Application of Quantum Calculations in the Chemical Industry—An Overview

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The field of quantum chemistry experienced huge progress in the past two decades. The drivers for this have been the availability of more and more powerful computer hardware, the development and implementation of improved methods with a better balanced compromise between accuracy and efficiency, as well as pioneering work how these methods are successfully applied to real-world problems. Thus, quantum calculations, in particular via density functional theory, became an essential tool in many branches of chemical research. This article tries to give an overview how quantum chemical modeling is used in chemical industry, which is done by reviewing papers written by authors from chemical companies. Various topics of particular industrial relevance are introduced together with strategies how to address them via quantum calculations. Examples are the computation of reaction thermodynamics and kinetics as the key ingredients to understand and predict chemical reactivity, but also solvation models as well as methods to describe electronically excited states. © 2014 Wiley Periodicals, Inc.

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Introduction

A much cited announcement of Mulliken in his Nobel Prize lecture in 1966 was that of “the era of computing chemists, when hundreds if not thousands of chemists will go to the computing machines instead of the laboratory for increasingly many facets of information is already at hand.” For this vision of molecular simulation being an integral part of both academic and industrial chemical research to become reality, a first requirement was the availability of computers to process a larger amount of numerical operations. Furthermore, in the case of quantum chemistry, also strategies that allow for an efficient approximate treatment of the Schrödinger equation had to be developed, for example, Hückel theory or the Hartree–Fock (HF) self-consistent field (SCF) method.

Although there are numerous earlier examples of semiempirical calculations performed by researchers in the chemical industry,[1] it is rather clear that the application of quantum chemistry at a broader level started in the 1990s. In the very same years, density functional theory (DFT) emerged as a more accurate alternative to HF at still moderate computational cost if compared to correlated ab initio methods like perturbation theory (e.g., as devised by Möller and Plesset, like the popular second order approach MP2) or coupled cluster theory (e.g., explicit single and double excitations plus perturbational triples, CCSD(T)). In fact, DFT accounts for the majority of quantum chemical publications from industry along with quantum chemical application papers from academia. Also this trend is reflected in the fact that the Nobel Prize in 1998 was awarded to Pople for establishing quantum chemical descriptions), although of high relevance, as documented by a number of papers in collaboration with industrial partners,[2,3] is also not covered in the following: quantum chemistry represents rather an auxiliary discipline for this research.
area, and its inclusion would go beyond the scope of this overview.

It should be noted that this compilation of topics cannot be comprehensive as the focus of industrial research is not scientific publishing but rather documentation in internal reports and patents. However, also from patents, which represent in many cases, the only externally visible evidence of an industrial research effort, it is typically not possible to conclude if, for example, input from mechanistic studies via molecular simulations supported the disclosed invention or if a computational screening was applied to identify or narrow down a class of claimed substances. A significant amount of industrial publications containing quantum chemical results has been written in collaboration with academic partners. In these often combined experimental and theoretical papers, the industrial partner can have performed either experiments or calculations; in the following, no differentiation is made with respect to who of the authors actually provided the computational part. Finally, the amount of literature is simply so large that a selection had to be made here anyway, which has been done with the intention to introduce application fields and used modeling techniques of larger interest plus a few noteworthy standalone publications.

This review article is organized as follows: first, some examples are given where method development (including the establishment of structure–property relationships with quantum chemical descriptors) was conducted by industrial researchers or where benchmark studies have been performed to assess the predictive quality of methods for an intended application. After this, calculations of chemical reactions are presented, which account by far for the largest number of industrial papers; due to partially differing methodological approaches, this topic is subdivided into homogeneous (reactions of molecular species, in the gas phase or in solution) and heterogeneous systems (e.g., reactions on surfaces of solid catalysts). Then, some publications are reviewed where quantum chemistry has been used as an “analytic technique” for characterization of (potential) molecular structures or as a tool to support experimental spectroscopic characterization. In a next section, application of quantum chemistry to electronically excited states is discussed; the property of interest can be here, for example, excitation energy or excited state reactivity. Finally, main trends are summarized and it is assessed how quantum chemistry is creating added value in industrial chemical research.

**Method Development and Benchmarking**

In contrast to the application of computational chemistry, method development does not have an immediate value-adding output with respect to, for example, generation of intellectual property or understanding of processes, but enables the computational chemist to do so in a next step. For this reason, method development in industry normally takes place only if for an application of sufficient interest there is no satisfying method available and if the implementation of the new method can be expected to occur at a reasonable time-scale. Developing novel electronic energy expressions or

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writing full quantum chemical program packages is, therefore, not the focus of industrial research.

**Accuracy of quantum chemical methods**

To assess if a method is really suitable for an intended application, it can be necessary to perform benchmark studies of methods for (model) systems of interest, which is documented by a number of publications. There are several such papers of Meier (DSM); one of them discusses the performance of DFT methods with respect to accuracy and reliability and their ability to give an “answer to real world molecular systems.” In another article, a protocol is given how quantum chemistry should be applied for a reliable prediction of vibrational spectra, including—if necessary—anharmonicity. Also methodological benchmarks on conformer stability of hexane have been performed as well as a comparison of DFT with coupled cluster calculations applied to rotational barriers around bonds with a conjugation to aryl systems.

Accuracy becomes a particularly critical issue for the prediction of chemical kinetics as rate coefficients derived via Eyring theory depend exponentially on activation energy and entropy. The high interest in this topic is documented by a paper of Green (Exxon), which compares several DFT methods and MP2 for the prediction of activation barriers of a unimolecular alkoxy radical rearrangement. It is concluded that although DFT works surprisingly well for these systems, it is not yet as accurate as required to be most useful to the chemist. MP2 does not perform better for the considered reaction, either. In a further paper of researchers from Exxon with Green (now as the academic partner), calculations of gas-phase hydrogen abstraction reactions (relevant to model processes like pyrolysis or combustion) are presented.

This example of bimolecular reactions represents a case where the activation entropy is markedly different from zero, therefore, its computation is crucial to achieve a correct description of the temperature dependence of chemical kinetics. The methods used in this work (standard statistic thermodynamic treatment via rigid rotor, harmonic oscillator plus a hindered rotor add-on to the partition function as well as a tunneling correction according to the Wigner formula), obviously, perform well in this respect, whereas for the DFT energetics, the aforementioned uncertainty in the activation energy remains.

Not only for chemical kinetics, but also for thermodynamics of chemical reactions as well as prediction of thermodynamic data like heats of formation highly accurate calculations are required. In a paper of Dobbs and Dixon (DuPont), the calculation of (a) the reaction enthalpy of amide hydrolysis and (b) the heat of formation of formamide via consideration of isodesmic reactions is described. This work also includes a methodological benchmark (up to CCSD(T) accuracy) and a basis set convergence study.

Furthermore, a series of papers should be mentioned, in which Dixon and Matsuzawa (SONY) present large benchmarks with respect to method (DFT, HF, MP2, and semiempirical techniques) and basis set for the computation of hyperpolarizabilities. Knowledge of this property is important in the design of materials for nonlinear optical applications. The authors recommend the use of DFT or MP2 in combination with sufficiently large basis sets (diffuse basis functions). Applications to isomers of 4-aminindoaniline (as a model for its substituted forms, which are used as dyes) and to metallorphophines are discussed in further papers.

Numerous further benchmark studies have been performed to assess methods not in general but rather their predictive quality for one specific chemistry; these papers will be discussed later in the context of other literature on the corresponding topic.

**QM/MM methods**

A big issue for the application of quantum calculations to chemical problems is the condensed-phase environment in which the majority of processes take place. There is still no generally applicable technique how to account for the dynamic solvation environment of a reacting system with quantum accuracy. The modeler has either to accept severe limitations of system size or of sampling quality. In the case of processes occurring at larger catalytic systems like enzymes even a static quantum chemical treatment becomes difficult if not impossible. Such problems require a multiscale description, which means a coupling of methods with differing accuracy and computational cost, for example, combining quantum mechanics and molecular mechanics (QM/MM) as mentioned in Introduction section.

Within a European project, a consortium of Norsk Hydro, ICI (Synetix), and BASF, together with numerous academic partners, developed a flexible QM/MM approach and implemented it in the computational chemistry scripting system ChemShell. In a paper of Sherwood et al., apart from its development, application of this tool to very diverse problems is described, for example, reactions on oxide surfaces and in zeolites as well as structure and reactivity of enzymes. Two different ways how QM and MM part can be defined are given in Figure 1. The choice of the quantum chemical inner part and the question if a boundary region with link atoms is required, depends on the need of electronically reasonable fragments for the quantum chemical calculation.

In another work, Thiel and authors from BASF introduce a specific type of coupling where CHARMm force fields are used to treat the enzymatic environment around the active site of triosephosphate isomerase, whereas the active site is described by quantum chemical methods. For the coupling, an electrostatic embedding approach is presented: point charges from the CHARMm force field are included into the one electron part of the QM Hamiltonian to polarize the wavefunction. The partitioning of the system into a QM part and an MM part requires a cut through chemical bonds. Formally dangling bonds in the QM part are saturated with hydrogen and additional dipoles are introduced into the MM part to model the electrostatics of these cut bonds correctly in the QM part. To assess the validity of the embedding model, different sizes of the QM region are compared. At the BP86 level of theory the same qualitative picture for the reaction
mechanism is observed independent of the size of the QM subsystem, Figure 2; geometry optimizations including large QM regions (275 atoms) do not result in new insights. Similar checks are performed for different sizes of the geometry-optimized region. Therefore, it is concluded, that the QM/MM-description with compact QM regions already provides a consistent picture of enzyme reactivity for triosephosphate isomerase.

Although in the following some work is contained where such QM/MM techniques are applied, by far most presented studies involve just a QM model. This may be the consequence of several reasons: first, most force field development has been performed for biological systems, thus, the MM description can be of doubtful quality if elements other than H, C, N, O, P, or S are involved (or also binding situations not encountered in biology). But also the improvement of DFT codes has significantly lifted the boundary with respect to the system size where a QM/MM treatment is really required. Finally, also in the field of solvation description, where QM/MM allows in principle for dynamics with a reasonable sampling, static solvation models have become quite popular, as discussed in the next subsection.

Treatment of condensed-phase effects via solvation models

A computationally much less demanding alternative to take into account intermolecular interactions represents the static description of molecular surroundings by a dielectric continuum like in polarizable continuum model (PCM) or advanced methods based on it[19] or in COSMO (conductor-like screening model).[20] The latter has been extended by a statistical thermodynamics treatment of the interactions of the molecular surface charge densities, known as COSMO-RS solvation model.[21] According to the number of publications, the latter approach is the most widely used solvation model beyond a continuous dielectric description based on first principle calculations in industrial chemical research and engineering. The focus of this section is, therefore, largely on such applications.

An advantage of the COSMO-RS solvation model is that it represents a link between quantum chemical calculations of single molecules and thermodynamic bulk properties, without requiring chemistry specific parameters (in contrast to the thermodynamic models typically used in chemical engineering). Furthermore, in the past years, COSMO-RS has also been used to compute thermodynamics of chemical reactions in the condensed phase as a more accurate alternative to a simple continuum solvation treatment, thus, extending the scope of quantum chemistry to problems where solvation effects on reactivity are complex and dominant.

Accuracy of COSMO-RS and Method Development. The need for methods that overcome the limitations of standard gas-phase calculations has triggered method development also in industry, although, as mentioned before, extensive software development is typically not done by industrial users. Thus, the implementation of COSMO in the program package

![Figure 1](image1.png)

**Figure 1.** Schematic representation of two different ways to define QM and MM part in QM/MM approaches.[15] Reproduced with permission from Sherwood, THEOCHEM, 2003, 632, 1, © Elsevier.

![Figure 2](image2.png)

**Figure 2.** Energy profile of the enzymatic triosephosphate isomerization in the active site.[17] Different sizes of the QM and optimized region (denoted by the used method and the number of atoms in brackets) are compared.
TURBOMOLE\textsuperscript{22} has been performed by Schäfer (BASF) et al.\textsuperscript{23} Franke and Friedrich (Evonik)\textsuperscript{24} reported on an advanced way to solve the integral equations in the COSMO-RS method. Besides these developments, further work has been devoted to the applicability and accuracy of the model. The original application field of COSMO-RS is chemical engineering, where computed activity coefficients of species in multinary fluid mixtures allow for a prediction of various kinds of phase equilibria (i.e., liquid-liquid, vapor-liquid and solid-liquid equilibria); applications are documented in a number of benchmark papers. In one work, Franke et al. compare the predictive quality of equations of state approaches as implemented in the ASPEN PLUS program system\textsuperscript{25} with COSMO-RS for Henry coefficients (infinite dilution vapor pressures) of hydrocarbons in alcoholic media.\textsuperscript{26} The authors observe that COSMO-RS performs well (or is even superior to the other approaches) if experimental pure component vapor pressures are included as anchor points (in this case, only the infinite dilution activity coefficients are determined by COSMO-RS), while the prediction of the pure component vapor pressure is somewhat less accurate.

In another paper of the same authors, infinite dilution activity coefficients are again the property of interest in a study on the suitability of different quantum chemical methods and basis sets for the computation of COSMO-RS surface charge density input.\textsuperscript{27} For an unbiased assessment of the different surface charge density profiles, also the COSMO-RS parameterization has to be adapted to each of the considered methods. It is concluded that reasonable predictions can already be made with basis sets of valence double zeta quality. With respect to quantum chemical methods, the considered standard DFT functionals (within the generalized gradient approximation GGA as well as hybrid-GGA, meta-GGA, meta-hybrid-GGA) all seem to perform similarly well, whereas HF and LDA functionals appear significantly less suitable. A slightly more accurate prediction is, at least for the considered examples, observed on the MP2 level of theory.

Again, the same authors also discuss a molecular-class-based parameterization of COSMO-RS, also here for mixtures of alcohols and hydrocarbons.\textsuperscript{28} For the example of infinite dilution activity coefficients, they achieve an accuracy compared to experimental data which is close to that of the UNIFAC(Do) group contribution method.\textsuperscript{29} Such chemistry specific adaption of COSMO-RS is, of course, at the expense of its general applicability and requires a sufficient amount of consistent experimental data.

Phase equilibria involving also species in their solid state (e.g., solubilities) are a more complex problem than mixtures composed of fluids alone, as in crystalline and amorphous solids the directionality of interactions matters significantly more than in fluid systems. However, Klamt et al., together with Bayer, devised a structure–property relationship (taking into account the solute descriptors volume, rigidity due to ring structure and chemical potential in water), which is able to predict aqueous solubility of typical active ingredients like drugs and pesticides with an accuracy of around 0.5 logarithmic units.\textsuperscript{30} Finally, Diedenhofen et al.\textsuperscript{31} together with BASF, discuss the computation of vapor pressures for the very special case of ionic liquids. Assuming that the gas phase consists of ion pairs, the authors observe a good correlation between experiment and theory, suggesting that at least far below thermal decomposition (via chemical reaction) this mechanism of evaporation prevails.

COSMO-RS can also serve as a method to parameterize other simulation methods like the Perturbed Chain Polar-Statistical Associating Fluid Theory (PCP-SAFT), \textsuperscript{32} as discussed by Sadowski et al. together with Heilig (BASF).\textsuperscript{33} They devise a strategy how to derive the association energy parameter from the hydrogen bonding enthalpy computed with COSMO-RS; this represents a way how to reduce the required amount of independent experimental data points when new compounds are included into thermodynamic modeling with equation of state approaches.

Application of COSMO-RS to Chemical Reactions. As already mentioned, the accuracy of COSMO-RS suggests that this method might also be useful to perform a reliable treatment of reaction thermodynamics and kinetics in the condensed phase. To this end, the solvation model is used in a thermodynamic cycle to describe the desolvation of nongaseous reactants and the solvation of nongaseous products of a chemical conversion, whereas the actual reactive step is treated with appropriate quantum chemical methods in the (ideal) gas phase (i.e., a consideration of thermodynamics via partition functions based, for example, on the rigid rotor and harmonic oscillator assumptions). A detailed description of this workflow, Figure 3, and its application to radical polymerization in different solvents has been given by Deglimann et al. (BASF).\textsuperscript{34} In spite of deficiencies to predict absolute rate coefficients, caused by the aforementioned exponential dependence of reaction kinetics on both activation enthalpies and entropies, the relative changes in rate upon transition from one medium to another are reproduced very well, as is shown in Figure 4 for the aqueous polymerization of N-vinyl pyrrolidone at varying monomer concentration.

Whereas for reactions of neutral species the inclusion of solvation effects typically leads to an improved prediction but is usually not mandatory to, for example, qualitatively compare reactive pathways, the situation changes as soon as ions are involved, even more so if within the chemical reaction a charge separation or recombination takes place. In the latter case, solvation effects are in a similar energetic range as bond dissociations, or even larger. It has been shown that for such systems solvation models beyond continuum approaches are required and that COSMO-RS represents a reasonable choice for a computation of thermodynamics (and kinetics) in aqueous and non-aqueous media.\textsuperscript{35} However, it should be noted that there are still cases where a straightforward application of this solvation protocol leads to inconsistencies, like in the prediction of aqueous pK\textsubscript{a} values where the general correlation between computed and experimental results is good but the slope of the correlation line systematically differs from one, which means that computed Gibbs free energies of dissociation suggest an overestimation of differences in acidity or basicity.\textsuperscript{36}

Altogether, the large number of industrial papers concerning the basics, application and advancements of COSMO-RS
suggests that there is a high interest to create links between quantum chemistry and chemical engineering, whereas there still appears to be a larger gap between these two disciplines in academia.

A multiscale model for charge transport in organic materials

One further example of method development in an industrial environment represents a technique to simulate charge transport through organic semiconductors via a combination of calculations at various levels as discussed by Lennartz (BASF) and coworkers.[37] Due to the focus of this review on quantum chemistry, mainly the quantum chemical part of this work is reported here and the multiscale nature of the chosen approaches is only very briefly touched. Unlike inorganic semiconductors, which can be described by periodic band structure calculations, a more localized picture is necessary for organic semiconductors. Usually, thin films of organic semiconducting molecules are deposited from the gas phase or by liquid processing onto a substrate, resulting in highly disordered nonperiodic packing motives. Simulation of charge carrier mobility is often based on Marcus theory of electron transfer and requires at least the three following steps:

- Generation of an amorphous thin film morphology by molecular dynamics methods involving several hundreds to a few thousands of molecules.
- Quantum chemical calculation of transport parameters.
- Simulation of charge transport on a 3D grid by kinetic Monte Carlo simulations.

One computational bottleneck of the simulation lies in the calculation of transfer integrals, since they have to be determined for every kind of molecular pair within a certain distance (corresponding approximately to the first coordination sphere) to calculate the bimolecular hopping rates. An efficient implementation of a direct coupling scheme helped to study the transport of electrons and holes in Alq3 (the aluminum salt of mer-(tris(8-hydroxyquinolinate))).[38] Specifically, the difference in mobility can be traced back to the difference in delocalization of spin density of anion and cation, which has been found also earlier on a less sophisticated level of theory regarding disorder and morphologies.[39] Also a molecular rationalization for the field dependence of charge carrier mobility is given. The charge carrier pathways are spatially very randomized due to the large disorder in the system at low fields while they tend to approach straight lines at high fields, thereby being faster. These findings confirm also earlier studies at a purely classical level.[40] With a similar approach electron and hole transport was analyzed for 2,8-bis(triphenylsilyl)dibenzo-furan.[41] This material is well-suited for deep blue phosphorescent emitter dyes. It could be shown, that delocalization of the anion density over the triphenylsilyl-groups supports electron transport and reduces molecular reorganization energies while keeping energetic disorder at a moderate level.

Structure–property relationships based on quantum chemical descriptors

Many application properties of interest are difficult to directly link in a general manner to one (computationally accessible) observable. However, within certain limits, structure–property relationships can be successful in correlating these properties in a one- or multidimensional form to descriptors, which are the outcome of either calculations or experiments that have the
advantage of being less elaborate or more reproducible than full application testing. Such relationships can be more or less intuitive, depending on how far the physical link between computed and application property is known. Two examples for the setting up of such relationships are given in the following.

Li (Chevron Texaco) and collaborators discuss concepts that link lubrication between sliding surfaces provided by a number of (mainly transition metal) oxides at elevated temperature to parameters like chemical potential, absolute electronegativity or chemical hardness (which is defined as the difference between ionization potential and electron affinity divided by two) as descriptors. They conclude that there is a correlation between the desired lowering of the friction coefficients and the fractional number of electrons transferred between two contacting solid oxide surfaces, which explains to a certain extent the similar dependence on all of these parameters.

A clearly more obvious relation is expected in the case of electrochemical properties of battery constituents and computable descriptors like orbital energies, ionization potentials, or electron affinities. In one paper, researchers from Mitsubishi Chemical present the preparation and electrochemical properties of electrolyte salts of formula \( \text{Li}(\text{C}_n\text{F}_{2n+1}\text{BF}_3) \) as well as their testing in Li-ion cells, and compare results to quantum chemical calculations of the corresponding anions. It is observed that main trends in oxidation potential can be correlated with either highest occupied molecular orbital (HOMO) energy or adiabatic ionization potential, but the more subtle perfluoro alkyl chain length dependence is not covered by these simple models. Another joint publication of Mitsubishi Chemical and the software company Accelrys describes the computational high throughput screening (more than 7000 structures) of lithium-ion battery electrolyte SEI (solid electrolyte interface) additives. These chemicals are intended to undergo film formation on electrochemical reduction at the carbon anode. Their performance is correlated to (a) the electrochemistry-related descriptors of a low-lying lowest unoccupied molecular orbital (LUMO) and a high (vertical) electron affinity, (b) chemical hardness, where a low value indicates a high chemical reactivity, and (c) a high dipole moment, which hints on a strong complexation of \( \text{Li}^+ \). Apart from physicochemical intuition, this choice of a descriptor profile is validated by the fact that the known additives butyl succinate and fluoroethylene carbonate fit to these requirements.

Many further (often obvious) structure–property relationships where the computed observable is the tendency to undergo a chemical reaction are discussed in the following section as well as structure–property relationships that try to predict chemical reactivity without actually treating the chemical reaction in an explicit manner (i.e., via thermodynamics between reactants and transition states or products).

Summary

As mentioned before, within industrial modeling method development is not the objective, but represents a means to be on a longer term more successful in projects where these novel methods are applied. This makes clear that method development will mostly take place in areas of high and constant interest. For the same reason, in such new techniques it will rather be tried to intelligently combine existing approaches (and implementations) rather than to perform fully new developments. For areas where academia offers a broad variety of solutions, there would be no benefit in an industrial method development (e.g., accurate electronic energy expressions); there will rather be activities in topics that are located in between different scientific communities, like the aforementioned two examples of coupling (originally) chemical engineering tools with quantum calculations on chemical reactions or simulating charge transport via Monte Carlo techniques parameterized by both MM and quantum chemical input.

Chemical Reactivity and Catalysis

A central discipline of quantum chemical modeling in both academia and industry is to rationalize and predict the course of chemical reactions. One major reason for this is that no other method exists to compute relative molecular energetics and (via application of statistic thermodynamics) also thermodynamic functions for species and chemical conversions without chemistry-dependent parameters. Such studies of chemical reactivity, in particular in the area of catalysis, represent a very important subject in industrial molecular modeling. Some publications on catalysis contain calculations of more or less complete catalytic cycles, whereas others consider only selected reactive steps within these cycles. A few papers even focus only on the question how a complex catalyst looks like at a molecular level under the process conditions, as will be described in Application to Catalysts subsection; this can already help to establish links between one class of catalytic site and a specific reactivity, which then enables in silico searches for similar structural features.

A typical quantum chemical study of chemical reactivity would start with the determination of relative energies of reactants, products and/or transition states and from these the computation of thermodynamics (enthalpies, entropies, and Gibbs free energies) and/or kinetics (activation barriers, rate coefficients, e.g., via Eyring theory), which can then be used in many ways:

- As input parameters for chemical engineering and process simulations (heat of reactions, equilibrium constants, and reaction kinetics).
- For comparison of activation barriers of elementary reactive steps to determine product selectivity of kinetically controlled reactions.
- For comparison of different postulated mechanisms to decide how a complex process actually takes place at a molecular level.
- For construction of full catalytic cycles including the identification of resting state, rate-limiting step and to estimate the thermodynamic barrier associated with it (→ catalytic activity).
- For guidance in the design or improvement of catalyst composition and structure, based on the gained insight.
For reactions involving well-defined species in one homogeneous phase, the choice of an appropriate molecular model is usually not very difficult. In contrast to this, when reactions at surfaces are studied, for example, within heterogeneous catalysis, there is typically no general or straightforward way to approach the problem: either periodic or cluster models have to be constructed which should cover the most important features of the reactive surface under application conditions. Due to the different challenges and routes to solution for these two cases, the topics of molecular and heterogeneous reactivity are discussed in two separate subsections.

**Molecular reactivity**

As mentioned before, the choice of a model to study homogeneous reactions is typically straightforward: either species are computed “as they are” (normally without surrounding solvent molecules) or as simplified models where side groups not thought to be involved in chemical reactions are simplified, for example, as –H or –CH₃. The latter strategy is, for example, applied to long alkyl chains which may serve to make a species hydrophobic but do not strongly influence its chemical behavior, or to study reactions of polymers via small oligomeric models.

**Olefin Insertion at Transition Metal Centers.** Olefin insertion and its reverse reaction, β-hydride elimination, represent crucial steps in many catalytic processes, for example, hydrogenation, hydroformylation, or olefin isomerization, Scheme 1. Furthermore, it also represents the propagation step of catalytic olefin polymerization, which is discussed in the Homogeneous Polyolefin Catalysis subsection.

In two papers, Meier and Coussens (DSM) present computational studies of olefin insertion into the metal hydride bond of cationic Pt catalysts carrying two monophosphine ligands. Their studies compare very different levels of theory: HF, MP2, DFT; in the latter case, results from static calculations are even compared to those of Car-Parinello molecular dynamics (CPMD) type investigations. At least with the used small model phosphine ligands PR₃ (R = –H, –Cl, –CH₃) it is found that insertion barriers are quite small (around 10 kJ/mol) and rather independent of substitution at P and the quantum chemical method used.[46] In another work on this topic, it is found that for the electron deficient phosphine PF₃, even smaller barriers are computed, but also the regioselectivity of insertion in the case of propylene as olefin substrate (for which linear insertion products are preferred over the branched isomers) decreases on transition from the more electron rich phosphines to PF₃.[47] Additionally, explicit solvent effects with the donor solvent acetonitrile are studied to probe the relevance of β-agostic interactions between alkyl substituents and the metal center for olefin isomerization in the condensed phase.

The same reaction is also the topic of a recent experimental and computational paper by Beller and scientists from Evonik that focuses on catalysts prepared from Fe(CO)₅, KOH, and H₂O (computational models: trinuclear anionic carbonyl hydrido complexes).[48] The remarkable selectivity of this catalyst for 2-olefin products is rationalized by the necessity of breaking up an agostic metal–alkyl interaction, which is computed to occur most easily for terminal methyl groups.

**Olefin Metathesis.** Olefin metathesis represents another catalytic reaction, which has experienced much attention in the past decades. It can, for example, be used to exchange alkylidene fragments from olefinic substrates or to build up macro-molecules via a ring opening polymerization of cyclic alkenes. For its mechanism, see Scheme 2.

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**Scheme 1.** Olefin insertion into transition metal–hydride bonds as relevant step for a number of subsequent catalytic reactions.

**Scheme 2.** Mechanism of olefin metathesis; in the paper of Meier and coworkers,[49] M represents Cl₂(PR₃)₂Ru with R = H, whereas in practice alkyl or aryl phosphines are used.
Meier (DSM) and coworkers\cite{49} describe CPMD simulations of this reaction for the (strongly simplified) model catalyst \( \text{Cl}_2\text{(PH}_3\text{)}_2\text{Ru} = \text{CH}_2 \). They confirm the mechanism postulated by Grubbs and coworkers,\cite{50} which involves phosphine dissociation, substrate coordination and formation of a metallacyclobutane. An interesting feature of this work is the application of various simulation temperatures to study either just bond flexibility and structural fluxionality or real chemical reactivity (also after dissociating one phosphine ligand from the catalyst model to facilitate olefin coordination and conversion).

Although more than 10 years later, computer power has very much increased, the approach to use \textit{ab initio} molecular dynamics not only to get an idea of structural features but also to identify potential pathways of chemical reactivity is still restricted to very small or strongly simplified reactive systems; however, this procedure can definitively help to create mechanistic ideas if entirely novel chemistries are considered in the absence of experimental evidence.

**Homogeneous Polyolefin Catalysis.** A larger number of industrial quantum chemical publications deals with catalytic olefin polymerization. In this field, heterogeneous Ziegler–Natta catalysts,\cite{51} which will be discussed in the Ziegler–Natta Polyolefin polymerization. In this field, heterogeneous Ziegler–Natta catalysis will be discussed in the Ziegler–Natta Polyolefin polymerization. In this field, heterogeneous Ziegler–Natta catalysis will be discussed in the Ziegler–Natta Polyolefin polymerization.

For the case of Si-bridged bis-indenyli zirconocenes, that is, formation of dinuclear adducts and of ion pairs for the case of Si-bridged bis-indenyli zirconocenes. They conclude that a certain amount of steric bulk at the appropiately positions should avoid both these side reactions, thus making olefin complexation (and subsequent conversion) the preferred mode of stabilization for the cationic metal center.

The actual catalytic propagation step of olefin polymerization is the subject of the first (full) \textit{ab initio} molecular dynamics study (using CPMD) of a chemical reactive step, which has been performed by researchers from DSM in collaboration with the IBM Centre for Scientific and Engineering Computing.\cite{55} The insertion of ethylene into the \( M – \text{CH}_2 \) bond of an \textit{ansa}-zirconocene is predicted to be an extremely fast event (occurring within 150 fs). It is, however, admitted that this finding results from a neglect of the equilibrium with agostically stabilized reactant or product species, which represent thermodynamic sinks and thus slow down the overall polymerization rate.

In a study of Resconi (Basell) together with academic partners, for (already activated) \textit{ansa}-zirconocene catalysts of \( C_2 \) and \( C_1 \) symmetry, the stereoselectivity of propagation steps is predicted.\cite{56} The higher isotacticity observed when polymerizing butene instead of propylene can be rationalized via QM/MM calculations. In the case of the \( C_2 \) symmetric catalysts, it is concluded that a “back-skip” of the polymer chain occurs to a significant extent and that the resulting increase of propagation steps from one specific out of two possible diastereomeric sites is responsible for the observed degree of isoselectivity.

In collaboration of Roesky et al. with Basell, in a combined experimental and theoretical work, heterobimetallic metalloenzyme—nonmetalloenzyme catalysts of Group IV metals of formula \( \text{Cp} + 2(\text{Me}) \text{Zr(\(\mu\)-O)Ti(NMe}_2)_3 \) and \( \text{Cp} + 2(\text{Me}) \text{Zr(\(\mu\)-O)Hf(NMe}_2)_3 \) \( M – \text{CH}_2 \) (\( M \) = Zr) are presented.\cite{57} DFT is used to compare stabilities of cationic products resulting from catalyst activation with MAO to get an idea of the actually formed active species and to study monomer (ethylene and styrene) bonding to these. For the mixed Zr/Ti-complex, it is predicted that ethylene polymerization will most probably be carried out by Zr centers, whereas simultaneous styrene polymerization rather takes place at Ti.

Supported molecular polyolefin catalysts are studied by Duchateau et al.\cite{58} (in collaboration with DSM), which are prepared from substituting cyclopentadienyl chloro complexes of Ti and Zr with \( R_5\text{SiOH} \) (\( \text{Ph}_3\text{SiOH} \) and cuboctameric...
hydroxysilsesquioxane (C_3H_4)_7Si_8O_{12}(OH)). DFT is used, in this
work, to rationalize electronic differences (—acidity) of these
two silicon compounds which are singly or doubly attached as
anionic ligand R_2SiO^- to the catalytically active species.

Nonmetallocene polyolefin catalysts, based on metal centers in
the oxidation state +3 are the subject in a series of studies con-
ducted at DSM. For aluminum amidinate complexes of general
formula [Al(CH_3)(RC(NR_2)]_3^+ oligomerization thermodynamics as
well as olefin insertion are studied. In one paper from 1999, static
DFT calculations of ethylene insertion at [Al(CH_3)_2CH(NH_3)_2]^+
and [CH_3C(NH_3)_2CH_2Al(CH_3)_2Al(CH_3)(CH_2CH(NH_3)_2]^3 are also
here compared to results from CPMD: both approaches are
found to yield similar results.[39] A comparison of the activation
barriers suggests a mononuclear active species due to prohibitive
barriers for ethylene insertion at the methyl-bridged dinuclear
complex. Experimental evidence obtained only slightly later and
quantum chemical consideration of side reactions (termination
via β-hydride transfer) as well as of oligomerization equilibria at
various levels of theory, however, rather hint that a dinuclear spe-
cies must be the active catalyst.[60] Finally, in a paper from 2003,
which represents an extensive study of dinuclear complex equili-
bria for several alkyl substitution patterns at the amidinate ligands,
another dinuclear species is identified, which is energeti-
cally within reach and should in fact allow for fast ethylene inser-
tion but still prevent hydride transfer; therefore, this species is
now thought to be the actually active catalyst for olefin polymer-
ization.[61,62] Also Sc has been considered as a metal center for
ethylene polymerization catalysts: in a benchmark study, the per-
formance of DFT methods to predict catalytic activity is com-
pared to CCSD(T) for methyl diketiminato complexes of Al and
Sc.[63] It is concluded that, although absolute values of activation
barriers are quite method dependent, the relative difference
between propagation reaction and β-hydride transfer is rather
the same at all levels of theory, which makes for this class of cat-
alysts also DFT an acceptable option for mechanistic studies.

Within Group IV transition metals, researchers from DOW
describe experimental and computational studies on a triden-
tate naphthyl–pyridyl–amide complex of Hf as catalyst for ethyl-
ene/α-olefin copolymerization.[64] Via DFT studies, the fact that
a bimodal product distribution can be obtained is rationalized
by the result that either ethylene or the α-olefin perform one
single fast (irreversible) insertion step into the Hf-naphthyl
bond. This leads effectively to two different classes of catalysts
(or 10 in principle separable species, taking regio- and stereoi-
somerism into account), which then exhibit different activity and
comonomer selectivity.

Also Fujita et al. from Mitsui Chemicals report on the design
and catalytic properties of Ti and Zr complexes for olefin poly-
merization. In their papers on systems with phenoxy-imine[65]
or pyrroliide-imine[66] chelate ligands, DFT is used to gain
insight into monomer coordination modi (i.e., the question if it
coordinates cis to the growing polymer chain as a prerequisite
to propagation) and strength; from this, conclusions on cata-
ytic activity are drawn. More recent results of the same
researchers, partially in collaboration with academic partners,
also involve computational protocols with the consideration of
transition states to rationalize a high tendency toward β-H-
transfer with ethylene monomer[67] or isotacticity on styrene
polymerization[68] for further phenoxy-imine catalyst systems.

Finally, in a comparative study between different polyolefin
catalysts (models for heterogeneous systems but also metallo-
cenes), researchers from DSM and SABIC discuss hydrogen sensi-
tivity, which is the reactivity ratio between metal alkyl
gydrogenolysis and the normal olefin insertion propagation, see
again Scheme 3.[69] From the calculations, it is concluded that
there is a correlation between this property and complexity of
the model donor ammonia, that is, the more exothermic the
reaction with ammonia (due to higher electrophilicity of metal
centers), the lower the hydrogen sensitivity of a catalyst.

Polymerization of Methacrylates, Acrylates, and Other Vinylic
Monomers. Several papers of Weiss (BASF), together with vari-
ous academic partners, consider coordinative methacrylic and
acrylic ester polymerization at catalytic centers similar to some
of the above systems. The interest in these unusual polymer-
ization conditions (acylates and methacrylates are typically
polymerized under radical conditions) comes from the poten-
tial access to novel material properties (due to, e.g., higher
tacticity or a lower polydispersity).

The focus of one paper, resulting from a collaboration with
Müller and coworkers,[71] is the "anionic" polymerization of
methacrylates, initiated by organolithium compounds, in the
presence of aluminum centers (provided by AlEt_3). One of these
combined nuclear magnetic resonance (NMR) spectroscopic and
quantum chemical studies aims at obtaining information on the
active species present in the nonpolar reaction medium: it is
concluded that unimeric and dimeric complexes between Li^+
and ester enolates prevail, with the aluminum alkyl bound to
the O-atom carrying the ester alkyl group; further (carbonyl) O-
atoms from the monomer or the product will then additionally
provide a coordinative saturation for Li^+. In another paper, it is
described how structures change on adding a quaternary
ammonium chloride to the reaction mixture—-it is predicted
that the halide will coordinate to AlEt_3 and that the most favor-
able interaction between aluminum trialkyl halide anion and Li^+
is via agostic interaction with the alkyl groups.[72]

It is also studied, how initiation of the same reaction occurs
in the case of a metal free system, that is, a tetrphenylphos-
phonium ester enolate (derived from methyl isobutyrte), see
Scheme 4.[69] The significant induction period under these
polymerization conditions can be rationalized by formation of
a rather stable ylide adduct between initiator anion and cation
(in which one former phenyl ring has lost its aromaticity),
which, however, is not a thermodynamic sink anymore in case
of the bulkier propagating polymer chain end ester enolates, see Scheme 4.

Another collaboration of Weiss with Ziegler et al. concerns coordinative polymerization of acrylic ester monomers by metallocenes with Sm and Zr centers. In one paper, differences between these two classes of metallocenes are compared, that is, the question if in the propagation step a mononuclear or a dinuclear mechanism is at work.\(^ {73}\) It turns out that samarocene as well as monocaticionic zirconocenes could be catalytically active in a mononuclear propagation step. In contrast to this, neutral zirconocenes are predicted to require dinuclear complexes for propagation. From computed thermodynamics and kinetics of elementary reactions, a process model is constructed, which seems capable to account for the selectivity of the propagating insertion step. In a further paper on the same topic, side reactions that could prevent a technical application of these catalysts for acrylic ester polymerization are studied.\(^ {74}\) As a result, monocationic ansa-zirconocenes appear to be most promising due to their ability to coordinate the substrate and to allow at the same time for a fast propagating addition of carbanionic centers of complexated ester enolates to it.

In a study of Ziegler and coworkers,\(^ {75}\) together with Bayer, investigations on the copolymerization of simple olefins with polar vinylic monomers, that is, \(CH_2=CHX\) with \(-X = -CN, -COOCH_3, -OC(O)CH_3, \text{and} -Cl\) are performed at the QM/MM level. In contrast to the polymerization catalysts presented so far, here reactions at a cationic Pd(II) complex of a neutral diimine ligand are considered. The late transition metal catalyst offers the advantage of a lower tendency to full saturation and deactivation by the free electron pairs provided from the functional groups of the polar comonomers. However, the calculations still suggest a certain preference for this undesired \(σ\)-complexation. Therefore, in search for a more suitable catalyst, results are presented for hypothetic anionically or even diionically modified diimine ligands, which look quite promising in the respect that a too small \(σ\)-complexation should be suppressed, thus allowing for the desired \(π\)-complexation plus propagating insertion for the polar monomers. However, this substitution raises the activation barriers for olefin propagation (at least for the considered ethylene) to such an extent that also with these modified catalysts a real coordinative \((co)polymerization of the two different types of monomers appears to be not possible as well.

A similar problem is addressed in another QM/MM study by the same authors: they look again into the feasibility of a copolymerization between a nonpolar and a polar monomer, ethylene and aroylnitrile, at the Pd(II) complex of a bidentate monoanionic ligand which exhibits a phenolato and a neutral diazo donor.\(^ {76}\) According to the calculations, coordination and propagating insertion steps for the two monomers are sufficiently similar from an energetic point of view, which represents one requirement for a copolymerization. However, on consideration of potential side reactions, the authors identify the formation of cyclic oligomers (in particular trimers) of species Pd\(\text{Ligand}\)[\(\text{CH(CH}_2\text{-Polymer})(\text{CN})\], linked via Pd—N bonds, as a deep thermodynamic sink. From this finding, it is concluded that also this type of catalyst is not suitable for the intended reaction.

Furthermore, molecular weight build up in the polymerization of ethyl-\(\alpha\)-cyanoacrylate—both free anionically and zwitterionically—has been studied at Henkel.\(^ {77}\) For the model initiators hydroxide and pyridine, activation barriers are computed for the first five consecutive monomer addition steps. In the few earliest steps, the two systems are predicted to behave quite differently: whereas the first hydroxide attack is computed to be highly exergonic and to proceed without an enthalpic barrier (i.e., as a diffusion controlled step), the first pyridine addition, leading to a zwitterionic intermediate, is predicted to be slightly endergonic and to exhibit a significant barrier at the considered reaction conditions (THF, modeled via the solvation model COSMO). It then requires a few further monomer addition steps before both systems are predicted to propagate similarly. With these results, kinetic modeling is performed to quantify consequences of different initiation on the overall polymerization process; thus, it can be understood why under certain conditions due to slow initiation but subsequent fast propagation the obtained molecular weight distribution of products is far from the originally expected averages.

For the anionic polymerization of butadiene and styrene in hydrocarbon solvents, Frischknecht and Milner (ExxonMobil) describe a multiscale modeling approach to shed light on the aggregation behavior of polar headgroups, the growing chain ends of polymers.\(^ {78}\) Whereas the competition in aggregation state between star-like micelles and long cylindrical micelles is covered by solving the self-consistent mean-field equations to obtain stretching energies of the polymer chains in these micelles, quantum chemical calculations are performed to gain access to headgroup structures and binding energies. The authors conclude that no free alkyl-lithium ion-pairs will be present under process conditions, over a large range of chain lengths highly aggregated states are predicted to be strongly favored; this aggregation will, therefore, also influence the kinetics of propagation steps.

But also for well-established industrial processes like free radical acrylic ester polymerization kinetics of side reactions are often hardly accessible by the experiment, which complicates a kinetic modeling based on real elementary reactive steps.\(^ {35}\) Quantum chemistry can also here try to complement kinetic schemes as described by Rappe and coworkers\(^ {79}\) together with scientists from Arkema and DuPont in an extensive study on the backbiting and \(β\)-scission reactions on polymerization of methyl acrylate. The authors observe for the prevailing 1:5 backbiting reaction a reasonable agreement between DFT results and estimated rate coefficients from macroscopic modeling and sample measurements.

### Aliphatic Polycarbonates from CO\(_2\) and Epoxides

Polymerization catalysis is also the topic of various publications of Rieger et al. and researchers from BASF, which describe experiments and quantum chemical calculations on the copolymerization of CO\(_2\) and epoxides to yield aliphatic polycarbonates. The industrial interest in this reaction reflects the promise of the “green” C\(_1\) building block CO\(_2\) (being not mineral-oil based),
which, however, requires suitably energy rich reaction partners to overcome its thermodynamic inertness. Scheme 5 shows the two-step mechanism of this copolymerization and an important side reaction, cyclic carbonate formation.

One paper together with Luinstra and coworkers \cite{80} studies the mechanism of this reaction carried out at a chromium–salen complex. From calculations performed for ethylene oxide as comonomer and a simplified catalyst model, it is concluded that epoxide ring opening by a carbonato terminated polymer represents a dinuclear step (with the anionic carbonato chain end and the epoxide being bound to different chromium centers), whereas CO$_2$ needs no external activation for insertion into the metal–alcoxide bond, which thus represents a mononuclear step. As a side reaction, backbiting leading to cyclic carbonate is predicted to preferentially take place via nucleophilic attack of carbonato chain ends.

In another paper with Deglmann and coworkers \cite{81} the reactivity of the comonomers cyclohexene oxide and propylene oxide is compared for a specific dinuclear Zn catalyst of Williams coworkers. \cite{82} Computed Gibbs free energy profiles of the catalytic cycles suggest that for the desired copolymerization with CO$_2$, both epoxide comonomers are in principle suitable. However, again as an undesired side reaction, backbiting is identified to cause the observed differences in reactivity: for propylene oxide, the backbiting reaction leading to cyclic propylene carbonate is computed to be even faster than propagation, whereas for cyclohexene oxide this pathway is found to be of no larger importance, see Scheme 6. From electronic differences in propagation and backbiting transition state, recommendations are given how to design catalysts with a preference for the copolymer also in the case of propylene oxide. One feature of this work is the solvation treatment via COSMO-RS as introduced in the Treatment of Condensed-Phase Effects via Solvation Models subsection: this level of accuracy beyond continuum solvation is necessary in this case, as for the catalytic cycles, pathways involving neutral catalysts are compared to others in which polymer chain ends temporarily dissociate from the catalyst giving rise to separated anion and cation (not shown in Schemes 5 and 6).

A second paper of the same authors focuses on zinc dialkanoate (e.g., zinc glutarate) catalysts, again for the copolymerization of CO$_2$ with propylene oxide. These are actually heterogeneous catalysts; however, the calculations within this work involve very simplified models of dinuclear catalyst sites at which the rate-limiting epoxide opening step is assumed to take place. Therefore, the results should be transferable to homogeneous systems as well. It is studied, how the distance of the two metal centers influences activation barriers of carbonate as well as alcoxide attack at the epoxide, which either leads to aliphatic polycarbonates or polyethers, respectively. Results indicate that an optimal selectivity plus reasonable

\[ 	ext{Zn} \quad \text{Zn} \]

Scheme 6. Comparison of predicted kinetics for (rate limiting) productive propagation step and competing backbiting reaction (to cyclic carbonate) for copolymerization of propylene oxide and cyclohexene oxide with CO$_2$ for a dinuclear zinc catalyst.\cite{81}
activity for the polymeric carbonate is obtained if the intermetallic distance assumes values between 4.3 and 5.0 Å, which is in fact, the case in the three catalytically more active of the considered systems.

Finally, in a recent paper, preparation, application, and mechanistic studies for another dinuclear Zn complex, again for the copolymerization of cyclohexene oxide and CO$_2$ are presented. This very active catalyst exhibits the unique feature that at moderate pressure the CO$_2$ insertion is rate limiting, which hints a high efficiency of the epoxide ring opening step that is ascribed to the flexible tether between the two metal centers. Calculations support this—it is observed that for the two potentially rate-limiting steps in the catalytic cycle Gibbs free energies are for entropic reasons quite similar, although enthalpies differ markedly: epoxide ring opening is a dimolecular event in contrast to the formally trimolecular CO$_2$ insertion.

**Poly(hydroxy butyrate) from Propylene Oxide and CO.** Three further papers by the Rieger group with Molnar and other authors from BASF discuss approaches toward a synthetic poly(hydroxy butyrate) from propylene oxide and CO. The interest in this product results from the potential biodegradability of this polyester—depending on its stereochemistry. The envisioned conversion is either achieved via a two-step process, that is, involving first a reaction between the two enucts to yield β-butyro lactone (isolated as intermediate) and its subsequent ring opening polymerization, or in one single step, see Scheme 7.

Within the first strategy, one paper discusses β-butyro lactone preparation via multisite catalysis, that is, a catalyst system composed of a Co center, assumed to be Co($\text{CO}_2$)$_4$, and a Lewis acidic site. It is shown via DFT calculations and experiments (infrared spectroscopic reaction monitoring) that epoxide ring opening is only possible by a collaboration between these sites, that is, that the nucleophilic attack by Co to form a Co–C bond requires electrophilic stabilization of the resulting alcoxide intermediate. The reaction proceeds via subsequent CO insertion into the Co–C bond, CO addition to the Co-center and ring closure. Another paper presents Cr catalysts with salophen ligands for the ring opening polymerization step of racemic β-butyro lactone leading to an isotactically enriched material via chain end control. It is postulated that the reaction proceeds in a dinuclear manner and that growing polymer chains are carboxylate terminated.

In a third paper, a catalyst system is presented that allows for the direct conversion of the comonomers to poly(hydroxy butyrate). Like the multisite catalyst for β-butyro lactone synthesis, it is composed of Co($\text{CO}_2$)$_4$ plus a Lewis acid and, additionally, a pyridine derivative. DFT and experimental mechanistic studies are used to track the difference resulting from the altered reaction conditions: first, suitable Lewis acids have to bind irreversibly to alcoxide groups resulting from propylene oxide ring opening, which avoids backbiting to form lactones. Apart from this, the pyridine acts as a nucleophile to take over (after CO insertion) the acyl terminated polymer chain end, thus releasing Co($\text{CO}_2$)$_4$ from the chain, which can then perform ring opening of the next propylene oxide, that is, electrophilically activated by the carbonyl C of the acyl pyridinium intermediate. A comparison of the differing mechanisms of lactone formation and polymerization is given in Scheme 8.

**(Poly)condensation.** In many technically relevant reactions, small molecules like water are released, which is either already thermodynamically favored by itself or which becomes favorable as soon as the water or other volatile products are removed from the reaction mixture. Mechanistically, these reactions are often more complex than suggested by organic chemistry textbooks as documented in a mechanistic study of amide formation out of organic amines and carboxylic acids [in the absence of stoichiometric coupling reagents] by Whiting and coworkers with partners from Syngenta. As the postulated zwittrionic adduct between amine and carboxylic acid turns out to be unstable, another route toward the tetrahedral carbonyl addition–elimination intermediate is required; this is found to be a concerted reaction involving a second carboxylic acid as a (catalytic) proton shuttle, which fits to the fact that also aryl boronic acids are experimentally known to promote amide formation.

The aforementioned fact that equilibria can be strongly shifted toward the product side under suitable process conditions also means that via condensation chemistry polymers with high molecular weight can be obtained; polycondensation accounts, for example, for the production of polyamide-66 or polyethylene terephthalate (PET). In a paper of Shigemoto (Toray Industries) et al., the mechanism of transesterification of dialkyterephetales (which, when reacted with diols, leads on release of volatile alcohol to polymers like PET), at Sb, Ge, and Ti alcoxide catalysts is studied. A clear preference is found for a sequence of alcoxide addition (from the diol or polymer chain end) to the ester carbonyl group (which coordinates with its O atom to the catalyst) and elimination of another alcoxide group from this tetrahedral intermediate to yield an ester with exchanged alkyl substituent. The computed activation barriers compare favorably with the experiment.

**Chemical Transformations of Vitamin E Derivatives.** Four articles by scientists of DSM and various academic groups address experimental and theoretical aspects within the chemistry of vitamin E (a mixture containing mostly tocopherols, in particular α-tocopherol, see Scheme 9).

In three of these publications, DFT thermodynamics are used to rationalize observed reactivity patterns. In one study, calculations are performed on the chemical equilibrium between 5-nitrosoγ-tocopherol and its ω-quinone monoxime...
tautomer, for which the relative stability is reversed if compared to (stable) \(\alpha\)-nitrosophenol, that is, in case of the tocopherol derivative, the \(\alpha\)-quinone monoxime is preferred, which then decomposes to 5,6-tocopherylidine.\(^{[90]}\) In another work, the computed thermodynamics of ketalization behavior for oxidation products of \(\alpha\), \(\beta\), \(\gamma\), and \(\delta\)-tocopherol model compounds are found to compare favorably with the experiment.\(^{[91]}\) In the third paper, bromination of tocopherols and the same model compounds is considered.\(^{[92]}\) As should be expected from the mechanism of electrophilic aromatic substitution, the regioselectivity of aromatic ring bromination can be rationalized from stabilities of the corresponding cyclohexadienyl cation intermediates of \(\delta\)-tocopherol, the only substrate allowing for differently substituted products at the aromatic core. However, no effort is made, to computationally treat the competing \(\alpha\)-methyl bromination as well, which is postulated to occur via \(\alpha\)-quinone methide species, and thus to compare between two mechanistically very different reactive pathways.

Furthermore, in a collaboration between Netscher and coworkers,\(^{[93]}\) one step within a novel synthetic route toward \(\alpha\)-tocopherol is investigated: the methyltrioxorhenium catalyzed oxidation of pseudocumene to trimethyl-\(p\)-benzoquinone. DFT is used to compute Gibbs free energies of intermediates and transition states involved in the catalytic cycle; as rate-limiting step, the epoxidation of pseudocumene by a Re-bis-peroxo intermediate is identified. The computed solvent dependence (modeled via PCM) of activation barriers for this step is in line with the experimental finding that the fastest oxidation takes place in nitromethane medium.

These papers nicely reflect how for a topic of interest—vitamin E synthesis and derivatization—quantum chemistry can be applied to support research and development at very different levels of complexity—from simple comparison of isomer stability to catalytic cycles and their solvation dependence.

**Prediction of Product Selectivity.** Further papers describe the application of quantum chemical techniques to support preparative chemistry by rationalizing the observed product composition. This can add great value, even if a certain reaction has already been technically established, as it represents one

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**Scheme 8.** Mechanism of reaction between propylene oxide and CO, leading—depending on the Lewis acid and the presence of a pyridine—either to \(\beta\)-butyrolactone or poly(hydroxy butyrate).

**Scheme 9.** Structure of tocopherols (\(R = \) isoprenoid side chain) and model compounds thereof (\(R = H\)): \(\alpha\)-tocopherol: \(R_1 = R_2 = Me\), \(\beta\)-tocopherol: \(R_1 = Me\) and \(R_2 = H\), \(\gamma\)-tocopherol: \(R_1 = H\) and \(R_2 = Me\), \(\delta\)-tocopherol: \(R_1 = R_2 = H\).
ingredient to clarify if this synthetic route has already arrived at a theoretical optimum or not.

In a combined NMR and DFT study, researchers from Ineos and cooperation partners discuss the product composition obtained when reacting dicyclopentadiene with bicyclononadiene. A computational treatment of all potential reactive pathways (including transition states) explains why out of eight potential product species, only three endo-isomers are formed.

DFT studies form also part of a paper that describes the first total synthesis of (R)-convolutamidine A by Garden et al. together with researchers from DSM. Calculations (PM3 to identify relevant conformers, then DFT) are performed for reactants, transition states and products of the aldol reaction between acetone and 4,6-dibromoisatin, that introduces an asymmetric carbon center, and which takes place in a stereo-specific manner due to an amino acid derived chiral auxiliary reagent. Although the general preference for the observed product enantiomer is in line with the calculations, the predicted and experimental selectivity differ, for which several possible reasons are discussed (one such reason might be the fact that gas-phase DFT is used).

There are, of course, cases where product selectivity is a complex function of process conditions, including reaction time. In such cases it cannot be avoided to develop a full mechanistic picture as done by researchers from ChevronTexaco in collaboration with academic partners for the alkylation of phenols with alkenes, catalyzed by benzene sulfonic acid (as a model for macroporous cation-exchange resins). The authors identify a reaction cascade via initial sulfonic ester formation, O-alkylation, and acid catalyzed (cationic) alkyl group migration (equilibration between ipso-, ortho-, meta-, and para-position) as most favorable pathway. This also accounts for the experimentally observed initial high phenyl ether concentrations.

Also for chemistry taking place at polymers, calculations can represent a convenient way to shed light on the selectivity for certain reactive sites. In one combined EPR and quantum chemical study, Gilbert and researchers from DSM consider hydrogen abstraction reactions from linear and branched alkanes as well as linear (terminal and internal) alkenes, which model the functionalities available for crosslinking of low molecular weight polyolefins. DFT calculations on H-abstraction by alkoxyl radicals are able to rationalize the selectivity of radical attack; it is found that the favored positions for abstraction are not necessarily determined by more or less favorable reaction enthalpies (i.e., stability of the resulting radical) but sometimes rather a consequence of accessibility, for example, for the more buried secondary and in particular tertiary H-atoms in polypropylene. In a DFT study of Marque and coworkers, with Arkema, the authors draw similar conclusions for the peroxidic degradation of polypropylene, modeled as 2,4,6-trimethylheptane.

**Deriving of Chemical Reactivity from Quantum Chemical Descriptors.** In contrast to the above examples, where chemical reactions are explicitly considered with the techniques described above, structure-activity relationships with descriptors derived from, for example, quantum chemistry can also serve to rationalize reactivity. For example, if a reactive step via the same mechanism can take place at various sites of a molecule (or at different substrates), a comparison of partial charges at these sites can already allow for an estimate of preferred positions (or reactants) for electrophilic or nucleophilic attack. Similar predictions via analyses of (frontier) orbitals are in many cases possible as well.

One methodological paper of Beck (Bayer) discusses the validity of such an approach, that is, the question if maxima of the electrophilic Fukui function (the local derivative of the electron density with respect to the total molecular electron number) are suitable to predict major sites of metabolic attack. This is done for the examples of numerous drugs and agrochemicals and it is concluded that the protocol represents a valid approach, being in many cases good for the purpose of rationalization, but still far from predictive, which at least in part results from the specificity of enzymatic processes.

Another example for such approaches represents a paper by researchers from Sumitomo Chemical, which studies the industrially important Beckmann rearrangement of cyclohexanone oxime to 2-Caprolactam (as the precursor of polyamide 6) on a zeolite catalyst. Here, the shape of orbitals (analyzed via the PIO technique proposed by Fujimoto et al.) and bond distances serve as descriptors to rationalize the influence of hydrogen bonding from water and the zeolite on the tendency to undergo the desired chemical reaction.

**General Trends in Studies of Molecular Reacting Systems.** Altogether, in most of these papers on chemical reactions, a static approach is chosen (actually, none of the above studies, after the year 2000, involves ab initio molecular dynamics); selected reactive pathways, derived from the literature or chemical intuition, are studied by optimizing structures of potential conformers of intermediates and transition states and conclusions are mainly drawn from consideration of the resulting lowest energy species (according to the Curtin–Hammel principle). This approach of course involves much shorter computation times than dynamic simulations and is thus applicable to larger species. It is obvious that the trend goes from investigations for model systems to calculations of the “real” system, for example, to study a homogeneous catalyst with the ligands actually applied in the experiment (but, typically without solvent molecules, unless very strong and directed interactions are expected). However, a clear drawback of this approach is that only if the pathway actually chosen by nature for a given set of reactions and reaction conditions has been included, correct conclusions can be drawn: either the originator of such a study or the modeler performing it should be acquainted with the chemistry under consideration (at the level of elementary reactions, which is often not fully covered by chemical standard literature). This also means that when modeling is used as a predictive tool, for example, to assess the potential of a new synthetic route or catalyst, the quantum chemical study must also cover typical side reactions as well and compare the barriers associated with them to those of the desired conversion.
Although for calculations of the presented homogenous systems any quantum chemical ground state method can be applied from a technical point of view (as far as it is computationally affordable), DFT is clearly the method of choice within these studies of chemical reactivity. If post-HF ab initio methods are involved, this is rather done for benchmark purposes to decide which density functional yields a realistic description or to compute specific corrections (i.e., energetic shifts) for DFT results within a certain chemistry. For most of the above applications, DFT is expected to yield reasonable results, that is, the considered systems are composed of species that can clearly be described by a single reference wave function. Mostly “old fashioned” DFT methods are used; to rather similar extent these are either the functional BP86\cite{18} (and similar expressions within the generalized gradient approximation) or the HF-exchange containing hybrid functional B3-LYP.\cite{102} In the near future, it is expected that more recent developments within DFT, for example, functionals belonging to the “M06 family”\cite{103} or more recent functionals developed by Truhlar et al., other meta-hybrid expressions or also double hybrid methods, containing perturbative contributions,\cite{104} will be applied to a larger extent due to their promise of higher accuracy at still affordable computational cost. It appears even possible that CCSD(T) might once become the single point energy method of choice if current developments to combine local approaches (as, e.g., implemented in the MOLPRO program\cite{105} with density fitting and explicit correlation\cite{106}) keep their promise of a much better scaling behavior than the seventh power with respect to the system size (as encountered for canonical CCSD(T) so far); of course, computational cost does not only depend on formal scaling behavior, an affordable prefactor, provided by an efficient implementation, is a crucial requirement as well. Most of the presented studies do not consider solvation effects, which is justified if thermodynamics or kinetics of neutral species in nonpolar media are considered or if ionic species undergo charge conserving reactions on which charge delocalization does not change markedly. However, for many industrially relevant processes, this is not the case; thus, the availability of reasonable solvation models and robust protocols how to apply them is essential for quantum chemistry to gain further importance as a standard tool in the study of chemical processes in solution.

**Heterogeneous reactivity**

Most chemical large-scale processes incorporate steps that involve a catalyst in solid form at which reactions take place on the outer surface or in its pores. Therefore, heterogeneous catalysis is industrially by far more important than homogenous catalysis. Modeling, however, is much more elaborate and difficult in the heterogeneous case for various reasons:

- Solid surfaces exhibit a large structural variety, for example, different crystal surfaces, steps, kinks, ad-atoms, defects, and so forth.
- Catalysts very often need tiny amounts of dopants to be active or selective; the location of these dopants in the active catalyst structure is usually not well-known.
- The composition and structure of solid surfaces may change with the reaction conditions (temperature, pressure, and composition of the surrounding media).
- The catalytic activity is usually dominated by the aforementioned structural features and not by ideal, plain crystal surfaces. Therefore, a realistic description of all relevant sites is crucial.
- Methodologically, the extended nature of solid materials requires the use of either periodic structure calculations (usually based on plane-wave DFT methods), or large-scale molecular calculations on cluster models of the catalyst active site (including QM/MM or similar techniques which also involve a QM cluster). Especially the periodic calculations for realistic catalyst models are computationally much more expensive than typical molecular calculations in homogeneous catalysis.

These difficulties explain why realistic studies of heterogeneously catalyzed reactions are more rarely encountered in literature as compared to homogeneous catalysis.

**A Common Shortcut—Correlations Between Binding Energy and Activity**. Although a detailed treatment of the catalyst is inevitable for the understanding of reaction mechanisms, the usually desired screening of a large variety of materials to find an improved catalyst requires more efficient approaches. Within the last decades, concepts have been developed, which relate the reactivity and selectivity of catalytic surfaces to simplified descriptors like bond dissociation energies of adsorbates, and make use of linear relations between reaction and activation energies (Brensted–Evans–Polanyi relations) as well as scaling relations between the adsorption energies of different chemical species, see Figure 5.\cite{107}

These concepts have first been successfully applied to describe trends of catalytic activity on metal surfaces, but have meanwhile been extended to metal oxides and other types of materials.\cite{108} Haldor Topsoe in collaboration with the group of Nørskov has been especially active in these developments. Among other reactions, there are detailed papers on the mechanisms of ammonia synthesis on Ru-catalysts, methanation, and steam reforming reactions.\cite{109}

**Reactions at Internal Surfaces: Zeolites**. The earliest realistic quantum chemical calculations used in industry for heterogeneous catalysis modeling are found in literature in the later 1990s for zeolites. These crystalline materials usually have a high porosity, and therefore, exhibit large unit cells, which makes it computationally expensive to treat them with periodic methods. However, due to their well-defined structure, which can be regarded as a super-molecule, cluster models have been very successful in describing their properties and reactivity, either in fully QM or in QM/MM-type calculations.

Industrially, the isomerization and cracking of hydrocarbons are the most important applications of zeolites. Mechanisms of these reactions have been studied at Shell using HF, MP2, and DFT (B3-LYP) methods for a minimal cluster model of the active site as shown in Figure 6a.\cite{110} Within these investigations, experimentally observed reaction kinetics and product
distributions are rationalized, and the influence of the strength of the Brønsted acidic sites is assessed.

Since acidity is crucial for catalyst behavior, attempts have also been undertaken at BASF, in cooperation with Sauer et al.,[111] to quantify this property for different active sites in various zeolites. Significantly larger structural models than in the case before were taken into account to realistically assess the effects of the different zeolite lattices, see Figure 6b. In spite of involving some of the largest post-HF calculations on realistic models at that time, the authors conclude that available methods do not allow for a quantitative calculation of relative energies of protonation, although trends in spectroscopic behavior (vibrational spectroscopy and NMR) are well-reproduced.

One possibility for the transition to even larger systems represent the aforementioned QM/MM schemes. These, then also allow for the application of computationally more expensive methods to the smaller QM subsystem where real chemical interactions are to be described. This approach has been chosen by Limtrakul and coworkers[112] in cooperation with DOW to compare the adsorption of ethylene, benzene, and ethyl benzene on faujasite zeolite models. The motivation of this study are by large-scale industrial processes in which ethylene and benzene are converted to ethyl benzene, which is a precursor of styrene. With a very small QM model alone, consisting of just one Al and two Si centers, all three substrates are predicted to bind with similar strength; in contrast to this, the full QM/MM model (altogether 84 centers) not only gives the correct ranking of interaction energies (ethylene < benzene < ethyl benzene) but also yields reasonable absolute values.

Ziegler-Natta Polyolefin Catalysis. For reactions taking place at (external) surfaces, studies involving periodic models emerged also end of the 1990s. The first periodic DFT code applied to these problems was CPMD,[113] which represents an implementation of the CPMD method[45] encountered in this review already in the Molecular Reactivity subsection. Among the earliest applications of this method were studies of heterogeneous Ziegler–Natta polyolefin catalysis.

A commonly used heterogeneous Ziegler–Natta-type catalyst involves TiCl₄ on a MgCl₂ support. There are several studies on the nature of the active site(s) and the mechanism of the catalytic reaction. Using CPMD, the stability of Ti centers on various MgCl₂ surfaces is discussed by Weiss (BASF) et al.[114] together with academic cooperation partners. It is found that there is a strong interplay between structure and stability of the active site and the catalytic activity.

Figure 5. (a) Calculated energy diagrams for reaction pathways, (b) Brønsted–Evans–Polanyi relations and (c) a volcano-relation for the CO hydrogenation reaction.[107] Reproduced with permission from Nørskov et al., Nat. Chem., 2009, 1, 37, ©Macmillan Publishers.

Figure 6. Strongly differing levels of abstraction in cluster models for zeolites.[110,111] Structure on the right hand side reproduced with permission from Sauer et al., Chem. Phys. Lett., 1999, 308, 147, © Elsevier.

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Furthermore, a good matching, that is, strong binding of the Ti sites to the underlying MgCl₂ surface is required to ensure stability of the catalytic sites during the reaction. Apart from this, factors governing the regioselectivity of the polymerization are elucidated.

Advanced Ziegler–Natta catalyst systems make use of special donor additives, for example, aromatic esters, whose function is still not completely understood. Computational studies at Basell[115] and Reliance,[116] using molecular DFT methods on cluster models, come to the conclusion that the donor molecules interact favorably with some of the MgCl₂ surfaces, and thereby, stabilize certain morphologies or phases, thus generating active sites at the corners of such crystallites, as shown in Figure 7.

However, certain aspects in Ziegler–Natta catalysis like the effects of external and internal donors on Ti centers can also be understood as a quasi-homogeneous reaction, which is documented in a combined calorimetric and theoretical paper by Cavallo, together with Basell, on the interaction of donors with TiCl₄.[117]

**Fischer-Tropsch Catalysis.** The production of bulk chemicals needs very efficient catalysts to meet economic and environmental requirements. Therefore, extensive resources are devoted to these systems in industrial research. To gain understanding about the catalytic reactions and to test hypotheses about the effects of changes in structure and composition, computational methods represent a valuable tool in these developments.[118]

One example is the Fischer–Tropsch process, which could be an economically attractive route for the production of chemicals and fuels from a variety of feedstocks. The primarily produced syngas (a mixture of carbon monoxide and hydrogen) is transformed into hydrocarbon products by suitable catalysts, usually based on Fe or Co. Critical issues represent the selectivity of the catalyst with respect to chain length of the produced hydrocarbons, and the ratio of saturated and unsaturated products. Researchers at Johnson-Matthey have been particularly active in modeling these topics.[119] For example, in one paper, they investigate in detail, the reaction mechanisms on a stepped Co(0001) surface via periodic DFT calculations.[120] From the calculated activation barriers for the C—C coupling and the hydrogenation reaction for different chain lengths, they derive a chain length-dependent probability of further growth, see Figure 8. In particular, the high amount of methane produced can thus be explained.

In a study at Sasol, the poisoning effect of sulfur on Fe-based Fischer-Tropsch catalysts is attributed to the endothermcity of this CO dissociation reaction.[121] Furthermore, Sasol and academic cooperation partners investigate the coverage-dependent adsorption of CO and the CO dissociation reaction at a Fe(100) surface by means of periodic DFT calculations for slab models.[122] It is found that the adsorption energies as well as the activation barriers for dissociation are only slightly changed with increasing coverage of the surface with CO. However, the thermodynamics of the dissociation reaction change markedly: in spite of being exothermic at low coverage, they become endothermic at 50% monolayer coverage.

The latter example, as many others, shows that investigations of idealized single-site events can be insufficient to understand the behavior of catalysts under actual, i.e. varying working conditions. Very often, a multiscale modeling strategy would be needed, coupling the microscopic reaction events with macroscopic phase equilibria and transport phenomena.[123]
C-H Activation. Selective alkane and especially methane activation is currently discussed as one of the “dream reactions” in catalysis: it would allow to use natural gases more efficiently as feedstocks for the production of chemicals.

Lercher and coworkers,[124] in collaboration with DOW, present investigations on a new class of La-based catalysts for the production of methyl chloride from methane, oxygen, and hydrogen chloride. By combining kinetic investigations, spectroscopic measurements, and periodic DFT calculations, they are able to show that the mechanism proceeds via surface oxidation of Cl atoms, without a change in the oxidation state of catalyst metal atoms, which is quite uncommon in oxidation catalysis.

Further Studies of Chemical Interactions with Surfaces. Understanding and prediction of interactions with surfaces can be beneficial for problems beyond catalytic reactive events. One such issue, still within the heterogeneous catalysis context, represents catalyst degradation. This is, for example, the focus of a paper of Neurock et al., together with researchers from Shell, which describes an ab initio study of adsorption and diffusion of Ag atoms on alumina (x-Al2O3); atomic migration from small catalytic silver clusters to form large agglomerates is thought to be responsible for deactivation of ethylene oxide catalysts over time.[125] DFT calculations of the (0001) surface suggest weak binding in case of Al-termination and much stronger binding in case of O-termination. This suggests that migration occurs much more easily on the former than on the latter surface. However, on transition from these idealized to more realistic partially hydroxylated surfaces, binding of Ag atoms becomes again much weaker compared to O-terminated surfaces, which makes it difficult to draw final conclusions about the importance of Ostwald ripening for the catalyst deactivation process.

In an investigation of Cheng and other researchers from Air Products and Chemicals, the adsorption of ammonia on the (100) surface of niobium (modeled as a simple cluster consisting of just nine atoms) is studied; this finally aims at understanding corrosion via nitride formation in ammonia reactors.[126] It is found that adsorption at hollow surface sites is energetically possible, whereas on-top adsorption is rather disfavored.

Cheng et al.[127] also report on the mechanism of hydrogen “spillover” onto carbon materials: this means the competition between physisorption and chemisorption of atomic hydrogen on carbonized hydrogen storage materials, which governs the flux and distribution on these surfaces from catalytic, H2 dissociating spots (e.g., Pt clusters) to actual chemical storage sites. Although there are some minor differences between the three surface models of extended graphite sheet, single-walled carbon nanotube, and hexabenzocoronene (treated with periodic DFT), it is stated that for all these systems, a transport at ambient temperature is only possible via physisorption; the energetically highly favored C–H bond formation on chemisorption is irreversible under these conditions.

Also lubrication and consequently wear inhibition represent properties that can be influenced by chemical interactions on surfaces. One important class of oil additives in automotive engines are dialkyl dithiophosphate salts (e.g., of Zn). In a series of papers, Goddard and coworkers,[128] together with researchers from Chevron, describe force field developments for these anions and their interaction with Fe(OH)3(H2O)3 as a model for Fe(III) surface species. Via this technique, binding energies for dithiophosphates with different alkyl groups on α-Fe2O3 are predicted and it turns out that binding strength of the resulting self-assembled monolayers per surface area in fact correlates with antiwear performance in engine tests.[128] It should be noted that in another theoretical study (at the semiempirical molecular orbital level of theory) by Roberts and coworkers[129] together with Paramins Exxon Chemical, another mode of action for this class of lubricants is suggested: they hypothesize a reaction between dithiophosphate anions and the (formal) O2− anion from the oxygen-rich steel surface and conclude that complexes with an S–O bond are the energetically most favorable products (which is chemically rather surprising in the absence of molecular oxygen).

General Trends in Studies of Heterogeneous Reactivity. In summary, studies of chemical reactions at external and internal surfaces are mostly performed at the DFT level, which currently appears to be the best compromise of reliability and efficiency. The sizeable amount of industrial publications suggest that there is a large interest in studies of heterogeneous chemistry in spite of the high computational cost and an uncertainty about the transferability of results obtained for simplified models. In the future, experimental techniques that allow for a surface characterization at realistic (i.e., not high vacuum) conditions would be beneficial to further advance modeling within this research area of high economic importance.

Structure and Characterization

Almost every quantum chemical modeling includes structure optimization steps. Although this is in many cases, a consequence of the fact that for a consistent description of energetics, structures obtained at the same level of theory and converged according to the same criteria have to be compared, the optimized structures can already contain interesting information by themselves: thus, quantum chemistry can be considered as an analytical tool for structure characterization, contributing to the questions:

- Is a chemical formula or crystal structure assignment correct: does it correspond to a minimum on the potential energy surface at all? Is it stable against certain reorganizations that occur in reality almost without any barrier, for example, changes in hydrogen bonding pattern?
- It provides 3D-structures to existing species as well as so far not yet prepared synthetic targets, thus guiding the chemist to establish and pursue concepts of structure–property relationship.
Based on the optimized structures, quantum chemistry can be used to compute further properties like molecular spectra, thus again being part of a characterization workflow to assign, for example, absorptions in infrared (IR) and Raman spectra to vibrations of atoms and groups thereof. Such contributions to spectroscopy are covered in this section as well, only spectroscopic properties related to electronic excitation are discussed in the Electronically Excited States section.

Molecular structure–property relationships

One example of an attempt to trace back a specific effect to the molecular conformation is the radical quenching (and thus, polymer stabilizing) capability of N-acylated hindered amine light stabilizers, see Scheme 10. For this class of compounds, it was postulated that structures which allow for intramolecular hydrogen bonding perform particularly bad. DeBellis (Ciba) and Hass\(^{[130]}\) present an extensive study of conformations for these systems. In contrast to the above expectation, it is shown that also those stabilizers which are in principle able to form intramolecular hydrogen bonds, will, in thermodynamic equilibrium, adopt to a much larger extent structures without such interactions. Thus, this principle of molecular design does not seem to be at work. The authors also compare different methods to predict conformational isomerism for this class of compounds, and conclude that HF, post-HF, or DFT accuracy is required for reasonable results, whereas force field and semiempirical methods are unreliable.

In another paper by Koning et al. from DSM and Teijin on polyamides made up from sebacic acid, 1,4-diamino butane and the bio-based diaminoisoidide, gas-phase molecular conformations of the latter comonomer are studied at both DFT and MP2 level\(^{[131]}\). It is found that nine conformers are within a range of 4 kcal/mol and could matter in amorphous or crystalline domains of the mixed polyamide. This larger number of possible conformations facilitates any structural disorder and explains the lower degree of crystallinity upon increasing the level of diaminoisoidide. Based on the most stable computed conformers, also an assignment of magic angle spinning \(^{13}\)C-NMR signals via comparison to computed DFT shifts is tried.

Verification and refinement of X-ray structures

Not only systems with high conformational flexibility, but also structural elucidation of fully crystalline materials can require quantum chemical input or benefit from it. There are cases where X-ray structural analysis alone does not yield unambiguous results, for example, caused by the fact that it typically does not resolve positioning of protons. A computational plausibility check or a comparative study of possible tautomers can, therefore, be necessary for a full structural assignment\(^{[132,133]}\).

This technique has been used in a work of Brodski et al.\(^{[134]}\) together with DSM, on the structure of melaminium dihydrogenphosphate, an intermediate on the condensation of melaminium dihydrogenphosphate to the flame-retardant melaminium polyphosphate. Periodic DFT calculations are able to support the suggested infinite chains of melaminium cations and pyrophosphate anions, both held together in a strongly hydrogen bonded network, although due to too small energetic differences, a definite assignment of all hydrogen atom positions within the pyrophosphate moieties is not possible.

A similar approach has also been chosen by Weiss and Bräu\(^{[135]}\) (BASF) to obtain insight into the structure of hemihydrate, CaSO\(_4\)\(\frac{1}{2}\)H\(_2\)O; the questions addressed by periodic DFT are the plausibility of the structure assigned from new X-ray data (the experiment being complicated due to twinning) and again the position of hydrogen atoms. The calculation fully confirms the proposed monoclinic structure, and having established position and orientation of water molecules, the authors conclude that hemihydrate in fact contains exactly half a formula unit of water (which also was a subject of debate, before).

What does a system look like under the application conditions?

The 3D structure of molecules plays also a central role in the development of active ingredients, for example, in agrochemistry (as it does, of course, in the not further considered pharmaceutical research, too): the biological targets, that is, molecular sites where an action, for example ligand binding, is desired to take place, will typically interact with only one or a few out of many conformers a synthetic ligand can adopt. If these desired conformers are not thermodynamically preferred (or at least accessible via an “affordable” energetic penalty) in the medium of interest, the active ingredient will be quite inefficient. The fact that a conformation is observed in the X-ray structure hints at least a certain stability; however, there is no guarantee that not significantly different conformers prevail in solution due to solvation effects. This is checked, for example, in a study of Beck and coworkers (Bayer)\(^{[136]}\) for the insecticide thiacloprid, and the authors confirm that the Z-configuration around a C=\(\equiv\)N bond, as found in the X-ray structure, is also clearly preferred in aqueous solution (the medium effect being taken into account via COSMO-RS). It is obvious that studies like this have to be performed on a regular basis in pharmaceutical or agrochemical active development although the outcome will often not be published due to the low scientific challenge.

Structural understanding represents also the first step of a rational approach to catalysis at a molecular level. In one paper, van Doremaele (DSM) and coworkers\(^{[137]}\) present a homogeneous half-sandwich dimethyl titanium \(k^1\)-amidate complex as a precursor for an ethylene-propylene...
polymerization catalyst. In addition to the X-ray structure, DFT calculations are used to study bonding within a dimeric dicarbonyl resting state from catalyst activation and suggest the presence of two doubly agostically bridging methyl groups. In another work of Duchateau et al. with DSM, aluminosilasequioxanes are studied as molecular models for Lewis and Bronsted acidic sites of zeolites and aluminosilicates. DFT is used to confirm the presence of a strong intramolecular hydrogen bond, which is suggested by $^1$H-NMR and IR spectroscopy for the Bronsted acidic \(((c\text{-}C_5H_9)\text{Si}_5\text{O}_{10}(\text{OSiMe}_3)(\text{OH}))\) for the calculations, a smaller model is used in which $c\text{-}C_5H_9$ is substituted by $H$.

Assignment of vibrational spectra

The assignment of bands in IR and Raman spectra can be an important contribution of quantum chemistry, as demonstrated by several papers. This type of study adds particular value when systems are considered where the vibrational spectrum cannot be easily understood as a combination of contributions from isolated functional groups for which accurate tabulated values are available.

Application to Small Species.

In a paper of Börner with cooperation partners from Evonik, the tautomerism between secondary phosphine oxide (R$_2$HP=O) and phosphinous acid (R$_3$P—OH) for several substituents R is investigated. One motivation of this study is that the latter form can coordinate via the lone pair at P to metal centers and thus serve as a novel class of ligands. Both NMR and gas-phase DFT energetics agree that the equilibrium is markedly on the side of the phosphine oxide unless particularly electron withdrawing R are employed. However, for the very electron deficient tetrafluoro-4-pyridyl substituent, calculations suggest that the phosphinous acid form can coexist or even represent the dominant species, which is confirmed by the experiment. For this choice of R, computed IR spectra are compared to the experiment in different solvents, which allows not only for a quantification of tautomers in the equilibrium but also to decide which rotamer of the phosphinous acid with respect to the P—O bond is present.

In another work, Chen et al. (DOW) consider Raman spectra of oligobromides, which have the potential to serve as a more manageable form of elemental bromine. For the first time, the authors detect via this spectroscopic method anions of formula Br$_7^-$, Br$_8^-$, and Br$_9^-$ and perform a structural assignment based on DFT calculations. It is concluded that for Br$_7^-$ and Br$_8^-$, structures with three or four Br$_2$-units attached to one central Br-atom are preferred, which agrees with the relative stabilities of isomers predicted by DFT.

Application to Catalysts.

Lennon and coworkers, together with Ineos, describe IR and inelastic neutron scattering studies of the interaction between $\gamma\text{-}Al_2O_3$ and methanol and substantiate their conclusion of adsorbed methoxy species on the (110) surface by periodic DFT calculations. A characteristic peak at about 2600 cm$^{-1}$ is found to arise as a combination band from the methyl rock and deformation of the adsorbed methoxy species.

Another paper of Selent and coworkers, together with Evonik, presents a very regioselective rhodium diphosphine catalyst for olefin hydroformylation. The authors show that for the hydrido dicarbonyl resting state, the most stable conformer exhibits a bis-equatorial arrangement of the diphosphine ligand, which is concluded from a comparison of computed and experimental position and intensity of C—O stretching vibrations of the two carbonyl ligands (i.e., in the spectral region between 1900 and 2100 cm$^{-1}$).

The fact that the applicability of quantum chemistry is not limited to stretching and bending vibrations of strong covalent bonds is demonstrated by Meier (DSM) et al. in a work on aluminum methyl chloride complexes (models for Ziegler–Natta cocatalysts). It is suggested that DFT calculations in fact also allow for an assignment of bands in the far infrared region.

Application to Polymers.

Also for polymers, the combination of vibrational spectroscopy and quantum chemistry allows for an insight into features beyond the often well-known “primary structure” of chemical connectivity; and it is these molecular conformation dependent intra- and intermolecular noncovalent interactions that govern many polymer properties.

In one study on the biodegradable polyesters poly(3-hydroxybutyrate) and poly(3-hydroxybutyrate-co-3-hydroxyhexanoate), Ozaki and coworkers together with Procter&Gamble explain the particularly high frequency of the $—\text{CH}_3$ asymmetric stretching mode in IR and Raman spectra of the crystalline material by a C—H:O hydrogen bonding between methyl groups and the carbonyl O of ester groups of two helical polymer chains in a parallel arrangement.

Further computational studies by Konica-Minolta and Procter&Gamble consider 2D vibrational dynamic compression modulation spectra of PET and a specific polyimide. DFT is
used to assign vibrational bands, and, in the case of PET, also to differentiate between gauche and trans conformer. However, no attempt is made to predict features of the 2D spectra or the effects from compression by quantum chemical means.

There are also several studies on perfluorinated polymers (or polymer precursors). Again, the influence of hydrogen bonding is discussed, here its consequences for the OH stretching region of IR spectra, which is studied in two papers by Radice (Solvay) et al. for macromeric perfluoropolyether diols. The property of interest is the preferred interaction partners of terminal OH groups, which are found to form, depending on medium and chemical structure of the perfluoropolyether, O–H . . . F hydrogen bonds to the neutral alkyl fluoride groups as rather uncommon hydrogen bridge acceptors.

Vibrational spectra of perfluorinated terminal amides (based on similar perfluoropolyethers), which represent corrosion inhibitors, are the subject of a further paper. These amides are studied in perfluorinated solvent at different concentrations, which has an influence on the intermolecular adducts formed between amide functionalities, again through hydrogen bonding. Via DFT calculations, spectra of free amides and oligomeric species thereof are predicted, which allows for an assignment of the experimentally observed concentration dependent peaks. Thus, the combination of IR spectroscopy and DFT can be used as a technique to obtain insight into intermolecular association.

The same authors also describe the application of DFT calculations to interpret Raman spectra (both applied in the classical manner and as 2D correlation spectroscopy) of perfluoropolyethers with peroxo groups in the backbone (resulting from their preparation via oxidative polymerization of tetrafluoroethylene). Although predicted frequencies of O–O stretching modes are somewhat lower than in the experiment, the computation allows also here for an unambiguous assignment of observed bands.

Finally, they also describe studies of one single partially halogenated ether of formula CClF2-CF(CF3)-O-CF2-CH3. With this well-defined molecular model for hydrofluoropolyethers, IR spectroscopy with assignment of bands from DFT predictions is again used as a tool to gain insight into conformational equilibria.

Another study of 3M compares perfluorinated proton exchange membranes for (fuel cell applications) with respect to IR spectra of the corresponding characteristic sulfonic acid group carrying side chains. Although DFT calculations are again successful in assigning spectral bands in the fingerprint region, the authors conclude that their original target to establish an IR spectroscopy-based assessment of membrane degradation cannot be achieved due to low intensities of bands associated with ether bonds.

Assignment of NMR spectra

Prediction and assignment of NMR spectra is another potential application of quantum chemistry; the available software allows for such studies at various levels of theory. There is, however, less literature on industrial application to NMR than to vibrational spectroscopy. This might be a consequence of the fact that chemical shifts are accessible at good accuracy via databases and parameterized empirical predictive tools, at least for (standard) organic chemistry.

Giesen and Zumbulyadis (Eastman Kodak) perform in one paper a benchmark of the accuracy obtained via HF, MP2, and DFT in the prediction of 13C-NMR shifts. As results obtained via the B3-LYP functional in combination with moderately sized basis sets exhibit already a systematic correlation with the experiment, they propose a linear fit function for optimal predictive power (including a special parameterization for C-atoms attached to halogen atoms to account for spin–orbit coupling effects).

Among published applications, there is one paper of Meier (DSM) et al. that performs a comparison of DFT methods for the quantum chemical prediction of 13C-NMR shifts for 2-amino benzothiazole and 2-methylamino benzothiazole (which respresent metabolites of the pesticide methabenzthiazuron) and 2-benzoylamino benzothiazole (a model compound for reaction products of these metabolites with hemic soil constituents). The authors observe that the dependence of results on density functional and basis set is small and recommend the use of the GIAO (gauge independent atomic orbital) or CSGT (continuous set of gauge transformations) methods.

One application of DFT to solid state NMR has already been mentioned in Molecular Reactivity subsection. Another paper of Bhaduri (Reliance) discusses functionalized MCM-41 mesoporous molecular sieves. The covalent linkages formed on reaction with various silyl chlorides and silicon-containing alkyl chlorides are studied via heteronuclear NMR spectroscopy (using fast magic angle spinning), and an assignment of 29Si, 13C, and 1H chemical shifts is performed based on DFT calculations.

Assignment of EPR spectra

There are also reports on industrial application of quantum chemistry to EPR spectroscopy, although not many organic sales chemicals exhibit a nonsinglet ground state as a prerequisite to apply these techniques. One such exception are N–O centered radicals, which can be present in the structurally isomeric N-alkoxyaminyl or aminoxyl form, see Scheme 11. These (sometimes) persistent radical species are the subject of two papers by Tanaka (Sumitomo Chemical) et al.; application of these substances can be, for example, in spin-labeling, as polymerization mediator or in radical batteries. One work deals with the question which DFT methods allow for the best prediction of 14N hyperfine coupling constants (a0N) and g-factors. It is observed that with respect to a0N, the predictive quality for aminoxyl radicals is highly dependent on the used
density functional (a high amount of HF exchange seems helpful, here), whereas for N-alkoxymaminyl radicals, the agreement is rather satisfying independent of the DFT method. For g-factors, the predictions for N-alkoxymaminyl radicals are generally better than for aminoxyl radicals. In a further publication, the authors not only discuss $\alpha_N$ and $g$-factor prediction but also the product selectivity of C-radical addition to organic nitroso compounds which yields—depending on substitution patterns—either aminoxyl of N-alkoxyamine isomer as also shown in Scheme 11.[159]

In a further DFT study by Yokojima (Mitsubishi Chemical) et al.[160] of an electrochemically oxidized diarylethene (which could, e.g., find application as part of a molecular switch), $^1$H and $^{19}$F hyperfine coupling constants are predicted (at the B3-LYP level) for the open and isomeric ring closed structure. From the resulting assignment of spectra, the ratio between these two isomers is derived.

**XPS assignment**

Although an X-ray absorption and subsequent core electron emission definitely leaves a molecule in an excited state, XPS is not discussed in the following section on excited state treatment but in the following subsection: the obtained spectra are typically interpreted on the basis of the initial ground state electronic structure. In a paper of Meier (DSM) and Pijpers,[161] Koopmans’ theorem is applied to HF orbital energies corresponding to the C$_1s$-level of various vinlyc, oxygen-containing polymers. It is concluded that the shift of these levels induced by neighboring O-atoms is reproduced. No improvements are recognized when applying the more complicated $\triangle$SCF procedure. Therefore, in a later paper, an interpretation based on HF orbital energies is also used to discern between trans- and gauche-conformation of PET.[162] Finally, in a further paper, a linear relation is established between atomic charges, calculated at the semiempirical AM1 level,[163] and XPS core level shifts of the elements C, N, O, and F.[164] With this established, also correlations for charges and finally XPS shift prediction at transition metal centers (attached to the ligand atoms C, N, O, and F) are presented.

**Application to mass spectrometry**

Quantum chemistry can also help to rationalize or predict mass spectrometric experiments, for example, by studying the aggregation (or fragmentation) behavior of ionized species. This is, for example, the case in a paper of Lammertsma and coworkers[165] in collaboration with researchers from DSM which studies the binding strength of various monocations (Na$^+$, K$^+$, and Cu$^{+}$) to ethylene glycol oligomers. From the smallest cationic metal–oligoxyglycol complexes observed in MALDI-TOF-MS experiments, a complexation energy threshold is derived, which is minimally required for a complex to be long-lived enough for detection. When comparing this threshold with complexation energies of a number of metal monocations by alkanes (up to dodecane), it becomes obvious that MALDI-TOF-MS detection of polyolefins with traditional ionization techniques is rather not expected (with some chance, one exception might be complex formation with late, first-row transition metals).

Also in a paper of researchers from Air Products and Chemicals, in cooperation with the software company Molecular Simulations, complex formation between metal cations (Na$^+$ and Ag$^{+}$) and a class of surfactants is studied.[166] These polyethylene glycol-based surfactants contain a C=C unit in their hydrophobic part, which accounts for a much stronger interaction with Ag$^+$ than with Na$^+$. Considering the fact that Ag$^+$ binds also slightly more strongly to the etheric O-atoms, it is rationalized why TOF-SIMS suggests higher maxima of the molecular weight distribution in case of ionization with Na$^+$ than with Ag$^+$.

**Summary**

Altogether, the applications collected in this section illustrate the large scope of useful information that can be extracted from insight into molecular structure and the understanding of molecular spectra by assignment of complex peaks. Compared to other cases (as encountered in the above and the following section), where choosing a suitable quantum chemical method is crucial for reasonable results, structure optimization is quite method insensitive, and thus, standard DFT with moderately large basis sets is expected to be fully sufficient for such studies. This also holds for the calculation of second energy derivatives for vibrational spectra. An exception represents of course systems where the description by a certain DFT method is not only inaccurate but also results in a qualitatively incorrect potential energy surface (e.g., if dispersive interactions are dominant but not taken into account by the chosen method or if a wrong electronic ground state is predicted).

**Electronically Excited States**

So far, all the above work considers only properties and interconversion of species in their electronic ground state. However, huge progress has been made in the past decades also for a description of excited states, and there are numerous examples of the industrial application of these methods (although clearly fewer than for the topics of the two sections before).

**Prediction of electronic excitation energies with time-dependent density functional theory**

Although the DFT formalism has been developed for electronic ground states, time-dependent density functional theory (TDDFT) represents a popular extension to treat electronically excited states as well.[167] Its promise of being computationally rather cheap (if compared to post-HF methods for excited states) has triggered its applications also by researchers from industry.

Guillaumont and Nakamura (Mitsubishi Chemicals)[168] report on the prediction of absorption spectra (wavelengths as well as intensities) for various classes of dye molecules and compare with experimental data. Overall, it is concluded that first transition energies are reproduced within a few tenths of eV.
A further paper discusses this requirement of structural rigidity upon electronic excitation as a prerequisite for efficient emission in the case of Cu(I)-tripod complexes. Emission from these complexes is usually limited due to a rotation in the excited state, yielding a planar excited state in contrast to the tetrahedral ground state. However, it could be shown by the support of DFT calculations, that the rotation is effectively hindered in caged Cu(I) tripod systems, shown in Scheme 13, which thus allows for emission in solution and in the solid state. Triplett geometries are optimized at the unrestricted Kohn–Sham level (using the BP86 functional) in both studies.

Less problematic with respect to emission quenching dynamics in the excited state are hexacoordinate Ir(III)-complexes, which are currently among the most promising candidates for phosphorescent emitters in the OLED industries. The accurate prediction of emission wavelength for potential emitter candidates is of great interest to focus lab resources on the most promising candidates. It is shown that again unrestricted Kohn–Sham DFT for the excited triplet state is a powerful tool to predict emission behavior of a series of Ir(III)-complexes. The peak wavelength is approximated by the vertical de-excitation energy at the optimized triplet geometry. Using a constant shift to correct for the too small band gap description inherent to the used BP86-functional, a good absolute correlation with experimental results is obtained, as shown in Figure 9. Moreover, the model is successfully applied to also predict emission wavelengths for a new class of carbene-based Ir(III)-emitter molecules in the deep blue spectral region, which is verified by a comparison to the experiment.

Besides wavelength and emission efficiency, also the emissive rate is of interest for these complexes. Here a relativistic treatment involving the zeroth-order regular approximation in combination with the B3-LYP functional is among the methods of choice. Excited singlet and triplet states are calculated via TD-DFT and spin–orbit coupling is accounted for via perturbation theory. For structure optimization, again unrestricted Kohn–Sham DFT is sufficient. The big difference in emissive rates between mer-tris(N-dibenzofuranyl)-N′-methylimidazole)Ir(III) (25 µs half-life time) and fac-tris(2-phenylpyridine)Ir(III) (3 µs half-life time) can be

Properties of organic light emitting diodes emitters

The area of organic electronics and the need of emitter molecules for the application in organic light emitting diodes (OLED) or absorber molecules for organic photovoltaic cells has triggered several quantum chemical studies on excited state properties. In this field, Lennartz and other scientists from BASF have been particularly active, which is documented in the following compilation of papers.

One topic of particular interest represents phosphorescent emitter molecules, since these allow for a conversion of 100% of the excitons formed by electron-hole recombination to light. In one work it is discussed that Pt(II) complexes containing 1,2-bis(diphenylphosphanyl)benzene as a chelating ligand and two anionic cyano ligands usually show no photoluminescence in solution. However, in the solid state, emission can be observed. DFT calculations reveal, that the quadratic planar ground state of the complex undergoes a geometric rearrangement to a distorted tetrahedral structure in the triplet state, see Scheme 12. The origin of this distortion and the character of the electronic states after the rotation are rationalized by an orbital correlation diagram. Since such a substantial change in the excited state geometry allows for efficient coupling to vibrational modes, consequently a nonradiative decay behavior is observed. The packing of the rigid crystal structure effectively prevents this distortion via specific stacking interactions.
well-reproduced and traced back to the differences in metal d-orbital contributions to the HOMO-level of the molecule, which is much more pronounced in the latter case. A comparable approach was used by Younker and Dobbs (DuPont) to calculate emissive lifetimes of nine phosphorescent Ir(III)-complexes. Good agreement with respect to the experiment could be achieved.\textsuperscript{[175]}

There are further studies on OLED emitters: Karatsu and coworkers\textsuperscript{[176]} together with scientists from Mitsubishi Chemicals, also report on absorption and emission properties of substituted tris(phenylbenzimidazolinato)Ir(III) complexes. Treatment of these systems with DFT and TD-DFT is observed to yield satisfying results where a comparison with the experiment is possible. Han and Lee (LG Chem)\textsuperscript{[177]} discusses in a paper, calculation of absorption and emission energies for a methylated derivative of the singlet emitter Alq\textsubscript{3} (which has already been mentioned in subsection 2.4). It is found that compared with the semiempirical ZINDO method\textsuperscript{[178]} and singlet excitation configuration interaction, the TD-DFT method (with the B3-LYP functional) yields the best agreement with the experiment.

**Figure 9.** Comparison of experimental and computationally predicted peak emission wavelengths for Ir(III)-based OLED emitters.\textsuperscript{[179]} Reproduced with permission from Erk et al., SID Symposium Digest of Technical Papers, 2006, 37, 131. © Wiley.

Charge transfer at organic interphases

Apart from the emissive fate of excited states, generated by recombining charges, also the opposite process, that is, an excited driven separation of charges is of great interest in the area of organic photovoltaics, where the aim is to harvest as many electrons as possible from incident photons. Calculations of the initial charge separation step, therefore, require at least two molecules, where in the initial state one molecule is in a local excited state and the neighboring molecule in its ground state. In the final charge-transfer state, one molecule is transformed into a radical-cation and the other into a radical-anion. Since the reaction is taking place in a solid state environment, very different stabilization effects can be expected for the local excited state compared to the extremely polar charge-transfer state.

Also for this issue, there are publications describing modeling activities at BASF. One paper discusses a QM/MM-type approach using an electrostatic embedding scheme, which is applied to account for environmental effects on the energetics of excited states.\textsuperscript{[179]} Specifically, charge separation at a merocyanine/C\textsubscript{60} interface is examined. Supramolecular calculations of the local and charge-transfer states for this molecular pair are performed at the approximate coupled cluster singles and doubles (CC2) level of theory. TD-DFT approaches are not used due to their well-known deficiency to describe charge-transfer states properly. The electrostatic environment is represented via atom centered point charges and dipoles. The point charge field is determined including polarization effects in a self-consistent manner in a purely classical calculation (i.e., classical representation of excited state and charge transfer (CT) state through fitting the quantum mechanical densities). It is shown that via this approach, the difference in performance measured for two types of geometric orientation of the merocyanine molecules relative to the C\textsubscript{60}-molecule correlates with the changes in energy difference between the local excited state and the charge-separated state, see Figure 10.

Whereas charge separation dynamics is important for organic photovoltaic cells, ground state charge separation mechanisms are of great interest with regard to electrical doping of organic semiconductors. In a further paper, also the role of charge-transfer states is examined for a well-known charge-transfer salt in the solid state, the system tetra-thiafulvalene/tetracyanoquinodimethane (TTF-TCNQ).\textsuperscript{[180]} It turns out to be necessary to choose a bilayer structure with coplanar orientation of the molecules as model to rationalize recent experiments involving colaminated crystals, as shown in Figure 11. Biradicalic charge-transfer ground states formally require multireference approaches, therefore, multireference configuration interaction calculations based on a complete active space SCF reference wavefunction (CAS-SCF/MRCI) are performed to generate a theoretical reference. It turns out, that the CT-state is well-above the ground state for QM-clusters of varying size, thus it is concluded that single reference techniques can be applied as well. Subsequently, besides standard density functionals also long-range corrected functionals are examined. Whereas standard hybrid density functionals fail to describe the interface electrostatics, the best fit with the theoretical reference data is observed with the \textit{ω}B97X functional.\textsuperscript{[181]}

The fate of excited states of UV absorbers

Another important application field of excited state methods is focused reaction dynamics. A detailed molecular picture of the photochemical and photophysical behavior of ortho-hydroxyphenyl benzotriazoles is of great industrial importance since they serve as the core of many UV absorbers. Debellis (Ciba) and Robb, together with further academic partners, have been active on this topic. In one paper, they examine details of the excited state dynamics of this lead structure as well as several derivatives by combined CAS-SCF and TD-DFT studies.

In a first study, TD-DFT calculations (B3-LYP) are used as a calibration point for CAS-SCF calculations.\textsuperscript{[182]} Although the
CAS-SCF treatment does not account for dynamical electron correlation in a balanced way, it can be shown that qualitative features of the excited states are well-reproduced. Based on the CAS-SCF potential energy surface the following conclusions about the mechanism can be drawn, which are also in agreement with experimental findings: first, a singlet charge-transfer state is generated via a $\pi\pi^*$ transition which transfers the OH-proton via a small barrier due to an avoided crossing between the CT-state and an $n\pi^*$-state to the ortho N-atom of the triazole. The resulting keto tautomer relaxes very efficiently to the ground state via a conical intersection, as depicted in Figure 12. In this work, the conical intersection is explicitly characterized using the initial relaxation direction$^{[183]}$ method.

The photostability of benzotriazoles can be further improved, if the triazole moiety is transformed into a triazine, as discussed by the same authors.$^{[184]}$ In contrast to triazoles, the first excited state is here not of CT-character but rather of $\pi\pi^*$-delocalized nature. This state transforms into the keto tautomer via a forbidden crossing due to an interaction with the higher lying charge-transfer state. Furthermore, computations suggest an extended seam of crossing for the $S_1$ and $S_0$ states all along the proton transfer coordinate, see Figure 13. Together with the shape of the $S_0$ surface, which always favors a return to the $S_0$ ground state structure, the outstanding stability of these triazines as UV absorber can be understood.

In another study, intramolecular proton transfer in ortho-hydroxybenzaldehyde is examined.$^{[185]}$ Whereas the papers discussed so far are semiquantitative with respect to the energetics as dynamic electron correlation is not taken into account at the CASSCF level, here CAS-SCF in combination

Figure 10. Two different scenarios for an interfacial system composed of mercocyanine and C60. The QM region in the discussed approach$^{[179]}$ consists of each one mercocyanine and C60 molecule. All close-by nonsymmetry equivalent pairs have to be calculated. Reproduced with permission from Ojala et al., Adv. Funct. Mater., 2012, 22, 86, © Wiley.

Figure 11. Relative orientation and size of the molecular aggregates constituting the interface of the system TTF-TCNQ.$^{[180]}$ Reproduced with permission from van Regemorter et al., J. Chem. Phys., 2012, 137, 174708, © AIP Publishing.
with perturbation theory (CASPT2) for the CAS-SCF optimized structures is applied. Barriers calculated for the excited state dynamics are in reasonable agreement with the experiment. In contrast to the above systems, decay channels leading to potential degradation of the absorber via an oxetene species are predicted.

Summary

The industrial application of excited state methods comprises (partially relativistic) TD-DFT, but also a larger amount of ab initio methods like CAS-SCF, partially in combination with perturbation theory or large-scale MRCI calculations, as well as approximative single reference coupled cluster approaches like CC2. Sometimes, electrostatic embedding schemes are used to account for the effect of surrounding media.

Obviously, these methods are not as regularly applied in the industry as, for example, calculations on chemical reactivity (Chemical Reactivity and Catalysis section), at least this is suggested by the smaller number of publications. One probable reason is the lack of a real black-box method to treat excited states. Furthermore, multireference methods are computationally very expensive and require expertise to obtain reasonable results at all.

Conclusions

In the past two decades, the scope of problems that can be seriously addressed by quantum chemistry has strongly broadened. This is the consequence of a huge increase in computer power, the development of robust and more accurate methods as well as their efficient implementation, and also progress in the way how chemical problems are translated into computational models.

However, any approach to a specific question will always represent a compromise between accuracy and expected computational effort. This is, in particular, the case for modeling in an industrial environment, where a reasonable answer is expected to be given in due time and at minimal cost with respect to required man and computer power. Such a compromise can look quite different from case to case: for process modeling and design, the highest possible accuracy (typically with respect to both energy method and entropic plus solvation treatment) may be required; however, there are other tasks where a qualitative thermodynamic estimate is fully sufficient or where only a rough virtual screening based on easy to calculate properties like molecular structure or dipole moments is needed.

The output of computational modeling is either prediction or better understanding; particularly in the latter case, modeling often provides complementary information to the experiment. Quantum chemistry can serve to close gaps where a decision from experimental data alone is not possible (or at least difficult) and—if based on this a selection criterion has been identified—as a screening technique to point out candidates for experimental synthesis and testing. Thus the added value of computational chemistry is not to replace the experiment but to serve as a key discipline for the transition from trial-and-error based to targeted research and development. It is expected that this synergism offered by a combined experimental and theoretical approach will in the future even more become a standard procedure to tackle fundamental questions in industrial chemical research.

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