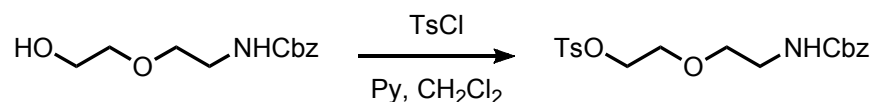


Supplementary Material for Chemical Communications

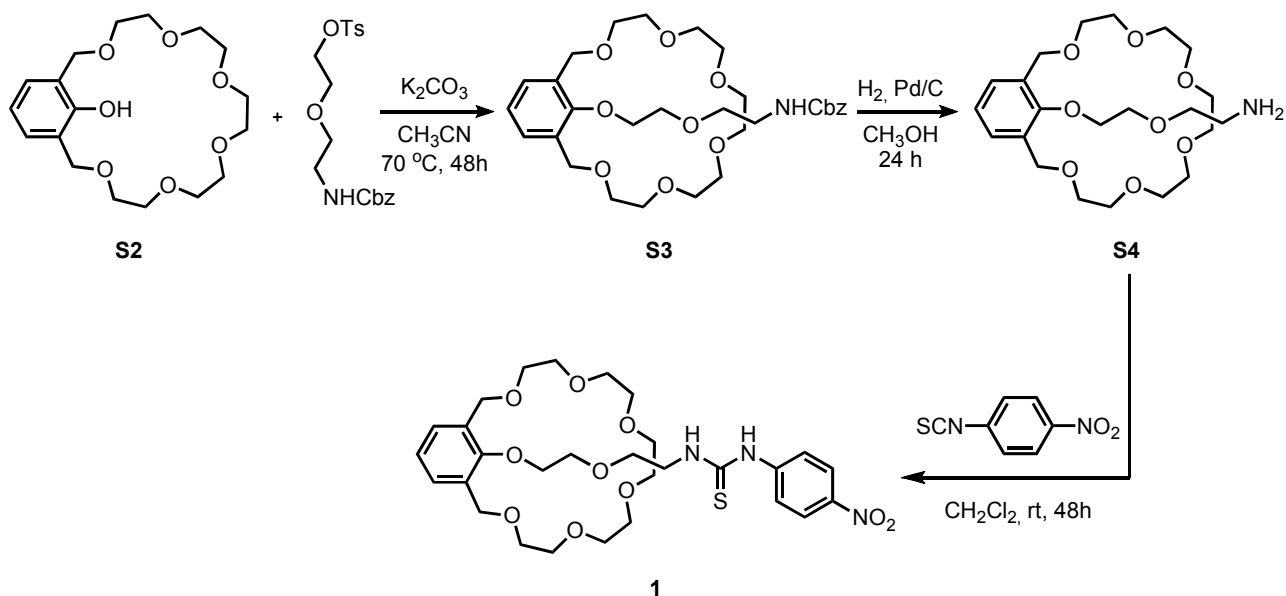
A selective chromogenic chemosensor for carboxylate salts recognition.

Piotr Piątek

1. Synthetic procedures.



To a stirred solution of 2-[N-(benzyloxycarbonyl)aminoethoxy]ethanol¹ (2 g, 8.37 mmol) and pyridine (5 mL) in dichloromethane (~40 mL) *p*-toluenesulphonyl chloride was added and the solution was stirred at room temperature overnight. The reaction mixture was washed two times with 1M HCl, then with water, dried over MgSO₄ and concentrated *in vacuo*. The crude residue was dissolved in 30% AcOEt/Hexanes solution (addition of a few drop of CH₂Cl₂ is needed for a complete dissolution) and vacuum filtered through short pad of silica gel eluting with 30% AcOEt/Hexanes solution (150 mL) then 50% AcOEt/Hexanes solution (200 mL). The fraction eluted with 50% AcOEt/Hexanes solution was evaporated to dryness, dissolved in a minimal amount of hot CH₂Cl₂, allowed to cool, and then Et₂O is added. The precipitation was collected by filtration to give 2-[N-(benzyloxycarbonyl) aminoethoxy]ethyl *p*-toluenosulfonate as white crystals (2.42 g, 74%).
 δ H(CDCl₃, 200MHz) 2.42 (2H, s, CH₃), 3.30-3.36 (2H, m, OCH₂), 3.48 (2H, t, J=4.8, CH₂N), 3.61-3.65 (2H, m, CH₂O), 4.11-4.18 (2H, m, TsOCH₂), 5.05 (1H, bs, NH), 5.11 (2H, s, PhCH₂O), 7.31 (2H, d, Ts), 7.34-7.39 (5H, m, Ph), 7.79 (2H, d, Ts).



Compound S3

2-hydroxy-1,3-xylyl-21-crown-6 **S2** (550 mg, 1.57 mmol) and dry K₂CO₃ (450 mg, 3.26 mmol, 2eq) were suspended in dry CH₃CN (~60mL). To this stirred suspension compound 2-(N-(benzyloxycarbonyl)aminoethoxy)ethyl *p*-toluenosulfonate (740 mg, 1.88 mmol, 1.2eq) was added, and the resulting mixture was heated at 70 °C (oil bath) under an inert atmosphere for 4 days. After this time, the suspension was allowed to cool, then solids were dissolved by addition of water. The solvent was removed in *vacuo* to give an oily

residue, which was extracted with CH_2Cl_2 (3 x 60mL). The combined extracts were dried over MgSO_4 , filtered, and the solvent removed *in vacuo* to give a crude material, which was purified by column chromatography (SiO_2 , 30% AcOEt/Hexanes) to give **S3** (634 mg, 71%) as a colorless oil. $\delta\text{H}(\text{CDCl}_3, 200\text{MHz})$ 3.47-3.72 (24H, m, macrocyclic- $\text{CH}_2\text{O} + 2\times\text{CH}_2\text{O}$), 3.84-3.88 (2H, m, CH_2O), 4.38-4.43 (2H, m, PhOCH_2), 4.52 (4H, bs, macrocyclic- PhCH_2O), 6.18 (1H, bs, NH), 7.05 (1H, t, $J=7.6$, macrocyclic-PhH), 7.27 (2H, d, $J=7.6$, macrocyclic-PhH), 7.34 (5H, bs, Cbz-Ph); $\delta\text{H}(\text{CDCl}_3, 50\text{MHz})$ 66.7, 69.2, 69.9, 70.3, 70.7, 71.1, 76.2, 114.4, 123.8, 128.6, 132.1, 155.1, 158.2; m/z (ESI) 600.2774 ($[\text{M}+\text{Na}]^+$ $\text{C}_{30}\text{H}_{43}\text{NO}_{10}\text{Na}$ requires 600.2785).

Compound **S4**

Compound **S3** (620 mg, 1.1 mmol) was dissolved in methanol (~70 mL), and 50 mg of 5% Pd/C was added. The reaction mixture was kept under H_2 atmosphere (balloon pressure) at room temperature for 24 h. The catalyst was filtered off, the solvent was evaporated to dryness, to give amine **S4** (429 mg, 87%), which was used without further purification. $\delta\text{H}(\text{CDCl}_3, 200\text{MHz})$ 1.81 (2H, bs, NH_2), 2.94 (2H, t, $J=5.2$, CH_2N), 3.54-3.69 (24H, m, macrocyclic- $\text{CH}_2\text{O} + 2\times\text{CH}_2\text{O}$), 3.84-3.90 (2H, m, CH_2O), 4.32-4.37 (2H, m, PhOCH_2), 7.07 (1H, t, $J=7.6$, PhH), 7.32 (2H, d, $J=7.6$, PhH); $\delta\text{H}(\text{CDCl}_3, 50\text{MHz})$ 42.1, 68.9, 69.8, 70.6, 70.7, 70.9, 71.1, 73.4, 75.7, 123.8, 131.7, 131.9, 157.8; m/z (ESI) 466.2421 ($[\text{M}+\text{Na}]^+$ $\text{C}_{22}\text{H}_{37}\text{NO}_8\text{Na}$ requires 466.2417).

Compound **1**

To the solution of amine **S4** (429 mg, 0.97 mmol) in dichloromethane (40 mL) 4-nitrophenylthioisocyanate (209 mg, 1.16 mmol, 1.2 eq) was added. The reaction mixture was stirred at room temperature for 48 h. The solvent was evaporated, and the crude material was purified by a column chromatography (SiO_2 , 20-40% Acetone/Dichloromethane) to give receptor **1** (430 mg, 64%) as pale-yellow crystals. $\delta\text{H}(\text{CDCl}_3, 200\text{MHz})$ 3.55-3.71 (20H, m, macrocyclic- CH_2O), 3.82 (2H, t, $J=4.8$, CH_2O), 3.90-4.05 (4H, m, $2\times\text{CH}_2\text{O}$), 4.41-4.45 (2H, m, PhOCH_2), 4.61 (4H, bs, macrocyclic- PhCH_2O), 7.09 (1H, t, $J=7.2$, macrocyclic-PhH), 7.31 (1H, d, $J=7.2$, macrocyclic-PhH), 7.74 (1H, bs, NH), 7.84 (2H, d_{AX} , $J=9.2$, Ph- NO_2), 8.15 (2H, d_{AX} , $J=9.2$, Ph- NO_2), 9.42 (1H, bs, NH); $\delta\text{H}(\text{CDCl}_3, 50\text{MHz})$ 68.2, 69.4, 70.6, 70.8, 70.9, 71.4, 120.7, 124.2, 124.7, 131.7, 132.5, 144.6, 146.4, 172.1, 195.7; m/z (ESI) 646.2405 ($[\text{M}+\text{Na}]^+$ $\text{C}_{22}\text{H}_{37}\text{NO}_8\text{Na}$ requires 646.2411).

2. Titration experiments.

^1H NMR titrations:

The ^1H NMR titrations were performed on a Varian UnityPlus 200MHz spectrometer, at 298K in CD_3CN solution. In each case, a 500 μL of 2 mM solution of receptor **1** was added to a 5mm NMR tube. Small aliquots of hexafluorophosphate cation salts or tetrabutylammonium anion salts stock solutions (containing 1 at 2 mM concentration) were added and a spectrum was acquired after each addition.

Mathematical analysis of titration data was performed using the HypNMR 2000 program.²

UV-vis titrations:

The UV-vis titrations were performed on a Thermo Spectronic Unicam UV500 spectrophotometer, at 298K, in CH_3CN solution. In each case, a 2000 μL of 4.8×10^{-5} M

solution of receptor **1** was added to a 10 mm cuvette. When necessary, 1:5 mixtures of the receptor and an alkali metal hexafluorophosphate salt were prepared. Aliquots of the anion solution were then added, the sample was mixed thoroughly and a spectrum was acquired after each addition.

Equilibrium constants were calculated using equation 4.5 of Connors.³

1. J. Marchand-Brynaert, M. Bouehet, R. Touillaux, C. Beauve and J. Fastrez, *Tetrahedron*, 1996, **52**, 5591-5606.
2. C. Frassinetti, S. Ghelli, P. Gans, A. Sabatini, M. S. Moruzzi and A. Vacca, *Anal. Biochem.*, 1995, **231**, 374.
3. K.A., Connors, *Binding Constants*; John Wiley & Sons: New York, 1987, p. 148.