Inorg. Chem. **2005**, *44*, 4475–4484

On the Nature of Carbon–Hydrogen Bond Activation at Rhodium and Related Reactions†

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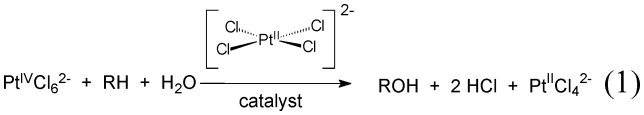
Received January 3, 2005

Over the past 20 years, substantial progress has been made in the understanding of the activation of C–H and other strong bonds by reactive metal complexes in low oxidation states. This paper will present an overview of the use of pentamethylcyclopentadienyl and trispyrazolylborate rhodium complexes for the activation of arene and alkane C–H bonds. Insights into bond strengths, kinetic and thermodynamic selectivities, and the nature of the intermediates involved will be reviewed. The role of η-2 arene complexes will be shown to be critical to the C–H activation reactions. Some information about the fleeting alkane σ-complexes will also be presented. In addition, use of these complexes with thiophenes has shown the ability to cleave C–S bonds. Mechanistic information has been obtained indicating coordination through sulfur prior to cleavage. Relevant examples of nickel-based C–S cleavage will also be given.

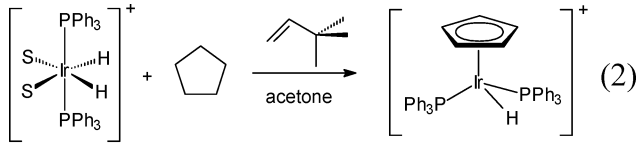
Introduction

The activation of C−H bonds in hydrocarbons is difficult due to the strength of and lack of polarity in these bonds. Over the past 25 years, significant advances have been made in using transition metal complexes to lower the barriers for cleavage of these bonds and for the inclusion of these reactions in useful organic transformations.[1] Many other elements form strong bonds to carbon, oftentimes rendering them inert to reaction also. In this paper, a historical summary is made in the use of rhodium complexes for discerning the kinetic and thermodynamic aspects of hydrocarbon activation. In addition, applications for the desulfurization of sulfur-containing hydrocarbons are included.

One of the earliest systems to provide evidence for alkane activation was published by Shilov in the 1960s.[2] This system used Pt(II) as a catalyst, with Pt(IV) as a stoichiometric oxidant, for the conversion of alkanes into alcohols and alkyl chlorides (eq 1).



While the initial reports provided few details about the mechanism of the activation, Shilov's early work paved the way for future investigations in this field. In the 1970s, Crabtree et al. reported a reaction in which an olefin was used to dehydrogenate an iridium(III) dihydride precursor.[3] The Ir(I) intermediate formed reacted with cyclopentane to give an η^5-cyclopentadienyl product that irrefutably involved alkane activation as the first step of the reaction (eq 2).



S = acetone

The work that initially attracted our attention was the report by L. Seiwell at DuPont regarding the use of $CpRh(C_2H_4)_2$ for the activation of aromatic C−D bonds in benzene-d_6.[4] In this system, reversible loss of ethylene generated a Rh(I) intermediate that could undergo oxidative addition to a C−D bond of benzene, insertion of ethylene into the Rh−D bond, β-elimination of a C−H bond, and reductive elimination of C_6D_5H. Consequently, this compound catalytically activated aromatic C−H bonds, although no intermediates could be observed. Upon arrival in Rochester in 1980, we elected to try to prepare stable derivatives of the C−H activation intermediates, with the ultimate goal of producing functionalized aromatic products catalytically. The progression of our investigations is described herein.

Results and Discussion

Fundamental Studies with Cp*Rh(PMe$_3$)(aryl)H. Our first reactions were aimed at synthesizing stable aryl hydride

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† This paper was delivered as the 2003 ACS Award in Organometallic Chemistry at the 225th National Meeting of the American Chemical Society in New Orleans, LA, March 24, 2003.

(1) For recent reviews, see: (a) Murai, S., Ed. *Topics Organometallic Chemistry*, Vol. 3; Springer: New York, 1999. (b) Goldberg, K. I., Goldman, A. S., Eds.; *Activation and Functionalization of C−H Bonds*; ACS Symposium Series 885; American Chemical Society: Washington, DC, 2004.

(2) Gol'dshleger, N. F.; Tyabin, M. B.; Shilov, A. E.; Shteinman, A. A. *Russ. J. Phys. Chem.* **1969**, *43*, 1222.

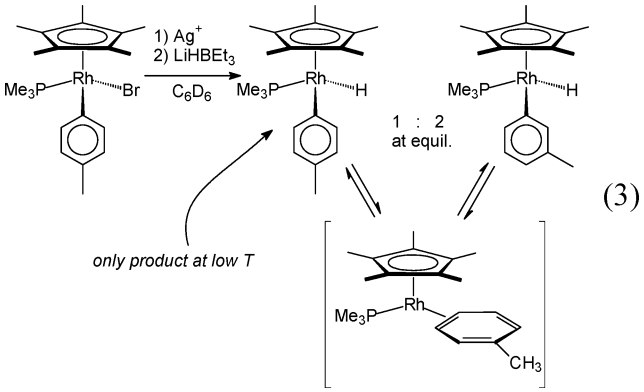
(3) Crabtree, R. H.; Mihelcic, J. M.; Quirk, J. M. *J. Am. Chem. Soc.* **1979**, *101*, 7738.

(4) Seiwell, L. P. *J. Am. Chem. Soc.* **1974**, *96*, 7134.

10.1021/ic050007n CCC: $30.25
Published on Web 05/06/2005

William D. Jones was born in Philadelphia, PA, in 1953 and was inspired to work in inorganic chemistry as an undergraduate researcher with Mark S. Wrighton at Massachusetts Institute of Technology (B.S., 1975). He obtained a Ph.D. in chemistry at California Institute of Technology (1979), working with Robert G. Bergman and completing his final year at Berkeley. He moved to the University of Wisconsin as an NSF postdoctoral fellow with 2004 ACS President Chuck Casey, and in 1980, he accepted a position as Assistant Professor at the University of Rochester. He was promoted to Associate Professor in 1984 and Professor in 1987 and is now the Charles F. Houghton Professor of Chemistry. Professor Jones has received several awards, including an Alfred P. Sloan Research Fellowship (1984), a Camille & Henry Dreyfus Foundation Teacher−Scholar Award (1985), a Royal Society Guest Research Fellowship (1988), a Fulbright−Hays Scholar (1988), a John Simon Guggenheim Fellow (1988), and the ACS Award in Organometallic Chemistry (2003). He also has served as an Associate Editor for *J. Am. Chem. Soc.* since 2003. Professor Jones' research interests include organometallic research in strong C−X bond cleavage, catalysis, model studies, mechanisms, kinetics, thermodynamics, and synthetic applications.

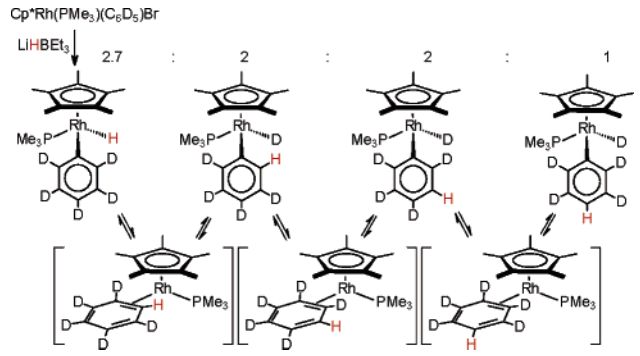
complexes and studying their reductive eliminations. We found that $Cp^*Rh(PMe_3)Cl_2$ could be used to prepare these complexes by reaction with aryl Grignard followed by triethylborohydride. In the reaction of *p*-tolyl Grignard, however, we observed both *p*- and *m*-tolyl hydride isomers. If the reaction was conducted at low temperature, using silver ion to remove chloride ion first, only the *p*-tolyl hydride product was produced. Upon warming to room temperature, equilibration with the *m*-tolyl isomer was observed until a 1:2 para:meta product ratio was obtained (eq 3).



(3)

The fact that the two isomers interconverted in benzene solvent indicated that the rearrangement was intramolecular and could not involve dissociation and readdition of the

Scheme 1



toluene. An η^2-arene complex was proposed as an intermediate, as had been suggested in earlier work by Parshall[5] and Chatt and Davidson.[6] Intermolecular exchange could be induced by heating the sample to 60 °C, and extrapolation of the rate to room temperature indicated a barrier to reductive elimination of 25.6 kcal/mol.[7]

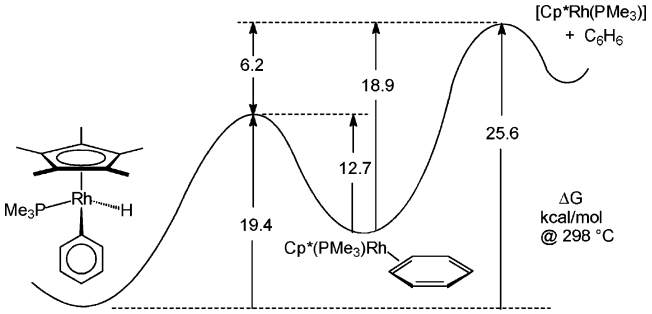
Further evidence for this η^2-arene intermediate came from preparation of the perdeuteriophenyl hydride complex, as shown in Scheme 1. The initial hydride complex was seen to convert first to the ortho-H species, then to the meta-H isomer, and then to the para-H isomer until at equilibrium a 2.7:2:2:1 ratio of the four isomers was observed. The intermediacy of distinct η^2-benzene intermediates accommodates the sequential migration around the ring. While the ratio of hydrogen on the phenyl ring is statistical, a preference for hydride on the metal center can be noted. By monitoring the rate of this migration, a barrier for the formation of the η^2-benzene complex from the phenyl hydride (reductive coupling) of 19.4 kcal/mol can be determined.[8]

In 1989, the author spent a sabbatical leave with Robin Perutz at the University of York. Perutz was actively investigating C−H activation with the corresponding CpRh complexes and undertook an experiment in which $Cp^*Rh(PMe_3)(C_2H_4)$ was irradiated in benzene solution using an excimer laser, and a transient was monitored ($\lambda_{max} = 370$ nm), having a lifetime of ~200 μs. This species was assigned as the η^2-benzene complex $Cp^*Rh(PMe_3)(\eta^2\text{-}C_6H_6)$, and the barrier to C−H oxidative cleavage was determined to be 12.7 kcal/mol.[9]

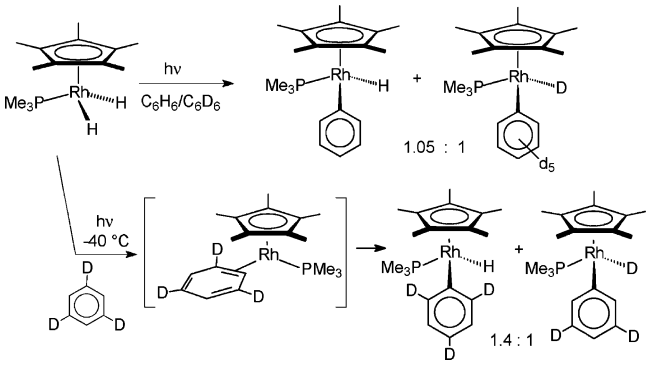
The experiment by Perutz allowed a complete kinetic and thermodynamic analysis of arene activation by the fragment $[Cp^*Rh(PMe_3)]$. As shown in Scheme 2, the η^2-benzene complex must lie 6.7 kcal/mol higher in energy than the phenyl hydride complex (= 19.4−12.7). Furthermore, the pathway leading to dissociation of the arene is 6.2 kcal higher in energy than the pathway for oxidative cleavage of the C−H bond. It is interesting to note that, since the pathway for oxidative addition of benzene to $[Cp^*Rh(PMe_3)]$ must be the same as that for reductive elimination of benzene from $Cp^*Rh(PMe_3)(C_6H_5)H$, the rate-determining step for arene activation involves coordination to the π-system of the arene, not cleavage of the strong C−H bond. Once the arene is coordinated to the metal, the cleavage of the C−H bond is the *lowest* energy process available to the intermediate, so C−H activation is observed.[8]

(5) (a) Parshall, G. W. *Homogeneous Catalysis*; John Wiley and Sons: New York, 1980; p 123. (b) Parshall, G. *Catalysis* **1977**, *1*, 334.
(6) Chatt, J.; Davidson, J. M. *J. Chem. Soc.* **1965**, 843.
(7) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 4240.
(8) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1984**, *106*, 1650.
(9) Belt, S. T.; Dong, L.; Duckett, S. B.; Jones, W. D.; Partridge, M. G.; Perutz, R. N. *J. Chem. Soc., Chem. Commun.* **1991**, 266.

Scheme 2



Scheme 3

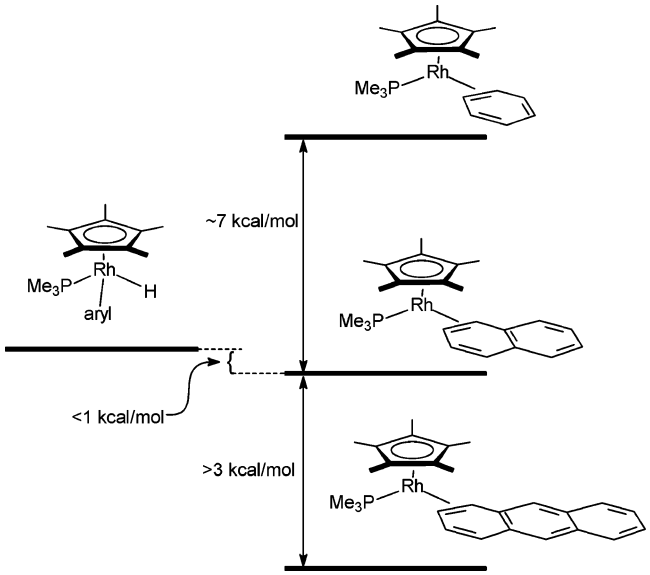


As mentioned above, we observed an equilibrium isotope effect in the scrambling of isomers generated from Cp*Rh(PMe$_3$)(η^2-C$_6$D$_5$H). The isotope effects on the individual steps in arene activation were investigated separately in two experiments (Scheme 3). First, irradiation of Cp*Rh(PMe$_3$)H$_2$ in a 1:1 mixture of C$_6$H$_6$/C$_6$D$_6$ gave a 1.05:1 ratio of C−H versus C−D activation products. The experimental conditions were such that once an arene is activated, it does not come off of the metal. Therefore, this ratio corresponds to the isotope effect for the binding of the 16-electron fragment [Cp*Rh(PMe$_3$)] to the arene (i.e., the barrier for formation of the η^2-arene complex). In the second experiment, Cp*Rh(PMe$_3$)H$_2$ was irradiated in a solution of 1,3,5-trideuteriobenzene in cyclopentane at −40 °C. In this case, only one η^2-arene complex can be formed, and the metal must now choose between breaking a C−H or a C−D bond. The ratio of products indicates that $k_H/k_D = 1.4$ for the step in which the C−H bond is broken. These experiments together demonstrate that the η^2-arene complex must lie along the reaction coordinate for C−H activation, because if there were a direct oxidative addition pathway, one would anticipate seeing the same isotope effect for each of the above benzene substrates.[10]

It was somewhat surprising for us to discover, in 1989, that η^2-arene complexes of [Cp*Rh(PMe$_3$)] could be directly observed in solution as stable species. In the activation of naphthalene, both the C−H activation product (β-position) and the η^2-naphthalene (1,2-position) were observed in a 1:2 equilibrium with each other. The intramolecular interconversion of these two species was sufficiently rapid that one could follow the interchange via spin saturation transfer by ^{31}P NMR spectroscopy, giving a barrier for interchange of 19.4 kcal/mol at 25 °C.[11]

Upon examination of anthracene as substrate, it was found that *only* the η^2-arene complex could be observed, indicating

Scheme 4

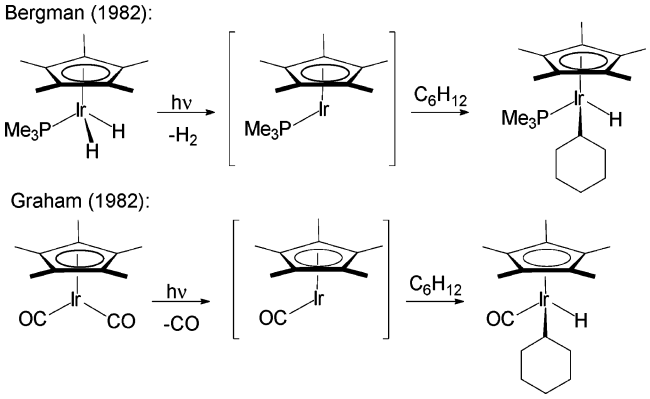


that now the η^2-complex was even more stable. The difference in energy of the complexes of these three substrates (benzene, naphthalene, and anthracene) is attributed to the relative energies of the η^2-arene complexes, because the C−H activation products are likely to be at very similar energies since the aryl−H and Rh−aryl bond strengths are likely to be similar. Scheme 4 shows a diagram of these relative energies. It was recognized that the stabilities of these complexes can be associated with the loss of resonance energy upon complexation. Indeed, calculation of the Huckel resonance energy of the bound versus free arene was found to be a good predictor of the product distribution (C−H activation vs η^2-coordination) for a whole series of fused polycyclic aromatic substrates. The balance point in terms of equilibrium energy corresponds to ~1.25 β, where β represents the interaction energy of two p-orbitals on adjacent carbon atoms in the Huckel energy model.[12] That is, if coordination of the metal to the arene costs more than 1.25 β in resonance energy, then C−H activation will be observed. Otherwise, the η^2-arene complex will be favored.

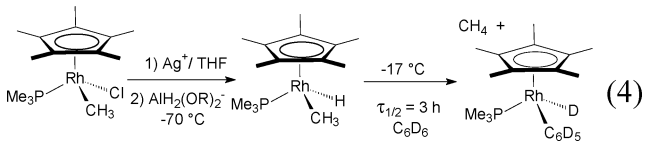
The above experiments provide evidence for formation of an η^2-arene complex prior to C−H activation but say little of the actual transition state for C−H cleavage. Parkin has examined the complex [Me$_2$Si(C$_5$Me$_4$)$_2$]W(Ph)H computationally and found that reductive elimination to give a σ-C−H complex that rearranges to the η^2-benzene complex is energetically favored over a "direct" pathway connecting the phenyl hydride and η^2-benzene complexes.[13] Oxidative addition therefore would proceed by rearrangement of the η^2-arene complex to a σ-C−H complex prior to oxidative cleavage of the bond. This study therefore suggests that it is likely that the rhodium systems also proceed through a σ-C−H intermediate, although no direct spectroscopic evidence was observed for such a species. Such an intermediate would likely have an extremely short lifetime. It is also worth noting that in the activation of ethylene by the fragment [Cp*Ir(PMe$_3$)], Bergman provided evidence that the π-complex was *not* an intermediate in the vinylic C−H activation (vide infra).[14]

(10) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1986**, *108*, 4814.
(11) (a) Jones, W. D.; Dong, L. *J. Am. Chem. Soc.* **1989**, *111*, 8722. (b) Chin, R. M.; Dong, L.; Duckett, S. B.; Jones, W. D. *Organometallics* **1992**, *11*, 871.
(12) Chin, R. M.; Dong, L.; Duckett, S. B.; Partridge, M. G.; Jones, W. D.; Perutz, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 7685.
(13) Churchill, D. G.; Janak, K. E.; Wittenberg, J. S.; Parkin, G. *J. Am. Chem. Soc.* **2003**, *125*, 1403.

Scheme 5



Fundamental Studies with Cp*Rh(PMe$_3$)(alkyl)H. Going back to our earliest studies with Cp*Rh aryl hydride complexes, we had also synthesized the analogous methyl hydride derivative. Its stability, however, was far different than that of its aryl hydride counterparts. In fact, treatment of Cp*Rh(PMe$_3$)MeCl with $LiAlH_2(OR)_2$ led initially to only decomposition products. It was discovered that preliminary removal of chloride ion using Ag^+ followed by reduction with $LiAlH_2(OR)_2$ at low temperature did indeed produce the methyl hydride, Cp*Rh(PMe$_3$)MeH. This species, however, was very unstable and decomposed at about −20 °C in the presence of benzene to give the more stable phenyl hydride complex and methane (eq 4).[15]

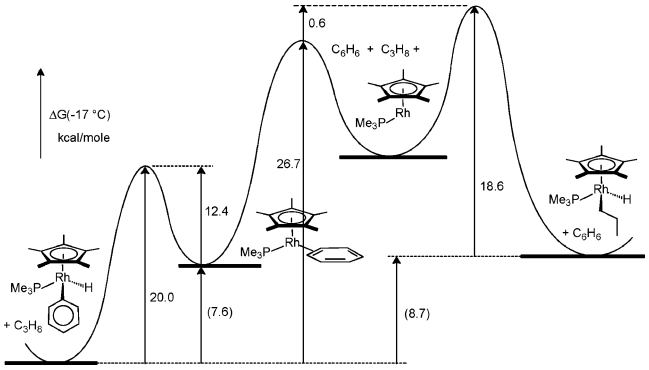


(4)

It was about this time in 1982 that Janowicz and Bergman[16] and Hoyano and Graham[17] reported their remarkable experiments with Cp*Ir complexes. In each case, irradiation of a precursor to [Cp*IrL] (L = PMe$_3$, CO) in cyclohexane solution led to the formation of stable alkyl hydride products (Scheme 5). Upon learning of these results, we realized that if the rhodium fragment we had been studying for arene activation were to be capable of alkane activation, then the fragment would have to be generated in alkane solvent at temperatures less than −20 °C. We accomplished this task by irradiation of Cp*Rh(PMe$_3$)H$_2$ in liquid propane at −50 °C. At this temperature, the product Cp*Rh(PMe$_3$)($CH_2CH_2CH_3$)H was stable, and the solvent could be evaporated at −40 °C without decomposition. The alkane activation product could then be taken up in THF-d_8 at low temperature and fully characterized spectroscopically. Just as in the case of the methyl hydride, alkane reductive elimination was observed at −17 °C in the presence of benzene to give propane plus Cp*Rh(PMe$_3$)(Ph)H ($\Delta G^{\ddagger}$ = 18.6 kcal/mol).[15]

One additional experiment allowed the connection to be made between alkane and arene activation, namely, the competitive activation of alkane versus arene C−H bonds. This selectivity was determined by irradiation of Cp*Rh(PMe$_3$)H$_2$ in a mixture of benzene/propane at −48 °C, producing a 4.2:1 ratio of Cp*Rh(PMe$_3$)(Ph)H:Cp*Rh(PMe$_3$)($CH_2CH_2CH_3$)H. This kinetic selectivity corresponds to only a 0.6 kcal/mol preference for activation of the much stronger aromatic C−H bonds. The addition of propane activation to the picture for benzene activation in Scheme 2 allows these two reactions to be compared. As shown in Scheme 6, there is a slightly higher barrier to activate propane than to activate benzene. The *n*-propyl hydride product, however, is fairly unstable and undergoes reductive elimination via a process that must be the microscopic reverse of oxidative addition with a barrier of 18.6 kcal/mol. These values can be combined with those established for benzene activation to establish that benzene activation is thermodynamically favored by 8.7 kcal/mol or ∼24 million × over alkane activation. This preference is observed despite the fact that the benzene C−H bond is almost 10 kcal/mol stronger than the propane primary C−H bond. The reason for this favorability must lie in the fact that the rhodium−aryl bond is so much stronger than the rhodium−alkyl bond that the difference in M−C bond strengths more than makes up for the difference in C−H bond strengths. Consequently, the kinetic and thermodynamic preference for cleavage of aromatic C−H bonds over aliphatic C−H bonds can be seen to be attributable to the following: (i) the formation of a stable η^2-arene complex rather than cleavage of the strong arene C−H bond and (ii) the formation of a rhodium−aryl bond that is much stronger than the rhodium−alkyl bond.[18]

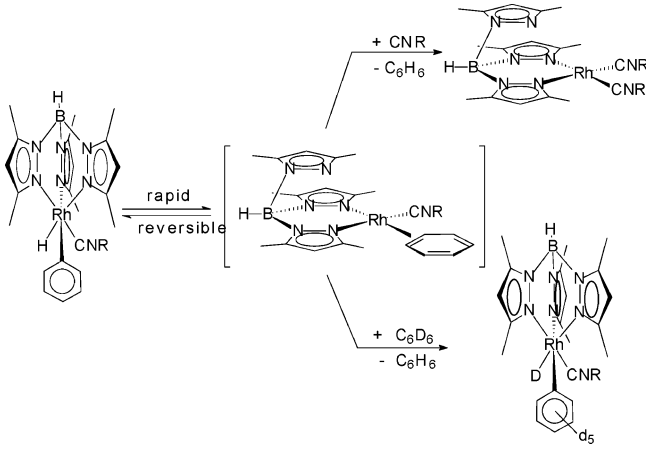
Scheme 6



Fundamental Studies with Tp′Rh(CNR)(R)H. It was generally recognized, largely due to the work of S. Trofimienko, that trispyrazolylborate complexes of metals were quite similar to cyclopentadienyl complexes of metals, based upon the large numbers of related compounds that had been synthesized.[19] In 1989, we initiated studies on tris-(3,5-dimethylpyrazolyl)borate (Tp′) complexes of rhodium. We initially succeeded by the reaction of [Rh(CNR)$_2$(μ-Cl)]$_2$ with KTp′ to isolate Tp′Rh(CNR)$_2$ (CNR = neopentylisocyanide), presumed to be analogous to Cp*Rh(CNR)$_2$, but soon discovered that the Tp′ was only κ^2 in this d^8 Rh(I) product.[20] Nevertheless, irradiation of the 16-electron square planar bis-isocyanide complex in benzene did yield the κ^3-phenyl hydride activation product Tp′Rh(CNR)(Ph)H in moderate yield. It was soon discovered that conversion of one of the isocyanide ligands to a carbodiimide ligand by treatment of the bis-isocyanide complex with phenyl azide gave a complex that was very photolabile. With this carbodiimide complex,

(14) Stoutland, P. O.; Bergman, R. G. *J. Am. Chem. Soc.* **1985**, *107*, 4581.
(15) Jones, W. D.; Feher, F. J. *Organometallics* **1983**, *2*, 562.
(16) Janowicz, A. H.; Bergman, R. G. *J. Am. Chem. Soc.* **1982**, *104*, 352.
(17) Hoyano, J. K.; Graham, W. A. G. *J. Am. Chem. Soc.* **1982**, *104*, 3723.
(18) (a) Jones, W. D. In *Activation and Functionalization of Alkanes*; Hill, C., Ed.; John Wiley and Sons: New York, 1989; Chapter 4, pp 111−149. (b) Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* **1989**, *22*, 91.
(19) See: Trofimenko, S. *Scorpionates, the Coordination Chemistry of Polypyrazolylborate Ligands*; Imperial College Press: London, 1999.
(20) Jones, W. D.; Hessell, E. T. *Inorg. Chem.* **1991**, *30*, 778.

Scheme 7

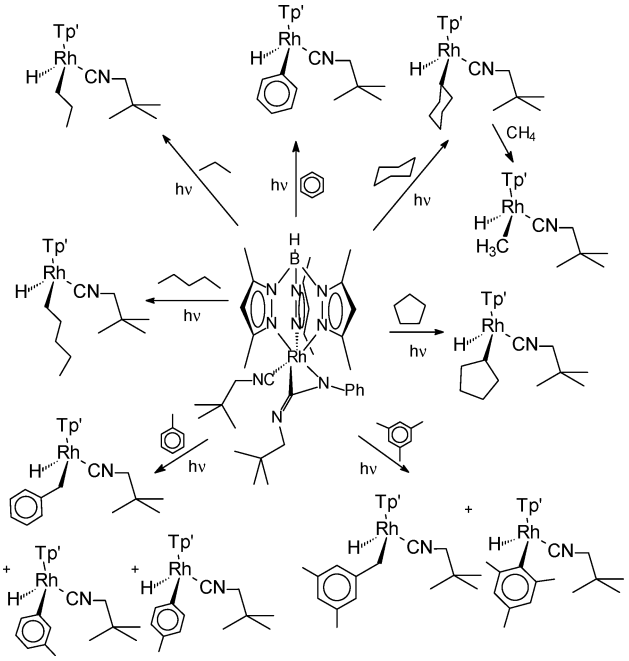


near quantitative formation of the phenyl hydride C−H activation product could be obtained.[21] This species was found to undergo exchange with C_6D_6 upon heating to ∼60 °C, with activation parameters consistent with a dissociative process ($\Delta H^{\ddagger} = 37.8$ kcal/mol; $\Delta S^{\ddagger} = +23$ e.u.). This large positive $\Delta S^{\ddagger}$ may reflect a κ^3 to κ^2 Tp′ coordination change prior to the rate-determining step. On the other hand, reaction with added isocyanide proceeded *more rapidly than benzene exchange* to give the bis-isocyanide complex. Activation parameters for this latter process were consistent with an associative mechanism ($\Delta H^{\ddagger} = 15.2$ kcal/mol; $\Delta S^{\ddagger} = -35$ e.u.), and the kinetics for the reaction showed a dependence upon the added isocyanide concentration. These observations led to the hypothesis of the intermediacy of an η^2-arene complex similar to that seen in the case of [Cp*Rh(PMe_3)] (Scheme 7). The intermediate η^2-benzene complex, now d^8 Rh(I), was presumed to be a 16-electron square planar intermediate. Consequently, associative substitution of benzene by isocyanide would be expected.[22]

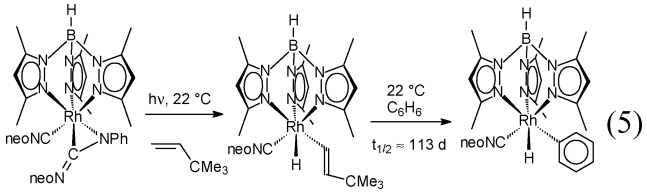
Further evidence for such an η^2-benzene intermediate came from a ring-walk experiment. The C_6D_6 activation product was first prepared and converted to the aryl chloride derivative prior to exchange of chloride for hydride. The perdeuteriophenyl hydride complex was then monitored by NMR spectroscopy to determine the location of the hydrogen in the arene ring as it appeared. In stark contrast to the Cp*Rh system, the hydrogen was observed to appear in ortho, meta, and para positions *at the same rate*. This observation led to the conclusion that the η^2-arene complex must be fluxional, not an unreasonable assumption in light of the greater stability of the d^8 square planar Rh(I) intermediate.[22]

As mentioned above, the high photolability of the carbodiimide ligand allowed the facile generation of the reactive fragment [Tp′Rh(CNR)] in almost any solvent. In fact, this fragment was observed to react with a wide variety of arene and alkane C−H bonds, as summarized in Scheme 8.[23] While the aryl hydride products were of similar stability to those of the [Cp*Rh(PMe_3)] fragment, the alkyl hydride products have reasonable stabilities at ambient temperature. Therefore, irradiation in pentane gave the *n*-pentyl hydride product (primary C−H activation only), which had a half-life for loss of pentane of about 1 h at 22 °C. This stability allowed a variety of reactions to be examined and the products

Scheme 8

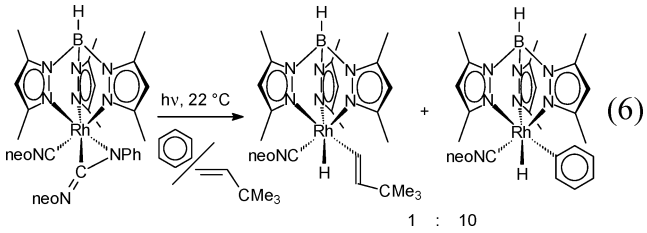


isolated. For example, vinylic C−H activation could now be seen with the substrate *tert*-butylethylene. The product is extremely stable, similar to the phenyl hydride product, losing *tert*-butylethylene over several months at 25 °C (eq 5).



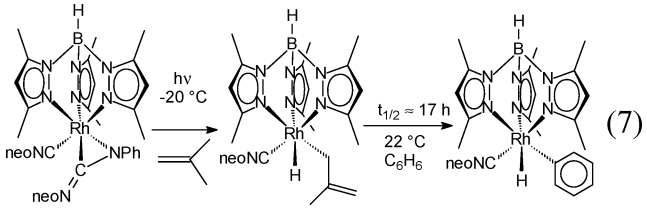
(5)

In terms of kinetic selectivity, irradiation of the carbodiimide in a mixture of benzene/*tert*-butylethylene produced a 10:1 mixture of C−H activation products (eq 6).



(6)

Similarly, irradiation of the carbodiimide complex in propylene gave only the allylic C−H activation product, which rearranged to the propene complex. Therefore, olefin complexation does not precede allylic C−H activation (cf. earlier work by Stoutland and Bergman[14]). Irradiation in isobutylene gives an analogous allylic activation product, but now reductive elimination to regenerate isobutylene and [Tp′Rh(CNR)] occurs rather than formation of the olefin complex (eq 7).[24]



(7)

(21) Hessell, E. T.; Jones, W. D. *Organometallics* **1992**, *11*, 1496.
(22) Jones, W. D.; Hessell, E. T. *J. Am. Chem. Soc.* **1992**, *114*, 6087.
(23) Jones, W. D.; Hessell, E. T. *J. Am. Chem. Soc.* **1993**, *115*, 554.

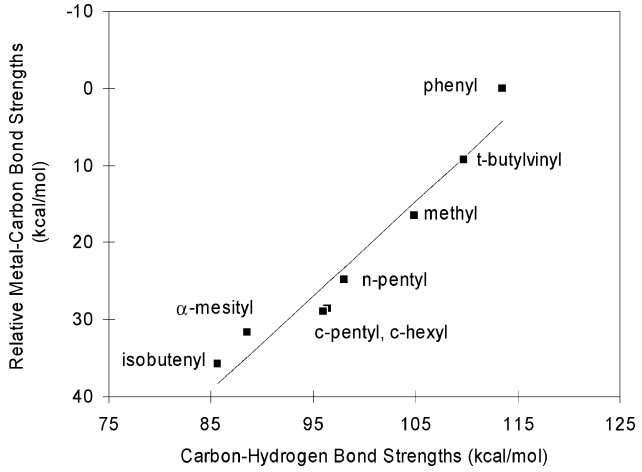
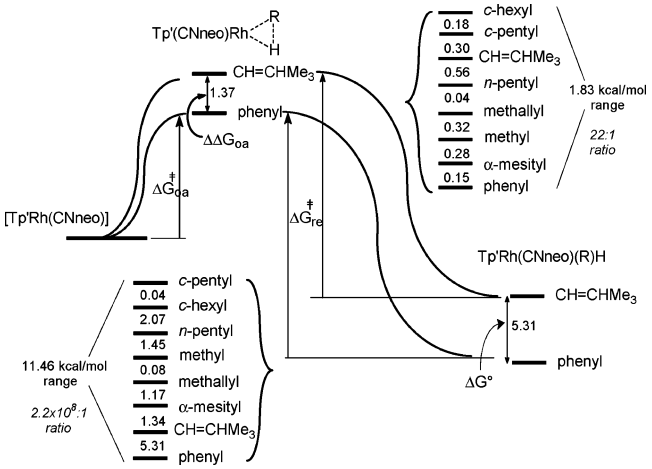


Figure 1. Plot of relative M−C vs C−H bond strengths. Slope = 1.22.

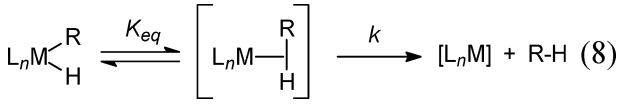
Scheme 9



On the basis of these competition and reductive elimination studies, one can generate a free energy diagram relating the competitive activation of these various substrates by combining the difference in free energy from the competition experiments ($\Delta\Delta G^{\ddagger}_{oa}$) with the barriers for reductive elimination ($\Delta G^{\ddagger}_{re}$) for each substrate. This is shown schematically in Scheme 9, where the results with eight different substrates are listed. One can see that the difference in kinetic selectivity is rather small, spanning a range of only 1.8 kcal/mol (which corresponds to 22:1 selectivity), whereas the difference in thermodynamic selectivity is immense, spanning a range of 11.5 kcal/mol (which corresponds to a 220 million:1 selectivity)! Therefore, the earlier conclusions made regarding C−H activation by the [Cp*Rh(PMe_3)] fragment appear to be applicable to the [Tp′Rh(CNR)] fragment as well.[24]

From a thermodynamic cycle relating M−C to M−H bond energies, one can determine relative rhodium−carbon bond strengths in this series of compounds. The results are shown in Figure 1, in which the M−C bond strength is plotted relative to the C−H bond strength. The slope of the best line drawn through these data is ∼1.2, consistent with the conclusion that the difference in metal−carbon bond strengths is larger than the difference in C−H bond strengths. There are some minor deviations from this trend. For example, a line joining the point for isobutenyl and cyclopentyl derivatives has a slope of only 0.8, which means that the difference in C−H bond strengths exceeds the difference in M−C bond strengths so that cleavage of the weaker C−H bond (butenyl) will be favored thermodynamically.[24]

One major advantage of exploring the trispyrazolylborate complexes over the cyclopentadienyl complexes has been their use in establishing the presence of σ-alkane complexes as intermediates. Following the initial discoveries of alkane activation in the 1980s, it became clear that there was ample evidence for the intermediacy of a metal-complexed alkane prior to cleavage of the C−H bond. Therefore, alkane oxidative addition is widely considered to take place in two steps: alkane coordination followed by C−H oxidative cleavage.[25] Likewise, alkane reductive elimination takes place via two steps: alkane reductive coupling followed by alkane dissociation (eq 8).



(8)

In this sense, alkane activation is similar to arene activation in that an intermediate is formed prior to cleavage of the C−H bond. Evidence for these species largely came from the observation of deuterium scrambling in alkyl deuteride complexes prior to dissociation of the alkane,[26] although transient spectroscopic techniques also provide evidence for these intermediates in related systems.[27,28] In one case, direct observation of a σ-alkane complex has been seen by NMR spectroscopy, although no C−H activation occurred in this case.[29] There are also two cases where interaction of an alkane with the vacant site of a metal is reported.[30]

We discovered that we could synthesize a *secondary* alkyl hydride complex of a linear alkane by using a very reactive reducing agent, Cp_2ZrH_2. This zirconium species is only sparingly soluble in benzene, but it rapidly undergoes metathesis of H for Cl, giving rise to insoluble Cp_2ZrHCl and Cp_2ZrCl_2. Therefore, we were able to rapidly convert Tp′Rh(CNR)(i-propyl)Cl to Tp′Rh(CNR)(i-propyl)H and monitor the changes that occurred in benzene-d_6 solution. The first thing we saw was that the isopropyl hydride complex had a lifetime of about 30 min at room temperature. This meant that, had secondary alkane activation occurred during the photolysis of the carbodiimide complex in liquid propane (Scheme 8), we should have easily seen it. We did not. Therefore selective activation of primary C−H bonds is kinetically preferred exclusively over secondary C−H bonds. The next thing we saw was the appearance and then slow disappearance of the *n*-propyl hydride complex. Because the reaction was conduc-

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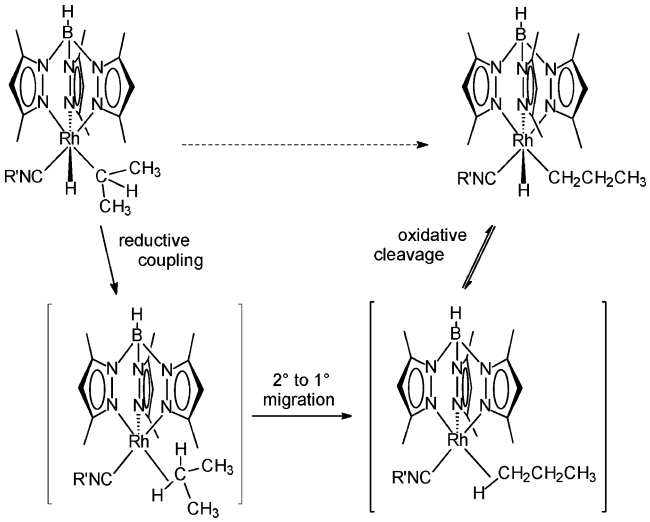
(26) Wick, D. D.; Reynolds, K. A. R.; Jones, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 3974.
(27) (a) Bromberg, S. E.; Yang, H.; Asplund, M. C.; Lian, T.; McNamara, B. K.; Kotz, K. T.; Yeston, J. S.; Wilkens, M.; Frei, H.; Bergman, R. G.; Harris, C. B. *Science* **1997**, *278*, 260. (b) Asplund, M. C.; Snee, P. T.; Yeston, J. S.; Wilkens, M. J.; Payne, C. K.; Yang, H.; Kotz, K. T.; Frei, H.; Bergman, R. G.; Harris, C. B. *J. Am. Chem. Soc.* **2002**, *124*, 10605.
(28) (a) Sun, X.-Z.; Grills, D. C.; Nikiforov, S. M.; Poliakoff, M.; George, M. W. *J. Am. Chem. Soc.* **1997**, *119*, 7521. (b) Childs, G. I.; Colley, C. S.; Dyer, J.; Grills, D. C.; Sun, X.-Z.; Yang, J.; George, M. W. *J. Chem. Soc., Dalton Trans.* **2000**, *12*, 1901.
(29) (a) Geftakis, S.; Ball, E. *J. Am. Chem. Soc.* **1998**, *120*, 9953. (b) Lawes, D. J.; Geftakis, S.; Ball, G. E.; *J. Am. Chem. Soc.* **2005**, *127*, 4134.
(30) (a) Evans, D. R.; Drovetskaya, T.; Bau, R.; Reed, C. A.; Boyd, P. D. W. *J. Am. Chem. Soc.* **1997**, *119*, 3633. (b) Castro-Rodriguez, I.; Nakai, H.; Gantzel, P.; Zakharov, L. N.; Rheingold, A. L.; Meyer, K. *J. Am. Chem. Soc.* **2003**, *125*, 15734.

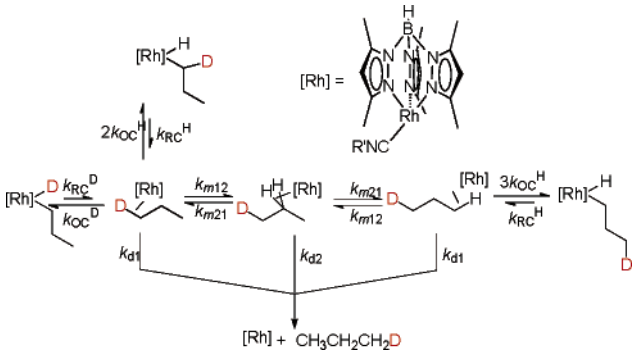
Scheme 10



ted in benzene solvent, the rearrangement had to occur intramolecularly without dissociation of alkane. This was proposed to occur via the secondary and primary σ-alkane complexes (Scheme 10).[31] We performed this same experiment using Cp_2ZrD_2 as reductant, resulting in a similar interchange of species at slightly different rates due to the deuterium that was present. Since the first step (reductive coupling) is irreversible in this system, the relative rates of disappearance of the starting isopropyl hydride/deuteride complexes must reflect the isotope effect on the reductive coupling step. This value was found to be ~ 2 ($= k_{rc}^{H}/k_{rc}^{D}$). The isotope effect for the reverse process, oxidative cleavage, was determined by irradiation of the carbodiimide complex in the presence of CH_2D_2. Once methane is bound, the metal must choose between C−H and C−D bonds, and the kinetic product distribution will then reflect the isotope effect on the oxidative cleavage step itself. From this experiment, $k_{oc}^{H}/k_{oc}^{D} \approx 4$.[32]

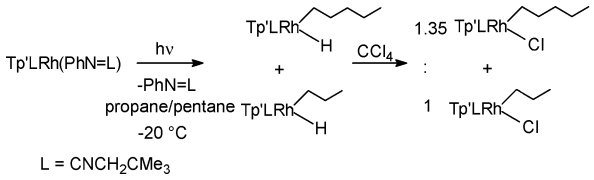
With these fundamental isotope effects in hand, we were then able to analyze a series of rearrangements of alkyl deuteride complexes. For example, rearrangement of the methyl deuteride Tp′Rh(CNR)(CH_3)D produces significant quantities of Tp′Rh(CNR)(CH_2D)H prior to elimination of CH_3D. There are five rate constants in the kinetic model describing this system (k_{oc}^{H}, k_{oc}^{D}, k_{rc}^{H}, k_{rc}^{D}, and $k_{dissociation}$), too many to be determined by simulation of the kinetics. However, one can successfully simulate the distribution of species by inclusion of the isotope effects described above and by restricting the simulation to give only relative rates for reaction. These relative rates are what describes he selectivity in the σ-methane complex. Likewise additional simulations of the *n*-propyl deuteride and isopropyl deuteride complex led to the establishment of the relative rates for the processes available to these complexes (Scheme 11). In consideration of larger linear alkanes, these processes include oxidative cleavage (k_{oc}), reductive coupling (k_{rc}), dissociation from a primary C−H bond (k_{d1}), dissociation from a secondary C−H bond (k_{d2}), migration from a primary C−H bond to a secondary C−H bond (k_{m12}), migration from a secondary C−H bond to a primary C−H bond (k_{m21}), and migration from a secondary C−H bond to a secondary C−H bond (k_{m22}). On the basis of the kinetic studies, the relative rates of these processes can be established for any given σ-alkane complex.[31,33]

Scheme 11



As shown in Figure 2, dissociation is the slowest process for all of the σ-alkane complexes. For methane, C−H oxidative cleavage is about 11× faster than dissociation. For ethane, C−H oxidative cleavage is about 4× faster than dissociation, and end-to-end migration is about 2× faster than dissociation. For propane, a similar selectivity in relative rates is seen, with C−H oxidative cleavage being the fastest process, migration from the methyl to the methylene intermediate in rate, and dissociation the slowest. Once the metal is attached to the middle of the propane (methylene), it can now migrate back to the end or dissociate with similar ease. (Remember, no oxidative cleavage takes place in the secondary position.) For butane, a similar set of relative rates is seen, but now migration from methylene to methylene is seen to be very rapid, much faster than dissociation. This means that if the rhodium binds to the middle of an alkane chain, the metal can quickly migrate to the end, where it then inserts. This rapid migration is consistent with the fact that only terminal C−H activation is seen in the linear hydrocarbons.[31,33]

One last area that has been addressed is the determination of the selectivity of the unsaturated metal fragment for coordination to a methylene group versus a methyl group. Which is faster (Scheme 12)? To address this question, we have looked at a competition between pentane and propane, two substrates containing the same number of methyl groups but different numbers of methylene groups. In the competition experiment, a 1.35:1 ratio of *n*-pentyl hydride:*n*-propyl hydride products is seen (eq 9).



(9)

Since the kinetic studies discussed above provide a basis for understanding the evolution of a σ-alkane complex once it is formed, one can simulate the selectivity for primary (k_{CH_3}) vs secondary (k_{CH_2}) coordination and adjust the ratio to match the experimentally observed result. We find that a methylene group must coordinate 1.5× faster than a methyl group in order to match the experimental observation. Therefore, while coordination to the secondary C−H bonds of an alkane is more rapid than to a primary C−H bond, activation is too slow at these positions to be observed, and the more rapid process of migration to the end leads to observation of only terminal activation products.[34]

(31) Northcutt, T. O.; Wick, D. D.; Vetter, A. J.; Jones, W. D. *J. Am. Chem. Soc.* **2001**, *123*, 7257.

(32) Jones, W. D. *Acc. Chem. Res.* **2003**, *36*, 140.

(33) See also Chapter 3 in ref 1b.

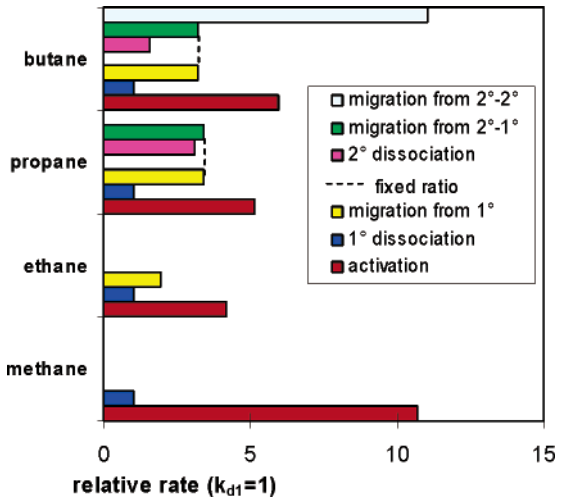
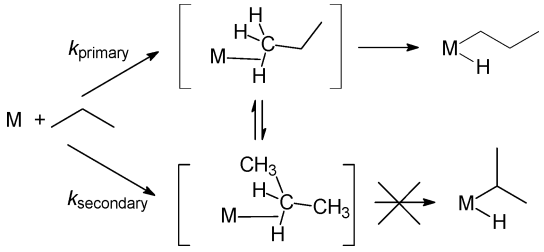


Figure 2. Bar graph of relative rates of processes in primary and secondary σ-alkane complexes of the type Tp′Rh(CNneopentyl)(σ-RH).

Scheme 12

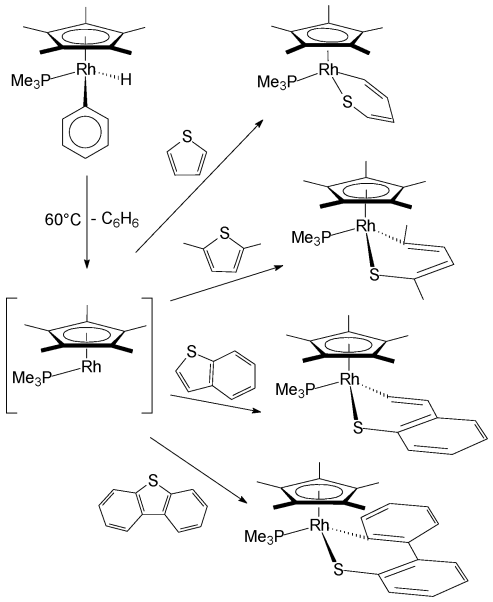


Homogeneous Models for the C−S Bond Cleavage Step in Hydrodesulfurization. In the course of examining the C−H bond activation reactions of arenes using the [Cp*Rh(PMe$_3$)] fragment, it was only natural that we examine reactions with heterocycles. While most heterocycles gave aryl hydride products via C−H activation, thermolysis of Cp*Rh(PMe$_3$)PhH in the presence of thiophene led to a product that did not contain a hydride ligand. Instead, the metal was found to insert into the C−S bond of the conjugated thiophene ring. This reaction was found to be quite general, with methylated thiophenes and dibenzothiophene also undergoing clean insertion reactions. Benzothiophene showed 100% selectivity for cleavage of the vinylic C−S bond, despite the fact that a stronger Rh−aryl bond could have been formed (Scheme 13).[35] Also, all of the metallacycles were found to be bent *except that with thiophene*, in which the metallacycle was planar. A theoretical investigation of the system showed the puckering to be attributable to steric interactions with any group attached to the carbon bound to the rhodium.[36]

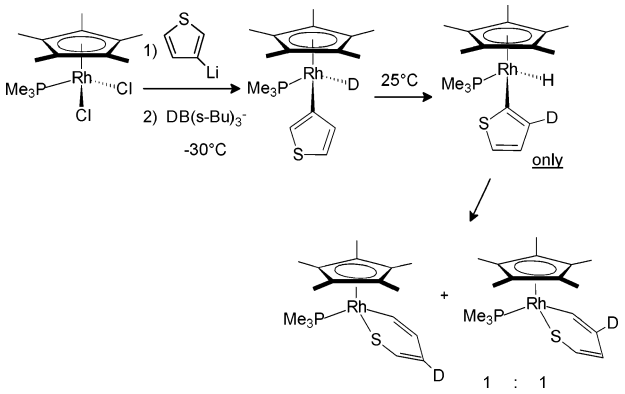
Several competition and labeling studies were examined to investigate the mechanism of the reaction. Upon irradiation of Cp*Rh(PMe$_3$)H$_2$ in the presence of thiophene at low temperature, a 3:1 ratio of C−S insertion and C$_\alpha$-H insertion were observed. Upon standing at room temperature, the α-thienyl hydride product converted into the more stable C−S insertion product. Further investigation of this rearrangement showed it to be intramolecular. One key experiment was the synthesis of the even less stable β-thienyl deuteride complex at −30 °C. Upon warming to RT, this species rearranges regiospecifically to the β-D-α-thienyl hydride product (Scheme 14). More slowly, the α-thienyl product rearranges to the C−S insertion product, but this latter step occurs with loss of regiospecificity. The mechanism proposed for these rearrangements is shown in Scheme 15, in which the reversible C−H/C−D activation reactions shuttle between the β-thienyl and α-thienyl hydride derivatives but always on the same double bond of the thiophene, thereby preserving regiospecificity in this rearrangement. More slowly, the metal in the η^2-thiophene complex migrates irreversibly to the sulfur, and then goes on to insert into the C−S bond. Since the S-bound intermediate has C_s symmetry, regiospecificity is lost in this step of the reaction.[37]

The rates of these various processes could be monitored, and from the rates the barriers to reactions were established. As shown in Scheme 16, the free energy diagram establishes the relative energies of the α-thienyl, β-thienyl, and C−S insertion products and also establishes the barrier heights to their interconversion. The η^2-thiophene and η^1-*S*-thiophene adducts are not seen directly but are the implied intermediates in the reaction that interconvert intramolecularly (i.e., without dissociation). It is interesting to compare this system with the [CpRe(CO)$_2$] system, in which no C−S or C−H cleavage

Scheme 13

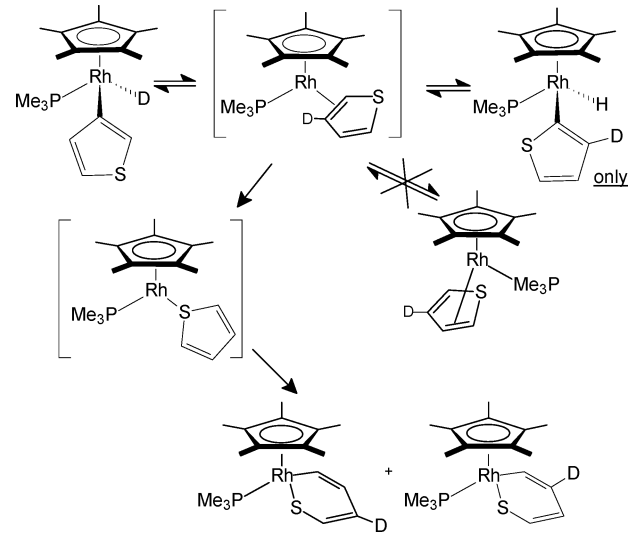


Scheme 14

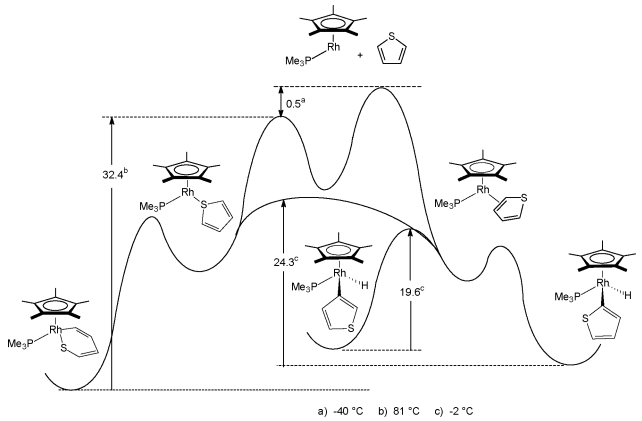


(34) Vetter, A. J.; Flaschenriem, C.; Jones, W. D. *J. Am. Chem. Soc.* (submitted for publication).
(35) Jones, W. D.; Dong, L. *J. Am. Chem. Soc.* **1991**, *113*, 559.
(36) (a) Blonski, C.; Myers, A. W.; Palmer, M.; Harris, S.; Jones, W. D. *Organometallics* **1997**, *16*, 3819. (b) See also: Sargent, A. L.; Titus, E. P. *Organometallics* **1998**, *17*, 65. (c) Maresca, O.; Maseras, F.; Lledos, A. *New J. Chem.* **2004**, *28*, 625.

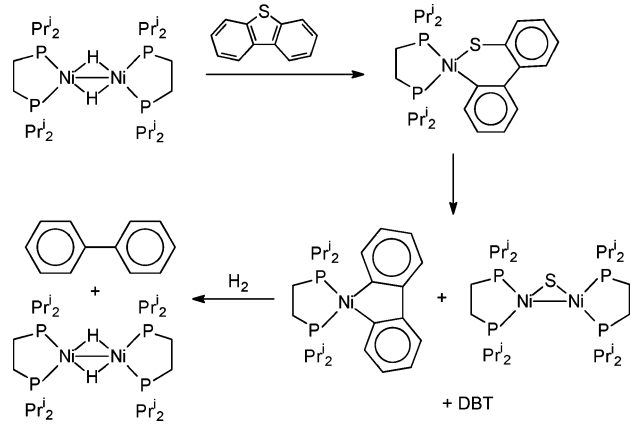
Scheme 15



Scheme 16

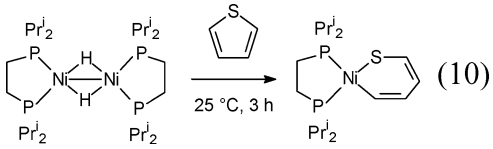


Scheme 17



occurs but in which the η^2-thiophene and *S*-thiophene adducts are observed to be in equilibrium.[38] It is worthwhile to note that as Scheme 16 indicates, the rate-determining step in thiophene activation is coordination to the sulfur, not the π-system of the thiophene. This may have implications for the manner in which thiophenes are desulfurized in the industrial HDS process, although this model system clearly lacks many of the features required for catalytic desulfurization. No further reaction of this compound with dihydrogen occurs, even at elevated temperatures, and the thiophene was found not to be very labile as well.

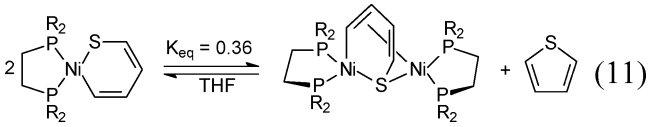
Homogeneous Models for the Catalytic Desulfurization of Dibenzothiophenes in Hydrodesulfurization. In considering further metal complexes that might more aptly serve as models for the heterogeneous HDS process, we realized that it was likely that two metal centers would be needed in order to cleave two C−S bonds.[39] We synthesized the new dinuclear dihydride $[Ni(dippe)H]_2$ (analogous to the Pörschke dihydride $[Ni(dtbpe)H]_2$[40]) with the idea that two metal centers might cleave both thiophene C−H bonds and that the hydride present might produce a reduced organic product. We discovered immediately that this dinuclear complex behaved as a source of mononuclear [Ni(dippe)], a highly reactive Ni^0 fragment, although apparently the species is only produced through an associative reaction of substrate with dimer. In the case of reaction with thiophene, the product is the C−S insertion adduct Ni(dippe)(η^2-C,S-thiophene) (eq 10).



(10)

The single-crystal X-ray structure of this product showed it to be planar with localized double and single bonds around the metallacycle ring, similar to the rhodium complex described earlier.[41]

One difference with the nickel system is that the thiophene was observed to be labile at room temperature, that is, the C−S cleavage was facile and reversible. This was discovered by observing that the [Ni(dippe)] fragment formed by thiophene elimination could coordinate to a second molecule of the insertion complex, giving a dinuclear species in which the ring-opened thiophene bridged the two metal centers (eq 11).



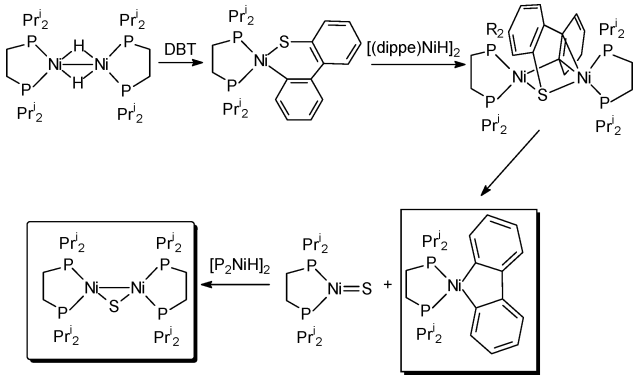
(11)

This equilibrium is quite remarkable in that the energetics are balanced ($K_{eq} = 0.36$) and the reaction involves ring-opening of a pseudo-aromatic ring. A similar activation of benzothiophene occurs and leads to a similar equilibrium ($K_{eq} = 1.3$).[42]

Reaction with dibenzothiophene also occurred at room temperature, but in this case, no equilibrium with a dinuclear counterpart was observed. Instead, loss of dibenzothiophene led to the formation of two new major products (75%), Ni(dippe)(biphenyl) and $Ni_2(dippe)_2(\mu$-S) (Scheme 17). Furthermore, reaction with H_2 led to the formation of free biphenyl and regeneration of the nickel hydride dimer. The sulfur ends up bridging two nickel centers in a very stable configuration and prevents catalytic desulfurization. On the basis of this model, the most difficult step in desulfurization is therefore the removal of sulfur bridging two adjacent metal

(37) Dong, L.; Duckett, S. B.; Ohman, K. F.; Jones, W. D. *J. Am. Chem. Soc.* **1992**, *114*, 151.
(38) Choi, Moon Gun; Robertson, M. J.; Angelici, R. J. *J. Am. Chem. Soc.* **1991**, *113*, 4005.
(39) For an example using $[Cp^*IrH_3]_2$, see: Jones, W. D.; Chin, R. M. *J. Am. Chem. Soc.* **1994**, *116*, 198.
(40) Bach, I.; Goddard, R,; Kopiske, C.; Seevogel, K.; Pörschke, K.-R. *Organometallics* **1999**, *18*, 10.
(41) Vicic, D. A.; Jones, W. D. *J. Am. Chem. Soc.* **1997**, *119*, 10855.
(42) Vicic, D. A.; Jones, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 7606.

Scheme 18

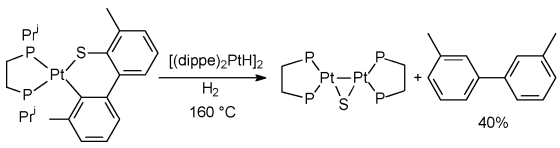


centers, a step that is widely believed to be important in the heterogeneous HDS process using MoCoS.[43]

But what is the mechanism of desulfurization in the nickel system? We believe that the missing link is the dinuclear complex that is seen with thiophene and benzothiophene but not dibenzothiophene. This complex, were it to form, could react further by extracting sulfur to directly generate the Ni−biphenyl product. The terminal nickel sulfido adduct would not be very stable and would be expected to react with more [Ni(dippe)] to give the observed μ-sulfido product (Scheme 18).[42] Alternatively, reaction with another [Ni(dippe)] fragment could lead directly to the μ-sulfido dinuclear product via a trinuclear intermediate.[44] Independent experiments provide evidence for the existence of such a terminal nickel sulfido adduct and for its reaction to give a μ-sulfido dimer.[45]

While dibenzothiophene reacts stoichiometrically with [Ni(dippe)] and dihydrogen to give biphenyl at ambient temperature, the presence of adjacent methyl groups slows this reaction. 4-Methyldibenzothiophene requires 5 days to react and gives a 90% yield of 3-methylbiphenyl. 4,6-Dimethyldibenzothiophene is one of the most difficult thiophenes to desulfurize industrially,[46] and its reaction with $[Ni(dippe)H]_2$ only occurs at 90 °C to give 46% yield of 3,3′-dimethylbiphenyl. Furthermore, no C−S insertion adduct could be seen with this sterically hindered dibenzothiophene.[47]

As such polyalkylated dibenzothiophenes represent a challenge to the modern HDS industry, we sought a metal complex that would provide evidence for the cleavage of these most resistant C−S bonds. The platinum analogue $[Pt(dippe)H]_2$ proved to be successful, reacting with 4,6-dimethyldibenzothiophene at 120 °C to give cleanly the C−S insertion adduct (Figure 3). This complex represents the only such structurally characterized species, and one can observe that the *o*-methyl group is indeed in a position to interfere with ligands attached to the metal center. In this case, the square planar Pt(II) complex has vacant sites above and below the square plane, and it is the region that the *o*-methyl group occupies. As with the nickel−DBT complex, reaction with dihydrogen liberates 3,3′-biphenyl and leaves behind a μ-sulfido dinuclear platinum complex (eq 12).[47]



(12)

While we believe these systems offer insights into what may be happening in the commercial HDS catalysts, further work will be required to make these systems catalytic. It

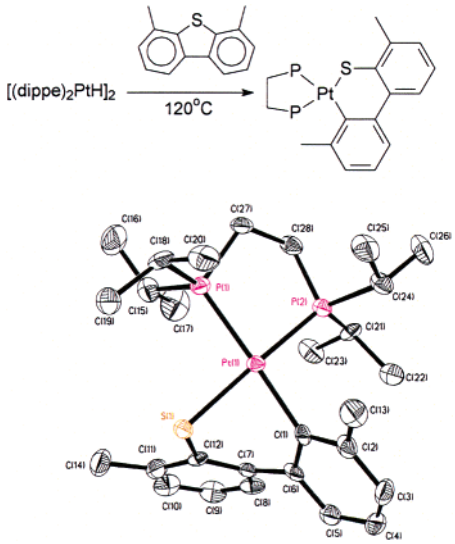


Figure 3. C−S cleavage of 4,6-dimethyldibenzothiophene and an ORTEP drawing of the insertion adduct. Ellipsoids are shown at the 30% level (hydrogens omitted for clarity).

may be that the true value of these studies lies in their ability to serve as models for what happens at the edge of the flat MoCoS particles, where sulfur vacancies are proposed to be required for HDS activity.[46] One can easily envision a ring-opened bridging thiophene complex such as those seen in these studies as being involved in this catalysis.

Conclusions. In the studies carried out in my research group over the past 20+ years, we have tried to take advantage of the ability to use physical organometallic studies to establish the kinetics and thermodynamics that relate to important chemical reactions: the cleavage of strong carbon−element bonds. We have made substantial progress in understanding several of these problems, as outlined here with respect to C−H and C−S activation. Other studies in our group also focus on C−C, C−N, and C−F bond activation, three other classes of strong C−X bonds. We will continue to take advantage of the insight provided by fundamental studies of organometallic reaction mechanisms as to the factors that control chemical reactivity and selectivity. With a better understanding of these factors, we will be able to rationally improve our ability to perform chemical reactions in the 21st century.

Acknowledgment. Acknowledgment is made to the U.S. Department of Energy, Grant FG02-86ER13569, for their support of this work, and to the National Science Foundation, Grant CHE-0414325, for partial support of this research. I also gratefully acknowledge the hard work and contributions of the 34 graduate students, 15 postdoctoral fellows, and 33 undergraduates who did the work that is presented herein. I thank Amy Vetter for her work on the cover graphic design accompanying this manuscript. The University of Rochester is acknowledged for the biography photo of WDJ. Finally, I thank my wife Heather for her support and encouragement throughout my career.

Note Added after Print Publication. A photo and biography were added. This article was originally released ASAP on May 6, 2005. The correct version was posted on July 19, 2005.

IC050007N

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