Electronic Supplementary Information

Taking Advantage of Co(II) Induced Enhanced VCD for the Fast and Sensitive Determination of Enantiomeric Excess

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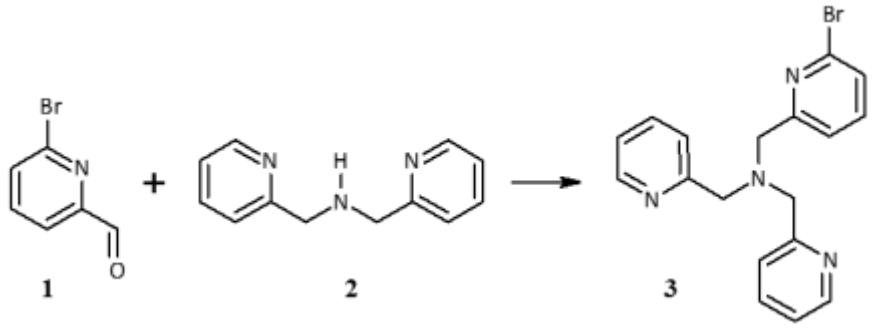
1. Experimental section

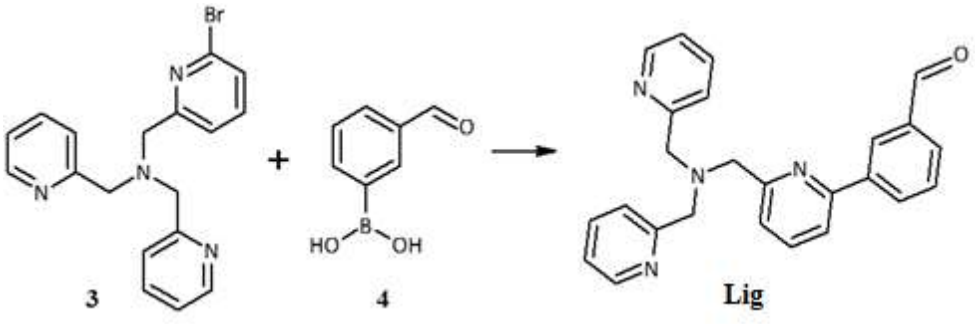
The syntheses of the ligand and of Co(II) stereodynamic probe were carried out according to the procedure reported by Zonta and coworkers.

1-(6-Bromopyridn-2-yl)-N,N-*bis*(pyridin-2-ylmethyl)methanamine (3)



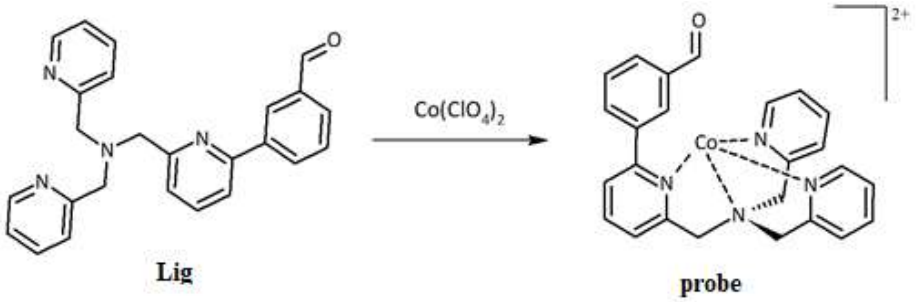
6-bromopyridine-2-carboxyaldehyde **1** (0.988 g, 5.33 mmol) and 2-pycolylamine **2** (960 µL, 5.33 mmol) were stirred for 1 hour in 40 mL of anhydrous THF under nitrogen. $Na(OAc)_3BH$ (1.127 g, 5.33 mmol) was then added. The mixture was stirred overnight at room temperature (r.t.) under nitrogen gas. The reaction solution was washed three times with a saturated $NaHCO_3$ aqueous solution and then the organic phase was dried on sodium sulphate and filtered. The solvent was removed under reduced pressure yielding the crude product **3** as a brown solid. The product was employed in the next synthetic steps without any purification. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.51 (d, 2H), 7.63 (t, 2H), 7.52 (m, 4H), 7.31 (d, 1H), 7.13 (dd, 2H), 3.9 (d, 6H). ^{13}C NMR (600 MHz, $CDCl_3$): δ = 161.1, 158.2, 148.9, 141.2, 138.6, 136.5, 126.2, 123, 122.1, 121.8, 60.1, 59.5.

[6-(3-formylphenyl)-2-pyridylmethyl]-*bis*(2-pyridylmethyl)amine (Lig)



1-(6-Bromopyridn-2-yl)-N,N-*bis*(pyridin-2-ylmethyl)methanamine **3** (1.6 g, 4.31 mmol), formylphenylboronic acid **4** (1.00 g, 6.7 mmol), $Pd(PPh_3)_4$ (0.505 g, 0.43 mmol) and anhydrous Na_2CO_3 (1.184 g, 11.11 mmol) were dissolved in a degassed 1/1/0.5 mixture of water/toluene/methanol (45 mL) under a nitrogen atmosphere. The mixture was stirred for 15 hours at 90 °C. the solvent was removed under vacuum and the obtained solid was dissolved in $CHCl_3$. The solution was extracted three times with a 5% HCl solution. The aqueous solution was then basified with NaOH and extracted three times with $CHCl_3$. The organic phase was dried over Na_2SO_3 and filtered. The solvent was removed under reduced pressure and the product **Lig** was obtained without further purification as a brownish oil (1.58 g, 4.14 mmol). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.11 (s, 1H), 8.53 (m, 3H), 8.30 (d, 1H), 7.92 (d, 1H), 7.76 (t), 7.64 (m), 7.57 (d), 7.11 (td,), 3.96 (s, 2H), 3.91 (s, 4H).

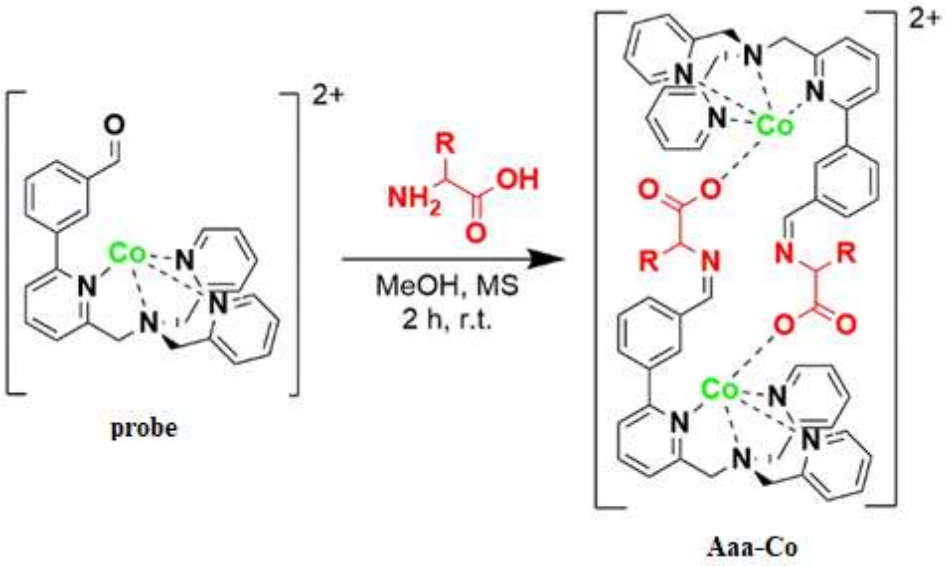
Stereodynamic Co(II) probe



Lig **probe**

1 equivalent of **Lig** was dissolved in the minimum amount of anhydrous acetonitrile and 1 equivalent of hexa-hydrated Co(II) perchlorate was added. The mixture was left standing for 15 minutes at room temperature and then the solvent was evaporated under reduced pressure. The product was obtained as a purple solid (80% yield) and was employed without any purification.

Probe-analyte complexes (Aaa-Co)



probe **Aaa-Co**

Enantiopure amino acids were dissolved in water to obtain standard solutions for each analyte. In a round-bottom flask the desired mixture of the solutions of the enantiomers of each amino acid was

added (1 equivalent). Water was removed under reduced pressure. Previously activated molecular sieves at 110 °C and the stereodynamic Co(II) probe (1 equivalent) were added. The reagents were dissolved in methanol to reach a final 7.5 mM concentration of the probe. The mixture was stirred for 2 hours at room temperature. The probe-analyte complex was obtained by solvent removing under reduced pressure.

2. Chiroptical analysis

ECD measurements

ECD spectra were recorded with a Jasco J-710 using a quartz cell with an optical pathlength of 1 cm. The samples were prepared by diluting 10 µL of the reaction solution to a final volume of 2.5 mL

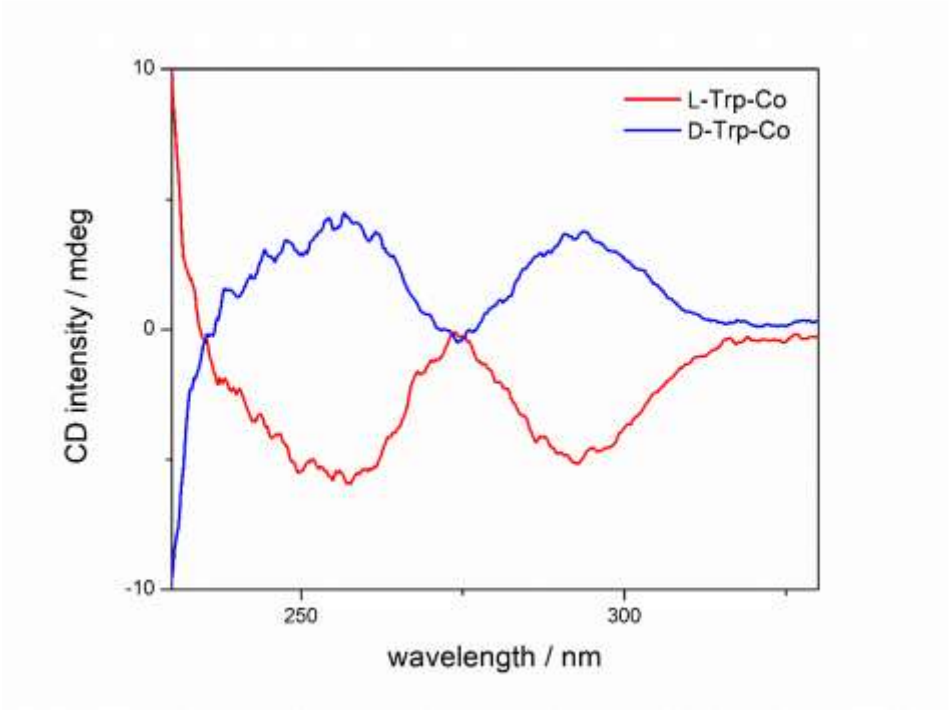


Fig. S1 ECD spectra normalized on the most intense UV/Vis band for the probe-analyte complexes of the enantiopure L-tryptophan (red) and D-tryptophan (blue).

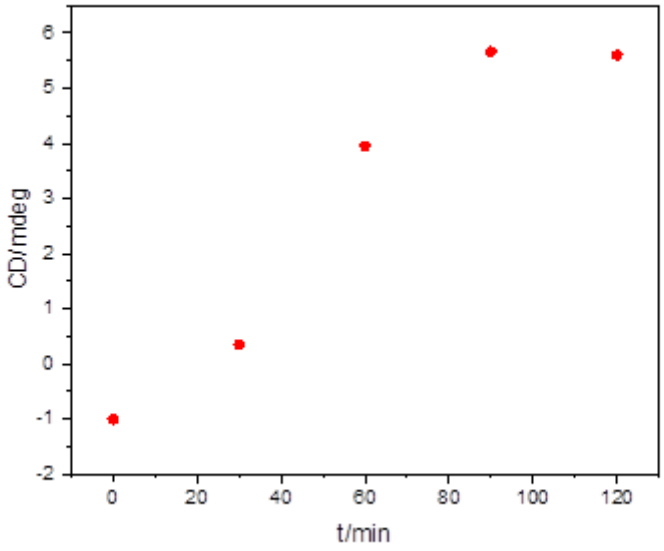


Fig. S2: plot of the CD intensity at 293 nm vs time for the assembly of the **Trp-Co** complex.

VCD measurements

VCD spectra were recorded on a spectropolarimeter Jasco FVS 6000 using KBr cell with an optical pathway of 64 µm. The samples were obtained by dissolving Aaa-Co in deuterated acetonitrile (150 µL every 10 mg of the starting stereodynamic probe). Because the spectra were recorded with not purified samples, each VCD spectrum is normalized on the most intense IR band.

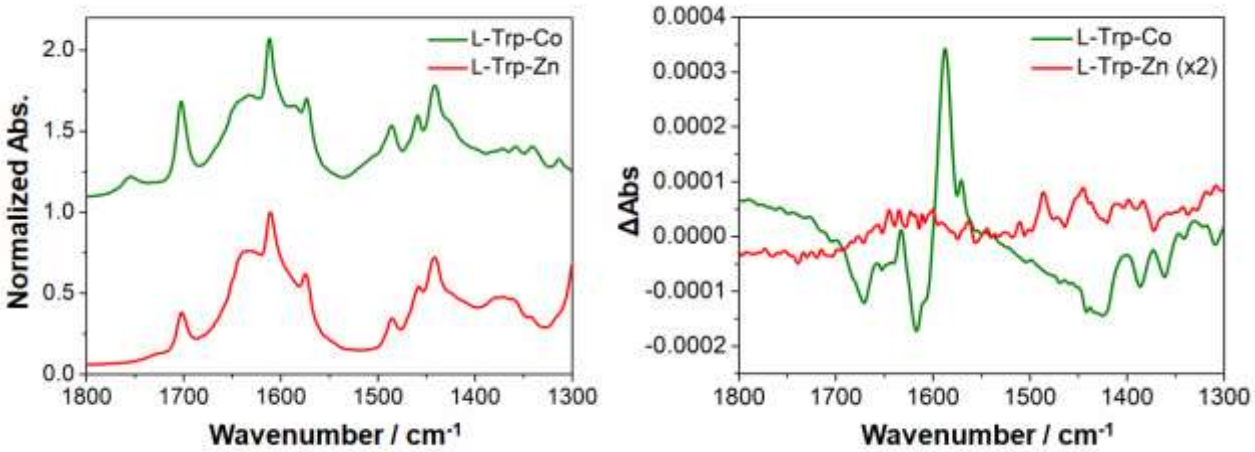


Fig. S3: offset normalized IR spectra (left) and normalized VCD spectra (right) of the enantiopure **Trp-Co** (green) and **Trp-Zn** (red) complexes. The Co(II)-induced signal enhancement is evident in the VCD spectra, while the IR absorptions are almost superimposable for both the Zn(II) and Co(II) systems.

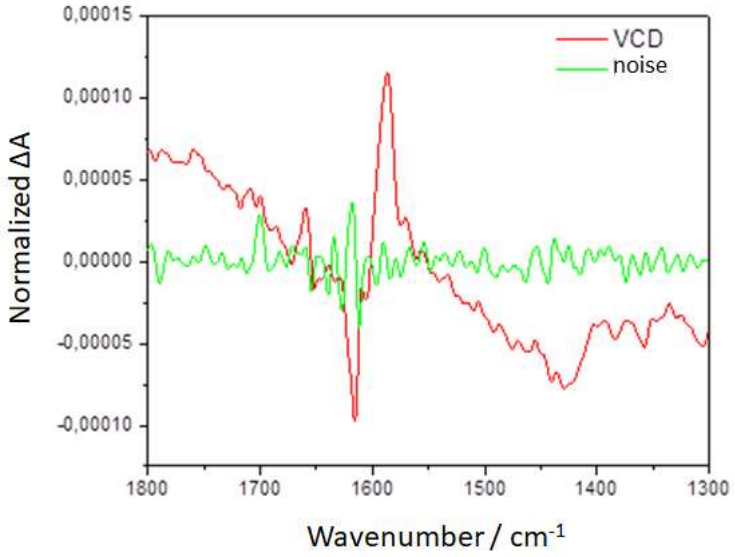


Fig. S4: normalized VCD spectra of the **Trp-Co** at 25% of enantiomeric excess (red) and the so-called "noise channel" of the VCD instrument, which measures the differences between the already accumulated VCD spectrum and the following VCD acquisition. The 1600 cm^{-1} centred bands are more intense than the green line.

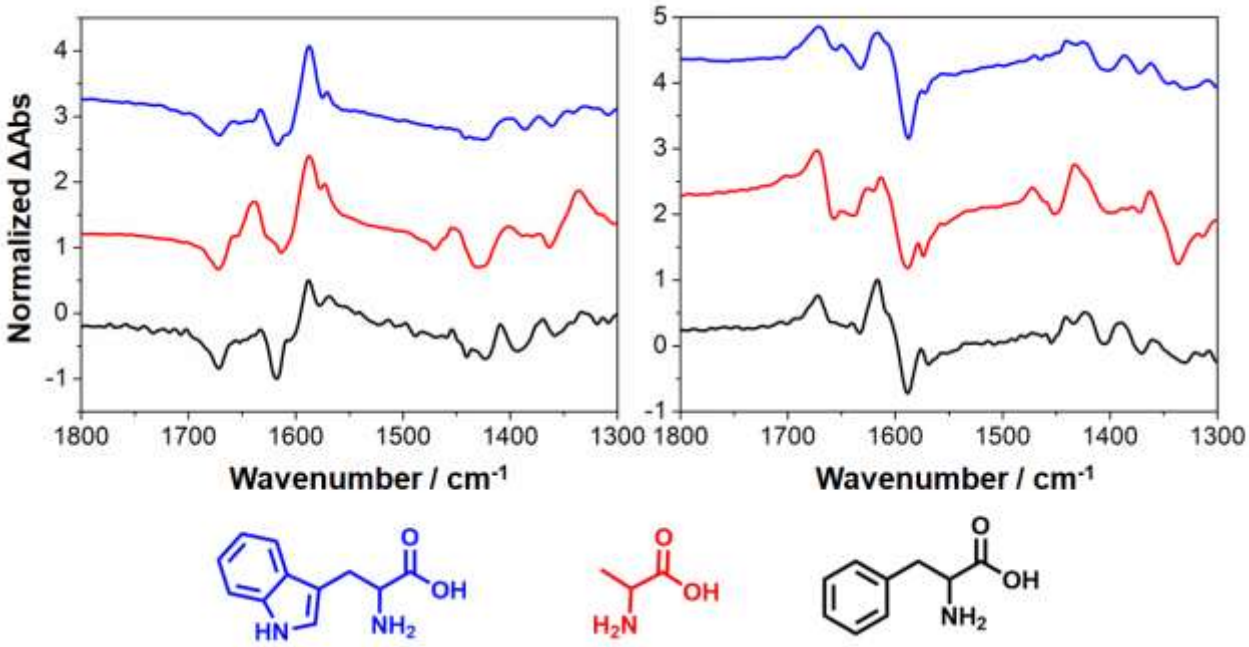


Fig. S5: normalized VCD spectra of the L-series (left) and D-series (right) of the **Aaa-Co** for the three tested amino acids: tryptophan (blue), alanine (red) and phenylalanine (black). It is evident that VCD signals pattern essentially depends on the absolute configuration of the analytes.

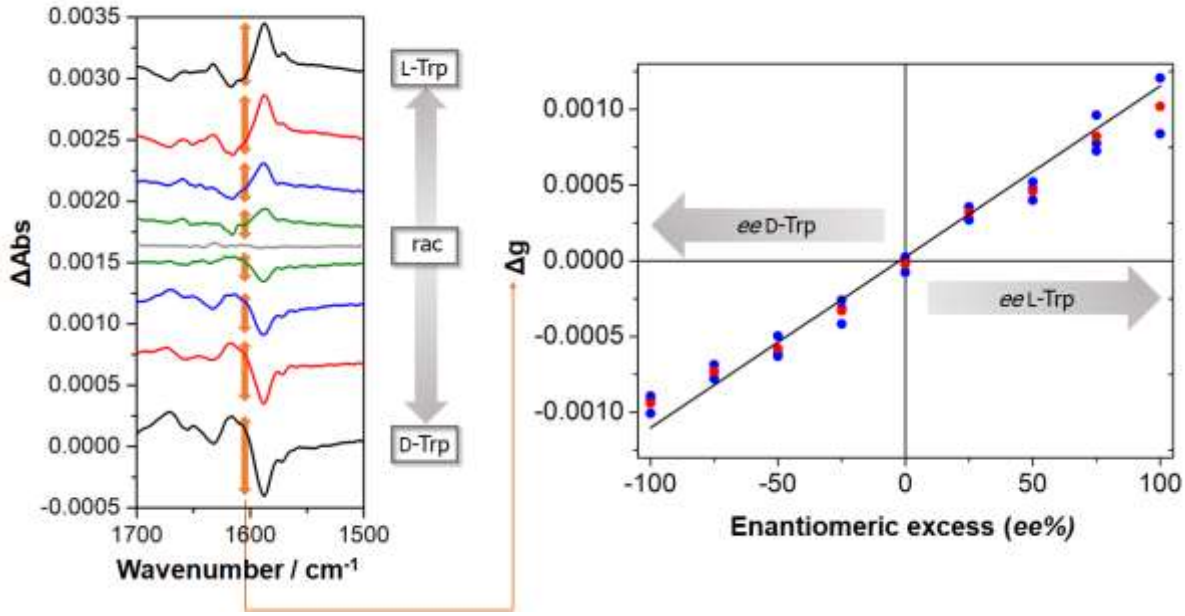


Fig. S6: normalized VCD spectra (left) of **Trp-C**o at different enantiomeric composition of the analyte (from pure L-Trp at the top to pure D-Trp at the bottom). The orange arrows indicate the nearby opposite signals whose g differences were employed to obtain the calibration curve showed at the right.