

Review Article

Applications of deuterium isotope effects for probing aspects of reactions involving oxidative addition and reductive elimination of H–H and C–H bonds[†]

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Abstract: The various types of deuterium isotope effects that are observed for reactions involving oxidative addition and reductive elimination reactions of H–H and C–H bonds with a transition metal center are reviewed. Copyright © 2007 John Wiley & Sons, Ltd.

Keywords: deuterium; kinetic; equilibrium; isotope effect; oxidative addition; reductive elimination; dihydrogen; σ -complex

Introduction

It is well known that the measurement of kinetic deuterium isotope effects (i.e. $k_{\text{H}}/k_{\text{D}}$) provides a useful means to ascertain details of the nature of the transition state for the rate-determining step of a reaction that involves cleavage of an X–H bond.¹ However, since many reactions are multistep, the observed kinetic isotope effect often represents a composite of the individual isotope effects for all steps (both forward and reverse) up to, and including, the rate-determining step. Therefore, an understanding of equilibrium deuterium isotope effects is of importance for the interpretation of kinetic deuterium isotope effects. Primary deuterium isotope effects are often rationalized using the guidelines illustrated in Figures 1 and 2, namely: (i) kinetic isotope effects are typically normal ($k_{\text{H}}/k_{\text{D}} > 1$)¹ and (ii) equilibrium isotope effects may be either normal ($K_{\text{H}}/K_{\text{D}} > 1$) or inverse ($K_{\text{H}}/K_{\text{D}} < 1$), with a value that is dictated by deuterium preferring to be located in the highest frequency oscillator.² In this review, the generality of these rules

as they apply to the various interaction of H–H and C–H bonds with transition metal centers will be discussed.

Prior to considering specific examples, however, it should be noted that the interaction between a transition metal (M) and X–H bonds may be represented by a continuum of structures, as illustrated in Scheme 1. Thus, if the X–H bond is completely cleaved, the species is referred to as the product of oxidative addition, $[\text{M}(\text{X})\text{H}]$, whereas it is described as a σ -complex, $[\text{M}(\sigma\text{-XH})]$, if the X–H bond remains intact.^{3,4,5}

In view of the existence of σ -complexes, the terms 'oxidative addition' and 'reductive elimination' do not correspond to elementary steps but are composites. Thus, oxidative addition consists of ligand association followed by oxidative cleavage, while the microscopic reverse, reductive elimination, consists of reductive coupling followed by dissociation, as illustrated in Scheme 1. The interaction of H–H and C–H bonds is, therefore, characterized by a variety of different types of isotope effects depending upon when the species under consideration is the product of oxidative addition or a σ -complex, as described in detail below.

Isotope effects pertaining to the interaction of a transition metal with dihydrogen

The interaction of dihydrogen with a transition metal center is of fundamental interest and plays an important role in many transition metal-catalyzed processes involving H_2 . For example, oxidative addition of

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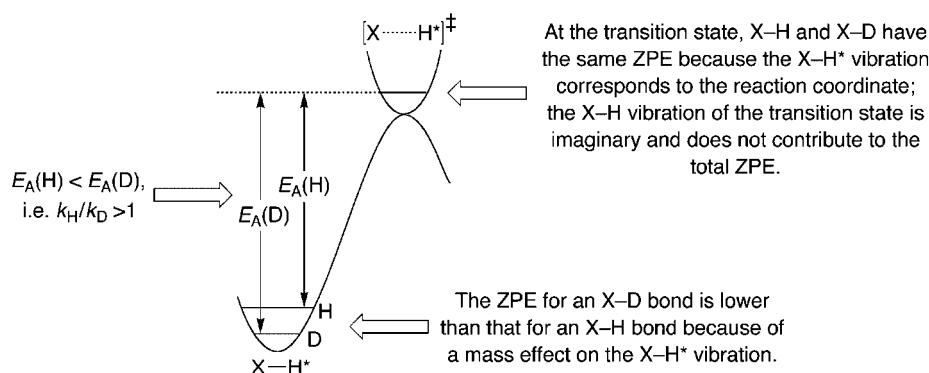


Figure 1 Simple rationalization of a normal primary KIE (i.e. $k_H/k_D > 1$) for cleaving X-H and X-D bonds.

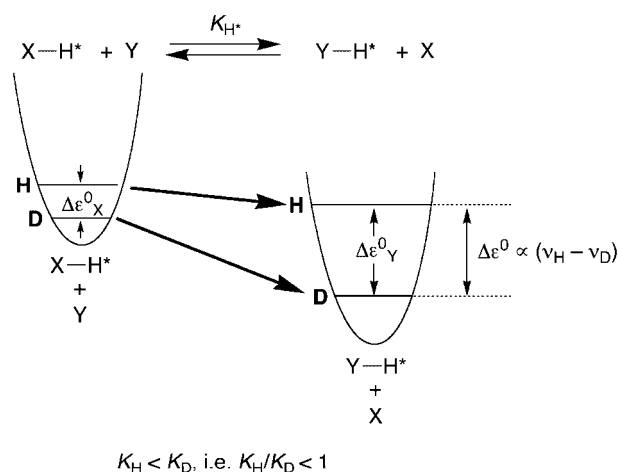


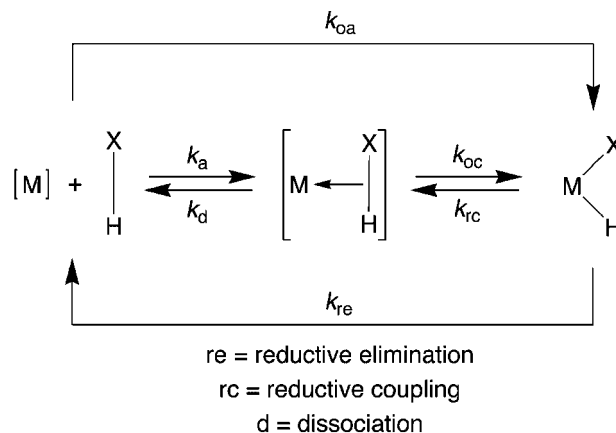
Figure 2 Simple illustration that deuterium prefers to reside in the site that corresponds to the highest stretching frequency (i.e. Y-H* versus X-H*).

dihydrogen is a crucial step in transition metal-catalyzed olefin hydrogenation and hydroformylation,⁶ with the former being exemplified by Monsanto's synthesis of L-DOPA.^{7,8} The most interesting facet of the reaction between a metal and dihydrogen, however, is that the aforementioned σ -complex may actually represent the most stable state of the system. Such species are termed dihydrogen complexes, $[M(\eta^2-H_2)]$, and have been extensively investigated.⁴ In many cases, dihydrogen complexes exist in facile equilibrium with their dihydride tautomers and so a complete analysis of the isotope effects pertaining to the interaction of H-H bonds with a transition metal requires consideration of both these species.

Isotope effects for oxidative addition of dihydrogen

An inverse equilibrium isotope effect for oxidative addition of H_2 to $W(PMe_3)_4X_2$. The position of the equilibrium involving oxidative addition of H_2 to a

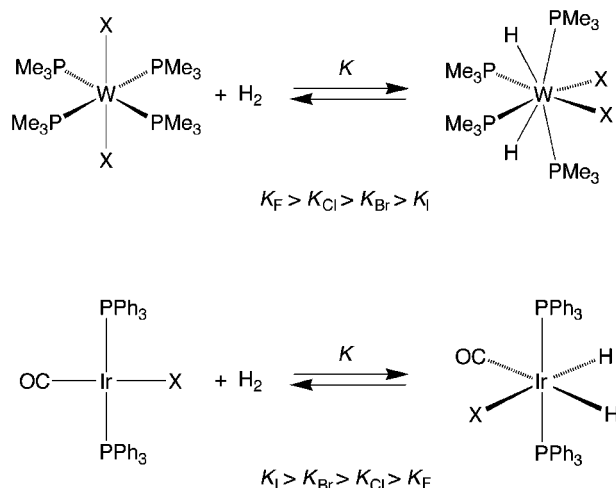
oa = oxidative addition
a = association
oc = oxidative cleavage



Scheme 1

metal center is highly dependent on the system (Scheme 2). For example, we previously demonstrated that the exothermicity of oxidative addition of H_2 to $W(PMe_3)_4X_2$ ($X = F, Cl, Br, I$) increases in the sequence $I < Br < Cl < F$,⁹ whereas experimental studies by Vaska on $Ir(PPh_3)_2(CO)X$,^{10,11} and a computational study by Goldman and Krogh-Jespersen on $Ir(PH_3)_2(CO)X$ ¹² indicate that the exothermicity of oxidative addition follows the opposite trend and increases in the sequence $F < Cl < Br < I$.

The existence of such markedly different substituent effects on the oxidative addition of H_2 to a metal center is counterintuitive, but a simple explanation was provided by recognizing that the overall effect of a π -donor depends critically on the geometry and electronic configuration of a metal center. For example, π -donation within four-coordinate 16-electron $Ir(PPh_3)_2(CO)X$ may stabilize the molecule by transforming it into an '18-electron' complex, whereas π -donation within 16-electron six-coordinate $M(PMe_3)_4X_2$ must occur in a

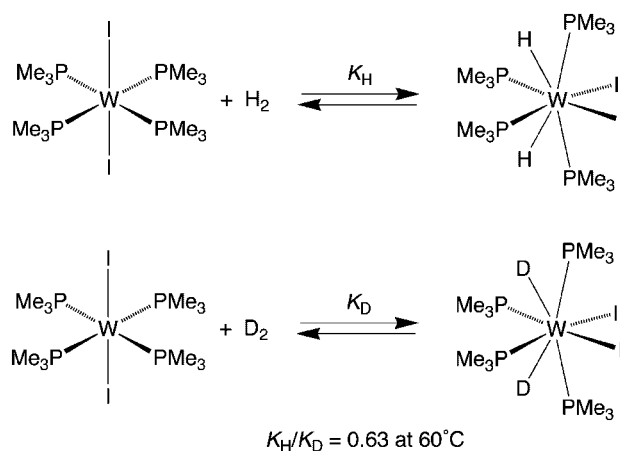
**Scheme 2**

pairwise manner and thereby destabilize the molecule by transforming it into a '20-electron' complex. With respect to the products of oxidative addition, both $W(PMe_3)_4H_2X_2$ and $Ir(PPh_3)_2(CO)(H)_2X$ have 18-electron configurations and are thereby destabilized by π -interactions, which are more extreme for the latter molecule because of the regular octahedral geometry that it adopts. Thus, consideration of the differential effects of π -interactions in both the reactants and products provides a simple explanation for the differing halide substituent effects: strong π -donors favor addition to $W(PMe_3)_4X_2$ but disfavor addition to $Ir(PPh_3)_2(CO)X$.

More fundamental than the influence of a ligand substituent on the equilibrium constant for oxidative addition of H_2 to a metal center, however, is how the equilibrium constant is perturbed upon isotopic substitution. Rather surprisingly, prior to 1993, there had been no detailed discussion in the literature pertaining to the equilibrium isotope effect for this elementary reaction.¹³ For this reason, effort was directed toward establishing the EIE for oxidative addition of H_2 and D_2 to $W(PMe_3)_4I_2$.⁹

Interestingly, the equilibrium isotope effect for oxidative addition of H_2 and D_2 to $W(PMe_3)_4I_2$ (Scheme 3) is characterized by a substantial *inverse* equilibrium deuterium isotope effect, with $K_H/K_D = 0.63(5)$ at $60^\circ C$. In particular, the inverse nature of the equilibrium isotope effect is counter to that which would have been predicted on the basis of the simple notion concerning primary isotope effects, namely that deuterium prefers to reside in the higher frequency oscillator.

Analysis of the temperature dependence of K reveals that the origin of the inverse equilibrium deuterium isotope effect is enthalpic, with oxidative addition of D_2

**Scheme 3**

being more exothermic than oxidative addition of H_2 [$\Delta H_D^0 = -21.6(7)$ kcal mol⁻¹ versus $\Delta H_H^0 = -19.7(6)$ kcal mol⁻¹]. The entropic contribution to the equilibrium isotope effect is small [$\Delta S_D^0 = -51(3)$ versus $\Delta S_H^0 = -45(2)$], but actually attempts to counter the inverse nature.

The magnitude of equilibrium isotope effects is normally evaluated by using the expression $EIE = K_H/K_D = SYM \cdot MMI \cdot EXC \cdot ZPE$ or a modification that employs the Teller-Redlich product rule, i.e. $KIE = SYM \cdot VP \cdot EXC \cdot ZPE$.^{14,15,16} In these expressions, SYM is the symmetry factor,¹⁷ MMI is the mass-moment of inertia term, EXC is the excitation term, ZPE is the zero point energy term, and VP is the vibrational product (Scheme 4). The SYM term is determined by the symmetry number ratio of the species involved and is unity for oxidative addition of H_2/D_2 to a metal center; the MMI term is determined by their structures (i.e. their masses and moments of inertia); and the VP, EXC, and ZPE terms are determined by their vibrational frequencies. Of these terms, SYM, MMI, and EXC relate to the entropy of the EIE, while ZPE provides the major contribution for the enthalpy.

Most commonly, the ZPE term dominates the EIE, which is the reason why the direction of the EIE can be predicted on the basis of vibrational frequencies alone. Specifically, since the difference in X-H and X-D zero point energies scales with ν_{X-H} , the zero point energy stabilization for a system is greatest when deuterium resides in the highest frequency oscillator (Figure 2). Thus, a normal EIE is predicted if ν_{Y-H} in the product is less than ν_{X-H} in the reactant, while an inverse EIE is predicted if ν_{Y-H} in the product is greater than ν_{X-H} in the reactant.

In this regard, because the inverse EIE for oxidative addition to $W(PMe_3)_4I_2$ is enthalpic in origin (see above),

$$\text{SYM} = \frac{\{(\sigma\text{n})^{\text{R}}_{\text{H}}/(\sigma\text{n})^{\text{R}}_{\text{D}}\}}{\{(\sigma\text{n})^{\text{P}}_{\text{H}}/(\sigma\text{n})^{\text{P}}_{\text{D}}\}}$$

$$\text{MMI} = \frac{(M^{\text{P}}_{\text{H}}/M^{\text{R}}_{\text{H}})^{3/2}(I^{\text{P}}_{\text{H}}/I^{\text{R}}_{\text{H}})^{1/2}}{(M^{\text{P}}_{\text{D}}/M^{\text{R}}_{\text{D}})^{3/2}(I^{\text{P}}_{\text{D}}/I^{\text{R}}_{\text{D}})^{1/2}} \quad \text{VP} = \prod (v^{\text{P}}_{\text{iH}}/v^{\text{P}}_{\text{iD}}) \prod (v^{\text{R}}_{\text{iD}}/v^{\text{R}}_{\text{iH}})$$

$$\text{EXC} = \frac{\prod \{[1 - \exp(-u^{\text{R}}_{\text{iH}})]/[1 - \exp(-u^{\text{R}}_{\text{iD}})]\}}{\prod \{[1 - \exp(-u^{\text{P}}_{\text{iH}})]/[1 - \exp(-u^{\text{P}}_{\text{iD}})]\}} \quad \text{ZPE} = \frac{\exp\{\sum (u^{\text{R}}_{\text{iH}} - u^{\text{R}}_{\text{iD}})/2\}}{\exp\{\sum (u^{\text{P}}_{\text{iH}} - u^{\text{P}}_{\text{iD}})/2\}}$$

where $u_{iX} = hv_{iX}/k_{\text{B}}T$, R = reactant, and P = product

Scheme 4

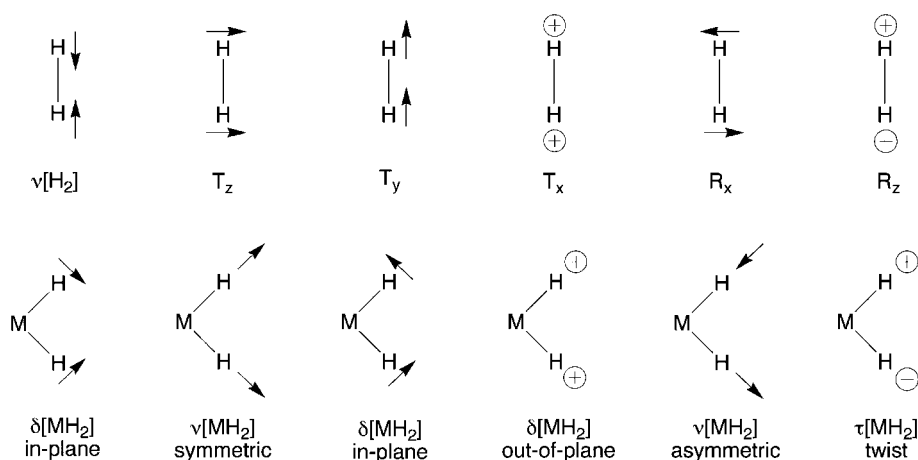


Figure 3 Vibrational modes associated with a C_2 -symmetric $[\text{MH}_2]$ fragment and the vibrational, translational, and rotational modes of H_2 from which they are derived.

it should be possible to rationalize the EIE in terms of the ZPE component and the relevant vibrational frequencies. Since one customarily focuses on stretching vibrations when evaluating primary isotope effects,¹⁸ a normal EIE would be expected for oxidative addition of H_2 and D_2 to $\text{W}(\text{PMe}_3)_4\text{I}_2$. Specifically, the observed $\nu_{\text{W-H}}$ and $\nu_{\text{W-D}}$ stretching frequencies of 1961 and 1416 cm^{-1} in $\text{W}(\text{PMe}_3)_4\text{H}_2\text{I}_2$ and $\text{W}(\text{PMe}_3)_4\text{D}_2\text{I}_2$, respectively, result in a zero point energy difference of 273 cm^{-1} for this vibrational mode. If the symmetric and asymmetric stretches have similar frequencies, the combined zero point energy lowering would be less than the difference between D_2 and H_2 zero point energies (630 cm^{-1}),¹⁹ so that a normal equilibrium isotope effect would have been predicted. Since this prediction is counter to the experimental result, it is evident that this simple appraisal is insufficient to provide an accurate evaluation of the EIE for oxidative addition of H_2 .

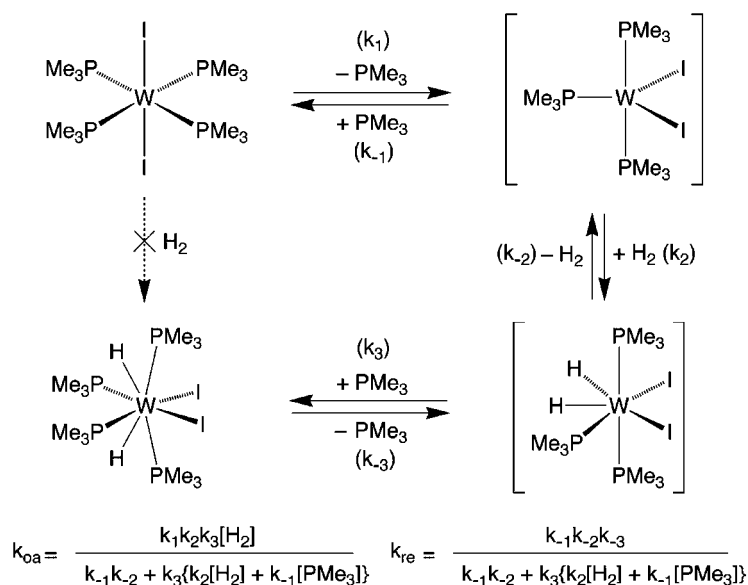
The inverse EIE may, however, be rationalized if *bending* modes associated with the dihydride moiety are included. Although bending modes are of sufficiently low energy that they are not normally invoked when discussing *primary* isotope effects, the fact that there are *four* such modes associated with the $[\text{WH}_2]$ moiety (Figure 3) means that, in combination, they may provide an important contribution. Inclusion of the bending modes, therefore, may result in a significant lowering of the zero point energy for $\text{W}(\text{PMe}_3)_4\text{D}_2\text{I}_2$ with respect to $\text{W}(\text{PMe}_3)_4\text{H}_2\text{I}_2$, to the extent that an inverse equilibrium isotope effect may result. In support of this suggestion, density functional theory calculations indicate that the ZPE level of $\text{W}(\text{PMe}_3)_4\text{D}_2\text{I}_2$ is 1049 cm^{-1} lower than that of $\text{W}(\text{PMe}_3)_4\text{H}_2\text{I}_2$.^{9b} The occurrence of an inverse deuterium equilibrium isotope effect is, therefore, a consequence of there being a *single* isotope sensitive vibrational mode in the reactant (H_2), yet *six* (albeit lower energy) isotope sensitive modes in the product.

Krogh-Jespersen and Goldman have provided a detailed analysis of the EIE for oxidative addition of H₂ and D₂ to Vaska's complex, which is also characterized by an inverse value.^{16c} Similar to W(PMe₃)₄I₂, the inverse EIE for oxidative addition of H₂ and D₂ to Ir(PH₃)₂(CO)Cl was calculated to be enthalpic in origin. Specifically, the combination of the three entropy determining contributions of SYM (1.0), MMI (5.66), and EXC (0.84) result in a normal contribution to the EIE (i.e. a positive value of $\Delta S_{\text{H}}^{\ddagger} - \Delta S_{\text{D}}^{\ddagger}$), such that the inverse nature of the EIE is essentially a consequence of a dominant zero point energy term (ZPE = 0.10) resulting in a positive value of $\Delta H_{\text{H}}^{\ddagger} - \Delta H_{\text{D}}^{\ddagger}$. Convincing evidence that the four bending modes are responsible for the inverse nature of the EIE is further indicated by the fact that eliminating them from the calculation results in the prediction of a normal EIE of 4.6. Using a similar approach, an inverse EIE of 0.73 at 60°C, comparable to the experimental value of 0.63, was calculated for W(PMe₃)₄H₂I₂.⁹ As with the Vaska system, the inverse nature of the EIE is the result of a dominant zero point energy term: ZPE (0.17), MMI (5.25), and EXC (0.80).

The inclusion of all isotope sensitive vibrations is also critical for evaluating KIEs for oxidative addition of H₂ and D₂. In this regard, although small KIEs have been postulated to be associated with an early transition state in which there is little lengthening of the H–H bond,²⁰ calculations by Goldman and Krogh-Jespersen concerned with the KIE for oxidative addition of H₂ to Vaska-type complexes, Ir(PH₃)₂(CO)X, indicates that the KIE is greatest for *early* transition states.^{16f} This result is counter to the notion that the KIE should be

greatest for late transition states in which the H–H bonds has been largely cleaved; as such, the result also provides a further caveat for focusing on the role of a single vibrational mode to rationalize isotope effects.

Kinetic isotope effects for oxidative addition of H₂ to W(PMe₃)₄I₂ and for reductive elimination of H₂ from W(PMe₃)₄H₂I₂. Kinetics studies indicate that oxidative addition of H₂ to W(PMe₃)₄I₂ is inhibited by PMe₃, thereby demonstrating that the reaction occurs via initial dissociation of PMe₃ forming a 5-coordinate [W(PMe₃)₃I₂] intermediate (Scheme 5).⁹ Further support for a mechanism involving rate-determining dissociation of PMe₃ is provided by the observation that there is no deuterium kinetic isotope effect for addition of D₂ to W(PMe₃)₄I₂; however, a deuterium kinetic isotope effect is observed in the presence of PMe₃ (Figure 4), under which conditions addition of PMe₃ to the 5-coordinate [W(PMe₃)₃I₂] intermediate becomes competitive with oxidative addition of H₂. Correspondingly, as required by microscopic reversibility, the reductive elimination of H₂ from W(PMe₃)₄H₂I₂ also proceeds via initial PMe₃ dissociation and a deuterium kinetic isotope effect is only observed in the presence of added PMe₃ (Figure 4). Analysis of the data indicates that the kinetic isotope effect for the step involving oxidative addition of H₂ is $k_{2(\text{H})}/k_{2(\text{D})} = 1.2$, while that for reductive elimination is $k_{-2(\text{H})}/k_{-2(\text{D})} = 2$ at 60°C. Both of these kinetic isotope effects are normal and are in accord with the aforementioned guideline pertaining to primary kinetic isotope effects.



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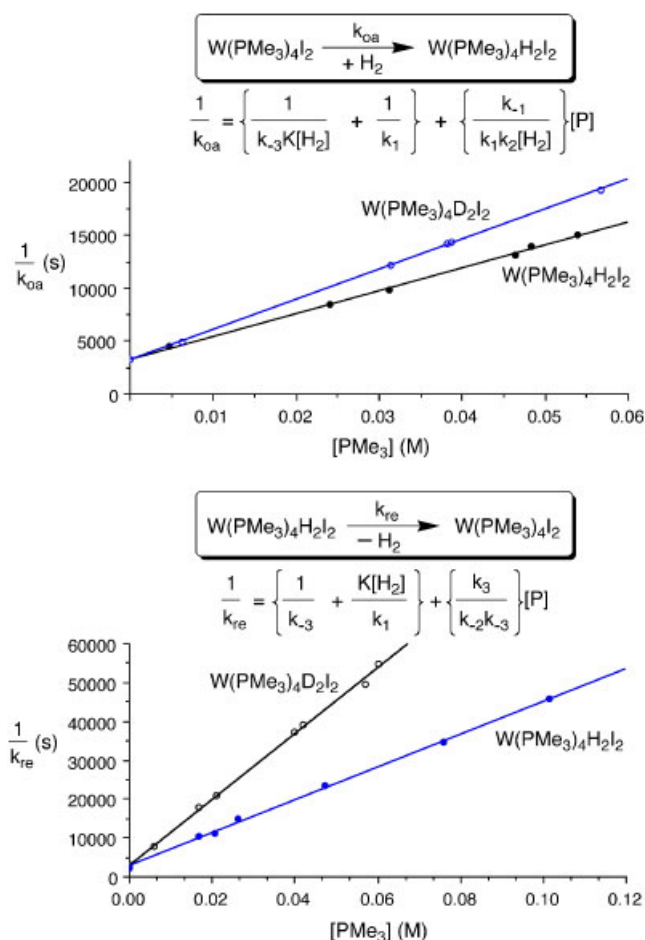


Figure 4 Variation of k_{ox} and k_{re} as a function of [PMe₃]. Modified with permission from ref. 9b. Copyright 1999 American Chemical Society.

Inverse-to-normal temperature dependent transitions for equilibrium isotope effects involving oxidative addition of dihydrogen

In addition to oxidative addition of H₂ and D₂ to W(PMe₃)₄I₂,⁹ inverse EIEs have been reported for oxidative addition to other metal complexes,²¹ and has thereby become a commonly accepted feature for this class of reaction. However, in view of reports that coordination of alkanes to a metal center can be characterized by both normal and inverse EIEs (see section "Equilibrium isotope effects for coordination of methane to {[H₂Si(C₅H₄)₂]W}"), the possibility that oxidative addition of H₂ to a single metal center could also be characterized by a normal EIE deserved further consideration. To examine this possibility, the EIE for oxidative addition of H₂ and D₂ to {[H₂Si(C₅H₄)₂]W} was calculated as a function of temperature (Figure 5).²² Interestingly, the calculations predicted that the EIE

for oxidative addition of hydrogen to {[H₂Si(C₅H₄)₂]W} does *not* vary with temperature in the simple monotonic manner predicted by the van't Hoff relationship, for which the EIE would be expected either to progressively increase or decrease and exponentially approach unity at high temperature.²³ Rather, the EIE exhibits a maximum, being *inverse* at low temperature and *normal* at high temperature.²⁴ The notion that an inverse-to-normal transition of the EIE could be a general phenomenon was confirmed by calculating the temperature dependence of the EIE for oxidative addition of H₂ and D₂ to Ir(PH₃)₂(CO)Cl (Figure 6).^{25,26}

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 the SYM and MMI terms are temperature independent, the occurrence of a maximum is a result of the ZPE and EXC terms opposing each other.²⁷ It is, however, more convenient to analyze the temperature dependence of the EIE in terms of the combined [SYM · MMI · EXC] term and the ZPE term. In this regard, the [SYM · MMI · EXC] term corresponds closely to the entropy component, while the ZPE term corresponds closely to the enthalpy component,²⁸ as illustrated by comparison of Figures 6 and 7.

The ZPE term increases from zero to a limiting value of unity as the temperature is increased, while the [SYM · MMI · EXC] entropy term decreases from a maximum value of MMI (for SYM = 1) at 0 K to a minimum value of unity at infinite temperature. Thus, at all temperatures the [SYM · MMI · EXC] entropy component favors a normal EIE, while the ZPE enthalpy component favors an inverse EIE. At high temperatures, the [SYM · MMI · EXC] entropy component dominates and the EIE is normal, while at low temperatures the ZPE enthalpy component dominates and the EIE is inverse.

As indicated above, the ZPE enthalpy component favors an inverse EIE because the [MH₂] fragment has a greater number of isotopically sensitive vibrations than that of the single stretch in H₂ and the energies of these vibrations are sufficient that they cause the total zero point stabilization of [MD₂] versus [MH₂] to be greater than that for D₂ versus H₂. The [SYM · MMI · EXC] entropy component favors a normal EIE because it is largely dominated by the different entropies of H₂ (34.0 e.u. at 300 K) and D₂ (39.0 e.u. at 300 K).^{29,30}

Experimental verification of the prediction that the EIE for oxidative addition of H₂ to a transition metal center could undergo a temperature-dependent transition from an inverse to a normal value was obtained by investigation of the Vaska system, which was chosen because it was anticipated that high temperatures would be required to observe the effect; the Vaska system is known to be thermally robust, with the

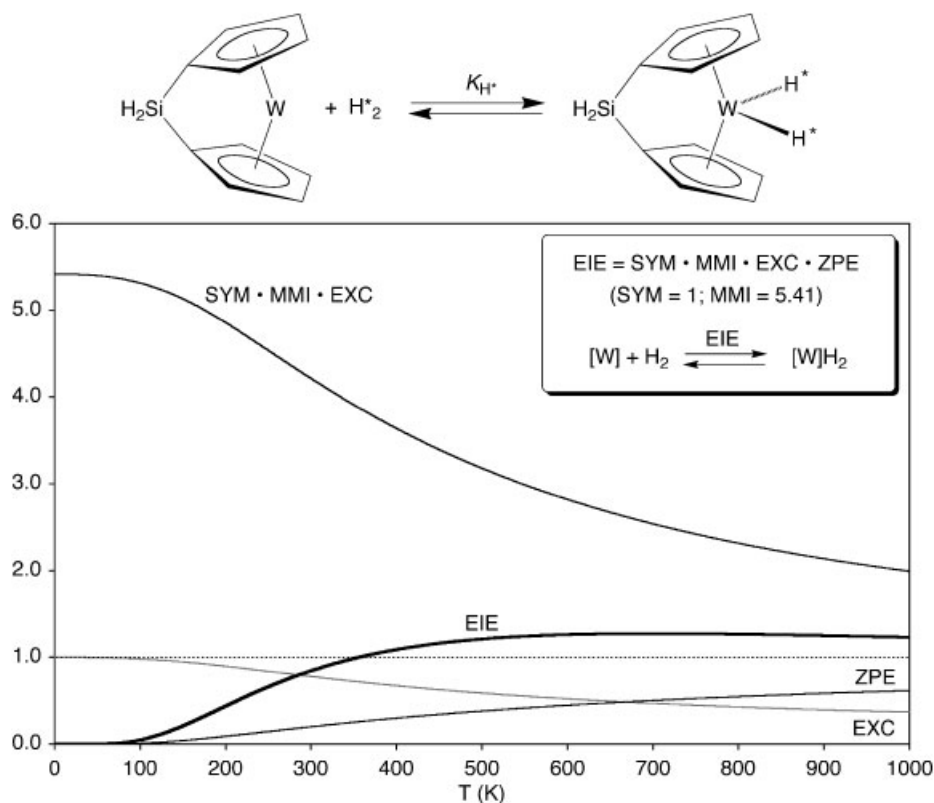


Figure 5 Calculated EIE as a function of temperature for oxidative addition of H_2 and D_2 to $\{[H_2Si(C_5H_4)_2]W\}$. The temperature dependence of the individual EXC and ZPE components, as well as the combined $[SYM \cdot MMI \cdot EXC]$ function, are also included.

interconversion of $Ir(PR_3)_2(CO)X$ and $Ir(PR_3)_2(CO)XH_2$ having been well characterized for a wide range of substituents (Scheme 2).^{21,31,32}

Significantly, the experimental EIE for the oxidative addition of H_2 and D_2 to $Ir(PMe_2Ph)_2(CO)Cl$ supports the theoretical prediction of a transition from inverse to normal as the temperature is raised.²⁵ Thus, while K_H is less than K_D at $25^\circ C$, K_D decreases more rapidly than does K_H upon raising the temperature, such that they become equal at ca. $90^\circ C$; above this temperature, K_H becomes greater than K_D (Figure 8). The strongly inverse EIE of 0.41(4) observed for oxidative addition of H_2 and D_2 to $Ir(PMe_2Ph)_2(CO)Cl$ at $25^\circ C$ becomes normal at temperatures greater than ca. $90^\circ C$ and reaches a maximum value of 1.41(6) at $130^\circ C$ (Figure 8), thereby providing important verification for the theoretical calculations.

Shortly after demonstrating that oxidative addition of H_2 and D_2 to $Ir(PMe_2Ph)_2(CO)Cl$ undergoes a transition from inverse to normal at high temperatures, a system was discovered for which the EIE for oxidative addition to a single metal center is normal at relatively low temperature ($40^\circ C$).³³ Specifically, the EIE for 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) is normal over virtually the entire temperature range ($30\text{--}90^\circ C$) measured (Table 1).^{34,35}

The important issue to address is concerned with the factors that influence the temperature of the inverse/normal EIE transition. Therefore, in an effort to establish the factors that influence the transition temperature, calculations were performed on $(\eta^4\text{-AnH})Mo(PH_3)_3H_2$ (Figure 9). Significantly, the calculated transition temperature for oxidative addition to $(\eta^6\text{-AnH})Mo(PH_3)_3$ is 223 K lower than that for $Ir(PH_3)_2(CO)Cl$, as illustrated in Figure 10, a result that is in accord with the experimental observation that the onset of a normal EIE for oxidative addition to $(\eta^6\text{-AnH})Mo(PMe_3)_3$ occurs at a significantly lower temperature than that for $Ir(PMe_2Ph)_2(CO)Cl$. For further comparison, the temperature dependence of the EIE for oxidative addition of dihydrogen to several other molecules is also illustrated in Figure 10. The data clearly illustrate that the transition temperature, which spans a range of 377 K, is a sensitive function of the system.

Consideration of the temperature dependence of the ZPE and combined $[SYM \cdot MMI \cdot EXC]$ components

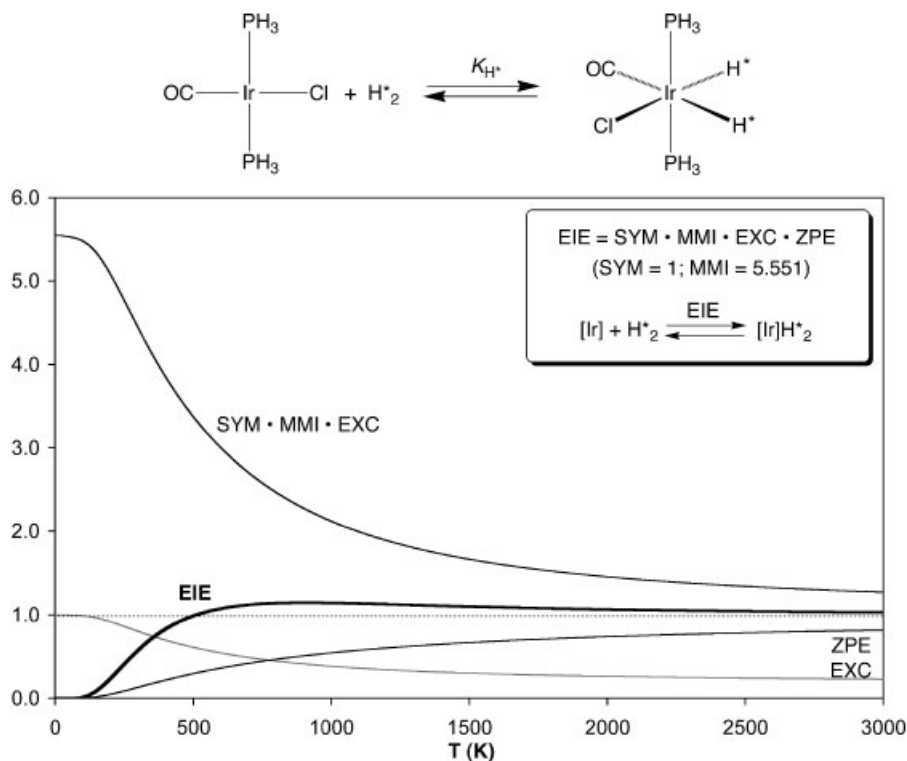


Figure 6 Calculated EIE as a function of temperature for oxidative addition of H_2 and D_2 to $\text{Ir}(\text{PH}_3)_2(\text{CO})\text{Cl}$ expressed in terms of $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ and ZPE components.

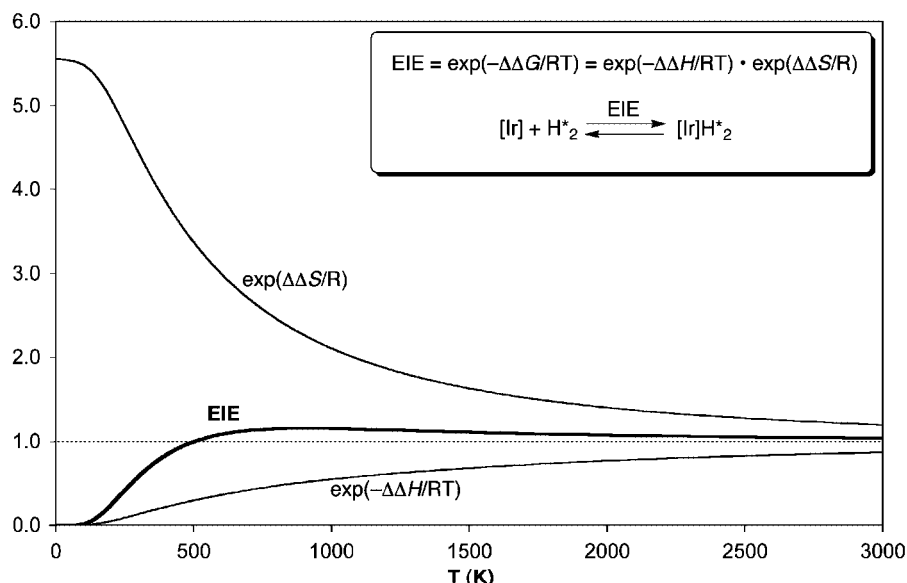


Figure 7 Calculated EIE as a function of temperature for oxidative addition of H_2 and D_2 to $\text{Ir}(\text{PH}_3)_2(\text{CO})\text{Cl}$, expressed in terms of $\exp(-\Delta\Delta H/RT)$ and $\exp(\Delta\Delta S/R)$.

indicates that the ZPE term exhibits greater sensitivity.²⁷ As such, it is largely responsible for determining the variation in transition temperature for the different systems. Since the ZPE term is an exponential function of the combined differences between vibrational

frequencies (ν_{H} and ν_{D}) for each mode within the isotopologues, the transition temperature correlates with $\Sigma(\nu_{\text{H}} - \nu_{\text{D}})$,³⁶ as illustrated in Figure 11. Specifically, as a result of the exponential form for the expression of the ZPE term, the inverse value approaches unity more

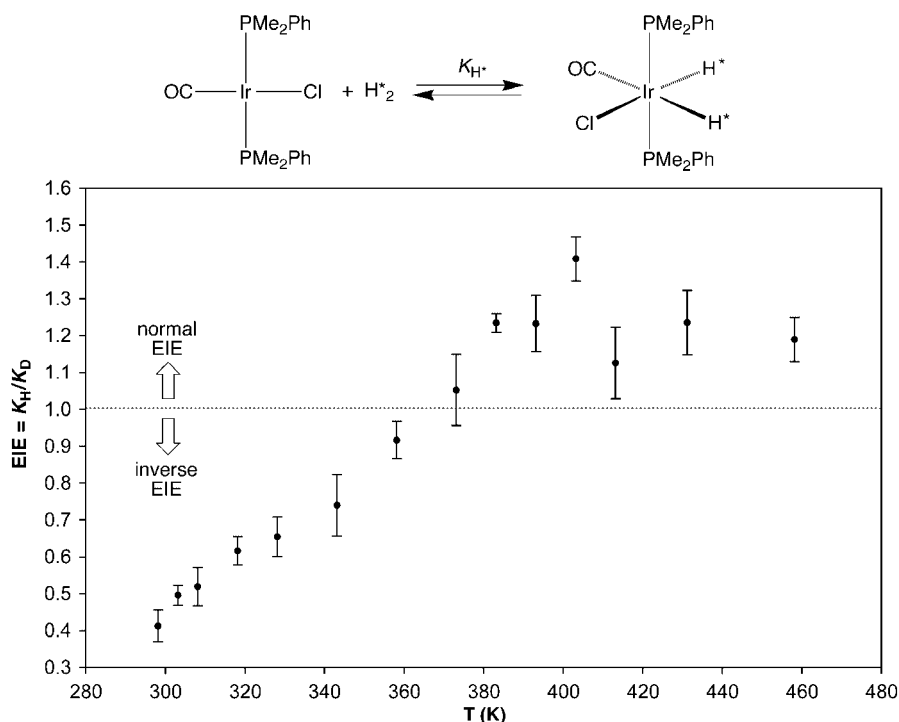
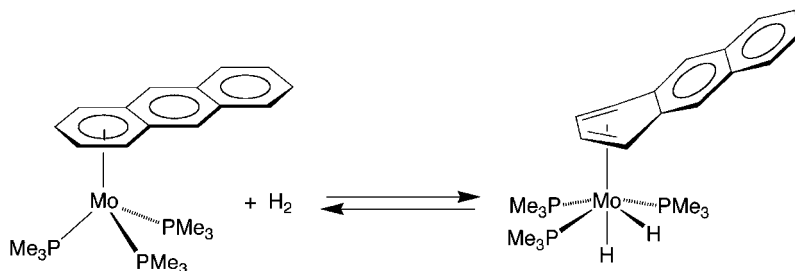


Figure 8 Temperature dependence of the EIE for oxidative addition of H_2 and D_2 to $Ir(PMe_2Ph)_2(CO)Cl$. Modified with permission from ref. 25. Copyright 2003 American Chemical Society.



Scheme 6

rapidly for molecules with small values of $\Sigma(v_H - v_D)$ than for molecules with higher values.

Although the sum $\Sigma(v_H - v_D)$ is performed over all vibrational frequencies, the two largest components are the M–H(D) stretches. As a consequence, the transition temperature is therefore more likely to be reached at an experimentally accessible temperature for molecules with low M–H(D) stretching frequencies. In accordance with this notion, the M–H stretches for $(\eta^4\text{-AnH})\text{-Mo}(\text{PH}_3)_3\text{H}_2$ (1863 and 1755 cm^{-1}) are of significantly lower energy than those of $Ir(\text{PH}_3)_2(\text{CO})\text{ClH}_2$ (2241 and 2043 cm^{-1}); correspondingly, the sum of the six principal isotopically sensitive modes for $(\eta^4\text{-AnH})\text{-Mo}(\text{PH}_3)_3\text{H}_2$ (6687 cm^{-1}) is considerably less than that for $Ir(\text{PH}_3)_2(\text{CO})\text{ClH}_2$ (7596 cm^{-1}).

As noted above, primary isotope effects are often rationalized in terms of ZPE arguments using the

Table 1 EIE data for oxidative addition of H_2 and D_2 to $(\eta^6\text{-AnH})\text{Mo}(\text{PMe}_3)_3$

Temperature ($^{\circ}\text{C}$)	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)

concept that deuterium prefers to be located in the highest frequency oscillator. On this basis, the observation of a normal isotope effect for oxidative addition of H_2 to $(\eta^6\text{-AnH})\text{Mo}(\text{PH}_3)_3$ could have simply been interpreted in terms of the two Mo–H stretching

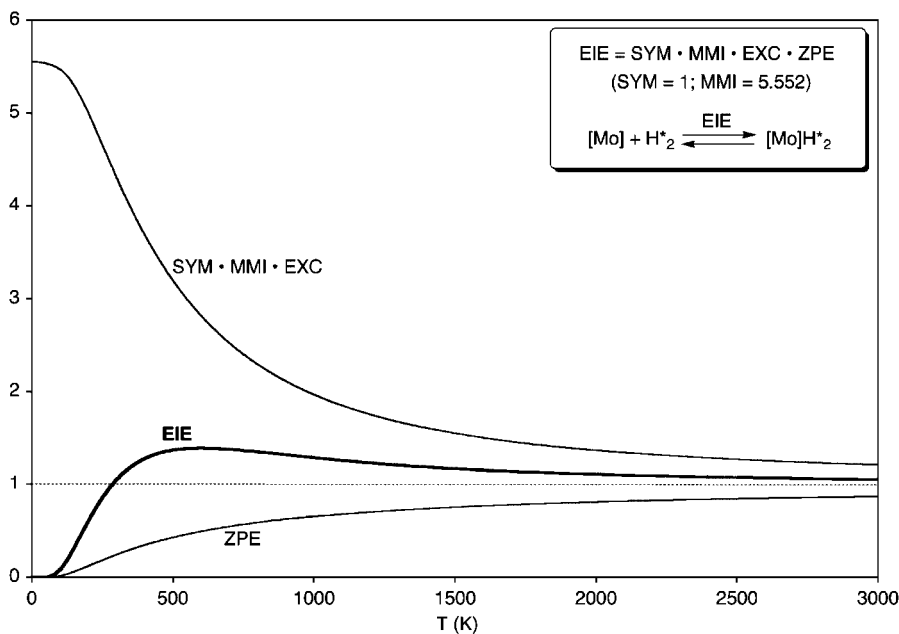


Figure 9 Calculated overall EIE as a function of temperature for oxidative addition of H₂ and D₂ to (η⁶-AnH)Mo(PH₃)₃ expressed in terms of [SYM · MMI · EXC] and ZPE components. Modified with permission from ref. 35. Copyright 2006 Royal Society of Chemistry.

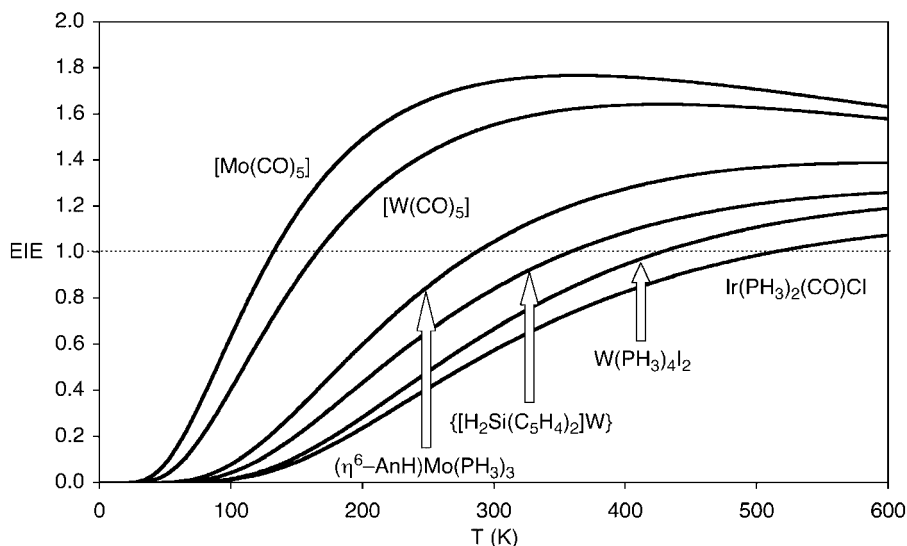


Figure 10 Calculated overall EIE as a function of temperature for oxidative addition of H₂ and D₂ to (η⁶-AnH)Mo(PH₃)₃ expressed in terms of SYM, MMI, EXC, and ZPE components. Reproduced with permission from ref. 35. Copyright 2006 Royal Society of Chemistry.

frequencies of (η⁴-AnH)Mo(PH₃)₃H₂ being lower than that of the H–H stretching frequency. However, such an analysis would be incorrect because the ZPE term actually favors an inverse EIE at *all* temperatures and the occurrence of a normal EIE is purely a consequence of the [SYM · MMI · EXC] (entropy) term. The important feature of (η⁴-AnH)Mo(PH₃)₃H₂ which results in a normal EIE at relatively low temperatures is that the M–H vibrational modes are of low energy and cause the ZPE term to approach unity rapidly. Thus, the

[SYM · MMI · EXC] entropy term is able to dominate the EIE at a relatively low temperature, thereby resulting in a normal EIE for oxidative addition of H₂ to (η⁶-AnH)Mo(PH₃)₃.³⁷

Equilibrium isotope effects for coordination of dihydrogen

In addition to the majority of EIEs for oxidative addition of H₂ and D₂ being inverse at ambient temperature, the

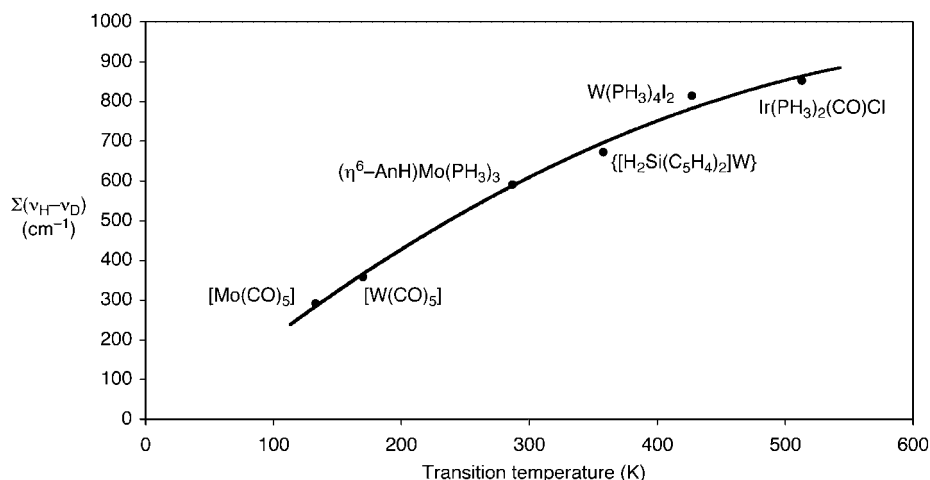


Figure 11 Correlation of the inverse to normal EIE transition temperature for oxidative addition of H₂ and D₂ with $\Sigma(v_{\text{H}}-v_{\text{D}})$. Reproduced with permission from ref. 35. Copyright 2006 Royal Society of Chemistry.

EIEs for formation of dihydrogen complexes are also inverse.³⁸ The first detailed analysis of the origin of the inverse deuterium EIE for coordination of dihydrogen was performed by Bender, Kubas, Hoff, and coworkers to rationalize the value of 0.70(15) at 22°C for the EIE for the formation of $\text{W}(\text{CO})_3(\text{PCy}_3)_2(\eta^2\text{-H}_2)$ from $\text{W}(\text{CO})_3(\text{PCy}_3)_2(\text{N}_2)$.^{16d} Significantly, the calculations indicate that the inverse EIE is primarily attributable to an inverse ZPE term (0.20).

However, in view of the transition between inverse and normal EIEs observed for oxidative addition of dihydrogen, we considered the possibility that the EIE for coordination of dihydrogen could also exhibit a similar behavior. Therefore, to evaluate this possibility, we performed calculations on the pentacarbonyl complex $\text{W}(\text{CO})_5(\eta^2\text{-H}_2)$,³⁹ a close relative of the first dihydrogen complexes, $\text{M}(\text{CO})_3(\text{PR}_3)_2(\eta^2\text{-H}_2)$ ($\text{M} = \text{Mo}, \text{W}; \text{R} = \text{Pr}^i, \text{Cy}$).⁴⁰ The temperature dependence of the EIE for the coordination of H₂ to $[\text{W}(\text{CO})_5]$ to form the dihydrogen complex $\text{W}(\text{CO})_5(\eta^2\text{-H}_2)$ is illustrated in Figure 12,⁴¹ which illustrates that the EIE is calculated to be inverse at ambient temperature, a result that is in accord with experimental reports of inverse EIEs for coordination of H₂ in other systems. At high temperatures, however, the EIE is calculated to become normal. In this regard, a normal EIE has also been calculated for coordination of H₂ and D₂ to $[\text{CpRu}(\text{H}_2\text{PCH}_2\text{PH}_2)]^+$ and $[\text{Os}(\text{H}_2\text{PCH}_2\text{CH}_2\text{PH}_2)]^+$ at 300 K, although the temperature dependence of the EIE was not discussed.⁴² On the basis of the reported ZPE terms (0.323 and 0.505, respectively), however, these EIEs should also become inverse at low temperature.

As noted for oxidative addition of H₂, the transition from an inverse to normal value and the existence of a

maximum is due to competition between the ZPE (enthalpy) and $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ (entropy) terms. The inverse ZPE term is a consequence of the fact that association with H₂ (be it forming either a dihydrogen or dihydride complex) creates *five* new isotopically sensitive vibrations (derived from the rotational and translational degrees of freedom of H₂ molecule) of sufficient energy that isotopic substitution results in a greater ZPE difference for the adduct than for H₂.

The temperature dependence of the EIE for oxidative addition of H₂ to $[\text{W}(\text{CO})_5]$ to form the dihydride $\text{W}(\text{CO})_5\text{H}_2$ exhibits a similar profile to that for coordination of H₂ (Figure 13),⁴¹ but a notable difference is that the transition from an inverse to a normal EIE occurs at a much lower temperature (170 K) than that for coordination (580 K). Since the combined $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ (entropy) terms are similar for both coordination and oxidative addition of H₂, the observation that the transition from an inverse to a normal EIE for oxidative addition occurs at a much lower temperature than that for coordination is a result of the ZPE (enthalpy) terms. Specifically, the ZPE (enthalpy) term for coordination of dihydrogen is more inverse than that for oxidative addition and so higher temperatures are required to effect the transition.

Although the complete set of isotope-sensitive vibrational frequencies for $\text{W}(\text{CO})_5(\eta^2\text{-H}_2)$ are not known experimentally, such data are, nevertheless, available for both $\text{W}(\text{CO})_3(\text{PCy}_3)_2(\eta^2\text{-H}_2)$ and $\text{W}(\text{CO})_3(\text{PCy}_3)_2(\eta^2\text{-D}_2)$.^{16d} As such, the experimental frequencies provide a means to predict the temperature dependence of the EIE for coordination of H₂ and D₂ to $[\text{W}(\text{CO})_3(\text{PCy}_3)_2]$. Thus, the experimentally determined vibrational frequencies predict that the EIE will pass from an inverse

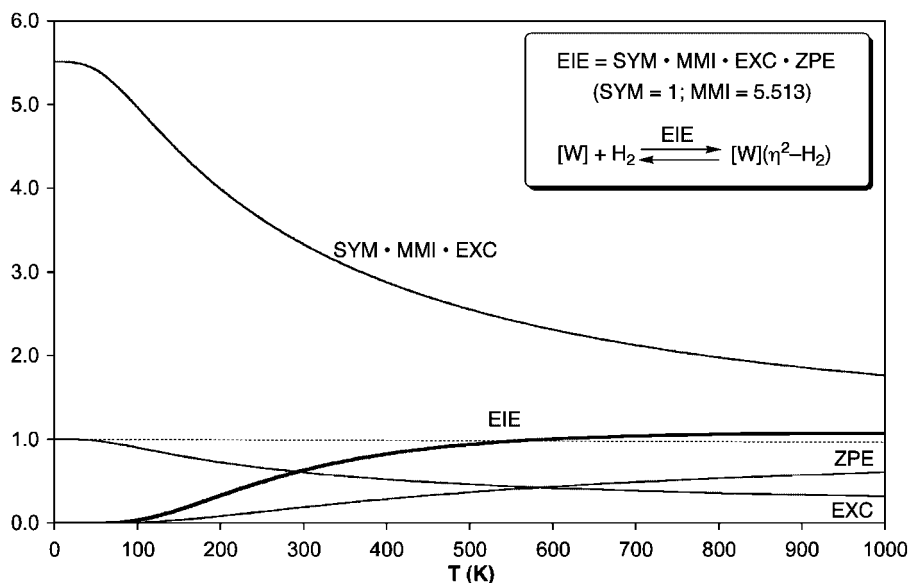
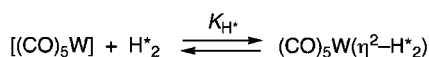


Figure 12 Calculated EIE as a function of temperature for coordination of H_2 and D_2 to $[\text{W}(\text{CO})_5]$. The temperature dependence of the individual EXC and ZPE components, as well as the combined $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ function, is also included. Modified with permission from ref. 41. Copyright 2003 American Chemical Society.

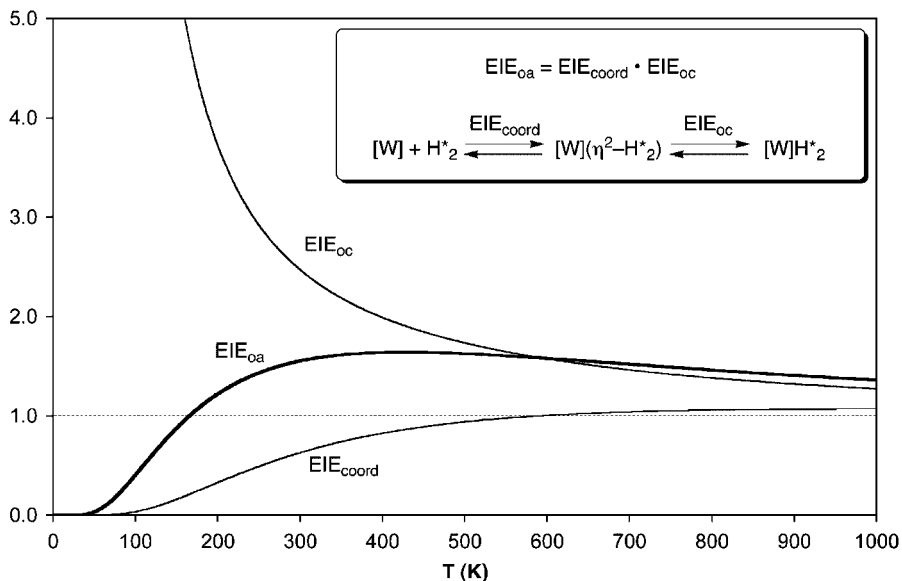


Figure 13 Calculated EIEs as a function of temperature for oxidative addition (EIE_{oxa}) and coordination ($\text{EIE}_{\text{coord}}$) of H_2 and D_2 to $[\text{W}(\text{CO})_5]$ and for oxidative cleavage of $\text{W}(\text{CO})_5(\eta^2\text{-H}_2)$ to $\text{W}(\text{CO})_5\text{H}_2$ (EIE_{oc}). Modified with permission from ref. 41. Copyright 2003 American Chemical Society.

value at ambient temperature to a normal value at high temperature, before returning to unity at infinite temperature (Figure 14).⁴¹ The similarity of the temperature dependence of the EIE for coordination of

H_2/D_2 to $[\text{W}(\text{CO})_5]$ using *calculated* frequencies to that for $[\text{W}(\text{CO})_3(\text{PCy}_3)_2]$ using *experimental* frequencies is significant since it provides excellent support for the use of calculated frequencies in predicting isotope effects.

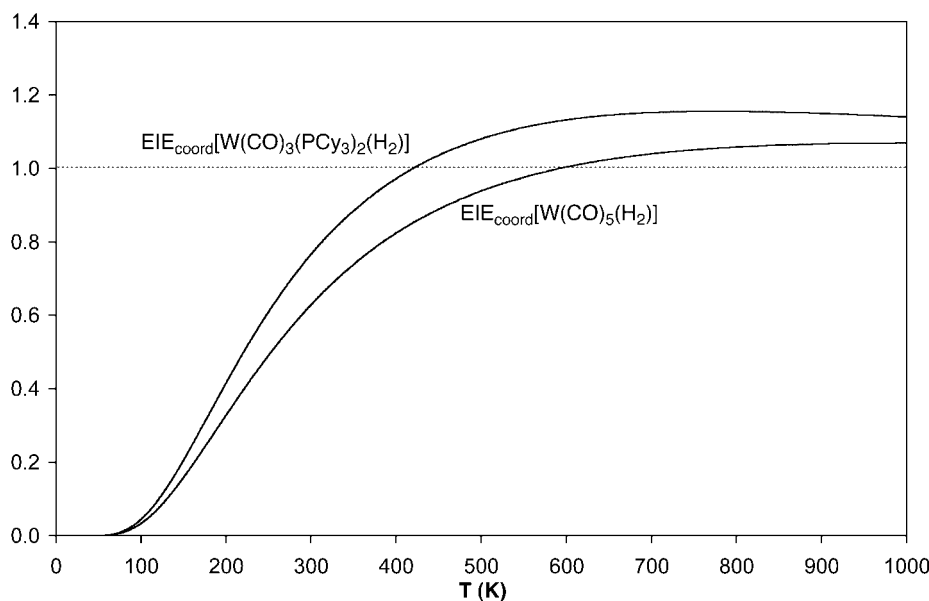


Figure 14 Comparison of the calculated EIE for coordination of H₂ and D₂ to [W(CO)₅] using computed frequencies with that for W(CO)₃(PCy₃)₂(η²-H₂) using experimentally determined frequencies. Modified with permission from ref. 41. Copyright 2003 American Chemical Society.

Equilibrium isotope effects for interconversion of dihydrogen and dihydride complexes

Another important aspect concerned with the EIEs for formation of W(CO)₅(η²-H₂) and W(CO)₅H₂ pertains to whether deuterium prefers to be located in the classical (dihydride) site or non-classical (dihydrogen) site. In this regard, the EIE for conversion of W(CO)₅(η²-H₂) to W(CO)₅H₂ is calculated to be normal at all temperatures, thereby demonstrating that deuterium favors the non-classical site in this system (Figure 13).⁴¹ This observation is noteworthy because there are contradictory reports in the literature concerned with the classical versus non-classical site preference of deuterium. For example, (i) experimental studies on CpNb(CO)₃(η²-H₂)/CpNb(CO)₃H₂⁴³ and [Re(PR₃)₃(CO)(η²-H₂)H₂]⁺/[Re(PR₃)₃(CO)H₄]⁺ (PR₃ = PMe₂Ph,⁴⁴ PMe₃⁴⁵), and calculations on W(CO)₃(PH₃)₂(η²-H₂)/W(CO)₃(PH₃)₂H₂⁴⁶ and {[H₂Si(C₅H₄)₂]Mo(η²-H₂)H}⁺⁴⁷ indicate that deuterium favors the non-classical site, while (ii) experimental studies on [TpIr(PMe₃)(η²-H₂)H]⁺⁴⁸ and [Cp₂W(η²-H₂)H]⁺⁴⁹ indicate that deuterium favors the classical site. Thus, while there is a preponderance of evidence that deuterium favors non-classical sites in polyhydride compounds, there are some examples in which the opposite preference has been suggested.

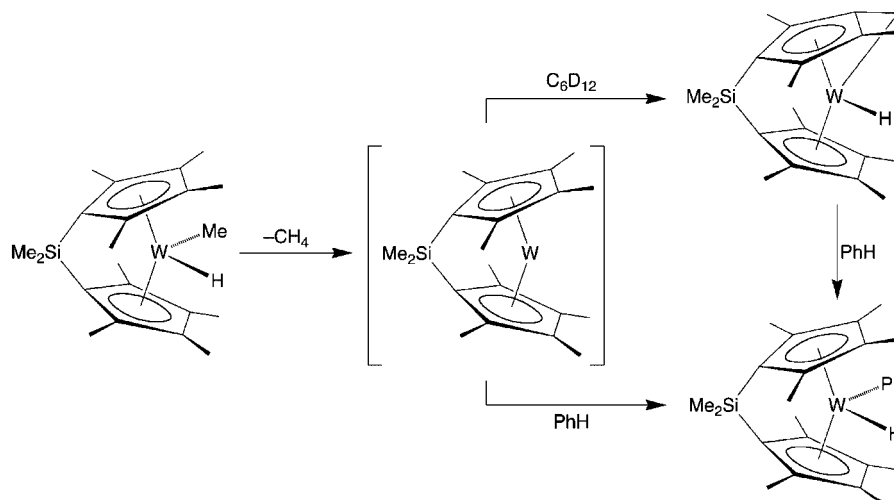
A detailed examination of the data indicates that the EIE for conversion of W(CO)₅(η²-H₂) to W(CO)₅H₂ is dominated by the ZPE term because substitution of the dihydrogen and hydride ligands by deuterium has relatively little impact on the MMI term due to the large

size of the molecules. Since W(CO)₅(η²-H₂) and W(CO)₅H₂ have the same number of isotopically sensitive vibrations, the normal ZPE term results purely from the fact that the ZPE associated with the H-H fragment in W(CO)₅(η²-H₂) is greater than that of the two W-H bonds in W(CO)₅H₂. Specifically, while there is a total of six isotopically sensitive normal modes associated with a [MH₂] moiety, the single most important mode is that which corresponds to the high energy H-H stretch in W(CO)₅(η²-H₂) (ν_{H-H} = 3330 cm⁻¹; ν_{D-D} = 2366 cm⁻¹) and becomes a low energy symmetric bend in W(CO)₅H₂ (ν_{HMH} = 784 cm⁻¹; ν_{DMD} = 600 cm⁻¹). The ZPE differences for these vibrations clearly favor deuterium residing in the non-classical site. An alternative way of interpreting the isotope effect for conversion of W(CO)₅(η²-H₂) to W(CO)₅H₂ is to recognize that the normal value for EIE_{oc} is a direct result of the fact that EIE_{oa} < EIE_{coord} (since EIE_{oc} = EIE_{oa}/EIE_{coord}).

Isotope effects pertaining to the interaction of transition metals with C-H bonds

Experimental measurement of isotope effects for reductive elimination of methane from [Me₂Si(C₅Me₄)₂]W(Me)H

The reductive elimination of methane from the tungstenocene methyl-hydride complexes, e.g. Cp₂W(Me)H⁵⁰ and Cp^{*}W(Me)H,⁵¹ is a well-known process. Similarly,



Scheme 7

we demonstrated that the *ansa*-complex $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2\text{W}(\text{Me})\text{H}]$ is also subject to reductive elimination and that the tungstenocene intermediate so generated may be trapped either intramolecularly to give $[\text{Me}_2\text{Si}(\eta^5\text{-C}_5\text{Me}_4)(\eta^6\text{-C}_5\text{Me}_3\text{CH}_2)]\text{WH}$,⁵² or intermolecularly by benzene to give $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2\text{W}(\text{Ph})\text{H}]$ (Scheme 7).^{53,54} Kinetics studies indicate that although intermolecular oxidative addition of benzene is thermodynamically favored, intramolecular C–H bond cleavage within $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2\text{W}]$ to give $[\text{Me}_2\text{Si}(\eta^5\text{-C}_5\text{Me}_4)(\eta^6\text{-C}_5\text{Me}_3\text{CH}_2)]\text{WH}$ is actually kinetically favored.

The kinetic isotope effect for reductive elimination of methane from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2\text{W}(\text{CH}_3)\text{H}]$ and $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2\text{W}(\text{CD}_3)\text{D}]$ is characterized by a substantial inverse KIE of 0.45(3) in benzene at 100 °C. Although a normal KIE may have been expected since this has a substantial primary component, the inverse value may be readily rationalized by recognizing that the reductive elimination reaction is not a single step, but is rather a two-step sequence involving formation of a σ -complex intermediate $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2\text{W}(\sigma\text{-MeH})]$ prior to rate-determining elimination of methane.⁵⁵

Specifically, for a situation involving a σ -complex intermediate, the rate constant for irreversible reductive elimination is a composite of the rate constants for reductive coupling (k_{rc}), oxidative cleavage (k_{oc}), and dissociation (k_{d}), namely $k_{\text{obs}} = k_{\text{rc}}k_{\text{d}}/(k_{\text{oc}} + k_{\text{d}})$. The latter expression simplifies to $k_{\text{obs}} = k_{\text{rc}}k_{\text{d}}/k_{\text{oc}} = K_{\sigma}k_{\text{d}}$, where K_{σ} is the equilibrium constant for the conversion of $[\text{M}](\text{R})\text{H}$ to $[\text{M}](\sigma\text{-RH})$ if methane dissociation is rate determining, i.e. $k_{\text{d}} \ll k_{\text{oc}}$ (Figure 15). As such, the kinetic isotope effect for overall reductive elimination is $k_{\text{H}}/k_{\text{D}} = [K_{\sigma(\text{H})}/K_{\sigma(\text{D})}][k_{\text{d}(\text{H})}/k_{\text{d}(\text{D})}]$, where $K_{\sigma(\text{H})}/K_{\sigma(\text{D})}$ is the equilibrium isotope effect for the conversion of $[\text{M}](\text{R})\text{H}$ to $[\text{M}](\sigma\text{-RH})$ (Figure 15). If the isotope effect for

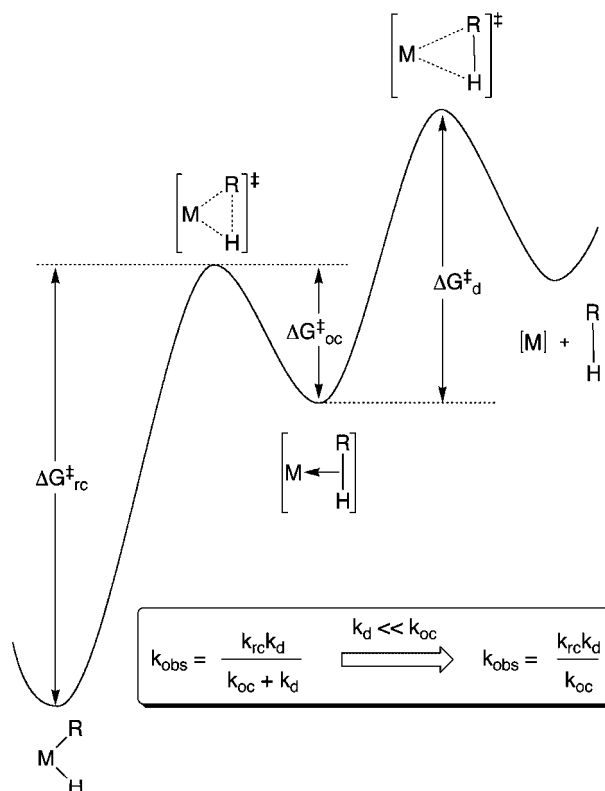


Figure 15 Free energy surface for reductive elimination of RH from a metal center via a σ -complex intermediate for which $k_{\text{d}} \ll k_{\text{oc}}$.

dissociation of RH (i.e. $[k_{\text{d}(\text{H})}/k_{\text{d}(\text{D})}]$) is close to unity (since the C–H bond is close to being fully formed), the isotope effect on reductive elimination would then be dominated by the equilibrium isotope effect $K_{\sigma(\text{H})}/K_{\sigma(\text{D})}$ for the formation of the σ -complex $[\text{M}](\sigma\text{-RH})$. The latter would be predicted to be inverse on the basis of the aforementioned simple notion that deuterium prefers

to be located in the higher frequency oscillator, i.e. C–D versus M–D. As such, an inverse KIE may result for the overall reductive elimination, without requiring an inverse effect for a single step (Figure 16).⁵⁶ Indeed, this explanation has been invoked to rationalize inverse KIEs for a variety of systems, e.g. Cp*Ir(PMe₃)(C₆H₁₁)H (0.7),⁵⁷ Cp*Rh(PMe₃)(C₂H₅)H (0.5),^{56d} Cp₂W(Me)H (0.75),^{50b} Cp*₂W(Me)H (0.70),⁵¹ [Cp₂Re(Me)H]⁺ (0.8),⁵⁸ [(Me₃tacn)Rh(PMe₃)(Me)H]⁺ (0.74),⁵⁹ (tmeda)Pt(Me)(H)(Cl) (0.29),⁶⁰ [Tp^{Me₂}]Pt(Me)₂H (0.81), and [Tp^{Me₂}]Pt(Me)(Ph)H (≤ 0.78).⁶¹ Normal KIEs are also known for reductive elimination reactions, e.g. (Ph₃P)₂Pt(Me)H (3.3), (Ph₃P)₂–Pt(CH₂CF₃)H (2.2), and (Cy₂PCH₂CH₂PCy₂)Pt(CH₂Bu^t)H (1.5),⁶² and these may be interpreted as either a single-step reaction or as a two-step reaction in which formation of the σ -complex intermediate is rate determining.

While the preequilibrium mechanism (Figure 16) provides a commonly accepted rationalization of inverse kinetic isotope effects for reductive elimination of RH, consideration must be given to the possibility that it could also correspond to the isotope effect for the reductive coupling step if that were to be rate determining. Since there is relatively little information pertaining to the individual isotope effects for the reductive elimination step, we considered it worthwhile to investigate this system in more detail. Although it is not possible to address this issue by studying the kinetics of reductive elimination of [Me₂Si(C₅Me₄)₂]W(CH₃)H and [Me₂Si(C₅Me₄)₂]W(CD₃)D, it is possible to address the issue by studying the elimination of CH₃D from [Me₂Si(C₅Me₄)₂]W(CH₃)D and [Me₂Si(C₅Me₄)₂]W(CH₂D)H.⁵² Specifically, [Me₂Si(C₅Me₄)₂]W(CH₃)D is observed to isomerize to [Me₂Si(C₅Me₄)₂]W(CH₂D)H⁶³ via the σ -complex intermediate [Me₂Si(C₅Me₄)₂]W(σ -CH₃D) on a time scale that is comparable to the overall reductive elimination of CH₃D, and a kinetics analysis of the transformations illustrated in Scheme 8 permits the KIE for reductive coupling to be determined. Significantly, assuming that secondary effects do not play a dominant role, the primary KIE for reductive coupling of [Me₂Si(C₅Me₄)₂]W(Me)X (X = H, D) to form the σ -complex intermediate [Me₂Si(C₅Me₄)₂]W(σ -XMe) is normal, with a value of 1.4(2). It is important to emphasize that it is only possible to extract the KIE for the formation of the σ -complex intermediate [Me₂Si(C₅Me₄)₂]W(σ -HMe) because the rate of isomerization is comparable to the overall reductive elimination of methane. Thus, if the reaction involved *only* interconversion of [Me₂Si(C₅Me₄)₂]W(CH₃)D and [Me₂Si(C₅Me₄)₂]W(CH₂D)H, without competitive loss of methane, the derived value of $k_{rc(H)}/k_{rc(D)}$ would be indeterminate, with multiple solutions existing. Dissociation of methane provides an

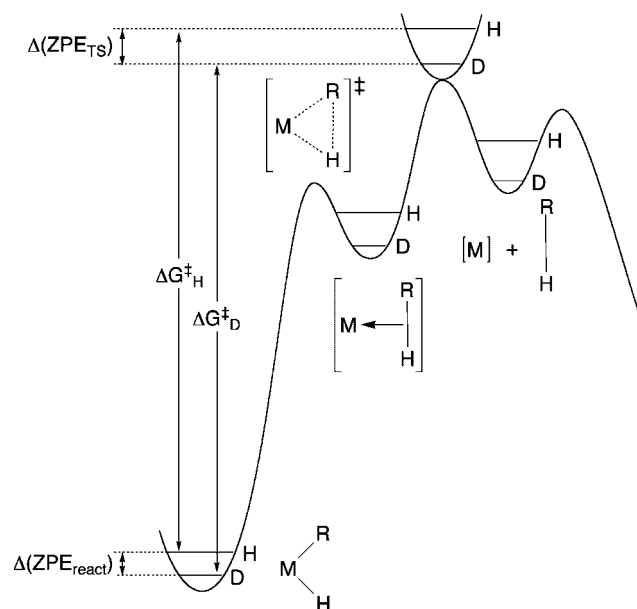
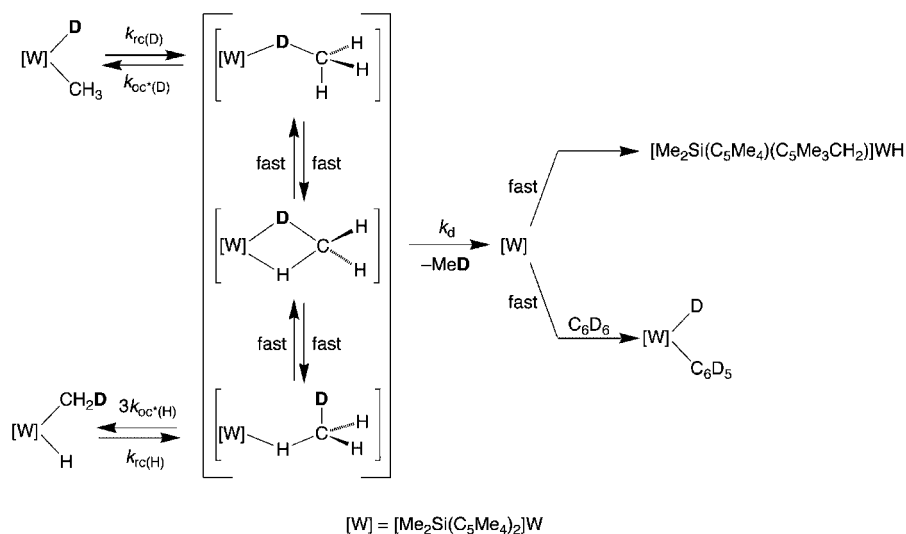


Figure 16 Origin of an inverse kinetic isotope effect for reductive elimination. The inverse kinetic isotope effect is essentially a consequence of an inverse equilibrium isotope being transferred to the rate-determining step.

additional kinetic constraint that allows $k_{rc(H)}/k_{rc(D)}$ to be ascertained.

Since formation of the σ -complex is characterized by a normal kinetic isotope effect, the observation of an inverse kinetic isotope effect 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, it is particularly pertinent to note that Jones has recently demonstrated that the EIE for the interconversion of [Tp^{Me₂}]Rh(L)(Me)X and [Tp^{Me₂}]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 = CNCH₂Bu^t; X = H, D).^{64,65}

Despite the fact that the reductive coupling steps for [Me₂Si(C₅Me₄)₂]W(Me)H and [Tp^{Me₂}]Rh(L)(Me)H are characterized by a normal KIE, an inverse KIE was proposed for [Tp]Pt(Me)H₂.⁶⁶ Specifically, the KIE for reductive coupling of [Tp]Pt(Me)H₂ was determined by comparison of (i) the rate constant for deuterium incorporation into the methyl group of [Tp]Pt(CH₃)H₂ when dissolved in CD₃OD (k_D) with (ii) the rate constant for hydrogen incorporation into the methyl group of [Tp]Pt(CD₃)D₂ when dissolved in CD₃OH (k_H). The ratio of these rate constants was proposed to correspond to the KIE for reductive coupling but, as noted above for the interconversion of [Me₂Si(C₅Me₄)₂]W(CH₃)D and [Me₂Si(C₅Me₄)₂]W(CH₂D)H, it is not possible to extract the KIE for reductive coupling from such a



Scheme 8

measurement. The isotope exchange reactions are multistep and the derived rate constants do not correspond to elementary steps and, as such, do not give the KIE for reductive coupling which is otherwise indeterminate.^{1c,53}

Computational determination of kinetic and equilibrium isotope effects for reactions involving [Me₂Si(C₅Me₄)₂]W(Me)H

The above discussion indicates that while it may be easy to measure an overall kinetic isotope effect for a reaction, there is considerable difficulty associated with extracting the kinetic isotope effects for the individual steps. Therefore, we employed computational methods to determine various isotope effects pertaining to the reductive elimination of methane from [Me₂Si(C₅Me₄)₂]W(Me)H.⁶⁷

Kinetic isotope effects for reductive elimination of methane from [Me₂Si(C₅Me₄)₂]W(Me)H. The mechanism for the reductive elimination reaction was computed by first performing a series of geometry optimizations that progressively couple the C–H bond, thereby generating the σ -complex intermediate [Me₂Si(C₅Me₄)₂]W(σ -HMe) via a {[Me₂Si(C₅Me₄)₂]–W(σ -HMe)}[‡] transition state (Figure 17). The second step of the reaction involves dissociation of methane from the σ -complex [Me₂Si(C₅Me₄)₂]W(σ -HMe) to generate the 16-electron tungstenocene intermediate, {[Me₂Si(C₅Me₄)₂]W}, a transformation that involves a spin crossover from a singlet to triplet manifold, as illustrated in Figure 17.⁵⁵ Significantly, the barrier to dissociation of CH₄ is higher in energy than the barrier

to accessing the σ -complex intermediate, a condition that is necessary if the kinetic isotope effect were to be dictated by a preequilibrium.

Since the calculation of vibrational frequencies is highly computationally intensive, the kinetic isotope effects were determined for a computationally simpler system in which the methyl groups of the [Me₂Si(C₅Me₄)₂] ligand were replaced by hydrogen atoms, i.e. [H₂Si(C₅H₄)₂]W(Me)H. The isotope effects calculated for the individual transformations pertaining to the overall reductive elimination of methane from [H₂Si(C₅H₄)₂]W(Me)H at 100°C are summarized in Table 2, from which several important points emerge. For example, the primary KIE for reductive coupling of [H₂Si(C₅H₄)₂]W(Me)X (X = H, D) to give the σ -complex [H₂Si(C₅H₄)₂]W(σ -XMe) is small, but *normal* (1.05). Likewise, the microscopic reverse, i.e. oxidative cleavage of [H₂Si(C₅H₄)₂]W(σ -XMe), is also *normal* (1.60). As a consequence of the fact that the KIE for oxidative cleavage is greater than that for reductive coupling, the equilibrium isotope effect (EIE) for the interconversion of [H₂Si(C₅H₄)₂]W(Me)X and [H₂Si(C₅H₄)₂]W(σ -XMe) is *inverse* (0.65). It is also evident from the data in Table 2 that secondary isotope effects do not play a significant role, with values close to unity for the interconversion of [H₂Si(C₅H₄)₂]W(CX₃)H and [H₂Si(C₅H₄)₂]W(σ -HCX₃). Analysis of the individual SYM, MMI, EXC, and ZPE terms indicates that it is the zero point energy enthalpy term that effectively determines the magnitude of the isotope effects for the interconversion of [H₂Si(C₅H₄)₂]–W(Me)H and [H₂Si(C₅H₄)₂]W(σ -HMe) at 100°C.

The KIE for dissociation of methane from the σ -complex is also close to unity, as has been postulated elsewhere.^{50b} Thus, by predicting both a normal kinetic

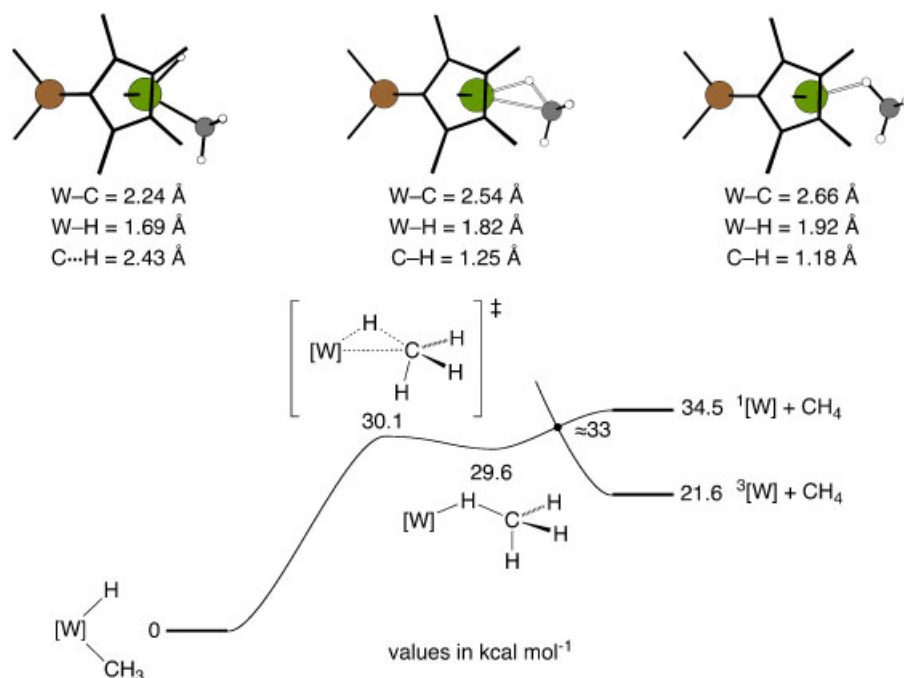


Figure 17 Calculated enthalpy surface for reductive elimination of CH_4 from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{Me})\text{H}$. Modified with permission from ref. 54. Copyright 2004 American Chemical Society.

Table 2 Primary (p) and secondary (s) isotope effects (IE) pertaining to reductive elimination of methane from $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$ at 100°C^a

		SYM	MMI	EXC	ZPE	IE
$k_{\text{rc}(\text{H})}/k_{\text{rc}(\text{D})}$	p	1	1.00	1.05	1.00	1.05
	s	1	1.00	0.98	1.04	1.02
	p&s	1	1.00	1.04	1.00	1.04
$k_{\text{oc}(\text{H})}/k_{\text{oc}(\text{D})}$	p	1	1.01	1.03	1.54	1.60
	s	1	1.00	1.05	1.04	1.09
	p&s	1	1.00	1.08	1.60	1.73
$K_{\sigma(\text{H})}/K_{\sigma(\text{D})}$	p	1	0.99	1.01	0.65	0.65
	s	1	1.00	0.94	1.00	0.94
	p&s	1	0.99	0.96	0.63	0.60
$k_{\text{d}(\text{H})}/k_{\text{d}(\text{D})}$	p	1	1.00	0.90	0.98	0.88
	s	1	0.98	0.92	1.23	1.11
	p&s	1	0.98	0.85	1.15	0.96
$k_{\text{re}(\text{H})}/k_{\text{re}(\text{D})}$	p	1	1.00	0.91	0.63	0.58
	s	1	0.98	0.86	1.23	1.04
	p&s	1	0.98	0.82	0.72	0.58

^aPrimary effects (p) correspond to reductive elimination of $\text{CH}_3\text{-H}$ versus $\text{CH}_3\text{-D}$; secondary effects (s) correspond to reductive elimination of $\text{CH}_3\text{-H}$ versus $\text{CD}_3\text{-H}$; primary and secondary effects (p&s) correspond to reductive elimination of $\text{CH}_3\text{-H}$ versus $\text{CD}_3\text{-D}$.

isotope effect for the reductive coupling step and an inverse kinetic isotope effect for the overall reductive elimination, the calculated isotope effects for the over-

all reductive elimination of methane from $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$ are in accord with the experimental study on $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{Me})\text{H}$. Specifically, the KIE calculated for reductive elimination of methane from $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{CH}_3)\text{H}$ and $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{CD}_3)\text{D}$ (0.58) compares favorably with the experimental value for $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{CH}_3)\text{H}$ and $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{CD}_3)\text{D}$ (0.45). Furthermore, analysis of the isotope effects for the individual steps demonstrates that the principal factor responsible for the inverse nature of the KIE for the overall reductive elimination is the inverse equilibrium isotope effect for the interconversion of $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$ and $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\sigma\text{-HMe})$. The calculations therefore reinforce the notion that inverse primary kinetic isotope effects for reductive elimination of alkanes imply the existence of a σ -complex intermediate prior to rate-determining loss of alkane.

Equilibrium isotope effect for coordination of methane to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$. The frequency calculations on $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\sigma\text{-HMe})$ and $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$ also permit computation of the EIEs for coordination and oxidative addition of methane to the tungstenocene fragment $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$. The calculations predict that the EIEs for both coordination (1.45) and oxidative addition (2.42) of methane to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$ are normal, such that the reactions of CH_4 are thermodynamically more favored than those of CD_4 . Although there are no experimental reports of the EIEs for

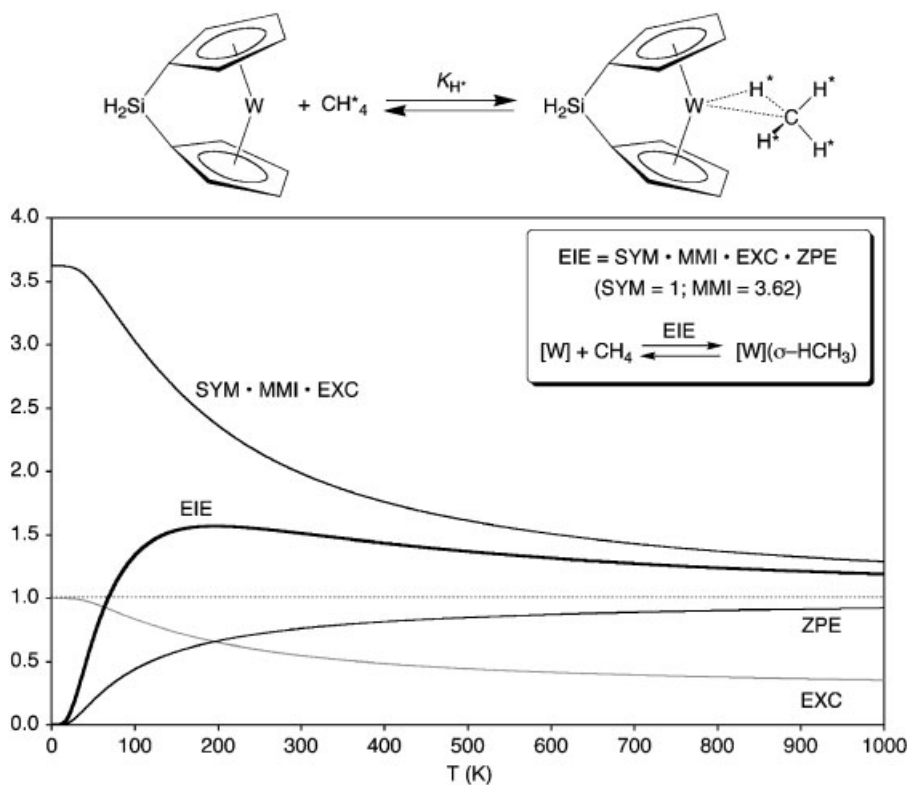


Figure 18 Calculated EIE as a function of temperature for coordination of CH_4 and CD_4 to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$. The temperature dependence of the individual EXC and ZPE components, as well as the combined $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ function, is also included.

coordination and oxidative addition of methane to a metal center for comparison with that for $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$, there are several conflicting reports of EIEs for coordination of other alkanes. Specifically, Gefதாக and Ball reported a normal EIE (1.33 at -93°C) for coordination of cyclopentane to $[\text{CpRe}(\text{CO})_2]$,⁶⁸ whereas Bergman and Moore reported inverse EIEs for the coordination of cyclohexane (≈ 0.1 at -100°C) and neopentane (≈ 0.07 at -108°C) to $[\text{Cp}^*\text{Rh}(\text{CO})]$.⁶⁹ The observation of both normal and inverse equilibrium isotope effects for coordination of alkanes to metal centers is counterintuitive and, in light of these observations, Bullock and Bender have commented that it is non-trivial to predict such isotope effects.^{1b}

An understanding of these disparate EIEs was, nevertheless, provided by evaluation of the temperature dependence of the EIE for coordinating methane to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$ (Figure 18). Thus, as described above for oxidative addition and coordination of dihydrogen, the EIE for coordination of methane to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$ exhibits a maximum: the EIE is 0 at 0 K, increases to a maximum value of 1.57, and then decreases to unity at infinite temperature. Both normal and inverse EIEs may therefore be obtained for coordination of a C–H

bond to the same metal center. As such, it provides a simple rationalization for the normal and inverse EIEs that have been reported for coordination of alkanes to different metal centers.

As with oxidative addition and coordination of dihydrogen, the unusual temperature dependence of the EIE for coordination of methane is a consequence of opposing $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ entropy and ZPE enthalpy terms: the $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ entropy component favors a normal EIE, while the ZPE enthalpy component favors an inverse EIE. At high temperatures, the $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ entropy component dominates and the EIE is normal, while at low temperatures the ZPE enthalpy component dominates and the EIE is inverse.

While the ZPE term is typically normal when the bond being broken is stronger than the one being formed, the ZPE term for coordination of methane 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.⁷⁰ The combined ZPE associated with these new isotopically sensitive vibrations is sufficient that it results in the ZPE change for $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\sigma\text{-HMe})$ upon isotopic substitution being greater than that for methane.

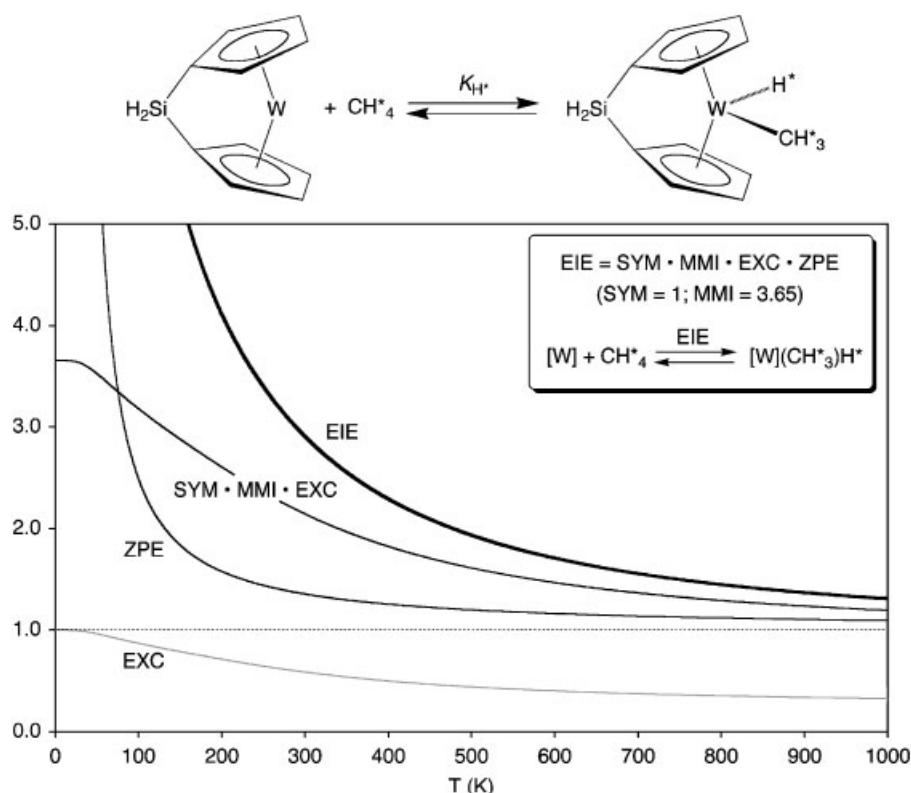


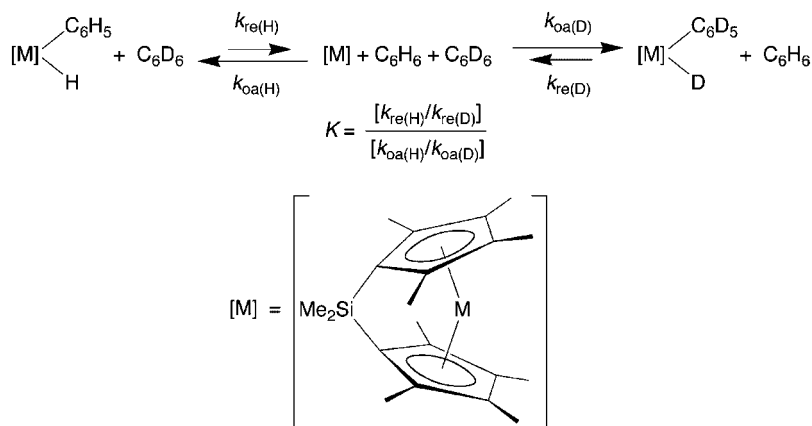
Figure 19 Calculated EIE as a function of temperature for oxidative addition of CH_4 and CD_4 to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$. The temperature dependence of the individual EXC and ZPE components, as well as the combined $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}]$ function, is also included.

Equilibrium isotope effect for oxidative addition of methane to $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$. In marked contrast to the EIE for coordination of methane which approaches zero at low temperature, the corresponding EIE for oxidative addition of methane to $\{[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}\}$ is normal at all temperatures and actually approaches infinity at low temperature (Figure 19).⁷¹ This dramatic difference is associated with the ZPE terms. Specifically, the ZPE term for coordination of methane is inverse at all temperatures (and zero at 0 K), while that for oxidative addition is normal at all temperatures (and infinity at 0 K).

While the total number of isotope sensitive vibrations are the same for both $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\sigma\text{-HMe})$ and $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$, the principal difference in the ZPE term is a consequence of the fact that the isotopically sensitive vibrations associated with the W–H bond of the methyl–hydride complex $[\text{H}_2\text{Si}(\text{C}_5\text{H}_4)_2]\text{W}(\text{Me})\text{H}$, namely a W–H stretch and two bends, are of sufficiently low energy that they do not counter those associated with the C–H bond that has been broken. As a result, the ZPE term for oxidative addition of the C–H bond is normal.

Kinetic isotope effects for reductive elimination of benzene from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{M}(\text{Ph})\text{H}$ ($\text{M}=\text{Mo}, \text{W}$)

Although the reductive elimination of methane from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{CH}_3)\text{H}$ is irreversible, the reductive elimination of benzene from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{C}_6\text{H}_5)\text{H}$ is reversible and may be studied by observing isotopic exchange with C_6D_6 solvent (Scheme 9). By analogy with reductive elimination of methane, reductive elimination of benzene from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{C}_6\text{H}_5)\text{H}$ and $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{C}_6\text{D}_5)\text{D}$ is also characterized by an inverse kinetic isotope effect, with $k_{\text{H}}/k_{\text{D}} = 0.65(10)$ at 182°C , an observation that is consistent with a preequilibrium involving the formation of an intermediate with an intact C–H bond prior to rate-determining loss of benzene (Figure 20). Two possibilities exist for this intermediate, namely (i) an $\eta^2\text{-}\pi$ -complex in which the benzene coordinates by a C=C double bond, and (ii) a σ -complex in which the benzene coordinates via a C–H bond. Of these possibilities, DFT calculations suggest that the preferred intermediate connecting $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{C}_6\text{H}_5)\text{H}$ and $\{[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}\}$ is the σ -complex, $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\sigma\text{-C}_6\text{H}_6)$.



Scheme 9

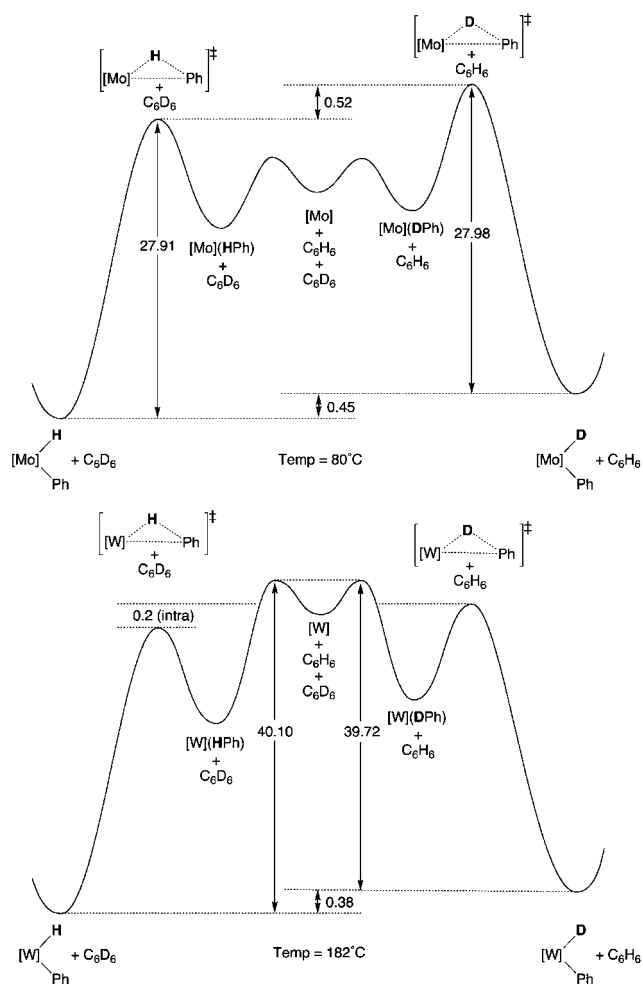


Figure 20 Comparison of the free energy surfaces for reductive elimination of benzene from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{M}(\text{C}_6\text{H}_5)\text{H}$ and $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{M}(\text{C}_6\text{D}_5)\text{D}$ in C_6D_{12} ($\text{M} = \text{Mo}$ at 80°C , W at 182°C). Energies in kcal mol^{-1} . Reproduced with permission from ref. 53. Copyright 2003 American Chemical Society.

In contrast to the inverse kinetic isotope effect for reductive elimination of benzene from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{W}(\text{Ph})\text{H}$, a *normal* KIE [$k_{\text{H}}/k_{\text{D}} = 1.14(10)$] is observed for the molybdenum analogue, $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{Mo}(\text{Ph})\text{H}$. The difference between the molybdenum and tungsten systems is a consequence of the reductive coupling step being rate determining for molybdenum, whereas dissociation of benzene is rate determining for tungsten (Figure 21).

Kinetic isotope effects for oxidative addition of benzene to $\{[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{M}\}$ ($\text{M} = \text{Mo}, \text{W}$)

Since the reductive elimination of benzene from $[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{M}(\text{Ph})\text{H}$ ($\text{M} = \text{Mo}, \text{W}$) is reversible, the nature of the energy surface has been probed in more detail by studying the microscopic reverse by using the tuck-in complexes $[\text{Me}_2\text{Si}(\eta^5\text{-C}_5\text{Me}_4)(\eta^6\text{-C}_5\text{Me}_3\text{CH}_2)]\text{MH}$ ($\text{M} = \text{Mo}, \text{W}$) as sources of the metallocenes $\{[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{M}\}$ (Scheme 10). Competition experiments with $\text{C}_6\text{H}_6/\text{C}_6\text{D}_6$ mixtures allow the intermolecular KIEs for oxidative addition to be determined in the absence of thermodynamic equilibration of the products. Significantly, the oxidative addition of benzene to the molybdenocene and tungstenocene fragments is characterized by very different KIEs (Table 3). Thus, a substantial KIE of 2.1(2) is observed for oxidative addition to the molybdenocene species, whereas no KIE is observed for oxidative addition to the tungstenocene analogue (Table 3). The difference in KIEs is a consequence of different rate determining steps for the oxidative addition reaction (Figures 20 and 22). Specifically, a significant KIE is observed for addition to $\{[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{Mo}\}$ because the rate-determining step involves cleavage of the C–H bond, whereas an insignificant isotope effect is observed for

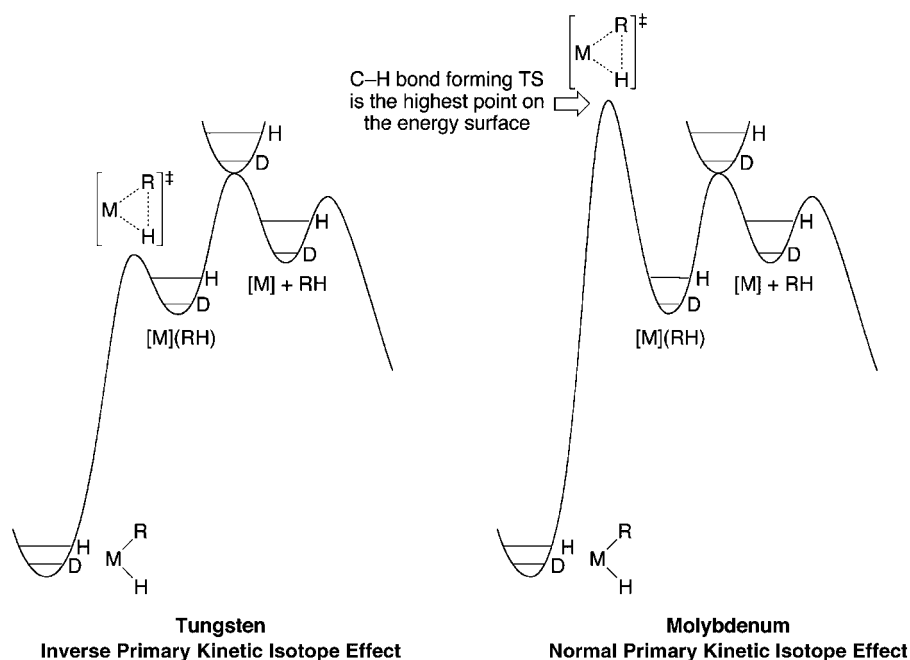
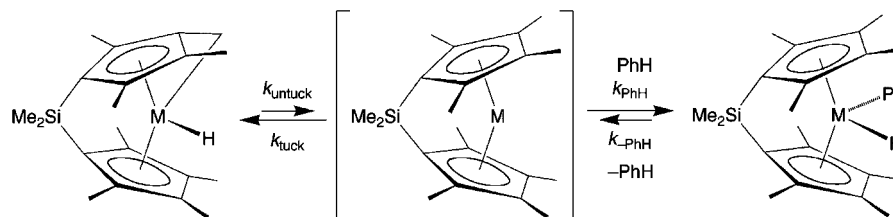


Figure 21 Explanation for a normal kinetic isotope effect for elimination of RH from molybdenum but an inverse kinetic isotope effect for tungsten. A normal isotope effect is observed for molybdenum because the rate-determining step is reductive coupling. Reproduced with permission from ref. 53. Copyright 2003 American Chemical Society.



Scheme 10

{[Me₂Si(C₅Me₄)₂]W} since the rate-determining step only involves coordination of benzene (Figure 22).

While the intermolecular C₆H₆/C₆D₆ competition experiment does not probe the step involving oxidative cleavage of the C–H bond for the tungsten system, this step may be probed via an intramolecular KIE employing selectively deuterated benzene, namely 1,3,5-C₆H₃D₃. Specifically, if there exists an intermediate in which the H/D benzene sites are either equivalent or interchange rapidly, the intramolecular KIE corresponds to the bond cleavage event, even though this occurs after the rate-determining step. Thus, the intramolecular KIE of 1.4(2) for addition of 1,3,5-C₆H₃D₃ to {[Me₂Si(C₅Me₄)₂]W} is distinct from the intermolecular KIE of 1.0(1) for intermolecular competition between C₆H₆ and C₆D₆ (Table 3) (Figure 22). The difference between intermolecular and intramolecular KIEs provides additional evidence for the existence of an intermediate.

Table 3 Isotope effects for [Me₂Si(C₅Me₄)₂]M(Ph)H (*T* = 80°C for Mo and 182°C for W)

	Mo	W
$k_{\text{re(H)}}/k_{\text{re(D)}}$	1.14(10)	0.65(10)
$[k_{\text{oa(H)}}/k_{\text{oa(D)}}]_{\text{inter}}$	2.1(2)	1.0(1)
$[k_{\text{oa(H)}}/k_{\text{oa(D)}}]_{\text{intra}}$	2.6(2)	1.4(2)
$K_{\text{calc}} = [k_{\text{re(H)}}/k_{\text{re(D)}}] / [k_{\text{oa(H)}}/k_{\text{oa(D)}}]_{\text{inter}}$	0.54	0.65
K_{obs}	0.53(2)	0.66(5)

Oxidative addition of 1,3,5-C₆H₃D₃ to the molybdenum complex is characterized by an intramolecular KIE of 2.6(2) at 80°C, a value that is comparable to the intermolecular KIE of 2.1(2) because the two KIEs probe the same C–H bond cleavage transition state (Table 3 and Figure 22).⁷²

The equilibrium constant for the interconversion of [Me₂Si(C₅Me₄)₂]Mo(C₆H₃D₂)D and [Me₂Si(C₅Me₄)₂]Mo(C₆H₂D₃)H is 1.96(8).⁷³ Consideration of a simple

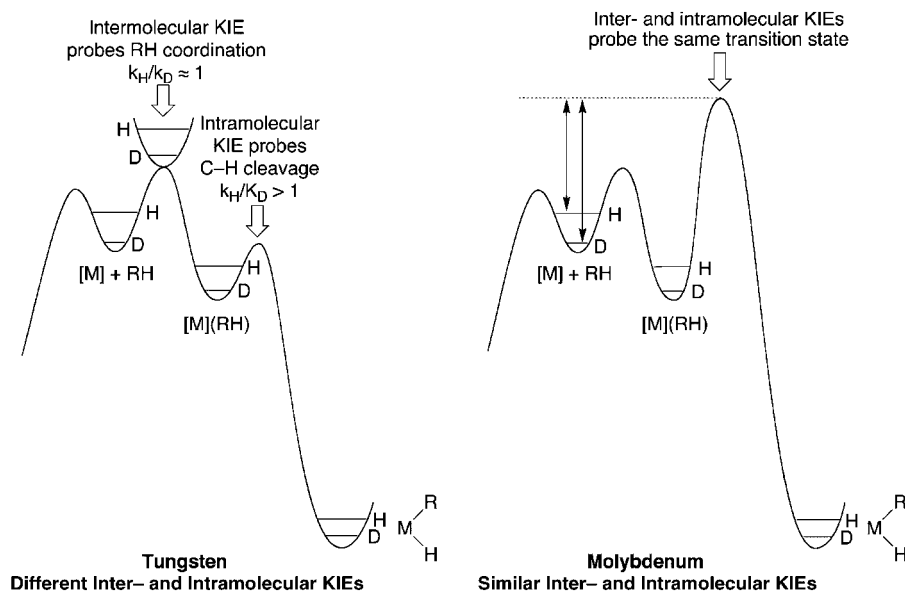


Figure 22 Different kinetic isotope effects for oxidative addition of benzene to $\{[Me_2Si(C_5Me_4)_2]Mo\}$ and $\{[Me_2Si(C_5Me_4)_2]W\}$. A significant kinetic isotope effect is observed for addition to $\{[Me_2Si(C_5Me_4)_2]Mo\}$ because the rate-determining step involves cleavage of the C–H(D) bond, whereas no isotope effect is observed for $\{[Me_2Si(C_5Me_4)_2]W\}$ since the rate-determining step involves coordination of benzene. However, an intramolecular kinetic isotope effect is observed for reaction of $C_6H_3D_3$ with $\{[Me_2Si(C_5Me_4)_2]W\}$ because it now probes the product-forming step, rather than the rate-determining step. For molybdenum, the inter- and intramolecular kinetic isotope effects are similar because they probe the same transition state. Reproduced with permission from ref. 53. Copyright 2003 American Chemical Society.

thermodynamic cycle indicates that this value also corresponds to (i) the EIE for C–H versus C–D cleavage of $C_6H_3D_3$ by $\{[Me_2Si(C_5Me_4)_2]Mo\}$ and (ii) the EIE for the conversion of the η^2 - π -complex to the phenyl hydride. Correspondingly, it is evident that the EIE for the reverse reaction, i.e. the formation of $[Me_2Si(C_5Me_4)_2]Mo(\eta^2$ - π - $C_6H_6)$ from $[Me_2Si(C_5Me_4)_2]Mo(Ph)H$, is 0.51(2). In this regard, a similar inverse EIE has been reported by Jones for the interconversion of $Cp^*Rh(PMe_3)(Ph)H$ and $Cp^*Rh(PMe_3)(\eta^2$ - π - $C_6H_6)$ [$K_H/K_D = 0.37$].⁷⁴

Comparison of the energy surfaces for oxidative addition of RH to $\{[Me_2Si(C_5Me_4)_2]Mo\}$ and $\{[Me_2Si(C_5Me_4)_2]W\}$ based on isotope effects

Evaluation of the various kinetic and equilibrium isotope effects pertaining to the interaction of benzene with the $\{[Me_2Si(C_5Me_4)_2]Mo\}$ and $\{[Me_2Si(C_5Me_4)_2]W\}$ moieties demonstrates that there is a significant difference in the energy surface for the two systems concerned with the relative barriers for the two steps. The difference in these barriers reflects the reactivity preferences of the hydrocarbon adducts $[Me_2Si(C_5Me_4)_2]M(RH)$. Specifically, oxidative cleavage of $[Me_2Si(C_5Me_4)_2]M(RH)$ is favored over RH dissociation for the tungsten system, whereas RH dissociation is favored for the molybdenum system. A simple rationa-

lization for this difference may be traced to the relative energies of $[Me_2Si(C_5Me_4)_2]M(R)H$ and $\{[Me_2Si(C_5Me_4)_2]M\}$ species. The difference in energies between $[Me_2Si(C_5Me_4)_2]M(R)H$ and $\{[Me_2Si(C_5Me_4)_2]M\}$ is greater for tungsten due to the existence of stronger W–X versus Mo–X bonds.⁷⁵ To a certain extent, the activation barriers for the formation of $[Me_2Si(C_5Me_4)_2]M(R)H$ and $\{[Me_2Si(C_5Me_4)_2]M\}$ from $[Me_2Si(C_5Me_4)_2]M(RH)$ will track the thermodynamic stabilities of the two products. Thus, as $[Me_2Si(C_5Me_4)_2]M(R)H$ becomes more stable (i.e. tungsten), the barrier for oxidative cleavage is lowered such that dissociation becomes rate determining. Conversely, as the relative stability of $[Me_2Si(C_5Me_4)_2]M(R)H$ is lowered (i.e. molybdenum), the barrier for the barrier for oxidative cleavage is raised and may become rate determining (Figure 23).

Conclusions

The magnitude of an isotope effect is often used to infer details of the reaction coordinate and corresponding structural changes of the molecules involved. However, since certain reactions, e.g. oxidative addition of dihydrogen, exhibit both normal and inverse EIEs for the same system, depending upon temperature, it is apparent that conclusions derived from the magnitude of an isotope effect at a single temperature may be more

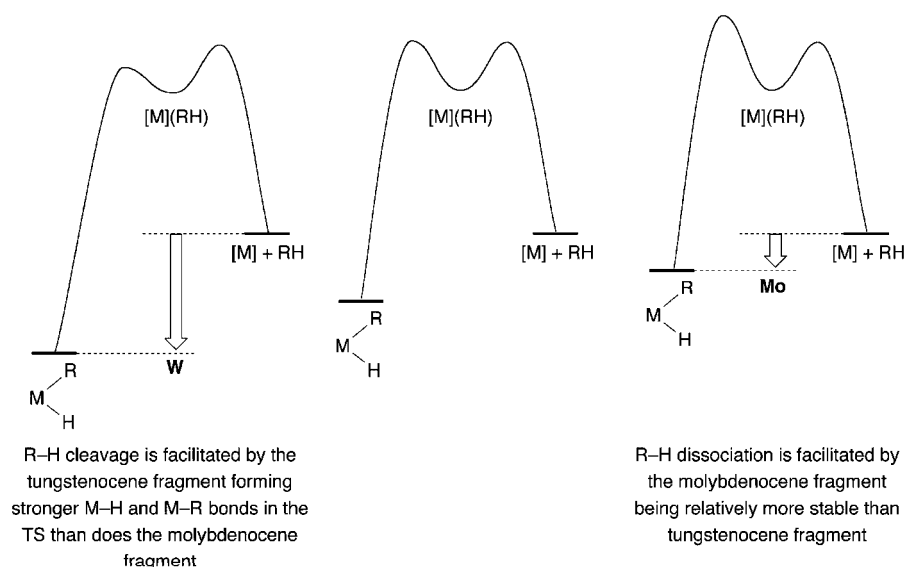


Figure 23 Rationalization of the different energy surfaces for Mo and W. The relative barriers for dissociation of R-H versus oxidative cleavage of a σ -complex are proposed to be influenced by the exothermicity of the overall transformation, with oxidative addition to tungsten being more exothermic than that to molybdenum. Reproduced with permission from ref. 53. Copyright 2003 American Chemical Society.

unreliable than previously considered. For example, on the basis of the typical explanation for the nature of an equilibrium isotope effect, i.e. deuterium prefers to be located in the highest frequency oscillator, the observation of a normal EIE for oxidative addition of H_2 at elevated temperatures could possibly have been interpreted as being due to a zero point energy effect resulting from the H_2 molecule having a higher stretching frequency than the combined frequencies associated with the $[MH_2]$ unit. However, the zero point energy term is actually inverse and the origin of the normal EIE at elevated temperature is purely due to entropy effects dominating.

The existence of σ -complex intermediates on the energy surface for oxidative addition and reductive elimination of X-H bonds may have profound consequences on KIEs. For example, the inverse KIE for reductive elimination of methane from $[Me_2Si(C_5Me_4)_2]W(CH_3)H$ is a consequence of a preequilibrium with the σ -complex intermediate $[Me_2Si(C_5Me_4)_2]W(\sigma-HMe)$, i.e. the inverse KIE is dictated by an inverse EIE for the preequilibrium.

Finally, it is important to recognize that closely related compounds may be characterized by very different isotope effects for the analogous transformation. For example, the reductive elimination of RH from $[Me_2Si(C_5Me_4)_2]M(R)H$ ($M = Mo, W$) is characterized by an inverse KIE for the tungsten system, but a normal KIE for the molybdenum system. Furthermore, oxidative addition of PhH to $\{[Me_2Si(C_5Me_4)_2]Mo\}$ and $\{[Me_2Si(C_5Me_4)_2]W\}$ exhibits different isotope effects,

with the molybdenum system exhibiting a substantial intermolecular KIE, while no effect is observed for the tungsten systems. These differences in KIEs are the consequence of the fact that the reactions are mediated by σ -complex intermediates $[Me_2Si(C_5Me_4)_2]M(RH)$ that have different reactivities. Thus, the tungsten complex $[Me_2Si(C_5Me_4)_2]W(RH)$ favors oxidative cleavage over RH dissociation, whereas the molybdenum complex $[Me_2Si(C_5Me_4)_2]Mo(RH)$ favors RH dissociation over oxidative cleavage. The rate-determining steps for the oxidative addition/reductive elimination energy surface for molybdenum and tungsten are, therefore, different, with the result that the KIEs are dictated by different transition states.

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17. The symmetry factor includes both external (σ) and internal (n) symmetry numbers. See: Bailey WF, Monahan AS. *J Chem Educ* 1978; **55**: 489–493.
 18. It is, however, important to consider bending modes in evaluating secondary isotope effects.
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 20. Collman JP, Roper WR. *Adv Organomet Chem* 1968; **7**: 53–94.
 21. See, for example: (a) Reference 16c; (b) Shin JH, Parkin G. *J Am Chem Soc* 2002; **124**: 7652–7653; (c) Yan SG, Brunschwig BS, Creutz C, Fujita E, Sutin N. *J Am Chem Soc* 1998; **120**: 10553–10554.
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 23. More generally, the EIE approaches SYM, the ratio of the symmetry numbers. For comparisons involving H_2 and D_2 , SYM is equal to unity.
 24. In terms of ΔH and ΔS , a simple exponential variation of K as a function of temperature, according $K = \exp(-\Delta H/RT) \exp(\Delta S/R)$, merely requires that ΔH and ΔS do not vary significantly over the temperature range studied. The existence of a maximum and a transition between normal and inverse EIEs is a result of ΔS being temperature dependent.
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 26. For other examples involving H_2 for which both normal and inverse EIEs have been discussed, see: Kotaka M, Okamoto M, Bigeleisen J. *J Am Chem Soc* 1992; **114**: 6436–6445.
 27. Both ZPE and EXC are components of the vibrational partition function and their temperature dependencies are influenced by the magnitude of the vibrational frequencies, but in opposing directions. Thus, while low-frequency vibrations in the product may favor a more inverse EXC term, they favor a less inverse ZPE term. In view of this competition, it is not possible *a priori* to discuss in a simple manner how a change in vibrational frequency would influence an EIE.
 28. It should be noted that the ZPE and enthalpy [$\exp(-\Delta\Delta H/RT)$] terms are not identical because the thermal population of vibrationally excited states also provides a contribution to the enthalpy term. Correspondingly, the [SYM·MMI·EXC] and entropy [$\exp(\Delta\Delta S/R)$] terms are not identical, but differ by a similar component to that relating ZPE and enthalpy. However, these differences are small such that $\text{ZPE} \approx [\exp(-\Delta\Delta H/RT)]$ and $[\text{SYM} \cdot \text{MMI} \cdot \text{EXC}] \approx [\exp(\Delta\Delta S/R)]$ are good approximations.
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 30. Specifically, the translational entropy of D_2 is greater than that of H_2 because of a mass effect, while the rotational entropy of D_2 is greater than that of H_2 because (i) the rotational levels of D_2 are more closely spaced than those of H_2 due to a mass effect via the moment of inertia and (ii) the degeneracy of the rotational levels for D_2 are greater than those for H_2 .
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 33. The addition of H_2 across the Cr–Cr bond in the dinuclear fulvalene complex $(\mu\text{-}\eta^5, \eta^5\text{-C}_{10}\text{H}_8)[\text{Cr}(\text{CO})_3]_2$ to give dinuclear $(\mu\text{-}\eta^5, \eta^5\text{-C}_{10}\text{H}_8)[\text{Cr}(\text{CO})_3\text{H}]_2$ is characterized by a normal EIE of 1.45(10) at 55°C. See: Vollhardt KPC, Cammack JK, Matzger AJ, Bauer A, Capps KB, Hoff CD. *Inorg Chem* 1999; **38**: 2624–2631.
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 37. In this regard, the normal EIE observed for oxidative addition to dinuclear $(\mu\text{-}\eta^5, \eta^5\text{-C}_{10}\text{H}_8)\text{-}[\text{Cr}(\text{CO})_3]_2$ (Reference [33]) is also most likely a consequence of the Cr–H vibrations being of low energy so that the transition temperature is relatively low.
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70. See Reference [1b] for a description of the six new vibrations. Note that although there are six new vibrations, they do not contribute equally to the EIE.
71. The oxidative addition of CH₄ to Ir(PH₃)₂(CO)H is also calculated to have a normal EIE of 3.64 at 300 K. See Reference [16c].
72. Note that even though the intramolecular and intermolecular KIEs probe the same transition state, they are not expected to be identical because the intramolecular KIE specifically probes *only* the oxidative cleavage step (because that is where the partitioning occurs) whereas the intermolecular isotope effect will also be influenced to a certain degree by the isotope effects on the rate constants for association and dissociation of benzene. In addition, differing contributions from the MMI, EXC, and ZPE terms result in different KIEs for the same fundamental reaction. See, for example Reference [16a].
73. $K = \frac{[[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{Mo}(\text{C}_6\text{H}_2\text{D}_3)\text{H}]}{[[\text{Me}_2\text{Si}(\text{C}_5\text{Me}_4)_2]\text{Mo}(\text{C}_6\text{H}_3\text{D}_2)\text{D}]}$.
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