Tweezer-Type Catechol and Resorcinol Derivatives: Preparation, Structures, and First Investigations Towards their Hydrogen Bonding Abilities

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Abstract: Tweezer-type molecules with an ester linkage between catechol or resorcinol and linear amino acid-based urea or amide derivatives are prepared. X-ray structures of representative compounds show, that the molecules are able to form intra- as well as intermolecular hydrogen bonds. In solution this hydrogen bonding donor/acceptor ability of the tweezers can be seen, on the one hand by interaction with anionic guest species (nitrate), and on the other hand by formation of gels in the case of the urea derivatives.

Key words: amino acids, esters, hydrogen bonds, molecular recognition, supramolecular chemistry

The selective recognition of cations, neutral molecules or anions plays an important role in many biological processes. To understand the basic principles of molecular recognition phenomena which occur in nature is an important goal on the way to design efficient artificial receptors. The selectivity of the binding of guest species hereby depends on a perfect geometric and electronic match between the host and the guest (receptor/substrate).[1]

Very often cyclic molecules are used to model the receptor abilities towards different guests.[2] However, as an alternative tweezer-type compounds, which possess a higher flexibility, also can act as receptors.[3] Recently we started to study tweezer-type compounds which possess an aromatic biphenol backbone to which two side chains are attached via ester linkages. The side chains should possess hydrogen bond donor/acceptor units to enable an interaction with appropriate guest species. We have already reported, that the 2,2′-biphenol derivatives **1**–**3** (Figure 1) are able to bind nitrate in a 1:1 fashion and that an additive effect of the number of hydrogen bonds[4] is observed in the binding of anions. Every additional hydrogen bond leads to an enhancement of the free enthalpy of complexation of 2–3 kJ/mol.[5]

However, the association constants which were observed for the binding of nitrate by **1–3** are very low.[5] In the present study we substitute the flexible 2,2′-biphenol backbone by the more rigid catechol and resorcinol backbone. The use of the two different backbones allows a fixation of the tweezer-arms in an 60° (**a**) or 120° (**b**) angle (Figure 2).

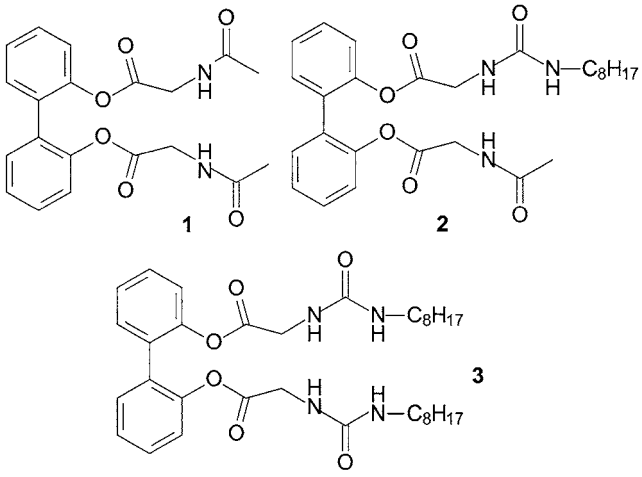

Figure 1 Tweezer-type receptor molecules based on 2,2′-biphenol and glycine derived side chains.

To enable some interaction with potential guest species, we introduce different side arms which bear hydrogen bond donor/acceptor moieties (indicated by the arrows in Figure 2 **A**–**E**).[6] The number of such potential binding units can be varied by introducing either amides (**B**) and carbamates (**A, C**) or ureas (**D, E**) and their distance can be altered by using different spacers. Additionally the steric hindrance (**C**) and the solubility (different substituents at the terminus **D**) of the system can be influenced and chirality can be introduced (R = Me, **D**).

The very simple dicarbamate **5a** is prepared by reaction of catechol **4a** with octyl isocyanate in acetonitrile and isolated after column chromatography (silica gel, ethyl acetate–hexane, 1:2) in 50% yield (Scheme 1).

The compounds, which are based on a catechol or a resorcinol backbone and on two *N*-acetylglycine side chains **7a**,**b** are prepared in a one-step procedure starting from the corresponding dihydroxybenzene derivative **4a** (catechol) or **4b** (resorcinol) and *N*-acetylglycine **6** (Scheme 2).

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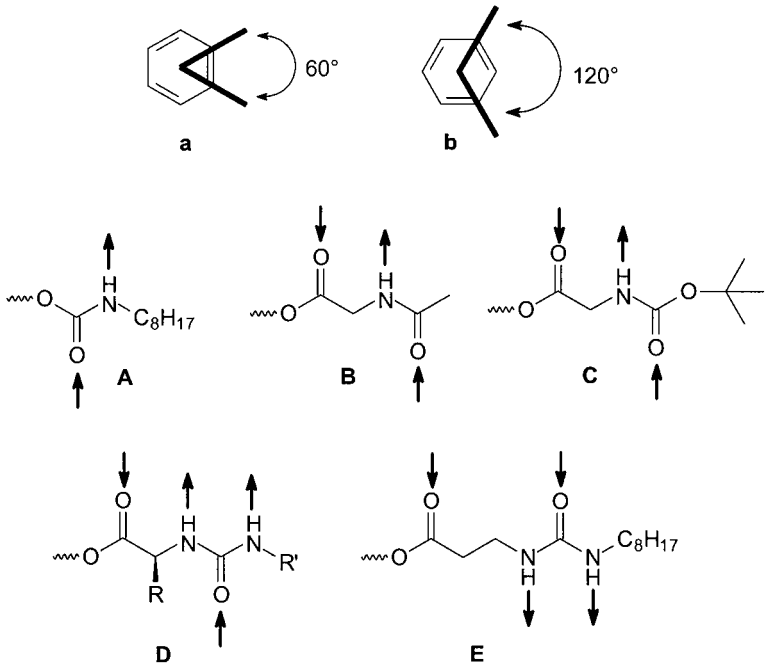
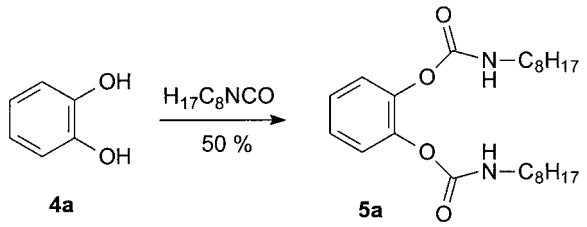


Figure 2 Comparison of the catechol **a** and resorcinol **b** backbone (top) and of the hydrogen bond donor/acceptor ability of different side arms (bottom).



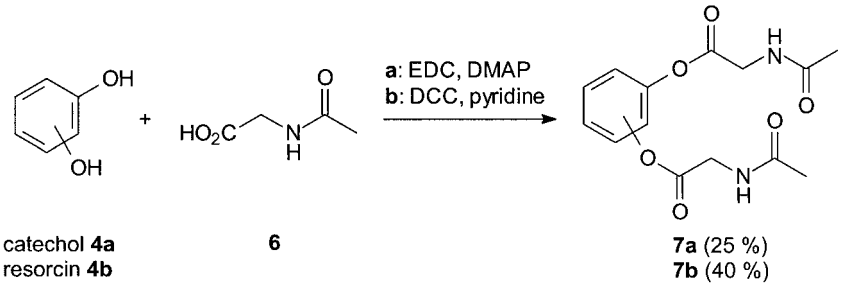
Scheme 1

The double ester formation to form **7a** proceeds in the presence of EDC [*N*-ethyl(*N*′-dimethylaminopropyl)carbodiimide] and DMAP (4-*N*,*N*-dimethylaminopyridine)[7] in dichloromethane at 0→25 °C. The compound **7a** is purified by crystallization from ethyl acetate–hexane and is obtained in 25% yield as a white solid.

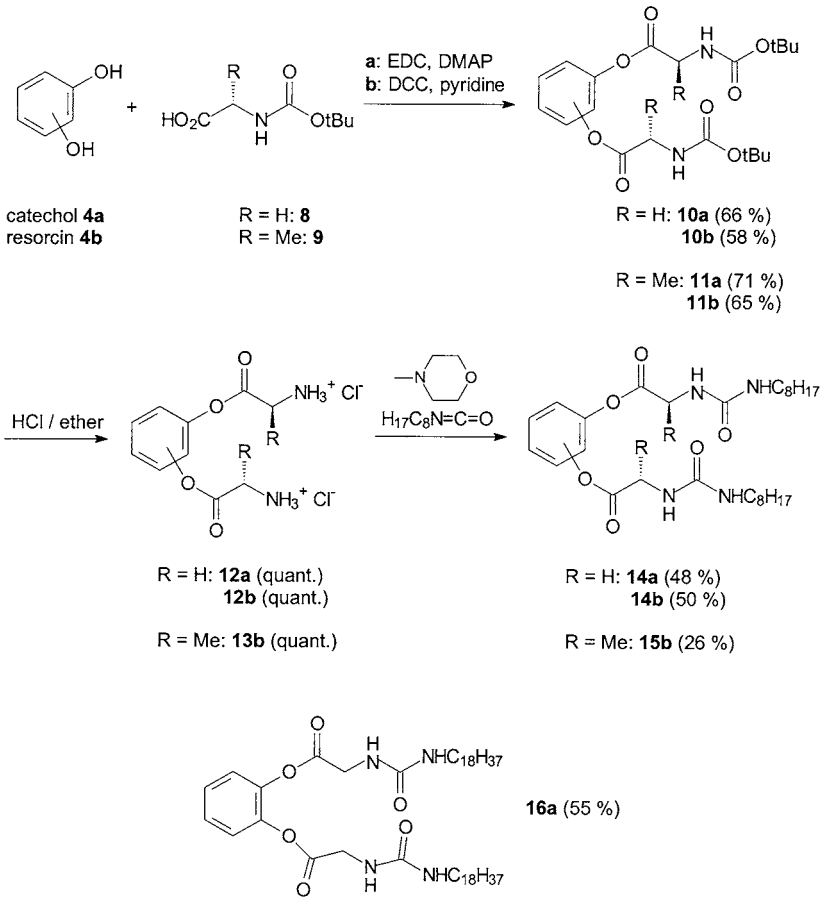
The resorcinol derivative **7b** is obtained best with DCC (*N*,*N*′-dicyclohexylcarbodiimide) and pyridine as coupling reagents.[8] Recrystallization is done from ethyl acetate–hexane 1:2 to obtain **7b** in 40%. The yields in the preparations of **7a/b** are relatively low due to the loss of material during the recrystallization. However, the compounds are obtained in high purity.

Related tweezer-type derivatives of catechol and resorcinol, which bear urea moieties in the side arms, can be prepared in three step sequences.

In the first step of the reaction sequence catechol (**4a**) or resorcinol (**4b**) are coupled with *N*-BOC-glycine **8** using the same coupling procedures as were applied to the corresponding *N*-acetyl derivatives **7a** and **7b**. The diester **10a** is obtained in 66% by EDC/DMAP coupling, while **10b** is formed in 58% by coupling with DCC/pyridine. Additionally we prepared the chiral derivatives **11a** (71%) or **11b** (65%) by reaction of catechol (**4a**) or resorcinol (**4b**) with *N*-BOC-alanine **9** in the presence of DCC and pyridine (Scheme 3). The BOC protecting groups are removed quantitatively by reaction of **10a**,**b** and **11b** with HCl in ether and the dihydrochlorides **12a**,**b** and **13b** are coupled directly with *N*-methylmorpholine[9] to liberate the amino functions which are trapped by octyl isocyanate to obtain the urea derivatives **14a** (48%), **14b** (50%) and **15b** (26%). The compounds precipitate from the reaction mixture and can be isolated in analytically pure form by filtra-



Scheme 2



Scheme 3

tion. Attempts to deprotect **11a** and subsequently couple the resulting amine with isocyanate failed due to decomposition of the material.

The derivative **16a** with octadecyl instead of the decyl substituent is prepared in a similar way from **12a** as a crude product. However, **16a** could not be purified and was not obtained in analytically pure form.

For comparison studies we also synthesized the catechol derivative **20a** with β-alanine in the spacer. The compound with β-alanine urea moieties in the side arms **20a** is prepared starting from catechol **4a** and forming the diester with *N*-BOC-β-alanine **17** in the presence of EDC and DMAP. The diester **18a** is obtained in 60% yield. The BOC protecting groups of **18a** are removed by reaction with HCl and subsequently the dihydrochloride **19a** is reacted with *N*-methylmorpholine and octyl isocyanate. Thus, the derivative **20a** is obtained in 56% yield (over two steps) (Scheme 4).

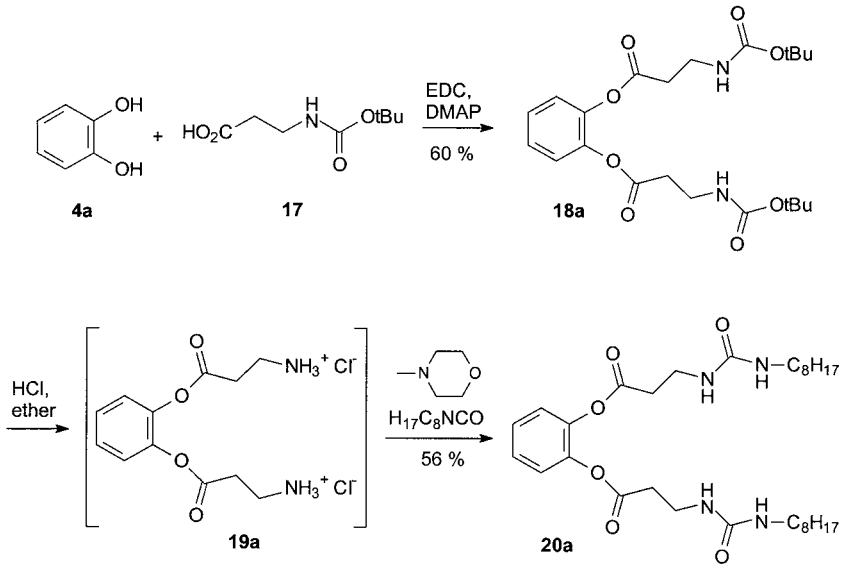
As described, we have several tweezer-type catechol (**5a**,**7a**,**10a**,**14a**,**16a** and **20a**) and resorcinol derivatives (**7b**,**10b** and **14b**) in our hands, which we can now investigate for their ability to form hydrogen bonds.

First we investigated representative X-ray structures of the catechol derivatives **11a**,**7a** and of the 'single-armed' intermediate **21a** in the solid state.[10] Compound **21a** is prepared by coupling of catechol (**4a**) with only one equivalent of **6** in 72% yield.

Figure 3 shows the structure of the BOC-protected bisalanyl catechol ester **11a** in the solid state. This compound forms a monomeric structure in the solid state with one intramolecular NH–O hydrogen bond bridging the two side arms (N...O = 2.902 Å). Hereby a 13 membered macrocycle results, which forms a saddle shaped structure with the two alanyl methyl groups more or less pointing towards the concave face of the molecule. A weaker intermolecular hydrogen bond is formed with N...O = 3.075 Å leading to a one-dimensional band in [100] directions.

The monomeric structure of the bis(*N*-acetylglycine)ester of catechol **7a** is presented in Figure 4a. The tweezer-type arrangement can be seen very nicely in this representation. No intramolecular hydrogen bonding can be observed for **7a** in the solid state.

Figure 4b on the other hand shows three molecules of **7a** forming a polymeric strand by hydrogen bonding.[6,11] Hereby the central molecule binds by its amide protons to two neighboring molecules. Additional hydrogen bonds are formed by the amide-oxygen atoms (Figure 4c) leading to a complicated three dimensional hydrogen bonded network with two different types of hydrogen bonds (N…O = 2.831 and 2.862 Å). The ester functionalities do



Scheme 4

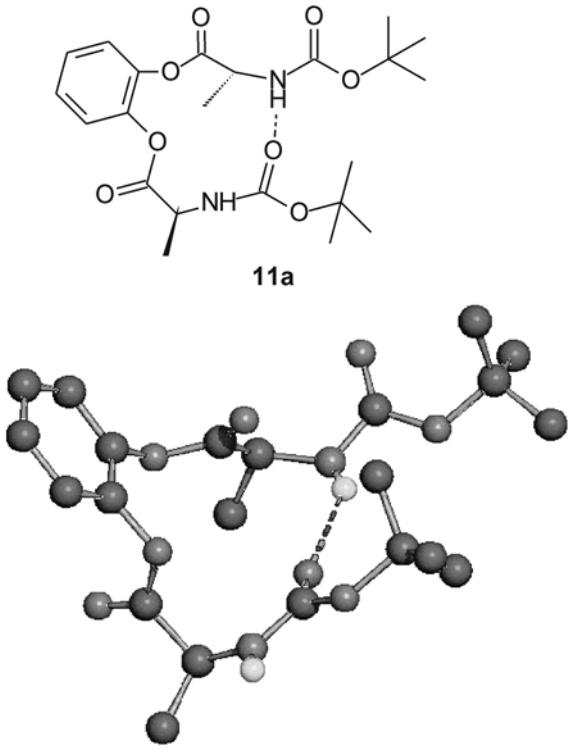


Figure 3 Molecular structure of **11a** as found in the solid state.

not interfere with the hydrogen bonding interactions. Here the ability of tweezer-type compounds like **7a** to act through their amide units of the side chains as hydrogen bond donor as well as acceptor molecules is nicely demonstrated.[6]

For comparison we prepared and crystallized compound **21a** with only one *N*-acetylglycine attached by ester linkage to catechol. One phenolic OH is able to form a hydrogen bond in addition to the amide of the acetylglycine moiety.

Figure 5a shows the monomeric structure of **21a** in the solid state. The acetylglycine is attached in a linear form to the aromatic ring with the ester twisted out of plane and the amide oriented in plane of the aromatic unit. The phenolic hydrogen does not form an intramolecular hydrogen bond to the neighboring ester unit but participates in intermolecular interactions. Hydrogen bonding between the amide oxygen atoms and the OH groups of two molecules **21a** leads to a macrocyclic dimer (Figure 5b), which by additional interaction of the amide oxygens with amide protons of neighboring molecules leads to a three-dimensional network in the solid state (Figure 5b/c). Hereby the O(2)-atom of the acetate undergoes two hydrogen bonding interactions; one with the phenolic OH group (O…O = 2.622 Å) and one with the amidic NH (N…O = 2.914 Å). Another weaker hydrogen bond (N...O = 3.142 Å) is observed between the amide proton and O(5).

The X-ray structural results show, that our compounds are able to undergo hydrogen bond interactions. Hereby bulky groups in the periphery seem to suppress or weaken intermolecular binding, while sterically less demanding derivatives lead to hydrogen-bridged polymeric structures in the solid state. The results observed in the solid state encouraged us to investigate into the ability of the tweezer-type complexes to form hydrogen bonds in solution: either with guest species or with each other.

In a preliminary study we tested the anion binding[12] by the tweezer-type compounds using nitrate anions[13] as guest species, which can be fixed in the tweezer by hydrogen bonding interaction. The results of the titration studies are summarized in Table 1 and Figure 6 shows as a representative example the Job plot for the system **7a**/NO_3^- and the corresponding titration curve. [NMR titration experi-

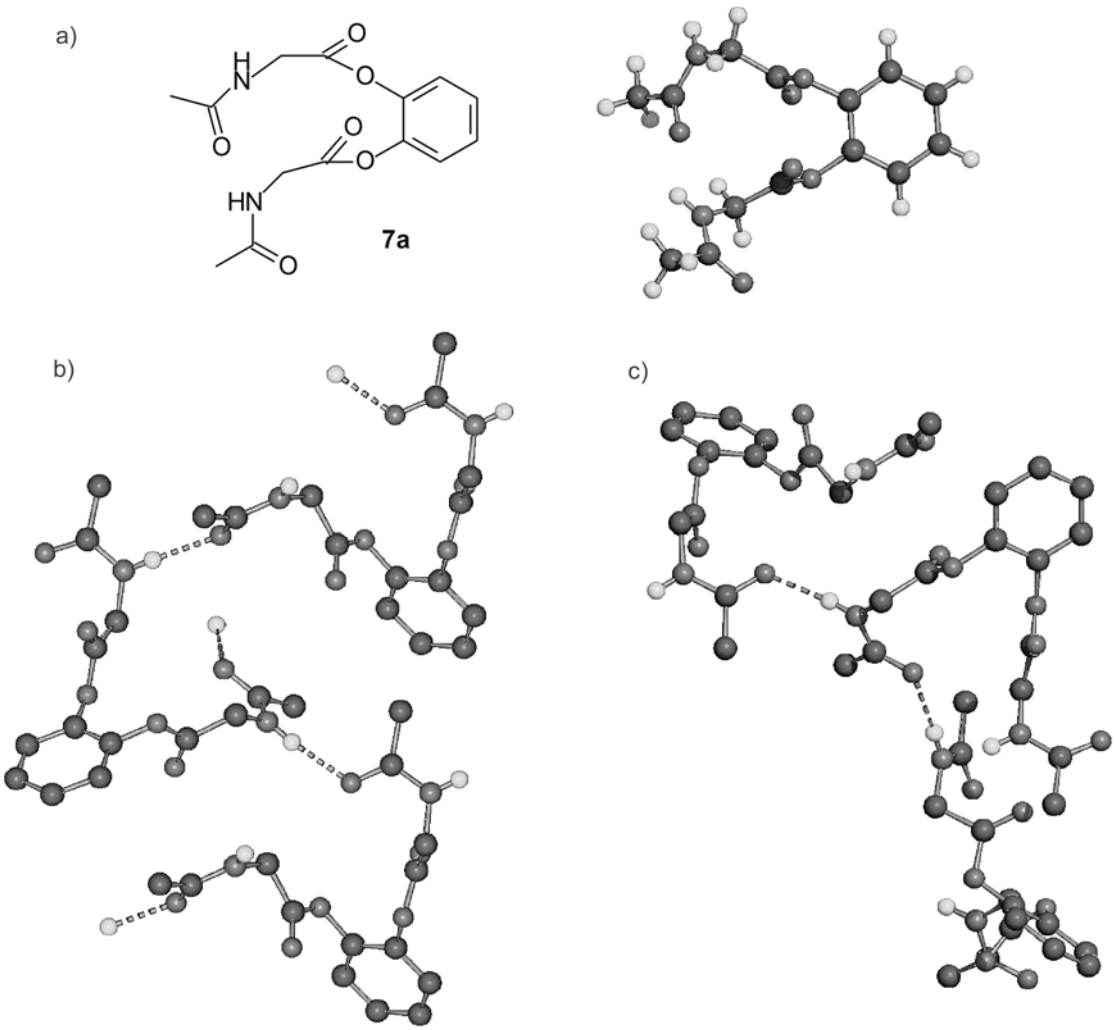


Figure 4 Molecular structure of **7a** as found in the solid state: a) the monomeric structure and b,c) different views of the hydrogen bonded network.

ments were performed in $CDCl_3$ at 297 K with subsequent addition of tetrabutylammonium nitrate (TBAN)].[14]

Titration plots for **5a**,**7a**,**14a**,**20a**,**7b**,**14b**, and **15b** with nitrate using Jobs method[14] show that a 1:1 complex is formed between the tweezer-type receptor and the anion. The titration experiments reveal, that the biscarbamate **5a** binds nitrate with a very low binding constant (K_a <25 mol^{-1}) while the bis-acetylglycine **7a** leads to a reasonable – but still weak – binding (K_a = 158 mol^{-1}). In the latter the distance between the two amide NH units seems to be more favorable for the binding of nitrate than in **5a** (Figure 7). Attempts to get stronger binding of the nitrate by introduction of further hydrogen binding sites in the ligands **14a**,**16a**, and **20a** does not lead to higher association constants.[5] Probably due to steric constrains in **14a** and poor preorganization in **20a** K_a values of 126 mol^{-1} (**14a**) and 102 mol^{-1} (**20a**) are observed for the binding of the anion. No association constant could be determined for the interaction of nitrate with **16a** (vide infra).

The resorcinol derivatives are also able to bind nitrate in a 1:1 fashion.[15] Hereby an enhancement of the binding constant is observed by switching from the simple bis-amide **7b** (K_a = 59 mol^{-1}) to the bis-urea derivative **14b** (K_a = 113 mol^{-1}). Comparison of the very similar receptors **14b** and **15b** shows that the methyl groups of the alanine residues of **15b** introduce conformations which are not favorable for the formation of a host/guest complex with nitrate. Binding of nitrate by the resorcinol derived tweezers strongly influences the chemical shift of the proton in 2 position of the resorcinol which is directed towards the anion binding site. Maximum high field shifts of 67 Hz (**7b**), 22 Hz (**14b**), and 58 Hz (**15b**) are observed in the titration experiments. For the protons H-4/6 and H-5 a less pronounced shifting occurs.

Although the observed association constants are all low, we can deduce some tendencies which should help us to design more effective receptors for anions in the future.

Hydrogen bonding in solution should not only occur with guest species, but hydrogen bonds should also be formed

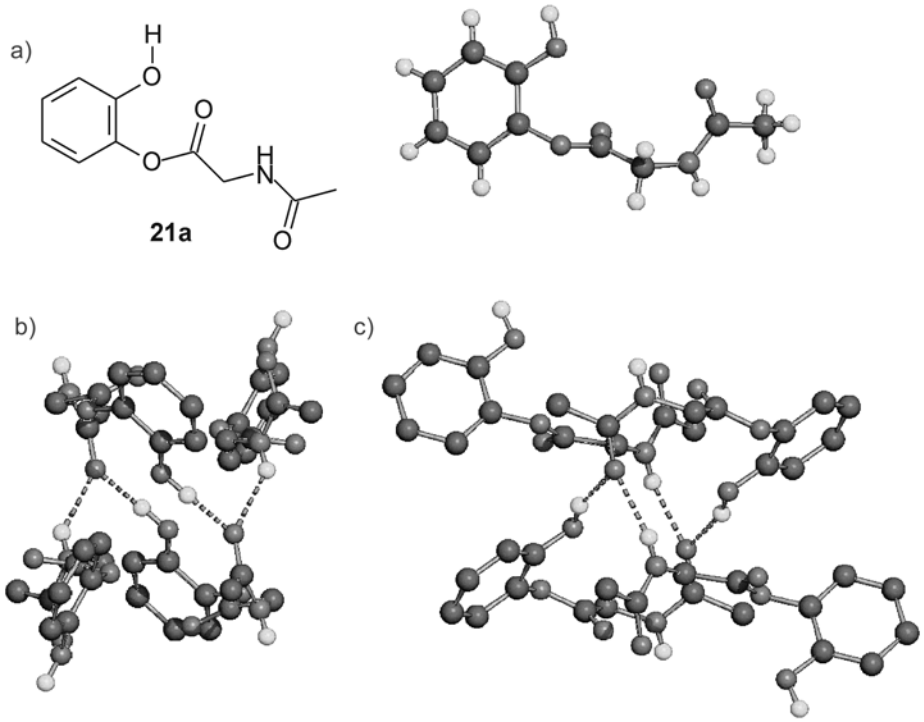


Figure 5 Molecular structure of **21a** as found in the solid state: a) the monomeric structure and b,c) different fews of the hydrogen bonded network.

between two or more tweezer-type molecules, leading to networks as observed in the solid state for **7a** or **21a**. Therefore we looked for possible gelating properties of the compounds and the results are summarized in Table 2. All experiments on the gelating properties were performed with 5 mg compound/1 mL solvent at room or at low (253 K) temperature.[16]

For simple amides like **5a** or **7a** no gelating could be observed in a series of different solvents. However, urea derivatives lead to gelation of a number of solvents. For example **14a** forms a gel in chloroform at room temperature, while a solution of **14a** in dichloromethane or ethyl acetate gelates upon cooling. Introducing longer alkyl chains in the periphery of the molecules as shown with compound **16a** leads to strong gelation in benzene. In dichloromethane and chloroform gelation proceeds at low temperature. Precipitation of **16a** as a fluffy – probably hydrogen bridged – solid from chloroform at room temperature is the reason, that no association constant with nitrate could be determined. Surprisingly, the β-alanyl derivative **20a** does not gelate any of the tested solvents.

Layering the gel, which is formed from **14a** in chloroform, with a few drops of a concentrated solution of tetrabutylammonium nitrate in chloroform, leads to a slow dissolution of the gel. Here the nitrate anions break up the hydrogen bonding network of the gel and form the already described 1:1 host guest complex $[\mathbf{14a}\cdot NO_3]^-$ with the receptor. The resorcinol derivatives **14b** and **15b** in chloroform only lead to organogels upon cooling the solutions.

In conclusion, we have presented the syntheses of tweezer-type compounds based on a catechol or resorcinol backbone and on two side arms which possess amide or urea functionalities as hydrogen bond donor/acceptor moieties. The use of either catechol or resorcinol as backbone allows the fixation of the arms at a defined angle to each other.

The solid state structures of **7a**, **11a** and **21a** show that the compounds are able to undergo hydrogen bonding. However, bulky groups like the BOC substituent of **11a** seems to prevent intermolecular hydrogen bonding.

In solution the ability of the tweezer-type compounds can be shown by host/guest interaction with nitrate. Low association constants were obtained by NMR titrations but some trends can be seen which might help in the design of more effective receptors. Additionally, in some cases gelation of solutions was observed, showing that the molecules can interact with each other to build up network structures.

In this paper we did not describe novel superior receptors but we have investigated a class of interesting tweezer-type compounds and showed that they are able to undergo hydrogen bonding interactions. In future studies this system has to be optimized and we hope that we can use the labile aryl ester linkages between the backbone and the side-arms to enter the field of 'dynamic combinatorial chemistry' based on libraries of related receptor molecules.[17]

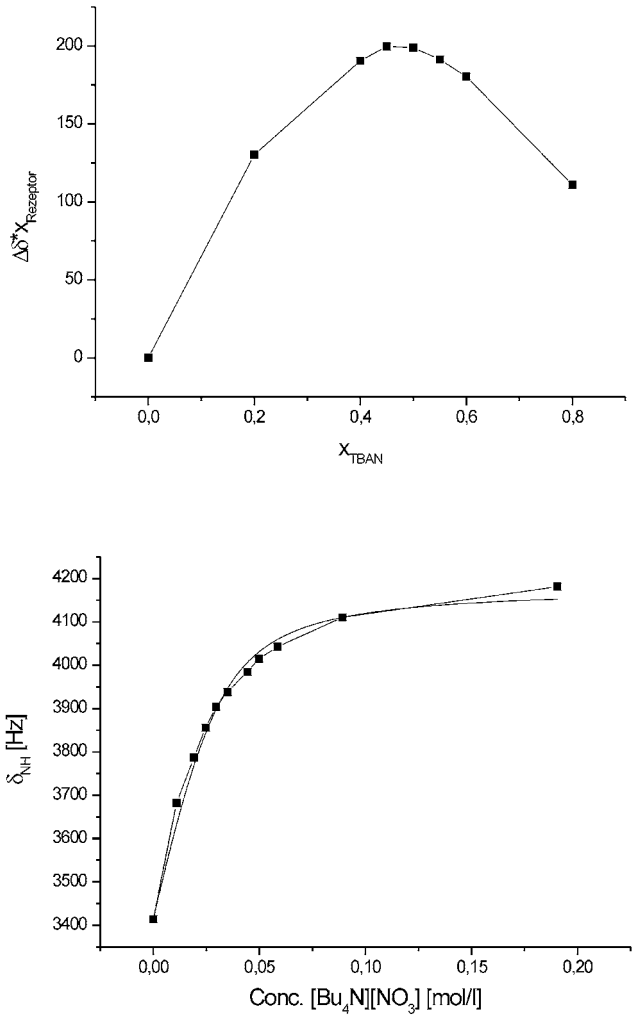


Figure 6 Jobs plot for the interaction of the receptor **7a** with tetrabutylammonium nitrate showing that a 1:1 complex is formed (X = molar fraction) (top). ^{1}H NMR titration curve (500 MHz) for the titration of **7a** (amide proton) with tetrabutylammonium nitrate in $CDCl_3$ at 297 K (bottom).

Table 1 Maximum ^{1}H NMR Shift Differences $\Delta\delta_{max}$ (500 MHz), Association Constants K_a and Free Enthalpy of Complexation ΔG_{HG} for the Formation of Receptor/Substrate Complexes with Nitrate

Nitrate Complex	$\Delta\delta_{max}$ ($CDCl_3$, 500 MHz) (Hz)	K_a (296 K) (mol^{-1})	ΔG_{HG} ($kJ \cdot mol^{-1}$)
5a·NO_3^-	143	< 25	> –8.1
7a·NO_3^-	768	158 ± 13	–12.5 ± 0.2
14a·NO_3^-	187	126 ± 40	–11.9 ± 0.8
16a·NO_3^-	–	–	–
20a·NO_3^-	338	102 ± 7	–11.4 ± 1.7
7b·NO_3^-	763	59 ± 6	–10.0 ± 0.3
14b·NO_3^-	398	113 ± 10	–11.7 ± 0.2
15b·NO_3^-	533	88 ± 6	–11.1 ± 0.2

Table 2 Gelating Properties of the Tweezer-Type Compounds in Different Solvents[a]

Compound	$CHCl_3$	CH_2Cl_2	EtOAc	Benzene
5a	–	–	–	–
7a	–	–	–	–
14a	++	+	+	–
16a	+	+	insoluble	++
20a	–	–	–	–
14b	+	–	–	–
15b	+	–	–	–

[a] – no gelating properties; + gelating at low temperatures; ++ gelating at room temperature.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX 500 spectrometer using DEPT techniques for the assignment of the multiplicity of carbon atoms. FT-IR spectra were recorded by diffuse reflection (KBr) on a Bruker IFS spectrometer. Mass spectra (EI, 70 eV) were taken on a Finnigan MAT 90 mass spectrometer. Elemental analyses were obtained with a Heraeus CHN-O-Rapid analyzer. Solvents were purified by standard methods. Melting points: Büchi B-540 (uncorrected).

***N*-Octyl[(2-(*N*-octylcarbamoyloxy)phenoxy]formamide (5a)**

Catechol (**4a**; 220 mg, 2.00 mmol) was dissolved in anhyd MeCN (20 mL) and under argon octyl isocyanate (706 μL, 4.00 mmol) was added. The mixture was refluxed for 16 h before the solvent was removed in vacuum. The residue was dissolved in EtOAc, washed with sat. aq $NaHCO_3$ (3 ×), dried ($MgSO_4$) and the solvent was removed. The crude product was purified by chromatography over silica gel (EtOAc–hexane, 1:2); yield: 420 mg (50%); white solid; mp 105 °C.

IR (KBr): 3339, 2959, 2923 2853, 1718, 1541, 1495, 1262, 1188, 761 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.19 (m, 4 H), 5.19 (br s, 2 H), 3.24–3.20 (m, 4 H), 1.53 (m, 4 H), 1.28 (m, 20 H), 0.88 (t, *J* = 6.9 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 153.9 (C), 143.1 (C), 126.1 (CH), 123.5 (CH), 41.4 (CH_2), 31.8 (CH_2), 29.8 (CH_2), 29.2 (CH_2, double intensity), 26.7 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

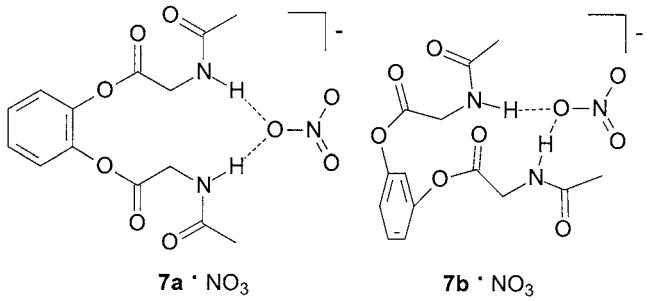
Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 421 $[M + H]^+$, 443 $[M + Na]^+$.

HRMS: *m*/*z* calcd for $C_{24}H_{41}N_2O_4$: 421.3066, found: 421.3057.

Anal. Calcd for $C_{24}H_{40}N_2O_4$ (420.59): C, 68.54; H, 9.59; N, 6.66: Found: C, 68.53; H, 9.24; N, 6.84.

2-[2-(Acetylamino)acetyloxy]phenyl-2-(acetylamino)acetate (7a)

Catechol (**4a**; 550 mg, 5.00 mmol), *N*-acetylglycine (**6**; 1.18 g, 10.0 mmol), and 4-*N*,*N*-dimethylaminopyridine (DMAP, 1.22 g, 10.0 mmol) were dissolved in CH_2Cl_2 at 0 °C. EDC (2.18 g, 11.4 mmol) was added and after 2 h at 0 °C, the mixture was allowed to warm to r.t. and stirred for additional 16 h. The solution was washed with sat. aq NH_4Cl (3 ×), dried ($MgSO_4$) and the solvent was removed in vacuum. The crude product was purified by recrystallization from EtOAc–hexane; yield: 384 mg (25%); white solid; mp 144 °C.



7a · NO_3 **7b** · NO_3

Figure 7 Comparison of possible nitrate binding modes of the catechol and resorcinol based receptors.

IR (KBr): 3247, 3069, 1794, 1653, 1571, 1490, 1407, 1376, 1242, 1158, 1149, 1119, 1038, 790, 781 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.27–7.24 (m, 2 H), 7.18–7.16 (m, 2 H), 6.93 (t, *J* = 5.9 Hz, 2 H), 4.22 (d, *J* = 5.9 Hz, 2 H), 2.06 (s, 6 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.3 (C), 167.6 (C), 141.8 (C), 127.1 (CH), 123.3 (CH), 41.3 (CH_2), 22.9 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 309 $[M + H]^+$.

Anal Calcd for $C_{14}H_{16}N_2O_6$ (308.29): C, 54.54; H, 5.23; N, 9.09. Found: C, 54.09; H, 5.31; N, 8.75.

X-Ray Structural Analysis of 7a[18]

Formula: $C_{14}H_{16}N_2O_6$, *M* = 308.29, colorless crystal 0.40 × 0.30 × 0.20 mm, *a* = *b* = 10.1776(2), *c* = 15.0922(3) Å, *V* = 1563.30(5) $Å^3$, ρ_{calc} = 1.310 g cm^{-3}, = 0.104 cm^{-1}, no absorption correction (0.960 < *T* < 0.980), *Z* = 4, tetragonal, space group $P4_1$ (No. 76), λ = 0.71073 Å, *T* = 173 K, ω and φ scans, 9971 reflections collected (±*h*, ±*k*, ±*l*), $[\sin\theta/\lambda]_{max}$ = 0.59 $Å^{-1}$, 2755 independent (R_{int} = 0.033) and 2555 observed reflections [$I \geq 2\sigma(I)$], 208 refined parameters, *R*1 = 0.045, *wR*2 = 0.109, Flack parameter 0.6(15), maximum residual electron density 0.16 (–0.20) e $Å^{-3}$.

3-[2-(Acetylamino)acetyloxy]phenyl-2-(acetylamino)acetate (7b)

Resorcinol (**4b**; 1.10 g, 10.0 mmol), *N*-acetylglycine (**6**; 2.36 g, 20.0 mmol), *N*,*N*′-dicyclohexylcarbodiimide (DCC, 4.56 g, 21.0 mmol) and pyridine (3 mL) in EtOAc (80 mL) were stirred for 3 d. Three drops of AcOH were added and after 30 min, the mixture was heated and was filtered hot. The solvent was removed in vacuum and the remaining crude product was recrystallized from hexane–EtOAc (2:1); yield: 1.22 g (40%); white solid; mp 139 °C.

IR (KBr): 3275, 3089, 2981, 2929, 2851, 1777, 1765, 1645, 1601, 1560, 1370, 1252, 1188, 806, 799, 605 cm^{-1}.

^1H NMR (DMSO-d_6, 500 MHz): δ = 8.46 (t, *J* = 5.7 Hz, 2 H), 7.46 (t, *J* = 8.2 Hz, 1 H), 7.03 (dd, *J* = 2.2, 8.2 Hz, 2 H), 6.94 (t, *J* = 2.2 Hz, 1 H), 4.06 (d, *J* = 5.7 Hz, 4 H), 1.88 (s, 6 H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ = 170.5 (C), 169.3 (C), 151.2 (C), 130.6 (CH), 119.7 (CH), 116.0 (CH), 41.5 (CH_2), 22.6 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 309 $[M + H]^+$.

Anal. Calcd for $C_{14}H_{16}N_2O_6 \cdot 3/2\ H_2O$ (335.29): C, 50.15; H, 5.71; N, 8.35. Found: C, 49.92; H, 5.73; N, 8.28.

2-{2-[(*tert*-Butoxy)carbonylamino]acetyloxy}phenyl-2-[(*tert*-butoxy)carbonylamino]acetate (10a)

Catechol (**4a**; 220 mg, 5.00 mmol) and *N*-BOC protected glycine **8** (1.93 g, 11.0 mmol) were dissolved in CH_2Cl_2 (10 mL) at 0 °C. EDC (2.18 g, 11.0 mmol) and DMAP (1.22 g, 10 mmol) were added. After warming to r.t., the mixture was stirred for 16 h, washed with sat. aq $NaHCO_3$ and brine and dried ($MgSO_4$). The solvent was removed in vacuum and the residue was recrystallized from EtOAc–pentane; yield: 1.40 g (66%); white solid; mp 126 °C.

IR (KBr): 3554, 3299, 3067, 3009, 2970, 2935, 2819, 1788, 1757, 1693, 1599, 1548, 1492, 983, 863, 846, 769, 667 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.29–7.27 (m, 2 H), 7.22–7.20 (m, 2 H), 5.51 (br s, 2 H), 4.15 (m, 4 H), 1.48 (s, 18 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 168.1 (C), 156.2 (C), 141.9 (C), 127.0 (CH), 123.3 (CH), 80.3 (C), 42.4 (CH_2), 28.4 (CH_3).

MS (EI/70 eV): *m*/*z* (%) = 425 (0.03) $[M]^+$, 110 (100).

HRMS: *m*/*z* calcd for $C_{20}H_{29}N_2O_8$.: 425.1924, found: 425.1929.

Analysis Calcd for $C_{20}H_{28}N_2O_8$ (424.45): C, 56.60; H, 6.65; N, 6.60. Found: C, 56.52; H, 6.69; N, 6.44.

2-(2-Aminoacetyloxy)phenyl-2-aminoacetate Dihydrochloride (12a)

Bis(*N*-*tert*-butoxycarbonylgylcine)catecholate **10a** (1.40 g, 3.30 mmol) was stirred overnight with a solution of sat. HCl in Et_2O at r.t. The solvent was removed in vacuum to obtain the product in quantitative yield (981 mg); white solid; mp 197 °C.

IR (KBr): 3308, 2993, 2949, 2682, 2606, 1789, 1768, 1694, 1576, 1547, 1493, 1428, 4102, 1305, 1254, 1196, 1170, 1133, 1111, 1099, 1045, 887, 791, 768, 758 cm^{-1}.

^1H NMR (CD_3OD, 500 MHz): δ = 7.39 (s, 4 H), 4.30 (s, 4 H).

^{13}C NMR (CD_3OD, 125 MHz): δ = 166.7 (C), 142.5(C), 128.7 (CH), 124.6 (CH), 41.3 (CH_2).

Pos. FAB MS (3-NBA, DMSO): *m*/*z* = 225 $[M - HCl_2]^+$.

Anal. Calcd for $C_{10}H_{14}Cl_2N_2O_4$ (297.14): C, 40.42; H, 4.75; N, 9.43: Found: C, 40.41; H, 5.19; N, 9.19.

2-{2-[(Octylamino)carbonylamino]acetyloxy}phenyl-2-[(octylamino)carbonylamino]acetate (14a)

The hydrochloride **12a** (100 mg, 0.34 mmol) and *N*-methylmorpholine (74 μL, 0.67 mmol) were stirred for 20 min in MeCN (10 mL) under argon. Octyl isocyanate (118 μL, 0.67 mmol) was added and the mixture was refluxed for 16 h. The product crystallized upon cooling and was isolated by filtration; yield: 87.1 mg (48%); white solid; mp 157–164 °C.

IR (KBr): 3330, 2955, 2924, 2854, 1767, 1752, 1628, 1586, 1496, 1255, 1165, 1098, 621 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.22 (m, 2 H), 7.16 (m, 2 H), 4.19 (s, 4 H), 3.15 (t, *J* = 7.2 Hz, 4 H), 1.47 (m, 4 H), 1.28–1.24 (m, 24 H), 0.87 (t, *J* = 6.9 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 168.4 (C), 159.1 (C), 141.7 (C), 127.0 (CH), 123.3 (CH), 42.2 (CH_2), 40.8 (CH_2), 31.8 (CH_2), 30.0 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 26.9 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 535 $[M + H]^+$.

Anal. Calcd for $C_{28}H_{46}N_4O_6 \cdot 1/2\ H_2O$ (543.70): C, 61.85; H, 8.71; N, 10.30: Found: C, 61.90; H, 8.40; N, 10.55.

2-{2-[(*tert*-Butoxy)carbonylamino]propanoyloxy}phenyl-2-[(*tert*-butoxy)carbonylamino]propanoate (11a)

Catechol (**4a**; 1.10 g, 10.0 mmol) and *N*-BOC-L-alanine (**9**; 3.78 g, 20.0 mmol) were dissolved in EtOAc (40 mL). DCC (4.56 g, 21.0 mmol) and pyridine (1.45 mL, 18.0 mmol) were added and the mixture was stirred at r.t. for 14 h. Three drops of AcOH were added and after stirring for another 30 min the precipitate was filtered off and the solvent was removed in vacuum. The crude product was purified by column chromatography (hexane–EtOAc, 2:1); yield: 3.21 g (71%); white solid; mp 93 °C.

IR (KBr): 3391, 3366, 2976, 2935, 1780, 1757, 1691, 1598, 1525, 1493, 1457, 1394, 1367, 1324, 1299, 1242, 1123, 1061, 1015, 949, 902, 884, 864, 846, 803, 788, 776, 756, 648 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.27–7.22 (m, 2 H), 7.18–7.16 (m, 2 H), 5.44 (d, *J* = 7.4 Hz, 2 H), 4.53 (quin, *J* = 7.4 Hz, 2 H), 1.55 (d, *J* = 7.4 Hz, 6 H), 1.45 (s, 18 H).

^{13}C NMR ($CDCl_3$): δ = 171.1 (C), 155.5 (C), 142.0 (C), 126.9 (CH), 123.3 (CH), 80.1 (C), 49.3 (CH_3), 28.4 (CH_3), 18.0 (CH).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 453 $[M + H]^+$.

Anal. Calcd for $C_{22}H_{32}N_2O_8$ (452.51): C, 58.40; H, 7.13; N, 6.19: Found: C, 58.08; H, 7.11; N, 6.11.

X-Ray Structural Analysis of 11a[18]

Formula $C_{22}H_{32}N_2O_8$, *M* = 452.50, colorless crystal 0.25 × 0.25 × 0.10 mm, *a* = 9.925(1), *b* = 12.997(1), *c* = 19.471(1) Å, *V* = 2511.7(3) $Å^3$, ρ_{calc} = 1.197 g cm^{-3}, μ = 7.61 cm^{-1}, absorption correction via ψ scan data (0.833 < *T* < 0.928), *Z* = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 2906 reflections collected (+*h*, +*k*, +*l*), $[\sin\theta/\lambda]_{max}$ = 0.62 $Å^{-1}$, 2906 independent (R_{int} = 0.000) and 2495 observed reflections [$I \geq 2\ \sigma(I)$], 304 refined parameters, *R*1 = 0.035, *wR*2 = 0.094, Flack parameter –0.3(2), maximum residual electron density 0.15 (–0.19) e $Å^{-3}$.

2-{2-[(Octadecylamino)carbonylamino]acetyloxy}phenyl-2-[(octadecylamino)carbonylamino]acetate (16a)

Under argon, the dihydrochloride **12a** (200 mg, 0.67 mmol) and *N*-methylmorpholine (148 μL, 1.35 mmol) were stirred for 20 min at r.t. in MeCN (10 mL). Octadecyl isocyanate was added and the mixture was stirred for an additional 16 h. The crude product precipitated and was isolated by filtration. However, the material upon cooling gelated in several organic solvents and therefore could not be purified by crystallization and was not obtained in an analytically pure form; yield: 300 mg (55%); white solid as a crude product; mp 165 °C.

IR (KBr): 3338, 2955, 2919, 2849, 1762, 1749, 1620, 1584, 1500, 1467, 1253, 1169, 1100 cm^{-1}.

^1H NMR ($CDCl_3$/CD_3OD (313 K), 500 MHz): δ = 7.17–7.14 (m, 2 H), 7.12–7.10 (m, 2 H), 4.06 (s, 4 H), 3.05 (m, 4 H), 1.35 (m, 4 H), 1.17 (m, 60 H), 0.79 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 168.9 (C), 159.0 (C), 141.7 (C), 126.6 (CH), 123.1 (CH), 41.8 (CH_2), 40.1 (CH_2), 31.7 (CH_2, double intensity), 30.0 (CH_2), 29.5 (CH_2, quadruple intensity), 29.5 (CH_2, triple intensity), 29.3 (CH_2), 29.2 (CH_2, double intensity), 26.8 (CH_2), 22.5 (CH_2, double intensity), 13.8 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 816 $[M + H]^+$.

HRMS: *m*/*z* calcd for $C_{48}H_{87}N_4O_6$: 815.6626, found: 815.6648.

3-{2-[(*tert*-Butoxy)carbonylamino]acetyloxy}phenyl-2-[(*tert*-butoxy)carbonylamino]acetate (10b); Typical Procedure

Resorcinol (**4b**; 1.10 g, 10.0 mmol), *N*-BOC-glycine (**8**; 3.50 g, 20.0 mmol), DCC (4.56 g, 21.0 mmol) and pyridine (3 mL) were stirred for 16 h in EtOAc (80 mL). After addition of 3 drops of AcOH and additional stirring for 30 min, the precipitated urea was filtered off, the solvent was removed and the residue was purified by column chromatography (silica gel, hexane–EtOAc, 2:1); yield: 2.45 g (58%); white solid; mp 145 °C.

IR (KBr): 3365, 2980, 2936, 1777, 1699, 1602, 1519, 1485, 1456, 1393, 1368, 1287, 1251, 1149, 1055, 965 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.36 (t, *J* = 8.2 Hz, 1 H), 7.01(dd, *J* = 2.1, 8.2 Hz, 2 H), 6.94 (t, *J* = 2.1 Hz, 1 H), 5.14 (br s, 2 H), 4.14 (d, *J* = 5.7 Hz, 4 H), 1.46 (s, 18 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 168.7 (C), 155.8 (C), 150.7 (C), 129.9 (CH), 119.1 (CH), 115.1 (CH), 80.4 (C), 42.6 (CH_2), 28.3 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 447 $[M + Na]^+$.

Anal. Calcd for $C_{20}H_{28}N_2O_8$ (424.45): C, 56.60; H, 6.65; N, 6.60: Found: C, 56.25; H, 6.85; N, 6.10.

3-{2-[(Octylamino)carbonylamino]acetyloxy}phenyl-2-[(octylamino)carbonylamino]acetate (14b); Typical Procedure

The bis(*N*-*tert*-butoxycarbonylgylcine)resorcinolate **10b** (2.45 g, 5.76 mmol) was first stirred in a sat. solution of HCl in Et_2O for 3 h at r.t. to quantitativly remove the BOC protecting group. The precipitated dihydrochloride **12b** (1.71 g) was used without characterization. The dihydrochloride **12b** (100 mg, 0.34 mmol) was stirred under argon for 20 min in MeCN (10 mL) in the presence of *N*-methylmorpholine (74 μL, 0.67 mmol). Octyl isocyanate (118 μL, 0.67 mmol) was added and the mixture was refluxed for 16 h . Upon cooling the product precipitated and was isolated by filtration; yield: 90.0 mg (50%); white solid; mp 147 °C.

IR (KBr): 3322, 2956, 2925, 2852, 1752, 1625, 1580, 1234, 918, 780, 685, 618 cm^{-1}.

^1H NMR (DMSO-d_6, 500 MHz): δ = 7.42 (t, *J* = 8.2 Hz, 1 H), 7.00 (m, 2 H), 6.91 (s, 1 H), 6.28 (m, 2 H), 6.20 (t, *J* = 5.7 Hz, 2 H), 4.00 (d, *J* = 5.7 Hz, 4 H), 2.97 (q, *J* = 6.5 Hz, 4 H), 1.30 (m, 4 H), 1.22 (m, 20 H), 0.83 (t, *J* = 6.8 Hz, 6 H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ = 170.5 (C), 158.4 (C), 151.3 (C), 130.5 (CH), 119.6 (CH), 116.0 (CH), 42.3 (CH_2), 39.5 (CH_2), 31.7 (CH_2), 30.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.8 (CH_2), 22.5 (CH_2), 14.4 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 535 $[M + H]^+$, 557 $[M + Na]^+$.

Anal. Calcd for $C_{28}H_{46}N_4O_6$ (534.70): C, 62.90; H, 8.67; N, 10.48: Found: C, 62.90; H, 8.27; N, 10.37.

3-{2-[(*tert*-Butoxy)carbonylamino]propanoyloxy}phenyl-2-[(*tert*-butoxy)carbonylamino]propanoate (11b)

Compound **11b** was prepared from **4b** (550 mg, 5.00mol) and **9** (1.89 g, 10.0 mol) as described for **10b**; yield: 1.46 g (65%); white solid; mp 120 °C.

IR (KBr): 3523, 3382, 3077, 2986, 2938, 1775, 1690, 1603, 1518, 1483, 1451, 1393, 1370, 1336, 1303, 1282, 1256, 1147, 1125, 1099, 1068, 1023, 1004, 963, 930, 904, 788, 756, 682 cm^{-1}.

^1H NMR ($CDCl_3$, 500 MHz): δ = 7.37 (t, *J* = 8.2 Hz, 1 H), 7.01 (d, *J* = 2.2 Hz, 2 H), 6.96 (m, 1 H), 5.10 (m, 2 H), 4.51 (m, 2 H), 1.52 (d, *J* = 7.2 Hz, 6 H), 1.45 (s, 18 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.6 (C), 155.1 (C), 150.9 (C), 129.8 (CH), 119.0 (CH), 115.0 (CH), 80.2 (C), 49.4 (CH), 28.3 (CH_3), 18.3 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 453 [M + H]$^+$, 475 [M + Na]$^+$.

Anal. Calcd for $C_{22}H_{32}N_2O_8 \cdot H_2O$ (470.52): C, 56.16; H, 7.28; N, 5.95. Found: C, 56.29; H, 6.92; N, 5.73.

3-(2-Aminopropanoyloxy)phenyl-2-aminopropanoate Dihydrochloride (13b)

Compound **13b** was prepared from **11b** (1.00 g, 2.21mmol) similar to the corresponding glycine derivative **12b**; yield: 717 mg (quant.); white solid; mp 225 °C.

IR (KBr): 3414, 2918, 1933, 1768, 1599, 1483, 1238, 1182, 1126, 1098, 884, 747, 685 cm^{-1}.

^{1}H NMR (DMSO-d_6, 500 MHz): δ = 8.89 (br s, 6 H), 7.55 (t, *J* = 8.1 Hz, 1 H), 7.20 (m, 1 H), 7.18 (m, 2 H), 4.33 (m, 2 H), 1.57 (d, *J* = 7.2 Hz, 6 H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ = 168.5 (C), 150.2 (C), 130.5 (CH), 119.7 (CH), 115.3 (CH), 40.0 (CH), 15.5 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 254 [M – HCl_2]$^+$.

Anal. Calcd for $C_{12}H_{18}Cl_2N_2O_4 \cdot 2\ H_2O$ (361.22): C, 39.90; H, 6.14; N, 7.76: Found: C, 39.73; H, 5.51; N, 6.96.

3-{2-[(Octylamino)carbonylamino]propanoyloxy}phenyl-2-[(*N*-octylcarbamoyl)amino]propanoate (15b)

Compound **15b** was synthesiszed from **13b** (150 mg, 0.47 mmol) as described for the corresponding glycine derivative **14b**; yield: 68.7 mg (26%); white solid; mp 185 °C.

IR (KBr): 3328, 2955, 2925, 2854, 1767, 1747, 1630, 1604, 1578, 1484, 1468, 1242, 1132 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.32 (t, *J* = 7.9 Hz, 1 H), 6.96 (m, 3 H), 5.77 (br s, 2 H), 5.54 (br s, 2 H), 4.60 (d, *J* = 6.1 Hz, 2 H), 3.16 (m, 2 H), 3.06 (m, 2 H), 1.41 (m, 10 H), 1.23 (m, 20 H), 0.86 (t, *J* = 6.4 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 172.4 (C), 158.2 (C), 151.0 (C), 129.6 (CH), 119.0 (CH), 115.7 (CH), 49.2 (CH), 40.4 (CH_2), 31.8 (CH_2), 30.2 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 26.9 (CH_2), 22.6 (CH_2), 17.9 (CH_3), 14.1 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 563 [M + H]$^+$, 585 [M + Na]$^+$.

HRMS: *m*/*z* calcd for $C_{30}H_{51}N_4O_6$: 563.3809, found: 563.3821.

Anal. Calcd for $C_{30}H_{50}N_4O_6 \cdot 1/2\ CHCl_3$ (622.44): C, 58.85; H, 8.18; N, 9.00. Found: C, 58.44; H, 8.14; N, 9.54.

3-{3-[(*tert*-Butoxy)carbonylamino]propanoyloxy}phenyl-3-[(*tert*-butoxy)carbonylamino]propanoate (18a)

A solution of catechol (**4a**; 1.10 g, 10.0 mmol) and *N*-BOC-β-alanine (**17**; 3.78 g, 20.0 mmol) in CH_2Cl_2 (40 mL) was cooled to 0 °C. EDC (4.03 g, 21.0 mmol) and DMAP (2.57 g, 21.0 mmol) were added and the reaction mixture was stirred for 16 h at r.t. The organic phase was successively washed with sat. aq NH_4Cl, sat. aq $NaHCO_3$ and brine. After drying ($MgSO_4$) the solvent was removed in vacuum and the residue is purified by column chromatography (silica gel, EtOAc–hexane, 1:5); yield: 2.73 g (60%); colorless waxy solid.

IR (KBr): 3360, 2978, 2917, 2849, 1769, 1712, 1516, 1494, 1458, 1392, 1367, 1275, 1243, 1167, 1103, 1074, 972, 922, 783, 757 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.25–7.20 (m, 2 H), 7.18–7.15 (m, 2 H), 5.18 (br s, 2 H), 3.42 (m, 4 H), 2.72 (t, *J* = 5.5 Hz, 4 H), 1.40 (s, 18 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 169.8 (C), 155.8 (C), 141.7 (C), 126.7 (CH), 123.4 (CH), 79.5 (C), 36.0 (CH_2), 34.5 (CH_2), 28.4 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 453 [M + H]$^+$.

HRMS: *m*/*z* calcd for $C_{22}H_{33}N_2O_8$: 453.2237, found: 453.2227.

Anal. Calcd for $C_{22}H_{32}N_2O_8$ (452.51): C, 58.40; H, 7.13; N, 6.19. Found: C, 58.26; H, 7.26; N, 5.68.

3-{3-[(Octylamino)carbonylamino]propanoyloxy}phenyl-3-[(octylamino)carbonylamino]propanoate (20a)

The BOC-protecting group of **18a** was removed quantitatively by stirring the compound in a sat. solution of HCl in Et_2O for 3 h at r.t. After removal of the solvent the dihydrochloride **19a** was obtained as a white solid which was used without characterization. The dihydrochloride **19a** (200 mg, 0.62 mmol) and *N*-methylmorpholine (135 μL, 1.23 mmol) were stirred for 20 min at r.t. under argon in MeCN (20 mL). After addition of octyl isocyanate (217 μL, 1.23 mmol), the mixture was refluxed for 16 h. The product precipitated upon cooling and was collected by filtration; yield: 195 mg (56%); white solid; mp 156 °C.

IR (KBr): 3347, 2954, 2923, 2850, 1755, 1623, 1584, 1252, 776 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.24–7.21 (m, 2 H), 7.19–7.17 (m, 2 H), 5.48 (br s, 2 H), 5.38 (br s, 2 H), 3.44 (t, *J* = 5.5 Hz, 4 H), 3.12 (t, *J* = 7.1 Hz, 4 H), 2.78 (t, *J* = 5.5 Hz, 4 H), 1.44 (quin, *J* = 7.1 Hz, 4 H), 1.29–1.24 (m, 20 H), 0.86 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 170.3 (C), 158.9 (C), 141.7 (C), 126.4 (CH), 123.4 (CH), 40.3 (CH_2), 35.5 (CH_2), 34.6 (CH_2), 31.8 (CH_2), 30.3 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 27.0 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

Pos. FAB MS (DMSO/3-NBA): *m*/*z* = 563 [M + H]$^+$, 585 [M + Na]$^+$.

Anal Calcd for $C_{30}H_{50}N_4O_6$ (562.75): C, 64.03; H, 8.96; N, 9.96: Found: C, 63.98; H, 8.63; N, 9.98.

2-Hydroxyphenyl-2-(acetylamino)acetate (21a)

Catechol (**4a**; 1.10 g, 10.0 mmol) and *N*-acetylglycine (**6**; 1.18 g, 10.0 mmol) were dissolved in EtOAc (40 mL). After addition of DCC (2.16 g, 10.5 mmol) and pyridine (1.45 mL, 18.0 mmol), the mixture was stirred for 14 h at r.t. Three drops of AcOH were added, the mixture was stirred for another 30 min, the precipitated urea was filtered off and the solvent was removed in vacuum. The crude product was purified by column chromatography (silica gel, EtOAc); yield: 1.50 g (72%); mp 133 °C.

IR (KBr): 3949, 3386, 3116, 2587, 1777, 1638, 1590, 1577, 1524, 1514, 1460, 1417, 1365, 1315, 1295, 1260, 1235, 1163, 1151, 1130, 1098, 1035, 941, 785, 759, 741, 633 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.17–7.13 (m, 1 H), 7.03–7.01 (m, 2 H), 6.89–6.86 (m, 1 H), 6.24 (br s, 1 H), 4.17 (d, *J* = 5.3 Hz, 2 H), 2.11 (s, 2 H).

^{13}C NMR ($CDCl_3$): δ = 172.4 (C), 167.8 (C), 147.9 (C), 137.7 (C), 127.6 (CH), 122.2 (CH), 120.2 (CH), 117.9 (CH), 42.7 (CH_2), 22.8 (CH_3).

MS (EI/70 eV): *m*/*z* (%) = 209 (2.72, [M]$^+$), 100 (100).

HRMS: *m*/*z* calcd for $C_{10}H_{11}NO_4$: 209.0688, found: 209.0677.

Anal. Calcd for $C_{10}H_{11}NO_4$ (209.20): C, 57.41; H, 5.30; N, 6.70. Found: C, 57.55; H, 5.42; N, 6.53.

X-Ray Structural Analysis of 21a[18]

Formula $C_{10}H_{11}NO_4$, *M* = 209.20, colorless crystal 0.70 × 0.50 × 0.20 mm, *a* = 12.804(1), *b* = 9.005(4), *c* = 9.176(2) Å, β = 94.33(1)°, *V* = 1055.0(5) Å^3, ρ_{calc} = 1.317 g cm^{-3}, μ = 8.70 cm^{-1}, absorption correction via ψ scan data (0581 < *T* < 0.845), *Z* = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, *T* = 223 K, ω/2 θ scans, 2244 reflections collected (+*h*, –*k*, ±*l*), $[(\sin\theta)/\lambda]_{max}$ = 0.62 Å^{-1}, 2148 independent(R_{int} = 0.038) and 2022 observed re-

flections [$I \geq 2\ \sigma(I)$], 144 refined parameters, $R1 = 0.052$, $wR2 = 0.156$, maximum residual electron density 0.30 (–0.28) e Å^{-3}.

Titration Experiments

The association constants K_a were obtained by stepwise addition of tetrabutylammonium nitrate to solutions of the receptors **5a** (0.027 molar), **7a** (0.030 molar), **14a** (0.032 molar), **20a** (0.028 molar), **7b** (0.032 molar), **14b** (0.028 molar), or **15b** (0.018 molar) in $CDCl_3$ at 297 K and the obtained data were analyzed with Wilcoxs method using Origin 6.0 (Microcal Software) for data fitting.

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