Catalytic C–H/Olefin Coupling

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ABSTRACT
The cleavage and addition of ortho C–H bonds in various aromatic compounds such as ketones, esters, imines, imidates, nitrile, and aldehydes to olefins and acetylenes can be achieved catalytically with the aid of ruthenium catalysts. The reaction is generally highly efficient and useful in synthetic methods. The coordination to the metal center by a heteroatom in directing groups such as carbonyl and imino groups is the key. The reductive elimination to form a C–C bond is the rate-determining step.

Introduction

Examination of an organic molecule reveals that it consists of a carbon skeleton and some functional groups. The remainder of the carbon framework in the molecule is covered with hydrogen atoms, which, of course, are usually inert and are generally regarded as unreactive parts of the molecule. Typically, synthetic operations are carried out with the aid of functional groups. If a synthetic method that allows the direct use of normally "unreactive" C–H bonds were to become available, an entirely new world in synthetic organic chemistry would be opened. This Account deals with such an innovation, largely developed by our research group.

The discoveries that soluble transition metal complexes are able to catalyze the cleavage of unactivated C–H bonds were made in 1960s. An ortho C–H bond of azobenzene was found to undergo cleavage in a reaction with a nickel complex to give the ortho-nickelated complex **1** (eq 1).[1] In 1965, naphthalene was found to undergo an oxidative addition to a Ru(0) complex (eq 2).[2] In 1965, an X-ray analysis of a ruthenium complex having "five ligands" showed, unexpectedly, that it was "six-coordinated" with a C–H bond as the sixth ligand.[3] These findings stimulated widespread interest in an entirely new field of organic synthesis where the manipulation of unreactive C–H bonds became a possibility. Extensive progress has been made during these 30 years, and as a result, more than 50 review articles[4,5] have appeared,
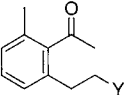
mostly dealing with the stoichiometric cleavage of C–H bonds by metal complexes. In contrast to the rich chemistry of these stoichiometric reactions, the development of catalytic reactions using this chemistry has been very slow. Two early examples (eqs 3 and 4) and two recent examples (eqs 5 and 6) are shown. The catalytic linear dimerization of acrylonitrile reported in the late 1960s[6] has been recently suggested[7] to involve the oxidative addition of a C–H bond β to the CN group onto the ruthenium, to give an intermediate such as **2** (eq 3).
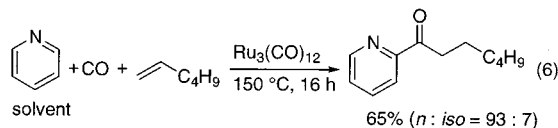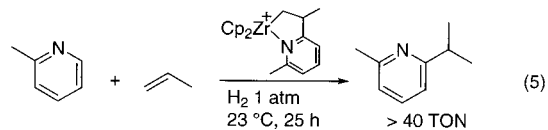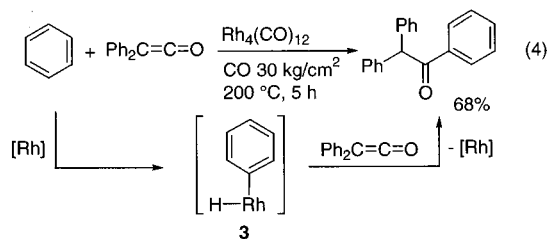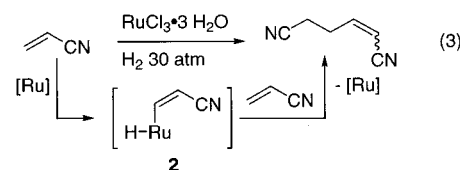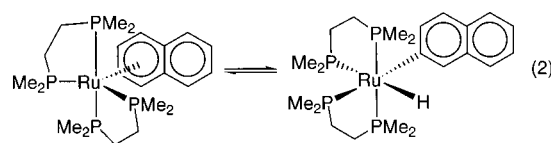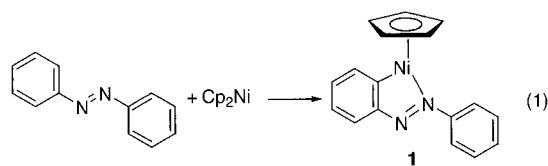
The addition of an aromatic C–H bond to an unsaturated function reported in 1978[8] (eq 4) likely involves an intermediate such as **3**. Recently, catalytic reactions involving the cleavage of the C–H bond at the α-position of pyridine (eqs 5 and 6) have been reported.[9,10] These

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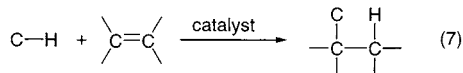
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Table 1. RuH$_2$(CO)(PPh$_3$)$_3$-Catalyzed Addition of Aromatic C—H Bonds in Aromatic Ketones to Olefins

aromtic ketone	olefins	mmols of ketones/olefins/catalyst (reaction time)	product yield
4			
	Y = H	2/ca.14/0.04 (24 h)	quant.
	Y = Bu^t	2/10/0.04 (8 h)	99%
	Y = o-tol	2/10/0.04 (5 h)	97%
	Y= SiMe$_2$(OEt)	2/2/0.04 (2 h)	quant.
	Y = CH$_2$SiMe$_3$	2/10/0.12 (4 h)	quant.

Table 2. Effect of Substituent Group on Product Distribution

	yields of products		
R = CF$_3$	0%	82%	0%
R = OMe	83%	10%	7%
R = F	77%	3%	11%

are exceptionally efficient, but the former suffered from a side reaction (hydrogenation of the olefin used)[9] and the latter often required the use of a large excess of one of the reactants.[10]
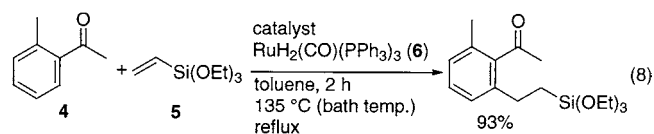
One of the most important goals of these efforts has been to achieve the one-step addition of a C—H bond across a double bond of an olefin (eq 7). If an unreactive C—H bond could participate in such a reaction without being converted into a reactive but sacrificing a functional group such as halogen, the overall transformation would find great utility in organic synthesis. The transformation for synthetic purposes must be highly efficient, i.e., high yield, highly selective, and catalytic. Recently, we reported on a breakthrough discovery for such a process, i.e., a series of ruthenium-catalyzed reactions for carbon—carbon bond formation at unactivated C—H bonds.[11–32] In this Account, we describe our findings to date with respect to the catalytic use of C—H bonds in organic synthesis using chelation assistance of a directing group.

$$C-H \ + \ \overset{}{\underset{}{}C}{=}\overset{}{\underset{}{}C} \ \xrightarrow{\text{catalyst}} \ -\overset{C}{\underset{}{}C}-\overset{H}{\underset{}{}C}- \qquad (7)$$
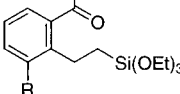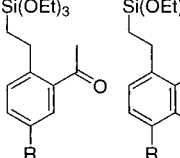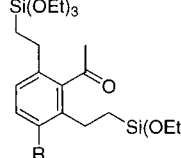
Aromatic Ketone/Olefin Coupling

The research was initiated by the finding of a ruthenium-catalyzed reaction of aromatic ketones with olefins. A representative example of the C—H/olefin coupling reaction is given in eq 8.[11] The reaction involves the cleavage and addition of an ortho C—H bond of acetophenone to an olefin. The reaction is operationally very simple, a simple mixing and refluxing (135 °C, oil bath temperature), generally resulting in nearly quantitative yields. Consequently, the new catalytic reaction satisfies the general requirements for a tool in organic synthesis, which is quite exceptional, if not for the first time, for this type of reaction involving the direct manipulation of C—H bonds.

Selected examples of the aromatic C—H/olefin coupling are given in Table 1. Ruthenium complexes having three triphenylphosphine ligands such as RuH$_2$(CO)(PPh$_3$)$_3$ (**6**)

or Ru(CO)$_2$(PPh$_3$)$_3$ are the best catalyst (or a catalyst precursor). Because of the high reactivity and the utility of the product, we often use triethoxyvinylsilane (**5**) in a test of the reactivity of a ketone. The 1:1 addition products in which the ortho C—H bond is cleaved and added regioselectively across the double bond of an olefin are obtained in excellent yields. In many cases, the yields are quantitative with respect to *both* starting materials. Olefins such as ethylene, *tert*-butylethylene, styrene derivatives, vinylsilanes, allylsilanes, and 1,1-disubstituted olefins can be used. In contrast, olefins with allylic hydrogens rapidly isomerize and give low yields of desired products. A large number of reactions including those of various substituted acetophenones have been examined.[13,22]

The reaction of heteroaromatic ketones with the vinylsilane **5** also affords the corresponding coupling product. The site selectivity for the reaction of 3-acetylthiophene is complete. This result suggests the importance of the existence of a conjugated enone character for this C—H bond cleavage.[11]

X = NMe, O, S
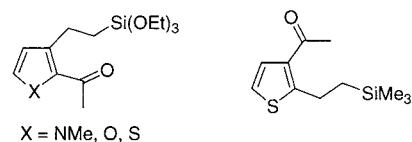
To better understand the new ruthenium-catalyzed reaction of C—H bonds in aromatic ketones with olefins, the effect of various substituents on the aromatic ring was examined. The present C—H/olefin coupling reaction tolerates both electron-donating (e.g., NMe$_2$, OMe, CH$_3$, NEtC(O)CH$_3$, and OC(O)CH$_3$) and electron-withdrawing (e.g., CF$_3$, CN, CO$_2$Me, F, and OCF$_3$) groups.[22,33]

As demonstrated previously,[12] a considerable amount of the 1:2 addition product is formed without dissociation of the 1:1 adduct from the ruthenium center; i.e., the binding of the carbonyl oxygen to the ruthenium center is maintained throughout the reaction.

Meta-substituted acetophenones have two different reaction sites. In many cases, C—C bond formation was observed to take place at the less congested position (Table 2). Steric crowding around the ortho position between the two substituents may prevent the ruthenium from approaching the C—H bond at this position. Interestingly, however, when the substituent is a methoxy or
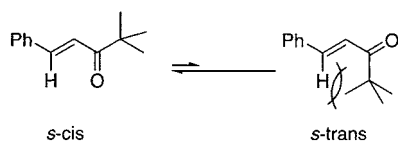

$$ \text{(8)} $$

catalyst RuH$_2$(CO)(PPh$_3$)$_3$ (**6**), toluene, 2 h, 135 °C (bath temp.) reflux, 93%

**FIGURE 1.** Equilibrium between s-cis and s-trans isomers.

fluoro group, C−C bond formation occurs at the sterically less favorable position, i.e., the 2-position. This unusual site selectivity might stem from electronic interactions between the ruthenium and the lone pair of electrons of the methoxy oxygen or fluoro atom.[34]

Olefinic C−H/Olefin Coupling

Not only aromatic C−H bonds but also olefinic C−H bonds can be added to olefins with the aid of ruthenium catalysts.[15] The reaction of acetylcyclohexene, which is an olefinic analogue of acetophenone, with the vinylsilane **5** in the presence of the same catalyst **6** gave the expected 1:1 olefinic C−H/olefin coupling product but in a low yield (50%) (eq 9). Interestingly and surprisingly, a more bulky ketone, i.e., pivaloylcyclohexene, reacted much faster and the yield was excellent, as shown in eq 9. The reason for this rate enhancement is not completely understood at present. Various olefins such as α-methylstyrene, vinylcyclohexene, and methyl methacrylate, which gave almost no addition products in the reaction of aromatic ketones, are applicable to olefinic C−H/olefin coupling.
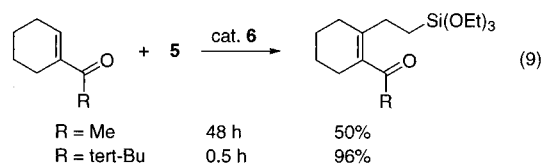
The use of acyclic enones for C−H/olefin coupling usually resulted in a complex mixture of products. For the chelation-assisted C−H bond cleavage, the s-cis conformation of the enone moiety is important, in terms of five-membered metalacycle formation (Figure 1). In the case of enone **7**, in which the corresponding s-trans conformation is destabilized by allylic strain between the olefinic C−H and the bulky *tert*-butyl group (Figure 1), the expected coupling product was obtained in high yield (eq 10).
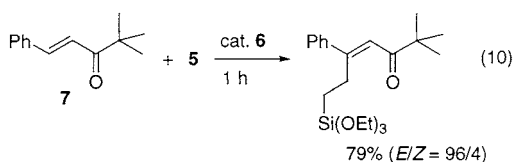
These reactions provide a new route to olefin−olefin cross-coupling. A similar strategy for the cross-coupling of acrylic esters with olefins using the same catalyst **6** has been reported by Trost.[35]

Aromatic Ketone/Acetylene Coupling and Olefinic Ketone/Acetylene Coupling

As the acceptor for the cleaved C−H bond, not only olefins but also acetylenes work well.[16,32] Thus, all four combina-

Table 3. RuH$_2$(CO)(PPh$_3$)$_3$-Catalyzed Addition of C−H Bonds in Aromatic Ketones and Conjugated Enones to Acetylenes

| acetylene	mmols of ketone/acetylene/catalyst (reaction time)	product yield
R━━━R'		
R = Pr ; R' = Pr	2/4/0.12 (4 h)	72% (E/Z = 94/6)
R = Me ; R' = SiMe$_3$	2/4/0.12 (3 h)	83% (only E isomer)
R━━━R'		
R = Ph ; R' = SiMe$_3$	2/4/0.12 (1 h)	96% (E/Z = 94/6)
R = Ph ; R' = Ph	2/4/0.12 (1 h)	71% (E/Z = 76/24)

tions, i.e., aromatic ketone/olefin coupling, olefinic ketone/olefin coupling, aromatic ketone/acetylene coupling, and olefinic ketone/acetylene coupling, can be used in this reaction.

Acetylenes are known to react with transition metal complexes in various ways, which include a C−H oxidative addition,[36] vinylidene complex formation,[37] the formation of metalacyclopentadiene,[38] and cyclotrimerization.[39] It would be interesting to observe whether the desired C−H/acetylene coupling competes successfully with these known reactions.[40,41] Therefore, it was not unexpected that terminal acetylenes did not react at all. Internal acetylenes, however, underwent smooth coupling under reaction conditions similar to those used for coupling with olefins. Representative examples are shown in Table 3.

The C−H bond of α-tetralone, which is one of the most reactive ketones in the coupling with olefins,[13] underwent addition to the triple bond of 1-(trimethylsilyl)-1-propyne in a completely regioselective, stereoselective manner in 83% yield. This indicates that the addition of a Ru−H (or, less likely, a Ru−C) bond to the acetylene proceeds in syn fashion. 4-Octyne reacted in a similar manner with high stereoselectivity (E/Z = 94/6). The olefinic C−H bond at the β-carbon atom of an α,β-unsaturated ketone is cleaved and added to triple bonds catalytically.[32] For this reaction, an aryl group on the acetylene carbon seems to be essential for achieving this reaction, although the roles of the aryl group are not clear at present. Highly congested trisubstituted olefins become available as the result of these recent findings.

Aromatic Ester/Olefin Coupling

In place of a ketone functionality, an ester group can participate in chelation-assisted C−H/olefin coupling.[17,31] The reaction of methyl benzoate with **5** completely failed to give the expected C−H/olefin coupling product (eq 11). Interestingly, however, the introduction of an electron-

Table 4. Addition of C–H Bonds in Aromatic Esters to Olefins Catalyzed by RuH₂(CO)(PPh₃)₃

|		
R = CN	83% (4 h)	28% (4 h)
R = CO₂Me	66% (6 h)	32% (6 h)
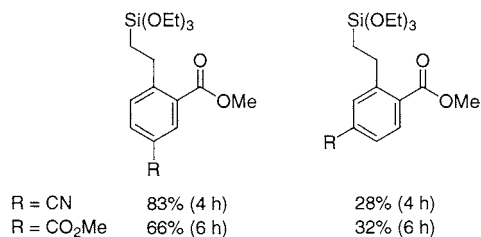
withdrawing group in the aromatic ring dramatically changed the reactivity. Selected results for other esters which contain an electron-withdrawing group are listed in Table 4.
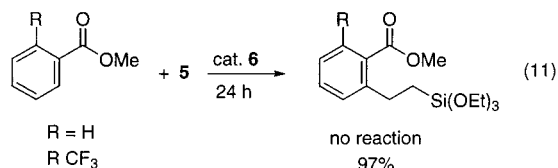
Nitrile and ester groups can be used as rate-accelerating substituents. One might suggest that the electron-withdrawing group would have facilitated the C–H bond cleavage step, but this appears not to be correct (vide infra). Compared with the reactivity among the meta- and para-substituted esters, esters having an electron-withdrawing group at the meta position are able to react with olefins much easier. This different reactivity may stem from the nature of the proposed intermediate that will be discussed below.

Reaction of Aromatic Imines with Olefins

An appropriate sp² nitrogen atom can also function as a directing group.[18,42] The catalytic reaction of aromatic imines **9** with the olefin **5** gave the corresponding 1:1 addition product (eq 12).[18] In addition, a side product, the unsaturated coupling product, was obtained (eq 12). Although the phosphine complex **6** also shows catalytic activity, Ru₃(CO)₁₂ (**8**), which was an ineffective catalyst for the reaction of ketones with olefins, shows the highest activity of the various transition metal complexes screened. The aldimines **9** react with some types of vinylsilanes, ethylene, *tert*-butylethylene, and aromatic olefins.
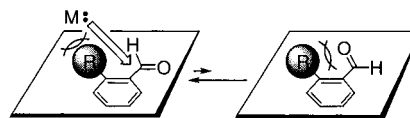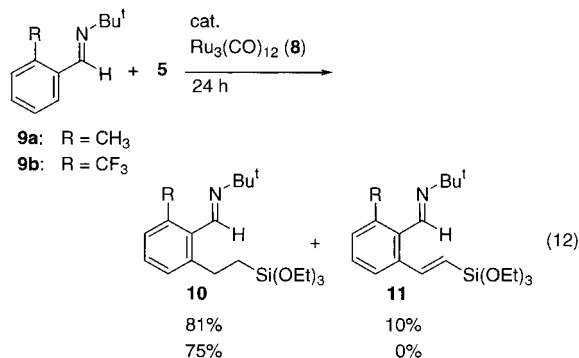
FIGURE 2. Suppression of reactivity of the formyl group by steric effects.
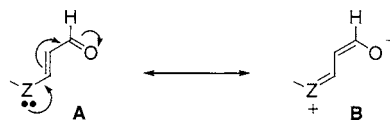
FIGURE 3. Suppression of reactivity of the formyl group by electronic effects.

Recently, Jun et al. have reported the similar alkylation reaction of aromatic ketimines with olefins using a rhodium catalyst.[43]

Reaction of Aromatic Nitriles with Olefins

Interestingly, a nitrile group can also serve as a directing group for the C–H/olefin coupling. In this case, the π-electrons of the nitrile group appear to participate in positioning the ruthenium close to the ortho C–H bond. The reaction of benzonitrile with **5** using **6** as a catalyst gave the corresponding 1:2 coupling product in 97% yield as the predominant product (eq 13).[27] This exclusive ortho selectivity implies that a nitrile group is able to direct the ruthenium to the ortho C–H bond. When the reaction was conducted using 1 equiv of the vinylsilane **5**, both the 1:1 addition product and the 1:2 addition product were obtained in 18% and 19% yields, respectively. This unusually high performance for the 1:2 adduct suggests that the second C–H bond cleavage takes place, to a great extent, prior to the dissociation of the 1:1 adduct from the ruthenium center.
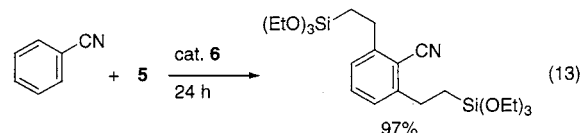
Addition of β-C–H Bonds in Aldehydes to Olefins

The use of a formyl group as a directing functionality is our next interest.[29] When aldehydes are exposed to low-valent ruthenium[44] and rhodium[45] complexes, decarbonylation usually takes place. In addition, the hydroacylation of olefins[46] becomes another competitor against the formyl group directed C–H/olefin coupling. To suppress these problems, the following two procedures were devised, one being steric (Figure 2) and the other electronic in nature (Figure 3).

Steric hindrance around the formyl moiety disturbs the approach of the ruthenium to the carbonyl carbon. Actually, the reaction of aldehydes having a sterically bulky group at a position ortho to the formyl group, i.e., 2,4-di-*tert*-butylbenzaldehyde and 2-(trimethylsilyl)benzaldehyde, gave the corresponding ortho alkylation product in good yield (eq 14). As an electronic control, the electron-

donating character of a heteroatom at a position β to the formyl group decreases the electrophilicity at the formyl carbon atom due to the contribution of resonance form **B**, and as a result, the formyl group cannot be attacked by the nucleophilic ruthenium center. The reaction of an aldehyde having a dihydropyran framework selectively gave the alkylation product (eq 15). These results indicate that both steric and electronic effects are important factors in preventing decarbonylation and in attaining C−H/olefin coupling.

(14)

(15)
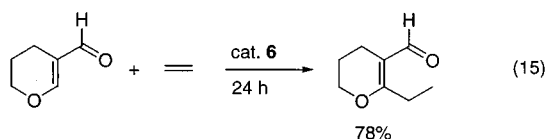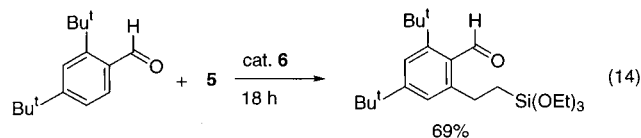
Intramolecular Cyclization of 1,*n*-Dienes via C−H Bond Cleavage

The transition-metal-catalyzed intramolecular cyclization of 1,5- and 1,6-dienes containing pyridyl, imidazolyl, or oxazolyl rings provides a new route for the construction of five- or six-membered carbocycles.[19,21,23] The intramolecular cyclization of 1,5-dienylpyridine (**12**) proceeded in the presence of RhCl(PPh$_3$)$_3$ as the catalyst to give the desired five-membered ring compound **13** in high yield (eq 16). Some 1,6-dienes containing a pyridyl moiety are applicable to this reaction. The C−H bond cleaved by the rhodium complex adds to both terminal and internal olefins resulting in a five- or six-membered carbocycle.

(16)
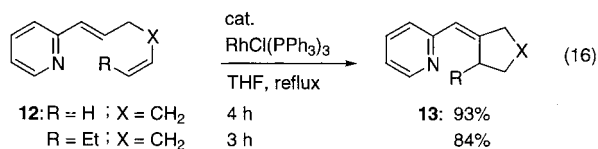
This catalytic cyclization can be extended to an asymmetric version.[21] When the [RhCl(coe)$_2$]$_2$/(*R*)-(*S*)-PFOMe catalyst system (coe = cyclooctene; (*R*)-(*S*)-PPFOMe = (*R*)-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethyl methyl ether) was employed in place of the [RhCl(coe)$_2$]$_2$/PCy$_3$ catalyst system, in the reaction of 1,5-dienylimidazoles, the corresponding five-membered carbocycle was obtained in 75% yield with 82% ee.

Mechanistic Aspect of C−H/Olefin Coupling

Preliminary studies with respect to the reaction mechanism of the ruthenium-catalyzed C−H/olefin coupling have been reported by us[12,13] and other groups.[47,48] These studies have revealed that initially hydrogenation of olefin with dihydrideruthenium catalyst **6** gives a zerovalent

Scheme 1. Preequilibrium in RuH$_2$(CO)(PPh$_3$)$_3$-Catalyzed Reactions of Ketones and Esters with a Vinylsilane
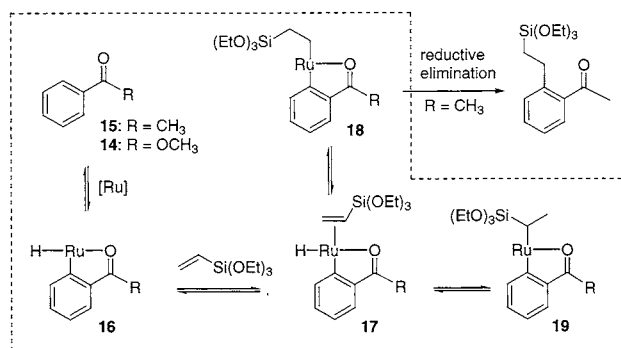
ruthenium species such as Ru(CO)(PPh$_3$)$_3$. Further mechanistic studies by means of deuterium-labeling experiments and the measurement of ^{13}C kinetic isotope effects (KIEs) were reported by us.[31,49,50]

A deuterium-labeling experiment using methyl benzoate (**14**-d_5) was carried out (eq 17). The ^{1}H NMR spectra of the recovered starting materials indicate that a complete scrambling occurred among the two ortho positions of the ester and three vinylic positions of the vinylsilane even though no coupling product was obtained.

(17)
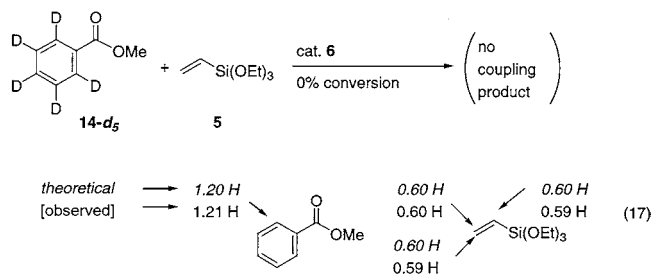
For obtaining information with respect to the rate-determining step in the reactions of ketones and esters, we measured the experimental ^{13}C kinetic isotope effects (KIEs) at natural abundance.[31,49,50] If a C−C bond formation step is rate-determining, the relative intensity of the ortho carbon in the starting material should be increased compared with those at natural abundance. The KIE of the ortho carbon was determined to be 1.033, while those of the other aromatic carbons were nearly 1.000 for each carbon atom. The same experiment was also applied to the reaction of aromatic ketones.[50] In this case, the KIE of the ortho carbon of the ketone was determined to be 1.023. These results strongly suggest that the C−C bond formation step is rate-determining in both (aromatic esters and ketones) catalytic reactions.

On the basis of these studies, a plausible reaction pathway for the ruthenium-catalyzed reactions of aromatic compounds with olefins can be proposed as shown in Scheme 1.

Since the H/D exchange occurred only at the ortho position, chelation assistance is critically important in C−H bond cleavage by the ruthenium complex, to give the ruthenium−hydride (Ru−H) species. The complexation of the vinylsilane and the addition of the Ru−H bond to olefins occur in both directions, and the reverse of these

Scheme 2. One- and Two-Step Mechanisms for Reductive Elimination
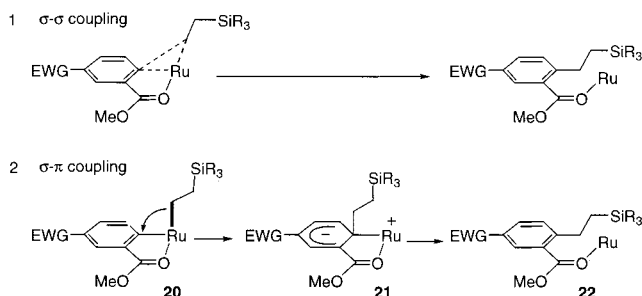
reactions, i.e., β hydride elimination, also takes place. In the present case, **19** can only return to **17**. In the case of the reaction of acetophenone, intermediate **18** undergoes reductive elimination to the corresponding coupling product, but in the case of methyl benzoate, **18** does not undergo reductive elimination. The hydride **17** returns to **16** and then to **14**. The deuterium scrambling experiments show that these equilibrium processes are occurring well ahead of reductive elimination. This means, surprisingly and in contrast to the generally accepted view, that the C—H bond cleavage step is an easy step in the present catalytic reactions. The ^{13}C kinetic isotope effects verify that the reductive elimination, resulting in C—C bond formation, is rate-determining in the $RuH_2(CO)(PPh_3)_3$-catalyzed reactions.

As discussed above, in the reaction of aromatic esters with olefins, reductive elimination is rate-determining. Typically, if the reductive elimination is the rate-determining step, an electron-withdrawing group on the leaving ligand (e.g., aromatic ring) would be expected to retard the rate of the reductive elimination step.[51] Interestingly, however, in the reaction of aromatic esters with olefins, the electron-withdrawing groups apparently facilitated reductive elimination. We propose that a migration mechanism (**20** to **21**, Scheme 2), i.e., $\sigma-\pi$ coupling, for the reductive elimination is favorable rather than usual $\sigma-\sigma$ coupling mechanism. In the case of $\sigma-\pi$ coupling, an alkyl group on the ruthenium first undergoes a 1,2-shift to the aromatic ring without extensive cleavage of the aromatic carbon—metal σ-bond (**20** to **21**).

The role of the electron-withdrawing groups in the reaction of aromatic esters with **5** (Table 4) can be attributed to an acceleration of this Michael addition-type migration. A meta-electron-withdrawing group is more efficient than ortho and para groups.

These results demonstrate the important features of the present C—H/olefin coupling. C—H bond cleavage, which has been often considered to be a rate-determining step, is a facial step compared with the C—C bond formation step, and a preequilibrium prior to a reductive elimination occurs in this catalytic cycle.[52]

Catalytic C—H/SiR₃ Coupling

The transition-metal-catalyzed addition of C—H bonds to C—C multiple bonds to give the alkylation products have been mentioned above.[11–32] The silylation of C—H bonds

Table 5. Site-Selective Silylation of Heteroarenes with VInylsilanes
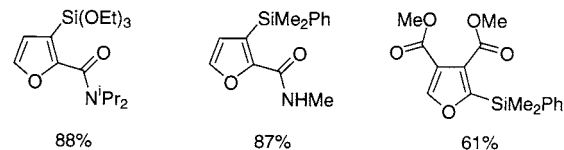
with vinylsilanes[53] and hydrosilanes[54] yielding heteroaryl- and arylsilanes will be discussed below.

The reaction of 2-acetylthiophene with trimethylvinyl-silane was carried out using $RuH_2(CO)(PPh_3)_3$ (**6**) as the catalyst, and the C—H/olefin coupling product was obtained in quantitative yield. Interestingly, however, the use of $Ru_3(CO)_{12}$ (**8**) as the catalyst, which is ineffective for the alkylation of the acetylthiophene with the vinylsilane, resulted in the efficient silylation of C—H bonds (eq 18).

The ruthenium—silyl intermediate might be formed by
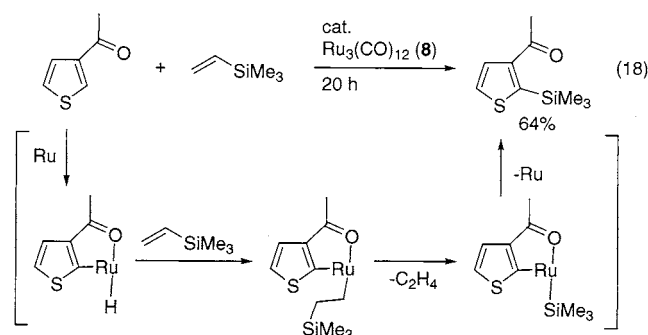
β-silyl elimination from the (2-(trimethylsilyl)ethyl)ruthenium intermediate, which was formed by the hydroruthenation of the trimethylvinylsilane. This type of silylation of the C—H bonds can be applied to a number of heteroaromatic compounds. Selected results are listed in Table 5. Furan derivatives having amide and ester functional groups were also found to be silylated with vinylsilanes. The presence of a free N—H moiety did not retard the reactivities of the heteroarenes.

Benzene derivatives cannot be silylated using vinylsilane. This can be overcome by the use of hydrosilanes as the silylating reagent; the silylation of aromatic compounds having a directing group was found to proceed to give the corresponding ortho silylation products (Table 6).[54,55] Berry reported on the similar silylation of aromatic compounds using hydrosilanes, but in their case a mixture of regioisomers (*o*-, *m*-, and *p*-isomers) was produced.[56] As shown in Table 6, this silylation procedure can be applied to various aromatic compounds. It should be emphasize that in the case of the ruthenium-catalyzed C—H/olefin coupling, a chelation assistance with π-conjugation (**C**) is important for attaining the coupling reaction, but in the case of the present silylation reaction heteroatoms which are not a component of the π-conjugation (**D**) are also able to function as a directing group.

During the catalytic reaction, two atoms of hydrogen must be removed. The reductive elimination of molecular hydrogen from a ruthenium center is a thermally difficult step because the free energy of this process is ca. +20 kcal/

Table 6. Site-Selective Silylation of Arenes with Hydrosilanes

93%   100%   98%

100%   58%   77%

C
an example of
chelation-assistance
with π-conjugation

D
an example of
chelation-assistance
without π-conjugation
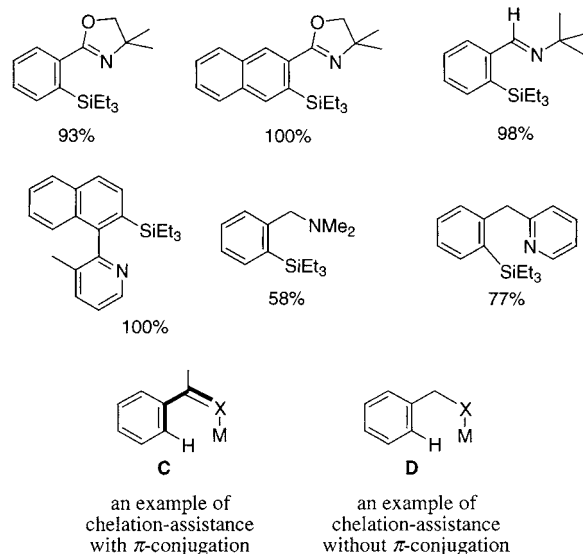
mol.[57] The use of an olefin as a hydrogen scavenger is essential for this catalytic reaction. In our C—H/SiR₃ coupling, *tert*-butylethylene and norbornene served as efficient hydrogen scavengers. This catalytic system is a new entry for the preparation of arylsilanes.

Concluding Remarks and Outlook

The ctalytic use of otherwise unreactive C—H bonds described above has already become a useful tool in organic synthesis. The reaction scheme is quite simple. A C—H bond is cleaved and then adds to olefins or acetylenes resulting in a new C—C bond. Functional group compatibility and the applicability of this reaction are wide. The formation of the new C—C bond occurs exclusively at a position ortho to the directing group, which includes carbonyl, imino, and nitrile groups. The efficiency of the reaction is high in many cases.

We have also developed procedures for the highly efficient carbonylation at C—H bonds, resulting in the formation of unsymmetrically substituted ketones.[58] These will be reviewed elsewhere. Recently, Ellman and Bergman has applied a mass spectrometric labeling strategy for a high-throughput reaction to the carbonylation at C—H bonds.[59] Other research groups have also studied these types of catalytic C—H/olefin coupling reactions. Trost reported on the RuH₂(CO)(PPh₃)₃-catalyzed addition of C—H bond in conjugated esters to olefins,[35] Grigg performed the alkylation of acetylpyridine,[60] Chaudret[61] and Leitner[62] have examined this type of coupling reaction using Ru(H₂)(H)₂(PCy₃)₂ as the catalyst at room temperature, and Brookhart reported on a rhodium-catalyzed reaction of aromatic ketones with olefins giving ortho alkylation products.[63] The RhCl(PPh₃)₃-catalyzed alkylation of arylpyridines with olefins has been reported by Lim et al.,[64] and Jun has reported the similar alkylation of aromatic imines with olefins.[65] The aromatic vinylation

of azobenzenes using acetylenes with the aid of RhCl-(PPh₃)₃ hs been reported by Kisch.[66]

The first stage of these types of catalytic reactions involving a C—H bond cleavage has been clarified. The second stage of this area will include applications of this methodology in the synthesis and preparation of highly valuable chemicals. Preliminary work has already been initiated. We investigated the practical scale (10−30 g of the starting ketone) synthesis of an ortho-alkylated aromatic ketone.[13,67] Sharpless reported that some of the reactions can be carried out in the absence of solvents.[68] In addition, Weber extended this coupling reaction to polymer synthesis[69] and Woodgate reported on the use of these types of coupling reaction in the synthesis of a natural product.[70]

A reference book summarizing the fundamental aspects and recent advances in this field has recently been published,[71] suggesting the presence of a new realm awaiting further development.

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