BINOL-strapped calix[4]pyrrole as a model chirogenic receptor for the enantioselective recognition of carboxylate anions

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Experimental section

Proton NMR spectra (400 MHz, Bruker DPX-400) were recorded using TMS as the internal standard. High resolution mass spectra were obtained on an Voyager-DE STR MALDI-TOF mass spectrometer. Column chromatography was performed over silica gel (Merck, 230-400 mesh). Pyrrole was distilled at atmospheric pressure from CaH₂. All other reagents were obtained from Aldrich and used as received unless noted otherwise. The experimental procedures and spectroscopic data for the corresponding enantiomeric compounds throughout the synthesis were identical each other. The retained enantiomeric purity was checked by CD spectra for the final receptors and synthetic procedure for only one stereoisomer is reported.

(S)-(-)-6-[2'(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (4S)

K₂CO₃ (2.0 g, 14.47 mmol) was added to a solution of (S)-(-)-1,1’-bi-2-naphthol (0.5 g, 1.75 mmol) in DMF (15 mL) and stirred for 1 hour at 60 °C, then 6-bromohexan-2-one (1.00 g, 5.56 mmol) was added to the reaction mixture and the stirring continued for an additional 24 h. The mixture was then combined with water (50 mL) and extracted with methylene chloride. The organic layer was dried (Na₂SO₄) and the solvent was removed in vacuo. The resulting viscous solid was purified by column
chromatography on silica gel (CH$_2$Cl$_2$: EtOAc = 9:1). Yield 0.82 g (96%); $^1$H NMR (CDCl$_3$) d 1.17 - 1.21 (m, 4H, CH$_2$), 1.38 - 1.43 (m, 4H, CH$_2$), 1.84 (s, 6H, CH$_3$), 1.94 - 1.98 (m, 4H, CH$_2$), 3.91 - 4.00 (m, 4H, CH$_2$), 7.13 - 7.15 (m, 2H, Ar-H), 7.18 - 7.22 (m, 2H, Ar-H), 7.29 - 7.33 (m, 2H, Ar-H), 7.38 - 7.41 (m, 2H, Ar-H), 7.83 - 7.85 (m, 2H, Ar-H), 7.91 - 7.94 (m, 2H, Ar-H); $^{13}$C NMR: 20.33, 28.66, 29.48, 42.99, 69.48, 115.73, 120.61, 123.59, 125.46, 126.19, 127.86, 129.21, 129.31, 134.14, 154.42, 209.06; MALDI-TOF MS Calcd. For C$_{32}$H$_{34}$O$_4$ 482.25, Found 482.21.

(R)-(+)-6-[2'-(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (4R)

K$_2$CO$_3$ (1.93 g, 13.97 mmol), (R)-(+)-1,1'-bi-2-naphthol (0.4 g, 1.40 mmol) and 6-bromohexan-2-one (1.00 g, 5.56 mmol) was treated identically as for the synthesis of (4S). All the spectroscopic data were identical with (4S).

Compound (5S)

(S)-(−)-6-[2'-(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (0.685 g, 1.42 mmol) was dissolved in pyrrole (3 mL, 43.24 mmol) and then TFA (0.11 mL, 1.41 mmol) was added. The mixture was stirred for 2 hr at 60 °C. The reaction was quenched by adding aqueous NaOH (0.1 N, 50 mL) and then extracted with CH$_2$Cl$_2$. The organic layer was dried (Na$_2$SO$_4$) and the solvent was removed in vacuo. The resulting viscous solid was purified by column chromatography on silica gel (CH$_2$Cl$_2$:EtOAc = 19:1). Yield 0.713 g (70%); $^1$H NMR (CDCl$_3$) d 0.84 - 0.93 (m, 4H, CH$_2$), 1.20 - 1.28 (m, 4H, CH$_2$), 1.31 (s, 6H, CH$_3$), 1.59 - 1.69 (m, 4H, CH$_2$), 3.78 (t, 4H, CH$_2$), 5.88 - 5.90 (m, 4H, pyrrolic-H), 6.05 - 6.08 (m, 4H, pyrrolic-H), 6.45 - 6.52 (m, 4H, pyrrolic-H), 7.08 - 7.10 (m, 2H, Ar-H), 7.16 - 7.20 (m, 2H, Ar-H), 7.27 - 7.32 (m, 4H, Ar-H), 7.50 (br s, 2H, NH), 7.61 (br s, 2H, NH), 7.82 - 7.89 (m, 4H, Ar-H); $^{13}$C NMR: 26.75, 30.26, 39.29, 41.10, 70.25, 105.09, 105.12, 107.91, 107.95, 116.28, 117.42, 117.46, 120.91, 123.97, 126.0, 126.65, 128.41, 129.62, 129.71, 134.62, 138.55, 155.0; MALDI-TOF MS Calcd. For C$_{48}$H$_{50}$N$_4$O$_2$ 714.39, Found 714.33.

Compound (5R)

(R)-(−)-6-[2’-(5-Oxo-hexyloxy)-[1,1’]binaphthalenyl-2-yloxy]-hexan-2-one (0.630 g, 1.31 mmol), pyrrole (3.5 mL, 50.4 mmol) and TFA (0.07 mL, 0.91 mmol) was treated identically as for the synthesis of (5S). All the spectroscopic data were identical with (5S).
Receptor (1S)

Compound (5S) (0.561 g, 0.78 mmol) was dissolved in acetone (200 mL) and then BF₃·OEt₂ (0.04 mL, 0.32 mmol) was added. The mixture was stirred for 50 min at room temperature. The reaction was quenched by adding aqueous NaOH (0.1 N, 50 mL) then, extracted with CH₂Cl₂. The organic layer was dried (Na₂SO₄) and the solvent was removed in vacuo. The resulting dark solid was purified by column chromatography on silica gel (CH₂Cl₂). Yield 67 mg (11 %). ¹H NMR (CDCl₃) d 0.85 - 0.94 (m, 4H, CH₂), 1.12 - 1.18 (m, 2H, CH₂), 1.22 - 1.28 (m, 2H, CH₂), 1.35 - 1.42 (m, 8H, CH₃ and CH₂), 1.48 (s, 6H, CH₃), 1.55 (s, 6H, CH₃), 1.62 - 1.69 (m, 2H, CH₂), 3.84 - 3.86 (m, 4H, CH₂), 5.45 - 5.46 (m, 2H, pyrrolic-H), 5.83 - 5.85 (m, 2H, pyrrolic-H), 5.93 - 5.94 (m, 2H, pyrrolic-H), 6.00 - 6.02 (m, 2H, pyrrolic-H), 6.73 (br s, 2H, NH), 6.97 (br s, 2H, NH), 7.23 - 7.24 (m, 4H, Ar-H), 7.31 - 7.36 (m, 2H, Ar-H), 7.48 - 7.50 (m, 2H, Ar-H), 7.89 - 7.91 (m, 2H, Ar-H), 8.00 - 8.03 (m, 2H, Ar-H); ¹³C NMR: 23.55, 27.90, 29.51, 29.83, 30.51, 35.52, 39.27, 40.46, 53.43, 71.20, 101.17, 102.91, 105.13, 105.97, 116.49, 121.12, 123.51, 125.45, 125.95, 127.85, 129.07, 129.47, 133.69, 134.06, 135.08, 138.40, 140.55, 155.08; MALDI-TOF MS Calcd. For C₅₄H₅₈N₄O₇ 794.46, Found 794.01.

Receptor (1R)

Compound (5R) (0.438 g, 0.61 mmol), acetone (120 mL) and BF₃·OEt₂ (0.04 mL, 0.32 mmol) was treated identically as for the synthesis of (1S). All the spectroscopic data were identical with (1S).
$^1$H NMR spectrum of 1S (CDCl$_3$)
$^{13}$C NMR spectrum of 1S (CDCl$_3$)
High resolution MALDI-TOF Mass spectrum of 1S
$^1$H NMR spectrum of 4S (CDCl$_3$)
$^{13}$C NMR spectrum of 4S (CDCl$_3$)
H NMR spectrum of 5S (CDCl₃)
$^{13}$C NMR spectrum of 5S (CDCl$_3$)
High resolution MALDI-TOF Mass spectrum of 5S
NMR binding study (1S with R-guest)
NMR binding study (1S with S-guest)
ITC

Isothermal Titration Calorimetry (ITC) measurements were performed as follows: Solutions of the chosen receptor in rigorously dry acetonitrile were made up so as to provide a receptor concentration range of 0.1–1 mM. These solutions were then individually titrated with the appropriate alkylammonium salts at 30 ± 0.01 °C. The original heat pulses were normalized using reference titrations carried out using the same salt solution but pure solvent, as opposed to a solution containing the receptor.

ITC plot (1S with R-guest)
ITC plot (1S with S-guest)