Enthalpy driven nitrate complexation by guanidinium-based macrocycles†‡

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NMR and isothermal calorimetric titrations, as well as X-ray structures, show the binding of a nitrate anion inside guanidinium-based macrocycles. All six lone pairs of nitrate are complemented by oriented hydrogen bond donors from a guanidinium and two urea subunits.

Introduction

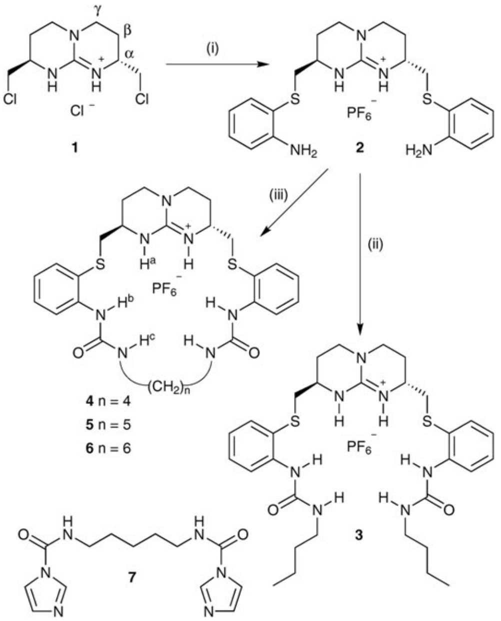
The molecular recognition of anions has become an important field of supramolecular chemistry.[1] Nevertheless, little attention has been given to weakly basic anions such as nitrate.[2] The use of macrocycles has the advantage of offering a preorganized scaffold, with convergent binding groups, to include a guest of complementary size and shape.[3] Although guanidinium-based systems have been widely used to recognise oxoanions like carboxylates or phosphates,[4] their use for nitrate binding has not been reported so far.[5]

From a recent theoretical study, the combination of both guanidinium and urea moieties should provide an almost ideal complement to the guest.[6] In this context, we describe herein the synthesis and binding properties of the open host **3**, and of three macrocycles **4**, **5** and **6**. Common to these designs is a bicyclic guanidinium scaffold, and two ureas are attached through an *ortho*-aminothiophenylene aromatic spacer in such a way that the first nitrogen atoms of both functions are located at an ideal distance (five atoms apart) for the hydrogen donors to complement both the *syn* and *anti* lone pairs of each oxygen.[7] Moreover, the aromatic ring increases the acidity of the urea and brings preorganization to the overall structure. Also, the sulfur atoms should contribute to shaping the host by chelation, while not introducing an overly electronegative atom that would cause electronic repulsion with the guest.[8] Regarding the linker between the ureas in the macrocycles, a five carbon chain (such as in **5**) should again be the best choice for nitrate encapsulation.

Results and discussion

The synthesis of the guanidinium-based receptors is described in Scheme 1. Guanidinium dichloride **1**[9] was transformed into diamine **2** (hexafluorophosphate salt) with 2-aminothiophenol in a 60% yield. Hexafluorophosphate, as a less competitive anion than chloride, was the counterion for all receptors. For compounds **3**, **4** and **6**, the appropriate isocyanate or diisocyanate reagents were employed. Thus, butylisocyanate reacted with **2** in a sealed vessel to form **3** in 85% yield, whereas hosts **4** and **6** resulted in a 40% yield under more dilute conditions, using 1,4-diisocyanatobutane and 1,6-diisocyanatohexane, respectively. For the synthesis of macrocycle **5**, a different procedure was followed, since 1,5-diisocyanatopentane is not commercially available. We used a bis-imidazolide intermediate **7**, prepared from 1,5-diaminopentane and 1,1′-carbonyldiimidazole (CDI), which was reacted with **2** in dry MeOH to obtain **5** in a modest 8% yield.

^{1}H NMR titrations with tetrabutylammonium (TBA) nitrate and hosts **3–6** were performed in CD_3CN. Saturation was observed for hosts **3** and **4** after addition of 1.5 equiv. of nitrate, whereas a control with diamine **2** did not show saturation, even after the addition of 10 equiv., accounting



Scheme 1 Synthesis of receptors **3–6**. Reagents and conditions: (i) 2-aminothiophenol, NaI, KO*t*Bu, acetone, room temperature, 4 h, then NH_4PF_6 0.1 M (60%); (ii) butylisocyanate, CH_2Cl_2, 45 °C, overnight, then NH_4PF_6 0.1 M (85%); (iii) diisocyanate (for **4** and **6**), CH_2Cl_2, 45 °C, overnight, then NH_4PF_6 0.1 M and Dowex ion-exchange resin (PF_6^-) (40%); or 1,5-diaminopentane (for **5**), CDI, 80 °C, 2 d, then Dowex ion-exchange resin (PF_6^-) (8%).

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† Dedicated to Professor George Gokel on the occasion of his 60th birthday.

‡ Electronic supplementary information (ESI) available: General methods and ITC/^{1}H NMR titration procedures. See 10.1039/b616409a.

Table 1 Association constants (/M^{-1}) and thermodynamic parameters for the binding of hosts **2–6** with TBA nitrate

	2	**3**	**4**	**5**	**6**
$K_a(/10^3)^a$	0.99	5.50	9.94	^{c}	^{c}
$K_a(/10^3)^b$	0.35	5.38	7.26	15.2	73.7
ΔH^d	−2.00	−3.73	−1.07	−3.02	−3.48
ΔS^d	5.06	4.72	14.2	9.16	10.8
ΔG^d	−3.53	−5.16	−5.37	−5.79	−6.75

[a] Determined by ^{1}H NMR titrations in CD_3CN at 298 K. [b] Determined by ITC titrations in CH_3CN at 303 K. [c] Not determined because of *in situ*-crystallization. [d] ΔH and ΔG in kcal mol^{-1}, ΔS in cal mol^{-1} K^{-1}.

for the importance of the additional hydrogen bonds (ureas) to stabilise the complex. Indeed, K_a values increased by one order of magnitude from 990 M^{-1} for **2** to 9.94 × 10^3 M^{-1} for **4** (Table 1). The macrocyclic effect was evidenced by the doubled binding constant for **4** compared to the linear analogue **3**. Both the urea and guanidinium NH protons involved in hydrogen bonding showed strong downfield shifts upon the addition of guest (Fig. 1). The titrations correspond to a widely studied[10,11] anion exchange process of the type:

$$\text{Host}\,(PF_6^-) + TBA^+\,(NO_3^-) \rightarrow \text{Host}\,(NO_3^-) + TBA^+\,(PF_6^-)$$

Single liquid–liquid extraction between **3** (in CH_2Cl_2) and $NaNO_3$ (saturated water solution) confirmed the strong host–guest interaction and a 1 : 1 stoichiometry for nitrate extraction.[12,13]

No accurate NMR binding data could be obtained for **5** and **6** due to *in situ*-crystallization at the concentrations of the titrations. To overcome this problem, we used isothermal titration calorimetry (ITC) at a much lower concentration as a tool for measuring binding constants and thermodynamic parameters.[14] The binding isotherms were characteristic of exothermic 1 : 1 complexes, and values for K_a were in good agreement with those obtained by ^{1}H NMR (Table 1).

An increase in cavity size results in a binding affinity enhancement between the macrocycle and nitrate. Hence, macrocycle **6** displays an increase of two orders of magnitude with respect to **2** and presents one of the highest K_a values reported so far.[15]

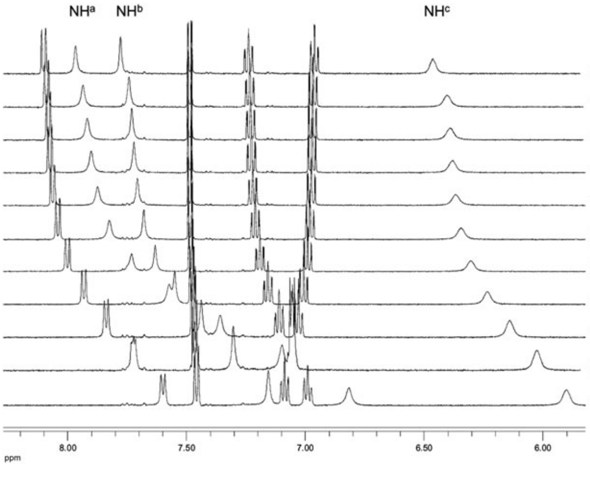

Fig. 1 ^{1}H NMR titration between **4** and TBA nitrate in CD_3CN.

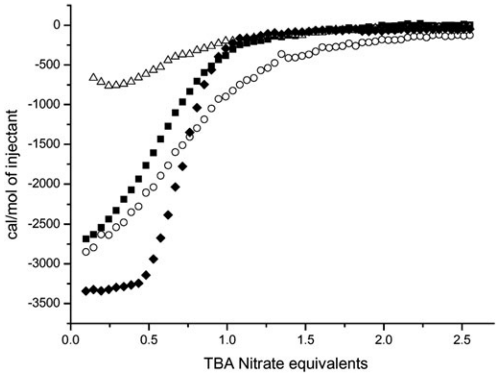

Fig. 2 ITC binding isotherms of **3–6** with TBA nitrate in CH_3CN at 303 K; **3** (○), **4** (Δ), **5** (■) and **6** (◆).

The binding isotherms reveal that the binding of nitrate with **4** is governed mainly by entropy (Fig. 2, see also Table 1), whereas for the other receptors, especially the macrocycles, both enthalpic and entropic contributions play a significant role. The strong negative enthalpy values indicate that hydrogen bonding with the oxygens of the guest is almost optimal, the entropic contribution being most likely due to solvent release from the cavity upon guest inclusion and increases as the conformational freedom of the macrocycle is reduced. In macrocycle **4**, the cavity is too small for optimal inclusion. Indeed, the hydrogen bonding is weaker and the smaller enthalpy change is compensated-by a stronger entropy contribution.

In the solid state (Fig. 3), all three macrocyclic nitrate salts behave as predicted and anticipated from the studies in solution. The asymmetric unit contains three independent macrocycles for **4** and two for **5** (only one structure is shown in Fig. 3 for each crystal). Salt **4** displays a distorted structure, with one urea twisted away from the cavity (hydrogen-bonded to a urea from another macrocycle), and only three identified hydrogen bonds with the nitrate. On the contrary, in both **5** and **6**, the nitrate nicely fits inside the cavity surrounded by six NH donors. Moreover, the X-ray structures of **5** and **6** show that the guest oxygen atoms form two hydrogen bonds with the host, in such a way that each oxygen shares its lone pairs with single NH donors from different functions (ureas or guanidinium).[16] This orientation (Fig. 4a) is preferred in the solid state over an alternative one where the oxygen lone pairs bind to NH donors from the same function (Fig. 4b). Those results are in good agreement with energy data from the computational study by Hay *et al.*,[6] which revealed that forcing urea to bind a single oxygen atom yields complexes that are 10% weaker than those involving hydrogen bonds from two oxygen atoms.

Experimental

Syntheses

(2*R*,8*R*)-2,8-Bis-[(2-aminophenylthio)methyl]-3,4,6,7,8,9-hexahydro-2*H*-pyrimido[1,2-*a*]pyrimidin-1-ium hexafluorophosphate (2). Sodium iodide (440 mg, 2.93 mmol), potassium

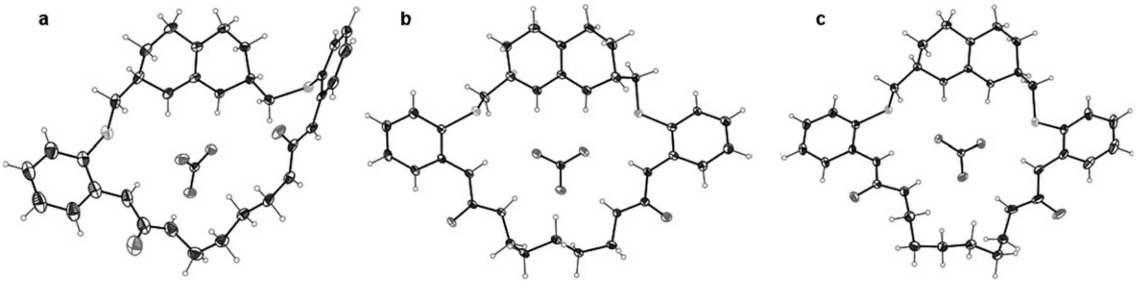

Fig. 3 ORTEP plots (50%) showing the structures of (a) **4**, (b) **5** and (c) **6** with nitrate as counterion.

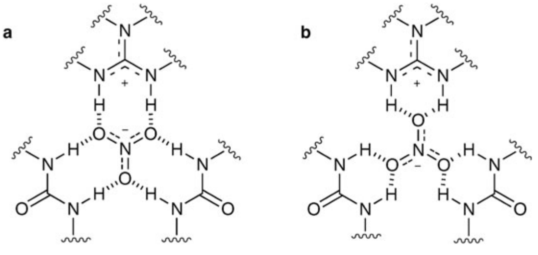

Fig. 4 Two binding modes for nitrate inclusion.

tert-butoxide (400 mg, 3.52 mmol) and 2-aminothiophenol (0.39 mL, 3.66 mmol) were added to a solution of **1** (200 mg, 0.73 mmol) in acetone (20 mL), and the mixture was stirred at room temperature for 4 h. After evaporation of the solvent, the resulting solid was dissolved in CH_2Cl_2 and the organic layer was washed with 0.1 M NH_4PF_6 solution, dried (Na_2SO_4), filtered over cotton and concentrated at reduced pressure. Purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 97 : 3) afforded **2** (190 mg, 60%) as a pale yellow solid. mp 162–164 °C; $[\alpha]_D^{25}$ −105.76 (*c* 0.5 in $CHCl_3$); δ_H (500 MHz, CD_3CN): 1.75–2.16 (4 H, m, $CH_{2\beta}$), 2.80 (2 H, dd, *J* = 7.43 and 1.13 Hz, CH_2S), 3.24 (10 H, m, $CH_{2\gamma}$, CH_2S, NH_2), 3.40 (2 H, m, CH_α), 6.61 (2 H, dt, *J* = 7.39 and 1.09 Hz, CH_{Ar}), 6.67 (2 H, dd, *J* = 7.87 and 1.19 Hz, CH_{Ar}), 6.81 (2 H, s, NH_{guan}), 7.09 (2 H, dt, *J* = 7.51 and 1.37 Hz, CH_{Ar}) and 7.35 (2 H, dd, *J* = 7.67 and 1.49 Hz, CH_{Ar}); δ_C (125 MHz, CD_3CN): 25.6 ($CH_{2\beta}$), 39.5 ($CH_{2\gamma}$), 45.4 (CH_2S), 47.9 (CH_α), 115.2 (C_{Ar}), 115.6, 118.3, 130.3, 136.1 (CH_{Ar}), 148.8 (CN) and 150.8 (C_{guan}); *m*/*z* (ESI) 414.2 ($M^+ - PF_6^-$).

General procedure for the synthesis of compounds 3, 4 and 6. The appropriate isocyanate (2 equiv.) or diisocyanate (1 equiv.) was added, under a nitrogen atmosphere, to a solution of **2** (1 equiv.) in dry CH_2Cl_2 (2 mL) in a sealed tube, and the mixture was stirred at 45 °C overnight. After evaporation of the solvent, the resulting solid was dissolved in CH_2Cl_2 and the organic layer was washed with 0.1 M NH_4PF_6 solution, dried (Na_2SO_4), filtered over cotton and concentrated at reduced pressure. After purification of the crude material by column chromatography on silica gel, the pure compound was obtained as a pale yellow solid. In the case of macrocycles **4** and **6**, this solid was further dissolved in acetonitrile and eluted through a Dowex ion-exchange resin (PF_6^-).

(2*R*,8*R*)-2,8-Bis-{[2-(3-butylureido)phenylthio]methyl}-3,4,6,7,8,9-hexahydro-2*H*-pyrimido[1,2-α]pyrimidin-1-ium hexafluorophosphate (3). Prepared from butylisocyanate (0.45 mL, 0.39 mmol) and **2** (100 mg, 0.18 mmol). Purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 98 : 2) afforded **3** (110 mg, 80%). mp 169–171 °C; $[\alpha]_D^{25}$ −175.76 (*c* 0.5 in $CHCl_3$); δ_H (500 MHz, CD_3CN): 0.89 (6 H, t, *J* = 7.64 Hz, CH_3), 1.39 (4 H, m, 4 H, CH_2), 1.58 (4 H, m, CH_2), 1.78–1.92 (4 H, m, $CH_{2\beta}$), 2.71 (2 H, dd, *J* = 7.51 and 1.05 Hz, CH_2S), 3.14 (2 H, dd, *J* = 7.43 and 1.13 Hz, CH_2S), 2.84–3.24 (10 H, m, $CH_{2\gamma}$, CH_α, CH_2), 5.91 (2 H, s, NH_{urea}), 7.09 (2 H, s, NH_{urea}), 7.12 (2 H, t, *J* = 7.41 Hz, CH_{Ar}), 7.26 (2 H, t, *J* = 7.15 Hz, CH_{Ar}), 7.37 (2 H, s, NH_{guan}), 7.50 (2 H, d, *J* = 7.80 Hz, CH_{Ar}) and 8.34 (2 H, d, *J* = 7.28 Hz, CH_{Ar}); δ_C (125 MHz, CD_3CN): 14.5 (CH_3), 19.7 (CH_2), 25.6 ($CH_{2\beta}$), 32.2 (CH_2), 39.5 ($CH_{2\gamma}$), 40.1 (CH_2), 45.4 (CH_2S), 47.9 (CH_α), 118.5 (C_{Ar}), 119.9, 122.1, 129.5, 134.2 (CH_{Ar}), 138.4 (NH_2C), 150.0 (C_{guan}) and 155.6 (C_{urea}); *m*/*z* (ESI) 612.4 ($M^+ - PF_6^-$).

Macrocycle 4. Prepared from 1,4-diisocyanatobutane (0.013 mL, 0.06 mmol) and **2** (30 mg, 0.06 mmol). Purification by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 98 : 2) afforded **4** (15 mg, 40%). mp 123–125 °C; $[\alpha]_D^{25}$ −76.24 (*c* 0.25 in $CHCl_3$); δ_H (500 MHz, CD_3CN): 1.51 (4 H, m, CH_2), 1.71–2.01 (4 H, m, $CH_{2\beta}$), 2.89 (4 H, m, CH_2), 3.06–3.24 (10 H, m, $CH_{2\gamma}$, CH_α, CH_2S), 5.92 (2 H, s, NH_{urea}), 6.82 (2 H, s, NH_{urea}), 6.98 (2 H, t, *J* = 11.0 Hz, CH_{Ar}), 7.09 (2 H, t, *J* = 7.63 Hz, CH_{Ar}), 7.15 (2 H, s, NH_{guan}), 7.48 (2 H, d, *J* = 7.80 Hz, CH_{Ar}) and 7.61 (2 H, d, *J* = 8.29 Hz, CH_{Ar}); δ_C (125 MHz, CD_3CN): 25.0 (CH_2), 25.9 (CH_2), 28.7 ($CH_{2\beta}$), 41.9 ($CH_{2\gamma}$), 44.4 (CH_2S), 46.9 (CH_α), 119.6 (C_{Ar}), 120.1, 121.8, 128.5, 133.5 (CH_{Ar}), 140.9 (NHC), 150.6 (C_{guan}) and 165.5 (C_{urea}); *m*/*z* (ESI) 554.2 ($M^+ - PF_6^-$).

Macrocycle 6. Prepared from 1,6-diisocyanatohexane (0.009 mL, 0.06 mmol) and **2** (30 mg, 0.06 mmol). Purification by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 98 : 2) afforded **6** (16 mg, 40%). mp 151–153 °C; $[\alpha]_D^{25}$ −17.20 (*c* 0.25 in CH_3CN); δ_H (500 MHz, CD_3CN): 1.25–1.39 (4 H, m, CH_2), 1.74–2.01 (4 H, m, $CH_{2\beta}$), 2.84–3.24 (12 H, m, $CH_{2\gamma}$, CH_α, CH_2S, CH_2), 3.40 (2 H, m, CH_2S), 5.82 (2 H, s, NH_{urea}), 6.90 (2 H, s, NH_{urea}), 7.05 (4 H, m, CH_{Ar}), 7.35 (2 H, s, NH_{guan}), 7.48 (2 H, d, *J* = 7.70 Hz, CH_{Ar}) and 7.70 (2 H, d, *J* = 8.11 Hz, CH_{Ar}); δ_C (125 MHz, CD_3CN): 24.8 (CH_2), 25.1 (CH_2), 25.8 (CH_2), 28.7 ($CH_{2\beta}$), 41.9 ($CH_{2\gamma}$), 44.1 (CH_2S), 47.1 (CH_α), 119.9 (C_{Ar}), 120.2, 122.3, 128.9, 132.8 (CH_{Ar}), 140.7 (NHC), 151.1 (C_{guan}) and 164.9 (C_{urea}); *m*/*z* (ESI) 582.3 ($M^+ - PF_6^-$).

Macrocycle 5. 1,5-Diaminopentane (0.114 mL, 0.978 mmol) was added dropwise to a solution of CDI (0.476 g, 2.978 mmol) in THF. After 30 min, the solvent was removed at reduced pressure and the crude material was purified by precipitation with ethyl acetate, affording **7** (280 mg, 96%) as a white solid. mp 89–91 °C; δ_H (500 MHz, CD_3OD): 1.67 (2 H, m, CH_2), 1.79 (4 H, q, J = 7.67 Hz, CH_2), 3.35 (4 H, t, J = 7.11 Hz, CH_2), 7.01 (2 H, s, CH), 7.60 (2 H, s, CH) and 8.24 (2 H, s, CH); δ_C (125 MHz, CD_3OD): 25.0 (CH_2), 29.9 (CH_2), 41.6 (CH_2), 130.0, 130.1, 137.4 (C_{Ar}) and 150.8 (CO).

Compound **7** (64 mg, 2.26 mmol) was added, under a nitrogen atmosphere, to a solution of **2** (100 mg, 2.26 mmol) in dry MeOH (6 mL) in a sealed tube, and the mixture was stirred at 80 °C for 2 d. After evaporation of the solvent, the resulting solid was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 98 : 2) and then precipitated in acetonitrile to afford **5** (as hydrochloride salt) as a white pure solid. The solid was dissolved in MeOH and eluted through a Dowex ion-exchange resin (PF_6^-) to yield **5** (PF_6^-) (20 mg, 8%). mp 136–138 °C; $[\alpha]_D^{25}$ −26.24 (c 0.25 in CH_3CN); δ_H (500 MHz, CD_3CN): 1.62 (6 H, m, CH_2), 1.81–2.21 (4 H, m, $CH_{2\beta}$), 2.89 (4 H, m, CH_2), 2.90–3.45 (10 H, m, $CH_{2\gamma}$, CH_α, CH_2S), 5.89 (2 H, s, NH_{urea}), 6.85 (2 H, s, NH_{urea}), 6.97 (2 H, t, J = 7.10 Hz, CH_{Ar}), 7.05 (2 H, t, J = 7.51 Hz, CH_{Ar}), 7.23 (2 H, s, NH_{guan}), 7.48 (2 H, d, J = 7.77 Hz, CH_{Ar}) and 7.62 (2 H, d, J = 7.90 Hz, CH_{Ar}); δ_C (125 MHz, CD_3CN): 25.0 (CH_2), 25.9 (CH_2), 26.2 (CH_2), 28.7 ($CH_{2\beta}$), 41.9 ($CH_{2\gamma}$), 44.4 (CH_2S), 46.9 (CH_α), 119.6 (C_{Ar}), 120.1, 121.8, 128.5, 133.5 (CH_{Ar}), 140.9 (NHC), 150.6 (C_{guan}) and 165.5 (C_{urea}); m/z (ESI) 568.3 ($M^+ - PF_6^-$).

Crystal data for 4 at 100 K

$C_{27}H_{36}N_8O_5S_2$ ($\frac{1}{4}H_2O$ for 3 molecules of **4**), 618.09 g mol^{-1}, orthorhombic, $P2_12_12_1$, a = 9.1246(10), b = 20.319(2), c = 47.951(5) Å, V = 8890.1(16) Å^3, Z = 12, ρ_{calc} = 1.385 Mg m^{-3}, R_1 = 0.0752 (0.1050), wR_2 = 0.1644 (0.1787), for 11 345 reflections with $I > 2\sigma(I)$ (for 15 128 reflections [R_{int} = 0.0753] with a total of 78 274 measured reflections), goodness-of-fit on F^2 = 1.091, Flack = −0.05(9), largest differential peak (hole) = 1.278 (−0.480) e Å^{-3}. The structure of **4** could be solved and refined in the higher symmetric orthorhombic chiral space group $P2_12_12_1$ or in the lower symmetric monoclinic chiral space group $P2_1$ as a monoclinic twin, which emulates a higher symmetric orthorhombic crystal with a β angle close to 90°. In the higher symmetric space group, the three independent refined structures were partly disordered, and the obtained R-values were higher (R_1 = 0.0752 ($F_o > 4\sigma F_o$)). In the lower symmetric space group, which refined with better R-values, by applying a twin matrix (1 0 0 0 −1 0 0 0 −1, basf 0.43), six different independent molecules could be refined without disorder (R_1 = 0.0654 ($F_o > 4\sigma F_o$)). In this case, the six independent molecules showed correlation effects. In order to discuss the crystal packing and the arrangement of the NO_3^- anions, the higher symmetrical and partly disordered structure solution was selected. CCDC 635651.

Crystal data for 5 at 100 K

$C_{28}H_{38}Cl_1N_8O_5S_2$, 630.78 g mol^{-1}, triclinic, $P1$, a = 10.8570(15), b = 12.4706(16), c = 12.9263(16) Å, α = 98.088(3), β = 112.786(3), γ = 107.966(3)°, V = 1465.8(3) Å^3, Z = 2, ρ_{calc} = 1.429 Mg m^{-3}, R_1 = 0.0812 (0.0863), wR_2 = 0.2163 (0.2213), for 20 146 reflections with $I > 2\sigma(I)$ (for 22 507 reflections [R_{int} = 0.0804] with a total of 38 109 measured reflections), goodness-of-fit on F^2 = 1.026, Flack = −0.07(4), largest differential peak (hole) = 0.437 (−0.408) e Å^{-3}. The different data obtained for compound **5** always corresponded to the overlap of the reflections of more than one crystal. The best R_1-value ($F_o > 4\sigma F_o$) reached was not lower than 11%. Using the program Gemini,[17] the overlapped data of two crystals could be first separated for integration and later refined as one data set, taking in account the overlapping reflections. If only the reflections without overlap were considered, the R_1-value ($F_o > 4\sigma F_o$) reached for 6182 independent reflections was 6.86%. If a factor was included for reflections overlapping more than 50%, a R_1-value ($F_o > 4\sigma F_o$) of 8.12% (20 146 reflections) was reached. If different factors were applied in correlation with the different degrees of overlapping of the reflections, a R_1-value ($F_o > 4\sigma F_o$) of 9.31% (35 238 reflections) could be reached. For the structure description, the refinement model with one overlapping factor was used. Additionally to the described overlapping of the crystals, pseudosymmetry from $P1$ to P-1 was detected. For a chiral structure, the correct space group being $P1$. CCDC 635652.

Crystal data for 6 at 100 K

$C_{29}H_{40}N_8O_5S_2$, 644.81 g mol^{-1}, monoclinic, $P2_1$, a = 12.8416(10), b = 8.7033(7), c = 13.7476(11) Å, β = 96.649(2)°, V = 1526.2(2) Å^3, Z = 2, ρ_{calc} = 1.403 Mg m^{-3}, R_1 = 0.0329 (0.0346), wR_2 = 0.0881 (0.0897), for 14 085 reflections with $I > 2\sigma(I)$ (for 14 681 reflections [R_{int} = 0.0406] with a total of 30 934 reflections), goodness-of-fit on F^2 = 1.032, Flack = 0.01(2), largest differential peak (hole) = 0.558 (−0.499) e Å^{-3}. CCDC 635653.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b616409a

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References

1 (*a*) F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609; (*b*) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486.
2 (*a*) A. P. Bisson, V. M. Lynch, M.-K. C. Monahan and E. V. Anslyn, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2340; (*b*) R. Herges, A. Dikmans, U. Jana, F. Köhler, P. G. Jones, I. Dix, T. Fricke and B. König, *Eur. J. Org. Chem.*, 2002, 3004.
3 K. Choi and A. D. Hamilton, *Coord. Chem. Rev.*, 2003, **240**, 101.
4 R. J. T. Houk, S. L. Tobey and E. V. Anslyn, *Top. Curr. Chem.*, 2005, **255**, 199.
5 For a X-ray structure of a nitrate–guanidinium salt, see: A. Gleich, F. P. Schmidtchen, P. Mikulcik and G. Müller, *J. Chem. Soc., Chem. Commun.*, 1990, 55.
6 (*a*) B. P. Hay, M. Gutowski, D. A. Dixon, J. Garza, R. Vargas and B. A. Moyer, *J. Am. Chem. Soc.*, 2004, **126**, 7925; (*b*) B. P. Hay, T. K. Firman and B. A. Moyer, *J. Am. Chem. Soc.*, 2005, **127**, 1810.

7 S. González, R. Peláez, F. Sanz, M. B. Jiménez, J. R. Morán and M. C. Caballero, *Org. Lett.*, 2006, **21**, 4679.

8 K. Kavallieratos, C. M. Bertao and R. H. Crabtree, *J. Org. Chem.*, 1999, **64**, 1675.

9 G.-Y. Lu, W.-J. He and H.-W. Hu, *Huaxue Xuebao*, 1996, **54**, 1214.

10 M. Berger and F. P. Schmidtchen, *J. Am. Chem. Soc.*, 1999, **121**, 9986.

11 M. Haj-Zaroubi, N. W. Mitzel and F. P. Schmidtchen, *Angew. Chem., Int. Ed.*, 2002, **41**, 104.

12 Single extractions were performed by shaking a 1 mg ml^{-1} host solution in CH_2Cl_2 and a saturated $NaNO_3$ solution in water for 5 min. The organic phase was isolated after centrifugation, the solvent removed and a ^{1}H NMR spectrum recorded. The other related guanidinium receptors' and carriers' (ref. 13) spectra, of both aqueous and organic phases, confirm the complete partition of the host into the organic phase in a 1 : 1 host–guest stoichiometry.

13 P. Breccia, M. Van Gool, R. Pérez-Fernández, S. Martin-Santamaria, F. Gago, P. Prados and J. de Mendoza, *J. Am. Chem. Soc.*, 2003, **125**, 8270.

14 (*a*) J. E. Ladbury and B. Z. Chowdhry, *Chem. Biol.*, 1996, **3**, 791; (*b*) I. Wadsö, *Chem. Soc. Rev.*, 1997, 79; (*c*) F. P. Schmidtchen, in *Macrocyclic Chemistry: Currents Trends and Future Perspectives*, ed. K. Gloe, Springer, Dordrecht, 2005, pp. 291.

15 (*a*) K.-J. Chang, D. Moon, M. Soo Lah and K.-S. Jeong, *Angew. Chem., Int. Ed.*, 2005, **48**, 7926; (*b*) K. Choi and A. D. Hamilton, *J. Am. Chem. Soc.*, 2003, **125**, 10241.

16 A full account on these and other related structures will be reported elsewhere.

17 *Gemini: Autoindexing program for twinned crystals*, Version 10.02, Bruker AXS Inc., Madison, Wisconsin, USA, release 5/2000.