A method of structure determination of organometallic complexes which uses a combination of molecular mechanics and X-ray crystallography is described. The method combines the strengths of molecular mechanics in the prediction of the conformation of organic structures with that of X-ray crystallography in the more ready determination of metal atom positions. Examples of the application of this combined approach to the structure determination of two different organometallic complexes are given.

**Introduction**

Molecular mechanics techniques have become widely used in recent years to predict the energies and three-dimensional structures of a large number of organic molecules. This success has spurred the development of numerous software packages and their use in academia and in industry, especially in the pharmaceutical industry where the three-dimensional stereochemistry is of great importance.

Molecular mechanics or the “force field” method can be traced back to concepts introduced by D. H. Andrews in 1930 [1]—basically that bonds tend to assume “natural” lengths and angles, and geometries of molecules will tend to adjust to take on these values while recognizing that steric interactions must be included using suitable van der Waals potential functions.

These ideas lay dormant until 1946 when explicit expressions for energy calculations including steric effects were suggested [2,3,4]. The field progressed, spurred by the development of computer programs by Allinger and other researchers, to studies involving the conformations and energies of hydrocarbons and their derivatives [5,6], to comparisons of conformations of hydrocarbons in the solid state to those predicted by molecular mechanics [7,8], and to studies in other diverse areas such as the prediction of rates and stereochemistries of selected chemical reactions [9].

In contrast to *ab initio* quantum mechanical methods, molecular mechanics is an empirical method for the calculation of molecular geometry and energy based on experimental data. Molecular mechanics, although certainly by no means as exact as quantum mechanics, does provide a means of rapidly calculating energies and molecular structures for larger molecules. As noted above, it does so by using potential functions, or force fields. These functions contain adjustable parameters which are optimized in order to obtain the best fit between calculated and experimental properties of a wide variety of molecules. (In some cases these “experimental” properties may actually be those calculated from accurate *ab initio* quantum mechanical methods.) For many molecules, molecular geometries may be defined in terms of potential functions involving only bond lengths, bond angles, torsional angles, and non-bonded (van der Waals) interactions. Energy minimization is carried out using an iterative optimization approach. (It should be noted that the minimum energy configuration found can depend on the starting geometry since convergence is always to the nearest local minimum.) An excellent overview of molecular mechanics is given in reference [10].

Encouraged by the success of molecular mechanics in these applications noted above, we decided to explore a combination of molecular mechanics with X-ray diffraction methods for the more ready elucidation of complex organometallic crystal structures.

**The Approach Used**

Present molecular mechanics methods, with their dependence on good empirical constants, are
typically much better at predicting the geometries and energies of pure organic molecules than those containing metal atoms; X-ray intensities on the other hand are well known to be more dependent to metal atom positions than those of the light atoms. The following approach therefore suggested itself:

(i) Determine the metal positions in the structure from Patterson or Patterson superposition methods and also, if possible, the positions of the coordinating atoms of the ligands.

(ii) Input these atomic positions into a molecular mechanics software package and sketch in the ligand or at least a major portion of the ligand. Refine the positions of the atoms that were added to obtain the lowest energy configuration while keeping the original atoms in a fixed configuration relative to one another. (Repeated trials with different starting "ligand sketches" are usually advisable to avoid selecting a local rather than a global minimum energy configuration.)

(iii) Use this molecular mechanics model as an initial trial model in a crystallographic refinement of the structure.

We selected the PCMODEL program [11] to use for our molecular mechanics calculations. It uses a force field which extends and improves upon the widely used MM2 force field of Allinger [12]. PCMODEL includes provision for transition metal atoms, has the ability to accept crystallographic atom positions of a structural fragment, and contains a provision for maintaining selected atoms in a fixed relationship to one another. Since such an entity can still rotate and/or translate as a group during the molecular mechanics minimization, an additional program was written to determine the rotation and translation matrices appropriate to describe these motions; these matrices were then used to convert the refined molecular mechanics model to crystallographic coordinates.

**Application to \([\text{FeP}_2\text{OC}_6\text{H}_3]\)_I**

Our first test of this approach was its application to the determination of the organometallic complex \([\text{FeP}_2\text{OC}_6\text{H}_3]\)_I. Data had previously been collected using a Rigaku AFC6R diffractometer and the compound was found to crystallize in the orthorhombic space group \(Pc2_1n\) with dimensions \(a=9.9101(3), b=16.5495(5)\) and \(c=18.3383(4)\) Å. The structure had originally been solved by determining the heavy atom positions using a Patterson superposition program [13] and then finding the remaining atoms by successive electron density and least squares refinement steps. The heavy atoms did a relatively poor job of phasing the structure and structure determination was consequently slow, requiring many map and refinement steps. Final results are reported in more detail in [14].

As a test of the usefulness of this molecular mechanics approach, the iron and two phosphorus atomic positions were used for the molecular modeling (the iodine only plays the part of the counter ion in the structure). The rest of the molecule was sketched onto the computer screen (Fig. 1) and allowed to shift to minimize its energy. The process was repeated using alternate starting configurations. The rotation and translation matrices pertaining to the resulting iron and phosphorus atomic displacements were determined and used to convert all the atomic positions after molecular mechanics refinement to fractional crystal coordinates. The resultant model crystallographically refined quickly to a final residual of \(R=4.4\%\). An ORTEP view of the molecule is shown in Fig. 2.

The deviations of the final X-ray fractional coordinates from those obtained via the molecular mechanics calculation averaged 0.014 (0.21 Å). The non-phenol atoms showed the smallest deviation with an average displacement of 0.009; for the phenols the agreement was within an average of 0.020. The latter would be expected to show greater deviation since their spatial orientations allow greater freedom of movement in response to packing forces in the solid. (Only the isolated molecule was modeled by the molecular mechanics program.)
Structural Solution of (OEP)Ti(η²-PhC≡C-Ph)

Shortly after we completed the studies described above, we were confronted with the task of carrying out the structural solution of (OEP)Ti(η²-PhC≡C-Ph) where OEP = octaethylporphyrinato. It crystallizes in the monoclinic system, space group C2/c, with a=49.367(7), b=13.734(9), c=36.622(4) Å, and β=136.63(1)°. Data (15,715 reflections within a 2θ sphere of 50°) were collected on an AFC6R diffractometer. There are two molecules of this titanium complex per asymmetric unit (218 atoms per asymmetric unit of which 110 are non-hydrogen). The structure resisted solution by standard techniques. Direct methods were unsuccessful and Patterson superposition procedures only readily yielded the positions of the titanium and coordinated nitrogen atoms. These alone were ineffective at phasing. We therefore decided to try the combined molecular mechanics and X-ray diffraction approach.

Each of the two sets of titanium and coordinated nitrogen atoms were input into PCMODEL. Since it was not known in which direction the ethyl arms attached to the porphyrin ligand would extend nor on which side of the porphyrin ring the diphenyl acetylene ligand would coordinate, only the twenty porphyrin carbon atoms on each ring were modeled and its energy minimized. Each molecule was treated separately and minimizations were carried out using a variety of starting configurations and also using different pairs of nitrogens as the anchor points to ensure that the lowest energy conformation would be found.

The positions of the atoms in the two modeled molecules were then converted back to fractional crystal coordinates and used as a starting model for crystallographic refinement. These atoms were enough to phase the experimental data such that the remaining carbon atoms could be then located from difference electron density map calculations. Refinement proceeded smoothly to yield a final residual of R = 6.1%. Figure 3 displays an ORTEP drawing showing the two molecules in the asymmetric unit. Further details on the structure can be found in reference [15].

The coordinates obtained from the molecular mechanics minimization and the final coordinates of these atoms from crystallographic refinement deviated by less than 0.4 Å on average. Although most agreed quite well, a few near the outer edge of the ligands were obviously affected by the neglect of the relatively large diphenylacetylene ligand and by distortions due to packing effects. As can be seen in Fig. 4, packing may lead to formation of intermolecular π–π interactions between pairs of porphyrins in the solid. Both effects were completely neglected in the molecular mechanics calculations. However, it should also be noted that even with the larger deviations that occurred in these few coordinates, the overall effect of adding those atoms improved the phasing such that the crystallographic structure could then be successfully refined.

Conclusion

We are quite encouraged by the results obtained thus far in using molecular mechanics as a means
to obtain a trial model of sufficient size and accuracy to facilitate refinement of complex organometallic structures. In the two cases studied to date, any significant deviations between molecular mechanics and X-ray coordinates appear to be readily accounted for by our neglect of steric effects due to other aspects of the structure left out in the modeling process. We plan to continue these studies and will also attempt to extend this approach by calculating ligand or ligand fragment positions using molecular mechanics and then searching for the best coordinates of these atoms.
in the crystal utilizing Patterson search techniques. In this way the necessity of first finding the metal and coordinated ligand atoms would be removed and the method could even be applied to structures involving no metal coordination.

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References