

Realistic Modeling of Ruthenium-Catalyzed Transfer Hydrogenation

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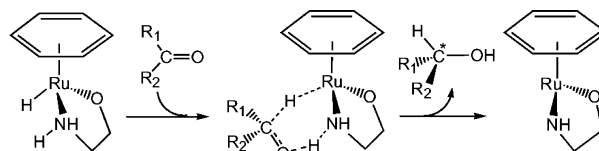
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Abstract: We report the first computational study of a fully atomistic model of the ruthenium-catalyzed transfer hydrogenation of formaldehyde and the reverse reaction in an explicit methanol solution. Using ab initio molecular dynamics techniques, we determined the thermodynamics, mechanism, and electronic structure along the reaction path. To assess the effect of the solvent quantitatively, we make a direct comparison with the gas-phase reaction. We find that the energy profile in solution bears little resemblance to the profile in the gas phase and a distinct solvation barrier is found: the activation barriers in both directions are lowered and the concerted hydride and proton transfer in the gas phase are converted into a sequential mechanism in solution with the substrate appearing as methoxide-like intermediate. Our results indicate that besides the metal–ligand bifunctional mechanism, as proposed by Noyori, also a concerted solvent-mediated mechanism is feasible. Our study gives a new perspective of the active role a solvent can have in transition-metal-catalyzed reactions.

Introduction

One of the most fundamental transformations in (bio)-chemistry is the asymmetric reduction of C=O and C=N bonds creating stereospecific centers in molecules. In this field, Noyori and co-workers initiated significant progress by introducing well-designed chiral ruthenium(II) (Ru) complexes that catalyze the transfer hydrogenation from 2-propanol to pro-chiral ketones with a high enantioselectivity under relatively mild reaction conditions.^{1,2} In particular, Ru complexes with aminoalcohol- and *N*-tosylated diamine-based ligands perform well with an enantiomeric excess of up to 99%.^{3–5} Ab initio calculations of model gas-phase complexes showed that a concerted transfer of a proton and a hydride from a Ru complex with an aminoalcohol ligand to the ketone is energetically favorable over other mechanisms proposed in the literature (Scheme 1).^{5–10}

Scheme 1. Scheme of Concerted Ru-Catalyzed Hydrogen Transfer via the Metal–Ligand Bifunctional Mechanism⁸



However, these studies did not incorporate explicitly the effect of the presence of the solvent alcohol molecules. Solvent molecules may play an important role as they actively take part in the reaction, being reactant or product. Moreover, they interact relatively strongly, via electrostatic and hydrogen bonding interactions, with the Ru complex. Here, we report on an ab initio molecular dynamics study of the formation of methanol via transfer hydrogenation from a Ru-complex hydride to formaldehyde (and the reverse reaction) in explicit methanol solvent. It has been demonstrated that the explicit role of the environment on chemical reactions can be well addressed by present day computational methods (see, e.g., refs 11 and 12).

Model and Methods

In the present computational study we considered a simplified form of a well performing Ru arene amino alcohol complex.¹³ The simplified complex consists of a Ru atom coordinated by a stabilizing benzene ligand and an amino alcohol ligand (Ru–C₆H₆–OCH₂CH₂NH) and is similar to the complex considered in earlier gas-phase computational studies.^{7,9} To model the solvated system, we considered a Ru complex and 40 methanol molecules. All molecules were placed in a periodically

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- (1) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.
- (2) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562–7563.
- (3) Fujii, A.; Hashiguchi, S.; Uematsu, N.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 2521–2522.
- (4) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97–102.
- (5) Petra, D. G. I.; Reek, J. N. H.; Handgraaf, J. W.; Meijer, E. J.; Dierkes, P.; Kamer, P. C. J.; Brussee, J.; Schoemaker, H. E.; van Leeuwen, P. W. N. *Chem. Eur. J.* **2000**, *6*, 2818–2829.
- (6) Alonso, D. A.; Brandt, P.; Nordin, S. J. M.; Andersson, P. G. *J. Am. Chem. Soc.* **1999**, *121*, 9580–9588.
- (7) Yamakawa, M.; Ito, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 1466–1478.
- (8) Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931–7944.
- (9) Handgraaf, J.-W.; Reek, J. N. H.; Meijer, E. J. *Organometallics* **2003**, *22*, 3150–3157.
- (10) The mechanistic aspects of transition-metal-catalyzed hydrogen-transfer reactions were very recently reviewed by Samec et al.²⁷

- (11) Villá, J.; Warshel, A. *J. Phys. Chem. B* **2001**, *105*, 7887–7907.
- (12) van Erp, T. S.; Meijer, E. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1660–1662.
- (13) Takehara, J.; Hashiguchi, S.; Fujii, A.; Inoue, S.; Ikariya, T.; Noyori, R. *Chem. Commun.* **1996**, 233.

replicated cubic box with an edge length of 14.12 Å. The box edge was obtained from a constant pressure and temperature simulation performed at ambient conditions using an empirical force field. For the reverse reaction we considered a Ru complex hydride coordinated by a formaldehyde molecule and 39 methanol molecules. We also considered a microsolvated system consisting of a Ru-complex hydride coordinated by a formaldehyde molecule and five hydrogen-bonded methanol molecules. Of the methanol molecules two are hydrogen-bonded to the oxygen ligand, two to the methanol/formaldehyde substrate and one to the NH ligand group. The calculations of the microsolvated system were performed in a periodic box of $15 \times 15 \times 13$ Å³, large enough to have negligible interactions among the periodic images.

The electronic structure was determined using the Kohn–Sham formulation of density functional theory (DFT). The DFT calculations were performed using the BLYP functional that combines a gradient correction term for the exchange energy as proposed by Becke¹⁴ with a correction for the correlation energy from Lee et al.¹⁵ The choice of the BLYP functional was guided by its accurate description of both the gas-phase Ru complex and liquid methanol. In refs 5 and 9 it was shown that gas-phase reaction energy profiles for the formation of methanol by transfer hydrogenation from a Ru-complex hydride were fully consistent with high-level electronic structure calculations (DFT-B3LYP and MP4) of ref 7. DFT-based molecular dynamics simulation studies of liquid methanol under ambient conditions provided an accurate description of structural and dynamical properties.^{16–18}

Pseudopotentials were used to restrict the number of electronic states to those of the valence electrons. The interaction with the core electrons is taken into account using semi-local norm-conserving Martins-Troullier pseudopotentials.¹⁹ The Ru pseudopotential was of the semi-core type including the highest s- and p-shell electrons as valence electrons. They were generated using an ionized configuration (Ru⁺) with the electrons treated relativistic in the scalar approximation. The pseudopotential cutoff radii for C, N, O, and H were 1.23, 1.12, 1.10, and 0.50 a.u., respectively. For Ru the radii of the s, p, and d part were 1.10, 1.20, and 1.24 a.u., respectively. The electronic states are expanded in a plane-wave basis including waves up to an energy of 70 Ry.

For the solvated system, DFT-based molecular dynamics simulations were performed using the Car-Parrinello method. In this ab initio molecular dynamics (AIMD) approach the calculation of the equations of motion for the atomic nuclei involves the introduction of a fictitious dynamics for the coefficients of the plane-wave basis set. The hydrogen nuclei were assigned a deuterium mass so that a larger time step could be used.^{20,21} The fictitious mass associated with the plane-wave coefficients was taken as 1100 a.u., which allowed for a time step in the numerical integration of the equations-of-motion of 0.169 fs, while maintaining adiabatic conditions for the electrons. The temperature was set at $T = 293$ K and imposed by a Nosé-Hoover thermostat²² with a frequency of 500 cm⁻¹. All calculations were performed with the CPMD package.²³

The rate of the Ru-catalyzed interconversion of methanol and formaldehyde was outside the time scale accessible to AIMD simulations. Therefore, the reactive event was enforced by a stepwise transfer

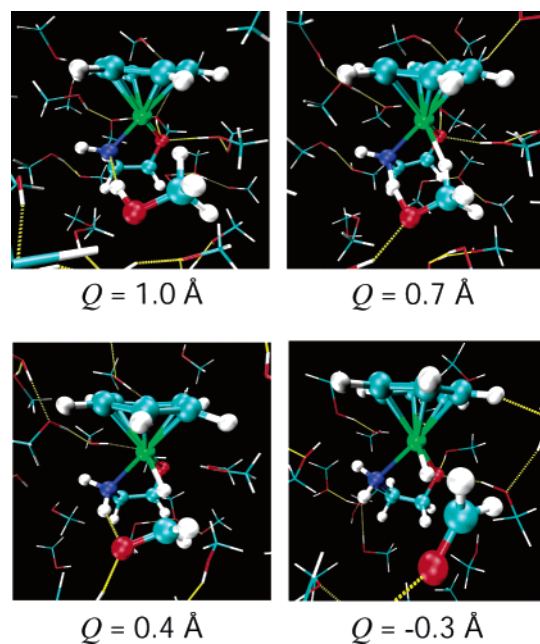


Figure 1. Snapshots of representative configurations of ab initio MD simulations of the Ru-catalyzed concerted hydrogen transfer in methanol solution. Molecules involved in the reaction are drawn in ball-stick representation. Other molecules are shown as lines and yellow dotted lines indicate hydrogen bonds. Green, red, blue, cyan, and white indicate ruthenium, oxygen, nitrogen, carbon, and hydrogen nuclei, respectively. Q is the hydrogen-transfer reaction coordinate. $Q = 1.0$: initial approach of one of the methanol solvent molecules, the donor, to the Ru complex. $Q = 0.7$: transfer of proton and hydride of the donor to the Ru complex. $Q = 0.4$: formaldehyde hydrogen-bonded to Ru complex. $Q = -0.3$: formaldehyde partially solvated.

of the hydride of the Ru complex to the formaldehyde carbon using the method of constraints. This was controlled by fixing the Ru–H–C asymmetric stretch coordinate $Q = r_{\text{Ru-H}} - r_{\text{C-H}}$. We performed 12 constrained AIMD simulations along the reaction path with Q -values in the range of 3.0 to -1.5 . The simulation trajectories were typically 4–5 ps. The free energy profile was obtained by integration of the calculated constraint force.^{24,25} The chosen reaction coordinate does not necessarily provide the best representation of the reaction pathway. Obviously, the pathway also involves the deprotonation of the hydroxide group of the methanol substrate and the coordination of solvent molecules. However, we have verified that with the employed reaction coordinate Q for all 12 constrained AIMD simulations the constraint force and structural properties are such that the hydroxide proton position does not show irreversible sudden changes, indicating that the Ru–H–C asymmetric stretch is a reasonable reaction coordinate.

Results and Discussion

Figure 1 shows four snapshots of the solvated system at key points along the reaction path. They show that the enforced transfer of the hydride results in a conversion of methanol into formaldehyde. Figure 2 shows the calculated constraint force and associated free-energy profile along the reaction path, as well as the gas-phase free-energy profile.⁹ In the following we will discuss the reaction path going from methanol to formaldehyde, i.e., on going from right to left in Figure 2. In the initial phase of the hydride transfer from the methyl C to Ru ($Q = 3.0$ – 1.0), the mean force of constraint increases, yielding an enhanced increase of the free energy. The hydroxyl proton

(14) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100.

(15) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789.

(16) Handgraaf, J. W.; van Erp, T. S.; Meijer, E. J. *Chem. Phys. Lett.* **2003**, *367*, 617–624.

(17) Pagliai, M.; Cardini, G.; Righini, R.; Schettino, V. *J. Chem. Phys.* **2003**, *119*, 6655.

(18) Handgraaf, J. W.; Meijer, E. J.; Gaigeot, M.-P. *J. Chem. Phys.* **2004**, *121*, 10111–10119.

(19) Troullier, N.; Martins, J. L. *Phys. Rev. B* **1991**, *43*, 1993–2006.

(20) Laasonen, K.; Sprik, M.; Parrinello, M.; Car, R. *J. Chem. Phys.* **1993**, *99*, 9080–9089.

(21) Silvestrelli, P. L.; Parrinello, M. *J. Chem. Phys.* **1999**, *111*, 3572–3580.

(22) Nosé, S. *J. Chem. Phys.* **1984**, *81*, 511–519.

(23) Hutter, J.; Alavi, A.; Deutsch, T.; Bernasconi, M.; Goedecker, S.; Marx, D.; Tuckerman, M.; Parrinello, M. *CPMD, version 3.4*; MPI für Festkörperforschung and IBM Zurich Research Laboratory, 1995–1999.

(24) Carter, E. A.; Ciccotti, G.; Hynes, J. T.; Kapral, R. *Chem. Phys. Lett.* **1989**, *156*, 472–477.

(25) Sprik, M.; Ciccotti, G. *J. Chem. Phys.* **1998**, *109*, 7737.

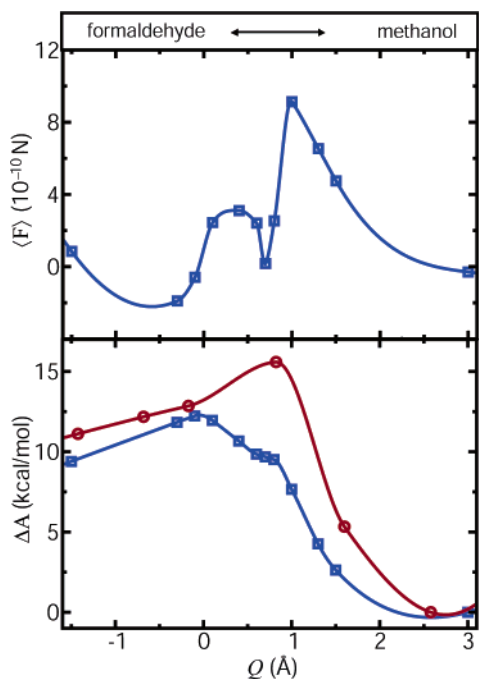


Figure 2. Average constraint force along the reaction path in solution (top). Statistical errors are $\approx 0.5 \times 10^{-10}$ N. Associated free-energy profile (blue, squares). For comparison the energy profile for the gas phase (red, circles) is also shown. The energy profiles are relative to the lowest energy value at $Q = 3.0$.

remains attached to the methanol O. Subsequently, for $Q = 1.0-0.5$, the constraint force shows a steep minimum reaching approximately zero at $Q = 0.7$. Consequently, the free-energy profile shows a small plateau. At $Q = 0.7$ the methanol hydroxyl proton transfers back and forth between the methanol O and the N of the amino alcohol ligand, with the proton bound predominantly to the N. Upon further transfer of the hydride the constraint force changes sign at $Q \approx 0.0$, indicating the location of the transition state. Compared to the gas-phase system, the transition state is lowered and shifted significantly toward the formaldehyde side of the reaction. The difference should be attributed to the presence of the solvating methanol molecules. This is further clarified by examining the structural and electronic changes along the reaction path.

Figure 3 shows, as a function of the reaction coordinate Q , the substrate C–O bond length and the bond lengths related to the proton and hydride transfer. The electronic changes are represented by Wannier function centers (WFCs).²⁶ These can be assigned a common chemical functionality such as being associated with a bonding pair or a lone pair of electrons. In Figure 4 we have plotted the distance between selected nuclei and associated WFCs. On going from methanol to formaldehyde, we can distinguish three stages: toward $Q = 1.0$, from $Q = 1.0$ to $Q = 0.6$, and smaller than $Q = 0.6$.

Beyond $Q = 1.0$: In the solution reaction the hydroxyl group of the methanol substrate remains in solution for Q larger than

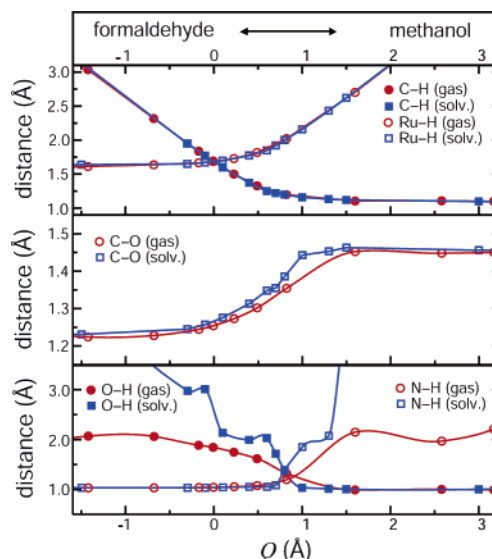


Figure 3. Average bond lengths along the reaction path. Top: hydride transfer C–H and Ru–H bonds; middle: substrate C–O bond; bottom: proton-transfer O–H and H–N bonds. Blue squares and lines indicate results for the reaction in solution. Red circles and lines indicate gas-phase results. Statistical errors for the bond lengths in solution are around 0.03 \AA .

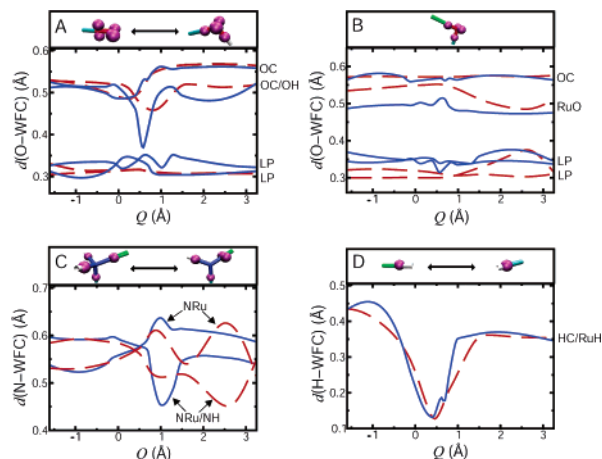


Figure 4. Distances between selected nuclei and associated Wannier function centers (WFCs). Blue lines indicate results for the reaction in solution. Red dashed lines shows results of the gas-phase reaction. (A) Oxygen nucleus of substrate; (B) oxygen nucleus of ligand; (C) nitrogen nucleus of ligand; (D) transferred hydrogen nucleus (Ru–H–C). Data points (not shown for simplicity) for the solvated system were obtained by averaging over six configurations of the respective constraint AIMD simulation. Statistical errors for the solvated system are around 0.005 \AA . For simplicity only two of the four WFCs associated with the nitrogen nucleus are shown; the ones associated with the N–C and N–H bond hardly change when going from gas phase to solution. Schematic diagrams in ball-stick representation of the nuclei with their respective WFCs (purple balls) are shown at the top of each plot.

1.5. For smaller values of Q it forms a hydrogen bond with the ligand amide group. This is accompanied by a change of the position of one of the nitrogen WFCs, reflected in a decrease of its distance to N from 0.55 to 0.45 \AA and its redirection toward the methanol hydroxyl hydrogen. This indicates that the electron pair associated with this WFC changes from a Ru–N bonding to a N lone pair. In the gas-phase system the methanol is hydrogen-bonded to the ligand N for Q larger than 1.5 . For smaller Q it shows the onset of the transfer of the hydroxyl proton to the ligand N, reaching the transition state just below $Q \sim 1.0$.

- (26) The method of maximally localized Wannier functions that transform the Kohn-Sham orbitals into Wannier functions whose centers (WFC) can be assigned with a chemical meaning such as being associated with an electron bonding or lone pair (LP).^{28,29} This method has proved to be a valuable tool in the investigation of the electronic charge distribution in condensed phase environment. Examples are hydrogen-bonded liquids.^{18,21}
- (27) Samec, J. S. M.; Bäckvall, J.-E.; Andersson, P. G.; Brandt, P. *Chem. Soc. Rev.* **2006**, *35*, 237–248.
- (28) Marzari, N.; Vanderbilt, D. *Phys. Rev. B* **1997**, *56*, 12847–12865.
- (29) Silvestrelli, P. L.; Marzari, N.; Vanderbilt, D.; Parrinello, M. *Solid State Commun.* **1998**, *107*, 7–11.

From $Q = 1.0$ to $Q = 0.6$: The free energy profile of the reaction in solution shows a plateau which is associated with a full proton transfer from the substrate O to the amine N. The N–H bond formation is reflected in the shift of the lone-pair WFC away from the N to ≈ 0.6 Å, making it a N–H bond WFC. The O–H bond WFC shifts toward the O to a value of 0.35 Å, typical for a lone pair. This yields an O with three lone pairs, indicating that the substrate is converted into a methoxide-like compound. It is stabilized by hydrogen bonds with solvent molecules. At $Q = 0.6$ the methoxide forms strong hydrogen bonds (1.6 and 1.9 Å) with solvent molecules, reflected in a shift of two lone-pair WFCs of the methoxide oxygen away from the oxygen. Also near the substrate C the electronic structure alters. The WFC of the methyl H that is transferred to Ru shifts toward the H, indicating that it is starting to lose its C–H bond character. In the gas-phase reaction the transition state is located in the range between $Q = 1.0$ and $Q = 0.6$ with the proton moving from the substrate O to the ligand N. However, in contrast to the reaction in solution the transfer is not yet fully completed. Also, the electronic state of the substrate differs from that in the solution reaction. As the hydroxyl O–H bond WFC shifts only slightly toward the substrate oxygen, the substrate does not acquire a methoxide character, but rather converts directly to formaldehyde. The WFC associated with the Ru–O bond shows a relatively sharp shift away from the oxygen at $Q = 0.6$. In the simplified picture provided by the WFCs this could be interpreted as a compensation of the shift of the WFC associated with the Ru–N bond toward the nitrogen, where, in turn, the latter is facilitated by the conversion of the nitrogen lone pair into a NH bonding pair. The shift of the RuO WFC away from the oxygen has implications for the hydrogen bonding of the ligand oxygen to solvent molecules. It is accompanied by a shift of one of the lone-pair WFCs toward the oxygen destabilizing the associated hydrogen bond such that it is broken in the region near $Q = 0.6$. The second solvent methanol remains strongly hydrogen-bonded.

When the proton is midway between the O substrate and amide N, the distance between O and N is rather short (≈ 2.7). It is known that for short distances between donor and acceptor a proton moves in a single well, see, e.g., ref 30 for the protonated water dimer. Extrapolating this to the proton between O and N in the present reaction would suggest that quantum tunneling effects are minor.

Below $Q = 0.6$: In solution, with the transition state at $Q = -0.1$, the methyl H is further transferred to Ru, converting the methoxide substrate into formaldehyde. In this process the lone-pair WFC of the substrate O involved in the hydrogen bond with the ligand N acquires C–O bond character. This is associated with the breaking of the hydrogen bond to the ligand N at $Q = -0.1$, near the maximum of the free energy profile.

The effect of the solvent molecules can be qualitatively reproduced by gas-phase calculations of a “microsolvated” complex with methanol molecules at hydrogen-bonding positions around the reacting complex. The energy profile for the microsolvated system is qualitatively similar to that of the solvated system. However, the plateau associated with the proton transfer from the substrate O to ligand N is more extended and yields a shallow minimum at $Q = 0.76$. As in full solution, this

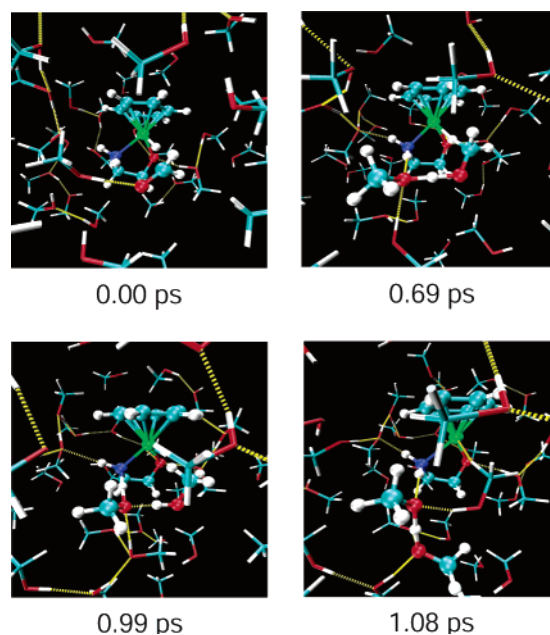
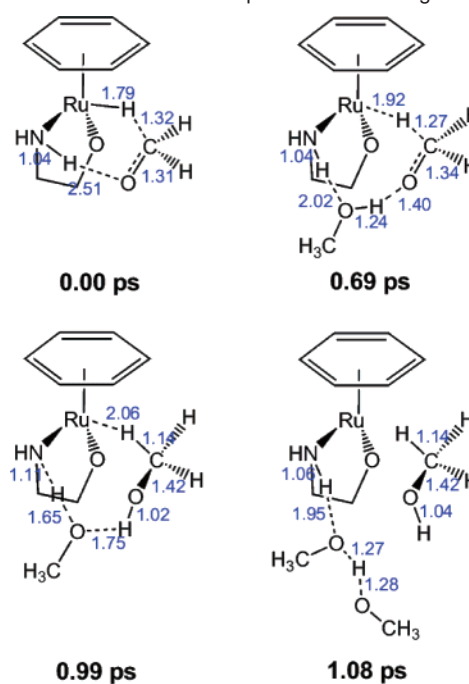


Figure 5. Snapshots of the solvated system after the constraint is released at $Q = -0.1$. Reacting molecules are shown in ball-stick representation. Solvent molecules are shown in thin lines and the dotted yellow lines indicate hydrogen bonds. See also caption of Figure 1. A movie of the simulation can be found in the Supporting Information.

Scheme 2. Structures of the Snapshots Shown in Figure 5^a



^a Only the reacting molecules are drawn. Averaged interatomic distances (blue) in Ångstrom are computed by taking time intervals around the snapshots. Statistical errors are smaller than 0.05 Å.

intermediate is a methoxide stabilized by hydrogen bonds to the ligand N and two methanol molecules.

We also performed a calculation of an actual reactive process in methanol solution, starting from an initial configuration of the constrained simulation at the transition state ($Q = -0.1$). Figure 5 shows four snapshots of the trajectory with the constraint released. Scheme 2 shows the corresponding pictures with the most important bond distances. In the initial configuration ($t = 0$ ps) the substrate has a formaldehyde character,

(30) Tuckerman, M. E.; Marx, D.; Klein, M. L.; Parrinello, M. *Science* **1997**, *275*, 817–820.

with the O hydrogen-bonded to a coordinating solvent molecule. After release of the constraint, the Ru-complex H moves immediately from Ru to the formaldehyde C, yielding for the subsequent 0.5 ps a methoxide-like substrate with a “long” C–H bond (1.2–1.4 Å) that is directed toward Ru. The substrate O is strongly hydrogen-bonded (1.4–1.7 Å) to a coordinating solvent molecule. The latter has two hydrogen bonds: one with the ligand N and the other with a second solvent molecule. At $t = 0.69$ ps simultaneously a shortening of the C–H bond to ≈ 1.1 Å and a proton transfer from the coordinated solvent molecule to the methoxide O occur (Figure 5, snapshot 2). This converts the coordinating solvent molecule into a methoxide. In the subsequent 0.3 ps there are several attempted proton transfers from the amine group (Figure 5, snapshot 3) and a second solvent molecule to the methoxide O. A persistent proton transfer occurs at $t = 1.08$ ps when the second solvent molecule donates a proton to the methoxide molecule followed by a chain of proton transfers showing a methoxide molecule migrating through the solution. After 1.71 ps a Ru complex with amine ligand and a solvent-stabilized methoxide molecule are formed, which will eventually exchange the proton to form the dehydrogenated Ru complex and methanol.

The reactive trajectory reflects to a large extent the mechanism observed in the constrained simulations. Both show the substrate appearing as a methoxide intermediate, being the main distinction from the mechanism calculated for the gas-phase reaction. In the reactive trajectory the methoxide exists for a short but finite time, which is consistent with the appearance of a plateau-like region in the free energy profile. The reactive trajectory suggests that the reaction may not necessarily occur via a bifunctional mechanism as put forward by Noyori et al.⁸ Our simulation suggests that the proton source for the ketone may be either a solvent methanol or the amine group of the Ru complex depending on the coordination of the ketone O.

A possible strategy for experimental verification of the existence of the methoxide intermediate could be the reaction of a non-deuterated hydrogenated catalyst and acetophenone in a deuterated alcohol solvent (e.g., R2CHOD) at catalytic conditions. If the methoxide intermediate is present, the chiral

product should contain a distribution of OH and OD. If it is not present, only the OH alcohol should appear in the product. A parallel control experiment should ensure that reaction conditions are such that no H/D exchange between solvent and the NH of the amine moiety (or OH of the product) occurs. Thus, the stability of these hydrogen atoms should be tested in advance by NMR for the Ru catalyst and product (e.g., 1-*S*-phenylethanol) dissolved in R2CHOD.

In conclusion, our ab initio molecular dynamics simulations show that methanol solvent molecules play an active role in a ruthenium-catalyzed transfer hydrogenation reaction converting formaldehyde into methanol. In the present case we have shown that the reaction in solution may follow a different mechanism than that in the gas phase. The explicit role of solvent molecules also indicates that the common computational approach of complementing a quantum-chemical description of the reacting species with a continuum model of the solvent will fail to capture important effects. More generally, our calculations show that a proper understanding of reactions in hydrogen-bonded solvents requires computational and experimental studies that probe the reacting species and nearest solvating molecules on an atomistic level.

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Supporting Information Available: A MPEG movie of the simulation after the constraint is released at $Q = -0.1$ Å. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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