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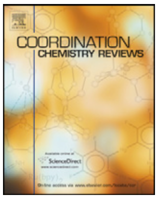

Review

Computation of structures and properties of transition metal compounds

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ABSTRACT

The computation of electronic structures of transition metal complexes has been developed in recent years to an extent where a large variety of spectroscopic properties and reactivities of mono- and oligonuclear transition metal compounds can be efficiently and reliably computed and interpreted with ab initio and semi-empirical quantum-chemical methods. These computations are often based on known structural data, and the interpretation of the electronic structures usually involves the comparison of computed and experimentally observed spectroscopic data and/or reactivities. The prediction of molecular properties, which eventually may lead to a rational design of novel complexes with given properties, requires as an important additional step a reliable structure prediction. The identification of factors which influence molecular structures of transition metal complexes and the ensuing approaches for a reliable structure optimization are an important basis for electronic structure calculations, and this is discussed in detail.

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1. Introduction

The discovery of novel transition metal complexes with exciting properties is often to a large extent based on serendipity and on the careful observation and interpretation of experimental data with classical models such as approaches derived from qualitative molecular orbital or ligand field theory, methods based on parameters related to donor-acceptor strengths or empirical concepts based on geometric and steric effects. It is quite general that, for compounds with novel and exciting properties, a subsequent thorough analysis of experimental data – state-of-the-art spectroscopy, magnetism, thermodynamic properties and/or detailed mechanistic information – with sophisticated electronic structure calculations is performed to interpret the experimental data and fully understand the novel compounds. As a result, new models and theories may emerge, possibly leading to rules how the relevant properties of the new class of compounds may be improved. There are also examples, where novel types of compounds or novel mechanistic ideas have emerged from theoretical studies or from a close collaboration of theoretically oriented chemists with experimentalists; recent examples include the discovery of the first molecular Fe^{VI} species [1], the experimental characterization of HgF_4 [2], the prediction and observation of multi-state reactivity in iron-based oxygen activation [3,4], the discovery of an elusive, biologically relevant $Cu–O_2$ complex [5,6], the investigation of copper-oxygen intermediates, capable of hydroxylating areas [7] and the search for

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the elusive high-spin $Fe^{IV}{=}O$ model system (an example, where the final *experimental* proof is still missing) [8–12]. In many other cases, it is the experience, intuition and creativity of experimentalists, based on the accumulated knowledge, often including biological systems and theory-based investigations, which lead to important achievements (selected examples, not discussed here in detail are given in references [13–16]).

From a general point of view, the still loose but in many areas increasingly efficient collaboration between experimentalists and theoreticians is satisfactory. However, in specific areas, there still is a hope and chance for improvement. An interesting example is that of single-molecule magnets (SMMs, see Section 2.3), where in the last decade enormous progress in terms of the theoretical and physical basis has been reported [17]. However, despite extensive preparative efforts [18], the first SMM, an Mn_{12}–oxo complex, in terms of efficiency is only outdone by one new compound and only by a very small margin [19–21]. Not only in this area, one therefore would hope that, the pure serendipity-based search for novel systems (believed to be the major way to success in the preparation of new SMMs) [17,18,22,23] will make way to a thorough theory-driven rational design, based on a reliable structure prediction and sophisticated electronic structure models.

We appreciate that there is an increasing overlap and cross-fertilization of preparative chemistry, the experimental investigation of molecular properties, theory and modeling. In many areas, a thorough interpretation of experimental data, often based on electronic structure calculations, has helped to create new models and rules, which then have inspired experimentalists to the synthesis and investigation of new compounds and reactions. The approach described here, which stresses the correlation of structures and properties, the possibility to enforce structures on transition metal centers by well designed organic ligands and, importantly, a reliable structure prediction, leading to a combination of theory, structural modeling and experiment, is in our view an accessible and scientifically appealing extension of the usual approaches but of course not the only possible route to success.

1.1. *Correlation of molecular structures and properties*

Structure correlation is a classical method for the thorough analysis and interpretation of molecular properties [24]. In transition metal coordination chemistry, the type of donor atoms and their arrangement around a metal center determine the properties of a complex to a large extent. Other factors related to the tuning of molecular properties by structural modifications are the variation of substituents at the periphery of a ligand to modify the solubility (used, e.g., for metal-ion-selective extractions [25]; note that hydrophobicity has also been proposed to change the properties of the metal center [26], and charged peripheral substituents have been shown to influence the electronics of the metal center in a similar way as electrostatic fields in metalloproteins are tuning the electronics of the reactive center [27]); substitution at the ligand periphery has also been used to modify the ligand conformation and therefore, e.g., the complex stability [28,29]; and the modulation of the shape of the active transition metal ion site has been used to stabilize specific substrate-catalyst interactions and destabilize others (used, e.g., in the area of enantioselective catalysis [30] and for the stabilization of meta-stable intermediates in mechanistic biomimetic studies [31]. The role of the protein in enzymes in shaping the environment is another well-appreciated structural aspect of importance, and there are various examples of modeling these particular structural features [32–34]. Here, we concentrate on the coordination geometry and its influence on the electronics of the coordination center.

Classical methods for interpreting the properties of transition metal complexes are the HSAB principle (*H*ard and *S*oft *A*cids and *B*ases), where the types of donor atoms and metal centers are classified and rules for preferences in metal–donor combinations have been derived [35–38], and ligand-field-theory-based approaches, where the geometric arrangement of the donors around the metal center is analyzed and used to interpret spectroscopic and magnetic data [39] and also stabilities and reactivities [40], e.g., using the empirical Irving–Williams series [41–43]. An example, which demonstrates how various properties can be derived from the type and geometric arrangement of the donors around a metal ion, is given in Table 1 and Fig. 1, where the redox potentials as well as electronic and EPR spectra of macrocyclic–ligand–copper(II) complexes are shown to be correlated with the donor set (N vs. S) and the size of the macrocycles (13- to 16-membered). The important observation is that the structure of these copper(II) complexes is enforced by the ligand (square pyramidal vs. square planar vs. tetrahedral, described by the angle θ in Fig. 1b; the 14-membered macrocycle has the right size for square planar coordination to Cu^{II}, the 13-memberd ring is too small and leads to a square pyramidal distortion, the 15- and 16-membered rings are too large and lead to tetrahedral distortions), and this defines the redox and spectroscopic properties, i.e. there is a good linear correlation of θ with the various molecular properties (Fig. 1c–f) [44–48]. These correlations might be accepted as a particularly well-behaved quantitative structure – property relationship (QSPR), others have been described in the area of metal-ion-selective extractions [52–55]. Empirical force-field calculations (molecular mechanics, MM) were quite expectedly shown in most of these examples to be a reliable predictive approach for the various QSPRs. Other not widely enough appreciated approaches related to structure correlations are those derived from the continuous symmetry measure (CSM) [56], which also include applications related to structure – property correlations similar to those shown in Fig. 1, and related to blue copper proteins [57], as well as applications involving enantioselective catalysis [58].

Table 1

Electronic parameters and redox potentials of copper(II) complexes containing macrocyclic ligands with various donor sets (the $Me(NO_2)[n]aneN_4$ ligands are those shown in Fig. 1a) [46,59,60]

Compound	Electronic transition (cm^{-1})	EPR		$E_{1/2}$ (V) vs. NHE
		$g_{\parallel}$	$g_{\perp}$	
$[Cu\{Me(NO_2)[13]aneN_4\}]^{2+}$	18,020	2.18	2.05	−0.34
$[Cu\{Me(NO_2)[14]aneN_4\}]^{2+}$	20,830	2.19	2.05	−0.54
$[Cu\{[14]aneN_4\}]^{2+}$	19,610	2.19	2.05	−0.47
$[Cu\{Me(NO_2)[15]aneN_4\}]^{2+}$	18,180	2.21	2.06	−0.42
$[Cu\{Me(NO_2)[16]aneN_4\}]^{2+}$	17,240	2.21	2.06	−0.22
$[Cu\{Me(NO_2)[14]aneN_2\text{-}cisS_2\}]^{2+}$	18,730	2.16	2.038	−0.025
$[Cu\{[14]aneN_2\text{-}cisS_2\}]^{2+}$	18,760	2.145		+0.075
$[Cu\{[14]aneS_4\}]^{2+}$	17,540	2.10		+0.60
$[Cu\{Me(NO_2)[14]aneN_2\text{-}cisO_2\}]^{2+}$	17,300			−0.51

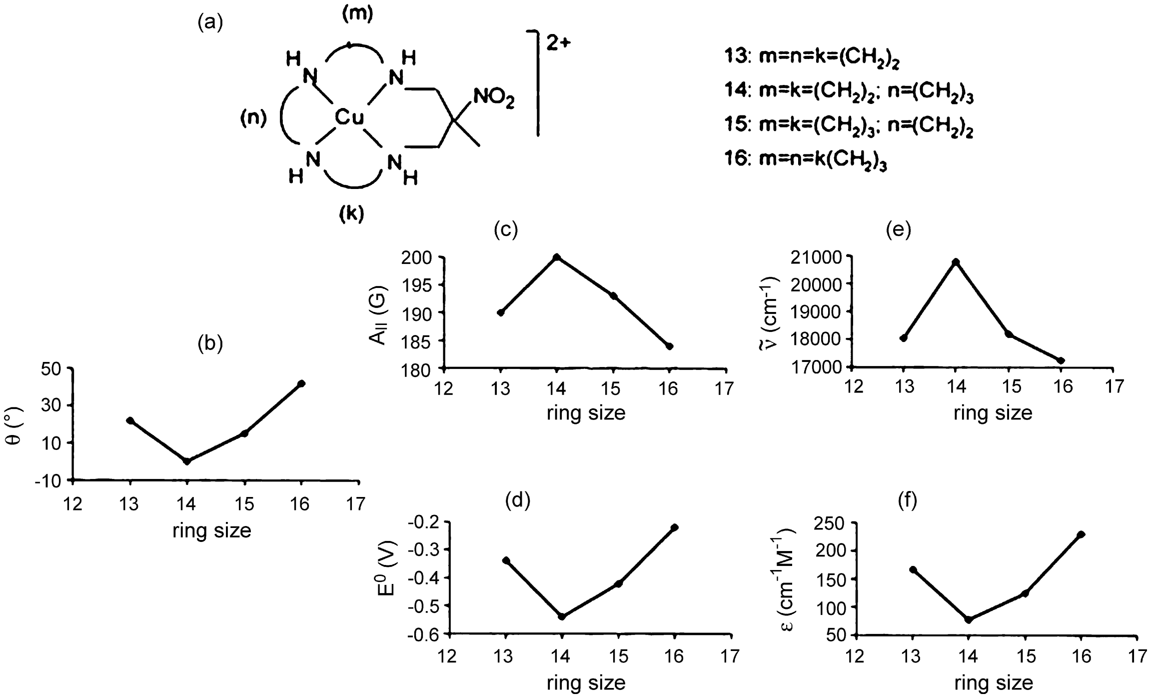


Fig. 1. Correlations of spectroscopic and electrochemical data of a series of copper(II) compounds (a); with the tetrahedral twist ($\theta = 0^\circ$ for planar, $\theta = 90^\circ$ for tetrahedral) (b); EPR parallel hyperfine coupling (c); redox potential (d); dd transition energy (e); dd transition intensity (f)[46].

Concluding this section we stress that thermodynamic and electronic properties as well as reactivities of transition metal complexes to a large extent depend on the coordination geometries. It follows that prediction and interpretation of properties imply a detailed understanding of and knowledge how to influence molecular structures. An important attribute of transition metal complexes is that the metal–ligand distances and to an even larger extent, the ligand–metal–ligand angles are much more elastic than the organic backbone of the ligands and, therefore, the coordination geometries and, consequently, the properties of the metal center may to a large extent be enforced by a careful choice of ligands [46,61–63].

1.2. Computation of molecular properties

MM may be used to compute properties directly derived from steric effects. In areas, where this is relevant, MM is not only an appropriate and efficient but also in terms of reliability and accuracy a competitive and often the only approach which allows to fully separate steric from electronic effects [64]. Major contributions to complex stabilities and metal ion selectivities such as ligand preorganization and complementarity, derived from the shape and size of ligand cavities (host molecules) and their flexibility and elasticity, as well as the corresponding preferences of metal ions (the guests) are among those features which have been successfully predicted by MM [62,65–67]. Redox potentials are related to complex stabilities (see above) and, for specific classes of metal complexes, MM has been used to compute redox properties with acceptable accuracies [50,68,69]. MM has also been used to optimize transition states and, in specific areas again, this can be useful as an efficient way to optimize catalyst selectivities [70]. Conformational searches, based on MM and data mining, have been used to elucidate interesting mechanistic details of metalloprotein-catalyzed reactions [71,72]. MM has also been used in combination with electronic and EPR spectroscopy (experiments and spectra simulations; ligand field theory, often based on the angular overlap model, AOM); with electronic parameter sets carefully fitted to experimental data and structures refined by MM, it was shown that it is possible to accurately and reliably predict spectroscopic parameters, and this was primarily used to determine structures of mono- and oligonuclear complexes in solution [45,73–76].

While there still are reasons to use some of these methods for specific applications, bonding, spectroscopy and reaction pathways are generally and often efficiently and reliably computed with quantum-chemical methods (QM); approximate density functional theory (DFT) is usually used for mechanistic work, and time-dependent DFT (TD-DFT), spectra-oriented CI (SORCI) and ligand-field-based DFT methods (LFDFT) are the appropriate methods for the computation of spectroscopic parameters which have been developed, validated and used in the last decade [77–89]. We do not dwell here on these methods; they are well described in the references cited here and discussed elsewhere in this special issue of Coordination Chemistry Reviews, and examples of specific applications will be discussed below.

In conclusion of this section, we note that, quite generally, electronic structure calculations are used for interpreting experimental data. Therefore, experimental structural data often are available and the QM methods then used are single point calculations based on experimental structural data. The question arises what the sources for accurate structural data are, when these are not available from experiments. Obvious possibilities are structures optimized by MM or QM methods, and advantages for each method in terms of efficiency, reliability and accuracy are discussed below. The main reason to perform single point QM calculations on given structural data is that a reliable calculation of the electronics often requires a setup which is too expensive to allow for a full structure optimization. Therefore, it is not uncommon that in examples, where the structure optimization is based on QM methods, the electronic properties are refined with a more expensive single point QM calculation, based on structural data obtained by a less costly QM model [90]. The general and obvious problem of deriving molecular properties from an electronic wavefunction computed from a structure which was not refined with the same model is that the structure is not a minimum on the potential energy surface (PES). The general opinion is that the approximations used in DFT lead to a situation where it is appropriate to use slightly different methods for structure optimization, the calculation of energetic properties and various electronic features, in particular in the field of transition metal complexes. That is, single point calculations of the electronics of transition metal complexes on structures derived from experiments, "cheap" DFT or MM calculations bear the problem that the wavefunction is slightly distorted because it does not describe a minimum on the PES but the errors generally are small and the reliability of the results usually is acceptable.

1.3. Molecular structure optimization

From the two sections above it immediately emerges that the design of novel compounds with desired properties and the fine-tuning of a known class of compounds with the aim to improve a certain property, in general and of transition metal complexes in particular, requires a reliable structure prediction. It is our experience and it also emerges from the literature that empirical force-field-based methods (MM) have considerable advantages in terms of efficiency, reliability and accuracy if appropriate methods for conformational analysis and structure optimization are used [63,91–97]. The higher *efficiency* of MM with respect to electronic-structure-based methods is undisputable and, for more than average-sized molecules, a QM structure optimization is with current hard- and software capacities not competitive for molecular design purposes. More importantly, the *reliability* of an optimized structure also is related to the global energy minimum structure on a warped potential energy surface or (even better) to a set of structures with similar energy, i.e. a conformational search may be required to define the relevant structure, [92,105] and this is, due to the computational expense, difficult to achieve with QM methods. Lastly, in terms of *accuracy*, it is our opinion that MM calculations may be equivalent or even superior to QM structure optimizations, provided a well-tuned force field is used [63,92,106–109]. It appears that for hexamine cobalt(III) complexes and a few other classes of classical coordination compounds [63,110] accurate enough general force fields are available, and in other areas custom-made specific force fields for specific classes of compounds have been reported [51,106,111–122]. The major draw-back of MM therefore is missing parameter sets for specific problems and the tedious parameterization procedure if published force fields are not available [123], although a variety of force-field fitting schemes have been described [116–118,124–133].

Generally, in QM studies, often using approximate density functional theory (DFT), the accuracy of the optimized structures is not a central point of contention. However, when accurate structural data are required, the tuning of the model used (functional and basis set) may also be difficult [134–136], and a thorough comparison of experimental with computed data based on MM on one hand and DFT on the other quite often indicates that the former are of superior quality [63,91,137]. It appears that the quality of both MM and DFT calculations depend on the method (force field, functions and parameterization; functional and basis set), and this emerges from the fact that both are empirical and semi-empirical methods, respectively.

MM was for a long time believed to be difficult if not impossible to apply to transition metal complexes [138]. Three major reasons discussed were the multifarious coordination numbers and geometries, leading to difficulties in defining the coordination angles and functional forms to describe them, the large variety of possible oxidation states and corresponding electronic structures, and the electronic influence exerted by the partially filled d-shell. The first of these problems is of entirely technical nature, and a variety of solutions have been developed [61,63,106]. The second problem, the fact that metal ions exist in various oxidation and electronic states implies that for each of these a separate parameter set needs to be defined and developed, much the same as carbon atoms in organic molecules have differing parameterization schemes in dependence of their electronic structure (e.g., sp^3, sp^2, sp^1 hybridization and the corresponding angular geometries) [139], i.e. the only problem resulting from the large diversity of transition metal complexes is the requirement for very extensive parameterization schemes [63,106,107,110,140].

The third reason given for a possible failure of MM in the area of transition metal compounds is related to the problem of properly describing d-orbital-based electronic effects and requires a more extensive discussion. Among the various approaches, the "points-on-a-sphere" model (POS) and the ligand-field-augmented MM model (LFMM) are the most significant [141]. Others, in particular the elegant valence-bond-MM approach, have for various reasons not attracted much attention in the field of coordination chemistry [125,143–145]. The basis of the POS approach is the observation that angular functions around a metal ion (L-M-L) have shallow potentials, and this also emerges from experimentally observed vibrational frequencies. The idea to replace the potential energy term for angular strain around metal ions by 1,3-repulsive forces [146–148] has the added advantage of a large simplification of the force field because metal–ligand stretching is then basically the only function which needs to be parameterized for each metal-center–donor-atom combination; also the problem of the need to pre-define the angular geometry disappears [63,140]. The idea of defining the angular geometry by donor-atom–donor-atom repulsion is derived from Kepert's geometric model with rigid ligands and constrained metal–donor distances [149,150], and the justification is that metal–ligand bonding in classical transition metal complexes is, due to the radial distribution of the *n*d orbitals in comparison with the corresponding $(n+1)$s and p orbitals, primarily governed by the spherically symmetrical s orbitals [151]. On a more qualitative basis, this might have been expected and is related to the general observation that multidentate ligands are successfully used to enforce specific coordination geometries (see Section 1.1). Minor deficiencies of the POS approach, due to subtle electronic effects, have been successfully treated with an additional ligand-field-based correction term with a generic parameterization [152], and a model for optimizing tetragonal copper(II) Jahn–Teller systems has also been developed [153]. However, the most elegant and for transition metal complexes generally applicable MM scheme is LFMM, based on a POS approach and including an AOM-derived potential added to the usual potential energy terms [154–156]. LFMM has been parameterized and extensively tested in the area of copper(II) complexes, where the extent and direction of Jahn–Teller distortions have been reliably predicted [157,158], and in the area of nickel(II) complexes, where a single parameterization scheme was used to accurately model complexes with $S=0$ and $S=1$ electronic ground states [159] (see also Section 2.2).

To conclude this section, it appears that MM is the method of choice for an efficient, reliable and accurate prediction of structures of transition metal complexes. The required methods are available but might need some adaption for specific types of complexes. MM is an interpolative approach. Therefore, the major problem is the appropriateness and accuracy of the force fields, and these include the functions used and their parameterization. Moreover, conformational searching and the modeling of effects emerging from the environment (solvation and crystal lattice) are not routinely considered. One final note for caution relates to the fact that quite often, force fields, especially those used in transition metal chemistry, are primarily fitted to structural data and therefore are not necessarily tuned to relative energies, which somewhat limits their use in the prediction of conformational equilibria [160,161].

2. Examples

There are many areas of transition metal chemistry where the concepts and combination of methods discussed above are relevant and where a considerable number of examples have been reported [63,92,163]. The three areas selected for the present account describe in Section 2.1 an example, where the coordination geometry is enforced by a very rigid ligand and the structure prediction as well as reasons for steric strain may be perfectly well computed by MM; the qualitative interpretation of the electronic properties and the observation of a rare example of a pentacoordinate cobalt(III) complex is based on qualitative ligand field theory arguments but a quantitative interpretation requires electronic structure calculations; in Section 2.2, an area, where state-of-the-art force-field calculations (LFMM) have recently been published and where a vast amount of experimental data has been interpreted by QM calculations in combination with the experiment; and in Section 2.3, an area, where it is implicit that the combination of electronic structure calculations along with structural modeling is much needed to define new directions for preparative work.

2.1. Rigid ligands

One of the central points made in this publication is that metal–ligand distances and the angular distribution of ligands around a transition metal center are more elastic than the geometries of the organic backbone of multidentate ligands. Rotation around single bonds is the major point of “weakness” of ligands, leading to flexibility (various possible conformations) and elasticity (adjusting of the shape and size of a cavity) in ligands [62]. Rigid ligands are reinforced with respect to single bonds in the ligand backbone, and this may be achieved by fused rings or multiple bonds [46,47,62,63,140,164–166]. An art in coordination chemistry is to design (and prepare) rigid ligands (and their complexes), which are able to enforce a desired coordination geometry and therefore a specific property. We have found in recent years that the extremely rigid bispidine-derived ligands (see Fig. 2) can enforce very specific structures and properties to metal ions. Various aspects of this chemistry have been reviewed [167], and some highlights include the stabilization of end-on-peroxo-dicopper(II) complexes [168], efficient catecholase [169,170] and aziridination [171,172] activities of copper–bispidine systems, efficient oxygenation catalysis of iron–bispidines [12,173] and the possibility to tune the spin states in high-valent iron–bispidines [10,11,136] and the Jahn–Teller distortion in copper–bispidine complexes [174–176]. The latter example (Jahn–Teller isomerism) and its reliable modeling (prediction) is another example of the efficiency of the LFMM model [160].

The example discussed here in some detail is that of the pentadentate bispidine L^3 which, in comparison to L^2 leads to six- instead of five-membered chelate rings involving py3, N7 and the metal center (see Figs. 2 and 3). There are drastic differences with respect to the structural and electronic properties and reactivities between $\{ML^2\}$ and $\{ML^3\}$ fragments. The most challenging observation is, that with cobalt L^3 is able to stabilize hexacoordinate cobalt(II) ($S = 3/2$), hexacoordinate cobalt(III) ($S = 0$) as well as pentacoordinate cobalt(III) ($S = 1$) complexes (see Fig. 3) [177]. Based on the assertion that the coordination geometry, specifically with rigid ligands such as the bispidines, is largely enforced by the ligand, and based on the claim that this is best modeled by MM, it is not astonishing that from an MM-based analysis (see Fig. 3d) the N7-M-py3 angle and repulsion between the coligand X and the α-protons of py3 emerge as the major factors for the destabilization of the hexacoordinate cobalt(III) structure (Fig. 3a vs. b) [177].

However, an analysis of this system, only based on MM, misses the important electronic aspects: the corresponding cobalt(II) complexes are hexacoordinate [178] and concomitant with the structural change of the cobalt(III) complexes there is a change of the electronic ground state (*low-spin* ($S = 0$) vs. *intermediate-spin* ($S = 1$), see Fig. 3c). The key is that there is a combination of steric and electronic effects leading to the bistability in the case of the cobalt(III) system of L^3. The point to make here is that it is possible to study the steric effects separately by MM (Fig. 3d) and the electronic effects by DFT (Fig. 3c and e) – a clear separation of the steric from the electronic effects is not possible with an electronic structure calculation alone [179].

2.2. Copper proteins

There is a rich literature on copper proteins and, for type 1 or blue copper sites in particular, there is an interesting history, specifically also in terms of structure-property correlations. Important

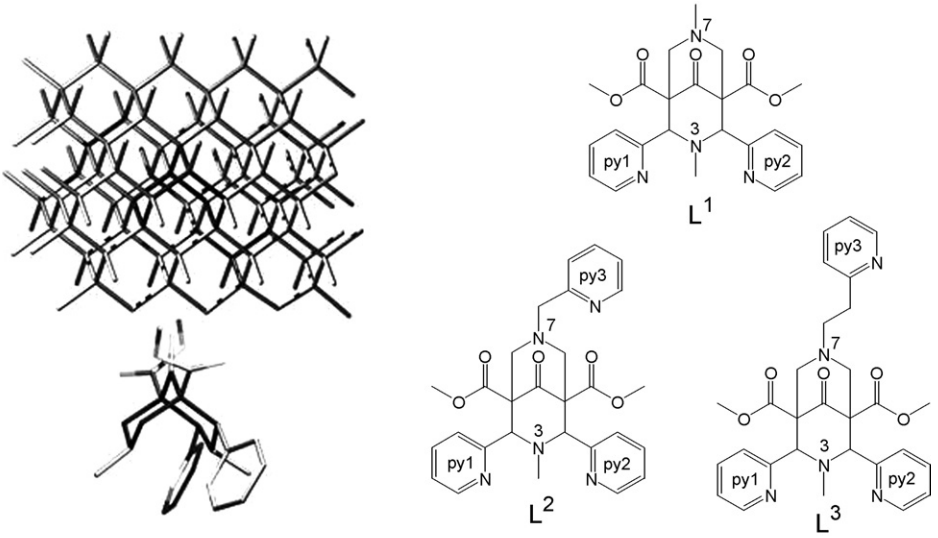


Fig. 2. The structure of diamond in comparison with the structure of the obviously rigid bispidine ligand L^1, and drawings of the bispidine ligands L^1, L^2 and L^3.

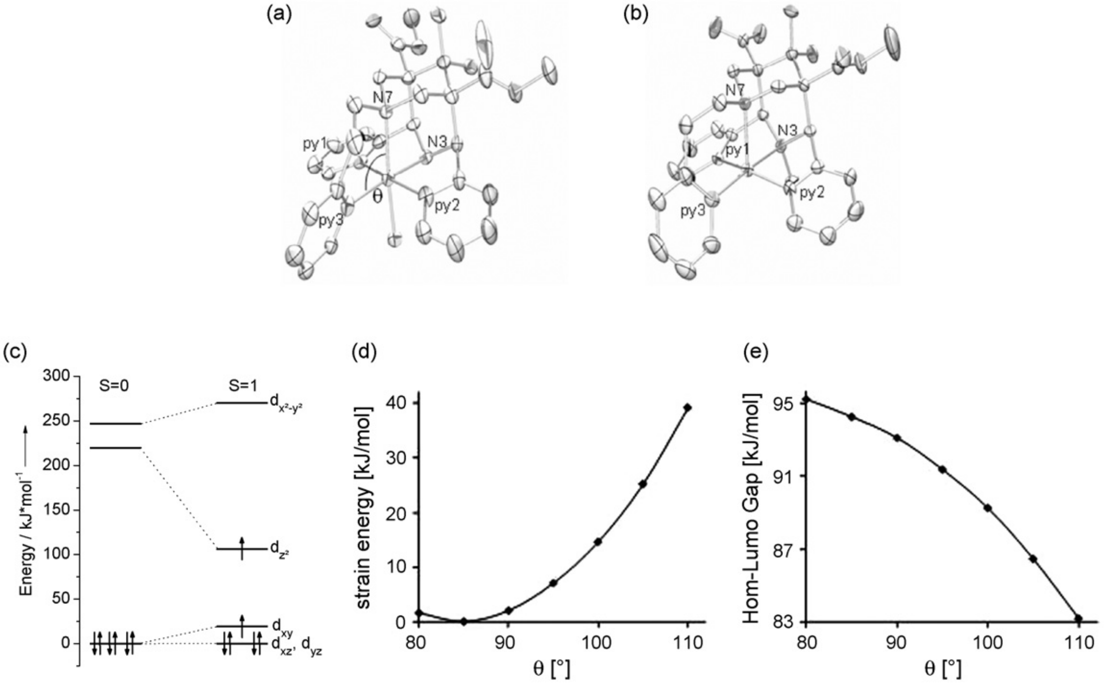


Fig. 3. Selected data of the cobalt–L^3 system (see Fig. 2): plots of the experimentally determined structures of the hexacoordinate $S = 0$ $[Co^{III}(L^3)(OH)]^{2+}$ (a) and the pentacoordinate $S = 1$ $[Co^{III}(L^3)]^{3+}$ (b) complexes, an energy level diagram (c), based on DFT calculations, the steric strain (d) and the homo-lumo gap ((e) see also diagram (c)) as a function of the angle θ, shown in (a) [177].

stations are the prediction of a trigonal pyramidal (tetrahedral) copper(II) site, based on spectroscopy [180,181] and its confirmation by X-ray crystallography [182], the formulation of the entatic state principle [183] and, finally, the observation that blue copper sites are not entatic [186] – at least not in the originally discussed sense [187–189]. An interesting experimental approach to assess the influence of the protein backbone on the properties of the active site is that of designing, preparing and characterizing loop mutants, a technique which has been used extensively in the area of blue copper proteins (see Fig. 4) [194–199], specifically also to probe the entaticity, electron transfer mechanisms and electronic properties [198,200,201]. A particularly interesting mutant is AmiPse (see Fig. 4, pseudoazurin loop engineered into the amicyanin protein), which changes the color from blue at ambient to green at low temperature [198]. Based on experimental observations and a series of quantum-chemical calculations [198,202–208], it appeared that there are two nearly degenerate structures with subtle differences in geometry and strikingly different electronics (see Fig. 5) [209]. The important questions, however, why this particular mutant (AmiPse) shows this interesting behavior and how structural modifications may be used to tune the structure and energetics of blue copper sites, are not yet answered.

A number of computational studies with the aim of structural predictions of blue copper proteins were done and, specifically, related to the loop mutants discussed here, MM and QM–MM studies were performed [213,214]. It appeared that MM was more efficient and not less reliable and accurate than QM–MM [215], and force fields were developed which were able to refine both isomers (axial and rhomb, see Fig. 5) of the blue copper sites [214]. Of interest in this context is the LFMM approach and in particular, its recent

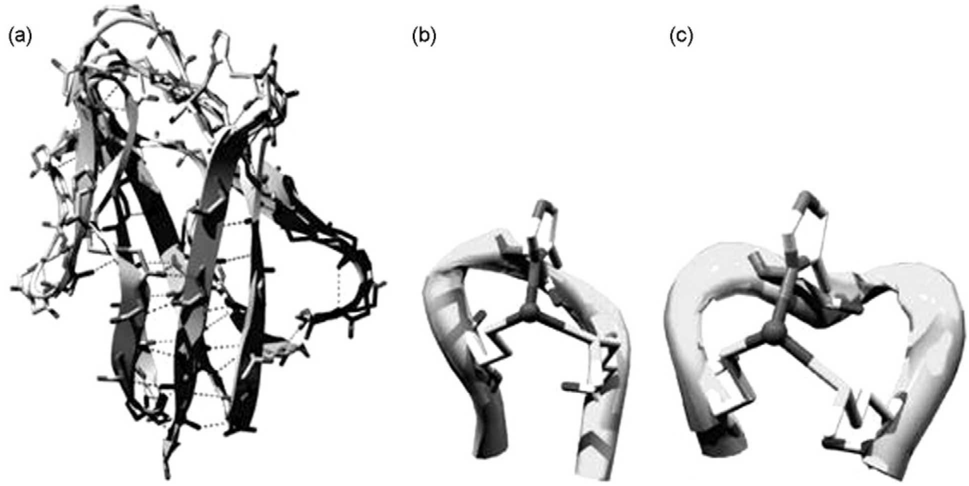


Fig. 4. The structure of amicyanin (a), and the structures of the C-terminal loops of amicyanin (b), and pseudoazurin (c) [202].

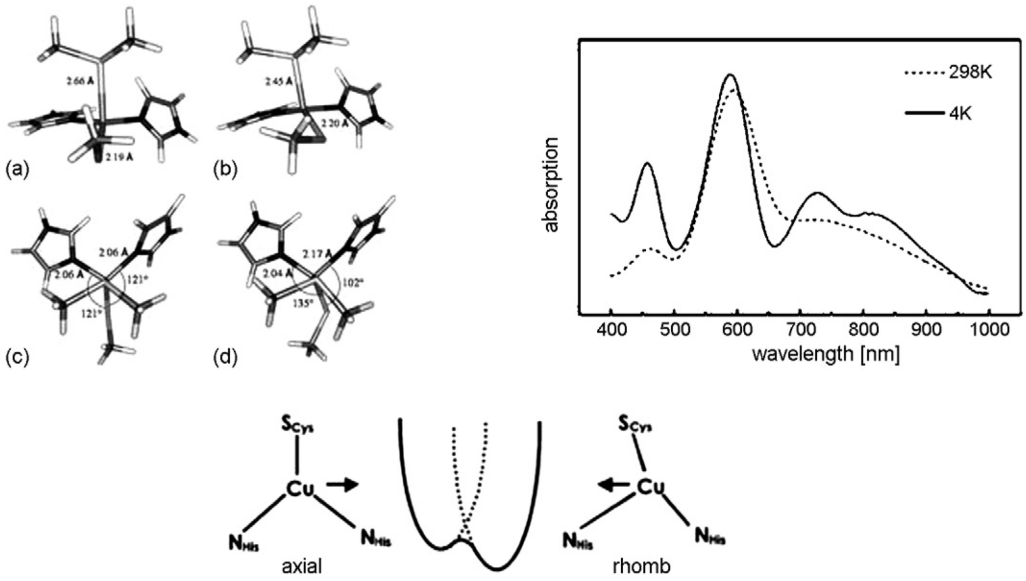


Fig. 5. Two views (perpendicular and parallel to Cu–S_{Met}) of the DFT optimized axial (a and c) and rhomb (b and d) active site models. Experimental UV–vis spectra of the amicyanin mutant AmiPse at room temperature and at 4 K. Schematic representation of the two DFT structures and the corresponding potential energy curve [202].

validation for blue copper proteins (see Fig. 6) [157,158,216,217]. While specific functions needed to be introduced to artificially tune the classical force fields towards the bistability of the blue copper site (see above), this does not seem to be necessary for the LFMM approach, which includes an AOM-based electronic term. It should be interesting to test the LFMM approach with the AmiPse mutant and others with similar structural peculiarities [218]. The LFMM approach might then be able to help to understand the fundamental reasons behind the degeneracy of the two states in AmiPse and, in combination with DFT-based calculations [82,202] unambiguously interpret the temperature-dependent color of this mutant.

An interesting recent development is the analysis of the performance of the LFMM model in the area of dinuclear type 3 copper enzymes (diamond-shaped $\{Cu_2O_2\}^{2+}$ dicopper sites, see Fig. 7) [137,219]. The importance of this result is that LFMM optimization leads to structures which are at least as accurate as those produced by DFT (also included in the overlay in Fig. 7), although explicit electronic coupling between the metal centers is neglected by LFMM.

The conclusion of this section is that MM – specifically LFMM – is able to accurately and reliably predict structures of metalloproteins. The first steps have been made with structural studies on the oxidized form of type 1 copper proteins and the active $\{Cu_2O_2\}^{2+}$ centers of dinuclear type 3 sites. There is good reason to assume that, provided the effort is made to carefully parameterize each system, metalloproteins in general may be reliably optimized by LFMM. However, although this particular MM approach includes an electronic term, fundamental reasons for specific distortions derived from electronic factors are not necessarily easy to derive.

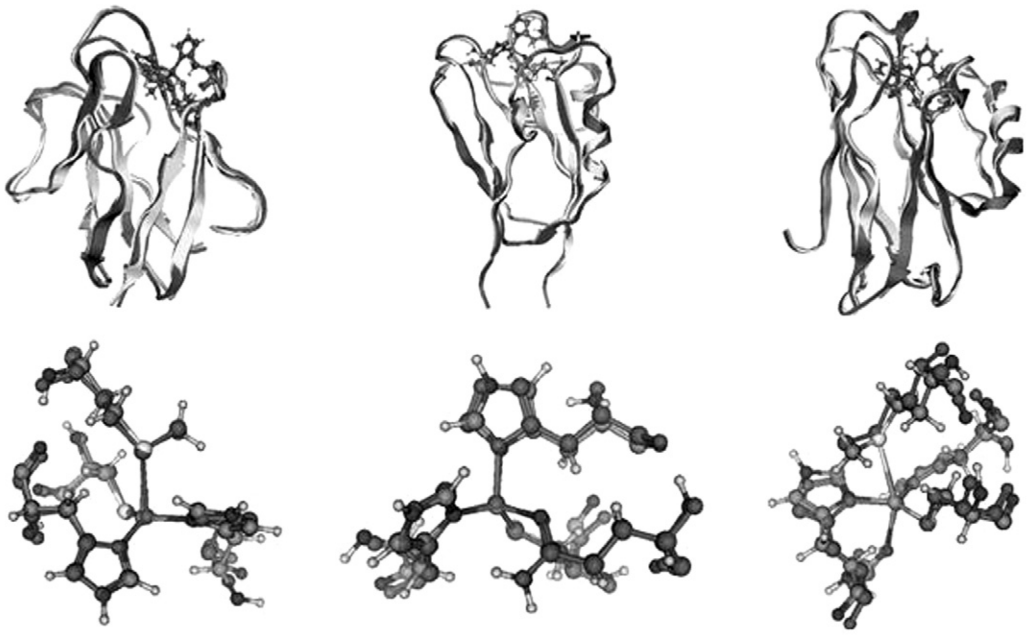


Fig. 6. Rmsd overlays of experimental (dark grey) and computed (light grey) backbone carbons (top) and active sites (bottom) of amicyanin (left), stellacyanin (middle) and azurin (right) (PDB codes 1AAC, 1JER, 1DYZ; copy from Ref. [217]).

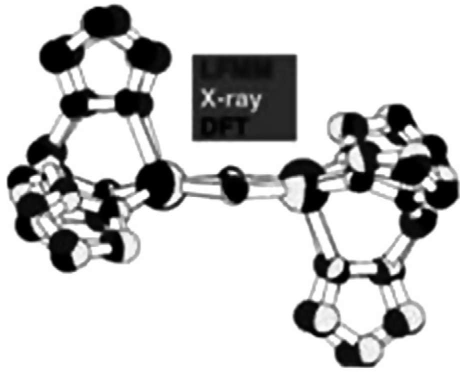


Fig. 7. Overlay structures of $[Cu(HB\text{-}(3,5\text{-}iPr_2pz)_3)]_2(O_2)$ [221], hydrogen atoms and isopropyl groups are omitted for clarity. (Copy from Ref. [137].)

Moreover, a prediction of molecular properties other than those derived from optimized structures and minimized steric strain has not yet been accomplished using LFMM. As in the other examples discussed here and similar to other MM approaches, an LFMM-based structure optimization seems to be a good and much needed basis for a thorough analysis of the electronic structures by single point QM calculations.

2.3. Molecular magnetism

In the early 1990s $[Mn_{12}O_{12}(OOCCH_3)_{16}(OH_2)_4]$ (see Fig. 8), known as Mn_{12} and first prepared and characterized in 1980 [222], was discovered to exhibit magnetic bistability [19,223–225]. The negative axial zero-field splitting D in this and other similar compounds leads to removal of the degeneracy of the M_s sublevels of the $S = 10$ ground state, such that those with the largest multiplicity are the lowest in energy (see Fig. 8), and the energy barrier for interconversion of the two spin ground states with $M_s = +10$ and $M_s = -10$ is $U = S^2|D|$ (for integer values of S, for half integer values $U = (S^2 - 1/4)|D|$). For Mn_{12}, with $S = 10$ and $D = -0.5\,cm^{-1}$, the experimentally determined value of the barrier U_{eff} is, as predicted, approximately $50\,cm^{-1}$, resulting in a blocking temperature of $T_B = 3.8\,K$ and a relaxation time τ of 2 months at 2 K [20,226]. Therefore, molecules like Mn_{12} behave at very low temperature much like small classical magnets and are called single-molecule magnets (SMMs) [227]. The bistability of SMMs together with their size of 2–5 nm may eventually open the way to magnetic information storage materials of ultimate density. SMMs are also of interest in fundamental science as excellent examples to study quantum effects and have attracted attention in the fields of quantum computing, magnetic refrigeration and spin-based molecular electronics [17,228].

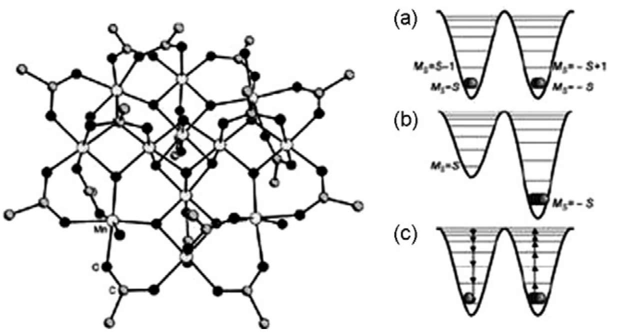


Fig. 8. Left: Experimental structure of Mn_{12} [222] (reproduced from [18]); right: energy levels for a spin state S with an easy axis magnetic anisotropy as in Mn_{12}. (a) Zero magnetic field: +M and −M levels are equally populated; (b) the magnetic field selectively populates the −M levels; (c) equilibration after removing the magnetic field (reproduced from [17]).

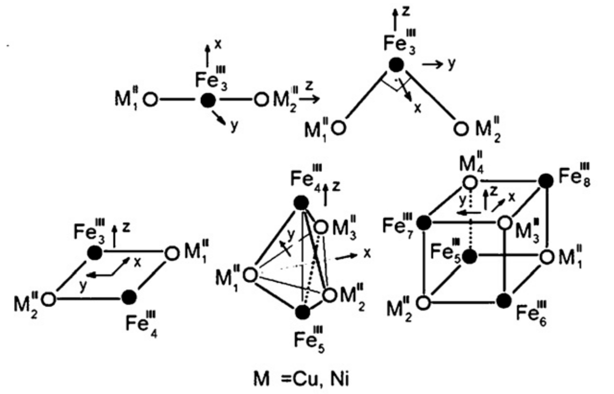
The field has seen much activity in the last decade and the physics and theoretical basis of SMM behavior as well as interesting experimental approaches for the characterization of novel materials have been developed. However, while a number of new SMMs were described in the literature, so far there is only one example with a slightly larger anisotropy barrier and blocking temperature than Mn_{12} ($U_{eff} = 86.4\,cm^{-1}$, $T_B = 4.5\,K$) [21]. One reason for the slow progress in the decisive preparative part is that, while the most crucial parameters for a significant increase of the anisotropy barrier are known – a large and negative value of the axial zero field splitting and a large total spin – a more than qualitative prediction of D has rarely been achieved, in contrast, to some extent at least, to the prediction of S, based on well understood magnetic coupling mechanisms [229]; lower than expected values of $|D|$ or the wrong sign of D have been shown to be a major reason for the missing success [230,231].

Cyanide-bridged oligonuclear complexes have the considerable advantage with respect to oxo-bridged compounds, to which Mn_{12} belongs, that they exclusively form linear M–CN–M′ subunits, which helps to assemble oligonuclear complexes with predictable structures [18,232,233]. Moreover, in cyanide-bridged spin clusters with low-spin Fe^{III} and Mn^{III}, the anisotropy term $\boldsymbol{S_1}\cdot D\cdot \boldsymbol{S_2}$ dominates over the Heisenberg exchange energy $-J\cdot \boldsymbol{S_1}\cdot \boldsymbol{S_2}$ ($|D| > J$) [234], and the expected relatively large negative D-values should allow to employ moderate-sized oligonuclear complexes, even for respectably large values of U_{eff}. Indeed, some moderate-sized cyanide-bridged SMM materials with various structural motives were reported but none has anisotropy barriers larger than that reported for Mn_{12} [235,236].

With a combined ligand-field-theory and broken-symmetry DFT approach (LFDFT) we have been able to show that the ground state Jahn–Teller coupling has strong implications for the isotropic and anisotropic magnetic exchange in oligonuclear cyanometalate complexes [230]. A pronounced magnetic anisotropy due to exchange is found for linear Fe^{III}–CN–M^{II} pairs with a four-fold pseudo-symmetry, which results from spin-orbit coupling of the $[Fe^{III}(CN)_6]^{3-}$ unit and is enhanced by the tetragonal field. In contrast, a trigonal field, e.g., due to Jahn–Teller angular distortions, leads to a reduction of the magnetic anisotropy. A large enhancement of the anisotropy is also found for the Fe^{III}–CN–Ni^{II} exchange pair, if anisotropic exchange combines with a negative zero field splitting energy of the $S = 1$ ground state of Ni^{II} in tetragonally compressed octahedra. In contrast, cancellation of the two anisotropic contributions is predicted for tetragonal elongations. A vector coupling scheme has been developed which allows combining the spin Hamiltonian parameters of the linear M–M′ pairs to yield the spin Hamiltonians for the entire spin clusters (see Fig. 9). The important and unique feature is that the vector coupling approach in combination with the LFDFT model allows treating large magnetic spin clusters on the basis of also accounting for subtle electronic effects such as ligand field distortions and spin-orbit coupling.

This model was used for the qualitative discussion of the magnetic properties of published oligonuclear transition metal complexes with ferromagnetic ground states [230] and for a thorough analysis of a series of linear and bent trinuclear hexacyanoferrate-based complexes [231]. The absence of SMM behavior in the latter examples was shown to be due to the large angular distortions of the $[Fe(CN)_6]^{3-}$ centers and the concomitant quenching of orbital angular momentum of the Fe^{III} ($^2T_{2g}$) ground state, imposed by ligand-based steric and/or crystal lattice effects.

While qualitative rules emerge from the LFDFT model [230,231], so far unpredictable subtle distortions lead to mag-



$$\hat{H}_{total} = \sum_{i\in Fe, j\in\{Cu\},\{Ni\}} [-J_{ij}\cdot \mathbf{S}_\mathbf{i}'\mathbf{S}_\mathbf{j} + \mathbf{S}_\mathbf{i}'\cdot(\mathbf{T}_\mathbf{ij}\mathbf{D}_{ij}\mathbf{T}_{ij}^*)\cdot\mathbf{S}_\mathbf{j} + \mathbf{S}_\mathbf{i}'\cdot(\mathbf{T}_\mathbf{ij}\mathbf{A}_\mathbf{ij}\mathbf{T}_{ij}^*)\cdot\mathbf{S}_\mathbf{j}] +$$
$$\sum_{j\in\{Cu\},\{Ni\}} [\mathbf{S}_\mathbf{j}\cdot(\mathbf{T}_\mathbf{j}\mathbf{D}_\mathbf{j}\mathbf{T}_\mathbf{j}^*)\cdot\mathbf{S}_j + \mu_B\mathbf{S}_\mathbf{j}\cdot(\mathbf{T}_\mathbf{j}\mathbf{g}_\mathbf{j}\mathbf{T}_\mathbf{j}^*)\cdot\mathbf{B}] + \sum_{i\in\{Fe\}}\mu_B\mathbf{S}_\mathbf{i}'\cdot(\mathbf{T}_\mathbf{i}\mathbf{g}_\mathbf{i}\mathbf{T}_\mathbf{i}^*)\cdot\mathbf{B}$$

Fig. 9. Visualization of the vector coupling model and the corresponding spin Hamiltonian (reproduced from Ref. [230]).

netic anisotropies which are much smaller than expected and required. It immediately follows that a reliable structure prediction is needed for an efficient design of novel cyanometalate-based SMMs, and it appears that only MM-based approaches will be able to efficiently and reliably lead to the desired results. Due to the importance of Jahn–Teller-labile centers such as $[Fe(CN)_6]^{3-}$, the LFMM approach [137,156,157,217] appears to be the method of choice although it has not yet been tested for this type of systems. Two additional challenges are that the modeling of complexes with simple monodentate ligands is particularly difficult (no forces exerted by the ligand backbone), and that from the experimental studies so far, it appears not unexpectedly that crystal lattice effects might be of importance. The optimization of crystal lattices is somewhat more difficult but the basic principles follow the same rules as those of MM of isolated molecules and corresponding approaches have been developed [99–101], and methods for the crystal structure prediction have also been described [102–104].

3. Conclusions

It appears that on the way to designing, preparing and understanding new transition metal complexes there is more than experiment on one and theory on the other side. An interpretation of experimental data with QM methods may help to understand electronic properties and reactivities and may also lead to rules which can be used by experimentalists to improve the performance of their compounds. What is not appreciated enough, however, is the fact that a rational design also involves a reliable structural prediction, and it is proposed that empirical force-field calculations (MM) are for structure optimization not only preferable due to their efficiency but also for their reliability and accuracy, provided a thoroughly fitted and validated force field is available for the specific problem. While combinations of MM with various experimental and empirical methods have been successfully used (spectroscopy, redox potentials, ligand field theory), potentially more attractive combinations of MM with QM-based electronic structure calculations such as DFT have only very rarely been used so far [74]. We hope to have shown that this is a potential which has not yet been fully realized [237].

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