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Perspective

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Potential of Metal-Catalyzed C−C Single Bond Cleavage for Organic Synthesis

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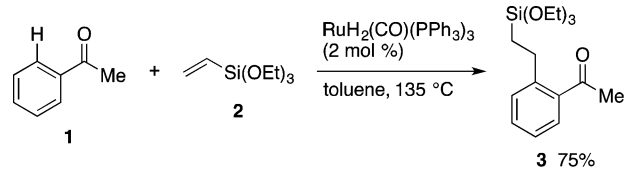
ABSTRACT: Conventional organic synthesis has been mainly based upon the reactivities of π-bonds and polar σ-bonds. Carbon−carbon single bonds are nonpolar and generally far less reactive. Although they remain intact under most reaction conditions, it is possible to activate and cleave them if suitable organometallic compounds or metal catalysts are applied. Such C−C single bond cleavage reactions are attracting increasing attention in the context of synthetic chemistry because they provide a unique and more straightforward route from readily available substances to targets, while requiring significantly fewer steps. The present Perspective aims to exemplify the potential of metal-catalyzed C−C single bond cleavage for organic synthesis.

INTRODUCTION

Most reactivities of organic molecules originate from their (i) π-bonds such as C═C and C═O, (ii) polar σ-bonds such as C−Br and C−Li, and (iii) nonbonding electron pairs. Their frontier orbitals are sterically as well as energetically accessible for the frontier orbitals of reagents and catalysts. Nonpolar σ-bonds such as C−H and C−C, on the other hand, are thermodynamically stable and far less reactive. Their HOMO energies are too low, and their LUMO energies too high, for interaction with the frontier orbitals of reagents and catalysts. Those frontier orbitals are considerably more constrained in space. Thus, they remain intact under most conventional reaction conditions. Nonetheless, if such nonpolar sigma-bonds can be site-selectively cleaved and utilized for the construction of organic skeletons, the reactions would develop into innovative synthetic maneuvers of enormous value. Accomplishing this would pave more straightforward synthetic pathways which derive from readily available chemical feedstocks—even hydrocarbons. It would become possible to dispense with a series of tedious functional group manipulations that were otherwise required for construction of target skeletons. If such approaches are applied to naturally occurring and therapeutically interesting compounds, their skeletal rather than functional-group modification may become feasible. Consequently, the site-selective "activation" of nonpolar σ-bonds not only presents a scientific challenge to organometallic chemists but also provokes the curiosity of many synthetic chemists.

One of the landmark reactions in the field of nonpolar σ-bond activation for organic synthesis is a ruthenium-catalyzed reaction of aromatic ketones with alkenes reported by Murai et al. in 1993 (Scheme 1).[1] In this example, an aromatic C−H bond ortho to an acyl group is site-selectively cleaved by a ruthenium catalyst and is added across an alkene intermolecularly to form a new C−C linkage in an atom-economical manner. This result demonstrated the synthetic potential of catalytic C−H bond transformations as well as their feasibility, inspiring countless chemists in the field of organometallic chemistry directed toward organic synthesis (OMCOS) to explore catalytic reactions of C−H bonds. Currently, a wide variety of C−H bond transformations are available and have been utilized for the synthesis of natural products and functional materials.[2] On the other hand, synthetic applications of C−C bond transformations remain limited. Interaction of a metal center with a C−C single bond is generally more difficult than that with a C−H bond because of their more constrained directionality. Nonetheless, direct functionalization of C−C bonds also create unique opportunities to significantly streamline synthetic pathways. This Perspective discusses the present scope of metal-catalyzed C−C single bond cleavage for organic synthesis. The first section explains the intrinsic difficulties of C−C bond cleavage. The second section deals with the examples selected from the early stages of this chemistry. The third section features recent examples that demonstrate the state-of-the-art of C−C single bond cleavage reactions for organic synthesis. The examples are limited to a few that explicitly convey intriguing and leading concepts related to C−C bond cleavage reactions. The paper closes with an outlook of the direction in the future. Comprehensive review articles, including stoichiometric reactions, are already available for reference.[3] Alkene and alkyne metathesis reactions, which also involve C−C bond cleavage, are beyond the scope of this Perspective. C−C bond cleavage reactions that do not involve direct interaction of a cleaving C−C bond with a metal center (e.g., Claisen rearrangement, retro-Aldol reaction, etc.) are likewise omitted.

Scheme 1



INTRINSIC DIFFICULTIES OF C−C BOND CLEAVAGE

Both thermodynamic and kinetic issues are relevant to the inert nature of C−C single bonds. The thermodynamic issue comes

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from the large bond energies of C−C σ-bonds. The final products of C−C bond cleavage reactions are often less stable than the reactants. The energy profiles of hydration reactions of ethylene and ethane are compared in Figure 1. Whereas an

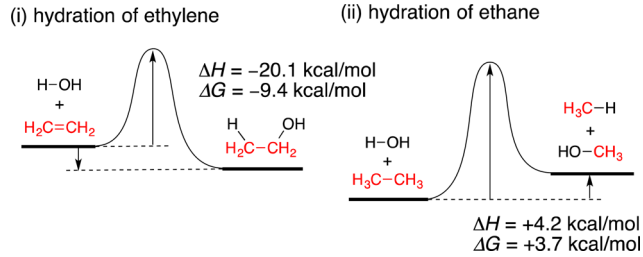


Figure 1. Comparison of hydration reactions of ethylene and ethane.

addition reaction of the O−H bond of water across the C−C double bond of ethylene is thermodynamically favored, addition to ethane with cleavage of the C−C single bond (hydrolysis) is thermodynamically disfavored.

In addition, the thermodynamic stability of an expected intermediate is also an issue. Bond energies of C−C σ-bonds are often much larger than those of metal−carbon (M−C) bonds; thus, conversion of C−C bonds into C−M bonds is likely to be thermodynamically disfavored. Consequently, the concentration of an organometallic intermediate containing C−M bonds is considerably low, even if such processes are kinetically feasible.

The kinetic issue is associated with the directionality of C−C σ-bonds and the energy levels of frontier bonding/antibonding orbitals. The σ-orbital of a C−C bond is highly constrained along the bond axis. Significant distortion is required for effective overlap of its frontier orbitals with metal orbitals (Figure 2). This distortion would demand considerable

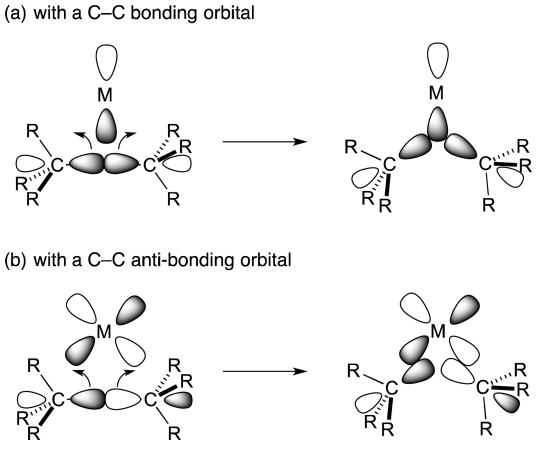


Figure 2. Interaction of metal orbitals with a C−C single bond for oxidative addition.

activation energy. In addition, the bonding orbital lies at a significantly low energy level, and the antibonding orbital lies at a high energy level. Interaction of these orbitals with a metal center is energetically cumbersome. In contrast, the frontier orbitals of other functionalities are much closer in energy to those of a metal center. It is difficult for metals to interact with C−C σ-bonds in preference to other functional groups. As a consequence, reactions with more exposed functionalities outcompete C−C bond cleavage reactions, leading to other reaction pathways.

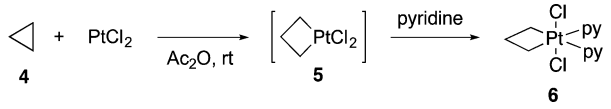
Another issue is side reactions which potentially occur after the C−C bond cleavage. Since the activation barrier of C−C bond cleavage is generally high, more forcing reaction conditions are often required for C−C bond cleavage. Under such circumstances, undesired reaction pathways, like β-hydride elimination, possibly occur with the alkylmetal intermediates.

Despite these intrinsic difficulties, synthetic chemists have devised various strategies for catalytic transformations involving C−C bond cleavage. The following sections deal with intriguing examples that clearly show the reaction scenarios and concepts which overcome the issues.

C−C BOND CLEAVAGE BY METALS: SEMINAL EXAMPLES

The pivotal example of C−C bond cleavage dates back more than a half century. In 1955, Tipper reported that cyclopropane (**4**) reacted with $PtCl_2$ to afford an adduct complex.[4] Although the structure was unclear at that time, the adduct was subsequently shown to be platinacyclobutane **6** resulting from oxidative addition of the C−C single bond onto the platinum center (Scheme 2).[5] This early example, and ensuing analogous

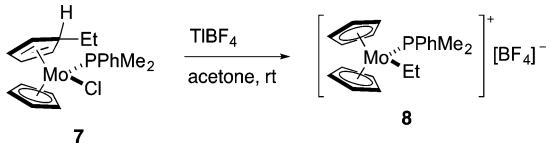
Scheme 2



reactions of small ring compounds,[6−11] demonstrated the viability of oxidative addition of strained C−C single bonds onto metals. The reactivity derives from strain, which destabilizes the starting substances. The destabilization contributes to lowering the activation barrier as well as gaining a driving force. In addition, the banana-type protruding σ-bond alleviates the directionality of bonding/antibonding orbitals, thus facilitating orbital interaction with the metal center.

Another interesting example of C−C bond cleavage was found in the synthesis of (cyclopentadienyl)metal complexes.[12] Treatment of the neutral molybdenum chloride **7** with thallium tetrafluoroborate produced the cationic molybdocene **8** (Scheme 3).[12a] Oxidative addition of the nonstrained C−C

Scheme 3



single bond between the η^4-cyclopentadiene ligand and the ethyl substituent occurred to generate the aromatic η^5-cyclopentadienyl ligand. The major driving force derives from stabilization by aromatization of the η^4-cyclopentadiene ligand.

Directing groups exert a proximity effect to provide a powerful strategy for C−C bond cleavage. In 1984, Jun and Suggs discovered a reaction between alkyl 8-quinolyl ketone **9** and the rhodium(I) complex **10** (Scheme 4).[13] The non-strained C(carbonyl sp^2)−C(sp^3) bond underwent oxidative addition onto the rhodium(I) center to afford the rhodacyclic compound **12**. Milstein et al. reported that a reaction of the

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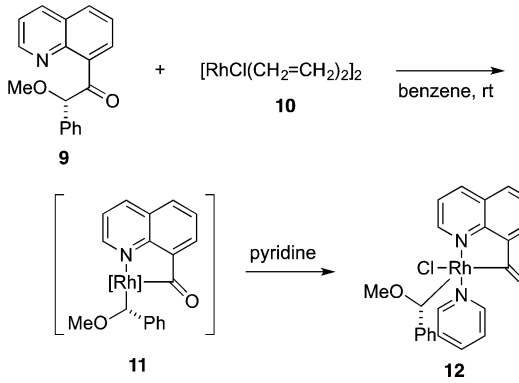
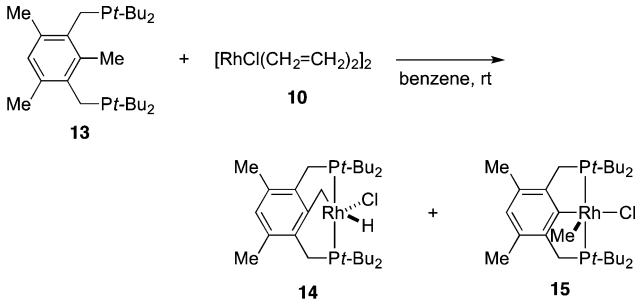
Scheme 4



bulky pincer-type diphosphine ligand **13** with $[RhCl(CH_2{=}CH_2)_2]_2$ (**10**) caused site-selective metal insertion into an aryl–methyl bond, even at room temperature (Scheme 5).[14] In these

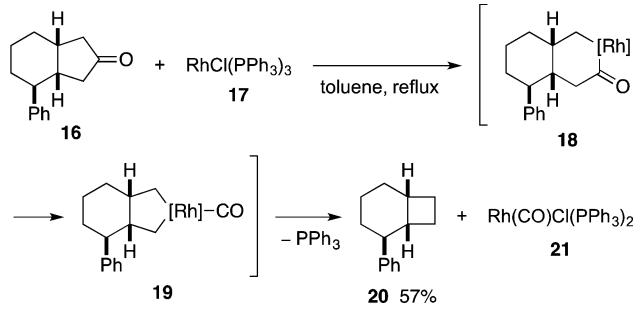
Scheme 5



examples, the Lewis basic atoms (nitrogen and phosphorus) coordinate to the rhodium center to locate it in proximity to the target C–C single bond. This constrained geometrical situation facilitates oxidative addition kinetically. In addition, coordination stabilizes the resulting five-membered ring metallacycles to assist the oxidative addition process thermodynamically.

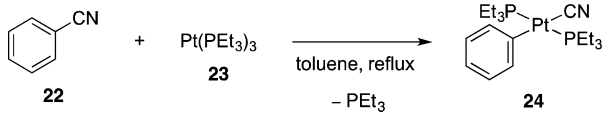
A nonstrained C–C single bond located next to a carbonyl group can be cleaved even without the assistance of directing groups. For example, cyclic ketone **16** reacted with an equimolar amount of $RhCl(PPh_3)_3$ (**17**) to furnish the decarbonylated cyclobutane **20** together with $RhCl(CO)(PPh_3)_2$ (**21**) (Scheme 6).[15,16] Mechanistically, the decarbonylation reaction would proceed through (1) oxidative addition of the C–C bond, (2) migratory deinsertion of carbon monoxide, and (3) reductive elimination of the cyclobutane.

Scheme 6



Similarly, a C–C single bond next to a cyano group undergoes oxidative addition.[16] For example, benzonitrile **22** reacted with the platinum(0) complex **23** to afford the phenylplatinum cyanide complex **24** (Scheme 7). Aroyl

Scheme 7



cyanides undergo decarbonylation upon catalytic treatment with rhodium.[17] Branched 2-methyl-3-butenenitrile isomerizes to linear 3-pentenenitrile with the aid of a nickel catalyst.[18] These results experimentally confirm the intermediacy of the oxidative adduct.

Another important elementary step to cleave a C–C single bond is β-carbon elimination. A seminal example is found in the reaction of trimethylaluminum (**25**) and isobutene (**26**) (Scheme 8).[19] When heated under pressurized conditions,

Scheme 8

the alkene underwent insertion into the carbon–aluminum bond to give tri(neopentyl)aluminum (**27**). On the other hand, when heated under an atmospheric pressure of nitrogen, the alkene **26** was eliminated, and the adduct **27** reverted back to trimethylaluminum (**25**). This reverse reaction indicates that a C–C single bond at the β-position to the metal center can be cleaved. This type of C–C bond cleavage is referred to as β-carbon elimination, which was later found with various organometallic compounds. Since the C–C bond to be cleaved is located in proximity to the metal center, this process can be sufficiently facile to occur without assistance of strain, directing groups, or π-functional groups.

FUNDAMENTAL STUDIES ON CATALYTIC REACTIONS VIA C–C BOND CLEAVAGE

Various catalytic transformations have been developed to construct new C–C bonds by way of C–C bond cleavage. Such reactions cause drastic changes in the connectivities of the carbon frameworks; thus, at a glance, with just a starting compound and a product, it is often difficult to understand what happens mechanistically. In many cases, however, the reaction pathway can be reasonably explained by assuming a *multi*-step mechanism involving the elementary steps mentioned in the preceding section. A typical example is shown in Scheme 9. When cyclobutenone **28** was treated with a rhodium catalyst, both the cyclobutenone and the cyclopropane ring were opened to combine into the cycloheptadienone **29**.[20] Mechanistically, the reaction is initiated by strain-assisted oxidative addition of the C(carbonyl sp^2)–C(sp^3) bond to produce the rhodacyclopentenone intermediate **30** (or rhodium–vinylketene complex). The cyclopropane ring is then opened through β-carbon elimination to release its ring strain. The eight-membered rhodacyclic intermediate **31** is generated, and subsequent reductive elimination affords the product **29**.

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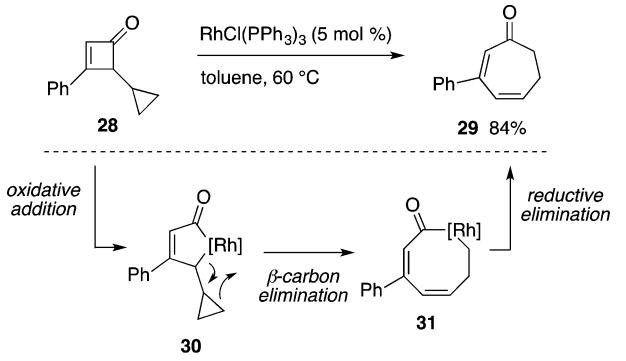
Scheme 9

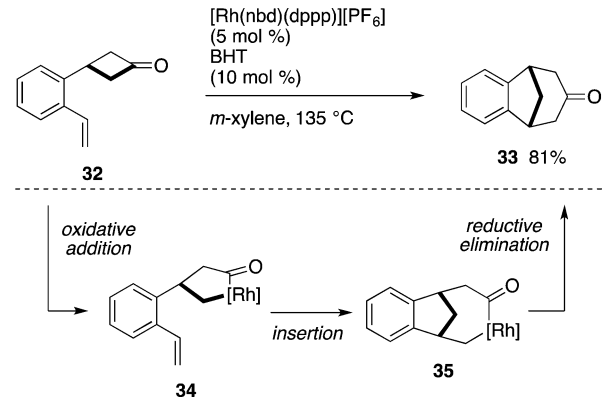


Likewise, skeletal rearrangement reactions involving C−C bond cleavage can be explained by assuming the oxidative addition reaction and the β-carbon elimination reaction assisted by strain, directing groups, and/or π-functional groups. The following section covers representative works on catalytic reactions.

Catalytic Reactions Initiated by Oxidative Addition and Related Processes. Very early examples are found of complex skeletal rearrangement reactions of highly strained molecules consisting of multiple small rings like cubanes and quadricyclane. This kind of chemistry is comprehensively reviewed by Bishop.[21] These reactions are, however, too complex to exemplify the fundamental reactivities, so they are not discussed further here.

Insertion of unsaturated functionalities into C−C bonds represents reactions which are advantageous for synthetic purposes. Cyclobutanone **32** underwent a skeletal rearrangement reaction to form benzobicyclo[3.2.1]octenone **33** upon treatment with a rhodium catalyst (Scheme 10).[22] In a formal

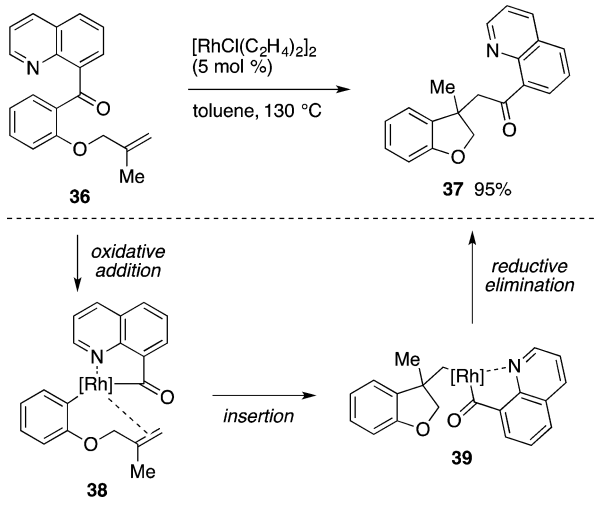
Scheme 10



sense, the C−C double bond of the pendant vinyl group is intramolecularly inserted into the C(O)−C σ-bond of the cyclobutanone moiety. Mechanistically, the reaction is initiated by strain-assisted oxidative addition of the C(O)−C bond onto rhodium, producing rhodacyclopentanone **34**. Intramolecular insertion of the C−C double bond into the resulting C−Rh bond follows, and the subsequent reductive elimination completes the insertion process.

The insertion reactions are not limited to strained ring systems. Insertion successfully takes place also with nonstrained C−C bonds if a directing group is available. For example, the C(O)−Ar single bond of 8-quinolyl ketone **36** underwent intramolecular 1,2-addition across the pendant alkene moiety (Scheme 11).[23] The quinoline nitrogen coordinates to the rhodium center to facilitate oxidative addition of the C(O)−Ar single bonds.

Scheme 11



Thus, catalytic cleavage of an unstrained C−C bond can be a useful strategy, if appropriate directing groups are deliberately exploited. It is often difficult, however, to remove a directing group from the product afterward, limiting the synthetic utility of such a process. It is desirable from a synthetic perspective to dispense with a process detaching a directing group. In this regard, it is particularly noteworthy that a cooperative catalysis of 2-amino-3-picoline and rhodium effects cleavage of an unstrained C(carbonyl sp^2)−C(sp^3) bond of ketones;[24] when a mixture of ketone **40** and 1-hexene (**41**) was heated in the presence of 2-amino-3-picoline and rhodium, 2-octanone (**42**) was produced, together with styrene (**43**) (Scheme 12).[24a] This groundbreaking reaction is initiated by condensation of aminopicoline with ketone **40** to form the imine **44**. The pyridine nitrogen serves as the directing group to facilitate the oxidative addition of the C(carbonyl sp^2)−C(sp^3) bond onto rhodium to furnish the five-membered rhodacyclic intermediate **45**. The subsequent β-hydrogen elimination extrudes styrene (**43**), and instead, 1-hexene (**41**) enters the coordination site of the rhodium center. The sequence of hydrorhodation (i.e., insertion of alkene **41** into the H−Rh bond), reductive elimination, and hydrolysis of the imine moiety affords the product **42** with regeneration of the aminopicoline.

Oxidative addition of C−CN bonds also extends to catalytic insertion reactions. For example, benzonitrile (**22**) was added across alkyne **48** in the presence of a nickel catalyst (Scheme 13).[25] The reaction is facilitated by addition of a catalytic amount of Lewis acids, which enables cleavage of the C−CN bond of acetonitrile. The nitrile nitrogen coordinates to the Lewis acid in the end-on mode, which facilitates the oxidative addition.

The oxidative addition of nitriles has also been applied to cross-coupling reactions with organometallic reagents like Grignard reagents and organoboronic acids.[26]

The C−CN bond of nitriles is cleaved also by silylmetal complexes to furnish metal isocyanide complexes.[27] This phenomenon found application to catalytic transformations. For example, benzonitrile **52** underwent a de-cyanative

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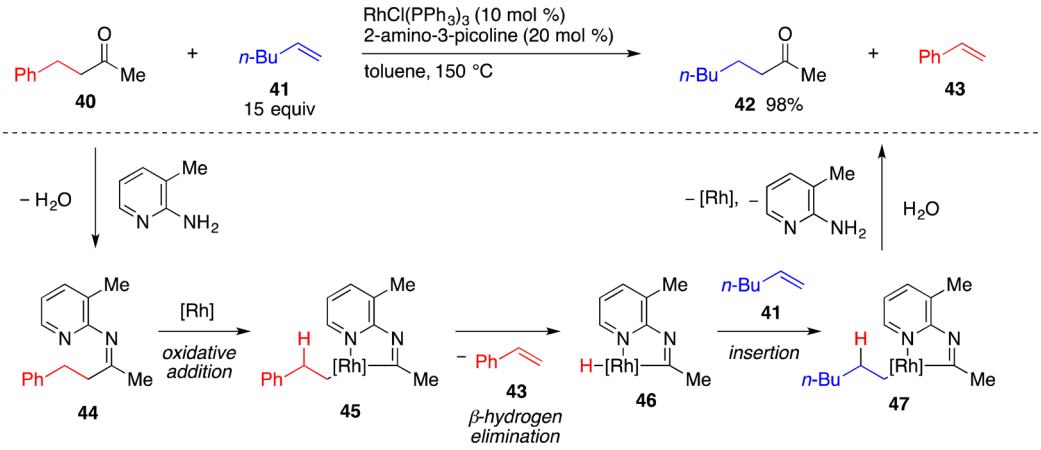
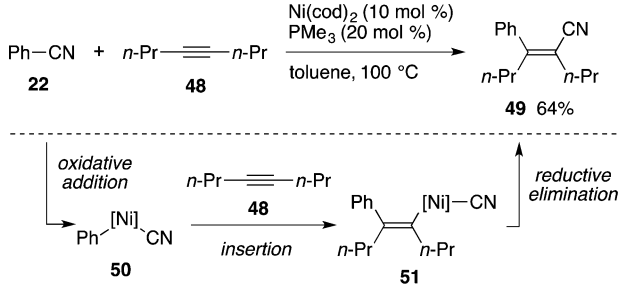
Scheme 12

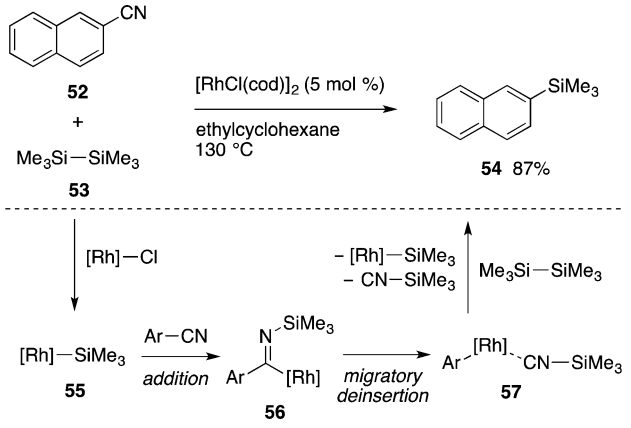


Scheme 13



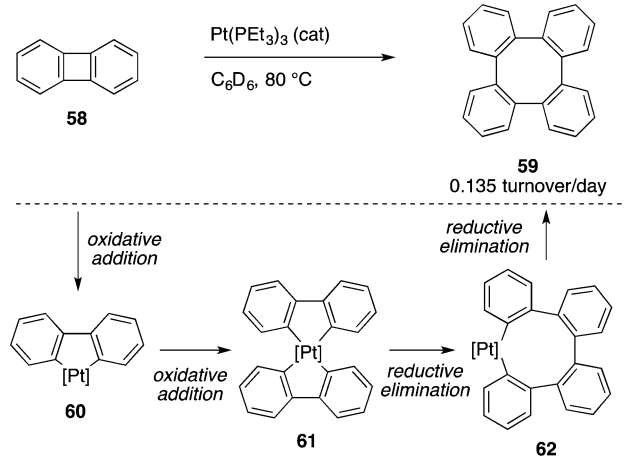
silylation reaction with disilane **53** in the presence of a rhodium catalyst (Scheme 14).[28] A related reductive de-cyanation reaction with hydrosilanes[29] and a de-cyanative borylation reaction with diboranes[30] have also been developed.

Scheme 14



Formal σ-bond metathesis reactions possibly occur through oxidative addition of strained C–C single bonds. A typical example is given by a dimerization reaction of biphenylene **58** to produce an eight-membered cyclic tetraphenylene, **59** (Scheme 15).[31] Mechanistically, oxidative addition of the strained C–C bonds occurred twice to form the platinum(IV) intermediate **61**. Then, reductive elimination followed also twice to afford the eight-membered ring product **59**, together with regeneration of the catalytically active platinum(0) species.[31b]

Scheme 15



In addition to σ-bond metathesis leading to homodimerization, the C–C bond of biphenylenes underwent formal cross-metathesis of σ-bonds when reacted with bismetallic compounds like Si–B, B–B, and Sn–B to form bismetalated biphenyl derivatives.[32] The C(O)–C bond of cyclobutanones underwent formal intramolecular σ-bond metathesis with a Si–Si bond of disilane[33] and a C–Si bond of silacyclobutane.[34]

Catalytic Reactions Involving β-Carbon Elimination. β-Carbon elimination is often found in catalytic transformations of tertiary alcohols. Miura et al. reported a palladium-catalyzed coupling reaction of *tert*-benzyl alcohol **63** with bromobenzene (**64**), giving biaryl **65** (Scheme 16).[35] The reaction proceeds through (1) oxidative addition of bromobenzene (**64**) onto palladium(0), (2) exchange of the bromo ligand on palladium(II) with the alkoxo ligand, (3) β-carbon elimination giving an di(aryl)palladium **68** with extrusion of acetone, and (4) reductive elimination. The bulkier aryl group underwent β-carbon elimination more readily. This result indicates that relief of steric congestion plays a key role in this C–C bond cleavage.

Homoallylic alcohols undergo analogous β-carbon elimination.[36] The reaction proceeds through a six-membered cyclic transition state rather than a more strained four-membered one, which would contribute to lowering the activation energy (Scheme 17).

It is difficult to cleave a C(sp^3)–C(sp^3) bond of simple aliphatic alcohols by way of β-carbon elimination. On the other hand, a C(sp^3)–C(sp^3) bond of four-membered cyclic alcohols

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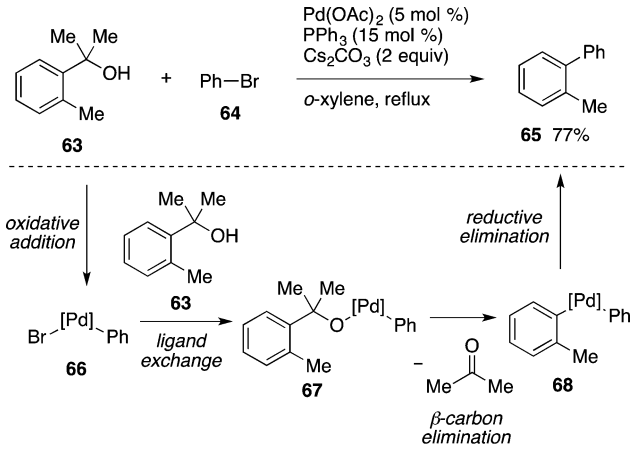
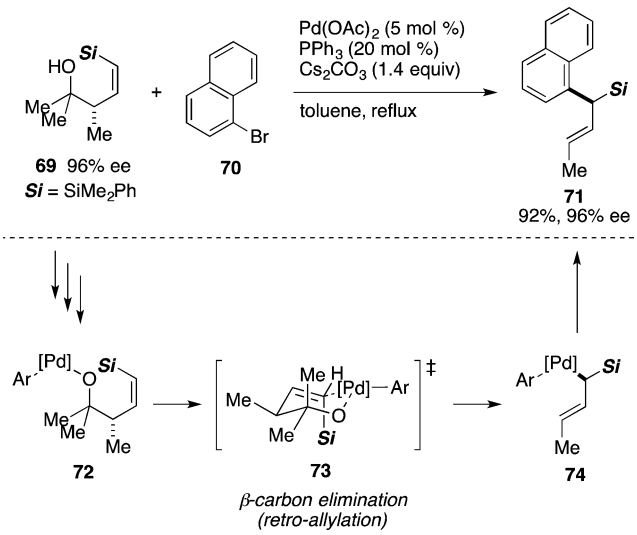
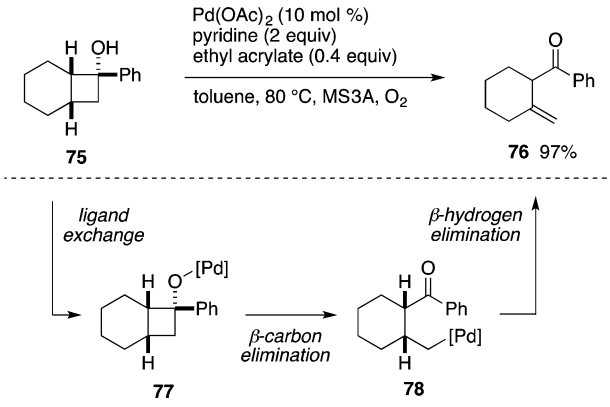
Scheme 16



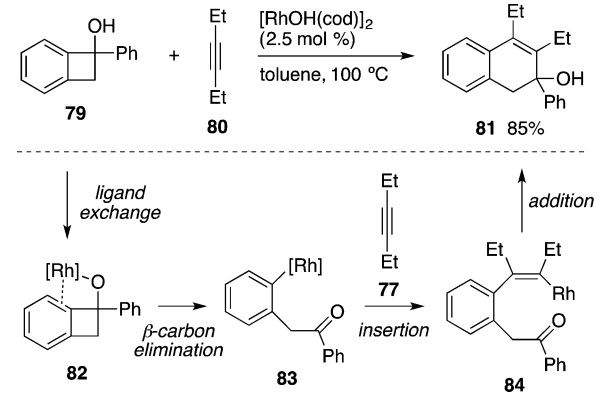
Scheme 17



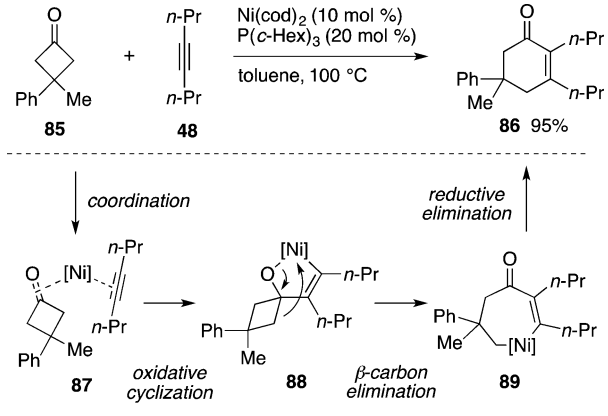
Scheme 18



Scheme 19



Scheme 20



is readily cleaved through β-carbon elimination. The facile cleavage is ascribed to the release of ring strain.[37] For example, treatment of cyclobutanol **75** with a palladium catalyst induced a ring-opening reaction through (1) exchange of the acetate ligand on palladium(II) with the cyclobutanolate ligand, (2) β-carbon elimination, and (3) β-hydrogen elimination, furnishing β,γ-unsaturated ketone **76** (Scheme 18).[37a] This ring-opening process has been applied to an arylation reaction with aryl halides[37b,f] and an isomerization reaction giving cyclopropyl ketones.[37c]

Benzocyclobutenol **79** underwent ring-opening with site-selective cleavage of the C(sp^2)−C(sp^3) bond upon treatment with a rhodium catalyst possessing electron-accepting ligands (Scheme 19).[38] The site selectivity is attributed to the participation of the π-orbitals of the benzene ring in the β-carbon elimination step.[39] It should be noted that this site selectivity is complementary to that of the thermal reaction, in which the C(sp^3)−C(sp^3) bond is cleaved through a 4π electrocyclic reaction.[40] The site-selective ring-opening process has been applied to insertion reactions of various unsaturated species, including alkynes,[38] alkenes,[41] and carbenes.[42] These reactions showcase an alternative approach to insertion of unsaturated bonds into C−C single bonds.

Another unique approach to alkyne insertion is found in a nickel-catalyzed reaction of cyclobutanone **85** and alkyne **48**, forming cyclohexenone **86** (Scheme 20).[43] The reaction is assumed to be initiated by an oxidative cyclization reaction between the carbonyl group and the alkyne on nickel. The resulting five-membered nickellacycle **88** undergoes β-carbon elimination to open the cyclobutane ring, facilitated by the release of ring strain. The seven-membered nickellacycle **89** is generated, and the subsequent reductive elimination affords the cyclohexenone product **86**.

Cleavage of a C−C single bond of far less strained cyclopentane rings was identified in a rhodium-catalyzed cycloisomerization reaction of allenyne **90** (Scheme 21).[44]

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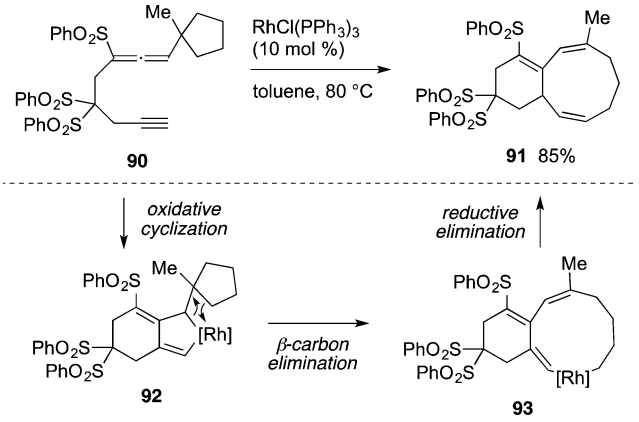
Scheme 21



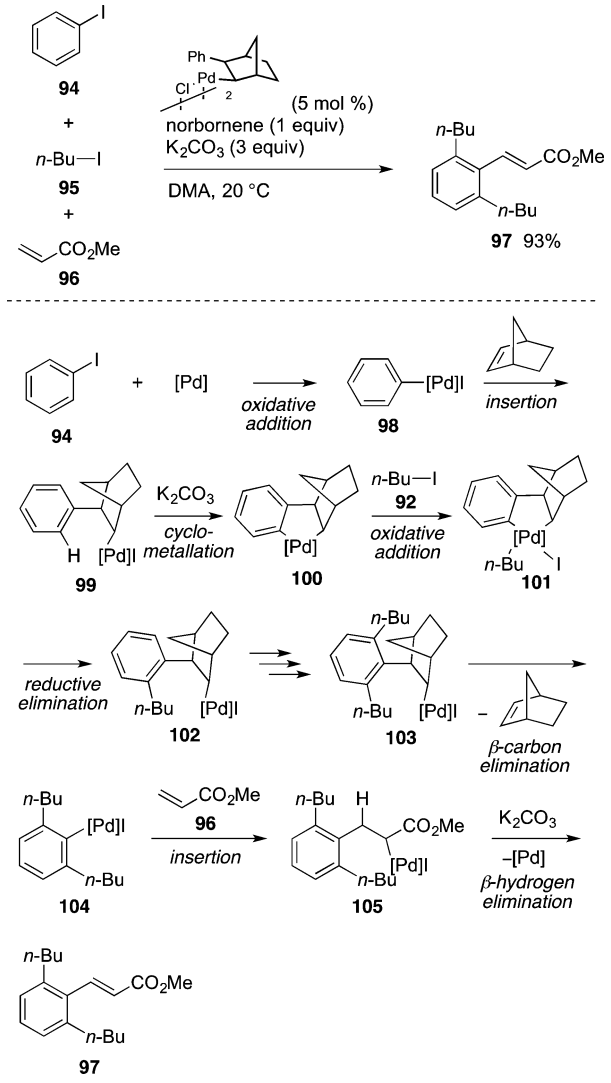
Oxidative cyclization of the allenyne **90** on rhodium provides rhodacyclic intermediate **92**, which undergoes β-carbon elimination to cleave the C−C bond. The 10-membered rhodacycle **93** is generated, and the subsequent reductive elimination gives rise to the product **91**. Relief of steric congestion by opening the cyclopentane ring may afford a driving force, although this promotive force is small.

A reversible alkene insertion/β-carbon elimination process repeatedly operates in a reaction of iodobenzene (**94**) with iodobutane (**95**) and acrylate **96** catalyzed by palladium and norbornene (Scheme 22).[45] Finally, *ortho*-difunctionalized arene **97** was produced with the formation of three C−C bonds. Mechanistically, the reaction is initiated by oxidative addition of the iodobenzene (**94**) onto palladium to generate phenylpalladium iodide **98**. A double bond of norbornene inserts into the C−Pd bond to furnish an alkylpalladium species **99**, which cleaves a nearby C−H bond to form palladacycle **100**. Iodobutane (**95**) then reacts with the palladacycle **100**. The resulting palladium(IV) intermediate **101** undergoes reductive elimination. Repetition of the cyclometalation/alkylation process leads to *ortho*,*ortho*-dialkylation. Ensuing β-carbon elimination with **103** affords the arylpalladium species **104** and norbornene. Subsequently, a Heck-type reaction occurs with acrylate **96**, giving rise to dialkylated cinnamate derivative **97**. Norbornene is a suitable traceless mediator for this unique reaction because of its high propensity to undergo insertion and the lack of hydrogen atoms that are amenable to β-hydrogen elimination after insertion.

C−C BOND CLEAVAGE FOR ORGANIC SYNTHESIS: RECENT EXAMPLES

On the basis of the fundamental reactivity disclosed over the past two decades, the focus of recent research in this field resides in applying the accumulated knowledge toward the target-oriented transformations/synthesis. One of the notable advances made over the past few years is extension to asymmetric synthesis of complex multicyclic compounds. For example, chiral benzobicyclo[2.2.2]octenone **107** was synthesized in an enantioselective manner through the nickel-catalyzed C−C bond cleavage reaction of 3-(2-styryl)-cyclobutanone **32** (Scheme 23a).[46] This method offers a more step-economical pathway to **107** than conventional methods previously reported. The constitutional isomer benzobicyclo[3.2.1]octenone **109** was also synthesized in a highly enantioselective fashion from the same starting substances through a chiral rhodium-catalyzed enantioselective

Scheme 22



C−C bond cleavage (Scheme 23b).[47] In addition, the tricyclic fused ring system **111** was enantioselectively constructed through intramolecular insertion of the alkene into the C(benzene)−C(carbonyl) bond (Scheme 23c).[48]

Various nitrogen heterocycles are synthesized in an enantiopure or -enriched form from small-ring compounds through C−C bond cleavage reactions. For example, chiral azetidines **112** (Scheme 24) and **116** (Scheme 25) were both available, with stereochemical integrity, from naturally occurring α-amino acids. They were successfully utilized for the synthesis of enantio-pure multiply substituted piperidine **115**[49] and benzosultam **117**,[50] respectively. Aminocyclopropanes (e.g., **118**), which are available from cyclopropanecarboxylates through Curtius rearrangement, serve as the intermediate for complex bicyclic amines and medium-sized cyclic amines like **119** (Scheme 26).[51]

A sophisticated mechanism, including reversible insertion/β-elimination of norbornene, operates in ortho-substitution of haloarenes. Palladium-catalyzed reactions of haloarenes with nucleophiles normally cause ipso-substitution.[52] When subjected to a palladium/norbornene catalyst system, however, the ortho position of *o*-iodotoluene (**120**) was selectively coupled with amine **121** (Scheme 27).[53] Direct functionalization of a C−H bond meta to the directing group was also realized by

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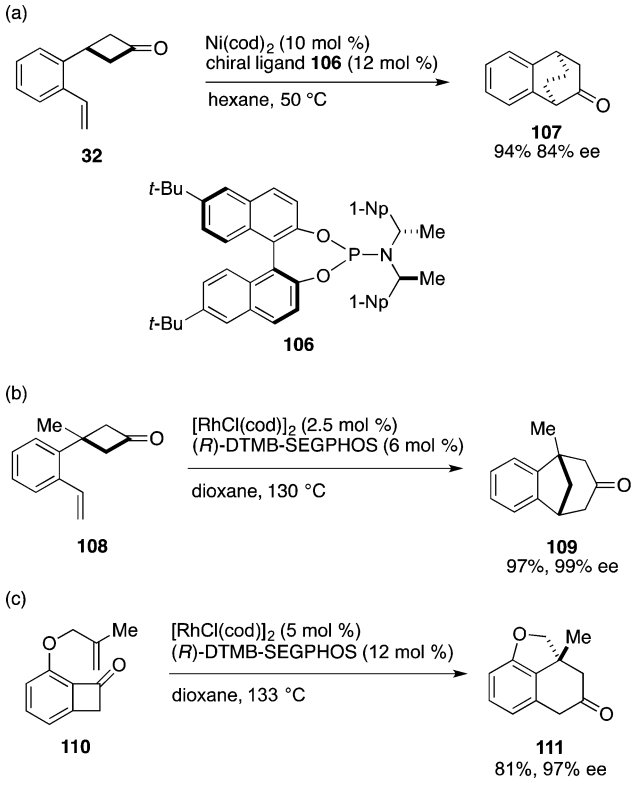
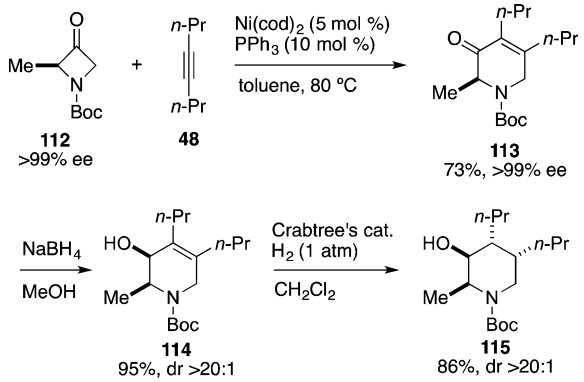
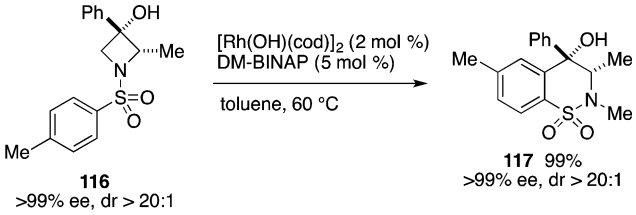
Scheme 23



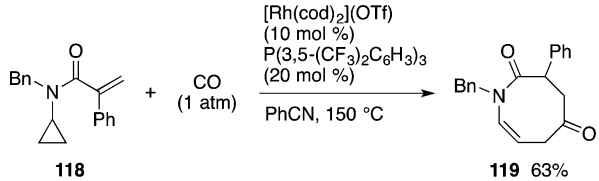
Scheme 24



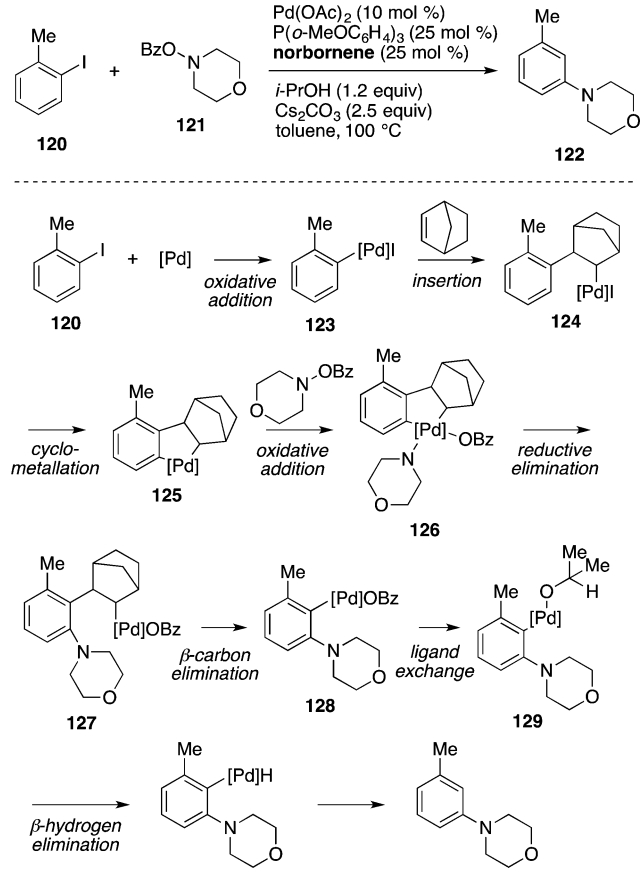
Scheme 25



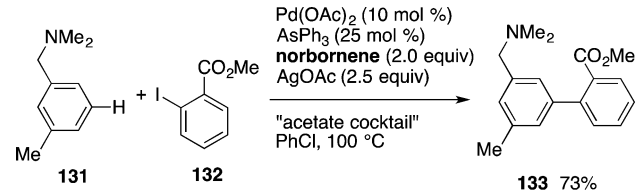
Scheme 26



Scheme 27



Scheme 28



means of an analogous palladium/norbornene system (Scheme 28).[54]

An allylic C−H bond of cyclohexene (**134**) is directly carboxylated with CO_2 by making use of C−C bond cleavage (Scheme 29).[55] The reaction pathway consists of two stages. The first stage is a photoreaction of ketone **135** with alkene **134** to furnish homoallyl alcohol **139**. The second stage is a copper-catalyzed allyl transfer reaction from homoallyl alcohol **139** to CO_2, in which the C−C bond of **139** is cleaved by β-carbon elimination.

OUTLOOK

In this Perspective, we have showcased selected examples of transition-metal-mediated C−C bond cleavage reactions. Such reactions present unique ways for the construction of organic skeletons with remarkable efficiencies that are otherwise unavailable. Disappointingly, however, the substrates are often limited to particular classes of molecules, like small-membered ring compounds with high strain energy stored within their chemical entities. It is not simple to expand those reactions to nonstrained substrates because catalytic reactions consist of

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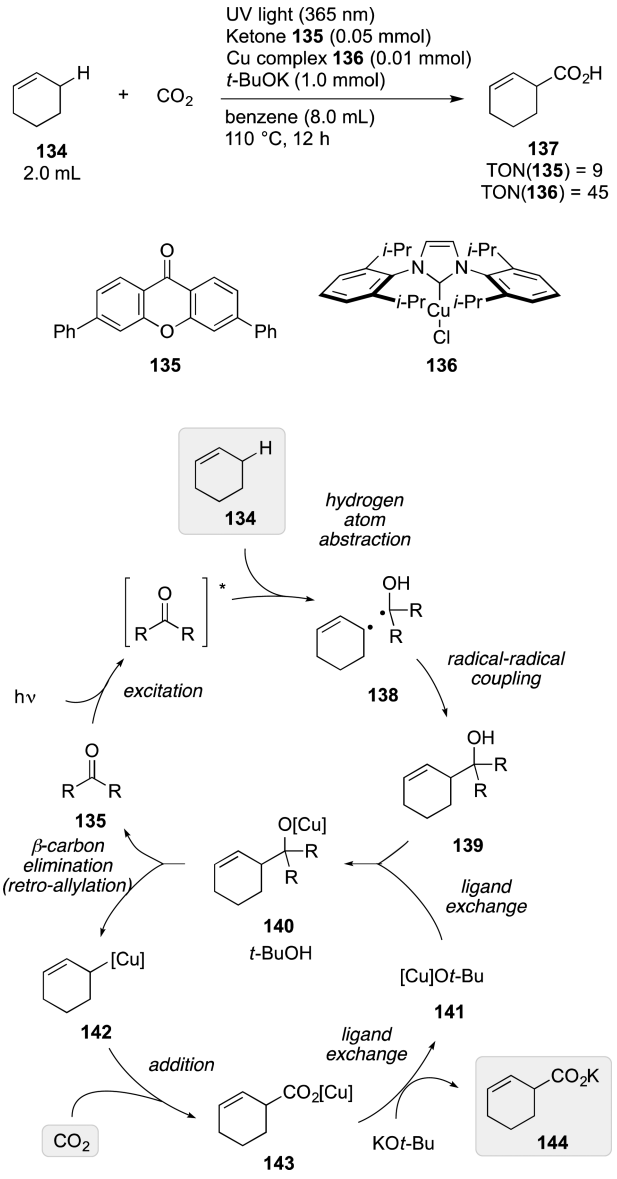
Scheme 29



multiple elementary steps, each of which possesses its own difficulty. There are multiple hurdles, including kinetic and thermodynamic ones, which must be overcome simultaneously. We believe that exploitation of light is one of the key tools to be explored in the chemistry of C−C single bond cleavage. Such processes are energetically assisted by the energy of photons and, thus, may allow thermodynamically disfavored (uphill) transformations. This would offer a means of activating thermodynamically stable C−C single bonds to generate a more energetic organometallic intermediate, which is reactive enough to surmount the activation barrier required for the following thermal pathway. Interestingly, such a process may afford products that are even thermodynamically less stable than the starting substances. A notable example of a light-driven C−C bond cleavage reaction has been reported by Jones et al. When platinum−arylalkyne complex **145** was irradiated with UV light, oxidative addition of the C(sp)−C(sp^2) bond onto the platinum center took place to afford alkynyl(aryl)platinum complex **146** (Figure 3a).[56] Upon heating, however, the complex underwent reductive elimination back to **145**. These

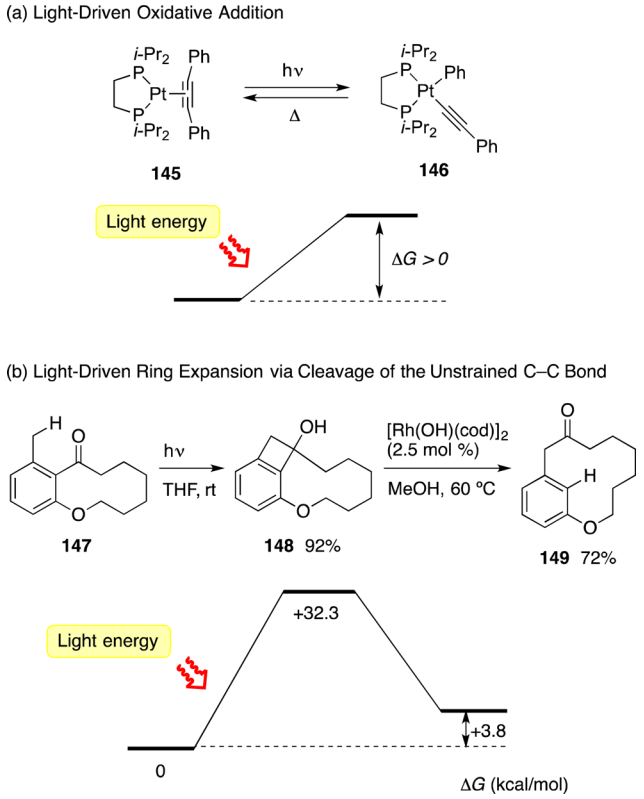


Figure 3. Light-driven C−C single bond cleavage reactions.

results explicitly demonstrate that the photoinduced oxidative addition is energetically uphill ($\Delta G > 0$). Light energy serves as the driving force for the energetically disfavored C−C bond cleavage reaction. Although further transformations of the resulting organoplatinum species **146** have not been studied, various thermal reactivities are expected from an energetic viewpoint. On the other hand, we have reported another way to exploit light energy for C−C bond cleavage: ring expansion of orthocyclophane **143** to metacyclophane **145** by sequential action of light and rhodium (Figure 3b).[57] In a formal sense, the benzylic C(sp^3)−H bond and the C(carbonyl sp^2)−C(aromatic sp^2) bond are both cleaved and exchanged to form new C(aromatic sp^2)−H and C(sp^3)−C(aromatic sp^2) bonds. The net process is energetically uphill (+3.8 kcal/mol according to DFT calculation at the B3LYP/6-31G(d) level); thus, the ring expansion process is not thermally feasible. Nonetheless, this transformation proceeds irreversibly by way of a photo-induced, energetically uphill reaction (**147** → **148**). Thus, exploitation of light in conjunction with transition metal complexes offers a unique opportunity for C−C bond cleavage and further reaction. We hope further exploration along this line would create new reactions and synthetic strategies and contribute to improving the efficiency of organic synthesis.

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Notes

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