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Catalytic Carbon–Carbon Bond Activation of Saturated and Unsaturated Carbonyl Compounds via Chelate-Assisted Coupling Reaction with Indoles

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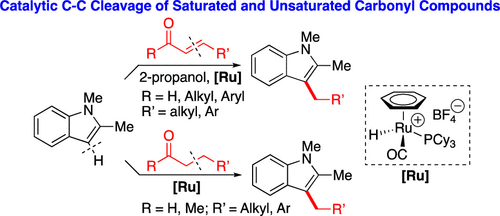
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# SUBJECTS:

[Ketones](https://pubs.acs.org/action/doSearch?ConceptID=291945), [Indoles](https://pubs.acs.org/action/doSearch?ConceptID=291862), [Crystal cleavage](https://pubs.acs.org/action/doSearch?ConceptID=291891), [Coupling reactions](https://pubs.acs.org/action/doSearch?ConceptID=291061), [Bond cleavage](https://pubs.acs.org/action/doSearch?ConceptID=290836)

# Abstract



The chelate assistance strategy was devised to promote a highly regioselective catalytic C–C bond activation reaction of saturated and unsaturated carbonyl compounds. The cationic Ru–H complex **1** was found to be an effective catalyst for mediating the coupling reaction of 1,2-disubstituted indoles with α,β-unsaturated aldehydes and ketones, in which the regioselective Cα–Cβ activation of the carbonyl substrates has been achieved in forming the 3-alkylindole products. The analogous coupling reaction of indoles with saturated aldehydes and ketones directly led to the Cα–Cβ cleavage of the carbonyl substrates in forming the 3-alkylindole products. The coupling reaction of 1,2-dimethylinole with (*E*)-3-nonen-2-one and 2-propanol-*d*8 showed 20–22% of deuterium incorporation to both α- and β-CH2 of the 3-alkylindole product. The coupling reaction of 1,2-dimethylinole with (*E*)-3-nonen-2-one exhibited the most significant carbon kinetic isotope effect on the α-carbon of the product (Cα = 1.046). The Hammett plot constructed from the reaction of 1,2-dimethylinole with a series of *para*-substituted enones *p*-X-C6H4CH═CHCOCH3 (X = OMe, Me, H, Cl, CF3) showed a modest promotional effect by an electron-donating group (ρ = −0.2 ± 0.1). Several catalytically relevant Ru–H species were detected by NMR from a stoichiometric reaction mixture of the Ru–H complex **1** with 1,2-dimethylindole and (*E*)*-*3-nonen-2-one in CD2Cl2. These results support a mechanism of the catalytic coupling reaction via conjugate addition of indoles to enones followed by the C–C bond activation and hydrogenolysis steps.

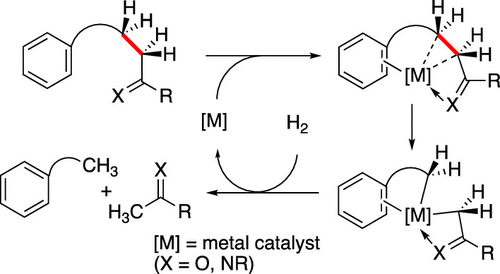
# KEYWORDS:

[C−C bond activation](https://pubs.acs.org/action/doSearch?action=search&AllField=C%E2%88%92C+Bond+Activation&qsSearchArea=AllField), [indole](https://pubs.acs.org/action/doSearch?action=search&AllField=Indole&qsSearchArea=AllField), [carbonyl compound](https://pubs.acs.org/action/doSearch?action=search&AllField=Carbonyl+Compound&qsSearchArea=AllField), [ruthenium catalyst](https://pubs.acs.org/action/doSearch?action=search&AllField=Ruthenium+Catalyst&qsSearchArea=AllField)

# Introduction

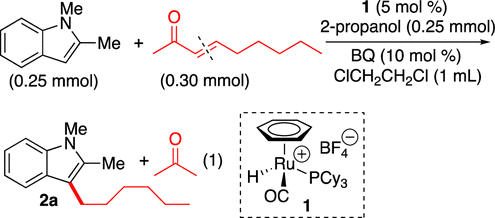
Designing selective C(sp3)–C(sp3) bond activation methods of saturated hydrocarbon compounds has been regarded as one of the most challenging problems in contemporary catalysis field.1 It has been widely recognized that the selective catalytic C–C bond activation methods would not only entail new opportunities for economically feasible and environmentally sustainable technologies ranging from petroleum and biomass reforming processes but also provide a powerful tool for the synthesis of complex organic molecules.1,2 In industrial cracking and reforming processes, heterogeneous metal catalysts are commonly used to convert petroleum and biomass feedstocks into high-value hydrocarbon commodities such as olefins, alcohols, and ethers. 3 Since such processes are inherently energy intensive and often lead to unselective products, they are seldomly employed for the synthesis of complex organic products requiring selective C–C bond cleavage reaction. Since Milstein’s pioneering discovery on a direct arene C(sp2)–CH3 bond activation reaction mediated by a pincer-ligated Rh complex, 4 a number of catalytic C–C bond activation methods have been devised by using soluble transition metal complexes. The chelate assistance methodology has been shown to be a particularly effective strategy for mediating regioselective CO–Cα bond activation reactions of arylketones and imines, where nitrogen chelate groups have been successfully employed for the synthesis of complex organic molecules via C–C bond cleavage.5 Ackermann and co-workers recently devised a chelation-assisted C–C activation protocol by using a nonprecious transition metal catalyst.6 By channeling a relief of strain energy as the driving force, catalytic C–C bond cleavage methods of cyclopropane and strained cyclic ketone derivatives have been shown to be a versatile synthetic tool for constructing a variety of cyclic compounds,7 as exemplified by recent asymmetric synthesis of biologically active chiral organic molecules.8 The catalytic β-carbon elimination method has also been shown to be effective for promoting regioselective C–C bond cleavage reactions for saturated and unsaturated hydrocarbon substrates bearing oxygen functional group.9 Dong and co-workers recently reported a series of catalytic C–C bond activation methods that are either driven by a relief of ring stain or are accompanied by insertion and elimination reactions.10 Despite such remarkable advances, the development of selective catalytic C(sp3)–C(sp3) bond activation methods of unstrained aliphatic compounds still largely remains as an elusive goal in the homogeneous catalysis field, as most of the current catalytic C–C cleavage technologies either employ strained cyclic substrates or are limited to C(sp2)–C(sp2) and C(sp2)–C(sp3) activation reactions on unsaturated hydrocarbons and carbonyl substrates. 11)

Inspired by both metal–organic cooperative catalysis and merging C–H and C–C bond activation methods,5,12 we envisioned a general strategy that exploits both arene and heteroatom chelate groups to promote unstrained C(sp3)–C(sp3) bond activation reactions, as illustrated in Scheme 1. We reasoned that a regioselective C–C bond activation reaction might be feasible when a metal catalyt can directly interact with the C–C σ-orbital without the interference from C–H bond orbitals, and this could be achieved when a metal catalyst is assisted by two chelate groups. By employing recently developed catalytic C–H coupling protocols using a well-defined cationic ruthenium-hydride catalyst [(C6H6)(PCy3)(CO)RuH]+BF4– (**1**),13 we have been exploring a number of catalytic coupling reactions of arenes with carbonyl compounds as a way to screen suitable template groups for promoting C–C cleavage reaction. Here we report a generally applicable catalytic coupling reaction of indoles with saturated and unsaturated carbonyl compounds, in which regioselective Cα–Cβ activation of the carbonyl compounds has been realized without employing any reactive reagents or forming toxic byproducts.



Scheme 1. Mechanistic Hypothesis for Chelate Assisted Catalytic C–C Cleavage Reaction

# Results and Discussion

While searching for a suitable heteroarene substrate that could serve as a chelate directing group for promoting C–C cleavage reactions, we initially discovered that the treatment of 1,2-dimethylindole with (*E*)-3-nonen-2-one in the presence of the catalyst **1** led to the regioselective Cα–Cβ bond cleavage of the enone substrate in forming the coupling product **2a** (eq 1). The formation of acetone byproduct was also detected by GC-MS in the crude reaction mixture. We subsequently found that the addition of both 2-propanol and 1,2-benzoquinone substantially improved the product yield of **2a**, and from a series of optimization study, we were able to establish the standard conditions for the coupling reaction of 1,2-dimethylindole with (*E*)-3-nonen-2-one (Table 1). Notably, we screened a number of different hydrogen source for the coupling reaction, in which both H2 (5 atm) and 2-propanol were equally effective as the hydrogen source, while other potential hydrogen donors such as formic acid and ethanol were completely ineffective in mediating the coupling reaction (entries 6,7). The catalyst **1** was found to exhibit the highest activity among the selected ruthenium catalysts (entries 8–13), and no catalytic activity was observed without Ru catalyst or with an acid catalyst (entries 14–16). 1,2-Dichloroethane was found to be the most suitable solvent for the coupling reaction among selected organic solvents. The catalytic method features a highly regioselective cleavage of unstrained Cα–Cβ bond of the enone substrate in forming the coupling product **2a**.

**Table 1. Catalyst and Additive Screening for the Coupling of 1,2-Dimethylindole with (*E*)-3-Nonen-2-onea**

|  |  |  |  |
| --- | --- | --- | --- |
| **entry** | **catalyst** | **deviation from the standard conditions** | **2a (%)b** |
| 1 | **1** | none | 81 |
| 2 | **1** | with H2 (5 atm) | 80 |
| 3 | **1** | in 2-propanol (1 mL) | 38 |
| 4 | **1** | no 2-propanol | 16 |
| 5 | **1** | no BQ | 72 |
| 6 | **1** | with HCO2H (0.3 mmol) | <5 |
| 7 | **1** | with EtOH (0.3 mmol) | <5 |
| 8 | [(PCy3)2(CO)(CH3CN)2RuH]BF4 |  | 46 |
| 9 | [(PCy3)(CO)RuH]4(O)(OH)2/HBF4·OEt2 |  | 26 |
| 10 | (PCy3)2(CO)RuHCl/HBF4·OEt2 |  | 20 |
| 11 | RuCl2(PPh3)3/HBF4·OEt2 |  | 0 |
| 12 | Ru3(CO)12/HBF4·OEt2 |  | 8 |
| 13 | [(COD)RuCl2]*x*/HBF4·OEt2 |  | 0 |
| 14 | PCy3/HBF4·OEt2 |  | 0 |
| 15 | AlCl3 |  | 0 |
| 16 | HBF4·OEt2 |  | <5 |

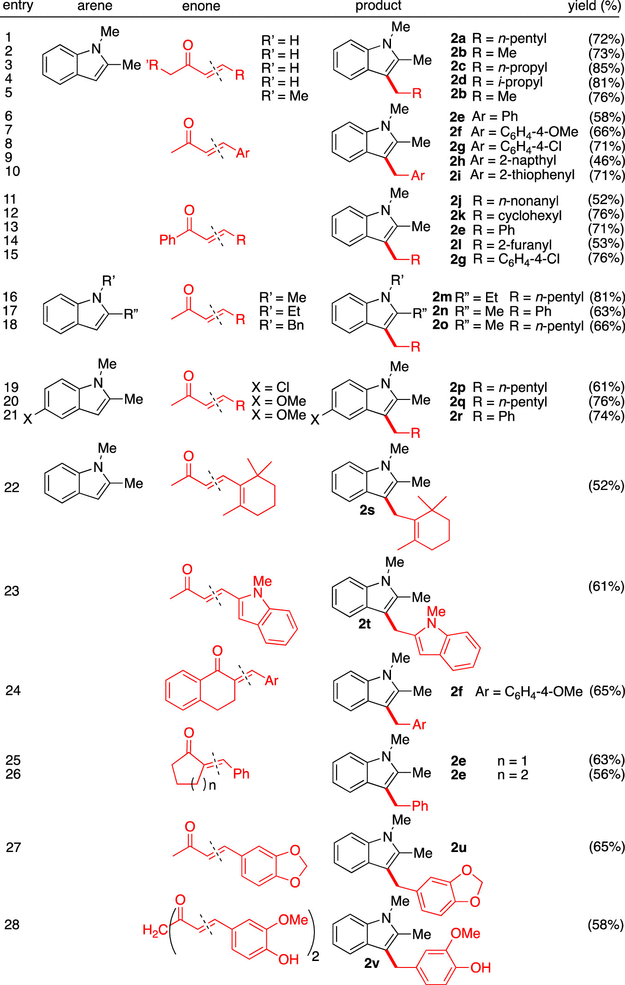
aStandard conditions: 1,2-dimethylindole (0.25 mmol), (*E*)-3-nonen-2-one (0.30 mmol), 2-propanol (0.25 mmol), catalyst (5 mol %), BQ (10 mol %), 1,2-dicholoroethane (1 mL), 125 °C, 36 h.

bThe product yield was determined by GC-MS by using hexamethylbenzene as an internal standard. BQ = 3,4,5,6-tetrachloro-1,2-benzoquinone.

## Reaction Scope

We examined the substrate scope for the C–C cleavage reaction under the optimized standard conditions (Table 2). For the sake of convenience, 2-propanol was used as the hydrogen source in most cases, even though both H2 and 2-propanol were found to be equally effective in giving the C–C cleavage products. Electron-rich 1,2-dimethylindole was found to be a suitable substrate for the coupling with both alkyl- and aryl-substituted enones to form the C–C cleavage products **2a**-**o** (entries 1–18). Both β-aryl-substituted aliphatic enones and aryl-substituted enones reacted smoothly with 1,2-dimethylindole, in which the Cα–Cβ bond of the enone substrates has been selectively cleaved in forming the coupling products **2e**-**i** and **2j**-**g**, respectively (entries 6–15). The coupling of 1,2-dimethylindole with 2-alkenylcyclic ketones selectively formed the C–C cleavage products **2e,f** along with the cyclic ketone byproducts (entries 24–26). A number of biologically active enone substrates such as (*E*)-β-ionone, 4-(1-methyl-1*H*-indol-2-yl)but-3-en-2-one and piperonylacetone predictively afforded the corresponding C–C cleavage products **2s,t,u** in good yields (entries 22, 23 and 27). Sterically demanding and electron-rich indole substrates were found to be essential for promoting the C–C cleavage reaction, as the analogous coupling reaction of 1-methylindole or 2-methylindole with the enones afforded less than 15% of the C–C cleavage products.

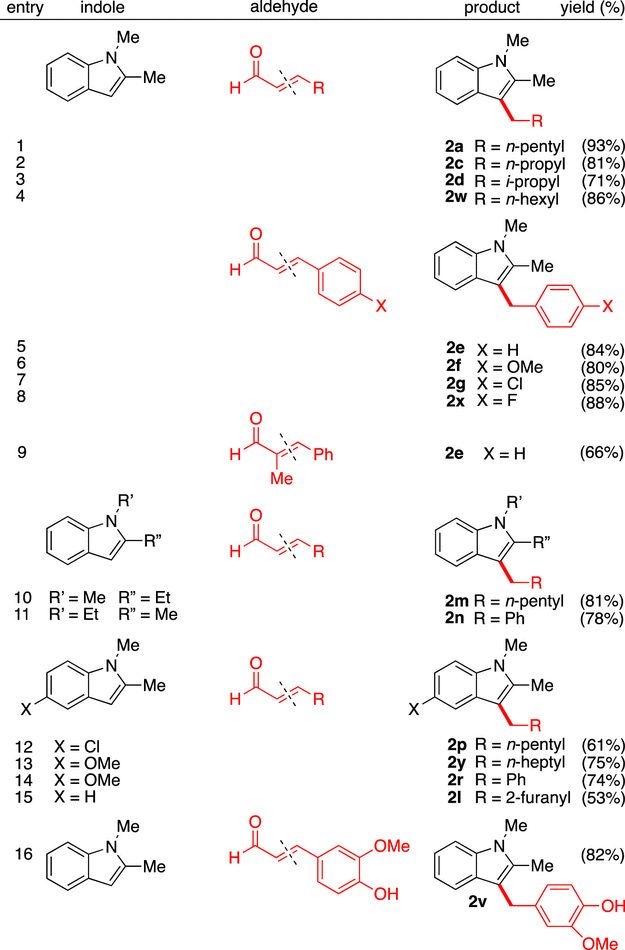
**Table 2. Catalytic C–C Cleavage Reaction of α,β-Unsaturated Ketones from the Coupling with Indolesa**



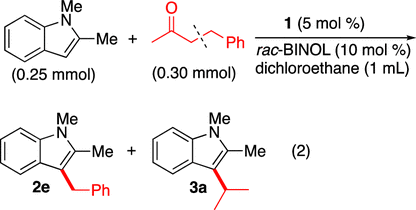
aReaction conditions: indole (0.25 mmol), ketone (0.30 mmol), 2-propanol (0.25 mmol), **1** (5 mol %), 3,4,5,6-tetrachloro-1,2-benzoquinone (10 mol %), 1,2-dichloroethane (1 mL), 125 °C, 36 h.

We next surveyed the aldehyde substrate scope by using the standard conditions (Table 3). Electron-rich 1,2-dimethylindole was found to be a suitable substrate for the coupling with both alkyl- and aryl-substituted α,β-unsaturated aldehydes to selectively give the C–C cleavage products **2** (entries 1–8). The coupling of 1,2-dimethylindole with 2-methylcinnamaldehyde also efficiently installed the C–C cleavage products **2e** (entry 9). The analogous coupling of 1,2,5-trisubstituted indoles with alkyl- and aryl-substituted enals predictively afforded the corresponding coupling products **2l**,**p**,**r**,**y**, which are resulted from the regioselective Cα–Cβ cleavage reaction (entries 12–15). Compared with the enone substrates, a substantially higher C–C cleavage product yield was obtained with the aldehydes in most cases. The coupling reaction of 1,2-dimethylindole with other unsaturated carbonyl compounds such as acrylic esters and amides gave a low C–C cleavage product yield (<20%) under similar conditions.

**Table 3. Catalytic C–C Cleavage Reaction of α,β-Unsaturated Aldehydes from the Coupling with Indolesa**



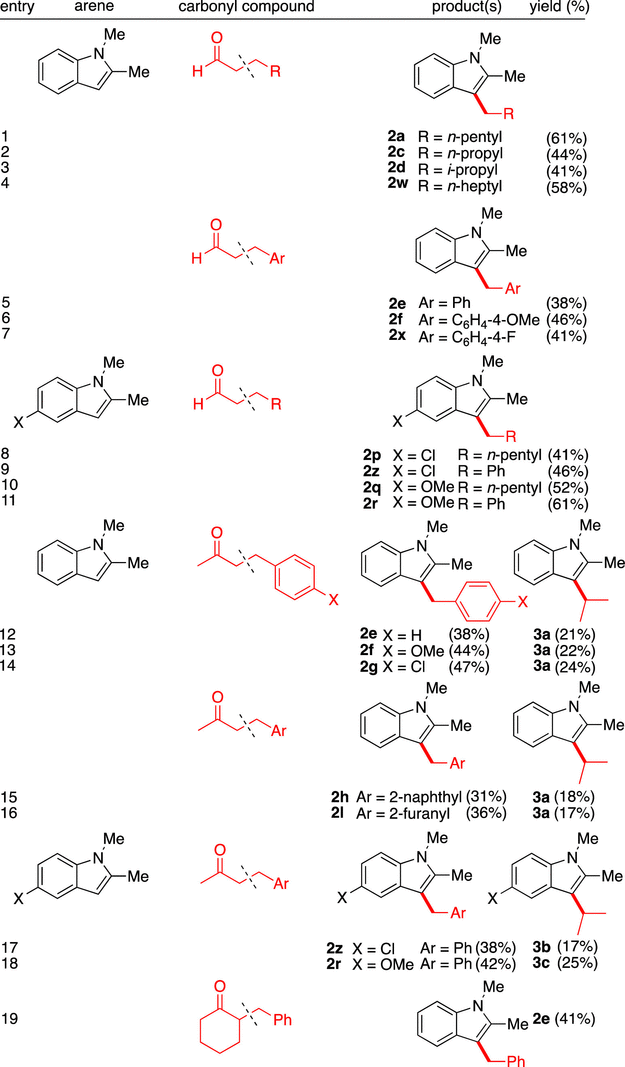
aReaction conditions: indole (0.25 mmol), aldehyde (0.30 mmol), 2-propanol (0.25 mmol), **1** (5 mol %), 3,4,5,6-tetrachloro-1,2-benzoquinone (10 mol %), 1,2-dichloroethane (1 mL), 125 °C, 36 h.



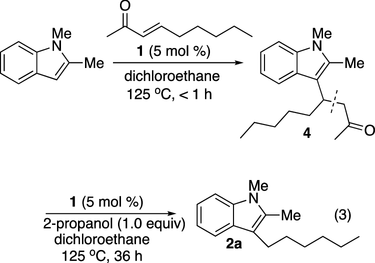
In light of the previously developed dehydrogenation of saturated of ketones and amines,14 we sought to combine the dehydrogenation and the coupling reaction to achieve a direct Cα–Cβ bond cleavage of the saturated carbonyl substrates. Thus, the treatment of 1,2-dimethylindole (0.25 mmol) with 4-phenyl-2-butanone (0.30 mmol) in the presence of **1** (5 mol %) and *rac*-1,1′-bi-2-naphthol (*rac*-BINOL; 10 mol %) in 1,2-dicholoroethane (1.0 mL) at 125 °C smoothly formed a mixture of the coupling product **2e** and **3a** (eq 2). In this case, no hydrogen donor additive was necessary for the coupling reaction. We screened a number of redox-active additives to promote the dehydrogenation of the ketone substrate and found that *rac*-BINOL is most effective in promoting the C–C cleavage reaction among selected catechol and benzoquinone additives (Table S3, Supporting Information).

The substrate scope of saturated carbonyl compounds was explored by using the optimized reaction conditions as described in eq 2 (Table 4). The coupling of 1,2-dimethylindole with both alkyl- and aryl-substituted saturated aldehydes smoothly formed the C–C cleavage products **2** (entries 1–11). In contrast, the coupling of 1,2-dimethylindole with saturated ketone substrates afforded a mixture of the products **2e**-**g,h,l,r,z** and **3a**–**c** (entries 12–18), in which 3-(2-propyl)indole product **3** was resulted from the coupling reaction with acetone byproduct. The coupling of 1,2-dimethylindole with 2-benzylcyclohexanone resulted in the C–C cleavage product **2e** and cyclohexanone byproduct. Compared to the unsaturated carbonyl substrates, a much narrower substrate scope of the saturated ketones was realized, as neither aliphatic ketones nor aryl-substituted ketones gave the desired C–C cleavage products presumably due to the difficulty in promoting the dehydrogenation for these saturated ketones. Moreover, the coupling reaction was quite sluggish for these saturated ketones, resulting in the formation of the product **3** from the coupling of unreacted indole with acetone byproduct. All of the C–C cleavage products were readily isolated after silica gel column chromatographic separation, and their structure was completely established by standard spectroscopic methods. To the best of our knowledge, the catalytic method represents a unique set of examples for achieving regioselective C(sp3)–C(sp3) cleavage of unstrained saturated carbonyl compounds.

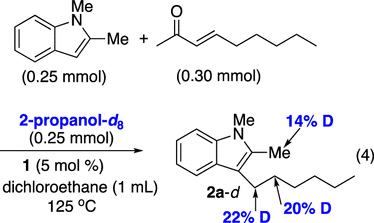
**Table 4. Catalytic C–C Cleavage Reaction of Saturated Aldehydes and Ketones from the Coupling with Indolesa**



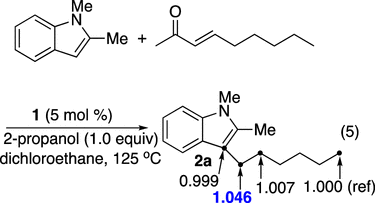
aReaction conditions: indole (0.25 mmol), carbonyl compound (0.30 mmol), **1** (5 mol %), *rac*-1,1′-bi-2-naphthol (10 mol %), 1,2-dichloroethane (1 mL), 125 °C, 36 h.



To probe whether the coupling reaction actually involves a direct C(sp3)–C(sp3) bond cleavage, we monitored the progress of coupling reaction of 1,2-dimethylindole with (*E*)-3-nonen-2-one by GC-MS. We observed a rapid formation of the initial coupling product **4**, which was isolated in 95% yield after the reaction was stopped at 30 min (eq 3). The treatment of the isolated **4** under the standard conditions slowly led to the C–C cleavage product **2a**. This experiment clearly demonstrates that the formation of the product **2a** was resulted from a two-step reaction sequence involving the initial conjugate addition of the indole to the carbonyl compounds, followed by the regioselective C(sp3)–C(sp3) bond hydrogenolysis.



## Deuterium Labeling Study

We have chosen the coupling reaction of 1,2-dimethylindole with (*E*)-3-nonen-2-one to probe the mechanism of the C–C cleavage reaction. First, the H/D exchange pattern was examined from the coupling reaction of 1,2-dimethylinole (0.25 mmol) with (*E*)-3-nonen-2-one (0.30 mmol) and 2-propanol-*d*8 (99.5% D, 0.25 mmol) in the presence of complex **1** (5 mol %) in 1,2-dichloroethane (1 mL), which was heated at 125 °C for 36 h (eq 4). In this case, benzoquinone was not added to the reaction mixture to avoid any potential complications. The isolated product **2a**-*d* showed nearly 20–22% of deuterium on both α- and β-CH2 of the alkyl group as analyzed by 1H and 2H NMR spectroscopic methods (Figure S1, Supporting Information). A significant amount of deuterium (14% D) was also incorporated to the 2-methyl group of the product **2a**-*d*. In a control experiment, the treatment of isolated product **2a** (0.25 mol) with 2-propanol-*d*8 (0.25 mmol) under otherwise standard conditions led to <5% deuterium on both α- and β-CH2 groups of **2a**, but with a substantially higher amount of deuterium incorporation to the 2-methyl group (9% D) (Figure S2, Supporting Information). These results suggest that an extensive H/D scrambling on both α- and β-alkyl carbons occurs during the C–C bond hydrogenolysis step from the exchange with 2-propanol-*d*8.

## Carbon Isotope Effect Study

To discern the rate limiting step of the reaction, we next measured the carbon kinetic isotope effect from the coupling reaction of 1,2-dimethylinole with (*E*)-3-nonen-2-one by employing Singleton’s high-precision NMR technique (eq 5).15 We obtained a high conversion sample of **2a** from three separate treatments of 1,2-dimethylindole (0.25 mmol), with (*E*)-3-nonen-2-one (0.30 mmol), 2-propanol (0.25 mmol) and complex **1** (5 mol %) in 1,2-dichloroethane (1 mL), which was compared with the low conversion sample of **2a** isolated from three separate 2.0 mmol scale of the reaction. The most significant carbon isotope effect was observed on the α-carbon of the indole product **2a** when the 13C ratio of the product from a high conversion was compared with the sample obtained from a low conversion (13C(avg 87% conversion)/13C(avg 11% conversion) at Cα = 1.046; average of three runs) (Table S4, Supporting Information). The significant carbon isotope effect on the α-carbon is consistent with the turnover limiting C–C bond cleavage step for the coupling reaction.

## Hammett Study

To probe electronic influence on the C–C cleavage reaction, we compared the reaction rates of 1,2-dimetylindole with a series of *para*-substituted enones *p*-X-C6H4CH═CHCOCH3 (X = OMe, Me, H, Cl, CF3) under the standard conditions. The *k*obs for each reaction was determined from a first-order plot of −ln[(1,2-dimethylindole)t/(1,2-dimethylindole)0] vs time. The Hammett plot of log(*k*X/*k*H) vs σp showed a linear correlation, in which the coupling reaction is moderately promoted by an electron-donating group (ρ = −0.2 ± 0.1) (Figure 1). A relatively small electronic effect from the β-aryl substituent of the enone substrate suggests of a metal-mediated nonelectrophilic C–C cleavage process. Similar moderate electronic effect with a relatively low Hammett ρ value has been observed for metal-mediated nonelectrophilic cleavage reactions of C–H, C–C and C–Si bonds.16

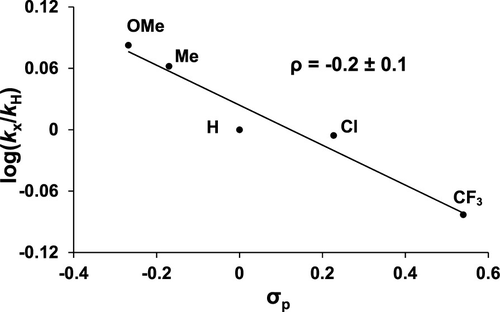
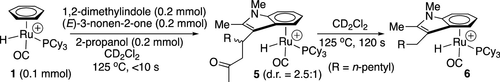


Figure 1. Hammett plot from the reaction of 1,2-dimethylindole with *p*-X-C6H4CH═CHCOCH3 (X = OMe, Me, H, Cl, CF3).

## Spectroscopic Detection of Catalytically Relevant Species

In an effort to detect catalytically relevant species, we monitored the coupling reaction of 1,2-dimethylindole with (*E*)-3-nonen-2-one by employing the NMR spectroscopic technique (Scheme 2). Thus, a stoichiometric mixture of the complex **1** (0.10 mmol), 1,2-dimethylindole (0.20 mmol), (*E*)*-*3-nonen-2-one (0.20 mmol), and 2-propanol (0.20 mmol) was dissolved in CD2Cl2 (0.5 mL) in a resealable NMR tube. The reaction tube was immersed in an oil bath set at 125 °C and was taken out periodically to record the NMR spectrum at an ambient temperature. After just 5 s of heating at 125 °C, four new sets of Ru–H signals rapidly appeared at δ −12.1 (d, *J*PH = 27.2 Hz), −12.2 (d, *J*PH = 27.6 Hz), −12.8 (d, *J*PH = 27.2 Hz) and −12.9 (d, *J*PH = 27.4 Hz) ppm in a 1:1:2.5:2.5 ratio as monitored by the 1H NMR, which were assigned to four diastereomeric mixtures of the arene-coordinated Ru–H complex **5** (Figure 2). The formation of free benzene molecule was also observed by the 1H NMR. The same diastereomeric mixture of the complex **5** was independently generated from the treatment of **1** with the isolated product **4**. The 13C{1H} NMR of independently formed **5** exhibited three sets of carbonyl peaks, at δ 207.5, 206.6, and 207.0 ppm, which are also consistent with four diastereomeric mixtures resulting from two chiral centers (the peak at δ 207.5 ppm consisted of two overlapping carbonyl peaks)(Figure S4, Supporting Information). Upon further heating for 120 s at 125 °C, a new set of Ru–H peaks began to appear at δ −12.4 (*J* = 27.5 Hz) and −12.8 (d, *J*PH = 27.3 Hz) ppm at the expense of the peaks due to **5**. These Ru–H peaks were identified as a diastereomeric mixture of the product-coordinated complex **6**, by comparing with an independently generated ones from the treatment of **1** with the product **2a**. Upon further heating for about 10 min, the peaks due to a diastereomeric mixture of the product-coordinated complex **6** eventually predominated at the expense of both **1** and **5**.



Scheme 2. Reaction of **1** with 1,2-Dimethylindole and (*E*)-3-Nonen-2-one

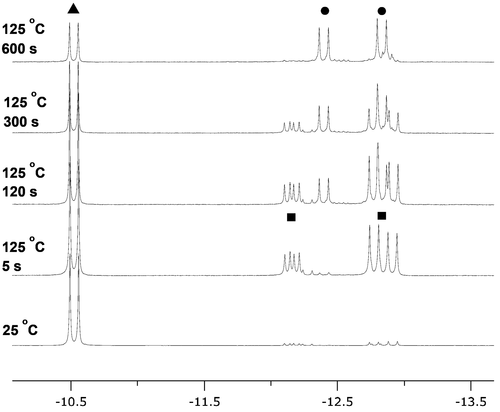
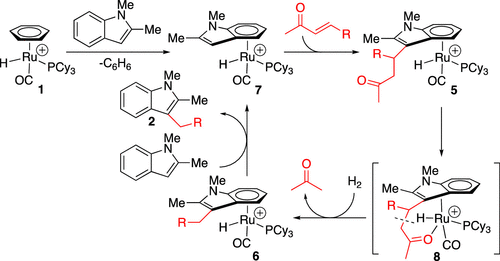


Figure 2. Partial 1H NMR spectra from the reaction of **1** with 1,2-dimethylindole and (*E*)-3-nonen-2-one. Complex **1** (▲), complex **5** (■) and complex **6** (●).

## Proposed Mechanism

We compiled a plausible mechanistic pathway for the coupling reaction of 1,2-dimethylindole with an enone substrate on the basis of these kinetic and spectroscopic data (Scheme 3). We propose that a catalytically active Ru–H species **7** is initially formed from the ligand substitution reaction with the indole substrate. The conjugate addition of **7** with the enone substrate, which was shown to be relatively facile under the catalytic conditions as illustrated in eq 3, would form the arene-coordinated complex **5**.17 Since the carbonyl coordination would require a vacant site on the Ru center, we hypothesize that a carbonyl-coordinated Ru-η3-indole species **8**, which is the key intermediate species for the C–C cleavage step, could be generated via an arene-to-indole coordination shift, in light of well-established ring-slippage modes of indole and related arene ligands.18 The carbon kinetic isotope effect data clearly indicates that the C–C bond cleavage is the turnover limiting step of the catalytic reaction. The subsequent C–C bond hydrogenolysis would form the product-coordinated complex **6** and acetone byproduct. The exchange reaction of **6** with another indole substrate would lead to the formation of the product **2** and the regeneration of **7**. A relatively moderate electronic effect from the β-aryl group of the enone substrate as probed by Hammett study supports a nonelectrophilic C–C bond cleavage step, while the deuterium labeling data indicates that the hydrogenolysis step may be rapid and reversible. Even with the direct spectroscopic detection of the Ru–H complexes **5** and **6**, which provides a supporting evidence for the proposed catalytic cycle, detailed kinetic, spectroscopic as well as computational studies are warranted to decipher the exact C–C bond cleavage mechanism.19



Scheme 3. Proposed Mechanism of the Coupling Reaction of 1,2-Dimethylindole with an Enone

# Conclusion

In summary, we have successfully developed a novel catalytic chelate assistance method to achieve a regioselective Cα–Cβ bond cleavage of saturated and unsaturated carbonyl compounds. We found that the coupling reaction of indoles with α,β-unsaturated aldehydes and ketones initially formed the coupling products, which subsequently underwent the regioselective C(sp3)–C(sp3) cleavage reaction that is assisted by both indole and ketone chelate directing groups. The analogous coupling reaction with saturated aldehydes and ketones led to the similar C–C cleavage products, which are resulted from the initial dehydrogenation of the carbonyl substrates prior to the coupling with indole substrates. We proposed a plausible mechanism of the coupling reaction on the basis of both kinetic and spectroscopic data, which features an initial conjugate addition of the indole substrate, the chelate assisted C–C activation and hydrogenolysis steps. We are continuing our efforts to explore other suitable double chelate groups for promoting selective catalytic C–C bond activation reactions.

# Notes

The authors declare no competing financial interest.

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**17** Though the complex **7** was not detected in the reaction mixture, it was independently generated from the reaction of **1** with 1,2-dimethylindole. The treatment of **7** with (*E*)-3-nonen-2-one rapidly formed the complex **5** within 30 min at 125 °C.

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**19** A reviewer suggested an alternative mechanism via a Brønsted acid-mediated *retro*-addition of an enol to an α,β-unsaturated iminium ion of the indole moiety. While we cannot completely rule out this possibility, the following experimental evidences are inconsistent with the acid-catalyzed mechanism. First, none of Lewis and Brønsted acid catalyst has been found to mediate the C–C cleavage reaction of the initially formed **4**. Second, the analogous coupling reaction of 1,2,5-trimethylpyrrole with (*E*)*-*3-nonen-2-one produced the conjugate addition product 3-(1,2,5-trimethyl-1*H*-pyrrol-3-yl)-2-nonanone but with a trace amount of the C–C cleavage product 1-(1,2,5-trimethyl-1*H*-pyrrol-3-yl)-2-propanone (<5%). This result indicates that the η6-arene coordination of Ru catalyst is essential for promoting the C–C cleavage reaction.