

Supplementary Information

Chiroptical Sensing of Unprotected Amino Acids, Hydroxy acids, Amino Alcohols, Amines and Carboxylic Acids with Metal Salts

Ciaran C. Lynch, Zeus A. De los Santos and Christian Wolf*
Department of Chemistry, Georgetown University, Washington DC, USA
cw27@georgetown.edu

Contents:

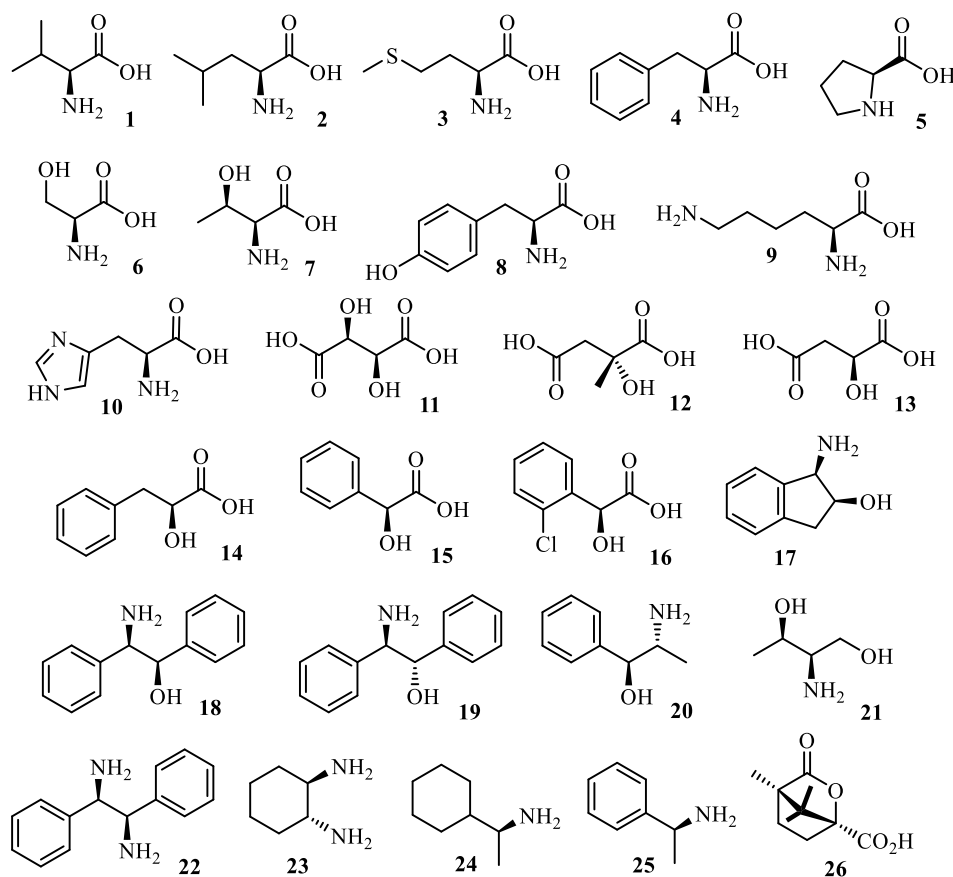
| | |
|---|----|
| 1. General Procedure | 2 |
| 2. Substrate Scope | 2 |
| 3. Mechanistic Studies | 31 |
| 3.1. UV Titration Analysis | 31 |
| 3.2. CD Titration Analysis | 33 |
| 3.3. Anion Effects | 36 |
| 4. Quantitative Chiroptical Sensing | 38 |
| 4.1 Ee Determination of Tartaric Acid with FeCl ₃ .6H ₂ O | 38 |
| 4.2. Ee Determination of <i>cis</i> -Aminoindanol with CuCl ₂ .2H ₂ O | 40 |
| 5. Colorimetric Detection | 42 |

1. General Sensing Procedure

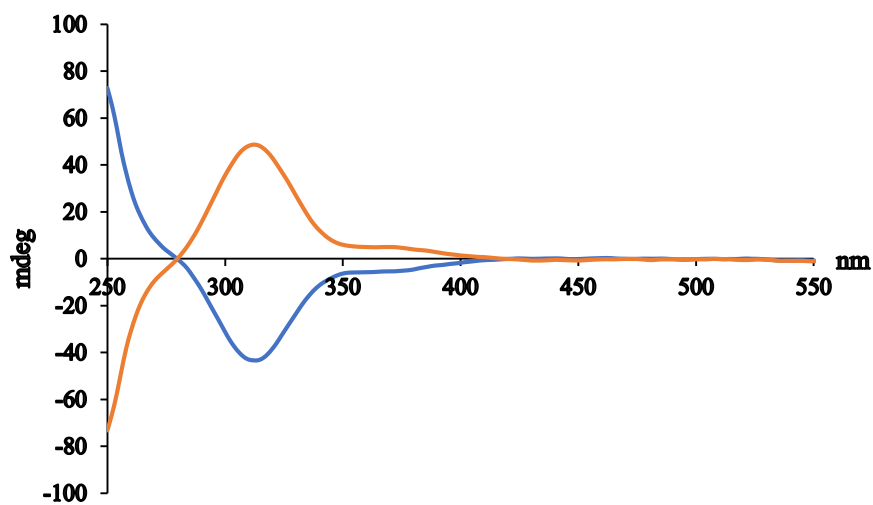
A stock solution of the metal salt (0.02 M) in either MeOH [$\text{Pd}(\text{NO}_3)_2$], DMSO [$\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, $\text{Ce}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$] or H_2O [$\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$] was prepared and portions of 0.5 mL were transferred into 4 mL vials. Solutions of the analytes were prepared in either MeOH or DMSO (0.50 M). For substrates carrying an acidic functional group, an equimolar amount of TBAOH (1.0 M in MeOH) was added. The mixtures were stirred for 1 hour at 25 °C and CD analysis was conducted after diluting the mixture with either MeOH, or DMSO to the final concentration given below. CD spectra were collected with a standard sensitivity of 100 mdeg, a data pitch of 2.0 nm, a band width of 2 nm, a scanning speed of 500 nm min^{-1} , 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. Control experiments with the chiral analytes showed that the free substrates are CD silent in the region of interest.

2. Substrate Scope

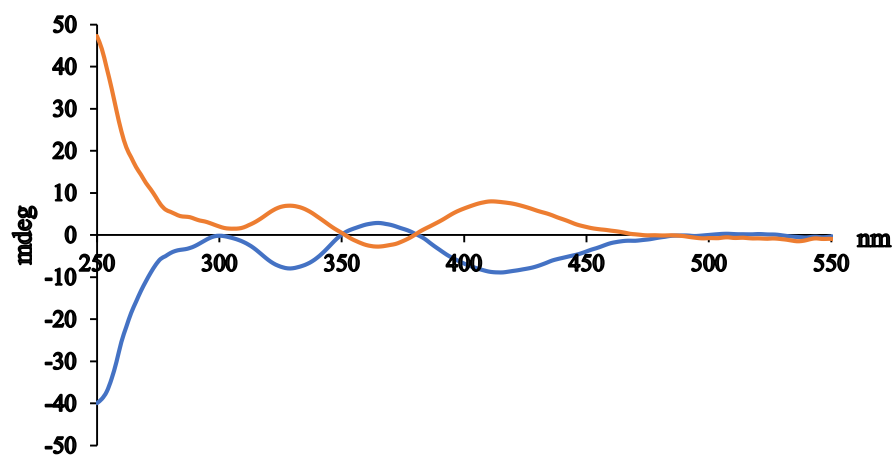
The scope of enantioselective chemosensing was tested with amino acids **1-10**, α -hydroxy acid **11-16**, amino alcohols **17-21**, amines **22-25** and carboxylic acid **26** (only one enantiomer shown).



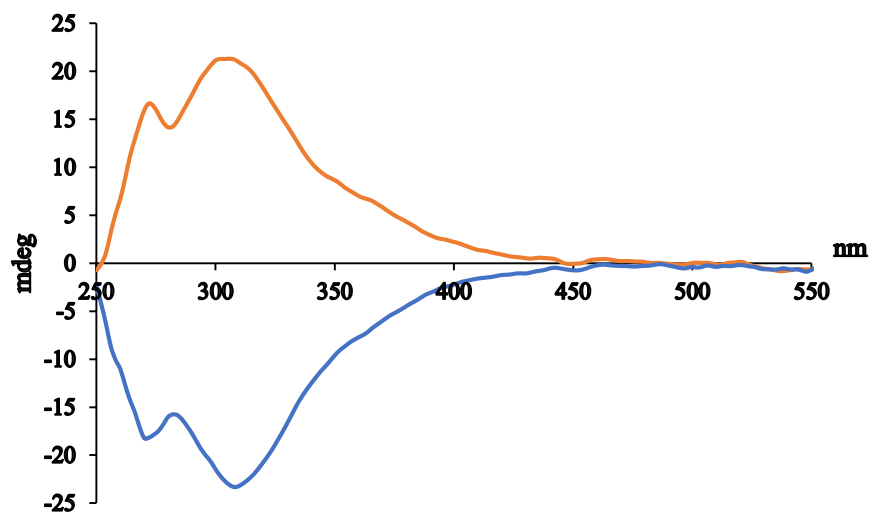
CD spectra of the assembly obtained from Pd(NO₃)₂, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in MeOH (1.8 mM Pd(NO₃)₂, 3 equivalents of **1**).



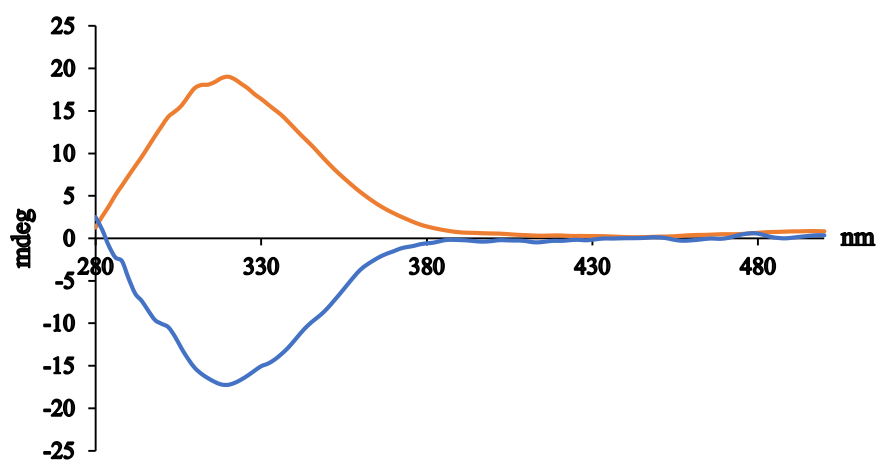
CD spectra of the assembly obtained from Pd(NO₃)₂, TBAOH, and (*S*)-**15** (blue) or (*R*)-**15** (orange) in MeOH (1.8 mM Pd(NO₃)₂, 3 equivalents of **15**).



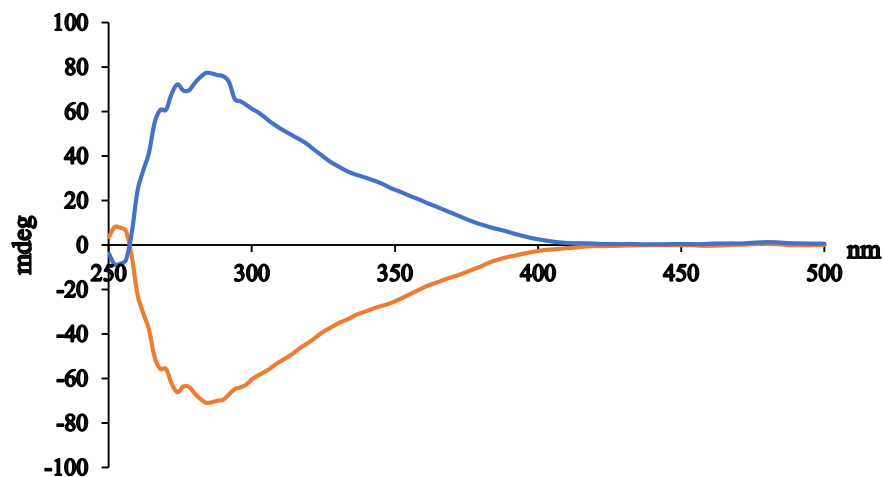
CD spectra of the assembly obtained from Pd(NO₃)₂, and (*S,R*)-**17** (blue) or (*R,S*)-**17** (orange) in MeOH (1.8 mM Pd(NO₃)₂, 3 equivalents of **17**).



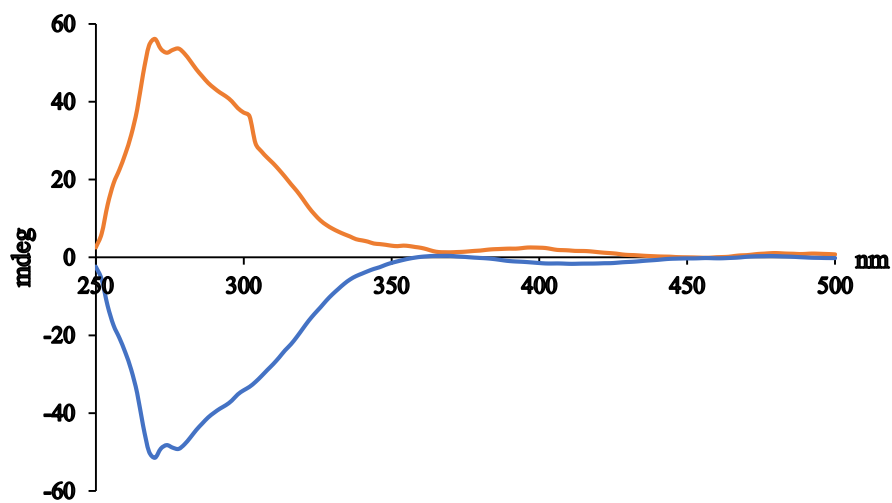
CD spectra of the assembly obtained from FeCl₂·4H₂O, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in DMSO (0.5 mM FeCl₂·4H₂O, 3 equivalents of **1**).



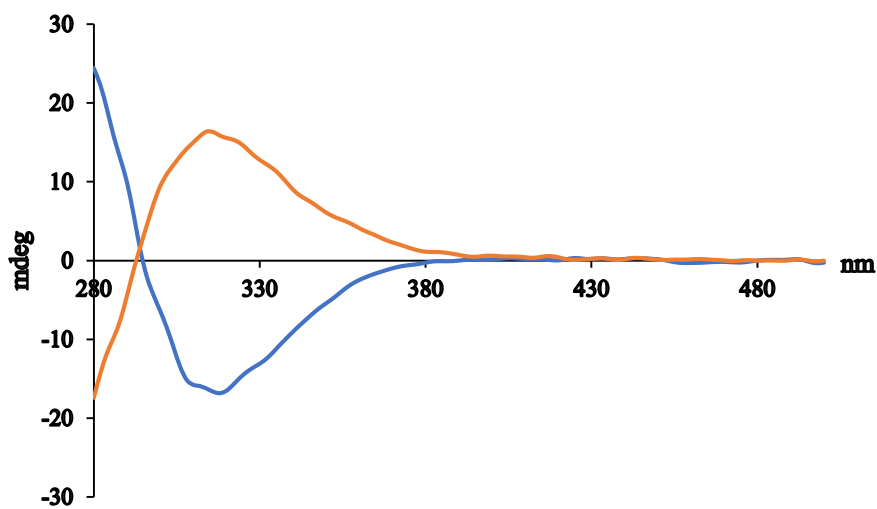
CD spectra of the assembly obtained from $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, TBAOH, and (*S*)-**15** (blue) or (*R*)-**15** (orange) in DMSO (0.5 mM $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, 3 equivalents of **15**).



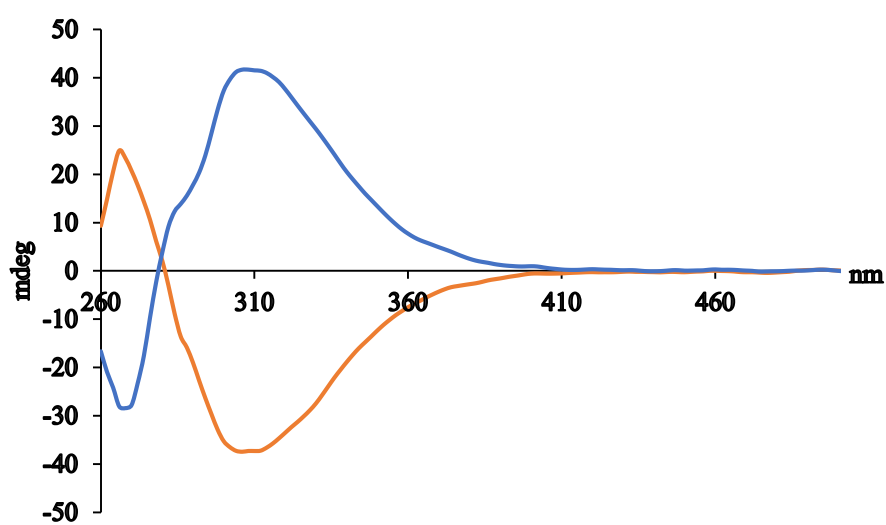
CD spectra of the assembly obtained from $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, and (*S,R*)-**17** (blue) or (*R,S*)-**17** (orange) in DMSO (0.5 mM $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, 3 equivalents of **17**).



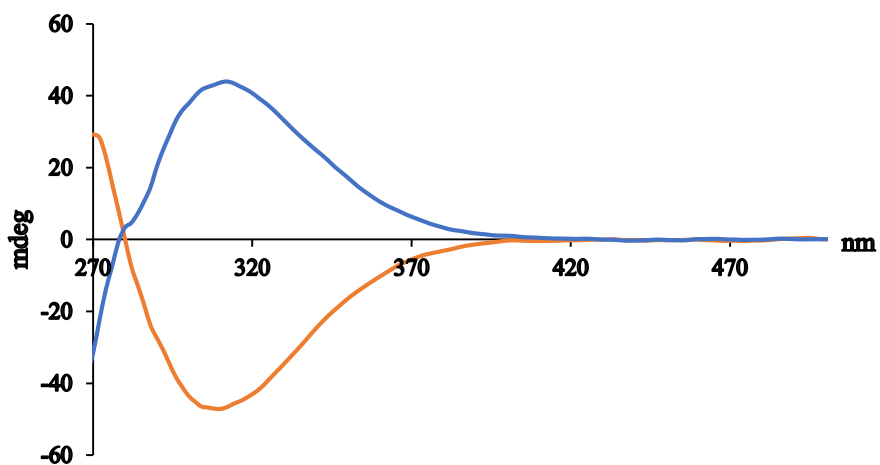
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **1**).



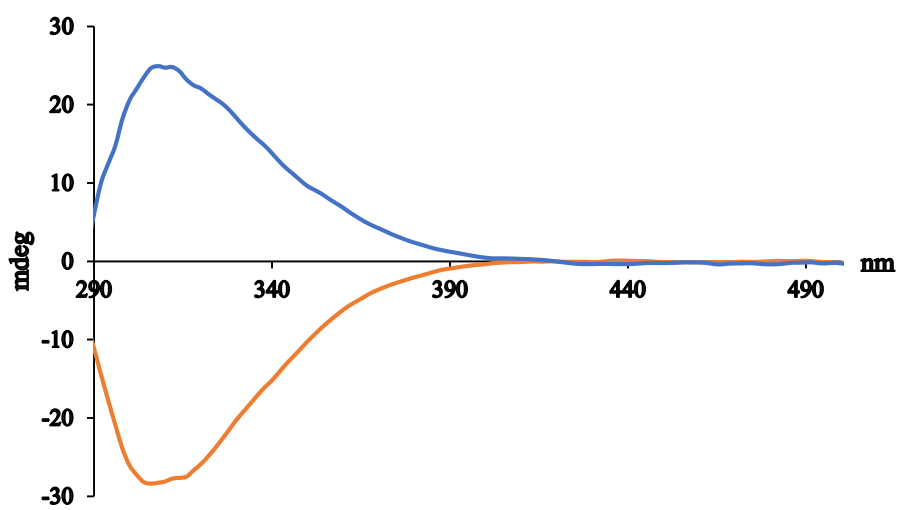
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**2** (blue) or (*R*)-**2** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **2**).



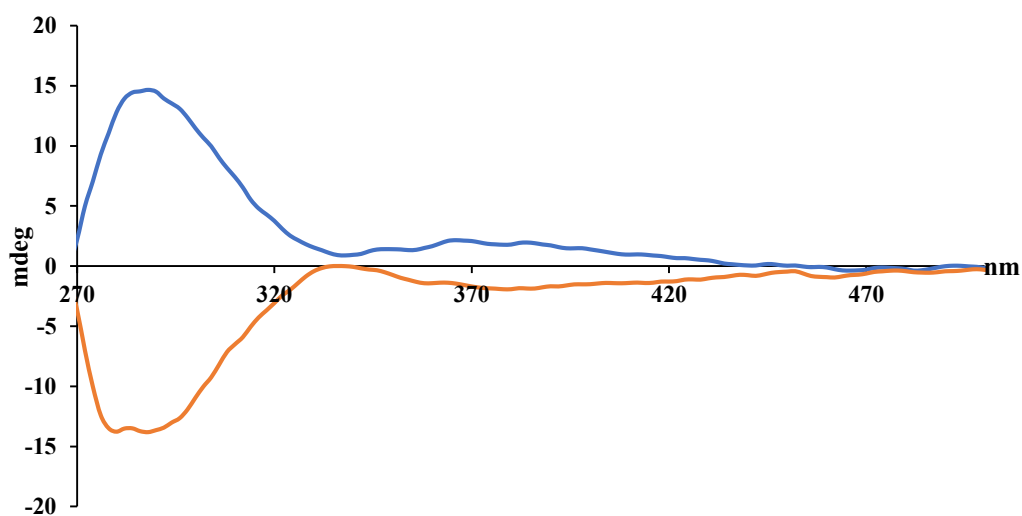
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**3** (blue) or (*R*)-**3** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **3**).



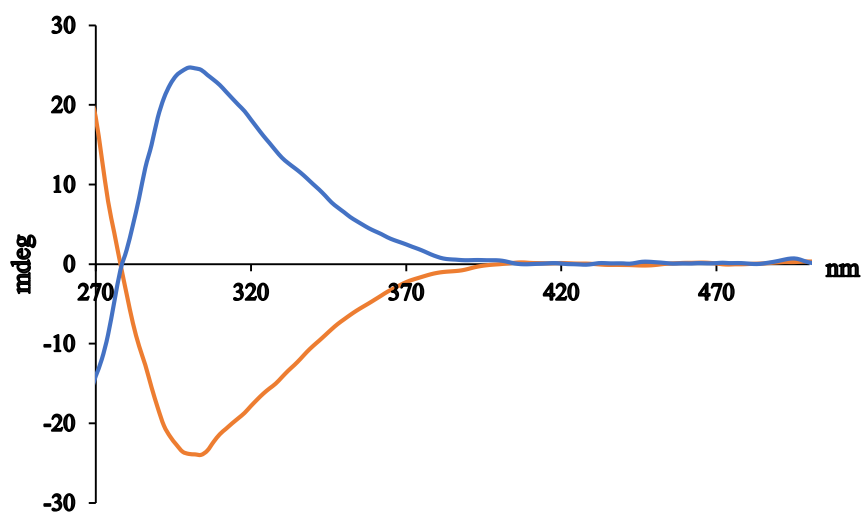
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**4** (blue) or (*R*)-**4** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **4**).



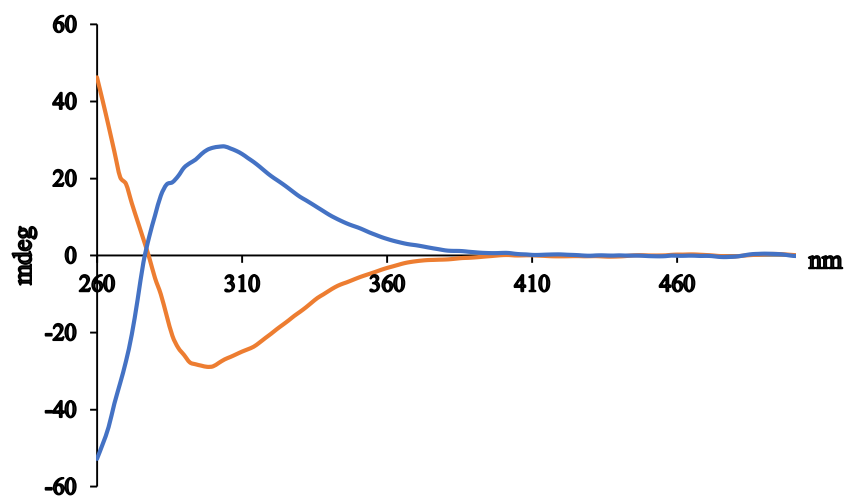
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**5** (blue) or (*R*)-**5** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **5**).



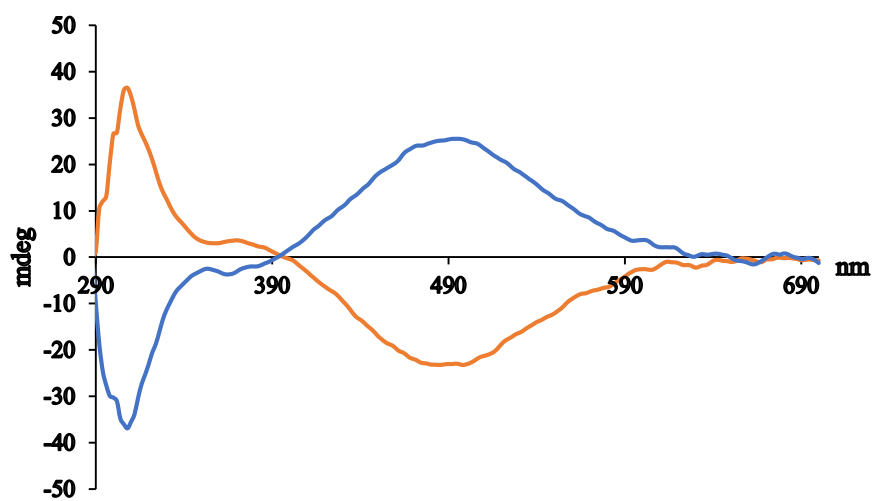
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**6** (blue) or (*R*)-**6** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **6**).



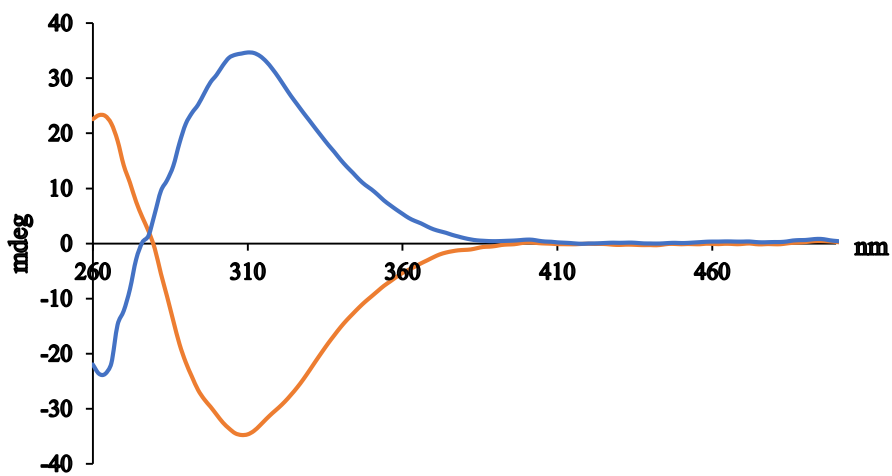
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S,R*)-**7** (blue) or (*R,S*)-**7** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **7**).



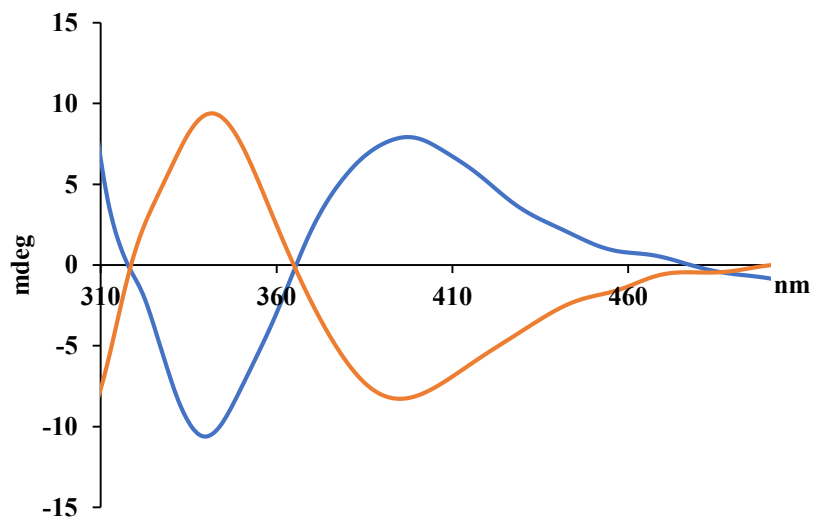
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**8** (blue) or (*R*)-**8** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **8**).



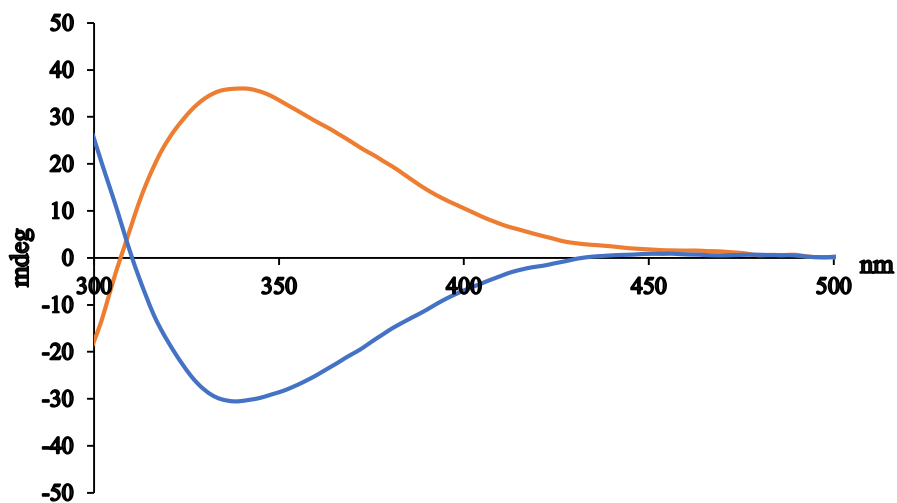
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**9** (blue) or (*R*)-**9** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **9**).



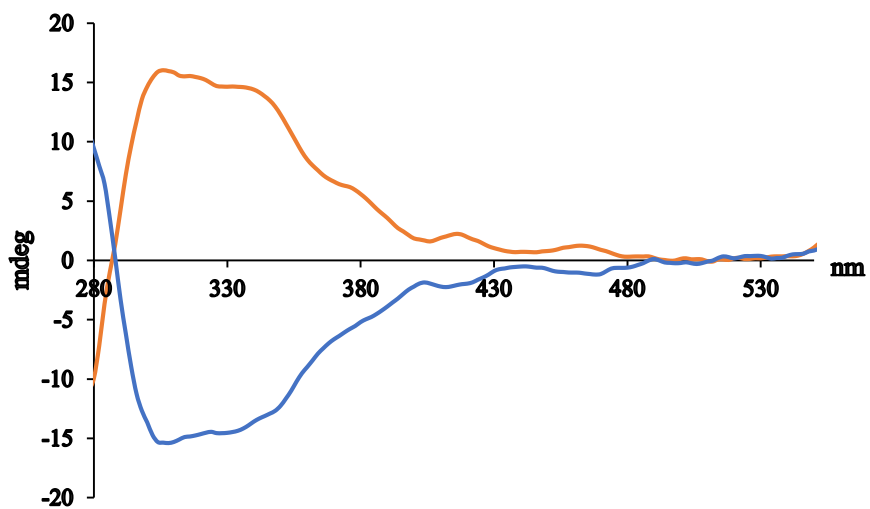
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**10** (blue) or (*R*)-**10** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **10**).



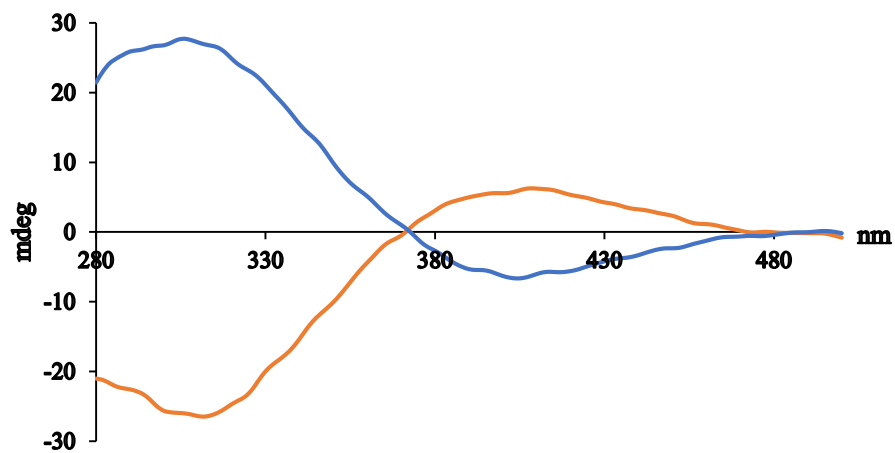
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S,S*)-**11** (blue) or (*R,R*)-**11** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **11**).



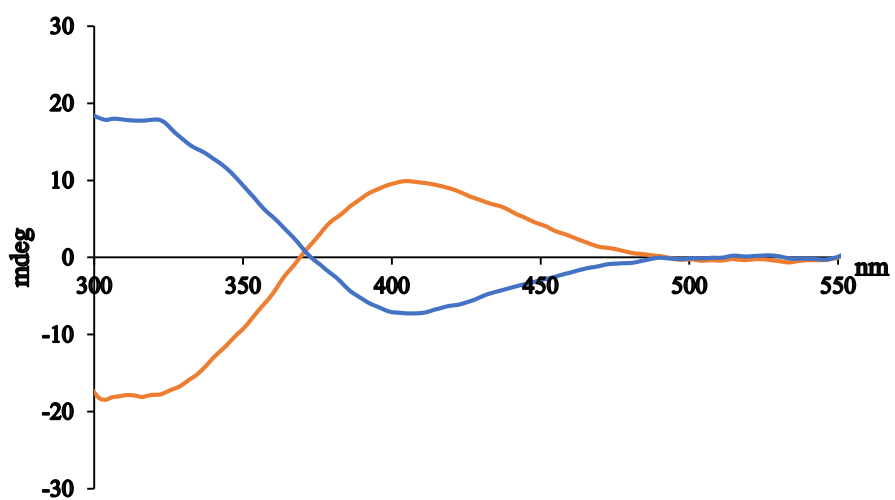
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**12** (blue) or (*R*)-**12** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **12**).



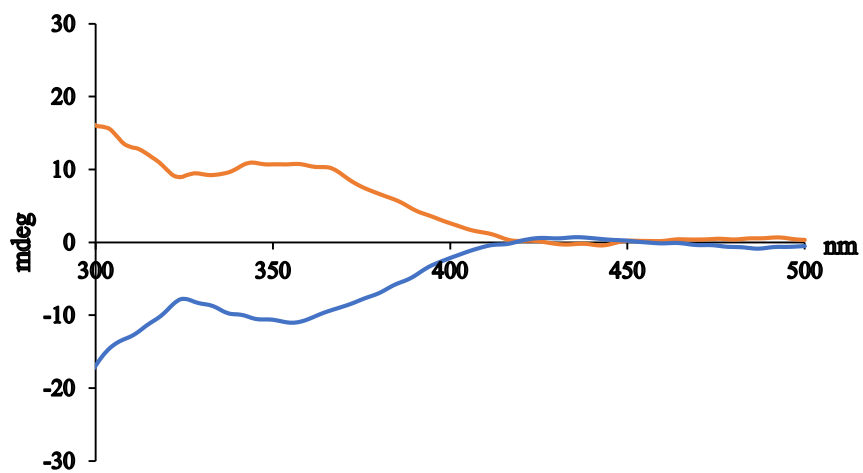
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**15** (blue) or (*R*)-**15** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **15**).



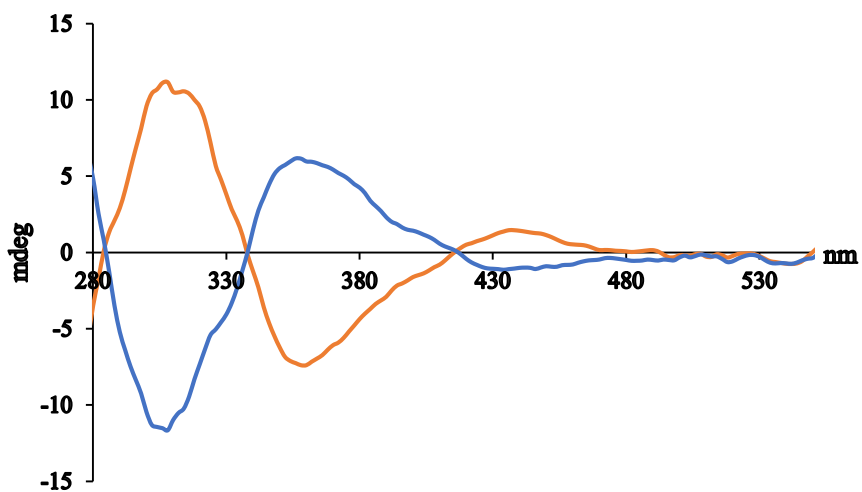
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**16** (blue) or (*R*)-**16** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **16**).



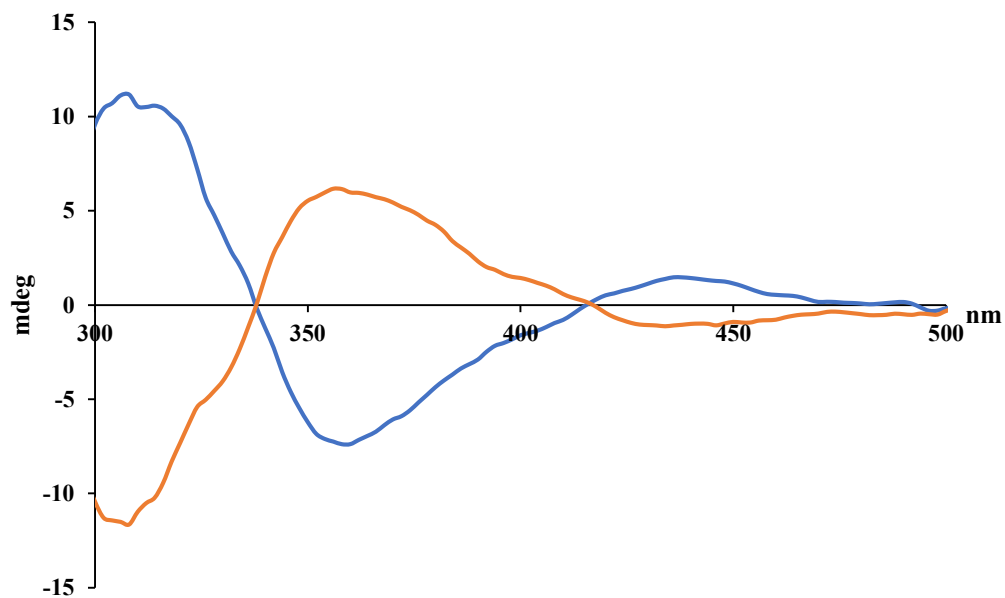
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and (*S,R*)-**17** (blue) or (*R,S*)-**17** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **17**).



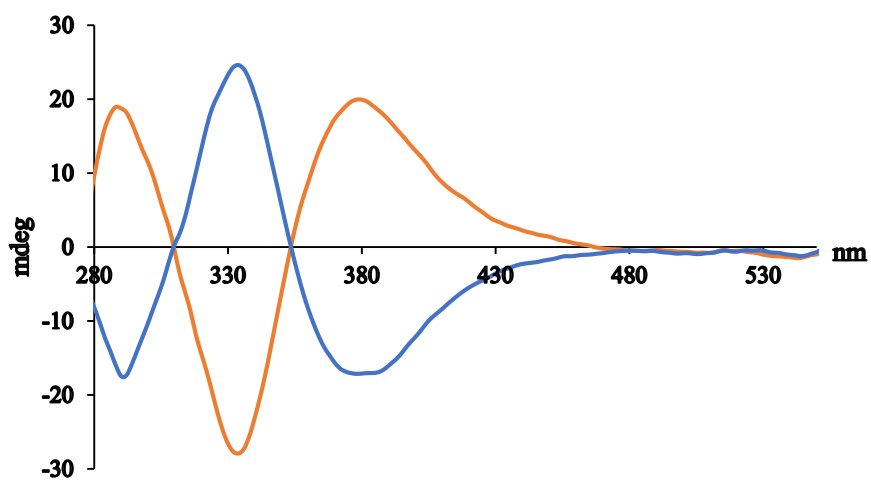
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and (*S,R*)-**18** (blue) or (*R,S*)-**18** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **18**).



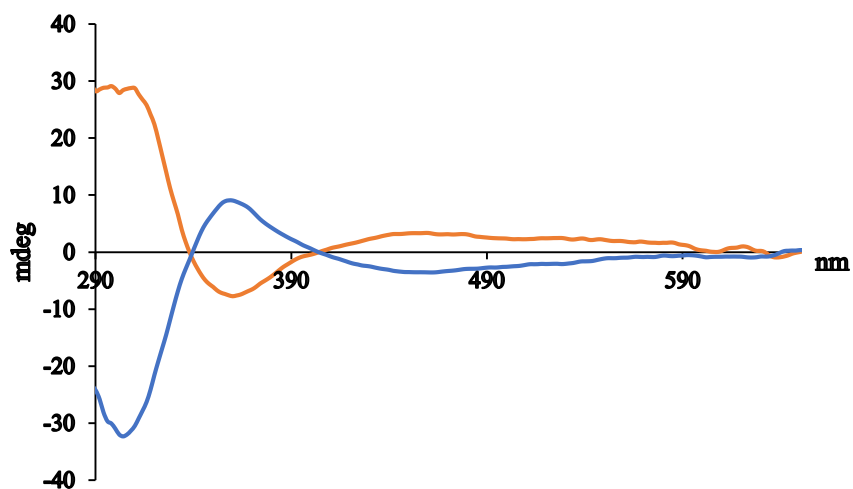
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*R,S*)-**20** (blue) or (*S,R*)-**20** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **20**).



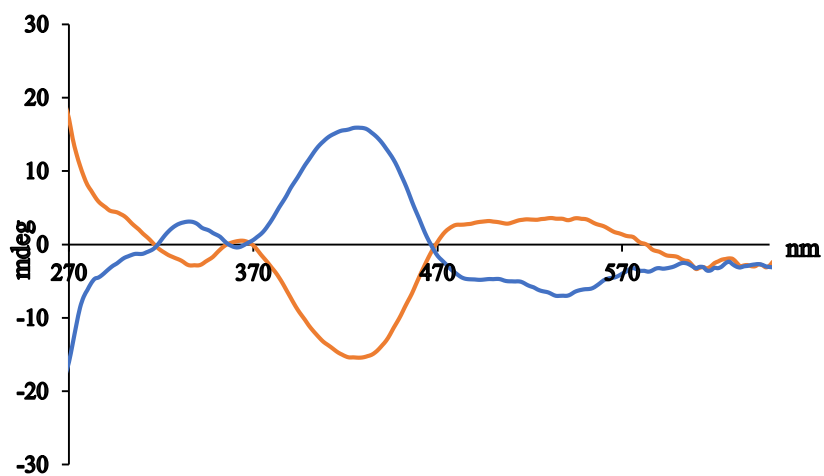
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and (*S,S*)-**21** (blue) or (*R,R*)-**21** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **21**).



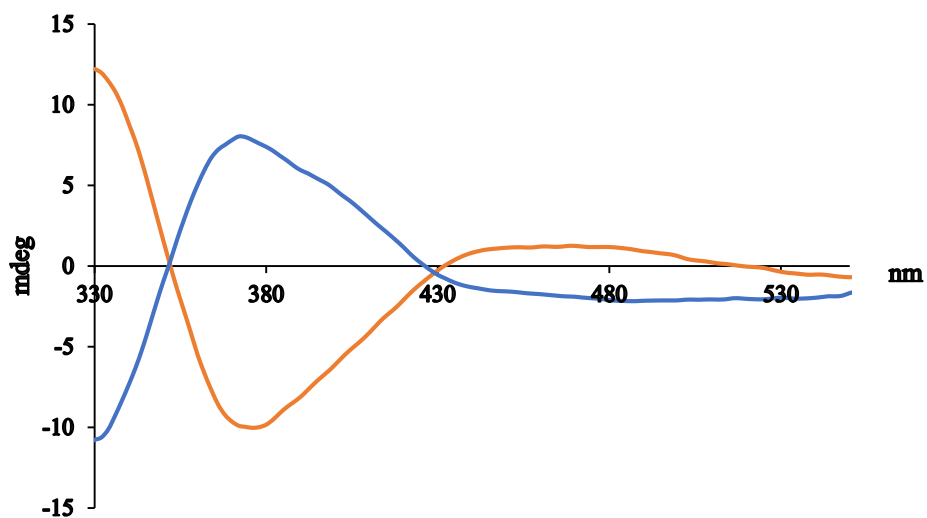
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and (*S,S*)-**22** (blue) or (*R,R*)-**22** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **22**).



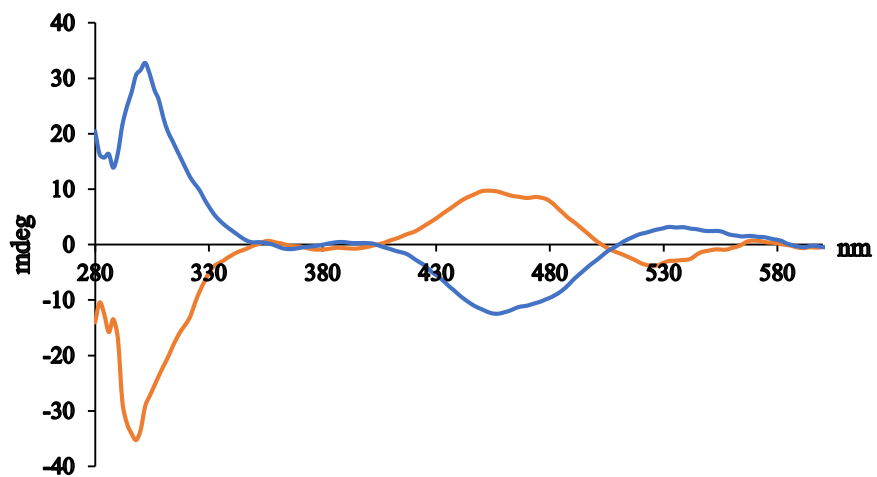
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and (*S,S*)-**23** (blue) or (*R,R*)-**23** (orange) in DMSO (0.5 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **23**).



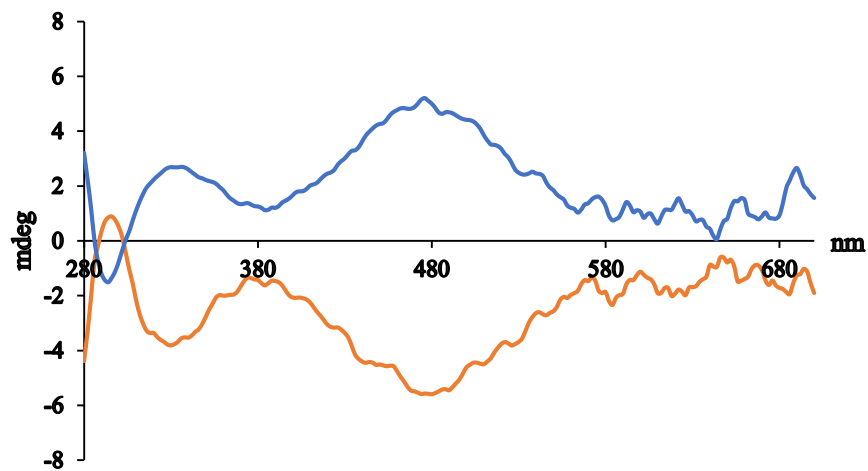
CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, TBAOH and (*S*)-**26** (blue) or (*R*)-**26** (orange) in DMSO (0.9 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **26**).



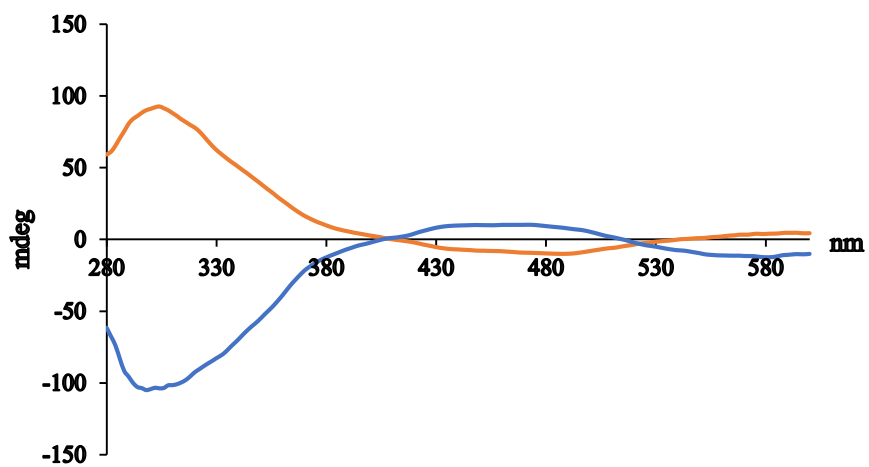
CD spectra of the assembly obtained from $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in DMSO (1.8 mM $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, 3 equivalents of **1**).



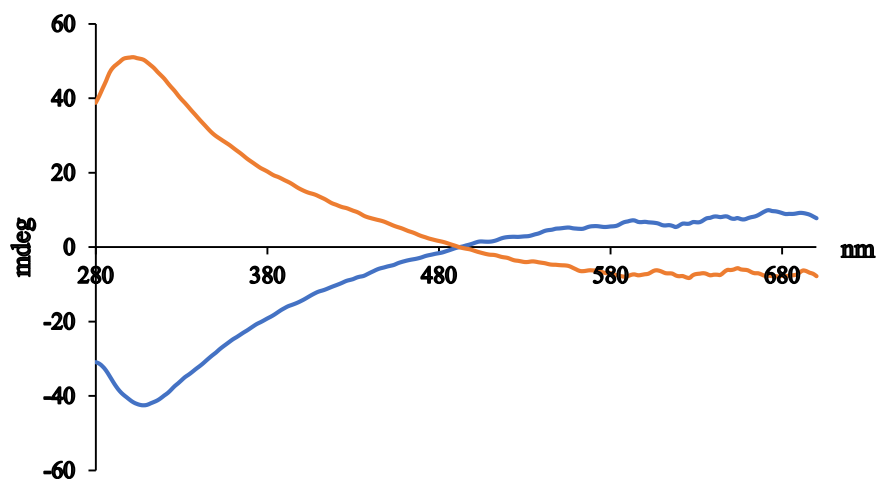
CD spectra of the assembly obtained from $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, TBAOH, and (*S*)-**15** (blue) or (*R*)-**15** (orange) in DMSO (1.8 mM $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, 3 equivalents of **15**).



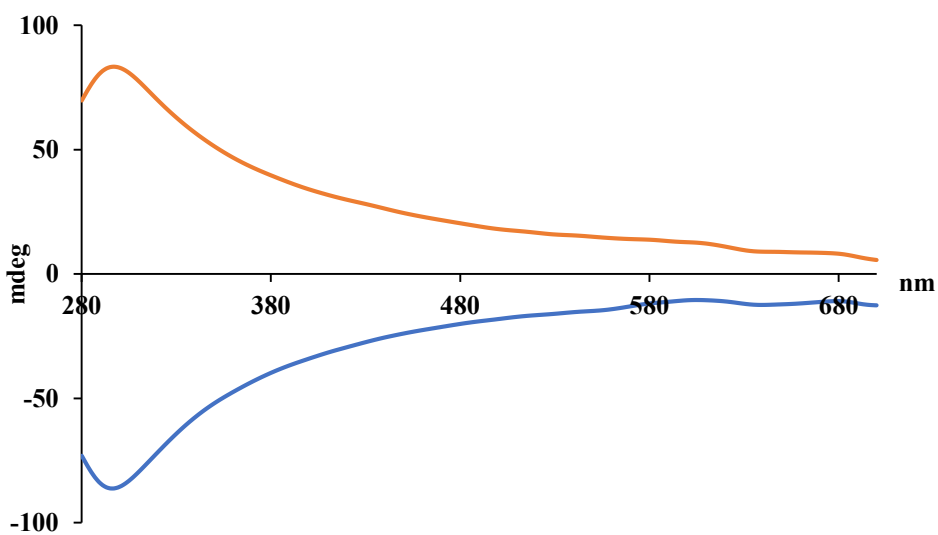
CD spectra of the assembly obtained from $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, and (*S,R*)-**17** (blue) or (*R,S*)-**17** (orange) in DMSO (1.8 mM $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, 3 equivalents of **17**).



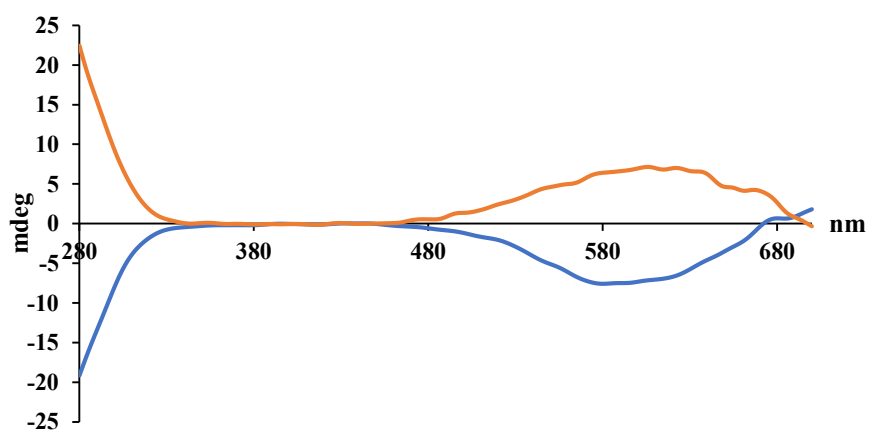
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in DMSO at (1.8 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **1**).



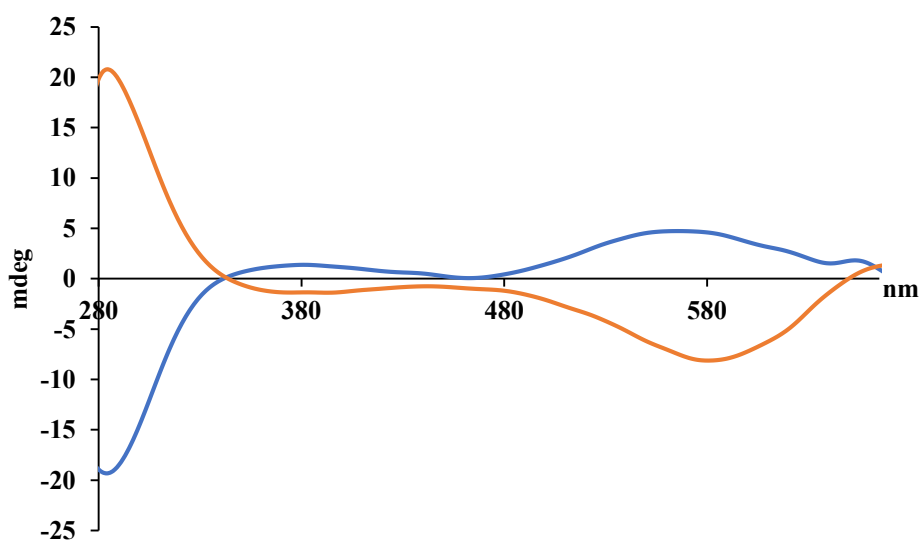
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*R*)-**2** (blue) or (*S*)-**2** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **2**).



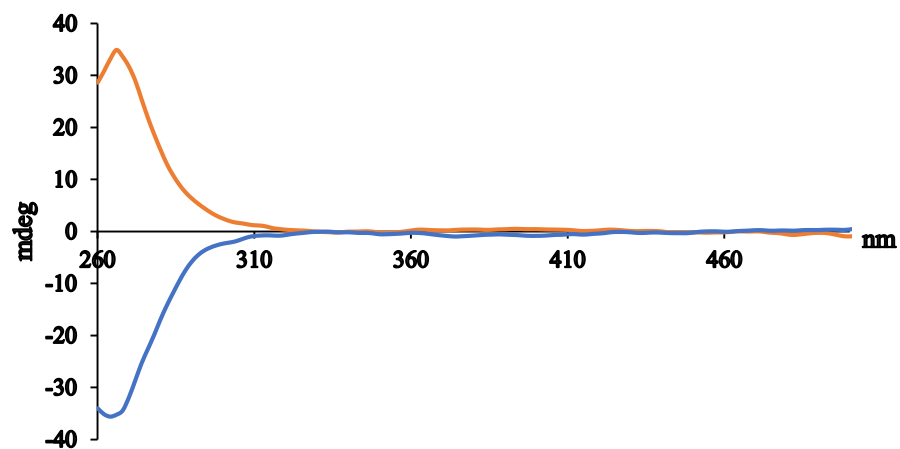
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S*)-**7** (blue) or (*R*)-**7** (orange) in DMSO (0.9 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **7**).



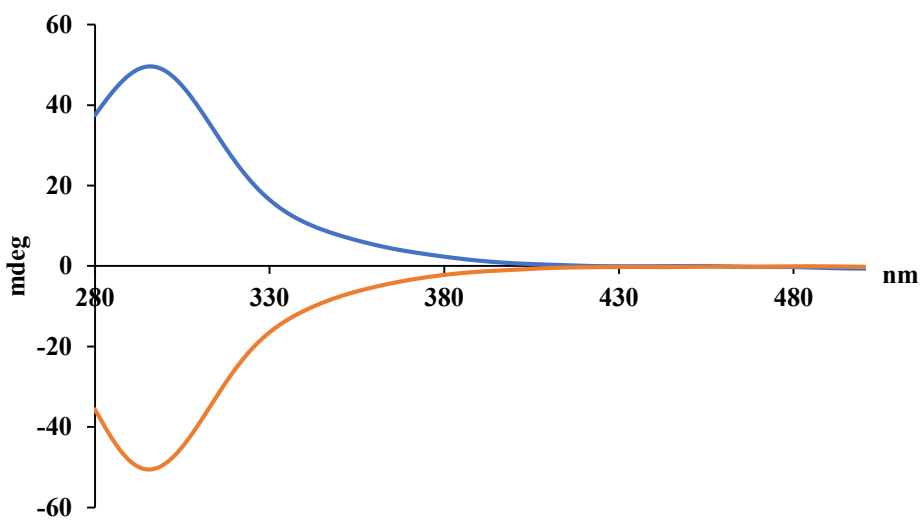
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*R*)-**10** (blue) or (*S*)-**10** (orange) in DMSO (0.9 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **10**).



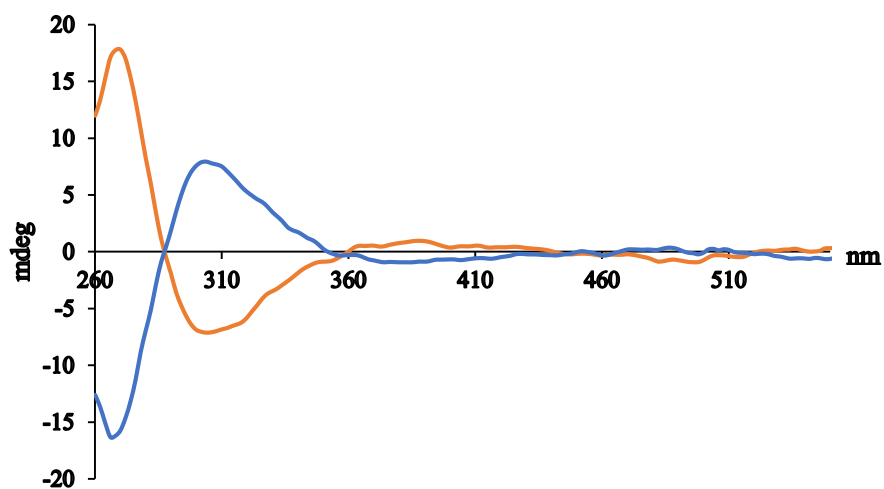
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S,S*)-**11** (blue) or (*R,R*)-**11** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **11**).



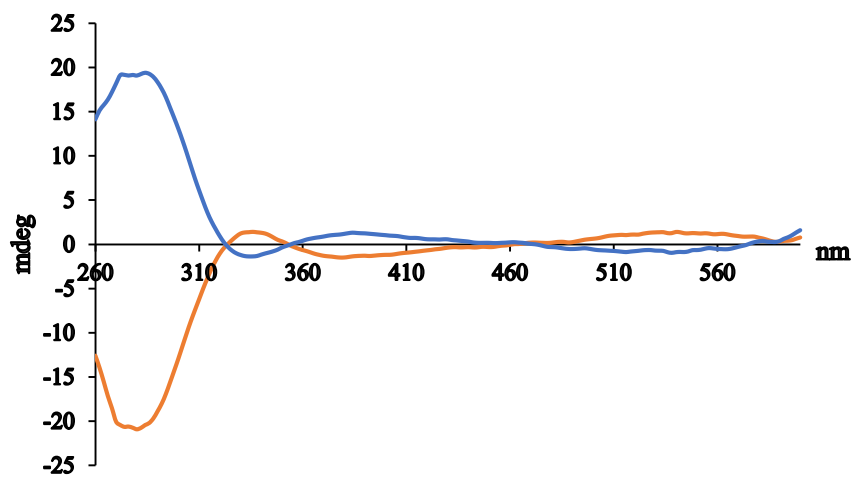
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*R*)-**12** (blue) or (*S*)-**12** (orange) in DMSO (0.9 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **12**).



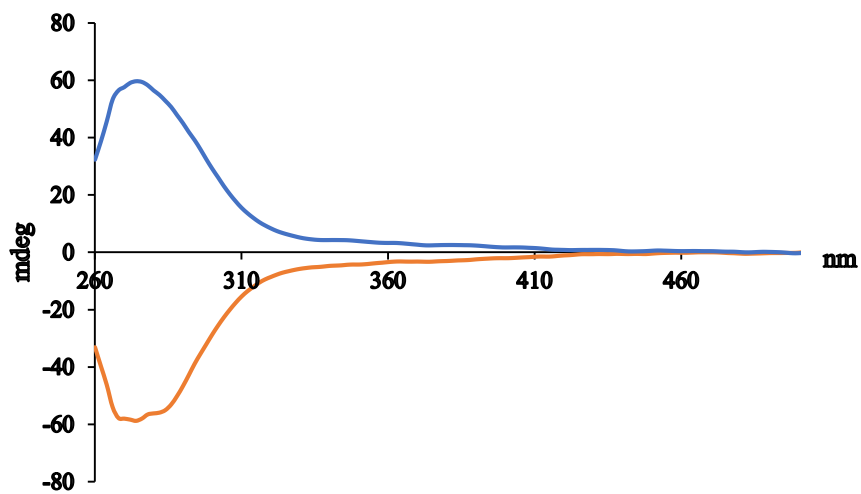
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S*)-**13** (blue) or (*R*)-**13** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **13**).



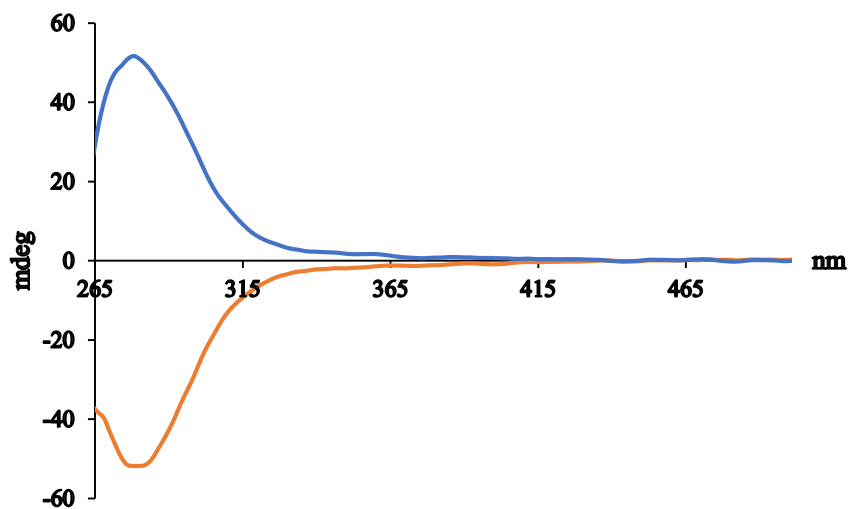
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S*)-**14** (blue) or (*R*)-**14** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **14**).



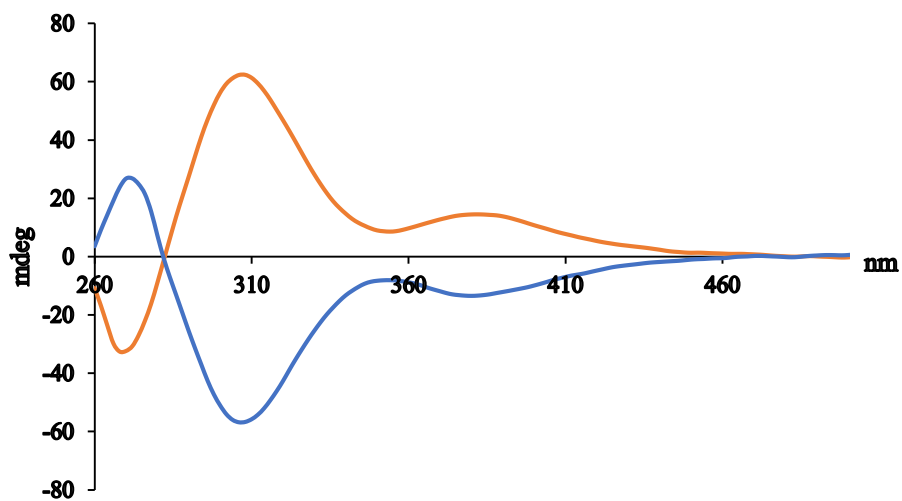
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S*)-**15** (blue) or (*R*)-**15** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **15**).



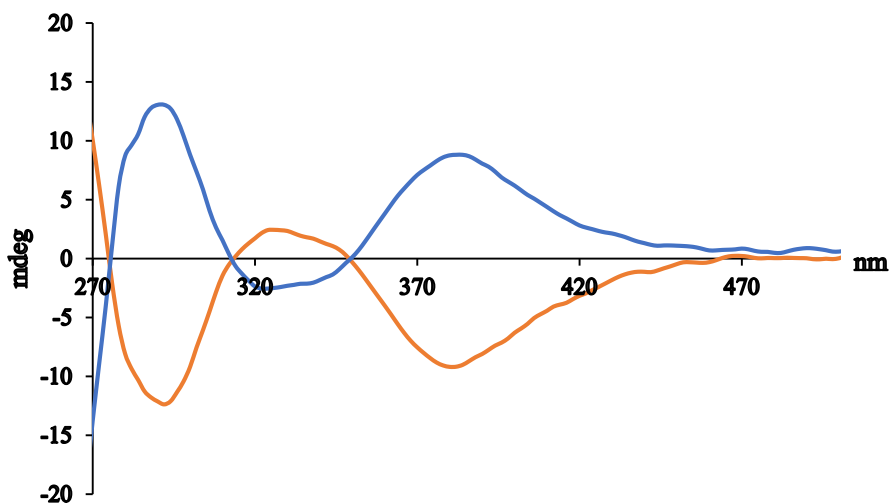
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S*)-**16** (blue) or (*R*)-**16** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **16**).



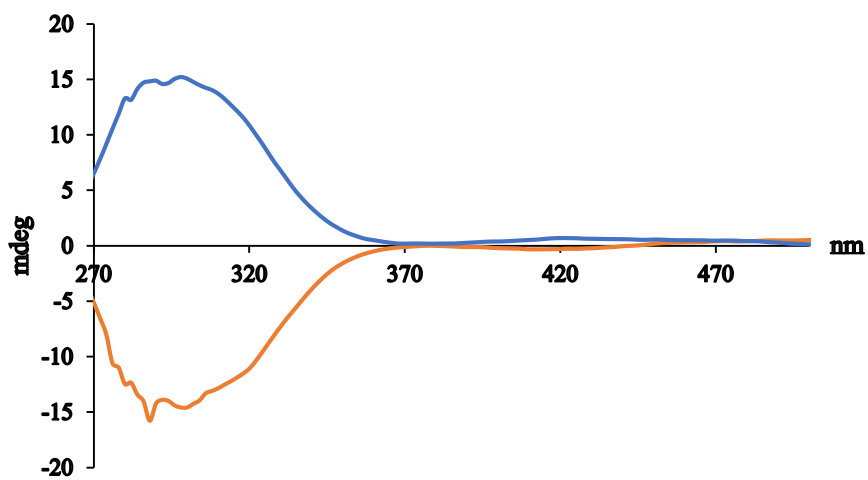
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S,R*)-**17** (blue) or (*R,S*)-**17** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **17**).



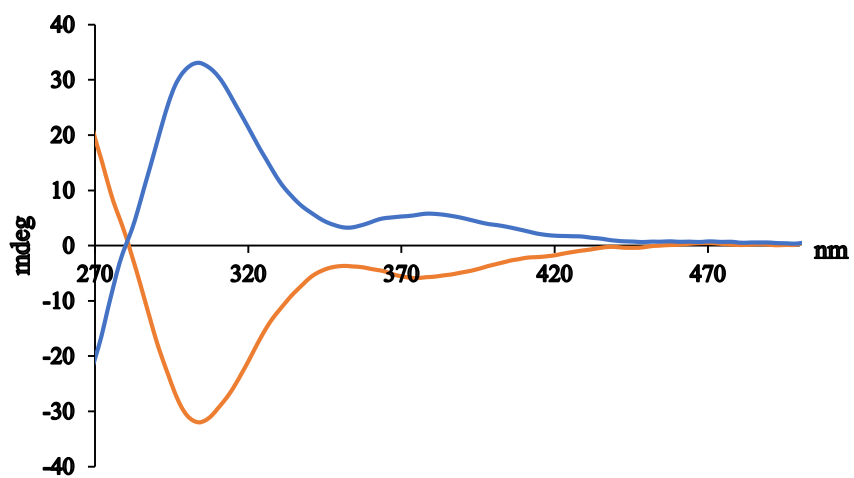
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S,R*)-**18** (blue) or (*R,S*)-**18** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **18**).



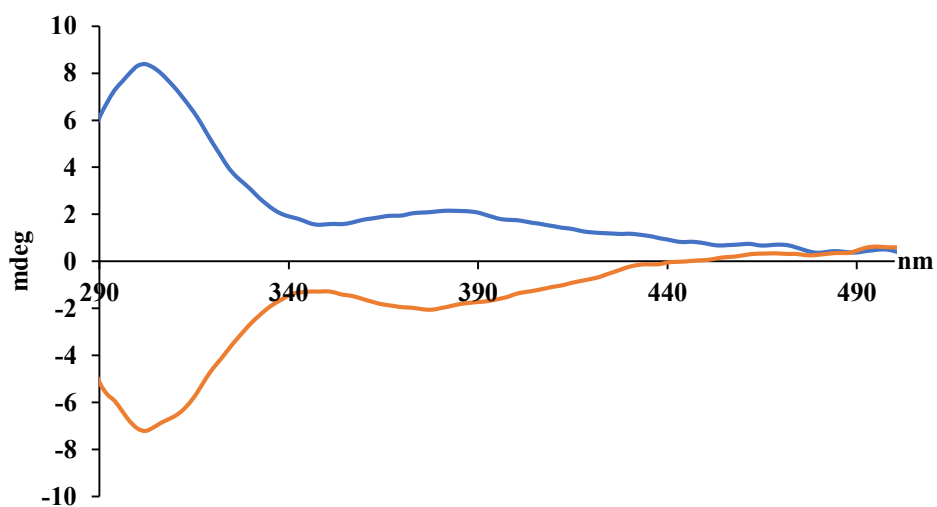
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S,S*)-**19** (blue) or (*R,R*)-**19** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **19**).



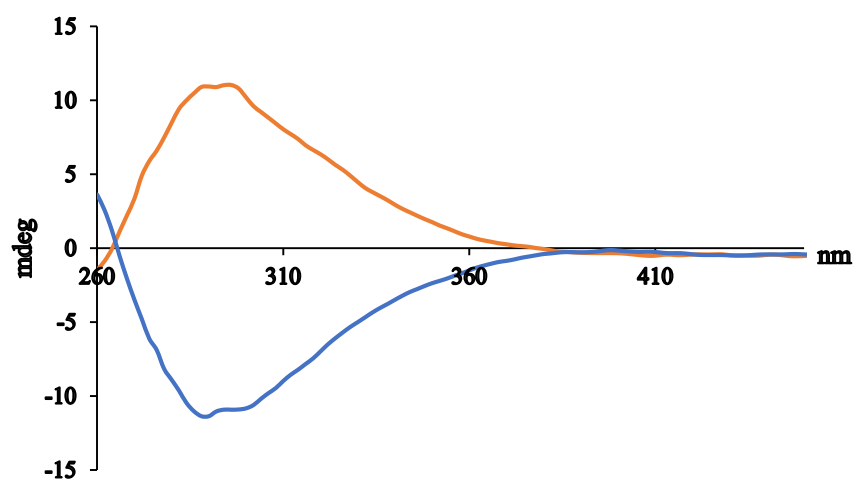
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S,R*)-**20** (blue) or (*R,S*)-**20** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **20**).



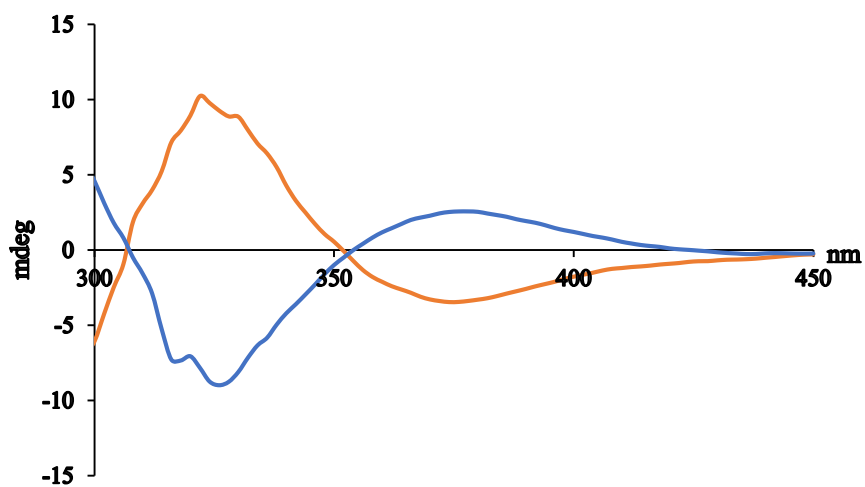
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, TBAOH, and (*S,S*)-**21** (blue) or (*R,R*)-**21** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 2.5 equivalents of **21**).



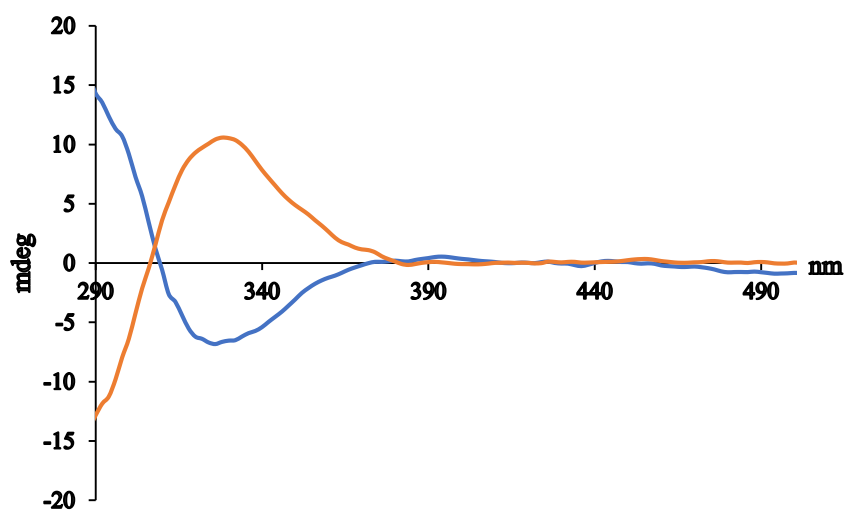
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S*)-**24** (blue) or (*R*)-**24** (orange) in DMSO (0.5 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 5 equivalents of **24**).



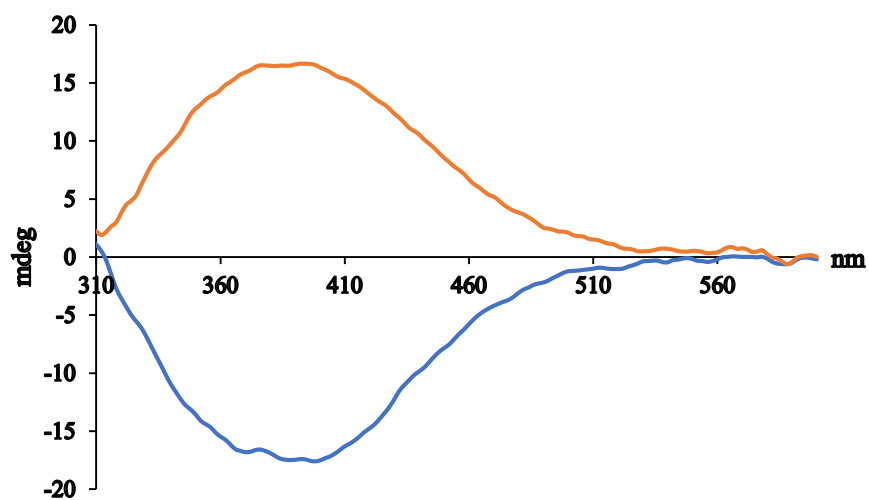
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S*)-**25** (blue) or (*R*)-**25** (orange) in DMSO (1.8 mM $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, 5 equivalents of **25**).



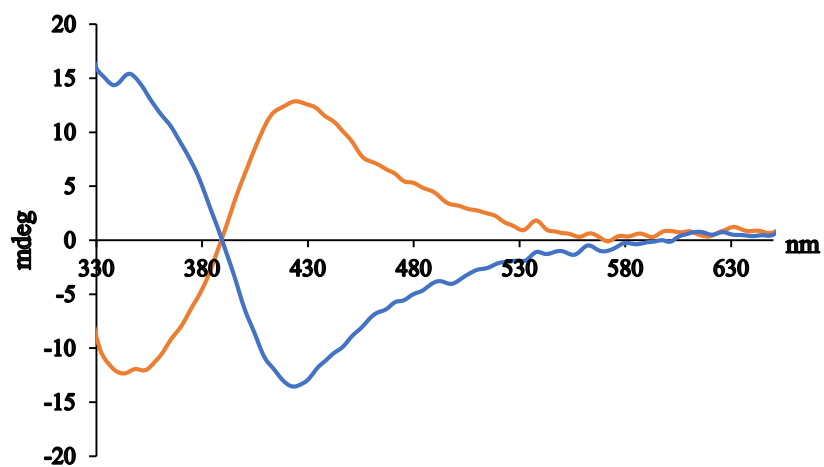
CD spectra of the assembly obtained from $\text{Ce}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in DMSO (1.8 mM $\text{Ce}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$, 3 equivalents of **1**).



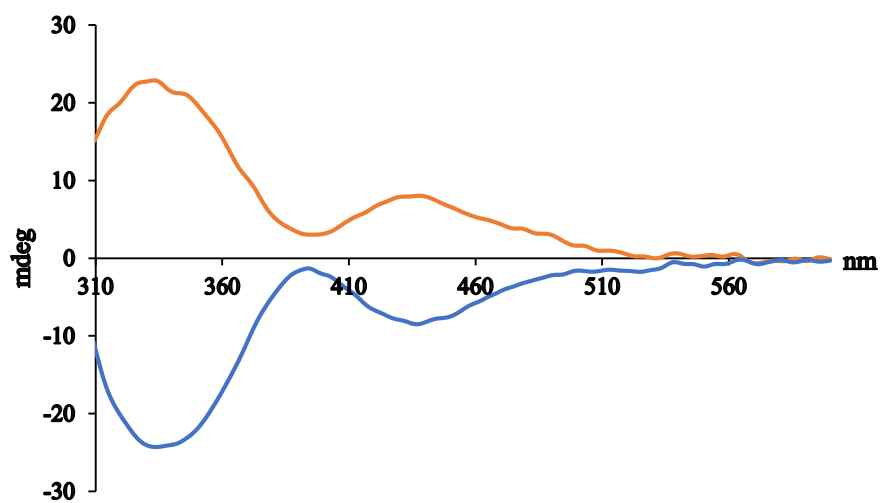
CD spectra of the assembly obtained from $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, TBAOH, and (*S*)-**1** (blue) or (*R*)-**1** (orange) in MeOH (1.8 mM $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, 3 equivalents of **1**).



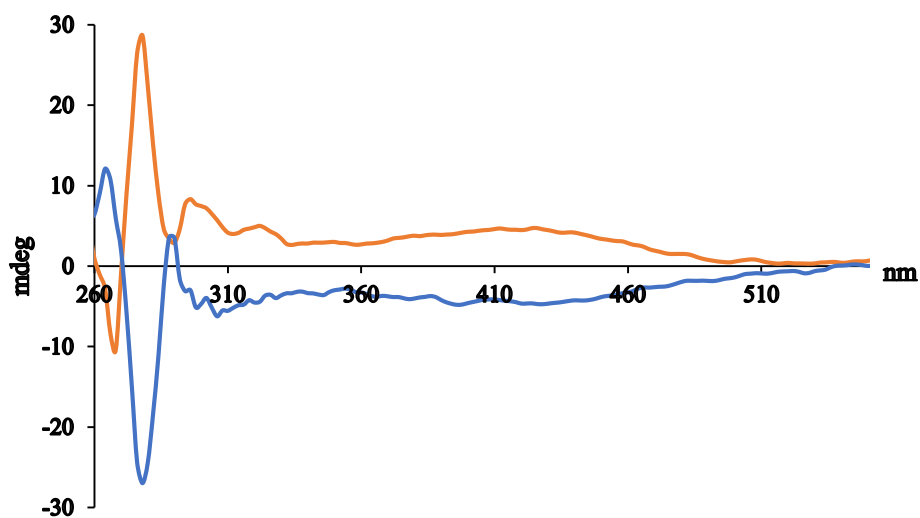
CD spectra of the assembly obtained from $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, TBAOH, and (*S*)-**15** (blue) or (*R*)-**15** (orange) in DMSO (1.8 mM $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, 3 equivalents of **15**).



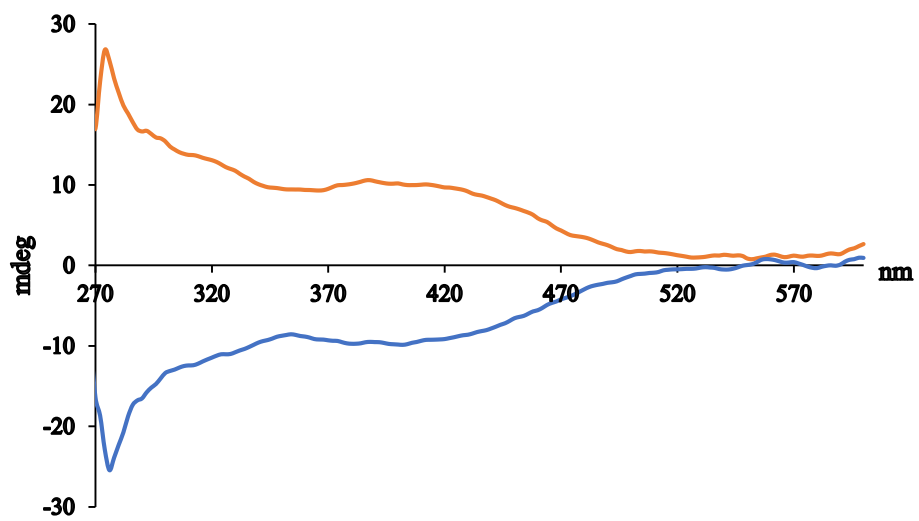
CD spectra of the assembly obtained from $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, and (*S,R*)-**17** (blue) or (*R,S*)-**17** (orange) in DMSO (1.8 mM $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, 3 equivalents of **17**).



CD spectra of the assembly obtained from $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, and (*S*)-**24** (blue) or (*R*)-**24** (orange) in MeOH at (0.9 mM $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, 6 equivalents of **24**).



CD spectra of the assembly obtained from $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, and (*S*)-**25** (blue) or (*R*)-**25** (orange) in MeOH (0.9 mM $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$, 6 equivalents of **25**).



Comparison of the chirality sensing with $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$

| Substrate | FeCl_3 | CuCl_2 |
|-----------|-----------------|-----------------|
| 1 | Green | Green |
| 2 | Green | Green |
| 3 | Green | Yellow |
| 4 | Green | Yellow |
| 5 | Green | Yellow |
| 6 | Green | Yellow |
| 7 | Green | Green |
| 8 | Green | Yellow |
| 9 | Green | Yellow |
| 10 | Green | Green |
| 11 | Green | Green |
| 12 | Green | Green |
| 13 | Red | Green |
| 14 | Red | Green |
| 15 | Green | Green |
| 16 | Green | Green |
| 17 | Green | Green |
| 18 | Green | Green |
| 19 | Red | Green |
| 20 | Green | Green |
| 21 | Green | Green |
| 22 | Green | Red |
| 23 | Green | Red |
| 24 | Red | Green |
| 25 | Red | Green |
| 26 | Green | Red |

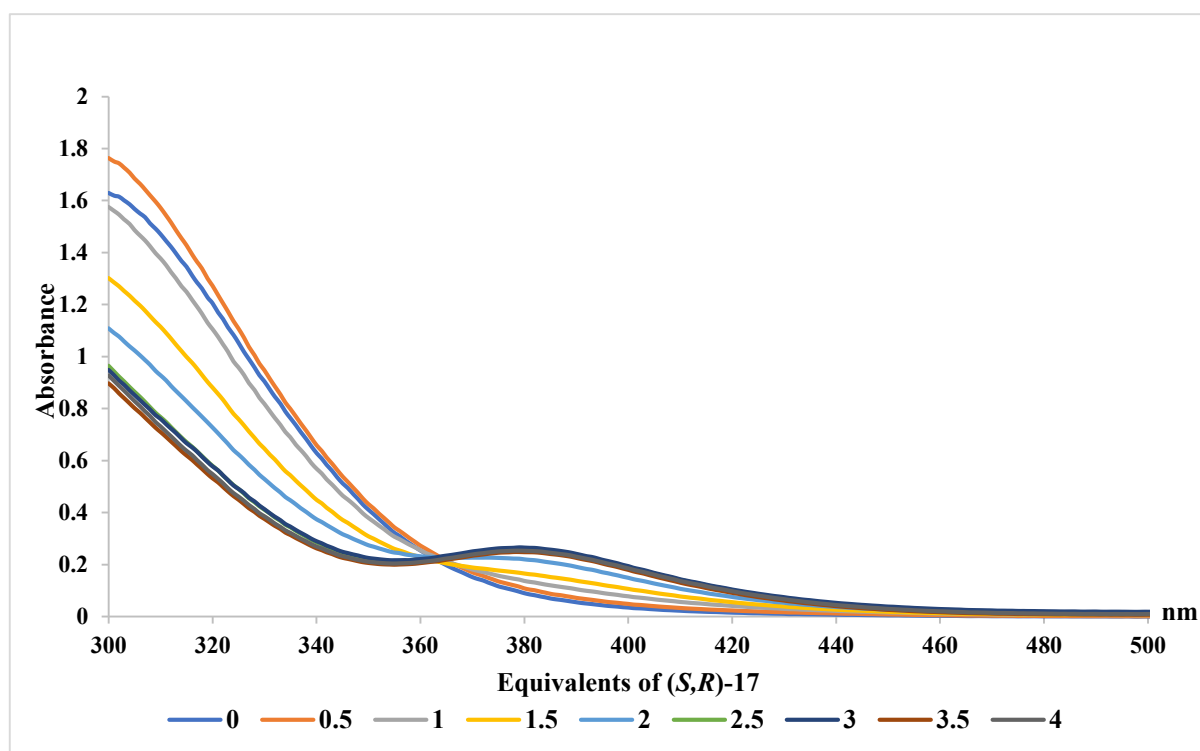
Green: Suitable for ee determination, yellow: insufficient ICD intensities, red: not suitable for ee quantification.

3. Mechanistic Studies

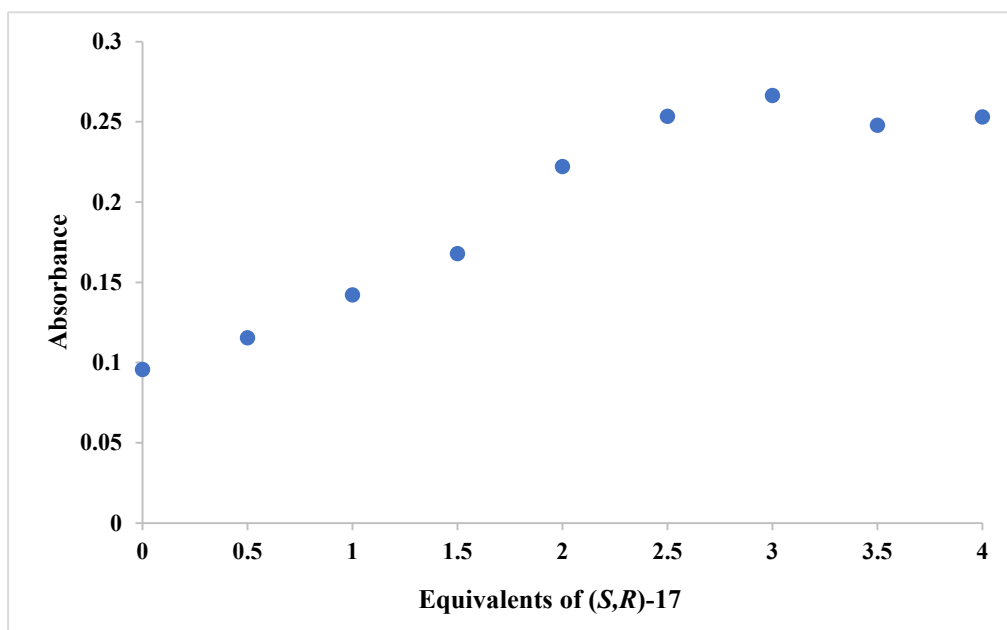
3.1 UV Titration Analysis

A stock solution of $\text{Cu}(\text{Cl})_2 \cdot 2\text{H}_2\text{O}$ or $\text{Fe}(\text{Cl})_3 \cdot 6\text{H}_2\text{O}$ (1 M) in DMSO was prepared and 0.1 mL portions were transferred into 4 mL vials. The portions were then diluted with 0.4 mL DMSO. A solution of (*S,R*)-**17** was prepared in DMSO (0.50 M). To each vial containing 0.5 mL of the Cu(II) or Fe(III) stock solutions were added increasing amounts of the substrate (0.0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 5.0 equivalents relative to Cu(II) or Fe(III)). UV analysis was performed at 0.5 or 0.25 mM in DMSO with an average scanning time of 0.1 s, a data interval of 1 nm, and a scan rate of 600 nm/min.

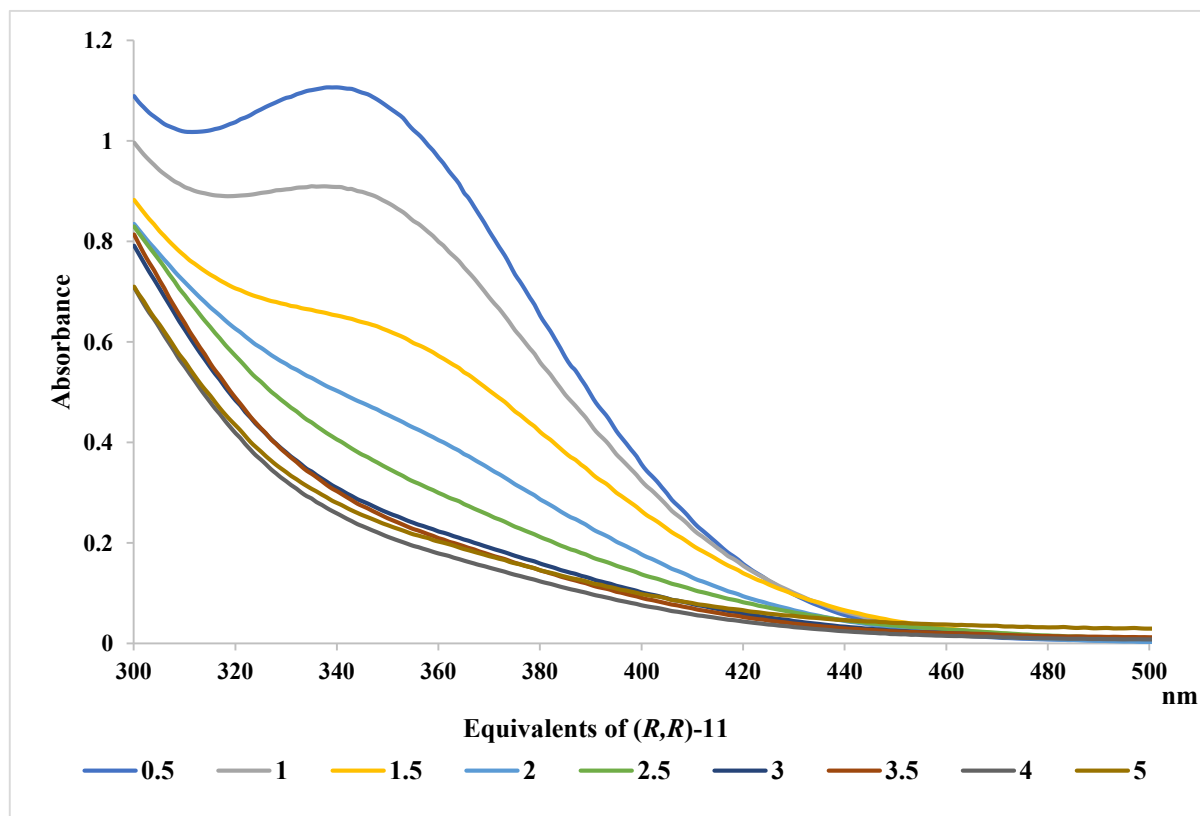
UV spectra of the assembly formed between $\text{Cu}(\text{Cl})_2 \cdot 2\text{H}_2\text{O}$ and (*S,R*)-**17** in DMSO (0.5 mM $\text{Cu}(\text{Cl})_2 \cdot 2\text{H}_2\text{O}$).



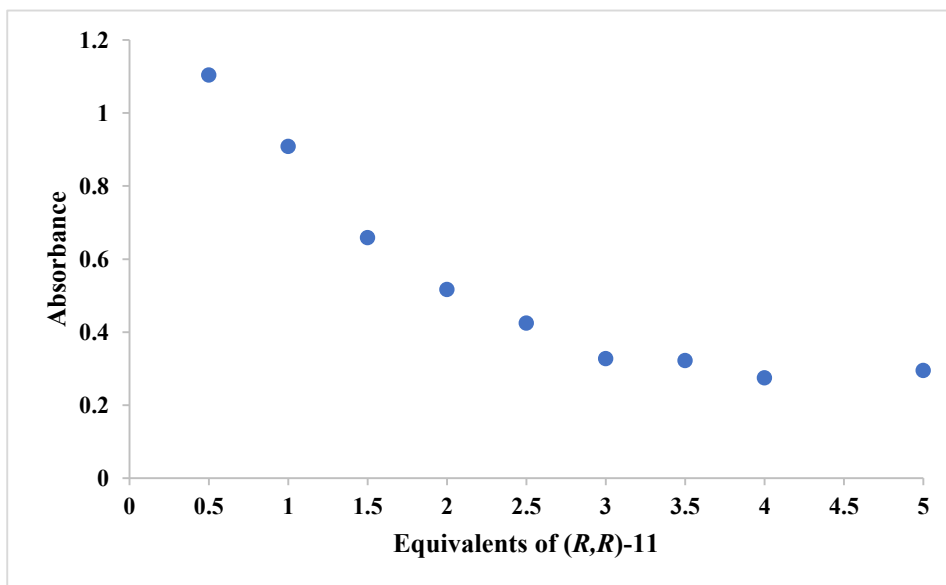
The UV maximum at 380 nm continuously increased upon addition of the substrate showing saturation upon addition of 2.5 equivalents of (*S,R*)-17.



UV spectra of the assembly formed between $\text{Fe}(\text{Cl})_3 \cdot 6\text{H}_2\text{O}$ and (*R,R*)-11 (0-5 equivalents) in DMSO (0.5 mM $\text{Fe}(\text{Cl})_3 \cdot 6\text{H}_2\text{O}$).

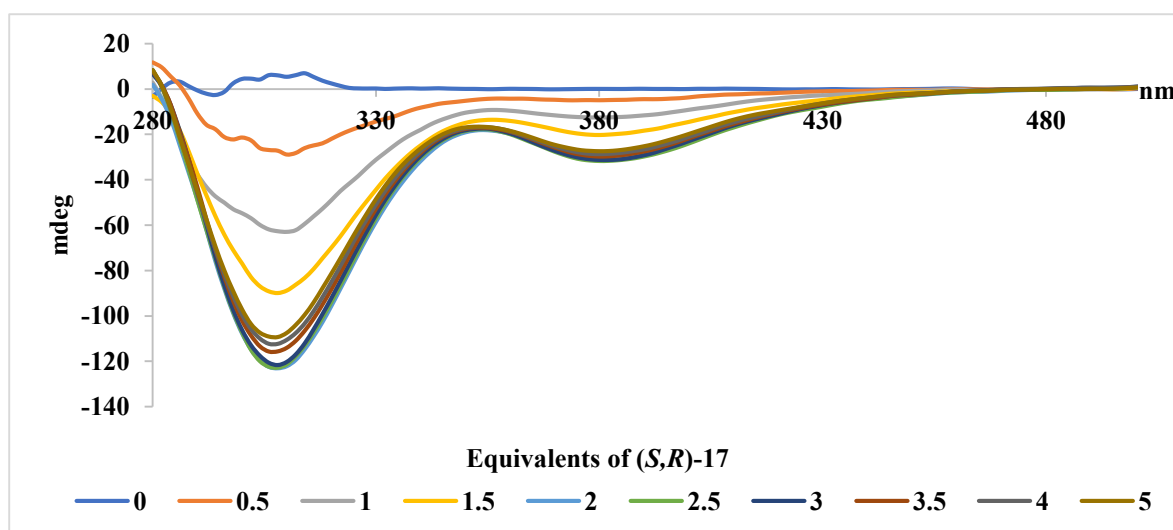


The UV signal at 337 nm continuously decreased upon addition of the substrate showing saturation upon addition of 3 equivalents of (*R,R*)-11.

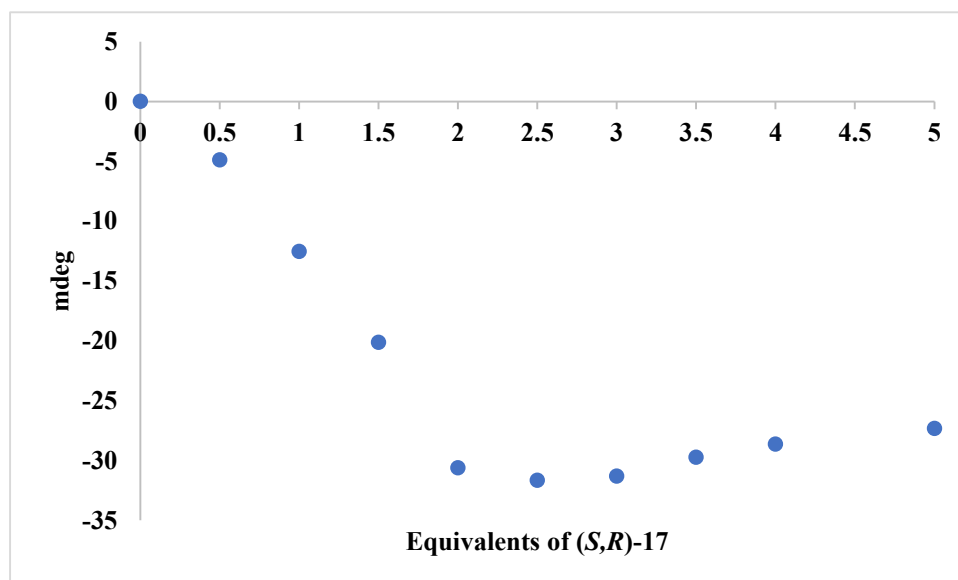


3.2 CD Titration Analysis

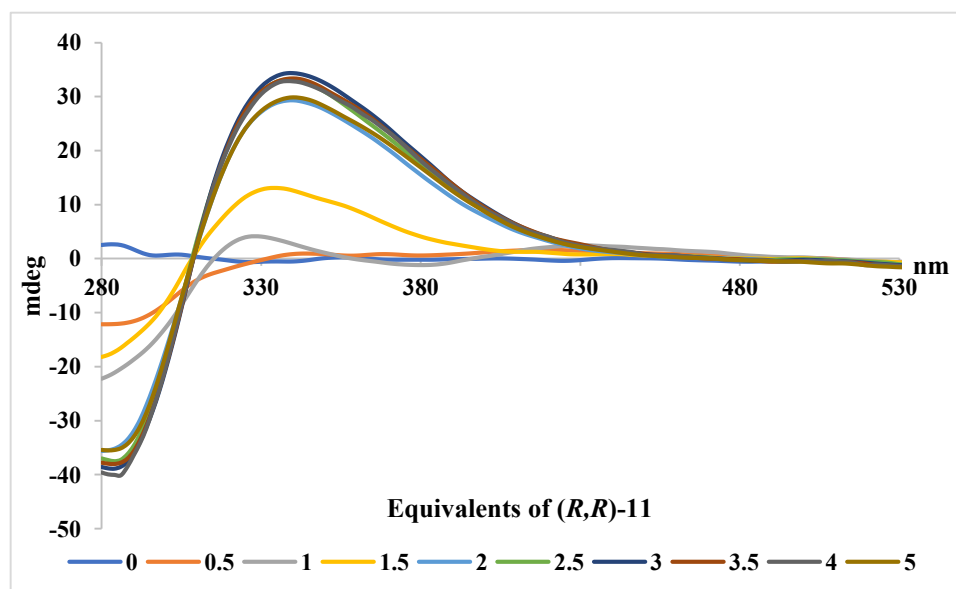
CD spectra of the assembly obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, and (*S,R*)-17 (0-5 equivalents) in DMSO at 0.9 mM.



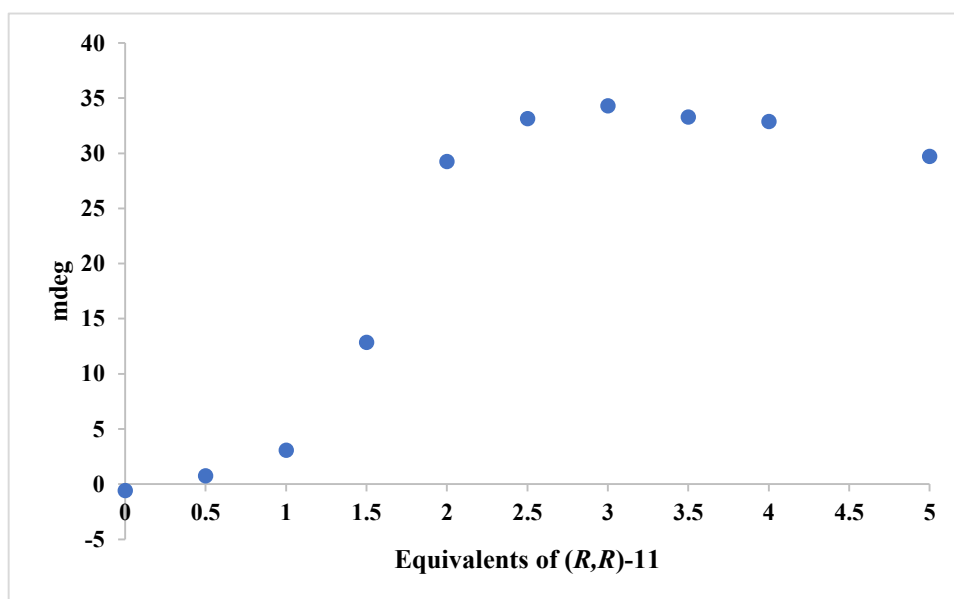
The CD signal at 380 nm increased steadily and reached a maximum in the presence of 2.5 equivalents of (*S,R*)-17.



CD spectra of the assembly obtained from $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, and (*R,R*)-11 (0-5 equivalents) in DMSO at 0.5 mM



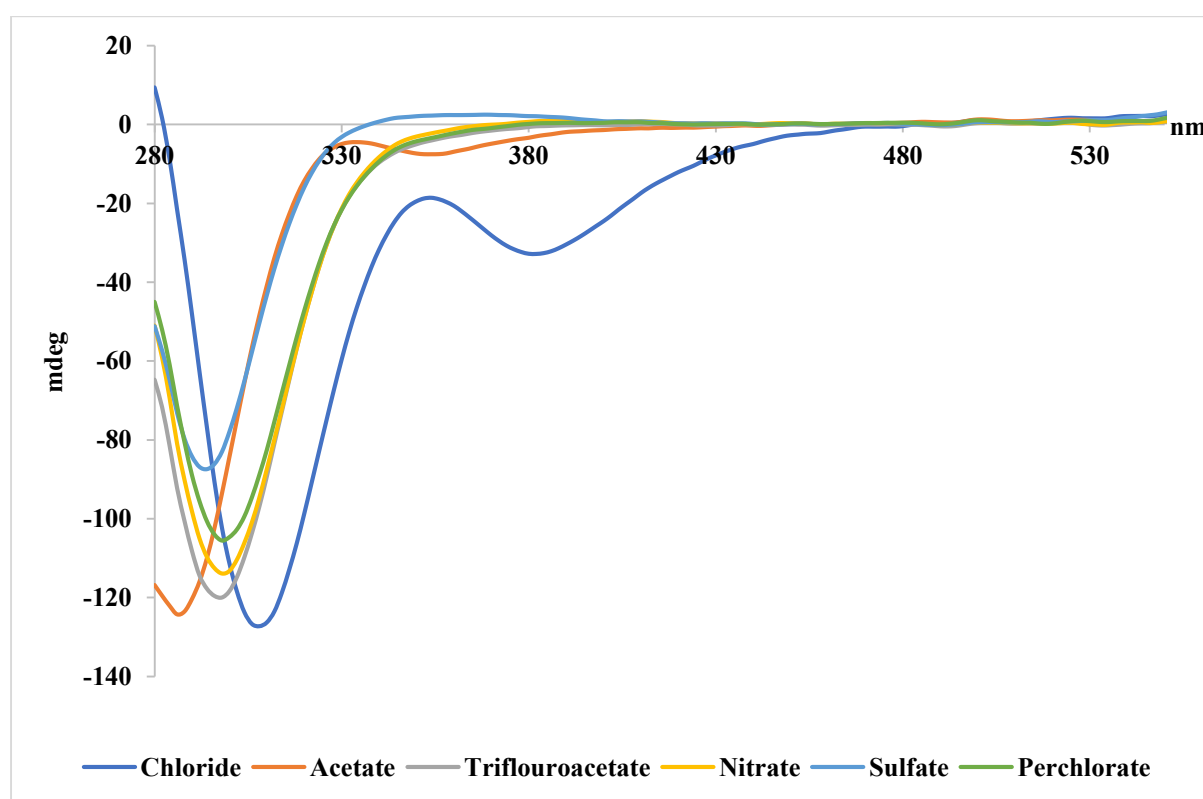
The CD signal at 338 nm increased steadily and reached a maximum in the presence of 3 equivalents of (*R,R*)-11.



3.3 Anion Effects

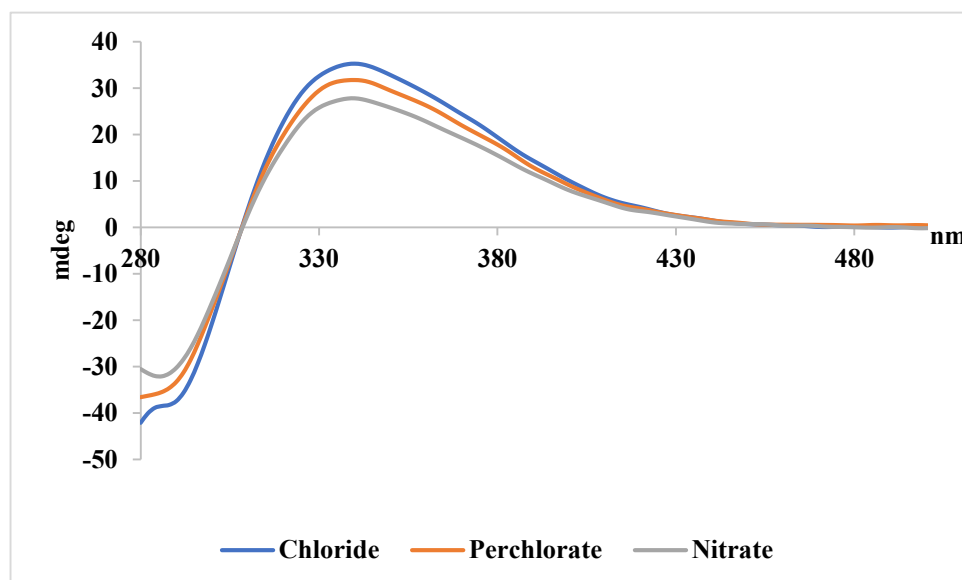
Stock solutions of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, $\text{Cu}(\text{OAc})_2$, $\text{Cu}(\text{CF}_3\text{CO}_2)_2$, $\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}$, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ and $\text{CuClO}_4 \cdot 6\text{H}_2\text{O}$ (0.02 M) in DMSO were prepared and 0.5 mL portions were transferred into 4 mL vials. A solution of **17** (0.50 M in DMSO) was prepared. To each vial containing 0.5 mL of the Cu(II) solution were added two equivalents (0.04 mL) of the substrate. CD analysis was performed by taking an aliquot (0.1 mL) of the reaction mixture and diluting it further with 2.0 mL of DMSO.

Anion effect study showing the CD spectra of different Cu(II) salts with (*S,R*)-**17** in DMSO at 0.9 mM.



Stock solutions of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{Fe}(\text{ClO}_4)_3$ and $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (0.0011 M) in DMSO were prepared and 0.5 mL portions were transferred into 4 mL vials. A solution of (*R,R*)-**11** (0.17 M in water) was prepared. An equimolar amount of TBAOH (1.0 M in MeOH) was also added. To each vial containing 0.5 mL of the Fe(III) solution were added three equivalents (0.06 mL) of the substrate. CD analysis was performed by taking an aliquot (0.05 mL) of the reaction mixture and diluting it further with 2.0 mL of DMSO.

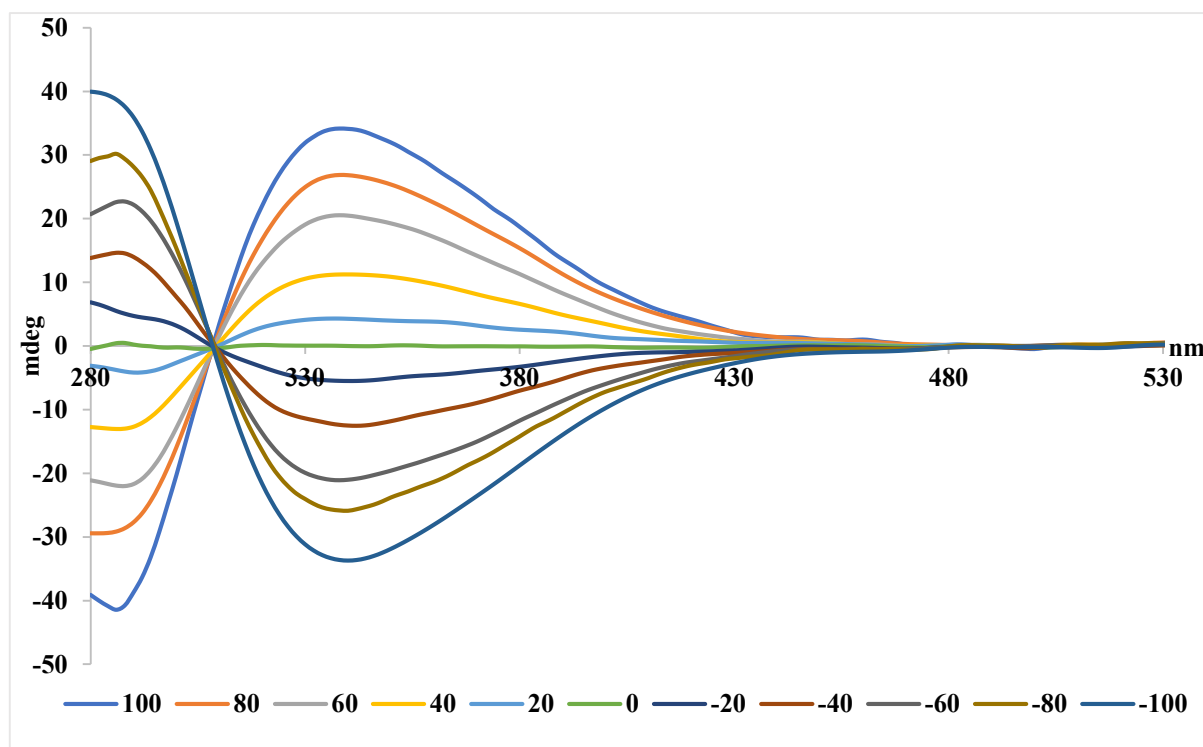
Anion effect study showing the CD spectra of different Fe(III) salts with (*R,R*)-**11** in DMSO at 0.5 mM.



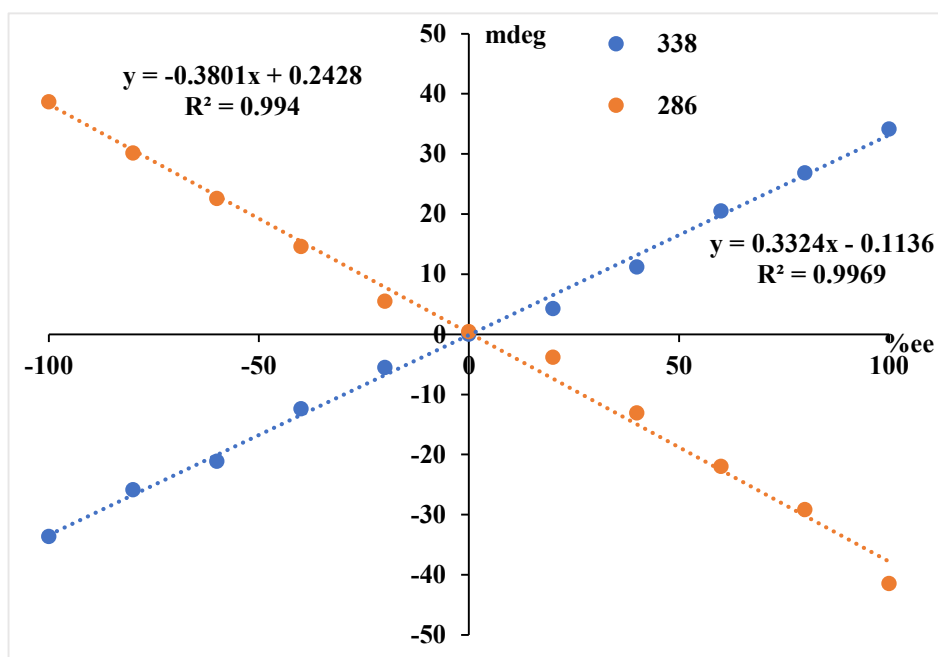
4. Quantitative Chiroptical Sensing

4.1 Ee Determination of Tartaric Acid with FeCl₃·6H₂O

A Stock solution of FeCl₃·6H₂O (0.0011 M) in DMSO was prepared and portions of 0.5 mL were transferred into 4 mL vials. Solutions of **11** (0.17 M in water) at varying ee compositions (+100.0, +80.0, +60.0, +40.0, +20.0, 0.0, -20.0, -40.0, -60.0, -80.0, -100.0) and an equimolar amount of TBAOH were prepared. To each vial containing 0.5 mL of the Fe(III) solution were added three equivalents of **11** (0.06 mL). The CD analysis was carried out as described above at a concentration of 0.5 mM. The CD amplitudes measured at 286 and 338 nm were plotted against %ee.



Linear relationship between the CD amplitudes at 286 and 338 nm and the enantiomeric excess of **11**



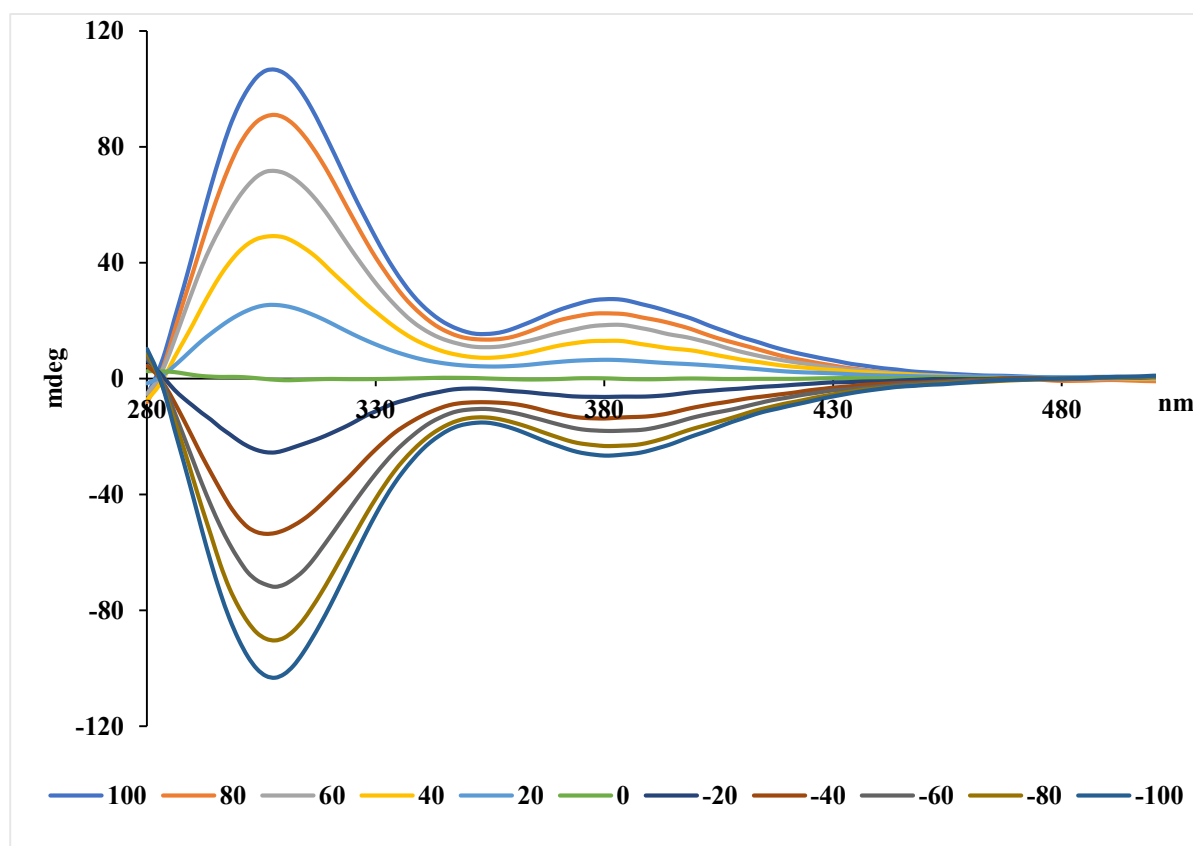
Ten scalemic samples of **11** were prepared and then treated with the Fe(III) salt as described above. Using the linear regression equations obtained from the calibration curves and the measured CD amplitudes at 286 and 338 nm, the enantiomeric excess and the absolute configuration of the major enantiomer were determined.

| Sample Composition | | Chiroptical Sensing (288 nm) | | Chiroptical Sensing (338 nm) | | Average |
|--------------------|------------|------------------------------|-----------------------------|------------------------------|-----------------------------|---------|
| Abs. Config. | Actual %ee | Abs. Config. ^a | Calculated %ee ^b | Abs. Config. ^a | Calculated %ee ^b | %ee |
| <i>R,R</i> | 88.0 | <i>R,R</i> | 85.2 | <i>R,R</i> | 84.8 | 85.0 |
| <i>R,R</i> | 82.0 | <i>R,R</i> | 80.3 | <i>R,R</i> | 83.8 | 82.0 |
| <i>R,R</i> | 61.0 | <i>R,R</i> | 59.0 | <i>R,R</i> | 59.1 | 59.1 |
| <i>R,R</i> | 46.0 | <i>R,R</i> | 38.6 | <i>R,R</i> | 34.5 | 36.5 |
| <i>R,R</i> | 27.0 | <i>R,R</i> | 22.4 | <i>R,R</i> | 17.9 | 20.1 |
| <i>S,S</i> | 16.0 | <i>S,S</i> | 15.3 | <i>S,S</i> | 12.8 | 14.1 |
| <i>S,S</i> | 33.0 | <i>S,S</i> | 27.5 | <i>S,S</i> | 29.7 | 28.6 |
| <i>S,S</i> | 57.0 | <i>S,S</i> | 66.3 | <i>S,S</i> | 64.4 | 65.4 |
| <i>S,S</i> | 76.0 | <i>S,S</i> | 75.3 | <i>S,S</i> | 72.6 | 74.0 |
| <i>S,S</i> | 94.0 | <i>S,S</i> | 97.2 | <i>S,S</i> | 98.5 | 97.9 |

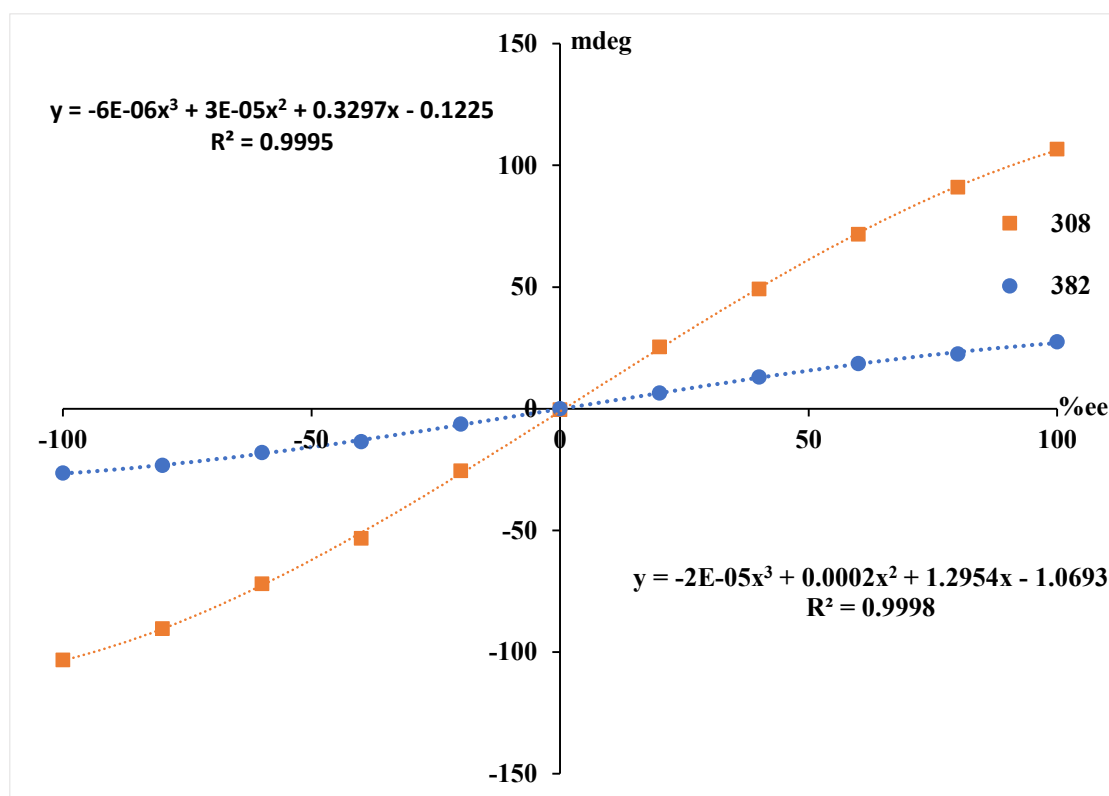
^aBased on the sign of the CD response. ^bBased on the amplitude of the CD response.

4.2 Ee Determination of *cis*-Aminoindanol with CuCl₂·2H₂O

A Stock solution of CuCl₂·2H₂O (0.025 M) in DMSO was prepared and portions of 0.5 mL were transferred into 4 mL vials. Solutions of **17** (0.50 M in DMSO) at varying ee compositions (+100.0, +80.0, +60.0, +40.0, +20.0, 0.0, -20.0, -40.0, -60.0, -80.0, -100.0). To each vial containing 0.5 mL of the Cu(II) solution were added three equivalents of **17** (0.06 mL). The CD analysis was carried out as described above at a concentration of 0.9 mM. The CD amplitudes measured at 308 and 382 nm were plotted against %ee.



Polynomial relationship between the CD amplitudes at 308 and 382 nm and the enantiomeric excess of **17**



Five scalemic samples of **17** were prepared and then treated with the Cu(II) salt as described above. Using the linear regression equations obtained from the calibration curves and the measured CD amplitudes at 308 and 382 nm, the enantiomeric excess and the absolute configuration of the major enantiomer were determined.

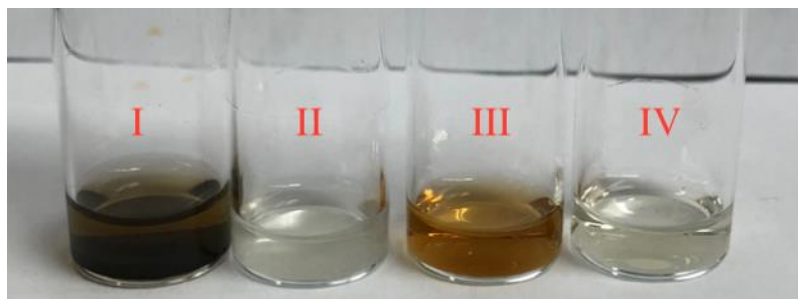
| Sample Composition | | Chiroptical Sensing (308 nm) | | Chiroptical Sensing (382 nm) | | Average |
|--------------------|------------|------------------------------|-----------------------------|------------------------------|-----------------------------|---------|
| Abs. Config. | Actual %ee | Abs. Config. ^a | Calculated %ee ^b | Abs. Config. ^a | Calculated %ee ^b | %ee |
| <i>RS</i> | 88.0 | <i>RS</i> | 88.1 | <i>RS</i> | 87.1 | 87.6 |
| <i>RS</i> | 46.0 | <i>RS</i> | 48.3 | <i>RS</i> | 48.2 | 48.2 |
| <i>SR</i> | 16.0 | <i>SR</i> | 14.2 | <i>SR</i> | 14.3 | 14.3 |
| <i>SR</i> | 76.0 | <i>SR</i> | 75.0 | <i>SR</i> | 73.3 | 74.2 |
| <i>SR</i> | 94.0 | <i>SR</i> | 95.2 | <i>SR</i> | 88.6 | 91.9 |

^aBased on the sign of the CD response. ^bBased on the amplitude of the CD response.

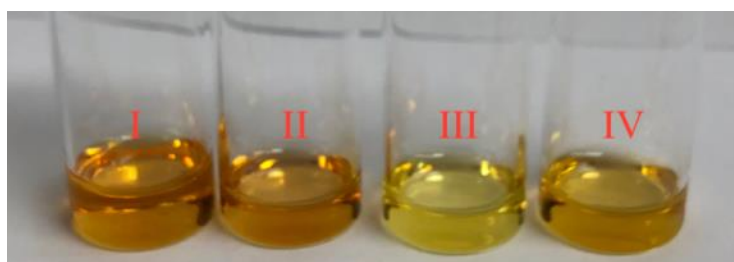
5. Colorimetric Detection

Samples were prepared as described above. The mixtures (2.0 mM) were stirred for 1 hour at 25 °C and the images were obtained. The $\text{Pd}(\text{NO}_3)_2$ samples were prepared in MeOH, while all other metal solutions were prepared in DMSO.

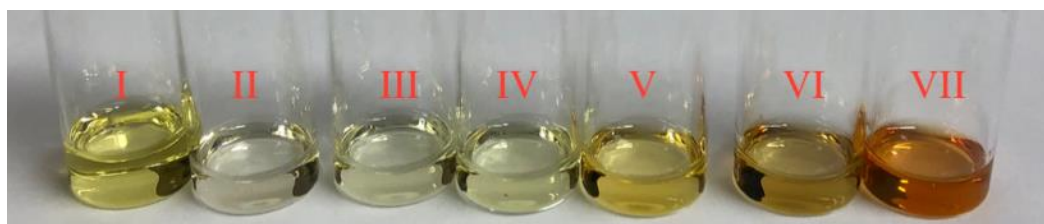
A) $\text{Pd}(\text{NO}_3)_2$: No substrate (I), (*R*)-**1** (II), (*R*)-**15** (III) and (*S,R*)-**17** (IV).



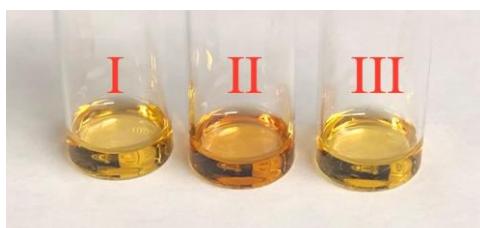
B) $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$: No substrate (I), (*R*)-**1** (II), (*R*)-**15** (III) and (*S,R*)-**17** (IV).



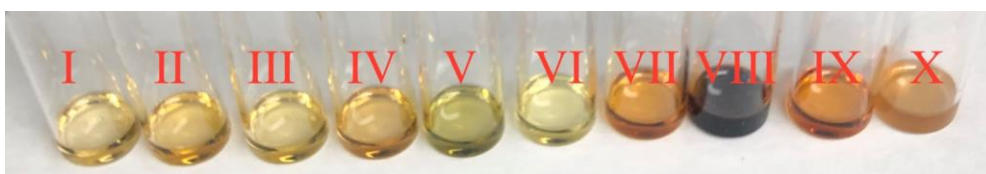
C) $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: No substrate (I), (*R*)-**1** (II), (*R*)-**15** (III), (*R,R*)-**11** (IV), (*S,R*)-**17** (V), (*R,R*)-**22** (VI) and (*R*)-**26** (VII).



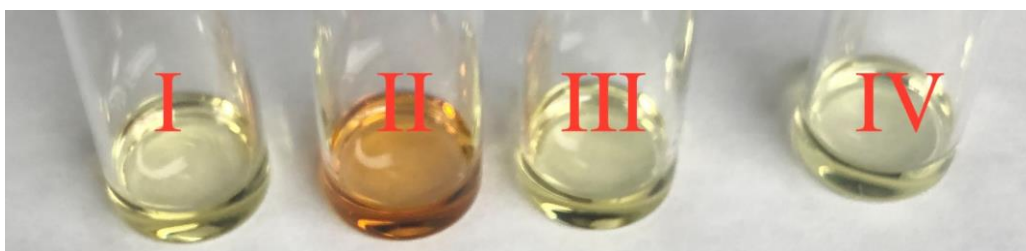
D) $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ in DMSO: (*R*)-**17** (I), (*S,R*)-**18** (II), (*R,R*)-**21** (III).



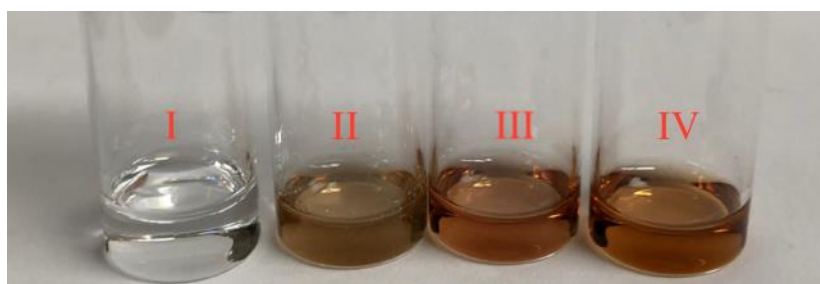
E) $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: (*R*)-**1** (I), (*R*)-**2** (II), (*R*)-**3** (III), (*R*)-**4** (IV), (*R*)-**5** (V), (*R*)-**6** (VI), (*R*)-**7** (VII), (*R*)-**8** (VIII), (*R*)-**9** (IX), and (*R*)-**10** (X).



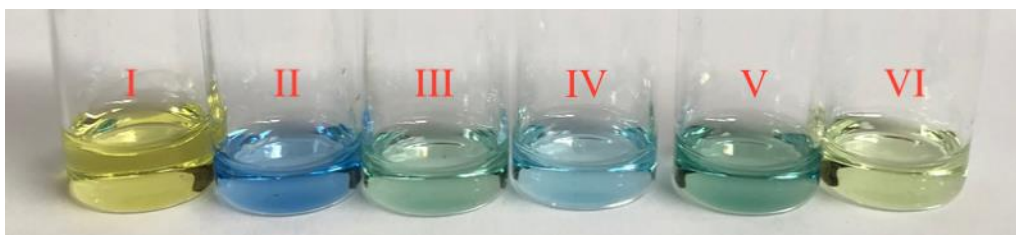
F) $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$: (*R,R*)-**11** (IV), (*R*)-**13** (III), (*R*)-**15** (IV) and (*R*)-**16** (IV).



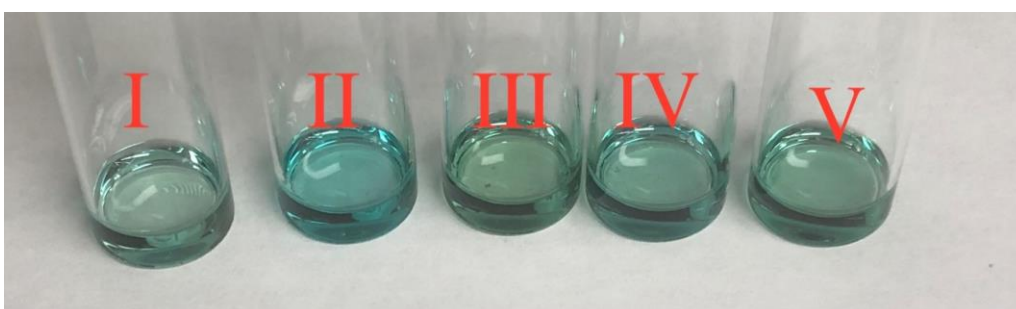
G) $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$: No substrate (I), (*R*)-**1** (II), (*R*)-**15** (III) and (*S,R*)-**17** (IV).



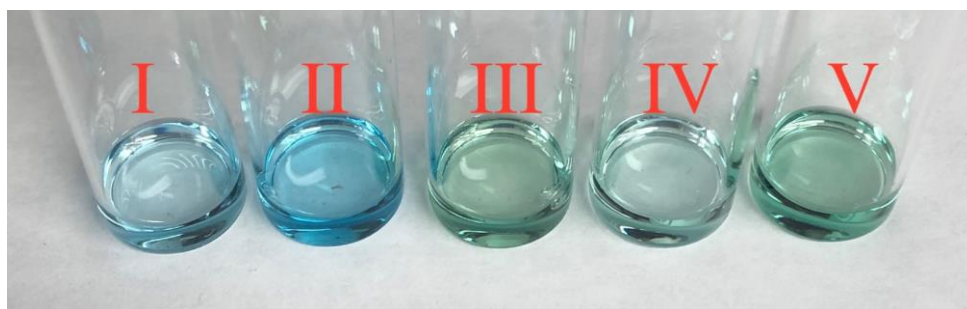
H) $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$: No substrate (I), (*R*)-**1** (II), (*R*)-**15** (III), (*R,R*)-**11** (IV), (*S,R*)-**17** (V) and (*R*)-**25** (VI).



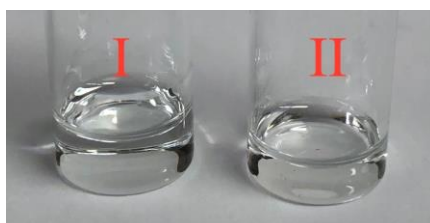
I) $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$: (*S,R*)-**17** (I), (*S,R*)-**18** (II), (*R,R*)-**19** (III), (*S,R*)-**20** (IV) and (*R,R*)-**21** (V).



J) $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$: (*R,R*)-**11** (I), (*R*)-**13** (II), (*R*)-**14** (III), (*R*)-**15** (IV) and (*R*)-**16** (V).



K) $\text{Ce}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$: No substrate (I), (*R*)-**1** (II).



L) $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$: No substrate (I), (*R*)-**1** (II), (*R*)-**15** (III), (*S,R*)-**17** (IV) and (*R*)-**25** (V).

