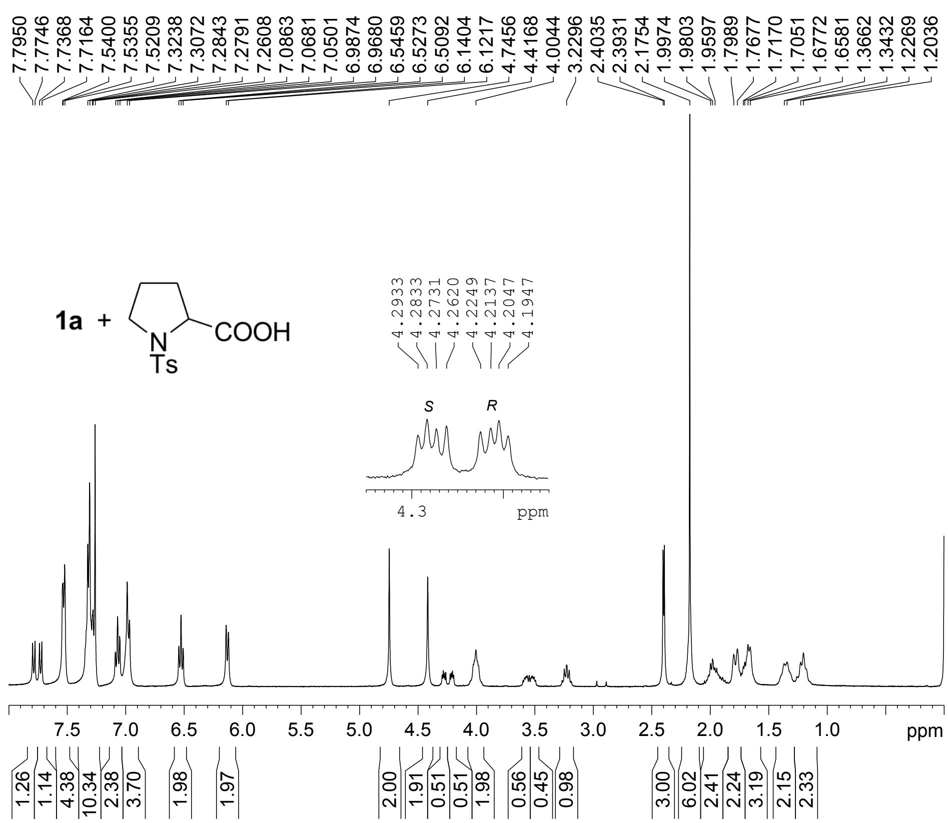


Figure S46. [1]H NMR spectrum of (±)-**13** with TAMCSA **1a** in $CDCl_3$ (400 MHz), [**1a**] = 10 mM.

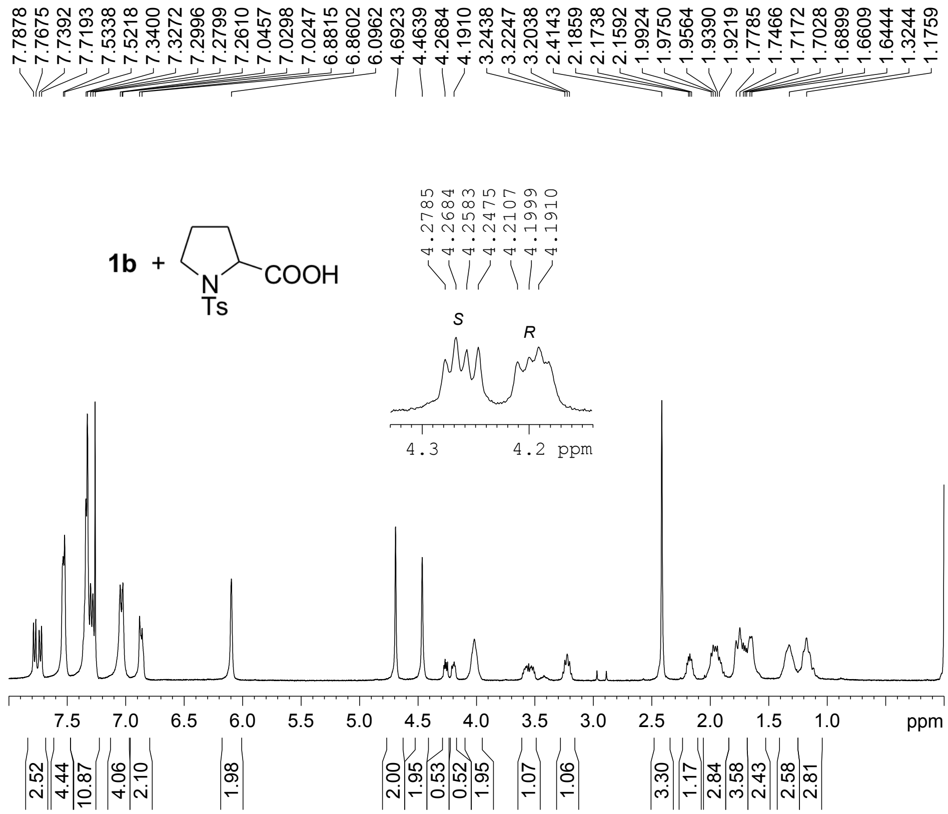


Figure S47. ^{1}H NMR spectrum of (±)-**13** with TAMCSA **1b** in $CDCl_3$ (400 MHz), [**1b**] = 10 mM.

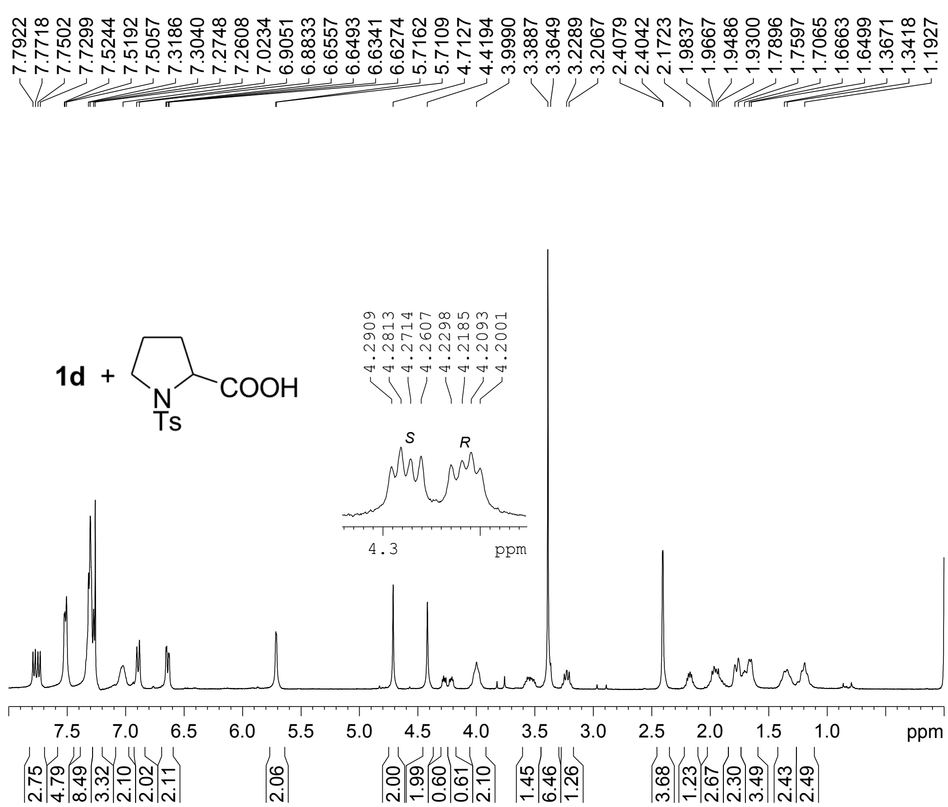


Figure S48. ^{1}H NMR spectrum of (±)-**13** with TAMCSA **1d** in $CDCl_3$ (400 MHz), [**1d**] = 10 mM.

[1]H NMR spectra of enantiomeric excesses.

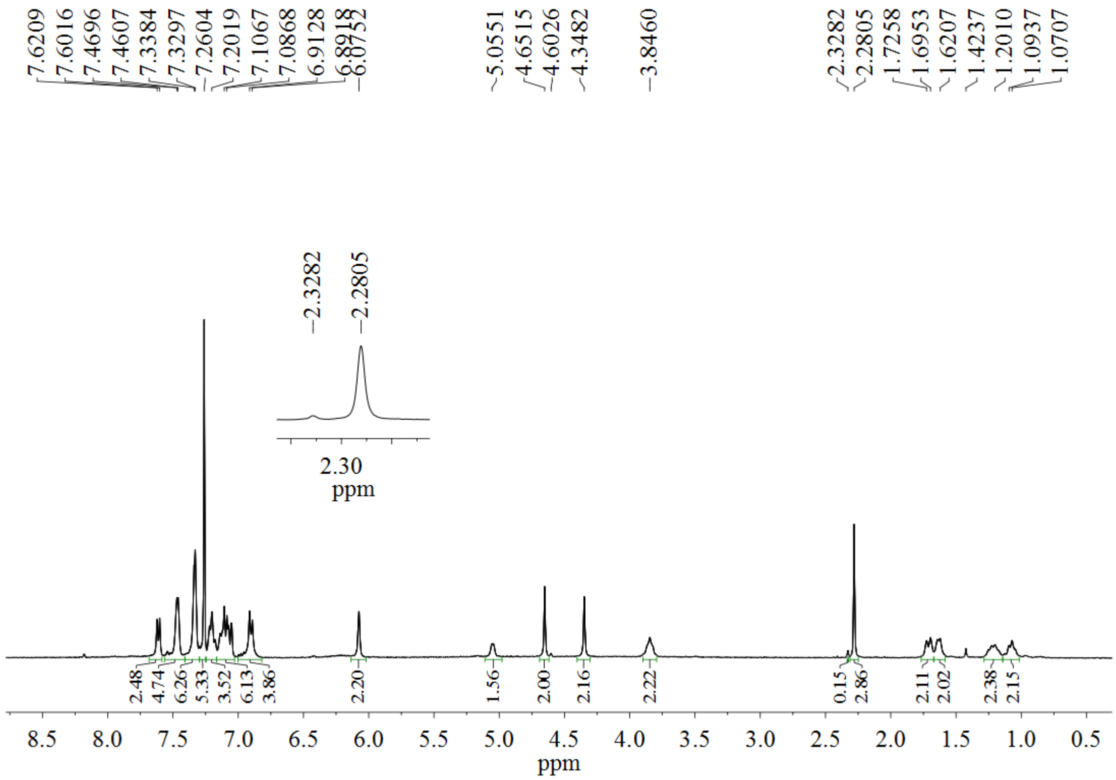


Figure S49. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (-90 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

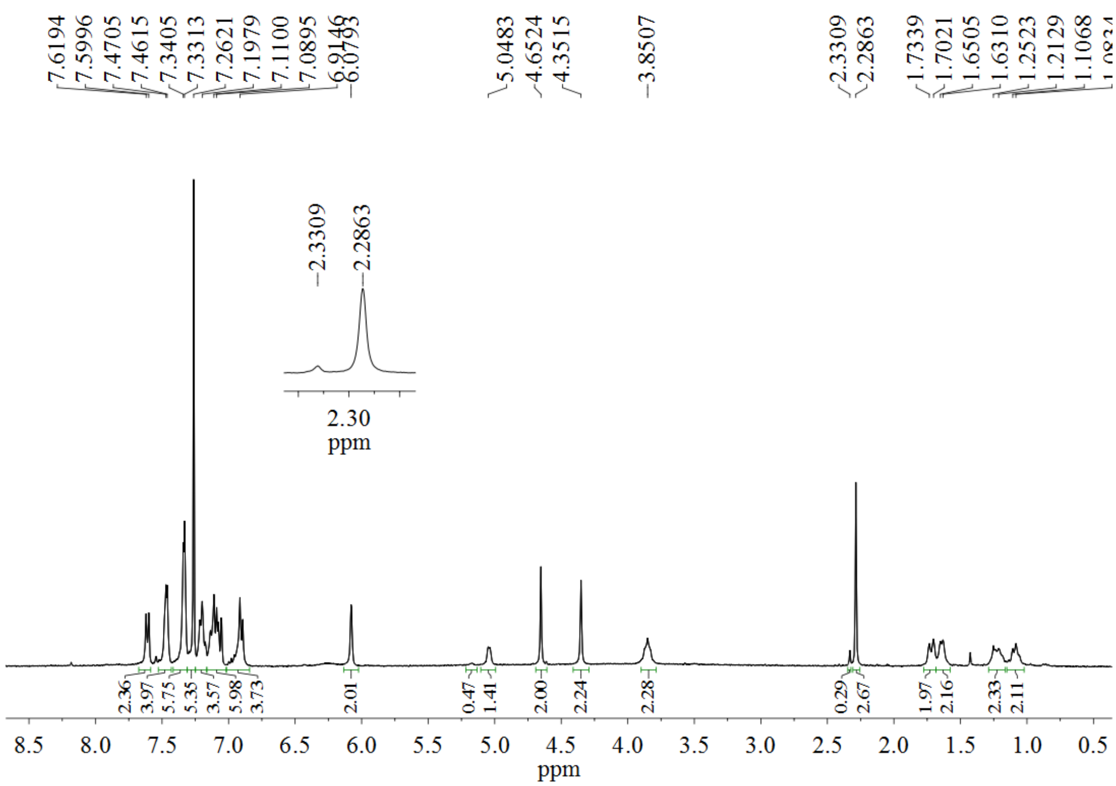


Figure S50. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (-80 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

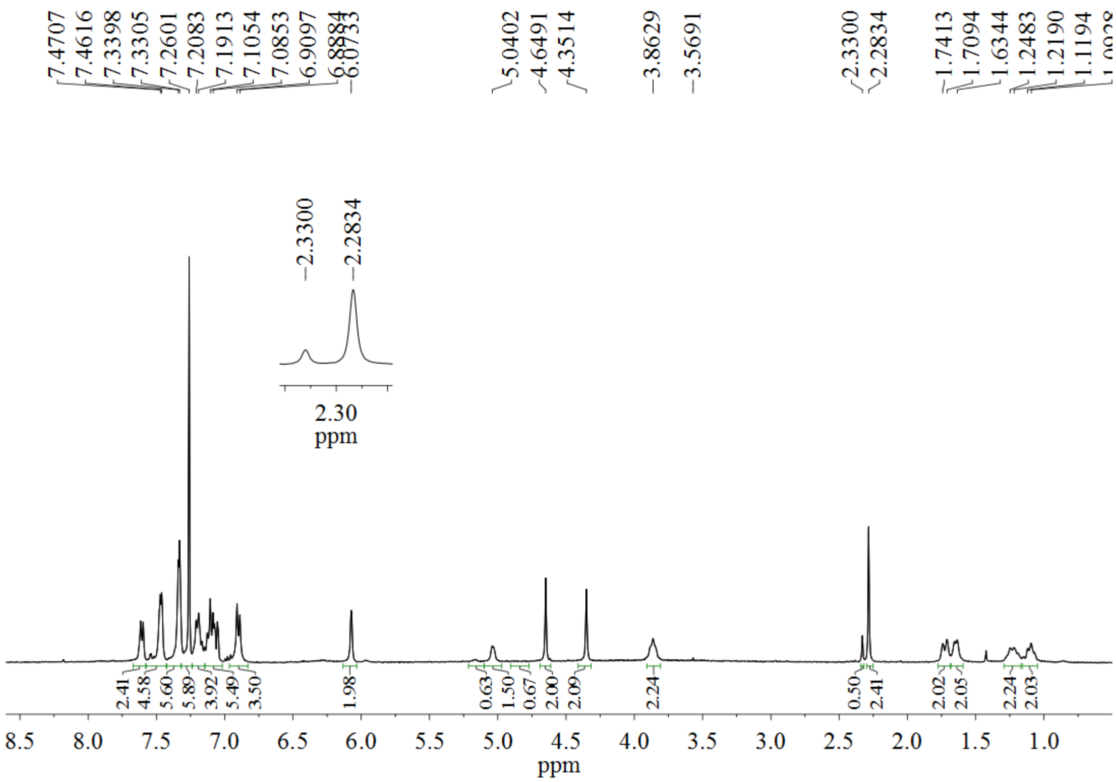


Figure S51. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (-65 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

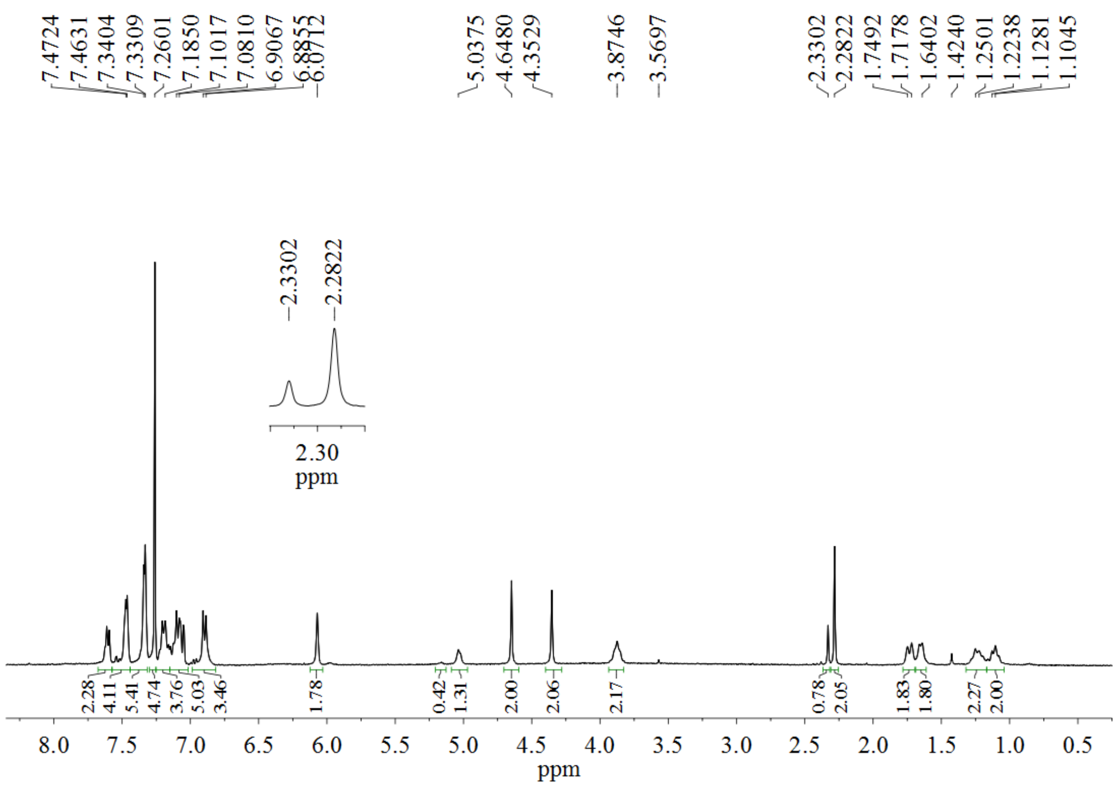


Figure S52. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (-45 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

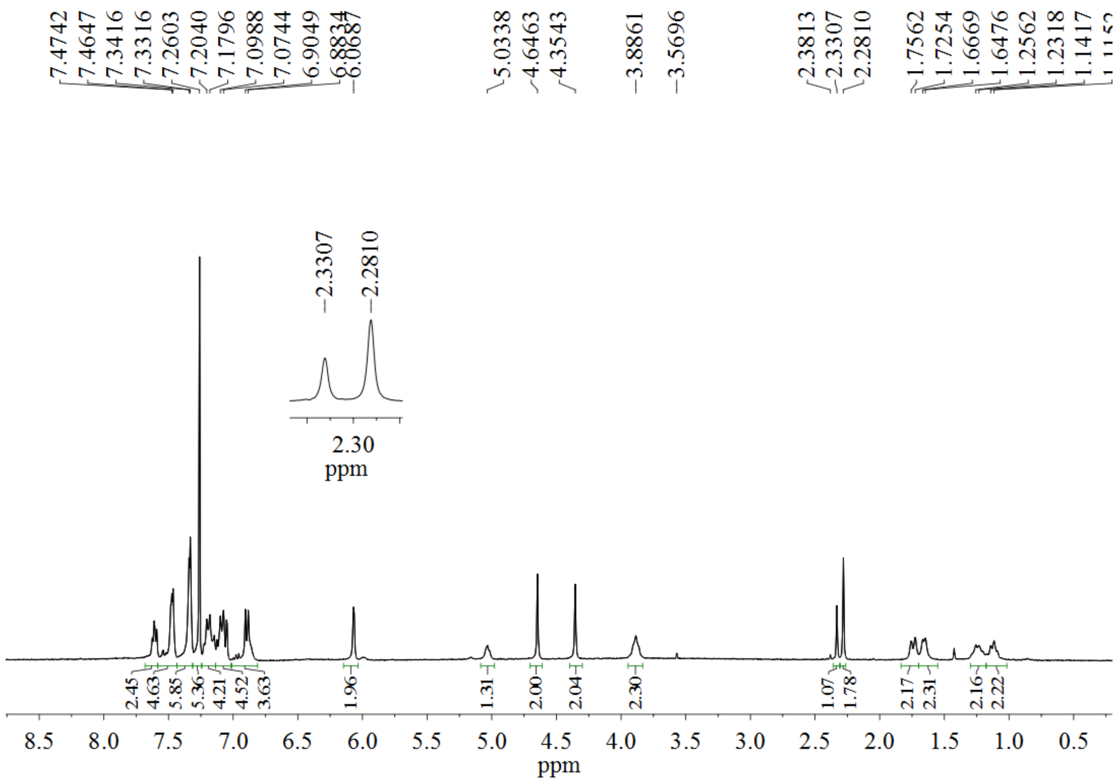


Figure S53. [1]H NMR spectrum of (*R*)**-11** and (*S*)**-11** (-25 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

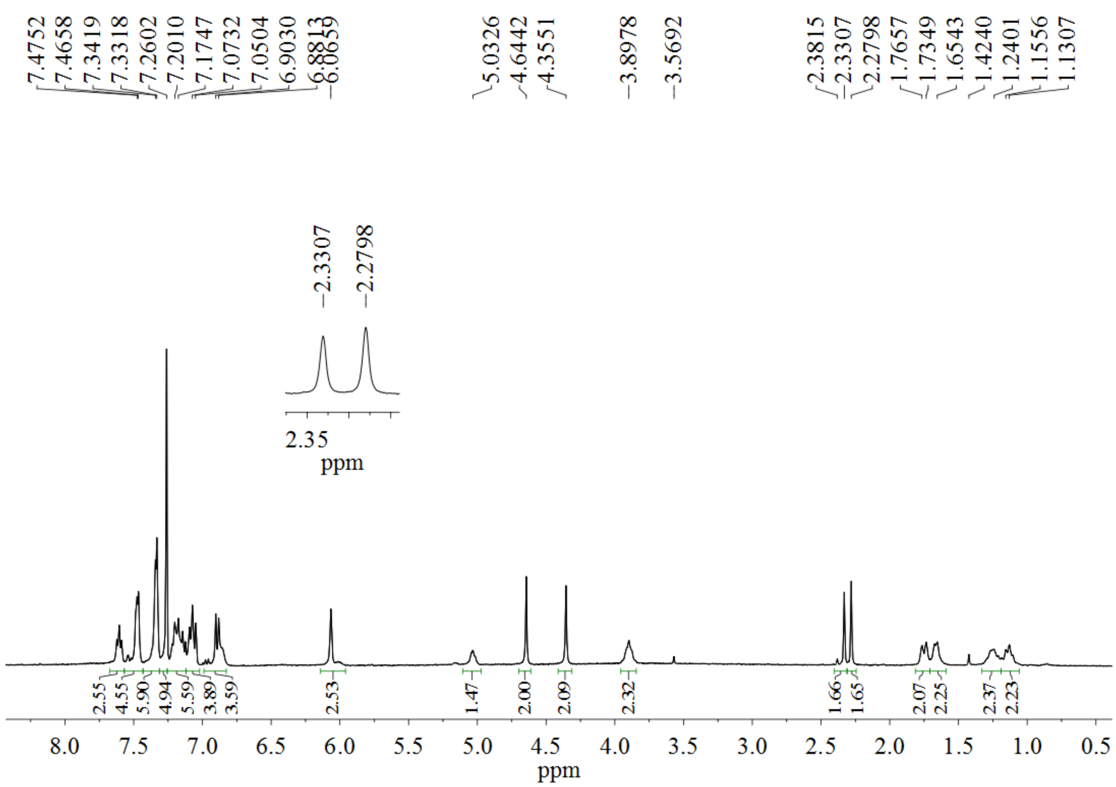


Figure S54. [1]H NMR spectrum of (*R*)**-11** and (*S*)**-11** (0 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

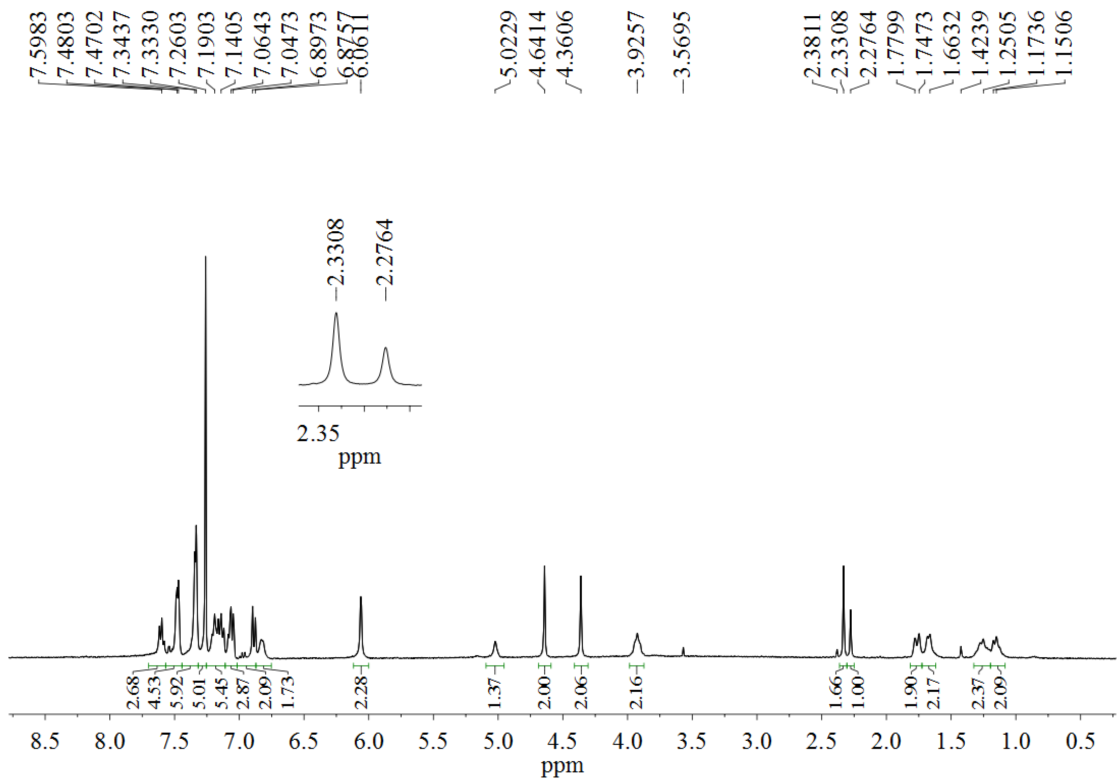


Figure S55. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (25 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

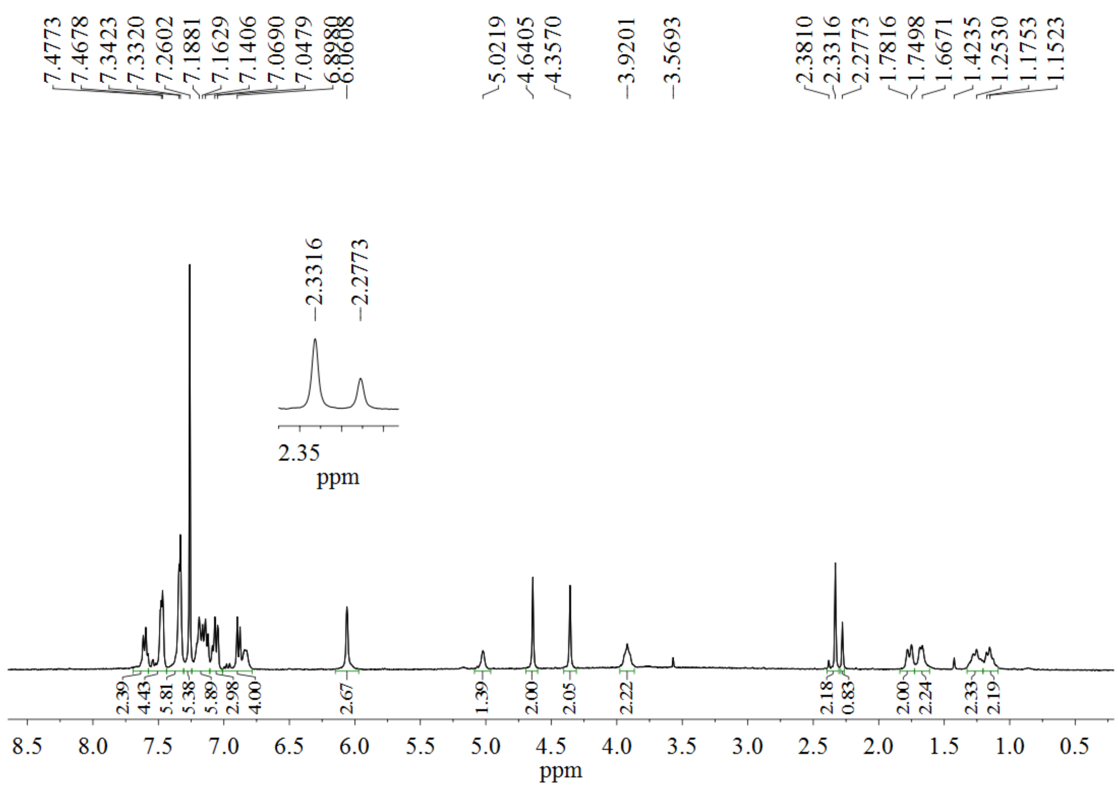


Figure S56. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (45 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

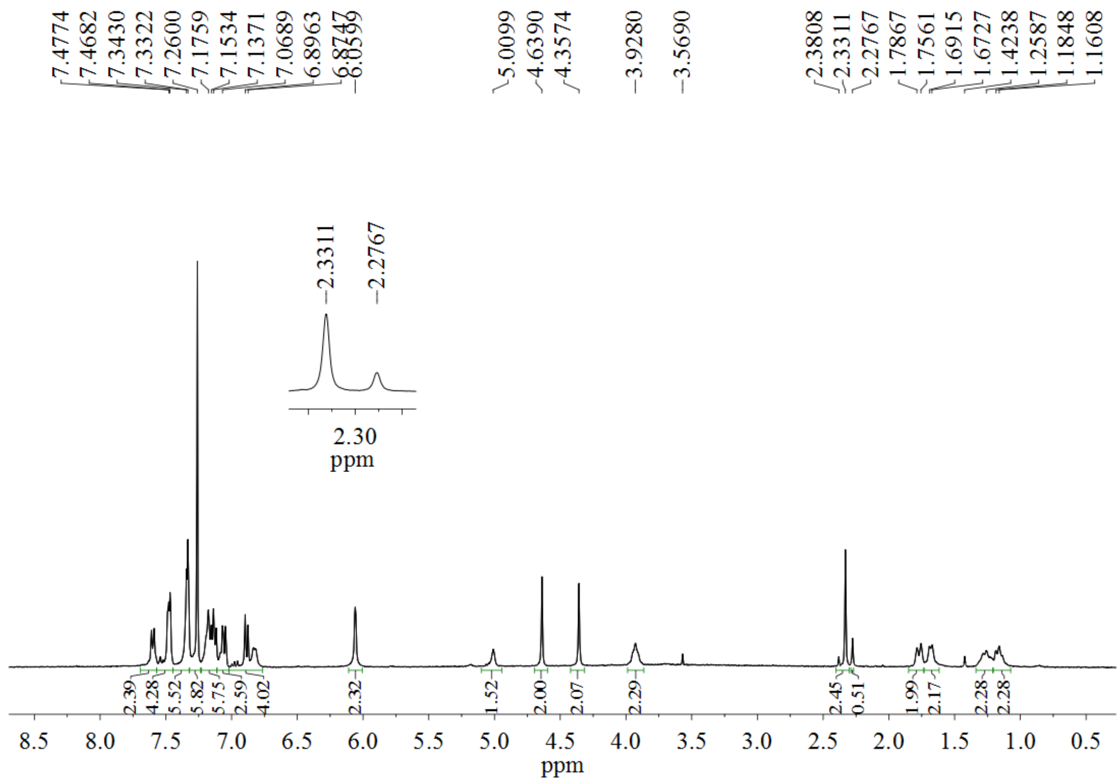


Figure S57. [1]H NMR spectrum of (*R*)-**11** and (*S*)-**11** (65 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

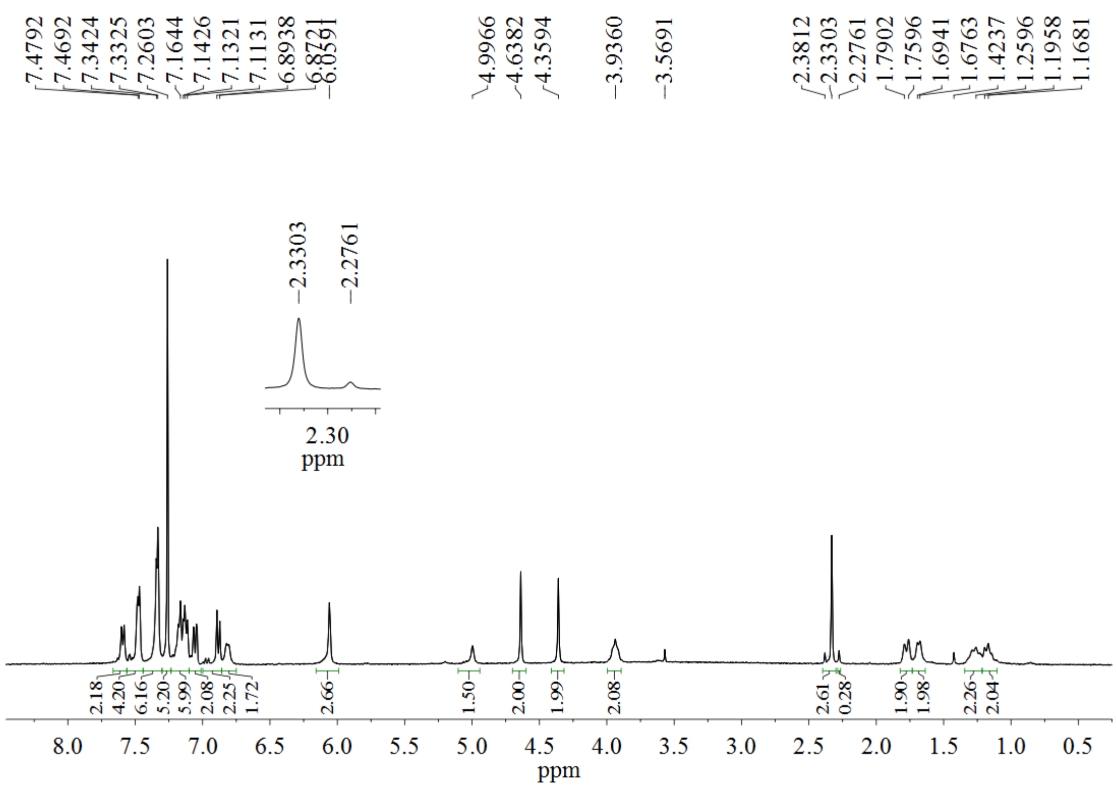


Figure S58. [1]H NMR spectrum of (*R*)-**11** and (*S*)-**11** (80 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

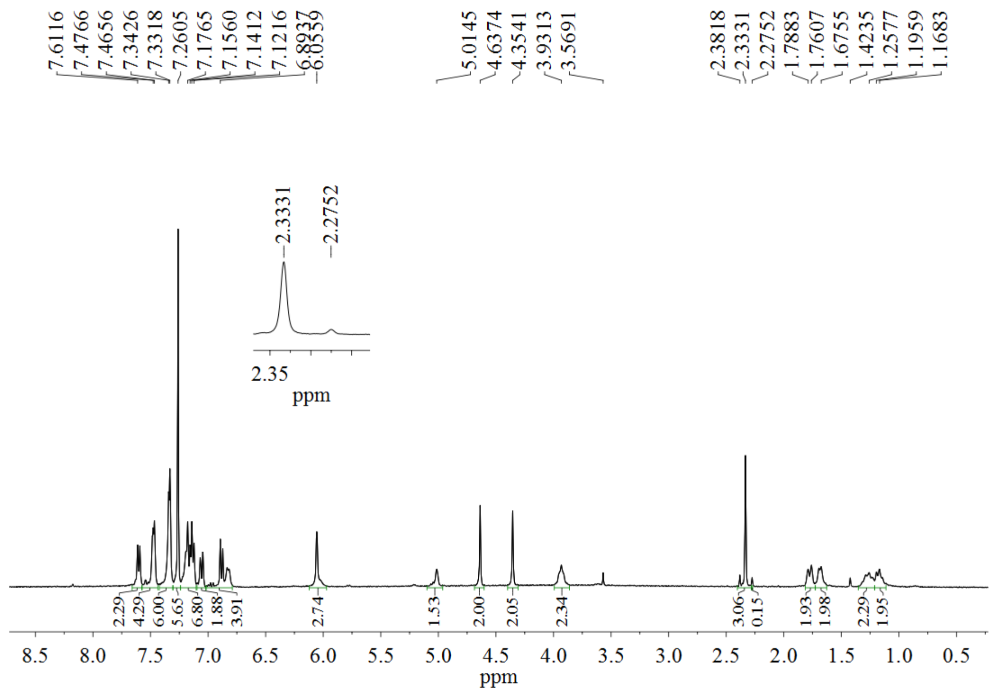


Figure S59. ^{1}H NMR spectrum of (*R*)-**11** and (*S*)-**11** (90 % ee) with TAMCSA **1b**, [**1b**] = 5 mM.

References

1. (a) Guangpeng Gao, Caixia Lv, Qiuju Li, Lin Ai, Jiaxin Zhang, *Tetrahedron Lett*., 2015, **56**, 6742; (b) Lixia Fang, Caixia Lv, Guo Wang, Lei Feng, Pericles Stavropoulos, Guangpeng Gao, Lin Ai, Jiaxin Zhang, *Org*. *Chem*. *Front*., 2016, **3**, 1716.