Selective carboxylate recognition using urea-functionalized unclosed cryptands – mild synthesis and complexation studies

Patryk Niedbala, Maciej Majdecki, Kajetan Dąbrowa, and Janusz Jurczak*

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland.
E-mail: jurczak_group@icho.edu.pl

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1. Crystal Data

1.1 Diffractometer and data collection

Single crystal X-ray diffraction measurements were carried out on an Agilent Supernova diffractometer, at 100K with graphite monochromated Cu Kα radiation (1.54184 Å). Colorless crystal in a form of long needle was used.

1.2 Structure refirements

The data reduction was made by using CrysAlisPro software. The structures were solved by direct methods and refined on F2 by full-matrix least-squares by using SHELXS97 and SHELXL97. All non-hydrogen atoms were refined as anisotropic while hydrogen atoms were placed in calculated positions, and refined in riding mode.

1.3 Crystallographic data

CCDC contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

1.4 Crystal data and structure refinement details

The crystal suitable for the x-ray measurement was obtained by a slow diffusion of water to the solution of receptor 4l in DMSO-d6.

Table S1. Crystal data and structure refinement details for 4l.

| Compound |
|-----------|
| Empirical formula | C₃₄H₃₅F₆N₇O₇ |
| Formula weight | 767.67 |
| CCDC No. | 1854521 |
| Wavelength | 1.54184 |
| Crystal system | monoclinic |
| Space group | P 2₁/n |
| Unit cell dimensions | a = 17.907(3) Å |
| | b = 9.0483(14) Å |
| | c = 25.336(5) Å |
| Volume | 3863.9 Å³ |
| Z | 4 |
| Density Calc. | 1.457 g/cm³ |
| Absorption coefficient | 1.131 |
| F(000) | 1752 |
| Crystal | Colorless needle |
| Crystal size | 0.3 × 0.05 × 0.02 mm |
| Index ranges | -22 ≤ h ≤ 18, -10 ≤ k ≤ 8, -26 ≤ l ≤ 31 |
| Reflections collected (all / independent) | 7412/3216 |
| Absorption correction | multi-scan |
| Refinement method | Full-matrix least-squares on F² |
| Restraints / parameters | 30 / 544 |
| Goodness-of-fit on F² | 1.068 |
Thermal ellipsoid plots (ORTEP) for reported crystal structure with the thermal ellipsoids shown at a 50% probability level.

Figure S1. Thermal ellipsoid plot (ORTEP) diagram for structure 41.
2. Computational studies

2.1 Conformational analysis of 4c-benzoate complex

The $^1$H NMR titration experiments performed in DMSO/water solvent mixtures reveal the unusual selectivity of hosts 4c and 4d for benzoate over more basic acetate. In order to rationalize these results and to elucidate the potential role of aryl ring of lariat arm on this process, we decided to perform extensive computational calculations. As a representative, we carried out the conformational search analysis for the 4c-PhCO$_2$ complex as implemented in program Spartan’18 Parallel Suite (method conformer distribution).$^3$

Briefly, 400 starting structures were obtained from the conformer distribution method implemented in Spartan program and using Merck Molecular Force Field (MMFF) for the given torsion angles (Figure S2).

![Figure S2](image)

**Figure S2.** Torsions and variances of the torsion angles used to generate the conformers.

All these conformers were then geometrically-optimized without any constrains using fast semi-empirical PM6 method. After that, energies of conformers were calculated at relatively fast DFT level of theory (B3LYP-D3/6-31(d)/gas-phase). From this set dozens of conformers with energy cut-off of 40 kJ/mol were selected, prior to removing the enantiomers and structurally similar conformers. These remaining ones were then fully geometrically-optimized without any constrains at DFT/B3LYP-D3/6-31(d)/gas-phase level of theory and 17 conformers with the lowest energies were further optimized at DFT/M06-2X/6-31G(d)$^{4,5}$ using a C-PCM approximation of the DMSO solvent which was used for the $^1$H NMR titrations experiments. Three lowest energy conformers are shown in Figure S3.
Figure S3. Three lowest-energy conformers of 4c-PhCO$_2^-$ complexes (a-c) obtained from the conformational search analysis; structures were fully geometrically-optimized at DFT/M06-2X/6-31G(d)/C-PCM:DMSO level of theory; non-acidic protons were omitted for clarity; the N-H···O-C hydrogen bond and C$_{Ar}$···C$_{Ar}$ and C-H···O/C interactions are color in green and gray, respectively.

Detailed analysis of this set suggest that in conformation with lowest energy the phenyl ring of benzoate is not involved in any particularly short π-π interactions with aromatic residues of the host (the distance between C-H proton of lariat arm and PhC-O moiety is 3.66 Å). However, analysis of the two next conformers (higher in energy by 10 and 16 kJ·mol$^{-1}$, respectively) reveal presence of such interactions, in particular π-π stacking between benzoate and pyridine moiety of the host ($d_{C\pi···C\pi} = 3.20 – 3.63$ Å, Figure S3b), edge-to-face interaction with pyridine moiety and aryl C-H proton from the lariat arm ($d_{C-H···N} = 3.49$ Å, Figure S3c), and C-H···O hydrogen bond between carboxylate and CH residue of lariat arm ($d_{O···H-C} = 3.35$ Å, Figure S3b). In addition, the latter type of interaction might explain the unexpected higher affinity of host 4d vs 4c for carboxylates. The host 4d has a para-substituted OMe group whereas host 4c has an unsubstituted phenyl group. For this reason, one could expect that binding affinities should be lower for host 4d possessing an electron-donating group. Analysis of the electrostatic surface potential for the simple analogs of hosts 4c, 4d, and 4l reveals that C-H protons of the lariat arm are in fact more polarized for host 4d than for hosts 4c and 4l (Figure S4). In addition 4l could not be engaged in edge-to-face interactions with benzoate due to steric factors.
Figure S4. The electrostatic potential surfaces EPS (a, calculated at DFT/M06-2X/6-31G(d)/C-PCM:DMSO level of theory, mapped at 0.001 au, inset - values are in kJ/mol) for analogs of lariat arm of receptors 4c (a), 4d (b), and 4l (c).
### 2.2 Cartesian coordinates of calculated structures

| Free 4c | E = -2.150 81444 au | 4c-PhCO2#1 (minimum) | E = -2.157 05124 au |
|---------|---------------------|----------------------|---------------------|
| O       | 0.075553            | -4.898483            | 0.855334             |
| O       | -1.232625           | -5.841433            | 3.749252             |
| O       | -1.222135           | 2.529312             | 4.736769             |
| O       | 0.001493            | 4.922806             | -1.804712            |
| O       | -3.083748           | 0.587178             | -5.097427            |
| O       | -1.743570           | -1.960149            | -3.090052            |
| O       | -0.778521           | 3.117613             | 2.677478             |
| O       | 0.478760            | 1.746069             | 3.415395             |
| N       | 0.269007            | 3.387979             | 1.407087             |
| N       | 1.065883            | 3.092341             | -0.940654            |
| N       | -0.969494           | 0.168846             | -4.309020            |
| C       | -2.016417           | -2.879289            | -2.038015            |
| C       | 0.908378            | -3.246167            | -1.257218            |
| C       | -1.064904           | -4.195012            | -0.235586            |
| C       | -0.047650           | 2.224719             | 1.674689             |
| C       | -0.756309           | -4.456079            | -2.799015            |
| C       | -1.469165           | -2.278077            | 3.654433             |
| C       | 0.954171            | 0.707744             | 3.421766             |
| C       | -0.584985           | 2.534736             | 3.675596             |
| C       | -0.964249           | 3.469869             | 2.549585             |
| C       | -2.021870           | 4.364841             | 2.731900             |
| C       | -2.362405           | 5.214343             | 2.710305             |
| C       | -1.638049           | 5.139642             | 0.492859             |
| C       | -0.600234           | 4.207364             | 0.408062             |
| C       | 0.181503            | 4.109688             | -0.888886            |
| C       | 1.945640            | 2.852160             | -2.073333            |
| C       | -0.308496           | 1.133220             | -4.926633            |
| C       | -2.287519           | -0.082521            | -4.431622            |
| C       | -2.815932           | -1.295893            | -3.607321            |
| C       | -3.272714           | -3.447840            | -1.811808            |
| C       | -3.409865           | -4.369734            | -0.773121            |
| C       | -2.326797           | -4.746405            | 0.021021             |
| H       | 0.561401            | -6.181382            | 1.534075             |
| H       | 0.979281            | -5.434009            | 1.968653             |
| H       | -0.384696           | -2.673765            | 1.846896             |
| H       | -1.306531           | -7.216099            | 4.644248             |
| H       | -2.551321           | -2.304271            | 3.463421             |
| H       | 2.045444            | 0.776920             | 4.387641             |
| H       | 0.869781            | 1.815317             | 2.483429             |
| H       | -2.551985           | 4.376656             | 3.676612             |
| H       | -3.180742           | 5.920467             | 1.784030             |
| H       | -1.858404           | 5.774617             | -0.357120            |
| H       | -1.129150           | 2.485527             | 3.650201             |
| H       | 2.126607            | 3.784188             | -2.581869            |
| H       | 2.896778            | 2.476803             | -1.669583            |
| H       | -1.042525           | 1.779381             | -5.586593            |
| H       | -0.431358           | -0.450932            | -3.716514            |
| H       | -3.561815           | -0.945157            | -2.948331            |
| H       | -3.314767           | -1.962743            | -3.483372            |
| H       | -4.125735           | -3.176147            | -2.242483            |
| H       | -4.384635           | -4.080159            | -0.597575            |
| H       | -2.471615           | -5.461522            | 0.821501             |
| N       | 0.353151            | -2.662774            | -1.528888            |
| N       | 0.601823            | -2.590366            | -2.508290            |
| N       | 0.538342            | 0.938455             | 5.305361             |
| N       | -0.965634           | -0.835978            | 3.625114             |
| N       | 0.212246            | 2.329400             | -3.903256            |
| N       | -0.613178           | 2.642768             | -3.853783            |
| N       | 0.539464            | 3.223248             | -4.450491            |
| N       | 0.540767            | -0.709761            | 3.896406             |
| N       | 0.835125            | -1.394138            | 4.703918             |
| N       | 1.101846            | 0.103631             | 3.005563             |
| N       | 1.382253            | 1.801960             | -3.063651            |
| N       | 2.198475            | 1.494728             | 3.273878             |
| N       | -1.528864           | -0.273523            | 4.379847             |
| N       | 0.520346            | 0.849559             | -5.546676            |
| N       | 0.946414            | -1.793713            | -0.624926            |
| O       | 0.477889            | -1.541755            | 0.474147             |
| H  | -1.201964 | -0.378413 | 2.656249 | H  | -2.758371 | 1.638103 | -3.910121 |
|----|-----------|-----------|----------|----|-----------|-----------|-----------|
| H  | 1.082232  | 0.906160  | -2.505622| N  | 2.025679  | -2.498403 | 0.356917  |
| N  | 2.116287  | -1.252255 | -1.126814| H  | 2.158032  | -1.656694 | -0.218883 |
| H  | 2.445678  | -1.607048 | -2.016630| C  | 3.121109  | -2.907494 | 1.122852  |
| C  | 2.945187  | -0.286949 | -0.529142| C  | 5.407324  | -3.544233 | 2.626630  |
| C  | 4.692572  | 1.656919  | 0.513431 | C  | 3.111436  | -4.012705 | 1.985163  |
| C  | 2.585803  | 0.445859  | 0.613487 | C  | 4.284935  | -2.128256 | 1.021026  |
| C  | 4.184631  | -0.038096 | -1.142498| C  | 5.413631  | -2.445689 | 1.766024  |
| C  | 5.046213  | 0.925993  | -0.624725| C  | 4.252865  | -4.316060 | 2.725937  |
| C  | 3.462027  | 1.406540  | 1.123525 | H  | 2.222509  | -4.622279 | 2.066757  |
| H  | 1.629896  | 0.255929  | 1.078737 | H  | 4.283700  | -1.268171 | 0.355024  |
| H  | 4.465239  | -0.599280 | -2.030618| H  | 6.302236  | -1.828123 | 1.673616  |
| H  | 5.998094  | 1.105424  | -1.116964| H  | 4.231199  | -5.175075 | 3.390650  |
| H  | 3.172169  | 1.969004  | 2.007729 | H  | 6.288480  | -3.793045 | 3.209173  |
| H  | 5.364299  | 2.408788  | 0.916452 | H  | 4.616331  | 3.959929  | -2.249378 |
| C  | 3.596633  | 3.738520  | 1.949054 | C  | 0.978760  | 3.171527  | -1.172868 |
| C  | 3.211958  | 2.421732  | -1.719080| C  | 2.671020  | 4.771969  | -1.803428 |
| C  | 1.360881  | 4.487328  | -1.418465| C  | 1.903621  | 2.132779  | -1.316869 |
| H  | 3.917789  | 1.605019  | -1.825555| H  | 2.970086  | 5.798872  | -1.991587 |
| H  | 0.638274  | 5.290544  | -1.309295| H  | -0.039371 | 2.934849  | -0.874122 |
| H  | 1.491916  | 0.704310  | -1.047861| O  | 0.358795  | 0.513828  | -0.515048 |
| O  | 2.290907  | -0.214129 | -1.370180| H  | -0.507613 | 1.933849  | -4.494819 |
### Table S2. Continuation.

|        | 4c=PhCO#2 (ΔE = +10.0 kJ/mol) | 4c=PhCO#3 (ΔE = +16.1 kJ/mol) |
|--------|-------------------------------|---------------------------------|
|        | E = 2571.0474 au              | E = 2571.0451 au                |
| O      |                               |                                 |
| 2.096533 | -1.385902                    | O                                |
| 3.660904 | -4.476703                    | -1.800107                      |
| -1.858498 | -2.683306                    | -2.560866                      |
| 2.919410 | -2.479250                    | 2.6019904                      |
| 0.890056 | 5.582959                     | 1.743970                       |
| -0.564682 | 2.427103                    | -1.207069                      |
| N       | 1.404206                     | -1.76343                        |
| -0.176103 | -2.500182                    | -0.044882                      |
| 0.655138 | -0.208343                    | 1.820582                       |
| 2.487028 | 2.150722                     | 2.039837                       |
| 0.737890 | 3.820354                     | -0.930481                      |
| C       | 0.587601                     | 1.93518                         |
| 0.817907 | 0.543083                     | 2.348084                       |
| C       | 0.406728                     | -0.871184                      |
| C       | 0.372543                     | 0.853444                       |
| C       | 0.280247                     | 0.770308                       |
| H       | 0.389344                     | 2.931759                       |
| C       | 0.587601                     | 4.352644                       |
| C       | 2.648894                     | 2.480908                       |
| N       | 0.403432                     | -0.981835                      |
| -0.176103 | -2.092712                    | -2.85313                       |
| -0.338569 | -0.849477                    | 3.016462                       |
| -0.873986 | -0.423312                    | -2.739829                      |
| -0.356208 | 0.278511                     | 3.170573                       |
| 0.263995 | 1.607303                     | -0.871184                      |
| 0.367177 | 1.556035                     | 2.221056                       |
| 1.820000 | -2.706407                    | 0.175174                       |
| 0.690434 | -4.499522                    | 1.146650                       |
| -0.674437 | 3.838917                     | -1.789877                      |
| 1.516649 | 2.609732                     | 0.1980275                      |
| 2.648881 | 1.952126                     | -2.583575                      |
| 2.879517 | 0.607616                     | 0.872772                       |
| H       | 4.076779                     | 0.391501                       |
| 3.61845 | -2.025557                    | 0.375015                       |
| H       | 0.770308                     | -1.821104                      |
| 0.893544 | -5.719413                    | 1.598103                       |
| 1.696493 | -5.628955                    | 0.767772                       |
| -1.591585 | 3.471801                    | 1.552044                       |
| 0.560313 | 1.889280                     | -0.326795                      |
| -1.681084 | -0.987376                   | -1.952587                      |
| -0.075530 | 1.096362                    | -3.616313                       |
| 1.104707 | 2.314112                     | -4.117752                      |
| 1.831511 | 0.525508                     | -1.635470                      |
| H       | 4.909315                     | 2.320827                       |
| 0.429469 | 0.419167                     | 0.631628                       |
| -0.634828 | -0.529874                    | 1.240610                       |
| C       | 0.511975                     | 0.987704                       |
| 3.982106 | 4.094143                     | 0.375015                       |
| 3.395101 | -0.395297                    | -0.047694                      |
| 0.071094 | 1.588147                     | -0.872772                      |
| 3.61845 | -2.025557                    | -2.345222                      |
| 3.61845 | -2.025557                    | -4.473233                      |
| 0.770308 | -3.094169                    | 0.872772                       |
| 3.373698 | 2.503522                     | 0.872772                       |
| 3.778419 | 0.119998                     | 0.631628                       |
| N       | 0.115343                     | -1.207069                      |
| C       | 0.406749                     | 0.327019                       |
| C       | 0.372543                     | -0.395185                      |
| C       | 0.280247                     | -0.891518                      |
| C       | 0.587601                     | -0.289153                      |
| C       | 2.648894                     | 1.745298                       |
| C       | 1.696493                     | 2.838577                       |
| -0.176103 | -1.632173                    | -1.789877                      |
| -0.338569 | -0.849477                    | 0.375015                       |
| -0.873986 | -0.423312                    | -1.789877                      |
| -0.356208 | 0.278511                     | 0.375015                       |
| 0.263995 | 1.607303                     | -1.789877                      |
| 0.367177 | 1.556035                     | -1.789877                      |
| 0.587601 | 0.543083                     | 0.375015                       |
| -0.186494 | 1.513185                     | -0.395185                      |
| -0.191268 | -0.965248                    | -1.207069                      |
| -2.699792 | -2.350686                    | 1.745298                       |
| -0.525691 | -3.396933                    | -5.628955                      |
| -0.323402 | -3.026275                    | 0.872772                       |
| -0.386205 | -2.493327                    | 0.375015                       |
| -0.499278 | -3.294256                    | 0.375015                       |
| -4.371220 | -3.826559                    | 0.375015                       |

S9
3. Copies of $^1$H and $^{13}$C NMR spectra

Figure S5. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4a in DMSO-$d_6$. 
Figure S6. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4b in DMSO-$d_6$. 
Figure S7. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4c in DMSO-$d_6$. 
Figure S8. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4d in DMSO-$d_6$. 
Figure S9. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4e in DMSO-$d_6$. 
Figure S10. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4f in DMSO-$d_6$. 
Figure S11. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4g in DMSO-$d_6$. 
Figure S12. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4h in DMSO-$d_6$. 
Figure S13. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4i in DMSO-$d_6$. 
Figure S14. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4j in DMSO-$d_6$. 
Figure S15. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4k in DMSO-$d_6$. 
Figure S16. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra of compound 4l in DMSO-$d_6$. 
4. Titration experiments

As the source of anions, commercially available tetrabutylammonium salts were used. HPLC grade water was added to the commercially available DMSO-d$_6$ of 99.9% isotopic purity to obtain the appropriate water concentration. The host solution was titrated in a NMR tube with the solution of the respective TBA salt in receptor aliquots (details are given in Table S3 and S4). The binding constants were calculated from the changes in chemical shifts of ligand protons which were shifted during titration. Nonlinear curve fitting was carried out with HypNMR 2008$^7$ (Version 4.0.71) program with fitting to the appropriate global binding model (see Table S3 and S4).

**Table S3.** Titration details, global stability constants $K_s$ (M$^{-1}$), and selected maximum signal shifts ($\Delta \delta_{\text{max}}$) of urea and amide protons for Receptors 4a, 4c,d,g with various anions in DMSO-d$_6$ + 0.5% H$_2$O$^a$

| Entry | Receptor | Anion       | $C_{\text{Host}}$ [M] | $C_{\text{Guest}}$ [M] | $K_s$ [M$^{-1}$] | $\Delta \delta_{\text{max}}$ [ppm] |
|-------|----------|-------------|------------------------|-------------------------|-----------------|----------------------------------|
| 1     | 4a       | Cl$^{-}$    | 0.26129                | 90                      | 0.15            | 0.30                             |
| 2     | 4a       | MeCO$_2^-$  | 0.27527                | 5970                    | 0.65            | -0.21                            |
| 3     | 4a       | PhCO$_2^-$  | 0.26129                | 5180                    | 0.74            | -0.22                            |
| 4     | 4c       | Cl$^{-}$    | 0.26106                | 140                     | 0.32            | -0.20                            |
| 5     | 4c       | MeCO$_2^-$  | 0.28629                | >10000$^b$              | 0.89            | -0.22                            |
| 6     | 4c       | PhCO$_2^-$  | 0.28960                | >10000$^b$              | 0.89            | -0.11                            |
| 7     | 4c       | Cl$^{-}$    | 0.25187                | 140                     | 0.27            | -0.15                            |
| 8     | 4c       | MeCO$_2^-$  | 0.17974                | >10000$^b$              | 0.81            | -0.18                            |
| 9     | 4c       | PhCO$_2^-$  | 0.17363                | >10000$^b$              | 0.81            | -0.18                            |
| 10    | 4c       | Cl$^{-}$    | 0.19430                | 310                     | 0.46            | -0.22                            |
| 11    | 4g       | MeCO$_2^-$  | 0.18456                |                          |                 | -0.22                            |
| 12    | 4g       | PhCO$_2^-$  | 0.19164                |                          |                 | -0.22                            |

$^a$ Values determined by $^1$H NMR titration experiments at $T = 298$ K using HypNMR 2008 software, $^b$ errors < 10%, TBA salts as the source of anions. $^c$ Stability constants above the limit of the $^1$H NMR titration technique ($\geq 10000$). $^d$ Not determined.

**Table S4.** Titration details, global stability constants $K_s$ (M$^{-1}$), and selected maximum signal shifts ($\Delta \delta_{\text{max}}$) of urea and amide protons for Receptors 4a, 4c,d,g,l, and 5 with various anions in DMSO-d$_6$ + 5% H$_2$O at 298 K$^a$

| Entry | Receptor | Anion       | $C_{\text{Host}}$ [M] | $C_{\text{Guest}}$ [M] | $K_s$ [M$^{-1}$] | $\Delta \delta_{\text{max}}$ [ppm] |
|-------|----------|-------------|------------------------|-------------------------|-----------------|----------------------------------|
| 1     | 4c       | MeCO$_2^-$  | 0.28717                | 1120                    | 0.83            | -0.26                            |
| 2     | 4c       | PhCO$_2^-$  | 0.28735                | 1780                    | 0.92            | -0.26                            |
| 3     | 4c       | Cl$^{-}$    | 0.19124                | 60                      | 0.25            | -0.07                            |
| 5     | 4d       | MeCO$_2^-$  | 0.18456                | 2400                    | 0.76            | -0.13                            |
| 6     | 4d       | PhCO$_2^-$  | 0.19164                | 4070                    | 0.86            | -0.05                            |
| 7     | 4d       | Cl$^{-}$    | 0.22237                | 120                     | 0.20            | -0.08                            |
| 8     | 4l       | MeCO$_2^-$  | 0.19700                | 7940                    | 0.75            | -0.21                            |
| 9     | 4l       | PhCO$_2^-$  | 0.17658                | 6760                    | 0.15            | -0.21                            |
| 10    | 5        | MeCO$_2^-$  | 0.24708                | 7                       | 0.73            | 0.43                             |
| 11    | 5        | PhCO$_2^-$  | 0.20065                | 10                      | 0.92            | 1.27                             |

$^a$ Values determined by $^1$H NMR titration experiments at $T = 298$ K using HypNMR 2008 software, $^b$ errors < 10%, TBA salts as the source of anions. $^c$ Not determined.

**Figure S17.** Labeling of the selected proton peaks of the receptors 4a, c, d, g, l, and 5.
Figure S18. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of Receptor 4a with increasing amount of (a) $n$-Bu$_4$NCl; (b) $n$-Bu$_4$NH$_2$PO$_4$; (c) $n$-Bu$_4$NCO$_2$Me and (d) $n$-Bu$_4$NCO$_2$Ph in DMSO-$d_6$ + 0.5% H$_2$O (v/v) (right).
Figure S19. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^3$H NMR titrations of Receptor 4c with increasing amount of (a) n-Bu4NCl; (b) n-Bu4NH2PO4; (c) n-Bu4NCO2Me and (d) n-Bu4NCO2Ph in DMSO-$d_6$ + 0.5% H2O (v/v) (right).
(a) Not determined.

(b) Fitting failed due to a complex binding model.

Figure S20. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of Receptor 4c with increasing amount of (a) $n$-Bu$_4$NCl; (b) $n$-Bu$_4$NH$_2$PO$_4$; (c) $n$-Bu$_4$NCO$_2$Me and (d) $n$-Bu$_4$NCO$_2$Ph in DMSO-$d_6$ + 5% H$_2$O (v/v) (right).
Figure S21. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of Receptor 4d with increasing amount of (a) $n$-Bu$_4$NCl; (b) $n$-Bu$_4$NH$_2$PO$_4$; (c) $n$-Bu$_4$NCO$_2$Me and (d) $n$-Bu$_4$NCO$_2$Ph in DMSO-$d_6$ + 0.5% H$_2$O (v/v) (right).
Figure S22. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of receptor 4d with increasing amount of (a) $n$-Bu$_4$NCl; (b) $n$-Bu$_4$NH$_2$PO$_4$; (c) $n$-Bu$_4$NCO$_2$Me and (d) $n$-Bu$_4$NCO$_2$Ph in DMSO-$d_6$ + 5% H$_2$O (v/v) (right).
Figure S23. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of receptor 4g with increasing amount of (a) n-Bu₄NCl; (b) n-Bu₄NH₂PO₄; (c) n-Bu₄NCO₂Me and (d) n-Bu₄NCO₂Ph in DMSO-$d_6$ + 0.5% H₂O (v/v) (right).
Fitting failed due to a complex binding model.

Figure S24. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of receptor 41 with increasing amount of (a) $n$-Bu$_4$NCl; (b) $n$-Bu$_4$NH$_2$PO$_4$; (c) $n$-Bu$_4$NCO$_2$Me and (d) $n$-Bu$_4$NCO$_2$Ph in DMSO-$d_6$ + 5% H$_2$O (v/v) (right).
Figure S25. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model (left); Stacked plots from $^1$H NMR titrations of receptor 5 with increasing amount of (a) $n$-Bu$_4$NCO$_2$Me and (b) $n$-Bu$_4$NCO$_2$Ph in DMSO-$d_6$ + 5% H$_2$O (v/v) (right).

Figure S26. Comparison of experimental shift changes (symbols) and calculated binding isotherms (lines) assuming 1:1 binding model for NH signals of 4c and 4d receptors.
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