Chiral Zn-Salen Complexes: A New Class of Fluorescent Receptors for the Enantiodiscrimination of Chiral Amines

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Electronic Supporting Information

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General experimental methods. The NMR experiments were carried out at 27° C on a Varian UNITY Inova 500 MHz spectrometer (^{1}H at 499.88 MHz, ^{13}C-NMR at 125.7 MHz) equipped with pulse field gradient module (Z axis) and a tuneable 5 mm Varian inverse detection probe (ID-PFG). ESI mass spectra were acquired on a ES-MS Thermo-Finnigan LCQ-DECA using MeOH (positive ion mode). A JASCO V-560 UV-Vis spectrophotometer equipped with a 1 cm path-length cell was used for the UV-Vis measurements. Luminescence measurements were carried out using a Cary Eclipse Fluorescence spectrophotometer with resolution of 0.5 nm, at room temperature. The emission was recorded at 90° with respect to the exciting line beam using 5:5 slit-widths for all measurements. All chemicals were reagent grade and were used without further purification. 3D minimized structures reported in the manuscript were obtained using HyperChem v8.0.7, MM+ force field.

General procedure for the synthesis of Zn-Salen complexes. Compounds **1** and **2** were obtained from the corresponding ligands using diethylzinc in toluene. Corresponding ligands were synthesised according to the literature procedure.[1] To 1 mmol of ligand dissolved in 25 ml of toluene dry, 1 mmol of diethylzinc (1 M in hexane, Aldrich) was added. Reaction was stirred under nitrogen for 24 h, thus the solvent was removed under reduced pressure. The crude product was dissolved in methanol and filtered, leading pure Zn-Salen complex (isolated yield 95% for **1**, 75% for **2**).

Procedure for fluorescence titrations. Two mother solutions of the appropriate receptor and guest (1.0×10^{-3} M) in toluene or methanol were prepared. From these, different solutions with different ratio receptor/guest were prepared as reported below, and emission spectra, normalized to eliminate dilution effect, were recorded. Fluorescence titrations with host **1** was carried out using λ_{exc} = 375 nm in toluene and 360 nm in methanol, recording at λ_{em} = 474 nm at 25 °C. Fluorescence titrations with host **2** was carried out using λ_{exc} = 380 nm and recording at λ_{em} = 486 nm in methanol at 25 °C. With this data treatment, the apparent binding affinities of receptors with selected guest were estimated using HypSpec (version 1.1.33),[2] a software designed to extract equilibrium constants from potentiometric and/or spectrophotometric titration data. HypSpec starts with an assumed complex formation scheme and uses a least-squares approach to derive the spectra of the complexes and the stability constants. χ^2 test (chi-square) was applied, where the residuals follow a normal distribution (for a distribution approximately normal, the χ^2 test value is around 12 or less). In all of the cases, $\chi^2 \leq 10$ were found, as obtained by 3 independent measurements sets.

Determination of Stoichiometry. Stoichiometry of the complexes were investigated by the Job's plot method, using spectrophotometric measurements. The samples were prepared by mixing equimolecular stock solutions (2×10^{-4} M) of the appropriate host and guest to cover the whole range of molar fractions keeping constant the total concentration (1×10^{-5} M). The changes in absorbance at 360 nm (for host **1**), and 380 nm (for host **2**) compared to uncomplexed receptor species ($\Delta I \times \chi^{-1}$) were calculated and reported versus the receptor mole fraction (χ). These plot show invariably a maximum at 0.5 mol fraction of receptor suggesting its 1:1 complex formation.

DOSY experiments. Diffusion-Ordered SpectroscopY (DOSY) NMR has been used to determine the presence of monomeric or higher species in solution. The DOSY technique provides information about the size of the molecular aggregate in solution. In fact, by means of the Stokes–Einstein equation, the diffusion coefficient of the compound can be converted into its hydrodynamic radius R_h and this value can be compared with the calculated radius obtained by Hyperchem-minimized structure of the complexes. Furthermore, diffusion coefficient value can be associated to the molecular weight, by the mathematic treatment recently described.[3] DOSY experiments on compound **1** in toluene-d_8 (10 mM) show a diffusion coefficient of 5.44×10^{-10} m^2 s^{-1}, corresponding to a calculated molecular weight of ca. 1174

(dimeric form, experimental molecular weight of dimer is 1192). While in methanol-d_4, a solution of **1** (10 mM) shows a diffusion coefficient of 6.51×10^{-10} m^2 s^{-1}, (calculated molecular weight of 587, experimental molecular weight is 596) corresponding to the monomeric form. Receptor **2** shows a diffusion coefficient of 5.97×10^{-10} m^2 s^{-1} (calculated molecular weight of 718, experimental molecular weight is 708), relative to monomer in methanol (10 mM), and a diffusion coefficient of 4.89×10^{-10} m^2 s^{-1} (calculated molecular weight of 1493, experimental molecular weight is 1416), relative to the dimer in toluene-d_8 (10 mM).

Synthesis of metal complex 1 and 2. Hosts **1** and **2** were synthesised following the general procedure. Characterization of metal complex **1**: ^{1}H NMR (500 MHz, CD_3OD): δ 8.13 (s, 2H), 7.26-7.33 (m, 12H), 6.94 (d, J = 3 Hz, 2H), 6.80 (d, J = 9 Hz, 2H), 5.05 (s, 2H), 1.22 (s, 18H). ^{13}C NMR (125.7 MHz, CD_3OD) 171.3, 132.7, 132.0, 129.96, 129.91, 129.2, 123.4, 120.2, 74.1, 72,4, 34.5, 31.8. δ ESI-MS: *m/z* 619.6 $[M+Na]^+$ (expected *m/z* 619.0). Anal. Calcd. for $C_{36}H_{38}N_2O_2Zn$: C, 72.54; H, 6.43; O, 5.37. Found: C, 72.51; H, 6.39; O, 5.32.

Characterization of metal complex **2**: ^{1}H NMR (500 MHz, CD_3OD): δ 8.00 (s, 2H), 7.26-7.33 (m, 12H), 6.64 (d, J = 2 Hz, 2H), 4.99 (s, 2H), 1.54 (s, 18H), 1.21 (s, 18H). ^{13}C NMR (125.7 MHz, CD_3OD) 170.8, 142.6, 137.2, 130.3, 129.7, 129.1, 128.4, 127,5, 120.1, 119.6, 81.2, 37.9, 35.9, 31.9, 30.1. ESI-MS: 731.6 $[M+Na]^+$ (expected *m/z* 731.3). Anal. Calcd. for $C_{44}H_{54}N_2NaO_2Zn$: C, 72.27; H, 7.44; O, 4.38. Found: 72.21; H, 7.41; O, 4.32.

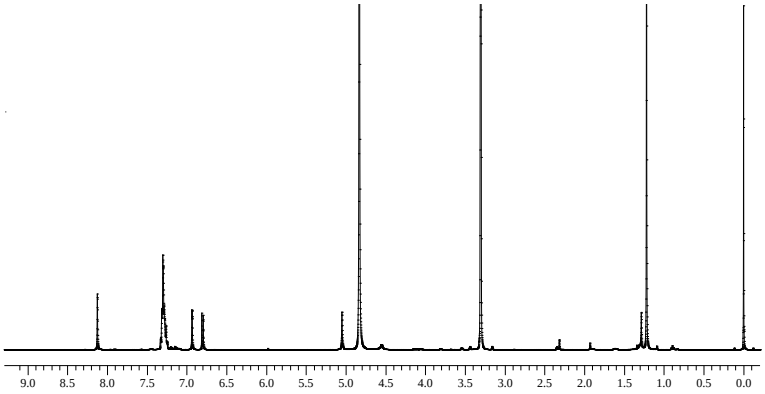

Figure S1. ^{1}H NMR spectrum of **1** in CD_3OD.

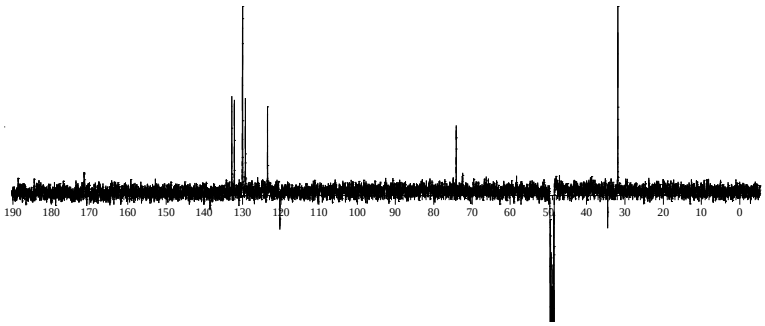

Figure S2. APT spectrum of **1** in CD_3OD

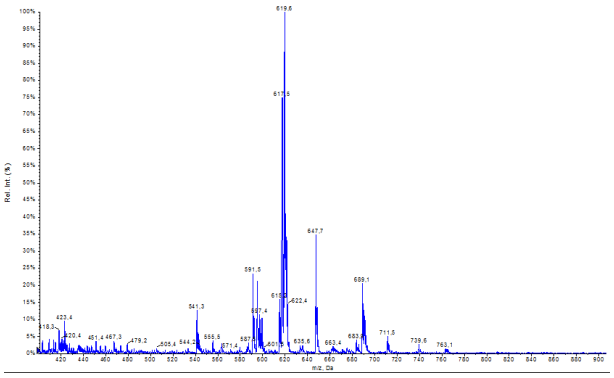

Figure S3. ESI-MS spectrum of **1.**

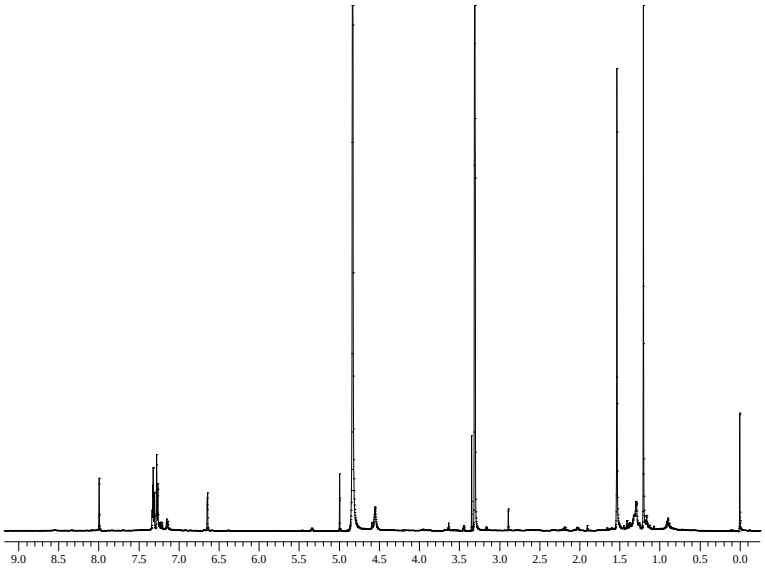

Figure S4. ^{1}H NMR spectrum of **2** in CD_3OD.

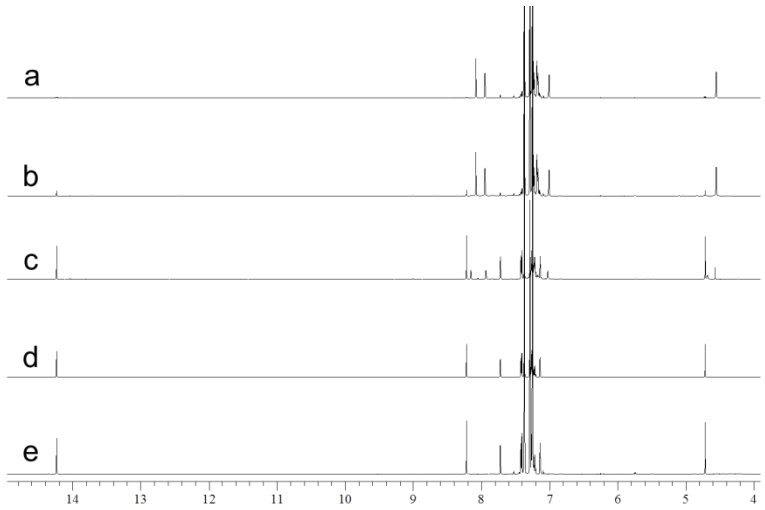

Figure S5. ^{1}H NMR spectra of **2** in toluene-d_8: a) freshly prepared; b) after 6h; b) after 12h; d) after 24h; e) corresponding salen ligand in toluene-d_8. The progressive increase of signals relative to the salen ligand (OH at 14.2 ppm and immine proton at 8.22 ppm are indicative) and the disappearance of original signal of the metal complex suggests the demetalation of Zn from the ligand in toluene.

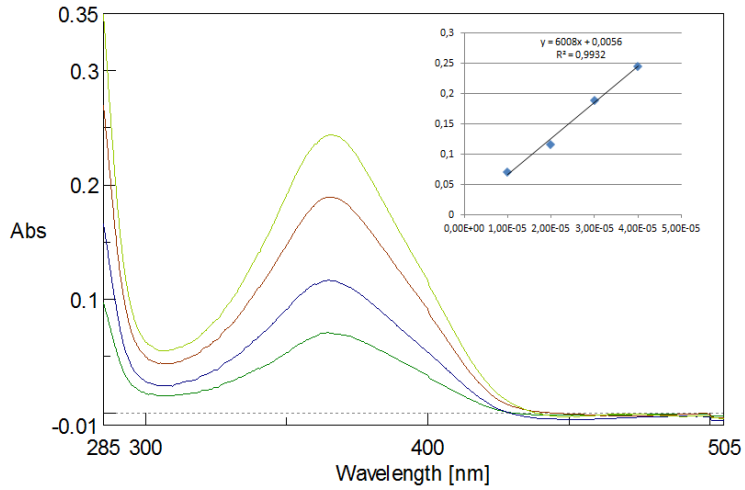

Figure S6. UV-VIS spectra of **1** in toluene at different concentrations (from 1×10^{-5} M to 4×10^{-5} M), inset shows the plot for the ε determination.

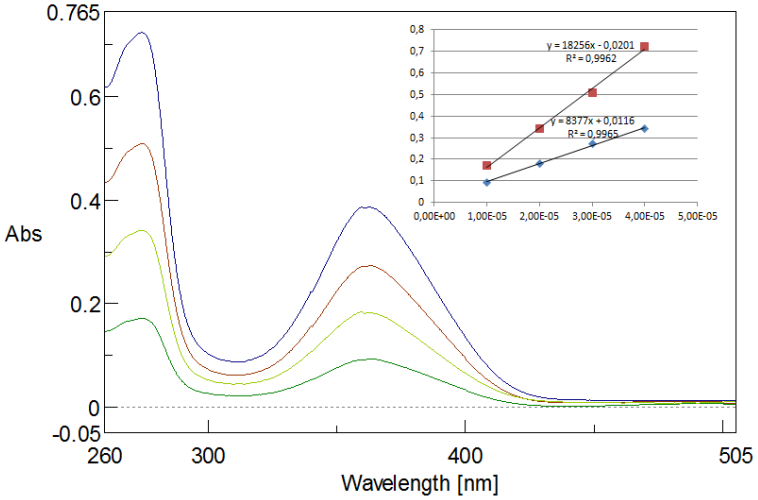

Figure S7. UV-VIS spectra of **1** in methanol at different concentrations (from 1×10^{-5} M to 4×10^{-5} M), inset shows the plot for the ε determination at 274 nm and 360 nm.

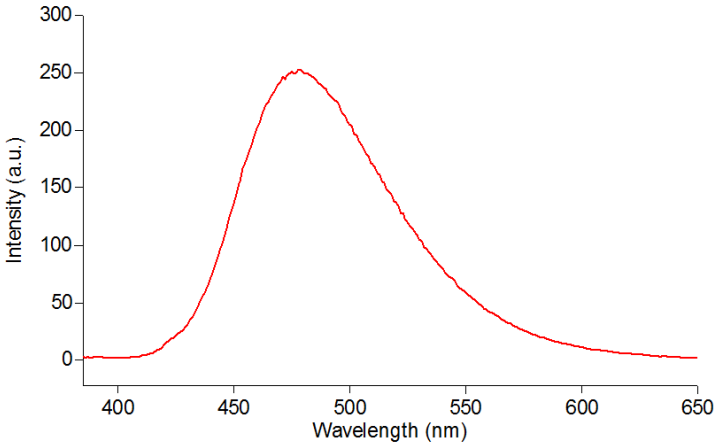

Figure S8. Emission spectrum of **1** in toluene (1×10^{-5} M, λ_{exc} = 375 nm).

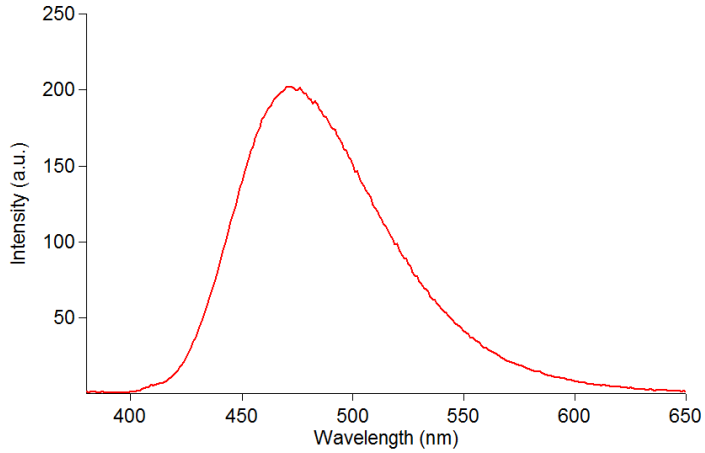

Figure S9. Emission spectrum of **1** in methanol (1×10^{-5} M, λ_{exc} = 375 nm).

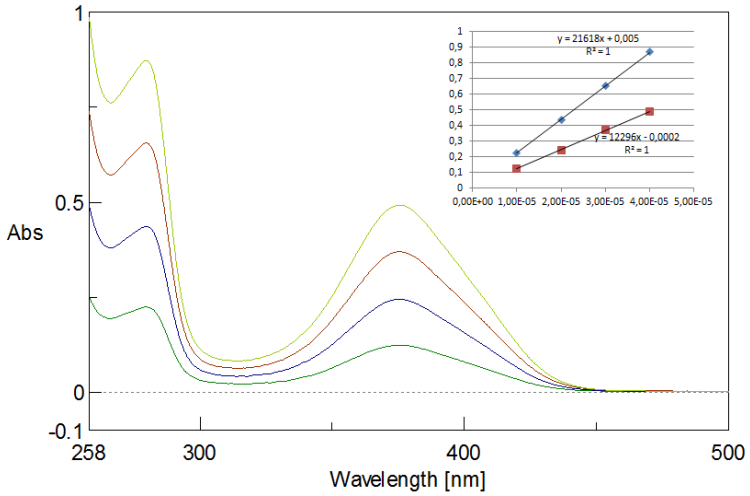

Figure S10. UV-VIS spectra of **2** in methanol at different concentrations (from 1×10^{-5} M to 4×10^{-5} M), inset shows the plot for the ε determination at 280 nm and 376 nm.

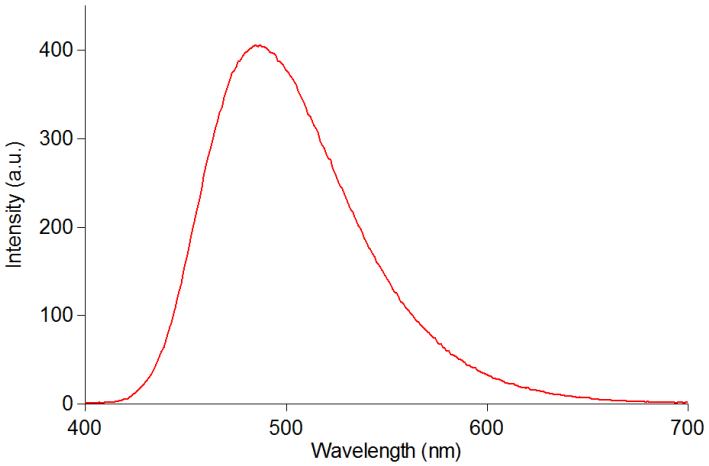

Figure S11. Emission spectrum of **2** in methanol (1×10^{-5} M, λ_{exc} = 375 nm).

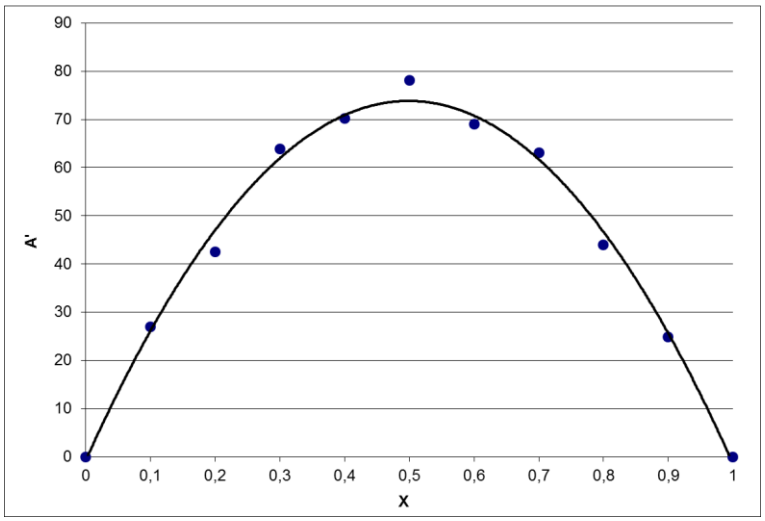

Figure S12. Job's Plot between **1** and *D*-Ala-Boc in toluene.

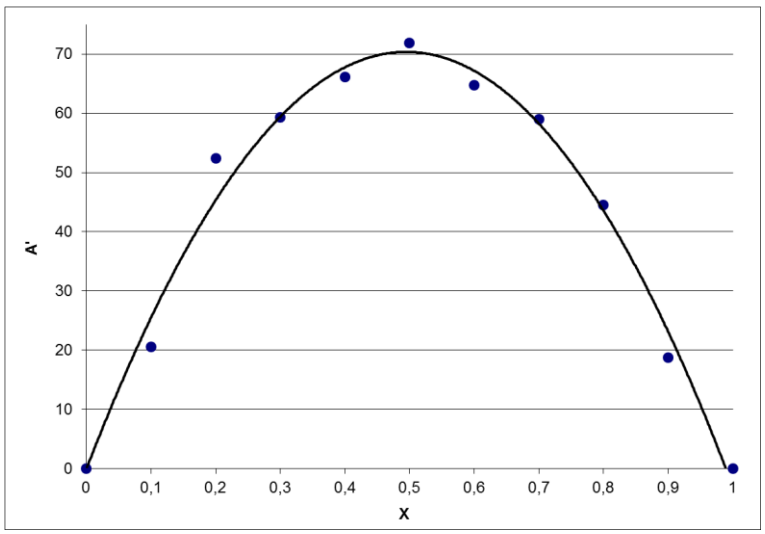

Figure S13. Job's Plot between **1** and acetone in toluene.

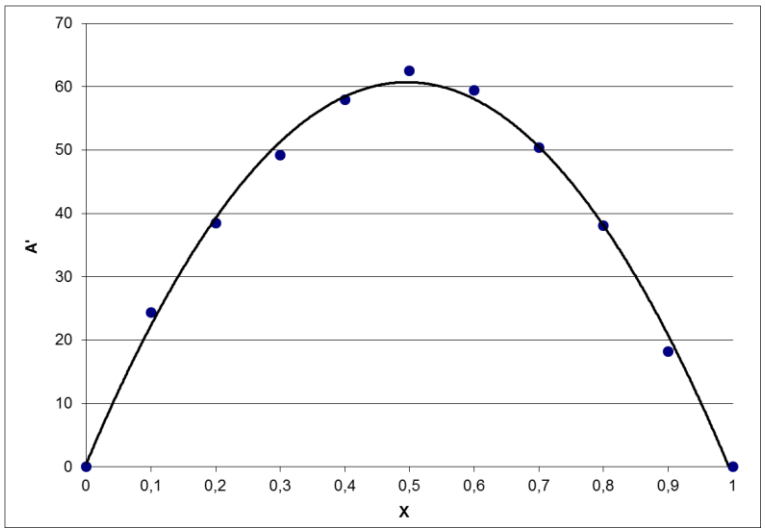

Figure S14. Job's Plot between **1** and 2-aminohexane in methanol.

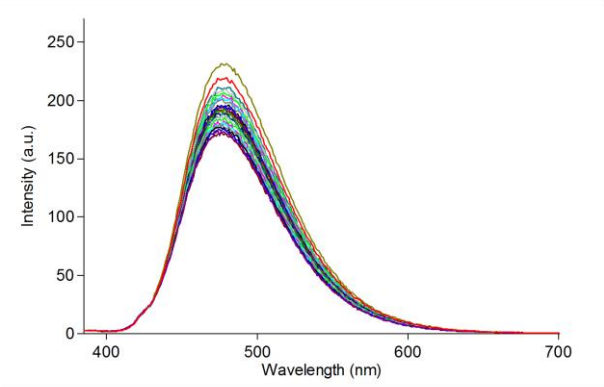

Figure S15. Representative fluorescence titration of receptor **1** with isobutylamine in toluene (1×10^{-5} M, 0 - 6 equivalents of guest added).

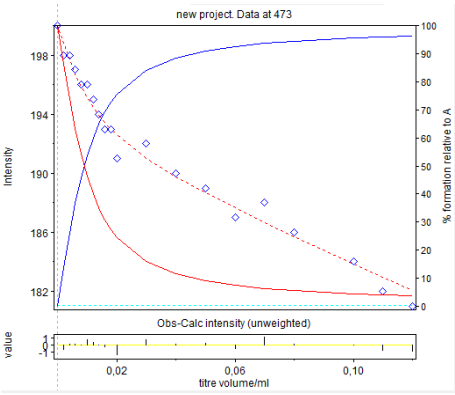

Figure S16. HypSpec plot of fluorescence titration between receptor **1** and (*S*)-1-(2-naphtyl)-ethylamine in methanol (blue points are experimental values, red dotted line is theoretical curve, blue and red line represent calculated concentrations of host-guest and host species, respectively).

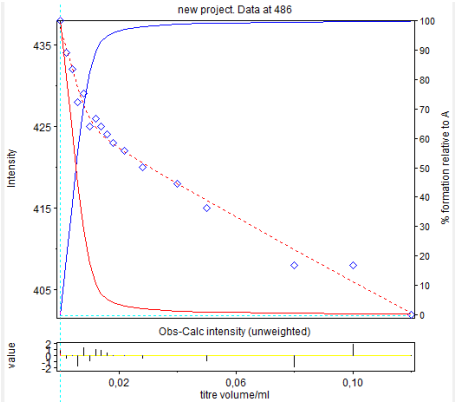

Figure S17. HypSpec plot of fluorescence titration between receptor **2** and (*S*)-1-(2-naphtyl)-ethylamine in methanol (blue points are experimental values, red dotted line is theoretical curve, blue and red line represent calculated concentrations of host-guest and host species, respectively).

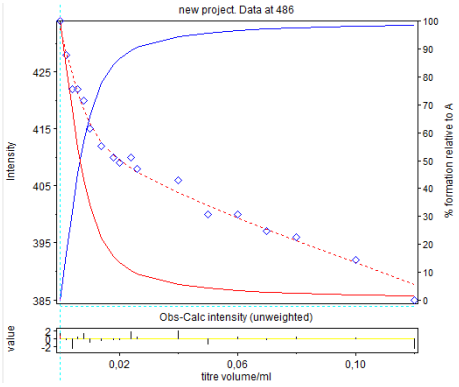

Figure S18. HypSpec plot of fluorescence titration between receptor **2** and (*R*)-1-(2-naphtyl)-ethylamine in methanol (blue points are experimental values, red dotted line is theoretical curve, blue and red line represent calculated concentrations of host-guest and host species, respectively).

Fluorescence titrations with receptor **1** in toluene.

HypSpec output files:

Receptor **1** vs. acetone

```
Project title: 1@acetone
Converged in 1 iterations with sigma = 2.5770

                      standard
Log beta    value     deviation
AB          5.7809    0.1289
```

Receptor **1** vs. benzophenone

```
Project title: 1@benzophenone
Converged in 2 iterations with sigma = 1.7177

                      standard
Log beta    value     deviation
AB          4.8021    0.1346
```

Receptor **1** vs. isobutylamine

```
Project title: 1@isobutylamine
Converged in 4 iterations with sigma = 2.2012

                      standard
Log beta    value     deviation
AB          6.3263    0.2056
```

Receptor **1** vs. *R*-2-aminohexane

```
Project title: 1@R-2-aminohexane
Converged in 1 iterations with sigma = 2.5492

                      standard
Log beta    value     deviation
AB          5.4383    0.1374
```

Receptor **1** vs. *S*-2-aminohexane

```
Project title: 1@S-2-aminohexane
Converged in 1 iterations with sigma = 2.6534

                     standard
Log beta   value     deviation
AB         4.6303    0.3513
```

Receptor **1** vs. *R*-1-cyclohexylethylamine

```
Project title: 1@R-1-ciclohexylethylamine
Converged in 3 iterations with sigma = 1.3227

                     standard
Log beta   value     deviation
AB         5.2841    0.1321
```

Receptor **1** vs. *S*-1-cyclohexylethylamine

```
Project title: 1@S-1-ciclohexylethylamine
Converged in 2 iterations with sigma = 0.87414

                     standard
Log beta   value     deviation
AB         4.8814    0.2986
```

Receptor **1** vs. *R*-1-(2-naphtyl)-ethylamine

```
Project title: 1@R-1-(2-naphtyl)-ethylamine
Converged in 3 iterations with sigma = 1.2194

                     standard
Log beta   value     deviation
AB         5.9405    0.1361
```

Receptor **1** vs. *S*-1-(2-naphtyl)-ethylamine

```
Project title: 1@S-1-(2-naphtyl)ethylamine
Converged in 7 iterations with sigma = 1.7324

                     standard
Log beta   value     deviation
AB         5.2148    0.1996
```

Receptor **1** vs. *D*-boc-ala

```
Project title: 1@D-boc-ala
Converged in 1 iterations with sigma = 1.0971

                     standard
Log beta   value     deviation
AB         5.9145    0.1054
```

Receptor **1** vs. *L*- boc-ala

```
Project title: 1@L-boc-ala
Converged in 1 iterations with sigma = 1.9672

                     standard
Log beta   value     deviation
AB         5.5801    0.0851
```

Fluorescence titrations with receptor **1** in methanol.

HypSpec output files:

Receptor **1** vs. *R*-2-aminohexane

```
Project title: 1@R-2-aminohexane
Converged in 6 iterations with sigma = 2.9959

                     standard
Log beta   value     deviation
AB         8.3315    0.5326
```

Receptor **1** vs. *S*-2-aminohexane

```
Project title: 1@S-2-aminohexane
Converged in 4 iterations with sigma = 0.9159

                     standard
Log beta   value     deviation
AB         6.3315    0.3841
```

Receptor **1** vs. *R*-1-cyclohexylethylamine

```
Project title: 1@R-1-ciclohexylethylamine
Converged in 1 iterations with sigma = 0.5530

                     standard
Log beta   value     deviation
AB         6.2552    0.4538
```

Receptor **1** vs. *S*-1-cyclohexylethylamine

```
Project title: 1@S-1-ciclohexylethylamine
Converged in 1 iterations with sigma = 0.6421

                     standard
Log beta   value     deviation
AB         5.7984    0.1437
```

Receptor **1** vs. *R*-1-(2-naphtyl)-ethylamine

```
Project title: 1@R-1-(2-naphtyl)-ethylamine
Converged in 1 iterations with sigma = 0.9141

                     standard
Log beta   value     deviation
AB         6.1704    0.2759
```

Receptor **1** vs. *S*-1-(2-naphtyl)-ethylamine

```
Project title: 1@S-1-(2-naphtyl)ethylamine
Converged in 1 iterations with sigma = 0.8551

                     standard
Log beta   value     deviation
AB         5.6980     0.2144
```

Receptor **1** vs. *D*-boc-ala

```
Project title: 1@D-boc-ala
Converged in 1 iterations with sigma = 0.84152
```

```
                    standard
Log beta   value    deviation
AB         5.5812   0.1659
```

Receptor **1** vs. *L*- boc-ala

```
Project title: 1@L-boc-ala
Converged in 1 iterations with sigma = 0.62625

                    standard
Log beta   value    deviation
AB         5.9069   0.1501
```

Fluorescence titrations with receptor **2** .

HypSpec output files:

Receptor **2** vs. *R*-2-aminohexane

```
Project title: 2@R-2-aminohexane
Converged in 1 iterations with sigma = 0.6492

                    standard
Log beta   value    deviation
AB         4.9908   0.1885
```

Receptor **2** vs. *S*-2-aminohexane

```
Project title: 2@S-2-aminohexane
Converged in 1 iterations with sigma = 0.7454

                    standard
Log beta   value    deviation
AB         6.1632   0.3364
```

Receptor **2** vs. *R*-1-cyclohexylethylamine

```
Project title: 2@R-1-ciclohexylethylamine
Not Converged in 50 iterations
```

Receptor **2** vs. *S*-1-cyclohexylethylamine

```
Project title: 2@S-1-ciclohexylethylamine
Converged in 1 iterations with sigma = 0.6421

                    standard
Log beta   value    deviation
AB         4.5285   0.2485
```

Receptor **2** vs. *R*-1-(2-naphtyl)-ethylamine

```
Project title: 2@R-1-(2-naphtyl)ethylamine
Converged in 1 iterations with sigma = 1.7441

                    standard
Log beta   value    deviation
AB         6.054    0.1999
```

Receptor **2** vs. *S*-1-(2-naphtyl)-ethylamine

```
Project title: 2@S-1-(2-naphtyl)ethylamine
Converged in 1 iterations with sigma = 1.0016

                     standard
Log beta   value     deviation
AB         6.7408    0.7148
```

Receptor **2** vs. *D*-boc-ala

```
Project title: 2@D-boc-ala
Converged in 1 iterations with sigma = 1.7019

                     standard
Log beta   value     deviation
AB         4.7728    0.1789
```

Receptor **2** vs. *L*-boc-ala

```
Project title: 2@L-boc-ala
Converged in 1 iterations with sigma = 1.7310

                     standard
Log beta   value     deviation
AB         4.2815    0.2854
```

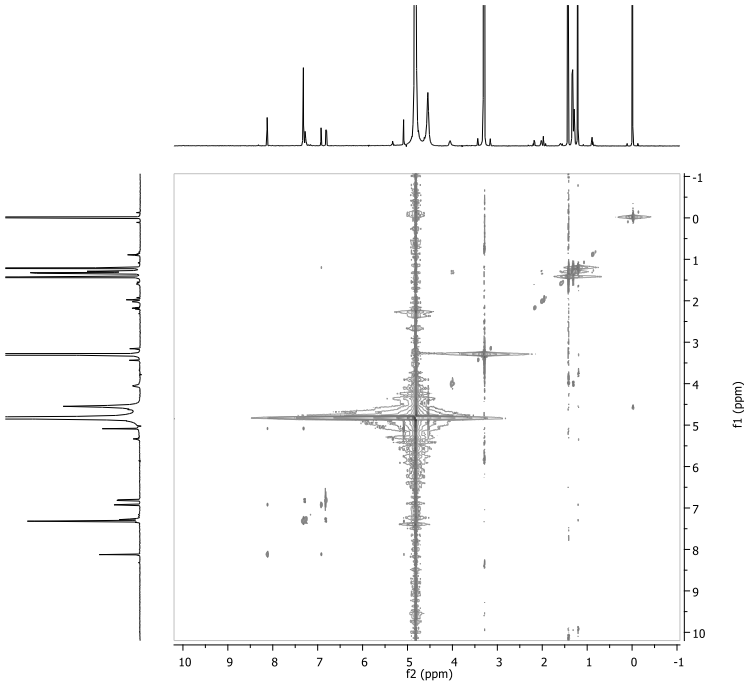

Figure S19. ROESY spectrum between receptor **1** and *D*-Boc-Ala (1:1, 1×10^{-3} M, CD_3OD, 27°C).

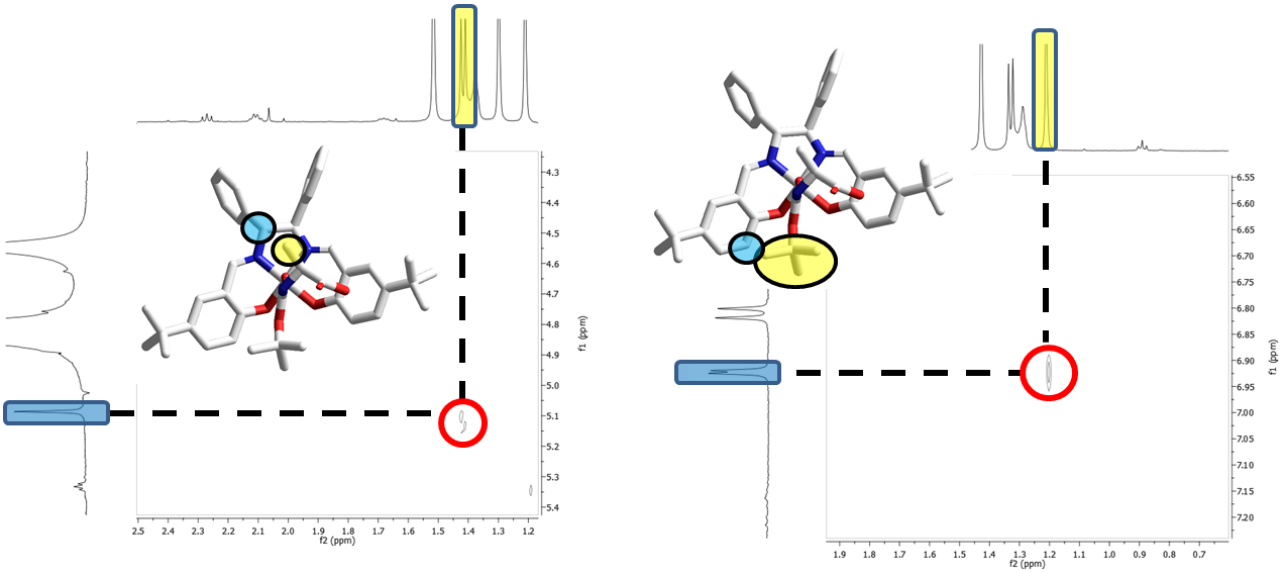

Figure S20. Details of ROESY spectrum of receptor **1** and *D*-Boc-Ala (1:1, 1×10^{-3} M, CD_3OD, 27°C) showing ROE contact between methyl group of the guest (highlighted in yellow) and methine proton of the host (in blue) (left); *t*-Butyl group of the guest and aromatic proton of the host (right).

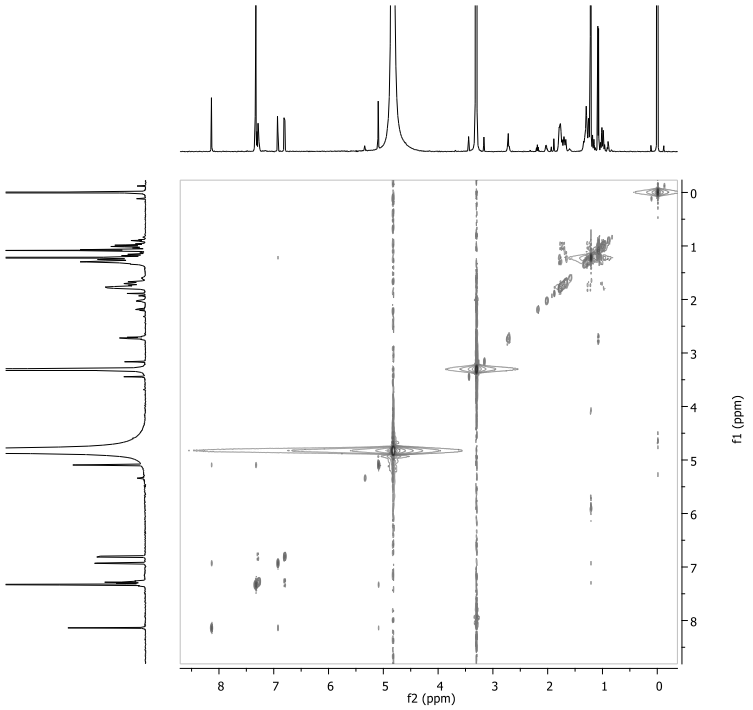

Figure S21. ROESY spectrum between receptor **1** and *R*-1-cyclohexylethylamine (1:1, 1×10^{-3} M, CD_3OD, 27°C).

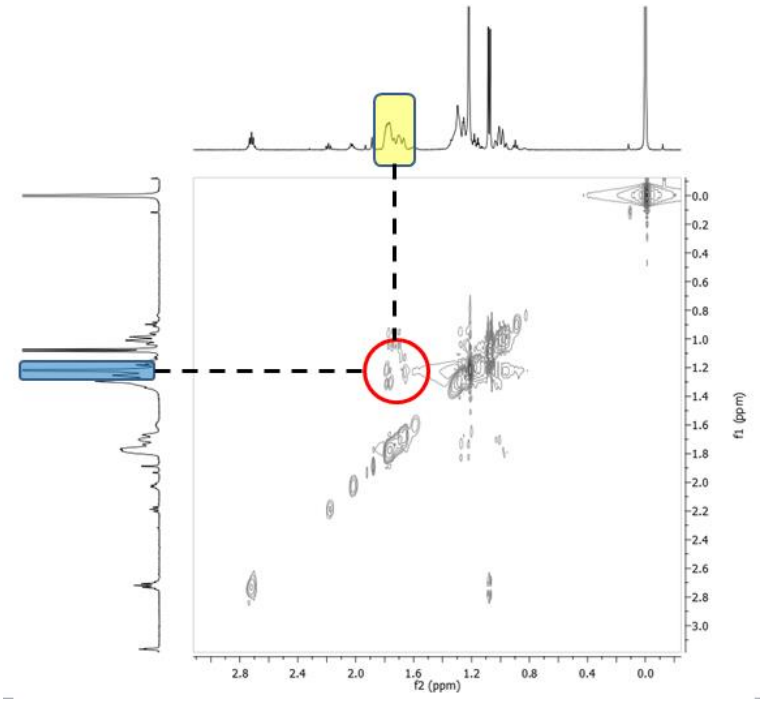

Figure S22. Detail of ROESY spectrum of receptor **1** and *R*-1-cyclohexylethylamine (1:1, 1×10^{-3} M, CD_3OD, 27°C) showing ROE contacts between *t*-Butyl group of the host (blue) and cyclohexyl protons of the guest (yellow).

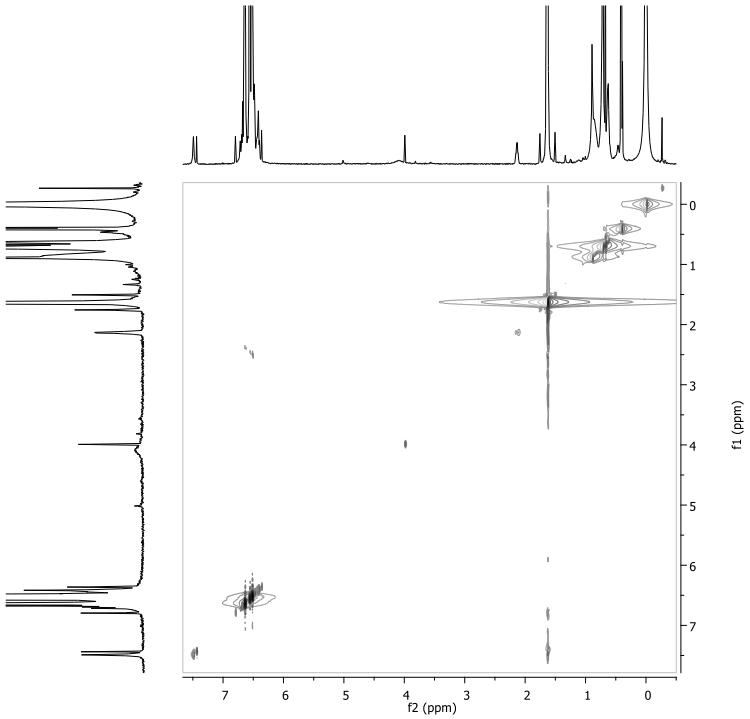

Figure S23. ROESY spectrum between receptor **1** and *R*-2-aminohexane (1:1, 1×10^{-3} M, toluene-d_8, 27°C).

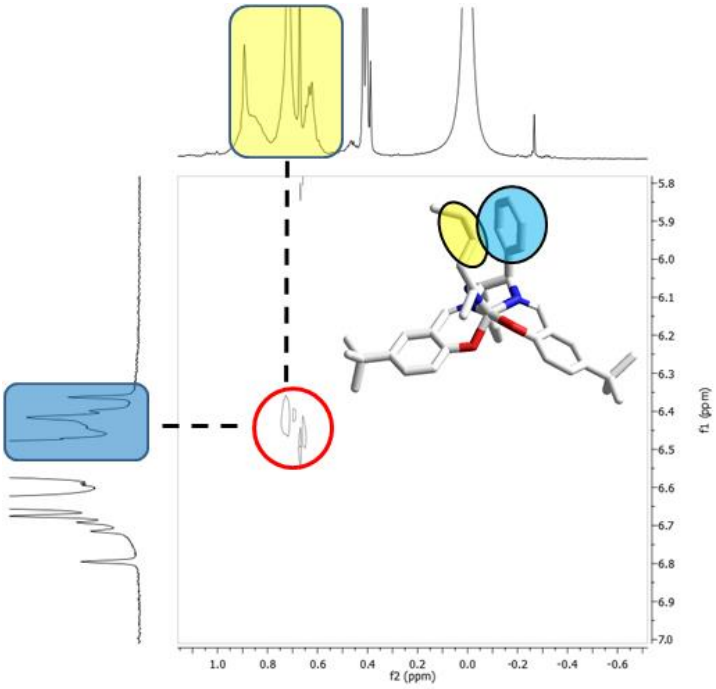

Figure S24. Detail of ROESY spectrum of receptor **1** and *R*-2-aminohexane (1:1, 1×10^{-3} M, toluene-d_8, 27°C) showing ROE contacts between aromatic proton of the host (blue) and aliphatic chain of the guest (yellow).

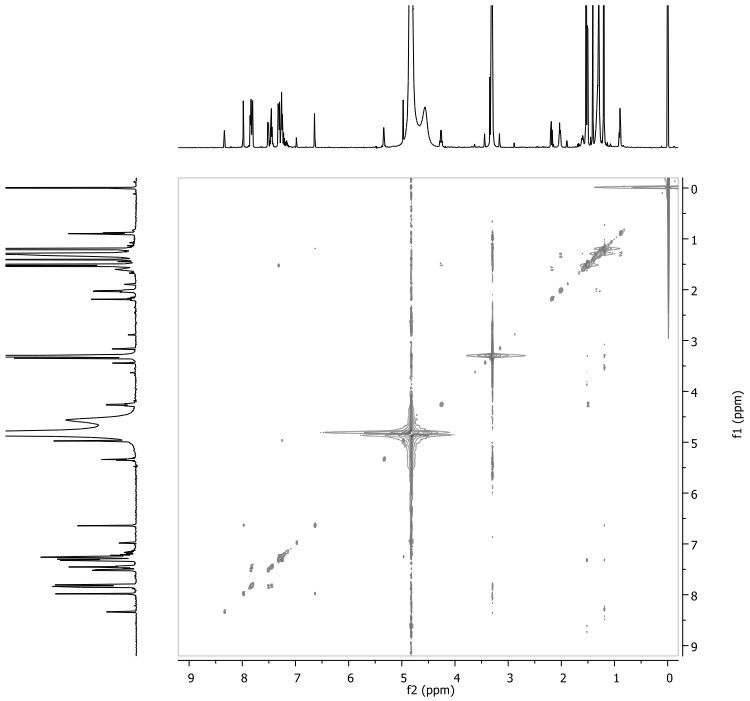

Figure S25. ROESY spectrum between receptor **1** and *R*-1-(2-naphtyl)-ethylamine (1:1, 1×10^{-3} M, CD_3OD, 27°C).

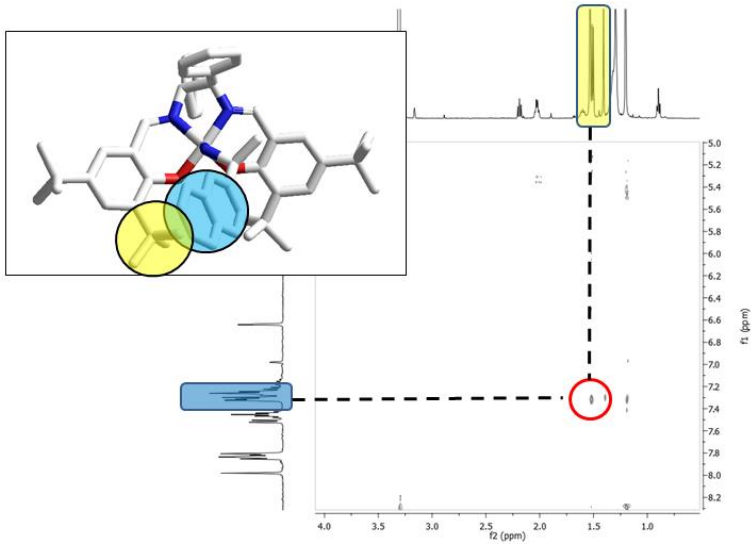

Figure S26. Detail of ROESY spectrum of receptor **1** and *R*-1-(2-naphtyl)-ethylamine (1:1, 1×10^{-3} M, CD_3OD, 27°C) showing ROE contacts between *t*-buthyl group protons of the host (yellow) and aromatic protons of the guest (blue).

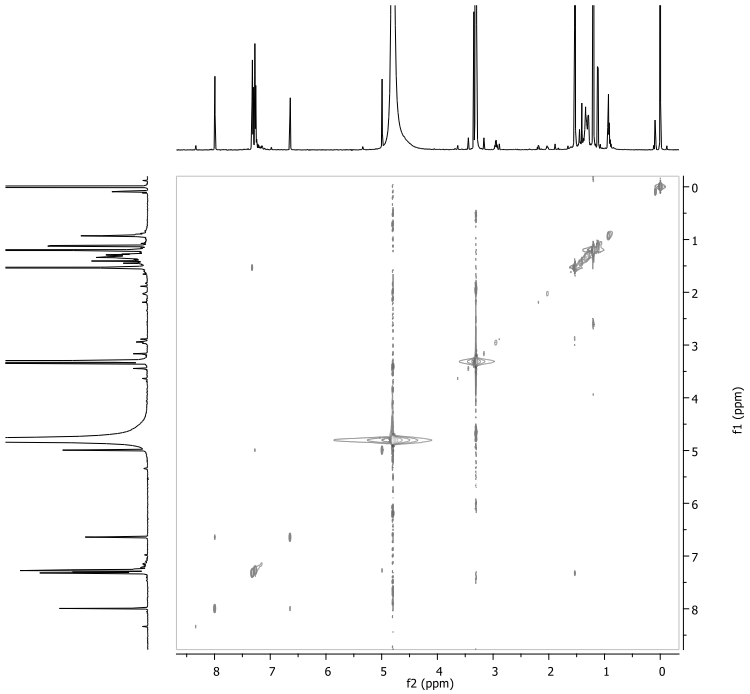

Figure S27. ROESY spectrum between receptor **1** and *R*-2-aminohexane (1:1, 1×10^{-3} M, CD_3OD, 27°C).

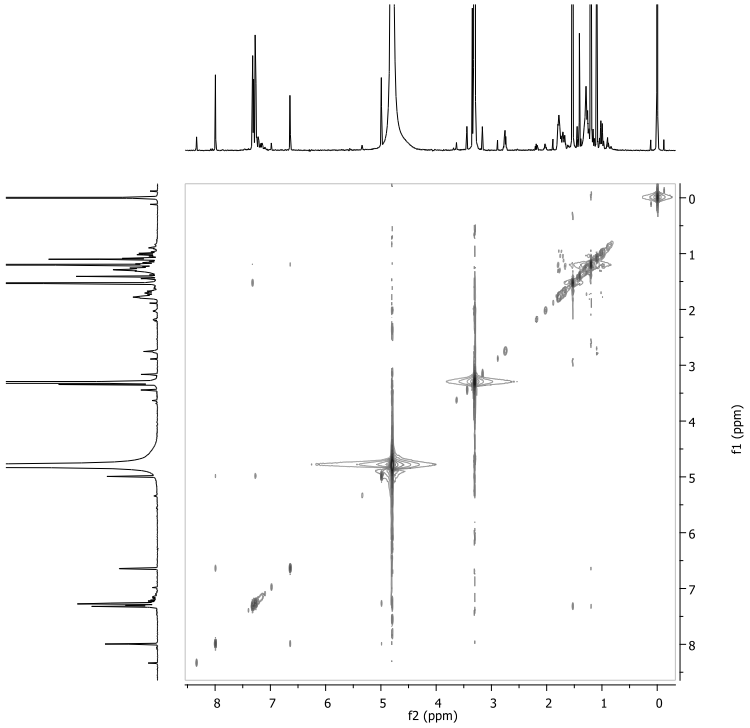

Figure S28. ROESY spectrum between receptor **1** and *R*-1-cyclohexylathylamine (1:1, 1×10^{-3} M, CD_3OD, 27°C).

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