Activation of Alkanes with Organotransition Metal Complexes

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Summary. Alkanes, although plentiful enough to be considered for use as feedstocks in large-scale chemical processes, are so unreactive that relatively few chemical reagents have been developed to convert them to molecules having useful functional groups. However, a recently synthesized iridium (Ir) complex successfully converts alkanes into hydridoalkylmetal complexes ($\mathrm{M + R{-}H \rightarrow R{-}M{-}H}$). This is a dihydride having the formula $\mathrm{Cp^*(L)IrH_2}$, where Cp* and L are abbreviations for the ligands $\mathrm{(CH_3)_5C_5}$ and $\mathrm{(CH_3)_3P}$, respectively. Irradiation with ultraviolet light causes the dihydride to lose $\mathrm{H_2}$, generating the reactive intermediate Cp*IrL. This intermediate reacts rapidly with C–H bonds in every molecule so far tested (including alkanes) and leads to hydridoalkyliridium complexes Cp*(L)Ir(R)(H). Evidence has been obtained that this C–H insertion, or oxidative addition, reaction proceeds through a simple three-center transition state and does not involve organic free radicals as intermediates. Thus the intermediate Cp*IrL reacts most rapidly with C–H bonds having relatively high bond energies, such as those at primary carbon centers, in small organic rings, and in aromatic rings. This contrasts directly with the type of hydrogen-abstraction selectivity that is characteristic of organic radicals. The hydridoalkyliridium products of the insertion reactions can be converted into functionalized organic molecules—alkyl halides—by treatment with mercuric chloride followed by halogens. Expulsion (reductive elimination) of the hydrocarbon from the hydridoalkyliridium complexes can be induced by Lewis acids or heat, regenerating the reactive intermediate Cp*IrL. Oxidative addition of the corresponding rhodium complexes Cp*RhL to alkane C–H bonds has also been observed, although the products formed in this case are much less stable and undergo reductive elimination at −20°C. These and other recent observations provide an incentive for reexamining the factors that have been assumed to control the rate of reaction of transition metal complexes with C–H bonds—notably the need for electron-rich metals and the proximity of reacting centers.

The usual requirements for organic feedstocks in large-scale metal-catalyzed processes are plentiful supply and reasonable reactivity toward transition metals. Alkenes (also called olefins or unsaturated hydrocarbons) fit these requirements well, since they are major constituents of petroleum and contain carbon-carbon double bonds, which are reactive toward a wide range of transition metal–based reagents (*1*, *2*). From the point of view of quantity, alkanes (saturated hydrocarbons) would also be very attractive feedstocks for catalytic synthesis of organic molecules; they are major constituents of natural gas, petroleum, and coal liquefaction processes. However, they are much less often used in this way for a simple reason: alkanes are among the least reactive organic molecules. This unreactivity is a consequence of the high C–H bond energies in alkanes. These values range from 90 to 98 kilocalories per mole for primary and secondary C–H bonds; in methane, the main constituent of natural gas, the C–H bond energy is 104 kcal/mole (*3*). This makes methane one of the most common but least reactive organic molecules in nature.

The large quantity and low reactivity of methane and higher alkanes has tantalized organic and organometallic chemists for several years. In 1968, when mechanistic theory in organometallic chemistry was just developing, one leader in this area stated that, "the development of successful approaches to the activation of carbon-hydrogen bonds, particularly in saturated hydrocarbons, remains to be achieved and presently constitutes one of the most important and challenging problems in this whole field" (*4*). This feeling, shared by many workers in the area, prompted many searches for clear-cut homogeneous metal-based alkane activation systems. However, only recently have soluble transition metal systems been found for which reaction with alkanes can be directly observed. These discoveries stimulated even greater interest in this problem. The purpose of this article is to summarize some of these discoveries, to discuss the advances they have led to in the fundamental understanding of reactions between alkanes and transition metal complexes, and to provide a general idea of the important and as yet unsolved questions that have been raised by this research.

Background

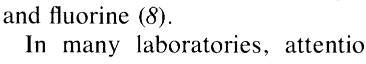
Alkanes are not completely unreactive. Free radicals capable of abstracting alkane hydrogen atoms [for example, chlorine atoms (Eq. 1)] have been known

$$\mathrm{Cl\cdot + R{-}H \longrightarrow HCl + R\cdot} \qquad (1)$$

for many years (*5*); these reactions lead to alkyl radicals, which may then be converted into other types of organic molecules (Eq. 2). In some cases, transi-

$$\mathrm{R\cdot + X{-}Y \longrightarrow R{-}X + Y\cdot} \qquad (2)$$

tion metals mediate the formation or reactions of free radicals (*6*). One problem with these systems is that they are either very unselective or, in more selective cases, tertiary hydrogens react much more readily than secondary or primary hydrogens. A typical example of a free-radical autoxidation, selective for tertiary hydrogens, is illustrated in Eq. 3.



(3)

It is much more difficult to activate secondary and primary hydrogens in such processes, and only a very few systems capable of causing methane to undergo free-radical reactions are known (*7*). Some organic reagents react with alkanes by apparent nonradical mechanisms; examples are ozone, superacids, and fluorine (*8*).

In many laboratories, attention has been focused on a specific goal: the discovery of a soluble complex capable of inserting a metal center into the C–H bond of alkanes (Eq. 4). This is one

$$\mathrm{M + R{-}H \longrightarrow R{-}M{-}H} \qquad (4)$$

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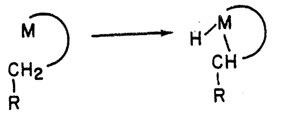
example of a general organometallic primary transformation called "oxidative addition" because the metal center is formally oxidized by two units in its conversion from starting complex to insert product (*9*). During the past 10 years, many examples of intramolecular C–H oxidative addition [that is, the metal and reacting C–H bond are located in the same molecule (Eq. 5)] have been



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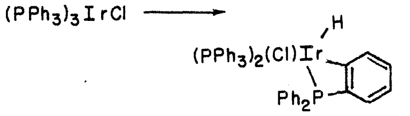
discovered (*10*). Some specific examples of this process are illustrated in Eqs. 6 to 8. The largest group involves so-called



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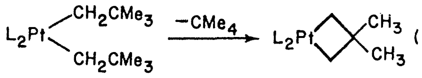

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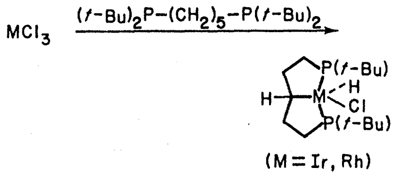
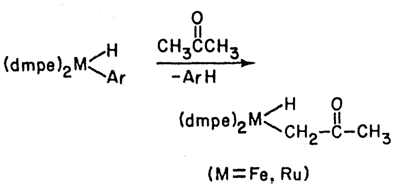


(8)

orthometallation processes, in which insertion takes place into the C–H bond of an aromatic ring attached to an atom directly bound to the metal (Eq. 6). A few cases are also known of insertion into a C–H bond of an alkyl chain located in the same molecule as the metal (Eqs. 7 and 8). Clearly, proximity of the reacting C–H bond to the metal center is a critical factor favoring such cyclometallation processes. In attempts to extend these reactions to intermolecular cases, a few reactions have been found in which metal centers that are relatively electron-rich react with organic compounds having C–H bonds with low bond energy or high acidity (Eqs. 9 and 10). However, before



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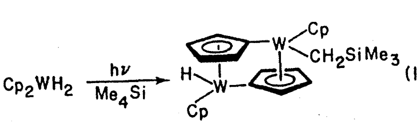
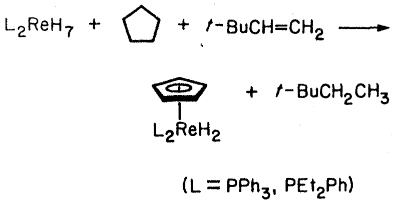


(10)

the work reported here was initiated, all attempts to find a clear example of Eq. 4 involving simple alkanes had been unsuccessful.

A few examples of multistep metal-based transformations of alkanes are known. One example, the work of Shilov and his group in the Soviet Union (*11*), was reported in the late 1960's. These reactions involve both alkane hydrogen-deuterium exchange and conversion to chlorides and acetates, catalyzed by soluble platinum salts. However, somewhat elevated temperatures (100° to 120°C) are required for these reactions. Little else is known about their mechanism, including whether they are truly homogeneous reactions. In much more recent work, Crabtree's group at Yale (*12*) and Felkin's at Gif-sur-Yvette in France (*13*)



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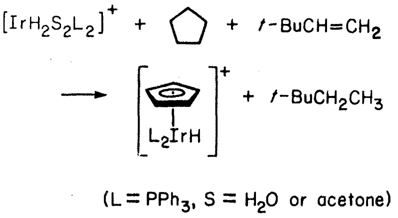
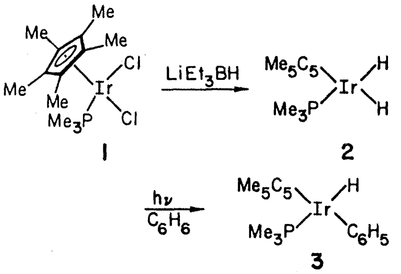


(12)

have reported the novel iridium- and rhenium-induced dehydrogenation processes exemplified by Eqs. 11 and 12. Crabtree has provided convincing evidence that these reactions are homogeneous and has proposed that they are initiated by insertion of the metal center into an alkane C–H bond. However, this hypothesis has not yet been confirmed by direct observation of the oxidative addition in these systems.

Generation and Oxidative Addition Reactions of (η^5-C_5Me_5)(PMe_3)Ir

In connection with a project aimed at examining the products of hydrogenolysis of metal alkyls, my co-workers and I had occasion to prepare dihydridoiridium complex **2** by the reaction shown in Eq. 13. Many dihydridometal complexes



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undergo reductive elimination of H_2 upon irradiation (*14*). In complexes related to **2** (for example, Cp_2MoH_2; Cp =C_5H_5) the type of intermediates generated in such reactions have been

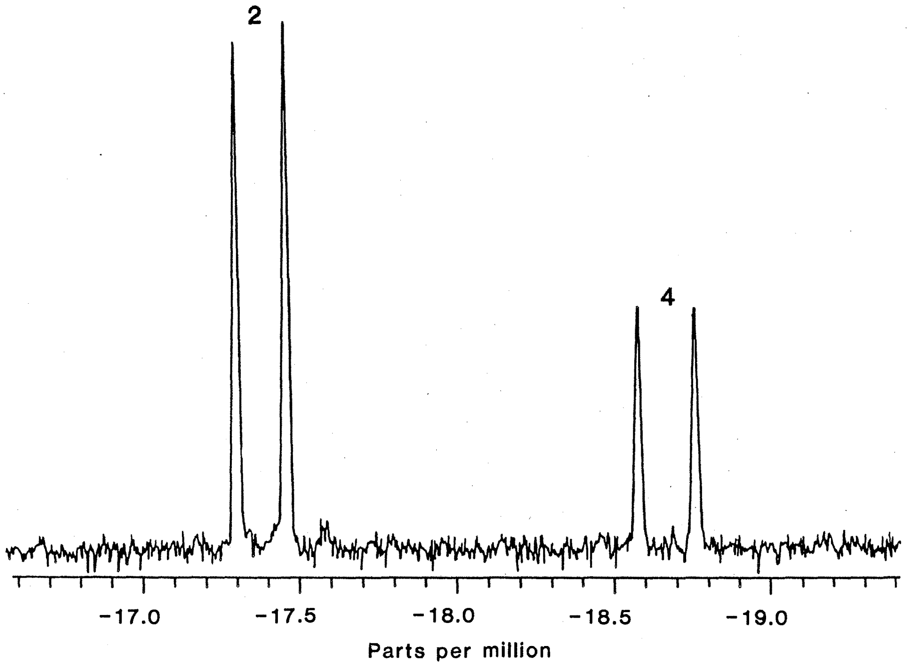
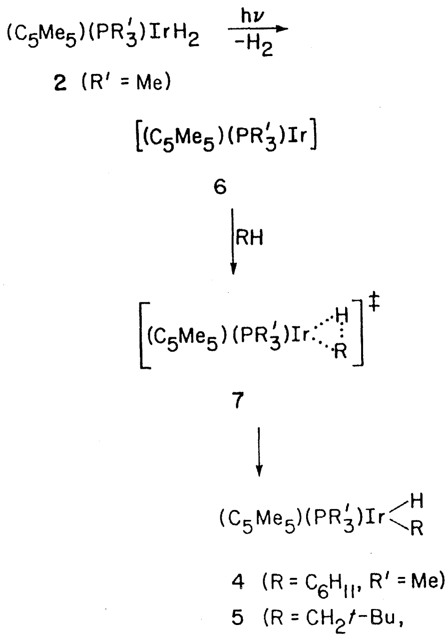


Fig. 1. Reproduction of the high-field portion of the proton nuclear magnetic resonance (NMR) spectrum of the mixture obtained during irradiation of Cp′(L)IrH_2 (complex **2**) with ultraviolet light in cyclohexane solvent. On the numbered axis at the bottom of the spectrum, the field increases toward the right. The position of each signal (that is, the chemical shift of the hydrogen atom producing that signal) is measured in parts per million distance from the single line observed for the internal standard tetramethylsilane, which appears at much lower field and is therefore not visible in this portion of the spectrum. Chemical shifts that appear at fields higher than tetramethylsilane are listed as negative numbers by convention. The lower-field doublet is due to the hydride signal for the starting dihydride **2**, and the higher-field doublet arises from the hydride signal for the C–H insertion product **4**.



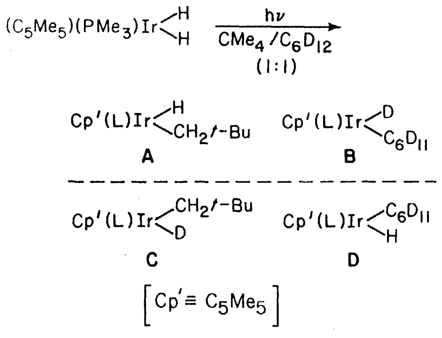
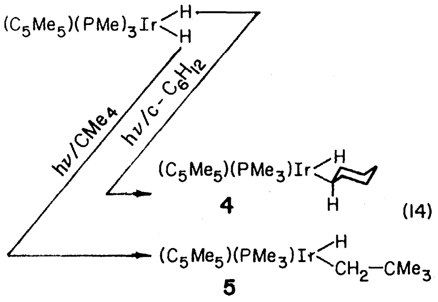


Fig. 2 (left). Proposed mechanism for the photochemical conversion of dihydride **2** to C–H insertion products. Fig. 3 (right). Schematic illustration of the crossover experiment (see text) carried out by irradiating dihydride **2** in a mixture of neopentane (CMe_4) and completely deuterated cyclohexane (C_6D_{12}).

shown to insert into at least some types of C–H bonds (see, for example, Eq. 10). We therefore decided to investigate the irradiation of **2**. We were encouraged to find that in benzene only **3**, the product of intermolecular C–H activation, was formed; no orthometallation product was observed. Benzene is reactive toward C–H activation, presumably because of involvement of its π-electrons in the insertion transition state. Our next step, therefore, was to attempt this reaction with somewhat less inherently reactive compounds. Exploratory experiments of this type are relatively simple because the presence of new metal hydride products can be detected by observing their characteristic resonances in the proton nuclear magnetic resonance (NMR) spectrum of the reaction mixture. The signals due to the metal-bound hydrogen atoms appear in the very-high-field region of the spectrum, and each signal is doubled as a result of spin-spin coupling between the hydride nucleus and the phosphorus nucleus also attached to the metal. Accordingly, we found that irradiation of **2** in acetonitrile gave H_2 and a new metal hydride product, and irradiation in tetrahydrofuran also gave new hydride products. We therefore proceeded immediately to alkanes. We found that irradiation of **2** in cyclohexane solvent gave a single new hydride in high yield. Figure 1 reproduces the high-field region of the proton NMR spectrum of the reaction mixture during irradiation. It shows the two-line pattern centered at −17.38 parts per million caused by the starting material, and the additional two-line pattern centered at −18.67 caused by the presence of the new hydride product. A similar result was obtained in neopentane solvent.

These products are the hydridoalkyl complexes **4** and **5** shown in Eq. 14. The



(14)

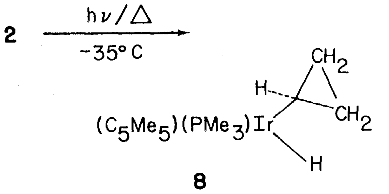
new complexes are extremely hydrophobic and are therefore very difficult to obtain pure. However, they can be isolated and purified, with some loss of material, and characterized fully by proton NMR, carbon-13 NMR, and infrared spectroscopic techniques. Furthermore, they can be converted to the corresponding bromoalkyliridium derivatives (see below), which can be characterized both by spectroscopic and elemental analysis techniques (*15*).

Mechanism of the C–H Oxidative Addition Reaction

The conventional mechanism for the C–H insertion is shown in Fig. 2. It is first assumed that, upon irradiation, an excited state of dihydride **2** is formed. This rapidly extrudes H_2, leaving behind the reactive, coordinatively unsaturated fragment **6**. Complex **6** then inserts into a C–H bond via transition state **7**, leading to the hydridoalkyliridium complexes **4** and **5**.

Although this mechanism is reasonable, supporting evidence for it appeared to be needed, especially since more complicated mechanisms involving free radicals have been established in certain other oxidative addition reactions (*16*). Many radical mechanisms proceed through a step in which the radical R· has independent existence. Thus the individual R and H groups located in each molecule of product **4** or **5** may not necessarily have been bound together in the starting hydrocarbon molecule. Information about this was obtained from the "crossover experiment" summarized in Fig. 3. We first irradiated **2** in a 1:1 mixture of neopentane and cyclohexane. This established that the two hydrocarbons have similar reactivity toward **6**, although the C–H bond in neopentane is slightly more reactive. Next, irradiation of **2** in a 1:1 mixture of neopentane and the deuterium-labeled alkane cyclohexane-d_{12} was carried out. As shown in Fig. 3, the products of this reaction were the hydridoneopentyl- and the deuterio(perdeuterocyclohexyl)iridium complexes **A** and **B**, with very small amounts of contamination from the crossed products **C** and **D**. Therefore, the R and H groups remain associated with one another during the process that converts the hydrocarbon to a hydridoalkyliridium complex.

This experiment rules out reactions involving radicals having a free existence and finite lifetime; however, it is more difficult to rule out processes proceeding predominantly through solvent-caged radical pairs. Our best evidence against such intermediates comes from relative reactivity studies. Hydrogen abstraction reactions of radicals favor C–H bonds with low bond energies; very strong bonds are nearly always inert (*5*). Cyclopropane may therefore be used as a diagnostic substrate since its C–H bond energy is 106 kcal/mole, even stronger than that of methane (*3*). Nevertheless, as shown in Eq. 15, irradiation of **2** in



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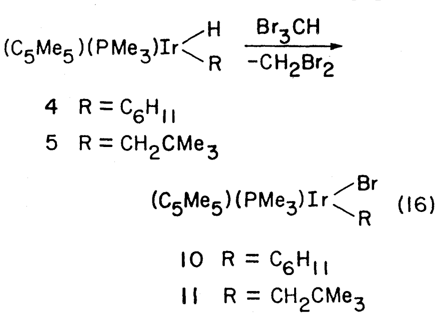
liquid cyclopropane at −35°C leads only to the C–H insertion product **8**. Thus, addition to the C–H bond is favored even over insertion into the relatively weak C–C bond, which would have led to a four-membered iridium-containing ring compound. In view of this result, a radical-cage mechanism seems extremely unlikely for these reactions.

Functionalization Reactions

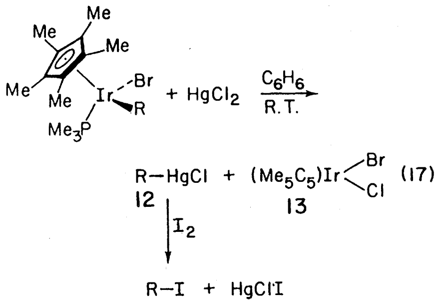
A primary goal of this work has been the conversion of the hydridoalkyliridium complexes to functionalized organic molecules. Unfortunately, many of the reagents that might be used to carry out such functionalizations promote only reductive elimination, simply regenerating the starting hydrocarbon. One solution to this problem is conversion of the hydrides to the corresponding bromoalkyliridium complexes **10** and **11**. This can be done smoothly at room temperature by treating the hydrides with the common reagent $CHBr_3$, as shown in Eq. 16. The bromine-containing products are somewhat easier to handle than their hydride precursors, and they do not easily undergo reductive elimination. As a result, functionalization of these materials has been more successful. The most convenient method we have found so far is summarized in Eq. 17. Treatment of bromoalkyliridium complex **10** or **11** with mercuric chloride leads to the corresponding alkylmercurial **12** and bromochloroiridium complex **13**. Conversion of **12** to organic halides can then be carried out with I_2 or Br_2 at room temperature. Thus overall conversion of an alkane to alkyl halide can be effected in good yield under mild conditions, in a nonradical process that completely avoids free radical intermediates.



$$(C_5Me_5)(PMe_3)Ir\begin{smallmatrix}H\\R\end{smallmatrix} \xrightarrow[-CH_2Br_2]{Br_3CH} (C_5Me_5)(PMe_3)Ir\begin{smallmatrix}Br\\R\end{smallmatrix} \qquad (16)$$

4 $R = C_6H_{11}$
5 $R = CH_2CMe_3$

10 $R = C_6H_{11}$
11 $R = CH_2CMe_3$



$$+ HgCl_2 \xrightarrow[R.T.]{C_6H_6} \underset{12}{R{-}HgCl} + \underset{13}{(Me_5C_5)Ir\begin{smallmatrix}Br\\Cl\end{smallmatrix}} \qquad (17)$$

$$\underset{12}{R{-}HgCl} \xrightarrow{I_2} R{-}I + HgCl{\cdot}I$$

Selectivity Studies

We next turned our attention to studies of the selectivity of the reactive intermediate $Cp'(PMe_3)Ir$ (**6**) ($Cp' = C_5Me_5$; Fig. 2). Irradiation of $Cp'(PMe_3)IrH_2$ (**2**) in the presence of solvents having different types of C–H bonds allowed the reactive intermediate $Cp'(PMe_3)Ir$ to react competitively with those bonds. At low conversion, the ratio of the products in such an experiment is directly equal to the ratio of rate constants for insertion into each type of C–H bond. Two types of selectivity experiments were carried out: those involving competition of the intermediate for C–H bonds in different molecules (intermolecular selectivity) and competition for different types of C–H bonds located in the same molecule (intramolecular selectivity).

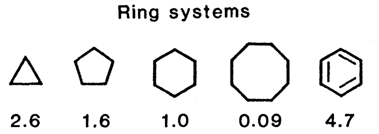


Fig. 4. Relative rates of reaction with Cp′IrL of one C–H bond in each of the cyclic organic molecules illustrated.

Intermolecular selectivities can be established readily because the individual oxidative addition products can be independently generated. Each selectivity experiment was carried out with solvents consisting of mixtures of two liquid hydrocarbons. First the dihydride **2** was irradiated in each pure solvent, and the NMR spectrum of the product was recorded. Then the irradiation was carried out in a mixture (usually 1:1) of the two solvents, and the ratio of the products was measured by repetitive integration of the hydride resonances in the high-field region of the spectrum. The rate ratio was calculated by correcting the ratio of product yields for the number of hydrogens available in each molecule. In this way, a neopentane-to-cyclohexane rate ratio of 1.4 and a cyclopropane-to-cyclohexane ratio of 2.6 were obtained. Similarly, we were able to determine the relative rates of attack by $Cp'Ir(PMe_3)$ on one C–H bond in each of the molecules in Fig. 4, with attack on cyclohexane set as 1.0. The results are interesting and, as far as we know, unprecedented: reactivity seems to vary with ring size, smaller rings showing higher reactivity toward C–H insertion and larger rings showing lower reactivity. The physical reason for this is not yet clear but may be related partially to the greater steric accessibility of the C–H bonds in the smaller rings, where the two carbon atoms attached to the reacting carbon are somewhat more tightly "tied back" than they are in the larger systems. A competition experiment with a cyclohexane-benzene mixture showed that the aromatic C–H bonds were 4.0 times as reactive as the cyclohexyl.

Intramolecular selectivities presented a more difficult problem. Reaction of $Cp'(PMe_3)Ir$ (**6**) with unsymmetrical hydrocarbons (that is, those having C–H bonds in different chemical environments) in general leads to several structurally different hydridoalkyliridium complexes. Because of the chemical similarity of these materials, it was not feasible to separate and identify them individually. Fortunately, however, NMR experiments on a wide range of C–H oxidative additions using symmetrical hydrocarbons (such as those summarized in the preceding paragraph) showed that the NMR line position (chemical shift) due to a particular metal-bound hydride in the hydridoalkylmetal products correlated quite reliably with the type of substitution at the carbon attached to the metal. That is, secondary hydridoalkyl complexes (for example, those formed from ring compounds such as cyclohexane and cyclopentane, having general structure $H{-}M{-}CHR_2$) exhibit hydride chemical shifts at relatively high field, whereas primary hydridoalkyl complexes ($H{-}M{-}CH_2R$) invariably exhibit hydride signals at significantly lower field in the proton NMR. Oxidative addition reactions carried out on simple unsymmetrical systems confirm that this dependence holds up in more complex molecules; for example, generation of **6** in *n*-propane, as predicted, gives two new

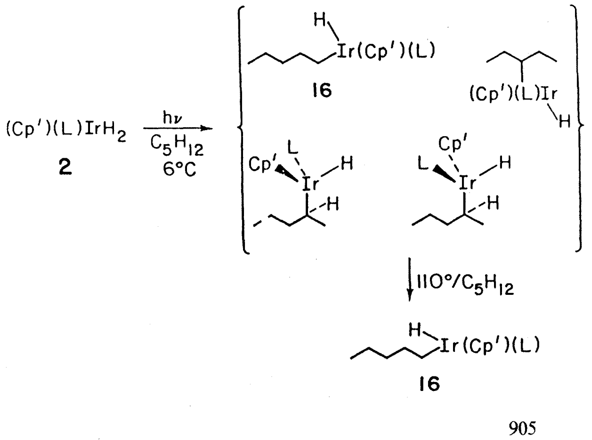
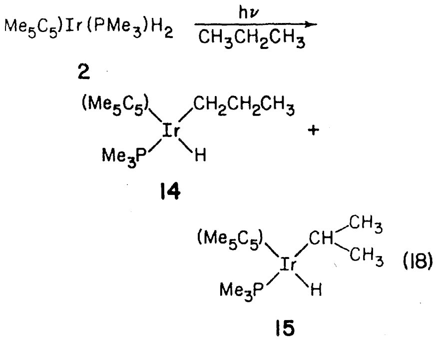


Fig. 5. The C–H insertion products formed on irradiation of dihydride **2** in *n*-pentane at 6°C and heating the resulting mixture to 110°C in the same solvent.

hydride signals, one in the lower-field "primary" and one in the higher-field "secondary" region of the spectrum. On the basis of this correlation, these signals can be assigned with some confidence to oxidative addition products **14** and **15**, respectively (Eq. 18). The results of experiments such as this one indicate that in simple acyclic systems such as *n*-propane, *n*-pentane, and 2-methyl-2-butane, **6** demonstrates measurable "antiradical" selectivity; it inserts into primary C–H bonds about twice as fast as into secondary, and insertion into tertiary C–H bonds is apparently so slow that we have never detected hydride signals due to this type of product.


(18)

Reductive Elimination and Thermochemical Studies

Regeneration (reductive elimination) of hydrocarbon R–H from hydridoalkyliridium complexes such as **4** and **5** can be induced by various oxidizing agents and Lewis acids. However, it can also be induced thermally. For example, heating hydridocyclohexyl complex **4** (see Eq. 14) to temperatures above 100°C in the presence of a solvent other than cyclohexane causes elimination of cyclohexane and (through the intermediacy of **6**) formation of the new hydridoalkyl complex resulting from insertion into a C–H bond of the solvent. This reaction proved to be especially useful in enhancing the effective primary-secondary selectivity of the C–H oxidative addition process. This is illustrated with the sequence of reactions carried out with *n*-pentane (Fig. 5). Irradiation of **2** in *n*-pentane gives four new hydride resonances in the NMR spectrum, one (that due to the major product **16**) in the primary and three in the secondary region of the spectrum. Three, rather than two, secondary products are observed because the insertion of iridium into the hydrogens at C-2 of this hydrocarbon can give rise to the two structurally distinguishable diastereomers shown in Fig. 5. Heating this mixture of hydridoalkyl complexes to 110°C in pentane causes disappearance of the resonances assigned to the secondary C–H insertion products and a corresponding increase in the resonances due to the primary insertion product **16**. This occurs because this temperature is sufficient to cause reversible reductive elimination from the secondary hydridoalkyl products; thus the product that is thermodynamically most stable (that is, the primary complex **16**) is formed. This is an extremely important result from a practical point of view because it suggests that a combination of photolysis followed by thermal equilibration will allow exclusive primary functionalization of linear alkanes. Supporting evidence for the reductive elimination-readdition mechanism has been obtained by heating the mixture of hydridopentyliridium complexes with cyclohexane instead of *n*-pentane, as shown in Fig. 6. Under these conditions, the secondary products again disappear but are converted into the cyclohexylhydridoiridium complex **4** instead of additional 1-pentylhydridoiridium complex **16**.

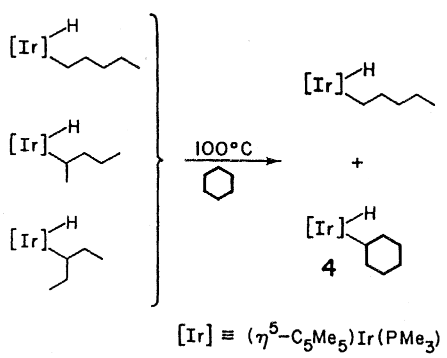
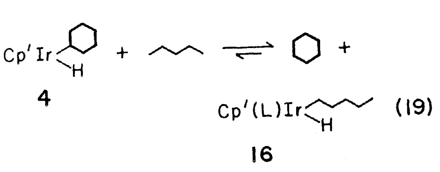
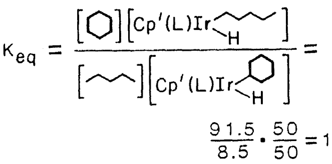


Fig. 6. Illustration of the result of heating the products formed on irradiation of **2** in *n*-pentane to 100°C in cyclohexane solvent.

Because different hydridoalkyliridium complexes are interconverting reversibly in these experiments, it is in principle possible to measure the equilibrium constants for the reactions and thus to obtain a quantitative measure of the relative iridium-carbon bond strengths involved. We have done this for the *n*-pentyl–cyclohexyl system. The reversible reaction under consideration and the equilibrium constant associated with it are illustrated in Eqs. 19 and 20. The equilibrium was studied by first dissolving the mixture of four hydridopentyliridium products illustrated in Fig. 5 in a 91.5:8.5 mixture of cyclohexane and *n*-pentane. This solution was then heated. At 120°C, reductive elimination and disappearance of the 2-pentyliridium complexes occurred. Heating to 140°C then brought the more stable complexes **4** and **16** into interconversion with one another via reversible reductive elimination–oxidative addition. In this solvent mixture and at this temperature, the system reached equilibrium after about 50 hours; 50 percent of the equilibrium mixture was **4** and 50 percent was **16**, and there were no detectable 2- or 3-pentyliridium complexes. With these equilibrium concentrations and the relative molar concentrations of the two solvents, the equilibrium constant was calculated to be 10.8, as shown in Eq. 20. This corresponds to a free energy difference of about 2 kcal/mole at 140°C. The primary C–H bond in *n*-pentane is about 4 kcal/mole stronger than the secondary C–H bond in cyclohexane (*3*). Using this number and the reaction free energy, and assuming a negligible entropy difference between reactants and products, we estimate the primary metal-carbon bond in the *n*-pentyliridium complex **16** to be about 6 kcal/mole stronger than the secondary metal-carbon bond in **4**. Clearly the secondary metal-carbon bonds in the 2-pentyliridium complexes are even weaker than that in **4**; we do not yet know the reason for this unusual result (*17*).

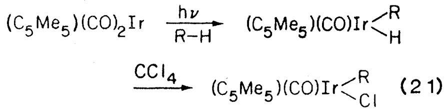

(19)



$$\frac{91.5}{8.5}\cdot\frac{50}{50}=10.8 \qquad (20)$$

Activation of Methane

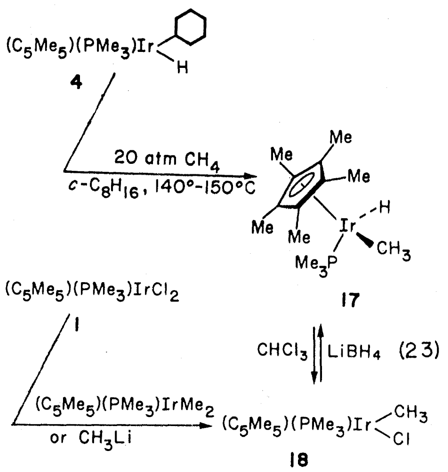
In considering various possible alkane substrates for C–H activation, the smallest hydrocarbon, methane (CH_4), is one of the most intriguing. The reasons for this, as mentioned earlier, are methane's very high bond dissociation energy (104 kcal/mole) (*3*), and its presence as a major constituent in natural gas. The fact that cyclopropane, despite its even higher bond energy, reacts readily with Cp'(PMe_3)Ir suggested that methane should be similarly reactive. However, there are serious technical problems in carrying out the irradiation of Cp'(PMe_3)IrH_2 (*3*) in methane. At normal pressures, such low temperatures are required to liquefy methane that the dihydride is insoluble in it. Attempts to find an inert solvent in which to carry out the methane reaction were not successful. For example, irradiation of dihydride **2** in perfluoroalkane solvents (in which it is only slightly soluble) under 4 atmospheres of CH_4 gave only decomposition to intractable materials, in contrast to the observations of Hoyano and Graham (*18*) and Watson (*19*) [Eqs. 21 ($R = CH_3$) and 22]. Photolysis in cyclooctane, a "slow" substrate for C–H insertion of the presumed intermediate Cp′(PMe_3)Ir, gave only the previously observed hydridocyclooctyl complex.



$$(C_5Me_5)(CO)_2Ir \xrightarrow[R-H]{h\nu} (C_5Me_5)(CO)Ir{<}^{R}_{H} \xrightarrow{CCl_4} (C_5Me_5)(CO)Ir{<}^{R}_{Cl} \quad (21)$$

$$(C_5Me_5)_2Lu{-}CH_3 + {}^{13}CH_4 \longrightarrow (C_5Me_5)_2Lu{-}{}^{13}CH_3 + CH_4 \quad (22)$$

It occurred to us that methane activation could be achieved thermally, under the reversible conditions described in the preceding section, by taking advantage of the presumption that the hydridomethyl complex **17** would be thermodynamically more stable even than primary alkyl complexes such as **2**. It turned out that application of this idea gave successful results. Thus, as shown in Eq. 23, heating hydridocyclohexyl complex **4** in cyclooctane solvent in a sealed Pyrex vessel under 20 atm of CH_4 at temperatures between 140° and 150°C for 14 hours led to a 58 percent yield of hydridomethyl complex **17** along with 8 percent of dihydride **2**. As with the other hydridoalkyl complexes, this material was quite sensitive, and therefore its identification by proton NMR was confirmed by conversion to the corresponding chloromethyl complex **18**, as well as by independent synthesis of **17** from dichloride **1** (via **18**) as shown in Eq. 23. In the methane thermal C–H oxidative addition experiment, we assume that the hydridocyclohexyl complex **4** and the corresponding hydridocyclooctyl complex are formed reversibly but do not build up because of their thermodynamic instability relative to the hydridomethyl complex **17**; that is, the hydridomethyl complex **17** is the "thermodynamic sink" for the system (*17*).



Preliminary Results on C–H Oxidative Addition with Rhodium Complexes

We prepared the rhodium complex **19**, analogous to dihydride **2**, and found that it, too, participates in C–H oxidative addition reactions (Fig. 7). Irradiation of **19** at room temperature leads only to an unidentified black substance. However, irradiation at −50°C produces new hydrides, again by observation of their absorptions in the high-field region of the low-temperature proton NMR spectrum. Preliminary studies have indicated that the C–H insertion reactions of the proposed intermediate Cp′RhL (Cp′ = C_5Me_5; L = PMe_3) shown in Fig. 7 are successful (*20*). With the exception of the hydridophenyl complex, warming the reaction solutions to −10°C causes reductive elimination of hydrocarbon and deposition of the black decomposition product. However, conversion of the hydridoalkyl complexes to the corresponding halides can be carried out at low temperature, and these products appear to be more stable than the hydrides.

Conclusions

We have found an example of the intermolecular reaction shown in Eq. 4, in which a soluble metal complex undergoes oxidative addition into the C–H bonds of alkanes, leading to hydridoalkylmetal complexes. Our most extensive work has been done with iridium, but preliminary results indicate that the analogous rhodium complexes undergo similar C–H insertions, although the products are considerably less stable. We have found it possible to convert the insertion products into organic halides, indicating that overall conversion of alkanes into functionalized organic molecules is feasible. Selectivity studies have shown that the reactive iridium complex favors insertion into aromatic, primary, and small-ring C–H bonds.

Development of catalytic processes will be more challenging. The difference between a catalytic and noncatalytic sequence of reactions is that the former is cyclic, so that the catalyst is regenerated in the final step of the sequence and can be automatically reused. Development of such a cyclic process, like methane activation, does not require substantial new fundamental information but still faces difficult practical roadblocks. One of these is the fact that reagents which convert the C–H insertion product to functionalized organic molecules often react irreversibly with the critical intermediate Cp′IrL, thus shutting down the cycle. However, research may uncover reagents that do not cause this problem.

On the fundamental side, we do not yet understand why the systems discussed here seem to favor intermolecular addition, whereas other metal complexes either favor intramolecular cyclometallation or do not react with unactivated C–H bonds at all. The search for additional systems that also engage in intermolecular addition should provide information that will be useful in answering this question. We also do not yet understand the physical basis for the selectivities we

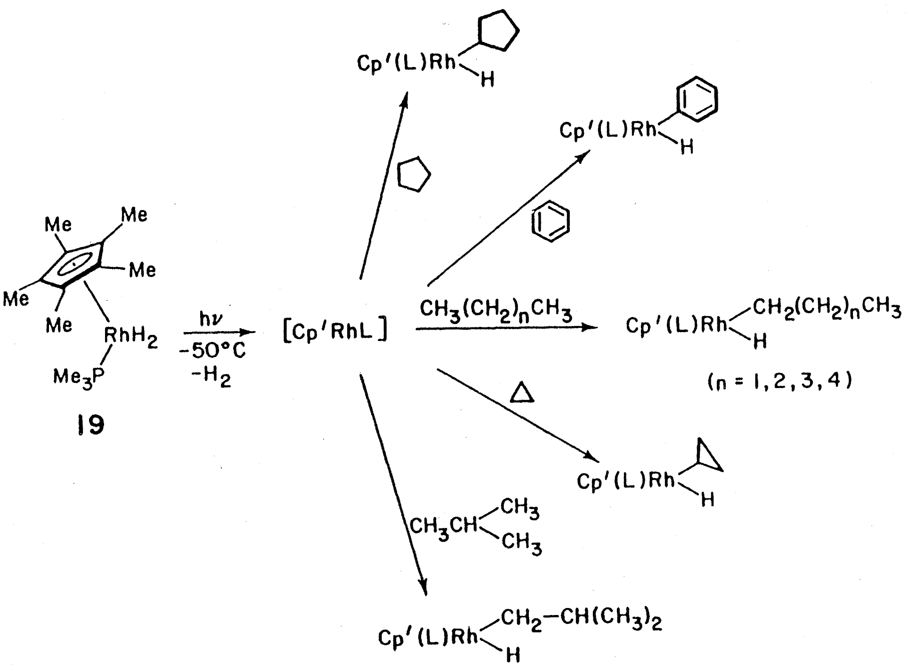


Fig. 7. The reactions observed on irradiation of the dihydridorhodium complex **17** at −50°C in various organic solvents.

have observed. Finally, our results raise questions about the supposed requirement for a very-electron-rich metal center to induce C–H activation. We have found that replacing PMe_3 with the more electron-withdrawing phosphine $P(OMe)_3$ gives a system that also effects oxidative addition. Independent work in Graham's laboratory, illustrated in Eq. 21, demonstrates that even a CO ligand is not electron-withdrawing enough to prevent C–H insertion (*18*, *21*). Finally, Watson's recent discovery of the reaction illustrated in Eq. 22 shows that methane (and other small hydrocarbons) will react with organometallic lutetium—a metal center normally considered to be very electrophilic (*19*). Intermolecular reactions between metal centers and alkanes are now being uncovered at an increasingly rapid rate and with metals having a wide range of electronic character. It seems likely that several different mechanisms for alkane oxidative addition will eventually be identified.

References and Notes

1. G. W. Parshall, *Homogeneous Catalysis* (Wiley, New York, 1980); P. Wiseman, *An Introduction to Industrial Organic Chemistry* (Applied Science Publishers, London, ed. 2, 1979).
2. H. A. Witcoff and B. G. Reuben, *Industrial Organic Chemicals in Perspective* (Wiley, New York, 1980), parts I and II.
3. S. W. Benson, *Thermochemical Kinetics* (Wiley, New York, ed. 2, 1976), p. 309.
4. J. Halpern, *Discuss. Faraday Soc.* **46**, 7 (1968). For reviews of the C–H activation area, see A. E. Shilov and A. A. Shteinman [*Coord. Chem. Rev.* **24**, 97 (1977)]; D. E. Webster [*Adv. Organomet. Chem.* **15**, 147 (1977)]; G. W. Parshall [*Acc. Chem. Res.* **8**, 113 (1975)].
5. C. Walling, *Free Radicals in Solution* (Wiley, New York, 1957); E. S. Huyser, *Free Radical Chain Reactions* (Wiley, New York, 1970); W. A. Pryor, *Free Radicals* (McGraw-Hill, New York, 1966).
6. J. T. Groves, *Adv. Inorg. Biochem.* **1**, 119 (1979); ———, T. E. Nemo, R. S. Myers, *J. Am. Chem. Soc.* **101**, 1032 (1979); J. T. Groves and M. Van Der Puy, *ibid.* **98**, 5290 (1976); C. K. Chang and M.-S. Kuo, *ibid.* **101**, 3413 (1979); J. T. Groves and W. J. Kruper, Jr., *ibid.*, p. 7613; C. L. Hill and B. C. Schardt, *ibid.* **102**, 6374 (1980); J. A. Sofranko, R. Eisenberg, J. A. Kampmeier, *ibid.*, p. 1163.
7. See (2), part I, pp. 110ff.
8. A. L. J. Beckwith and T. Duong, *J. Chem. Soc. Chem. Commun.* (1978), p. 413; Z. Cohen, E. Keinan, Y. Mazur, T. Haim Varkony, *J. Org. Chem.* **40**, 2141 (1975), and references cited therein; N. C. Deno, E. J. Jedziniak, L. A. Messer, M. D. Meyer, S. G. Stroud, E. S. Tomezsko, *Tetrahedron* **33**, 2503 (1977).
9. J. P. Collman and L. S. Hegedus, *Principles and Applications of Organotransition Metal Chemistry* (University Science Books, Mill Valley, Calif., 1980), pp. 176–258.
10. See, for example, M. I. Bruce, *Angew. Chem. Int. Ed. Engl.* **16**, 73 (1977); P. Foley and G. M. Whitesides, *J. Am. Chem. Soc.* **101**, 2732 (1979); H. D. Empsall, E. M. Hyde, R. Markham, W. S. McDonald, M. C. Norton, B. L. Shaw, B. Weeks, *J. Chem. Soc. Chem. Commun.* (1977), p. 589; R. A. Andersen, R. A. Jones, G. Wilkinson, *J. Chem. Soc. Dalton Trans.* (1978), p. 446; H. Werner and R. Werner, *J. Organomet. Chem.* **209**, C60 (1981); J. W. Rathke and E. L. Muetterties, *J. Am. Chem. Soc.* **97**, 3272 (1975).
11. N. F. Gol'dshleger, M. B. Tyabin, A. E. Shilov, A. A. Shteinman, *Zh. Fiz. Khim.* **43**, 2174 (1969). For a review of this work, see A. E. Shilov and A. A. Shteinman [*Coord. Chem. Rev.* **24**, 97 (1977)].
12. R. H. Crabtree, J. M. Mihelcic, J. M. Quirk, *J. Am. Chem. Soc.* **101**, 7738 (1979); R. H. Crabtree, M. F. Mellea, J. M. Mihelcic, J. M. Quirk, *ibid.* **104**, 107 (1982).
13. D. Baudry, M. Ephritikhine, H. Felkin, *J. Chem. Soc. Chem. Commun.* (1980), p. 1243; *ibid.* (1982), p. 606.
14. G. L. Geoffrey and M. S. Wrighton, *Organometallic Photochemistry* (Academic Press, New York, 1979).
15. A. H. Janowicz and R. G. Bergman, *J. Am. Chem. Soc.* **104**, 352 (1982); *ibid.*, **105**, 3929 (1983).
16. See, for example, J. A. Labinger, R. J. Braus, D. Dolphin, J. A. Osborn [*J. Chem. Soc. Chem. Commun.* (1970), p. 612]; F. R. Jensen and B. Knickel [*J. Am. Chem. Soc.* **93**, 6339 (1971)]; J. A. Labinger and J. A. Osborn [*Inorg. Chem.* **19**, 3230 (1980)].
17. These results have been discussed in a recent manuscript (M. J. Wax, J. M. Stryker, J. M. Buchanan, C. A. Kovac, R. G. Bergman, *J. Am. Chem. Soc.*, in press).
18. J. K. Hoyano and W. A. G. Graham, *ibid.*, in press.
19. P. L. Watson, *ibid.* **105**, 6491 (1983).
20. R. A. Periana and R. G. Bergman, in preparation. Similar work has been reported independently by another group [W. D. Jones and F. J. Feher, *Organometallics* **2**, 562 (1983)].
21. J. K. Hoyano and W. A. G. Graham, *J. Am. Chem. Soc.* **104**, 3723 (1982).
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