Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**.

Chemical Involvement of Solvent Water Molecules in Elementary Steps of the Fenton Oxidation Reaction**

Bernd Ensing, Francesco Buda, Peter Blöchl, and
Evert J. Baerends*

The proposed reaction mechanisms for the oxidation of organic substrates with the Fenton reagents (a mixture of ferrous ions and hydrogen peroxide) can roughly be divided into two groups. The first group regards Fenton chemistry as the production of free hydroxyl radicals by the metal-catalyzed decomposition of the peroxide,[1] whereas the second group involves the formation of a highly reactive iron–oxo complex, such as the ferryl ion ($[Fe^{IV}O]^{2+}$), as the oxidative intermediate.[2] The issue is clearly of interest for both biooxidation research, in view of the prominent role of Fe ions, and for oxidation catalysis in general. However, despite the numerous studies over more than 60 years,[3–10] the controversy remains, since the extremely short lifetimes of the intermediates make definitive experiments very difficult. The major complication with quantum chemical calculations is that the water solvent has to be included in the study. Not only are the Fe^{2+} ions coordinated by six water molecules, but conceivable reaction products such as OH^-, H^+, and $OH^\bullet$ will also be solvated and/or propagate through the solution by chain reactions. It is therefore impossible to treat the solvent by just model potentials that describe interactions between intact H_2O molecules with other H_2O molecules and Fe^{2+} ions (let alone by a continuum model).

The explicit incorporation of the water solvent in the computational study is no longer an elusive goal. Indeed, the ab initio molecular dynamics (AIMD) method[11] allows for a parameter free, finite temperature simulation in which, at each time step, the forces are computed directly from the electronic structure determined by density functional theory (DFT). Therefore, within this approach there are no restrictions on reactive processes at the Fe center or in the solution.

Recently, we performed DFT calculations on the isolated (gas-phase) Fenton reactants,[12] and found that dissociation of the O–O bond of hydrogen peroxide molecule coordinated to pentaaqua Fe^{II} ions to form $[Fe(OH)(H_2O)_5]^{2+}$ and a $OH^\bullet$ cannot readily occur since this reaction is endothermic by 27 kcal mol^{-1}. This value is in fact already smaller than the approximate 60 kcal mol^{-1} required to break the O–O bond in isolated hydrogen peroxide. The reduction of the dissociation energy occurs because the $OH^\bullet$ that remains coordinated to the iron center leads to an Fe^{II}–$OH^\bullet$ bond (formally Fe^{III}–OH^-), which is stronger by about 30 kcal mol^{-1} than the original Fe^{II}–H_2O_2 bond. Nevertheless, there is still an endothermicity of 27 kcal mol^{-1}, and homolytic dissociation of the coordinated H_2O_2 molecule can only become exothermic through the energy gain associated with a second Fe–OH bond replacing a much weaker Fe–H_2O bond. This process occurs in the gas phase by the leaving $OH^\bullet$ abstracting a hydrogen atom from an adjacent coordinated H_2O molecule. A water molecule and a second strong Fe–OH bond is formed, and this process provides enough energy to make the reaction exothermic [Eq. (1)]. Hence, no $OH^\bullet$ results.

$$[Fe^{II}(H_2O)_5(H_2O_2)]^{2+} \rightarrow [Fe^{IV}(OH)_2(H_2O)_4]^{2+} + H_2O \tag{1}$$

We now turn to the study of this reaction in solution. We had already observed in the gas phase that a single water molecule, when added in a "second solvation shell" position, reacts with the $[Fe(OH)_2(H_2O)_4]^{2+}$ complex to form the presumably reactive iron–oxo (ferryl) ion $[FeO(H_2O)_5]^{2+}$ and an H_2O molecule. The energy barrier for this transformation would be too high without the chemical involvement of the "solvent" water molecule. Hence, solvent simulation is necessary since solvent molecules may be chemically involved in the formation of the ferryl ion. Moreover, they may be involved in the alternative pathway of $OH^\bullet$ formation, since solvent molecules may react with the $OH^\bullet$ and propagate it through the solution by a chain reaction. We have, therefore, performed spin-polarized AIMD simulations of (high spin, $S=2$) Fe^{2+}/H_2O_2 in water using the CP-PAW code[13] with the BP[14, 15] exchange-correlation functional. We applied periodic boundary conditions, as usually done in MD simulations,[16] to a relatively small cubic unit cell containing an Fe^{2+} ion, a H_2O_2 molecule, and 31 water molecules to emulate the infinite bulk environment but keep the computation feasible. The formal concentration of the reactants is therefore high but not unrealistic (technical details of AIMD simulations of solvation and (radical) reactions in water may be found in ref. [17–21]). The same parameters for the basis set and dynamics were used as in our previous study of the S_N2 reaction in water,[17] namely, a constant temperature[22] of $T = 300$ K, a fictitious electron mass of $\mu_e = 1000$ a.u.; a MD time step of $\Delta t = 8$ a.u.; and a plane-wave cut-off of $k^2_{max} = 30$ Ry. The box size was $L =$

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[*] Prof. Dr. E. J. Baerends, Ir. B. Ensing, Dr. F. Buda
Theoretical Chemistry, Faculty of Exact Sciences
Vrije Universiteit Amsterdam
De Boelelaan 1083, 1081 HV Amsterdam (The Netherlands)
Fax: (+31) 20-44-47-629
E-mail: baerends@chem.vu.nl

Prof. Dr. P. Blöchl
Clausthal University of Technology
Clausthal-Zellerfeld (Germany)

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9.900 Å. The accuracy of the BP functional to describe reactions in water has previously been discussed.[17]

After a 1.16-ps equilibration run (using bond constraints to avoid any reaction occuring beforehand), the MD simulation was started (without any bond constraints) and the evolution of the coordinated Fenton reagents in water was followed for 10.2 ps. Almost immediately, the peroxide dissociates into an OH group coordinated to the iron center and an $OH^{\bullet}$, which now does not attack an adjacent coordinated H_2O molecule (as in the gas-phase study) but instead attacks a solvent water molecule that was hydrogen bonded to the β-oxygen atom of hydrogen peroxide (see snapshots 1 and 2 in Figure 1). Snapshots 2 and 3 show that in a fast chain reaction the reactive radical is passed on via two solvent water molecules and the reaction is terminated by abstraction of a hydrogen atom from a water ligand of the aqua–iron complex in the neighboring cell, which, as a consequence of the periodic repetition, is identical to the complex from which the $OH^{\bullet}$ originated. The process may be looked upon as a concerted reaction rather than a chain reaction since the abstraction of a hydrogen atom from a coordinated H_2O molecule occurs virtually simultaneously with the breaking of the O–O bond. This mechanism agrees with the energy cost being too high for just an $OH^{\bullet}$ splitting off from a coordinated H_2O_2 molecule. A second OH ligand has to be formed simultaneously, either at the same Fe center, as happens in the gas phase, or at an adjacent Fe center, as observed in the present simulation in solution. As a matter of fact, since there is only one Fe complex in the unit cell, the net effect is still formation of a dihydroxide species, a result which is similar to abstraction of an H atom from an H_2O molecule coordinated at the same Fe center [Eq. (1)]. Of course, if more Fe complexes were present in a unit cell, abstraction of an H atom from a H_2O ligand in a nearby complex at which the hydrogen peroxide had not yet dissociated, or which did not have a hydrogen peroxide molecule coordinated at all, would lead to two monohydroxide complexes. The important point is that the formation of a free $OH^{\bullet}$ is not thermodynamically favorable, and the hydrogen peroxide only dissociates if an $OH^{\bullet}$ "shunt" through the solution to a coordinated H_2O molecule, either at the same center or an adjacent Fe center, quenches the radical. Although, in principle, monohydroxide complexes may result if the $OH^{\bullet}$ shunt ends at a different Fe center to where it started, the more likely reaction path, in particular with a low concentration of Fe complexes, will be a chain involving a few solvent water molecules and ending at the same Fe center as where the hydrogen peroxide was coordinated, a process which leads to a dihydroxide complex. The high concentration of Fe^{2+} ions in our simulation, which leads to dihydroxides since the $OH^{\bullet}$ abstracts a H atom from an Fe center in a neighboring cell which already had an OH group present from the dissociation of H_2O_2, yields the same product. In establishing the high probability of formation of iron(IV) dihydroxide rather than free $OH^{\bullet}$ radicals, we also note that it remains to be seen whether the $OH^{\bullet}$ shunt, possibly through a chain of solvent molecules, could terminate at an organic substrate if that were in the neighborhood. This requires further investigation. If this were to occur, similar reaction products should arise, as in the case of the production of free $OH^{\bullet}$ radicals from, for example, radiation. The probability of such a mechanism occurring with a high concentration of an organic substrate might be sufficient to explain some of the experimental findings.

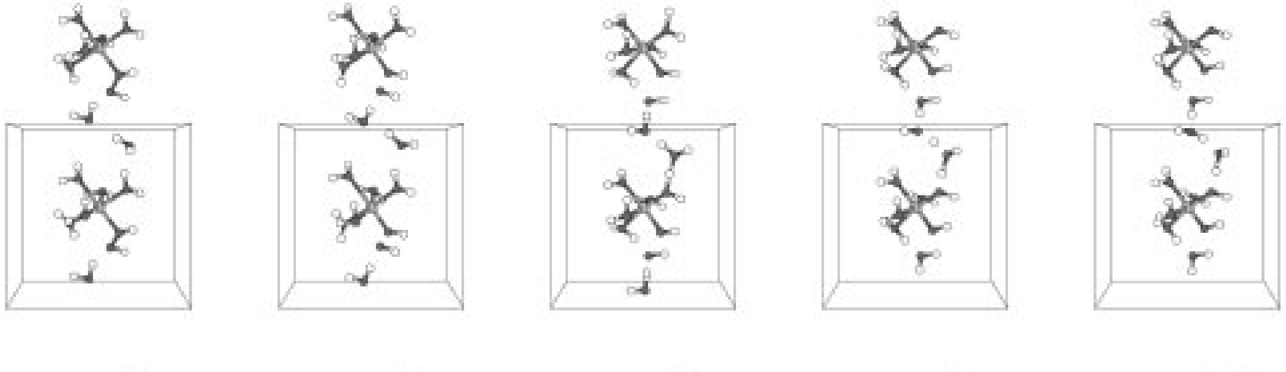
We observed in the simulations that the formed iron(IV) dihydroxide complex is in equilibrium with its conjugate base through proton donation from a water ligand to the solvent [Eq. (2)].

$$[Fe^{IV}(OH)_2(H_2O)_4]^{2+} + H_2O \rightleftharpoons [Fe^{IV}(OH)_3(H_2O)_3]^{+} + H_3O^{+} \quad (2)$$

Formation of the Fe(IV) dihydroxide complex also occurred in our gas-phase study, but of course the apparent acidity of the Fe^{IV} complex according to Equation (2) could not be observed in the gas phase. The dihydroxide complex is transformed in our simulation 1.7 ps after step 1 (during which time reaction (2) is going back and forth) into an iron–oxo complex by donation of a proton from a coordinated OH group to the solvent [Eq. (3)].

$$[Fe^{IV}(OH)_2(H_2O)_4]^{2+} + H_2O \rightarrow [Fe^{IV}O(OH)(H_2O)_4]^{+} + H_3O^{+} \quad (3)$$

We note that again the presence of solvent is crucial for this pathway to form the ferryl species, and enable an H^+ ion to



$t = 2$ fs　　$t = 41$ fs　　$t = 126$ fs　　$t = 137$ fs　　$t = 144$ fs

Figure 1. Five snapshots of step 1 of the reaction, starting at the moment that the R(OO) and R(FeO) constraints of H_2O_2 coordinated to $[Fe(H_2O)_5]^{2+}$ were released ($t = 0$). The hydrogen peroxide coordinated to the pentaaquairon complex is drawn in the center of the unit cell. One periodic image of the unit cell is drawn above it. The two solvent water molecules that are involved in the reaction are also shown but, for simplicity, the other solvent water molecules are left out. See text for further information.

diffuse into the solvent. The ferryl species is also formed in the gas-phase simulation (being the thermodynamically favored end product), but in this case by migration of an H^+ ion to the second OH^- ligand. As mentioned before, the solvent involvement was already indicated by the introduction of a single water molecule into the second coordination sphere in the gas-phase study. This water molecule aided migration of the H^+ ion to form $[Fe^{IV}O(H_2O)_5]^{2+}$, but the present complete picture could only be obtained by the explicit introduction of the solvent at finite temperature.

In conclusion, the simulations in water solution confirm our gas-phase calculations of the formation of the iron(IV) – oxo complex from the Fenton reagents. We have assumed the formation of the pentaaquairon – hydrogen peroxide complex as the initial necessary step. Our results demonstrate the importance of full incorporation of the water as both a solvent and reagent in the initial reaction steps. The oxo complex is found to be the important oxidative intermediate in the Fenton reaction. How it acts as the reactive species in, for example, hydroxylation of aliphatic and aromatic substrates,[23–25] oxidation of alcohols, and in other reactions will be the subject of further study.

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[1] F. Haber, J. Weiss, *Proc. R. Soc. London* **1934**, *147*, 332.
[2] W. C. Bray, M. H. Gorin, *J. Am. Chem. Soc.* **1932**, *54*, 2124.
[3] P. Wardman, L. P. Candeias, *Radiat. Res.* **1996**, *145*, 523.
[4] C. Walling, *Acc. Chem. Res.* **1998**, *31*, 155.
[5] D. T. Sawyer, A. Sobkowiak, T. Matsushita, *Acc. Chem. Res.* **1996**, *29*, 409.
[6] M. L. Kremer, *Phys. Chem. Chem. Phys.* **1999**, *1*, 3595.
[7] J. D. Rush, W. H. Koppenol, *J. Inorg. Biochem.* **1987**, *29*, 199.
[8] D. A. Wink, R. W. Nims, J. E. Saavedra, W. E. J. Utermahlen, P. C. Ford, *Proc. Natl. Acad. Sci. USA* **1994**, *91*, 6604.
[9] J. P. Hage, A. Llobet, D. T. Sawyer, *Bioorg. Med. Chem.* **1995**, *3*, 1383.
[10] C. Kim, K. Chen, J. Kim, L. Que, Jr., *J. Am. Chem. Soc.* **1997**, *119*, 5964.
[11] R. Car, M. Parrinello, *Phys. Rev. Lett.* **1985**, *55*, 2471.
[12] F. Buda, B. Ensing, M. C. M. Gribnau, E. J. Baerends, *Chem. Eur. J.* **2001**, in press.
[13] P. Blöchl, *Phys. Rev. B* **1994**, *24*, 17953.
[14] A. D. Becke, *J. Chem. Phys.* **1992**, *96*, 2155.
[15] J. P. Perdew, *Phys. Rev. B* **1986**, *33*, 8822, erratum: *Phys. Rev. B* **1986**, *34*, 7406.
[16] See, for example, D. Frenkel, B. Smit, *Understanding Molecular Simulation*, Academic Press, San Diego, **1996**.
[17] B. Ensing, E. J. Meijer, P. E. Blöchl, E. J. Baerends, *J. Phys. Chem. A* **2001**, *105*, 3300.
[18] M. Mohr, D. Marx, M. Parrinello, H. Zipse, *Chem. Eur. J.* **2000**, *6*, 4009.
[19] E. J. Meijer, E. J. Sprik, *J. Am. Chem. Soc.* **1998**, *120*, 6345.
[20] E. J. Meijer, M. Sprik, *J. Phys. Chem. A* **1998**, *102*, 2893.
[21] M. Tuckerman, K. Laasonen, M. Sprik, M. Parrinello, *J. Chem. Phys.* **1995**, *103*, 150.
[22] S. J. Nosé, *J. Chem. Phys.* **1984**, *81*, 511.
[23] D. Schröder, H. Schwarz, *Angew. Chem.* **1995**, *107*, 2126; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1973.
[24] K. Yoshizawa, Y. Shiota, T. Yamabe, *J. Am. Chem. Soc.* **1998**, *120*, 564.
[25] K. Yoshizawa, Y. Shiota, Y. Kagawa, T. Yamabe, *J. Phys. Chem. A* **2000**, *104*, 2552.

Insights into the Aryl – Aryl Exchange between Palladium and Phosphane Ligands in Pd^{II} Complexes: Preparation of Phthalocyanine-Containing Phosphonium Salts**

Gema de la Torre, Andreas Gouloumis,
Purificación Vázquez, and Tomás Torres*

The employment of modern synthetic methods in the phthalocyanines (Pc) field[1] can provide a large variety of functionalized derivatives and complex structures based on these macrocycles which may have interesting applications in materials science. In the last few years many scientists, ourselves included, have concentrated on the preparation of unsymmetrically functionalized phthalocyanines[2, 3] and binuclear Pc derivatives in which the macrocyclic units are fused to each other[4, 5] or bridged through different kinds of spacers.[6–8] Our interest in noncentrosymmetric and octupolar[9] systems for nonlinear optical (NLO) applications[10] as well as in the preparation of molecular materials with multiple functions led us to the synthesis of phosphonium salts containing one phthalocyanine unit (Figure 1). Pc-containing phosphonium cations are targets of choice for the preparation of hybrid materials that combine magnetism with NLO properties.[11]

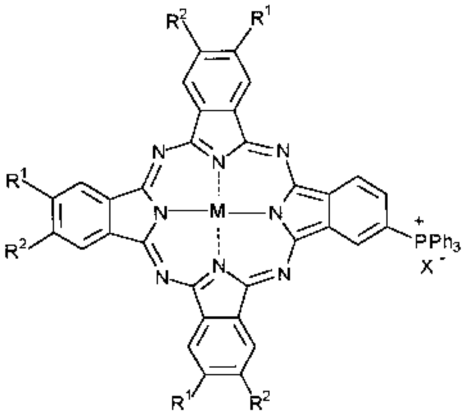

Figure 1. Phthalocyanine-phosphonium salts.

Tetraarylphosphonium salts can be formed by a palladium-catalyzed reaction between triphenylphosphane and an aryl bromide or iodide.[12] The mechanism of the quaternization reaction seems to involve oxidative addition of the aryl halide (ArI) to a palladium(0) – phosphane complex, followed by the reductive elimination of the phosphonium ion and a loss of the halide ion from the metal center (Scheme 1).

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[*] Prof. T. Torres, Prof. P. Vázquez, Dr. G. de la Torre, A. Gouloumis
Departamento de Química Orgánica
Universidad Autónoma de Madrid
Cantoblanco, 28049-Madrid (Spain)
Fax: (+34) 91-397-3966
E-mail: tomas.torres@uam.es

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