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Mechanism of the Palladium-Catalyzed Carbohydroxylation of Allene-Substituted Conjugated Dienes: Rationalization of the Recently Observed Nucleophilic Attack by Water on a (π-Allyl)palladium Intermediate

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Abstract: The mechanism of the palladium-catalyzed oxidative carbohydroxylation of allene-substituted 1,3-cyclohexadiene was studied by DFT calculations. All intermediates and transition states of the reaction were identified and their structures were calculated. The calculations confirm the mechanism previously proposed and show that the C–C bond-forming step occurs via insertion of one of the double bonds of 1,3-cyclohexadiene into a Pd–vinyl bond of a vinylpalladium intermediate. This reaction leads to a (π-allyl)palladium intermediate, and coordination of benzoquinone and a double bond in the molecule to Pd creates a highly reactive cationic π-allyl complex, which is readily attacked by water according to the calculations.

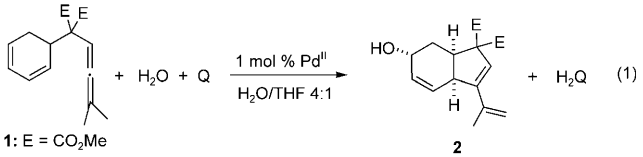
Keywords: density functional calculations · homogeneous catalysis · palladium · water

Introduction

Water is an environmentally friendly solvent of low cost, and recently organic reactions in water have attracted considerable interest.[1] Transition-metal-catalyzed reactions in water have emerged as a viable alternative to reactions in traditional organic solvents.[1a,2] In particular, various palladium-catalyzed reactions in water have been reported in the literature.[3–6] In most of these reactions water serves only as the solvent and does not participate in the reaction. Water is such a poor nucleophile that nucleophilic attack by water on coordinated unsaturated hydrocarbons is rare. One exception is the Wacker oxidation in which external *trans* attack by water on coordinated olefins has been demonstrated.[7] However, nucleophilic attack by water on (π-allyl)palladium complexes is very unfavored[8] and has been unprecedented for practical use until recently when we reported one such example.[9] We found that an unusually selective and fast water attack on a (π-allyl)palladium intermediate occurs in a palladium-catalyzed oxidative carbocyclization of allene-substituted conjugated dienes. In the present study we have carried out DFT calculations on this reaction, which confirms the high reactivity of this (π-allyl)palladium complex.

Results and Discussion

In the previously reported palladium-catalyzed carbohydroxylation of allene-substituted conjugated dienes,[9] allene–diene **1** reacts with water in the presence of *p*-benzoquinone (Q) and catalytic amounts of a Pd^{II} salt to give product **2** [Eq. (1)]. The proposed mechanism of the reaction is shown in Scheme 1.



Coordination of allene–diene **1** to Pd^{II} (complex **A**) followed by nucleophilic attack by the allene on the metal and transfer of a proton from one of the methyl groups to the TFA ligand produces intermediate **B**. Exchange of TFA for water produces the vinyl–palladium complex **C**, which undergoes insertion of the diene double bond into the Pd–vinyl bond. This generates a σ-allyl palladium complex **D** which then isomerizes, via the intermediate **E** where the car-

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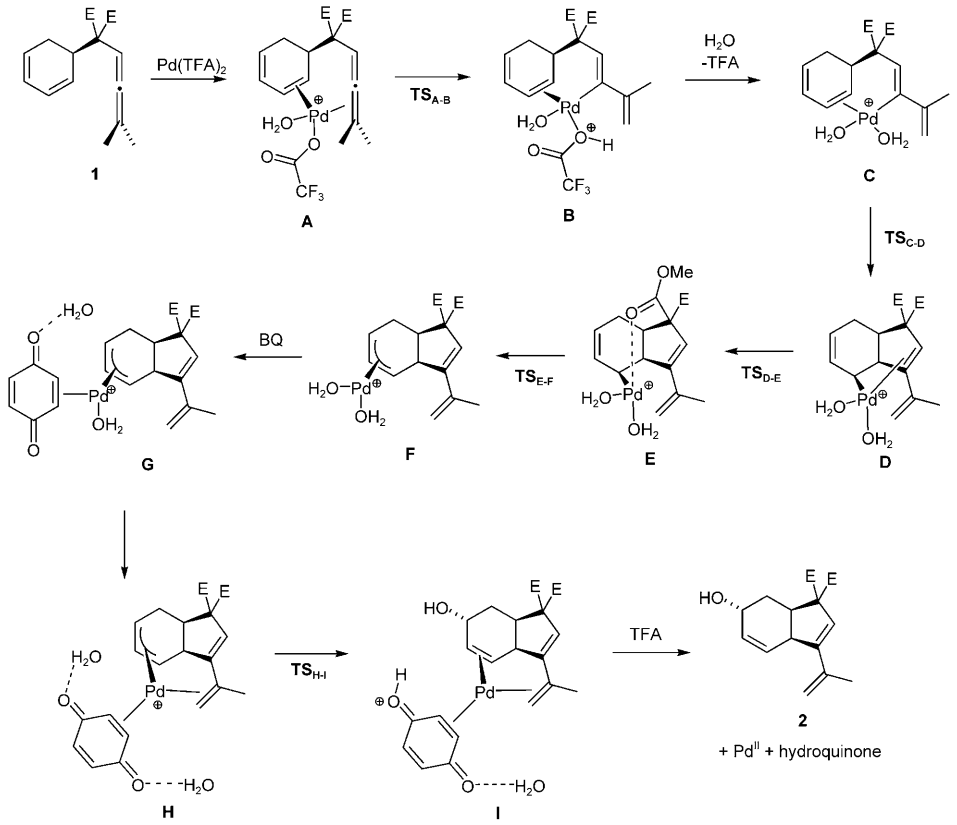

Scheme 1. Mechanism of the Pd^{II}-catalyzed oxidative carbocyclization of allene–diene (E = CO_2Me, TFA = trifluoroacetate).

bonyl oxygen coordinates to Pd, forming the *endo* (π-allyl)-palladium intermediate **F**. One of the water ligands is then exchanged for benzoquinone forming complex **G**. A possible explanation for the high reactivity of (π-allyl)palladium complex **G** is that the terminal double bond coordinates to palladium, which would lead to displacement of water and formation of a more electrophilic cationic complex **H**. Water attack on the π-allyl complex **H** from the *exo* face would produce **I**, which after decoordination releases the product **2**.

In the present investigation we have carried out density functional theory (DFT) calculations to elucidate the reaction pathway for the palladium-catalyzed carbohydroxylation of allene-substituted conjugated dienes and to find out whether **H** is a reasonable intermediate. All stable intermediates in the proposed mechanism above were optimized using DFT calculations (B3LYP/lacvp**) in the gas phase. The optimized gas-phase structures were then used for solvent calculations using Poisson–Boltzman self-consistent reaction field (PBF).[10] In the experimental work[9] mixtures of THF and water in different ratios were used. We therefore decided to calculate solution energies for both water and THF.

The calculated structure of the initial complex **A** is shown in Figure 1. From the structure one can see that the allene unit is bent with an angle of 153° (cf. 178° in the free allene). The double bond coordinating to Pd is also elongated and there is a short bond of 2.15 Å between Pd and the central carbon of the allene.

The transition state of the nucleophilic attack on Pd by the allene ($\mathbf{TS_{A-B}}$) was found and is shown in Figure 2. The energy is 8.8 kcal mol^{-1} above the ground state **A**. In this transition state a proton is transferred from the methyl group to the TFA ligand and the central carbon of the allene binds to Pd forming the vinyl palladium complex **B** (Figure 3). The trifluoroacetic acid ligand is then exchanged for water forming a more stable vinyl palladium complex **C** (Figure 4).

The next step is a migratory insertion of the diene double bond into the Pd–vinyl double bond. The transition state $\mathbf{TS_{C-D}}$ of the step was found with an energy of 5.5 kcal mol^{-1} above **C** (Figure 5). This is an early transition state with a very low

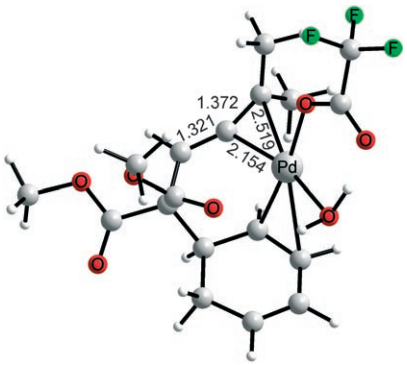

Figure 1. Calculated structure of complex **A**.

activation energy. The reaction is also exothermic with 24.5 kcal mol^{-1}.

The initial product of the migratory insertion is the σ-allyl palladium complex **D** (Figure 6). In this intermediate the coordination site that becomes vacant in the course of the migratory insertion is occupied by the C–C double bond in the newly formed ring. The σ-allyl palladium complex then rearranges to a more stable π-allyl palladium complex **F** (see Figure 10) via the transition state $\mathbf{TS_{D-E}}$ (Figure 7), the intermediate **E** (Figure 8) and a second transition state $\mathbf{TS_{E-F}}$ (Figure 9).

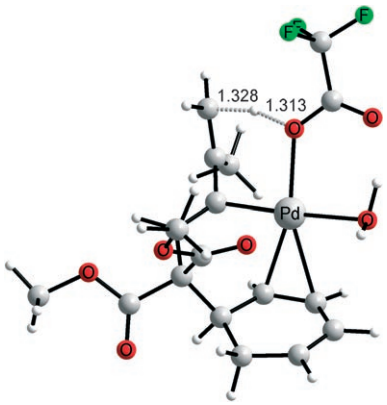

Figure 2. Calculated structure of transition state $\mathbf{TS_{A-B}}$.

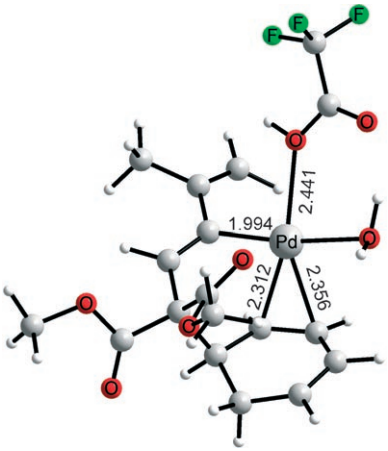

Figure 3. Calculated structure of complex **B**.

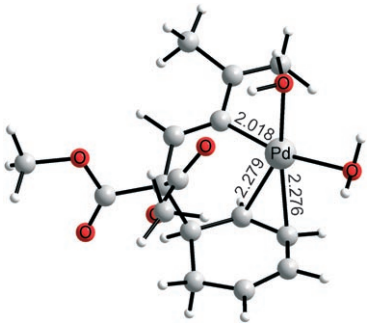

Figure 4. Calculated structure of complex **C**.

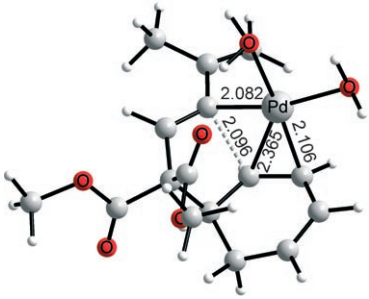

Figure 5. Calculated structure of transition state $\mathbf{TS_{C-D}}$.

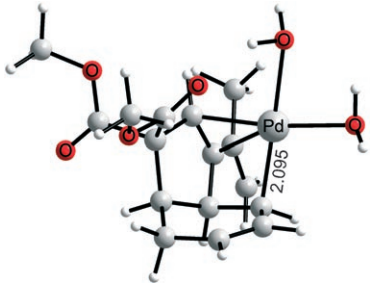

Figure 6. Calculated structure of complex **D**.

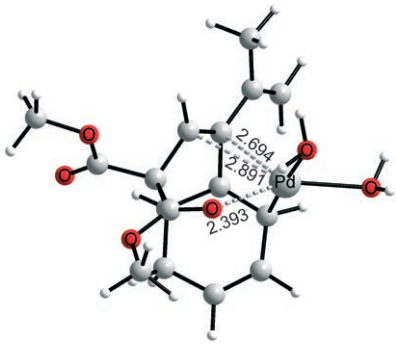

Figure 7. Calculated structure of transition state $\mathbf{TS_{D-E}}$.

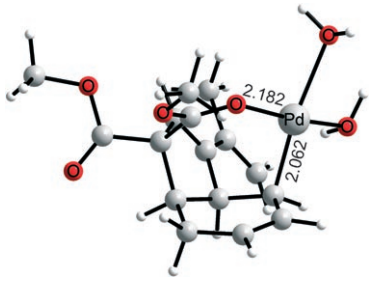

Figure 8. Calculated structure of complex **E**.

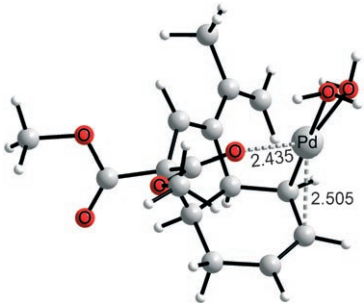

Figure 9. Calculated structure of transition state $\mathbf{TS_{E-F}}$.

The next step would be the attack of water on the π-allyl palladium complex **F** leading to formation of the product **2**. However, water is too poor a nucleophile to react with unactivated π-allyl palladium complexes such as **F**. The water attack requires the presence of the reoxidant, benzoquinone,

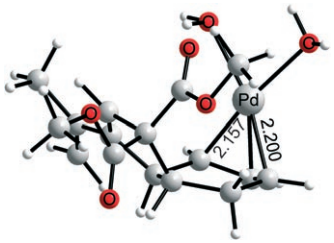

Figure 10. Calculated structure of complex **F**.

which is assumed to coordinate to palladium displacing one of the water ligands, forming complex **G** (Figure 11). According to the gas phase calculations the energy of **G** is 1.7 kcal mol^{-1} below **F**.

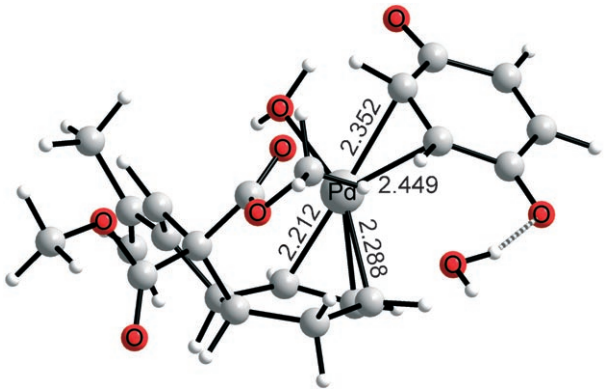

Figure 11. Calculated structure of complex **G**.

The terminal double bond of **G** could then coordinate to palladium displacing the other water ligand leading to the formation of the chelated complex **H** (Figure 12) with an energy of 8.8 kcal mol^{-1} above **G**.

The coordinated terminal alkene of **H** has Pd–C distances of 2.35 and 2.60 Å, the shorter being to the terminal methylene. The palladium–carbon bond lengths of the Pd–allyl moiety in **H** are: Pd–C2 2.16 Å, Pd–C3 2.27 Å, and Pd–C4 2.72 Å. The long Pd−C4 bond indicates a very high reactivity towards nucleophilic attack in the 4-position. The structure of complex **G** gives the corresponding Pd−C2 and Pd−C4 bond lengths 2.21 and 2.29 Å, respectively. This shows that the coordination of the terminal double bond to form **H** dramatically increases the reactivity at C4 by creating a cationic complex with an elongated Pd−C4 bond. The charge of complex **H** should be divided between Pd and the C4 carbon, and therefore C4 should have a very high carbocation character.

An interesting feature of complex **H** is the different coordination of the two double bonds. We can define a coordination plane in (π-allyl)PdL$_2$ complexes where the terminal carbons of the π-allyl group and the ligands L are located in the same plane.[11] From Figure 12 one can see that the quinone double bond is "in-plane" coordinated, whereas the terminal alkene is perpendicular to the coordination plane.

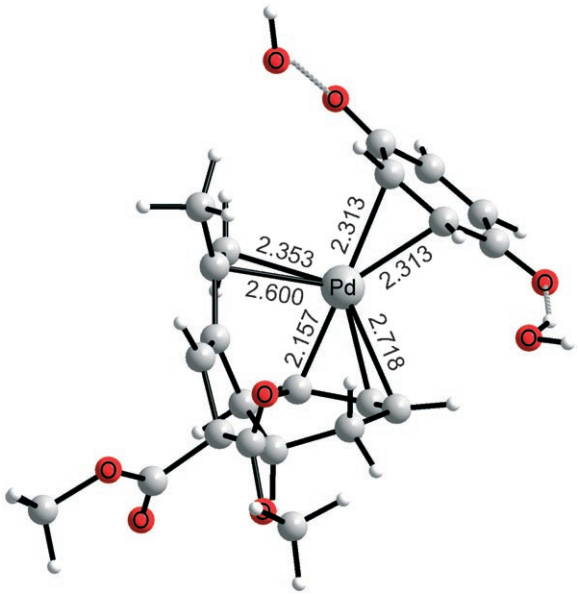

Figure 12. Calculated structure of complex **H**.

When an olefin is coordinated to a metal in a square planar complex the carbon–carbon double bond prefers to bind perpendicular to the coordination plane, but there are examples on "in-plane" coordination.[12]

The transition state for the water attack ($\mathbf{TS_{H-I}}$) was found and its structure is shown in Figure 13.

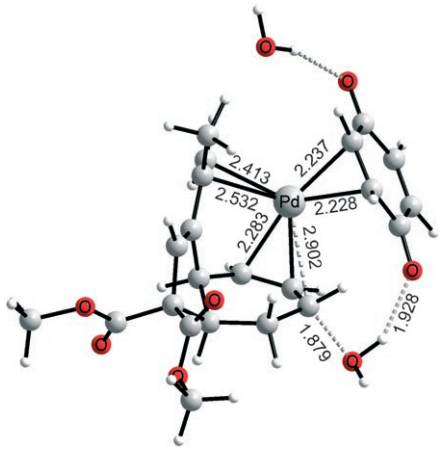

Figure 13. Calculated transition state structure $\mathbf{TS_{H-I}}$.

As predicted from structure **H**, there is a favorable energy pathway for water attack at C4. The calculated energy of this transition state, $\mathbf{TS_{H-I}}$ is 18.6 kcal mol^{-1} in relation to the π-allyl complex **H**. After the attack by water, complex **I** is formed and the energy relaxes down to −10.6 kcal mol^{-1} relative to complex **H**. The calculated structure of **I** is shown in Figure 14.

The energy profile of the entire reaction sequence in the gas phase is given in Figure 15 and the energy profile in water obtained from PBF calculations of the gas phase

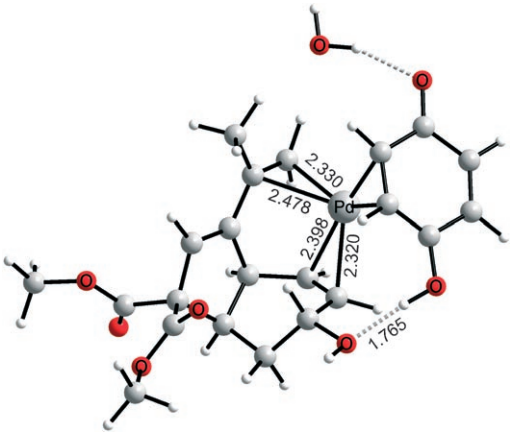

Figure 14. Calculated structure of complex **I**.

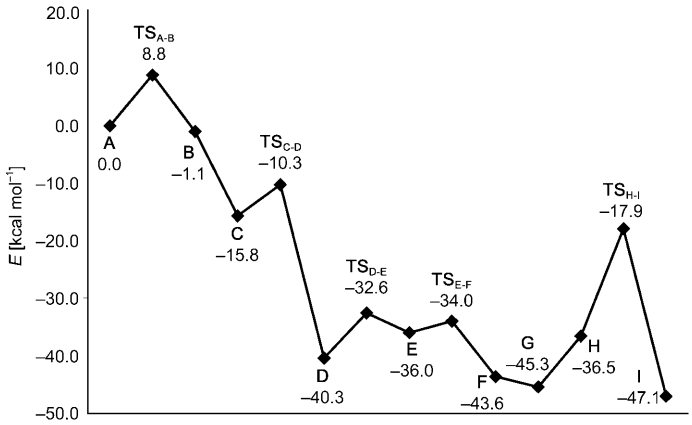

Figure 15. Energy profile of the reaction in gas phase.

structures is given in Figure 16. The PBF calculations in THF are quite similar to the PBF calculations in water and are given in the Supporting Information. The most stable species according to the calculations are the π-allyl complexes **F** and **G**, which are approximately 37–45 kcal mol^{-1} below the starting point (**A**). In the PBF calculation in water the most stable π-allyl complex is **F**, which is 43.4 kcal mol^{-1} below **A**. Transformation of **F** to product has to pass over a barrier that is 23.4 kcal mol^{-1} above **F** according to the calculations. Once the terminal double bond is coordinated (**H**) the nucleophilic attack by water is facile and occurs with an activation energy of 10.7 kcal mol^{-1} in the PBF calculations.

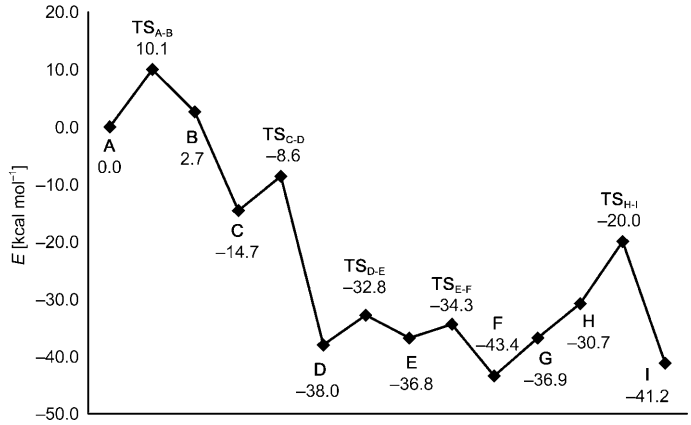

Figure 16. Energy profile for the reaction in water.

We have not calculated the transition states for the ligand exchanges converting **F** → **G** and **G** → **H**, since these transition states are supposed to be quite low and will not change the overall energy profile. It would also be difficult to find the transition states for the ligand-exchange reactions, due to the big changes in molecular geometry and the exchange of ligands. The ligand exchange reactions might also proceed through a multi-step dissociative or associative mechanism which would be highly affected by solvation and thus not possible to study using geometry optimization in the gas phase.

Conclusion

In summary, we have found that the palladium-catalyzed reaction of allene-substituted 1,3-cyclohexadiene in water proceeds via the pathway proposed in our previous experimental work. Coordination of a carbon-carbon double bond in the *endo*-(π-allyl)palladium complex, obtained from intramolecular *syn*-carbopalladation of a 1,3-cyclohexadiene, is a highly likely intermediate according to DFT calculations. The calculations predict the formation of intermediate **H**, which is attacked by water on the allyl carbon. The transition state for this attack in the PBF calculations of the gas phase structure is 10.7 kcal mol^{-1} above **H**.

Computational Details

Gas-phase geometry optimizations of all intermediates and transition states were performed using the B3LYP functional[13] with the lacvp**/6-31G(d,p) basis set.[14,15] All degrees of freedom were optimized. The transition states were characterized by a single imaginary vibrational frequency along the reaction coordinate. All computations were performed using Jaguar v. 4.0 and v. 6.0.[16] Vibrational frequencies were calculated in Jaguar 6.0. Gas phase optimized structures were used in solvent calculation using the Poisson–Boltzman self-consistent reaction field (PBF) with water: dielectric constant = 80.37, probe radius = 1.4 Å, and THF: dielectric constant = 7.58, probe radius = 2.531 Å as solvents ($E = E$(SCF) + E(solv)). All PBF calculations were performed in Jaguar 6.0.

Acknowledgements

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[10] a) Norrby et al.[10b] have shown that it is important to optimize the transition states in solution in nucleophilic attack on cationic (π-allyl)palladium complexes. They found that this is of particular importance for anionic nucleophiles where separated charges are brought together to form a neutral molecule. In the latter cases no transition state was obtained in the gas phase and the energy difference between product and starting material was unreasonably large ($>100\ kcal\,mol^{-1}$). For ammonia as nucleophile the effect was much smaller, and a transition state could be located at $2\ kcal\,mol^{-1}$ and the reaction was essentially thermoneutral with both gas phase and solution models. The latter reaction barrier is increased on solvation but it is still low ($8–10\ kcal\,mol^{-1}$). In our case we have attack by a neutral molecule on a charged species. All our intermediates and transition states have the same charge (+1) which gave good results in gas phase calculations. b) H. Hagelin, B. Åkermark, P. O. Norrby, *Chem. Eur. J.* **1999**, *5*, 902.
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