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Homo- and Hetero-Dinuclear Anion Complexes

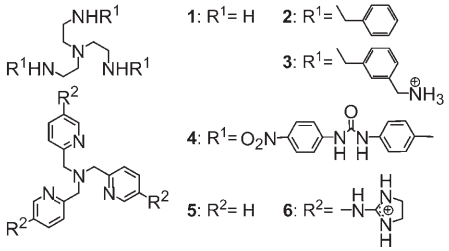
Michela Allevi, Marco Bonizzoni, and Luigi Fabbrizzi*[a]

Abstract: The tripodal system **4**, in which urea fragments are appended to the three terminal amine nitrogen atoms of a tris(2-aminoethyl)amine (tren) subunit, includes a Cu^{II} ion and two anions X^-, according to a cascade mechanism through three well defined stepwise equilibria in a DMSO solution. The first anion X^- (halide, N_3^-, NCS^-, NO_2^-, $H_2PO_4^-$) seeks the Cu^{II} centre coordinated by the tren moiety; the second anion X^- interacts with the trisurea cavity, but this occurs only if the stronger H-bond acceptors, such as N_3^- and $H_2PO_4^-$, are used. Binding of the second X^- ion is favoured by the preorganising effect exerted by the metal and disfavoured by the steric and electrostatic repulsions between the anions. Under the appropriate conditions, heterodinuclear complexes of formula $[Cu^{II}(\mathbf{4})(Cl)(H_2PO_4)]$ can be obtained in solution, in which Cl^- is bound to the metal centre and $H_2PO_4^-$ interacts with the trisurea compartment.

Keywords: anions · dinuclear complexes · hydrogen bonds · molecular recognition · polyamines

Introduction

Artificial receptors for anions typically present a concave space containing several interaction sites that have been strategically positioned within the cavity to fulfil the binding and geometrical requirements of the envisaged analyte.[1] Receptor–anion interactions have to be reversible and can be of various types, such as metal–ligand, electrostatic and hydrogen bonding. A number of metal based anion receptors contain a quadridentate-coordinating subunit, such as tris(2-aminoethyl)amine (tren, **1**)[2] and tris(2-pyridylmethyl)amine (TPA, **5**).[3] Tripodal ligands such as tren and TPA tend to impose a trigonal-bipyramidal geometry on the metal, leaving an apical position available for the coordination of the anion. As an example, bistren ligands, in which two tripodal tetramine subunits are covalently linked by spacers of varying length, have been shown to selectively include and recognise halides,[4] ambidentate polyatomic anions (e.g., N_3^-)[5] and dicarboxylates (including L-glutamate).[6,7] Moreover, positively charged fragments (e.g., ammonium,[8] guanidinium,[9] pyridinium,[10] imidazolium)[11] can be supported by a given organic scaffold (e.g., 1,3,5-triethylbenzene),[12] thus providing a cavity suitable for establishing both electrostatic and multipoint hydrogen-bonding interactions with the anion. In this case, selectivity is based on the intensity of the interaction and on matching the geometrical features of the receptor (cavity size and position of the binding sites) and anion (size and shape, if polyatomic). Anion binding fragments, such as amides,[13] ureas,[14] and pyrroles,[15] can also be neutral H-bond donors. In this case, the energy of the receptor–anion interaction is lower than that observed for positively charged receptors and, in most cases, recognition studies have to be carried out in aprotic media (CH_2Cl_2, MeCN, DMSO, in order of increasing polarity).



More recently, Anslyn et al. have designed systems in which positively charged groups, either ammonium or guanidinium, were linked to a quadridentate tripodal subunit, either tren or TPA, to give **3** and **6**, respectively.[16] The corresponding Cu^{II} complexes are able to establish both metal–

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ligand and electrostatic-hydrogen-bonding interactions with one polyatomic anion (e.g., phosphate), giving rise to 1:1 complexes of various stabilities, in a neutral aqueous solution. The metal centre is important for both anion binding, which affords a favourable enthalpy contribution, and its role in preorganising the positively charged fragments to generate a cavity suitable for anion inclusion (which ensures an entropic advantage). The thermodynamic contributions to the solution stability of the Cu^{II} complexes of **1** and **3** with phosphate have been investigated through isothermal calorimetry studies.[17]

We have considered a receptor containing two separate compartments suitable for the interaction with a pair of anions of either the same or different nature. In particular, we designed the tripodal system **4**, in which a nitrophenylurea subunit was linked to each terminal amine group of a tren platform. It is expected that coordination of a Cu^{II} ion by the tren subunit preorganises system **4** for the interaction with a pair of anions: the first interaction site is available on the axial position of the $Cu^{II}(tren)^{2+}$ moiety, followed by a second site to be provided by the three favourably arranged nitrophenylurea fragments.

We describe here the formation of the complexes of the $[Cu^{II}(\mathbf{4})]^{2+}$ receptor with a variety of anions in DMSO. The investigations were carried out by conducting spectrophotometric titration experiments. We observed the changes 1) in the d–d region of the spectra (to monitor the anion interaction at the metal centre), and 2) in the UV region by looking at the band of the nitrophenyl chromophore (to monitor the hydrogen bonding interactions of the anion with the urea fragments).[18] On this basis, we tried to answer the following questions: 1) How do the receptors' two binding sites compete for the coordination of the first anion? 2) To what extent do repulsive electrostatic and steric interactions affect the coordination of the second anion? 3) How do the different anions affinities toward metal–ligand and hydrogen-bonding interactions affect the stability of the 1:2 receptor–anion complexes and how could the conditions be addressed to favour the formation of complexes with two anions of different nature? Figure 1 illustrates the cascade mechanism for the hypothesised formation of the heterodianionic complex $[Cu^{II}(\mathbf{4})\leftarrow X\cdots Y]$ ($\leftarrow$ symbolises the coordinative bond and $\cdots$ the hydrogen-bonding interaction).

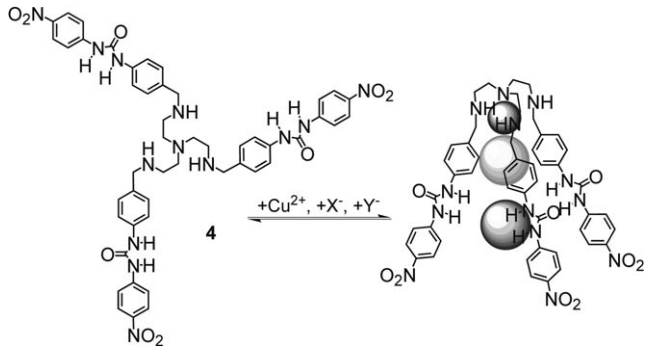


Figure 1. Cascade mechanism for the formation of the heterodianionic complex $[Cu^{II}(\mathbf{4})(X\cdots Y)]$. Spheres from the top: Cu^{II} ion, X^- anion, Y^- anion.

Results and Discussion

Anion interactions with the metal-free receptor 4: The tripodal receptor **4** provides three urea fragments suitable for the interaction with anions. A single urea subunit can donate two directional hydrogen bonds to a given anion (either mono- or poly-atomic). The energy of the receptor–substrate interaction is strictly related to the acidity of the urea subunit (which can be modulated through substituents of various electron-withdrawing properties) and to the intrinsic basicity of the anion. In this sense, the nitrophenyl substituent is expected to enhance the H-bond-donor tendencies of **4** and, conveniently, provide optical evidence of the occurrence of the receptor–anion interaction. In fact, the formation of the H-bond complex and the associated flow of negative charge from the anion to the $-NO_2$ group stabilises the excited state of the nitrophenyl chromophore, inducing a red-shift of the intense charge-transfer band centred at $\approx$350 nm. Selected spectra recorded over the course of the titration of a 1.99×10^{-5} M solution of **4** in DMSO with $[Bu_4N]H_2PO_4$ are reported in Figure 2. DMSO was chosen as a medium because it ensures a fairly high solubility of **4** ($\approx5\times10^{-3}$ M).

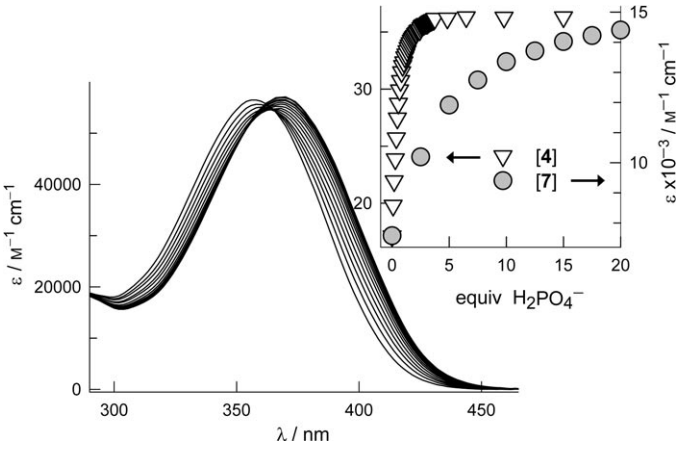


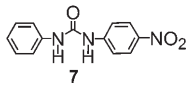
Figure 2. Spectra taken over the course of the titration of a solution of **4** (1.99×10^{-5} M) in DMSO against $[Bu_4N]H_2PO_4$. Inset are titration profiles: **4** (▼), at 400 nm, left vertical axis; **7** (●), at 400 nm, right vertical axis.

Anion addition causes a significant red-shift of the nitrophenyl band, indicating the occurrence of a rather strong H-bond interaction with the urea fragments. The titration profile at a selected wavelength, shown in the inset of Figure 2 (▽, left vertical axis), gives evidence of the formation of a 1:1 receptor–anion complex. Non-linear least-squares fitting of titration data,[19] over the 300–450 nm spectral range, gave a $\log K = 6.05 \pm 0.03$ for the association Equilibrium (1):

$$\mathbf{4} + H_2PO_4^- \rightleftharpoons [\mathbf{4} \cdots (H_2PO_4)]^- \quad (1)$$

The fact that excess addition of $H_2PO_4^-$ did not induce any further modification of the spectrum indicates the presence at equilibrium of the sole 1:1 complex, over the entire titration range, and would indicate that in the H-bond complex the anion interacts with all the urea fragments of **4**. In addition, models analysing the formation of 1:2 and 1:3 receptor–anion complexes were rejected by the least-squares fitting of the titration data.

The occurrence of a proton transfer from the $H_2PO_4^-$ ion to a secondary amine group of **4** should be also considered. However, the distinct red-shift of the nitrophenyl charge-transfer band indicates anion interaction at the trisurea compartment under definite stoichiometry. The proton transfer from the $H_2PO_4^-$ acid to a secondary amine, according to a Brønsted equilibrium, is an energetically favoured process that, in the present case, is in competition with and prevented by the establishment of rather strong H-bond interactions of the anion with the three urea fragments.



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For comparative purposes, the interaction of $H_2PO_4^-$ with the urea derivative **7**, corresponding to a single arm of the tripodal receptor **4**, was investigated under the same conditions. The pertinent titration profile at 400 nm is shown in the inset of Figure 2 (●, right vertical axis). Notice that the curvature of the profile is much smoother than that observed for **4**, and an association constant $\log K = 4.05 \pm 0.03$ was calculated. This finding reinforces the hypothesis that the tripodal receptor **4** interacts with $H_2PO_4^-$ through more than one arm. The advantage in favour of **4** by two orders of magnitude, with respect to **7**, results from the balance between the exoergonic contribution of H-bond interactions and the endergonic term associated to the organization of **4**, upon creating a cavity.

Similar titration experiments were carried out on the tripodal receptor **4** by using a variety of inorganic anions (Cl^-, Br^-, I^-, N_3^-, NCS^-, NO_3^-, NO_2^-), but no significant changes were observed in the UV-visible spectra, even after a large excess addition of the anion, ruling out the occurrence of any anion–urea H-bond interaction. Lack of interaction has to be ascribed to the relatively low basicity of the envisioned anions, in the presence of the highly competing solvent DMSO.

Anion interactions at the $[Cu^{II}(tren)]^{2+}$ cavity: Copper(II) complexes with tren derivatives tend to bind an X^- anion, to give five-coordinate ternary species, of compressed trigonal-bipyramidal geometry. Such an arrangement has been observed in the solid state for a number of complexes, in particular with those of the tribenzyl derivative **2**, with $X^- = Cl^-$,[20] NCS^-,[21] $S_2O_3^{2-}$.[22] On this basis, we carried out preliminary equilibrium studies on the interaction of the $[Cu^{II}(\mathbf{2})]^{2+}$ complex with anions in a DMSO solution. $[Cu^{II}(\mathbf{2})]^{2+}$ was considered an appropriate system for modelling the interaction of anions at the metal centre in the two-compartment $[Cu^{II}(\mathbf{4})]^{2+}$ receptor. Typically, a $2–5 \times 10^{-3}$ M solution of $[Cu^{II}(\mathbf{2})](ClO_4)_2$ was titrated with a standard solution of X^- (in general, from a tetralkylammonium salt). Figure 3 displays the spectra obtained over the course of the titration with N_3^-. On azide addition, a new, rather strong band develops at 410 nm, while two less intense bands at 675 and 850 nm strengthen moderately. The two latter bands have a d–d origin and correspond to the $d_{z^2} \rightarrow d_{x^2-y^2}, d_{xy}$ and $d_{z^2} \rightarrow d_{xz}, d_{yz}$ transitions, respectively, in a d^9 complex of trigonal-bipyramidal geometry. In contrast, the absorption band centred at 410 nm has a ligand-to-metal charge transfer (LMCT) nature, arising from the transfer of an electron from a π^* level of the anion to the half-filled d_{z^2} orbital of the metal centre. Plots of the absorbance at 410 and 675 nm, shown in the inset of Figure 3, clearly indicate the formation of a 1:1 adduct, and multiwavelength least-squares treatment of titration data gave a $\log K = 4.57 \pm 0.04$ for the Equilibrium (2):

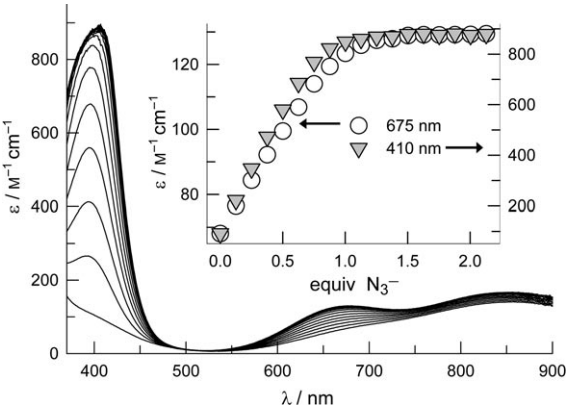


Figure 3. Visible spectra taken over the course of the titration of a solution of $[Cu^{II}(\mathbf{2})](ClO_4)_2$ (3.74×10^{-3} M) in DMSO against NaN_3. Inset: titration profiles at selected wavelengths.

$$[Cu^{II}(\mathbf{2})]^{2+} + N_3^- \rightleftharpoons [Cu^{II}(\mathbf{2})(N_3)]^+ \quad (2)$$

It is suggested that N_3^- replaces a DMSO molecule that is axially coordinated to the metal. The formation of the ternary complex can be perceived visually, as the pale-blue solution of $[Cu^{II}(\mathbf{2})(DMSO)]^{2+}$, on azide addition, takes a bright blue-green colour.

Similar behaviour was observed on titration with tetraalkylammonium salts of halides and pseudohalides. On addition of X^-, the solution of the $[Cu^{II}(\mathbf{2})]^{2+}$ complex took a colour varying from blue to green, essentially depending upon the energy of the LMCT band. In particular, such a band was distinctly observed at relatively high wavelengths with I^- (430 nm) and NCS^- (375 nm). For Cl^- and Br^-, due to their lower tendency to release electrons, the LMCT

band was displaced toward lower wavelengths and perceived as a shoulder of the band associated to the amine-to-copper(II) charge-transfer transition. In all cases, the formation of a 1:1 complex was ascertained. Log$K$ values for the general equilibrium $[Cu^{II}(\mathbf{2})]^{2+} + X^- \rightleftharpoons [Cu^{II}(\mathbf{2})(X)]^+$ are reported in Table 1.

Table 1. Equilibrium constants for the interaction of inorganic anions X^- with receptors $[Cu^{II}(\mathbf{2})]^{2+}$, **4** and $[Cu^{II}(\mathbf{4})]^{2+}$ in DMSO at 25 °C. The uncertainty for the last figure is given in parentheses.

Anion	**4** log$K$	$[Cu^{II}(\mathbf{2})]^{2+}$ log$K$	$[Cu^{II}(\mathbf{4})]^{2+}$ logK_1	$[Cu^{II}(\mathbf{4})]^{2+}$ logK_2
N_3^-	–	4.57(4)	3.86(3)	2.2(1)
NCS^-	–	4.16(2)	4.7(1)	–
Cl^-	–	3.48(3)	4.7(1)	–
Br^-	–	3.74(1)	3.48(7)	–
I^-	–	2.18(1)	2.13(2)	–
NO_2^-	–	4.79(4)	4.91(2)	–
$H_2PO_4^-$	6.05(3)	>5	>5	≈ 2

Titration experiments were carried out also with some oxoanions. By using $H_2PO_4^-$, distinct modifications of the d–d bands were observed and the high-energy LMCT band appeared as a shoulder. A 1:1 titration profile was obtained, but it was too steep for an accurate determination of the log$K$ value. In particular, at the investigated concentration (10^{-3} M), we can state only that the log$K$ value is >5. However, very poor spectral modifications were observed upon titration with $[Bu_4]NO_3$, for which a log$K$ value of <2 was estimated. A special case was that of the oxoanion NO_2^- for which a well-defined low-energy LMCT band was observed (see spectra in Figure 4) and a relatively high association

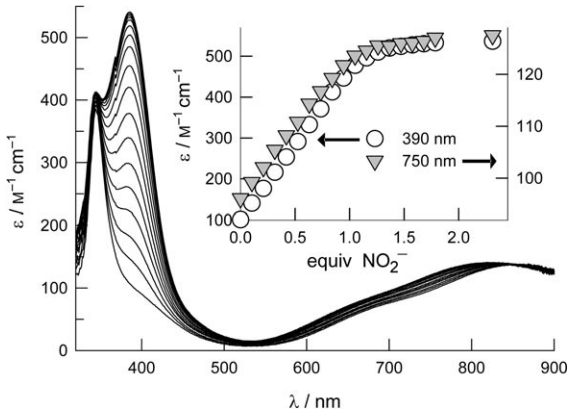


Figure 4. Visible spectra taken over the course of the titration of a solution of $[Cu^{II}(\mathbf{2})](ClO_4)_2$ (3.74×10^{-3} M) in DMSO against $[Bu_4N]NO_2$. Inset: titration profiles at selected wavelengths.

constant ($\log K = 4.79 \pm 0.04$) was determined. These findings may suggest the coordination of NO_2^- to the metal through the nitrogen atom (*nitro* mode), rather than through one of the oxygen atoms (*nitrito* mode).

Interaction of anions of the same nature at the two compartments of the $[Cu^{II}(\mathbf{4})]^{2+}$ receptor: The tendencies of the tripodal system **4** to interact with Cu^{II} were investigated by titrating a DMSO solution of **4** (2.075×10^{-3} M) with a standard solution of $Cu^{II}(CF_3SO_3)_2$ in DMSO. Figure 5 displays the family of spectra obtained over the course of the titration.

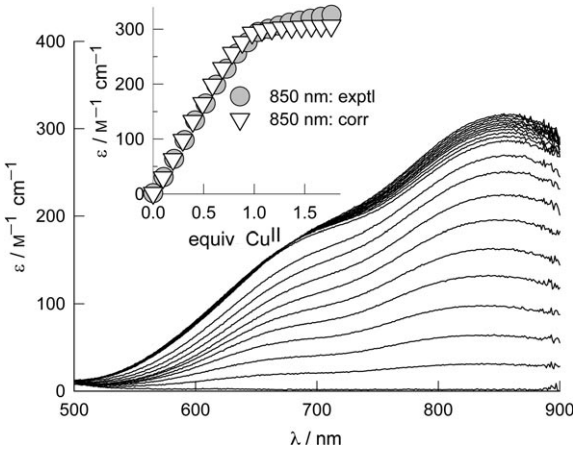


Figure 5. Visible spectra taken over the course of the titration of a solution of **4** (2.075×10^{-3} M) in DMSO against $Cu^{II}(CF_3SO_3)_2$. The two bands at 750 and 850 nm indicate the formation of a trigonal-bipyramidal complex. Inset are titration profiles of the band at 850 nm: experimental values (●); values corrected for the absorbance of the $[Cu^{II}(dmso)_4]^{2+}$ species (▼).

The 1:1 stoichiometry of the $[Cu^{II}(\mathbf{4})]^{2+}$ complex should be demonstrated by the titration profiles of the two d–d bands. As an example, the profile of the absorbance at 850 nm is shown in the inset of Figure 5 (circles). However, this is not a definitive profile, as the measured absorbance includes the contribution of the $[Cu^{II}(DMSO)_4]^{2+}$ complex, present in solution after the addition of one equivalent of Cu^{II}. The corrected titration profile (triangles in the inset of Figure 5) definitely demonstrates the 1:1 stoichiometry of the metal complex. Furthermore, the steep titration profile and the sharp discontinuity at one equivalent indicate the formation of a very stable coordination complex that has a stability constant that can only be estimated to be $>10^5$ (at 10^{-3} M). Titration experiments with anions were carried out on a DMSO solution containing equimolar amounts of $[Cu^{II}(CF_3SO_3)_2]$ and **4**. Within the employed formation range ($2\text{–}5\times10^{-3}$ M) the percent concentration of the $[Cu^{II}(\mathbf{4})]^{2+}$ receptor is $>99\,\%$.

Figure 6a shows the visible portion of the spectra taken over the course of the titration of a 2.075×10^{-3} M solution of $[Cu^{II}(\mathbf{4})]^{2+}$ in DMSO with $[Bu_4N]N_3$. The strong absorption of the nitrophenyl chromophore prevents the observation of the LMCT band expected upon interaction of N_3^- with the $[Cu^{II}(tren)]^{2+}$ subunit. However, the interaction of the N_3^- anion with the $[Cu^{II}(tren)]^{2+}$ moiety is unambiguously demonstrated by the strengthening of the two d–d bands in the 600–900 nm region. The intensity of the two d–d bands starts to increase noticeably upon the initial additions of the

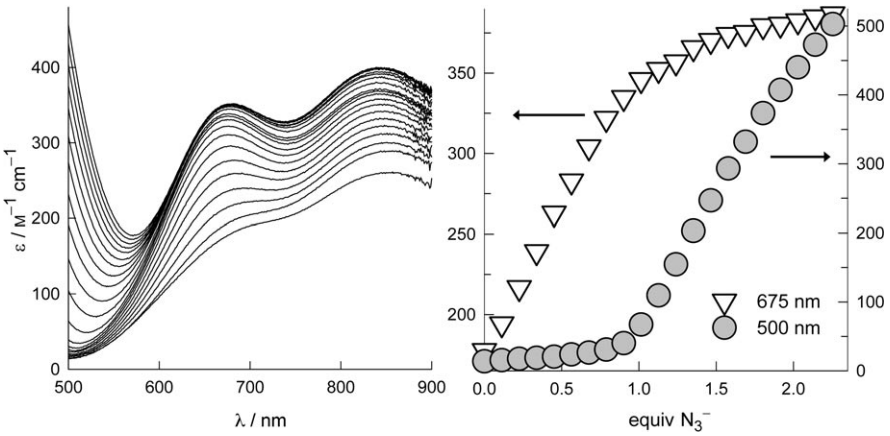


Figure 6. a) Visible spectra taken over the course of the titration of a solution of $[Cu^{II}(\mathbf{4})]^{2+}$ (2.075×10^{-3} M) in DMSO against NaN_3. b) Titration profiles at selected wavelengths: the d–d band at 675 nm gives evidence of the coordination of the first N_3^- ion at the metal centre; the absorbance at 500 nm, tail of the band of the nitrophenyl chromophore, indicates the entry of the second N_3^- ion and its hydrogen-bonding interaction with the three urea fragments.

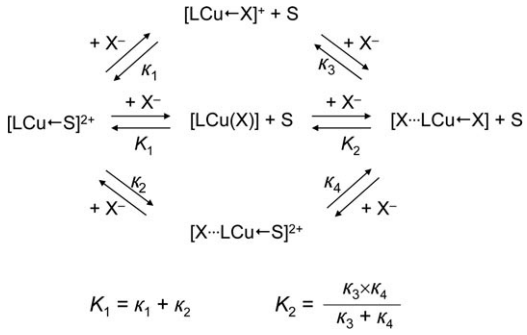
anion, indicating that the N_3^- first seeks the metal centre. The titration profiles of the bands at 675 nm (see Figure 6 b, triangles) and at 850 nm (not shown) correspond to the formation of a 1:1 complex, with an association constant $\log K_1 = 3.86 \pm 0.03$. In contrast, the absorbance at 500 nm begins to increase only after the addition of the first equivalent of N_3^- (see the titration profile in Figure 6 b). This spectral region pertains to the tail of the very intense absorption band of the nitrophenyl chromophore, which is in most part out of scale at this concentration level. Nevertheless, after the addition of one equivalent of the anion, a red-shift of the band was induced. It has been previously mentioned that a red-shift of the nitrophenyl absorption indicates the occurrence of a hydrogen-bonding interaction at a covalently linked urea fragment. Correspondingly, the increase of the absorption at 500 nm documents the interaction of N_3^- with the urea fragments, which are hypothesised to be spatially disposed to donate up to six hydrogen bonds to the anion. Multipoint interactions of the N_3^- ion with a polyammonium cage that donates six hydrogen bonds have been described.[23] In the present case, $\log K_2 = 2.2 \pm 0.1$ was calculated through non-linear least-squares fitting of spectral data. Therefore, the interaction of the metal-containing receptor $[Cu^{II}(\mathbf{4})]^{2+}$ with N_3^- can be described by the following two distinct stepwise Equilibria (3) and (4).

$$[Cu^{II}(\mathbf{4}) \leftarrow DMSO]^{2+} + N_3^- \rightleftharpoons [Cu^{II}(\mathbf{4}) \leftarrow N_3]^+ + DMSO \quad (3)$$

$$[Cu^{II}(\mathbf{4}) \leftarrow N_3]^+ + N_3^- \rightleftharpoons [(Cu^{II}(\mathbf{4}) \leftarrow N_3) \cdots N_3] \quad (4)$$

Although Equilibria (3) and (4) describe what happens in the investigated solution, as monitored through the spectrophotometric response, the equilibria involving the interaction of a receptor (LCu), containing two non-equivalent binding sites, with two anions X^- should be discussed in terms of microconstants, as illustrated in Scheme 1. In particular, the thermodynamic constants K_1 and K_2 are related to the microconstants κ_1 and κ_2, and κ_3 and κ_4, respectively, through the equilibria reported in Scheme 1. In the present case, in view of the much greater propensity of the anion X^- for the coordinative interaction rather than for the hydrogen-bonding interaction, it happens that: 1) $\kappa_1 >> \kappa_2$, from which: $K_1 = \kappa_1$, and 2) $\kappa_4 >> \kappa_3$, from which $K_2 = \kappa_3$.

Interestingly, the metal-free receptor **4** does not bind the N_3^- ion, ($\log K < 2$), probably because the intrinsically small energy associated to the urea–azide H-bond interaction does not compensate the conformational energy spent by the receptor on organizing a cavity for anion inclusion. However, the conformational energy term does not have to be spent by the metal-containing receptor $[Cu^{II}(\mathbf{4})]^{2+}$, in which the trisurea compartment is preorganised (at least in part), thanks to the metal coordination of the tren subunit.



Scheme 1. Interaction of the $[LCu\leftarrow S]^{2+}$ receptor with two X^- anions; S represents a solvent molecule, ($\leftarrow$) indicates the coordinative bond, ($\cdots$) indicates the hydrogen-bonding interaction.

A further example of stepwise anion recognition is provided by $H_2PO_4^-$. As observed in the titration with N_3^-, anion addition induces spectral modifications first in the d–d bands of the $[Cu^{II}(tren)]^{2+}$ subunit, then in the region of the nitrophenyl chromophore. Figure 7 displays the titration profiles at wavelengths pertaining to the two spectral regions.

On addition of the first equivalent of $H_2PO_4^-$, a steep increase of the band at 820 nm indicates phosphate coordination at the Cu^{II} centre. The sharp discontinuity at one equivalent prevents the determination of the constant of the Equilibrium of type (3), which can be estimated to be $>10^5$.

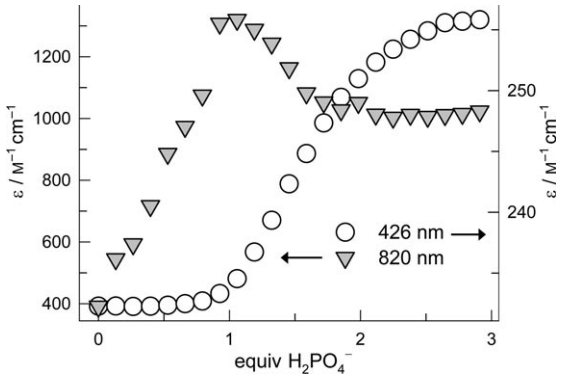


Figure 7. Titration profiles at selected wavelengths taken over the course of the titration of a solution of $[Cu^{II}(\mathbf{4})]^{2+}$ (2.00×10^{-3} M) in DMSO against $[Bu_4N]H_2PO_4$: the absorbance at 650 nm gives evidence of the coordination of the first $H_2PO_4^-$ ion at the Cu^{II} centre ($\log K > 5$); the absorbance at 426 nm indicates the establishing of H-bond interactions of the urea compartment of $[Cu^{II}(\mathbf{4})]^{2+}$ with the second $H_2PO_4^-$ ion ($\log K = 2.0\pm0.1$).

Upon addition of the second equivalent of phosphate, the absorbance at 425 nm begins to increase, providing evidence of the interaction of $H_2PO_4^-$ with the urea compartment. The smooth profile corresponds to a $\log K_2$ value of 2.0 ± 0.1, for an equilibrium of type (4). Noticeably, this value is nearly four orders of magnitude lower than that observed for the metal free receptor **4**. Such a huge difference should reflect a significant repulsive effect between the two $H_2PO_4^-$, of both steric and electrostatic nature. In this regard, a concomitant change in the d–d spectral region takes place, shown in Figure 6 by the decrease in the absorbance at 820 nm. This may indicate a distortion of the geometry of the $[Cu^{II}(tren)]^{2+}$ subunit, as part of a general conformational rearrangement of the receptor for accommodating the second $H_2PO_4^-$ anion. It is concluded that the unfavourable energy terms associated with electrostatic and steric repulsions and to the conformational rearrangement of the receptor cancel the favourable term associated with the metal-driven preorganisation of the urea compartment.

Upon titration of a 2.00×10^{-3} M solution of $[Cu^{II}(\mathbf{4})]^{2+}$ with Cl^-, Br^- and I^-, respectively, spectral changes were observed only in the d–d region, whereas no shift of the nitrophenyl band was observed. This excludes any interaction at the urea compartment and reflects the intrinsically weak H-bond acceptor tendencies of halide ions. LogK_1 values that have been determined through least-squares processing of spectral data in the d–d region are reported in Table 1. Most $\log K_1$ values for anions are similar to those determined for the model system $[Cu^{II}(\mathbf{2})]^{2+}$, whereas those for anions Cl^- and N_3^- are more than one order of magnitude higher. This may suggest the occurrence of an additional interaction of the metal bound anion with the N–H groups of the proximate urea fragments.

Interaction of anions of different nature at the two compartments of the $[Cu^{II}(4)]^{2+}$ receptor: The occurrence of the cascade interaction of the $[Cu^{II}(\mathbf{4})]^{2+}$ receptor with two different anions X^- and Y^- would require that 1) the anion X^- exhibits a pronounced penchant for metal–ligand interactions and a poor affinity for hydrogen bonding, and 2) the opposite were true for the anion Y^-. Although there are a number of anions that fulfil requirement (1), for example Cl^-, we have not found an anion that satisfies requirement (2). In fact, $H_2PO_4^-$, which establishes strong interactions at the urea subunits, also shows a high affinity for the Cu^{II} centre. To circumvent this problem, we prepared a diluted solution 2.00×10^{-5} M in $[Cu^{II}(\mathbf{4})]^{2+}$ and 3.00×10^{-3} M in $[Et_3Bn]Cl$. From the value of K_1, one can calculate that the $[Cu^{II}(\mathbf{4})\leftarrow Cl]^+$ complex is present in solution at 99% (the formation of this complex cannot be monitored spectrophotometrically at this concentration level, in view of the intrinsically poor intensity of the d–d bands) In contrast, chloride addition did not significantly modify the intense band of the nitrophenyl chromophore centred at 355 nm. The solution containing the $[Cu^{II}(\mathbf{4})\leftarrow Cl]^+$ complex was then titrated with $[Bu_4N]H_2PO_4$, inducing a distinct red-shift of the nitrophenyl absorption band, indicating anion interaction at the urea compartment.

The titration profile at 400 nm is shown in Figure 8 (▼). Multiwavelength non-linear fitting of titration data indicated

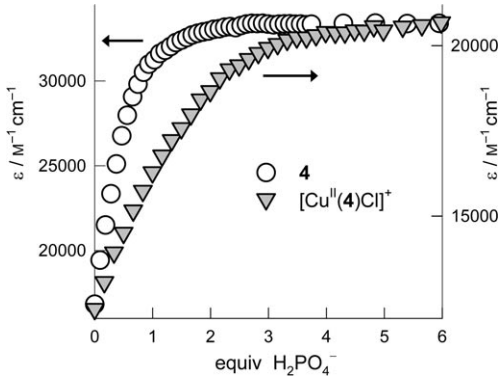


Figure 8. Titration profiles: at 400 nm for a solution of $[Cu^{II}(\mathbf{4})\leftarrow Cl]^+$ (2.00×10^{-5} M) against $[Bu_4N]H_2PO_4$ (▼); at 400 nm for a solution of **4** (2.00×10^{-5} M) against $[Bu_4N]H_2PO_4$ (●).

the formation of a 1:1 adduct, with a $\log K_2 = 4.83\pm0.01$. The constant corresponds to the following Equilibrium (5):

$$[Cu^{II}(\mathbf{4}) \leftarrow Cl]^+ + H_2PO_4^- \rightleftharpoons [(Cu^{II}(\mathbf{4}) \leftarrow Cl)\cdots H_2PO_4] \quad (5)$$

Surprisingly, the K_2 value is ≈700-fold higher than that associated with the formation of the corresponding homodianionic complex $[(Cu^{II}(\mathbf{4})\leftarrow H_2PO_4)\cdots H_2PO_4]$. This pronounced advantage is probably related to the smaller size of the chloride anion, which is expected to exert less pronounced steric and electrostatic repulsions toward the incoming $H_2PO_4^-$. However, this value is still 17-fold lower than that observed for the interaction of $H_2PO_4^-$ at the tris-urea compartment of the metal free receptor **4**. This indi-

cates that, in the $[(Cu^{II}(\mathbf{4})\leftarrow Cl)\cdots H_2PO_4]$ complex, interanion repulsions are still working and cancel, in part, the energy gain due to the metal-induced organization of the receptor. The distinctly higher affinity of the metal free receptor **4** toward $H_2PO_4^-$ with respect to that containing the $Cu^{II}Cl^+$ ion pair can be seen in Figure 8, in which the two titration profiles taken under the same conditions are compared.

The experiments described above may contribute to the impression that in the $[Cu^{II}(\mathbf{4})]^{2+}$ system, the first anion binds irreversibly to the metal centre, giving rise to a rigid and unalterable receptor that provides an H-bond-donating cavity. Indeed, the system investigated here should not differ too much from previously described anion receptors, in which a metal ion plays a mere architectural role in preorganising the organic receptor's framework. However, the anion interacting with the metal centre in the $[Cu^{II}(\mathbf{4})]^{2+}$ system is not irreversibly bound. This is not unexpected in view of the intrinsic lability of the Cu^{II} metal ion. Consequently, an X^- anion bound to Cu^{II} in the $[Cu^{II}(\mathbf{4})]^{2+}$ system should be replaced by an anion Y^-, under appropriate equilibrium conditions, according to a fast-exchange process. Indeed, this has been demonstrated by adding one equivalent of $[Bu_4N]H_2PO_4$ to a DMSO solution of $[Cu^{II}(\mathbf{4})]^{2+}$ (2.00×10^{-3} M). The high binding constant ($K_1>10^5$) ensures the formation of 100% of the $[Cu^{II}(\mathbf{4})\leftarrow H_2PO_4]^+$ complex, in which all the dihydrogenphosphate ion is bound to the metal centre. To this solution, aliquots of a standard concentrated solution of $[Et_3Bn]Cl$ in DMSO (0.620 M) were added. Upon chloride addition, a distinct shift of the nitrobenzyl charge transfer absorption band was observed, as shown in Figure 9 (left).

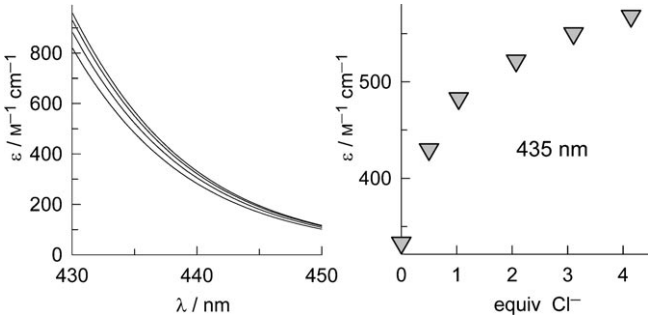


Figure 9. Spectra (left) taken over the course of the titration of a solution of $[Cu^{II}(\mathbf{4})]^{2+}$ (2.00×10^{-3} M) and $[Bu_4N]H_2PO_4$ in DMSO against $[Et_3Bn]Cl$. Titration profile (right) at 435 nm.

Only the very final portion of the tail of the nitrophenyl band could be distinctly monitored, due to the relatively high concentration of the chromophore, which caused optical saturation. However, a definite red-shift of the band was observed, which indicates the occurrence of an H-bond interaction at the trisurea compartment. As the Cl^- anion is not able to interact with the trisurea cavity of the $[Cu^{II}(\mathbf{4})]^{2+}$ receptor, even at high concentration, the spectral change has to be ascribed to the binding of the $H_2PO_4^-$ ion. Therefore, due to a mass effect, Cl^- displaces from the metal centre the $H_2PO_4^-$ anion, which translocates to the trisurea compartment, according to Equilibrium (6):

$$[Cu^{II}(\mathbf{4})\leftarrow H_2PO_4]^+ + Cl^- \rightleftharpoons [(Cu^{II}(\mathbf{4})\leftarrow Cl)\cdots H_2PO_4] \quad (6)$$

The progress of the $H_2PO_4^-$ sliding from one compartment to another is illustrated by the titration profile in Figure 9 (right).

The anion exchange process described by Equilibrium (6) emphasises the lability and reversibility of the non-covalent interactions responsible for the anion binding properties of the $[Cu^{II}(\mathbf{4})]^{2+}$ receptor, either metal–ligand or hydrogen bonding, and provides a further example of supramolecular dynamics.

Conclusion

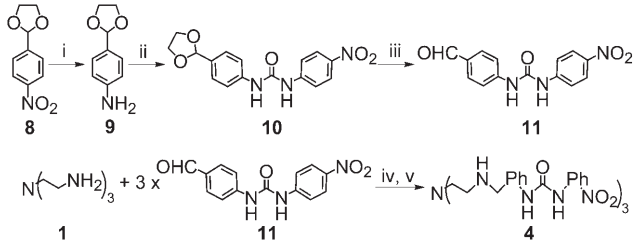
This work has shown that in a receptor containing two unequivalent recognition sites, the anion first seeks to bind at the metal centre, then to form H-bond interactions at the urea compartment. The latter interaction suffers from 1) the competition from the solvent and 2) the interanion repulsive effects of both electrostatic and steric nature. In particular, the trisurea compartment is able to host only anions displaying pronounced H-bond acceptor tendencies. On this basis, the formation of a heterodinuclear anion complex can be designed, firstly by saturating the metal containing subunit with a poor H-bond acceptor (e.g., Cl^-), through a concentration effect, then allowing the trisurea compartment to interact with a powerful H-bond acceptor (e.g., $H_2PO_4^-$). Moreover, due to the labile and reversible nature of metal–ligand and hydrogen-bonding interactions, hetroditopic systems such as those investigated here offer the opportunity to carry out fast anion interexchange processes, such as the sliding of $H_2PO_4^-$ from the metal centre cavity to the trisurea compartment, to leave room for Cl^- (present in excess concentration).

Anion-coordination chemistry is the younger sister of the traditional and well-established discipline of transition-metal coordination chemistry.[24] A number of examples of anions inside receptors that imitate the role of metals inside multidentate ligands have been reported recently. These include chelate, macrocyclic and cage complexes, helicates,[25] rotaxanes[26] and catenates.[27] In this work, we have explored the design of homodinuclear and heterodinuclear anion complexes. Dinuclear metal complexes display interesting properties in magnetism, [28] catalysis, [29] biochemistry[30] and medicinal chemistry. [31] It is difficult to forecast equally dominant roles for anion analogues, which nevertheless, deserve investigation. Here, we have tried to outline the principles governing the formation of stable homo- and hetero-dinuclear anion complexes in solution.

Experimental Section

General procedures: The spectra for the UV/Vis titration experiments were recorded by using either a Hewlett–Packard 8452 A diode-array or a scanning Varian Cary 100 spectrophotometer. The temperature of the cell holder was maintained at 25.0 °C by a thermostat. Typically, aliquots of a fresh tetrabutylammonium salt standard solution of the respective anion were added and the UV/Vis spectra of the samples were recorded. For chloride, the $[Et_3Bn]Cl$ salt was used, for azide, NaN_3 was used The HYPERQUAD program was used to fit all of the spectrophotometric titration curves.[19]

Synthesis of ligands and complexes: Reagents were bought from Sigma-Aldrich. Reagents and solvents were used without further purification. N^1-benzyl-N^2,N^2-bis(2-(benzylamino)ethyl)ethane-1,2-diamine (**2**) was synthesised by following a reported procedure.[32] Deionised water was used throughout. NMR spectra were recorded by using a Bruker Avance at 400 MHz, mass spectra were acquired by using a Thermo-Finnigan ion-trap LCQ Advantage MAX instrument equipped with an ESI source. Catalytic hydrogenations were carried out in a Parr stainless steel-pressure vessel with mechanical stirring. The synthetic route to **4** is outlined in Scheme 2.



Scheme 2. Synthetic route to the receptor **4**. i) H_2, 7 atm, PtO_2 5 mol%, $CH(OEt_3)_3$, THF; ii) 1.01 equiv 4-nitrophenylisocyanate, THF; iii) $HClO_4$ in THF, 2 h, RT; iv) MeOH, RT; v) $NaBH_4$, MeOH, 60 °C.

2-(4-Nitrophenyl)-[1,3]-dioxolane (8): 4-Nitro-benzaldehyde (4 g, 26.5 mmol) was dissolved in benzene (160 mL) with magnetic stirring (toluene was also tried, but yielded inferior results). To this solution, ethylene glycol (7.3 mL, 132 mmol) and *p*-toluenesulfonic acid (60 mg, 0.59 mmol, catalytic) were added and the solution refluxed for 4.5 h; after which TLC (SiO_2, AcOEt:hexanes = 3:7) showed the reaction to be complete. Once cooled to RT, the solution was washed with water (3 × 20 mL), then brine (3 × 20 mL). The combined aqueous phases from these extractions were washed with CH_2Cl_2 (3 × 20 mL). The combined organic phases from all the extraction steps were then dried with Na_2SO_4 (45 min) and the solvent was removed in vacuo to give the desired protected aldehyde in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.25$ (d, 2H), 7.65 (d, 2H), 5.95 (s, 1H), 4.15 ppm (m, 4H).

2-(4-Aminophenyl)-[1,3]-dioxolane (9): The pressure reactor was purged with nitrogen, then charged with **8** (9.75 g, 50 mmol), $CH(OEt)_3$ (14.8 g, 100 mmol) and dry THF (125 mL), to obtain a solution in which PtO_2 (1 g, 4 mmols, catalytic) was suspended. The reactor was then sealed, placed in a water/ice bath, evacuated and charged with H_2 to 7 atm (100 psi). Mechanical stirring was maintained throughout the reaction. Hydrogen consumption was compensated by repressurisation every 15 min. After ≈1.5 h hydrogen absorption ceased and the pressure remained constant. The reactor was then opened and the catalyst removed by filtration. After drying over Na_2SO_4, the solution was concentrated in vacuo (water bath ≈65 °C) to obtain a yellow viscous liquid that solidifies on cooling (yield 63%). The product was pure enough for the subsequent reaction steps. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.30$ (d, 2H), 6.70 (d, 2H), 5.70 (s, 1H), 4.20 (m, 2H), 4.00 (m, 2H), 3.60 ppm (br s, 2H; NH_2).

1-(4-(1,3-Dioxolan-2-yl)phenyl)-3-(4-nitrophenyl)urea (10): Compound **9** (2 g, 8.21 mmol) was dissolved in THF (50 mL). To this solution, 4-nitrophenyisocyanate (1.36 g, 8.29 mmol, 1.01 equiv) dissolved in THF (50 mL) was added dropwise with constant stirring. After ≈40 min a yellow-white precipitate began to develop. After 2.5 h stirring was discontinued and the solid isolated by filtration. The mother liquor was evaporated to half its volume and some more solid was collected. The combined solids were dried in a desiccator overnight (yield 61%). ^{1}H NMR (400 MHz, $[D_6]$DMSO): $\delta = 9.45$ (s, 1H; urea NH), 9.05 (s, 1H; urea NH), 8.20 (d, 2H), 7.60 (d, 2H), 7.30 (m, 4H), 5.60 (s, 1H), 4.10 (m, 2H), 3.90 ppm (m, 2H); negative-ion ESI-MS: *m*/*z*: 328.3 $[M-H]^-$, 364.2–366.2 $[M+Cl]^-$.

1-(4-Formylphenyl)-3-(4-nitrophenyl)urea (11): Complex **10** (2 g, 6.08 mmol) was dissolved in THF (350 mL). To this, $HClO_4$ (19 mL, 70%) was added and the solution was left stirring overnight at ≈30 °C, during which time the solution turned orange. Solid NaOH was added to neutralise the excess acid: the colour changed abruptly to brownish-red and a solid precipitated (inorganic salts). The solution was dried three times over fresh Na_2SO_4, then evaporated to a reddish solid, still containing inorganic salts. Assuming nearly quantitative yield, a purity of around 50% was estimated. Further purification was not undertaken and the product was used directly for the formation of the Schiff base mentioned above; a trial run showed that in this step, only the desired product precipitates out of the reaction mix. ESI-MS: *m*/*z*: 286.2 $[M+H]^+$, 308.3 $[M+Na]^+$.

Schiff base condensation between 11 and tren: Crude **11** (3.5 g, containing ≈6 mmol of **11**) was suspended in MeOH (1 L) and thoroughly sonicated accompanied by heating, then the insoluble matter was filtered off. To this solution, tris(2-aminoethyl)amine (tren) (300 μL, 2 mmol) was added and the mixture was left stirring overnight. During this time a solid separated, which was isolated and stored in a desiccator (yield 55% based on tren). ^{1}H NMR (400 MHz, $[D_6]$DMSO): $\delta = 9.55$ (s, 1H; urea NH), 9.20 (s, 1H; urea NH), 8.20 (d, 2H), 8.10 (s, 1H; imine CH), 7.65 (d, 2H), 7.48 (m, 4H), 3.60 (t, 2H), 2.75 ppm (t, 2H); ESI-MS: *m*/*z*: 948.2 $[M+H]^+$.

Reduction of the Schiff base to give 4: The Schiff base (969 mg, 1.02 mmol) was suspended in MeOH (180 mL). The suspension was stirred at 60 °C while $NaBH_4$ (1.16 g, 31 mmol) was added in small portions. The mixture was refluxed for another 2.5 h; then left stirring overnight at RT. The solvent was removed completely to give an orange solid that was taken up in dilute aqueous NaOH (200 mL) to give a suspension that was washed with CH_2Cl_2 (2 × 40 mL). The organic phases were discarded. The bright-yellow solid in the water phase was filtered off and dried to constant weight in a vacuum desiccator (yield 73%). ^{1}H NMR (400 MHz, $[D_6]$DMSO): $\delta = 9.60$ (s, 1H; urea NH), 9.20 (s, 1H; urea NH), 8.15 (d, 2H), 7.70 (d, 2H), 7.30 (d, 2H), 7.15 (d, 2H), 3.60 (br m, 4H; benzylic and aliphatic CH_2), 2.75 ppm (t, 2H); ESI-MS: *m*/*z*: 954.3 $[M+H]^+$.

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