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Rhenium-Catalyzed Acceptorless Dehydrogenative Coupling via Dual Activation of Alcohols and Carbonyl Compounds

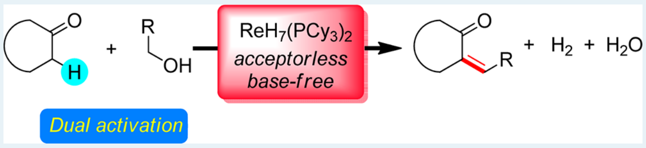
Hongming Jin,[†] Jin Xie,[†] Changduo Pan,[†] Zhengbo Zhu,[†] Yixiang Cheng,[†] and Chengjian Zhu*,[†,‡]

[†]State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210093, People's Republic of China

[‡]State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Shanghai 200032, People's Republic of China

Ⓢ *Supporting Information*

ABSTRACT: The rhenium hetaphydride complex was found to be a versatile, homogeneous catalyst for dehydrogenative functionalization of alcohol. The dehydrogenative C−C coupling of alcohols and carbonyl compounds was carried out in the absence of base and hydrogen acceptors to afford a series of α,β-unsaturated carbonyl compounds. A possible dual activation pathway was proposed by mechanistic investigations.



KEYWORDS: *alcohol, dehydrogenation, rhenium, homogeneous catalysis, C−H activation*

■ INTRODUCTION

Formulating sustainable, atom-economical strategies to construct C−C bonds has emerged as a perennial topic in organic chemistry.[1] Alcohol as an inexpensive and green coupling partner is much favored in terms of its ease of operation and storage.[2] In recent years, transition metal-catalyzed dehydrogenative coupling of alcohol represents an efficient and general method to construct intricate scaffolds.[3,4] Despite significant contributions to C−X bonds forming[5,6] having been made by dehydrogenative functionalization of alcohol, base and hydride acceptors were usually required,[3a,d,4c] which was not environmentally friendly. In this aspect, the development of base-free and acceptorless dehydrogenative coupling for the formation of C−C bonds is highly desirable. To meet the challenge, herein, we disclose an unprecedented dehydrogenative C−C coupling by rhenium complex-catalyzed dual activation of different substrates.

Recently, Klankermayer reported rhenium hydride complexes as promising dehydrogenative catalysts that were applied to dehydrogenative esterification and amidation.[7] Moreover, a rhenium hydride complex-catalyzed Thorpe−Ziegler reaction has been lately described by Takaya's group, in which a Re−C species, generated through direct C−H activation, was proposed

Scheme 1. Rhenium-Catalyzed Dehydrogenative C−C Coupling via the Dual Activation Model

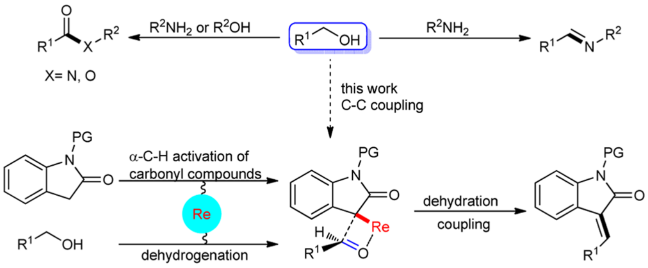
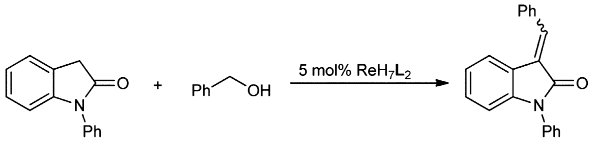


Table 1. Screening for Optimal Reaction Conditions[a]



1a **2a** **3a**

entry	L	solvent	additive	yield	*E/Z*
1	PCy$_3$	THF		64%	3:1
2	PPh$_3$	THF		31%	3:1
3	P(tolyl)$_3$	THF		37%	3:1
4[b]	dppe	THF		none	ND
5[b]	dppf	THF		none	ND
6[c]	PCy$_3$	THF		43%	1:1
7	PCy$_3$	CHCl$_3$		trace	ND
8	PCy$_3$	CH$_3$CN		trace	ND
9	PCy$_3$	anisole		71%	3:1
10	PCy$_3$	toluene		63%	7:2
11	PCy$_3$	DMF		none	ND
12	PCy$_3$	anisole	LiCl	75%	25:3
13	PCy$_3$	anisole	nBu$_4$NBr	77%	3:1
14	PCy$_3$	anisole	KCl	71%	3:1
15	PCy$_3$	anisole	4 Å MS	73%	3:1

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.8 mmol), additive (0.4 mmol), ReH$_7$L$_2$ (5 mol %), and solvent (0.5 mL) under N$_2$ atmosphere at 150 °C, isolated yield. [b]ReH$_7$L. [c]130 °C.

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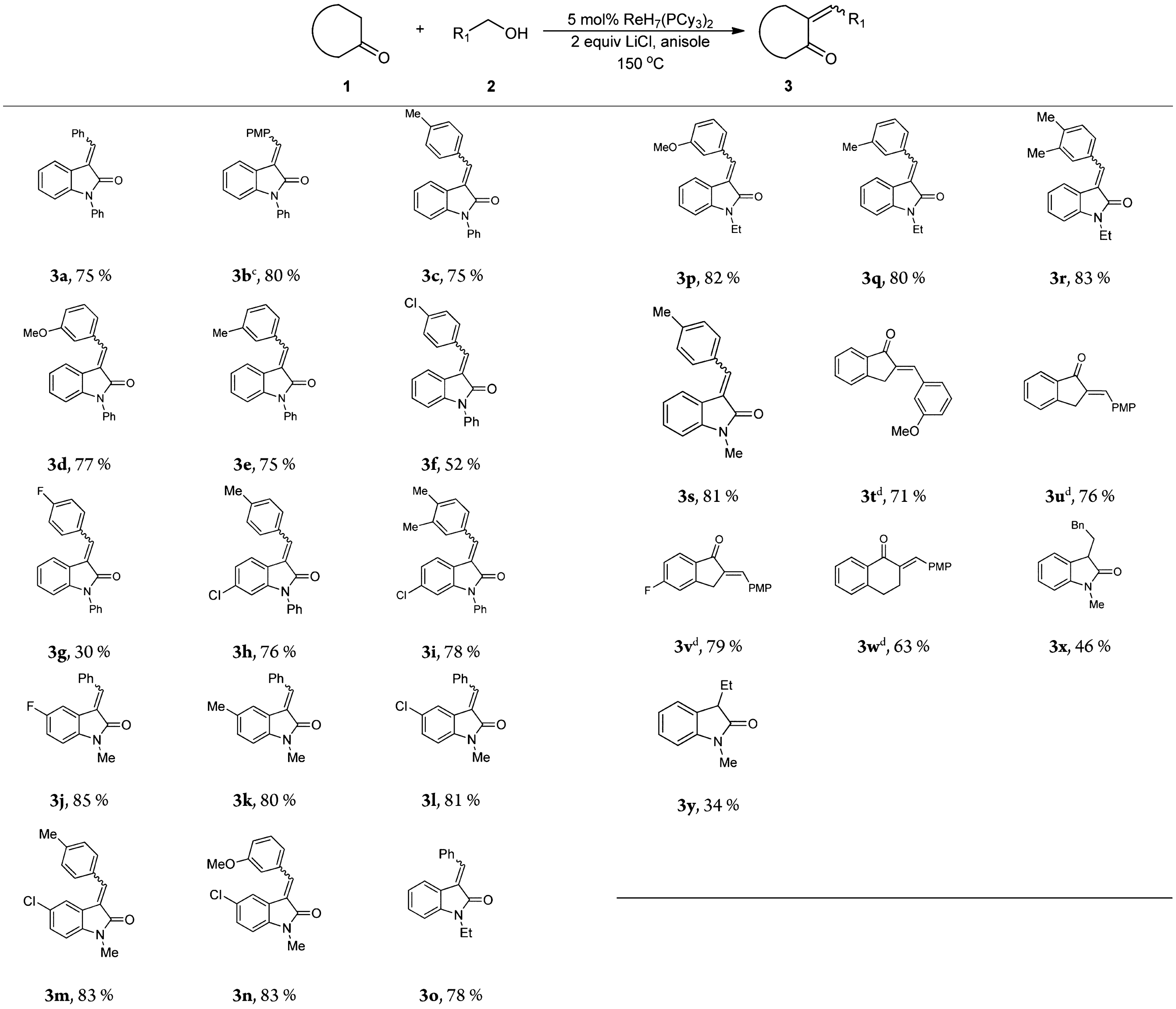
Table 2. Substrate Scope[a,b]



3a, 75 %; **3b**[c], 80 %; **3c**, 75 %; **3d**, 77 %; **3e**, 75 %; **3f**, 52 %; **3g**, 30 %; **3h**, 76 %; **3i**, 78 %; **3j**, 85 %; **3k**, 80 %; **3l**, 81 %; **3m**, 83 %; **3n**, 83 %; **3o**, 78 %; **3p**, 82 %; **3q**, 80 %; **3r**, 83 %; **3s**, 81 %; **3t**[d], 71 %; **3u**[d], 76 %; **3v**[d], 79 %; **3w**[d], 63 %; **3x**, 46 %; **3y**, 34 %

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.8 mmol), LiCl (0.4 mmol), $ReH_7(PCy_3)_2$ (5 mol %), and anisole (0.5 mL) under N_2 atmosphere for 24−36 h at 150 °C, isolated yield. [b] *E*/*Z* ratio ~ 25:3. [c] PMP = 4-methoxy phenyl. [d] Additional $ReH_7(PPh_3)_2$ (5 mol %) was added. Only the *E* isomer was obtained.

as the key intermediate.[8] Inspired by these reports, we envisaged a possible dehydrogenative coupling of alcohol to achieve α-olefination of carbonyl compounds via a dual activation model (Scheme 1). During our study, it was found that rhenium hetpahydride complexes as versatile catalysts integrated separate catalytic moieties into dehydrogenation coupling without a traditional base and hydrogen acceptors. To the best of our knowledge, there has been little success of the rhenium-catalyzed dehydrogenative C−C coupling reaction, although rhenium-catalyzed transformations have made outstanding achievements in the past decades.[7−11]

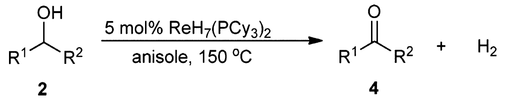
■ RESULTS AND DISCUSSION

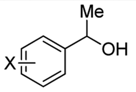
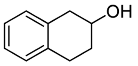
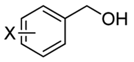
Initially, the reaction of *N*-phenyl oxindole **1a** and benzyl alcohol **2a** was chosen as the model reaction to screen the reaction conditions (Table 1). To our delight, 5 mol % of $ReH_7(PCy_3)_2$ gave **3a** in a yield of 64% at 150 °C for 36 h, whereas $ReH_7(PPh_3)_2$ afforded the product in only 31% yield (entries 1−2). When the reaction temperature was decreased to 130 °C, a lower yield was obtained (entry 3). Further optimization showed that the yield could be increased to 71% when anisole was used as a solvent. Unfortunately, the *E*/*Z* selectivity was not significantly improved by altering the solvent and temperature. Then, different additives were screened (entries 9−12), and it was found that **3a** could be isolated in 75% yield with a good *E*/*Z* selectivity by addition of anhydrous LiCl (entry 9), which may form a more stable transition state via Li^+ chelation. The optimal reaction condition is catalyzed by 5 mol % $ReH_7(PCy_3)_2$ under N_2 atmosphere at 150 °C.

We next explored the scope of this transformation using the optimized catalytic condition. The results are summarized in Table 2. Gratifyingly, a series of oxindoles bearing different substitutes (*R* = F, Me, Cl) furnished the desired 3-alkylene-oxindoles in good yields. Other carbonyl compounds also worked well and afforded only *E* isomers (**3t−w**). Subsequently, we screened a range of alcohols. The reaction of benzyl alcohols bearing electron-donating groups (**3a−e**) proceeded more smoothly than those bearing electron-withdrawing substitutes (**3f–g**) at the aromatic ring. A substrate bearing a strong electron-withdrawing group, such as NO_2, was not engaged in this reaction.[14] Aliphatic primary alcohols were also used in this reaction. Surprisingly, a few of dehydrogenative coupling products were isolated, while hydrogen autotransfer products were obtained as major products (**3x–y**). We therefore considered that the carbon–carbon double bonds seem to be stabilized by the conjugated and steric effect of an aromatic ring to avoid the following reduction reaction.

To gain insight into the reaction mechanism, several experiments were carried out. First, recatalyzed acceptorless dehydrogenation of alcohols was tested (Table 3). It was found that the dehydrogenation of 1-arylethanols under the standard conditions proceeded successfully to give the corresponding acetophenone derivatives in good yields (entries 1–3). Other secondary alcohols, such as 1,2,3,4-tetrahydronaphthalen-2-ol, also afforded **4o** in 62% yield (entry 4); however, the dehydrogenation of primary alcohols was less efficiently catalyzed and was also impacted by the electronic effect on the aromatic ring (entries 4–8).

Table 3. Recatalyzed Acceptorless Dehydrogenation of Alcohols[a]

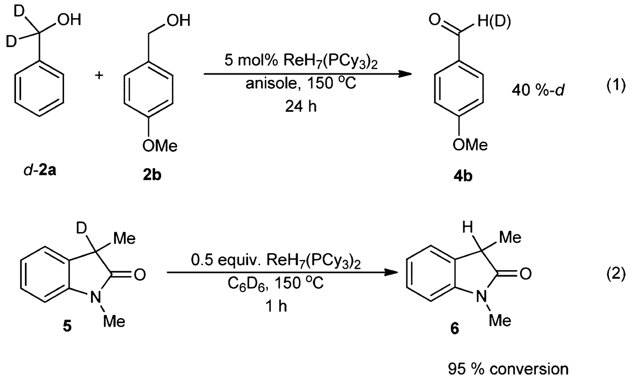


entry	alcohol		product	yield (%)
				
1	X = H	**2l**	**4l**	80
2	X = 3-MeO	**2m**	**4m**	84
3	X = 4-Me	**2n**	**4n**	85
4		**2o**	**4o**	62
				
5	X = H	**2a**	**4a**	46
6	X = 4-MeO	**2b**	**4b**	52
7	X = 4-Me	**2c**	**4c**	48
8	X = 3-Me	**2e**	**4e**	45
9	X = 4-Cl	**2f**	**4f**	19

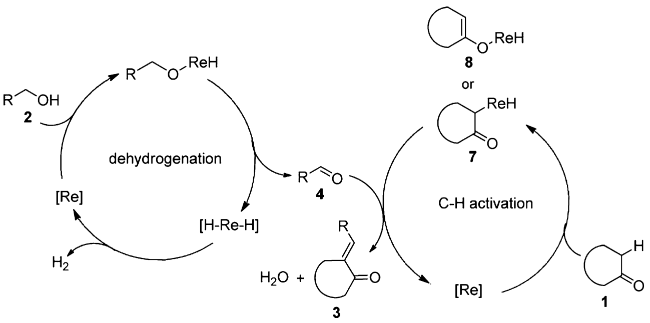
[a] Reaction conditions: **2** (0.2 mmol), $ReH_7(PCy_3)_2$ (5 mol %), and anisole (0.5 mL) under N_2 atmosphere at 150 °C, isolated yield.

Until now, there have been few reports on dehydrogenative oxidation of alcohol for homogeneous rhenium complexes.[12b] Thus, to disclose the detailed mechanism of this reaction, a deuterium labeling study was proposed [Scheme 2, eq (1)]. The 1:1 mixture of α, α-d_2-benzyl alcohol d-**2a** and **2b** was heated at 150 °C for 24 h. H/D scrambling was detected in 4-methoxy-benzaldehyde, suggesting that the alcohol dehydrogenation step was reversible.[6c,12,13] Upon our hypothesis for catalytic C–H activation moiety, Re–C species as the key intermediates have been proposed.[8−11,15] In this view, a deuterium experiment was devised to further substantiate our mechanistic pathway (Scheme 2, eq 2). Compound **5** was treated with 0.5 equiv of rhenium hydride complex at 150 °C for 1 h. Detected by ^2H NMR spectroscopy, the deuterium-labeled substrate nearly vanished, and **6** was isolated in 95% yield.[13] Therefore, we speculated the H/D exchanging between the carbonyl compounds and rhenium hydride complex probably underwent Re–C intermediate forming or an enolate type transition state. However, the definite intermediate was still unclear. Moreover, the aldehyde hardly condensed with carbonyl compounds in the absence of the rhenium complex. The proposed mechanism is depicted in Scheme 3. Oxidative addition of the rhenium complex to the α-C–H of carbonyl compounds **1** could furnish Re–C species **7** or enolate derivative **8**. Aldehyde **4** generated in situ by alcohol **2** dehydrogenation inserts the Re–C bond, followed by reductive elimination and dehydration to give the desired product **3**.

Scheme 2. Deuteration Experiments



Scheme 3. Proposed Mechanism



■ SUMMARY

In summary, we have developed the first example of homogeneous rhenium-catalyzed dehydrogenative C–C coupling. The rhenium-catalyzed dual activation process may occur in this transformation. The novel, acceptorless and base-free catalytic system makes this reaction more benign and step-economical. Moreover, it is a new development for rhenium chemistry. Further studies on rhenium-catalyzed dehydrogenation and the mechanistic details are under way in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and spectroscopic characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: cjzhu@nju.edu.cn.

Notes

The authors declare no competing financial interest.

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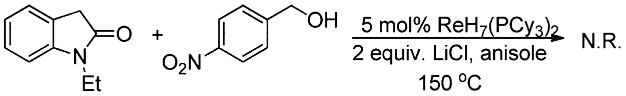
(13) For details, see the Supporting Information.

(14) For example:



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