Supporting Information

Rapid Organocatalytic Chirality Analysis of Amines, Amino Acids, Alcohols, Amino Alcohols and Diols with Achiral Iso(thio)cyanate Probes

Eryn Nelson, Jeffrey S. S. K. Formen and Christian Wolf*
Department of Chemistry, Georgetown University, 37th and O St., Washington DC 20057, USA.
Email: cw27@georgetown.edu

Contents **Page**

1. Optimization of reaction conditions **2**

2. Sensing scope: amines **16**

3. Sensing scope: amino acids **22**

4. Sensing scope: amino alcohols **26**

5. Sensing scope: alcohols **31**

6. Quantitative amine and alcohol sensing: absolute configuration, enantiomeric excess, and total concentration **37**

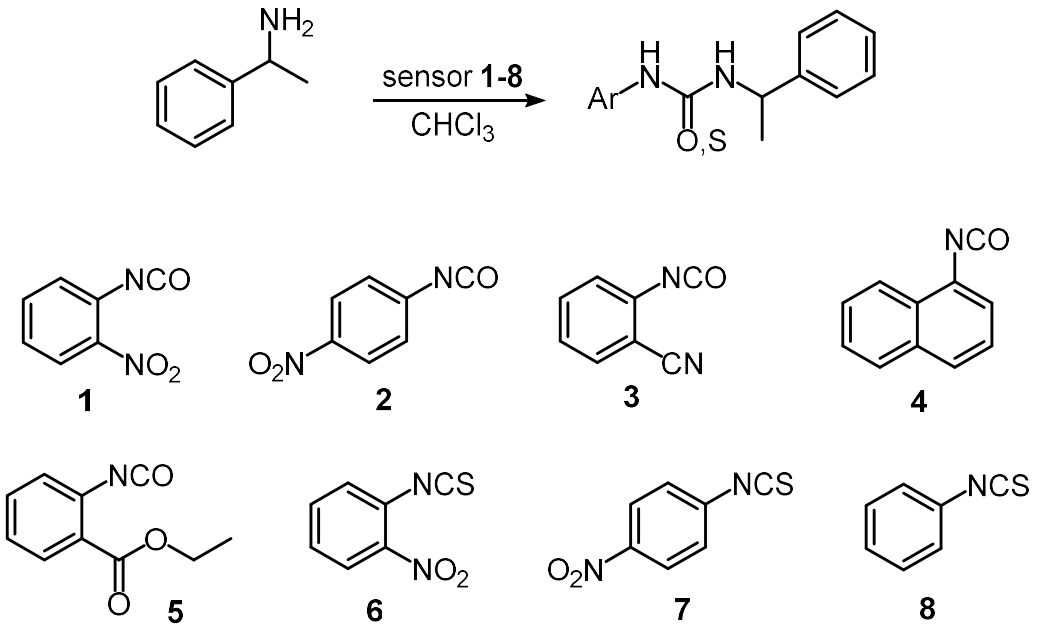
7. Crystallographic analysis **43**

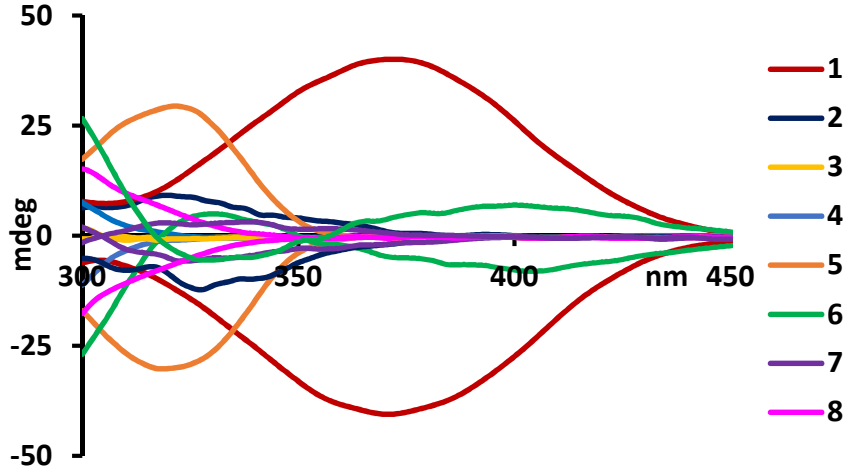
1. Optimization of reaction conditions

Probe screening

1-Phenylethylamine (82.5 mM) and an iso(thio)cyanates **1-8** (99.0 mM) were mixed in 1.0 mL of $CHCl_3$ and the reaction was stirred overnight followed by CD analysis in 2.0 mL of ACN (0.10–1.24 mM). The urea derived from **1** yielded the strongest red-shifted CD signal. Thus, further reaction optimization was carried out with probe **1**.

Scheme 1. Chiroptical sensing of phenylethylamine with **1-8**



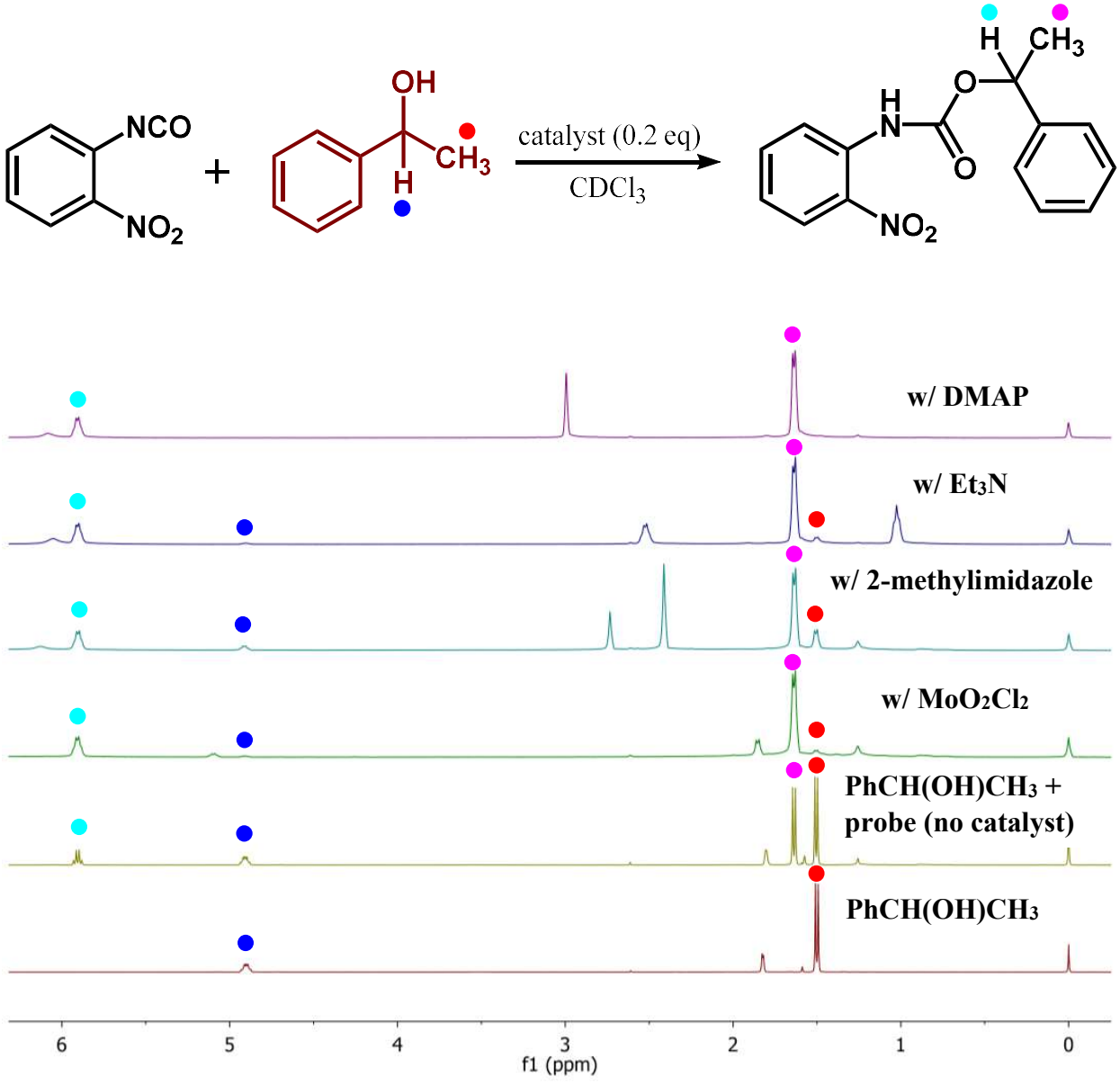


Individual CD concentrations were as follows: **1** (0.50 mM), **2** (0.12 mM), **3** (0.74 mM), **4** (0.37 mM), **5** (0.37 mM), **6** (0.50 mM), **7** (0.10 mM), **8** (1.24 mM).

Catalyst screening for alcohol reaction

(*R*)-Phenylethanol (81.9 mM), probe **1** (98.2 mM) and a catalyst (0.2 equivalents, 16.4 mM) were mixed in 1.0 mL of $CDCl_3$ and the reaction was stirred overnight. Based on ^1H NMR analysis, only DMAP resulted in complete conversion of alcohol to product. For all subsequent reactions with alcohols and amino alcohols, DMAP (20 mol%) was used as catalyst.

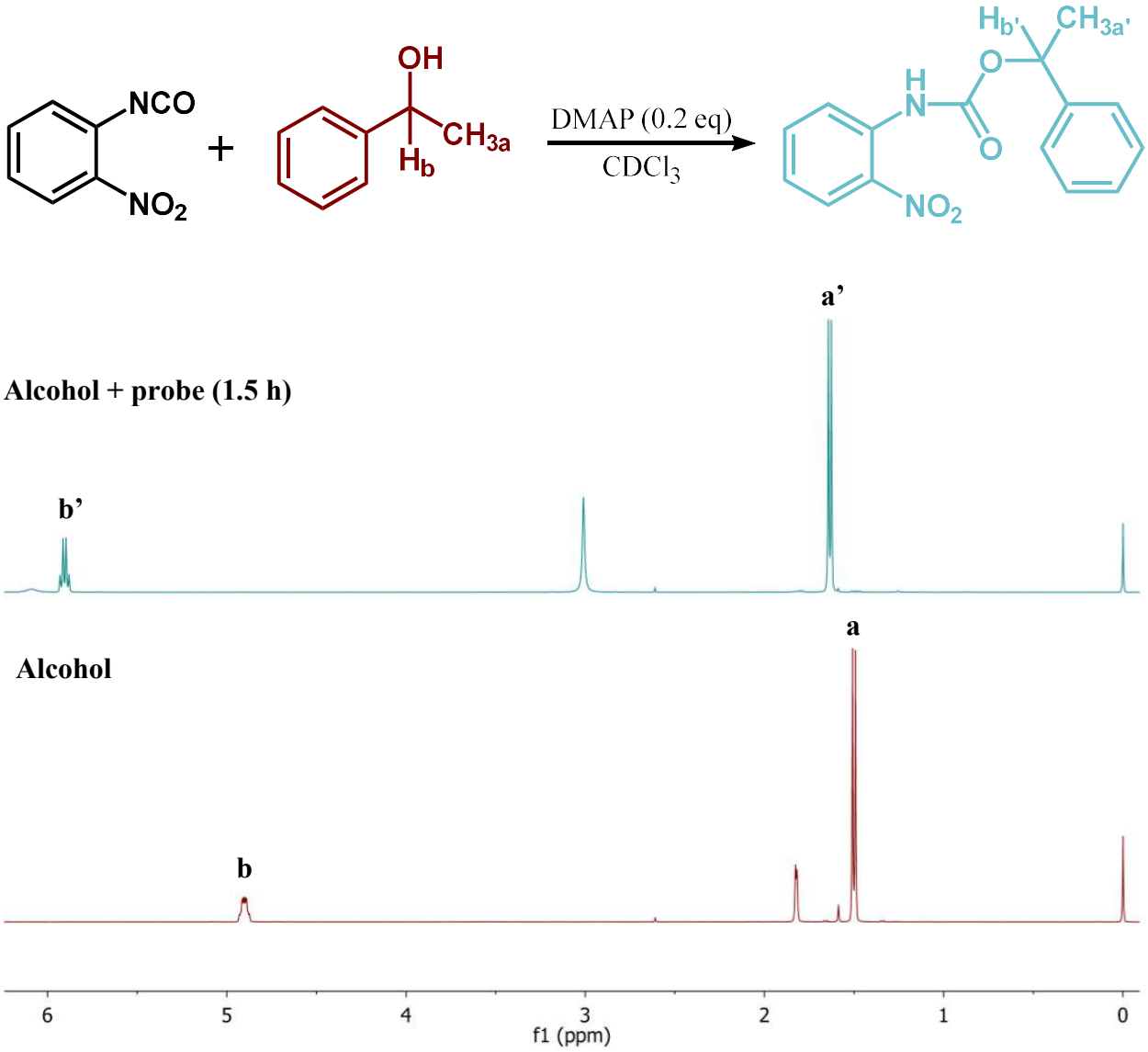
Figure 1. NMR reaction analysis



NMR analysis of alcohol reaction

(*R*)-Phenylethanol (81.9 mM) and probe **1** (98.2 mM) were mixed in 1.0 mL of $CDCl_3$ with 0.2 equivalents of DMAP (16.4 mM) and the reaction was monitored by ^1H NMR. The reaction was complete within 1.5 hours.

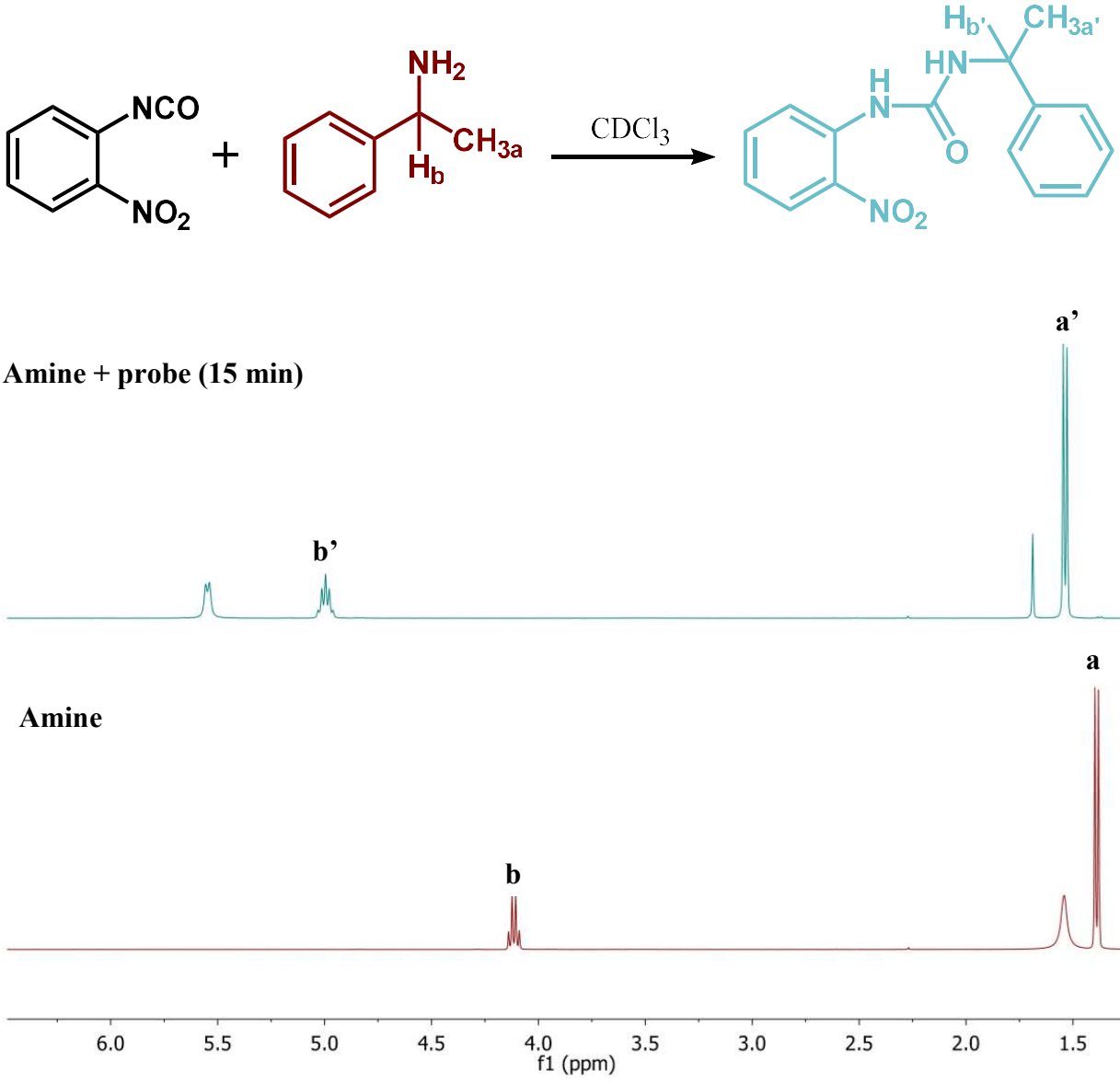
Figure 2. NMR analysis of the reaction between **1** and (*R*)-phenylethanol



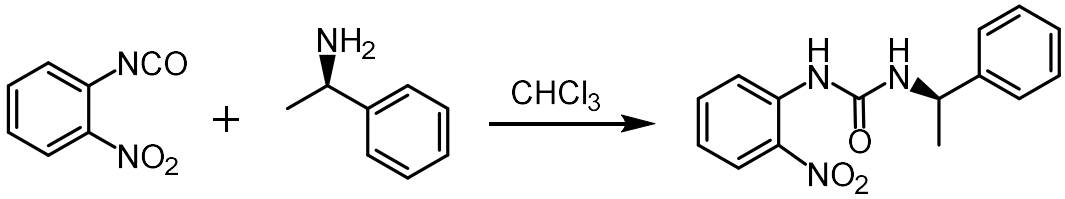
Reaction with amines

(*S*)-Phenylethylamine (82.5 mM) and probe **1** (99.0 mM) were mixed in 1.0 mL of $CDCl_3$ and the reaction was monitored by ^1H NMR. The reaction was complete within 15 minutes.

Figure 3. NMR analysis of the reaction between **1** and (*S*)-phenylethylamine



Representative urea and carbamate synthesis



(*R*)-Phenylethylamine (49.9 mg, 0.4 mmol) and probe **1** (81.2 mg, 0.5 mmol) were mixed in 3.0 mL of $CHCl_3$ and the reaction was stirred for one hour. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel with hexanes/ethyl acetate (6%) to afford the urea product as a yellow solid (112.2 mg, 96%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.60 (dd, *J* = 8.7, 1.3 Hz, 1H), 8.12 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.52 (ddd, *J* = 8.7, 7.1, 1.3 Hz, 1H), 7.40 – 7.20 (m, 5H), 7.00 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 5.34 (d, *J* = 7.3 Hz, 1H), 4.99 (m, *J* = 7.0 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 141.2, 135.9, 135.8, 135.4, 128.6, 128.1, 126.1, 125.8, 122.2, 120.7, 74.3, 22.3.

Figure 4. ^{1}H NMR spectrum of (*R*)-1-(2-nitrophenyl)-3-(1-phenylethyl)urea.

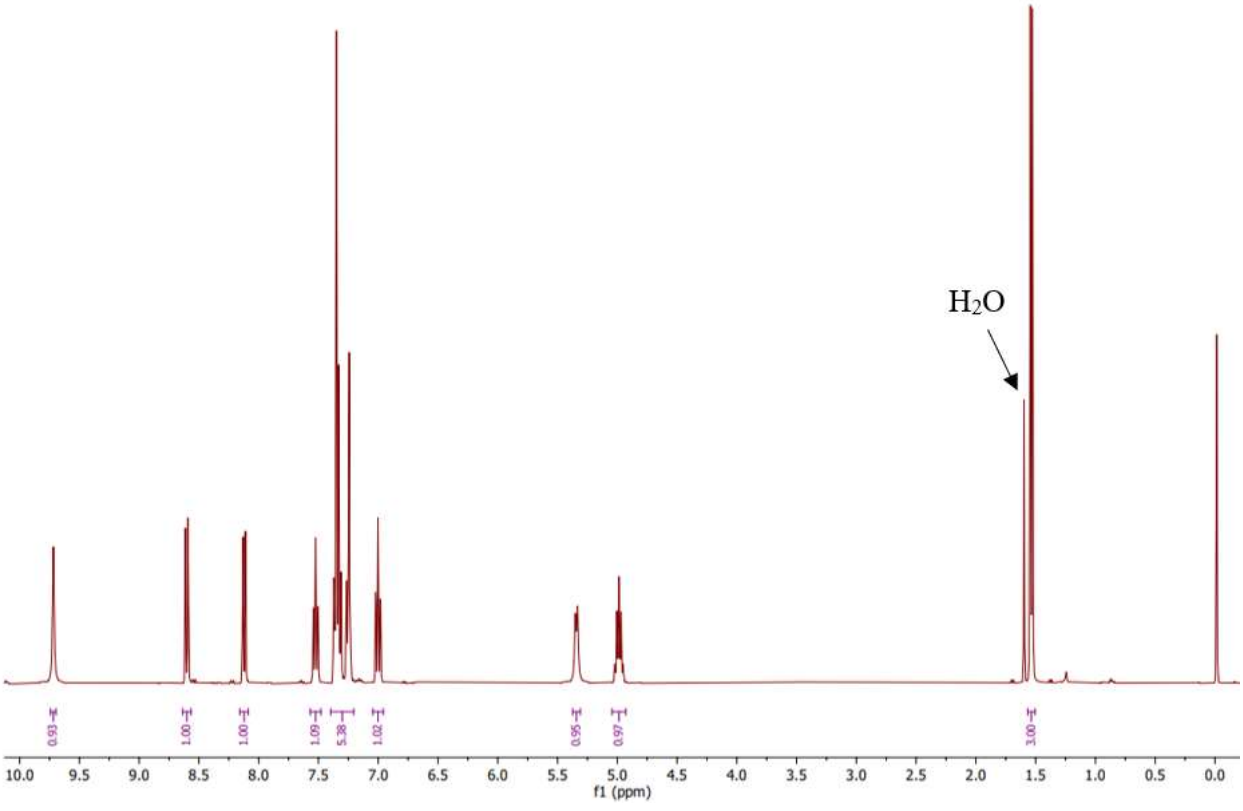
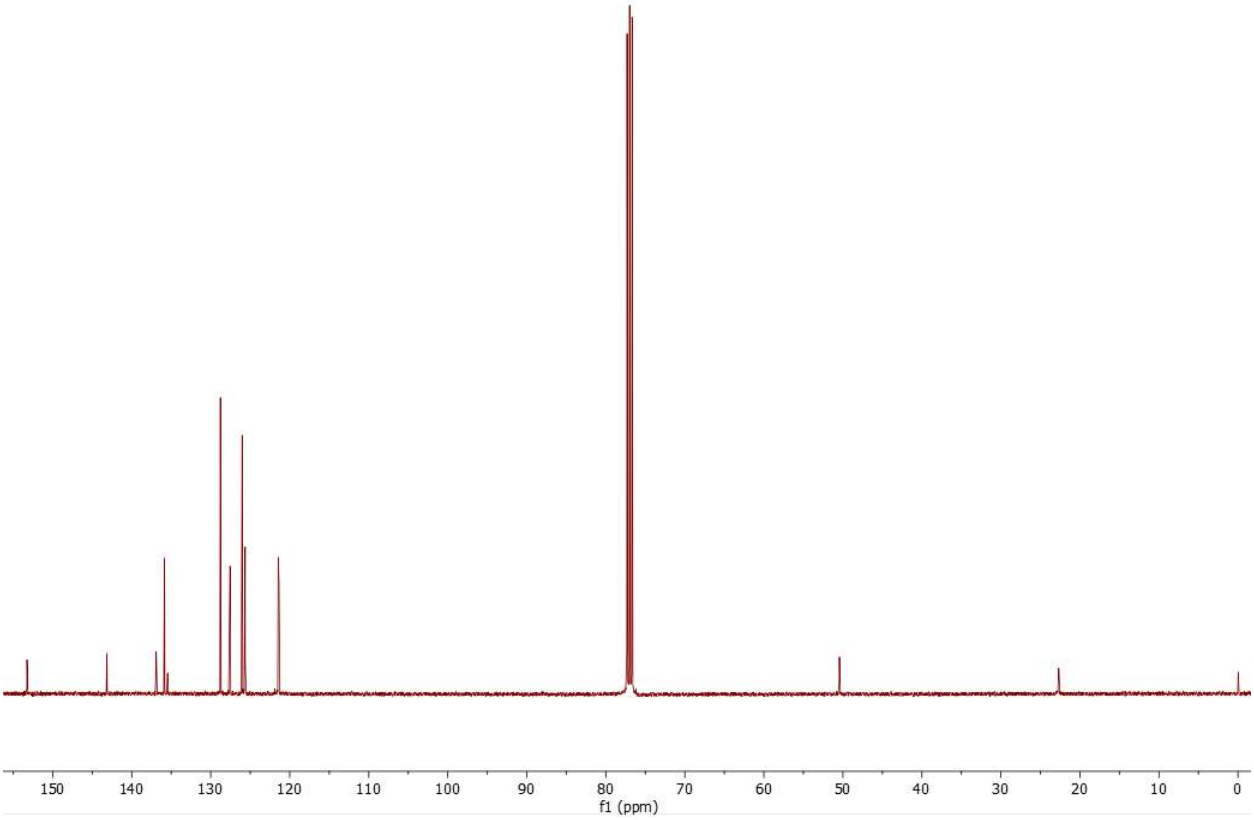
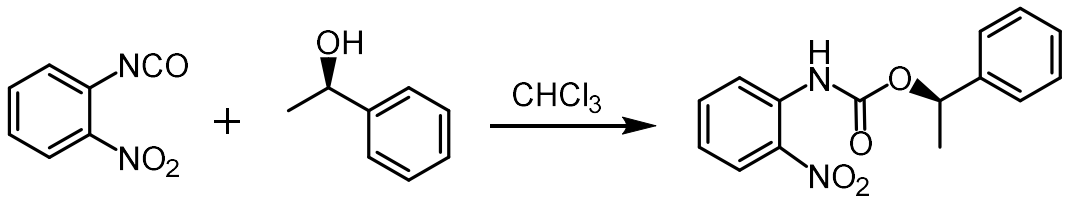


Figure 5. ^{13}C NMR spectrum of (*R*)-1-(2-nitrophenyl)-3-(1-phenylethyl)urea.





(*R*)-Phenylethanol (51.4 mg, 0.4 mmol), probe **1** (82.5 mg, 0.5 mmol), and DMAP (11.1 mg, 0.09 mmol) were mixed in 3.0 mL of $CHCl_3$ and the reaction was stirred overnight. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel with hexanes/ethyl acetate (6%) to afford the carbamate product as a yellow solid (120.1 mg, 100%), ^1H NMR (399 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.54 (dd, J = 8.7, 1.4 Hz, 1H), 8.17 (dd, J = 8.5, 1.6 Hz, 1H), 7.57 (ddd, J = 8.7, 7.2, 1.6 Hz, 1H), 7.45 – 7.26 (m, 5H), 7.08 (ddd, J = 8.5, 7.1, 1.4 Hz, 1H), 5.91 (q, J = 6.6 Hz, 1H), 1.63 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 141.2, 135.9, 135.8, 135.4, 128.6, 128.1, 126.1, 125.8, 122.2, 120.7, 74.3, 22.3..

Figure 6. ^{1}H NMR spectrum of (*R*)-1-phenylethyl (2-nitrophenyl)carbamate.

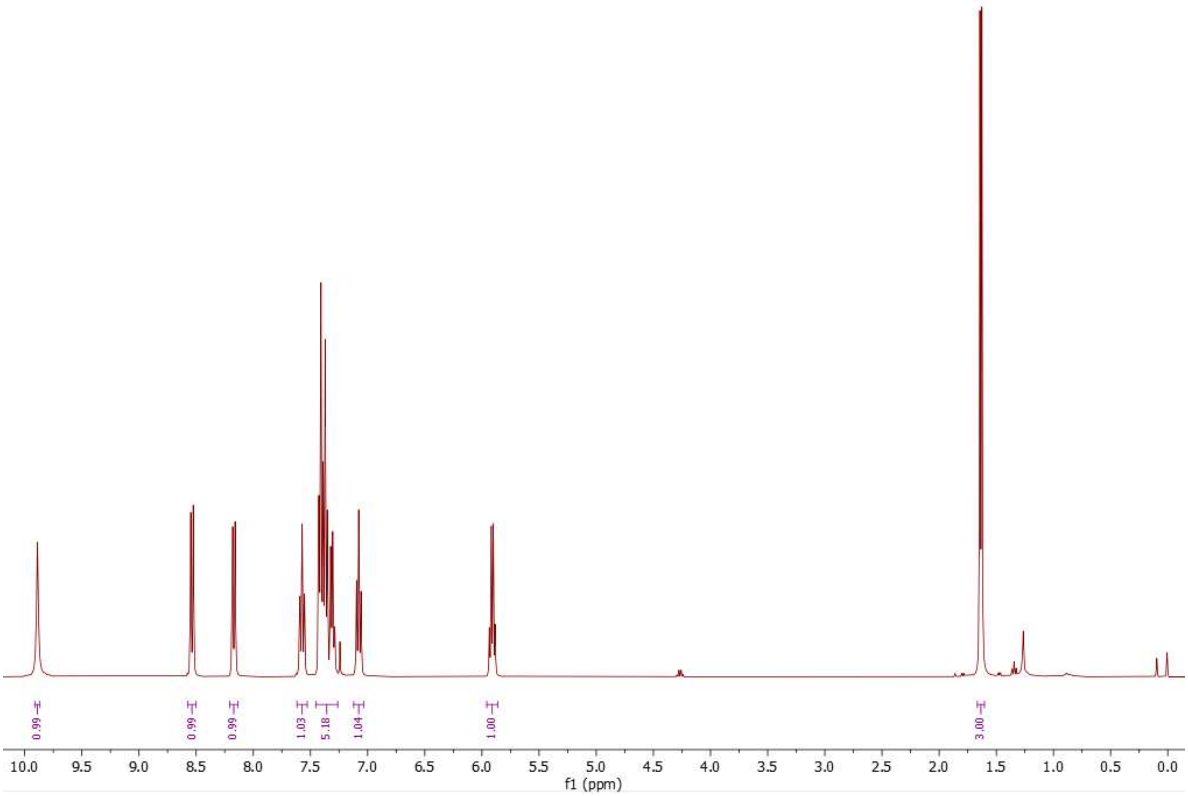
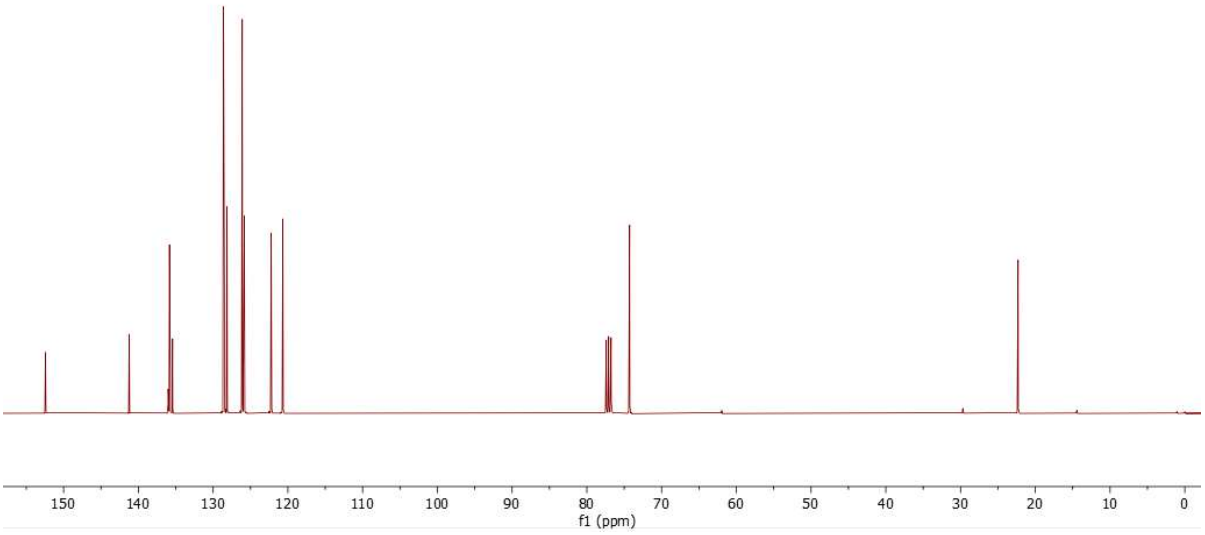


Figure 7. ^{13}C NMR spectrum of (*R*)-1-phenylethyl (2-nitrophenyl)carbamate.



Solvent screening for CD analysis

(*S*)-Phenylethylamine (82.5 mM) and probe **1** (99.0 mM) were mixed for 15 minutes in either 1.0 mL of $CHCl_3$ or 1.0 mL of ACN, then diluted to a final volume of 2.0 mL with ACN, $CHCl_3$, EtOH, or hexanes (0.41 mM) for CD analysis. The reaction run in $CHCl_3$ followed by dilution with ACN yielded the strongest CD signal. All subsequent reactions were thus run in $CHCl_3$ and diluted with ACN for CD analysis.

Figure 8. CD spectra of the reactions run in $CHCl_3$

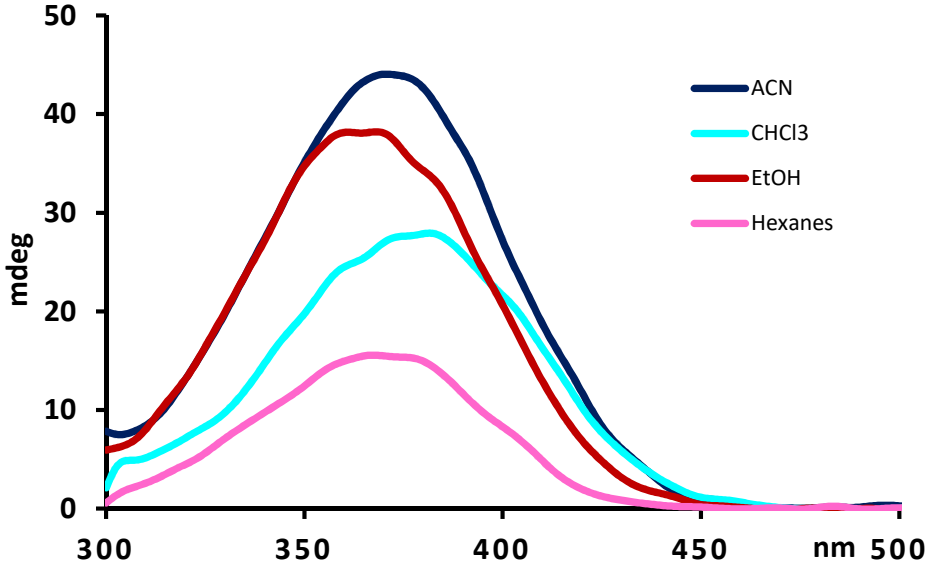
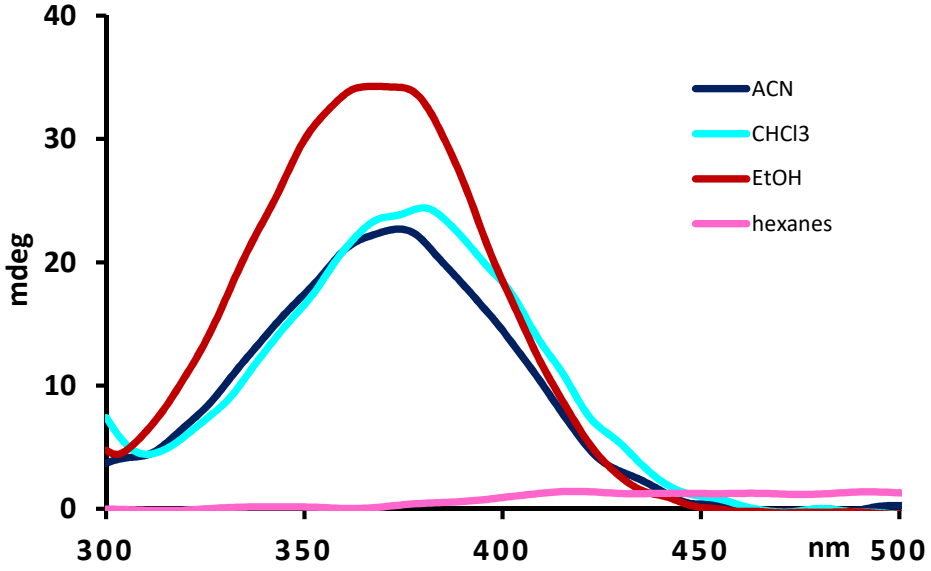


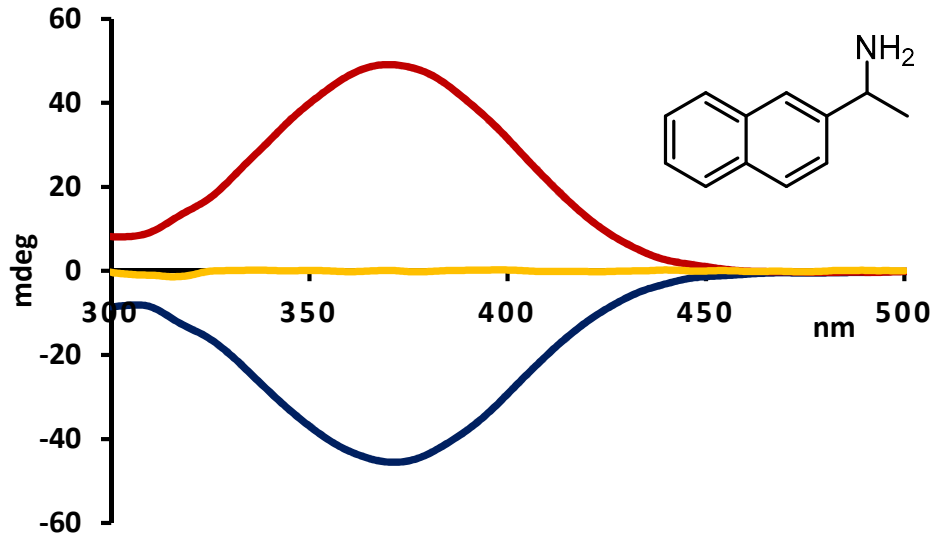
Figure 9. CD spectra of the reactions run in ACN



Efficiency of the organic reaction based CD induction

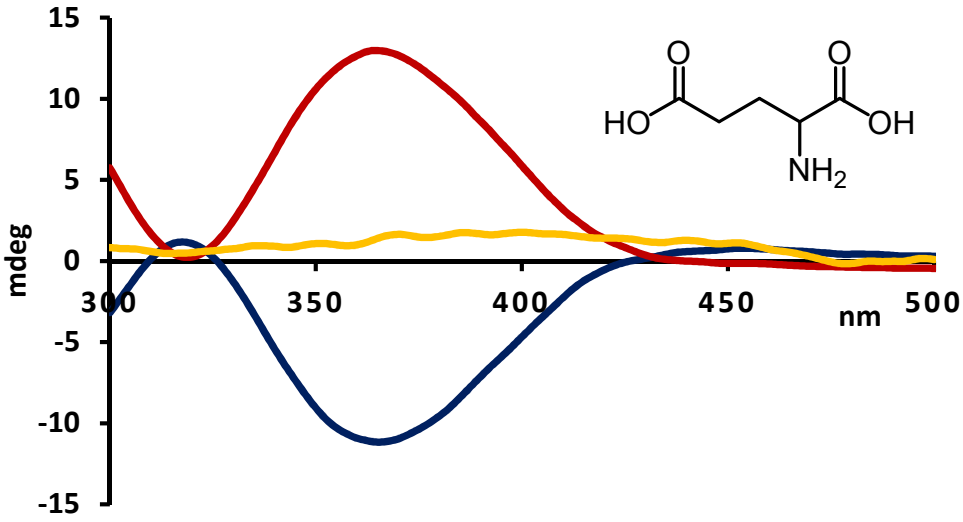
The CD signal induction with probe **1** was compared to the inherent CD properties of selected analytes. The analytes do not show CD signals above 300 nm where the probe is effective. In addition, we did not observe any or only very weak CD signals when we adjust the concentration to allow CD analysis in the region between 200 and 300 nm. At best these could be used for qualitative analysis purposes but not for accurate *er* and concentration determination.

Figure 10. CD spectra obtained by applying probe **1** to (*R*)-**13** (blue) and (*S*)-**13** (red). The CD spectrum obtained with free (*R*)-**13** under the same conditions but in the absence of a probe is shown in orange.



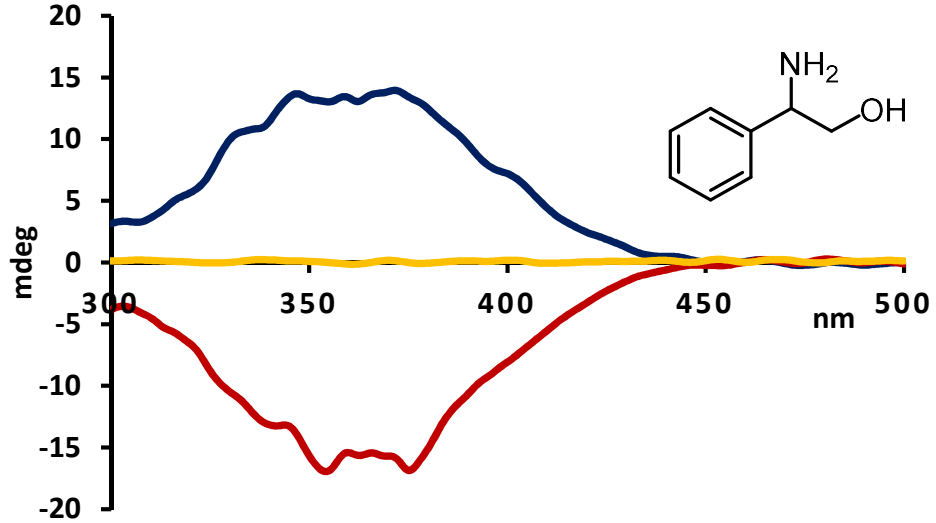
CD measurements were taken at 0.58 mM in acetonitrile.

Figure 11. CD spectra obtained by applying probe **1** to (*R*)-**25** (blue) and (*S*)-**25** (red). The CD spectrum obtained with free (*S*)-**25** under the same conditions but in the absence of a probe is shown in orange.



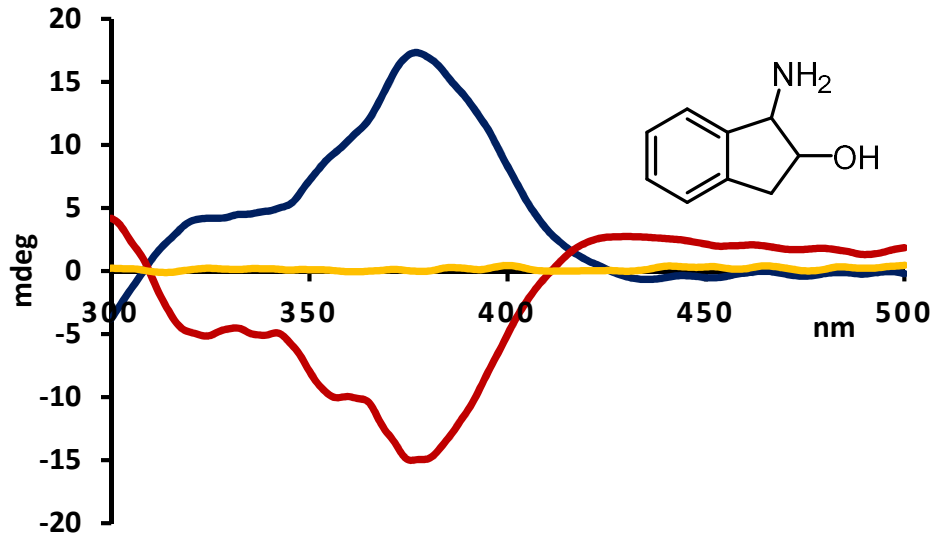
CD measurements were taken at 0.41 mM in acetonitrile.

Figure 12. CD spectra obtained by applying probe **1** to (*R*)-**26** (blue) and (*S*)-**26** (red). The CD spectrum obtained with free (*R*)-**26** under the same conditions but in the absence of a probe is shown in orange.



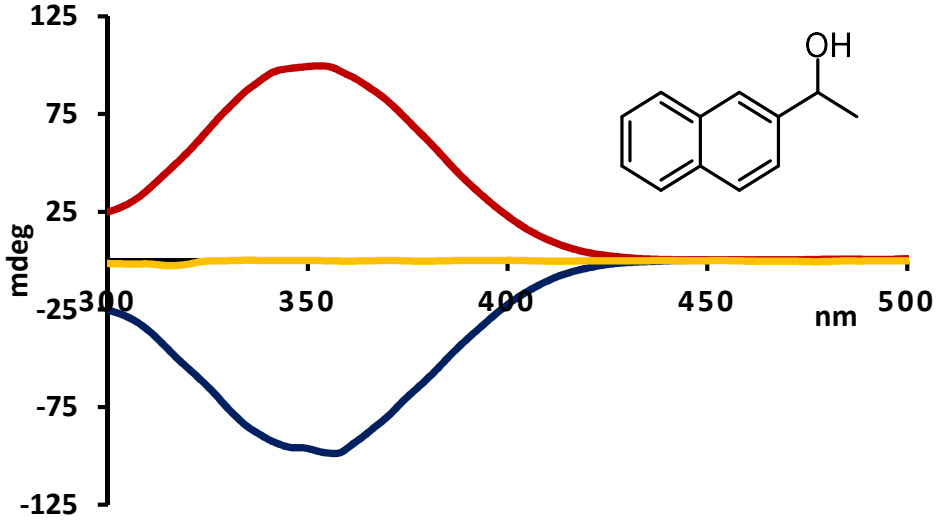
CD measurements were taken at 0.36 mM in acetonitrile.

Figure 13. CD spectra obtained by applying probe **1** to (1*R*,2*S*)-**28** (blue) and (1*S*,2*R*)-**28** (red). The CD spectrum obtained with free (1*R*, 2*S*)-**28** under the same conditions but in the absence of a probe is shown in orange.



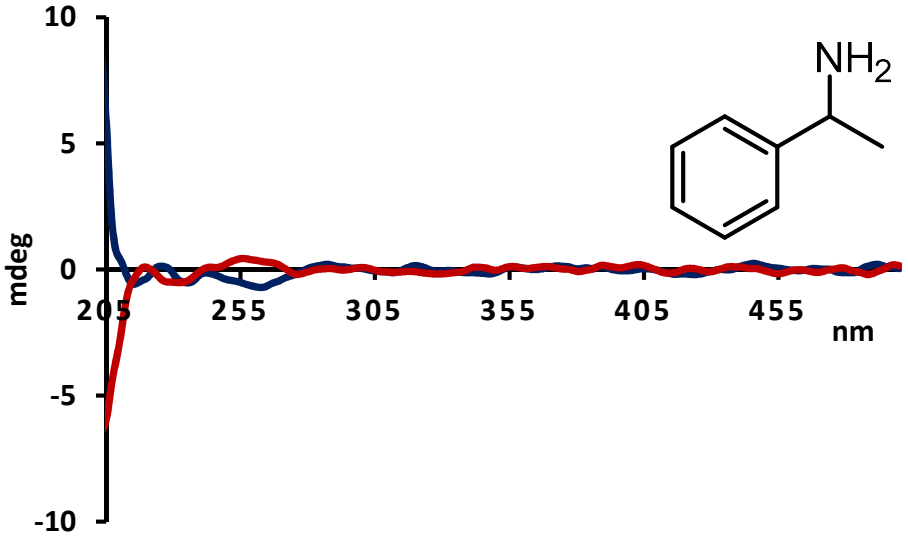
CD measurements were taken at 0.34 mM in acetonitrile.

Figure 14. CD spectra obtained by applying probe **1** to (*R*)-**38** (blue) and (*S*)-**38** (red). The CD spectrum obtained with free (*R*)-**38** under the same conditions but in the absence of a probe is shown in orange.



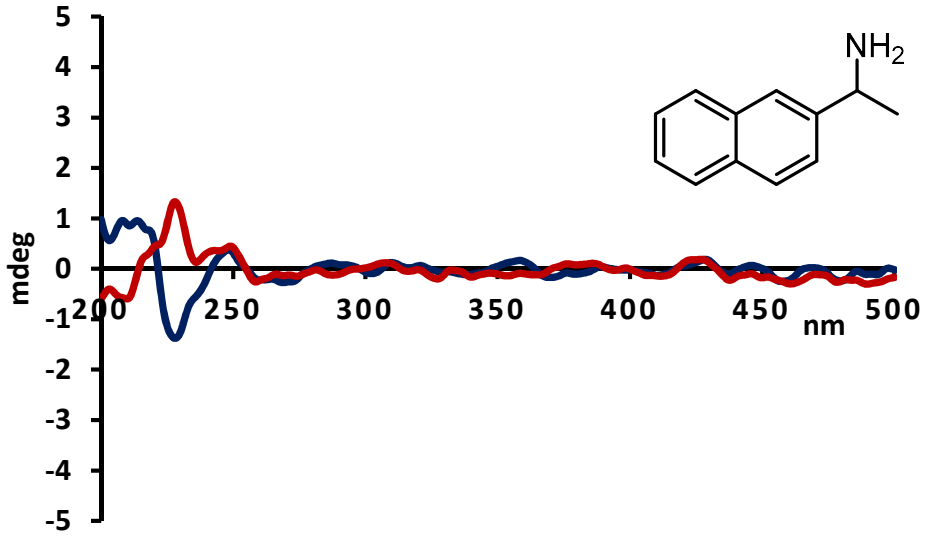
CD measurements were taken at 0.75 mM in acetonitrile.

Figure 15. CD spectra obtained with free (*R*)-**9** (blue) and (*S*)-**9** (red).



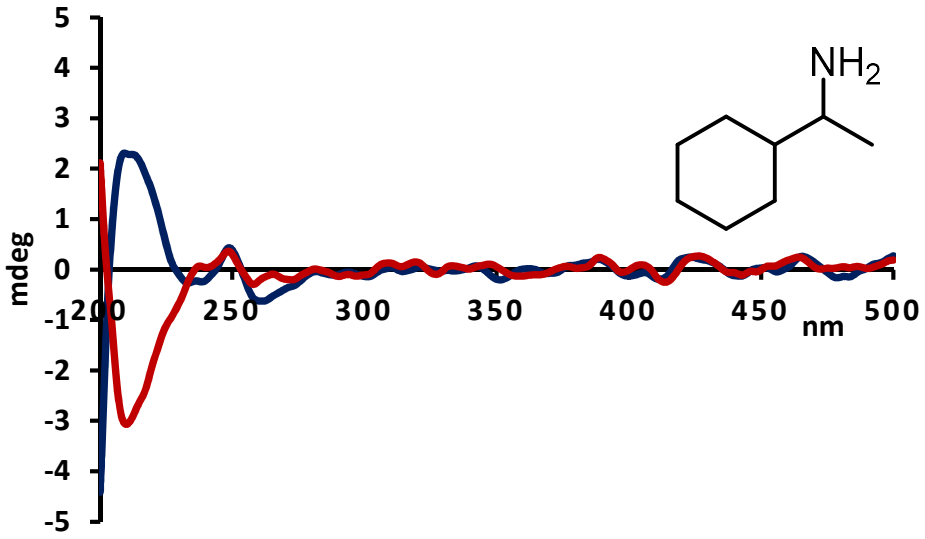
CD measurements were taken at 0.21 mM in acetonitrile.

Figure 16. CD spectra obtained with free (*R*)-**13** (blue) and (*S*)-**13** (red).



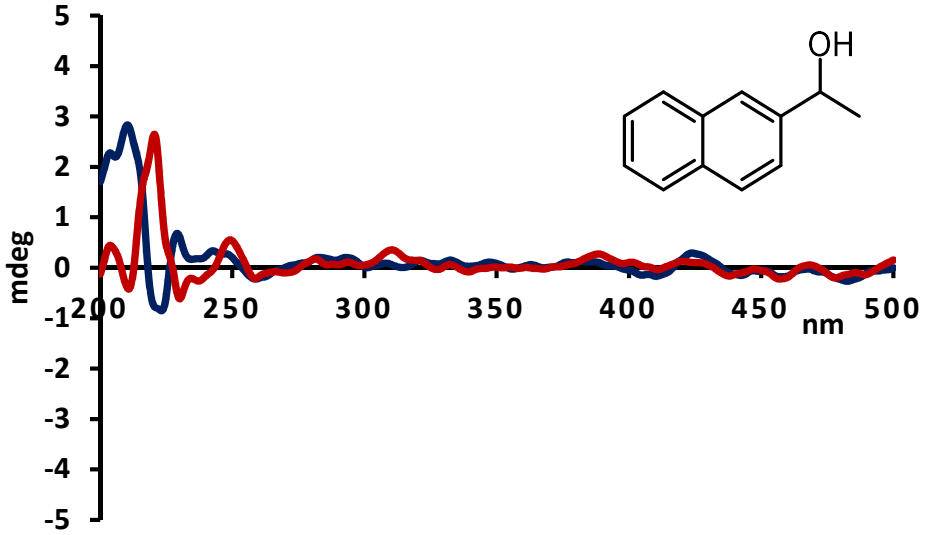
CD measurements were taken at 0.02 mM in acetonitrile.

Figure 17. CD spectra obtained with free (*R*)-**16** (blue) and (*S*)-**16** (red).



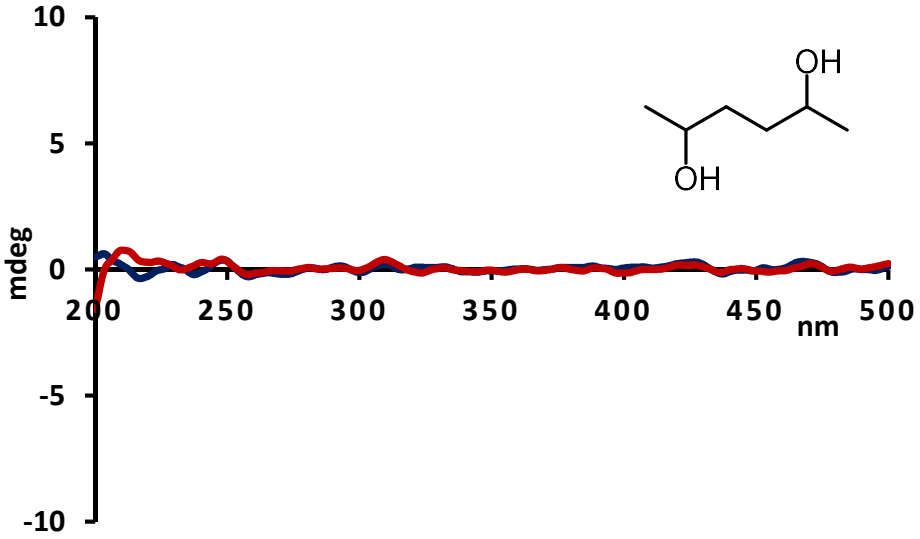
CD measurements were taken at 0.79 mM in acetonitrile.

Figure 18. CD spectra obtained with free (*R*)-**38** (blue) and (*S*)-**38** (red).



CD measurements were taken at 0.03 mM in acetonitrile.

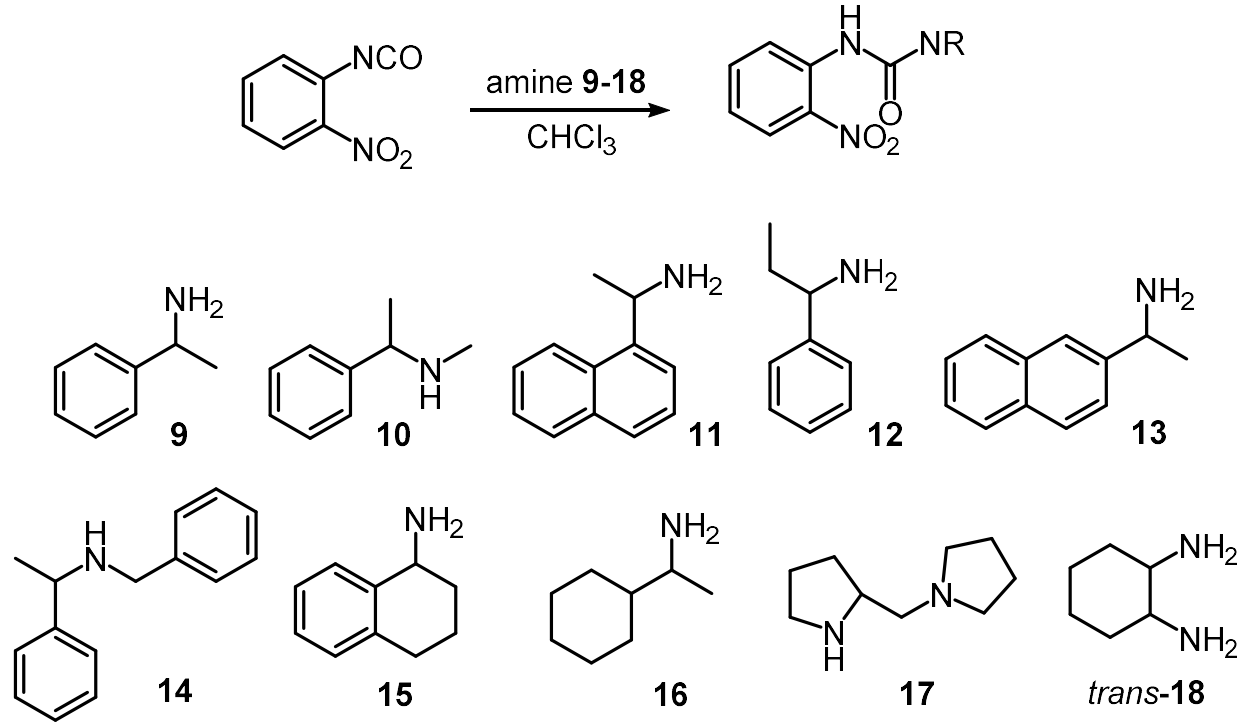
Figure 19. CD spectra obtained with free (2*R*,5*R*)-**43** (blue) and (2*S*,5*S*)-**43** (red).



CD measurements were taken at 0.76 mM in acetonitrile.

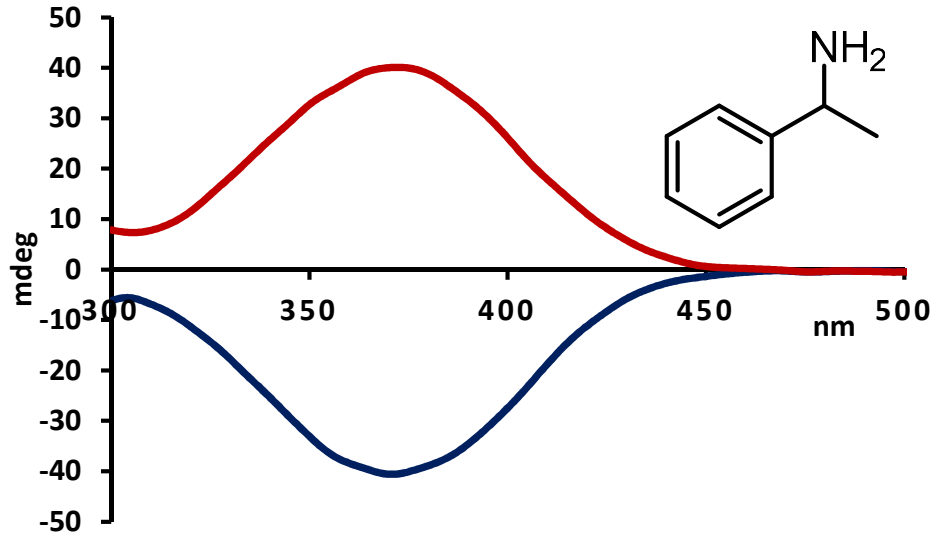
2. Sensing scope: amines

Scheme 2. Amine substrate scope



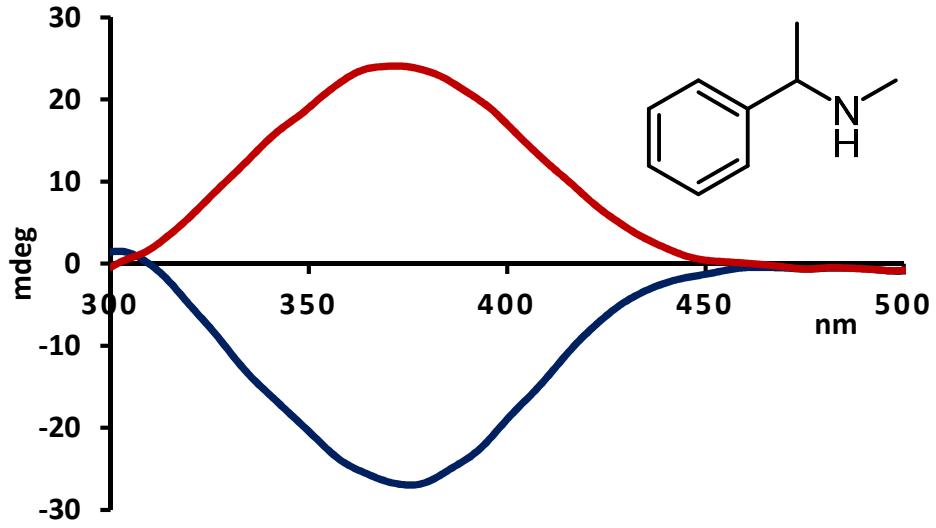
A solution of chiral amines **9-17** (45-85 mM) and probe **1** (1.2 equivalents) in 1.0 mL of chloroform was stirred for 15 minutes. For chiral diamine **18**, 2.4 equivalents of the probe were used. CD analysis was performed after dilution with ACN to the final concentration indicated under each Figure (20.0 μL of the reaction mixture added to 2.0 mL ACN). The CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, and a bandwidth of 1 nm in a continuous scanning mode with a scanning speed of 500 nm/min and a response of 1 s (1 cm path length). The data were baseline corrected and smoothed using a binomial equation.

Figure 20. CD spectra obtained by applying probe **1** to (*R*)-**9** (blue) and (*S*)-**9** (red)



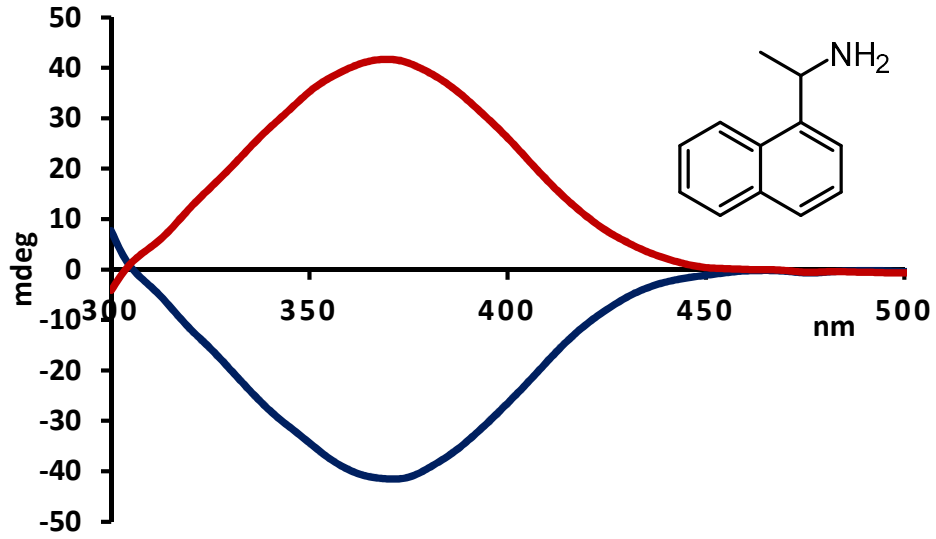
CD measurements were taken at 0.83 mM in acetonitrile.

Figure 21. CD spectra obtained by applying probe **1** to (*R*)-**10** (blue) and (*S*)-**10** (red)



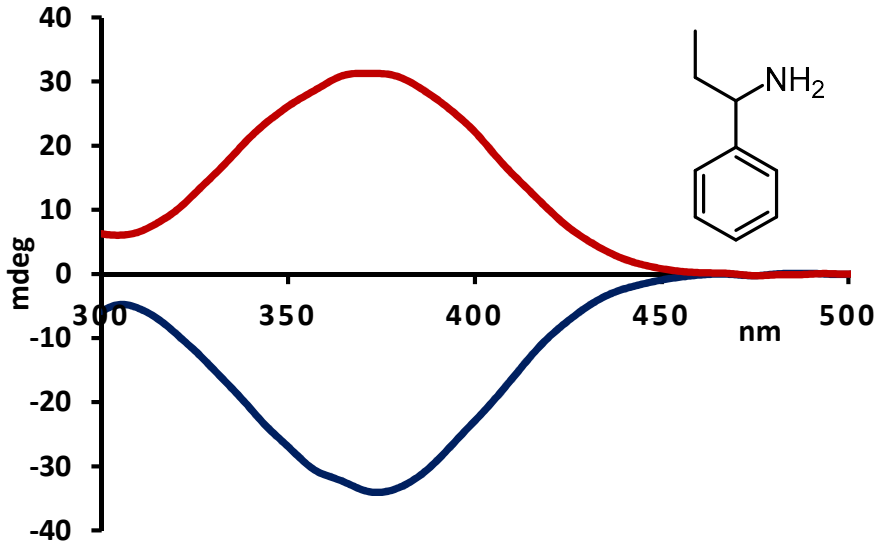
CD measurements were taken at 0.74 mM in acetonitrile.

Figure 22. CD spectra obtained by applying probe **1** to (*R*)-**11** (blue) and (*S*)-**11** (red)



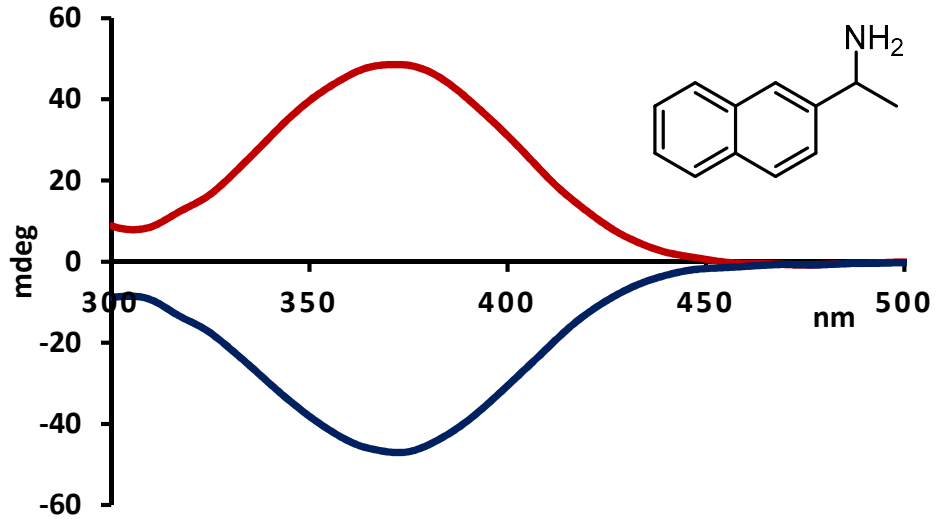
CD measurements were taken at 0.58 mM in acetonitrile.

Figure 23. CD spectra obtained by applying probe **1** to (*R*)-**12** (blue) and (*S*)-**12** (red)



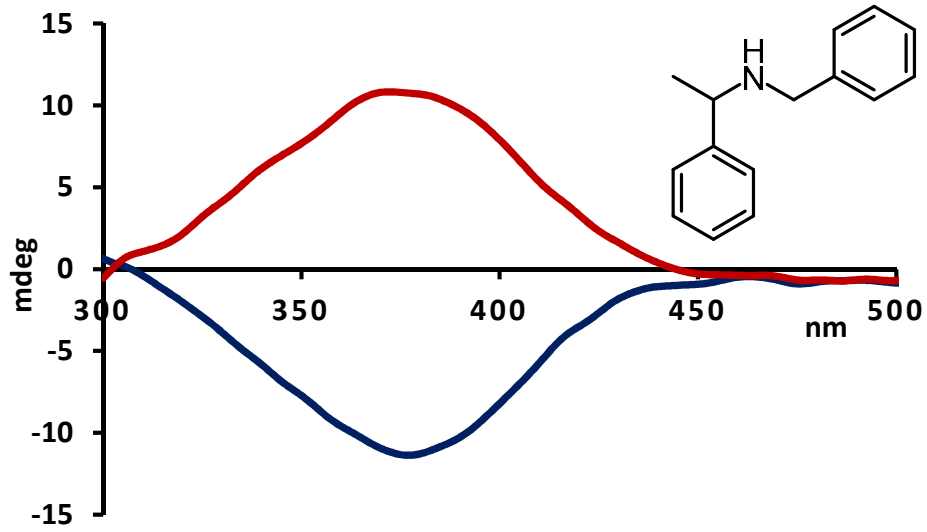
CD measurements were taken at 0.74 mM in acetonitrile.

Figure 24. CD spectra obtained by applying probe **1** to (*R*)-**13** (blue) and (*S*)-**13** (red)



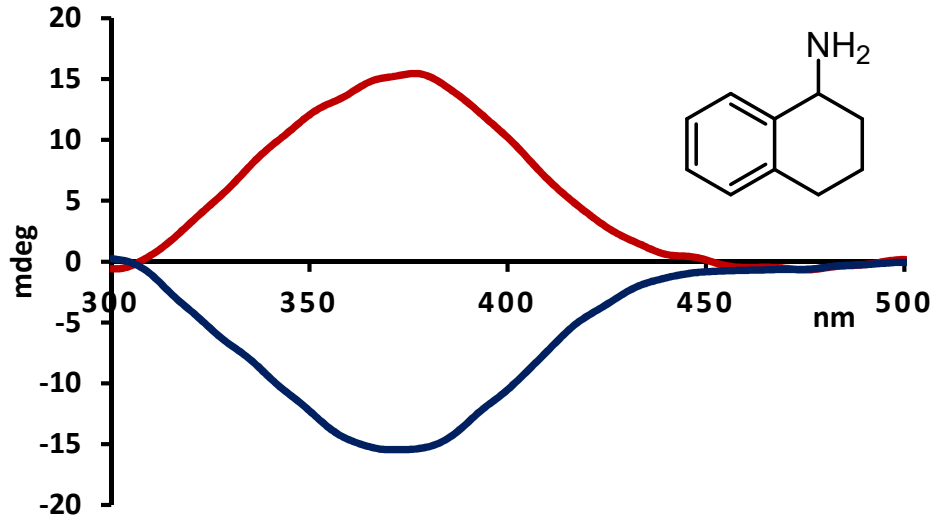
CD measurements were taken at 0.58 mM in acetonitrile.

Figure 25. CD spectra obtained by applying probe **1** to (*R*)-**14** (blue) and (*S*)-**14** (red)



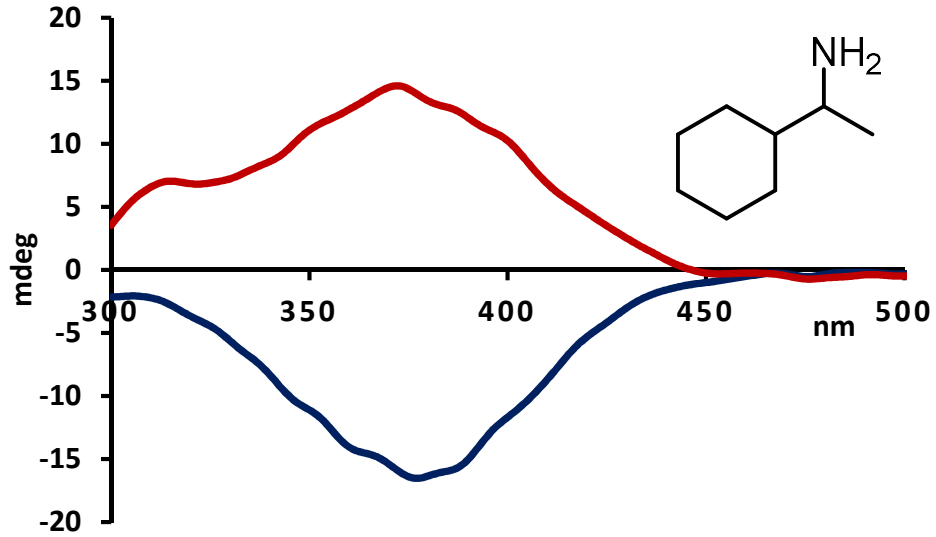
CD measurements were taken at 0.47 mM in acetonitrile.

Figure 26. CD spectra obtained by applying probe **1** to (*R*)-**15** (blue) and (*S*)-**15** (red)



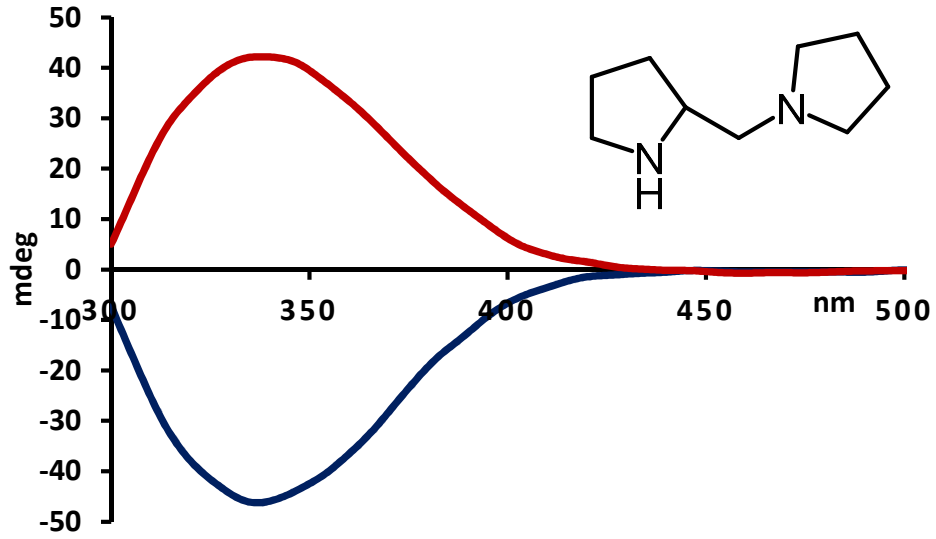
CD measurements were taken at 0.68 mM in acetonitrile.

Figure 27. CD spectra obtained by applying probe **1** to (*R*)-**16** (blue) and (*S*)-**16** (red)



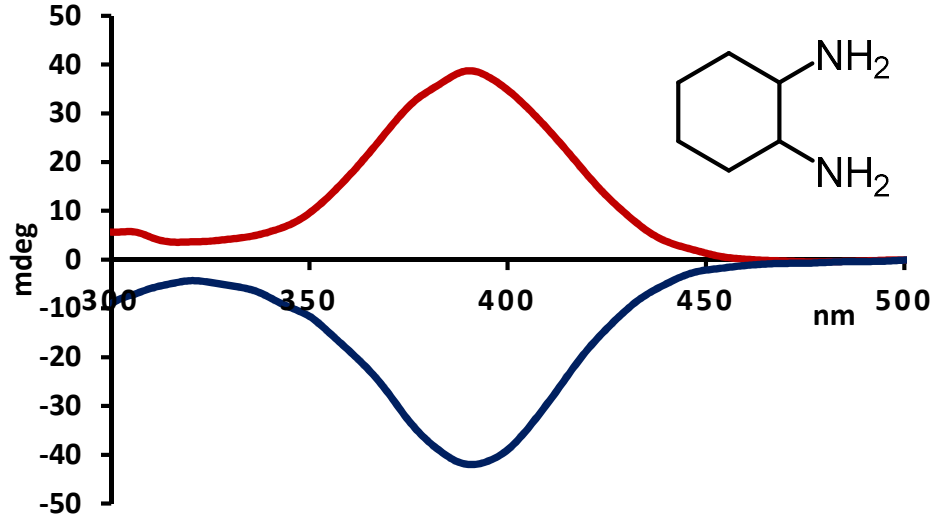
CD measurements were taken at 0.79 mM in acetonitrile.

Figure 28. CD spectra obtained by applying probe **1** to (*R*)-**17** (blue) and (*S*)-**17** (red)



CD measurements were taken at 0.65 mM in acetonitrile.

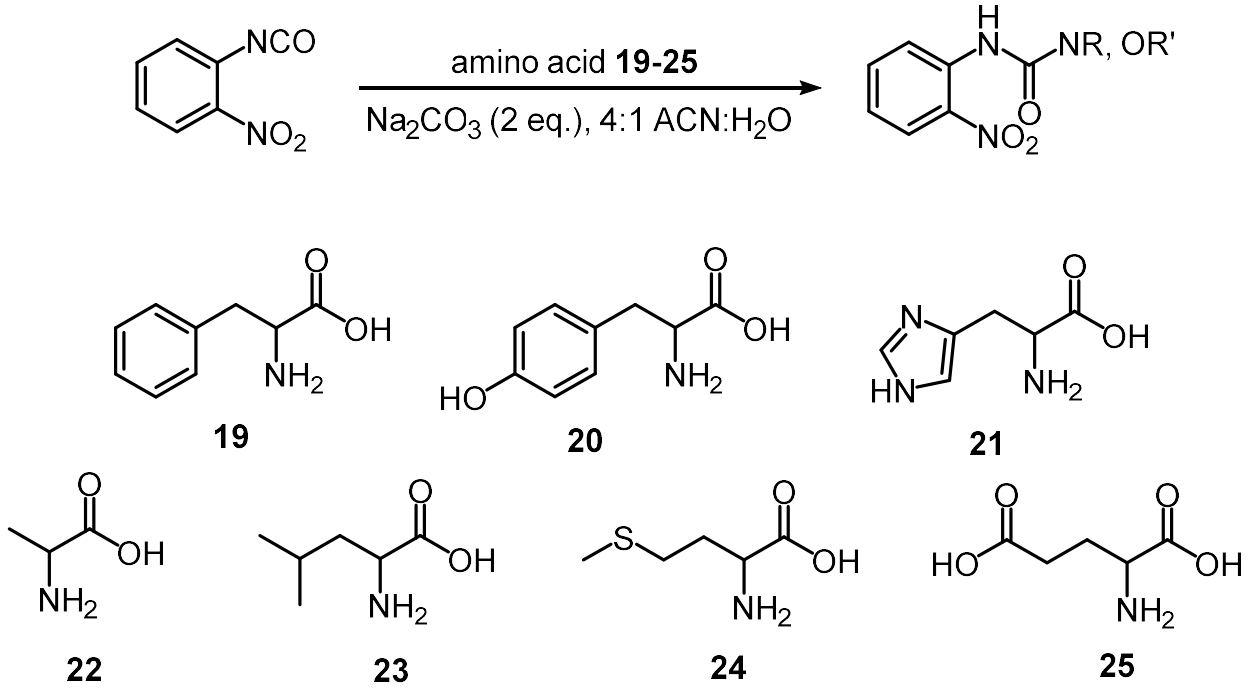
Figure 29. CD spectra obtained by applying probe **1** to (*R,R*)-**18** (blue) and (*S,S*)-**18** (red)



CD measurements were taken at 0.88 mM in acetonitrile.

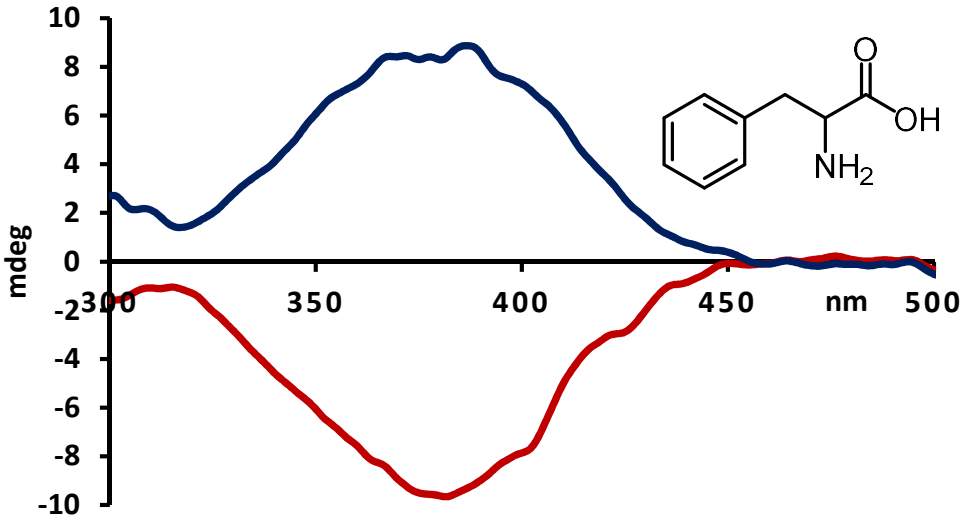
3. Sensing scope: amino acids

Scheme 3. Amino acid substrate scope



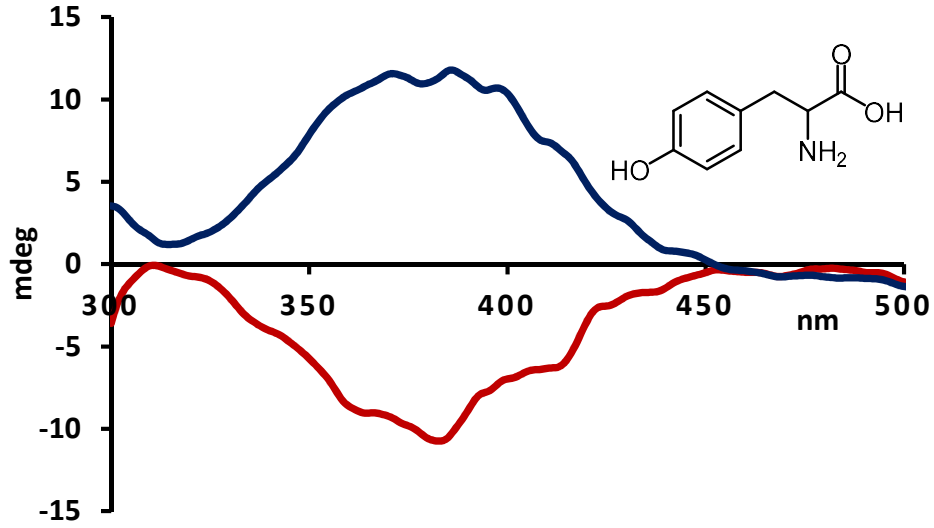
A solution of amino acids **19-25** (9.0 mM), probe **1** (10.8 or 21.6 mM), and Na_2CO_3 (18.0 mM) in 1.0 mL of a 4:1 ACN:water mixture was stirred overnight. For amino acids **19** and **22-25**, 1.2 equivalents of the probe (10.8 mM) were used. For amino acids **20** and **21**, 2.4 equivalents of the probe (21.6 mM) were used. For tyrosine (**20**), DMAP (0.2 equivalents) was used as a catalyst. CD analysis was performed after dilution with ACN to the final concentration indicated under each Figure (50.0-150.0 μL of the reaction mixture added to 2.0 mL ACN). The CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, and a bandwidth of 1 nm in a continuous scanning mode with a scanning speed of 500 nm/min and a response of 1 s (1 cm path length). The data were baseline corrected and smoothed using a binomial equation.

Figure 30. CD spectra obtained by applying probe **1** to (*R*)-**19** (blue) and (*S*)-**19** (red)



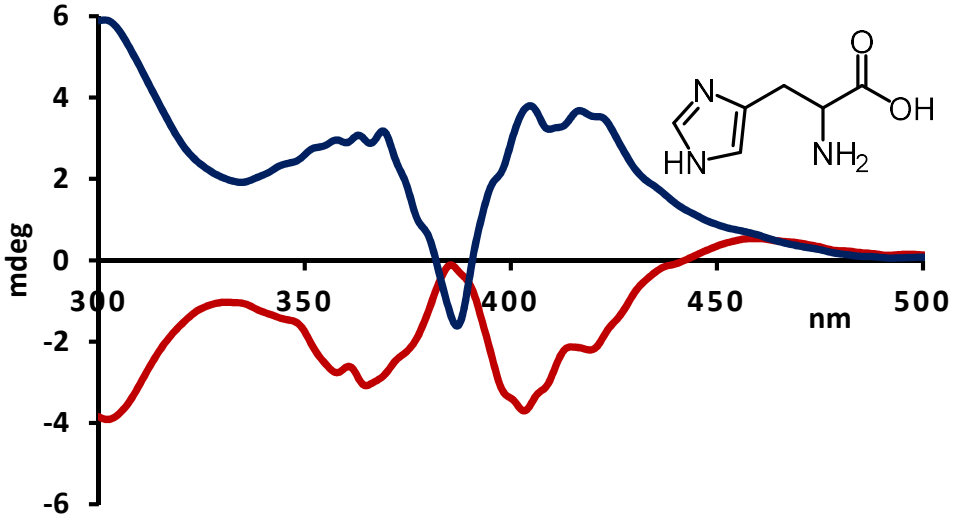
CD measurements were taken at 0.41 mM in acetonitrile.

Figure 31. CD spectra obtained by applying probe **1** to (*R*)-**20** (blue) and (*S*)-**20** (red)



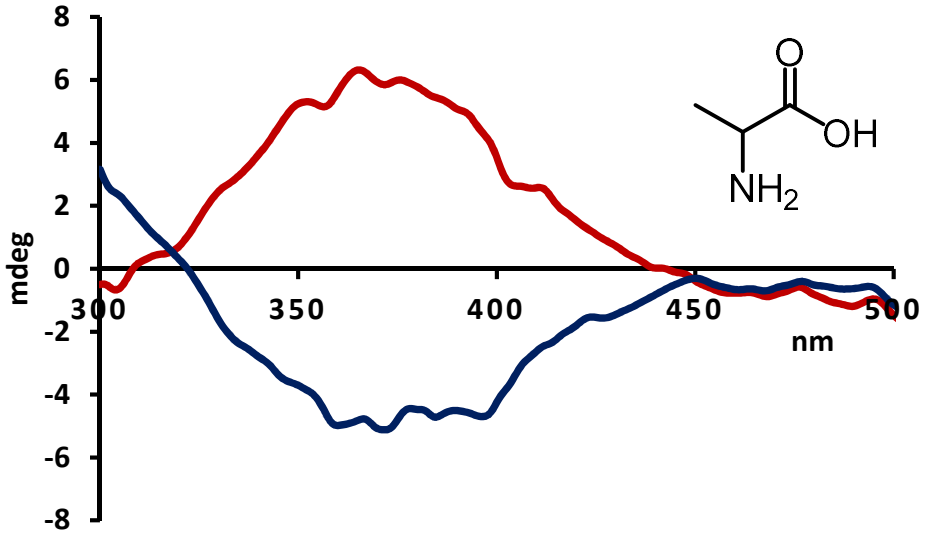
CD measurements were taken at 0.23 mM in acetonitrile.

Figure 32. CD spectra obtained by applying probe **1** to (*R*)-**21** (blue) and (*S*)-**21** (red)



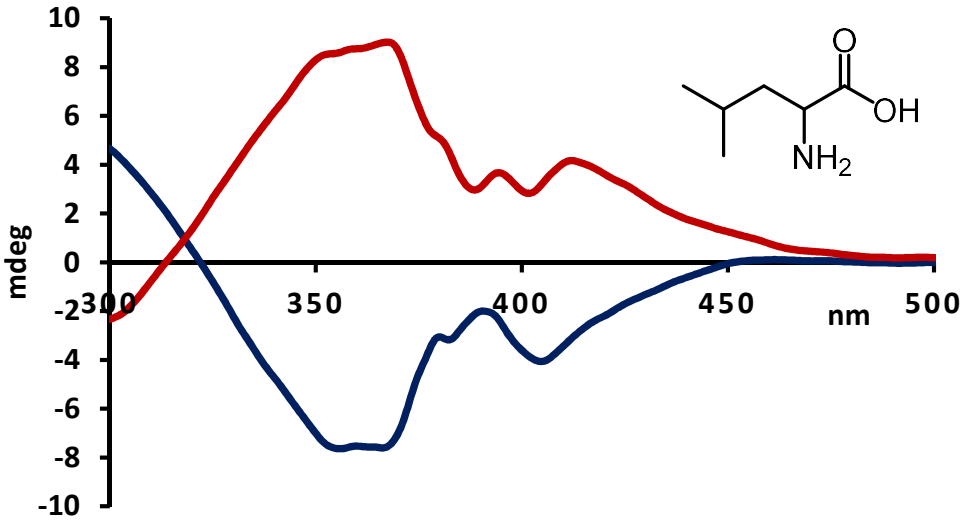
CD measurements were taken at 0.41 mM in acetonitrile.

Figure 33. CD spectra obtained by applying probe **1** to (*R*)-**22** (blue) and (*S*)-**22** (red)



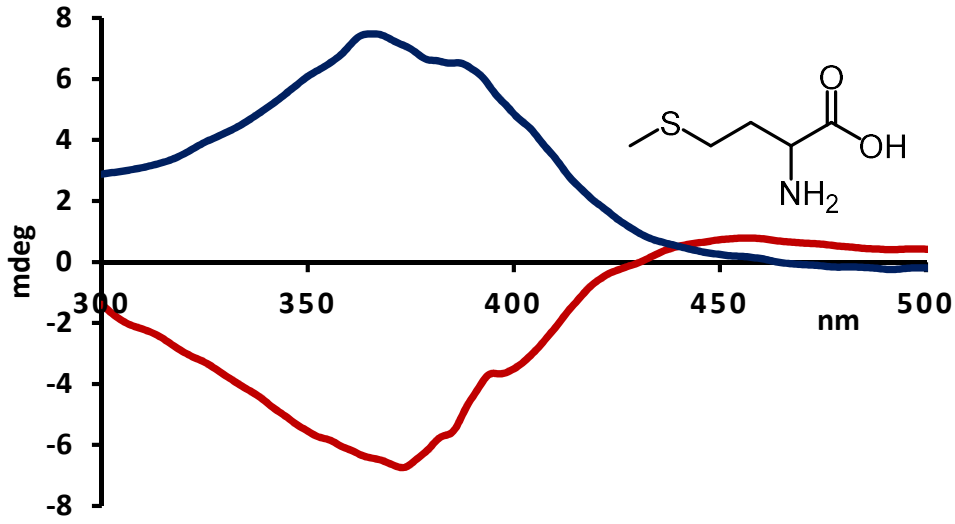
CD measurements were taken at 0.41 mM in acetonitrile.

Figure 34. CD spectra obtained by applying probe **1** to (*R*)-**23** (blue) and (*S*)-**23** (red)



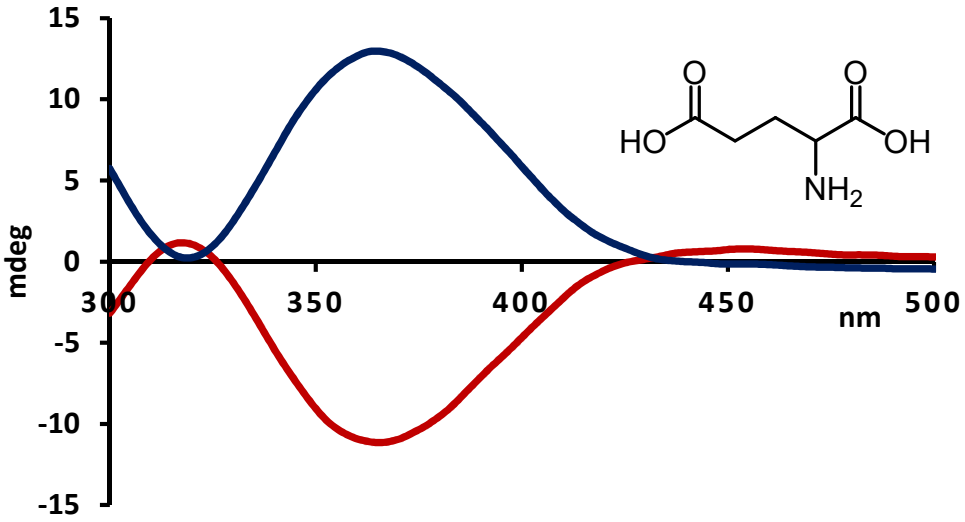
CD measurements were taken at 0.41 mM in acetonitrile.

Figure 35. CD spectra obtained by applying probe **1** to (*R*)-**24** (blue) and (*S*)-**24** (red)



CD measurements were taken at 0.68 mM in acetonitrile.

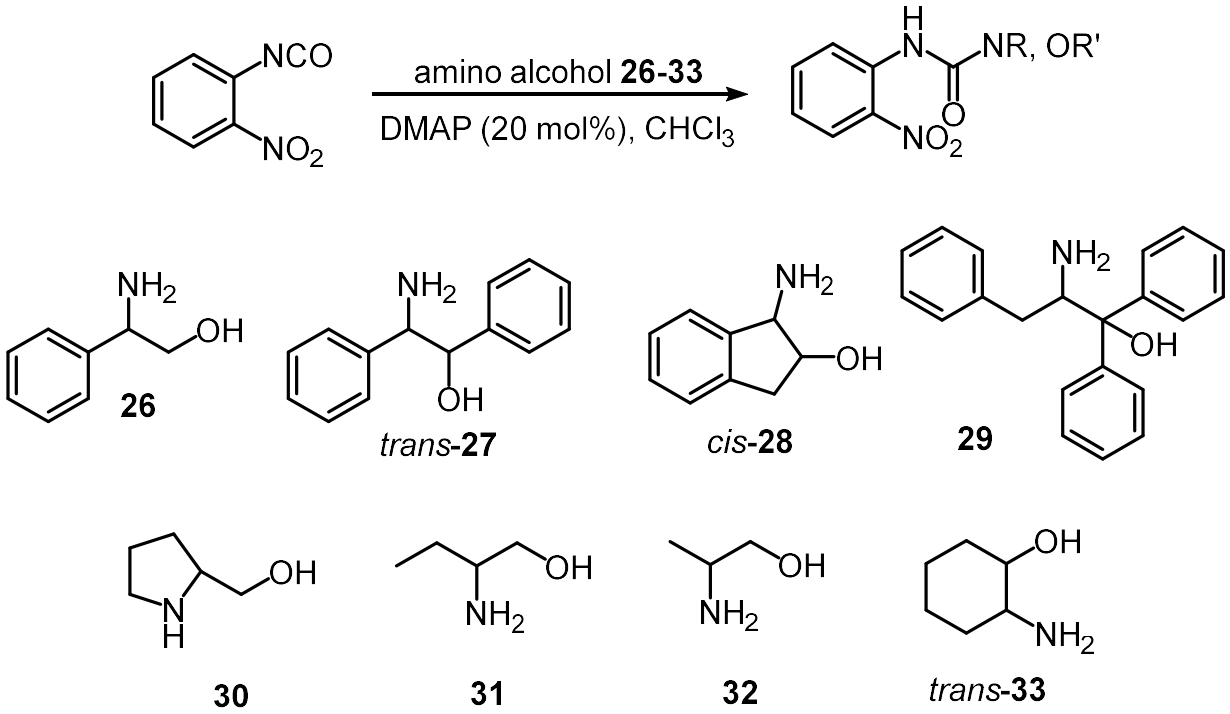
Figure 36. CD spectra obtained by applying probe **1** to (*R*)-**25** (blue) and (*S*)-**25** (red)



CD measurements were taken at 0.41 mM in acetonitrile.

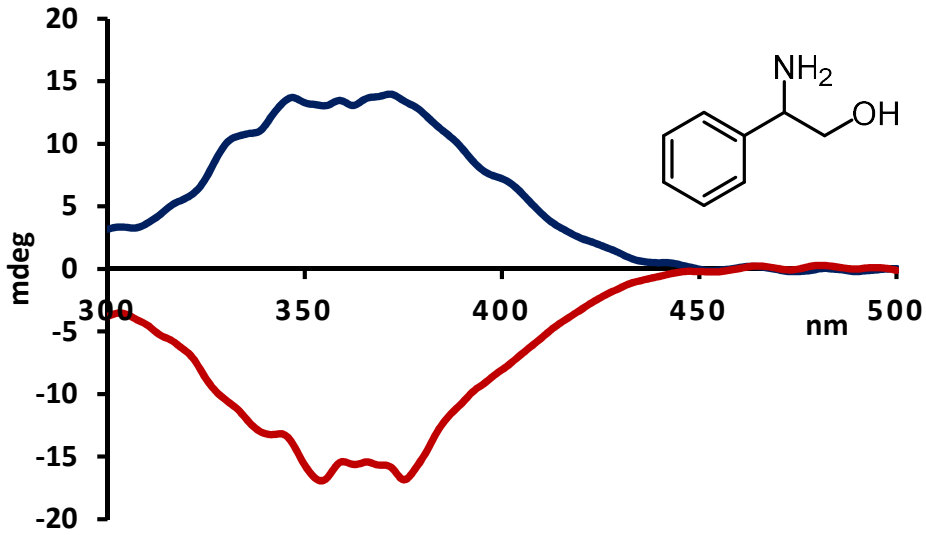
4. Sensing scope: amino alcohols

Scheme 4. Amino alcohol substrate scope



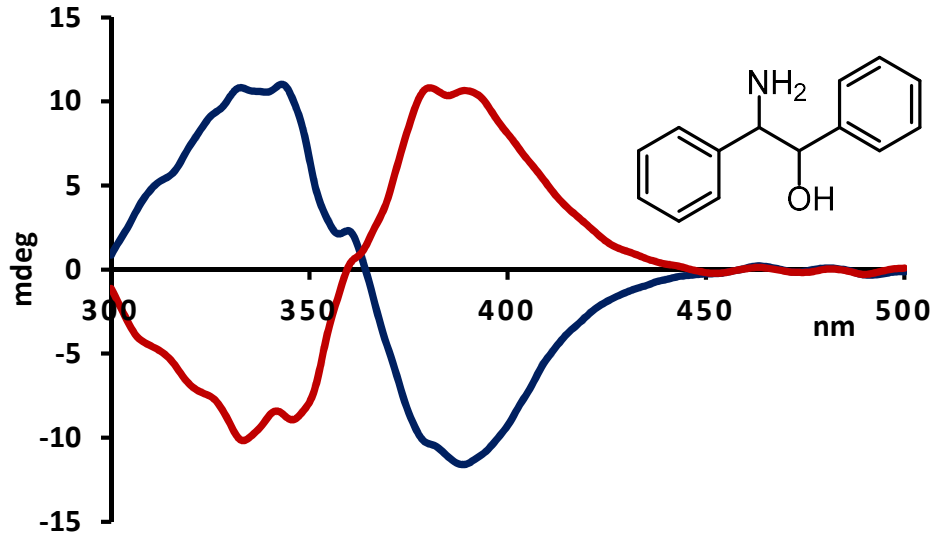
In a glovebox, a solution of chiral amino alcohols **26-33** (27-100 mM), probe **1** (2.4 equivalents), and DMAP (0.2 equivalents) in 2.0 mL of chloroform was stirred overnight. CD analysis was performed after dilution with ACN to the final concentration indicated under each Figure (15.0 – 40.0 µL of the reaction mixture added to 2.0 mL ACN). The CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, and a bandwidth of 1 nm in a continuous scanning mode with a scanning speed of 500 nm/min and a response of 1 s (1 cm path length). The data were baseline corrected and smoothed using a binomial equation.

Figure 37. CD spectra obtained by applying probe **1** to (*R*)-**26** (blue) and (*S*)-**26** (red)



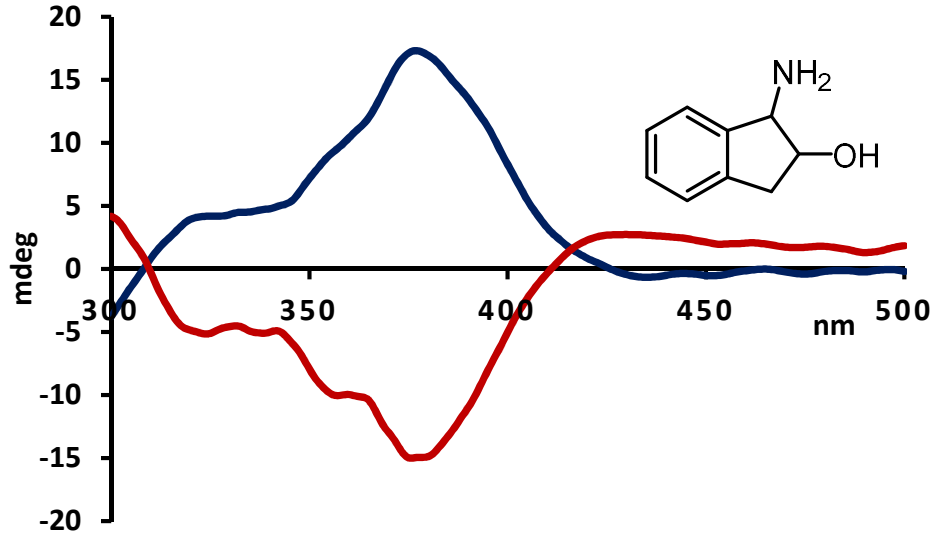
CD measurements were taken at 0.36 mM in acetonitrile.

Figure 38. CD spectra obtained by applying probe **1** to (*1R*,2*S*)-**27** (blue) and (1*S*,2*R*)-**27** (red)



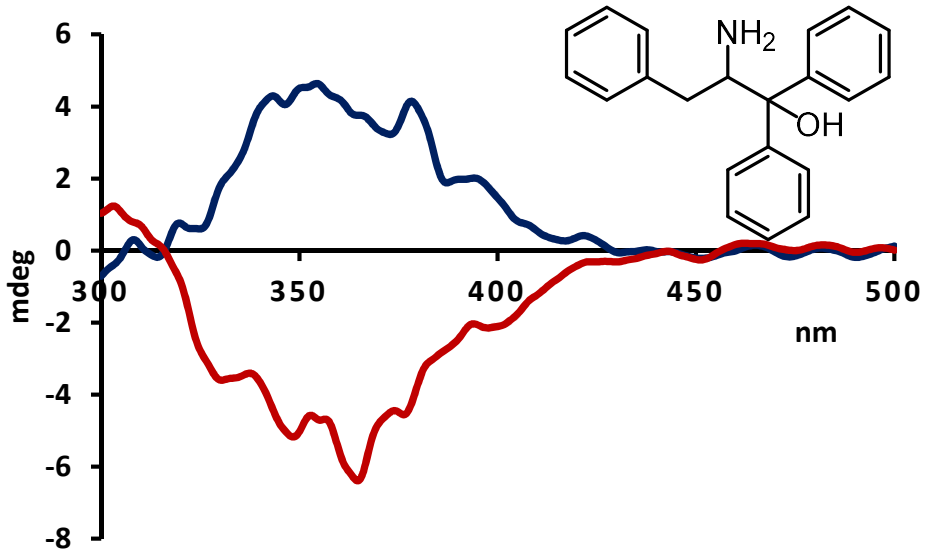
CD measurements were taken at 0.36 mM in acetonitrile.

Figure 39. CD spectra obtained by applying probe **1** to (1*R*,2*S*)-**28** (blue) and (1*S*,2*R*)-**28** (red)



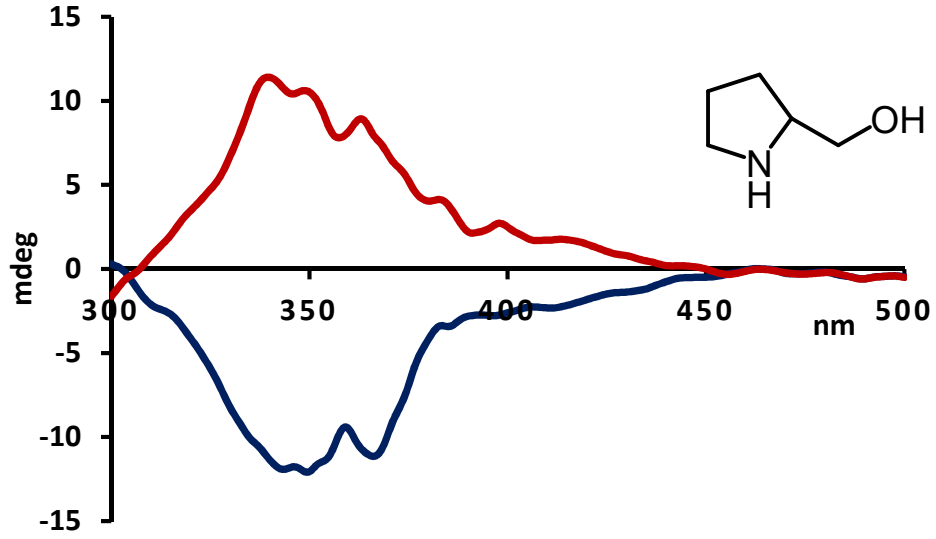
CD measurements were taken at 0.34 mM in acetonitrile.

Figure 40. CD spectra obtained by applying probe **1** to (*R*)-**29** (blue) and (*S*)-**29** (red)



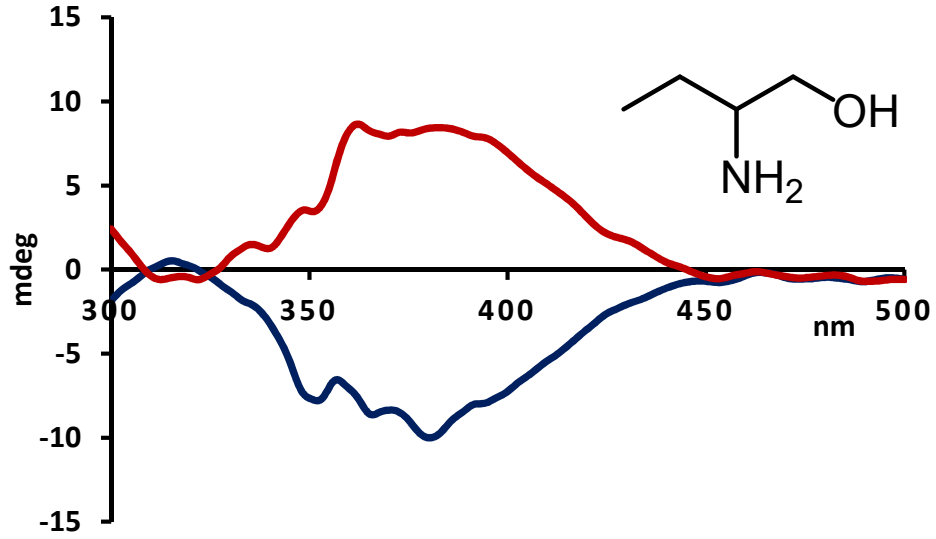
CD measurements were taken at 0.49 mM in acetonitrile.

Figure 41. CD spectra obtained by applying probe **1** to (*R*)-**30** (blue) and (*S*)-**30** (red)



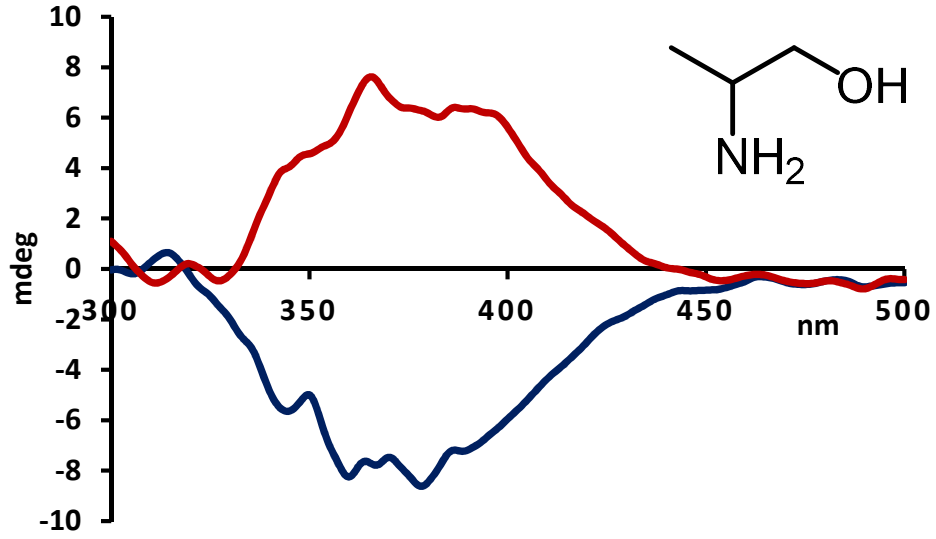
CD measurements were taken at 0.39 mM in acetonitrile

Figure 42. CD spectra obtained by applying probe **1** to (*R*)-**31** (blue) and (*S*)-**31** (red)



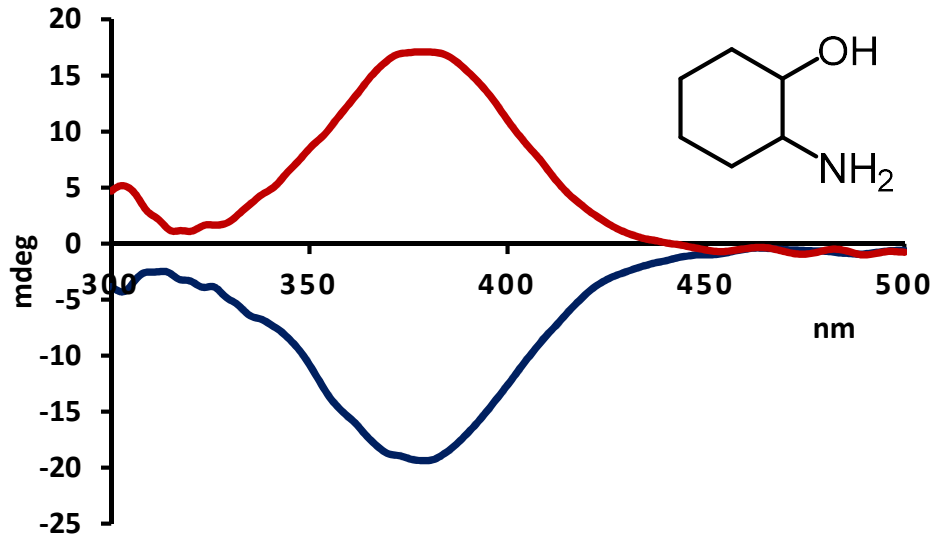
CD measurements were taken at 0.39 mM in acetonitrile.

Figure 43. CD spectra obtained by applying probe **1** to (*R*)-**32** (blue) and (*S*)-**32** (red)



CD measurements were taken at 0.37 mM in acetonitrile.

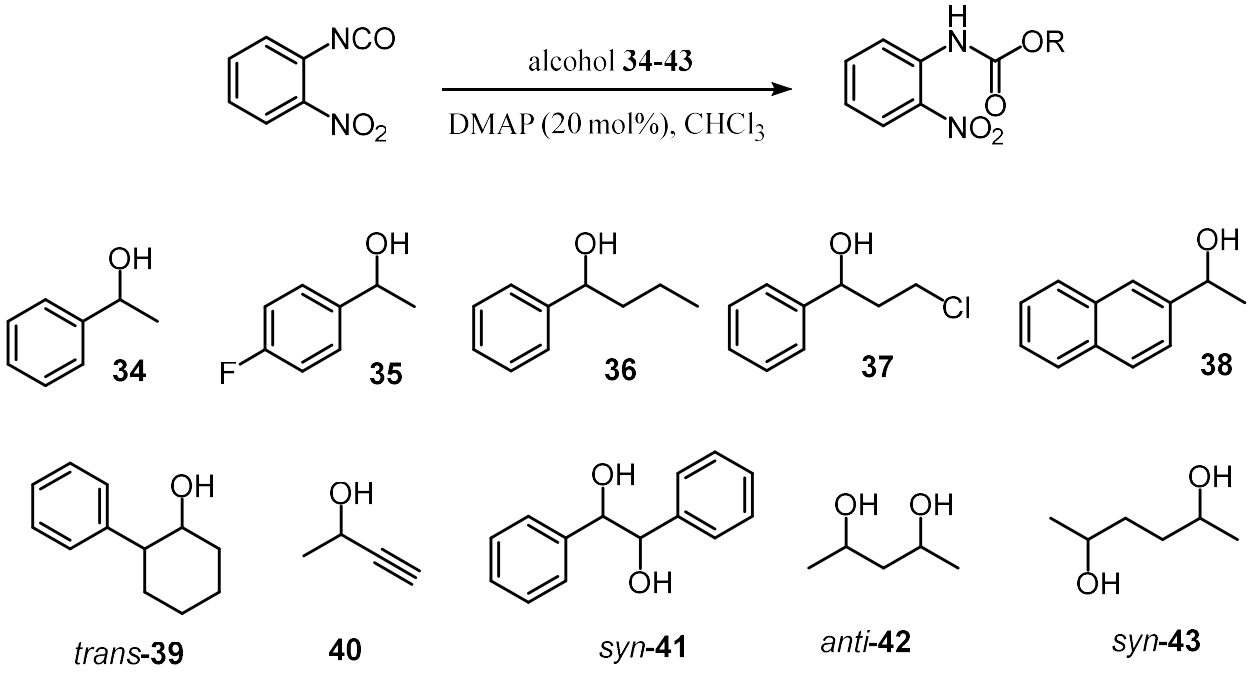
Figure 44. CD spectra obtained by applying probe **1** to (1*R*,2*R*)-**33** (blue) and (1*S*,2*S*)-**33** (red)



CD measurements were taken at 0.45 mM in acetonitrile.

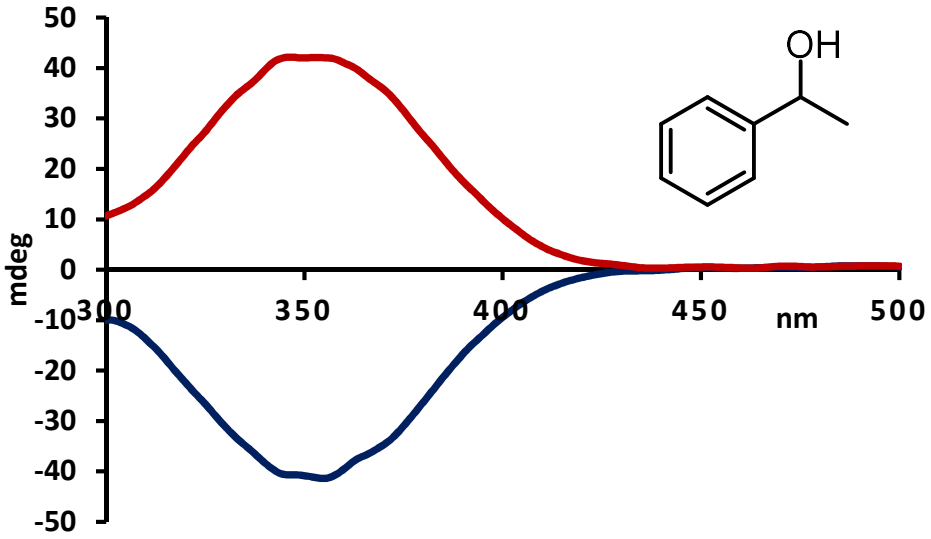
5. Sensing scope: alcohols

Scheme 5. Alcohol substrate scope



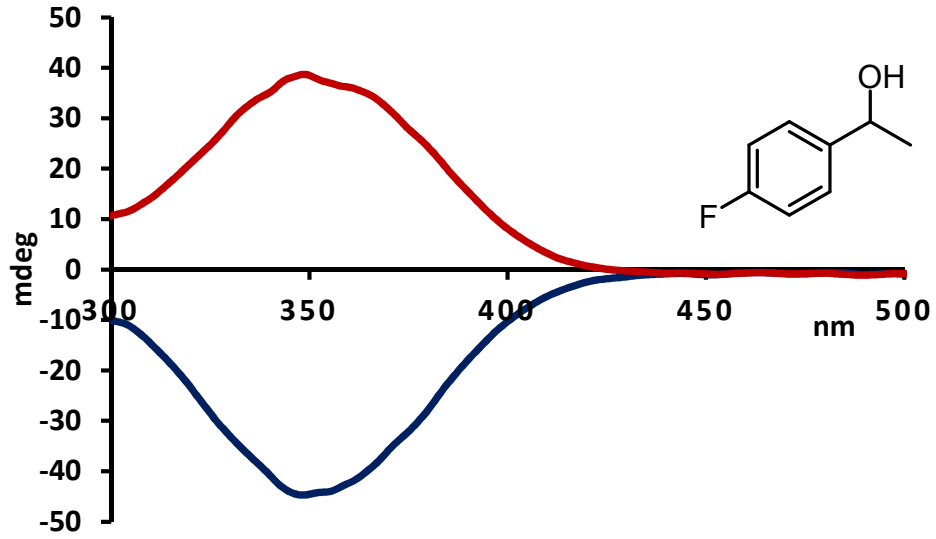
In a glovebox, a solution of chiral alcohols **34-43** (70-130 mM), probe **1**, and DMAP (0.2 equivalents) in 1.0 mL of chloroform was stirred overnight. For chiral alcohols **34-40**, 1.2 equivalents of the probe were used; for diols **41-43**, 2.4 equivalents of the probe were used. CD analysis was performed after dilution with ACN to the final concentration indicated under each Figure (5.0 – 20.0 µL of the reaction mixture added to 2.0 mL ACN). The CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, and a bandwidth of 1 nm in a continuous scanning mode with a scanning speed of 500 nm/min and a response of 1 s (1 cm path length). The data were baseline corrected and smoothed using a binomial equation.

Figure 45. CD spectra obtained by applying probe **1** to (*R*)-**34** (blue) and (*S*)-**34** (red)



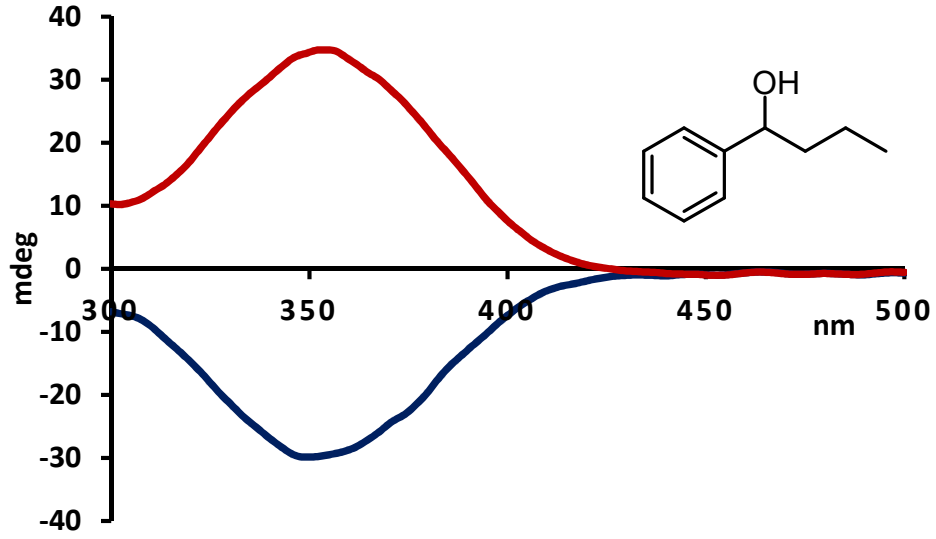
CD measurements were taken at 0.50 mM in acetonitrile.

Figure 46. CD spectra obtained by applying probe **1** to (*R*)-**35** (blue) and (*S*)-**35** (red)



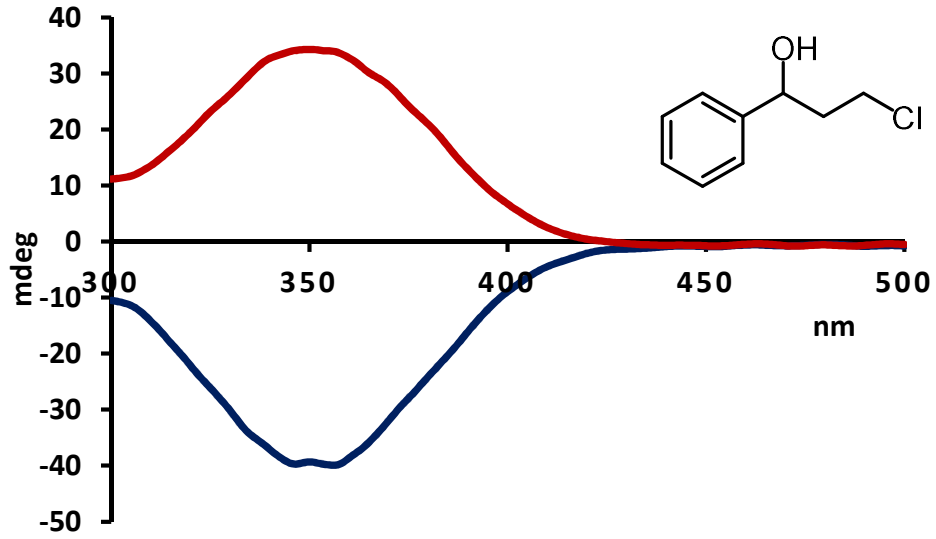
CD measurements were taken at 0.50 mM in acetonitrile.

Figure 47. CD spectra obtained by applying probe **1** to (*R*)-**36** (blue) and (*S*)-**36** (red)



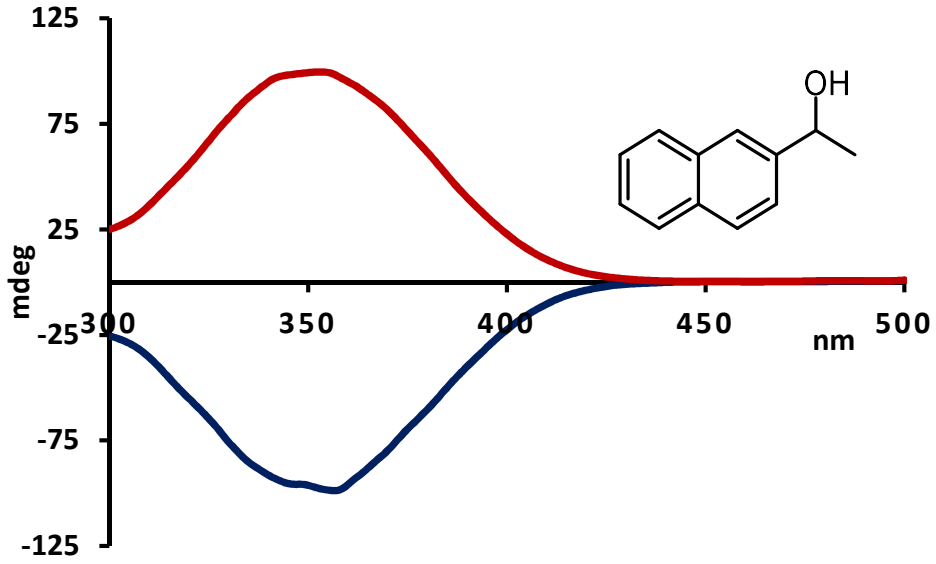
CD measurements were taken at 0.50 mM in acetonitrile.

Figure 48. CD spectra obtained by applying probe **1** to (*R*)-**37** (blue) and (*S*)-**37** (red)



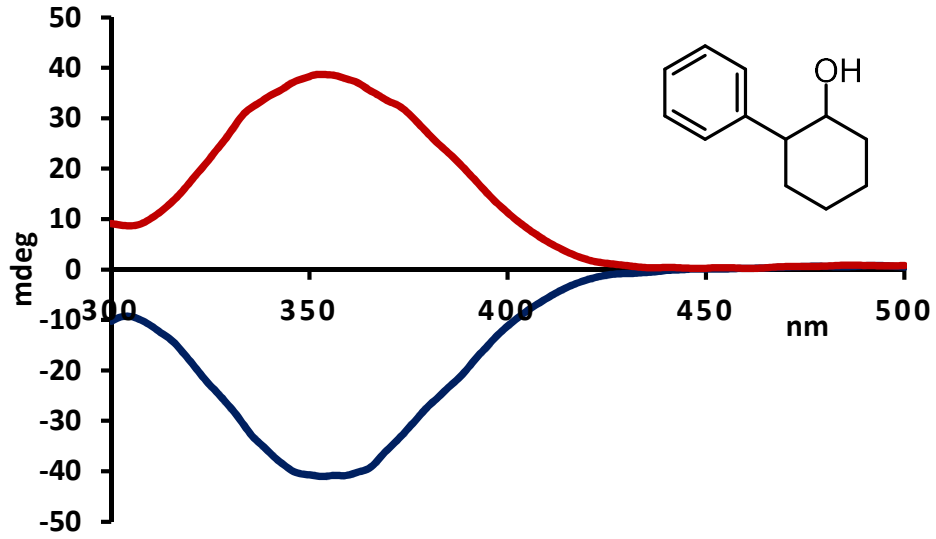
CD measurements were taken at 0.50 mM in acetonitrile.

Figure 49. CD spectra obtained by applying probe **1** to (*R*)-**38** (blue) and (*S*)-**38** (red)



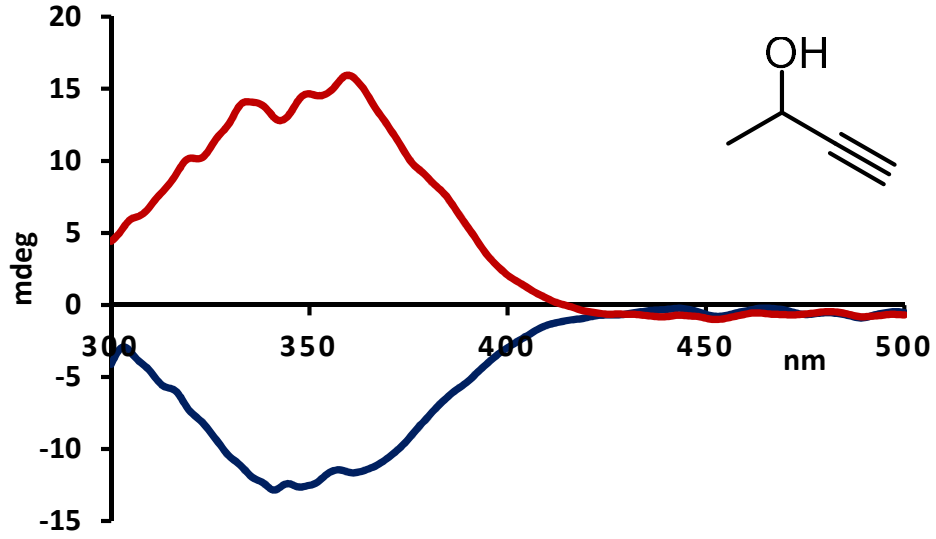
CD measurements were taken at 0.75 mM in acetonitrile.

Figure 50. CD spectra obtained by applying probe **1** to (1*R*,2*S*)-**39** (blue) and (1*S*,2*R*)-**39** (red)



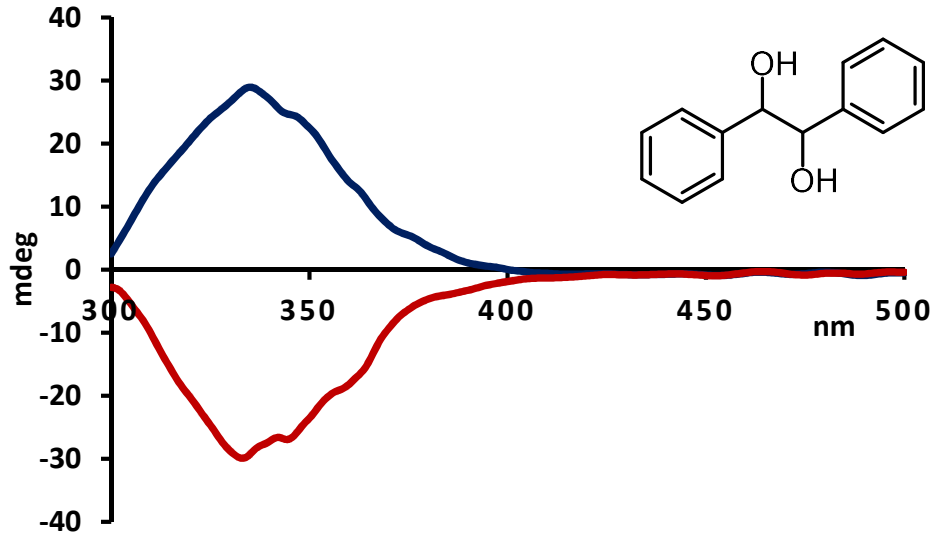
CD measurements were taken at 0.60 mM in acetonitrile.

Figure 51. CD spectra obtained by applying probe **1** to (*R*)-**40** (blue) and (*S*)-**40** (red)



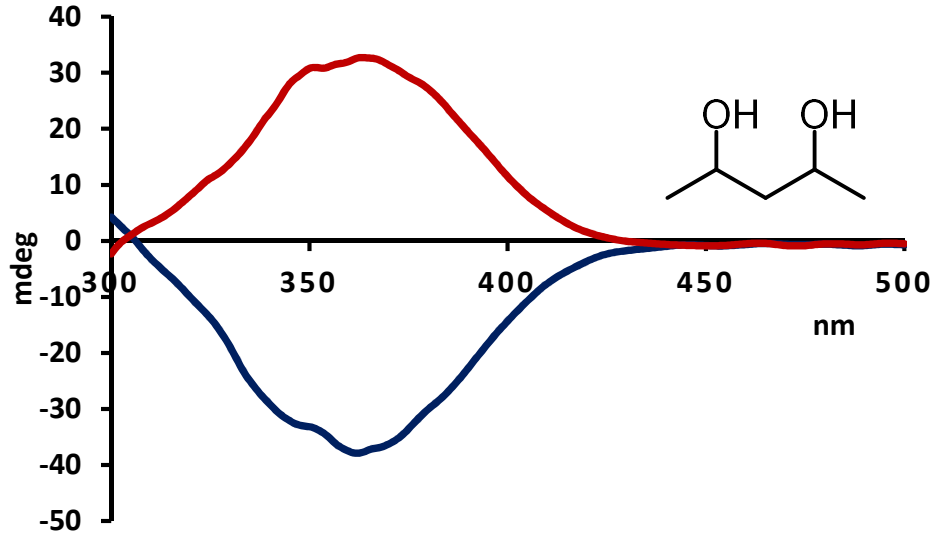
CD measurements were taken at 0.71 mM in acetonitrile.

Figure 52. CD spectra obtained by applying probe **1** to (1*R*,2*R*)-**41** (blue) and (1*S*,2*S*)-**41** (red)



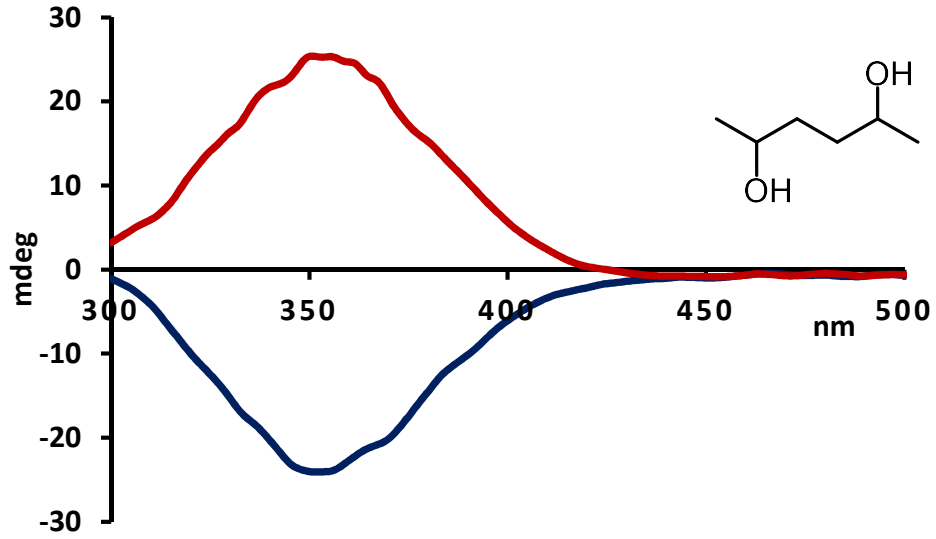
CD measurements were taken at 0.27 mM in acetonitrile.

Figure 53. CD spectra obtained by applying probe **1** to (2*R*,4*R*)-**42** (blue) and (2*S*,4*S*)-**42** (red)



CD measurements were taken at 0.34 mM in acetonitrile.

Figure 54. CD spectra obtained by applying probe **1** to (2*R*,5*R*)-**43** (blue) and (2*S*,5*S*)-**43** (red)



CD measurements were taken at 0.27 mM in acetonitrile.

6. Quantitative amine and alcohol sensing: absolute configuration, enantiomeric excess, and total concentration

CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, and a bandwidth of 1 nm in a continuous scanning mode with a scanning speed of 500 nm/min and a response of 1 s (1 cm path length). The data were baseline corrected and smoothed using a binomial equation. UV spectra were collected with an average scanning time of 0.0125 s, a data interval of 1.00 nm and a scan rate of 4800 nm/s.

Quantitative sensing of phenylethylamine

The change in the UV absorbance upon addition of (*R*)-phenylethylamine to probe **1** was measured. Probe **1** (120.0 mM) and (*R*)-phenylethylamine in varying concentrations (0, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 mM) were dissolved in 1.0 mL of $CHCl_3$ and stirred for 15 minutes. Each mixture was diluted with ACN (4.0 μL aliquot added to 2.0 mL of ACN) for UV analysis. The absorbance wavelength shifted from 328 nm to 375 nm as the substrate concentration increased from 0 to 100 mM. Plotting the intensity at 375 nm versus each concentration of phenylethylamine yielded a polynomial with $R^2 = 0.9961$ and $y = -3E\text{-}05x^2 + 0.009x + 0.2261$.

Figure 55. Calibration curve for concentration analysis of (*R*)-phenylethylamine with probe **1**

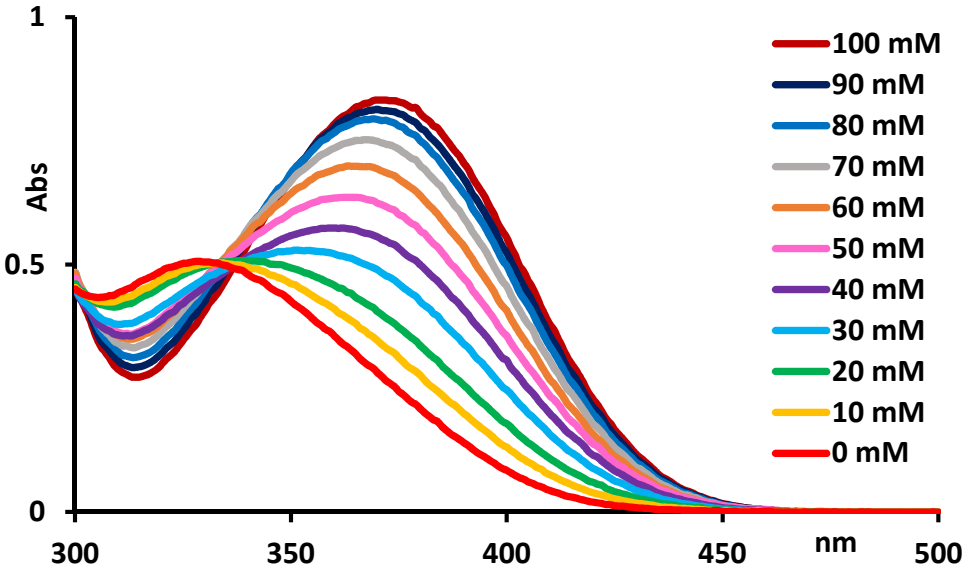
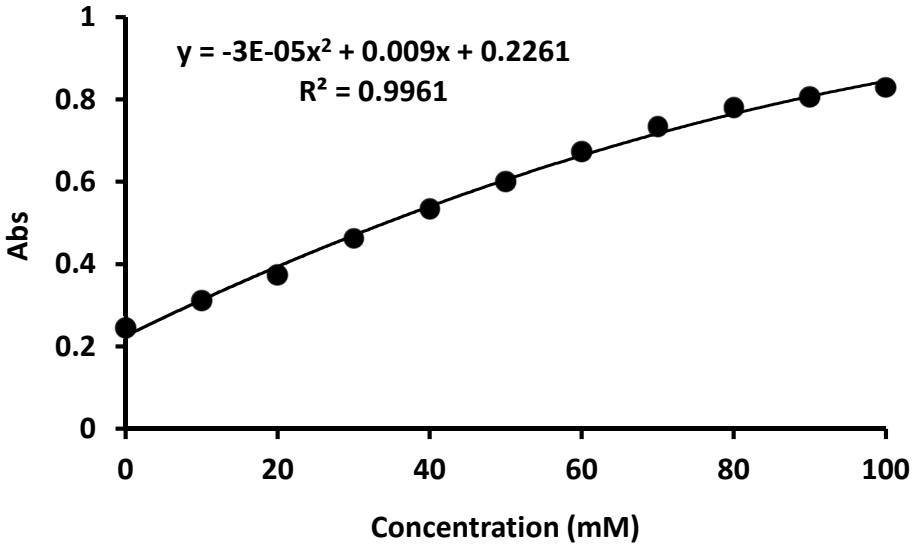


Figure 56. UV absorbance at 375 nm vs. concentration of (*R*)-phenylethylamine



The change in the CD amplitude of probe **1** upon addition of phenylethylamine in varying enantiomeric composition was measured. Probe **1** (99.0 mM) and phenylethylamine (total 82.5 mM) with varying *ee*'s (+100, +80, +60, +40, +20, 0, -20, -40, -60, -80, and -100%) were dissolved in 1.0 mL of $CHCl_3$ and stirred for 15 minutes. Each mixture was diluted with ACN for CD analysis (10.0 µL aliquot added to 2.0 mL of ACN). Plotting the CD amplitude at 375 nm against the enantiomeric excess of phenylethylamine yielded a straight line with $R^2 = 0.9885$ and $y = -0.3868x + 0.2678$.

Figure 57. Chiroptical response of probe **1** to scalemic samples of phenylethylamine

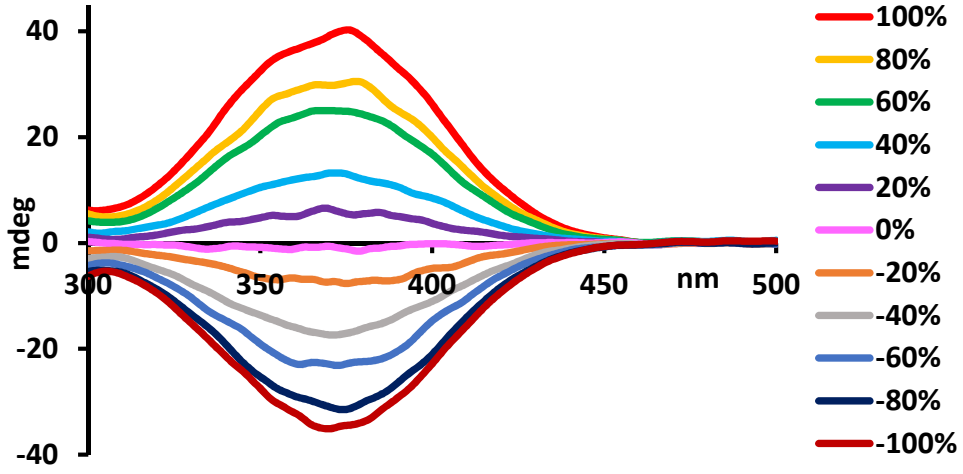
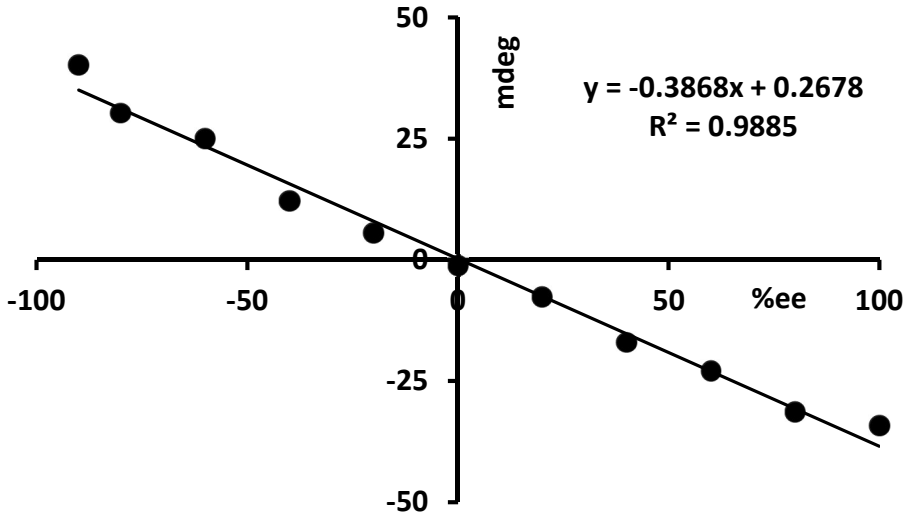


Figure 58. CD amplitude at 375 nm vs. sample *ee*



Simultaneous *ee* and concentration determination

Ten scalemic samples of phenylethylamine at varying concentrations and *ee* in $CHCl_3$ were prepared and subjected to simultaneous analysis of the concentration, enantiomeric excess, and absolute configuration using probe **1**. First, a UV spectrum was obtained as described above and the concentration was calculated using the intensities at 375 nm and the equation shown in Figure 42. Then, a CD spectrum was obtained as described above. The CD intensities were normalized to the concentrations obtained from UV analysis and the enantiomeric ratio was

calculated using the intensities at 375 nm and the equation shown in Figure 44. The absolute configuration was determined using the sign of the Cotton effect.

Table 1. Concentration, enantiomeric ratio, and absolute configuration of samples of phenylethylamine determined by simultaneous UV and CD responses of probe **1**.

Sample composition			**Sensing results**		
Abs. Config.	**Concentration (mM)**	***S/R***	**Abs. Config.**	**Concentration (mM)**	***S/R***
R	100.0	40.0:60.0	*R*	94.5	41.6:58.4
S	100.0	75.0:25.0	*S*	96.9	78.7:21.3
S	75.0	82.0:18.0	*S*	68.2	88.7:11.3
R	60.0	2.0:98.0	*R*	62.1	1.1:98.9
S	50.0	95.0:5.0	*S*	50.1	96.9:3.1
R	50.0	35.0:65.0	*R*	54.4	33.9:66.1
S	40.0	70.0:30.0	*S*	35.5	68.8:31.2
R	80.0	22.0:78.0	*R*	70.3	23.8:76.2
R	25.0	10.0:90.0	*R*	21.0	8.1:91.9
S	25.0	80.0:20.0	*S*	22.3	78.7:21.3

Quantitative sensing of 1-(2-naphthyl)ethanol

The change in CD amplitude of probe **1** upon addition of 1-(2-naphthyl)ethanol in varying enantiomeric composition was measured. In a glovebox, probe **1** (120.0 mM), DMAP (20.0 mM), and 1-(2-naphthyl)ethanol (total 100 mM) with varying *ee*'s (+100, +80, +60, +40, +20, 0, -20, -40, -60, -80, and -100%) were dissolved in 1.0 mL of $CHCl_3$ and stirred overnight. Each mixture was diluted with ACN for CD analysis (15.0 μL added to 2.0 mL of ACN). Plotting the CD amplitude at 350 nm against the enantiomeric excess of 1-(2-naphthyl)ethanol yielded a straight line with $R^2 = 0.997$ and $y = 0.9783x + 2.528$.

Figure 59. Chiroptical response of probe **1** to scalemic samples of 1-(2-naphthyl)ethanol

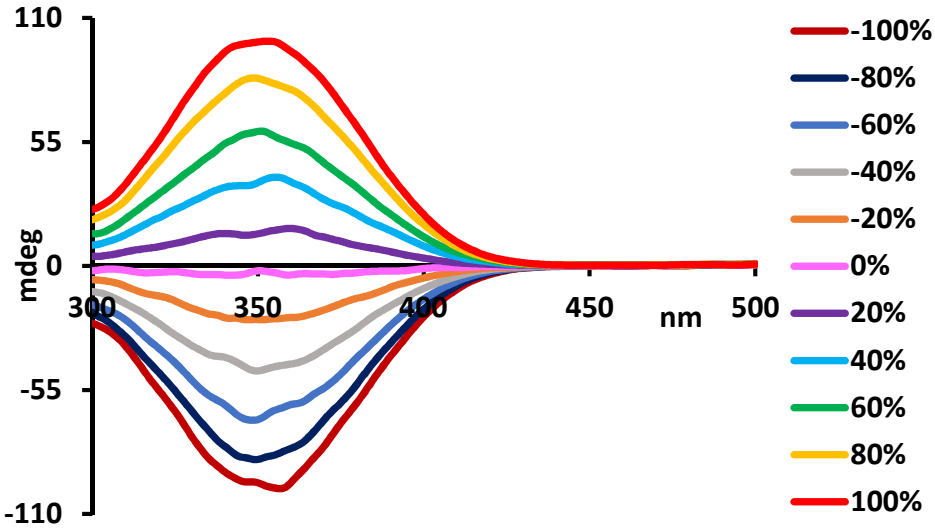
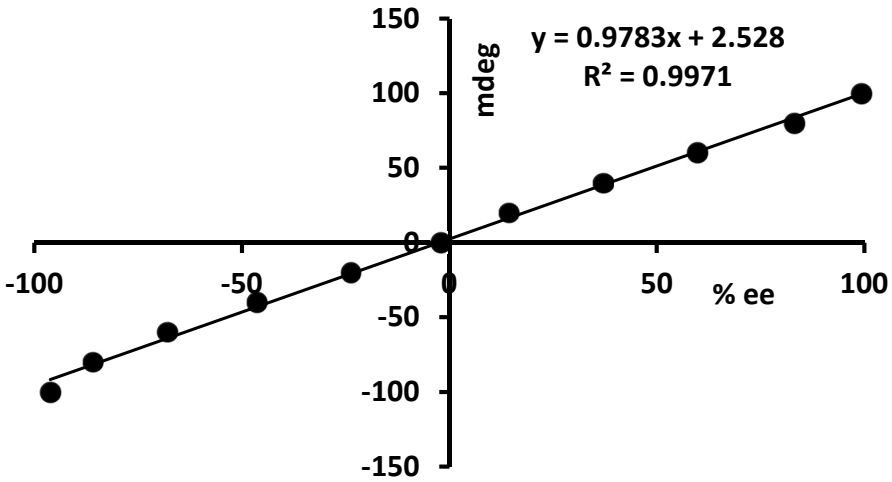


Figure 60. CD amplitude at 350 nm vs. sample *ee*



The change in the UV absorbance upon addition of (*R*)-1-(2-naphthyl)ethanol to probe **1** was measured. In a glovebox, probe **1** (120.0 mM) and (*R*)-1-(2-naphthyl)ethanol in varying concentrations (0, 20, 40, 60, 80, and 100 mM) were dissolved in 1.0 mL of $CHCl_3$ and stirred overnight. Each mixture was diluted with ACN (5.0 µL aliquot added to 2.0 mL of ACN) for UV analysis. The absorbance wavelength shifted from 319 nm to 354 nm as the substrate concentration increased from 0 to 100 mM. Plotting the intensity at 350 nm versus each concentration of 1-(2-naphthyl)ethanol yielded a polynomial with $R^2 = 0.9989$ and $y = -2E\text{-}05x^2 + 0.0067x + 0.309$.

Figure 61. Calibration curve for concentration analysis of (*R*)-1-(2-naphthyl)ethanol with probe **1**

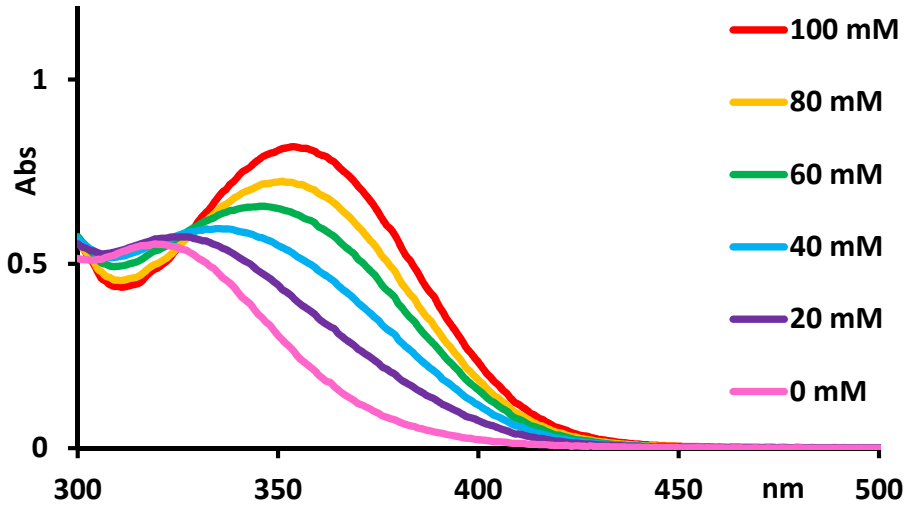
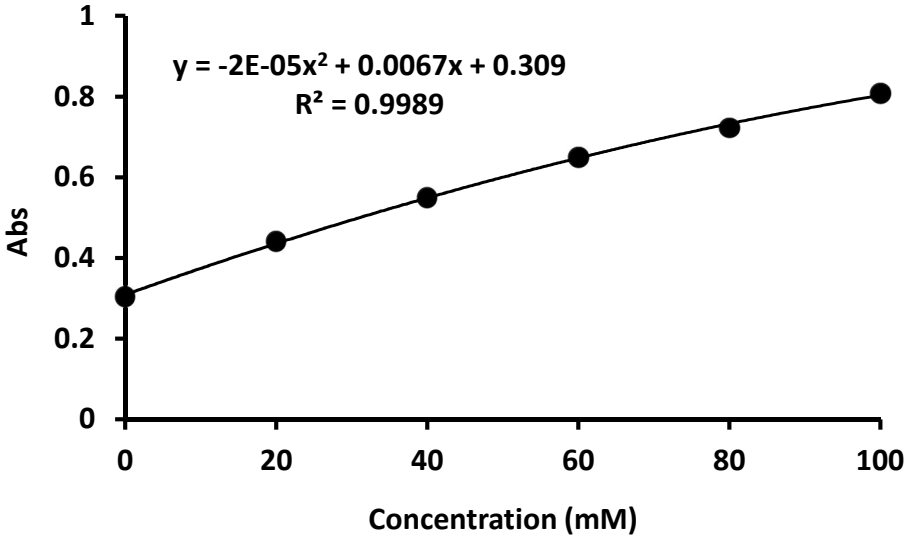
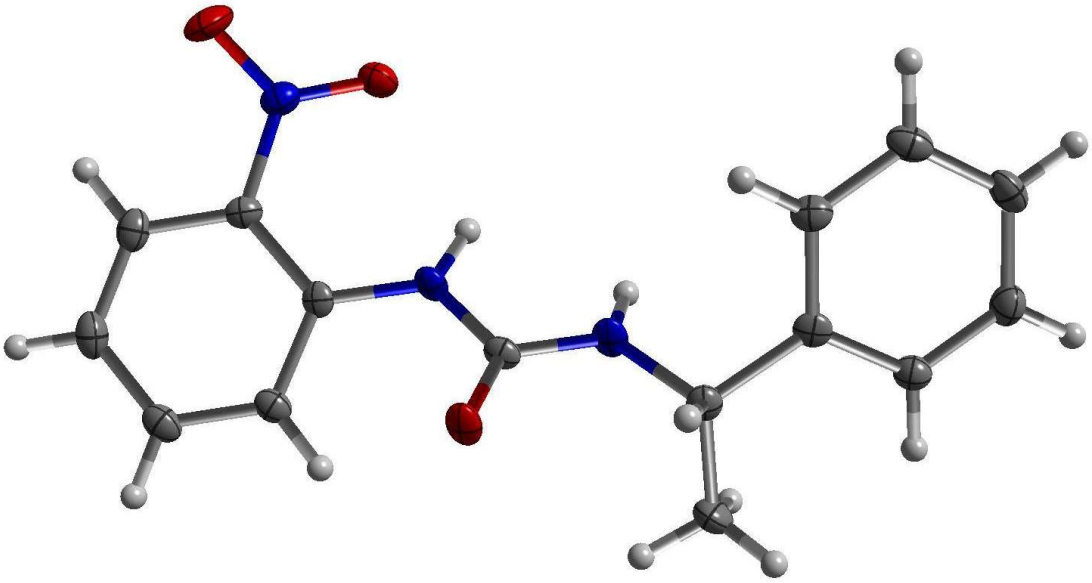


Figure 62. UV absorbance at 350 nm vs. concentration of (*R*)-1-(2-naphthyl)ethanol



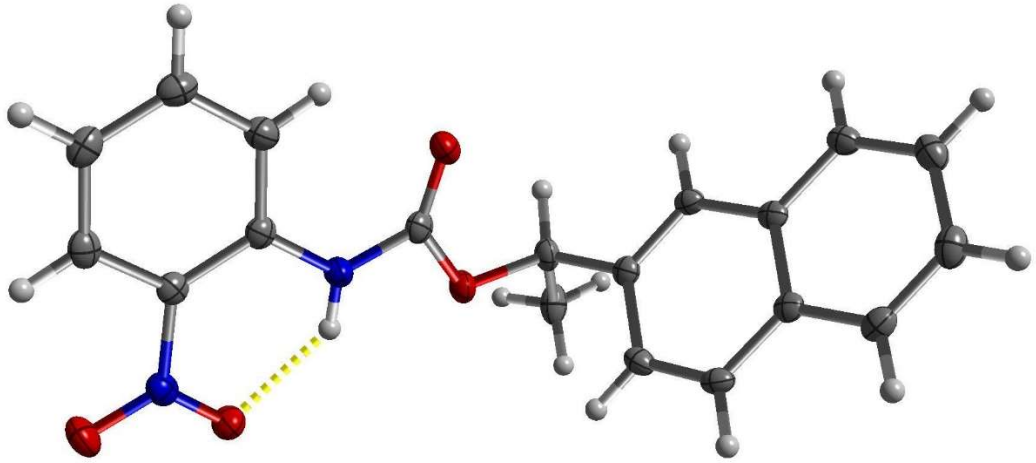
7. Crystallographic analysis

(*S*)-1-(2-Nitrophenyl)-3-(1-phenylethyl)urea



A single crystal was obtained by slow evaporation of a solution of the chiral product in dichloromethane:hexanes (1.5:1). Single crystal X-ray analysis was performed at 100 K using Bruker APEX DUO equipped with a Cu-Kα (λ = 0.154178 Å) microfocus source, an ApexII detector, and an Oxford 700 Cryostream. Data were integrated with the Bruker SAINT program. Structure solution and refinement were performed using the SHELXTL/PC suite and ShelXle. Intensities were corrected for Lorentz and polarization effects and an empirical absorption correction was applied using Blessing's method as incorporated into the program SADABs. Non-hydrogen atoms were refined with anisotropic displacement parameters. Crystal data: $C_{15}H_{15}N_3O_3$, *M* = 285.30, yellow needle, 0.034 x 0.082 x 0.529 mm3, monoclinic, space group P21, a = 4.64130(10), b = 11.0456(3), c = 13.6158(4) Å, V = 693.65(3) Å3, Z = 2. Absolute structure parameter = 0.2(2).

(*R*)-1-(Naphthalen-2-yl)ethyl (2-nitrophenyl)carbamate



A single crystal was obtained by slow evaporation of a solution of the chiral product in dichloromethane:hexanes (1:1). Single crystal X-ray analysis was performed at 100 K using Bruker APEX DUO equipped with a Mo-Kα radiation (λ = 0.71073 Å) microfocus source, an ApexII detector, and an Oxford 700 Cryostream. Data were integrated with the Bruker SAINT program. Structure solution and refinement were performed using the SHELXTL/PC suite and ShelXle. Intensities were corrected for Lorentz and polarization effects and an empirical absorption correction was applied using Blessing's method as incorporated into the program SADABs. Non-hydrogen atoms were refined with anisotropic displacement parameters. Crystal data: $C_{19}H_{16}N_2O_4$, *M* = 336.34, yellow block, 0.258 x 0.307 x 0.467 mm3, orthorhombic, space group P212121, a = 5.8533(12), b = 7.9653(17), c = 34.781(8) Å, V = 1621.6(6) Å3, Z = 4. Absolute structure parameter = -0.9(5).