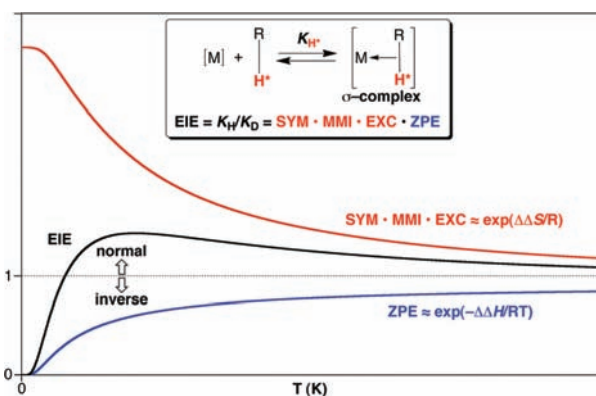# Temperature-Dependent Transitions Between Normal and Inverse Isotope Effects Pertaining to the Interaction of H−H and C−H Bonds with Transition Metal Centers

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CONSPECTUS

Deuterium kinetic isotope effects (KIEs) serve as versatile tools to infer details about reaction mechanisms and the nature of transition states, while equilibrium isotope effects (EIEs) associated with the site preferences of hydrogen and deuterium enable researchers to study aspects of molecular structure. Researchers typically interpret primary deuterium isotope effects based on two simple guidelines: (i) the KIE for an elementary reaction is normal ($k_H/k_D > 1$) and (ii) the EIE is dictated by deuterium preferring to be located in the site corresponding to the highest frequency oscillator.
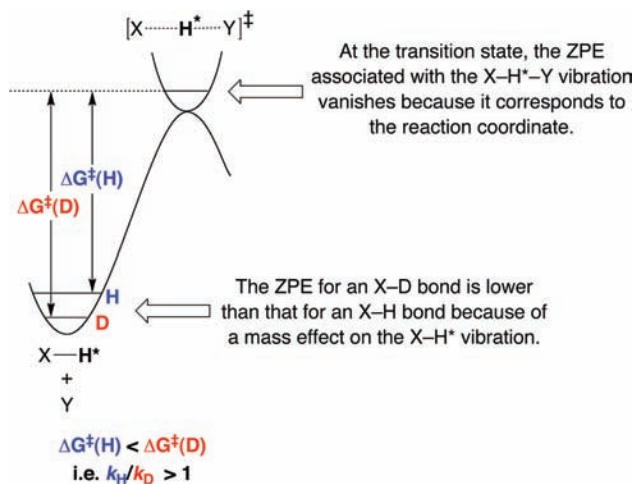
In this Account, we evaluate the applicability of these rules to the interactions of H−H and C−H bonds with a transition metal center. Significantly, experimental and computational studies question the predictability of primary EIEs in these systems based on the notion that deuterium prefers to occupy the highest frequency oscillator. In particular, the EIEs for (i) formation of σ-complexes by coordination of H−H and C−H bonds and (ii) oxidative addition of dihydrogen exhibit unusual temperature dependencies, such that the same system may demonstrate both *normal* (i.e., $K_H/K_D > 1$) and *inverse* (i.e., $K_H/K_D < 1$) values. The transition between a normal and inverse EIE indicates that these systems do not demonstrate the typical monotonic variation predicted by the van't Hoff relationship. Instead, the calculated EIEs in these systems are 0 at 0 K, increase to a value greater than 1, and then decrease to unity at infinite temperature. This unusual behavior may be rationalized by considering the individual factors that contribute to the EIE.

Specifically, the EIE may be expressed in the form EIE = SYM × MMI × EXC × ZPE (where SYM is the symmetry factor, MMI is the mass-moment of inertia term, EXC is the excitation term, and ZPE is the zero-point energy term), and the distinctive temperature profile results from the *inverse* ZPE (enthalpy) and *normal* [SYM × MMI × EXC] (entropy) components opposing each other and having different temperature dependencies. At low temperatures, the ZPE component dominates and the EIE is inverse, while at high temperatures, the [SYM × MMI × EXC] component dominates and the EIE is normal. The inverse nature of the ZPE term is a consequence of the rotational and translational degrees of freedom of RH (R = H, CH_3) becoming low-energy isotopically sensitive vibrations in the product, while the normal nature of the [SYM × MMI × EXC] component results from deuterium substitution having a larger impact on the moment of inertia of the smaller molecule.
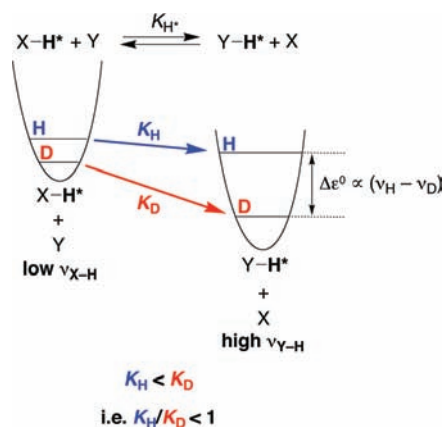
1. Introduction

The incorporation of deuterium into selected sites of a molecule provides a powerful means to probe both molecular structure and reaction mechanism. For example, the different thermodynamic site preferences of hydrogen and deuterium enable NMR spectroscopy to be used to determine whether a fluxional metal alkyl compound adopts an agostic structure with a three-center−two-electron M−H−C interaction.[1] While the impact of deuterium on the NMR spectroscopic properties is a manifestation of an equilibrium isotope effect (EIE),[2] more commonly encountered are studies pertaining to kinetic isotope effects (KIEs), which are used routinely to afford insight into the nature of the transition state for the rate-determining step of a reaction.[3,4] For multistep reactions, however, the KIE is a composite of the isotope effects for all forward and reverse steps up to and including the rate-determining step. As a consequence, a knowledge of EIEs is essential for the proper interpretation of KIEs. In this regard, primary deuterium isotope effects are often interpreted by using the two simple guidelines illustrated in Figures 1 and 2. Thus, (i) KIEs for an elementary reaction are normal ($k_H/k_D > 1$)[3,5] and (ii) EIEs are dictated by deuterium preferring to be located in the site corresponding to the highest frequency oscillator and, as such, may be either normal ($K_H/K_D > 1$) or inverse ($K_H/K_D < 1$).[6] In this Account, the applicability and limitation of these simple guidelines as they relate to the interaction of H−H and C−H bonds with transition metal centers will be discussed via consideration of specific examples.

Prior to discussing isotope effects, however, it is important to emphasize that the interaction between a transition metal and an X−H bond is characterized by a continuum of structures that are differentiated by the M···X, M···H, and H···X

FIGURE 2. Simple illustration that deuterium prefers to reside in the site that corresponds to the highest stretching frequency (i.e., Y−H* versus X−H*; H* = H, D).

distances (Scheme 1). In the extreme that the X−H bond is completely cleaved, the species corresponds to the product of oxidative addition, i.e. [M(X)H]. Intermediate situations, in which the X−H bond is not completely cleaved, correspond to species that have three-center−two-electron bonding interactions and are described as σ-complexes, [M(σ-XH)].[7] As will be seen, the nature of the isotope effect pertaining to the interaction of X−H bonds with a metal depends critically upon (i) whether the species involved is the σ-complex [M(σ-XH)] or the product of oxidative addition [M(X)H] and (ii) whether X is hydrogen or carbon.

SCHEME 1. Oxidative Addition and Reductive Elimination of X−H Bonds Occur via σ-Complex Intermediates
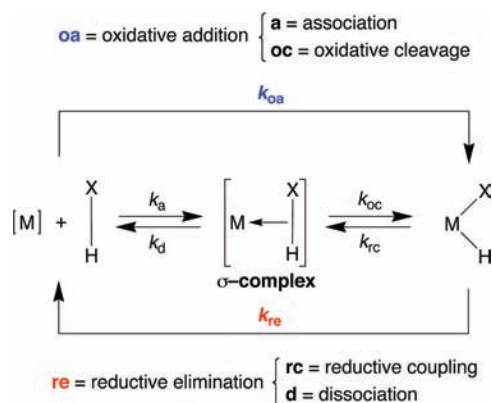
2. Equilibrium Isotope Effect for the Oxidative Addition of Dihydrogen to a Transition Metal: Early Studies

The oxidative addition of dihydrogen is an important elementary transformation that plays a critical role in many processes involving H_2 (e.g., metal-catalyzed hydrogenation and hydroformylation) and the position of the equilibrium is highly dependent on the system. For example, the equilibrium constant for oxidative addition of H_2 to $W(PMe_3)_4X_2$ (X = F, Cl, Br,
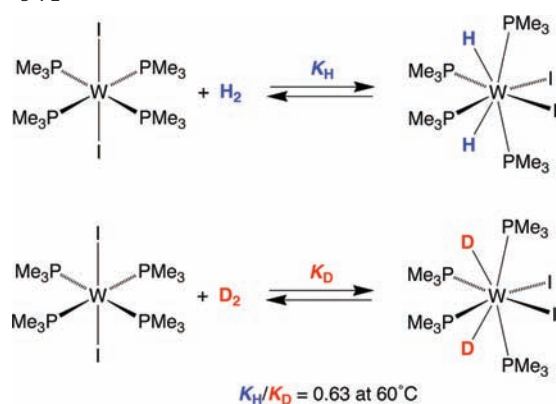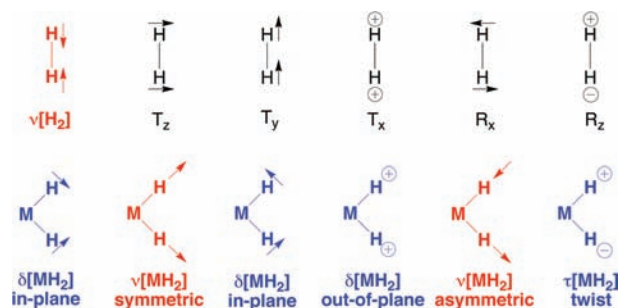

FIGURE 1. Simple rationalization of a normal primary KIE (i.e. $k_H/k_D > 1$) for cleaving X−H and X−D bonds.

SCHEME 2. An Inverse EIE for Oxidative Addition of H_2 and D_2 to $W(PMe_3)_4I_2$

$K_H/K_D = 0.63$ at 60°C

FIGURE 3. Vibrational modes associated with a C_2-symmetric $[MH_2]$ fragment and the vibrational, translational, and rotational modes of H_2 from which they are derived. In addition to the two stretching modes (red), the $[MH_2]$ fragment has four low energy modes (blue).

SCHEME 3. Expressions for Calculating an EIE from the Vibrational Frequencies and Moments of Inertia

$$EIE = K_H/K_D = SYM \cdot MMI \cdot EXC \cdot ZPE$$

$$SYM = \frac{\{(\sigma n)^R_H/(\sigma n)^R_D\}}{\{(\sigma n)^P_H/(\sigma n)^P_D\}} \qquad MMI = \frac{(M^P_H/M^R_H)^{3/2}(I^P_H/I^R_H)^{1/2}}{(M^P_D/M^R_D)^{3/2}(I^P_D/I^R_D)^{1/2}}$$

$$EXC = \frac{\prod\{[1 - \exp(-u^R_{iH})]/[1 - \exp(-u^R_{iD})]\}}{\prod\{[1 - \exp(-u^P_{iH})]/[1 - \exp(-u^P_{iD})]\}} \qquad ZPE = \frac{\exp\{\sum(u^R_{iH} - u^R_{iD})/2\}}{\exp\{\sum(u^P_{iH} - u^P_{iD})/2\}}$$

$$\text{where } u_{iX} = h\nu_{iX}/k_BT, \ R = \text{reactant, and } P = \text{product}$$

I) increases in the sequence I < Br < Cl < F,[8] whereas that for $Ir(PPh_3)_2(CO)X$ exhibits the opposite trend.[9] More fundamental than the influence of a ligand, however, is the question of how the equilibrium constant is perturbed upon isotopic substitution. It is, therefore, significant that we observed that oxidative addition of H_2 and D_2 to $W(PMe_3)_4I_2$ (Scheme 2) is characterized by a substantial *inverse* EIE, with $K_H/K_D = 0.63(5)$ at 60 °C,[8] a result that was initially rather surprising in view of the aforementioned notion that deuterium prefers to reside in the site corresponding to the higher frequency oscillator. Specifically, ν_{M-H} stretching frequencies of metal hydrides are much lower than the ν_{H-H} stretching frequency of dihydrogen, so that the zero-point energy (ZPE) difference for $W(PMe_3)_4H_2I_2$ and $W(PMe_3)_4D_2I_2$ would be expected to be less than that for H_2 and D_2. Since this prediction was counter to the experimental result, it was evident that this simple evaluation of the EIE for oxidative addition of H_2 and D_2 was inadequate.

The inverse EIE was, nevertheless, rationalized by taking into account *bending* and related low frequency modes associated with the dihydride moiety. Thus, although these modes are of sufficiently low energy that they are not normally invoked when discussing *primary* isotope effects, they do provide an important contribution for oxidative addition of H_2 because the $[WH_2]$ moiety possesses *four* such modes (Figure 3). The occurrence of an inverse deuterium EIE is, therefore, a consequence of there being *six* isotope-sensitive modes in the dihydride which, in combination, result in the total ZPE stabilization being greater than that for the single isotope-sensitive vibrational mode in H_2. In other examples of primary EIEs, there is not such a large difference in the number of isotope-sensitive modes and so the magnitude and direction of the isotope effect is governed principally by the *stretching* frequencies of the bonds that are broken and formed.

A more complete analysis of isotope effects, however, focuses on factors other than the ZPE term. Specifically, EIEs are determined from the molecular translational, rotational, and vibrational partition function ratios, according to the expression $EIE = SYM \times MMI \times EXC \times ZPE$, where SYM is the symmetry number that is factored out of the rotational partition function, MMI is the mass-moment of inertia term that is factored out of the translational and rotational partition functions, EXC is the excitation term that takes into account vibrationally excited states, and ZPE is the traditional zero-point energy term (Scheme 3).[3,10,11] Goldman and Krogh-Jespersen used this approach to delineate the factors responsible for the inverse EIE for oxidative addition of dihydrogen to Vaska's complex, $Ir(PPh_3)_2(CO)Cl$, and also concluded that the inverse nature of the EIE is a consequence of a dominant ZPE term.[11c]

## 3. Isotope Effects for Transformations Involving C−H Bonds

In addition to oxidative addition and reductive elimination of the H−H bond, we also have an avid interest in the corresponding processes involving C−H bonds. Here, we focus attention on the isotope effects pertaining to methane, a study which revealed interesting subtleties that shed new light on the interpretation of isotope effects pertaining to the interaction of both C−H and H−H bonds with metal centers.

SCHEME 4. Reductive Elimination of Methane from [Me$_2$Si(C$_5$Me$_4$)$_2$]W(CH$_3$)H and [Me$_2$Si(C$_5$Me$_4$)$_2$]W(CD$_3$)D Is Characterized by an Inverse KIE
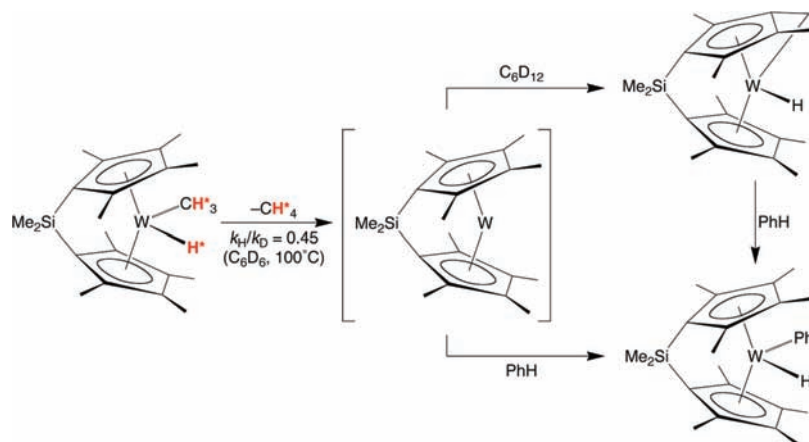
Isotope Effects for Reductive Elimination of Methane from [Me$_2$Si(C$_5$Me$_4$)$_2$]W(Me)H. Reductive elimination of methane from [Me$_2$Si(C$_5$Me$_4$)$_2$]W(CH$_3$)H and [Me$_2$Si(C$_5$Me$_4$)$_2$]-W(CD$_3$)D to generate the tungstenocene intermediate {[Me$_2$Si-(C$_5$Me$_4$)$_2$]W} is characterized by a substantial inverse KIE of 0.45(3) in benzene at 100 °C (Scheme 4).[12] Although a normal KIE may have been expected since this has a primary component, the inverse value is readily rationalized by the conventional explanation that reductive elimination is not a single step, but is rather a two-step sequence involving formation of a σ-complex intermediate prior to rate-determining elimination of methane (Figure 4).[4] For such a situation, the rate constant for reductive elimination simplifies to $k_{obs} = K_\sigma k_d$, where K_σ is the equilibrium constant for the conversion of [M](R)H to [M](σ-RH). If the KIE for dissociation of RH (i.e., $k_{d(H)}/k_{d(D)}$) were to be close to unity (since the C–H bond is almost fully formed), the KIE for reductive elimination would then be dominated by the *equilibrium* isotope effect $K_{\sigma(H)}/K_{\sigma(D)}$ for formation of the σ-complex, [M](σ-RH). On the basis of the premise that deuterium prefers to be located in the higher frequency oscillator, that is, the C–D versus M–D bond, the EIE for formation of the σ-complex would be inverse, thereby resulting in an inverse KIE for the overall reductive elimination of RH.

Although the pre-equilibrium mechanism is often invoked to rationalize inverse KIEs for reductive elimination of RH,[4,13] there is actually very little information in the literature pertaining to the isotope effects for the individual steps illustrated in Figure 4. Therefore, we viewed it as important to obtain the KIE for the reductive coupling step involving formation of the σ-complex, [Me$_2$Si(C$_5$Me$_4$)$_2$]W(σ-CH$_4$). However, because the σ-complex intermediate is not spectroscopically observable, it is not possible to measure the KIE for this step by comparison of [Me$_2$Si(C$_5$Me$_4$)$_2$]W(CH$_3$)H

and [Me$_2$Si(C$_5$Me$_4$)$_2$]W(CD$_3$)D. The KIE could, nevertheless, be obtained by investigating the monodeutero complex [Me$_2$Si-(C$_5$Me$_4$)$_2$]W(CH$_3$)D because isomerization to [Me$_2$Si(C$_5$Me$_4$)$_2$]-W(CH$_2$D)H, via the σ-complex intermediate [Me$_2$Si(C$_5$Me$_4$)$_2$]W(σ-CH$_3$D), proceeds on a time scale that is comparable to the overall reductive elimination of CH$_3$D. Significantly, a kinetics analysis of the transformations illustrated in Scheme 5 revealed that the KIE for reductive coupling of [Me$_2$Si(C$_5$Me$_4$)$_2$]W(Me)X (X = H, D) is *normal*, with a value of 1.4(2).
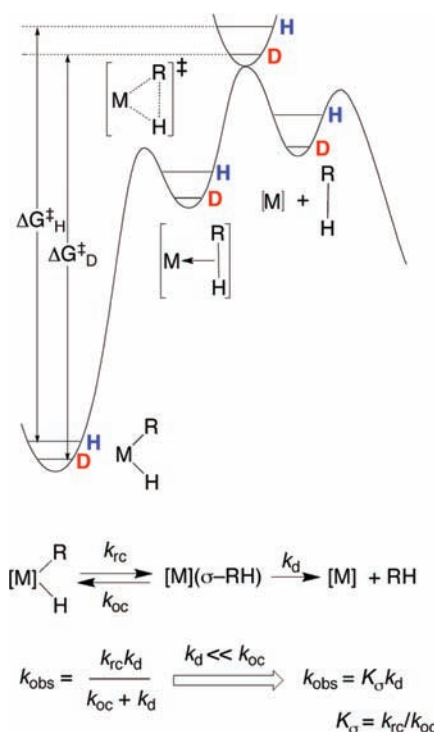
FIGURE 4. Origin of an inverse kinetic isotope effect for reductive elimination. The inverse kinetic isotope effect is essentially a consequence of an inverse equilibrium isotope being transferred to the rate-determining step.

SCHEME 5. Competitive Dissociation of Methane from the σ-Complex Enables $k_{rc(H)}/k_{rc(D)}$ to be Determined[a]
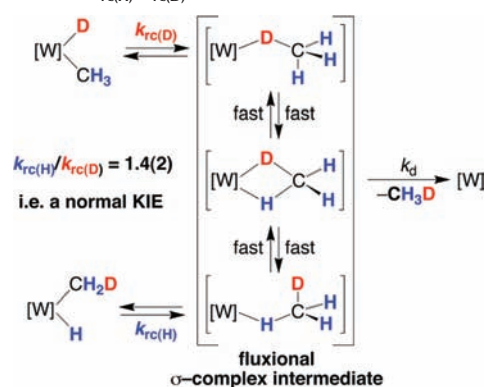
[a] [W] = {[Me$_2$Si(C$_5$Me$_4$)$_2$]W}.
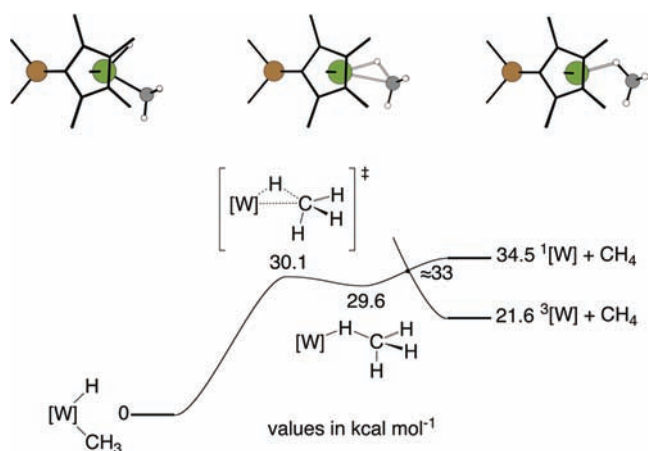
FIGURE 5. Calculated enthalpy surface for reductive elimination of CH$_4$ from [Me$_2$Si(C$_5$Me$_4$)$_2$]W(Me)H; vibrational frequencies were calculated for computationally simpler [H$_2$Si(C$_5$H$_4$)$_2$]W(Me)H. The transition state is the singlet/triplet crossing point.

Since formation of the σ-complex is characterized by a normal KIE, the inverse KIE for the overall reductive elimination can only be rationalized in terms of an inverse *equilibrium* isotope effect for the formation of the σ-complex. In this regard, Jones has also demonstrated that the EIE for the interconversion of [Tp^{Me_2}]Rh(L)(Me)X and [Tp^{Me_2}]Rh(L)(σ-XMe) is inverse (0.5), even though the individual KIEs for oxidative cleavage (4.3) and reductive coupling (2.1) are normal (L = CNCH$_2$Bu^t; X = H, D).[14]

In view of the experimental difficulty in extracting KIEs for individual steps of a multistep process, we turned our attention to using computational methods to complement the investigation. The calculated energy surface for reductive elimination of methane from [Me$_2$Si(C$_5$Me$_4$)$_2$]W(Me)H is shown in Figure 5, illustrating that the transition state for the reductive coupling step is lower than that for dissociation of methane, a condition that is necessary if the KIE were to be dictated by a pre-equilibrium.[15] Since the calculation of vibrational fre-

quencies is highly computationally intensive, the KIEs were determined for a simpler system in which the methyl groups of the [Me$_2$Si(C$_5$Me$_4$)$_2$] ligand were replaced by hydrogen atoms, i.e. [H$_2$Si(C$_5$H$_4$)$_2$]W(Me)H. In accord with the experimental results, the calculations predicted a small, but *normal*, KIE (1.05) for reductive coupling of [H$_2$Si(C$_5$H$_4$)$_2$]W(Me)X (X = H, D). Furthermore, the KIE for the microscopic reverse, that is, oxidative cleavage of [H$_2$Si(C$_5$H$_4$)$_2$]W(σ-XMe), was also predicted to be *normal* (1.60), such that EIE for the interconversion of [H$_2$Si(C$_5$H$_4$)$_2$]W(Me)X and [H$_2$Si(C$_5$H$_4$)$_2$]W(σ-XMe) is *inverse* (0.65) and becomes the dominating factor in the KIE for the overall reductive elimination of methane.

Equilibrium Isotope Effects for Coordination of Methane. Since the computational study proved to be of considerable benefit to analyzing the observed isotope effect for reductive elimination of methane, we considered it worthwhile to use this approach to investigate steps involved in the reverse reaction. In this regard, the EIEs for both coordination (1.45) and oxidative addition (2.42) of CH$_4$ and CD$_4$ to {[H$_2$Si(C$_5$H$_4$)$_2$]W} were calculated to be normal at 100 °C (the temperature at which reductive elimination was studied in the experimental system). Although there are no experimental reports of EIEs for coordination and oxidative addition of methane for comparison with the present system, there are several conflicting reports for coordination of other alkanes. For example, coordination of cyclopentane to [CpRe(CO)$_2$] is characterized by a normal EIE (1.33 at −93 °C),[16] whereas coordination of cyclohexane to [Cp*Rh(CO)] is characterized by a large inverse EIE (∼0.1 at −100 °C).[17] The existence of both normal and inverse EIEs for coordination of alkanes is a very interesting and counterintuitive result, and one that caused Bullock and Bender to conclude that it is nontrivial to predict such isotope effects.[4b]

Since the normal EIE calculated for coordination of methane to {[H$_2$Si(C$_5$H$_4$)$_2$]W} corresponded to the value at 100 °C, we were intrigued to determine whether it could become inverse upon lowering the temperature. However, rather than becoming inverse, the EIE increased slightly to a value of 1.57 upon lowering the temperature to −100 °C! Puzzled by this result, we determined the full temperature dependence of the EIE over a large temperature range (Figure 6), from which it became evident that the apparent insensitivity of the EIE between −100 and 100 °C is deceptive. Specifically, the EIE for coordination of methane to {[H$_2$Si(C$_5$H$_4$)$_2$]W} exhibits a maximum and does *not* vary with temperature in the simple monotonic manner predicted by a typical van't Hoff relationship. Thus, the EIE is 0 at 0 K, increases to a maximum value of 1.57, and then decreases to unity at infinite temperature.
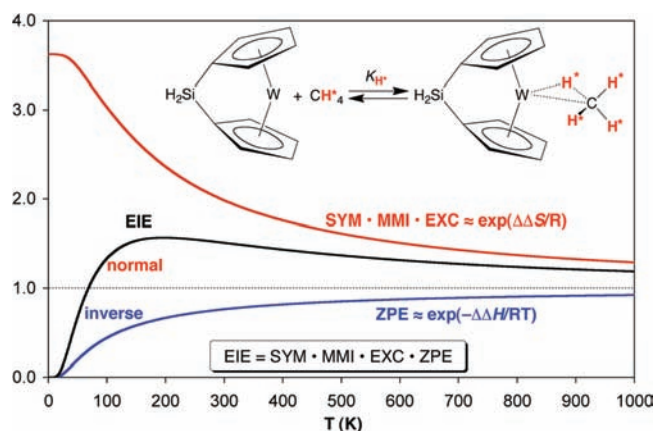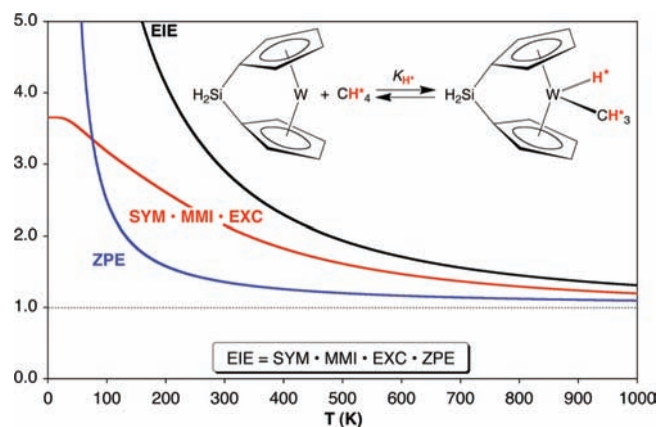
FIGURE 6. Calculated EIE as a function of temperature for coordination of CH_4 and CD_4 to $\{[H_2Si(C_5H_4)_2]W\}$. The ZPE term dominates at low temperature and the EIE is inverse, while the combined $[SYM \times MMI \times EXC]$ function dominates at high temperature and the EIE is normal.

FIGURE 7. Calculated EIE as a function of temperature for oxidative addition of CH_4 and CD_4 to $\{[H_2Si(C_5H_4)_2]W\}$. Both the ZPE term and the combined $[SYM \times MMI \times EXC]$ function are normal, thereby resulting in a normal EIE at all temperatures.

This form of the temperature dependence is highly significant because it demonstrates that, depending upon the temperature, *both normal and inverse EIEs may be obtained for coordination of a C−H bond in the same system*. As such, it provides a simple rationalization for the aforementioned literature reports of both normal and inverse EIEs.

The precise form of the temperature dependence of the EIE is determined by the values of the individual SYM, MMI, EXC, and ZPE terms. Since SYM and MMI are temperature independent, the occurrence of a maximum is a result of the ZPE and EXC terms opposing each other and having different temperature dependencies.[18] It is, however, convenient to analyze the temperature dependence of the EIE in terms of the combined $[SYM \times MMI \times EXC]$ term and the ZPE term, especially since the former corresponds approximately to the entropy component, while the latter corresponds approximately to the enthalpy component.[19] In this regard, while it is commonly recognized that isotopic substitution influences the enthalpy of a reaction by a mass effect on the ZPE level, the change in mass may also exert an effect by virtue of the fact that the *spacing* of the vibrational (and rotational) energy levels depends on the masses of the atoms involved. Specifically, the energy levels become more closely spaced as the mass increases,[20] such that more states may be accessed at a given temperature, which thereby influences the entropy. For example, the entropy of D_2 (39.0 eu at 300 K) is greater than that of H_2 (34.0 eu at 300 K).

When the coordination of methane to $\{[H_2Si(C_5H_4)_2]W\}$ is analyzed in these terms, it is evident that, at all temperatures, the $[SYM \times MMI \times EXC]$ entropy component favors a normal EIE, while the ZPE enthalpy component favors an inverse EIE. The $[SYM \times MMI \times EXC]$ entropy component dominates at

high temperatures and the EIE is normal, while at low temperatures the ZPE enthalpy component dominates and the EIE is inverse (Figure 6).

The $[SYM \times MMI \times EXC]$ term is normal because substitution by deuterium exerts a greater impact on the moments of inertia of the smaller molecule (i.e., methane) than the larger metal complex. Conversely, the ZPE term is inverse because coordination results in the creation of six additional isotope-sensitive vibrations that are derived from rotational and translational degrees of freedom of methane.[4b] As such, the ZPE change for $[H_2Si(C_5H_4)_2]W(\sigma\text{-HMe})$ upon isotopic substitution is greater than that for methane, a situation that is closely analogous to the origin of the inverse EIE for oxidative addition of H_2 to $W(PMe_3)_4I_2$.

Equilibrium Isotope Effects for Oxidative Addition of Methane. Interestingly, the temperature dependence of the calculated EIE for oxidative addition of methane to $\{[H_2Si(C_5H_4)_2]W\}$ (Figure 7) is quite distinct from that for coordination of methane (Figure 6), being normal at *all* temperatures. The origin of this difference resides with the ZPE term, which is inverse for coordination of methane and is normal for oxidative addition. Thus, for oxidative addition, the $[SYM \times MMI \times EXC]$ and ZPE terms operate in concert to give a normal EIE at all temperatures, whereas these terms oppose each other for coordination of methane, such that the EIE becomes inverse at low temperature.

The important issue is, therefore, concerned with why the ZPE terms are so different for coordination and oxidative addition of methane, especially in view of the fact that the total number of isotope-sensitive vibrations are the same for both $[H_2Si(C_5H_4)_2]W(\sigma\text{-HMe})$ and $[H_2Si(C_5H_4)_2]W(Me)H$. In this regard, the ZPE term for oxidative addition is normal because
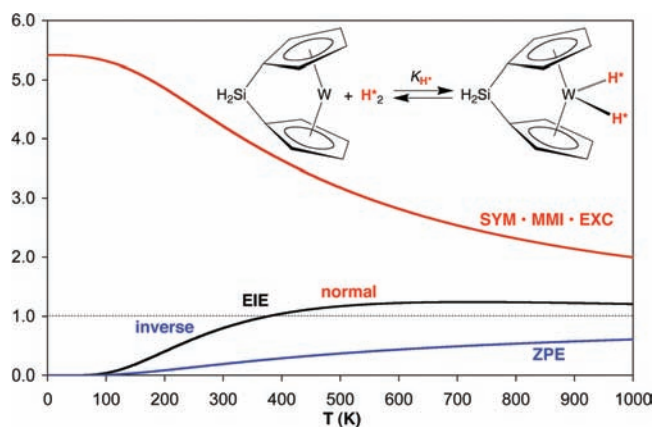
FIGURE 8. Calculated EIE as a function of temperature for oxidative addition of H_2 and D_2 to {$[H_2Si(C_5H_4)_2]W$}. The ZPE term dominates at low temperature and the EIE is inverse, while the combined [SYM × MMI × EXC] function dominates at high temperature and the EIE is normal.

the isotopically sensitive vibrations associated with the W–H bond, namely, a W–H stretch and two bends, are of sufficiently low energy that they no longer counter those associated with a C–H bond in methane.

## 4. Equilibrium Isotope Effects for Oxidative Addition of Dihydrogen: A Reappraisal

In addition to $W(PMe_3)_4I_2$,[8] other metal centers were reported to exhibit inverse EIEs for oxidative addition of H_2.[21] Furthermore, *coordination* of H_2 to give dihydrogen complexes, $[M(\eta^2\text{-}H_2)]$, was also characterized by inverse EIEs.[22] As such, the interaction of dihydrogen with a transition metal, be it to form a dihydride or to form a dihydrogen complex, was generally characterized by an inverse EIE. However, in view of the unusual temperature dependence of the EIE that we discovered for coordination of methane, our curiosity was piqued as to whether oxidative addition of dihydrogen could also be possibly characterized by a normal EIE.

To evaluate this possibility, we initially calculated the EIE for oxidative addition of H_2 and D_2 to {$[H_2Si(C_5H_4)_2]W$} as a function of temperature, thereby revealing that the EIE becomes normal at high temperature with a profile that is similar to that for coordination of methane (Figure 8).[23] At low temperatures, the ZPE enthalpy component dominates and the EIE is inverse because the $[MH_2]$ fragment has six isotopically sensitive vibrations that are of sufficient energy to cause the total zero point stabilization of $[MD_2]$ versus $[MH_2]$ to be greater than that for D_2 versus H_2. At high temperatures, the [SYM × MMI × EXC] entropy component dominates and the EIE is normal because the entropy of D_2 is greater than that of H_2.

Significantly, experimental verification of an inverse to normal temperature-dependent transition was obtained by con-
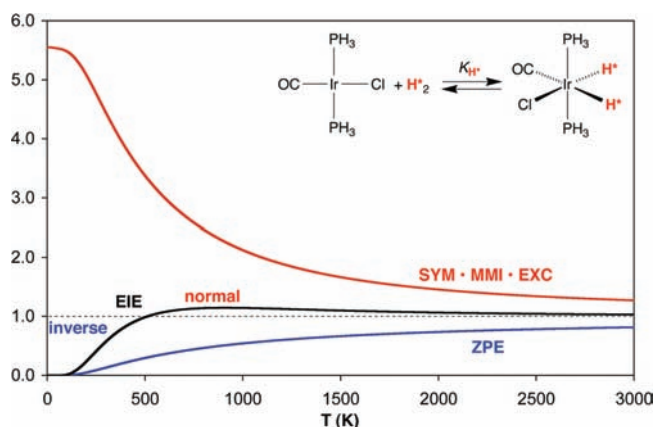

FIGURE 9. Calculated EIE as a function of temperature for oxidative addition of H_2 and D_2 to $Ir(PH_3)_2(CO)Cl$ expressed in terms of [SYM × MMI × EXC] and ZPE components.
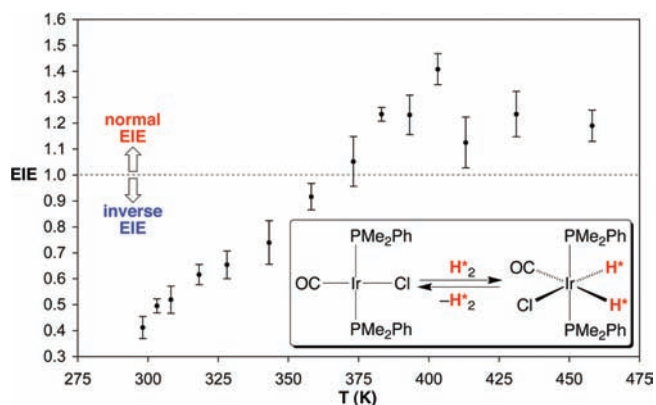
FIGURE 10. Experimental temperature dependence of the EIE for oxidative addition of H_2 and D_2 to $Ir(PMe_2Ph)_2(CO)Cl$ in benzene.

SCHEME 6. Oxidative Addition of H_2 and D_2 to $(\eta^6\text{-AnH})Mo(PMe_3)_3$ (AnH = Anthracene) Exhibits a Normal EIE at Relatively Low Temperatures
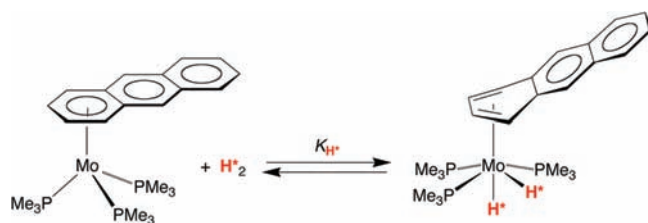
sideration of the Vaska system, $Ir(PMe_2Ph)_2(CO)Cl$ (Figures 9 and 10),[19] for which the strongly inverse EIE of 0.41(4) at 25 °C became normal at temperatures greater than ca. 90 °C and reached a value of 1.41(6) at 130 °C (Figure 10). Shortly thereafter, we discovered that oxidative addition of H_2 and D_2 to the anthracene complex $(\eta^6\text{-AnH})Mo(PMe_3)_3$ (AnH = anthracene) giving $(\eta^4\text{-AnH})Mo(PMe_3)_3H_2$ (Scheme 6)[21c,24] is characterized by a normal EIE at relatively low temperatures (Table 1).

It was, therefore, apparent that the generality of inverse EIEs for oxidative addition of H_2 and D_2 to a single transition
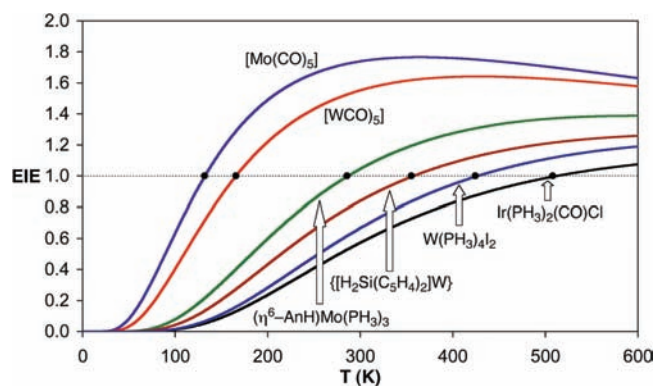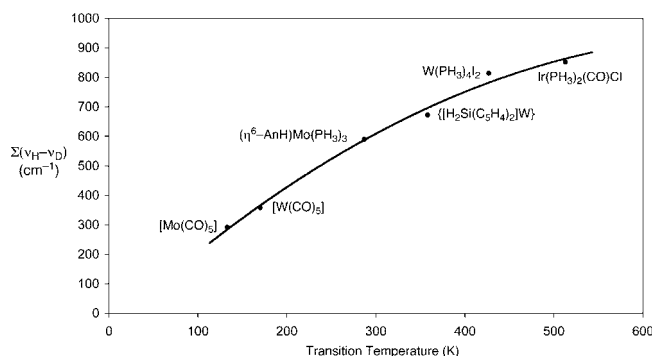
TABLE 1. EIEs for Oxidative Addition of H_2 and D_2 to (η^6-AnH)Mo(PMe$_3$)$_3$

temp,°C	EIE
30	0.99(1)
40	1.03(2)
50	1.07(3)
60	1.13(5)
70	1.20(4)
80	1.27(8)
90	1.25(9)

metal center no longer held. Since an appreciation of the factors that influence the temperature of the inverse/normal EIE transition is essential for enabling one to predict whether a normal or inverse EIE would be expected for a specific system, calculations were performed on a series of dihydride compounds. These calculations indicate that the transition temperature is a very sensitive function of the system (Figure 11) and examination of the ZPE and [SYM × MMI × EXC] components indicates that it is the ZPE term that largely determines the transition temperature. As such, the transition temperature correlates with $\Sigma(\nu_H - \nu_D)$, as illustrated in Figure 12, with the inverse EIE approaching unity more rapidly for molecules with small values of $\Sigma(\nu_H - \nu_D)$ than for molecules with larger values (Figure 11). While $\Sigma(\nu_H - \nu_D)$ is performed over all vibrational frequencies, the two largest components are the M−H(D) stretches, such that the transition temperature is more likely to be reached at an experimentally accessible temperature for molecules with low M−H(D) stretching frequencies, as exemplified by the fact that the M−H stretches for (η^4-AnH)Mo(PH$_3$)$_3$H$_2$ are significantly lower than those of Ir(PH$_3$)$_2$(CO)ClH$_2$.

It is important to emphasize that the normal EIE observed for oxidative addition of H_2 to (η^6-AnH)Mo(PMe$_3$)$_3$ is *not* due to the ZPE factor but is specifically due to the [SYM × MMI × EXC] (entropy) term. Thus, while the normal EIE is in accord with the simple rule of thumb that deuterium favors the higher frequency oscillator site (i.e., H−H rather than Mo−H), such

FIGURE 11. Calculated EIEs for oxidative addition of H_2 to various metal centers, illustrating the large range of transition temperatures.

FIGURE 12. Correlation of the inverse to normal EIE transition temperature for oxidative addition of H_2 and D_2 with $\Sigma(\nu_H - \nu_D)$.

agreement is purely coincidental and is not the true explanation. The origin of a normal EIE for formation of (η^4-AnH)Mo(PMe$_3$)$_3$H$_2$ is a consequence of the Mo−H vibrational modes being of relatively low energy such that the ZPE term rapidly approaches unity, thereby enabling the [SYM × MMI × EXC] entropy term to dominate the EIE at a relatively low temperature.

## 5. Equilibrium Isotope Effects Involving Dihydrogen Complexes

Coordination of H_2 and D_2 to form dihydrogen complexes is also characterized by an inverse EIE,[22] with the first detailed analysis being provided by Bender, Kubas, Hoff, and co-workers to rationalize the value of 0.70 for formation of W(CO)$_3$(PCy$_3$)$_2$(η^2-H$_2$) from W(CO)$_3$(PCy$_3$)$_2$(N$_2$).[11d] Consistent with oxidative addition, the inverse EIE for coordination of dihydrogen is primarily attributable to an inverse ZPE term (0.20). As such, we anticipated that coordination of dihydrogen could also be characterized by a normal EIE at high temperature when the [SYM × MMI × EXC] term would dominate. Indeed, this notion is supported by calculations on W(CO)$_5$(η^2-H$_2$), as illustrated in Figure 13.[25]

Dihydride and dihydrogen complexes are tautomers, and a remaining issue pertains to the site preference of deuterium, a subject that is of relevance because there are contradictory reports concerned with the classical versus nonclassical site preference of deuterium in polyhydride compounds.[26] In this regard, the EIE for conversion of W(CO)$_5$(η^2-H$_2$) to W(CO)$_5$H$_2$ is calculated to be normal at *all* temperatures, thereby demonstrating that deuterium favors the nonclassical site in this system (Figure 14). This preference is dictated by the ZPE term because substitution of the dihydrogen and hydride ligands by deuterium has relatively little impact on the MMI term due to the large size of the molecules. Furthermore, because W(CO)$_5$(η^2-H$_2$) and W(CO)$_5$H$_2$ have the same number of isotopically sensitive vibrations, the normal ZPE term is largely a
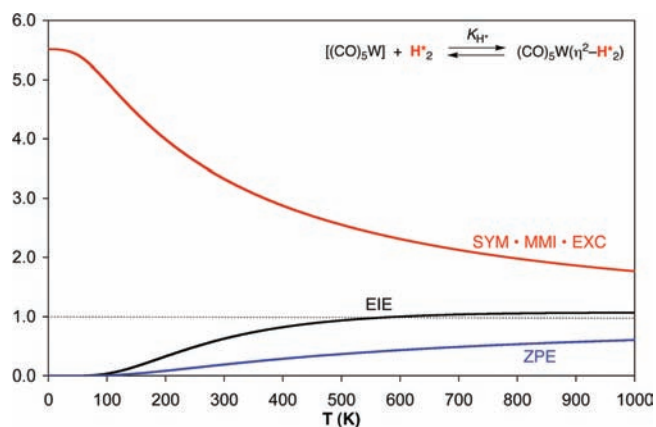
FIGURE 13. Calculated EIE as a function of temperature for coordination of H_2 and D_2 to $[W(CO)_5]$. The temperature dependence of the individual ZPE and the combined $[SYM \times MMI \times EXC]$ function are also included.
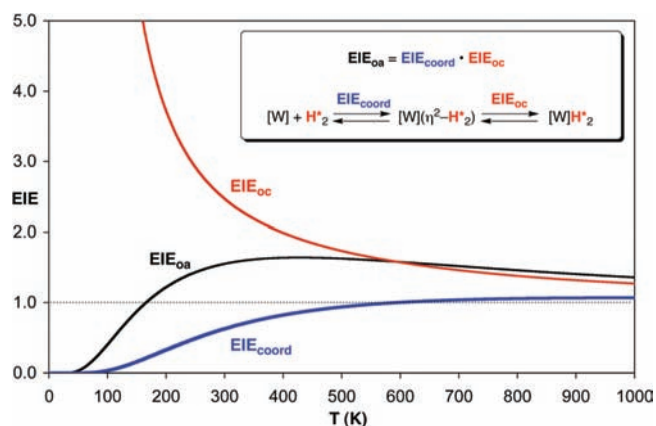
FIGURE 14. Calculated EIEs as a function of temperature for oxidative addition (EIE_{oa}) and coordination (EIE_{coord}) of H_2 and D_2 to $[W(CO)_5]$ and for oxidative cleavage of $W(CO)_5(\eta^2\text{-}H_2)$ to $W(CO)_5H_2$ (EIE_{oc}).

consequence of the high-energy H–H stretch in $W(CO)_5(\eta^2\text{-}H_2)$ becoming a low-energy symmetric bend in $W(CO)_5H_2$.

6. Concluding Remarks

Primary EIEs have been traditionally rationalized by appealing to enthalpy arguments based on ZPE differences and the derived EIE is expected to either increase or decrease with temperature. However, the results described here indicate that the EIEs for transformations involving the interaction of H–H and C–H bonds with a transition metal exhibit unusual temperature dependencies in which the EIE exhibits a maximum and may be both inverse and normal for the same system. This behavior is a consequence of the fact that the ZPE (cf., enthalpy) and $[SYM \times MMI \times EXC]$ (cf., entropy) terms oppose each other and have different temperature dependencies. The ZPE and $[SYM \times MMI \times EXC]$ terms for the various reactions

TABLE 2. Nature of the ZPE and $[SYM \times MMI \times EXC]$ Terms and the EIEs at High and Low Temperature for the Various Interactions of H_2/D_2 and CH_4/CD_4 with a Metal Center

equilibrium	ZPE	$[SYM \times MMI \times EXC]$	EIE (low T)	EIE (high T)
$M + H_2 \rightleftarrows M(\eta^2\text{-}H_2)$	inverse	normal	inverse	normal
$M + H_2 \rightleftarrows MH_2$	inverse	normal	inverse	normal
$M(\eta^2\text{-}H_2) \rightleftarrows MH_2$	normal	normal	nomal	normal
$M + CH_4 \rightleftarrows M(\sigma\text{-}HCH_3)$	inverse	normal	inverse	normal
$M + CH_4 \rightleftarrows M(CH_3)H$	normal	normal	nomal	normal
$M(\sigma\text{-}HCH_3) \rightleftarrows M(CH_3)H$	normal	normal	normal	normal

studied, and the nature of the limiting EIEs at high and low temperatures, are summarized in Table 2.

Although the nature of the ZPE term for primary EIEs is often predicted by considering only the high-energy stretching frequencies, the impact of low-energy isotopically sensitive vibrations becomes critical when there are several such modes that are created from the rotational and translational degrees of freedom of one of the molecules. For example, coordination of H_2 to a metal center is accompanied by a large increase in the number of isotopically sensitive modes, which thereby results in a inverse ZPE term rather than the normal ZPE term that would be predicted if one only focused attention on the high-energy stretching frequencies. Consideration of *all* isotopically sensitive vibrations is, therefore, essential for correctly predicting the nature of the ZPE term.

While the $[SYM \times MMI \times EXC]$ term is not usually invoked when rationalizing EIEs because it is typically a minor component, it can become a dominant factor when either the reactants or products are small so that isotopic substitution has a significant impact on the moment of inertia of one of the molecules. As such, the influence of the $[SYM \times MMI \times EXC]$ term is particularly germane to reactions involving H_2 and CH_4, and the situation is such that the MMI component favors deuterium residing in the smaller molecule.

An understanding of EIEs is also important for rationalizing the KIEs for multistep reactions. KIEs are often used to infer details pertaining to the structure of a transition state, but the subtleties presented here serve as a caveat against such interpretations. For example, consider the EIEs for coordination and oxidative addition of methane (Figures 6 and 7). At high temperature, the EIEs for both coordination and oxidative addition of methane are normal, so a logical conclusion could be that the σ-complex has a structure in which the C–H bond was largely broken and was approaching that of a methyl hydride. At low temperature, however, the EIE for coordination of methane is inverse while that for oxidative addition is normal. In this case, a reasonable inference could be that the σ-complex has a very different structure from that of the methyl hydride complex. Obviously one of these conclusions must be wrong!

The σ-complex has only one structure, as does the methyl hydride complex, and thus neither the similarity nor dissimilarity of two EIEs can be used reliably to indicate whether two species have either similar or dissimilar structures.

In summary, the interactions of H−H and C−H bonds with transition metal centers are characterized by interesting temperature-dependent deuterium EIEs. It is, therefore, evident that the correct analysis of primary KIEs and EIEs in systems of this type cannot simply be achieved by considering only the ZPEs associated with the high-energy stretching frequencies. As such, it is prudent to consider *all* isotopically sensitive vibrations before attempting to interpret the significance of an isotope effect. Although the determination of the frequencies of all isotopically sensitive vibrations is experimentally challenging, good estimates may be obtained by using computational methods and the use of the frequencies so obtained provides a useful approach for analyzing isotope effects.

BIOGRAPHICAL INFORMATION

Gerard Parkin received his B.A. (First Class), M.A., and D.Phil. degrees from the Queen's College, Oxford University. Both his graduate and undergraduate research was carried out under the guidance of Professor Malcolm L. H. Green. In 1985, he moved to the California Institute of Technology as a NATO postdoctoral fellow to work with Professor John E. Bercaw. He joined the faculty of Columbia University as Assistant Professor in 1988 and was promoted to Associate Professor in 1991 and to Professor in 1994. He served as Chairman of the Department from 1999−2002. Among other awards, he is a recipient of the Presidential Faculty Fellowship Award, the ACS Award in Pure Chemistry, the ACS Award in Organometallic Chemistry, the RSC Corday Morgan Medal, the RSC Award in Organometallic Chemistry, and the Columbia University Presidential Award for Outstanding Teaching. His principal research interests are in the areas of synthetic, structural, and mechanistic inorganic chemistry.

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