

Critical Evaluation of Metal Complex Molecular Mechanics. Part 1. Cobalt(III) Hexaamines

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The ability of available molecular mechanics programs to calculate structures and relative energies of metal complexes is examined via a comparative study of five different force fields: Molmec, Momec91(H), Momec91-(C), Xnviron, and Spartan. The method used for assessing the validity of the force fields showed that four of the force fields were able to reproduce successfully the structures of various Co(III) hexaamine cations determined by X-ray analysis, even when these structures were considerably distorted. In certain cases, the calculated relative steric energies were not reliable. Small variations in force fields parameters sometimes led to large changes in the calculated steric energies, and in some instances, in the order of steric strain for different isomers. The most notable changes occurred when metal-dependent parameters were altered.

Introduction

The basic premise of force field calculations is that the conformational potential energy of a molecule, V_{total} , can be expressed as a simple function of the orientation of the atoms relative to a hypothetical strain-free molecule having the same constitution. The force field represents the bond stretching (V_b), bond angle bending (V_θ), torsion angle deformations (V_ϕ), and nonbonded interactions (V_{nb}) along with other relevant terms. (See ref 1 and the Supporting Information for more information.) The geometry of the molecule is optimized by minimization of V_{total} , the general form of which is given by eq 1¹.

$$V_{\text{total}} = \sum V_b + \sum V_\theta + \sum V_\phi + \sum V_{\text{nb}} + \text{other relevant terms} \quad (1)$$

Molecular mechanics is now a very popular tool for describing the structures and relative energies of many classes of molecules.^{1–42} While Allinger's MM2^{7,8} is the most commonly chosen force field for the description of purely organic

molecules, especially hydrocarbons, the choice of force field for the chemist wishing to study molecules containing a metal is not clear-cut. The general lack of experimental data, especially thermodynamic, to which force field parameters can

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Table 1. Brief Comparison of the Five Force Fields

force field	key authors	basis	minimization technique	selected references
Molmec	Adam, Lindoy	Extension of MM2	quasi-Newton minimization algorithm with the BFGS update method using analytical first derivatives	12, 27, 30, 31, 43, 46
Momec91(H) and Momec91(C)	Hambley for Momec91(H); Comba and Bernhardt for Momec91(C)	extension of Snow's work incorporating modifications suggested by Allinger	Newton-Raphson	1, 5, 26, 28, 29, 32-37, 44
Xnviron Spartan 3.0 ^a	Snow, Maxwell, Dwyer, Geue, Hehre	extension of Snow's work extension of TRIPOS 5.2; present authors did not have access to parameters ⁴⁹	Newton-Raphson	19, 24, 38-41, 45 13, 47, 48

^a Spartan 3.0 is a suite of programs⁴⁷ including a graphical user interface, *ab initio* and semi-empirical modules, and a properties module. As part of the module responsible for the preparation of input for various calculations, several molecular mechanics force fields such as MM2 and MM3 are included. To simplify the discussion, the module responsible for the MM calculations on metal complexes will be called Spartan. This extension of the TRIPOS 5.2 force field has not been parametrized with a view to providing reliable energies, and the present authors did not have access to the parameters, but the force field is commercially available and likely to be used by coordination chemists. For these reasons Spartan was only included in the structure-predicting study.

be fitted, the variability in coordination mode of the metal center, the problem in defining reference angles around the metal center, as well as the effect of the molecule having an overall charge, are all factors which make developing a set of transferable force field parameters more difficult for metal containing molecules than for organic molecules. Consequently, numerous molecular mechanics (MM) force fields for metal complexes have appeared in the literature as research groups have parametrized their own force field for the problems at hand. Several comparisons of force fields for organic molecules have appeared in the literature,^{13,21,22} and it is now time that more attention be spent on evaluating the ability of currently available force fields to model transition metal complexes.

The aim of this work was to determine how well several existing force fields (Molmec, Momec91(H), Momec91(C), Xnviron, and Spartan) are able to generate reliable structures and isomer distributions for a series of metal complexes. The aim was also to examine the effect of variations in selected force field parameters on these structures and energies. The force fields described below were chosen to provide a sample of the different approaches being taken to model metal complexes. For evaluation purposes, it was decided that part 1 of the comparative study would be limited to one of the most well studied and historically important classes of complexes, the Co(III) hexaamines. Compared to other systems, much more experimental data is available, the complexes are unequivocally six coordinate, approximately octahedral, and all have the low-spin d^6 electronic configuration and there are already a number of force fields which contain parameters for Co(III) hexaamines. These complexes should be a good probe for examining how the MM force fields duplicate the balance that exists between the demands of the metal ion and those of the ligands.

Later work will consider molecular mechanics applications to metal complexes of Co(II), Zn(II), Cd(II), Hg(II), Mn(II), and Fe(II).

Description of the Force Fields Used in This Study

A brief description of the five force fields used can be found in Tables 1 and 2. Further details can be found in the Supporting Information.

Computational Details

General. Molmec⁴³ calculations were performed on an Apple Macintosh IIfx. Momec91(H),⁴⁴ Momec91(C),^{26,44} and Xnviron⁴⁵ calculations were performed on a Digital VAX Worksta-

tion 3100. Spartan calculations were carried out on a Silicon Graphics Iris Workstation. Output was analyzed with the graphics program Chem3D 3.1.1.⁵⁰ Data analysis was carried out using Excel 4.0, Kaleidograph 3.0, and the Compar program contained in the Molmec suite of programs.⁴³

Force field files were supplied by the authors of Molmec, Momec91(H) and Momec91(C). The parameter set for Xnviron was taken from ref 39. Calculations from recent publications were duplicated as a check of the parameters supplied.^{26,28,30,39} Version 3.0 of Spartan was employed.⁴⁷

Trial input coordinates were obtained from the Cambridge Structural Database (CSD),⁵¹ unpublished local work and from manipulation of computer graphics (Chem3D and Spartan). The coordinates were orthogonalized, and missing hydrogen atoms were added with Chem3D or AdAtom (a component of the Molmec suite of programs). Minimization was carried out with the relevant force field and the output was examined using Chem3D graphics. To confirm that the conformation so achieved was not an artifact, minimization was repeated with readjusted sets of trial coordinates.

Structural Study. The calculated structures were compared to that observed in the crystal by examining the differences in bond lengths, valence angles, torsion angles, and atom positions for non-hydrogen atoms.

Study of the Energetics. To assess the ability of Molmec, Momec91(H), Momec91(C), and Xnviron to predict the relative stabilities of isomers, five molecules were chosen in which the experimental isomer distributions were measured using equilibration methods: $[\text{Co}(\text{trap})_2]^{3+}$,³⁶ $[\text{Co}(\text{dien})_3]^{3+}$,^{32,52} $[\text{Co}$ -

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Table 2. Overview of the Functional Form of the Potential Energy Functions

force field	bond stretching	valence angle deformations	torsion angle term ^a	nonbonded interactions	other terms which are included
Molmec	quadratic and a cubic term	quadratic reference angles differ according to terminal atoms L–M–L' valence angle bending terms included	three cosine terms constants differ according to terminal atoms	Buckingham potential nonbonded terms involving the metal included	dipole–dipole interactions which are given by Jean's formula ⁷ bend–stretch cross term
Momec91(H) and Momec91(C)	quadratic	quadratic no L–M–L' valence angle bending terms are included	one cosine term only two torsional constants used: X–C–N–Y and X–C–C–Y	Buckingham potential L··L geminal nonbonded terms are included no nonbonded terms involving the metal 91(H) and 91(C) differ only in the constants associated with nonbonded interactions involving H atoms	
Xnviron	quadratic	quadratic cis L–M–L terms included	one cosine term only two torsional constants used; X–C–N–Y and X–C–C–Y	Buckingham potential no nonbonded terms involving the metal softer nonbonded interactions than the MM2 based force fields nonbonded distances greater than 1.2 times the sum of the van der Waals radii of the relevant atoms are neglected	

^a None of the force fields includes barriers to rotation around M–L bonds.

(chxn)₃³⁺,⁵³ [Co(±bn)₃]³⁺,^{54,55} and [Co(pn)₃]³⁺.^{56,57} A further five molecules were chosen where it is not possible to isolate the isomers because of conformational flexibility but where the conformation is known in the solid state and can be evaluated in solution: [Co(en)₃]³⁺,⁵⁸ [Co(tmen)₃]³⁺,^{59–61} [Co(sar)]³⁺,³⁷ [Co((NH₃)₂-sar)]⁵⁺,⁶² and [Co((NMe₃)₂-sar)]⁵⁺.⁶² Minimization of each isomer was carried out using the method described above. The isomer with the lowest steric energy was assigned an energy value of 0 kJ mol⁻¹ and the other isomers were assigned an energy value equal to their own steric energy minus the steric energy of the isomer with the lowest steric energy. In this way, the results are presented as differences, Δ*V*. A statistical correction due to symmetry was applied to the steric energies in order to obtain a calculated free energy term, Δ*G*_c, which was then compared to experimental free energy differences.^{1,32} For example, a factor of *RT* ln(2) must be added to the steric energy of the *s-fac* isomer because the *mer* and *u-fac* isomers of [Co(dien)₂]³⁺ are asymmetric and have a 2:1 preference over the *s-fac* isomer.³² The percentage distribution of the isomers of a particular molecule at a specified temperature was calculated from the calculated free energies of all conformers.¹

Sensitivity of the Force Fields to Changes in the Parameters. To determine the influence of any one parameter on the results, variations were made in selected force field parameters, and the results were compared with the original in terms of both structures and energies.

Results

To compare the calculated and observed structures, a set of 17 crystal structures was chosen which satisfied the following criteria:⁶³ (i) *R* factor less than 5%; (ii) standard deviations in the Co–N bond lengths less than 0.01 Å; (iii) no obvious structural distortion of the cation due to strong nonbonding or hydrogen bonding interactions with the anions; and (iv) only Co(III), N(sp³), C(sp³), and H atoms. Other structures were eliminated because close inspection revealed that large anisotropic temperature factors in the ligand backbone were due to the presence of more than one conformation. It has been demonstrated elsewhere⁴² that the variation between X-ray structures of Co(III) hexaamines with anions such as chloride, bromide, perchlorate, nitrate and tetrachlorozincate was small despite the different arrangements of counterions, implying that the cation structure is not influenced significantly by these anions. Hence comparing the isolated cation structure in an experimental structure with that which has been calculated by MM seems valid. The chosen set (Table 3, ligand structures for all Co(III) complexes considered in this work are depicted in Figure 1) included very simple ions such as [Co(NH₃)₆]³⁺, more complicated structures with four-membered rings, distorted geometries around the metal, and large macropolycycles such as [Co(Et₂-Me₆-N₆tetracosane)]³⁺. Overall, this is a challenging set of structures to reproduce because of the range of distortions arising from compromises between the demands of the ligand and of the metal.

The rms differences in atom positions (rms(total)) for the 17 structures ranged from 0.010 to 0.088 Å for the Molmec force

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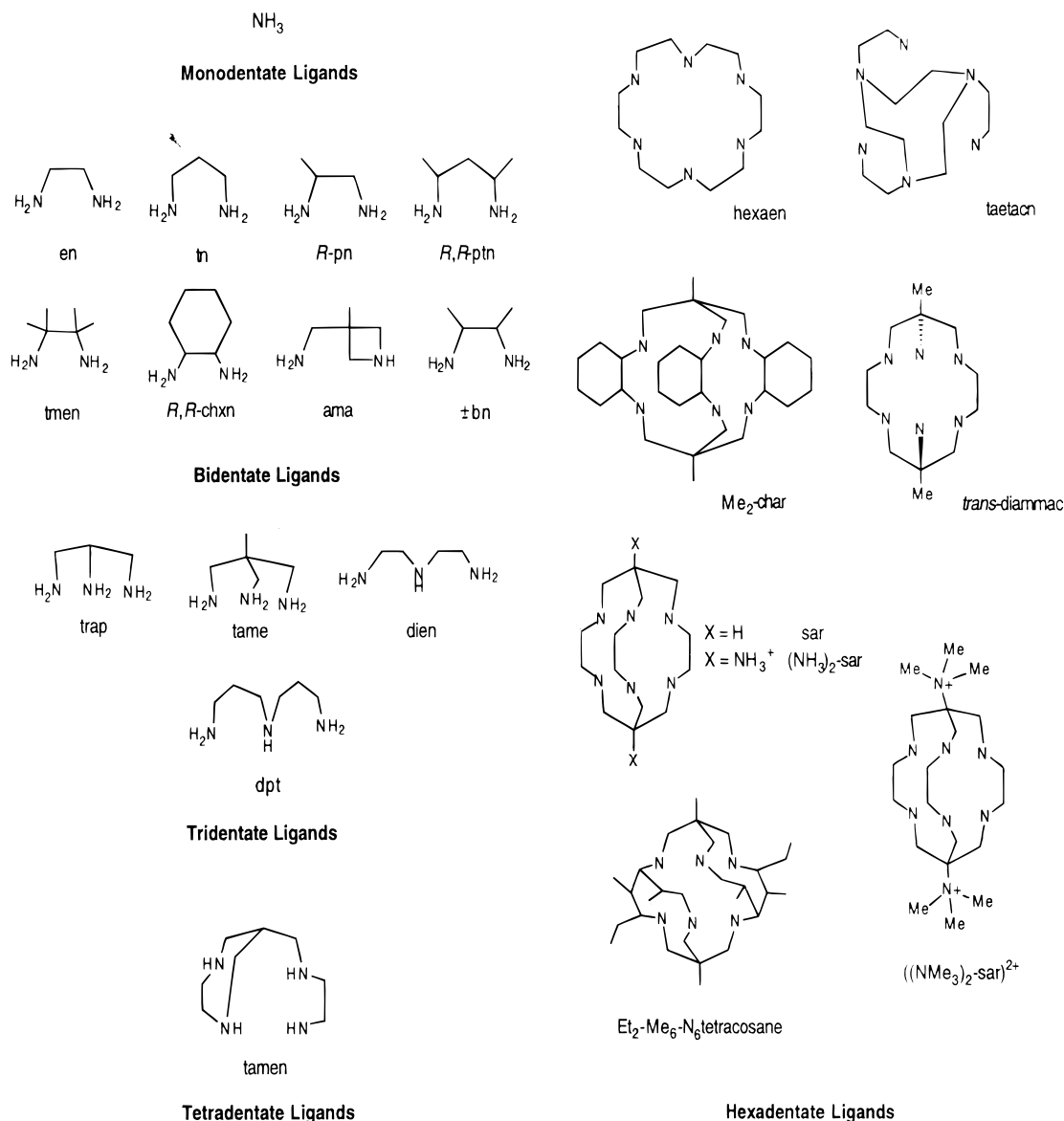


Figure 1. Ligand structures.

Table 3. Chosen Set of Co(III) Hexaamine Crystal Structures

structure	max Co-N		reference
	R (%)	errors (Å)	
[Co(NH ₃) ₆ (anion)] ^a	—	—	—
[Co(en) ₃](tartrate)Cl·5H ₂ O	2.2	0.001	64
[Co(trap) ₂]Cl ₃	2.6	0.002	65
(-) ₅₄₆ -[Co(R,R-ptn) ₃]Cl ₃	3.9	0.009	66
[Co(dpt) ₂](ClO ₄) ₃	4.2	0.006	67
[Co(tame) ₂](tartrate) H ₂ O	2.5	0.003	68
(+) ₅₈₉ -mer-[Co(dien) ₂]Br ₃ (C) ^b	3.8	0.009	69
meso-[Co(hexaen)]Cl ₃	2.0	0.001	70
[Co(tamen)(en)](ClO ₄) ₃	4.6	0.003	71
(-) ₄₈₇ -[Co(taetaen)](ClO ₄) ₃	4.0	0.004	72
[Co(trans-diammac)]Cl ₂ (ClO ₄)	2.9	0.002	73
(-) ₅₈₉ -[Co(R-pn) ₃]Br ₃	3.7	0.006	74
rac-[Co((NH ₃) ₂ -sar)]Cl ₅ ·1.5H ₂ O (B) ^b	3.1	0.005	75
mer-[Co(ama) ₃]Cl ₃ ·3H ₂ O	4.3	0.005	76
ob ₃ -[Co(R,R-chxn) ₃]Cl ₃ ·3H ₂ O	2.5	0.003	77
Δ-lel ₃ -[Co((CH ₃) ₂ -char)]Cl ₂ (ClO ₄)	3.9	0.004	78
[Co(Et ₂ -Me ₆ -N ₆ -tetracosane)]Cl ₃ ·4H ₂ O	3.5	0.002	79

^a An average of nine structures was used (see ref 42). ^b More than one independent cation was found in the observed structure, and one was chosen for comparison.

field, from 0.030 to 0.118 Å for Momec91(H), from 0.020 to 0.098 Å for Momec91(C), from 0.027 to 0.100 Å for Xnviron,

and from 0.014 to 0.104 Å for Spartan. The overall rms differences (between the calculated and observed structures) in bond lengths, valence angles, and torsion angles, when all seventeen structures are considered together, are shown in Table 4.

On a global level, these indicators imply that Spartan provides a poorer fit than the other force fields. The magnitude of some of these values are of the same order as the experimental uncertainty in some of the crystal structures. At this level, the accuracy of the experimental data must be taken into consideration when assessing the reliability of the force fields. The statistics given in Table 2 compare favorably with molecular mechanics calculations on alkane systems using both MM2 and the force field of Engler, Andose, and Schleyer, in which agreements of 0.001 Å for bond lengths, 1–2° in valence and torsional angles were achieved.²¹ Nevertheless, the overall statistics only provide a rough global view and do not pinpoint systematic problems in the force fields. To locate such errors, each type of bond and angle was examined. The results of the comparison of MM-calculated Co–N bond lengths with the corresponding bond lengths observed in the 17 crystal structures are shown graphically for all five MM models in Figure 2.

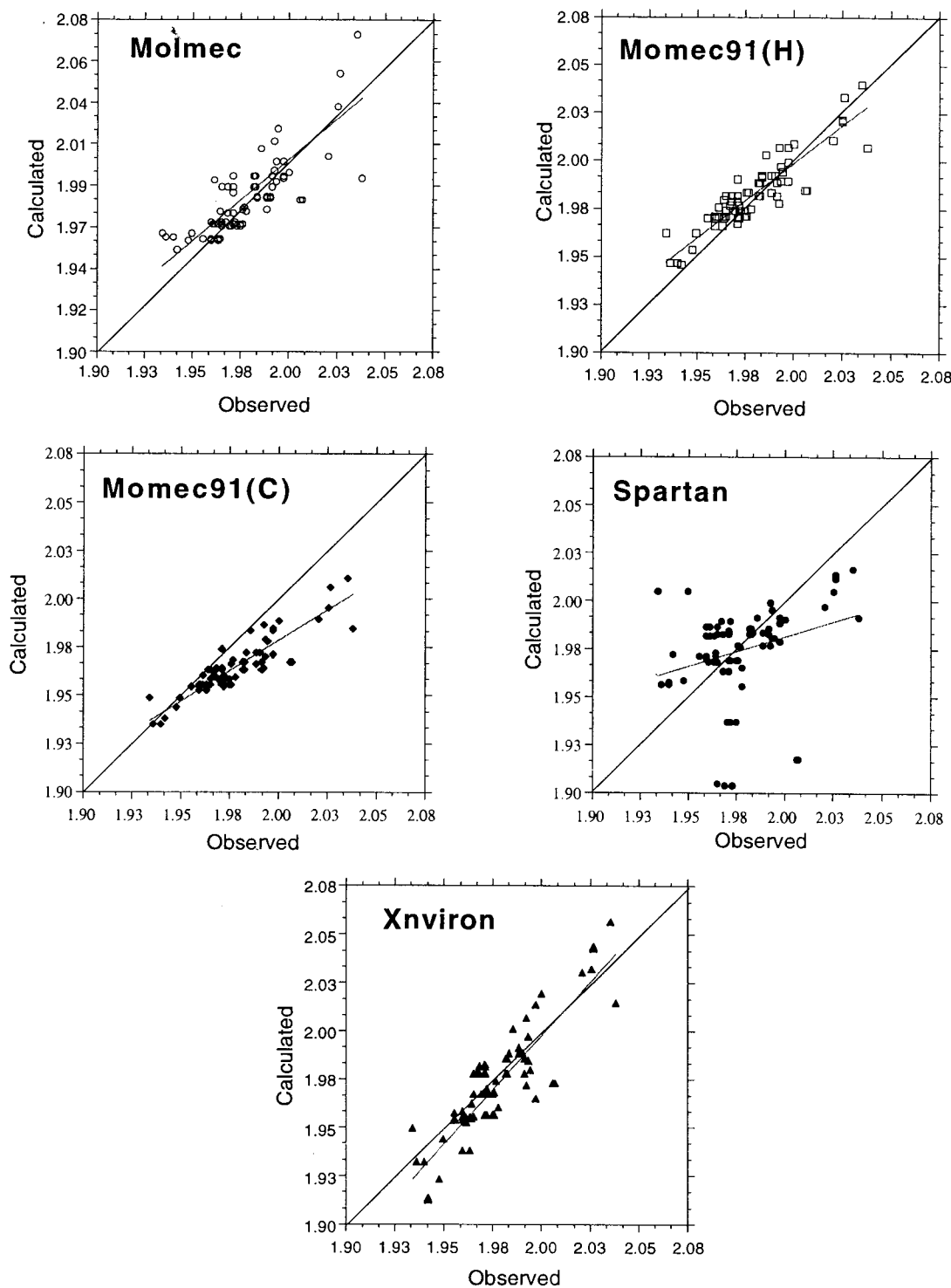


Figure 2. Comparison of 102 crystallographically observed $\text{Co}^{\text{III}}\text{-N}$ bond lengths (\AA) with those calculated using the five different MM force fields.

Table 4. Overall Statistics

statistic	no. of bonds or angles	Molmec	Momec 91(H)	Momec 91(C)	Xnviron	Spartan
$\text{rms}(r)$ (\AA)	405	0.024	0.015	0.017	0.015	0.036
$\text{rms}(\theta)$ (deg)	763	1.5	2.2	1.8	1.7	2.4
$\text{rms}(\phi)$ (deg)	554	2.7	3.9	2.9	3.6	4.1

Momec91(H) and Xnviron acceptably reproduced the observed Co-N bond lengths. Molmec gave a poorer fit for some of the longer bonds, and this is reflected in the lower correlation coefficient (0.82 versus 0.91 for Momec91(H) and Xnviron). However, Momec91(C) systematically underestimated the Co-N bond lengths (slope of the line through the data = 0.62) even

after allowing for a ± 0.01 \AA uncertainty. The bond lengths calculated by Spartan were highly noncorrelated (correlation coefficient = 0.31).

A very surprising result was that no force field reproduced the observed N-C bond lengths (Figure 3). Molmec appeared to be reproducing the *trends* in N-C distances (slope, 0.41;

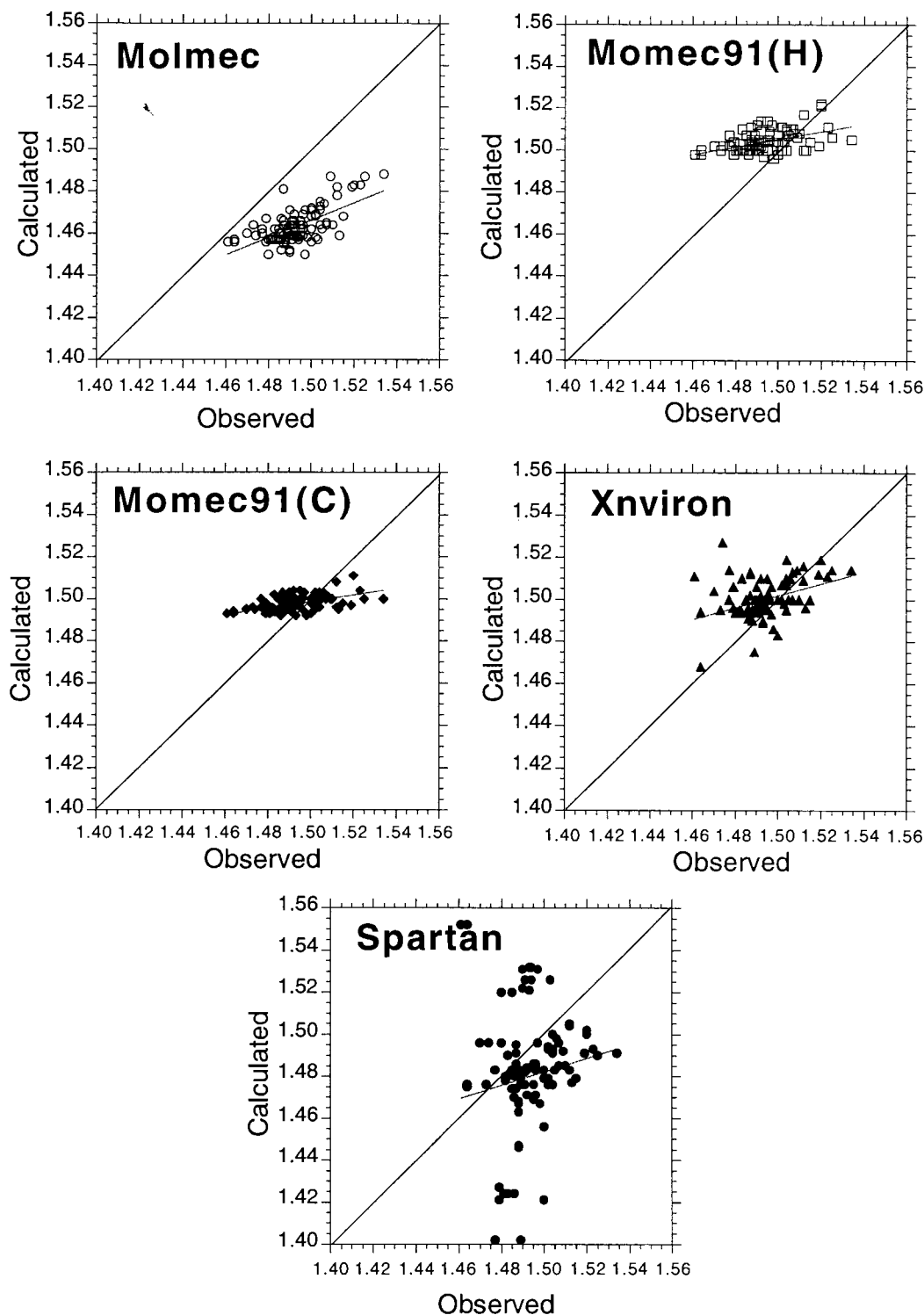


Figure 3. Comparison of observed and calculated C–N bond lengths (Å).

correlation coefficient, 0.66) but underestimated all of the values. All C–N bond lengths calculated with Momec91(H) were between 1.496 and 1.522 Å, and between 1.492 and 1.511 Å for Momec91(C). The Xnviron data appears clustered at 1.50 Å with a circular spread (correlation coefficient, 0.44). The spread in the C–N distances was almost random for Spartan with the lowest correlation coefficient, 0.14, and a range of distances from 1.396 to 1.552 Å.

Similar trends were observed for the C–C bond lengths in which four of the force fields were invariant relative to the

observed values, which spanned 0.105 Å, from 1.47 to 1.575 Å. Again, the bond lengths calculated using Spartan were highly noncorrelated with some distances being up to 0.15 Å in error. Clearly, this force field does not reproduce bond lengths satisfactorily.

The Molmec force field most accurately reproduced the N–Co–N valence angles. The two Momec91 force fields underestimated the trans N–Co–N valence angles by as much as 10°, while overestimating large cis N–Co–N valence angles by as much as 10°. The Xnviron force field was intermediate

between the Momec91 and Molmec force fields in this respect. Spartan consistently overestimated the trans N–Co–N valence angles.

In the observed structures, the Co–N–C angles were clumped in two regions, with one near the ideal tetrahedral angle and the other around 117°. All of the force fields were able to model this parameter rather well.

All force fields reproduced the observed C–C–C angles, even though these spanned the range 85–120° (unstrained angles are tetrahedral). Similarly, the N–C–C and C–N–C angles were well reproduced. Interestingly, all of the models were able to reproduce the observed C–C–C angles of 85°, N–C–C angles of 89°, and C–N–C angles of 86° for the complex with three four-membered rings, [Co(ama)₃]³⁺.

Twist angles⁸⁰ are another measure of the environment around the metal ion. A twist angle of 60° indicates perfect octahedral symmetry for the CoN₆ core while one of 0° represents a trigonal prismatic environment. In general, the structures calculated with the two Momec91 force fields were twisted further away from octahedral symmetry than the observed structures, while Xnviron and Spartan predicted twist angles closer to 60° than those observed. As an example, the observed twist angle in the observed structure of [Co(en)₃]³⁺ was 54(1)° while the calculated values were 54° for Molmec, 50° for Momec91(H), 52° for Momec91(C), 56° for Xnviron, and 55° for Spartan.

Comparison of Observed and Calculated Isomer Distributions. In the following examples, the experimental results have been determined by aerial oxidation of mixtures of the relevant ligand and Co(II) salts over charcoal. It has been shown that this method generally leads to equilibrium distributions of Co(III) hexaamines.^{53,56}

The MM results for the [Co(trap)₃]³⁺ molecule³⁶ are reported in Table 5. In this simple example, all force fields predicted small energy differences between the isomers and the correct order of the isomer stability, although Xnviron overestimated the stability of the racemic form.

The [Co(dien)₂]³⁺ system is one of the most extensively studied systems, both experimentally and by MM.^{81,82} Three

Table 5. MM Energy Differences, V (kJ mol⁻¹), ΔV (kJ mol⁻¹), relative ΔG_c (kJ mol⁻¹), and Isomer Distributions (%) of [Co(trap)₃]³⁺ (Note that V Has Been Rounded to the Nearest kJ mol⁻¹)

model	V (ΔV)		ΔG_c		%	
	racemic	meso	racemic	meso	racemic	meso
Molmec	67 (1)	66 (0)	0	0.7	55	45
Momec91(H)	113 (1)	112 (0)	0	0.7	55	45
Momec91(C)	73 (0.5)	73 (0)	0	1.2	62	38
Xnviron	79 (0)	80 (2)	0	0.3	79	21
H ₂ O/Cl ⁻ ^a					55	45

^a Reference 36.

Table 6. MM Energy Differences, ΔV (kJ mol⁻¹), and ΔG_c (kJ mol⁻¹) of [Co(dien)₂]³⁺

model	ΔV^a			ΔG_c (298 K)		
	<i>mer</i>	<i>u-fac</i>	<i>s-fac</i>	<i>mer</i>	<i>u-fac</i>	<i>s-fac</i>
Molmec	0	31	30	0	31	32
Momec91(H)	0	9	11	0	9	13
Momec91(C)	0	4	6	0	4	8
Xnviron	0	1	0	0	1	2

^a To simplify the comparison, for each geometric isomer the energy result shown is for the lowest energy conformer: λ -NH-*mer*- $\lambda\delta, \lambda\delta$ for the meridional form, *s-fac*- $\lambda\delta, \lambda\delta$ for the symmetrical facial form, and Δ -*u-fac*- $\delta\lambda, \delta\lambda$ for the unsymmetrical facial form. All force fields predicted these conformers to be the lowest energy form of each isomer.

diastereoisomers exist (meridional (*mer*), unsymmetrical-facial (*u-fac*) and symmetrical-facial (*s-fac*)) and for each of these several conformations are possible. One conformer of the *mer* form (λ -NH-*mer*- $\lambda\delta, \lambda\delta$), four *s-fac* conformers, and six *u-fac* conformers were calculated, this being the same conformer set as that used in the published Molmec study.³⁰ This is also the same set of conformers as that used in an earlier Momec91(H) study³² for the *u-fac* isomer but four fewer for the *mer* isomer and three fewer for the *s-fac* isomer. However, the conformers neglected here were found to be significantly less stable and did not contribute significantly to the stability of these two isomers. In general, a full conformational analysis should be performed and subsequent calculations with the Momec91(C) force field using a full conformational analysis reported slightly different results although the trends were identical.¹ The MM energy differences, ΔV and ΔG_c , are shown in Table 6. All conformations considered were included in the calculation of the percentage distribution. A comparison of the calculated isomer distributions with experimental results obtained in the presence of a variety of counterions and solvents⁵² is shown in Table 7.

All of the molecular mechanics results predicted that the order of isomer stability is *mer* > *u-fac* > *s-fac*, but to different degrees. Molmec, Momec91(H), and Momec91(C) predicted that the *mer* isomer is significantly more stable than the other two forms, while Xnviron predicted almost equal amounts of the *mer* and *u-fac* forms. It is clear that ion pairing and solvation can influence the thermodynamic isomer distribution, especially in cases where the anion can associate in a specific manner (e.g. phosphate and sulfate).⁵² However, it has been shown for this system that ion association with certain anions (chloride, nitrate, perchlorate, hexafluorophosphate) in water is seemingly unimportant and that the association in dimethylacetamide or dimethylsulfoxide with perchlorate is expected to be minimal.⁵² Thus the isomer distributions obtained in the presence of these species have been argued to approximate isolated state values.³² In this context, Momec91(C) gave the best agreement with the experimental results. Molmec and Momec91(H) were skewed

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Table 7. Calculated^a and Experimentally Determined⁵² Isomer Distributions (%) at 298 K for [Co(dien)₂]³⁺

	<i>mer</i>	<i>s-fac</i>	<i>u-fac</i>
Molmec	100	0	0
Momec91(H) ^b	93	6	1
Momec91(C) ^c	72	25	4
Xnviron ^d	45	40	15
acetone/PF ₆ ⁻	74	17	9
DMA/Me ₂ SO/ClO ₄ ⁻	79	14	7
H ₂ O/Cl ⁻	65	28	7
H ₂ O/ClO ₄ ⁻	62	30	8
H ₂ O/0.1M PO ₄ ³⁻	20	25	55
H ₂ O/2M SO ₄ ³⁻	37	38	25
H ₂ O/CH ₃ COO ⁻	66	27	7
<i>t</i> -C ₄ H ₉ OH/CH ₃ CO ₂ ⁻	35	45	20

^a All conformers considered in the analysis were taken into consideration in the calculation of the percentage distribution. ^b An earlier version of Momec91(H) considering 18 conformers calculated the distribution to be 87% (*mer*), 11% (*u-fac*), and 2% (*s-fac*) (see ref 32). ^c The same version of Momec91(C) employing a full conformational analysis found 66%, 32%, and 2% (see ref 1). ^d An earlier version of Xnviron, considering only three conformers, found 20%, 40%, and 40% (see ref 81). Note that, except for the Molmec and recent Momec91(H) calculations, all of the MM results can be found to be in satisfactory agreement with at least one of the reported experimental distributions.

too far toward the *mer* isomer while the Xnviron results were closest to the distribution obtained in the presence of sulfate in water or acetate in *t*-BuOH. However, it is worthwhile to bear in mind that the experimental results for the anions, with the least association with the cation, vary by ~8%, and that a kJ mol⁻¹ here or there in the MM results can significantly alter the percentage distributions.

The [Co(chxn)₃]³⁺ complex has also been studied previously experimentally^{53,77,83–85} and by MM.⁸⁶ The experimentally observed distribution (Cl⁻, H₂O, 373 K) consisted of 47% *lel*₃, 35% *lel*₂*ob*, 14% *lelob*₂, and 3% *ob*₃.⁵³ All of the force fields predicted small energy differences between the conformers (<6 kJ mol⁻¹), and all predicted that the *ob*₃ conformer was the least abundant (5–9%) followed by the *lelob*₂ conformer (19–27%). The two Momec91 force fields predicted a larger presence of the *lel*₂*ob* conformer compared with the *lel*₃ conformer, while the Molmec and Xnviron force fields predicted almost equal amounts of both (~35% for each isomer).

The racemic form of [Co(±bn)₃]³⁺ is very similar to [Co(chxn)₃]³⁺ (four isomers: *lel*₃, *lel*₂*ob*, *lelob*₂, and *ob*₃). The MM results obtained for this molecule were very similar to those obtained for the [Co(chxn)₃]³⁺ complex, with all force fields predicting small energy differences (<5 kJ mol⁻¹) between the conformers and all predicting the *lel*₂*ob* conformer to be most abundant and the *ob*₃ to be least abundant. These results are quite similar to those reported (±10%) in a study using a force field developed by DeHayes and Busch.^{17,55} Two conflicting sets of experimental results have been obtained for this system. One study⁵⁵ (Cl⁻, H₂O, 333 K) found that the distribution was *lel*₃ (60%), *lel*₂*ob* (28%), *lelob*₂ (12%), and *ob*₃ (0%) while a more recent study⁵⁴ (Cl⁻, H₂O, 343 K) found that the distribution was *lel*₃ (46%), *lel*₂*ob* (35%), *lelob*₂ (15%), and *ob*₃ (4%). It is interesting to note that the more recent results are identical to within 1% of those obtained for the distribution of [Co(chxn)₃]³⁺ obtained at 373 K. However, tests for equilibration were not carried out in either study on the [Co(±bn)₃]³⁺ system. That

is, the isomer distribution obtained by taking a racemic pair of any one isomer and equilibrating it over charcoal should be the same as the distribution obtained by taking a racemic pair of any one of the other isomers.⁵⁶

For the [Co(pn)₃]³⁺ molecule all force fields made the same predictions and the results agreed to within ±10% with those determined experimentally.⁵⁶ (See also the Supporting Information.)

Predictions of Conformer Distributions. NMR experiments⁵⁸ on the [Co(en)₃]³⁺ molecule indicated that the ligands undergo rapid inversion between *lel* and *ob* conformations and that there is extensive conformational averaging of the signals. A relatively crude analysis of the NMR spectrum using the Karplus relations implies that the proportion of the *ob*₃ species is negligible and that, if the *lelob*₂ form is neglected in the calculations, the proportion of the *lel*₂*ob* to *lel*₃ would be ~2:1.⁵⁸ All force fields predicted small energy differences between conformers (<5 kJ mol⁻¹) with the order of conformer stability being *lel*₂*ob* > *lel*₃ ~ *lelob*₂ > *ob*₃. The calculated conformer distributions for each force field were the same to within 7% and largely in conformity with the expectations derived from the [Co(pn)₃]³⁺ system.

Larger relative energy differences (up to 21 kJ mol⁻¹) were calculated between the conformers of [Co(tmen)₃]³⁺.^{59–61} Three of the force fields predicted the ordering of isomer stability to be *lel*₃ > *lel*₂*ob* > *lelob*₂ > *ob*₃, while the Molmec force field predicted the order *lel*₂*ob* > *lel*₃ > *lelob*₂ > *ob*₃.

For the three cage complexes studied, [Co(sar)]³⁺, [Co((NH₃)₂-sar)]⁵⁺ and [Co((NMe₃)₂-sar)]⁵⁺, there are significant differences in the predictions of each force field (Tables 8 and 9). A description of each of the conformers can be found elsewhere.³⁷

The energy differences between conformers vary considerably between force fields. The calculated Momec91(C) energy differences (Δ*G*_c) for the cages are of the order of ~3 kJ mol⁻¹ with a maximum of 15 kJ mol⁻¹, whereas for the Xnviron force field the differences are of the order of ~30 kJ mol⁻¹ with a maximum of 44 kJ mol⁻¹. For all three cages, Xnviron predicts that the *D*₃*ob*₃ conformer is the most stable, and that at 298 K there is <2% of the *C*₂*lelob*₂ conformer and none of the other conformers. The Molmec force field predicts that the *C*₂*lelob*₂ and *D*₃*ob*₃ conformers are the most stable forms of all three cages and that the other three conformers are of negligible importance. Both Momec91 force fields predict that significant amounts of the *C*₂*lel*₂*ob* and *C*₂*lelob*₂ conformers are present for all three cages, but very little of the *D*₃*ob*₃ conformer.

Sensitivity of the Force Fields to Changes in the Parameters. It is important to know how sensitive the structures and energies of the molecular mechanics models are to changes in the parameters. In addition, some systematic errors in the models were detected and these need to be addressed. The main systematic errors with the Molmec force field were that the C–N bond length was underestimated at ~1.46 Å when the average observed value was 1.49 Å, and that the average C–C bond length was slightly overestimated at 1.537(7) Å compared to the average observed value of 1.523(17) Å. The C–N reference bond length (*r*₀(C–N)) was therefore increased from 1.45 to 1.48 Å while the remainder of the force field was unchanged, and this modified Molmec force field was used to recalculate the 17 test structures. The overall rms difference in bond lengths rms(*r*)_{total} for the structures was 0.016 Å compared to 0.024 Å for the original force field, the rms(θ)_{total} improved from 1.5 to 1.3°, while the rms(φ)_{total} remained the same at 2.7°. The trends

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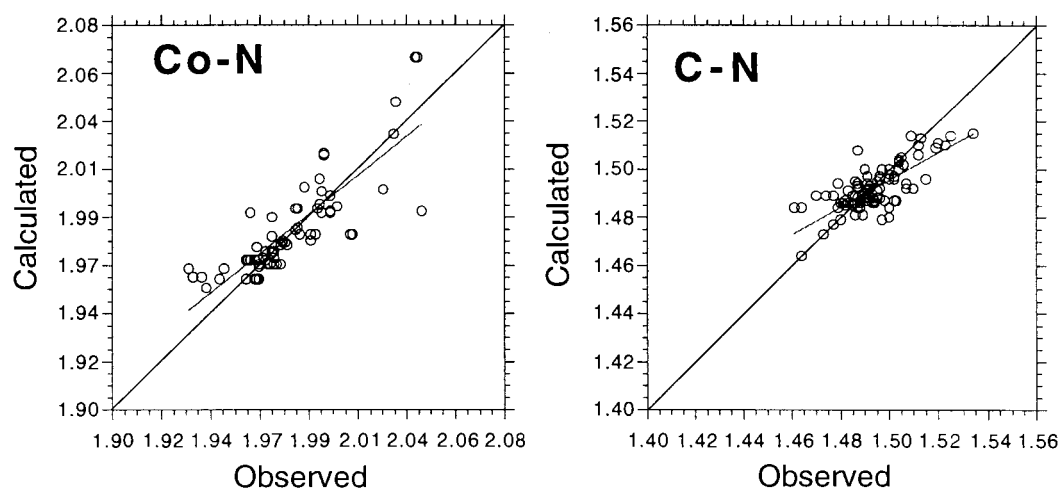
Table 8. MM ΔG_c (kJ mol⁻¹) and % Distribution at 298 K of [Co(sar)]³⁺ ^a

	ΔG_c^b					%				
	D_{3ob3}	C_{2lelob_2}	C_{2lelob}	C_{3lel_3}	D_{3lel_3}	D_{3ob3}	C_{2lelob_2}	C_{2lelob}	C_{3lel_3}	D_{3lel_3}
Molmec	2	0	10	<i>c</i>	9	36	60	2	0	2
Momec91(H)	10	2	0	3	11	1	27	55	16	1
Momec91(C)	6	0	0	2	5	4	36	37	18	5
Xnviron	0	9	26	25	26	98	2	0	0	0

^a The results are almost identical to those calculated for [Co((NH₃)₂-sar)]⁵⁺. ^b The statistical factors, *n*, used to convert the MM steric energies (ΔV) into ΔG_c using $RT \ln(n)$ are $D_{3lel_3} = D_{3ob3} = 1$; $C_{3lel_3} = 2$; $C_{2lelob} = C_{2lelob_2} = 3$. ^c Reverted to D_{3lel_3} .

Table 9. MM ΔG_c (kJ mol⁻¹) and % Distribution at 298 K of [Co((NMe₃)₂-sar)]⁵⁺

	ΔG_c					%				
	D_{3ob3}	C_{2lelob_2}	C_{2lelob}	C_{3lel_3}	D_{3lel_3}	D_{3ob3}	C_{2lelob_2}	C_{2lelob}	C_{3lel_3}	D_{3lel_3}
Molmec	0	2	17	20	24	71	29	0	0	0
Momec91(H)	6	0	0	4	24	4	42	45	9	0
Momec91(C)	4	0	3	4	15	11	57	21	11	0
Xnviron	0	13	37	33	44	99	1	0	0	0

**Figure 4.** Comparison of observed and calculated Co–N and C–N bond lengths (Å) for the Molmec force field upon alteration of the C–N r_0 value.

in the Co–N and N–C bond lengths are depicted in Figure 4. The modified Molmec force field reproduced the trends in both the Co–N and C–N bond lengths, although the average C–C distance was still a little overestimated. However, many of the calculated C–C distances were within the experimental uncertainties and further improvements would need to consider the accuracy of the experimental data. The relative energy differences between the conformers of [Co((NMe₃)₂-sar)]₅₊ were calculated with the modified Molmec force field and were found to be almost identical to those calculated using the original force field. In this example, the structures were found to be sensitive to the parameter change, but the energies were not.

For the cage molecules, large energy differences were calculated using the Xnviron model. Consequently, it was of interest to examine the effect of variations in the parameters on the calculations (Table 10).

There was very little difference between the results when a nonbonded cutoff was employed and when all of the interactions were included, but changes in the valence angle deformation terms had a significant effect on the energies. Analogous analyses of the sensitivities of the parameters were carried out on the [Co(sar)]³⁺ molecule and similar conclusions were obtained. However, there was virtually no change in the results for the [Co(en)₃]³⁺ molecule.

To determine if the Momec91(C) force field was also sensitive to the value of certain valence angle deformation force constants, the value of the Co–N–C valence angle force

Table 10. Effect of the Xnviron Parameter Changes on ΔG_c (kJ mol⁻¹) for [Co((NMe₃)₂-sar)]₅₊ ^a

Conformer	A	B	C	D	E	F	G
D_{3ob3}	0	0	0	0	0	0	0
C_{2lelob_2}	13	12	8	11	10	9	7
C_{2lelob}	37	37	28	35	30	27	22
C_{3lel_3}	33	32	30	31	26	23	17
D_{3lel_3}	44	46	44	47	33	29	21

^a For calculations B–F, only one change was made to the original force field. For calculation G, two simultaneous changes were made to the original force field. (A) No changes to original force field; (B) all nonbonded interactions included; (C) N–Co–N valence angle force constant halved; (D) C–N–C valence angle force was increased from 0.4 to 1.0 mdyne Å⁻¹ was used; (E) C–C–N valence angle force constant halved; (F) Co–N–C valence angle force constant decreased from 0.7 to 0.3 mdyne Å⁻¹; (G) both changes in E and F incorporated simultaneously.

constant was increased from 0.2 to 0.4 mdyne Å⁻¹ and the calculations on the [Co(sar)]³⁺ molecule were repeated. The calculated ΔG_c and % distribution at 298 K with the modified model were D_{3ob3} (4 kJ mol⁻¹, 13%), C_{2lelob_2} (0 kJ mol⁻¹, 61%), C_{2lelob} (3 kJ mol⁻¹, 16%), C_{3lel_3} (6 kJ mol⁻¹, 6%), and D_{3lel_3} (9 kJ mol⁻¹, 1%). Small energy differences were calculated with the original force field (Table 8) and the differences with the modified force field were only a little larger, but the effect was to alter significantly the populations of the conformers.

The sensitivity of the Xnviron and Momec91(C) calculated structures to changes in the Co–N–C force constant was assessed by recalculating five of the seventeen structures.

The alterations made to the Co–N–C force constant had a negligible effect (± 0.001 Å) on the bond lengths. For Co–N–C angles which were very distorted from tetrahedral ($> 115^\circ$), the agreement for both force fields was better with the smaller force constant but angles which were less than 115° were better reproduced with the larger constant. In any case, the changes were very small and either set of structures would be acceptable. In summary, it can be seen that for these two force fields alterations to the Co–N–C force constant result in an insignificant effect on the calculated structures but a large effect on the relative energies.

The results here are in contradiction to the conclusions of a previous study using a slight variation on the present Xnviron force field, where it was found that both the energy differences between isomers and the structures of a series of Co(III) amino acid complexes were *not* sensitive to the choice of Co–N–C force constant.⁴⁰

Discussion

The first aim of this work was to examine how well several existing force fields were able to generate reliable structures by comparing the calculated results with a test set of experimental structures. Root-mean-square differences in the bond lengths, valence angles, torsion angles, and atom positions were useful in providing an overall measure but the graphical plots of the calculated versus observed bond lengths or angles were far more useful in detecting systematic errors. Ideally, these graphs should be of the form $y = x$, and any deviation from this relationship points to either systematic errors in the force field and/or some problem with the experimental data.

The reasons for the very surprising result that none of the force fields reproduced the trends in the N–C and C–C bond lengths were examined. It may be the case that the force constants associated with stretching and compressing these bonds and/or the “strain free” bond length are not set correctly and/or that there is a problem with the experimental data. Very short observed bond lengths can be the result of disorder if, for example, the structure is the average of two or more conformations, and this can sometimes be detected in unusually large thermal parameters.⁸⁷ In this data set, problems of this nature were avoided as much as possible, but of course many of the structures that were being modeled are conformationally flexible and labile. The crystal structures (*mer*-[Co(dien)₂]³⁺ and [Co(R-pn)₃]³⁺, which gave rise to the outliers at the small end of the range, were reexamined. In the *mer*-[Co(dien)₂]³⁺ structure, all but one of the C–N bond lengths were less than 1.48 Å. In addition, there were some unusually short Co–N bond lengths (~ 1.91 to 1.93 Å) even though nothing unusual was noted in the publication of this structure.⁶⁹ However, disorder does not account for unusually long observed values. In the report on the structure of Co[(*lel*₃-R-pn)₃]³⁺, it is noted that the C–C bond lengths are longer in this structure than in the *ob*₃ structure.⁸⁷ Most of the long C–N bonds (> 1.51 Å) were from the structure⁷⁶ of [Co(ama)₃]³⁺ which contains three four-membered rings. Difficulties in reproducing the structures of four-membered rings have been reported for some force fields²¹ so perhaps it is not surprising that all force fields studied here underestimated these bond lengths. Allinger has attempted to deal with this problem by including an explicit bend–stretch

interaction potential in order to account for the increase in C–C bond lengths along the series cyclohexane, cyclopentane, cyclobutane.²¹ Of the five force fields examined here, only Molmec explicitly includes a stretch–bend potential. It is interesting to note that this is the only force field which reproduced the *trends* in the N–C bond lengths; and after a correction to the N–C reference bond length, Molmec reproduced both the trends and the values of the N–C and C–C bond lengths. For the other force fields this factor is implicit in the parametrization of the bond stretch and the valence angle bending terms.

Three of the force fields use MM2 force constants to model the “organic” valence angles (C–C–C, N–C–C, and C–N–C) whereas Xnviron uses the larger force constants obtained from normal coordinate analyses. This difference appeared to have no effect on the results as all four force fields reproduced the observed angles even though these spanned the range 85 – 120° .

One area that is of particular interest to coordination chemists is how well the force fields can model the geometry around the metal center. Both the Molmec and Xnviron force fields use a harmonic potential to describe all angle bending interactions, whereas Momec91(H) and Momec91(C) have replaced the L–M–L’ angle bending term with a geminal nonbonding interaction, all other angles being modeled with the usual harmonic potential. So it is interesting to note that the twist angles were most accurately reproduced by Molmec as were the *cis* and *trans* N–Co–N and Co–N–C valence angles, with both the trends and the actual values being correctly predicted even over a wide range of angles. Xnviron gave a good fit to the *cis* and *trans* N–Co–N valence angles, but there was a slight underestimation of the Co–N–C angles. The two Momec91 force fields were able to reproduce all of the angles except the N–Co–N angles and work is in progress to replace these geminal nonbonded interactions with a Fourier potential which has minima at 90 and 180° .⁸⁸ The SHAPES force field also uses this type of potential.⁶

In this work only the non-hydrogen atoms were considered in the structural comparisons. H atom positions are difficult to determine with any accuracy from electron density difference maps unless the X-ray structure is particularly good and in most X-ray crystallographic analyses, the H atoms positions are placed at calculated positions. In addition, the Momec91 force fields position the hydrogen atoms at the center of electron density (C–H = 0.97 Å, N–H = 0.91 Å), while the Xnviron force field places the hydrogen atoms where the nucleus is expected to be (C–H = 1.06 Å, N–H = 0.99 Å). However, the Momec91(H) force field uses a harder nonbonded potential to describe interaction between H atoms and other atoms than Xnviron.

The second aim of this work was to test the ability of the force fields to calculate energies by: (i) correctly predicting the order of isomer stability for a series of Co(III) hexamines whose isomer distributions have been measured experimentally and; (ii) by examining the differences in the calculations in their predictions on systems for which rigorously experimentally determined conformer distributions are not known. Many MM studies^{1,27,30,32,36} have based the validity of their force fields to predict energies on a comparison of calculated results with isomer distributions determined from equilibration studies and the assumption made is that the dominant contribution to the isomer distribution is the steric strain, and that other contribu-

(87) Rae, A. D., Australian National University, personal communication.

(88) Hambley, T. W., University of Sydney, personal communication.

tions such as solvation and ion pairing are very similar for all isomers and can therefore be ignored. One of the problems here is that there are few rigorous studies of isomer distributions of Co(III) hexaamines, even though they have been the most thoroughly investigated types of complexes. This is in contrast to the situation in organic chemistry where considerable thermodynamic data exists, especially for hydrocarbons, which greatly assists researchers wishing to test the validity of MM force fields destined for organic molecules.

In this work it was found for the simple systems that the force fields predicted small energy differences (~ 4 kJ mol⁻¹) and generally were able to predict the correct order of the known distributions give or take a few kJ mol⁻¹. As such, this analysis did not readily discriminate between the force fields, and one could be led to believe that predictions of isomer distributions (of molecules belonging to the same class as the test systems) would be reliable. However, substantial differences in the calculated relative energies were found between the force fields for the conformers of the cage molecules [Co(sar)]³⁺, [Co((NH₃)₂-sar)]⁵⁺, and [Co(NMe₃)₂-sar)]⁵⁺. This was a surprise given that the structures of the cage complexes included in the 17 test structures, [Co((NH₃)₂-sar)]⁵⁺, [Co(CH₃)₂-char)]³⁺, and [Co(Et₂-Me₆-N₆tetracosane)]³⁺, were satisfactorily modeled by all four force fields. The Momec91(C) force field predicted small energy differences between conformers in all cases, while Xnviron predicted large differences in energy between the conformers.

A detailed study of a variety of Co(III) cage complexes by NMR, CD, and UV/vis spectroscopy indicated that [Co((NMe₃)₂-sar)]⁵⁺ in solution adopts the *D*₃*ob*₃ conformation in conformity with the solid-state structure, while [Co((NH₃)₂-sar)]⁵⁺ and [Co(sar)]³⁺ exist mainly as *lel* conformers.⁶² However, it is not possible at the present time to say if the latter are exclusively *D*₃*lel*₃, *C*₃*lel*₃, or *C*₂*lel*₂*ob*, or combinations of these, as a result of conformational flexibility. There are therefore conflicting results between the force field calculations and the solution conformational results at least for these cage complexes.

It has been said that the choice of nonbonded potentials is of utmost importance to the force field.^{21,40,89} In this work, this was assessed by evaluating two versions of the Momec91 force field. The only difference between Momec91(H) and Momec91(C) is that the Momec91(C) force field employs softer C···H, H···H, and N···H interaction potentials than Momec91(H), and it can be seen that these differences *do* influence the results of the calculations. Energetically, the Momec91(C) force field predicted much smaller energy differences between isomers compared to the Momec91(H) force field, which in some cases led to quite different populations of conformers. In terms of structure, the Momec91(H) force field reproduced the Co–N bond lengths much better than Momec91(C) which consistently underestimated them. But, the Momec91(C) force field reproduced angles involving the metal atom slightly better than Momec91(H). This is just one example of the fact that many parameters are correlated and a change in one parameter can alter other parameters, thus making it quite difficult to fit all aspects of a structure.

Molecular mechanics force fields employ a pairwise nonbonding potential even though some of the long range interactions are through bonds or atoms and employing a cutoff is an attempt to avoid this problem. The Xnviron force field is the only force field that ignores nonbonded interactions which are

further away than 1.2 times the sum of the van der Waals radius of the relevant atoms. This was originally incorporated into the program when the available computing power could not adequately cope with the large number of interactions which needed to be calculated.²⁴ Two sets of calculations were considered, one where all force fields gave more or less the same result ([Co(en)₃]³⁺), and one where the force fields contradicted each other ([Co(NMe₃)₂-sar)]⁵⁺). However, it was found that there was no significant difference in the predictions made with Xnviron when all of the nonbonded interactions were included and when a cutoff was employed. A comparison of the nonbonded functions used showed that Xnviron was employing a much softer set of potentials than the other force fields, except for the H···H potential which is intermediate between those of the two Momec91 force fields. At the cutoff distance, the vast majority of interactions are very weakly attractive so that inclusion of every interaction results in the addition of a large number of values ~ 0.002 kJ mol⁻¹, and the sum of all of the nonbonded interactions consequently becomes negative. However, if the same cutoff were employed in the Momec91(H) force field, many of the interactions being ignored would still be positive.

From the above examples, it can be seen that seemingly slight variations in the parameters can sometimes have a significant effect on either the structures predicted by the force fields and/or the relative energies between isomers. So it would seem that *sometimes* errors in the models are canceling. In this work, most of the parameters altered were those for which it is difficult to find experimental sources (nonbonding parameters, angle bending terms involving the metal atom) and in the original force field parametrization, these parameters were estimated and then adjusted to give a good fit to the available data. Unfortunately, this type of sensitivity in the models is a serious problem for applications of MM to metal-containing species and may be one of the major limiting factors in developing reliable force fields for these types of molecules.

The balance between different components of the total steric energy found for the 17 test structures as well as the isomer distribution calculations was examined and it was noted that there were trends in the ordering of the energy terms that occurred for almost every molecule for all four force fields. For the majority of molecules calculated with Molmec, the order of the energy terms was $V_\phi > V_{nb} > V_\theta > V_b > V_{dd}$ (dipole–dipole interactions) $> V_{bs}$ (bend–stretch cross-term). For Momec91(H), the order was $V_{nb} \gg V_b \sim V_\theta \sim V_\phi$; for Momec91(C) the ordering was $V_{nb} \gg V_\phi \sim V_b \sim V_\theta$; and for Xnviron, $V_\theta \sim V_{nb} > V_\phi > V_b$. In other words, the Molmec force field is unbalanced toward very large torsional angle deformations, Momec91(H) and Momec91(C) are skewed toward large nonbonded interactions, whereas the nonbonded and valence angle deformations dominate the Xnviron calculations. Evidently, one reason for the difference between the last three models is the description of the interactions of the ligand donor atoms with the metal ion. In the Momec91(H) model these interactions are described by geminal nonbonding terms which are mostly repulsive. In the Xnviron model these interactions are modeled by L–M–L valence angle bending terms. This would confirm the view that due to the different ways that the MM models partition V_{tot} and the correlation between parameters, it is unwise to examine each individual energy component (V_b , V_{nb} , V_θ etc) in the hope of understanding how the molecule distorts in order to minimize strain.⁹⁰ The actual values of the individual energy components are quite

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dependent on the way in which the force field has been parametrized. However, this type of analysis was quite useful in shedding light on the contradictory conformer distribution results found for the cage complexes.

Each set of isomer calculations was examined in order to assess how the balance of terms influenced the overall energy differences between the isomers. Although there was no one term in any force field which varied significantly among the isomers for the calculations of $[\text{Co}(\text{trap})_2]^{3+}$, $[\text{Co}(\text{chxn})_3]^{3+}$, $[\text{Co}(\pm\text{bn})_3]^{3+}$, $[\text{Co}(\text{R-pn})_3]^{3+}$, and $[\text{Co}(\text{en})_3]^{3+}$ the situation was quite different for the cage complex calculations. Calculations using the Molmec force field found that V_b , V_{dd} , and V_{bs} were more or less the same for the five conformations of $[\text{Co}(\text{NMe}_3)_2\text{-sar}]^{5+}$, but there were quite large variations in V_θ , V_{nb} , and V_ϕ . Most noticeable were a 32 kJ mol⁻¹ difference in V_θ between the D_{3ob3} and $C_{2lel2ob}$ conformers, a 24 kJ mol⁻¹ difference between the D_{3ob3} and D_{3lel3} in favor of the D_{3ob3} conformer in both cases, and a 22 kJ mol⁻¹ difference in V_ϕ between the D_{3ob3} and $C_{2lel2ob}$ conformer in favor of the $C_{2lel2ob}$ form. Calculations using the Momec91(H) and Momec91(C) force field found that V_b and V_{nb} were more or less the same but there were differences in V_θ and V_ϕ of ~10 to 20 kJ mol⁻¹. Xnviron calculations found that V_b was constant but a variation of ~10 kJ mol⁻¹ was found in V_{nb} and V_ϕ . The most striking difference was that the V_θ component of the calculation on the D_{3lel3} conformer was 48 kJ mol⁻¹ lower than the V_θ component of the D_{3ob3} conformer. Similarly, the analogous differences for $[\text{Co}(\text{NH}_3)_2\text{-sar}]^{5+}$ and $[\text{Co}(\text{sar})]^{3+}$ were 38 and 35 kJ mol⁻¹, respectively. The effect of lowering the Co–N–C valence angle force constant on the Xnviron calculations of $[\text{Co}(\text{sar})]^{3+}$ and $[\text{Co}(\text{NMe}_3)_2\text{-sar}]^{5+}$ was reexamined. It was found that V_θ was unchanged for the D_{3ob3} conformer, whereas for the D_{3lel3} conformers, V_θ was lowered by ~15 kJ mol⁻¹ compared to the original set of calculations. A similar but reduced effect was found for the Momec91(C) force field.

However, in other cases, the defects in the models did cancel. When $r_0(\text{C–N})$ was increased in the Molmec model for all conformers of $[\text{Co}(\text{NMe}_3)_2\text{-sar}]^{5+}$, V_b lowered by 8 kJ mol⁻¹, V_{nb} lowered by 30 kJ mol⁻¹, V_θ by 7–10 kJ mol⁻¹, V_ϕ by 0–2 kJ mol⁻¹, V_{bs} by 1 kJ mol⁻¹, and V_{dd} was unchanged, thus resulting in a drop in V_{tot} by 46–49 kJ mol⁻¹. Considering that the total energy differences between conformers were reasonably large, there was neither a reordering of conformer stability nor a significant change in conformer populations. Similarly, when all nonbonded interactions were included in the Xnviron calculations on $[\text{Co}(\text{en})_3]^{3+}$, V_{tot} decreased by 22 kJ mol⁻¹ for each conformer due exclusively to a decrease in V_{nb} . Thus it would seem that the various defects in the models are not always canceling when comparisons are made between isomers, which is in contrast to recent work.¹

Conclusions

MM calculations using Molmec, Momec91(H), Momec91(C), and Xnviron were found to reliably reproduce the structures of Co(III) hexaamines although some systematic errors were detected in each model, and the user would need to be aware of them when choosing a force field. The best use for Spartan is as a sophisticated graphics package to create input structures for other applications. Spartan does not produce accurate structures. Plotting calculated versus observed structural parameters for each type of bond is better than comparing average values and rms differences only provide a crude global view.

A report on extensions of MM2 to give Molmec notes that “as a consequence of the usual lack of thermodynamic data available for calibrating the parts of the force field involving the metal, strain energies calculated using the corresponding (extended) force field cannot be expected to have high quantitative precision. This appears not to have been appreciated in the past.”⁴⁶ The conclusions of the work described here are in agreement with this statement. This work has demonstrated that four different force fields made generally correct predictions about five molecules whose isomer distributions have been determined experimentally. For these calculations the quantitative precision was found to be of the order of a few kJ mol⁻¹. Alarmingly, these same four force fields made quite different predictions for the three cages molecules, and it was not a clear-cut matter to determine which was making the most correct predictions.

Users of molecular mechanics who wish to study metal complexes should be aware (i) that it is important to be sure that the molecule under study belongs to the class of molecules for which the force field was parametrized; (ii) that there may be limitations in the particular model they are using because the results may be quite sensitive to small changes in certain parameters and that the defects in the models do not always cancel; (iii) that it is unwise to read too much into the individual energy terms in V_{tot} in the hope of understanding exactly how the molecule balances strain because these depend on the way that the force field has been parametrized; and (iv) that when the relative energy differences are small (<4 kJ mol⁻¹), the unknown solvation and ion-pairing effects are probably important. The effects of solvation and ion-pairing on the overall energies have not been treated in this work. At this stage, very little experimental (or computational^{36,91–96}) data exists as to solvation contributions to the energies of metal complexes, and it is unlikely that much more will become available soon. MM is an empirical technique and thus, without precise experimental data it is not possible to accurately account for ion-pairing and solvation effects.

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Supporting Information Available: Descriptions of the force fields, listings of force field parameters, rms statistics, molecular mechanics component energies and plots of calculated versus observed bond lengths and angles and plots of the nonbonded potentials used by the force fields are available (54 pages). Ordering information is given on any current masthead page. †Present address: The Australian Permanent Mission to the United Nations Office at Geneva, 56 Rue de Moillebeau, 1211 Geneva 19, Switzerland.

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