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RESEARCH ARTICLE

CO-Enabled Rhenium Hydride Catalyst for Directed C(sp²)-H bond Alkylation with Olefins†

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Dedicated to Professor Ei-ichi Negishi for his 80th birthday

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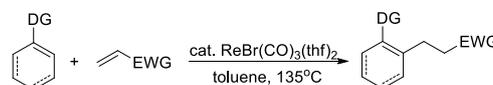
We have reported the first example of CO-enabled rhenium hydride complex-catalyzed inter- and intramolecular hydroarylations of activated alkenes. It has a broad reaction scope. α , β -unsaturated ketones, esters and amides are all suitable for this transformation. It affords a novel and convenient protocol to construct 3-methylindolones. In addition, the mechanism investigation suggests that rhenium carbonyl hydride species may act as a key intermediate.

Introduction

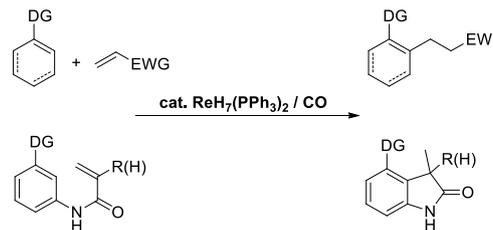
Transition metal-catalyzed insertion reaction of unsaturated compounds into C-H bonds has been increasingly esteemed as an efficient and atom-economic strategy to construct C-C bonds.^{1, 2} In the past decade, considerable attention has been attracted by rhenium carbonyl compounds-catalyzed C-H transformations.³ Despite outstanding achievements, the development of simple, accessible and novel rhenium catalysts to accomplish these transformations is still highly desirable to the chemical society.^{4a} Based on previous works on rhenium chemistry, it was found that rhenium hydride complexes, which could be easily prepared from cheap potassium perrhenate,^{4b, c} had significant advantages in handling, storing and availability. In 2009, Moehring's group has obtained *ortho*-metalated compound through rhenium hydride complex promoting sp² C-H activation.⁵ Recently, rhenium hydride complex were also reported to be an excellent and elegant catalysts for α -C-H activation of carbonyl compounds^{6a} and dehydrogenation of alcohol.^{6b, c} However, to the best of our knowledge, the instance about rhenium hydride complex-promoted inert C(sp²)-H functionalization is very rare. Herein, we found CO enabled rhenium hydride catalyst for directed C(sp²)-H bond activation

(Scheme 1). Moreover, the intramolecular transformations afford a novel and efficient strategy to construct 3-methylindolone frameworks,^{7a, b} which are essential building blocks in organic synthesis.^{7c, d}

Kuninobu's work



This work

Scheme 1 Re-catalyzed sp² C-H bonds alkylation with olefins

Results and discussion

Initially, the reaction of 2-phenylpyridine **1a** and pent-1-en-3-one **2a** was chosen as model reaction to seek the reaction conditions (Table 1). The influence of different atmosphere was evaluated in the presence of 5 mol % ReH₇(PPh₃)₂ at 150 °C in THF. To our delight, although the transformation does not proceed under N₂, Ar, and air atmosphere (entries 1-3), **3aa** could be obtained in 68 % yield when CO was stuffed (entry 4). During the attempting of several commercial ligands (entries 5-8), we found that the PPh₃ showed the higher efficiency than P(tolyl)₃, but the other phosphine ligands led to unsatisfactory results. Furthermore, the yield of **3aa** could be improved to 83% by using toluene as solvent (entry 9). Notably, increasing the

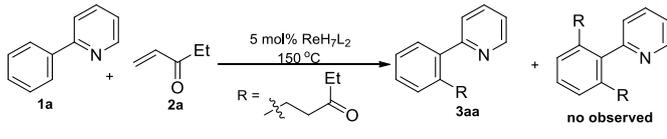
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dosage of catalysis to 10 mol % provided the desired product in 92% yield (entry 10). It should be noticed that the di-substituted product was not observed, although the pent-1-en-3-one **2a** was excess. However, the product was only got in 58% yield, when 1 equiv. **2a** was used (entry 11). Thus, the optimal reaction conditions is catalyzed by 10 mol% $\text{ReH}_7(\text{PPh}_3)_2$ under 1.5 atm CO atmosphere in toluene.

Table 1 Screening for optimal reaction conditions.^a

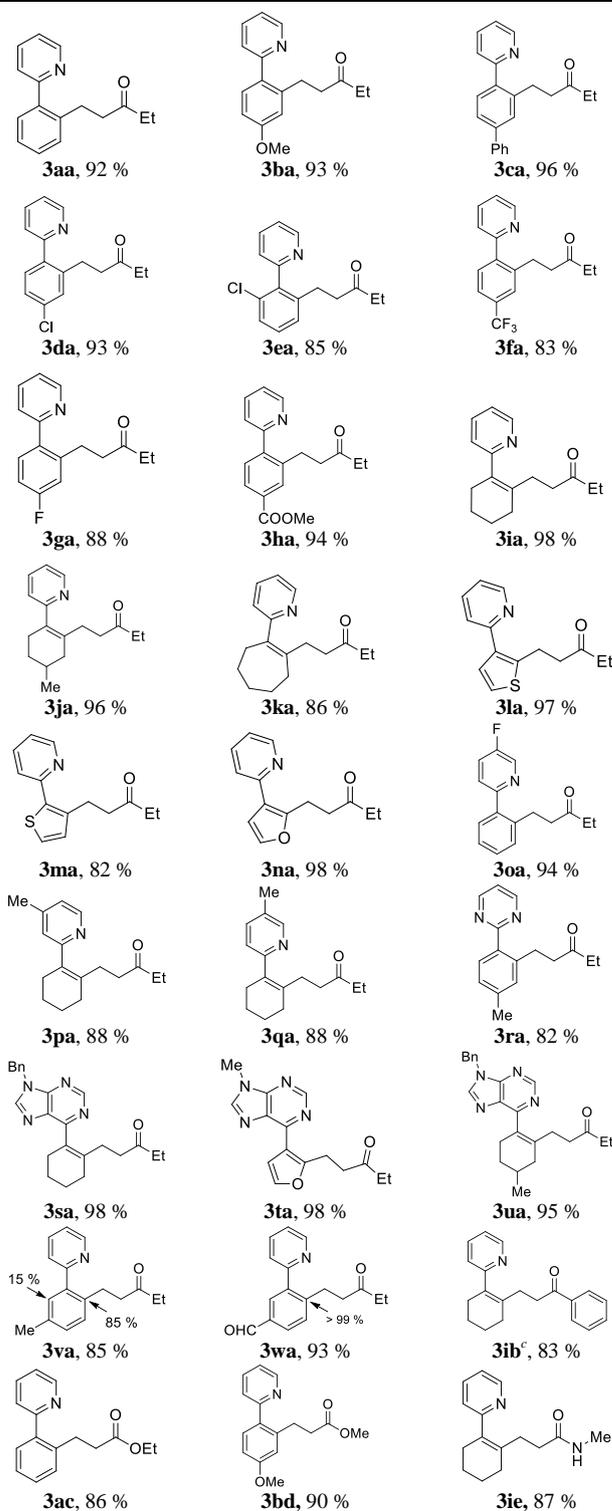
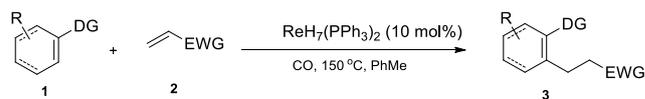


Entry	L	Solvent	Atmosphere	Yield (%)
1	PPh_3	THF	N_2	0
2	PPh_3	THF	Ar	0
3	PPh_3	THF	Air	0
4	PPh_3	THF	CO	68
5 ^b	dppe	THF	CO	0
6 ^b	dppp	THF	CO	0
7	PCy_3	THF	CO	0
8	$\text{P}(\text{tolyl})_3$	THF	CO	62
9	PPh_3	Toluene	CO	83
10 ^c	PPh_3	Toluene	CO	92
11 ^d	PPh_3	Toluene	CO	58
12	PPh_3	CH_3CN	CO	0
13	PPh_3	anisole	CO	74
14	PCy_3	1,4-dioxane	CO	31

^aReaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), ReH_7L_2 (5 mol%), CO (1.5 atm) and solvent (0.5 mL) 150 °C for 24 h. Isolated yield. The reactions were carried out in a 10 mL sealed tube. ^b ReH_7L . ^c10 mol % $\text{ReH}_7(\text{PPh}_3)_2$ was used. ^d**2a** (0.2 mmol)

With the optimized conditions in our hand, the scope of substrates has been investigated. Firstly, all kinds of substituent substrates were applied to achieve this transformation (Table 2). To our delight, the reaction smoothly proceeded in high yield, regardless of electron-donating or electron-withdrawing groups. The sp^2 C-H bonds on simple cycloalkenes were also successfully employed to explore the scope of substrates with excellent yield (**3ia-3ka**). Moreover, heterocycles, examples for thiophene and furan (**3la-3na**), were also easily alkylated to produce a series of functional molecules. Some of functional groups, such as methoxy (**3ba**), trifluoromethyl (**3fa**), ester (**3ha**) and formyl (**3wa**), were all tolerated, which was beneficial to further decoration. Meanwhile, when m-substituted arenes were employed (**3va**, **3wa**), high regioselectivity was revealed, favoring to functionalization of the less-hindered C-H bond. Secondly, different directing groups were detected. The reaction was not restricted by pyridine derivatives (**3oa-3qa**), and then pyridine containing electron-withdrawing group could lead to higher yield. Pyrimidine and purine have been also demonstrated to be great directing groups (**3ra-3ua**), which widely exist in biological molecules and natural products.

Table 2 Scope of different substituted substrates.^{a,b}

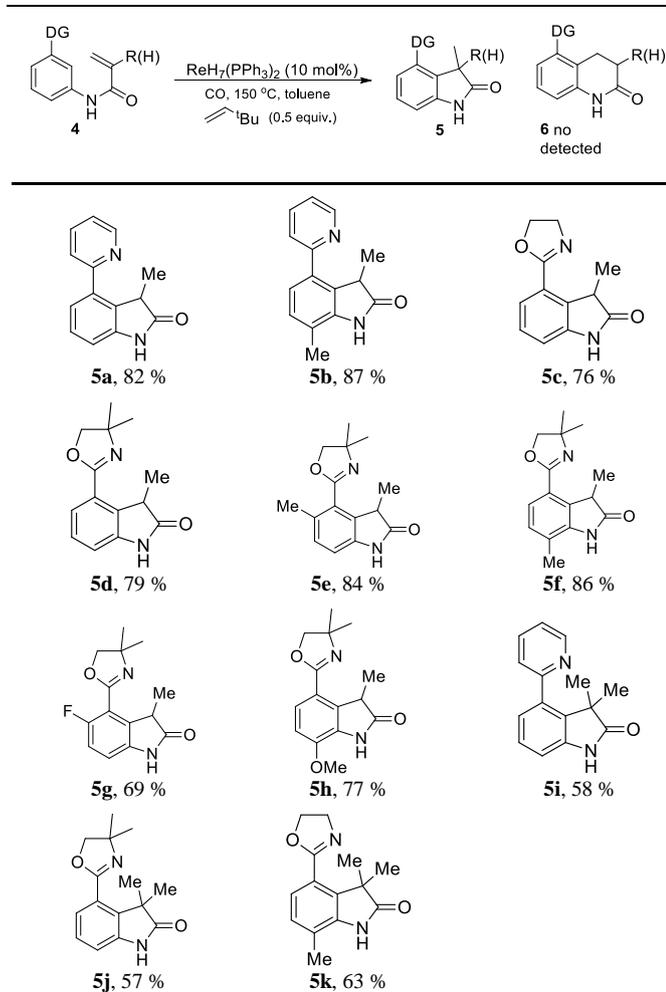


^aReaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), $\text{ReH}_7(\text{PPh}_3)_2$ (10 mol%), CO (1.5 atm), and toluene (0.5 mL), 150 °C for 24 h. The reactions were carried out in a 10 mL sealed tube. ^bIsolated yield. ^c**2b** (0.3 mmol)

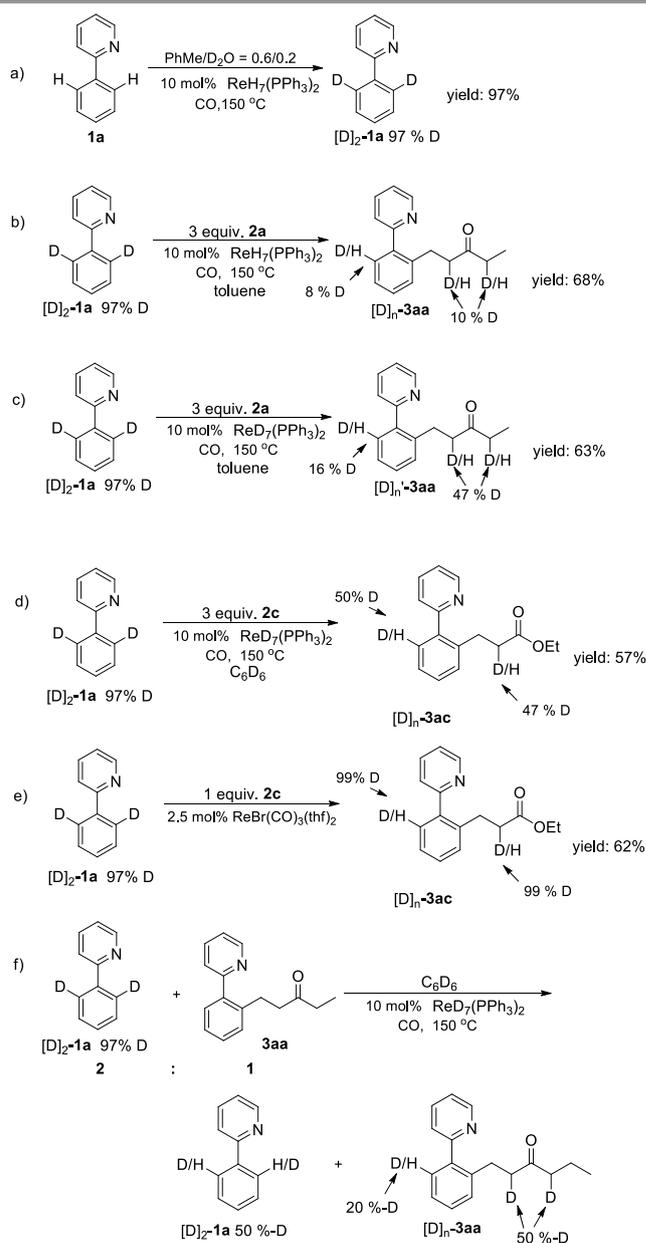
We further explored the range of α , β -unsaturated compound. Phenylvinylketone was also suitable for this transformation (**3ib**). Particularly, lowly electro-philic α , β -unsaturated ester (**3ac**, **3bd**) and amide (**3ie**) proceeded smoothly to afford moderate yields.

In order to apply rhenium-catalyzed C-H activation to construct heterocyclic frameworks, the intramolecular transformations have been surveyed. Interestingly, the sp^2 C-H bonds selectively inserted into the α -site of the double bond to display the indolones **5**, and the product **6** has not been detected. Additionally, 3, 3-dimethylbut-1-ene was utilized as hydrogen acceptor, protecting the double bonds of substrates from being reduced by *in-situ* generated reductive H species.⁸ The catalytic system was applied to synthesize a series of indolones (Table 3). Different substituted products have been obtained in moderate to excellent yields. To convert these frameworks to more general structures, the removable directing groups have been considered. Oxazolines as benign directing groups can be reduced to aldehydes or turned into carboxylic acids by hydrolysis, which is in favour of further functionalization.⁹

Table 3 Construction of indolones.^{a, b}



^aReaction conditions: **4** (0.2 mmol), 3,3-dimethylbut-1-ene (0.1 mmol), $\text{ReH}_7(\text{PPh}_3)_2$ (10 mol %), toluene (0.5 mL), CO (1.5 atm), 150 °C for 24 h. The reactions were carried out in a 20 mL sealed tube. ^bisolated yield.

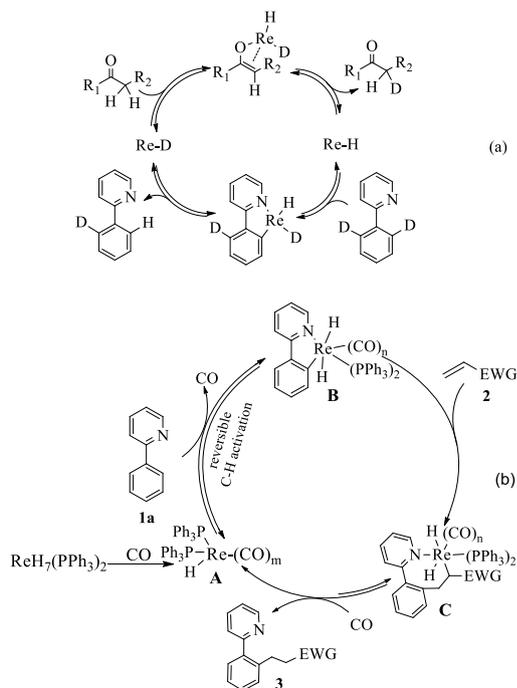


Scheme 2 Mechanistic experiments.

To gain insight into the Re-catalyzed C-H alkylation reaction,^{10a} several mechanistic experiments were carried out to elucidate the mechanism. Firstly, rhenium-catalyzed *ortho*-directed C-H deuteration with D_2O has indicated the C-H bond metalation step should be involved (Scheme 2a).^{10b} Furthermore, the obvious H/D scrambling has been examined during the reaction of $[\text{D}]_2\text{-1a}$ with **2a**, which suggested C-H bond metalation to be reversible (Scheme 2b).^{2a, 2d, 2j} In order to monitor the influence of hydrogen on catalyst, the $\text{ReD}_7(\text{PPh}_3)_2$ was used (Scheme 2c and 2d). Obvious H/D scrambling at the *ortho*-positions of phenylpyridine moiety, the similar results indicated the hydrogen on catalyst has few influence on the mechanistic experiments ($[\text{D}]_n\text{-3aa}$), and also demonstrated that C-H bond activation was reversible^{11a}, in stark contrast to rhenium

carbonyl compound-catalyzed C-H activation that was a rate determining step^{11b} (Scheme 2e). In addition, the apparent H/D exchange has been observed, when the mixture of [D]₂-**1a** and **3aa** was stirred under standard condition (Scheme 2f). It suggested that a key Re-H species might enable the H/D transfer between different substrates (Scheme 3a).

Finally, a tentative mechanism has been proposed upon these experiments and previous work (Scheme 3b). Initially, the rhenium hydride catalyst reacted with CO to generate Re-H species **A**.¹² Subsequently, the intermediate **B** was generated by a reversible C-H metalation, which could be stabilized by CO coordination under high temperature. Then, the alkene **2** inserted into Re-C bonds giving intermediate **C**. The intermediate **C** underwent reductive elimination to recover Re-H species **A**.



Scheme 3 Proposed mechanism.

Summary

In summary, we have reported the first example of CO-enabled rhenium hydride compound-catalyzed directed sp² C-H alkylation. Different directing groups and substrates were all suitable for this catalytic system. The intramolecular transformation also provides a new and efficient protocol to construct indolone frameworks. The research of mechanism has suggested that Re-H species might play a key role in catalytic cycle, which provided a further perspective for rhenium-catalyzed C-H functionalization. Further studies on rhenium hydride complexes-catalyzed transformations are under way in our laboratory.

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