Guest Exchange

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Guests on Different Internal Capsule Sites Exchange with Each Other and with the Outside**

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In memory of Hans Georg von Schnering

In the section "*Dynamics of Guest Exchange in Cavitates*" of the text book "*Supramolecular Chemistry*"[1a] the study of "guest entry and exit from 'open' container molecules" is considered as a challenge. A further challenge is to study the entry and exit processes for guests which can also exchange sites within the container—to date unprecedented, and the subject of the present investigation. The compartmentalization, which corresponds in a formal sense, to the biological cell,[1b] can be realized based on structurally well-defined, discrete spherical metal oxide based porous nanocapsules/containers of the type $(\text{pentagon})_{12}(\text{linker})_{30} \equiv [\{(Mo)Mo_5O_{21}(H_2O)_6\}_{12}\{Mo_2O_4(\text{ligand})\}_{30}]^{n-}$ **(1)**[2a–q] (for "organic type" nanocontainers see Refs. [2r–u]). Their use allows cation transport through biological membranes to be modeled[3,4a]—or generally speaking to study transport of metal ions acting as charge carriers in small spaces.[4b] Most importantly, the 20 $\{Mo_9O_9\}$-type pores of **1**, exhibiting crown-ether like function, can be closed[5] and opened stepwise[3e] based on pore plugging with cationic guests.[5,6a] The pores are flexible, which can lead to passage of substrates that are (a little bit) larger than the pores[7] with the consequence that uptake–release processes can be studied over a wider range. Herein uptake–release processes—based on **1** where ligand = acetate ion—which are connected with internal exchange equilibria, are studied by ^{1}H and especially EXSY NMR spectroscopy. The results are supported by a crystal structure clearly demonstrating the presence of ligands positioned on two different internal sites. The uptake–release processes are influenced by the type of solvent, pH value, temperature, as well as the presence of other substrates.

The porous anionic nanocapsules of type **1** can be synthesized with different internal ligands, such as acetate ions (**2**; see for example, Refs. [2i,j,l]). Correspondingly, the exchange processes in solutions of compound **2** (Figure 1) in D_2O were investigated by ^{1}H and EXSY NMR spectroscopy (**2** was studied by several groups in context with different problems of materials science[2o]). Remarkably, in the ^{1}H NMR spectra the expected signal at $\delta = 0.7$ ppm for the structurally important "linker-type acetates" (coordinated to the $\{Mo^V_2\}$ linkers; Figure 1) is accompanied by a weak downfield signal at $\delta = 0.9$ ppm (Figure 2), which is caused by

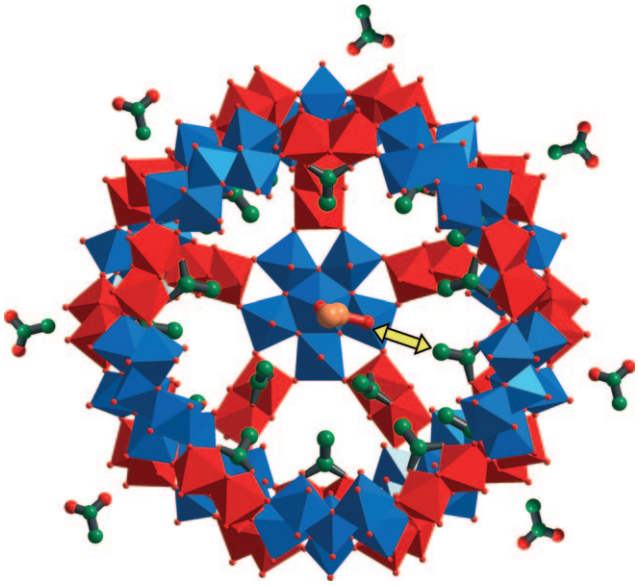

Figure 1. Polyhedral representation of the anionic capsule of compound **3** which is the same as that of the corresponding compound **2** (pentagonal $\{(Mo^{VI})Mo^{VI}_5O_{21}(H_2O)_6\}^{6-}$ units/ligands[2q] in blue, $\{Mo^V_2\}$ linkers in red (one of the $\{(Mo^{VI})Mo^{VI}_5O_{21}(H_2O)_6\}^{6-}$ units and five of the $\{Mo^V_2\}$ linkers are removed for clarity). C and O atoms of the acetate ions in ball-and-stick representation are depicted either in green (coordinated to $\{Mo^V_2\}$ linkers) or given enlarged in orange (coordinated to the pentagonal units). The yellow double arrow indicates the exchange equilibrium between the two types of internal acetate ligands.

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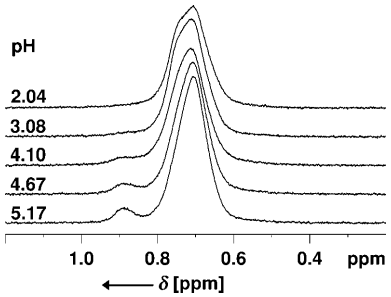

Figure 2. The pH-dependence—varied by addition of diluted hydrochloric acid—of the ^{1}H NMR spectra of solutions of **2** in D_2O (1 mM) at 293 K shows two signals belonging to acetate ligands bound to the capsule's two different internal sites (see Figure 1). The intensity ratio of the signals at room temperature of ca. 1:9 is extremely sensitive to the solution conditions; for further details see text. The two peaks are, as expected, similar to those measured for a solution of **3** (see values in the Experimental Section). The interest here refers to the peaks at lower pH values; for details and for the shoulder at higher pH, see the Supporting Information.

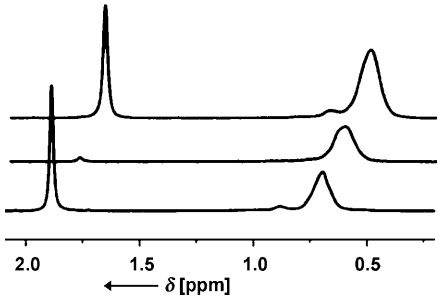

Figure 3. Reversible binding/loading of acetate ligands to pentagonal units inside the capsule (all at pH values of ca. 5). Top: ^{1}H NMR spectrum of a solution of **2**[2j] (NH_4^+ salt) in D_2O: accordingly, approximately 13 acetate equivalents are present in the bulk D_2O outside the capsule, along with approximately 23 acetate equivalents bound to $\{Mo^V_2\}$ linkers and approximately 4 to pentagonal units (error limit ± 1). Middle: If the Na^+ salt[7] (prepared from **2a**) is dialyzed against pure water, the number of "linker-type acetate" ligands inside the capsule decreases to 21 according to the ^{1}H NMR spectrum. Important: Also the signal assigned to the more labile acetate ligands bound to pentagonal-unit binding sites ($\delta = 0.9$ ppm) is no longer observed. Bottom: Upon addition of a larger amount of acetate buffer to the solution (used for the Middle spectrum) the equilibrium is shifted towards higher occupancy of the inside binding sites, and the weaker signal at $\delta = 0.9$ ppm is again observed. According to the related ^{1}H NMR spectrum, approximately 23 acetate equivalents are present in the bulk solution outside the capsule and approximately 32 are found inside. Of those inside the capsule approximately 28 are bound to the $\{Mo^V_2\}$ linkers and approximately 4 to pentagonal units. (Reported equivalents were quantified using a coaxial tube containing an integration standard consisting of methane sulfonic acid in D_2O. The three spectra are offset from one another for clarity, the chemical shift scale is thus only accurate for the bottom spectrum.)

a small number of additional acetate ions coordinated to the second internal sites, that is, to the pentagonal units (Figure 1). This type of coordination was now also confirmed by an X-ray crystallographic study of the corresponding compound **3** containing $[(CH_3)_2NH_2]^+$ ions (Figure 1). This study was possible because **3** crystallizes in the space group $R\bar{3}$, exhibiting less crystallographic disorder than **2**, which crystallizes in a higher-symmetry cubic space group[21] and therefore did not allow (though taken into consideration[21]) in the earlier study a clear demonstration of the second coordination type. For the preparation and crystal data of **3** see the Experimental Section. The stability of **2a** in solution—a requirement for the present studies—was reported several times (see for example, Refs. [2m,n] and the cited publications in the review Ref. [2o]). It can also easily be confirmed by Raman spectroscopy (Supporting information, Figure S1).

$$(NH_4)_{42}[\{(Mo^{VI})Mo^{VI}_5O_{21}(H_2O)_6\}_{12}\{Mo^V_2O_4(CH_3COO)\}_{30}]\cdot ca.\{300\,H_2O + 10\,CH_3COO^- + 10\,NH_4^+\} \equiv (NH_4)_{42}\cdot \mathbf{2a}\cdot ca.\ \{300\,H_2O + 10\,CH_3COO^- + 10\,NH_4^+\} \quad \mathbf{2}^{[2j,l]}$$

$$Na_{15}[(CH_3)_2NH_2]_{33}[\{(Mo^{VI})Mo^{VI}_5O_{21}(H_2O)_5(CH_3COO)_{0.5}\}_{12} Mo^V_2O_4(CH_3COO)\}_{30}]\ ca.\{300\,H_2O + 7\,CH_3COO^- + 4\,(CH_3)_2NH_2^+ + 3\,Na^+\} \quad \mathbf{3}$$

(formal formulation of the crystal lattice ions!)

Referring in more detail to the implications of the ^{1}H NMR spectra in Figure 2: the acetate ligands coordinated to the pentagonal units are most easily released in solution, and preferentially liberated with decreasing pH value. This is logical as ligands linked to the negatively charged pentagonal units are more weakly bound and therefore more easily protonated (then released in form of the acids) than the acetate ligands coordinated to the positively charged $\{Mo_2O_4\}^{2+}$ linkers (see Figure 1 and formula of **1**). More details regarding the change of the spectra resulting from the addition of acids to the solution of **2a** are given in the Supporting Information. Moreover, it can nicely be shown that the complete release of labile acetate ligands from the pentagonal-type binding sites is reversible (Figure 3).

Figure 3 shows that on equilibration of the (dynamic) ligand-exchange the number of "linker type acetates" inside **2a** is smaller in solution (ca. 23; Figure 3, top) than in the crystalline state (30, see formula)[2j] while upon release to the bulk solution each linker-type acetate is replaced by two H_2O ligands; see also Ref. [7]. Important in this context, the loss of acetate ligands from the linker positions leads to stronger interactions between (resultant) positively charged linkers, $\{Mo_2O_4(H_2O)_2\}^{2+}$, and the negatively charged pentagonal units/ligands.

Another line of (quantitative) evidence for exchange of acetate ions between the bulk solution and the interior of the capsule is obtained by adding deuterated acetate ions to the solution whose NMR spectrum is shown at the bottom of Figure 2, and analyzing the decrease in equilibrium intensities of the proton signals of normal acetates inside the capsule, and the commensurate increase in intensity of the signal arising from acetate outside the capsule (Supporting Information, Figure S2). The dynamic nature of the exchange processes—and especially the preferable release of acetate ligands from the pentagonal sites of **2a**—can also be revealed by the variable-temperature NMR spectra (Figure 4). Moreover, as the temperature increases from 25 to 95 °C, the

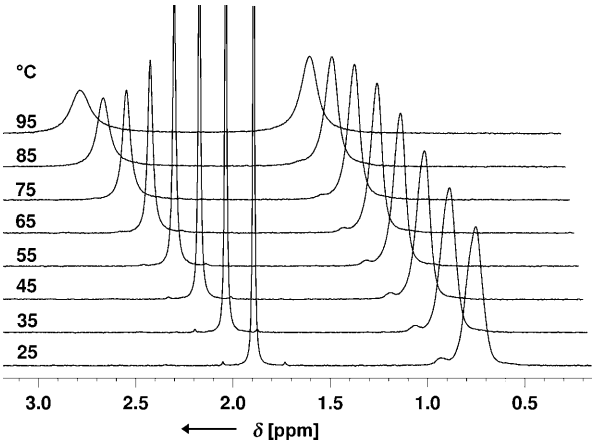

Figure 4. Variable temperature ^{1}H NMR spectra of solutions of **2** in D_2O (pH 5.25). The sharper signals correspond to external acetate ions, while the signals at $\delta = 0.7$ and 0.9 ppm (at 25 °C) are due to the two different internal acetate ligands; see also Figure 2. (The chemical shift variations are due to the shift variation of the lock signal.)

signals associated with the external and internal acetate ions broaden considerably, indicative of an increase in the rate of internal/external exchange; but the energy barrier is too high to achieve the interpretable coalescence.

The ^{1}H EXSY spectrum of the solution of **2** (Figure 5) shows most convincingly that there is an exchange between the inside and outside acetate ions, even at room temperature.

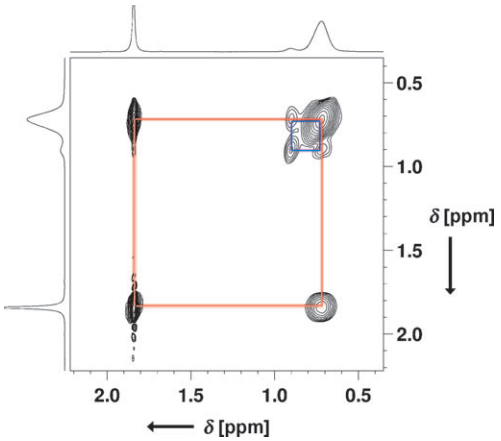

Figure 5. Room temperature ^{1}H EXSY spectrum of a solution of **2** in D_2O (1 mM) indicating the existing equilibria according to Equation (1) (pH 5.10; mixing time 1 s).

This result is in contrast to the scenario of solutions of the capsule **1** containing butyrate ligands,[8] where no ligand exchange could be detected at this temperature. The result can be explained in part by the different sizes of acetate and butyrate ions but more significantly by the hydrophobic interactions between the encapsulated butyrate ligands.[8] More importantly, there is not only an exchange between internal and external acetate ions (peaks at $\delta = 0.71$, 1.85 ppm), but also between the two different internal "guests" (peaks at $\delta = 0.71$, 0.89 ppm). However the exchange of the few acetate ligands bound to the pentagonal units with the external acetate is not easily detectable. This may be due to a sensitivity problem of the measurement, but also due to the fact that the "linker-type acetates" show a preferable exchange with the outside as they are positioned near to the pores (Figure 1). The overall exchange equilibrium may be—based on the EXSY spectrum—schematically represented by Equation (1)

$$\text{internal acetate ligands[pentagon} \rightleftharpoons \text{linker]} \rightleftharpoons \text{external acetate ions} \quad (1)$$

Exchange scenarios of the present type depend, according to the ^{1}H NMR spectra, on the type of solvent, a problem which will be studied in detail in the future. An exchange between the interior and exterior acetate ions is not detectable for solutions of **2** in DMSO. Interesting observations in this context were made with the dimethylammonium (DMA) salt **3**: Whereas in aqueous solution the same "acetate exchange behavior" was observed as for **2a**, no plausible interaction of DMA with the capsule was detectable. In contrast, in DMSO solutions, the DMA cations interact with the capsule, or more plausibly, with the pores giving rise to a characteristic extra ^{1}H NMR signal ($\delta = 0.40$ ppm) found besides that for the "free cations" ($\delta = 2.61$ ppm). An analogous scenario with respect to the two solvents DMSO and H_2O was observed for amidinium cations which close the capsule pores in DMSO solution but not in H_2O.[3e] In this context the unprecedented competing of substrates for the passage through the pores or interaction with them will be a subject of future studies. These should show that the relative hydrophobic/-philic properties of both solvents and substrates play a significant role.

To conclude, the "inside–outside type exchange" of acetate ions together with the unprecedented connection with the related internal site-exchange equilibria could be detected as a result of their compartmentalization, within porous nanocapsules of type **1**. The "communication" between the ions is controlled/influenced by the strength of their coordination to the capsule interior, the flexibility of the capsule pores, and other "signals" from the outside, such as variations in the H^+ concentration. These results suggest that such systems offer the chance to learn about exchange processes in small spaces following "local laws", that is, different from those valid for bulk media, and to perform related studies based on different solvents and different substrates inside the capsule. This includes the possible reactions between the substrates.

Experimental Section

3: A stirred solution of $Na_2MoO_4 \cdot 2H_2O$ (7.67 g, 31.7 mmol) and $CH_3COONa \cdot 3H_2O$ (12.5 g, 91.9 mmol) in H_2O (250 mL) was treated with $N_2H_4 \cdot H_2SO_4$ (0.8 g, 6.1 mmol) and 50% (v/v) CH_3COOH (65 mL). The mixture was stirred for 10 min (gradual color change from colorless to green, pH ca. 4.0, later to brown). After addition of dimethylammonium chloride (6.97 g, 85.6 mmol), the reaction solu-

tion was left in an open wide beaker (400 mL) in the fume hood. The dark brown, needle-like precipitated crystals were collected by filtration after 3 days, and washed with a small amount of cold water. Yield: 1.75 g (18% based on Mo).

Elemental analyses (%) calcd for **3**: C 7.11, H 3.14, N 1.91, Na 1.53 (values refer to 150 H_2O corresponding to the relevant (for the analysis) loss of crystal water, see below); found: C 6.8, H 2.9, N 2.1, Na 1.5. The chemical formula of **3** refers to the maximum possible number of crystal water molecules, which correspond to the related volume calculated from the cell volume and the sum of volumes of all cell ingredients excluding those of the crystal water molecules. Characteristic spectroscopic data: IR (solid, KBr disk): $\tilde{\nu} = 1620$ (m, δ_{H_2O}), 1545 (m, ν_{asCOO}), 1415 (doublet, w-m, ν_{sCOO}, δ_{CH_3}, δ_{NH_2}), 970 (s) and 939 (sh, $\nu_{Mo=O}$), 857 (s), 791 (s), 724 (s), 626 (w-m), 570 (s), 511 cm^{-1} (w), ^1H NMR of **3** in D_2O: $\delta = 2.76$ (Me, dimethylammonium), 1.87 (Me, external acetate ions), 0.85 (Me, internal pentagon-based acetate ligands), 0.71 ppm (Me, internal "linker-type acetate") and in [D_6]DMSO: $\delta = 8.23$ (NH, dimethylammonium), 2.61 (Me, external dimethylammonium), 1.90 (Me, external acetate ions), 0.57 (Me, internal "linker-type acetate"; the peak for the other internal site is not clearly resolved), 0.40 ppm (Me, coordinated dimethylammonium).

Crystal data for **3**: $C_{160}Mo_{132}N_{37}Na_{18}O_{718}H_{945}$, $M = 27958.43\ g\,mol^{-1}$, rhombohedral, space group $R\bar{3}$, $a = 32.855(2)$, $c = 74.682(6)$ Å, $V = 69815(8)$ Å^3, $Z = 3$, $\rho = 1.995\ g\,cm^{-3}$, $\mu = 1.824\ mm^{-1}$, $F(000) = 40950$, crystal size $= 0.24 \times 0.2 \times 0.1\ mm^3$. A total of 128081 reflections ($1.46 < \Theta < 26.98°$) were collected, of which 33374 were unique ($R(int) = 0.0782$). An empirical absorption correction using equivalent reflections was performed with the program SADABS 2.10. The structure was solved with the program system SHELXS-97 and refined using SHELXL-97 to $R = 0.0618$ for 17923 reflections with $I > 2\sigma(I)$, $R = 0.1364$ for all reflections; max/min residual differential electron density 1.627 and $-1.734\ e\,Å^{-3}$. Crystals of **3** were removed from the mother liquor, immediately cooled to 183(2) K, and mounted to a Bruker AXS SMART diffractometer (three circle goniometer with 1 K CCD detector, MoK_α radiation, graphite monochromator; hemisphere data collection in ω at 0.3° scan width in three runs with 606, 435, and 230 frames ($\phi = 0$, 88, and 180°) at a detector distance of 5 cm). (SHELXS/L, SADABS from G. M. Sheldrick, University of Göttingen, 1997/2003; structure graphics with DIAMOND 3.0, http://www.crystalimpact.com/ and with POV-Ray 3.6, http://www.povray.org/). The formula is based on crystallographic measurements and analytical data (for cation disorder see Supporting Information). There is additional electron density which could not be refined under the pentagonal units (4 × 6 positions). CCDC 783497 (**3**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[5] The first published example referred to the closing of the 20 $\{Mo_9O_9\}$ pores/receptors of a type **1** capsule by the 20 $[C(NH_2)_3]^+$ ions/guests, which leads to a structuring of the initially disordered H_2O molecules.[6a] (The O···H-N hydrogen bonding within a pore is comparable to that between a classical crown-ether host and the guanidinium cation.[6b]) In the closed capsule a well-defined three-shell highly symmetrical $\{H_2O\}_{100}$ cluster was found;[6a] the presence of a different crystallographically independent closed capsule containing another encapsulated H_2O cluster was first mentioned in: T. Mitra, P. Miró, A.-R. Tomsa, A.

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