Ligand-Exchange Processes on Solvated Beryllium Cations

Part III[1])

Which Model Reaction is Preferable for Quantum-Chemical Investigations of a Water-Exchange Mechanism?

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On the basis of DFT calculations (B3LYP/6-311 + G**), the possibility to include solvent effects is considered in the investigation of the H_2O-exchange mechanism on $[Be(H_2O)_4]^{2+}$ within the widely used cluster approach. The smallest system in the gas phase, $[Be(H_2O)_4(H_2O)]^{2+}$, shows the highest activation barrier of $+15.6$ kcal/mol, whereas the explicit addition of five H-bonded H_2O molecules in $[\{Be(H_2O)_4(H_2O)\}(H_2O)_5]^{2+}$ reduces the barrier to $+13.5$ kcal/mol. Single-point calculations applying CPCM (B3LYP(CPCM:H_2O)/6-311 + G**//B3LYP/6-311 + G**) on $[Be(H_2O)_4(H_2O)]^{2+}$ lower the barrier to $+9.6$ kcal/mol. Optimization of the precursor and transition state of $[Be(H_2O)_4(H_2O)]^{2+}$ within an implicit model (B3LYP(CPCM:H_2O)/6-311 + G** or B3LYP(PCM:H_2O)/6-311 + G**) reduces the activation energy further to $+8.3$ kcal/mol but does not lead to any local minimum for the precursor and is, therefore, unfavorable.

Introduction. – Despite the very high toxicity of beryllium and its compounds [2 – 5], beryllium plays an important role in the modern world. For quantum-chemical mechanistic investigations, the beryllium dication has interesting aspects: it is the smallest metal ion (0.35 Å), it is normally four-coordinate in solution with a tetrahedral structure as shown by calculations and experiments [6], and kinetic studies on its mechanistic behavior are known from *Merbach* and co-workers [7].

The most fundamental process that a metal ion in an aqueous medium can undergo in general is exchange of its coordinate H_2O molecules by H_2O molecules in the second coordination sphere. Although this exchange process does not lead to any chemical conversion since reactants and products are identical, it usually controls the rate and mechanism of complex-formation and ligand-substitution reactions of such solvated metal ions since most reactions with metal ions are carried out in solution, often in aqueous solution [8]. Thus the mechanistic understanding of such processes is of fundamental importance to comprehend the role that solvated metal cations can play in industrial, environmental, and biological processes. Our present mechanistic understanding mostly comes from experimental H_2O-exchange studies performed over the past three decades as reviewed in detail recently [8].

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[1])   For Part II, see [1].

Parallel to the experimental studies, theoreticians tried to model and predict the mechanism of such H_2O-exchange processes by using a variety of theoretical techniques [9][10]. The level applied today in such calculations leads in general to a very good agreement between the suggested mechanism based on experimental data (especially volumes of activation) and that predicted theoretically [9][10].

Quantum-chemical investigations of such solvent-exchange mechanisms can follow two strategies: *i*) Examination of a cluster model where the solvation sphere around the hydrated metal ion is usually only considered explicitly for the first and to some extent for the second coordination spheres (usually for only one additional H_2O molecule). Up to now, only very few studies exist, based on pure quantum-mechanical methods in which it was possible to take into account a complete second coordination sphere for aquated metal ions [11].

ii) Molecular-dynamics (MD) simulations – classical or *Carr-Parinello* (CPMD). Most simulations of ligand-exchange processes or solvent organization around a metal center have used pure classical MD simulations [12–17], mixed quantum-mechanics/ molecular-mechanics (QM/MM) approaches [12][18–20], or CPMD simulations [21–27]. These methods were successfully used to study the behavior and dynamics of a metal ion in solution but only in a few cases to explore the details of a ligand-exchange mechanism because of the rare-event problem and general methodic limitations [10]. To the best of our knowledge, only the very fast H_2O exchange around Ca^{2+} [28] and Sr^{2+} [29] was observed during unconstrained CPMD simulations. An overview of widely used computational methods is given in recent reviews [9][30].

While experimental methods investigate reactions under real conditions in a very large ensemble of molecules, quantum-chemical calculations focus on one molecule and are outstandingly applicable to investigate a reaction in detail without disturbing side effects. We recently demonstrated the impressive advantage of the application of modern quantum-chemical methods for the investigation of the mechanism of solvent-exchange reactions around lithium [31–33], beryllium [1][34], aluminum [35], titanium [36], and zinc [37] cations. In all cases, we applied cluster models. The weakest point of these cluster models is the almost complete neglect of solvent influences. To improve this point, two possible ways can be followed: One can try to perform the calculations in an implicit solvent model, *e.g.*, PCM, CPCM, *etc.*, or add additional H_2O molecules to the solvation shells. These additional H_2O molecules do not necessarily have to be involved in the investigated reaction. For the first time, we studied the influence of such an explicit solvent sphere on a H_2O-exchange process while calculating the dissociative H_2O exchange on $[Al(H_2O)_6]^{3+}$. We considered up to four additional H_2O molecules explicitly in the second coordination sphere. The additional four H-bonded H_2O molecules were not directly involved in the mechanism and acted as spectator ligands. In this particular case, we found – even for an incomplete solvent sphere – a stabilizing effect of the additional solvent molecules for the dissociative exchange process for all systems, *e.g.*, the activation energy was reduced to nearly 50% by taking only two extra H_2O molecules into account. On the other hand, the energy was not lowered systematically as this approach was spoiled by secondary steric effects [35].

In the present study, we compare the two different concepts to model solvent influences with earlier published gas-phase results for H_2O exchange on

$[Be(H_2O)_4]^{2+2})$. A previous study based on $[Be(L)_4(L)]^{2+}$ showed that H_2O exchange, as well as the exchange of other solvents, *e.g.*, NH_3, CO_2, CO, N_2, *etc.*, also follows an associative interchange mechanism [34]. While we utilized for the implicit treatment the CPCM and PCM model as implemented in Gaussian 03, we adopted for the explicit treatment the approach of *Bertrán*, *Lledós*, and *Revetllat*, who connected the entering H_2O molecule *via* H-bonded H_2O molecules to the leaving halogen ion of tetrahedral CH_3F [38]. For this study, we furnished tetrahedral $[Be(H_2O)_4]^{2+}$ not only with one entering H_2O molecule but with five extra H_2O molecules; the latter do not directly participate in the reaction but model the surrounding solvent shell.

Results and Discussion. – Earlier studies had shown that $[Be(H_2O)_4]^{2+}$ exchanges its H_2O ligands *via* an associative interchange pathway [34]. As the most sensitive part of a reaction is the nature of the transition state, we first investigated its structure. A structural comparison of **ts** (transition state calculated (B3LYP/6-311 + G**) in the gas phase), **ts-wc** (transition state calculated (B3LYP/6-311 + G**) in a cluster of five extra H_2O molecules), **ts-CPCM** (transition state calculated within the CPCM-solvent model (B3LYP(CPCM)/6-311 + G**)), and **ts-PCM** (transition state optimized within the PCM-solvent model (B3LYP(PCM)/6-311 + G**), shows no large differences (see *Fig. 1* and *Table 1*). Modeling solvent effects shrinks in all cases the Be – O bonds of the entering/leaving H_2O molecules. Taking into account that **ts-wc** has C_2 symmetry, while **ts-CPCM** and **ts-PCM** show no symmetry, the average bond distances are very similar. In contrast, the three equatorial spectator solvent molecules show no effect at all when considering solvent influences. The structures of **ts-CPCM** and **ts-PCM** are identical within the computational accuracy for the transition state and the precursor (*vide infra*).

The precursor complexes show the same behavior (see *Table 2* and *Fig. 2*). The Be – O bonds are in all cases slightly shorter than in the calculation without the environment. Whereas all four transition states show one negative frequency in the calculated vibrational spectra, characteristic for transition states, we were able to find a local minimum without a negative frequency only for the precursor in the gas phase **pc** and for the H_2O cluster approach **pc-wc**. Despite intensive search, we were not able to locate an arrangement of the fifth H_2O molecule that did not show a negative frequency. The motion associated with this negative frequency moves the H_2O of the second coordination sphere above or below the plane spanned by the Be^{2+} cation and the O-atoms of the H_2O molecules that coordinate the fifth H_2O molecule. This movement does not break the H-bonds between the H_2O molecules. On pulling the fifth H_2O molecule to one side, a new optimization leads again to the starting structure with the same negative frequency. Therefore, we attribute this behavior to an artifact of the CPCM and PCM models.

Experimental mechanistic investigations benefit from the measurement of activation volumes. Based on the calculated structures, *Rotzinger* proposed the nowadays well accepted quantum-chemical descriptor 'difference of sums of $r(M-O)$', $\Delta\Sigma r$, for

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2)　Since the pK_a value of $[Be(H_2O)_4]^{2+}$ is 6.5, we focused on the H_2O exchange reaction on $[Be(H_2O)_4]^{2+}$ as in our previous publication [34] and did not consider possible parallel reactions like deprotonation and formation of species like $[Be(H_2O)_3(OH)]^+$.
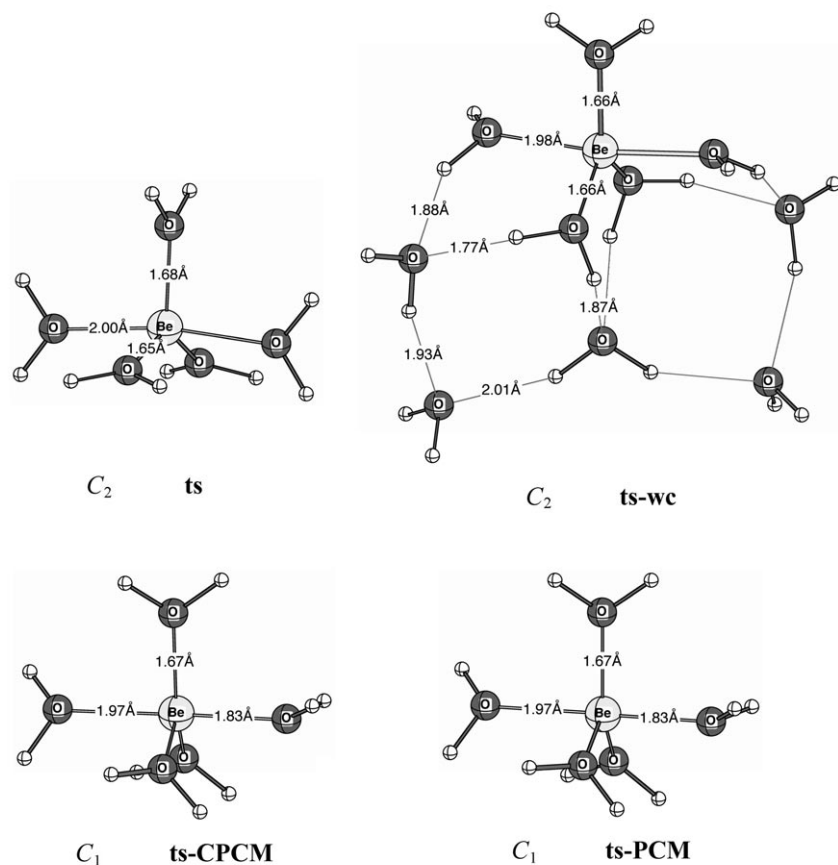
Fig. 1. *Calculated structures of the transition states within different environment models*

Table 1. *Bond Distances in the Calculated Structures of the Transition States within Different Environment Models*

	ts (C_2) [Å]	ts-wc (C_2) [Å]	ts-CPCM (C_1) [Å]	ts-PCM (C_1) [Å]
Be−OH$_2$ (entering/leaving)	2.00, 2.00	1.92, 1.92	1.97, 1.83	1.97, 1.83
Be−OH$_2$ (spectator)	1.68, 1.65, 1.65	1.66, 1.66, 1.66	1.67, 1.67, 1.67	1.67, 1.67, 1.67

the volume of activation, $\Delta V^{\ddagger}$ [39]. As can be seen from *Table 3*, this descriptor is in all four cases identical. This is not surprising as the structures are very similar (*vide supra*).

The highest activation energy for H$_2$O exchange on [Be(H$_2$O)$_4$(H$_2$O)]$^{2+}$ is calculated in the gas phase, independent of the selected method. All approaches to include solvent effects clearly reduce the energy barrier. While the addition of five extra H-bonded H$_2$O molecules reduces the activation barrier to *ca.* 5/6 (13.5 kcal/
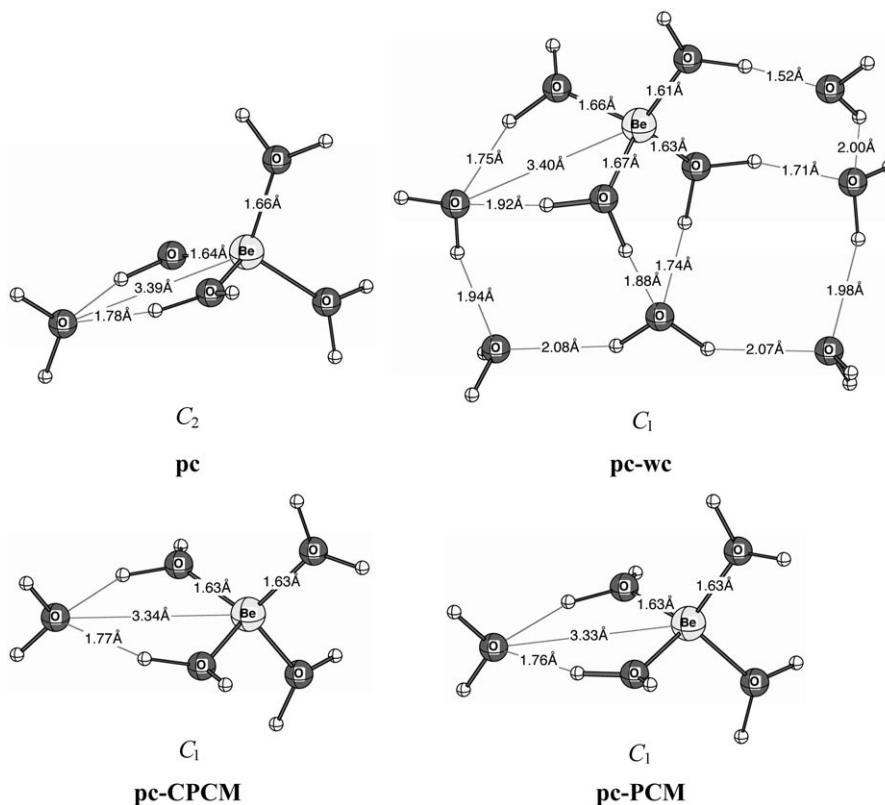
Fig. 2. *Calculated structures of the precursor complex within different environment models*

Table 2. *Bond Distances of the Calculated Structures of the Precursor Complex within Different Environment Models*

	pc (C_2) [Å]	**pc-wc** (C_1) [Å]	**pc-CPCM** (C_1) [Å]	**pc-PCM** (C_1) [Å]
Be−OH₂	1.64, 1.66,	1.61, 1.63,	1.63, 1.64,	1.63, 1.63,
	1.64, 1.66	1.67, 1.66	1.63, 1.63	1.63, 1.63
H-Bond (entering H₂O)	1.78, 1.78	1.75, 1.92	1.76, 1.77	1.76, 1.77

Table 3. *Calculated Changes of the Volume Descriptor $\Delta\Sigma r$ for the H_2O-Exchange Process*

pc [Å]	**pc-wc** [Å]	**pc-CPCM** [Å]	**pc-PCM** [Å]
1.01	1.03	1.05	1.04

mol), single-point calculations applying implicit solvent models reduce the barrier to less than 4/6 (CPCM: 9.4 kcal/mol; IPCM: 9.8 kcal/mol, see *Table 4*). The lowest barrier (8.3 kcal/mol), a little bit more than 3/6 of the barrier, can be obtained by
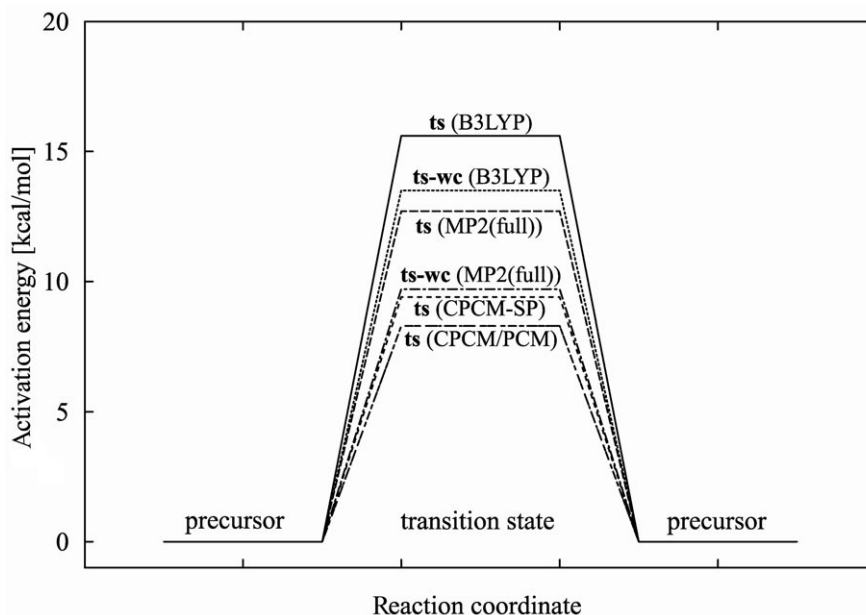
Fig. 3. *Energy profiles for the H₂O exchange processes.* **ts** (B3LYP): **ts** B3LYP/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); **ts-wc** (B3LYP): **ts-wc** B3LYP/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); **ts** (MP2(full)): **ts** MP2(full)/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); **ts-wc** (MP2(full)): **ts-wc** MP2(full)/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); **ts** (CPCM-SP): **ts** B3LYP(CPCM:H₂O))/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); **ts** (CPCM): **ts-CPCM** B3LYP(CPCM:H₂O)/6-311 + G**//B3LYP(CPCM:H₂O)/6-311 + G** + ZPE (B3LYP(CPCM:H₂O)/6-311 + G**); **ts** (PCM): **ts-PCM** B3LYP(PCM:H₂O)/6-311 + G**//B3LYP(PCM:H₂O)/6-311 + G** + ZPE (B3LYP(PCM:H₂O)/6-311 + G**). The 'product' is denoted as 'precursor' since the overall reaction does not include a net chemical conversion.

optimizing the precursor and transition states within the PCM- and CPCM-solvent models (see *Fig. 3*).

All compared methods corroborate the transition state for H₂O exchange *via* an interchange mechanism and show nicely the motion of the interchange process. In the case of the H₂O cluster modeled by five extra H₂O molecules, the transition state is stabilized in **ts-wc** by ten H-bonds between 1.77 and 2.01 Å. To obtain an acceptable equation and meaningful results, it is an essential prerequisite to have the same number of H-bonds in the precursor reference. This we realized in **pc-wc**, where the eleventh bond can be addressed as the replacement of the entering/leaving Be−OH₂ interaction in **ts-wc**. Here we successfully investigated around [Be(H₂O)₄]²⁺ an ordered H₂O cluster that confirmed the mechanism investigated with **pc** and **ts**. Therefore, the concept of a H₂O cluster that connects the entering and leaving H₂O molecules by H-bonded H₂O molecules, is appropriate but not really necessary. The explicit consideration of a full coordination sphere will lead to special problems related to the determination of the number, the orientation, and the interaction (H-bonds) of the

Table 4. *Calculated Activation Energies for the H_2O-Exchange Process*

Method[a])	ts [kcal/mol]	ts-wc [kcal/mol]	ts-CPCM [kcal/mol]	ts-PCM [kcal/mol]
B3LYP	+ 15.6	+ 13.5	–	–
MP2(full)	+ 12.7	+ 9.7	–	–
CPCM-SP	+ 9.4	–	–	–
IPCM-SP [34]	+ 9.8	–	–	–
CPCM	–	–	+ 8.3	–
PCM	–	–	–	+ 8.3

[a]) B3LYP: B3LYP/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); MP2(full): MP2(full)/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); CPCM-SP: B3LYP(CPCM:H_2O)/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); IPCM-SP: B3LYP(IPCM:H_2O)/6-311 + G**//B3LYP/6-311 + G** + ZPE (B3LYP/6-311 + G**); CPCM: B3LYP(CPCM:H_2O)/6-311 + G**//B3LYP(CPCM:H_2O)/6-311 + G** + ZPE (B3LYP(CPCM:H_2O)/6-311 + G**); PCM: B3LYP(PCM:H_2O)/6-311 + G**//B3LYP(PCM:H_2O)/6-311 + G** + ZPE (B3LYP(PCM:H_2O)/6-311 + G**).

H_2O molecules or solvents in general. In addition, for a larger number of H_2O molecules around a metal center, one can expect a larger number of conformations to be local minima, such that a variety of pathways for solvent-exchange processes could be possible, depending on the starting structure selected for the simulation. We fear that this can lead to biased mechanistic conclusions. Of course, the final goal is always to obtain simulations as close as possible to the real system, although even for a complete second and third solvation sphere the concentration of the solvated metal ion will be far too high. Hopefully, this can be solved in the near future by *ab initio* MD simulations. The alternative approach utilizes the optimizations and calculations of the vibrational spectra within implicit solvent models, *e.g.*, CPCM or PCM. As shown above, we were not able to obtain a local minimum on the potential hypersurface within these solvent models. As this is an absolute prerequisite for studying an unknown reaction, we do not consider this a favorable approach.

Taking all these observations into account, and against the background of successful earlier studies by ourselves and others (*vide supra*), we still suggest to investigate solvent exchange reactions with traditional small solvent clusters where the second coordination sphere is denoted, *e.g.*, by one solvent molecule, that probably will be involved in the investigated reaction. As shown in previous studies, solvent effects can be included easily and successfully by single-point calculations of implicit solvent models, *e.g.*, CPCM, IPCM, or PCM [31–34].

Conclusion. – In this study, we compared the possibility to include additional solvent effects in the study of solvent-exchange mechanisms by DFT and *ab initio* calculations within the widely used cluster approach. As a test case, we selected the interchange mechanism at $[Be(H_2O)_4]^{2+}$. While the smallest system in the gas phase, $[Be(H_2O)_4(H_2O)]^{2+}$, shows the highest activation barrier, all approaches to include solvent effects reduce the barrier. The addition of five additional H-bonded H_2O molecules in $[\{Be(H_2O)_4(H_2O)\}(H_2O)_5]^{2+}$ reduced the barrier by only 15%, whereas the application of implicit models, *e.g.*, CPCM, even as a single-point calculation,

reduced the barrier to *ca.* 50 – 60%. The study of the reaction by calculating all necessary structures (transition state and precursor) within the implicit solvent models is severely hampered as no local minima for the precursor could be found. The transition state was corroborated easily in all cases.

Experimental Part

Quantum-Chemical Methods. All structures were fully optimized at the B3LYP/6-311 + G** level [40] and characterized by computation of vibrational frequencies. Gas-phase-reaction energies were evaluated by MP2(full)/6-311 + G** single-point calculations (all electrons were included in the correlation treatment) [41], and the influence of bulk solvent was probed, if not otherwise noted, also by single-point calculations by means of the CPCM formalism [42][43] with H_2O as solvent, *i.e.*, B3LYP(CPCM:H_2O)/6-311 + G**//B3LYP/6-311 + G**. In addition, for the small system [Be(H_2O)$_4$(H_2O)]$^{2+}$, we performed geometry optimizations and characterized the structures by computation of vibrational frequencies within the B3LYP(PCM:H_2O)/6-311 + G** [43][44] and B3LYP(CPCM:H_2O)/6-311 + G** solvent model. The Gaussian 03 suite of programs was used throughout [45].

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