

## PERSPECTIVE

## Molecular Modeling of Catalysts and Catalytic Reactions

Thomas R. Cundari,\* Jun Deng, Wentao Fu, Thomas R. Klinckman, and Akihiko Yoshikawa

Department of Chemistry, The University of Memphis, Memphis, Tennessee 38152-6060

Received August 27, 1998

## I. INTRODUCTION

With the exception of drug design, few things have attracted the interest of theorists as has the promise of employing computation to probe catalysts and catalytic reactions. Experimental chemists employ catalysts not only to “improve” reactions kinetically (obtain a faster rate) but also to effect transformations with very high regiospecificity and/or stereospecificity. Historically, catalyst development has been approached in an Edisonian fashion, with numerous reaction conditions (catalyst, coligands, solvent, temperature, pressure, catalyst loading, etc.) being analyzed to find a system with optimum activity and selectivity. Computation holds the promise of achieving molecular level understanding of catalysts and catalytic reactions. Such information, particularly when it can be integrated with experiment, should be of great utility in the rational design of new and improved catalysts.

The great attention paid to computer-aided design and analysis of catalysts and catalytic reactions is undoubtedly due in large part to their importance in academia and industry. Catalysis is a “grand challenge” and “critical technology” area, designations emphasizing its economic importance.<sup>1</sup> A National Research Council report<sup>2</sup> states that computation must provide “a framework for understanding...catalyst composition, structure and performance”. Hence, there is a great fiscal incentive to find improved catalysts. Additionally, if one considers a typical catalytic process, then computation is, in some respects, an ideal analysis tool. There is a maxim among experimentalists that if one can retrieve a chemical entity from a catalytic reaction then it most likely is not an active species. By its very nature, catalysis involves highly reactive species which are thus often formed in low concentrations with short lifetimes. Hence, important intermediates are often not amenable to direct observation and evaluation by powerful experimental methods such as X-ray crystallography. Furthermore, it is not profitable to slow down a catalyst to make it more amenable to experimental study as one is changing the very chemical properties that make most catalysts of interest, i.e., great reactivity.

As most of us recall from our first college chemistry course<sup>3</sup> a catalyst is a substance that changes the speed of a chemical reaction without itself undergoing a permanent chemical change in the process. The Arrhenius equation thus immediately suggests transition states (TSs) as important points in catalytic cycles since their energies relative to ground state reactants largely determines the rate of a reaction. Direct information about the bonding and structure of these ephemeral chemical species is limited. Experimen-

talists can probe the structure of transition states indirectly through determination of quantities such as activation parameters and isotope effects, but it is not possible to put them “in a bottle” and study TSs with the full arsenal of experimental techniques. Computational chemists can directly calculate the geometries of transition states. Comparison of calculated information (e.g., activation parameters and kinetic isotope effects) with experimental data gives confidence in a computational model. Once confidence in a model is established, computation can provide a window on portions of the catalytic cycle unseen by the experimentalists. Thus, theory and experiment can work together synergistically for the development of better catalysts.

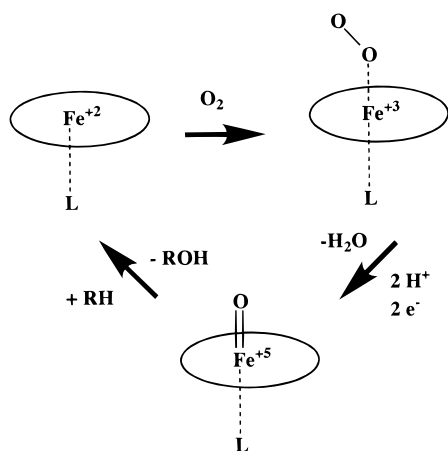
## II. FOCUS

The field of catalysis is vast, and thus so are the interests of those who model it. For the sake of brevity and clarity, this Perspective will focus on a subset of catalytic processes. The examples chosen are illustrative of challenges and opportunities in molecular modeling of catalysts. First, this contribution will focus on homogeneous catalysts. These involve molecular species which are usually the most well understood experimentally and computationally. Industrially, heterogeneous catalysts are generally more important. Marks has recently written a review delineating the connections between homogeneous and heterogeneous catalysis.<sup>4</sup> Second, d-block metals will form the primary focus of this Perspective. These metals have the ability to stabilize many, diverse chemical environments. It is this ability that give d-block metals a central role in catalysis. Consider any of the many catalysts with a d-block metal and the changes in oxidation state, spin state, and coordination number involved. An example is the catalytic cycle in Scheme 1 for alkane hydroxylation by cytochromes P-450 or its metalloporphyrin mimics.<sup>5</sup>

## III. CHALLENGES

It is not without justification to assert that the importance of d-block metals in catalysis has provided considerable driving force for the advancement of molecular modeling techniques for these elements. The challenges in quantum and classical modeling of d-block chemistry have been delineated in reviews of the research of the many groups whose work has led to the splendid growth in modeling the d-block metals.<sup>6–12</sup> Briefly, the main challenges in modeling d-block metals with quantum methods are (1) the large number of electrons and orbitals (molecular orbital calcula-

Scheme 1



tions scale geometrically with the power typically ranging from two to seven depending on the specific method employed), (2) the importance of electron correlation (a problem exacerbated by the presence of low-energy excited states), and (3) relativistic effects (particularly for metals of the third transition series). The development and application of molecular mechanics (MM) techniques for d-block metals has also recently undergone considerable growth as a research area.<sup>9–12</sup> Classical techniques engender new modeling challenges, in particular finding suitable experimental information for force field parameterization, treating systems with high coordination numbers, and the transferability of metal-dependent force field parameters from one complex to another.

If one were to sum up the situation as succinctly as possible, it would be to state that the challenges inherent in the molecular modeling of d-block metals arise from the very chemical properties that make them of such utility in catalysis, i.e., the wide array of chemical environments that they can stabilize. One finds transition metals coordinated to soft and hard donor ligands with multiple oxidation states, different spin states, and variable stereochemistry. The nature of the chemical environment can exert exquisite control over the chemistry of d-block metal systems. For example, the family of enzymes the cytochromes P-450 have an axial thiolate ligand ( $\text{L} = \text{RS}^-$  in Scheme 1) from a cysteine residue and effect catalytic oxidation of xenobiotics. Related enzymes in which the axial ligand is the nitrogen-donor histidine comprise the oxygen-binding heme proteins such as hemoglobin and myoglobin.

#### IV. WHAT IS REQUIRED?

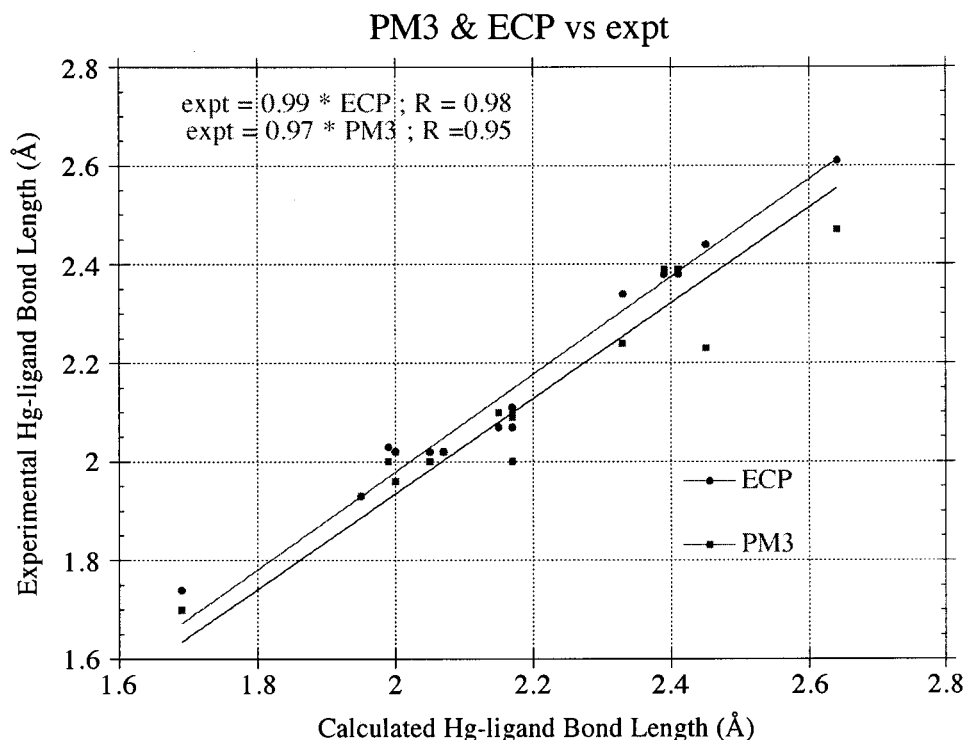
In modeling catalysts and catalytic systems, the computational chemist has several targets in the quest to understand existing systems and help design improvements. For the purposes of this Perspective, we will divide these task into four areas: (1) correct description of the molecular and electronic structure of catalysts, catalyst precursors, and intermediates, (2) reliable modeling of potential energy surfaces, (3) evaluation of spectroscopic parameters, and (4) accurate prediction of energetic quantities. We will investigate each in turn.

**i. Structural Determination.** In many respects, the ability to reliably predict the structure of a catalyst or catalyst intermediate has the same value to the computational chemist

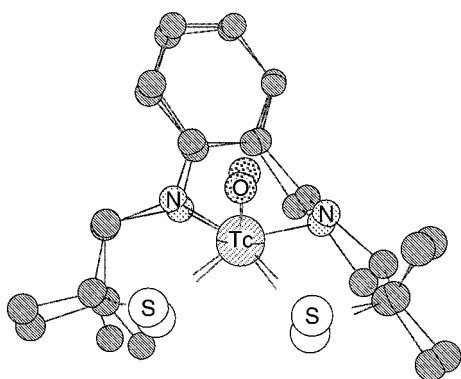
as a crystal structure has to an experimentalist. Chemists have learned since the time of Pauling<sup>13</sup> and his seminal work “The Nature of the Chemical Bond”, there is perhaps no more valuable piece of information about a chemical species than the three-dimensional arrangement of the atoms which comprise it. This information is directly available from a variety of diffraction experiments (X-ray, neutron, and electron being the most common) or can be inferred indirectly from spectroscopy (NMR, EXAFS, infrared, etc.). Increasingly, structural information can be garnered from computation.

Accurately predicting geometries is perhaps one of the easiest tasks that a modeler can be called on to perform. At a minimum, if a particular level of theory cannot perform admirably in this regard, it is not worthwhile applying it to other portions of the computational exercise. For the computational chemist with an interest in modeling catalysts the ability to accurately predict geometries is important in several respects. It provides the most straightforward initial clues that the computational methods being used are accurately describing the underlying electronic structure of the system of interest. As the other chemical information (atomic charges, orbital energies, propensity to attack by nucleophiles/electrophiles, etc.) one may wish to extract from a computational study of a catalyst is derived from this, it is important that the suitability of the model be established as early as possible in the computational process. For example, in a study of carbon–hydrogen bond activation by divalent mercury complexes, our group evaluated a series of 16, chemically diverse ligands. As is evident from Figure 1 (a comparison of two levels of theory versus experiment), the agreement is near ideal for one method (high-level *ab initio* calculations employing effective core potential, ECP, methods at the Hartree–Fock level of theory<sup>14</sup>) and less so for the other (a semiempirical PM3 Hamiltonian).<sup>15</sup> Hence, one can proceed to other reliable experimental quantities, e.g., reaction enthalpies or heats of formation, to further assess the *ab initio* approach, while the results in Figure 1 suggest caution with further investigations utilizing the semiempirical method.

An exercise in structural prediction also provides useful calibration of the level of accuracy that can be expected when modeling a catalyst. Determination of an appropriate level of accuracy is dependent on the particular modeler’s comfort level and the specific application. For example, in our research with ECPs we typically find that these techniques can predict geometries to within 1–3% as long as a suitable wave function (i.e., is electron correlation needed or not?) is utilized.<sup>7,8</sup> Anything greater is worrisome. Figure 1 raises another important issue that must weigh into any molecular modeling of catalysts, the time requirement. The PM3 calculations each took less than a minute for full geometry optimization (those in Figure 1 were done on a 266 MHz personal computer), as compared to an hour or so for each ECP calculation (utilizing a UNIX workstation). The PM3-predicted mercury–ligand bond lengths are, on average, too long by 3%. It is quite conceivable that this level of agreement may be acceptable given the huge time savings that can be realized from using an approximate modeling method. Indeed, the modeler may wish to utilize the results of the PM3 calculation to provide an initial guess for a more computationally intensive *ab initio* calculations.



**Figure 1.** Comparison of *ab initio* based effective core potential method and semiempirical PM3 Hamiltonian for describing Hg(II) complexes.



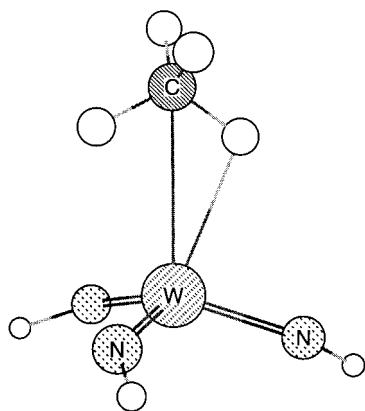
**Figure 2.** Overlay of MM-predicted and experimental geometry for Tc(V)-oxo complex (hydrogen atoms omitted for clarity).

Another reason that reliable structural prediction is an important primary step in catalyst modeling is that it gives the modeler confidence, by comparing with experimental data, before embarking on unknown systems. With respect to this final point, it is relatively easy to model a series of highly related complexes with quantum or classical techniques. This can, however, prove dangerous given the chemical diversity seen in d-block systems. The greatest confidence in a computational model is obtained when good metric predictability is obtained for a wide range of d-block complexes. In the mercury example, since the chemistry of mercury is dominated by the divalent state, this goal is achieved by evaluating Hg(II) systems with anionic ligands that span a range of hard (e.g., hydroxide), soft (e.g., bisulfide), and intermediate (e.g., bromide) bases.<sup>14</sup> For other d-block metal complexes, particularly those from the middle portion of the series, different bond and ligand types can often be found within a single complex! As an example, consider the Tc complex shown in Figure 2. There are bonds to “hard” nitrogen and oxygen donors along with bonds to

“soft” sulfur donors. Additionally, this complex contains single, double, and dative bond types. Thus, the ability of the new force field to accurately predict the geometry of this Tc complex is very encouraging.<sup>16</sup> The computational chemists best chance of accurate structural prediction lies in the use of the most flexible approaches (large basis sets with explicit inclusion of electron correlation). However, seldom are such techniques computationally feasible for realistic catalyst models. Cases in which there is a diversity of ligand types within a single complex type are expected to present the greatest challenge to approximate modeling techniques such as molecular mechanics and semiempirical quantum mechanics. However, the great savings in computational time that can be achieved provide considerable motivation for the development of reliable, approximate modeling methods in catalysis.

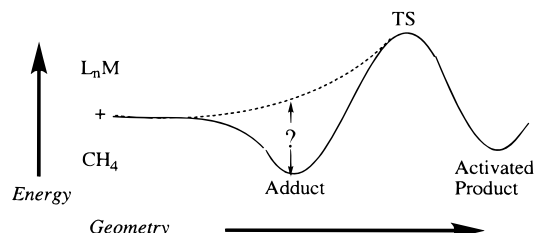
**ii. Reaction Trajectories.** Catalysis is, by definition, a dynamic process. Following geometric changes (as well as the underlying orbital changes) as reactants pass through the transition state and on to products yields very important clues as to interactions that govern a catalytic reaction. Modeling of intrinsic reaction coordinates<sup>17</sup> (IRCs) can also be used to study whether a particular intermediate lies along a reaction coordinate and if it is a local minimum or a nonstationary point. For example, there has been much interest in catalysis in the initial stages of carbon–hydrogen bond activation by transition metal complexes.<sup>18,19</sup> Carbon–hydrogen activation plays a pivotal role in many catalytic cycles and is of interest in connection with the transformation of hydrocarbon petrofeedstocks to more valuable, functionalized products.<sup>20</sup> Experiments suggested the intermediacy of weakly-bound adducts between alkanes and activating complexes prior to C–H scission. Alkane adducts (Scheme 2 shows an example), even if they form, are expected to be ephemeral, and hence their analysis by computation is a

## Scheme 2



natural. Computations<sup>21</sup> indicate that methane adducts are feasible for early d-block complexes in which the metal is in its highest ( $d^0$ ) oxidation state in addition to more electron-rich complexes<sup>18</sup> for which the evidence, experimental and computational, is clearer. In terms of utilizing reaction coordinate techniques, it was possible to isolate the TSs for C–H activation by many  $d^0$  complexes and then to follow the IRCs back toward reactants. Calculated IRCs indicate that methane remains in the coordination sphere of the metal and hence it lies along the reaction path for C–H activation, Scheme 3. Similarly, in a study of olefin metathesis between

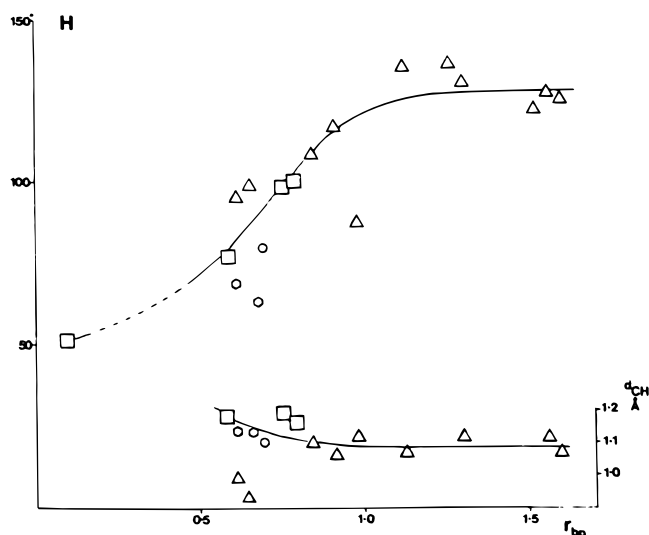
## Scheme 3



ethylene and the model catalyst,<sup>22</sup>  $W(OH)_2(=CH_2)(=NH)$ , following the reaction coordinate back toward reactants indicates that the substrate, ethylene, remains within the W coordination sphere, supporting experimental inferences as to formation of an olefin-catalyst precursor that plays a role in determining regioselectivity and stereoselectivity.

The study of reaction coordinates, although profitable, raises a dilemma. How does one validate a calculated reaction trajectory? Experiments using molecular beam and ion-beam techniques reveal much about reaction dynamics. Real catalysts typically have large ligands, with a multitude of vibrational degrees of freedom, to engender regioselective control over a reaction. However, d-block systems whose dynamics are best understood experimentally<sup>23</sup> (e.g.,  $Co^+ + CH_4$ ) are usually considerably less complicated than those of interest to catalytic chemists.

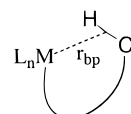
One potential route to validation of reaction coordinate techniques lies within the realm of crystallography, in particular the method known as a Bürgi–Dunitz analysis.<sup>24</sup> Briefly, the Bürgi–Dunitz analysis is an attempt to extract dynamic information from static structures. Different ligand and metal combinations are presumed to model low-energy points along a hypothetical reaction coordinate. One of the best examples of the Bürgi–Dunitz analysis of a catalytically important reaction is that reported by Crabtree and co-



**Figure 3.** Plot of both  $H$  (the angle C–H–M in deg) and  $d_{CH}$  (Å) against  $r_{bp}$  (Å) from Table IV. Squares and hexagons refer to neutron data, triangles and circles to X-ray data. Hexagons and circles refer to  $\alpha$ -CH bridges that are more constrained geometrically than  $\beta$  and higher types (squares and triangles); more weight is attached to the latter, particularly with regard to  $H$ . Only when  $r_{bp}$  falls appreciably below 1.0 does  $H$  fall below  $130^\circ$  and  $d_{CH}$  rise significantly above the value in the free C–H bond (ca. 1.08 Å). The calculated value of  $H$  for a cis alkyl hydride complex (entry 21 of Table IV) is also included; the corresponding value of  $d_{CH}$  (2.68 Å) is too large to include in this plot. See ref 25.

workers. These researchers looked at X-ray and neutron diffraction structures of agostic TM complexes, Scheme 4,

## Scheme 4

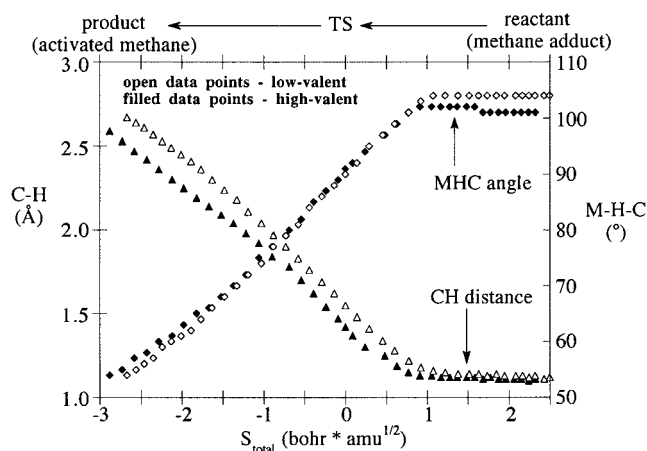


to model a trajectory for oxidative addition. By investigating two metric parameters (C–H distance and M–H–C angle) as a function of a derived reaction coordinate ( $r_{bp}$ , the distance from the metal to the C–H bond centroid) from X-ray and neutron data they derived the trajectory in Figure 3.<sup>25</sup> This trajectory and the insight it has provided have made a seminal contribution to the way in which chemists view this important catalytic process.

Our group investigated oxidative addition processes using reaction coordinate-following techniques.<sup>26</sup> Oxidative addition has been well studied computationally, so our main goal was to provide a base of comparison for the less well studied  $\sigma$ -bond metathesis. The results from calculated IRCs are shown in Figure 4. Notice the good correspondence with the experimental trajectory<sup>25</sup> (Figure 3)—the C–H bond distance remains constant until near the TS and then rises abruptly, and the M–H–C angle remains constant and then rapidly declines in the vicinity of the transition state. Furthermore, these geometric changes seem to be correlated. This point, which we term the “break point”, is generally in the vicinity of the TS for C–H bond activation.

Figure 4 shows a typical, calculated “Crabtree trajectory” for oxidative addition of methane to a 14-electron, three-coordinate  $Ir^I$  complex ( $Ir(H)(PH_3)_2 \cdots H-CH_3 \rightarrow Ir(H)_2-(CH_3)(PH_3)_2$ ) and  $\sigma$ -bond metathesis to a three-coordinate,  $W^{VI}$  complex ( $W(=NH)_3 \cdots H-CH_3 \rightarrow W(=NH)_2(NH_2)-$





**Figure 4.** C–H distances and M–H–C angles along a calculated methane activation trajectory by prototypical high-valent ( $\text{W}^{\text{VI}}(\text{=NH})_3$ ) and low-valent ( $\text{Ir}^{\text{I}}(\text{H})(\text{PH}_3)_2$ ) complexes.

( $\text{CH}_3$ ). What is surprising is that the behavior of C–H and M–H–C is nearly identical for oxidative addition and  $\sigma$ -bond metathesis. This is despite the fact that in the latter reaction both ends of the cleaved C–H bond end up on two different atoms (tungsten and nitrogen) but on the same atom (iridium) in the former. The similarity is greatest in the “early” portion of the activation event, i.e., before the TS (set by definition to  $S_{\text{total}} = 0 \text{ bohr amu}^{1/2}$  on the reaction coordinate) or  $S_{\text{total}} > 0$ .

Analyses of calculated electronic properties along the IRCs reveal an interesting picture of C–H activation.<sup>26</sup> Regardless of mechanism, the charge on the methane fragment increases (becomes more positive) until the “break point” after which it decreases. Interactions between C–H bonds and TM centers arise from a synergistic donation of electron density from the C–H bond to a vacant TM orbital (with  $\sigma$  local symmetry) combined with backdonation from a filled TM orbital (with  $\pi$  local symmetry) to the C–H  $\sigma^*$ .<sup>27</sup> The IRC analysis thus suggests that for the early portion of the reaction coordinate, the metal acts as an electrophile toward the substrate. This is reasonable since  $d^0$  systems are in their highest stable formal oxidation state and hence electron deficient. Low-valent C–H activators are 14- or 16-electron complexes and thus electron-deficient relative to the 18-electron count observed for most organometallics with metals from the late transition series. Thus, in each case there is considerable impetus for the metal to act as an electrophile.

After the break point the activating complex acts as a nucleophile/base, donating electron density to populate the C–H  $\sigma^*$ . It is this interaction that finally causes the C–H bond to rupture. This simple “donation/backdonation” picture of bond activation is satisfying in several regards. First, it rationalizes why the IRC is so similar early on—the metal acts as the electrophilic center in each case. Second, it helps to clarify the role of the adduct—it helps to bring the substrate and complex into intimate contact and in the vicinity of the TS with minimal energetic expense. Almost invariably, complexes where adduct formation cannot occur (e.g., neutral  $d^2$  and  $d^{10}$  complexes)<sup>14,28</sup> have higher C–H activation barriers than related systems in which adduct formation is favorable. Third, this simple two-step mechanism provides a simple explanation for why the reactions of low- and high-valent complexes deviate after the break

point. For low-valent complexes, the frontier orbitals are metal-based and thus the metal acts as both nucleophile and electrophile resulting in both ends of the C–H bond being ligated to the metal. For the multiply bonded, high-valent complexes that we have investigated the frontier molecular orbitals are metal–ligand  $\pi$  orbitals that are more heavily polarized toward the electronegative ligand and away from the electropositive, early TM. Thus, the C–H bond in these high-valent complexes ends up being added across the bond.

If the modeler can establish confidence in reaction coordinate techniques for catalytic reactions, there are several advantages as compared to Bürgi–Dunitz analyses. First, computed trajectories do not require changing metals and ligands to model different points along a reaction coordinate. As a result, there are less variables in a computed trajectory. Second, the calculated trajectory can be used to easily investigate intermolecular interactions, while experiments are often limited to intramolecular interactions. Intermolecular processes are typically more relevant to catalysis. Third, geometric changes along the computed trajectory can be correlated with the energetic changes these perturbations engender. Fourth, computed trajectories can be sampled in the neighborhood of the transition states, arguably the most important points on a catalytic cycle. Fifth, the wave function describing the catalytic process is available for each step along the reaction coordinate. The wave function can thus be analyzed to correlate geometric changes with the underlying “orbital dynamics” as was done above for the example of C–H bond activation.

**iii. Spectroscopy.** To the experimentalist, spectroscopic techniques are valuable in two respects. First, to confirm/exclude potential catalytic intermediates. Second, as a tool to reveal chemical information about a catalytic intermediate. This section will focus on infrared (IR) spectra as this is one of the least well studied in the area of d-block catalysis, and our group has experience in this area. Infrared spectra, arising from the vibrations of atoms within a molecule, are perhaps the easiest to be modeled. Ostensibly, one only needs a stationary point geometry (see section i) and the second derivatives of the total energy with respect to atomic coordinates. The coordinates can be Cartesian or, if atom connectivity is specified, internal. The change in dipole moment with respect to changes in coordinates is used to derive IR intensities.

There has been considerable research on the use of quantum methods to estimate the IR spectra of main group (MG) compounds.<sup>29</sup> What has emerged from this work is that calculation with the harmonic approximation, done for computational tractability, tends to overestimate vibrational frequencies as compared to experiments (which, of course, include anharmonicity). The degree of overestimation varies with the method employed, generally approaching unity for *ab initio* methods as the treatment of electron correlation is improved but being less sensitive to basis set effects. However, for a single computational model the overestimation is relatively constant for different types of modes (stretches, angular deformations, etc.). Thus, application of a simple scaling factor ( $\lambda$ ), eq 1, quite often leads to

$$\nu_{\text{est}} = \nu_{\text{calc}} * \lambda \quad (1)$$

reasonable estimation of IR frequencies. Other procedures

using more involved scaling procedures (exponential, mode sensitive, neural networks, etc.) have also been investigated.<sup>30</sup>

Surprisingly, there has been relatively little research in the use of molecular modeling to describe the IR spectra of transition metal (TM) complexes. Russo et al.<sup>31</sup> and Frenking and co-workers<sup>32</sup> investigated the ability of *ab initio* techniques (coupled with effective core potentials) to predict the vibrational frequencies of several TM complexes. To some extent the modeling efforts are hampered by a lack of reliable experimental data and the sensitivity of the vibrational modes to environmental factors—solvent, counterion—when they cannot, as is usually the case for d-block complexes, be measured in gas phase. The most extensive investigation of *ab initio* ECP techniques for estimation of vibrational frequencies is that conducted in our group by Phil Raby.<sup>33</sup> Nearly 100 complexes (50 for PM3) and  $\approx 200$  ( $\approx 100$  for PM3) metal–ligand stretching modes were investigated for chalcogenido complexes,  $L_nM=Ch$  ( $Ch = O, S, Se, Te$ ), species important in catalytic oxidations ( $Ch = O$ ), and hydrodesulfurization of fuel oil ( $Ch = S$ ). Several results issued from this research that are significant with respect to modeling the IR spectra of d-block complexes. First, similar behavior is seen for TM and MG systems with respect to the use of the harmonic approximation for vibrational frequencies, i.e., a systematic overestimation of experimental frequencies ( $\lambda \approx 0.86$  (ECP);<sup>33</sup>  $\lambda \approx 0.88$  (PM3)). Second, the use of scaling and linear corrections to bring ECP-calculated frequencies into closer correspondence with experiment yields similar predictive ability for TM and MG systems. The PM3 technique performs distinctly worse for the prediction of vibrational frequencies ( $\approx 64\%$  higher in terms of the average absolute error). Third, the variability of  $\lambda$  for specific subsets of complexes can be significant for TM cases, quite possibly due to the great chemical diversity seen in these systems. Fourth, the coupling of vibrational, structural, and electronic data, with experimental information, can be a powerful analysis tool for catalytic intermediates. For example, previous computations<sup>34</sup> and experiments<sup>35</sup> suggest a fundamental difference in the  $TM=Ch$  bond for the lightest congener (oxygen) versus its sulfur and selenium analogues. This conjecture is given greater weight by analysis of the vibrational spectra of these complexes which show that  $\lambda \approx 1$  for the heavier chalcogenidos, while the vibrational scaling factor ( $\lambda$ ) is considerably lower for the oxos.

The calculation of spectroscopic properties of d-block complexes is perhaps the area in which the least effort has been placed by those with an interest in catalyst modeling and is an area where additional research would be most welcome. This is especially so given the crucial role that transient species play in catalysis. Such species are typically not stable enough or formed in sufficient concentration to permit isolation and analysis by a direct technique such as X-ray crystallography. However, it is often possible to probe such species through spectroscopic techniques. The stringency required for accurate calculation of spectroscopic information (where one must provide a balanced description of ground and excited state(s)) often limits the study of these quantities to the highest levels of theory—*ab initio* techniques often with post-Hartree–Fock treatments or density functional methods. However, there has been progress in the utilization of semiempirical techniques for modeling of the

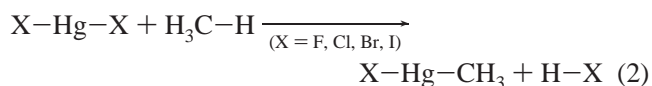
**Table 1.** Calculated Reaction Enthalpies (kcal mol<sup>-1</sup>) for Eq 2

X	$\Delta H_{\text{expt}}$	$\Delta H_{\text{ECP}}$	$\Delta H_{\text{PM3}}$	$ \Delta H_{\text{expt}} - \Delta H_{\text{ECP}} $	$ \Delta H_{\text{expt}} - \Delta H_{\text{PM3}} $
F	3	1	-11	2	14
Cl	26	21	22	5	4
Br	31	29	44	2	13
I	39	35	56	4	17
			av	3	12

electronic spectroscopy of TM complexes, most notably by Zerner and his colleagues using the ZINDO parameterization of the INDO/1 technique.<sup>36</sup> Additionally, the Comba group<sup>37</sup> have coupled the rapid molecular mechanics method with the angular overlap model (AOM) technique to provide rapid prediction of electronic spectra. Deeth and co-workers have applied similar techniques for modeling of EPR (electron paramagnetic spectroscopy) spectra.<sup>38</sup>

**iv. Energetics.** Calculation of accurate reaction energies is crucial in the analysis and design of catalysts and catalytic reactions. A recent review<sup>39</sup> of organometallic thermochemistry has the provocative title “Transition Metal–Hydrogen and Metal–Carbon Bond Strengths: The Keys to Catalysis”. If this is indeed true, the difficulties encountered in calculation of accurate energies suggests that the keys are not yet in the pocket of the computational chemist! Higher levels of theory are generally required—larger basis sets and more extensive treatment of electron correlation. Indeed, this is the primary reason that density functional theory (DFT) techniques promise to revolutionize the study of reaction energetics involving metal complexes. The published version of Ziegler’s ALCAN award lecture is an excellent overview of the application of DFT to metal complexes with catalytic applications.<sup>40</sup> Another complication in the development of accurate and efficient techniques for d-block complexes is that the great wealth of enthalpic data available for organic compounds is much more sparse for metal-containing species. Additionally, metal–ligand bond-energies are typically more sensitive to chemical environment than for organic compounds.<sup>39</sup>

From a computational point of view, calculation of energetics is much more demanding than structure determination. As an example, let us return to the Hg(II) complexes discussed above (Figure 1), for which accurate prediction of geometries was found. It is evident from the calculated enthalpies for methane activation, eq 2, in Table 1 that the *ab initio* ECP techniques



(Hartree–Fock optimized geometries and energies calculated with Møller–Plesset second-order perturbation theory) do a very good job<sup>14</sup> (as was the case for geometric prediction). The semiempirical PM3 technique is not suitable with respect to accurate modeling of the reaction energetics for even this relatively simple metathesis reaction. For the chloride and fluoride complexes, the PM3-predicted enthalpies are low but too high for the bromide and iodide, Table 1. Additionally, the average absolute difference in  $\Delta H$  between PM3 and experiment is 12 kcal mol<sup>-1</sup>, four times larger than obtained with ECP methods, Table 1.

As an alternative approach to the prediction of bond energies involving TMs, a former Ph.D. student in our group,

Eddie Moody, investigated artificial intelligence techniques, specifically neural networks (NNs), for the prediction of energetic data.<sup>41,42</sup> Diatomics were chosen for this preliminary research as there is considerable, reliable experimental information available for compounds incorporating elements from across the entire periodic table. Furthermore, diatomics afforded an excellent opportunity to compare the predictive ability of neural networks with traditional quantum techniques.

In a study of 52 diatomic element-oxos<sup>41</sup> (EO, chosen given the importance of oxidic species in catalytic oxidations), it was found that a trained NN could predict bond energies (using the atomic number, first and second ionization potentials, covalent radius, polarizability, atomization energy, and electronegativity of E as inputs) to within 12.5 kcal mol<sup>-1</sup>. Although this agreement is not spectacular it must be compared to 24.8 kcal mol<sup>-1</sup> for quantum calculations employing correlated wave functions. Moreover, many dozens of NN simulations can be run in the time it takes to perform a single quantum mechanical calculation even for a diatomic. Perhaps more importantly, if one assesses the predictive ability of the neural network approach as a function of the position of E in the periodic table (main group, d-block versus f-block) it is found that bond energies are predicted with commensurate accuracy for main group oxos ( $\Delta = 12$  kcal mol<sup>-1</sup>, 29 examples), d-block oxos ( $\Delta = 14$  kcal mol<sup>-1</sup>, 17 examples), and f-block ( $\Delta = 10$  kcal mol<sup>-1</sup>, six examples), where  $\Delta$  is the average absolute difference between theory and experiment. It is typically observed with quantum and classical techniques that accurate modeling of chemical properties becomes increasingly difficult and more expensive in the order main group < d-block < f-block. Thus, the development of modeling approaches that can accurately model main group, d-block, and f-block chemistry is particularly exciting given the growing importance of all these elements in catalysis.

In a follow-up to our neural network research on oxos,<sup>41</sup> a more comprehensive study of 199 diatomic species (XY) was conducted.<sup>42</sup> The valence electron configurations, atomic number, and atomic mass of both X and Y were used as inputs to the NN to describe the diatomic. The ability to predict molecular properties *individually* was investigated as well as NN prediction of bond energies ( $D_e$ ) *simultaneously* with other molecular properties, i.e., equilibrium bond distances ( $r_e$ ) and equilibrium stretching frequencies ( $w_e$ ). The neural network results were compared with those from ECP calculations employing multiconfiguration self-consistent field (MCSCF) wave functions. The NN techniques outperformed the MCSCF calculations, at a considerable savings in computational time, particularly for bond energies. Furthermore, although individual NN prediction of  $D_e$ ,  $w_e$ , or  $r_e$  was superior to simultaneous prediction of all three, as expected, the drop off in predictive ability was not large and still superior to the results obtained with MCSCF calculations.

#### SUMMARY, CONCLUSION, AND PERSPECTIVE

The modeling of catalysts and catalytic reactions is a complex, often multistep, process. This Perspective has just scratched the surface of some of the issues involved in modeling the chemistry of catalysts and the reactions they

participate in with an emphasis on d-block metal-based systems. In this contribution, catalyst modeling has been decomposed into four activities—structural prediction, reaction trajectories, spectroscopy, and energetics—although other researchers might prefer different organization schemes. Each portion of the computational exercise has challenges pertinent to it if accurate modeling is to be achieved. At its most basic level, computational characterization of a catalytic cycle (such as that shown in cartoon format in, for example, Scheme 3) can be reduced to identification of not only the relative geometries (i.e., relative position along the abscissa) of the important points but also their energetic relationships (i.e., relative position along the ordinate). The molecular and electronic structure at these points is also clearly of interest, and the agreement of the model with known, high-quality experimental information (e.g., structural information, equilibrium or kinetic data, spectroscopic parameters, etc.) provides confidence when the model is applied to portions of the catalytic cycle invisible to experiment. As has been stressed in several places, modeling the bonding and reactivity of catalysts involving d-block metals necessitates that the models employed (be they quantum, classical, etc.) be validated against a series of diverse complexes as opposed to a narrow set of related systems. Traditionally, in quantum mechanical analyses of catalytic processes, geometries are typically determined at a lower level of theory. Subsequently, single-point calculations with larger basis sets and/or more extensive correlation treatments are used for determination of accurate energetics and/or evaluation of spectroscopic properties. Thus, the identification of procedures for simultaneously predicting several molecular properties is perhaps the area in which the greatest research is needed in the modeling of catalysts and catalytic reactions.

#### ACKNOWLEDGMENT

The authors acknowledge the Department of Energy (DE-FG02-97ER14811) for support.

#### REFERENCES AND NOTES

- (1) (a) Grand Challenges 1993: High Performance Computing and Communications; Federal Coordinating Council: Washington, D.C., 1992. (b) Critical Technologies: The Role of Chemistry and Chemical Engineering; National Research Council, National Academy Press: 1992.
- (2) Catalysis Looks to the Future; NRC, National Academy Press: Washington, D.C., 1992.
- (3) Brown, T. L.; LeMay, H. E.; Bursten, B. E. *Chemistry: The Central Science*; 6th ed.; Prentice Hall: Englewood Cliffs, NJ, 1994; p 517.
- (4) Marks, T. J. Surface-Bound Metal Hydrocarbyls: Organometallic Connections between Heterogeneous and Homogeneous Catalysis. *Acc. Chem. Res.* **1992**, 25, 57.
- (5) *Cytochrome P450: Structure, Mechanism, and Biochemistry*, 2nd ed.; Ortiz de Montellano, P. R., Ed.; Plenum: New York, 1995.
- (6) Frenking, G.; Antes, I.; Böhme, M.; Dapprich, S.; Ehlers, A. W.; Jonas, V.; Neuhaus, A.; Otto, M.; Stegmann, R.; Veldkamp, A.; Vydroishchikov, S. F. Pseudopotential Calculations of Transition Metal Compounds: Scope and Limitations. In *Reviews in Computational Chemistry*; Boyd, D., Lipkowsky, K., Eds.; 1996; Vol. 8, p 63.
- (7) Benson, M. T.; Cundari, T. R.; Lutz, M. L.; Sommerer, S. O. Effective Core Potential Approaches to Computational Inorganic Chemistry. In *Reviews in Computational Chemistry*; Boyd, D., Lipkowsky, K., Eds.; 1996; Vol. 8, p 145.
- (8) Cundari, T. R.; Gordon, M. S. Effective Core Potential Studies of Transition Metal Chemistry. *Coord. Chem. Rev.* **1996**, 147, 87.
- (9) Comba, P.; Hambley, T. W. *Molecular Modeling of Inorganic Compounds*; VCH: New York, 1995.



- (10) Hay, B. P. Methods for Molecular Mechanics Modeling of Coordination Compounds. *Coord. Chem. Rev.* **1993**, 126, 177.
- (11) Cundari, T. R. Molecular Modeling of d- and f-block Metal Complexes. *J. Chem. Soc., Dalton Trans.* **1998**, 2771.
- (12) Landis, C. L.; Root, D. M.; Cleveland, T. Molecular Mechanics Force Fields for Modeling Inorganic and Organometallic Compounds. In *Reviews in Computational Chemistry*; Boyd, D. B., Lipkowitz, K. B., Eds.; 1995; Vol. 6, p 73.
- (13) Pauling, L. The Nature of the Chemical Bond, 3rd ed.; Cornell University Press: Ithaca, NY, 1960.
- (14) Cundari, T. R.; Yoshikawa, A. Methane Activation by Mercury(II) Complexes. *J. Comput. Chem.* **1998**, 19, 902.
- (15) Cundari, T. R.; Deng, J. Unpublished results.
- (16) Cundari, T. R.; Fu, W. Unpublished results.
- (17) Gonzalez, C.; Schlegel, H. B. An Improved Algorithm for Reaction Path Following. *J. Chem. Phys.* **1989**, 90, 2154.
- (18) Wasserman, E. P.; Moore, C. B.; Bergman, R. G. Gas-Phase Rate of Alkane C-H Oxidative Addition to Transient CpRh(CO). *Science* **1992**, 255, 315.
- (19) (a) Schafer, D. F.; Wolczanski, P. T.  $d^0$  Alkane Complexes ( $(\text{Bu}_3\text{SiN}=\text{Si}=\text{W}(\text{R}(\text{H}))_2)_2$ ) Precede C-H Activation and Formation of  $(\text{Bu}_3\text{SiN}=\text{Si}=\text{W}(\text{R}(\text{H}))_2)_2$ . *J. Am. Chem. Soc.* **1998**, 120, 4881. (b) Schaller, C. P.; Bonnano, J. B.; Wolczanski, P. T. Does Methane Bond to  $d^0$   $(\text{Bu}_3\text{SiN}=\text{Si}=\text{Zr}=\text{NSi}(\text{Bu}_3)_2)$  Prior to C-H Bond Activation? An Inter vs Intramolecular Isotope Effect Study. *J. Am. Chem. Soc.* **1994**, 116, 4133.
- (20) Parkyns, N. D. Methane Conversion-A Challenge for Industrial Chemists. *Chem. Br.* **1990**, 9, 841.
- (21) (a) Cundari, T. R. Methane Adducts of  $d^0$  Transition Metal Complexes. *Organometallics* **1993**, 12, 1998. (b) Cundari, T. R.; Klinckman, T. R. Reduced Variational Space Analysis of Methane Adducts. *Inorg. Chem.* **1998**, 37, 5399.
- (22) Cundari, T. R. Unpublished results.
- (23) Koga, N.; Musaev, D. J.; Morokuma, K.; Cundari, T. R.; Nguyen, K. A.; Gordon, M. S. The Reactions of  $\text{Co}^+$  ( $^3\text{F-d}^8$ ) with  $\text{H}_2$  and  $\text{CH}_4$ . *J. Phys. Chem.* **1993**, 97, 11435.
- (24) Bürgi, H. B.; Dunitz, J. D. From Crystal Statics to Chemical Dynamics. *Acc. Chem. Res.* **1983**, 16, 153.
- (25) Crabtree, R. H.; Holt, E. M.; Lavin, M.; Morehouse, S. M. Inter- vs. Intramolecular C-H Activation: A C-H-Ir Bridge in  $[\text{IrH}_2(8\text{-methylquinoline})\text{L}_2]\text{BF}_4$  and a  $\text{C-H} + \text{M} \rightarrow \text{C-H-M}$  Reaction Coordinate. *Inorg. Chem.* **1985**, 24, 1986. Reprinted from ref 25. Copyright 1985 American Chemical Society.
- (26) Cundari, T. R. Calculation of a Methane C-H Oxidative Addition Trajectory: Comparison to Experiment and Methane Activation by High-Valent Complexes. *J. Am. Chem. Soc.* **1994**, 116, 340.
- (27) Saillard, J. Y.; Hoffmann, R. C-H and H-H Activation in Transition Metal Complexes and on Surfaces. *J. Am. Chem. Soc.* **1984**, 106, 2006.
- (28) Cundari, T. R. C-H Activation by a  $d^2$  W-imido Complex: Comparison of [2+2] and Oxidative Addition Pathways. *Organometallics* **1993**, 12, 4971.
- (29) Pople, J. A.; Scott, A. P.; Wong, M. W.; Radom, L. Scaling Factors for Obtaining Fundamental Vibrational Frequencies and Zero-Point Energies from HF/6-31G\* and MP2/6-31 G\* Harmonic Frequencies. *Isr. J. Chem.* **1993**, 33, 345.
- (30) Rauhut, G.; Pulay, P. For example: Transferable Scaling Factors for Density Functional Derived Vibrational Force Fields. *J. Phys. Chem.* **1995**, 99, 3093.
- (31) Russo, T. V.; Martin, R. L.; Hay, P. J. Effective Core Potentials for DFT Calculations. *J. Phys. Chem.* **1995**, 99, 17085.
- (32) Neuhaus, A.; Veldkamp, A.; Frenking, G. Oxo and Nitride Complexes of Molybdenum, Tungsten, Rhenium and Osmium. A Theoretical Study. *Inorg. Chem.* **1994**, 35, 5278.
- (33) Cundari, T. R.; Raby, P. D. Theoretical Estimation of Vibrational Frequencies Involving Transition Metal Compounds. *J. Phys. Chem. A* **1997**, 101, 5783.
- (34) Benson, M. T.; Cundari, T. R.; Lim, S. J.; Nguyen, H. D.; Pierce-Beaver, K. An Effective Core Potential Study of Transition Metal Chalcogenides. Part I. Molecular Structure. *J. Am. Chem. Soc.* **1994**, 116, 3955-3966.
- (35) Parkin, G.; Howard, W. A. Terminal Oxo, Sulfido, Selenido, and Tellurido Complexes of Zirconium,  $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Zr}(\text{E})(\text{NC}_5\text{H}_5)$ : Comparison of Terminal Zr-E Single and  $\text{Zr}=\text{E}$  Double Bond Lengths. *J. Am. Chem. Soc.* **1994**, 116, 606.
- (36) Stavrev, K. K.; Zerner, M. C. Spin-Averaged Hartree-Fock Procedure for Spectroscopic Calculations: The Absorption Spectrum of  $\text{Mn}^{2+}$  in ZnS Crystals. *Int. J. Quantum Chem.* **1997**, 65, 877. Cory, M. G.; Stavrev, K. K.; Zerner, M. C. An Examination of the Electronic Structure and Spectroscopy of High- and Low-Spin Model Ferredoxin via Several SCF and CI Techniques. *Int. J. Quantum Chem.* **1997**, 63, 781.
- (37) Bernhardt, P. V.; Comba, P. Prediction and Interpretation of Electronic Spectra of Transition Metal Complexes via the Combination of Molecular Mechanics and Angular Overlap Model Calculations. *Inorg. Chem.* **1993**, 32, 2798.
- (38) Deeth, R. J.; Paget, V. J. Molecular Mechanics Calculations on Imine and Mixed-Ligand Systems of  $\text{Co}^{\text{III}}$ ,  $\text{Ni}^{\text{II}}$ , and  $\text{Cu}^{\text{II}}$ . *J. Chem. Soc., Dalton Trans.* **1997**, 527-546.
- (39) Simoes, J. A. M.; Beauchamp, J. L. Transition Metal-Hydrogen and Metal-Carbon Bond Strengths: The Keys to Catalysis. *Chem. Rev.* **1990**, 90, 629.
- (40) Ziegler, T. Density Functional Theory as a Practical Tool in Studies of Organometallic Energetics and Kinetics. *Can. J. Chem.* **1995**, 73, 743-761.
- (41) Cundari, T. R.; Moody, E. W. Prediction of Bond Dissociation Energies using Neural Network, Statistical, and Quantum Mechanical Approaches. *J. Mol. Struct. (THEOCHEM)* **1998**, 425, 43.
- (42) Cundari, T. R.; Moody, E. W. A Comparison of Neural Networks and Quantum Mechanics for Inorganic Systems. *J. Chem. Inf. Comput. Sci.* **1997**, 37, 871.

CI9802171