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 bipheno1 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 bonds4 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).

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).
The double ester formation to form 7a proceeds in the presence of EDC [N-ethyl(N’-dimethylaminopropyl)carbodiimide] and DMAP (4-N,N-dimethylaminopyridine) 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. 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 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 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 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-
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 /c98-alanine in the spacer. The compound with /c98-alanine urea moieties in the side arms 20a is prepared starting from catechol 4a and forming the diester with N-BOC-/c98-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 bis-alanyl 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 3
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.5

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 amide 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 binding12 by the tweezer-type compounds using nitrate anions13 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/NO3− and the corresponding titration curve.
ments were performed in CDCl$_3$ at 297 K with subsequent addition of tetrabutylammonium nitrate (TBAN).\textsuperscript{14}

Titrations plots for 5a, 7a, 14a, 20a, 7b, 14b, and 15b with nitrate using Jobs method\textsuperscript{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.\textsuperscript{5} Probably due to steric constraints 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.\textsuperscript{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 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.
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 tetramethylammonium 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 [14a·NO₃]⁻ 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 linkage between the backbone and the side-arms to enter the field of ‘dynamic combinatorial chemistry’ based on libraries of related receptor molecules.17

Figure 5 Molecular structure of 21a as found in the solid state: a) the monomeric structure and b,c) different views of the hydrogen bonded network.
H NMR and 13C 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 c109/L, 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 NaHCO3 (3 c180/L), dried (MgSO4) 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.

1H NMR (CDCl3, 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).

13C NMR (CDCl3, 125 MHz): δ = 153.9 (C), 143.1 (C), 126.1 (CH), 123.5 (CH), 41.4 (CH2), 31.8 (CH2), 29.8 (CH2), 29.2 (CH2, double intensity), 26.7 (CH2), 22.6 (CH2), 14.1 (CH3).


HRMS: m/z calcd for C24H41N2O4: 421.3066, found: 421.3057.

Anal. Calcd for C24H40N2O4 (420.59): C, 68.54; H, 9.59; N, 6.66; Found: C, 68.53; H, 9.24; N, 6.84.

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

Catechol (4a; 220 mg, 2.00 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 CH2Cl2 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 NaHCO3 (3 ×), dried (MgSO4) and the solvent was removed in vacuum. The crude product was purified by recrystallization from EtOAc–hexane; yield: 420 mg (50%); white solid; mp 105 °C.

Figure 6 Jobs plot for the interaction of the receptor 7a with tetra-butylammonium nitrate showing that a 1:1 complex is formed (X = molar fraction) (top). 1H NMR titration curve (500 MHz) for the titration of 7a (amide proton) with tetrabutylammonium nitrate in CDCl3 at 297 K (bottom).

<table>
<thead>
<tr>
<th>Compound</th>
<th>CHCl3</th>
<th>CH2Cl2</th>
<th>EtOAc</th>
<th>Benzene</th>
</tr>
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<tbody>
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<td>–</td>
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<tr>
<td>7a</td>
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<td>14a</td>
<td>++</td>
<td>+</td>
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<td>–</td>
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<tr>
<td>16a</td>
<td>+</td>
<td>+</td>
<td>insoluble</td>
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<tr>
<td>20a</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>14b</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>15b</td>
<td>+</td>
<td>–</td>
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* – no gelating properties; + gelating at low temperatures; ++ gelating at room temperature.

1H NMR and 13C 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).

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

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<td>14a</td>
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<td>15b</td>
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2/[2-(Acetylamino)acetoxy]phenyl-2-(acetylamino)acetate (7a)

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

IR (KBr): 3275, 3069, 1794, 1563.30 (5) Å⁻³, 0.033) and 2555 observed reflections [20 refined parameters, R₁ = 0.045, wR₂ = 0.104, no absorption correction (0.960 < T < 0.980), Z = 4, tetragonal, space group P4₁ (No. 76), λ = 0.71073 Å, T = 173 K, and 2067, 1694, 1576, 1493, 1428, 4102, 1305, 1254, 1196, 1170, 1133, 1111, 1099, 1045, 877, 791, 768, 758 cm⁻¹.

X-Ray Structural Analysis of 7a¹⁸

Formula: C₁₄H₁₆N₂O₆, M = 308.29, colorless crystal, c = 15.0922 (3) Å, V = 1563.30(5) Å³, pD = 1.310 g cm⁻³, = 0.104 cm⁻¹, no absorption correction (0.960 < T < 0.980), Z = 4, tetragonal, space group P4₁ (No. 76), λ = 0.71073 Å, T = 173 K, and 2067, 1694, 1576, 1493, 1428, 4102, 1305, 1254, 1196, 1170, 1133, 1111, 1099, 1045, 877, 791, 768, 758 cm⁻¹.

Comparison of possible nitrate binding modes of the catechol and resorcinol based receptors.
H), 1.45 (s, 18 H).

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


Found: C, 58.08; H, 7.11; N, 6.11.

HRMS: m/z calcd for C\(_{22}\)H\(_{32}\)N\(_2\)O\(_8\): 452.50, colorless crystal.

IR (KBr): 3391, 3366, 2976, 2935, 1780, 1757, 1691, 1598, 1525, 1299, 1191, 1115, 1084, 1045, 976 cm\(^{-1}\).

IR (KBr): 3523, 3382, 3077, 2986, 2938, 1775, 1699, 1602, 1485, 1456, 1368, 1287, 1251, 1149, 1055, 965 cm\(^{-1}\).

HRMS: m/z = 247 [M + Na]^+.


Found: C, 61.90; H, 8.40; N, 10.55.

HRMS: m/z = 447 [M + Na]^+.

Anal. Calcd for C\(_{28}\)H\(_{46}\)N\(_4\)O\(_6\): 534.70; C, 62.90; H, 8.67; N, 10.48.

Found: C, 61.90; H, 8.40; N, 10.55.

HRMS: m/z = 447 [M + Na]^+.

Anal. Calcd for C\(_{28}\)H\(_{46}\)N\(_4\)O\(_6\): 534.70; C, 62.90; H, 8.67; N, 10.48.

Found: C, 61.90; H, 8.40; N, 10.55.
Anal. Calcd for C25H24N2O8: C, 56.16; H, 7.28; N, 5.95. Found: C, 56.29; H, 6.92; N, 5.73.

3-[(O-tolyaminocarbonyl)amino]propanoic acid (15b)
Compound 15b was synthesized 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): 3347, 2954, 2923, 2850, 1755, 1623, 1584, 1252, 776 cm\(^{-1}\).

1H NMR (CDCl\(_3\), 500 MHz): \(\delta = 7.32\) (br s, 1 H), 6.96 (m, 3 H), 5.77 (br s, 2 H), 5.45 (br s, 2 H), 3.60 (d, \(J = 6.1\) Hz, 2 H), 3.16 (m, 2 H), 2.06 (m, 2 H), 1.41 (m, 10 H), 1.23 (m, 20 H), 0.86 (t, \(J = 6.4\) Hz, 6 H).

13C NMR (CDCl\(_3\), 125 MHz): \(\delta = 168.5\) (C), 150.2 (C), 130.5 (CH), 119.7 (CH), 115.3 (CH), 40.0 (CH), 15.5 (CH2).

Pos. FAB MS (DMSO/3-NBA): m/z = 254 [M – HCl]+.
Anal. Calcd for C10H11NO4: C, 57.55; H, 5.42; N, 6.53. Found: C, 57.38; H, 5.28; N, 6.54.

2-Hydroxyphenyl-2-(acetylamino)acetate (21a)
Catechol (4a, 1.10 g, 10.0 mmol) and N-acetyl-L-ala-

PAPER
Synthesis of Tweezer-Type Catechol and Resorcinol Derivatives

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X-Ray Structural Analysis of 21a\(^a\)
Formula C\(_{10}\)H\(_{10}\)O\(_{4}\), M\(_r\) = 189.20, colorless crystal 0.70 \(\times\) 0.50 \(\times\) 0.20 mm, \(a = 12.804(1)\) \(\AA\), \(b = 9.005(4)\) \(\AA\), \(c = 9.176(2)\) \(\AA\), \(\beta = 94.33(1)^\circ\), \(V = 1055.0(5)\) \(\AA^3\), \(\mu = 8.70\) cm\(^{-1}\), absorption correction via \(\psi\) scan data (0581 < \(\psi\) < 8045), \(Z = 4\), monoclinic, space group P2\(_1\)/c (No. 14), \(\lambda = 1.54\) Å, \(\theta = 223\) K, \(\omega/2\theta\) scans, 2244 reflections collected (+h, +k, +l), \(|\sin(\theta)/\lambda|_{max} = 0.62\) Å, 2148 independent (R\(_{int}\) = 0.038) and 2022 observed re-

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

1H NMR (CDCl\(_3\), 500 MHz): \(\delta = 7.25–7.20\) (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).

13C NMR (CDCl\(_3\), 125 MHz): \(\delta = 169.8\) (C), 155.8 (C), 141.7 (C), 126.7 (CH), 123.4 (CH), 79.5 (C), 36.0 (CH2), 34.5 (CH2), 28.4 (CH2).

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

HRMS: m/z calcd for C\(_{22}\)H\(_{24}\)N\(_2\)O\(_8\): 563.2237, found: 563.2227.

Anal. Calcd for C\(_{12}\)H\(_{18}\)Cl\(_2\)N\(_2\)O\(_4\): C, 58.26; H, 7.26; N, 5.68.

2-Hydroxyphenyl-2-(acetylamino)acetate (21a)
Catechol (4a, 1.10 g, 10.0 mmol) and N-acetyl-L-ala-

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reflections \[ I \geq 2 \sigma(I) \], 144 refined parameters, \( R_1 = 0.052 \), \( wR_2 = 0.156 \), 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), 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.

**Acknowledgement**

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**References**


(18) Data sets were collected with Enraf-Nonius CAD4 and Nonius KappaCCD diffractometer. Programs used: data collection EXPRESS (Nonius B.V., 1994) and COLLECT (Nonius B.V., 1998), data reduction MolEN (K. Fair, Enraf-Nonius B.V., 1990) and Denzo-SMN, absorption correction for CCD data SORTAV, structure solution SHELXS-97, structure refinement SHELXL-97 (G.M. Sheldrick, Universität Göttingen, 1997). Crystallographic data (excluding structural factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 180408, 180409 and 180410. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, CambridgeCB2 1EZ, UK [fax: int. code: +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].