Tris(acetylacetonato)rhodium(III)-Catalyzed α-Alkylation of Ketones, β-Alkylation of Secondary Alcohols and Alkylation of Amines with Primary Alcohols

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Abstract: The tris(acetylacetonato)rhodium(III) catalyst is shown to be a versatile catalyst in the presence of DABCO (1,4-diazabicyclo[2.2.2]octane) as ligand for the α -alkylation of ketones followed by transfer hydrogenation, for the one-pot β -alkylation of secondary alcohols with primary alcohols and for the alkylation of aromatic amines in the presence of an inorganic base in toluene.

Keywords: alcohols; amines; 1,4-diazabicyclo-[2.2.2]octane (DABCO); ketones; transfer hydrogenation; tris(acetylacetonato)rhodium(III) complex

tion resulting in the loss of a water molecule, and subsequent hydrogenation of the resulting enone to yield

the coupled secondary alcohol as product (see

Scheme 2). Both the α -alkylation of ketones and the

β-alkylation of sec-alcohols with primary alcohols

were first reported by Cho et al. with RuCl₂(PPh₃)₃

catalyst at 80-100 °C in dioxane.^[3] In this work, it was

mandatory to use stoichiometric amounts of a sacrifi-

cial hydrogen acceptor such as 1-dodecene as hydro-

gen trap to avoid reduction of the product ketones.

Cho et al. have reported that in the absence of a sacri-

Introduction

Alcohols are one of the most basic and important classes of organic compounds because they have a wide range of applications.^[1] α -Alkylation of enolates derived from ketones with electrophiles such as alkyl halides is the conventional method to form alcohols with extended C–C bonds.^[1,2] The metal-catalyzed α -alkylation of ketones and/or β -alkylation of sec-alcohols with primary alcohols is attracting much attention (Scheme 1) lately because of its critical advantage over the conventional α -alkylation method involving enolates, which suffers from problems with waste salts.

The metal-catalyzed alkylation reaction has positioned itself as a green process in terms of atom economy, avoidance of protecting groups, and waste minimization. It is to be noted that the β -alkylation of *sec*alcohols with primary alcohols is a multistep process that involves a dehydrogenation reaction of the alcohol to the ketone or aldehyde, followed by aldol reac-



Scheme 1. General scheme for C-C coupling of alcohols.

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alcohols.

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Scheme 2. Borrowing hydrogen process in C-C coupling of



Ru^[3a,b,5] and Ir^[6] metal-based catalysts have also been reported for this purpose, and they have shown sensible reactivity by modest alterations of the original reaction conditions. For example, a chiral bimetallic Ru-Ir catalyst combination has enabled the enantioenriched α -alkylation of ketones.^[7a] Both iridium and ruthenium complexes with chelating N-heterocyclic carbene^[7b] complexes as well as ruthenium and iridium terpyridine^[7c] complexes have also been reported for the direct β -alkylation of a secondary alcohol with primary alcohols. Saito et al. has reported using a Cu(I)/H₂/NaOH system for the direct β-alkylation of secondary alcohol with primary alcohols.^[8] Reactions involving metal nanoparticles of Ni,^[9] Pd^[10] (viologen polymers) and heterogeneous Pd/AlO(OH)^[11] catalysts have also been reported for ketone and alcohol coupling reactions allowing ketones to become the major products. It is to be noted that here the carbonyl functionality remains unreduced, and thus the corresponding alcohols are very rarely produced. Recently it has been reported that pincer-type N-heterocyclic carbene/Pd complexes^[12] give high yields of the corresponding alcohols. The Ag/Al₂O₃ heterogeneous catalyst system has also been reported for the selective synthesis of ketones but not alcohols using a β-alkylation method.^[13] Ryu et al. have reported the selective ketone product formation using RuHCl(CO)(PPh₃)₃ catalyst for the α -alkylation reaction for a variety of ketones and primary alcohols.^[14] Interestingly, Ru-based catalysts in general have been shown to give either a mixture of alcohols and ketone or alcohols as the major component of the product mixture.^[5]

Alkylation of Amines with Primary Alcohol

Nitrogen-containing molecules, particularly amines and their derivatives, have more important functions in chemical and biological sciences.^[15] Direct metalcatalyzed N-alkylation of amines with primary alcohols provides an efficient route to new sec-amines. Grigg et al. and Watanabe et al. independently reported the first examples of direct C-N bond formation with alcohols.^[16] Recent reports have led to more active catalysts and milder conditions, which were based on various metal ions such as Ru,^[17] Ir,^[6f,7b,18] Pt,^[19] Au,^[20] Ag,^[21] Pd,^[22] Ni,^[23] Cu,^[24] and Fe.^[25] A drawback of some of these reported catalytic systems is that the reaction tends to give a mixture of both imine and sec-amine as products^[6f,7b,21c,27,30] The formation of imines from the reaction can be understood from the fact that an alcohol can be activated by the metal ion as the corresponding aldehyde, then in situ condensation of amine with aldehvde to give imines which is followed by a transfer hydrogenation reaction to yield the secondary amine as final product.



Scheme 3. Borrowing hydrogen concept illustrated for *N*-alkylation of amine.

This overall process is termed *borrowing hydrogen*^[26] which is clearly elaborated in the mechanistic scheme shown in Scheme 3. Recently Xu et al. reported that the direct alkylation of amines was catalyzed by Wilkinson's catalyst and promoted by air.^[27] This reaction has been shown to provide a mixture of both *sec*-amine and imine.

Given the critical importance of both alcohols and sec-amines, herein, we report a phosphorus-free, very low loading (1.0 mol%) of commercially available tris(acetylacetonato)rhodium(III) complex/DABCO/ base-based catalytic system for the α -alkylation of ketones, and direct one-pot β -alkylation of secondary alcohols with primary alcohols. These reactions produce alcohols as the final product, no ketone was formed during the reaction. These reactions are atom economical as we use only stoichiometric amounts of reagents. Notably, our reaction requires the use of DABCO which is a sterically hindered, mild base which is eco-friendly, highly reactive, and inexpensive.^[28] Using the same catalytic system we also report the direct C-N bond formation via N-alkylation of aromatic amines under mild conditions using an inorganic base and DABCO. These studies form the focus of this paper.

Results and Discussion

Initial experiments were carried out by choosing acetophenone, 1-phenylethanol and 4-methoxyphenylmethanol as model substrates for optimizing the reaction conditions for the α -alkylation of ketones and for the β-alkylation of secondary alcohols with primary alcohols in the presence of 1 mol% rhodium as metal source, with DABCO as organic ligand additive, base and toluene as solvent. Two different rhodium catalysts were evaluated for this study and they are tris(acetylacetonato)rhodium(III) (A) and trichlororhodium(III) hydrate (B). When the latter catalyst (B) was used in the presence of a ligand and a strong base such as KO-t-Bu in toluene, the desired coupled product 3-(4-methoxyphenyl)-1-phenylpropan-1-ol was obtained in 55% yield (Table 1, entry 1). By employing identical reaction conditions, when 1-phenyl-

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Table 1. Optimization of reaction conditions for the α -alkylation of ketone and β -alkylation of secondary alcohols with primary alcohol.^[a]

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Entry	Metal source	Base	Ligand	Yield ^[b]
1	RhCl ₃ ·3 H ₂ O	KO- <i>t</i> -Bu	DABCO	55
2	RhCl ₃ ·3 H₂O	KO- <i>t-</i> Bu	DABCO	42 ^[c]
3	RhCl ₃ ·3 H₂O	КОН	DABCO	61
4	RhCl₃·3 H₂O	КОН	DABCO	32 ^[d]
5	RhCl ₃ ·3 H ₂ O	КОН	-	15
6	RhCl ₃ ·3 H ₂ O	КОН	-	10 ^[c]
7	RhCl ₃ ·3 H₂O	K ₂ CO ₃	DABCO	nd ^[e]
8	RhCl ₃ ·3 H ₂ O	-	DABCO	nd ^[e]
9	_	KO- <i>t</i> -Bu	DABCO	trace
10	-	K ₂ CO ₃	DABCO	nd
11	Rh(acac) ₃	KOtBu	DABCO	91
12	Rh(acac) ₃	кон	DABCO	98
13 14	Rh(acac) ₃ Rh(acac) ₃	КОН КОН	DBU DABCO	70 98 ^[c]

^[a] Reaction conditions: acetophenone (1 mmol, 0.5 M in toluene) 4-methoxyphenylmethanol (1 mmol, 0.5 M in toluene), metal source (1.0 mol%), base (1 mmol), DABCO (50 mol%) and 2 mL of toluene at 110 °C, for 4–6 h.
 ^[b] Isolated violated of addition product

^[b] Isolated yield of addition product.

^[c] Phenylethanol (1 mmol), 4-methoxyphenylmethanol (1 mmol) and reaction time was 14-16 h

^[d] Acetonitrile used as solvent.

^[e] Considerable amount of aldehyde obtained.

ethanol (secondary alcohol) was used as substrate in place of a ketone, a direct β -alkylation of the secondary alcohol with a primary alcohol readily occurs, and this results in the C-C coupled product of 3-(4methoxyphenyl)-1-phenylpropan-1-ol in 42% yield (Table 1, entry 2). It is clear from Table 1, entries 1 and 2, that both the reactions give rise to same coupled alcohol product. When the α -alkylation reaction was carried out in the presence of KOH as base, the yield of addition product has been slightly increased to 61% (Table 1, entry 3). When the same reaction was carried out in acetonitrile as solvent, a significant drop in yield of the product to 32% was observed (Table 1, entry 4). When the α -alkylation reaction was performed in the absence of DABCO we have obtained only a very poor yield (15%) of the coupled alcohol product (Table 1, entry 5). Similar results with poor yield of the product were obtained with β -alkylation reactions under similar reaction conditions (Table 1, entry 6). From the above results it can be inferred that DABCO plays a crucial role in promoting the reaction. It is also clear that the solvent toluene is the best solvent for both α -alkylation of ketones and β-alkylation reactions of secondary alcohol with primary alcohol to get good yields of the coupled alcohol products. Instead of strong inorganic bases, we have also employed the much milder potassium carbonate as base; interestingly, no detectable products were obtained. (Table 1, entry 7). We have also performed the reaction in the absence of inorganic base and absence of rhodium source, for the α -alkylation reaction (Table 1, entries 8–10), once again no detectable C-C coupled products were obtained. Therefore, for these reactions both inorganic base and rhodium metal source are essential to promote the reaction. Interestingly, when the rhodium metal source is changed from trichlororhodium(III) (B) to tris(acetylacetonato)rhodium(III) (A), in the presence of DABCO and KO-t-Bu base, we have obtained yields as high as 91% for the coupled product 3-(4-methoxyphenyl)-1phenylpropan-1-ol (Table 1, entry 11). However, we have noted when the inorganic base used for this reaction is KOH instead of KO-t-Bu, the yield of the coupled product rose to 98% for the α -alkylation reaction (Table 1, entry 12). Similarly, the β -alkylation reaction under similar reaction conditions gave yields as high as 98% for the coupled alcohol product (Table 1, entry 14) but at the expense of the required reaction time which was 14-16 h. When the reaction was performed in the presence of DBU as organic ligand additive instead of DABCO, we obtained only 70% yield of the α -alkylated alcohol product (Table 1, entry 13).

Thus, the optimum reaction conditions for both α alkylation and β -alkylation reactions are the use of equimolar amounts of ketone or sec-alcohol with primary alcohols, tris(acetylacetonato)rhodium(III) (A), KOH base, DABCO ligand in toluene solvent at 110°C. Using the optimized reaction conditions in hand, α -alkylation reactions of ketones with primary alcohols using various ketones were examined to explore the scope of the reaction (Scheme 4, Table 2). As can be seen, this protocol is applicable for the reactions of a variety of aromatic ketones as well as aliphatic ketones with aromatic alcohols, and these studies illustrate the scope of the present catalytic system. Among various ketone substrates studied, to our delight the reaction proceeded smoothly, and excellent vields were obtained between aromatic ketones like acetophenone, 1-(4-methoxyphenyl)ethanone and 1-(6-methoxynapthalen-2-yl)ethanone with aromatic alcohols like phenylmethanol, 4-(methoxyphenyl)methanol and p-tolylmethanol (Table 2, entries 1-6 and



Scheme 4. α -Alkylation of ketones and β -alkylation of secondary alcohols with primary alcohols.

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Table 2. Rh(III)-catalyzed α -alkylation of ketones with primary alcohols.^[a]

Entry	Ketones	Alcohol	Product	Yield ^{[b] [%]}
		́п́∼∕∩н	он	ו
1	°		он	95
2	Ċ	°€	С	1 ₀ . 98
3	۲ ۵	ГОН	С	L 94
4	`o [©] °	-O OH	о он	o 96
5		Стон) ₉₅
6	, DI	СТОН		94 ک
7		°о€стон		o 75 ^[c,d]
8		Стон	ОН	57 ^[c,d]
9		он	C C C C C C C C C C C C C C C C C C C	56 ^[c]
10	\bigcirc^{o}	°о€стон	ÓC	1 ₀ - ⁶²
11	¥,	°€	У) O 61
12	¥ Y	Стон		58
¹³ `(СОН		95

^[a] *Reaction conditions*: ketone (1 mmol, 0.5M in toluene), primary alcohol (1 mmol, 0.5M in toluene), KOH (1 mmol), catalyst **A** (1 mol%) DABCO (0.5 mmol) and 2 mL of toluene.

^[b] Isolated yields.

entry 13). When the reaction was performed between propiophenone and 4-methoxyphenylmethanol, we have obtained 3-(4-methoxyphenyl)-2-methyl-1-phenylpropan-1-ol as product in good yields with a longer reaction time (24 h). In this case, the product was elucidated as a mixture of diastereomers in a 50:50 ratio (Table 2, entry 7). The best diastereoselectivity ever noted for this compound, synthesized *via* the same approach, is approxiately 50:50.^[8] However, when the reaction was conducted between propiophenone and 3-phenylpropan-1-ol we have obtained 2-methyl-1,5diphenylpentan-1-ol only in moderate yield (57%) as the diastereomeric product in a 50:50 ratio (Table 2 entry 8). When the reaction was performed using pro-

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piophenone and 2-methylpropan-1-ol, only a moderate yield of product 2,4-dimethyl-1-phenylpentan-1-ol was obtained (Table 2, entry 9) as a mixture of diastereomers in a 50:50 ratio. We could not find literature references that have descriptions about observed diastereoselectivity ratios for entries 8 and 9 in Table 2. It is very likely that no one has synthesized these compounds before in the literature. The α -alkylation of cyclohexanone with phenylmethanol also gave a moderate yield of 62% of alcohol product as 2-(4-methoxybenzyl)cyclohexanol (Table 2, entry 10). It can be clearly seen that when the reaction is conducted between an aliphatic ketone such as 4-methylpentan-2one with an aromatic alcohol like phenylmethanol and 4-(methoxyphenyl)methanol, the isolated yields of the desired products were nearly 58-61%. (Table 2, entries 11 and 12). Thus, the conclusion drawn from these studies is that aromatic ketones and aromatic primary alcohols give highest yields for the C-C coupled product, however, we have obtained only a moderate yields when aliphatic ketones are used with aromatic and aliphatic primary alcohols under our optimized experimental conditions (Table 2, entries 10-12). As discussed earlier, Ryu et. al. have reported selective ketone product formation using the $Ru(H)(Cl)(CO)(PPh_3)_3$ catalyst for α -alkylation reactions of a variety of ketones and primary alcohols using similar substrate stoichiometry (1:1) and catalyst loading (1.0 mol%).^[14] In contrast, in our work, we use a similar substrate stoichiometry and catalyst loading and have obtained exclusively alcohols as the product during α -alkylation reactions using a commercially available catalyst A. This result strongly suggest that a Rh(III) species even in small amounts promotes the reduction of not only the double bond but also the keto functionality during the reaction.

Being encouraged by the above results, we next examined the one-pot β -alkylation of various secondary alcohols with primary alcohols under our optimized reaction conditions (Scheme 4). The β -alkylation of secondary alcohols like 1-phenylethanol, and 1-(4-methoxyphenyl)ethanol with primary alcohols like phenylmethanol, 4-(methoxyphenyl)methanol and *p*-tolylmethanol gave excellent yields of the corresponding coupled alcohol products (Table 3, entries 1–5).

When the reaction was performed between an aromatic secondary alcohol like 1-(6-methoxynapthalene-2-yl)ethanol and a primary aromatic alcohol such as *p*-tolylmethanol also gave excellent yield as high as 92% (Table 3 entry 7). Notably, a previous report for this reaction gave only 65% yield with $\text{RuCl}_2(\text{PPh}_3)_3$ catalyst^[3a] whilst we have obtained a much higher yield using the commercially available $\text{Rh}(\text{acac})_3$ catalyst. The use of a secondary alcohol, such as 1-phenylpropanol with 4-methoxyphenylmethanol, for the reaction gave a good yield of the desired product which is elucidated as a diastereoisomeric mixture in a 50:50

^[c] Reaction time was 24 h and 50:50 diastereomeric mixtures of products formed

Table 3. Rh(III)-catalyzed β -alkylation of secondary alcohols with primary alcohols.^[a]



^[a] Reaction conditions: Secondary alcohol (1 mmol, 0.5 M in toluene), primary alcohol (1 mmol, 0.5 M in toluene), catalyst A (1.0 mol%), KOH (1 mmol), DABCO (0.5 mmol) and 2 mL of toluene at 110 °C, for 12–16 h.

^[b] Isolated yield of addition product.

^[c] Diastereomeric mixture.^[3a,5a]

ratio (Table 3, entry 6). For this reaction, the previous report by S. Saito et al. has shown a similar 50:50 diastereoselectivity for the product.^[8] Similarly, the reaction of α -tetralol with 4-(methoxyphenyl)methanol and phenylmethanol gave the corresponding alkylated alcohols as diastereoisomeric mixtures in a 50:50 ratio in good yields (Table 3, entries 8 and 9).^[6a] For reactions between 1-phenylpropanol and 3-phenylpropanol only a 47% yield of a 50:50 diastereomeric product was obtained (Table 3, entry 10). Similar diastereomeric product formation in a 50:50 ratio has been reported previously by other researchers for the reaction of α -tetralol with 4-methoxyphenylmethanol and phenylmethanol as well as reaction of 1-phenylpropanol with 4-methoxyphenylmethanol.^[8,6a] Given that excellent results were obtained for the α -alkylation of ketones and the β -alkylation of secondary alcohols with primary alcohols, it is apparent that the catalytic system is very efficient at low catalyst loading (1 mol%) under benign reaction conditions in toluene at 110 °C.

It is to be noted that with the exception of entries 8-10 in Table 3, the reactions of all the substrates have been reported in the literature. However, the yields obtained with many of our substrates with our catalyst system are much higher than those reported in the literature. Given the fact that the β -alkylation reaction is very important, we have made a comparison of our work with those of important works that were reported previously using the substrates described in Table 3. The details of these results are shown in Table 4. As can be seen in Table 4, a large excess of base and catalyst is needed to promote the reaction for Ru- and Ir-based catalysts. In these works, it has been reported that the yields for the products are much lower than those reported in the present work when aromatic sec-alcohols, alicyclic alcohols are used with aromatic alcohols.[3a,5b,6a] In addition, our catalyst system is both commercially available and it requires only stoichiometric use of reagents using 1.0 mol% of the catalyst for promoting the β -alkylation reaction.

During the course of this study, we have discovered that the optimized reaction conditions for both α -al-kylation of ketones and β -alkylation of secondary alcohols can also be extendable to the direct N-alkylation of various aromatic amines with aromatic alcohols to synthesize exclusively *sec*-amines (Scheme 5).

The results of this study are presented in Table 5. Quite notably, when the direct amination reaction was performed in the presence of catalyst **B** between *p*-toluidine and 4-(methoxyphenyl)methanol no product was isolated (Table 5, entry 1). Interestingly when the same reaction was performed in the presence of

Table 4. Comparison of the β -alkylation of secondary alcohols by different methods.

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R´, `	+ R'		R' 🗸
1	2		3

Entry	Catalyst loading (mol%)	Conditions ^[a]	Yield [%] ^[ref.]
1	[RuCl ₂ (PPh ₃) ₃] (5)	1 (100), 2 (200), KOH (300), 1-dodecene (500),dioxane, 80 °C, 40 h	34–90 ^[3a]
2	[RuCl ₂ (dmso) ₄] ₂ (5)	1 (100), 2 (100), KOH (200), neat, 100 °C, 74 h	47–98 ^[5b]
3	[IrCpCl ₂] ₂ (2)	1 (100), 2 (120), NaO- <i>t</i> -Bu (300), toluene, 110 °C, 1 7 h	58–88 ^[6a]
4 ^[b]	Rh(acac) ₃ (1)	1 (100), 2 (100), KOH (100), DABCO (50), toluene,110 °C, 17 h	47–98

^[a] *Conditions:* reagents loading in mol%, R=Ph, Nap, PhCH₂; R[']=Ph, PhCH₂CH₂.

^[b] Present work.

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$$R-NH_{2} + R^{I} \frown OH \qquad \frac{KOH (1 \text{ mol})}{DABCO (0.5 \text{ mmol})} R^{-N} \swarrow R^{I}$$

Scheme 5. N-Alkylation of amines with primary alcohols.

Table 5. Rh(III)-catalyzed N-alkylation of amines with primary alcohols^[a]



[a] Reaction conditions: aromatic alcohol 1 mmol (0.5 M in toluene), aromatic amine 1 mmol (0.5 M in toluene), catalyst A (1.0 mol%), KOH, (1 mmol), DABCO (0.5 mmol), toluene 2 mL.

- ^[b] Isolated yields;
- [c] Reaction performed in the presence 1.0 mol% of catalystB; product not detected (n.d).
- ^[d] Solvent used is acetonitrile

catalyst **A** instead of catalyst **B** using acetonitrile as solvent only the imine [(E)-4-methoxy-*N*-(4-methylbenzylidene)aniline] was isolated as product (Table 5, entry 2). However, when the same reaction was conducted in toluene we have discovered that only 4-methoxy-*N*-(4-methylbenzyl)aniline, a *sec*-amine, is formed as major product (Table 5, entry 3). As can be seen from Table 5, 4-ethylaniline reacts smoothly under our experimental conditions with 4-methoxyphenylmethanol and gives an excellent yield of 4ethyl-*N*-(4-methoxybenzyl)aniline (Table 5, entry 4). Similarly, the reaction performed between 4-ethylaniline and phenylmethanol has given good yields as high as 92% of N-benzyl-4-ethylaniline product (Table 5, entry 5). When thereaction was conducted between aniline with phenylmethanol and 4-methoxyphenylmethanol, excellent yields of the corresponding amines were obtained - as high as 95% (Table 5, entries 6 and 7). Under our optimized reaction conditions, 4-iodoaniline also reacts smoothly with p-tolylmethanol and gives an excellent yield of the product 4-iodo-*N*-(4-methylbenzyl)aniline (Table 5, entry 8). Interestingly, our methodology is also suitable for sulfonamides in a coupling reaction with primary aromatic alcohols which are an important class of compounds in agrochemical and pharmaceutical chemistry.^[29,25a] In addition, this reaction could be used as a protecting group strategy for amines due to the easily removable sulfonyl group on the nitrogen so that they lead to the formation of primary amines.

For example, when the reaction was performed between 4-methylbenzenesulfonamide and 4-(methoxyphenyl)methanol, the C–N cross-coupled *N*-(4-methylbenzyl)-4-methylbenzenesulfonamide product was obtained in 88% yield (Table 5, entry 9). To the best of our knowledge, the only work to date that reports such high yields for *sec*-amines from 4-methylbenzenesulfonamide and 4-methoxyphenyl)methanol is that by Yu and Xu et al.^[27]

We wish to propose a possible mechanism for the β-alkylation reaction on the lines that are reported using [IrCpCl₂]₂ complexes.^[6a] The probable mechanism of Rh(III) complex-catalyzed β-alkylation of secondary alcohols with primary alcohols is described in Scheme 6. We propose that the first step of the reaction would involve the oxidation of primary and secondary alcohols to aldehydes and ketones accompanied by the generation of a hydrido rhodium species. We propose that this step occurs upon the reaction of alcohols in the presence of KOH and Rh(acac)₃ to generate a Rh(alkoxide) species which undergoes a β -hydrogen elimination reaction to provide ketones, aldehydes, and hydrido rhodium species. Then, the base-mediated cross-aldol condensation between aldehyde and ketone would occur to give an α,β -unsaturated ketone. Then, the successive transfer hydrogenation of C=C and C=O double bonds of the α,β -unsaturated ketone by the hydrido rhodium species would occur to give the product. In this catalytic system, the hydrido rhodium species generated at the stage of the oxidation of alcohols are consumed at the stage of the reduction of α,β -unsaturated ketone. Hence, additions of hydrogen donor and acceptor are not required; thereby making our Rh(III)-based catalytic system a highly atom economical process.



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Scheme 6. Possible mechanism for Rh(III) complex-catalyzed β -alkylation of secondary alcohols with primary alcohols.

Conclusions

In summary, we have demonstrated that the Rh- $(acac)_3$ /DABCO/KOH catalyst is very efficient and useful system for the α -alkylation of ketones, the β -al-kylation of secondary alcohols and also the alkylation of amines with primary alcohols in the absence of any extra additives or external H₂ source. We have also shown that the present catalyst system enables a highly atom economical process that can be extendable to the direct N-alkylation of various aromatic amines with aromatic alcohols to synthesize exclusive-ly *sec*-amines.

Experimental Section

Materials and Analysis

All chemicals and solvents were purchased from commercial vendors and used as received. The ¹H NMR and ¹³C NMR spectra were recorded on a Varian (400 MHz) or an Avance (300 MHz) spectrometer. Tetramethylsilane (δ =0.00 ppm) was used as internal standard for ¹H NMR. ¹³C NMR were referenced to the residual solvent signal (CDCl₃, 77.0 ppm). Merck silica gel 60–120 mesh was used for column chromatography using hexanes/ethyl acetate solvent mixture.

Typical Procedure for α-Alkylation of Ketones with Primary Alcohols

A pressure tube was charged with a mixture of acetophenone (1 mmol, 0.5 M in toluene) and 4-methoxyphenylmethanol (1 mmol, 0.5 M in toluene), DABCO (50 mol%), KOH (1 mmol) and catalyst **A** (1.0 mol%). The reactants were stirred in 2 mL of toluene at 110 °C for 4 h. The progress of the reaction was monitored by TLC. After the completion of reaction, it was quenched using brine solution and extracted with ethyl acetate (3×50 mL). The combined organic extracts were dried over anhydrous sodium sulfate and filtered. Then, the solvent was evaporated under reduced pressure to give the crude product which was subjected to silica gel column chromatography using hexanes/ethyl acetate mixture as eluent to afford 3-(4-methoxyphenyl)-1-phenylpropan-1-ol; yield: 98%.

Typical Procedure for β-Alkylation of Secondary Alcohols with Primary Alcohols

A pressure tube was charged with a mixture of 1-phenylethanol (1.0 mmol, 0.5 M in toluene), (4-methoxyphenyl)methanol (1.0 mmol, 0.5 M in toluene), DABCO (50 mol%), KOH (1.0 mmol), and catalyst **A** (1.0 mol%). The reactants were stirred in 2 mL of toluene at 105–110 °C for 12–16 h. The progress of the reaction was monitored by TLC analysis. After the completion of reaction, it was quenched using brine solution, and extracted with ethyl acetate (3×50 mL). The combined organic extracts were dried over anhydrous sodium sulfate and filtered. Then, the solvent was evaporated under reduced pressure to give the crude product which was subjected to silica gel column chromatography using hexanes/ethyl acetate mixture as eluent to afford 3-(4-methoxyphenyl)-1-phenylpropan-1-ol; yield: 98%.

Typical Procedure for N-Alkylation of Amines with Primary Alcohols

A pressure tube was charged with a mixture of *p*-toluidine (1.0 mmol, 0.5 M in toluene), 4-(methoxyphenyl)methanol 1.0 mmol (0.5 M in toluene), DABCO (50 mol%), KOH (1.0 mmol) catalyst **A** (1.0 mol%). The reactants were stirred in 2 mL of toluene at 105–110 °C for 12–16 h. The progress of the reaction was monitored by TLC analysis. After the completion of reaction, it was quenched using brine solution, and extracted with ethyl acetate (3×50 mL). The combined organic extracts were dried over anhydrous sodium sulphate and filtered. Then, the solvent was evaporated under reduced pressure to give the crude product which was purified by column chromatography using hexanes/ethyl acetate mixture as eluent to afford 4-methoxy-*N*-(4-methylbenzyl)aniline; yield: 94%.

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FULL PAPERS

10 Tris(acetylacetonato)rhodium(III)-Catalyzed α-Alkylation of Ketones, β-Alkylation of Secondary Alcohols and Alkylation of Amines with Primary Alcohols

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