Two compartmentalized Inner Receptors for the Tetramethylammonium Guest within Keplerate-Type Capsule

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SUPPORTING INFORMATION

SI-1. Analytical treatment of the variable concentration $^1$H NMR data. Calculation of the equilibrium constant $K_t$ of NMe$_4^+$ cation transfer into the Keplerate capsule.

SI-2. Titration experiment: variable NMe$_4^+$/Keplerate ratio $^1$H NMR dependence.

SI-3. Variable temperature $^1$H EXSY NMR experiments.
**SI-1. Analytical treatment of the variable concentration $^1$H NMR data. Calculation of the equilibrium constant $K_t$ of NMe$_4^+$ cation transfer into the Keplerate capsule.**

The $^1$H NMR resonance of the NMe$_4^+$ cations results from two separate processes: i) a two-site diffusion system in a fast exchange regime (already described in Watfa et al. J. Am. Chem. Soc. 2015, 137, 5845–5851); and ii) an inclusion process into the capsule in slow exchange regime with respect to the NMR time scale.

i) The binding process involves the solvated cations NMe$_4^+$aq as well as the counter-ion NH$_4^+$, both in competition at the {Mo$_9$O$_9$} porous sites P. Assuming that the 20 {Mo$_9$O$_9$} sites are independent, the binding process is expressed by following equilibriums and the binding constants are given by equations (1) and (2).

\[
P + NH_4^+ = P-NH_4^+ \quad K_{NH_4}^{\text{plug}} = \frac{NH_4^+_{\text{plug}}}{P \cdot NH_4^+_{\text{aq}}} \quad (1)
\]

\[
P + NMe_4^+_{\text{aq}} = P-NMe_4^+ \quad K_{TMA}^{\text{plug}} = \frac{NMe_4^+_{\text{plug}}}{P \cdot NMe_4^+_{\text{aq}}} \quad (2)
\]

ii) The transfer reaction can be described as follows:

\[
NMe_4^+_{\text{aq}} + [Mo_{132}] = NMe_4^+@[Mo_{132}] \quad K_t = \frac{NMe_4^+_{\text{in}}}{K_{\text{tep}} \cdot NMe_4^+_{\text{aq}}} \quad (3)
\]

The following equations (4), (5), (6) and (7) correspond to the conservation equations in P, NMe$_4^+$, NH$_4^+$, and {Mo$_{132}$} capsule respectively:

\[
20C^\circ = [P] + [NMe_4^+]_{\text{plug}} + [NH_4^+]_{\text{plug}} \quad (4)
\]

\[
nC^\circ = [NMe_4^+]_{\text{in}} + [NMe_4^+]_{\text{plug}} + [NMe_4^+]_{\text{aq}} \quad (5)
\]

\[
52C^\circ = [NH_4^+]_{\text{aq}} + [NH_4^+]_{\text{plug}} \quad (6)
\]

\[
C^\circ = [K_{\text{tep}}] + [NMe_4^+]_{\text{in}} \quad (7)
\]

where $C^\circ$ is the concentration in Keplerate {Mo$_{132}$} and $n$ the equivalent number of NMe$_4^+$ substrate per {Mo$_{132}$} capsule. The number of equivalent in cationic substrate NMe$_4^+$ is fixed to $n \approx 3$ in the variable concentration samples studied.

The plugging processes has been studied in a previous work (Watfa et al. J. Am. Chem. Soc. 2015, 137, 5845), and the equilibrium constants were determined as follows: $K_{NH_4} = 370 \text{ M}^{-1}$; $K_{NMe_4} = 1550 \text{ M}^{-1}$. To determine the value of $K_t$, one has to determine $[NMe_4^+]_{\text{in}}$, $[NMe_4^+]_{\text{aq}}$, and $[K_{\text{tep}}]$.

**Determination of $[NMe_4^+]_{\text{in}}$ and $[K_{\text{tep}}]$.**

From the NMR spectrum, the integration of S1 (2.9 ppm) and S2 (3.0 ppm) should represent the amount of integrated NMe$_4^+$ into the capsule and the corresponding fraction ($\alpha$) is deduced by comparison to the integration of the NMe$_4^+$ signal at 3.2-3.3 ppm that should correspond to the fraction of outside NMe$_4^+$ (solvated and plugged forms in fast chemical exchange). One then can conclude:

\[
[NMe_4^+]_{\text{in}} = 3\alpha C^\circ \quad (8)
\]
\[
[NMe_4^+]_{aq} + [NMe_4^+]_{plug} = 3(1-\alpha)C^o
\]  
(9)

From (7) one can deduce the amount of [Kep]:

\[
[Kep] = C^o - [NMe_4^+]_{in} = (1-3\alpha)C^o
\]
(10)

**Determination of \([NMe_4^+]_{aq}\).**

By combining (1) and (6):

\[
[NH_4^+]_{aq} = \frac{52C^o}{1 + P \ K_{NH_4}}
\]
(11)

and combining (1) and (11):

\[
[NH_4^+]_{plug} = P \ K_{NH_4} \ [NH_4^+]_{aq} = \frac{52C^o \ P \ K_{NH_4}}{1 + P \ K_{NH_4}}
\]
(12)

In similar way, combining (2) and (9):

\[
[NMe_4^+]_{aq} = \frac{3(1-\alpha)C^o}{1 + P \ K_{TMA}}
\]
(13)

and combining (2) and (13):

\[
[NMe_4^+]_{plug} = P \ K_{NMe_4+} \ [NMe_4^+]_{aq} = \frac{3(1-\alpha)C^o \ P \ K_{NMe_4+}}{1 + P \ K_{NMe_4+}}
\]
(14)

The amount of \([P]\) can be calculated from the numerical resolution of the following polynomial equation derived from (4), (12) and (14):

\[
a [P]^3 + b [P]^2 + c [P] + d = 0
\]
(15)

with:

\[
\begin{align*}
a &= K_{NMe_4+} K_{NH_4} \\
b &= K_{NMe_4+} + K_{NH_4} + (32 + 3(1-\alpha))C^o K_{NMe_4+} K_{NH_4} \\
c &= 1 + 32C^o K_{NH_4} + (3(1-\alpha)-20)C^o K_{NMe_4+} \\
d &= -20C^o
\end{align*}
\]

By introducing the values of \([P]\) in equations (11), (12), (13), and (14), one can calculate the quantities of \([NH_4^+]_{aq}\), \([NH_4^+]_{plug}\), \([NMe_4^+]_{aq}\), and \([NMe_4^+]_{plug}\) respectively.
Variable concentration experiment for determination of equilibrium constant $K_t$.

By plotting the $[\text{NMe}_4^+]_{\text{in}} = f([\text{NMe}_4^+]_{\text{aq}}(\text{Kep}))$ from variable concentration experiment one can expect according to eq (3) a straight line plot starting from the origin with a slope corresponding to the equilibrium constant for the NMe$_4^+$ transfer reaction. Such a result is presented in Figures S1 and S2 for the two types of encapsulated NMe$_4^+$ responsible of signals S1 and S2 respectively.

**Figure S1:** $([\text{NMe}_4^+]_{\text{in}})_{\text{S1}}$ plot as a function of $([\text{NMe}_4^+]_{\text{aq}}(\text{Kep}))$, i.e., $C_{\text{in}}(\text{S1}) = f(C_{\text{solv}}-C_{\text{Kep}})$, from variable concentration (0.2-5 mM) $^1$H NMR spectra of $(\text{NH}_4)_4[\text{Mo}_{132}\text{O}_{372}(\text{H}_2\text{O})_{72}(\text{CH}_3\text{COO})_{30}]$ in D$_2$O solution containing 3 equivalents of NMe$_4^+$ ion. The amount of plugged pores by NMe$_4^+$ and NH$_4^+$, according to equations (12) and (14) are also plotted in red and the horizontal line (20 pores) represent the total number of pores per Keplerate.

**Figure S2:** $([\text{NMe}_4^+]_{\text{in}})_{\text{S2}}$ plot as a function of $([\text{NMe}_4^+]_{\text{aq}}(\text{Kep}))$, i.e., $C_{\text{in}}(\text{S2}) = f(C_{\text{solv}}-C_{\text{Kep}})$, from variable concentration (0.2-5 mM) $^1$H NMR spectra of $(\text{NH}_4)_4[\text{Mo}_{132}\text{O}_{372}(\text{H}_2\text{O})_{72}(\text{CH}_3\text{COO})_{30}]$ in D$_2$O solution containing 3 equivalents of NMe$_4^+$ ion.

While a straight line is obtained with the signal S2 ($K_t = 132 \pm 3 \text{ M}^{-1}$), the plot for signal S1 is linear only at low concentrations ($K_t = 84 \pm 7 \text{ M}^{-1}$). When all the pores are plugged with NMe$_4^+$ and NH$_4^+$, the stability constant $K_t$ drops as a consequence of decrease in the affinity towards those specific sites probably due to the electrostatic repulsion effect.
Titration experiment: variable NMe₄⁺/Keplerate ratio ¹H NMR dependence.

Figure S3. Variation of the amount of incorporated NMe₄⁺ in the Keplerate capsule as the function of the equivalent amount of NMe₄⁺ introduced in a 5 mM solution of (NH₄)₄₂[Mo₁₃₂O₃₁₂(H₂O)₇₂(CH₃COO)₃₀].

Figure S4. ¹H NMR spectra of D₂O solution of (NH₄)₄₂[Mo₁₃₂O₃₂₇(H₂O)₇₂(CH₃COO)₃₀] in presence of NMe₄Br at fixed {Mo₁₃₂} concentration of 5 mmol/l and various NMe₄⁺/{Mo₁₃₂} ratio: a) 1.5, b) 3, c) 6, and d) 9. In the inset a vertical expansion (x16) is displayed around ca. 3 ppm.
SI-3. Variable temperature $^1$H EXSY NMR experiments.

$^1$H EXSY NMR experiments were acquired by using the NOESY sequence, setting a relaxation delay of 1 s, an acquisition time of 2 s, and mixing time values ($t_m$) between 0 and 500 ms. The number of data points (8192x1024) and the number of transients (16) were kept constant for all experiments to be compared between each other quantitatively. Microscopic rate constants ($k$, s$^{-1}$) were calculated from the integration of the 2D spectra by using the EXSYCALC software (http://desoft03.usc.es/mmartin/software.html). At least two experiments with different $t_m$ values were acquired to extract the magnetization exchange rates, which correspond to the rate constant values of exchange equilibriums in our case (species A and B in exchange are the same).

**Basic principle of determination of exchange rates from EXSY NMR.**

Multisite exchange rates can be computed from 2D-EXSY NMR data and the details of the method are well documented in the literature (see for example the review of Perrin and Dwyer Chem. Rev. 1990, 90, 935).

The method is based on the general Eq. (1), which relates the cross-peak intensities $I_{ij}$ of two exchanging species, i and j, at a mixing time $t_m$ to the rate matrix $R$ and the bulk magnetization vector $M^0$.

$$I_{ij} = (\exp(-R_{ij}t_m))_{ij} M^0_j$$

A solution for the rate-constant matrix $R$ whose off-diagonal elements are $R_{ij} = -k_{ji}$, where $k_{ji}$ is the first-order rate constant for chemical exchange from site j to site i, is given by Eq. (2).

$$R = -t_m^{-1} \ln A = -t_m^{-1} X(\ln \Lambda)X^{-1}.$$  

Here, $A$ is the matrix with the elements $A_{ij} = I_{ij}(t_m)/M^0_i$, and $X$ is the square matrix of eigenvectors of $A$, such that $X^{-1}AX = \Lambda = \text{diag}(\lambda_i)$, and $\ln A = \text{diag}(\ln \lambda_i)$. $\Lambda$ is therefore a matrix with the eigenvalues of $A$ in the diagonal and the rest of the terms 0, $X$ and its inverse $X^{-1}$ are the eigenvectors of $A$.

The solution of Eq. (2) gives the exchange matrix $R$, where the off-diagonal elements correspond to the kinetic parameters ($R_{ij} = -k_{ji}$) while the diagonal elements are a combination of the chemical exchange rates and the longitudinal relaxation rates ($-(1/T_1)_i - \Sigma_i R_{ij}$).
2D-EXSY NMR with various mixing time at 27°C.

Figure S5. EXSY NMR spectra (NMe$_4^+$ and acetate chemical shifts ranges) of a 5 mM solution of (NH$_4$)$_{42}$[Mo$_{132}$O$_{372}$(H$_2$O)$_{72}$(CH$_3$COO)$_{30}$] in presence of 9 equivalent NMe$_4$Br, recorded for various mixing times, $t_m = 0, 50, 100,$ and $500$ ms.
2D-EXSY NMR with mixing time $t_m = 500$ ms at various temperature.

![EXSY NMR spectra](image)

**Figure S6.** EXSY NMR spectra (NMe$_4^+$ chemical shifts range) of a 5 mM solution of (NH$_4$)$_4$[Mo$_{132}$O$_{372}$(H$_2$O)$_{72}$(CH$_3$COO)$_{30}$] in presence of 9 equivalent NMe$_4$Br, recorded with a mixing time $t_m = 500$ ms, at various temperatures, 27, 33, 37, 42, 46°C.

**Table S1.** Rate constants (s$^{-1}$) obtained from $^1$H EXSY NMR experiments for exchange processes involving NMe$_4^+$ at different temperatures. A three sites exchanging model was applied: A-B-C for NMe$_4^+$aq-S2-S1 (see Fig. S6). Values in red are not considered in the thermodynamic analysis because are lowly reliable; i) because of their low intensity cross peaks of S1 and S2 along F1 ($K_{BA}$ and $K_{BC}$) are superimposed with the residual signal of NMe$_4^+$aq due to its very long $T_2$ relaxation time (F1 truncation), ii) the very low intensity of the cross peaks between B and C ($K_{BC}$ and $K_{CB}$) hampered a correct integration. The exchange rates between A and B, and between A and C are therefore represented by their forward reaction rates.

<table>
<thead>
<tr>
<th>T (°C)</th>
<th>$k_{AB}$</th>
<th>$k_{BA}$</th>
<th>$k_{AC}$</th>
<th>$k_{CA}$</th>
<th>$k_{BC}$</th>
<th>$K_{CB}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.1</td>
<td>0.33</td>
<td>0.14</td>
<td>1.59</td>
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<td>0.19</td>
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<td>42.4</td>
<td>1.09</td>
<td>0.25</td>
<td>5.22</td>
<td>0.20</td>
<td>0.67</td>
<td>0.15</td>
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<td>45.8</td>
<td>1.87</td>
<td>0.20</td>
<td>7.05</td>
<td>0.13</td>
<td>0.32</td>
<td>0.06</td>
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Figure S7. EXSY NMR spectra (acetates chemical shifts range) of a 5 mM solution of [(NH₄)₄₂[Mo₁₃₂O₃₇₋₂(H₂O)₇₋₂(CH₃COO)₃₀] in presence of 9 equivalent NMe₄Br, recorded with a mixing time $t_m = 500$ ms, at various temperatures, 27, 33, 37, 42, 46°C.

Table S2. Rate constants (s⁻¹) obtained from $^1$H EXSY NMR experiments for exchange processes involving acetate at different temperatures. A three sites exchanging model was applied: A-B-C for AcO$_{aq}$-AcO$_{linker2}$-AcO$_{linker1}$ (see Figure S7). Values in red are not considered in the thermodynamic analysis because are lowly reliable; due mainly of the low intensity of signal B and their partial superimposition between resonances B and C.

<table>
<thead>
<tr>
<th>T (°C)</th>
<th>$k_{AB}$</th>
<th>$k_{BA}$</th>
<th>$k_{AC}$</th>
<th>$k_{CA}$</th>
<th>$k_{BC}$</th>
<th>$k_{CB}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.1</td>
<td>0.09</td>
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<td>33.3</td>
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<td>0.96</td>
<td>0.19</td>
<td>0.92</td>
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<tr>
<td>37.0</td>
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<td>1.23</td>
<td>0.19</td>
<td>0.95</td>
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<td>42.4</td>
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<td>1.67</td>
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<td>0.24</td>
<td>0.92</td>
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</table>
Eyring plots.

**Figure S8.** Eyring plot obtained from rate constants of $A \rightleftharpoons B$ ($\text{NMe}_4^{+\text{aq}} \rightleftharpoons S1$) and $A \rightleftharpoons C$ ($\text{NMe}_4^{+\text{aq}} \rightleftharpoons S2$) exchanges.

**Figure S9.** Eyring plot obtained from rate constants of $A \rightleftharpoons B$ ($\text{AcO}_{\text{aq}} \rightleftharpoons \text{AcO}_{\text{linker2}}$) and $A \rightleftharpoons C$ ($\text{NMe}_4^{+\text{aq}} \rightleftharpoons \text{AcO}_{\text{linker1}}$) exchanges.