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The relation between ligand structures, coordination stereochemistry, and electronic and thermodynamic properties

Peter Comba

Institut für Anorganische Chemie, Universität Basel, Spitalstrasse 51, 4056 Basel (Switzerland)

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Correspondence to: P. Comba, Anorganisch-chemisches Institut, Universität Heidelberg, Im Neuenheimer Feld 270, 6900 Heidelberg, Germany.

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A. INTRODUCTION

One of the most prominent and fascinating features of transition metal complexes is their large variability of molecular geometry. This is in contrast to organic compounds, and can largely be attributed to the electronic structures of the metal ions possessing partially filled d (and f) orbitals. The geometric flexibility is not only due to the variability of d-electron configurations, viz. a large choice of metal centres, but, with a given metal ion, a number of different geometries may be observed. Taking nickel(II) as an example, four-coordinate (tetrahedral, square planar), five-coordinate (square pyramidal, trigonal bipyramidal) and six-coordinate (octahedral, trigonal prismatic) complexes are known. Moreover, with a "given" geometry, the angles between the ligand atoms and the metal centre are rather flexible. In hexacoordinated species, "trans" angles of between 180° (octahedral) and ~140° (trigonal prismatic; a limit of 135° may be assumed, although the elongation about the C_3 axis of a trigonal prism is not strictly defined) have been observed. In four-coordinate complexes, the valence angle around the metal centre may vary from 90° (square planar) to 109° (tetrahedral), and the bite angle in octahedral complexes, defined by two chelated cis ligand atoms and the metal, for example in cobalt(III) complexes, varies from values as low as ~68° for four-membered rings to over ~82° for five-membered rings and around 95° for six-membered rings. The flexibility of the coordination angles is obviously the result of rather small force constants and the respective bending modes in vibrational spectra appear at rather low frequencies (~100–300 cm^{-1} for amino complexes as opposed to ~800 cm^{-1} for C—C—C bending). The metal ligand bonds are usually more rigid but still rather flexible compared with carbon–carbon bonds. It therefore is expected that the long axes of the thermal ellipsoids in crystal structures of metal complexes are oriented perpendicular to the metal–ligand vector, and this is generally observed except for bonds in the direction of Jahn–Teller active modes.

The ligand sphere and the coordination geometry obviously have a large influence on the kinetic, thermodynamic and electronic properties of transition metal complexes. Ligand exchange reactivities, isomer stabilities and selectivities and spectroscopic properties are often related to structural parameters. But what determines the coordination geometry of a transition metal complex? The obvious answer is that each structure is a compromise between the desire of the metal ion (mainly electronic effects) and the ligand demand (primarily steric effects). The discussion above might lead to the conclusion that the demands of the metal ion are rather weak in this competition and the limit of ligand influence is only given by chemical instability of the resulting structure. Indeed, models have been proposed which interpret and predict structures of metal complexes while completely ignoring any electronic effects. These models, much to the annoyance of spectroscopists, have, within certain limits, led to reasonably successful results.

In this article a number of models and methods for the interpretation and/or prediction of coordination geometries are reviewed. Recall that there is an important difference between interpretation and prediction which, in many studies, has been ignored, viz. a number of models proposed for the interpretation of structures, thermodynamics and spectroscopy have been applied without thorough evaluation for predictions. Within a given parameterization the *interpretation* of data usually involves the variation of some parameters to fit the experimental data, followed by an interpretation of the resulting parameter values. For a successful *prediction* of properties, the parameters involved must be known in advance, and this usually means that these parameters must be transferable from a known and well-understood system to the properties of compounds to be predicted. Obviously, this can be a complex problem and may lead to large uncertainties and inaccuracies. However, the prediction of properties of new materials which may eventually lead to the design of new compounds with tailor-made properties is tempting and certainly of importance. Much time and resources may be saved if one can be fairly certain that the compounds prepared in the laboratory will have the properties that one wishes them to have. This must lead to a pragmatic approach which takes the above-mentioned problems into account, viz. to know and appreciate the error limits caused by various uncertainties.

Among the various models discussed here, molecular mechanics calculations are unique in many ways. They have been applied to a range of problems in chemistry in general and coordination chemistry in particular. This popularity is based on the simplicity of the model which sometimes might be misleading in the sense that the high degree of parameterization still allows a number of effects not explicitly treated by the model to be accounted for. The ready availability of corresponding programs, computers and the success of the method in a number of areas have certainly helped to boost the standing of molecular mechanics. I do not intend to write just another review on molecular mechanics; the area of coordination chemistry has been covered by some recent articles on this topic [1–4]. I will (i) present a range of well-known methods for the prediction of geometries, structures, thermodynamics and electronics of transition metal complexes, (ii) show in detail the main areas of application of molecular mechanics calculations in the field of coordination chemistry, (iii) give a detailed view of the parameterization of the molecular mechanics model and the problems thereof, with particular reference to applications in coordination chemistry, and (iv) discuss a selected number of examples of calculations with various models.

It is the aim of this article to discuss a large range of models used in the area of the stereochemistry, spectroscopy and thermodynamics of coordination compounds and their applications. Obviously, there are approximations and resulting limitations inherent to each of these models. It is my intention to discuss possible oversimplifications and dangers of overinterpretations in detail, without undue judgement and criticism of the specific examples reviewed.

B. INTERPRETATION AND PREDICTION. A SURVEY OF MODELS

(i) Shape

Chemists are usually visually oriented, and for most of us it is rather easy to relate the shape of a molecule, depending on the personal interest, to properties such as stability, reactivity, selectivity, and electronic properties. For the determination of the shape of molecules, exact structural information (e.g. X-ray data) is often needed. However, for the *description* of the shape of a molecule it is often more efficient to involve methods based on topology and graph theory [5–11]. The geometry of a coordination complex is usually described relative to an idealized polyhedron. All non-isomorphic convex polyhedra with 4–8 vertices have been tabulated [6]. For the detailed analysis of the shape, additional geometric parameters are required, and this may then lead to important details in the interpretation of the relation between geometric reaction paths and idealized geometries [5]. With this type of analysis, it is then possible, for example, to interpret intramolecular rearrangements.

Graph theory has also been used in the design of multidentate ligand systems [7]. This may be a rather complex method and it has not yet been applied in many cases. If only the number of isomers needs to be known, relatively simple methods based on combinatorial relations have been described [12].

Topology is of importance in a number of other areas. For example, topologically determined charge distributions lead to important information in relation to relative stabilities and reactivities [8,9].

(ii) Graphics

Computer graphics are more and more replacing simple molecular model kits. However, they are not only superior from an aesthetic point of view or when it comes to the presentation of ideas and results; when employed in connection with calculations using or producing atomic coordinates, they are an indispensable tool [13–16]. Geometrical and topological considerations are clearly of basic importance in the analysis of computer graphics. An increasing number of graphics packages with various levels of sophistication and in different price ranges are available [17].

(iii) Geometry

Based on purely geometrical models, i.e. with no "chemistry" involved, structural and thermodynamic properties can quite often be understood and explained in some detail. An example in this area is the geometrical description of the trigonal twist of hexacoordinate transition metal complexes [18–20], which will be discussed in a separate section below.

The detailed analysis of steric effects may also relate geometric parameters with reactivities and stabilities. This has been rather successful in the case of the cone angles, where the steric demand of any ligand, usually a phosphine, is related to thermodynamic properties [21–23]. The concept of cone angles has been quantified and has resulted in the seat-ligand-fitting model, which again is a purely geometrical analysis of the coordination space [24–26].

Selective complexation of metal ions is becoming a rather competitive topic, mainly in the area of cyclic ligands. A main objective here is a fit of the macrocycle hole size with the metal ion size. In a purely geometrical model, methods were developed to calculate the hole size radius and a goodness of fit parameter (hole size vs. Pauling radius) [27–30]. A range of methods in this area based on molecular mechanics calculations has been established, and will be discussed in a separate section below.

(iv) Electrostatics

A purely electrostatic model of ligand–ligand repulsion is based on the idea that geometrically fixed chelate ligands are floating on the surface of a sphere with the metal centre as origin and a constant radius. The optimum position is found by minimizing the interligand repulsion U [31–34].

$$U \propto \frac{1}{d^n} \qquad n \sim 6$$

Intraligand repulsion is usually neglected but was found to be of importance in some examples [34]. The repulsion model has been used for a number of different stereochemistries and coordination numbers, and it was recently adopted for the calculation of boranes and carbonyl cluster compounds [35]. In the latter case, the ligand (carbonyl) structure was calculated with the conceptionally very similar valence shell–electron pair repulsion (VSEPR) model [36,37]. Clearly, the complete neglect of ligand flexibility (stereochemically rigid ligands) and the fact that electronic effects are basically ignored are a drawback of this model and are replacing it somewhat outside "real chemistry". However, the relative success of this method in some areas of coordination chemistry indicates that such a simple model might be useful in a limited area of research if the results are not overinterpreted.

(v) Mechanics

Molecular mechanics calculations will be discussed in detail in the next section. There, and in the related methods reviewed here, electronic interactions are at least partly included. From a careful analysis of the structural data of a series of similar molecules, it emerges that changes in bond distances and valence angles are generally correlated [38]. This may be interpreted in terms of structural reaction coordinates for conformational interconversions and bond breaking and bond making. Fractional bonds and bond orders have been defined, calculated and interpreted in the CNPE model [38–41]. The corresponding relationships between bond lengths, bond energies and bonding force constants are based on modified Morse functions. Structural, vibrational and kinetic properties of related molecules which undergo the same type of reaction may be correlated through a simple model of reaction profiles. This concept has been used successfully to analyze reaction paths and rates in a number of areas.

Chirality forces have been widely discussed, and there is some argument whether these are 6- or 8-point forces [42,43]. A comparison of the resulting chirality forces between homo- and heterochiral molecules is a measure of chiral recognition, and this has been studied in some detail. Quantitative analyses have involved quantum mechanical and molecular mechanical methods, and it was demonstrated that chiral phases for racemate resolution may be understood or designed in this way. An important result in this field was that through-space field and other second-order effects are more important than generally has been assumed [44].

(vi) Electronics

Models describing the electronic structures of transition metal ions have been used to interpret or predict the reactivity, structural, thermodynamic and spectroscopic properties of coordination compounds. Crystal field theory was the first attempt to quantify the influence of the ligand sphere to the electronic properties of the transition metal ion [45]. In the crystal field and ligand field theories, the degeneracy of the set of five d orbitals is lifted by their interaction with the point charges or dipoles of the ligands. Important aspects are the strength of the ligands and the symmetry of the ligand sphere. Thus, the number of energy levels can be related to the coordination geometry and the separation between the energy levels is a function of the ligand strength. Thermodynamic properties, reactivities and spectroscopic properties have been successfully interpreted with these models which are still widely used [46–49].

The angular overlap model is, in some respects, just a different parameterization of much the same theory [50–52]. However, the fact that in angular overlap model calculations the e_σ and e_π parameters, representing σ and π bonds between metal and ligand atoms, are used instead of the less directly interpretable parameters D_q, D_s, D_t, etc., makes this model much more appealing to chemists. The energies of the various states are calculated based on a set of e_σ and e_π parameters for each ligand atom and the action of a symmetry-adapted angular overlap matrix on these terms. The main applications of the angular overlap model are in the area of transition metal ions, especially in the field of spectroscopy and magnetism [53–55]. However, it has also been used to calculate the shapes of molecules containing main group elements [56].

Reaction modes and reactivities of a number of systems in various areas have been analyzed with ligand field theory and related models [46–49,57,58]. In the area of electronic–structural relationships, Jahn–Teller effects, mainly in relation with copper(II) complexes, are among the most prominent examples where the ligand field, the angular overlap model, and related theories have been used successfully to interpret distortions of the coordination geometry very precisely [59–61]. Also, the trigonal twist of octahedral complexes [62–66] and the tetrahedral distortion of square planar complexes [67–72] were modelled with some measure of accuracy.

It has been demonstrated that structural changes occurring due to electron rearrangements (e.g. light absorption or high spin–low spin interconversions) may be calculated by a single expansion of the potential energy difference of the two states of the molecule as a function of a totally symmetrical metal ligand stretching mode of the Jahn–Teller active ε_g vibration [73,74]. It is of importance that the model used is purely electronic, viz. for the calculation of the structure of the excited state one needs only the structural parameters and force constants of the ground and not of the experimentally less available excited state, although there are examples where these parameters have been thoroughly determined [75].

A number of computer programs are available for the interpretation of electronic and EPR spectra and the magnetic properties of transition metal complexes. These usually relate the geometries of the chromophores and a set of ligand field parameters to the energies of the various electronic states [49,54,76,77]. In addition, programs that are used in the simulation of EPR spectra of monomeric and oligomeric paramagnetic complexes are growing in importance [78–82].

Molecular orbital theory is usually applied in the area of spectroscopy of coordination compounds when orbitals other than the metal-centred d orbitals are of importance [83]. This is the case, for example, for charge transfer spectra and metal–metal bonding. In the area of interpretations of structural effects, Hückel theory calculations have proven to be very successful, especially with organometallic compounds [84,85].

C. MOLECULAR MECHANICS

(i) History and background

Molecular mechanics calculations lead to relatively precise quantitative information on intramolecular steric effects. In organic chemistry they are a routine tool and have been applied to interpet and predict structures, and vibrational and thermodynamic data [86,87]. The first application in the area of coordination chemistry appeared more than 20 years ago [88], and since then molecular mechanics, force field calculations, or conformation analysis as they are also called, have become well established in this area [1–4].

In the molecular mechanics model, the positions of the atoms of a molecule are determined by a number of forces (the force field). The energy lost by moving atoms away from equilibrium positions is given by the sum $U_{total} = \Sigma_i U_i$ (see Fig. 1). Included in these potentials are usually bonding, valence angle, atom repulsion and various other terms. Force fields will be described in some detail in the next section. They obviously represent mainly steric effects but electronics are also included, for example in the bonding and valence angle terms. However, since a force field has to be as general as possible, viz. independent of the connectivity and resulting geometry, a number of electronic effects such as Jahn–Teller distortions, trans effects and others are not generally included, and this is a problem which will be discussed in later sections.

Molecular mechanics calculations usually involve the refinement of a structure by modification of trial coordinates in order to minimize the strain energy. Minimization may be achieved by a number of different algorithms such as steepest decent, Newton–Raphson, simplex, and others. Most of the programs used in the area of coordination chemistry minimize the strain energies with a modified Newton–Raphson procedure, which allows a simultaneous variation of all coordinates [89]. This usually leads to relatively fast convergence and rather stable structures, especially if the trial coordinates are close to an energy minimum, viz. if they represent a chemically reasonable structure.

One major problem with molecular mechanics calculations is that the species calculated usually do no have any environment included. However, it also is not fully consistent with the model to call them "gas-phase molecules" since most of the force field parameters have been fitted to solid state or solution properties (see below). Problems which are directly related to environmental properties include crystal lattice effects, which lead to subtle distortions of otherwise highly symmetrical structures [90] and selectivity in solvation or ion-pairing. Solvent-dependent equilibria between square planar and octahedral nickel(II) complexes [91,92] and between

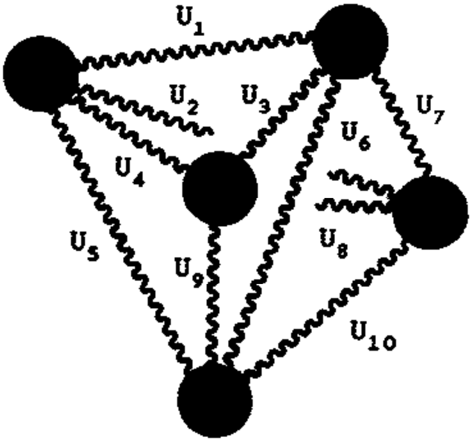


Fig. 1. Schematic representation of the molecular mechanics model.

monomers and dimers [93] are prominent examples of solvation effects, and selective ion-pairing is of practical importance in isomer and enantiomer separation procedures based on fractional crystallization and chromatography [94–98]. Some preliminary attempts in the modelling of the first aquation shell of complex cations have been published [99], but it is clear that much more work needs to be done in this area. A study of crystal packing effects based on crystal force field calculations in order to evaluate the stability of conglomerates has recently appeared [98]. The problems in modelling solvation and crystal lattice effects are similar and related to the number of interactions which have to be minimized. In the crystal lattice, at least 27 unit cells have to be included in a meaningful model of the crystal environment. With an approximate square dependence of the CPU time on the number of atoms, the required computer time increases for average size molecules (50–100 atoms) from a couple of minutes to hours.

Another important problem is related to the application of molecular mechanics calculations to relative stabilities. The differences in strain energies between conformers or isomers may be related, if electronic effects can be neglected (or accounted for, see below), to $\Delta\Delta H$. For the calculation of isomer (or conformer) distributions, the important question is then how one accounts for entropy effects. Models to calculate entropy terms have been used [16,89,100–102], but they often require additional sets of parameters and approximations. In the known examples involving simple coordination compounds [100–102], the entropy differences are quite small, viz. within the error limit of their calculated values. With similar cobalt(III) hexaamines, the decision was therefore to completely neglect them [103]. For very large molecules, the direct calculation of entropy was also found to be too inaccurate, and there the entropy was deducted from fluctuations of the internal coordinates, calculated by Monte-Carlo or molecular dynamics simulations [104–107].

Some of the more important applications of molecular mechanics calculations in the field of coordination chemistry will be discussed in detail and based on a number of selected examples in a separate section. Here, I will just present a short summary. The area of application in coordination chemistry is relatively large. However, in terms of the quality of the interpretations and their relevance, there clearly are large differences, and this will also be apparent in the section reporting the selected examples.

Molecular mechanics calculations have been used to calculate vibrational spectra [89], and many available computer programs have this facility included. However, this feature is frequently not used. The neglect of interaction constants and small inconsistencies in the force field, which may not be of importance in terms of the minimized strain energies or optimized structures (cancellation of errors), might lead to quite large differences between calculated and experimental frequencies. This may be partly due to the fact that the force fields used in molecular mechanics have usually been fitted to structural, less frequently to thermodynamic and very seldom to spectroscopic, data and therefore are not necessarily directly related to the force fields used in spectroscopy (see also next section). Moreover, normal coordinate analysis of vibrational spectra is a more direct method for the analysis of spectroscopic properties. Indeed, molecular mechanics has mainly been used in this field for testing of force field parameters [89,108]. An interesting point is that calculated vibrational frequencies along with the moments of inertia, calculated from the final coordinates, may be used to compute some entropy terms [89,101].

The other two types of data resulting from molecular mechanics calculations are structural (optimized geometries) and thermodynamic (minimized strain energies). The calculation of structures of simple coordination compounds by molecular mechanics has been used in a number of areas [90,93,109–115]. The difficulty in obtaining accurate geometries increases with the size and flexibility of the molecules, and additional (experimental) information is often needed. With binuclear copper(II) compounds, a system was recently developed which involves the simulation of EPR spectra based on structural parameters resulting from molecular mechanics calculations [93]. Experimental structures which, for various reasons, have a lack of precision may be further refined with force field calculations [109,110]. This is a rather ambitious task and clearly depends strongly on the quality of the force field. The *analysis* of structural disorder is, in terms of accurate quantitative calculations, a less delicate problem, and this has been shown to be an important application of molecular mechanics calculations [90]. A promising extension in the area of applications of molecular mechanics calculations is the use of calculated structural data in electronic calculations for the prediction or interpretation of electronic properties (electronic and EPR spectra of coordination compounds) [71,72,111,112]. The calculation of structures of short-lived intermediates [113,114] and of electronically excited states [115] is of some interest. The problem here is that the calculated structures cannot be compared with experimental data and therefore rather large uncertainties have to be appreciated. The same is true, maybe to an even larger extent, for the calculation of relative stabilities of putative intermediates or transition states, as this was recently done to analyze a stereoselective synthesis [116]. An additional problem in this borderline area between semi-quantitative calculation and pure speculation arises when additional electronic effects, which cannot be accounted for by molecular mechanics, might be of importance, as was discussed in numerous studies on the hydrolysis of cobalt(III) pentaamines, modelled in the above-mentioned calculations [113,114].

The pioneering work in molecular mechanics in coordination chemistry was a conformational analysis [88], and this topic has found wide application in recent years [92,100–103,117–126]. An important study in this area was the analysis of the energy surface related to the interconversion of all possible conformers of five-membered chelate rings [127,128]. The agreement of the calculated activation energies with experimental data [129] is only fair but possibly not less than one can really expect based on the approximations needed for these studies. Similar investigations, viz. the analysis of the ligand strain along a normal coordinate (metal–ligand bond), are the basis of a number of other investigations, including the analysis of trigonal twist angles [90,130], and complex stabilities as a function of the ligand hole size [4,90,122,131–146]. Isomer stabilities and selectivities have been studied extensively [103,147–155], and they are usually based on a complete conformational analysis. Detailed analyses of redox potentials have also been based on isomer distributions calculated by molecular mechanics calculations, and electron transfer reactions were related to steric strain [115,156–160].

There are a number of interesting new methodological developments in the area of molecular mechanics in general. Carbonyl ligands may occupy a number of geometrically different coordination sites in cluster compounds: terminal, semi-, doubly-, or triply-bridging. With a "surface force field" approach [161], including partial bridging [162], it has become possible to *interpret* these geometries. An obvious lack of accuracy in the accurate *prediction* of these geometries is cleary due to the neglect of electronic effects, and these might be implemented to the model. Relatively small molecules usually have a tractable number of conformers, and it is then possible to minimize every conformer separately. This is especially true for complexes of chelate ligands. However, for simple asymmetrical monodentate ligands such as methylamine coordinated to metal ions, a full analysis can already become rather complex, and large molecules such as peptides or peptide complexes are clearly intractable with this simple method. For the stochastic analysis of energy surfaces aiming at the analysis of the global energy minimum and/or the particle distribution in the isomer and/or conformer space, there exist a number of methods [163–168]. They usually involve a Monte-Carlo type algorithm to scan the conformation space and, due to the excessively large number of structures to analyze, the minimization procedure has to be simplified. An interesting method in this respect is the "pure central force field approach" where valence and torsional angles are represented by forces between two atoms such that all strain energy terms may now be represented by a set of two body central forces [166]. Clearly, such a force field (as yet it has been used for pure carbohydrates only) is not directly related to any experimentally available physical parameters, and as such it is an interesting extreme case in the discussion of the parameterization which follows. In addition, conformational searches using internal instead of cartesian coordinate systems were shown to have some advantage in terms of performance, especially when some of the coordinates are constrained [167]. However, with the state-of-the-art computational facilities, a limit in terms of the size of molecules seems to be reached with chain lengths of ~20 atoms [167]. A recent development based on rigid geometry refinement with internal coordinates and involving an algorithm based on random torsional search seems to overcome some of these limitations [168].

(ii) Parameterization

A molecular mechanics program generally comprises four parts, viz. (i) an input/output section, which deals with the molecular model (coordinates and connectivities) and the calculated strain energies, (ii) a strain energy section, where the various energy terms are calculated, (iii) a force field, which obviously depends on the functional form of the potentials and is responsible for their exact shape, and (iv) a "minimizer" which optimizes the molecular structure by minimizing the total strain energy. This section deals with the closely related points (ii) and (iii), which are possibly the most critical and controversial points of molecular mechanics calculations, partly because they are completely empirical.

$$U_{\mathrm{total}} = \Sigma(E_{\mathrm{b}} + E_{\mathrm{nb}} + E_\theta + E_\phi + E_\delta + E_\sigma + E_{\mathrm{hb}}) \tag{1}$$

$$E_{\mathrm{b}} = \tfrac{1}{2}k_r(r_{ij} - r_0)^2 \tag{2}$$

$$E_{\mathrm{nb}} = a\mathrm{e}^{-br_{ij}} - \frac{c}{r_{ij}^6} \tag{3}$$

$$a = 2014(\varepsilon_i\varepsilon_j)^{1/2} \tag{4}$$

$$b = \frac{12.50}{\mathrm{vndr}_i + \mathrm{vndr}_j} \tag{5}$$

$$c = \frac{2.55(\varepsilon_i\varepsilon_j)^{1/2}(\mathrm{vndr}_i + \mathrm{vndr}_j)^6}{144} \tag{6}$$

$$E_\theta = \tfrac{1}{2}k_\theta(\theta_{ijk} - \theta_0)^2 \tag{7}$$

$$E_\phi = \tfrac{1}{2}k_\phi(1 + \cos(m(\phi_{ijkl} + \phi_{\mathrm{off}})) \tag{8}$$

$$E_\delta = \tfrac{1}{2}k_\delta\delta^2 \tag{9}$$

$$E_\sigma = \frac{q_i q_j}{\sigma r_{ij}} \tag{10}$$

$$E_{\mathrm{hb}} = \frac{c}{r_{ij}^{12}} - \frac{d}{r_{ij}^{10}} \tag{11}$$

Most programs used in the area of coordination chemistry optimize the structure of a molecule by minimizing the total strain energy, consisting of bonding interactions (E_{b}), repulsion (E_{nb}), valence (E_θ) and torsion angle terms (E_ϕ), out-of-plane (E_δ) and electrostatic interactions (E_σ) and hydrogen bonding (E_{hb}) (see eqns. (1)–(11) and Fig. 2).

(a) Bonding energy

The bonding energy function should represent the experimentally known relatively steep repulsion between two atoms and the relatively flat attraction, which with a large separation of the two atoms should become zero. A Morse function fulfils these requirements relatively well. Nevertheless, in molecular mechanics calculations, bonding interactions are, with only a few exceptions, usually calculated based

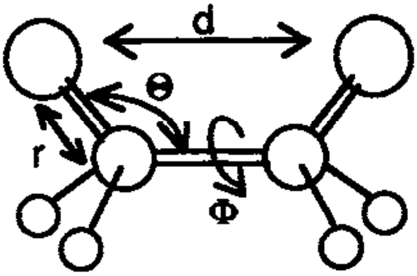


Fig. 2. Schematic representation of the force field (see eqns. (1)–(11), k_r, k_θ, k_ϕ, k_δ are force constants, r_0, θ_0, ϕ_0 are strain-free values, vndr are van der Waals radii, a, b, c are constants used in the Buckingham functions, q are partial atomic charges, σ are dielectric constants).

on harmonic potentials. There are two important reasons for this approximation: (i) the parameterization for a Morse function can not usually be based on experimental data, and (ii) harmonic paraboloids represent the potential in the proximity of the energy minimum with relatively high precision. Moreover, the anharmonic character of the non-bonded interactions (usually represented by Buckingham potentials, see eqn. (3)) results in a certain degree of anharmonicity in the bonding even if the bonds are described with harmonic potentials. Additional anharmonicity is introduced in cases where valence angle bending is modelled by Urey–Bradley functions (1,3-non-bonded interactions around the metal centre). However, calculations based on harmonic bonding functions clearly cannot give any information related to the absolute stability of a compound (e.g. dissociation of a ligand).

A qualitative comparison with spectroscopic data is of some interest here. If one considers a series of metal complexes with a constant M—L unit (e.g. Co^{III}—NH_3) and variable M—L bond lengths, it is apparent that the (spectroscopic) force constant for the M—L stretching mode with a_{1g} symmetry varies, as expected, with the M—L bond length, viz. the corresponding potential must have an anharmonic component [169]. However, for a given molecule one usually observes that the vibrational structure of electronic absorption bands with a_{1g} symmetry displays up to about five progressions [170]. Clearly, the exact form of the potentials is rather subtle, but these observations indicate that the approximation of the potentials with harmonic functions is reasonable for the rather crude molecular mechanics approach.

(b) Valence angles involving the metal centre

The valence angles involving metal ions are rather flexible, and force constants used for these terms are invariably small, typically ~0.05–0.5 mdyn rad^{-1} [1–4,117]. For a number of reasons, in a series of recent studies, these valence angle bending terms were replaced by 1,3-non-bonded (geminal) interactions of the ligating atoms, which are not usually included in force field calculations, modelled by Urey–Bradley functions (linear plus quadratic term) [126]. This approach was shown to lead to excellent results in a number of systems [90,92,93,103,115,126,151–155,157–160].

More importantly, based on a series of transition metal hexaamine cage complexes, subtle structural differences, which were originally believed to be due to electronic effects [65], were well reproduced with this modified force field [130] (see next section). An important advantage of this modification is that the coordination geometry now can be described by fewer parameters, and therefore the development of force fields for metal ions and ligand atoms is much easier and thus more accurate. I have to emphasize that the replacement of the valence angle bending potential around the metal ion by pure repulsion must also lead to some metal–ligand atom elongation which obviously has to be corrected with smaller metal–ligand strain-free distances (this does not imply, however, that strain-free metal–ligand distances are generally smaller for force fields which include 1,3-interactions than for others; they depend on many other parameters). Therefore, the whole parameterization, especially in terms of metal–ligand distances, is not strictly comparable between "conventional" force fields and those which involve the approach discussed here. It will be seen that the strain-free parameters fitted with a force field using Urey–Bradley functions around the metal centre are in good agreement with expectations based on experimental results. These general aspects will be discussed in detail in one of the following sections.

(c) Bond torsion

The rotation around a single and a multiple bond are two completely different properties. Whereas a change of the torsion angle around a double bond might involve bond breaking and formation of a new isomer, the rotation around a single bond is a more or less hindered transformation between conformers. Nevertheless, the two potentials are often expressed by the same function involving a cosine term, and the steepness of the potential and the size of the energy barrier are then tuned with the force constant k_ϕ (see eqn. (8)).

Hindered rotation around single bonds and the corresponding energy barriers have been determined experimentally [171]. The bonds in question are primarily σ bonds, therefore in terms of hindered rotation there should not be any electronic effects present. The barrier must primarily be due to repulsion, i.e. atom repulsion (vicinal or 1,4-interactions) which are included in the non-bonded interaction term, and bond or electron repulsion ("charge clouds" of the 1,2- and 3,4-bonds) which are the basis for the additional correction by the bond torsion potential. Rotation around the metal–ligand axis does not seem to be measurably restricted [172] and the corresponding potential is therefore generally omitted.

(d) Electrostatic interactions

With compounds involving metal cations, it would seem to be sensible to include an electrostatic potential. With alkali metal ions and oxygen donors, metal ligand bonding has been described with a purely electrostatic term [173]. With complexes of uncharged ligands such as amines, electrostatic correction terms are usually not included. Even with charged ligands, such as halogen or pseudo-halogen ions and carboxylates, electrostatic interaction is often neglected (or accounted for in other ways) [1–4,117]. The introduction of electrostatic interactions in a "well balanced" force field would imply a factorization of bonds and angles into a "covalent" and an "electrostatic" part, and this does not seem to be sensible. Electrostatic potentials were used in some cases [153,174] but the results imply that this is not generally necessary [175,176]. A major problem with electrostatic interactions is the determination of partial charges on all the atoms. Although a number of approaches for this problem are available [8,9,177–183], it still is, in most cases, a rather cumbersome procedure and also leads to additional uncertainties.

(e) Hydrogen bonding

A number of different functions describing hydrogen bonding are available [184–189]. The question of whether an angular dependence of hydrogen bonds has to be introduced explicitly in the function expressing the hydrogen bond potential, or whether it is already inherent to the rest of the force field, is still debated. It can be argued that hydrogen bonds are a priori electrostatic interactions and therefore isotropic [186–190]. However, based on an extensive analysis of a large amount of data, it seems to emerge that a certain degree of angular dependence is evident in the sense that preferred geometries are experimentally detected [184]. Also, these observed geometries can be reproduced satisfactorily with a function involving an angular term. Indeed, modelling of the geometries is possible if the electrostatic contribution is completely neglected [184]. Still, the question remains as to whether this is a proof for "lone-pair directionality" in hydrogen bonds. It is rather illustrative that experimentally observed structures are also reproduced accurately with a purely electrostatic approach [109,153,174,186–191]. Here, the angular dependence is a result of neighbour effects due to repulsion of the substituents on the hydrogen donor and acceptor atoms.

(f) Electronic effects

In a molecular mechanics parameterization including, among others, repulsion as well as bonding and angle bending terms, steric as well as general electronic effects are considered. However, more specific electronic effects such as Jahn–Teller distortions, trans effects, π bonding and the electronic preference of metal ions for certain coordination numbers (e.g. square planar vs. octahedral nickel(II)) are usually not included in the force field. If a basis for the structural prediction or interpretation of Jahn–Teller active copper(II) complexes and σ and π donors or acceptors such as carboxylates or imines (e.g. pyridine) is intended to be introduced in the force field, it should be as general and simple as possible. Otherwise, the molecular mechanics approach loses much of its appeal to coordination chemists, since the simplicity of the model compared with the relatively accurate predictions that may be made despite neglect of electronic effects are its strength.

Force field parameters in most of the above-mentioned systems have been published [1–4], but they have generally been restricted to rather narrow fields of application. Such a limitation clearly allows for a complete neglect of electronic effects, or these may become part of the parameterization. However, every class of compound then requires a new force field, and the whole model loses generality and its predictive power. Therefore, additional work is clearly needed in this area. Some preliminary results and ideas for the treatment of mixed chromophores and of Jahn–Teller labile copper(II) complexes will now be discussed.

It is obvious that the complexes $M{-}L_x^{n+}$ and $M{-}L_{x-y}L'^{m+}_y$ may have different properties with respect to the M–L bond, viz. $M{-}L_y$ and $M{-}L'_y$ are not identical "metal centres" for the ligand L. If these differences are only steric in nature, then the different structures and strain energies are well described by the properties of any reasonable force field. Differences in the charge of L and L′ may be accounted for by addition of electrostatic potentials. For reasons outlined above, and because additional charges on the ligand usually also lead to additional π and/or σ bonding, electrostatic interactions have not been used to model such effects. The case of carboxylates and of imine-containing ligands such as pyridine has recently been studied in some detail [93,112,116,175] (see also Table 1).

Hexa- and pentacoordinate copper(II) complexes usually exhibit characteristic tetragonal chromophores with axial elongation. The amount of axial elongation (or compression) is, to a large extent, due to electronic effects. However, the coordination geometry of the in-plane ligands is only moderately dependent on the exact position of the axial ligand(s), and therefore their refinement is straightforward with a well-balanced force field. In the past, the axial ligands have often been fixed to experimentally known or assumed positions [108,192], and this is clearly possible if the geometry of the in-plane ligands is of primary interest. However, if the target is the whole chromophore, a more general procedure, which includes a model of the electronic effects, must be applied. To first order, this problem has been solved for copper(II) complexes with tetragonal (or rhombic) geometries, enforced by the ligand environment (e.g. copper(II) tetraamines with axial anions or solvent molecules). In these cases, the bonds to axial ligands are modelled with a rather small force constant, k, and a relatively large strain-free bond distance, r_0, reflecting the usually observed elongation [175]. With this simple model, the general agreement between calculated and experimentally observed structural parameters of the entire chromophore is surprisingly good. However, the model must be improved in two ways: (i) for general copper(II) complexes, without inherent ligand field distortions (e.g. CuL_6^{n+}), a method has to be found to predict the mode of distortion. Here, electronic considerations have to be taken into account [59,60]. (ii) The magnitude of the distortion, i.e. the exact position of the (axial) ligands, might have to be refined more precisely. Possibilities include the earlier proposed linear relationship between in-plane and axial bonds [193–195], bond length-dependent (variable) force constants, and an extension of the recently proposed model for the calculation of Jahn–Teller coupling constants

TABLE 1

Metal–ligand bonding force field parameters [175]

Bond type	Force constant, k_b (mdyn Å^{-1})	Strain-free value, r_0 (Å)
$Cr^{III}–N_{amine}$	1.10	2.045
$Cr^{III}–N_{imine}$	1.00	1.985
$Fe^{III}–N_{amine}$	1.70	1.950
$Fe^{III}–N_{imine}$	1.70	1.925
$Co^{III}–N_{amine}$	1.75[a]	1.905[a]
$Co^{III}–N_{amine(carboxylate)}$	1.75	1.915
$Co^{III}–N_{imine}$	1.75	1.865
$Co^{III}–O_{carboxylate}$	1.40	1.860
$Co^{II}–N_{amine}$	0.82[b]	2.120[b]
$Co^{II}–N_{imine}$	0.82	2.100
$Ni^{II}–N_{amine}$	0.60	2.090
$Ni^{II}–N_{amine(carboxylate)}$	0.60	2.035
$Ni^{II}–N_{amine(imine)}$	0.60	2.050
$Ni^{II}–N_{imine}$	0.60	2.025
$Ni^{II}–O_{carboxylate}$	0.65	2.040
$Cu^{II}–N_{amine}$	0.60	1.970
$Cu^{II}–N_{amine(carboxylate)}$	0.60	1.970
$Cu^{II}–N_{amine(imine)}$	0.60	1.940
$Cu^{II}–N_{imine}$	0.60	1.940
$Cu^{II}–O_{carboxylate}$	0.80	1.900
$Cu^{II}–S_{thioether}$	0.60	2.290
$Cu^{II}–O_{axial(tetragonal)}$	0.10	2.500
$Cu^{II}–O_{axial(nitro)}$	0.10	2.670
$Cu^{II}–O_{axial(pyramidal)}$	0.10	2.150
$Zn^{II}–N_{amine}$	0.35	2.220
$Rh^{III}–N_{amine}$	1.75	2.050

[a] Ref. 126.

[b] Ref. 157.

of hexacoordinate complexes, based on ground state properties [74]. Also, ligand strain effects may be calculated via molecular mechanics calculations and then included in the calculation of Jahn–Teller coupling by the recently proposed method involving non-random strain effects [60,196,197], and this is presently being tested [198].

(g) Transferability of force field parameters

There are three important aspects in relation to the transferability of parameters which emerge from the above discussions and that need to be discussed here: the questions are whether parameters within a certain molecular mechanics force field can be transferred from one compound to another, whether parameters from one particular parameterization can be transferred to another force field, and whether experimental force constants can be directly transferred into molecular mechanics force fields. In other words, is there one "correct" molecular mechanics force field and can the corresponding force constants be directly extracted from experimental data?

Experimental force constants for any specific bond are clearly dependent on the environment and are therefore molecule specific. In molecular mechanics, however, generally applicable and therefore molecule-independent force constants are needed. Therefore, the two types of parameter are not related in a simply way. Moreover, in molecular mechanics calculations, relatively large deviations from a strain-free geometry are described. However, the force constants used in .vibrational spectroscopy represent general situations involving relatively small changes from a geometry that, at least in the case of strained molecules, can deviate considerably from the ideal structure. Again, the two types of force constant are conceptually different parameters. Therefore, force constants used in molecular mechanics calculations are not directly related to experimental observables. Indeed, they are usually the result of extensive fitting of structural and/or thermodynamic properties of a series of compounds to the corresponding experimental data.

As outlined above, the pure central force field approach [166] is an interesting method that completely ignores the usual parameterization described here, which is based on the connectivity of the molecule. This, together with the fact that there is no direct relation between experimental force constants and molecular mechanics parameters (the strain-free bond lengths and angles are not experimentally available either), indicates that there is no such thing as "one ultimate and correct" force field parameterization. The quality of a force field is rather determined by a range of application which is as wide as possible and an agreement between calculated and experimentally available data within this field of applications which is as good as possible.

We have recently developed a force field for a range of metal ions and ligand donor atoms [175] that is based on a well-established parameterization for cobalt(III) hexaamines [126] (see Table 1). I am aware that a number of force fields for some of the metal–ligand combinations described there have already been available [1–4,199]. However, these have all been limited to rather small areas (although they admittedly have used rather consistent parameterization schemes) and were not directly transferable to our general parameterization.

(h) Force field parameters and physical properties

I have outlined above that a force field has just to be consistent within itself, and the isolated parameters are not necessarily *directly* related to physical properties. A conventional force field based on eqns. (1)–(11) might lead to the hope that there is, for example, a strict relation between an ideal metal ion size (value of a specific metal–ligand distance) and the corresponding parameter value of r_0. However, in any force field there is some degree of cross-correlation, i.e. these parameters are dependent on the molecular mechanics model and the corresponding force field as a whole, and this is seen in the variation of a number of available metal–ligand r_0 values (Table 2) which are based on generally rather similar parameterization schemes. Clearly, r_0, k (and other force field parameters) may only be varied within certain limits in the scheme based on eqns. (1)–(11) (see Table 2).

It emerges that a judgement of the quality of a particular r_0 value is confined to a comparison between calculated strain energies and structures with respective experimental data, and any comparison of a particular r_0 value with observed metal–ligand distances is not really warranted. Nevertheless, strain-free metal–ligand parameters, r_0, have been compared with physical properties, mainly in the areas of spectroscopy and thermodynamics such as chelate, macrocyclic and cryptate effects, and metal ion selectivities of macrocyclic ligands [3,4,131,192,200]. In these cases, "exact" values of strain-free parameters ("ideal sizes of metal ions") were of some importance. (In a later section I will show that with a modified model this is not really the case.)

The data presented in Table 2 indicate that the variation may be rather large compared with the bond length differences interpreted in terms of spectroscopic and thermodynamic effects and with the usual agreement of observed and calculated M−L distances of ±0.01 Å [3,175]. Again, it seems to be impossible and also immaterial to judge the quality of isolated r_0 values. What matters is the performance of the respective *entire* force fields, and satisfactory results have been published with parameterizations including all of the values presented in Table 2. Our recently published force field Table 1 [175] is based on a model where angle-bending terms involving the metal centre are replaced by the usually neglected 1,3-interactions. As outlined above, this is expected to lead to a small compression of the corresponding

TABLE 2

Variation of published strain-free metal-ligand distances, r_0

Bond type	Strain-free value, r_0 (Å)		
$\mathrm{Cr^{III}{-}N_{amine}}$	2.045[a]	2.050[b]	
$\mathrm{Co^{III}{-}N_{amine}}$	1.905[a]	1.925[c]	1.950[d]
$\mathrm{Co^{II}{-}N_{amine}}$	2.120[e]	2.180[b]	
$\mathrm{Ni^{II}{-}N_{amine}}$	2.090[a]	2.100[f]	2.010[g]
$\mathrm{Cu^{II}{-}N_{amine}}$	1.970[a]	2.030[h]	2.000[i]
$\mathrm{Cu^{II}{-}S_{thioether}}$	2.290[a]	2.380[j]	
$\mathrm{Cu^{II}{-}O_{carboxylate}}$	1.900[a]	1.950[i]	
$\mathrm{Zn^{II}{-}N_{amine}}$	2.220[a]	2.170[b]	
$\mathrm{Rh^{III}{-}N_{amine}}$	2.050[a]	2.040[b]	

[a] Ref. 175. [b] Ref. 3. [c] Ref. 117. [d] Ref. 201. [e] Ref. 157. [f] Ref. 202. [g] Ref. 123. [h] Ref. 3 (a value of 2.000 (2.160) was proposed for square planar (octahedral) coordination). [i] Ref. 199. [j] Ref. 2.

r_0 values. It is interesting to see that this trend is not observed *generally*, indicating again that the variation seen in Table 2 is not only due to the differences in the molecular mechanics model used.

D. APPLICATIONS. SELECTED EXAMPLES

(i) Trigonal twist

The widespread opinion that coordination chemistry is essentially concerned with octahedral complexes is misconceived. A range of available coordination numbers other than six are common and moreover, exact octahedral geometry is rarely observed, for example many complexes exhibit trigonal prismatic geometry rather than octahedral [65]: A species with a twist angle ϕ (see Fig. 3) of 30° is as much a distorted trigonal prism as it is a distorted trigonal antiprism or octahedron. What is responsible for the fact that some hexacoordinate structures are trigonal prismatic and others are octahedral? Clearly, this must, in any case, be the result of a compromise between ligand and metal centre dictation, no matter what the size of these effects is.

The trigonal twist is of particular interest to spectroscopists since it is a distortion along a normal mode, as are Jahn–Teller [59,60] and tetrahedral distortions [67–70] in copper(II) complexes, and it might therefore be treated in much the same way. Also, the trigonal twist is an interesting example in terms of structural interpretation and/or prediction since a considerable range of approaches, including purely geometrical considerations [18–20], repulsion-based calculations [31–34], ligand-field theory [62–65], the angular overlap model [66], molecular orbital [203], and molecular mechanics [130] models, have been used.

The differences in destabilization energies between octahedral and trigonal prismatic chromophores of tris-bidentate metal complexes have been calculated as

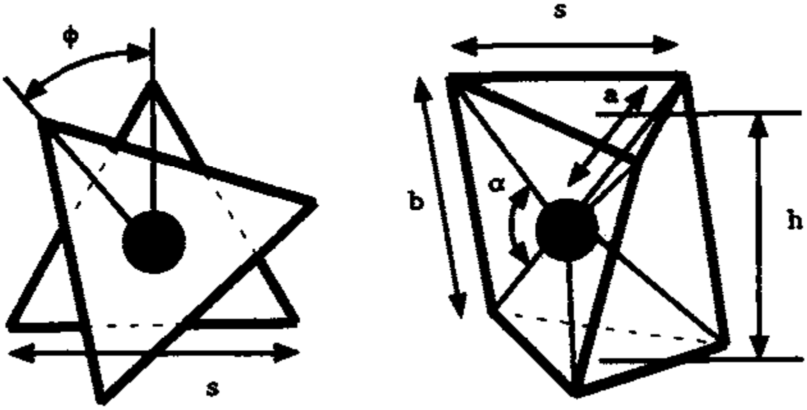


Fig. 3. Definition of structural parameters of D_3 polyhedra with six vertices.

a function of d electron occupancy (low spin and high spin) and for various bite angles α, based on a ligand-field approach [62,63] and with the angular overlap model [66] (see Fig. 4). It may be assumed that these energy differences are the electronic driving force for octahedral geometry. The fact that electronic preference in this model is for octahedral geometry agrees with the observation that octahedral coordination is generally more abundant than trigonal prismatic geometry. Based on geometrical relations, it emerges that an increase in metal–ligand distance will twist the hexahedron towards a trigonal prism if the normalized bite b/a and the normalized trigonal side s/a of a bidentate ligand are kept constant (ligand dictation). Based on the electronic stabilization of octahedral geometry and experimentally available or assumed ligand field parameters, the twist angles ϕ of the whole series of complexes with similar ligands and various electronic configurations may be calculated, provided that the twist angle ϕ of two extreme cases are known (ligand dictation, for example high-spin d^5; maximum electronic preference for octahedral geometry, for example low-spin d^6). This type of analysis was performed with a series of 19 transition metal cage complexes (**1**), (**2**) with a large range of d electron configurations and twist angles ϕ between ~60° and ~20° [65].

The fact that the calculated twist angles were in good agreement with the experimental angles (within 5°) was interpreted as the structures being the result of a compromise between ligand and metal ion dictation [65]. Elongation of the metal–ligand bond must also clearly lead to a twist towards trigonal prismatic geometry. However, no simple correlation was found in this case (see Fig. 5, below), and this effect was therefore neglected. The reason for the missing correlation is clearly due to the subtle changes in ligand conformation, and the fact that ligand flexibility cannot be accounted for in this model is a major problem.

In a purely geometrical approach, the twist angle of tris-bidentate metal com-

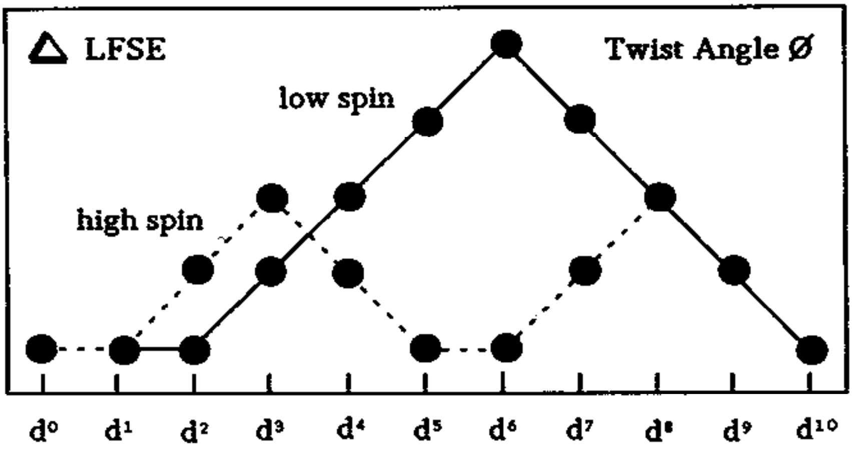
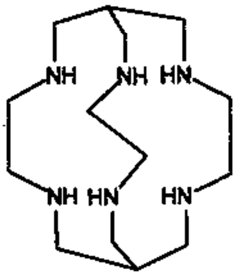
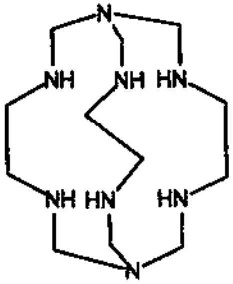


Fig. 4. Twist angle, ϕ, as a function of the d electron occupancy (ligand-field model [62–65]. Calculations with the angular overlap model produce qualitatively similar curves [66]).



sar (1)



sep (2)

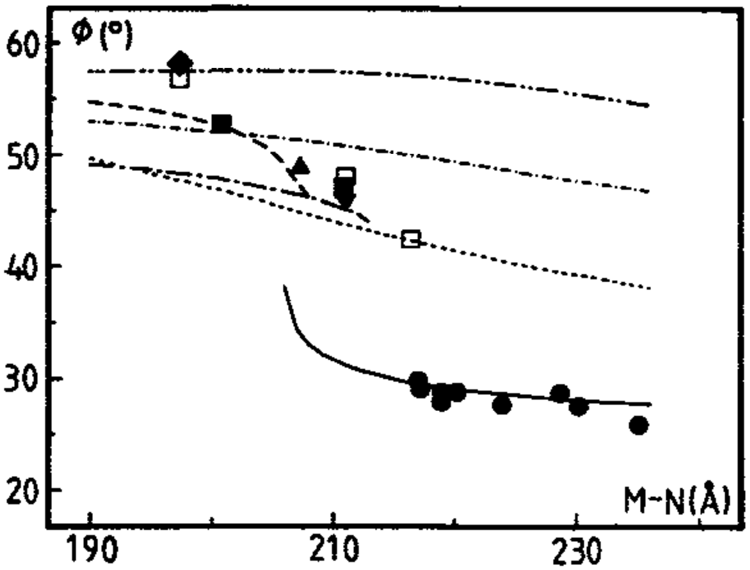


Fig. 5. Twist angle, ϕ, of $[M(sar)]^{n+}$ (1) as a function of the metal–amine bond length. (Reproduced with permission from ref. 130.)

plexes was analyzed based on the structural parameters b/a (normalized bit distance) and s/a (normalized trigonal side; see Fig. 3 for definitions) [18–20]. Interestingly, the twist angles ϕ of a large series of complexes with trigonal symmetry are in good agreement with curves described by the geometrical

$$\left(\frac{b}{a}\right)^2 = 4\left[1 - \frac{1}{3}\left(\frac{s}{a}\right)^2 \cos^2\left(\frac{\phi}{2}\right)\right]$$

function. It also was pointed out [20] that these curves are largely superimposable with calculated energies based on a pure ligand–ligand repulsion approach [31–35]. This is not unexpected since the repulsion potential expressed in terms of the geometrical parameters

$$U \propto \frac{1}{d^n}$$

has a mathematically similar form to the pure repulsion model. Here, the optimum geometry of chelates with fixed metal–ligand bond lengths, a, and bite distances, b, are found by minimization of the repulsion potential, U. The geometrical model only has been used for interpretations, but the ligand atom repulsion method has some predictive power. The major problem in both approaches is that, again, the ligand geometry is fixed. Also, metal centre-based electronic effects are totally neglected, and this is difficult to understand in the context of the results discussed above [65].

We now come back to the cage complexes mentioned earlier. These structures have also been analyzed by molecular mechanics calculations [130]. The method used involves the variation of fixed metal–ligand bond lengths and the replacement of angle-bending terms around the metal ions by Urey–Bradley potentials (ligand–ligand repulsion). Thus, the force field is metal ion-independent (see also next section). The calculated and experimental twist angles ϕ are shown in Fig. 5. There is excellent agreement between calculated and experimental structures. One of the advantages of this method is that the ligand structure is flexible, and different conformers have been refined. It is obvious from Fig. 5 that, within each conformer, there is the expected linear correlation between the twist angle ϕ and the metal–ligand distance.

One of the more interesting points here is that the two conceptually completely different models used to analyze and predict the twist angles of the cage complexes lead to results of similar quality. In the ligand-field approach, electronic effects are introduced explicitly, whereas in the molecular mechanics parameterization, they have seemingly been largely excluded with the substitution of the relevant angle-bending potentials by ligand–ligand repulsion. However, an analysis of the force field in terms of purely steric and electronic terms is not warranted. Therefore, one might not be all that astonished that two different models lead to similar results. Also, in a more general way, the two approaches are formally quite similar in terms of the parameterization:

$$\underbrace{V \cdot Q}_{\text{LF}} = \underbrace{k \cdot Q^2}_{\text{MM}}$$

(ii) Macrocycle hole size

The chemistry of metal ion complexes of macrocyclic and macropolycyclic ligands has developed rapidly over recent years. Macrocyclic complexes generally exhibit greater stability and inertness than acyclic analogues. The application of these complexes to host–guest chemistry, medical chemistry, metal ion selectivities and stabilization of normally inaccessible oxidation states has been reviewed recently [204]. The size of the macrocycle is an important factor in a number of properties and applications. Together with the donor set and (coordinating) side chains, the ring size is an important determining factor for metal ion selectivity. However, other effects such as solvation have been analyzed to be of similar importance, and they also need to be included in a thorough evaluation of the relative complex stabilities [205]. I am aware of five different methods for the determination and interpretation of the macrocycle hole size, and these will be discussed now.

The simplest method uses crystal structure data to calculate the hole radius, determined by the mean distance of the donor atom positions from their centroid (see Fig. 6) [27–30]. The main drawback of this purely geometrical method is that the ligand structure is not flexible and therefore cannot adjust to the demand of the metal ion (it might not have been at its strain energy minimum in the crystal structure anyway). Another important point is the fact that at least one structure of each ligand studied this way has to be known in advance, thus this method is not useful for ligand design.

The other four methods all involve molecular mechanics calculations. The best fit of a metal ion M into a macrocycle L obviously occurs when the total strain energy of ML is at a minimum. Therefore, U_{total} (see above) as a function of M–L has to be plotted for all conformers, i.e. the global minimum as a function of M–L has to be found considering the whole conformation space. U_{total} is not a symmetrical potential (see above). This is obvious in the example shown in Fig. 7. Therefore, the often-used model [132–146] for explaining the best fit with the metal–ligand bonding potential, E_{ML}, which is usually described by a harmonic function, is misleading. This oversimplification, which does not account for strain energy differences due to a

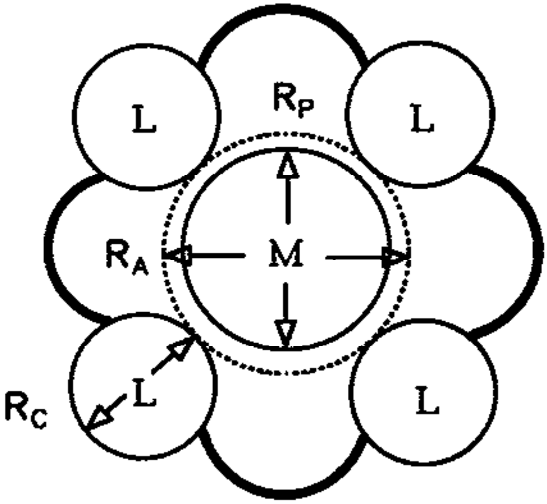


Fig. 6. Geometrical determination of the macrocycle hole size [28].

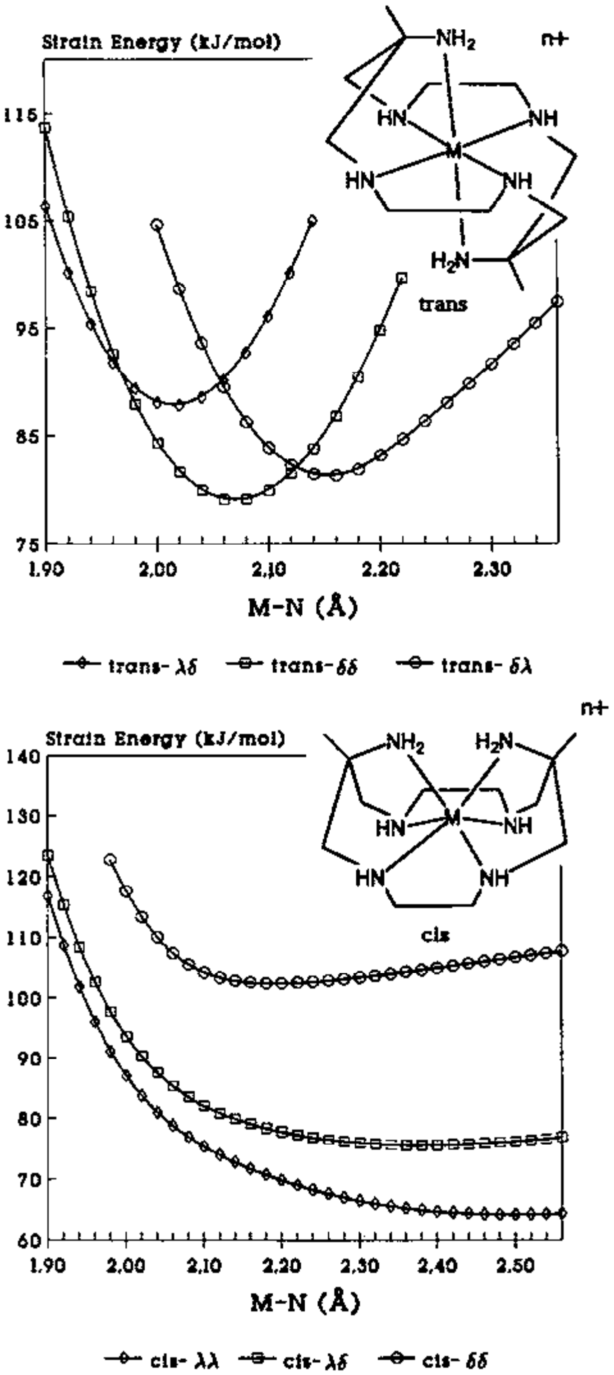


Fig. 7. Total strain energy as a function of M–L for the conformers of *trans*- and *cis*-[M(diammac)]$^{n+}$ [90].

relaxation of the ligand, might be partly responsible for some of the controversy that this method has caused.

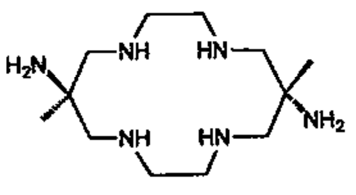
$$E_{ML} = \frac{1}{2}k_{ML}(r_{ML} - r_0)^2$$

It was concluded that, in this approximation, the best fit of a metal ion into a macrocycle is at the minimum of the metal-ligand potential, viz. $E_{ML} = 0$. This condition is fulfilled with either $k_{ML} = 0$ or $r_{ML} = r_0$. The corresponding two methods of finding a size-matching metal ion for a macrocycle involve molecular mechanics calculations with $k_{ML} = 0$ [132,133] or the determination of the minimum of the curve of U_{total} vs. r_0 [139–142]. There has been some controversy on how to calculate the latter curves.

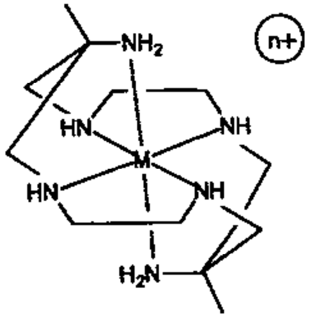
It was argued that an absolute calculation as a function of r_0 [3,141] relies on a well-balanced and accurate force field which, in terms of k_{ML}, is not given [142]. Also, the interpretation of the resulting functions relies on an accurate knowledge of the strain-free bond distance, r_0, and this is certainly not warranted (see above). It was therefore proposed to fix r_{ML} with an exceedingly large force constant and then calculate U_{total} as a function of r_{ML} [139–142]. Obviously, the resulting strain energies cannot be analyzed in an absolute way [141], but this is a problem common to all molecular mechanics calculations. The more serious problem is that the considerable increase in strain energy produced by a small deviation of the restrained M−L distance produces unrealistically steep curves. Thus, relative energy differences between conformers at a given M−L distance are meaningless. Also, the claim that these calculations are independent of a metal force field is not entirely true since an accurate estimate of the L−M−L valence angle bending force constant is of critical importance [140].

All these problems vanish if the metal-ligand distance is fixed mathematically, rather than by restraints imposed by large force constants or by variation of r_0, and by a substitution of the L−M−L bending function by 1,3-repulsion of the ligand atoms [90,130]. So far, we have used this method for the analysis of subtle structural effects rather than for purely thermodynamic considerations, but an application of this model to metal ion selectivities would seem to be appropriate. The method of fixing internal coordinates by Langrangian multipliers [128] has the advantage that the constrained M−L bonds do not necessarily contribute to the strain energy, hence neither k_{ML} nor r_0 have to be included in the force field. Furthermore, the difference in the parameterization concerning angle terms around the metal ion has the advantage that the only other set of parameters involving the metal ion disappears. Considering the M−L−R bending function as metal ion-independent (which is a generally accepted approximation), the whole force field becomes metal ion-independent. Clearly, the calculations are dependent on the function used for the 1,3-interactions. However, the implemented Urey–Bradley function is widely accepted and the parameters involved are identical to the rest of the organic part of the molecules, and this whole parameterization [126] has been thoroughly tested [130].

The advantage of this method is that the calculated hole size is completely independent of the metal ion to be coordinated. The desire of the metal centre is for maximum orbital overlap, and this is based on electronic effects included in the parameter values of r_0 and k of the metal–donor atom bond. However, the calculated M–L distance at the minimum energy of any calculated conformation (e.g. $U_{\text{total}} = 88\ \text{kJ mol}^{-1}$; M–L = 2.02 Å for the trans-$\lambda\delta$ conformer shown in Fig. 7) is representing the ligand desire and therefore independent of the parameterization of the metal chromophore. This also has important implications in terms of the much discussed problem of metal ion compression (see above). Taking the same U_{total} vs. M–N curve (trans-$\lambda\delta$ in Fig. 7), in every structure (be it calculated or experimental) with M–L larger than the best fit of 2.02 Å the ligand will try to compress the metal ion and in every structure with a smaller value than 2.02 Å the ligand will try to elongate the metal–ligand bond. Thus, the corresponding Co(III) and Fe(III) complexes with M–L ~ 1.94 and 1.98 Å, respectively, have elongated but still comparably short bonds. The important point here is that, based on $r_0^{\text{Co(III)}} = 1.95$ Å (see Table 2) or Co(III)–$\text{N}^{\text{average}} = 1.97$ Å [3], one might be tempted to interpret a Co(III)–amine bond length of 1.94 Å as being compressed. The analysis based on the corresponding curve in Fig. 7 indicates that this clearly is not the case. The only *trans*-$[\text{M(diammac)}]^{n+}$ complexes with genuinely compressed M–L bonds characterized so far are *trans*-$\delta\delta$-$[\text{Zn(diammac)}]^{2+}$ with M–L ~ 2.15 Å and *trans*-$\delta\delta$-$[\text{Ni(diammac)}]^{2+}$ with M–L ~ 2.10 Å [90]. With *cis*-$[\text{M(diammac)}]^{n+}$, one concludes that the ligand is leading to elongated M–L bonds for virtually all metal ions (Fig. 7). Although the M–L bond lengths may be estimated quantitatively, the metal–ligand compression or elongation analyzed this way is clearly only qualitative, viz. any quantitative analysis would have to involve a definition of r_0. However, as I will show later, even in terms of spectroscopy there is no real need to quantify the amount of compression or elongation. I have to stress here again that the above analysis (Fig. 7) is based on the force field used. Any variation of parameters of the ligand backbone (metal-based parameters are not involved) will lead to a modification of



diammac (3)



$[\text{M(diammac)}]^{n+}$ (4)

the analyzed curves. However, this does not seem to be a problem since there is broad agreement on the parameterization of organic molecules, and, more importantly, all the experimentally observed structures are in good agreement with the predictions in Fig. 7 [90]. Also, good agreement was found in a similar study with transition metal hexamine cage complexes (see above and ref. 130).

(iii) Isomer distribution

Questions concerning the isomerism of metal complexes have fascinated coordination chemists since Werner's early work [206]. In simple systems it is easy to determine the number of topologically possible isomers and computer programs based on combinatorial methods have been developed for more complex problems [12]. In recent years it has become routine to analyze the relative stabilities of isomers of a given system by molecular mechanics calculations. Clearly, the whole conformation space has to be considered in such an analysis, viz. each conformer contributes to the total isomer distribution. The abundance of each isomer may be calculated from the partition function of the corresponding system [155].

$$N_i[\%] = 100\,\frac{e^{-(E_i/RT)}}{Q_{\text{total}}}$$

$$Q_{\text{total}} = \sum_i e^{-(E_i/RT)}$$

The accuracy of the calculated isomer distribution is determined by the accuracy of the calculated relative stabilities E_i of all the isomers. The accuracy needed for meaningful interpretations may be exemplified with a two-particle system, where at 298 K the relative energy differences of 1, 2, 5, 10 and 15 kJ mol^{-1} lead to 60/40, 69/31, 88/12, 98/2 and 100/0 distributions, respectively. Thus, errors in the relative energies of around 1 kJ mol^{-1}, will lead to large errors in the calculated isomer distributions. It also emerges that a conclusive test for an approach aiming at the analysis or prediction of isomer distributions should involve systems with only partial selectivity, where the resulting errors are most important.

Isomer distributions determined by molecular mechanics calculations are found from the relative stabilities, E_i, which are related to strain energy differences. The basis for reliable results is clearly a well-balanced force field. However, even with a reasonable force field there are a number of problems which need to be addressed. Firstly, a non-uniform set of ligand atoms may lead to isomers with different chromophores, and electronic effects in addition to the calculated strain energy differences may then lead to the stabilization or destabilization of certain isomers. Such effects have been studied, to some extent, in relation to the calculation of strain energy minimized structures [175], but the effect on the strain energies has not been investigated quantitatively so far. It is questionable whether a simple spectroscopic analysis may be informative since any ligand field analysis is based on electronic as well as structural properties, and the latter might be the result of the stabilization to be analyzed. Secondly, the strain energies used in the calculation of isomer distributions are enthalpy rather than free energy terms. Corrections with calculated entropy terms have been included in a few studies [16,100–102]. However, these corrections are based on a number of additional uncertainties and approximations, and, at least for simple cobalt(III) hexaamines, the corrections are small with respect to the overall error limits [103]. Apart from statistical corrections, entropy effects are therefore usually neglected. Thirdly, molecular mechanics calculations usually involve "naked" molecules. It is conceivable that differences in solvation and/or ion-pairing might lead to the stabilization of certain isomers and/or conformers. However, these effects are not easy to quantify. Experimentally, they are often applied in separation and purification procedures based on chromatography or fractional crystallization. The substrates used are often oxo anions, such as tartrate, leading to selective hydrogen bonding [97]. Since environmental effects are generally neglected in molecular mechanics calculations, the respective experiments should involve "innocent" environments, viz. counter ions that do not lead to isomer selection.

In a recent series of studies with simple cobalt(III) hexaamines we have found that within this limited range of compounds there is generally an excellent agreement between calculated and experimental isomer distributions. These results are summarized in Table 3. Other results of satisfactory quality have been found for a range of cobalt(III) complexes including $[Co(dien)_2]^{3+}$ (**5**) [157], $[Co(dpt)_2]^{3+}$ (**6**) [151], $[Co(dien)(dpt)]^{3+}$ [152] and $[Co(ppm)((R),(S)\text{-ala})]^{2+}$ (**14**) [150] (for further examples, see ref. 2). Some of these results are not directly comparable with the systems presented in Table 3 since different force fields have been used for some of the studies and, in most of the cases, not all conformers have been included in the analysis, and this clearly is a necessity in a thorough analysis.

An interesting application in this area is racemate separation by stereoselective coordination of racemic ligands to a chiral matrix consisting of an optically pure ligand coordinated to a transition metal ion. The basic idea is shown schematically in Fig. 8.

Here the separation of enantiomers is reduced to a comparably simple isomer separation. Based on the results of simple cobalt(III) hexaamines, it should be possible to analyze the quality of a chiral matrix with molecular mechanics calculations with some measure of accuracy. This is an important point since every racemic substrate must have a different optimum chiral matrix, and their syntheses may be rather tedious and expensive. It is obvious that chiral matrices used for racemate separations should involve labile metal ions rather than the inert cobalt(III) centres discussed above. The systems studied experimentally have usually involved copper(II) [208,209]. Chromatography or extraction processes (stereoselective transport through liquid membranes) have been used or proposed for the separation of the resolved substrate from the matrix complex [92,209]. A number of recent examples for the design of chiral matrices with square planar nickel(II) complexes are presented

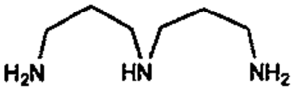
TABLE 3

Comparison between calculated and experimental isomer distribution of some cobalt(III) hexaamines[a]

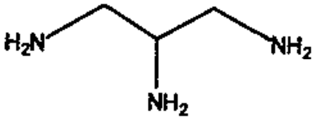
Compound	Isomer	%		Ref.
		Calc.	Expd.	
$Co(trap)_2^{3+}$	meso	40	45	103
	rac	60	55	
$Co(dipa)_2^{3+}$	meso	5	0	207
	rac	95	100	
$Co(trab)_2^{3+}$	A	21	21	154
	B	16	15	
	C	16	15	
	D	4	4	
	E	43	45	
$Co(trab)(en)X^{2+}$	A	58	60	155
	B	24	22	
	C	18	18	
$Co((R)\text{-}trab)(pn)X^{3+}$	(R)-pn	56	54	155
	(S)-pn	44	46	

[a] Ligands involved include trap (**7**), dipa (**8**), trab (**9**), en (**10**) and pn (**11**).

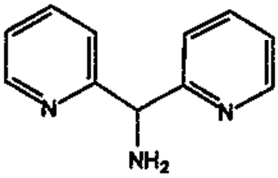
dien (5)



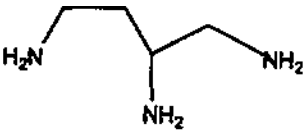
dpt (6)



trap (7)

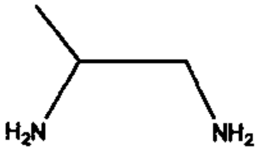


dipa (8)

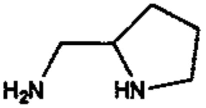


trab (9)

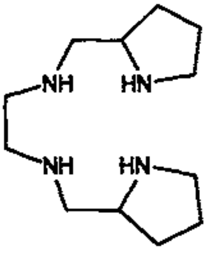
en (10)



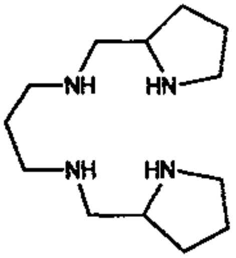
pn (11)



pam (12)



epm (13)



ppm (14)

in Table 4. Here the solvent-dependent equilibrium between square planar and octahedral coordination is used to coordinate the racemic substrate stereoselectively. After separation of the excess substrate from the now octahedral matrix complex, the (partly) resolved coordinated substrate is then obtained by enforced square planar coordination of the nickel(II) species (solvent change) [92].

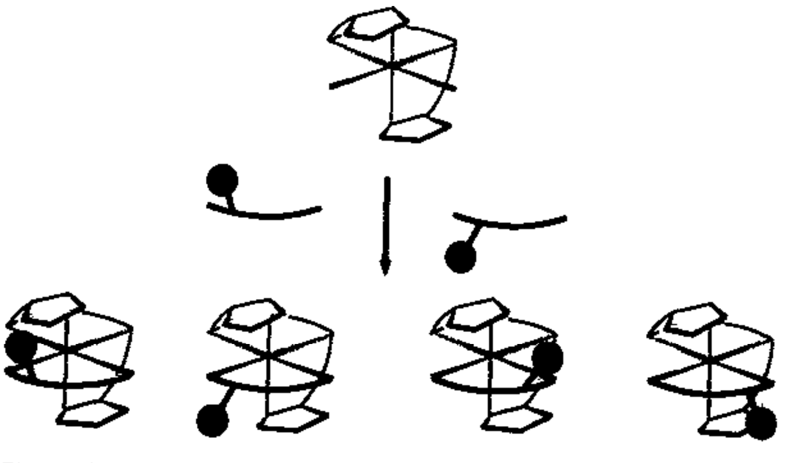


Fig. 8. Schematic presentation of a racemate separation by a stereoselective ligand exchange reaction.

TABLE 4

Calculated and experimental stereoselectivities with the matrix ligands ppm and epm [92][a]

Matrix	Substrate	Calculated		Experimental	
		% S	% R	% S	% R
Co(III)/ppm	pn	55	45	51	49
Co(III)/ppm	pam	64	36		
Ni(II)/ppm	pn	44	56	43	57
Ni(II)/ppm	pam	53	47	56	44
Ni(II)/epm	pn	62	38	57	43
Ni(II)/epm	pam	27	73	30	70

[a] Ligands involved include epm (**13**), ppm (**14**), pn (**11**) and pam (**12**).

The stability differences are obviously due to subtle changes of all terms involved in the total strain energy, and a prediction without a determination of the relative strain energies does not seem to be possible [155]. This also emerges from a comparison of the data presented in Table 4, where substitution of the metal centre or of the substrate lead to seemingly unpredictable variations. The optimum enantiomeric excess of ~45% still seems to be rather modest. However, optically pure material may be obtained with such systems in few cycles. Also, in chromatography good separations are obtained with separation factors $\alpha \approx 2$, and recently it has been demonstrated [210] that, depending on a number of parameters related to the stationary phase, this corresponds to only ~10% enantiomeric excess.

(iv) Electron transfer

The sizes of metal ions generally vary between oxidation states. Therefore, the steric strain enforced by the ligand backbone is dependent on the oxidation state of the metal centre. Thus, the strain energy difference within a given metal ion and set of oxidation states clearly is dependent on the ligand sphere. This property has been used in qualitative and quantitative analyses of thermodynamic and kinetic properties of electron transfer reactions.

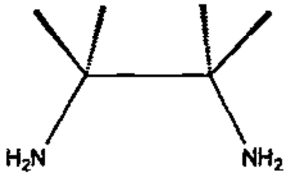
The cobalt(III/II) redox potentials of hexaamine complexes cover a wide range [115,211,212]. The data indicate that the most negative potential belongs to a couple where the ligand allows shorter than average Co—N bonds ($[\mathrm{Co(diammac)}]^{3+/2+}$ (**4**) −0.63 V; Co(III)—N ~1.94 Å; Co(II)—N ~2.08 Å) whereas the largest potential belongs to a couple with relatively long Co—N bonds ($[\mathrm{Co(dpt)_2}]^{3+/2+}$ (**6**) 0.28 V; Co(III)—N ~2.03 Å; Co(II)—N ~2.22 Å). It emerges that ligands preferring a large metal ion are easier to reduce than ligands with small preferred hole sizes. This interpretation has been analyzed with molecular mechanics calculations [115,159,160,213,214]. A correlation of the strain energy differences between the cobalt(III) and cobalt(II) structures of a series of ten hexaamines complexes with the corresponding redox potentials was found [115]. A quantitative analysis revealed that, although steric relaxation is a major component, additional effects such as the Lewis basicity of the ligand atoms might be of some importance. In addition, the analysis of redox potentials of transition metal complexes (Ni(II), Cu(II), Pd(II), Cr(III)) of linear tetraamines and tetraaza-macrocyclic ligands and their *N*-methylated analogues has indicated that increasing hydrophobicity of the ligands may lead to stabilization of the lower valent complexes (Ni(I), Cu(I), Pd(I), Cr(II)) [215,216].

Usually, electrode processes involving a reduction are treated as one-step reactions described by the standard redox potential E^0, the heterogeneous rate constant, k, and the charge transfer coefficient, α. Recently, it was argued that such a treatment must be inadequate if the relative stabilities of the conformers of the oxidized form O_i are different from the stabilities of the conformers of the reduced form R_i. In this case, the redox couple must be described by a multistep process (charge transfer coefficients omitted) [157].

$$\begin{tikzcd}
O_1 + n\cdot e \arrow[r, shift left, "{E_1^0,\ (k_s)_1}"] \arrow[d, shift right] & R_1 \arrow[l, shift left] \arrow[d, shift right] \\
O_2 + n\cdot e \arrow[u, shift right, "K_1"'] \arrow[r, shift left, "{E_2^0,\ (k_s)_2}"] \arrow[d, shift right] & R_2 \arrow[l, shift left] \arrow[u, shift right, "K'_1"'] \arrow[d, shift right] \\
O_3 + n\cdot e \arrow[u, shift right, "K_2"'] \arrow[r, shift left, "{E_3^0,\ (k_s)_3}"] \arrow[d, shift right] & R_3 \arrow[l, shift left] \arrow[u, shift right, "K'_2"'] \arrow[d, shift right] \\
O_i + n\cdot e \arrow[u, shift right, "K_i"'] \arrow[r, shift left, "{E_i^0,\ (k_s)_i}"] & R_i \arrow[l, shift left] \arrow[u, shift right, "K'_i"']
\end{tikzcd}$$

This model has been used to analyze the couples $[\mathrm{Co(sep)}]^{3+/2+}$ (**2**) [157], $[\mathrm{Co(dien)_2}]^{3+/2+}$ (**5**) [157] and $[\mathrm{Co((\pm)\text{-}pn)_3}]^{3+/2+}$ (**11**) [158], based on conformational analyses by molecular mechanics calculations. For $[\mathrm{Co(sep)}]^{3+/2+}$ and $[\mathrm{Co(dien)_2}]^{3+/2+}$ no conformational changes were predicted to occur and, indeed, single-step reductions were observed experimentally. For $[\mathrm{Co((\pm)\text{-}pn)_3}]^{3+/2+}$, the calculated equilibrium constants, K_i, between the various conformers were predicted to be different in the Co(III) and Co(II) states and four different E^0 values were predicted to lie within a range of 20 mV. Qualitatively, this is in good agreement with the experimental data. However, a lack of resolution and of independent experimental information and the presence of unpredictable dependencies of the experimental parameters on environmental factors prevent a quantitative analysis [158].

The rate of electron transfer of $\mathrm{CoN_6^{3+/2+}}$ couples span an extremely wide range from $\leqslant 10^{-7}\ \mathrm{M^{-1}\,s^{-1}}$ ($[\mathrm{Co(NH_3)_5}]^{3+/2+}$, $[\mathrm{Co(tmen)_3}]^{3+/2+}$ (**15**), [Co-



tmen (15)

$(dpt)_2]^{3+/2+}$ (**6**)) to ~10^3 M^{-1} s^{-1} ($[Co(diammac)]^{3+/2+}$ (**4**) [159,160,212,217–219]). The kinetics of the outer-sphere electron processes of $Co^{3+/2+}$ couples are usually described with semiclassical models based on the Marcus theory [220,221].

$$k = K_0 \nu_n \chi_{el} \chi_n$$

Here K_0 is the collision constant (dependent on charge and size of the reactants), ν_n is the effective nuclear frequency and χ_n and χ_{el} describe nuclear and electronic components. Usually it is assumed that the Franck–Condon barrier predominates, and electronic contributions have only rarely been assessed [156], and are often neglected (adiabatic electron transfer for $CoN_6^{3+/2+}$ couples). The main contributions are then related to structural reorganizations which are mainly dependent on bond length differences and to the force constants of the respective breathing modes. Additional factors such as changes in angle bending and torsional strain and trigonal twist are usually assumed to be of secondary importance. In addition, the closest approach of the two substrates and solvent reorganization have to be considered [220,221]. Qualitatively, it emerges that $Co^{3+/2+}$ couples with relatively similar structures (enforced Co–N bond lengths) as in the case of $[Co(sep)]^{3+/2+}$ (5.1 M^{-1} s^{-1} (**2**) [219]), $[Co(sar)]^{3+/2+}$ (2.2 M^{-1} s^{-1} (**1**) [217]) and $[Co(diammac)]^{3+/2+}$ (900 M^{-1} s^{-1} (**4**) [219]) lead to fast electron transfer rates. These steric contributions to the Franck–Condon barrier have been modelled with some success with molecular mechanics calculations [115,156,159,160].

(v) Spectroscopy

(a) Ligand-field strength

The ligand field strength of any particular metal ion is dependent on the ligand atoms and the geometry of the ligand sphere. With a given set of ligand atoms, the ligand-field strength is dependent on their basicity, that is on their substitutents. Experimentally, this emerges, for example, from series of amine complexes where the ligand-field strength increases with the number of primary, secondary and tertiary amines [3,200,222]. Other factors influencing the ligand-field strength include the metal–ligand bond length, the coordination angle and the angle between the metal–ligand bond and the direction of the lone pair on the ligand atom. Hydrophobicity of the ligands has also been proposed to influence the ligand-field strength [215,216]. The geometric factors have been analyzed spectroscopically and with molecular mechanics calculations [3,71,72,132,200,213,222,223]. The angular dependencies are basically related to optimum orbital overlap. Based on the effects of the hole size of series of hexaaza macrocyclic complexes of Co(III) on the spectroscopic properties, it was suggested that shortening of the metal–ligand bond length leads to an increase in the ligand-field strength [132,213]. This is in agreement with the observation that the ligand-field and angular overlap model parameters D_q and e_σ and e_π increase with decreasing bond length ($1/r^n$, $n = 5, 6$ dependency [224]). There is some controversy regarding the question of whether short bonds are really compressed. It was argued that the high ligand-field strengths observed with short bonds are the result of the best fit of the metal into a macrocycle resulting in an optimum oribal overlap, and that compressed bonds are observed very rarely [3,200,222]. The question of whether any bond is relaxed ("best fit"), compressed, or elongated depends on the strain-free value of this particular bond and not on the respective parameter used in a molecular mechanics force field (see above). Spectroscopically, this is not of importance since the ligand-field parameters do increase with decreasing metal–ligand distances, whether the bonds are compressed or not, and this is in agreement with the observations.

An interesting observation is that there is a correlation of the ligand-field strengths and the corresponding redox potentials [115,212,225–227]. This was debated in a number of cases [228–230]. Clearly, based on theoretical considerations, the two properties cannot be expected to correlate in a simple way, since the redox potentials are related to energy differences between the ground states of the oxidized and reduced forms, whereas the ligand-field strength depends on the energies of the ground and excited state of a given oxidation state. In the case of cobalt(III) hexaamines, the cobalt(III/II) redox potential has been fitted to the release of steric strain upon reduction to cobalt(II), and this is related to the strain energy of the cobalt(III) ground state. Clearly, the ligand-field strength is also dependent of the geometry of the ground state. Therefore, it is not astonishing that a trend between redox potentials and ligand-field strengths is observed, but their description as a simple linear correlation is not warranted.

In an attempt to quantify these observations, the redox potentials and ligand-field strengths of cobalt(III) hexaamines have both been fitted to strain energy differences between Co(III) and Co(II) ground states and between Co(III) ground states and approximated Co(III) excited states (force field not known) [115]. The observation of a correlation found in the latter case is rather fortuitous since electronic transitions between d orbitals are, based on the Franck–Condon principle, energetically dependent only on the bond lengths of the ground state structure. Indeed, there is a good correlation between the ground state structures and the frequency of the d–d transitions, and this has been demonstrated above.

Clearly, the structure of the excited state is in many cases different from the ground state structure (see Fig. 9). However, according to the Franck–Condon principle, the electronic transition generally does not occur to the equilibrated excited state but rather to higher vibrational levels, and this therefore leads to the usually observed broad absorption bands. A simple method to estimate the change in metal–ligand bond lengths accompanying electronic transitions in transition metal complexes has been proposed [73].

$$\delta r \sim \frac{nm\Delta}{fr_0N}$$

Here the change in bond length δr, is only dependent on ground state properties, viz. the energy separation Δ, the force constant, f, of the symmetric stretching mode, the number of ligand atoms, N, and of electrons, m, involved in the change and the usually used dependency of Δ on the nth power of the bond length ($n \sim 5$ [224]). Therefore, this method to determine the excited state structure needs fewer approximations than molecular mechanics calculations. Indeed, one could imagine developing force fields for excited states based on structures calculated with this simple and solid model. If a constant force constant $f \approx 2.49$ mdyn Å for the series of cobalt(III) hexaamines studied [115] is assumed (spectroscopically this is not entirely correct, of course), then δr (values between 0.064 and 0.076 Å are the result) is proportional to Δ/r_0, viz. the geometry of the excited state (and therefore also the strain energy difference between excited and ground state) is correlated to the ground state structure. This might be the reason for the observed dependency [115].

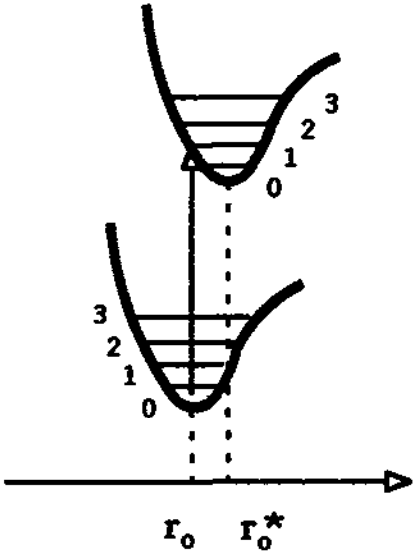


Fig. 9. Electronic absorption to an excited state with an equilibrium structure that is different from the ground state.

(b) Structure of copper(II) dimers

There is a considerable interest in binuclear metal complexes. In particular with copper(II), a growing number of systems are available where metal–metal interactions and multi-electron processes have been studied in order to obtain some information on the reaction modes and structures of metalloproteins [231]. Since the solid state structures of many of these natural compounds are still not known, solution techniques such as spectroscopy, correlatable with electronic or structural models, are of considerable interest. We have recently developed a method for the structural analysis of weakly coupled binuclear copper(II) complexes in solution based on the simulation of EPR spectra coupled with molecular mechanics calculations [93].

Some years ago, a simulation program for EPR spectra of coupled paramagnetic dimers was developed using a set of the *g* and *A* values of the two sites and geometric parameters that unambiguously define the geometry of the binuclear chromophore (see Fig. 10) [82]. In the simplest case with two equivalent sites of tetragonal symmetry, eight parameters, not including line shape parameters, have to be fitted to the spectrum. Clearly, such a structural analysis based on EPR spectra simulation alone might be ambiguous, especially if the spectra are, as is often the case, ill-resolved [232].

A recently developed force field for copper(II) complexes was shown to lead to rather accurate structural predictions [175]. However, molecular mechanics calculations alone do not seem to be appropriate for the prediction of structures of binuclear complexes, since the number of torsional degrees of freedom can quite often lead to

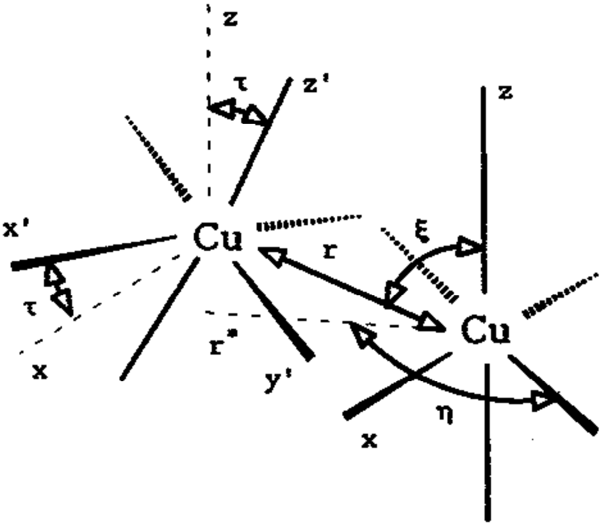


Fig. 10. Definition of structural parameters used to simulate EPR spectra of weakly coupled dinuclear copper(II) complexes.

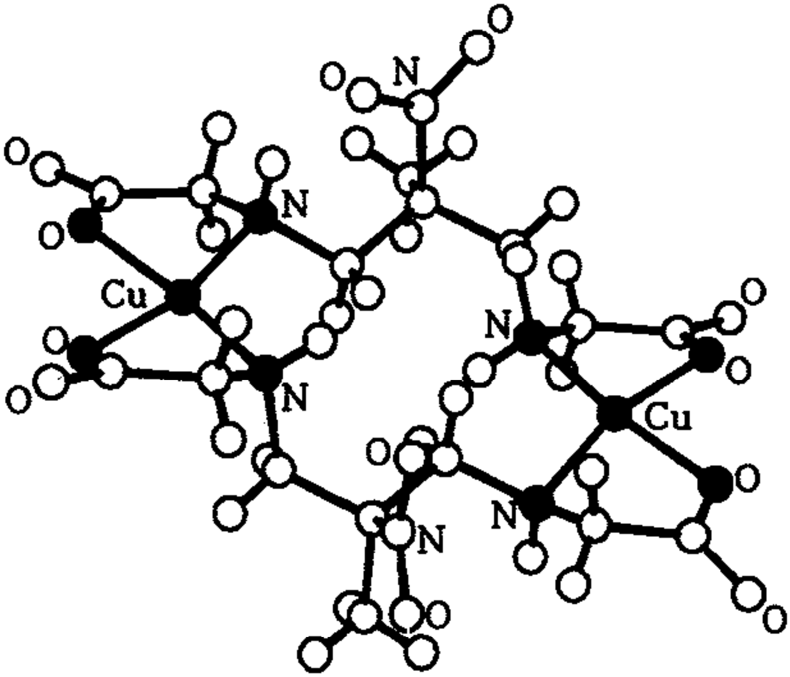


Fig. 11. Solution structure of [Cu(mnpgly)] [93].

a large number of conformers. It therefore occurred to us that EPR spectroscopy and spectra simulation combined with molecular graphics and molecular mechanics should lead to an unambiguous determination of the structure of weakly coupled binuclear copper(II) complexes.

In the course of preparative work on (chiral) quadridentate ligands based on animo acids by template condensation around copper(II), we observed (via EPR spectroscopy) a dimeric species which we were unable to crystallize [233]. The analysis based on spectra simulation and molecular graphics and mechanics yields the solution structure shown in Fig.11 with the parameters presented in Table 5.

It is interesting to note that the strain energy of the dimer (per mole) is less than half of the corresponding monomer strain energy, suggesting that the dimer is more stable than the respective monomeric structure. Reduction of the nitro substituents to amines, and substitution of one glycine residue per ligand by alanine (mixed glycine/alanine ligand) still leads to dimer formation in solution, whereas any higher degree of substitution on the ligand backbone prevents dimer formation. These observations are also in good agreement with the molecular mechanics results.

It is important to note that this simple and efficient method for the determination of solution structures of weakly coupled binuclear copper(II) complexes has also been tested successfully on examples where structural data based on X-ray crystallography are available [93]. Moreover, it is not restricted to binuclear copper(II)

TABLE 5

Solution EPR and structural parameters of [Cu(mnpgly)]$_2$ [93]

Parameter	EPR simulation	Molecular mechanics
$g_\perp$	2.07	
$g_\parallel$	2.25	
$A_\perp$ [10^4 cm^{-1}]	35	
$A_\parallel$ [10^4 cm^{-1}]	80	
ζ (°)	73	68
τ (°)	5	4
η (°)	6	4
d (Å)	6.7	6.7

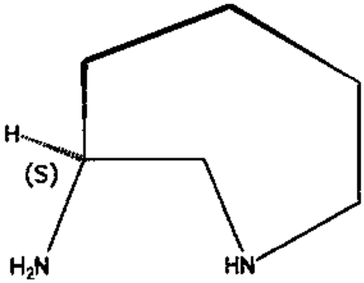
complexes, and it might be extended to homo- and heterobinuclear complexes with one unpaired electron per chromophore. Also, the predictive power of the model might be of importance for the design of binuclear complexes with given spectroscopic properties.

(c) Combined molecular mechanics and angular overlap model calculations

Angular overlap model calculations allow term energies (d–d spectra) and magnetic properties such as *g*-tensor parameters to be calculated, based on a set of e_σ and e_π paramters and the structure of the chromophore. It is tempting to use a combination of molecular mechanics and angular overlap model calculations to interpret or predict structural and spectroscopic properties of transitional metal compounds [71,72,111,112]. Our aim is to use this combination to design metal complexes with specific spectroscopic properties, e.g. as spectroscopic models for biologically relevant compounds. The two important problems that are addressed in a first stage are: (i) whether the geometries of the chromophores are modelled sufficiently well by molecular mechanics and (ii) whether the angular overlap model parameters are transferable, viz. whether there exists a consistent set of parameters for a specific M–L bond.

A demanding test for the application of the combination of molecular mechanics and angular overlap model calculations was copper(II) where considerable problems exist in relation to the geometries of the chromophores, mainly due to Jahn–Teller lability [175]. A series of macrocyclic copper(II) complexes [234] and additional complexes with ligands blocking the axial sites, studied spectroscopically in solutions, glasses, powders and single crystals, has produced data of chromophores including square planar, octahedral and square pyramidal geometries with various degrees of tetragonal and tetrahedral distortions [71,72]. The calculated structures of the chromophores are generally in good agreement with the experimental data.

The angular overlap model calculations of the series of copper(II) complexes revealed that the e_σ parameters have not only to be corrected for variations in the bond lengths ($1/r^6$) but, independent of whether experimental or calculated structural data were used, some correction for misaligned valencies have to be included. These so-called "bent bonds" have recently been reviewed [235], and a simple model which does not need any additional parameters has been proposed [71]. Based on this model and a constant set of electronic parameters, there is good agreement between the experimentally observed and the calculated (MM-AOM) spectroscopic properties. This emerges from the data presented in Table 6, where the experimental and calculated electronic properties (AOM calculations based on both experimental (AOM) and calculated (MM-AOM) structural parameters) of two isomers of a copper(II) tetramine with strikingly different structures (square planar and distorted square pyramidal, Fig. 12) and electronic properties (orange and purple colours) are tabulated [71].



(S)-ahaz
(16)

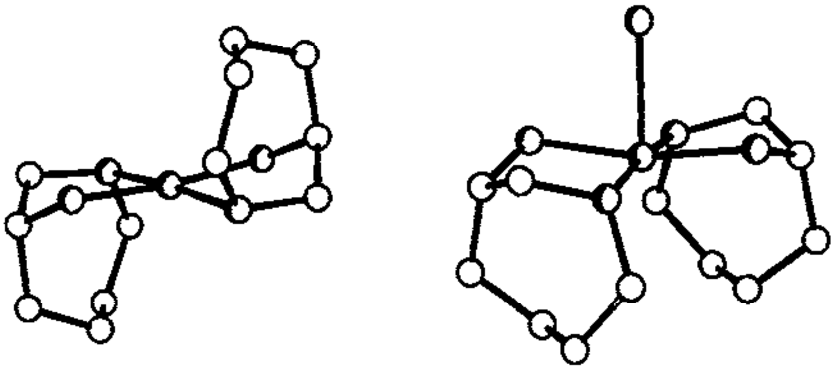
We have shown recently that the g-tensor parameters of iron(III) compounds are extremely sensitive to structural distortions and that the g values calculated with

TABLE 6

Observed and calculated electronic properties of the $[Cu(ahaz)_2]^{2+}$ chromophores [71]

Parameter	$[Cu((R)\text{-ahaz})((S)\text{-ahaz})]^{2+}$ (17)			$[Cu((S)\text{-ahaz})_2(X)]^{n+}$ (18)		
	Exptl.	AOM	MM/AOM	Exptl.	AOM	MM/AOM
$^2B_1$ (d_{xy}) (cm^{-1})	22217	21994	21178	19304	19944	20545
$^2E^{(1)}$ (d_{xz}) (cm^{-1})	22217	20985	20160	19304	18837	19372
$^2E^{(2)}$ (d_{yz}) (cm^{-1})	22217	21804	20987	19304	19645	20190
$^2A_1$ (d_{z^2}) (cm^{-1})	19878	19876	18716	16425	16817	16090
g_1	2.038	2.025	2.030	2.048	2.019	2.038
g_2	2.063	2.050	2.047	2.048	2.067	2.042
g_3	2.142	2.149	2.155	2.159	2.160	2.159
$\|A_1\|$ (10^{-4} cm^{-1})	−(11)[a]	11	16	31 (26)[a]	5	26
$\|A_2\|$ (10^{-4} cm^{-1})	−(40)[a]	49	42	31 (26)[a]	68	29
$\|A_3\|$ (10^{-4} cm^{-1})	−(207)[a]	207	205	200 (203)[a]	194	205

[a] Calculated using experimentally observed transition energies.



[Cu((R)-ahaz)((S)-ahaz)]$^{2+}$
(17)

[Cu((S)-ahaz)$_2$]$^{2+}$
(18)

Fig. 12. Calculated structures of [Cu((R)-ahaz)((S)-ahaz)]$^{2+}$ (17) and [Cu((S)-ahaz)$_2$X]$^{n+}$ (18) [71].

the angular overlap model are in excellent agreement with experiment [77]. Iron(III) therefore seemed to be another demanding example to test the applicability of molecular mechanics calculations in this context. The results of the combined molecular mechanics/angular overlap model (MM-AOM) predictions of the *g* values of a range of published low-spin Fe(III) hexaamine and hexakispyridyl systems indicate that the predictions are quite satisfactory. However, two major problems arise: (i) there are areas with very strong dependencies of certain *g* values on particular modes of distortion, and these may be identified by AOM model calculations as functions of these normal modes [77,112]; and (ii) the question of Jahn–Teller active vibrations and their influence on the energy levels has to be addressed. Obviously, this is especially important in cases with highly symmetrical chromophores leading to near degeneracy in the ground state. The experience with the copper(II) systems discussed above leads to the hope that this problem might be solved, even in the rather simplistic frame of the molecular mechanics model.

From studies with low spin iron(III) and copper(II) complexes, it emerges that the agreement between the calculated spectroscopic parameters based on experimental and with molecular mechanics-modelled geometries is satisfactory. Since the calculation of the electronic properties of the comparably difficult sytems of low spin iron(III) and copper(II) complexes seems to be tenable, it is anticipated that similar studies with a range of (first row) transition metal ions might be feasible.

E. CONCLUDING REMARKS

The interpretation and also the prediction of structural properties, reactivity, thermodynamic and electronic properties of compounds in general, and of transition metal complexes as discussed in this chapter, are a central feature in chemistry. The models used in these areas are becoming more and more sophisticated. However, some of the rather simple methods lead to precise results in a limited area of application. It is well known that an increase in the parameterization may lead to an improved fit but additional approximations might then bury some of the basic aspects. This can be much the same with an increase in the sophistication in a model. Most of the concepts discussed here are readily available and it has been my intention to indicate approximations, limitations and possible applications of a number of basic methods and models in this area.

All the models, be they purely geometrical, related to shape, involving electrostatics, electronics or molecular mechanics may lead to useful data. The question is just what one does with these results; that is, how precise and how relevant are they? The question of relevance is clearly linked to the model chosen and the precision is related to approximations inherent to the model. If the "numbers" resulting from model calculations are thoroughly interpreted, with care and appreciation of the limitations and approximations of the model, important new insights may be gained. Clearly, these calculated data usually have to be compared with experimental results, produced before (interpretation) or after (design) the calculations. One can even go a step further and realize that any measurement needs compounds, and this very clearly shows that one of the most important tasks in our field still is preparative chemistry.

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