A new look at the chemical reaction

At the heart of chemistry has always been the chemical reaction, and numerous analytical tools, such as NMR, UV-vis spectroscopy and mass spectrometry, are commonly used to elucidate reaction mechanisms. These conventional techniques have, however, an important limitation: they measure ensembles of millions of molecules at the same time and give only an average picture of a reaction mechanism, which might be incomplete and misleading because certain molecules might react whilst others are inactive. It is for this reason that during the past decade the interest is increasingly focusing on studying chemical reactions at the level of single molecules, and the stormy development of methods that allow such single molecule investigations, in particular Scanning Probe Microscopy, makes totally new insights in reaction mechanisms possible.

Johannes A. A. W. Elemans
Institute for Molecules and Materials, Radboud University Nijmegen, Heyendaalseweg 135, 6525 AJ Nijmegen, The Netherlands
E-mail: j.elemans@science.ru.nl

Is it possible to really ‘see’ individual molecules in action as they are involved in a chemical reaction? And can we, in this way, get a complete understanding of reaction mechanisms, at the resolution of atoms? The importance of studying chemical reactions in such high detail has been highlighted by Gerhard Ertl, who was awarded the Nobel Prize in chemistry in 2007 for elucidating mechanisms of chemical processes on heterogeneous catalytic surfaces. He was one of the pioneers in applying the world’s most powerful microscope, the Scanning Tunneling Microscope (STM), to visualize atoms and molecules in action, while they are involved in a chemical reaction.

The STM is still a relatively new tool to image matter down to the atomic level. Since its invention in 1981 by Binnig and Rohrer at IBM[1,2], its impact for materials science has been tremendous. It had suddenly become possible to truly visualize single atoms and molecules at a surface, and it is no surprise that this rapidly led to new insights in the fields of surface physics and chemistry. An STM operates by scanning an atomically sharp metallic needle along a flat conductive surface, without contacting it. Upon applying a bias voltage between the sample and the tip, a tunneling current may start to run when the two electrodes are in very close proximity (nanometer range). Because >95% of this tunneling current travels through the terminal atom of the tip, extremely high spatial resolution can be obtained of the surface and of atoms or molecules adsorbed on it. While scanning, the STM tip can be maintained at constant height, or alternatively, a feedback loop retracts or approaches the tip to keep the tunneling current at a

ISSN:1369 7021

constant value. An STM image therefore not only provides a detailed topographic picture of a surface, but also information about its local electronic density of states.

In contrast to electron microscopes, STMs can operate in a wide variety of environments, such as in air, in liquids, in ultrahigh vacuum (UHV), at ultralow temperatures (4 K), or under high pressures of gases. In the first years after its conception, the STM was principally used to investigate well-defined metal and semiconductor surfaces, until in the late 1980s Foster and Frommer published the first study of well-organized layers of organic molecules adsorbed on a graphite surface[3]. Since then, numerous STM studies have appeared in which molecules adsorbed to surfaces have been characterized down to the submolecular level. Many of these studies involve steady state imaging of surfaces that are (partially) covered with monolayers of immobilized molecules, but in recent years STM research is getting more and more directed toward observing dynamic processes. These can vary from rotational and translational movement of atoms and molecules to observing complete chemical reactions in real-space and real-time. In particular the latter research area is one of the holy grails of surface science, because what is more appealing than studying chemical reactions in the most direct way possible, i.e. by visualizing them? Ertl, being one of the pioneers, investigated in detail the molecular mechanisms of catalytic reactions in an STM operating in UHV[4]. Following a different approach, Somorjai applied STMs at high pressures and temperatures to monitor in situ the reaction-induced restructuring at the interface of metals and gases[5]. Although being of fundamental importance, these studies have in common that they are carried out under rather extreme conditions, far removed from the environments in which many reactions in the laboratory and biological systems usually take place, namely in a liquid under ambient conditions. Although STM studies of molecules at the liquid-solid interface are very popular[6], so far surprisingly little work has been done on investigating reactivity in this environment at the molecular level. Only recently have the first single molecule studies of catalysis at liquid-solid interfaces been described, viz. fluorescence microscopy has been applied to monitor, by single turnover counting, chemical reactions carried out on crystal facets[7,8] and by enzymes on a surface[9-11]. However, these techniques still lack the extremely high spatial resolution that can be achieved by STM. This insight will focus on the first examples of chemical reactions at the liquid-solid interface that are studied with the highest resolution possible, by using dedicated liquid STMs.

STM at the liquid-solid interface

Many chemical reactions observed in an STM have been studied under highly inert UHV conditions, where molecules are generally evaporated or a solution of them is sprayed onto a surface with spray valve. A key advantage of a UHV environment is that a wide temperature window, varying from 4 to hundreds of Kelvins, can be applied, so that the mobility of molecules on the surface can be tuned. Another advantage of working in UHV is that superior control can be obtained over surface coverage, and sub-monolayer structures, isolated clusters, and single molecules can be studied. At first sight, when compared to UHV, performing STM at a liquid-solid interface (Fig. 1) seems to be accompanied with quite some limitations. The temperature window is limited to the melting and boiling point of the liquid, and molecules dissolved in that liquid generally adsorb to the surface in closely packed monolayers, in particular if the interaction between molecules and surface is based on physisorption (i.e. no chemical bonds are formed or broken upon adsorption). In that case the adsorption process often relies on self-assembly, which involves a continuous adsorption and desorption of molecules at the liquid-solid interface until thermodynamic equilibrium is reached. I will be no surprise that such dynamic processes are not straightforward to control. It must also be realized that the solvent is not always an innocent factor. In the case of STM studies it is generally chosen for practical reasons: it should dissolve the molecules, but not compete with them for adsorption at the surface; it should have a low vapour pressure so that during the experiment a stable liquid phase is maintained which does not suffer from continuously changing conditions due to evaporation; and it should be chemically inert, a property of critical importance when reactivity is studied. Popular liquid media nowadays are high boiling organic solvents like 1-phenyloctane, *n*-tetradecane, 1,2,4-trichlorobenzene and 1-octanoic acid, which all have a relatively low polarity so that they do not interfere with the tunneling current. This does not exclude the possibility to carry out STM experiments in highly polar liquids such as water. By making use of an electrochemical STM (EC-STM), in which two additional electrodes are employed to

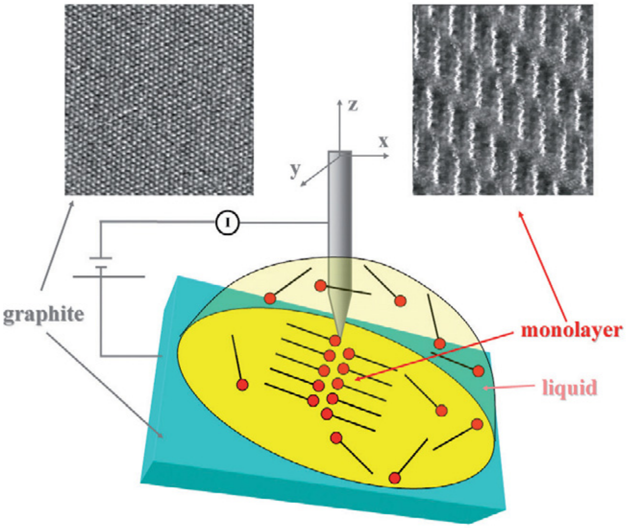

Fig. 1 Schematic representation of an STM tip immersed in a droplet of a solution of molecules on a surface and is scanning the interface. On the top left an STM image is shown of a clean graphite surface at atomic resolution, and on the top right a self-assembled monolayer of molecules adsorbed at the liquid-graphite interface. Image reproduced with permission of the Royal Society of Chemistry.

gain independent control over the electrochemical potentials of tip and sample, surfaces can be imaged in highly polar and aqueous conditions under potential control. Finally it must be noted that, although still only a few systematic studies have appeared dealing with the influence of the solvent, 2D self-assembled structures at the liquid-solid interface can be highly dependent on slight changes in solvent polarity and on variations in the concentration of the molecules in solution[12,13].

Despite the complications involved with using a liquid, there are of course also many advantages, for example the easy experimental setup which does not involve the use of high vacuum or high pressure chambers. An STM experiment at a liquid-solid interface can be simply carried out by placing a droplet of a solution onto a flat surface and immersing the STM tip into that droplet. In addition, working in such an easily accessible environment as the liquid-solid interface allows easy administration to or withdrawal of chemicals, which is of particular interest for the study of chemical reactions: reactants can be added, and the liquid phase can be easily analyzed by other techniques by withdrawing a sample, and all these manipulations can be carried out in situ while the scanning is continued.

Monitoring the conversion of reactants into products

Initial approaches to image reactivity in an STM involved the immobilization of reactive molecules at a liquid-solid interface and follow changes in their appearance during the course of a reaction. Typical examples are the conversion of hexaphenylbenzene into coronone derivatives by an oxidative cyclodehydrogenation reaction[14] and light-induced photo-isomerizations[15,16]. In those cases STM images revealed clear differences between the reactants and the products. It is even more exciting to specifically design molecules that self-assemble in a specific supramolecular arrangement at the liquid-solid interface, in a way that reactive groups become organized in such close proximity that, for example, a coupling reaction can be carried out. Following this approach, isophthalic acid molecules functionalized with diacetylene-containing alkyl chains were self-assembled at the 1-undecanol-graphite interface in lamellar arrays in which the diacetylene functions were organized close together, in an ideal geometry for a so-called topochemical polymerization (Fig. 2a)[17]. After initiation of the polymerization with light, the resulting π-conjugated polyacetylene chains could be clearly recognized in the STM images as bright strands (Fig. 2b). In a similar fashion it was possible to monitor with STM the photodimerization of cinnamate derivatives[18]. In more recent work, a monolayer of aniline molecules was imaged in an electrochemical STM (EC-STM) at the liquid-solid interface of a gold surface and aqueous 0.1 M H_2SO_4[19]. When the bias potential of this surface was increased, an oxidative polymerization of the adsorbed aniline molecules, which had a clear impact on the surface topography, was induced. Elongated structures of aligned polyaniline chains were observed with an internal structure revealing a zig-zag ordering of the monomers (Fig. 2c-e).

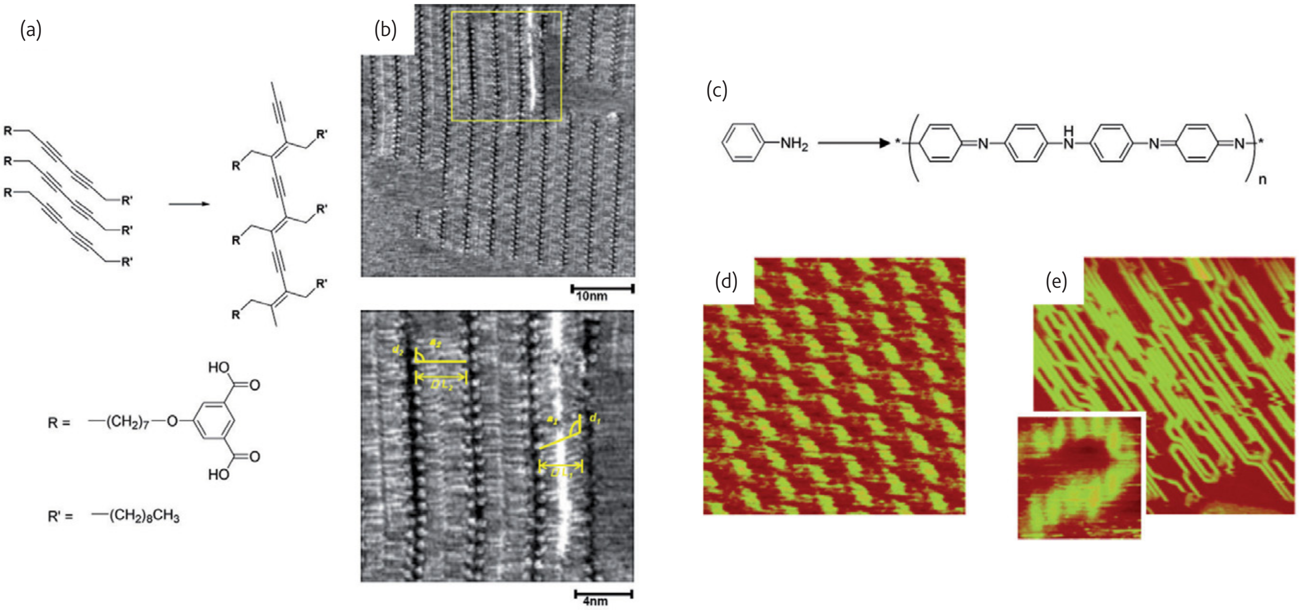

Fig. 2 (a) Topochemical polymerization of diacetylene compounds into polydiacetylenes, (b) STM image (top) and a magnification (bottom) of a monolayer of lamellar arrays of the self-assembled diacetylenes; a bright strand of polymerized molecules is clearly recognizable. (c) Polymerization of aniline. (d) STM image of aniline molecules at the interface of gold and 0.1 M H_2SO_4. (e) STM image of the interface after polymerization; the inset shows a magnification in which the ordering of the monomers within the polymers is revealed. Images reproduced with permission of Wiley-VCH Verlag GmbH and Co. KGaA, and the American Chemical Society.

Monitoring multistep reactions

A couple of years ago our group decided to explore a completely different approach of monitoring reactivity in an STM, by imaging molecular catalysts during a multistep reaction. A carefully chosen reaction, which had already been extensively studied in our chemistry laboratories, viz. the catalytic oxidation of alkenes into epoxides (Fig. 3a), was transferred to the liquid-solid interface in a home-built liquid-cell STM[20]. Instead of the reactants and products, the catalysts of the reaction, manganese(III) porphyrins, were adsorbed at the liquid-solid interface. These flat molecules expose their reactive metal centers to the STM tip and changes in their oxidation state and coordination geometry could be nicely monitored during the various steps of the reaction (Fig. 3b-d). Under an argon atmosphere, the catalysts appear as bright dots, but upon admission of molecular oxygen (O_2) to the system, they visibly undergo a reaction: the centers of several of the catalysts suddenly appeared 3 times higher in the STM image. And here, immediately the additional value studying a reaction with STM became apparent: its superior lateral resolution allows the elucidation of reaction mechanisms that remain hidden when conventional ensemble techniques are applied. In this case, statistic analysis of the reactive

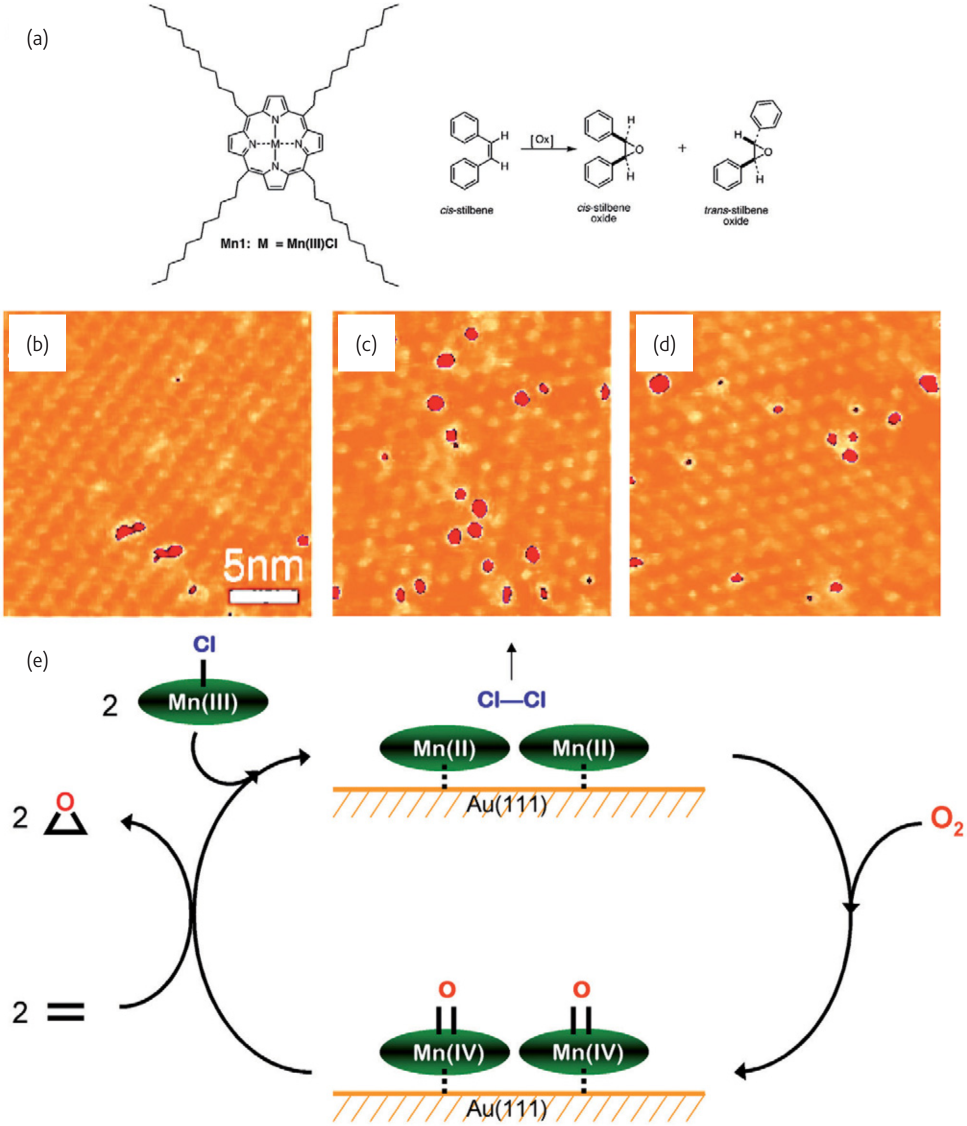

Fig. 3 Multistep reaction at the interface between gold and n-tetradecane studied by STM. (a) Manganese porphyrin catalyst Mn1 and the reaction it catalyzes in which cis-stilbene is oxidized to cis- and trans-stilbene oxide. (b) STM image of Mn1 catalysts at the liquid-solid interface under argon; note the two pairs of oxidized catalysts (red dots) between the native catalysts (yellow dots). (c) The same interface after admission of O_2 to the system. (d) The same interface after the addition of cis-stilbene to the liquid phase. (e) Catalytic cycle showing changes in the porphyrin catalyst that were concluded from the observations in the STM images.

surface indicated that each molecule of O_2 had oxidized two adjacent catalysts at the surface, by a homolytic O-O splitting and distribution of the oxygen atoms over the two catalysts. This reaction, which according to control experiments in the bulk does not occur in solution, was proposed to be activated by the gold surface by an initial reduction of the manganese centers from Mn^{III} to Mn^{II} upon their adsorption. Both this reduction and the subsequent oxidation to generate $Mn^{IV}=O$ particles were confirmed by in situ UV-vis reflectance measurements of the surface. The $Mn^{IV}=O$ species are active catalysts in the epoxidation of alkenes, and addition of *cis*-stilbene to the liquid phase resulted in a strong decrease in the number of oxidized catalysts (Fig. 3d). This observation suggested a reaction of the oxidized catalysts with the alkene molecules, which was confirmed by gas-chromatographic analysis of the liquid layer in which indeed the *cis*-stilbene epoxide product was present.

Limitations, challenges and outlook

The above examples illustrate the exciting possibilities of STM to look at the level of atoms and molecules during chemical reactions at the liquid-solid interface. However, the new approach is accompanied with several limitations, the most important one being the time resolution of the technique. Typically, scanning a surface of square nanometers with STM takes at least multiple seconds, which is very slow when compared to the time frame of many chemical reactions. Faster scanning is in principle possible, but it is generally also accompanied with a loss in resolution. Although efforts have been undertaken to develop STMs that work at video rate speeds[21], they have so far not been applied at the liquid-solid interface. To obtain increased time-resolution with STM will therefore be a major future challenge, although a careful choice of the reaction might still yield valuable results. The earlier described oxidation reaction with the manganese porphyrin catalysts is an illustrative example, since their turnover times lie in the range of multiple seconds. A second point of attention is that, in order to get a reliable view of surface reactivity, confinement of the active species to the 2D environment of the liquid-solid interface is essential[22]. When adsorption and desorption of the molecules is highly dynamic, it might be unclear if a reaction has truly occurred at the surface or in the supernatant solution. This issue can be solved by taking care that molecules are adsorbed strongly to the interface so that no exchange with molecules from solution occurs. To accomplish this, one could also change the supernatant solution by a different one in which the adsorbed molecules do not dissolve. Finally, one should always keep in mind that scanning by the STM tip is not necessarily innocent; apart from mechanical effects it can also have electronic effects on the adsorbed molecules, since nearby the tip a considerable electric field is present. For that reason it is advisable, if possible, to always correlate results obtained by STM with results obtained by complementary techniques.

Despite its limitations, I foresee an exciting future for STM as a tool to study reactivity at a liquid-solid interface. Numerous reactions from the bulk are waiting to be studied at the single molecule level at a surface, and not only will STM reveal new insights about reaction mechanisms, it might also unravel the influence of the interface itself, in terms of activity and selectivity of a specific reaction. Given the importance of active surfaces in everyday life, such fundamental insights into reactivity at the nanoscale might pave the way to the rational development of increasingly efficient functional materials.

Acknowledgments

I would like to express thanks to my colleagues from the IMM, in particular Prof. Roeland J.M. Nolte and Prof. Alan E. Rowan for laying the foundation of my scientific career, and Prof. Sylvia Speller for giving me the opportunity to develop cutting edge research in the Nano*Lab* Nijmegen; Dr. Bas Hulsken, Jan Gerritsen, Duncan den Boer, Michiel Coenen, Minko van der Maas and Thomas Habets for forming a great team of creative co-workers; Prof. Steven De Feyter (K.U. Leuven, Belgium) for being an inspiring colleague; and the Netherlands Organization for Scientific Research (CW-NWO), for financing my research via a Vidi grant. mt

REFERENCES

1 Binnig, G., *et al., Phys. Rev. Lett.* (1982) **49**, 57

2 Binnig, G. *et al., Appl. Phys. Lett.* (1982) **40**, 178

3 Foster, J. S., and Frommer, J. E., *Nature* (1988) **333**, 542

4 Ertl, G., Angew. *Chem. Int. Ed.* (2008) **47**, 3524

5 Somorjai, G., *Appl. Surf. Sci.* (1997) **121**, 1

6 Elemans, J. A. A. W., and De Feyter, S., *Soft Matter* (2009) **5**, 721

7 Roeffaers, M. B. J., *et al., Nature* (2006) **439**, 572

8 Roeffaers, M. B. J., *et al., Proc. Natl. Acad. Sci. USA* (2007) **104**, 12603

9 Lu, H. P., *et al., Science* (1998) **282**, 1877

10 Velonia, K., *et al., Angew. Chem. Int. Ed.* (2005) **44**, 560

11 Martínez Martínez, V., *et al., J. Am. Chem. Soc.* (2008) **130**, 13192

12 Kampschulte, L., *et al., J. Am. Chem. Soc.* (2008) **130**, 8502

13 Lei, S., *et al., Angew. Chem. Int. Ed.* (2008) **47**, 2964

14 Samorì, P., *et al., Langmuir* (2002) **18**, 4183

15 Heinz, R., *et al., Angew. Chem. Int. Ed. Engl.* (1994) **33**, 2080

16 P. Vanoppen, *et al., J. Phys. Chem.* (1996) **100**, 19636

17 Grim, P. C. M., *et al., Angew. Chem. Int. Ed. Engl.* (1997) **36**, 2601

18 Abdel-Mottaleb, M. M. S., *et al., Nano Lett.* (2001) **1**, 353

19 Yang, L. Y. O., *et al., J. Am. Chem. Soc.* (2007) **129**, 8076

20 Hulsken, B., *et al., Nat. Nanotechnol.* (2007) **2**, 285

21 Rost, M. J., *et al., Rev. Sci. Instrum.* (2005) **76**, 053710

22 Piot, L., *et al., Adv. Funct. Mater.* (2007) **17**, 3689