Electronic Supplementary Material (ESI) for Chemical Communications
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Supplementary Information

Sensing of the Concentration and Enantiomeric Excess of Chiral Compounds with Tropos Ligand Derived Metal Complexes

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Content:

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1. Synthetic Procedures

All commercially available reagents and solvents were used without further purification. NMR spectra were obtained at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) using CD_3CN or $CDCl_3$ as solvent. Chemical shifts are reported in ppm relative to TMS. Electrospray ionization mass spectra (ESI-MS) were collected on a Thermo Finnigan LCQ instrument. Samples were dissolved in ACN for MS analysis (1 mg/mL).

[Bis(2-(diphenylphosphino)phenyl)ether]palladium(II) dichloride.[1]
To a solution of (1,5-cyclooctadiene)palladium(II) dichloride (540 mg, 1 mmol) in 25 mL of CH_2Cl_2 was added bis[2-(diphenylphosphino)phenyl]ether (285 mg, 1 mmol) dissolved in 6 mL of CH_2Cl_2. After stirring at room temperature for 3.5 hours, the mixture was filtrated and the precipitate was washed with 3 mL of CH_2Cl_2 followed by 20 mL of hexanes. After drying under vacuum, 586 mg (0.82 mmol, 82%) of [bis(2-(diphenylphosphino)phenyl)ether]palladium(II) dichloride was obtained. ^{1}H NMR ($CDCl_3$) δ = 6.73 (dd, *J* = 8.0 Hz, 8.0 Hz, 2H), 6.86 (dd, *J* = 7.5 Hz, 7.5 Hz, 2H), 6.96 (m, 2H), 7.26-7.42 (m, 16H), 7.56-7.63 (m, 6H). ^{13}C NMR ($CDCl_3$) δ = 121.5, 124.9, 127.8, 128.8, 129.4, 130.7, 132.8, 134.9, 135.1.

Bis(acetonitrile)[bis(2-(diphenylphosphino)phenyl)ether]palladium(II) hexafluoroantimonate, 1.[2]
To a solution of [bis(2-(diphenylphosphino)phenyl)ether]palladium(II) dichloride (286 mg, 0.4 mmol) in 5 mL of ACN was added $AgSbF_6$ (274.4 mg, 0.8 mmol, 2 equivalents) dissolved in 3 mL of ACN. After stirring at room temperature for 20 minutes, the mixture was filtrated through a short celite column using CH_2Cl_2 as mobile phase. The solvents were removed and the residue was passed through another celite column using CH_2Cl_2. After redissolving in 3 mL of CH_2Cl_2, recrystallization upon addition of 20 mL of hexanes gave 468 mg (0.4 mmol, 98%) of **1** as a yellow solid. ^{1}H NMR (CD_3CN) δ = 1.97 (s, 6H), 6.81 (m, 2H), 7.09 (ddd, *J* =1.2 Hz, 7.4 Hz, 7.4 Hz, 2H), 7.20 (m, 2H), 7.53-7.72 (m, 22H). ^{13}C NMR (CD_3CN) δ = 1.8, 118.9, 123.6, 126.8, 127.4, 127.8, 130.9, 134.7, 135.5, 137.3, 137.4, 160.1. Anal. Calcd. for $C_{40}H_{34}F_{12}N_2OP_2PdSb_2$: C, 40.08; H, 2.86; N, 2.34. Found: C, 40.44; H, 2.87; N, 2.21.

Bis(acetonitrile)[1,1′-bis(diphenylphosphino)ferrocene]palladium(II) hexafluoroantimonate, 2.[3]
To a solution of $AgSbF_6$ (75.6 mg, 0.22 mmol, 2.2 equivalents) in 3 mL of ACN was added 81.6 mg (0.1 mmol) of [1,1′-bis(diphenylphosphino)ferrocene]palladium(II) dichloride (complex with dichloromethane) under nitrogen. After stirring at room temperature for 30 minutes, the mixture was filtrated through a short celite column using CH_2Cl_2 as mobile phase. The solvents were removed and then residue was passed through another celite column using CH_2Cl_2. Removal of solvents gave 118 mg (0.1 mmol, 98%) of **2** as a purple solid. ^{1}H NMR (CD_3CN) δ = 1.97 (s, 6H), 4.57 (s, 4H), 4.77 (s, 4H), 7.56-7.62 (m, 8H), 7.72-7.83 (m, 12H). ^{13}C NMR (CD_3CN) δ = 1.8, 69.0, 78.0, 80.2, 118.9, 130.2, 131.3, 135.2, 135.4.

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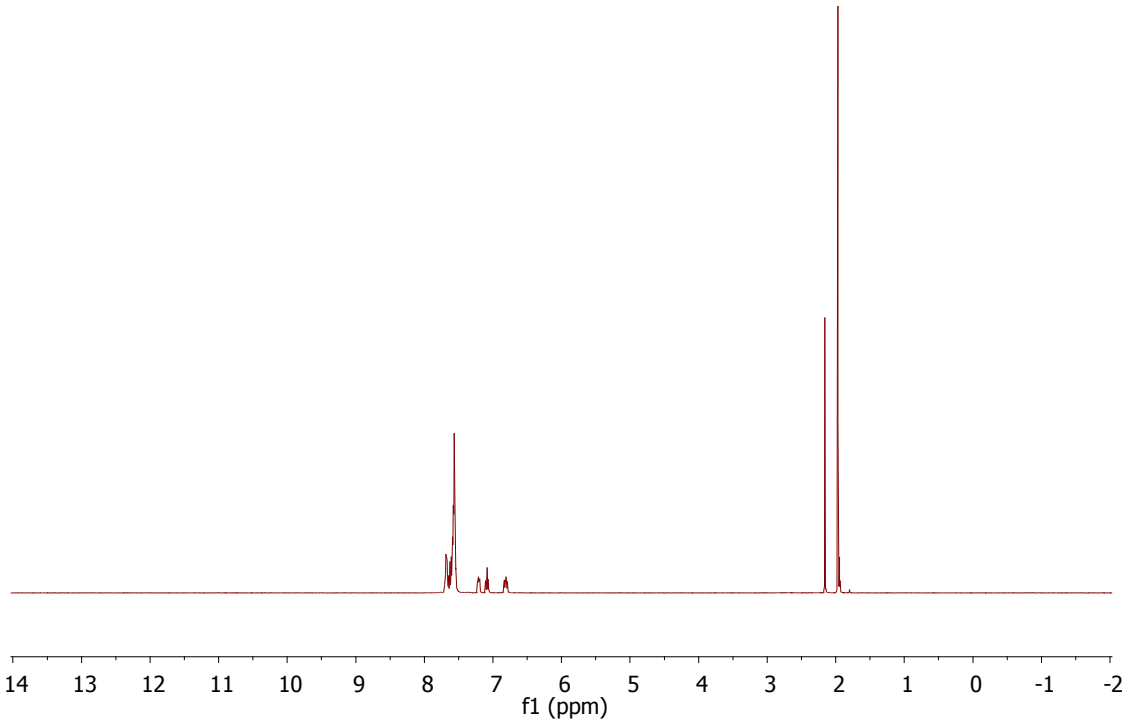
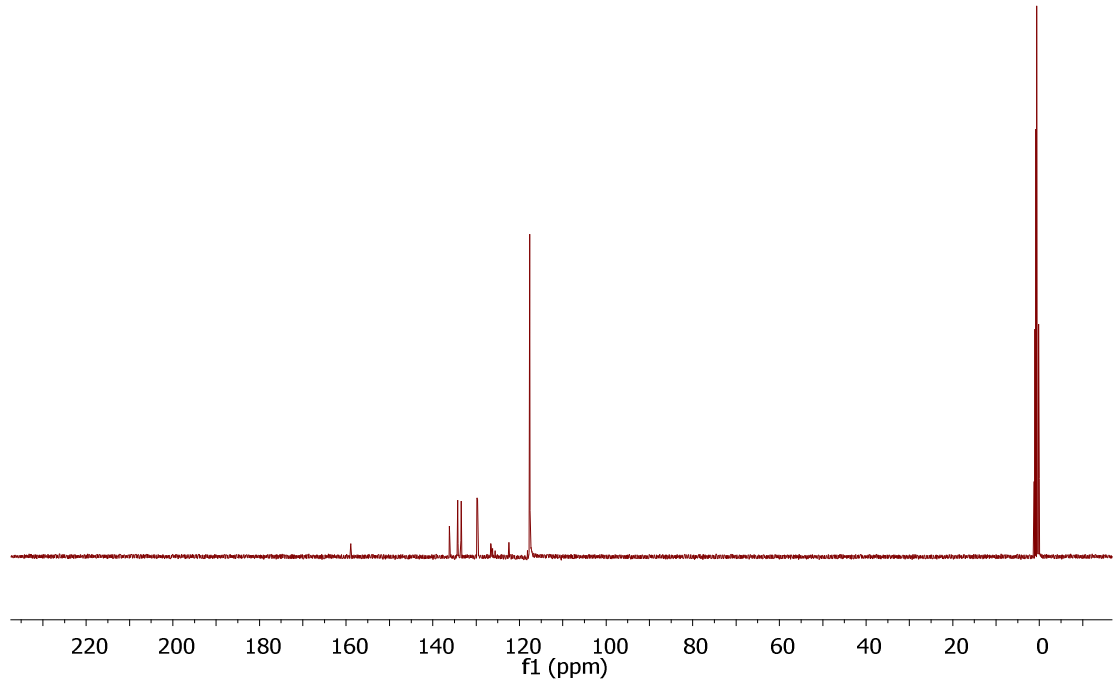
^{1}H and ^{13}C NMR spectra of bis(acetonitrile)[bis(2-(diphenylphosphino)phenyl)ether] palladium(II) hexafluoroantimonate, **1**.





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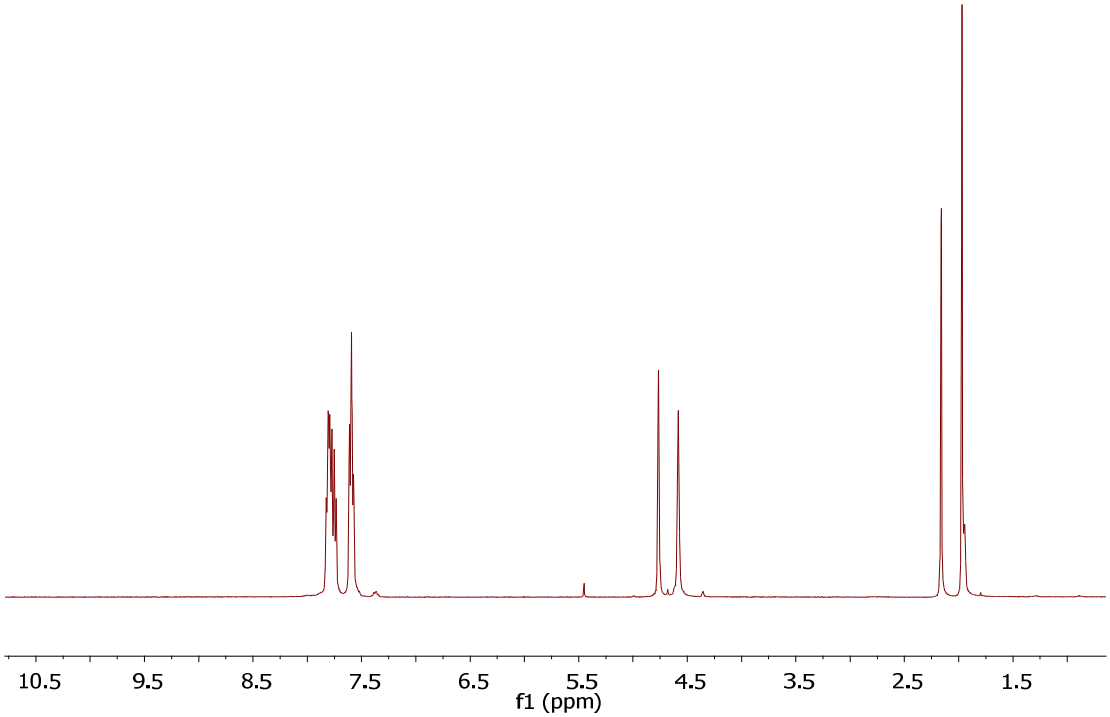
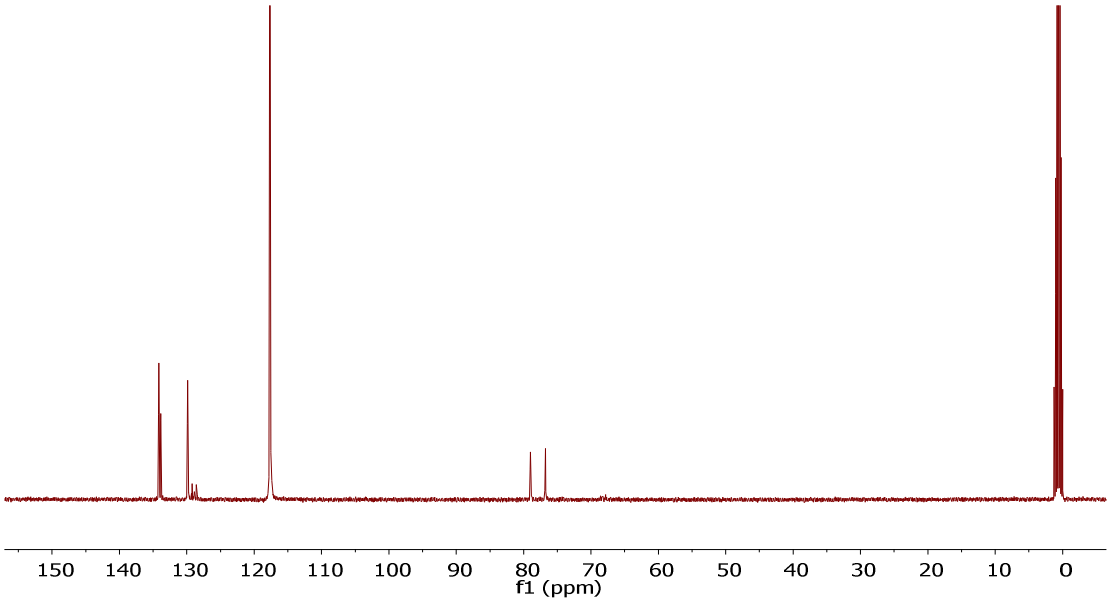
^{1}H and ^{13}C NMR spectra of bis(acetonitrile)[1,1′-bis(diphenylphosphino)ferrocene] palladium(II) hexafluoroantimonate, **2**.





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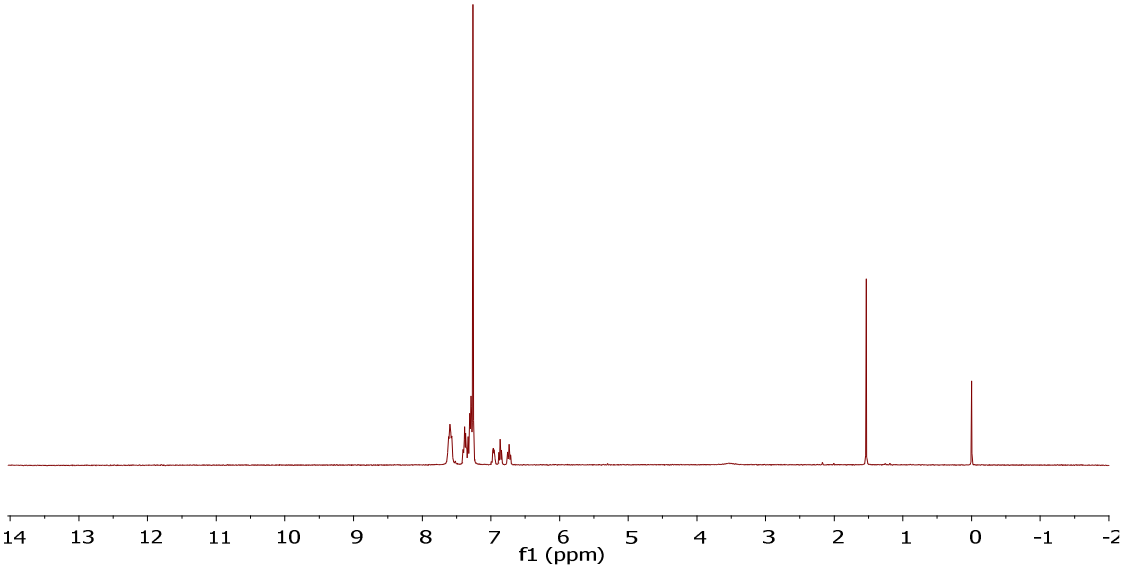
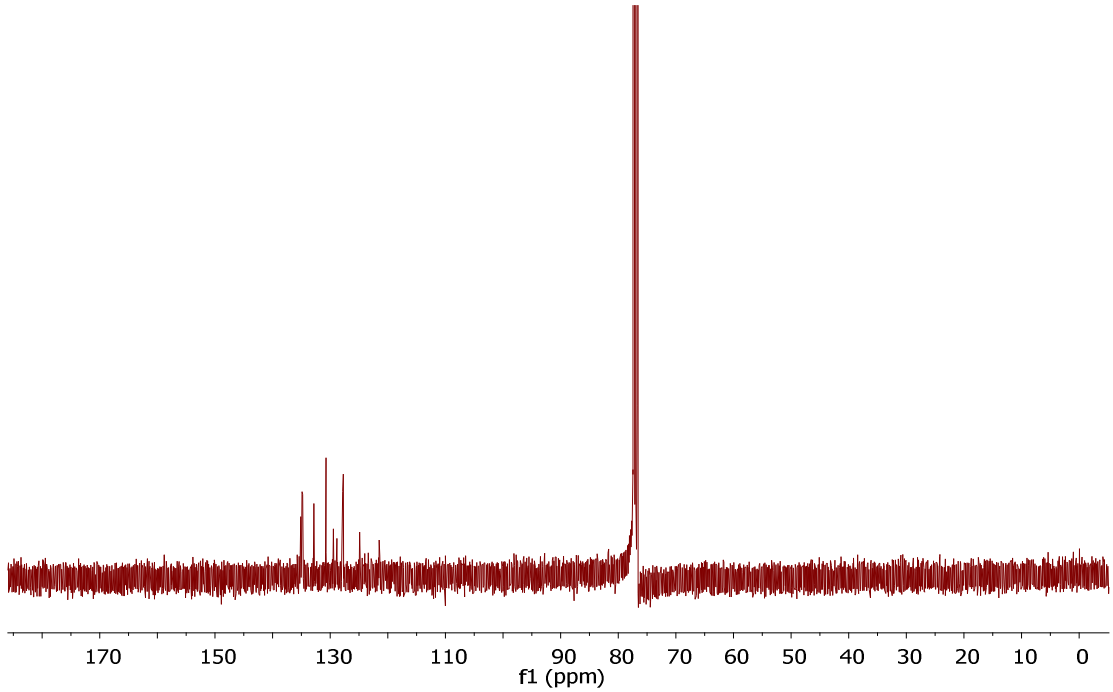
^{1}H and ^{13}C NMR spectra of [bis(2-(diphenylphosphino)phenyl)ether]palladium(II) dichloride.





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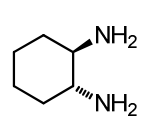
2. Sensing Experiments

A stock solution of sensor **1** or **2** (0.01 M) in ACN was prepared and 100 µL of this solution was placed into a 4-mL vial. Then, solutions of substrates (0.01 M for diamines and 0.02 M for amino alcohols) in ACN were prepared, and 100 µL of a substrate solution was placed in the vial containing 100 µL of the sensor stock solution. The mixture was diluted to 1.25×10^{-4} M for CD analysis unless noted otherwise. CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, a band width of 1 nm, a scanning speed of 500 nm/s and a response of 0.5 s using a quartz cuvette (1 cm path length). The data were baseline corrected and smoothed using a binomial equation. The following amines and amino alcohols (only one enantiomer shown) were analyzed.



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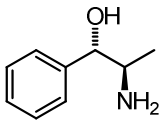

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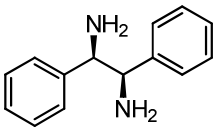

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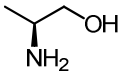

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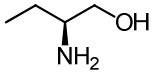

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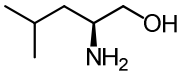

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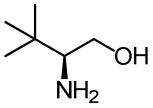

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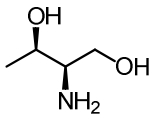

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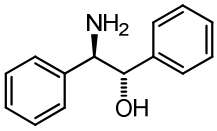

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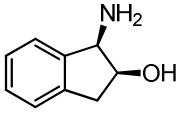

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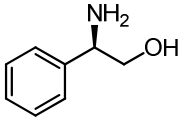

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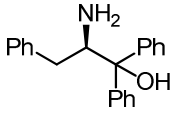
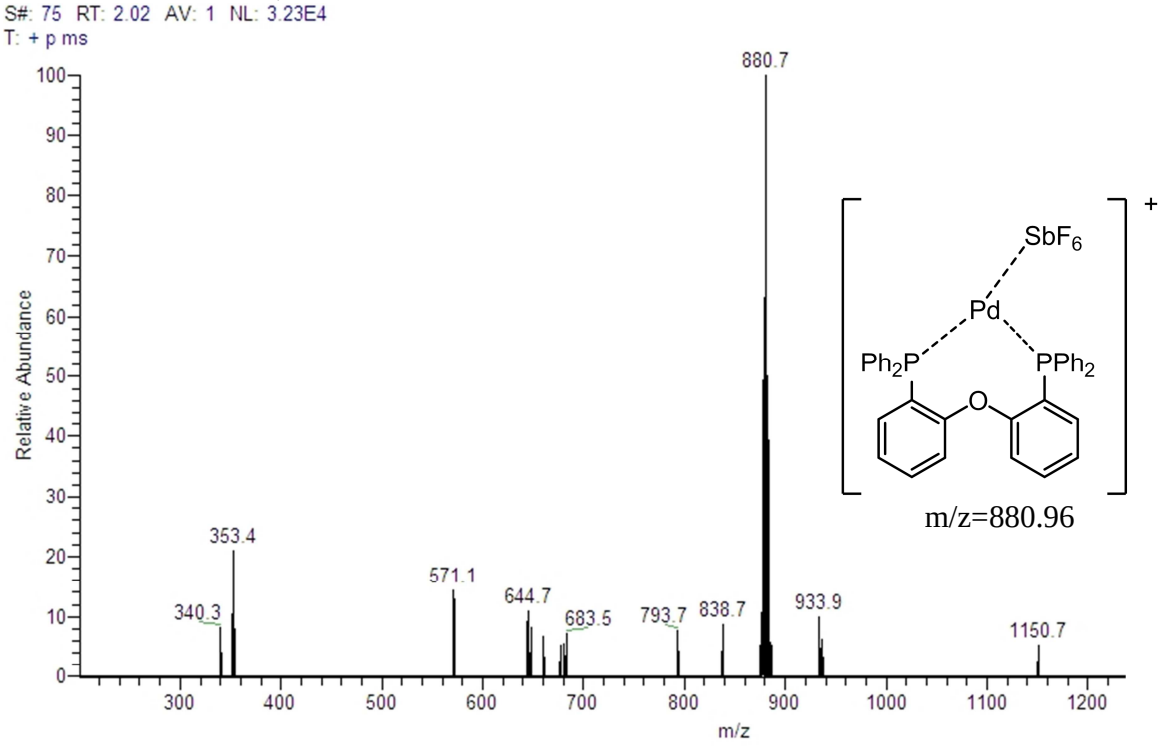


17

2.1. MS and NMR Analysis of the Substrate Coordination

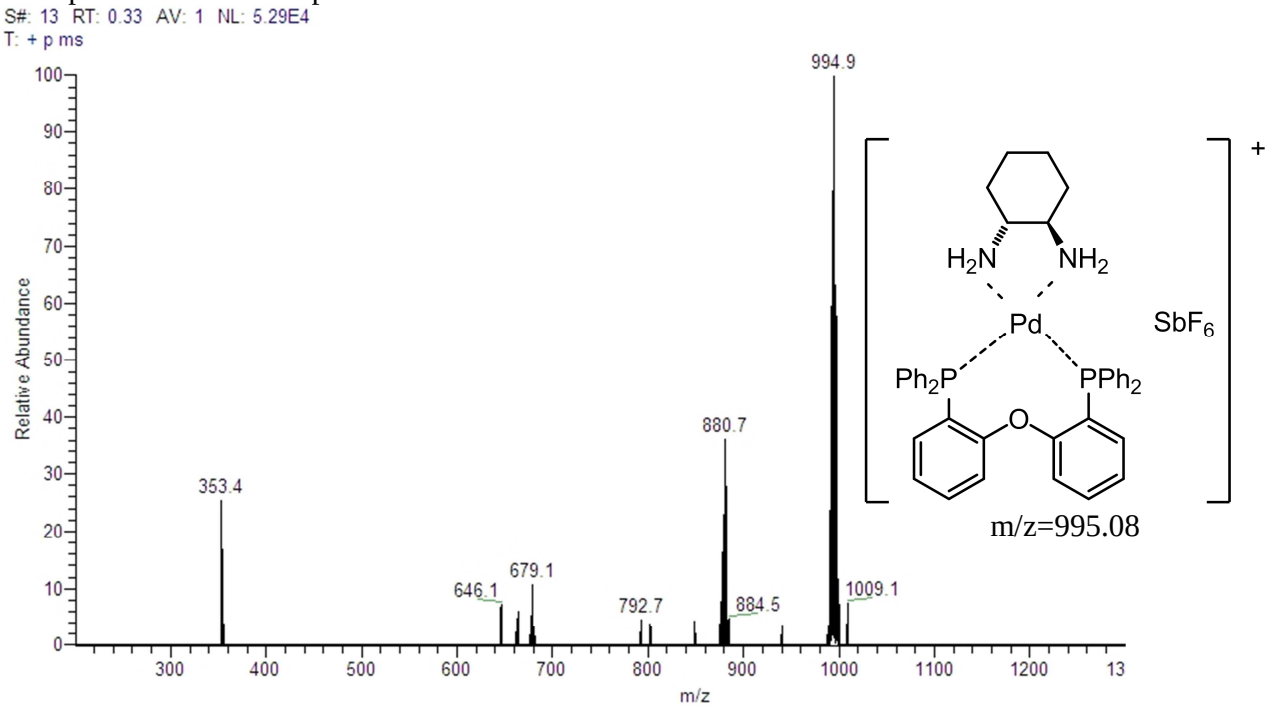
MS analysis in ACN (1 mg/mL) of a mixture containing the palladium complex **1** or **2** and either diamine **6** or **8** showed formation of a 1:1 complex. Mass spectrometric detection of the corresponding amino alcohol complexes was unsuccessful due to the formation of a palladium hydride species formed through oxidation of the alcohol group. The coordination of the substrate to the palladium center was also evident by NMR analysis.

MS spectrum of bis(acetonitrile)[bis(2-(diphenylphosphino)phenyl)ether]palladium(II) hexafluoroantimonate, **1**.



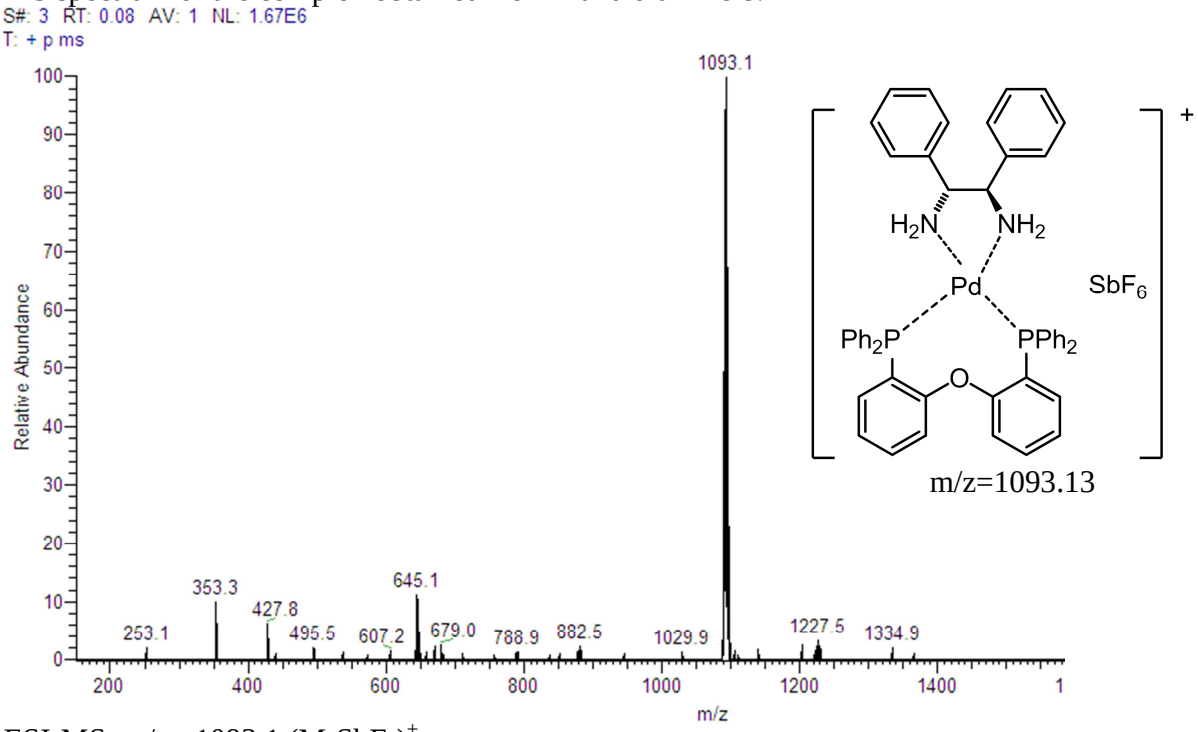
ESI-MS: m/z= 880.7 $(M\text{-}2ACN\text{-}SbF_6)^+$

MS spectrum of the complex obtained from **1** and diamine **6**.



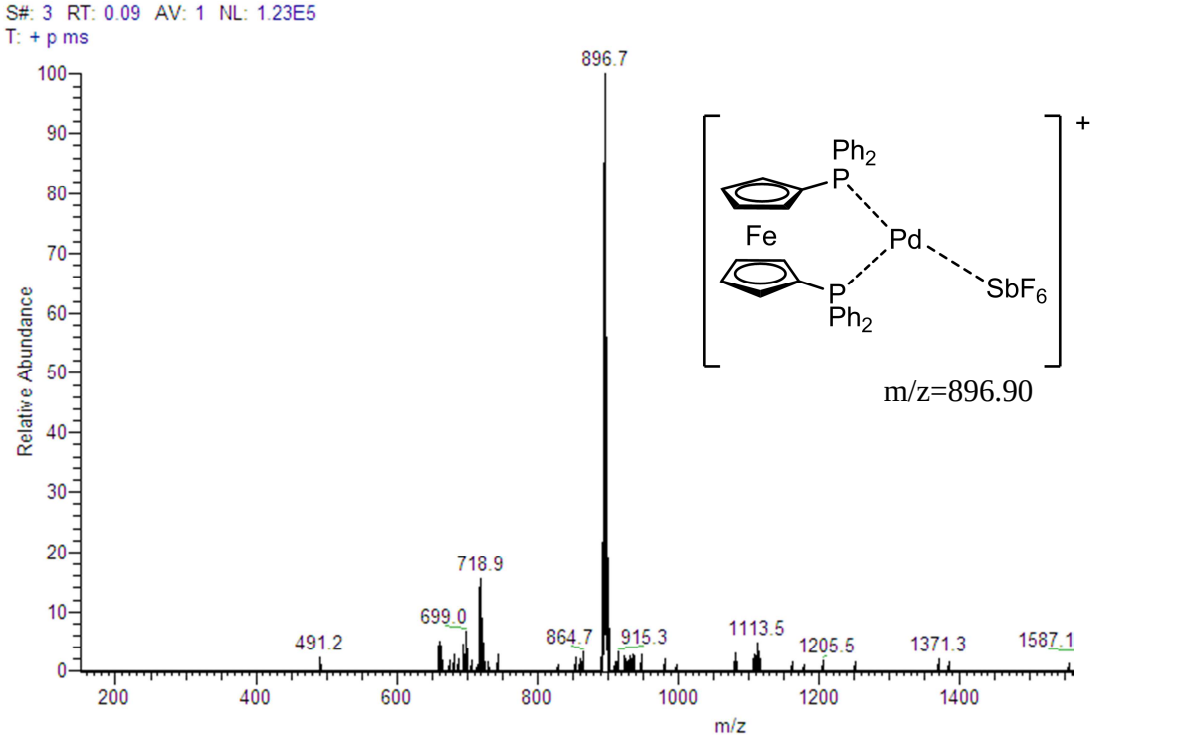
ESI-MS: m/z= 994.9 $(M\text{-}SbF_6)^+$

MS spectrum of the complex obtained from **1** and diamine **8**.



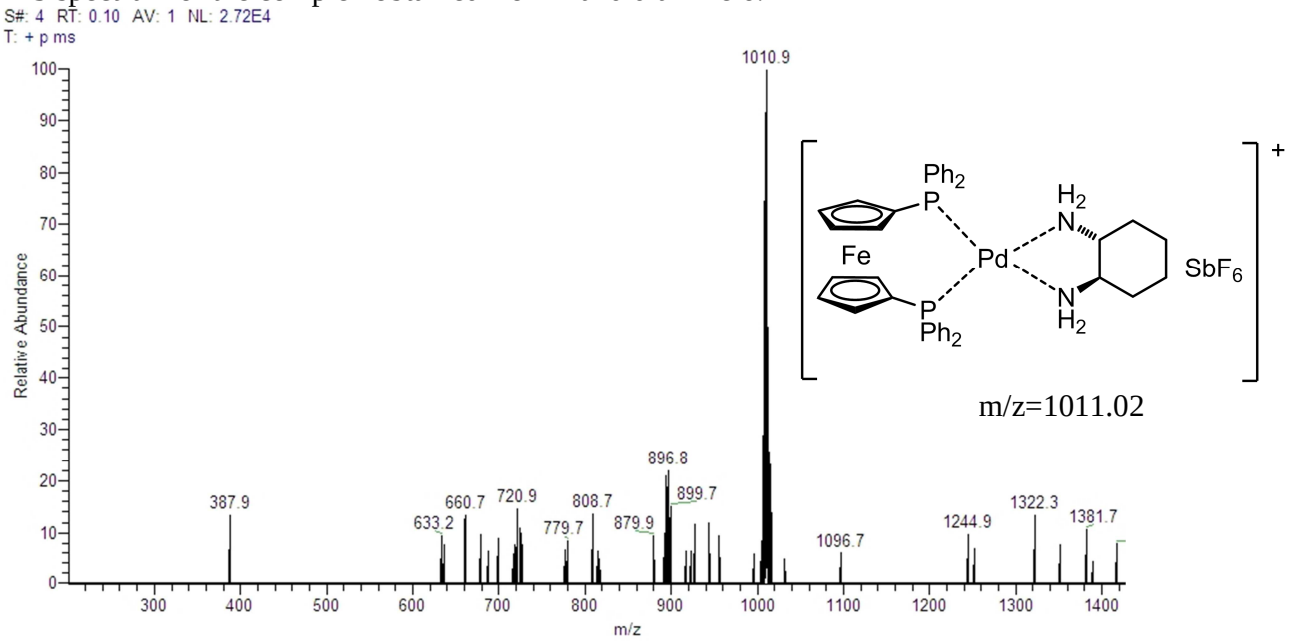
ESI-MS: m/z= 1093.1 $(M\text{-}SbF_6)^+$

MS spectrum of bis(acetonitrile)[1,1′-bis(diphenylphosphino)ferrocene]palladium(II) hexafluoroantimonate, **2**.



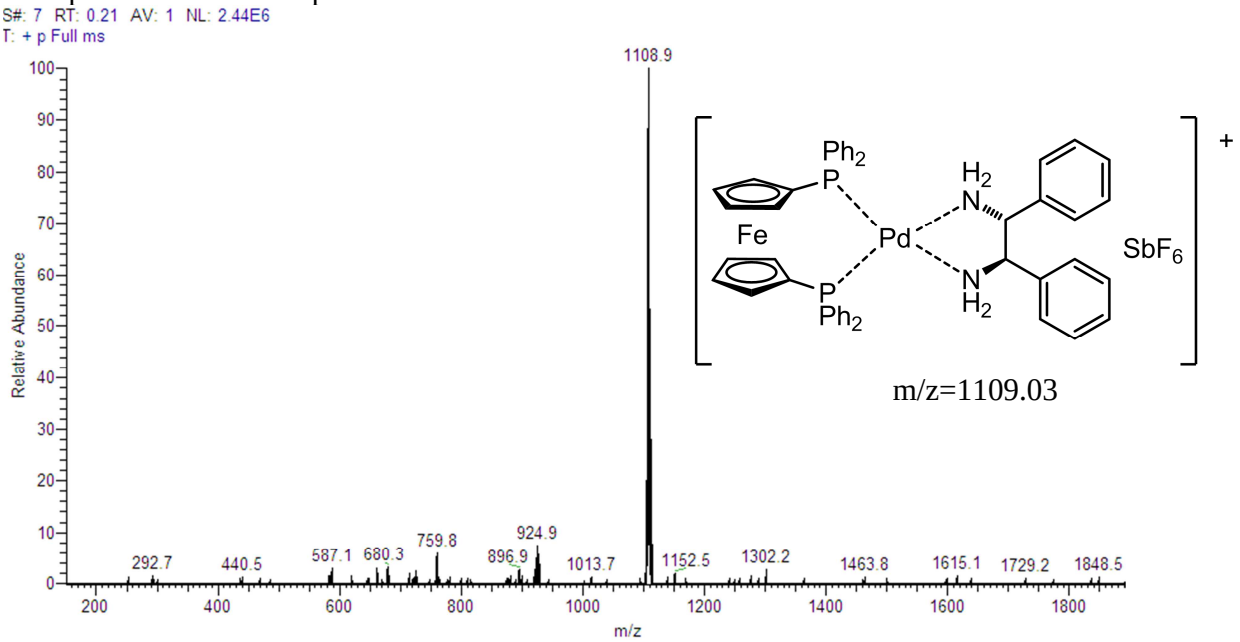
ESI-MS: m/z= 896.7 $(M\text{-}2ACN\text{-}SbF_6)^+$

MS spectrum of the complex obtained from **2** and diamine **6**.



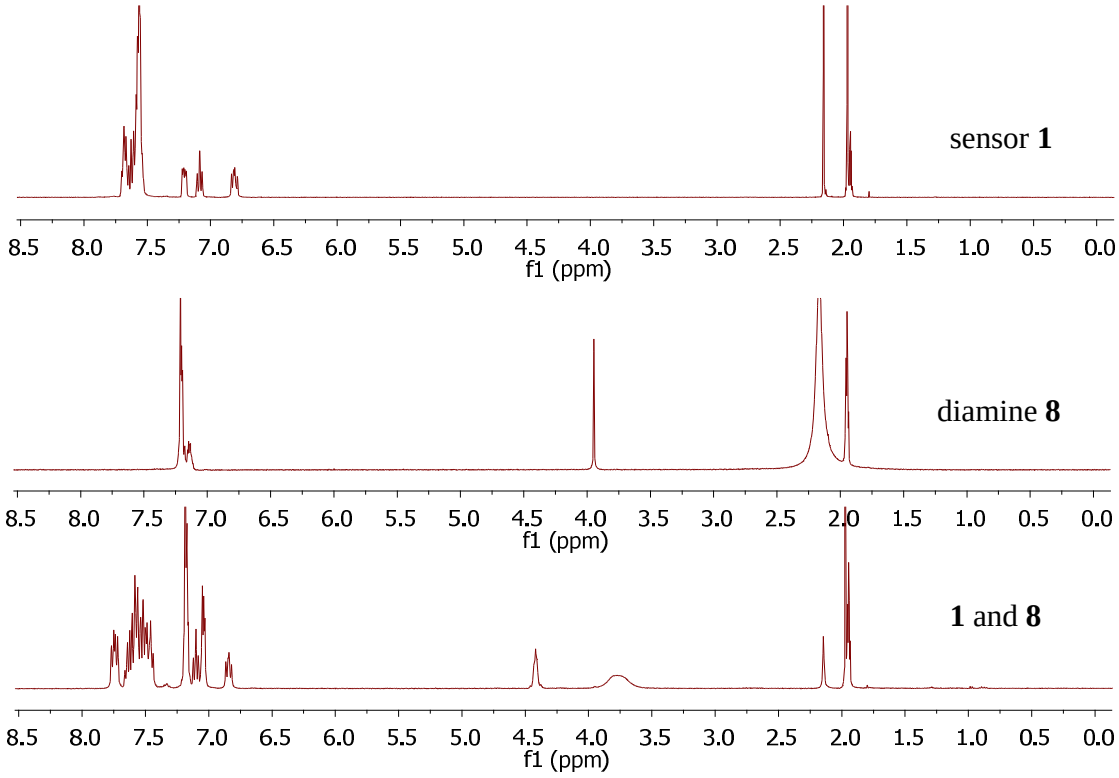
ESI-MS: m/z= 1010.9 $(M\text{-}SbF_6)^+$

MS spectrum of the complex obtained from **2** and diamine **8**.

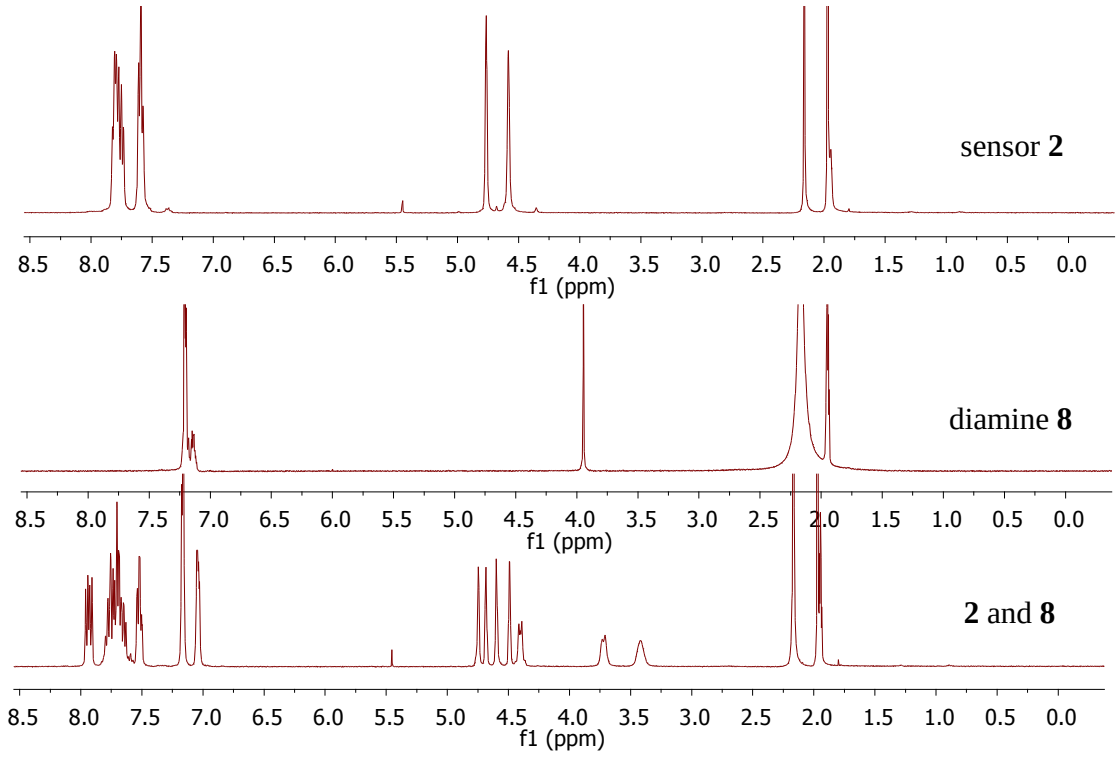


ESI-MS: m/z= 1108.9 $(M\text{-}SbF_6)^+$

^{1}H NMR Spectra of sensor **1**, diamine **8**, and a 1:1 mixture in CD_3CN.

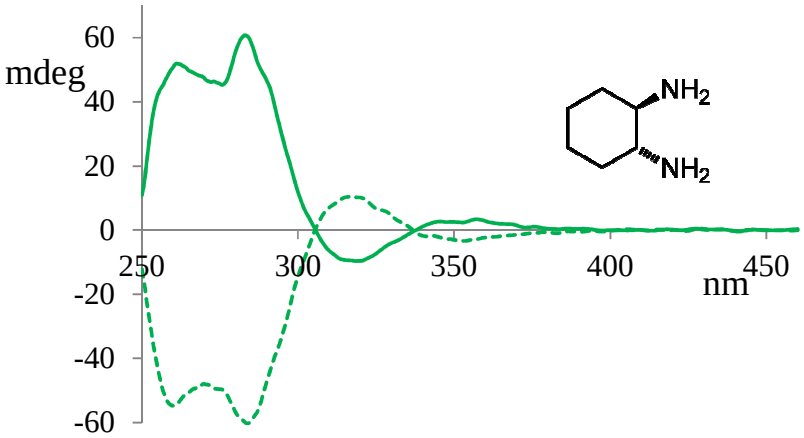


^{1}H NMR Spectra of sensor **2**, diamine **8**, and a 1:1 mixture in CD_3CN.

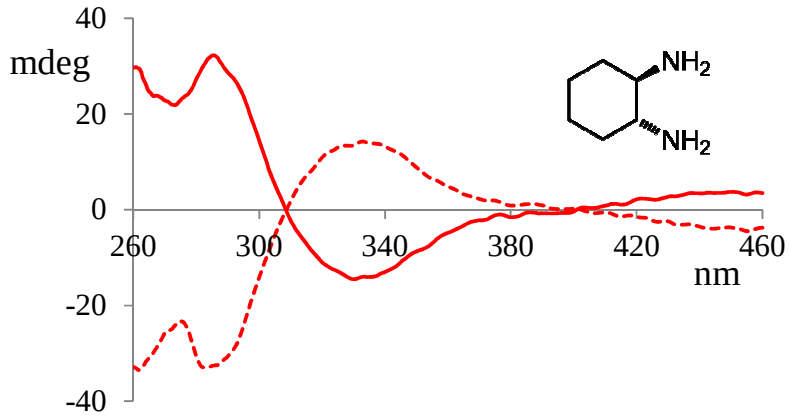


2.2. CD Spectroscopy

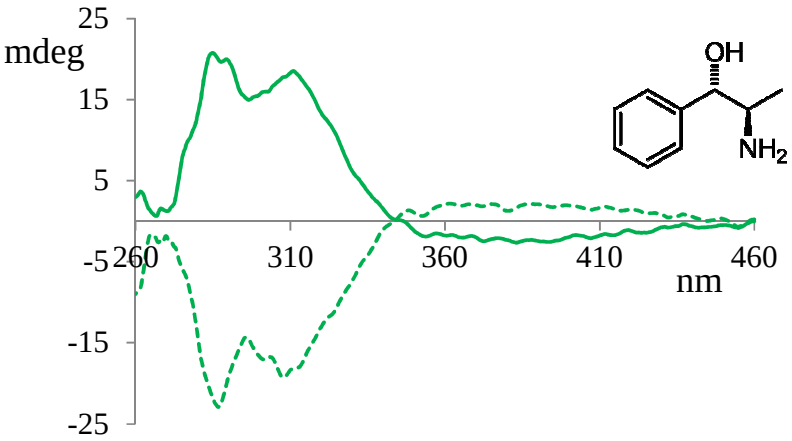
CD spectra of the complex formed from **1** and (1*R*, 2*R*)-**6** (solid line) or (1*S*, 2*S*)-**6** (dashed line) in ACN (1.25×10^{-4} M).



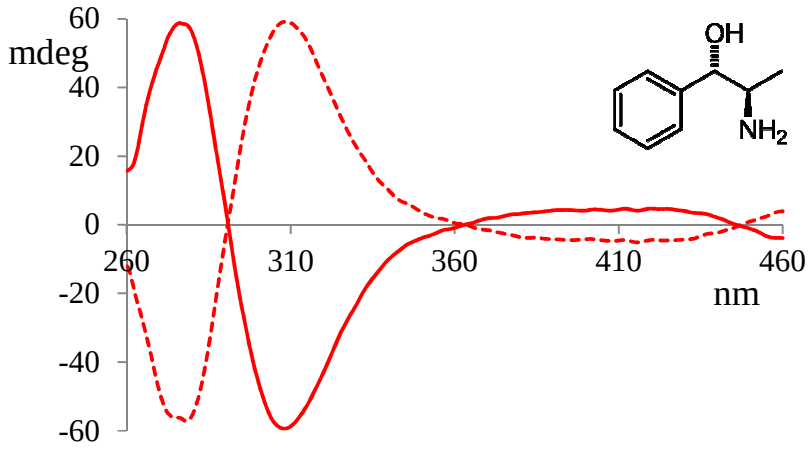
CD spectra of the complex formed from **2** and (1*R*, 2*R*)-**6** (solid line) or (1*S*, 2*S*)-**6** (dashed line) in ACN (1.25×10^{-4} M).



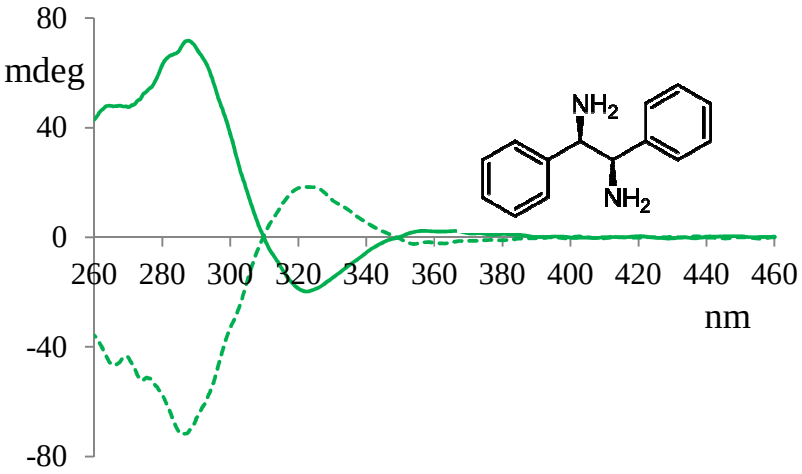
CD spectra of the complex formed from **1** and (1*R*, 2*S*)-**7** (solid line) or (1*S*, 2*R*)-**7** (dashed line) in ACN (1.25×10^{-4} M).



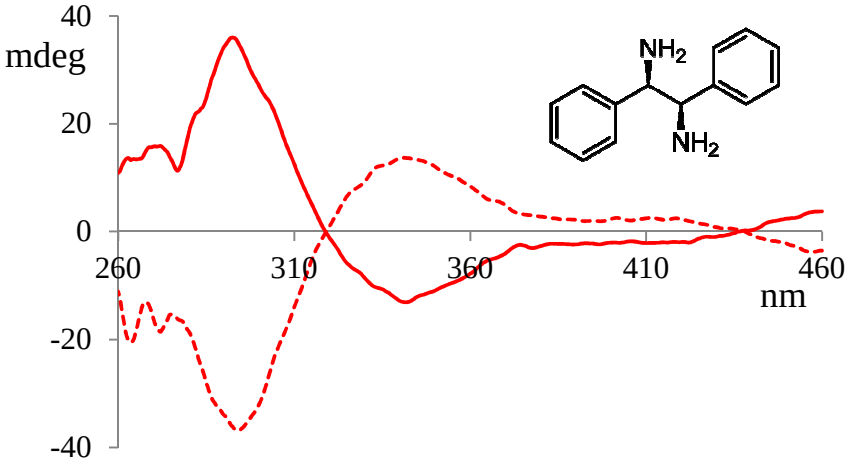
CD spectra of the complex formed from **2** and (1*R*, 2*S*)-**7** (solid line) or (1*S*, 2*R*)-**7** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **1** and (1*R*, 2*R*)-**8** (solid line) or (1*S*, 2*S*)-**8** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **2** and (1*R*, 2*R*)-**8** (solid line) or (1*S*, 2*S*)-**8** (dashed line) in ACN (1.25×10^{-4} M).



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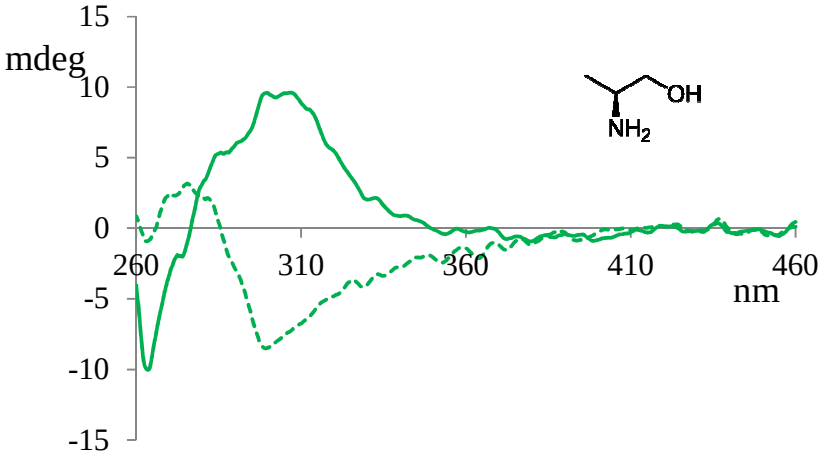
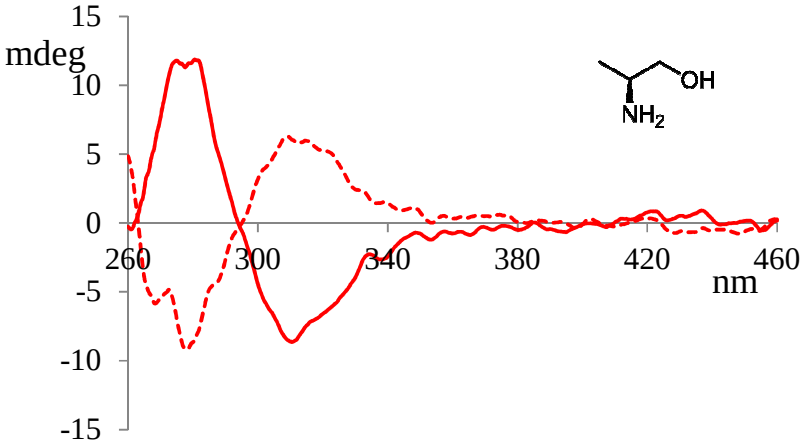
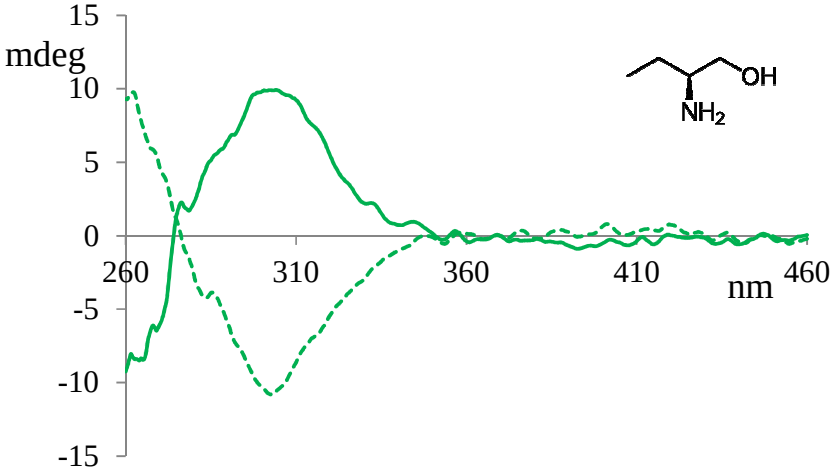
CD spectra of the complex formed from **1** and (*R*)-**9** (solid line) or (*S*)-**9** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **2** and (*R*)-**9** (solid line) or (*S*)-**9** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **1** and (*R*)-**10** (solid line) or (*S*)-**10** (dashed line) in ACN (1.25×10^{-4} M).



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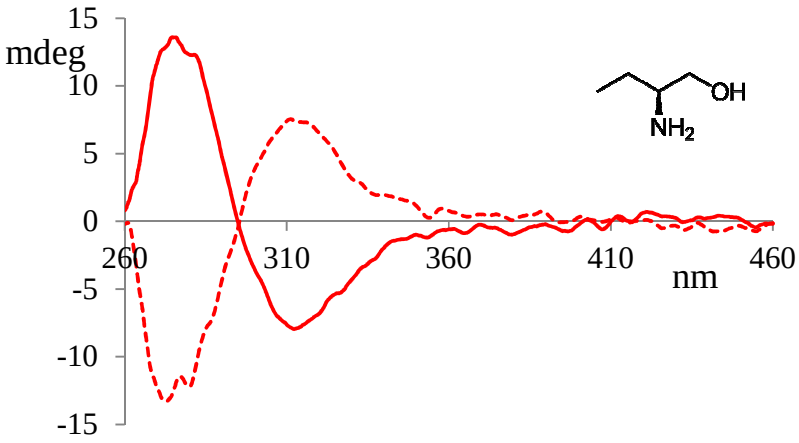
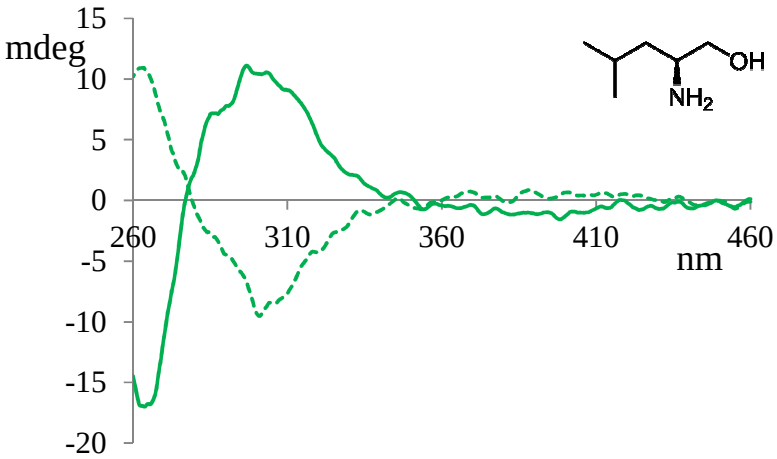
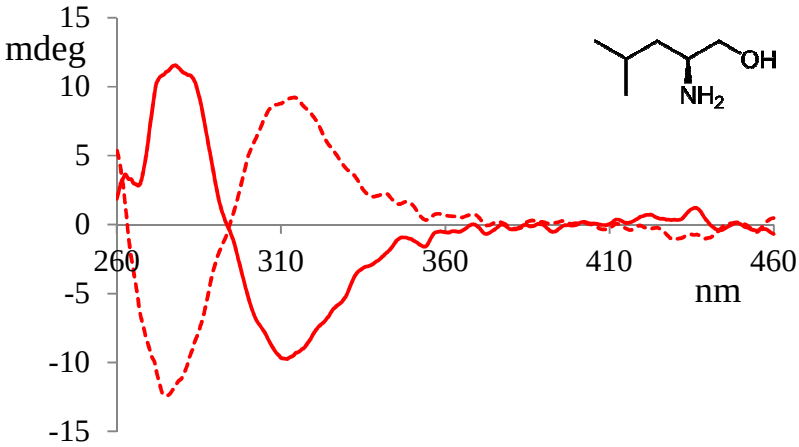
CD spectra of the complex formed from **2** and (*R*)-**10** (solid line) or (*S*)-**10** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **1** and (*R*)-**11** (solid line) or (*S*)-**11** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **2** and (*R*)-**11** (solid line) or (*S*)-**11** (dashed line) in ACN (1.25×10^{-4} M).



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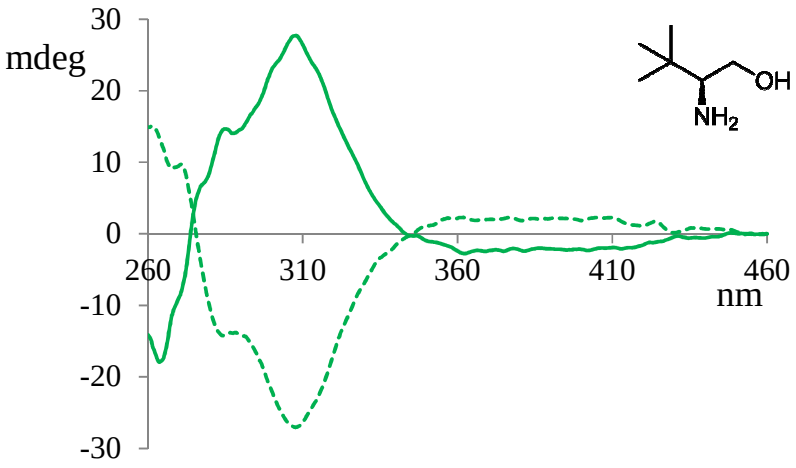
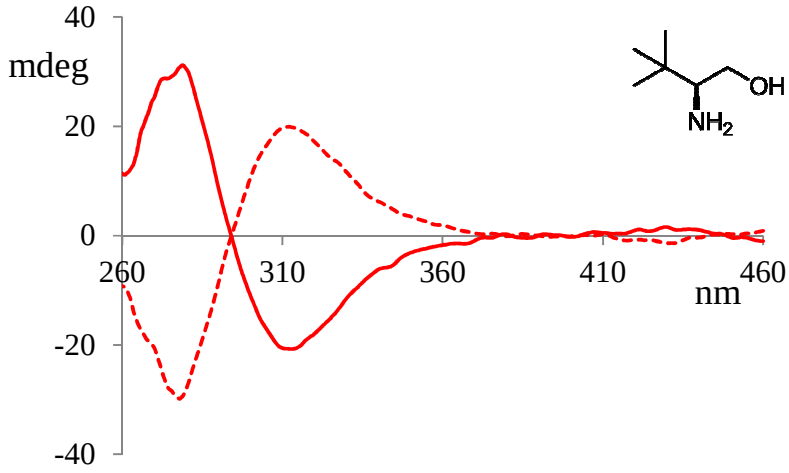
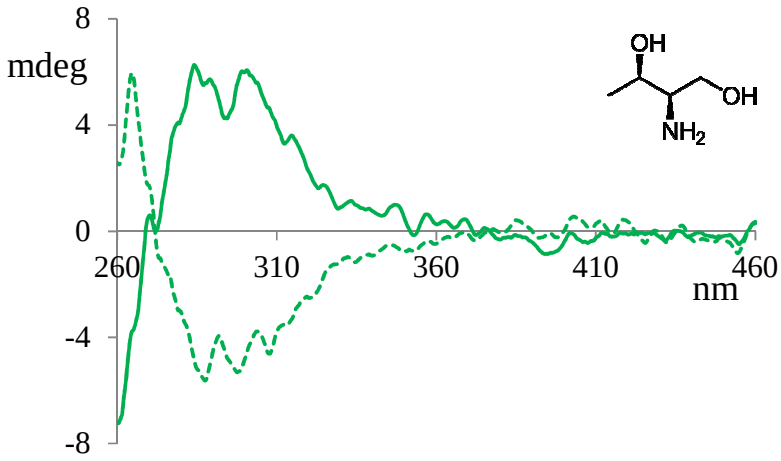
CD spectra of the complex formed from **1** and (*R*)-**12** (solid line) or (*S*)-**12** (dashed line) in ACN (1.25×10^{-4} M).



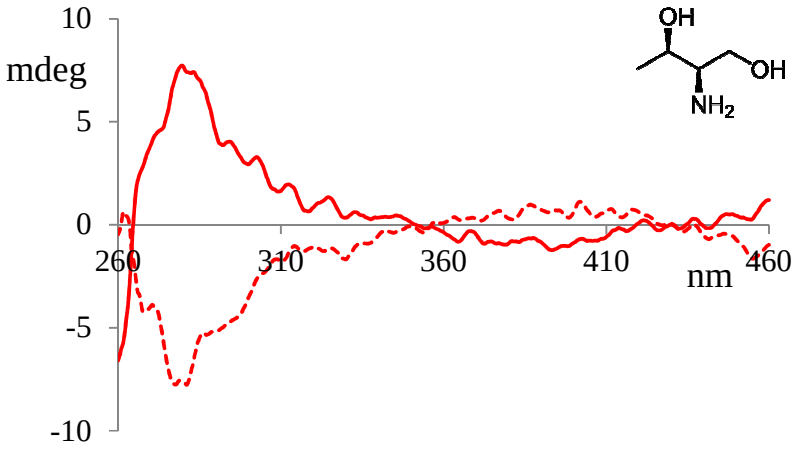
CD spectra of the complex formed from **2** and (*R*)-**12** (solid line) or (*S*)-**12** (dashed line) in ACN (1.25×10^{-4} M).



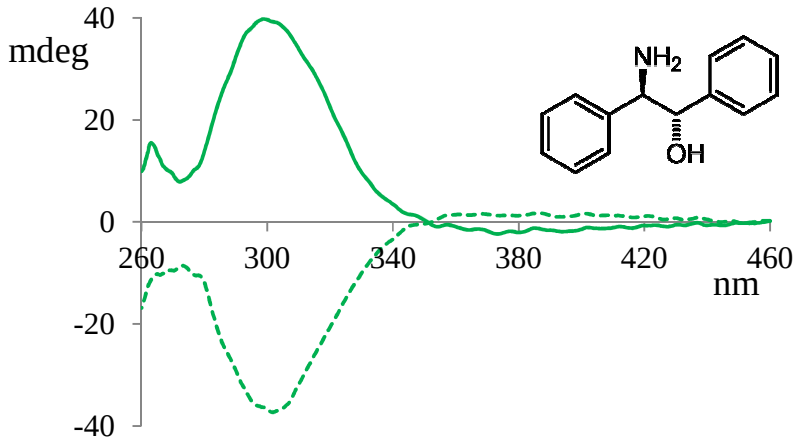
CD spectra of the complex formed from **1** and (2*R*,3*R*)-**13** (solid line) or (2*S*,3*S*)-**13** (dashed line) in ACN (1.25×10^{-4} M).



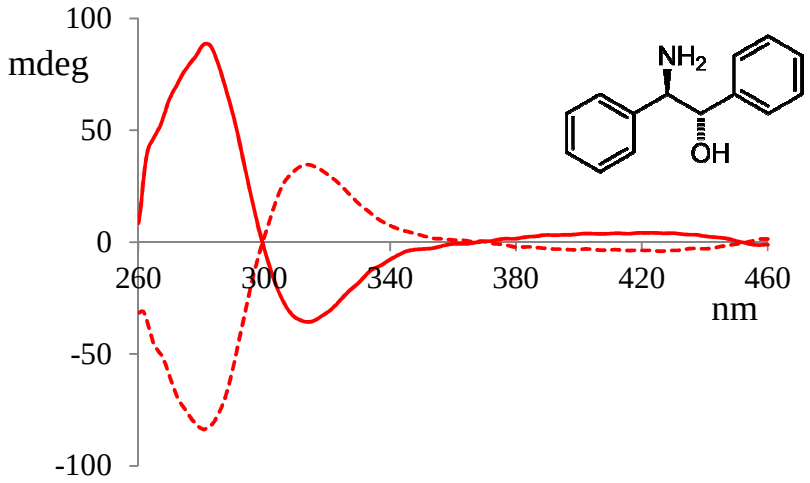
CD spectra of the complex formed from **2** and (2*R*,3*R*)-**13** (solid line) or (2*S*,3*S*)-**13** (dashed line) in ACN (1.25×10^{-4} M).



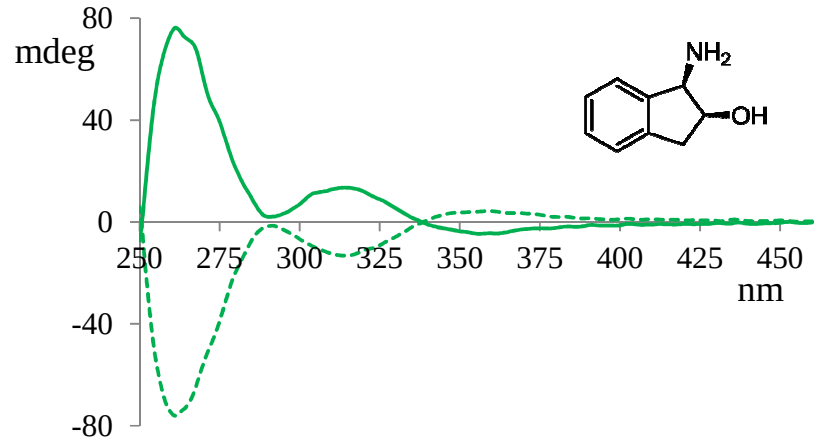
CD spectra of the complex formed from **1** and (1*R*,2*S*)-**14** (solid line) or (1*S*,2*R*)-**14** (dashed line) in ACN (1.0×10^{-4} M).



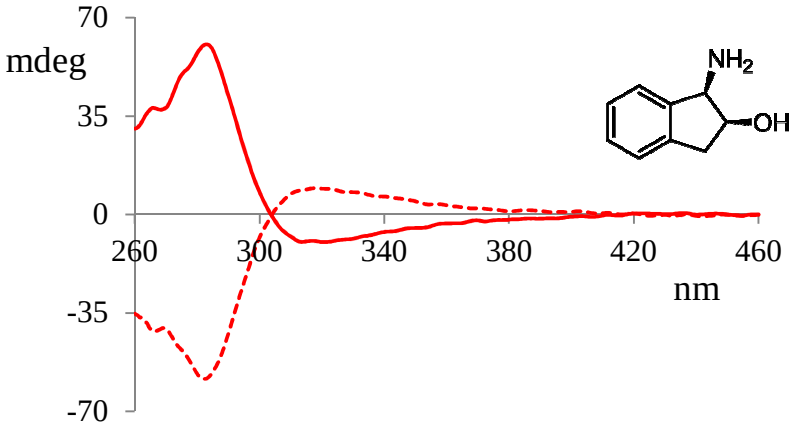
CD spectra of the complex formed from **2** and (1*R*,2*S*)-**14** (solid line) or (1*S*,2*R*)-**14** (dashed line) in ACN (1.25×10^{-4} M).



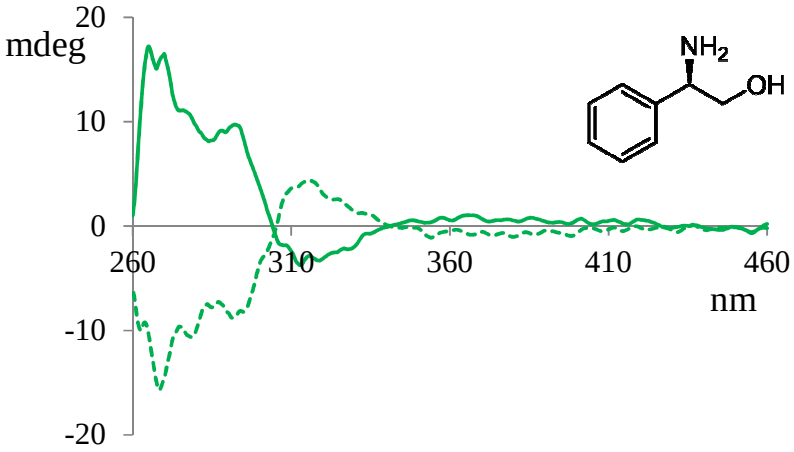
CD spectra of the complex formed from **1** and (1*S*,2*R*)-**15** (solid line) or (1*R*,2*S*)-**15** (dashed line) in ACN (1.0×10^{-4} M).



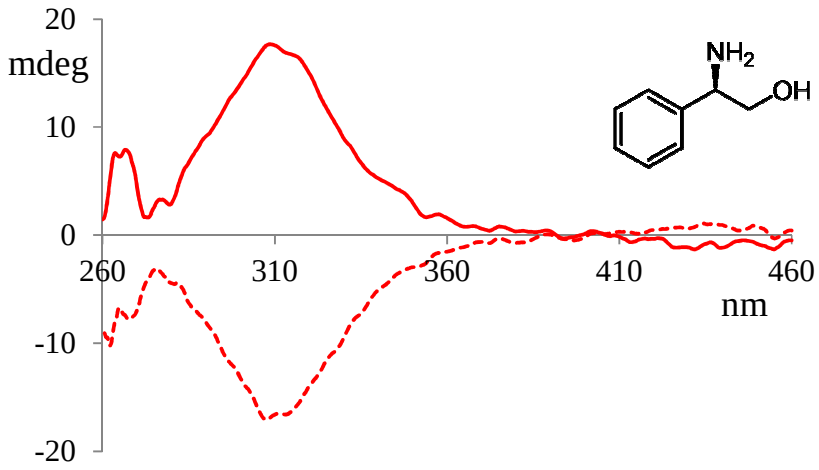
CD spectra of the complex formed from **2** and (1*S*,2*R*)-**15** (solid line) or (1*R*,2*S*)-**15** (dashed line) in ACN (1.25×10^{-4} M).



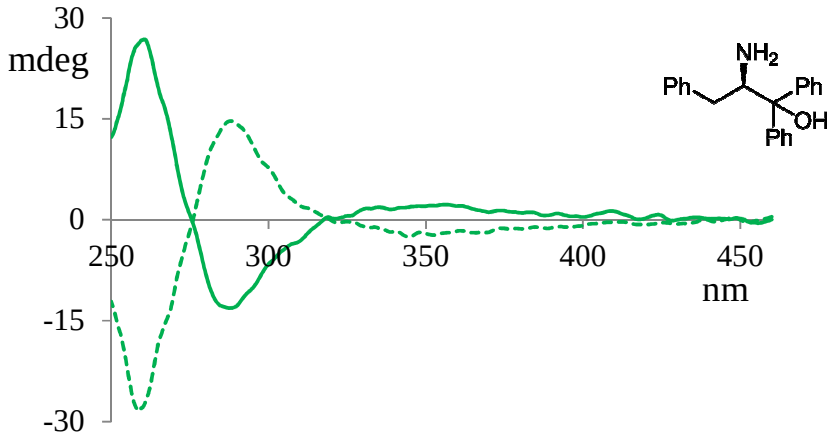
CD spectra of the complex formed from **1** and (*S*)-**16** (solid line) or (*R*)-**16** (dashed line) in ACN (1.25×10^{-4} M).



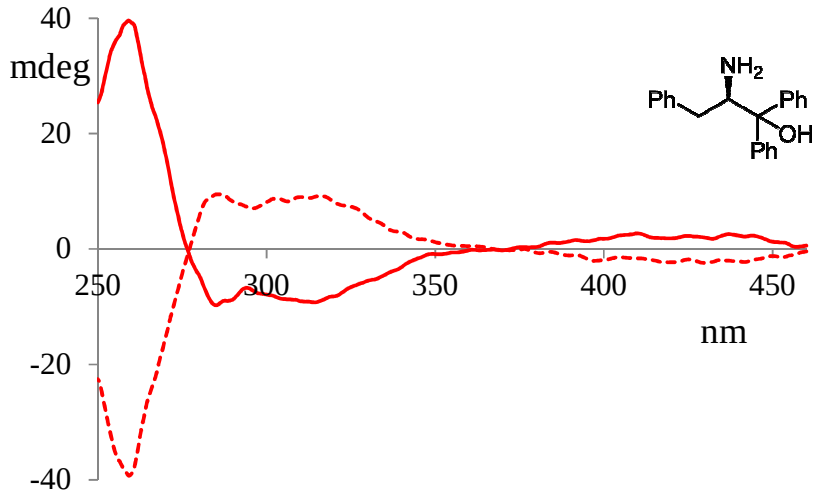
CD spectra of the complex formed from **2** and (*S*)-**16** (solid line) or (*R*)-**16** (dashed line) in ACN (1.25×10^{-4} M).



CD spectra of the complex formed from **1** and (*R*)-**17** (solid line) or (*S*)-**17** (dashed line) in ACN (7.5×10^{-5} M).



CD spectra of the complex formed from **2** and (*R*)-**17** (solid line) or (*S*)-**17** (dashed line) in ACN (1.0×10^{-4} M).



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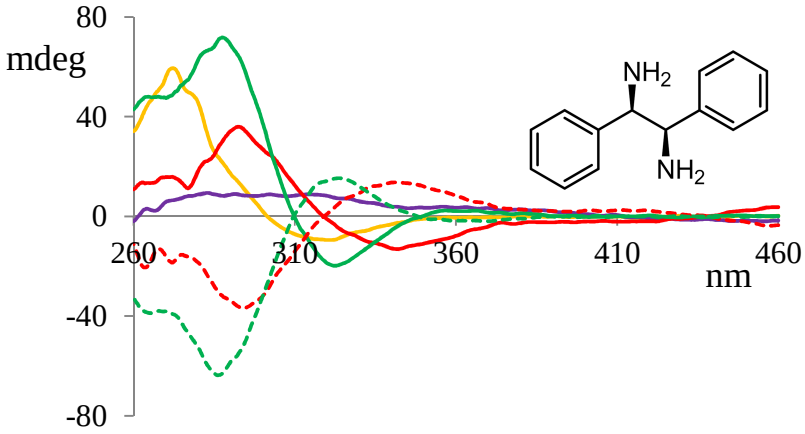
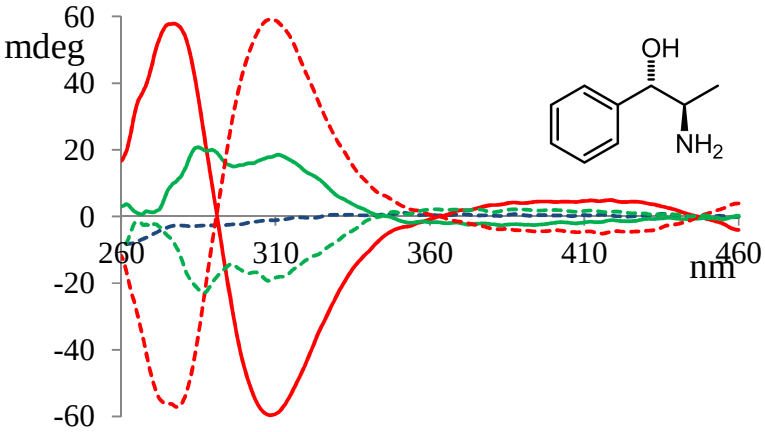
CD spectra of the complexes obtained upon addition of diamine **8** to Pd complexes **1-4** in ACN (1.25×10^{-4} M).



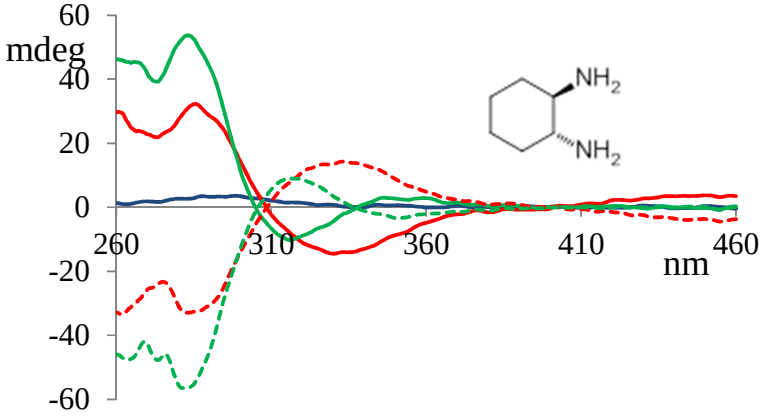
green: **1** and **8**
red: **2** and **8**
purple: **3** and **8**
yellow: **4** and **8** (7.5×10^{-5} M)

Comparison of the CD spectra obtained upon addition of amino alcohol **7** to either **1** or **2** and to $Pd(SbF_6)_2$ in the absence of a tropos ligand in ACN (1.25×10^{-4} M).



green: **7** and **1**
red: **7** and **2**
blue: **7** and $Pd(SbF_6)_2$ (1.0×10^{-4} M)

Comparison of the CD spectra obtained upon addition of diamine **6** to either **1** or **2** and to $Pd(SbF_6)_2$ in the absence of a tropos ligand in ACN (1.25×10^{-4} M).



green: **6** and **1**
red: **6** and **2**
blue: **6** and $Pd(SbF_6)_2$ (1.0×10^{-4} M)

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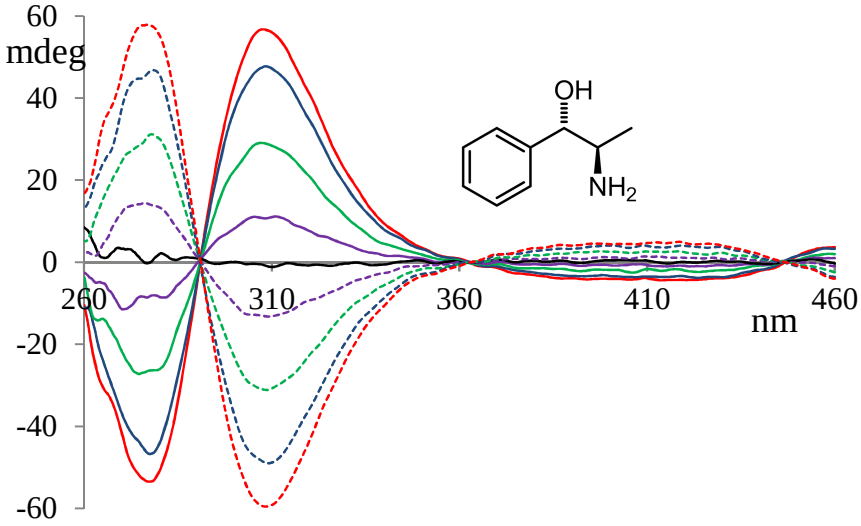
3. Quantitative Analysis of Concentration and Enantiomeric Composition

3.1. Calibration Curve and Ee Determination Using Palladium Complex 2 and Amino Alcohol 7

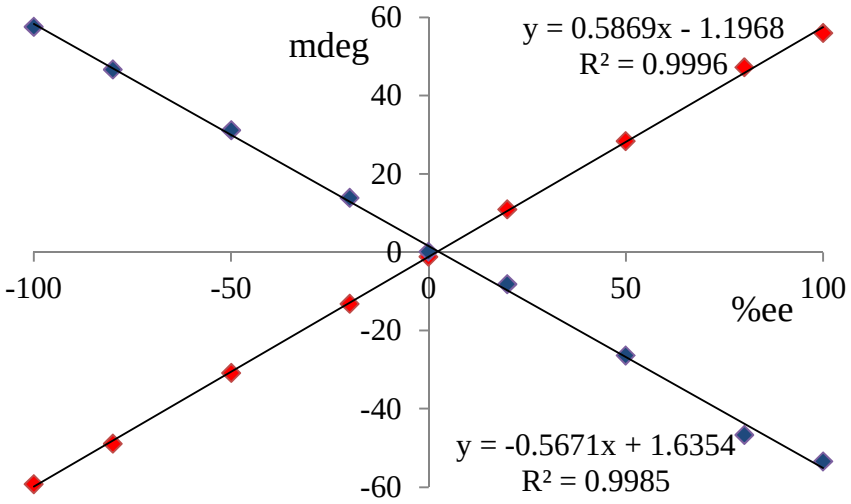
To determine the practical use of the sensors, the chiroptical response of palladium complex **2** to the coordination of amino alcohol **7** was investigated. Stoichiometric mixtures were prepared in ACN (1.25×10^{-4} M) with varying ee of substrate **7** (100%, 80%, 50%, 20%, 0%, -20%, -50%, -80%, -100%). The CD amplitudes (mdeg) at 310.0 nm and 278.0 nm were plotted versus %ee. The calibration curves showed a linear relationship at both wavelengths ($mdeg_{310nm}=0.5869\times ee-1.1968$, $R^2=0.9996$, $mdeg_{278nm}=-0.5671\times ee+1.6354$, $R^2=0.9985$).

CD spectra of the complex formed from **2** and **7** with varying ee in ACN (1.25×10^{-4} M).



Ee of amino alcohol **7**. Red: 100%ee, blue: 80%ee, green: 50%ee, purple: 20%ee, black: 0%ee.

Plots of CD amplitude at 310.0 nm and 278.0 nm versus %ee of **7**



Red: 310.0 nm, blue: 278.0 nm.

Five scalemic samples of amino alcohol **7** with varying ee were prepared and treated with **2** as described above. Using the linear equation developed above and measuring the CD amplitudes at 310.0 nm and 278.0 nm, the ee of the samples was determined. Experimentally obtained average data were within 3.0% of the actual values.

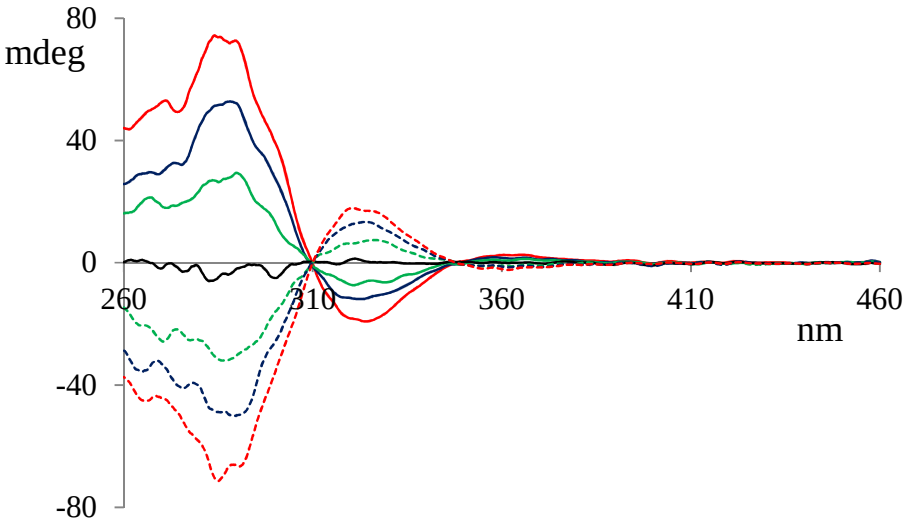
Experimental vs. actual ee's of 5 scalemic samples of amino alcohol **7** determined with Pd complex **2**

Actual ee%	Calculated %ee at 310.0 nm	Calculated %ee at 278.0 nm	Average %ee
60.0	62.0	64.0	63.0
40.0	42.3	40.9	41.6
30.0	31.0	33.9	32.0
-40.0	-40.3	-41.1	-40.7
-60.0	-61.2	-61.2	-61.2

3.2. Linear CD Response Using Palladium Complex 1 and Diamine 8

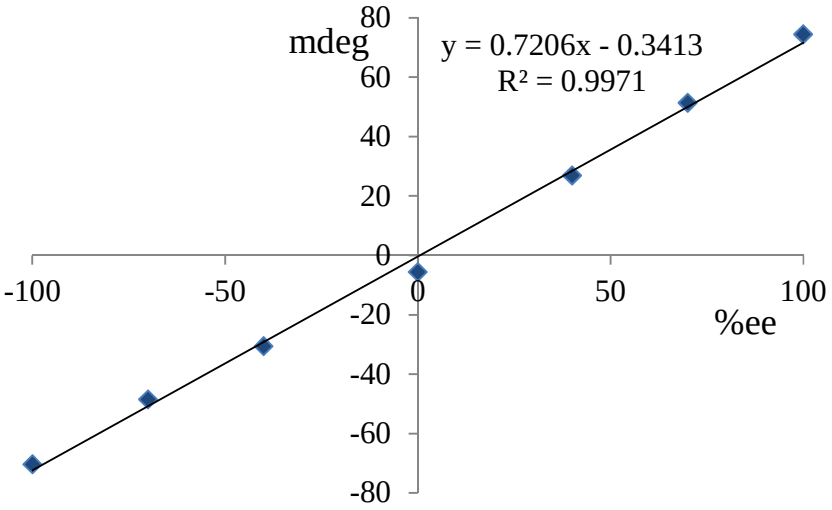
The chiroptical response of **1** to the coordination of diamine **8** was investigated. Solutions containing equimolar amount of the sensor and the substrate with varying ee (100%, 70%, 40%, 0%, -40%, -70%, -100%) in ACN (1.25×10^{-4} M) were prepared. The CD amplitude (mdeg) at 284.0 nm was plotted versus %ee. The calibration curve showed a linear relationship (mdeg=0.7206×ee-0.3413, R^2=0.9971).

CD spectra of the complex formed from **1** and **8** with varying ee in ACN (1.25×10-4 M).



Ee of diamine **8**. Red: 100%ee, blue: 70%ee, green: 40%ee, black: 0%ee.

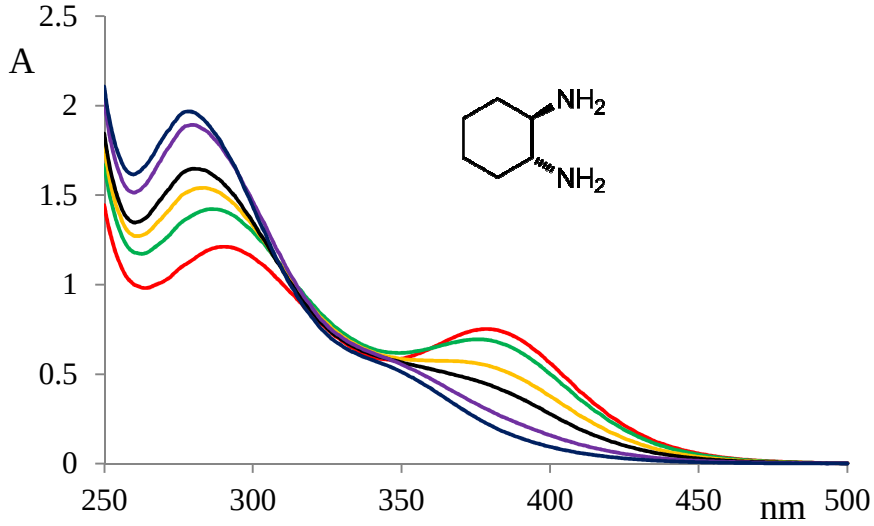
Plot of CD amplitude at 284.0 nm versus %ee of **8**



3.3. Determination of Both Enantiomeric Excess and Concentration of Diamine 6 Using Sensor 1

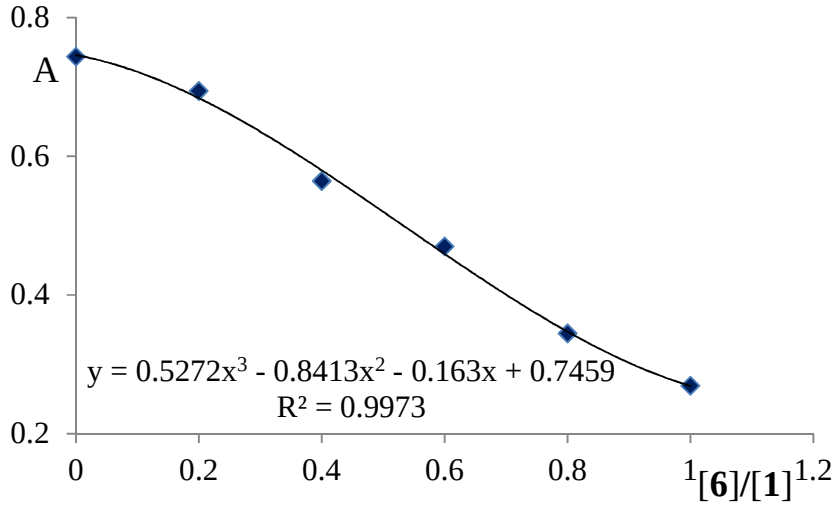
To investigate the possibility of determination of the concentration and ee, a UV calibration curve was plotted using **1** (1.25 $\times 10^{-4}$ M) and diamine **6** with varying ratio (0.0/0.2/0.4/0.6/0.8/1.0 equivalent). The calibration curve showed a sigmoidal relationship at 374.0 nm (**A**=0.5272[**6**/**1**]^3-0.8413[**6**/**1**]^2-0.163[**6**/**1**] +0.7459, R^2 = 0.9973).

UV-Vis spectra of sensor **1** upon addition of various amounts of diamine **6**.



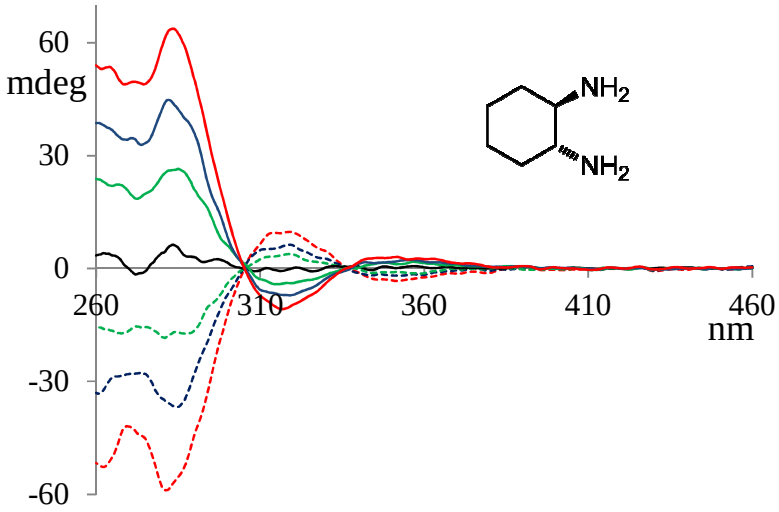
Sensor **1** (1.25 ×10^{-4} M) and varying amounts of diamine **6** in ACN. Red: 0 equiv., green: 0.2 equiv., orange: 0.4 equiv., black: 0.6 equiv., purple: 0.8 equiv., blue: 1.0 equiv.

Plot of the absorption maximum at 374 nm versus equivalents of **6**



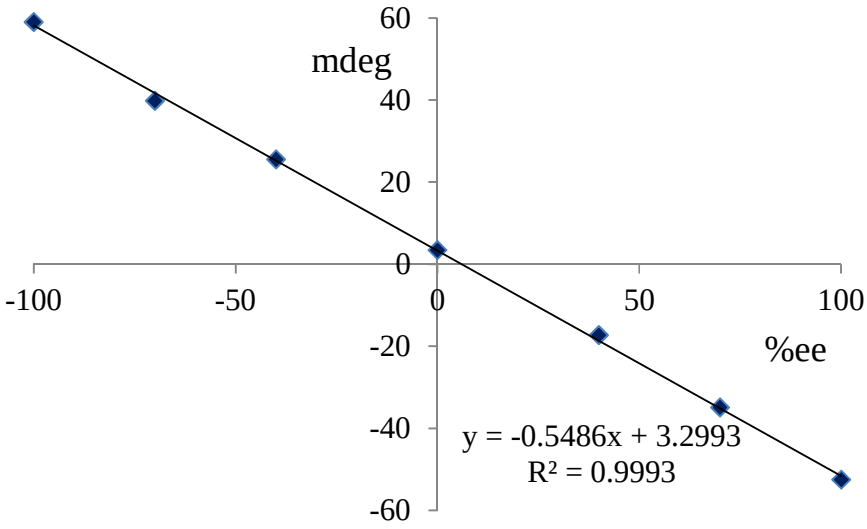
The chiroptical response of **1** to the coordination of diamine **6** was investigated. Solutions containing equimolar amount of the sensor and the substrate with varying ee (100%, 70%, 40%, 0%, -40%, -70%, -100%) in ACN (1.25 ×10^{-4} M) were prepared. The CD amplitude (mdeg) at 287.0 nm was plotted versus % ee. The calibration curve showed a linear relationship (mdeg=-0.5486×ee+3.2993, R^2 = 0.9993).

CD spectra of the complex formed from **1** and **6** with varying ee in ACN (1.25×10^{-4} M).



Ee of diamine **6**. Red:100% ee, blue: 70% ee, green: 40% ee, black: 0% ee.

Plot of CD amplitude at 287.0 nm versus %ee of **6**



Four scalemic samples of diamine **6** with varying concentration and ee were prepared and treated with **1** as described above. Using the UV and CD calibration curves developed above, the concentration and ee of each sample were determined experimentally. This was achieved by fast UV and CD measurements using the same sample solution in ACN (1.25×10^{-4} M). The measured UV response was first used to calculate the concentration

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of **6**. Based on the observation that the CD response of the palladium complex increases linearly with relative concentration of the substrate at a given ee, the concentration value determined by UV analysis was then applied in the calculation of the sample ee.

Experimental vs. actual concentrations and ee's of 4 scalemic samples of diamine **6** obtained using palladium complex **1**

Actual ratio [**6**]/[**1**]	Actual % ee	Calculated concentration	Calculated % ee
0.90	80.0	0.91	85.9
0.70	60.0	0.63	67.7
0.50	50.0	0.49	49.6
0.50	-60.0	0.53	-66.7

4. References

1 Bonazzi, S.; Eidam, O.; Guttinger, S.; Wach, J. Y.; Zemp, I.; Kutay, U.; Gademann, K. *J. Am. Chem. Soc*. **2010**, *132*, 1432-1442.
2 Aikawa, K.; Miyazaki, Y.; Mikami, K. *Bull. Chem. Soc. Jpn*. **2012**, *85*, 201-208.
3 Mikami, K.; Aikawa, K. *Org. Lett*. **2002**, *4*, 99-101.