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Catalysis

Bifunctional Ru^{II}-Complex-Catalysed Tandem C–C Bond Formation: Efficient and Atom Economical Strategy for the Utilisation of Alcohols as Alkylating Agents

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Abstract: Catalytic activities of a series of functional bipyridine-based Ru^{II} complexes in β-alkylation of secondary alcohols using primary alcohols were investigated. Bifunctional Ru^{II} complex (**3 a**) bearing 6,6′-dihydroxy-2,2′-bipyridine (6DHBP) ligand exhibited the highest catalytic activity for this reaction. Using significantly lower catalyst loading (0.1 mol %) dehydrogenative carbon–carbon bond formation between numerous aromatic, aliphatic and heteroatom substituted alcohols were achieved with high selectivity. Notably, for the synthesis of β-alkylated secondary alcohols this protocol is a rare one-pot strategy using a metal–ligand cooperative Ru^{II} system. Remarkably, complex **3 a** demonstrated the highest reactivity compared to all the reported transition metal complexes in this reaction.

Introduction

The efficient synthesis of long chain alcohols as biofuels from renewable sources is an indispensable component of alternative energy production and has lately received much attention as a viable, greener alternative to conventional fuels such as petrol and diesel.[1] Considering the demand of environmentally benign processes, modified Guerbet-type coupling of alcohols using various transition-metal catalysts has recently been explored by many groups.[2] Synthesis of β-alkylated secondary alcohols by using primary alcohols following the hydrogen-borrowing or hydrogen-autotransfer strategy has significant advantages over conventional methods, which typically require a multistep process and produces stoichiometric amount of halide wastes.[3]

In 2003, the Cho group reported $[RuCl_2(PPh_3)_3]$-catalysed direct β-alkylation of secondary alcohols using primary alcohols in the presence of sacrificial hydrogen acceptors.[4] Inspired by this result, significant efforts have been made to explore this transformation using several transition metal complexes.[5] Thus far, the most frequently used homogeneous catalysts are based on ruthenium and iridium and they have shown higher reactivity and selectivity compared to other systems. For this transformation, Peris and co-workers found that pyrazolin-3-ylidene containing Ru^{II} was more active in β-alkylation compare to other Ru^{II}NHC complexes.[6] Ru complexes bearing cyclopentadienyl (Cp), trispyrazolylborate (Tp), and bipyridine ligands were also found to be effective for this reaction.[7] Crabtree et al. reported terpyridine and NHC pyrimidine containing Ru^{II} and Ir^{III} complexes for β-alkylation of secondary alcohols with primary alcohols in which terpyridine-based complexes showed enhanced catalytic activity compare to other complexes.[8] Ruthenacycles derived from phenylmethanamine, *N*-methylphenylmethanamine, *N*,*N*-dimethylphenylmethanamine, and naphthalen-1-ylmethanamine ligands were also used for the same purpose.[9] Recently, Ru^{III}-promoted β-alkylation of secondary alcohols and Ru^{II}NHC-catalysed α-alkylation of methylene ketones was revealed by the groups of Yu and Glorious, respectively.[10] Iridium complexes such as $[Ir(cod)Cl]_2$,[11] $[Cp^*IrCl_2]_2$,[12] iridium-NHC,[13] pincer-(PCP)Ir[14] and benzoxazolyl iridium(III) complexes,[15] were also reported for this alkylation reaction. Despite significant advancements, these systems still have many limitations, and in most cases it requires high catalyst loading, more than stoichiometric amount of bases, high temperature, and long reaction time.

Metal–ligand cooperation has become a powerful strategy in activation of various bonds and catalysis.[16] For efficient molecular transformations, ligands in bifunctional catalysts directly take part in substrate bond activation and subsequent bond-formation steps. Among the numerous cooperative ligands, 6,6′-dihydroxy-2,2′-bipyridine (6DHBP) have received a great deal of attention and various transition-metal complexes containing this ligand are known.[17] 6DHBP-based iridium complexes have been reported to catalyse CO_2 hydrogenation and formic acid dehydrogenation,[18] dehydrogenative oxidation of alcohols,[19] dehydrogenation and hydrogenation of heterocycles,[20] hydrogen production from a methanol/water solution under weakly basic conditions,[21] water oxidation,[22] and chemoselective dehydrogenation of alcohols in lignin model compounds.[23] Recently, Cp*Ir(6DHBP)-promoted synthesis of α-alkylated ketones from ketones and primary alcohols, and from secondary alcohols and primary alcohols were demonstrated by Li and co-workers.[24] They also reported the synthesis of quinazolinones and quinolines following acceptorless dehydro-

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genative coupling protocol using the same catalyst.[25] Surprisingly, only few examples of 6DHBP-based Ru^{II} catalysed reactions such as transfer hydrogenation of ketones[26] and alcohol oxidation[23] have been reported, which showed moderate to poor activity.

Final turnover frequencies of the recently reported catalysts in cross-coupling reaction of alcohols are listed in Figure 1. Despite considerable efforts that have been devoted to this reaction, the efficiency of these catalytic systems is still significantly low. Hence, development of a new, more effective and sustainable process for C–C bond formation reaction using alcohols is highly desirable. Inspired by the pioneering work by Fujita and Yamaguchi with a series of Cp*Ir complexes bearing hydroxypyridine motif in the acceptorless dehydrogenation of alcohols,[27] we envisioned that Ru-complexes containing bifunctional 6,6′-dihydroxy-2,2′-bipyridine ligand may have the potential to promote the cross-coupling reaction of alcohols. Our proposed strategy for the utilisation of alcohols as alkylating agents is listed in Scheme 1.

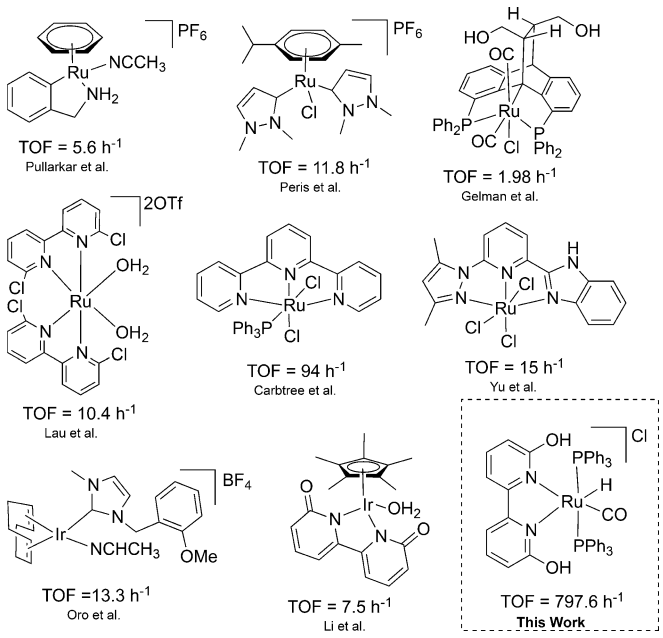
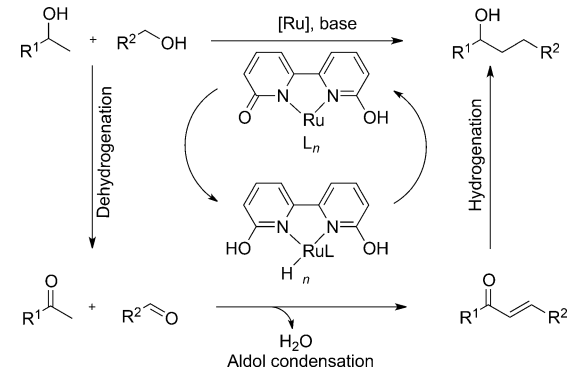


Figure 1. Final turnover frequency (TOF) of recently reported complexes in cross-coupling reaction of alcohols.

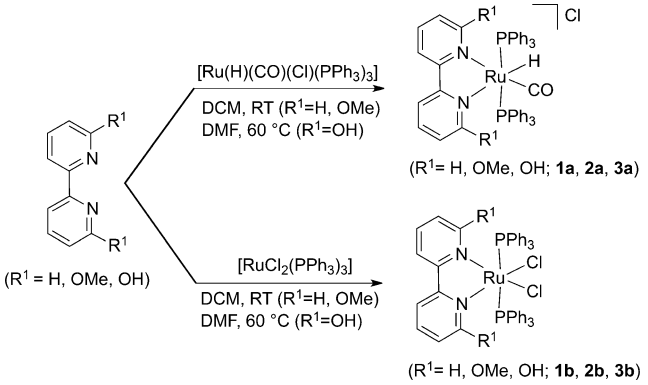
This is the first example of 6,6′-dihydroxy-2,2′-bipyridine-based ruthenium complex catalysed alcohol coupling reaction. In this study, we compare catalytic activities of a series of functional bipyridine-based ruthenium complexes and report a remarkably efficient, atom economical bifunctional Ru^{II}-based catalytic system for the cross-coupling between a range of different alcohols with high selectivity.

Results and Discussion

6,6′-Dimethoxy-2,2′-bipyridine (6DMeOBP) and 6,6′-dihydroxy-2,2′-bipyridine (6DHBP) were synthesised in good yields following the reported literature.[26] Treatment of 6DMeOBP with $[RuHCl(CO)(PPh_3)_3]$ in DCM at room temperature afforded complex **2a** in 64% yield (Scheme 2). Due to poor solubility of the 6DHBP in DCM, reaction of equimolar amount of $[RuHCl(CO)(PPh_3)_3]$ with 6DHBP was carried out in DMF at 60 °C which produced air stable Ru^{II} complex **3a** in 81% yield. Complexes **2b** and **3b** were also synthesised in good yield by reacting $[RuCl_2(PPh_3)_3]$ with the corresponding ligands in DCM and DMF in similar fashion.



Scheme 1. Proposed bifunctional Ru^{II}-promoted strategy for the utilisation of alcohols as alkylating agents.



Scheme 2. General scheme for the synthesis of bipyridine-based Ru complexes.

In the ^1H NMR spectrum, the hydride of complexes **2a** and **3a** appeared as a triplet at $\delta = -11.11$ ppm ($J_{HP} = 19.9$ Hz) and -13.19 ppm ($J_{HP} = 15.5$ Hz), respectively. The ^{31}P NMR resonances of **2a** and **3a** appeared at $\delta = 46.64$ and 46.59 ppm, respectively; this indicates the presence of one kind of phosphorous environment around the Ru centres. The ν_{CO} of complexes **2a** and **3a** appeared at 1938 and 1947 cm^{-1}, respectively, suggesting greater electron density over the ruthenium centre in complex **2a** compared to **3a**. The molecular structure of complexes **2a** and **3a** were established by single X-ray crystal structure analysis (Figure 2). The solid state structure and ^1H and ^{31}P NMR spectra of **2a** and **3a** further confirmed the formation of an Ru^{II} hydride carbonyl complex where two PPh_3 molecules were attached to the octahedral Ru centre in *trans*

geometry containing one bidentate NN ligand. The P-Ru-P bond angles of complexes **2a** and **3a** were 170.73° and 170.38°, respectively, indicating axial arrangement of the two PPh_3 molecules and a longer Ru–P bond length compared to the other four Ru–ligand bonds (Ru–N, Ru–CO and Ru–H); this further suggests a distorted geometry around the Ru centre. The chloride ion was present outside the primary coordination sphere for both complexes.

Initially, β-alkylation of 1-phenylethanol with benzyl alcohol was picked as a model reaction to screen the performance of a series of Ru^{II}-bipyridine-based complexes. The reactions were carried out for 45 min in refluxing toluene, employing various Ru^{II} precatalysts (0.1 mol%) and the results are summarised in Table 1. With $[RuCl_2(PPh_3)_3]$ and $[RuHCl(CO)(PPh_3)_3]$ complex yields as well as selectivity for the β-alkylated alcohol product were poor (Table 1, entries 1 and 2). Significant improvement in both conversion and selectivity were achieved with isolated Ru^{II} complexes bearing various 2,2′-bipyridine derived ligands (Table 1, entries 4–9). Among these catalysts, complex **3a** bearing bifunctional 6,6′-dihydroxy-2,2′-bipyridine exhibited the maximum reactivity with 70% conversion of 1-phenylethanol within 45 min (Table 1, entry 6), and after 1 h it showed 94% conversion with 92% selectivity for 1,3-diphenylpropan-1-ol (Table 1, entry 7). But, complexes **3b** and **6** showed only 11 and 21% conversion, respectively (Table 1, entries 3 and 10). Most of these substituted bipyridine-Ru^{II} complexes were not fully soluble in toluene at room temperature. However, under the reaction condition in the presence of base, they produced a homogenous solution except with **3b** as indicated by the Hg-poisoning test. Complex **3b** showed significantly lower catalytic activity compare to other complexes probably due to poor solubility (Table 1, entry 10). The same reactions with these Ru^{II} complexes were carried out in more polar solvents like dioxane and *tert*-amyl alcohol, which showed significantly lower conversion of 1-phenylethanol compared to toluene, probably due lower boiling point (Supporting Information, Table S3). This suggests that the α-hydroxyl substituent in the 2,2′-bipyridine ligand as well as other ligands bound to the ruthenium centre were crucial for the high catalytic performance. Importantly, in this cross-coupling reaction, ruthenium-based complex **3a** displayed significantly higher activity compare with all the previously reported catalysts including many iridium complexes (Figure 1).

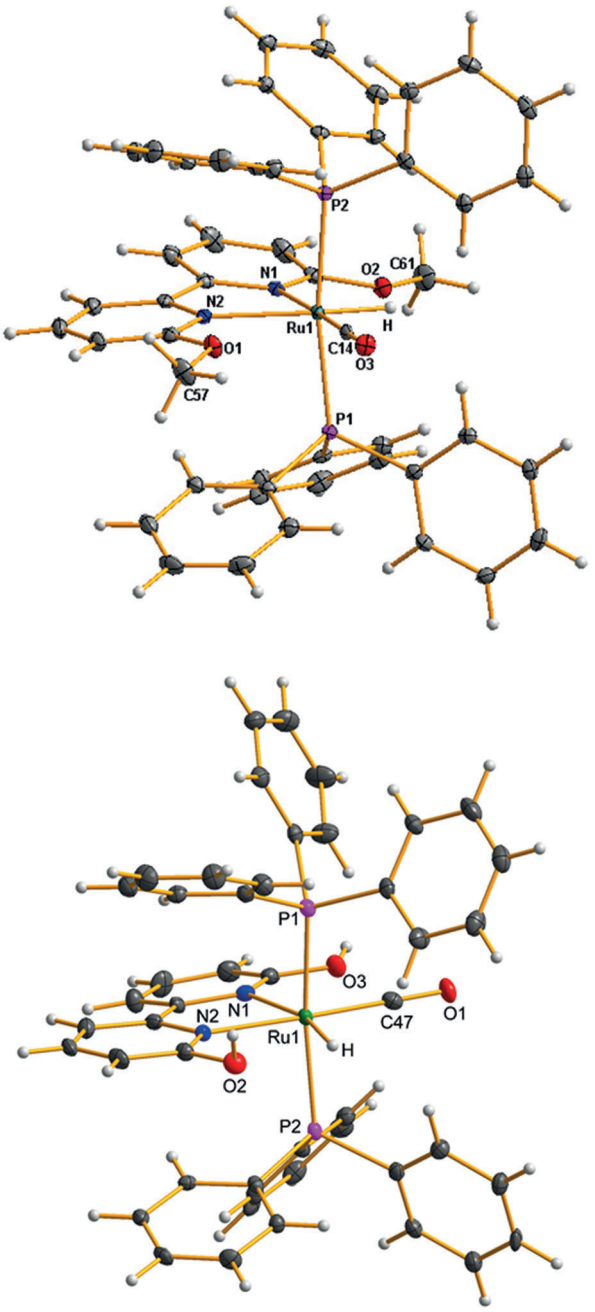
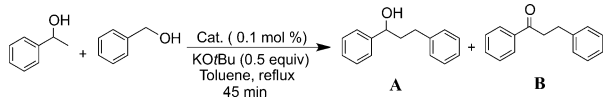


Figure 2. Molecular structure of $[6DMeOBP)Ru(H)(CO)(PPh_3)_2]Cl$ (**2a**; top) and $[6DHBP)Ru(H)(CO)(PPh_3)_2]Cl$ (**3a**; bottom); 30% thermal ellipsoids; counter chloride anion of both complexes were omitted for clarity.

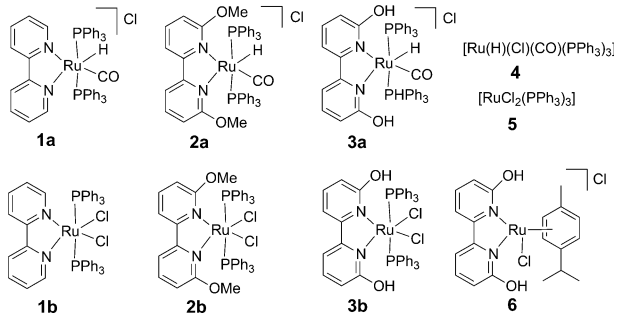
Next, β-alkylation of 1-phenylethanol with benzyl alcohol was carried out with 0.1 mol% catalyst **3a** using various bases to optimize the reaction condition, and the results are listed in Table 2. Carbonate bases showed poor conversion in the given reaction condition (Table 2, entries 1–3). Based on the superior performance, KO*t*Bu was selected as base for this reaction, although KOH and NaOH also worked effectively. Subsequently, the **3a**-catalysed cross-coupling reaction of 1-phenylethanol with benzyl alcohol was carried out in the presence of different equivalent KO*t*Bu to determine the ideal amount of base required for this reaction (Table 2, entries 6–11). Based on the conversion of 1-phenylethanol, 0.5 equiv KO*t*Bu was found to be optimum. As anticipated, no β-alkylation was observed without the base or the catalyst (Table 2, entries 12 and 13). Probably due to the higher boiling point of toluene, the yield of the C–C coupling product was much higher in toluene compare to dioxane as solvent (Table 2, entry 8).

β-Alkylation of 1-phenylethanol with a range of primary alcohols was conducted under the optimised conditions to determine the substrate scope and the results are presented in Table 3. The reaction of *para*-substituted benzyl alcohols with both electron-withdrawing atoms (chloro, bromo, and fluoro) and electron-donating groups (methyl and methoxy) proceeded smoothly to give the corresponding β-alkylated secondary alcohols in excellent yields with high selectivity (Table 3, en-

Table 1. β-Alkylation of 1-phenylethanol with benzyl alcohol using various Ru^{II} complexes.[a]

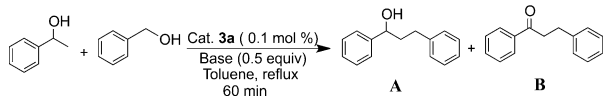


Entry	Catalyst	Conversion[b]	A/B ratio[c]
1	**4**	45	76:24
2	**5**	29	58:42
3	**6**	21	92:8
4	**1a**	48	86:14
5	**2a**	49	86:14
6	**3a**	70	90:10
7[d]	**3a**	94	92:8
8	**1b**	52	86:14
9	**2b**	54	85:15
10	**3b**	11	81:19



[a] Reaction condition: catalyst (0.1 mol%), 1-phenylethanol (1.25 mmol), benzyl alcohol (1.25 mmol) and KO*t*Bu (0.625 mmol) in reflux condition in toluene for 45 min. [b] Determined by GC analysis based on secondary alcohol. [c] Determined by ^{1}H NMR spectroscopy. [d] 1 h reflux.

Table 2. β-Alkylation of 1-phenylethanol with benzyl alcohol in the presence of different bases.[a]



Entry	Base [equiv]	Conversion [%][b]
1	Cs_2CO_3(0.5)	14
2	K_2CO_3 (0.5)	2
3	Na_2CO_3 (0.5)	4
4	NaOH (0.5)	90
5	KOH (0.5)	92
6	KO*t*Bu (0.5)	94
7	KO*t*Bu (0.7)	95
8[c]	KO*t*Bu (0.5)	40
9	KO*t*Bu (0.4)	75
10	KO*t*Bu (0.2)	38
11	KO*t*Bu (0.1)	28
12	No base	0
13[d]	KO*t*Bu (0.5)	0

[a] Reaction condition: catalyst **3a** (0.1 mol%), 1-phenylethanol (1.25 mmol), benzyl alcohol (1.25 mmol) and base (0.625 mmol) in reflux condition in toluene for 60 min. [b] Determined by GC analysis based on secondary alcohol. [c] Dioxane as solvent. [d] No catalyst.

tries 1–5). Substituents in *ortho*- and *meta*-positions of the benzyl alcohols were also converted to the desired secondary alcohols in good to high yields (Table 3, entries 6–8).

In addition, β-alkylation of naphthalen-1-ylmethanol and heteroatom-substituted 2-thiophenemethanol and cyclohexylmethanol generated the desired products in moderate to excellent yields with slightly longer heating (Table 3, entries 9–11). Notably, this method was also successfully applied to challenging aliphatic long-chain alcohols such as 1-butanol and 1-hexanol which selectively afforded the corresponding alcohol products in good yields within 4 h (Table 3, entries 12 and 13).

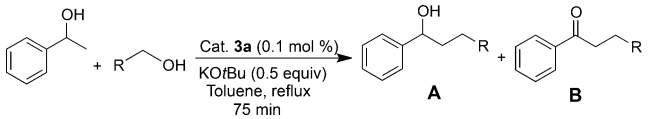
The substrate scope for the β-alkylated secondary alcohols with primary alcohols was further expanded by treating benzyl alcohol with various secondary alcohols. These results are summarised in Table 4. Similar to the alcohol cross coupling reactions listed in Table 3, reaction of substituted 1-phenylethanols bearing both electron-withdrawing atoms (chloro, bromo, and fluoro) and electron-donating groups (methyl and methoxy) progressed efficiently to provide the corresponding long-chain secondary alcohols in excellent yields with high selectivity (Table 4, entries 2–7). 1-(Naphthalen-2-yl)ethanol was also smoothly coupled with benzyl alcohol (Table 4, entry 8). In the case of 1-tetralinol, conversion and selectivity towards the alcohol products was moderate (Table 4, entry 9). In the same fashion, treatment of 1-phenyl-1-propanol with benzyl alcohol in the presence of **3a** resulted in 1,5-diphenylpentan-3-ol in 61% yield with high selectivity (Table 4, entry 10). The reaction of aliphatic secondary alcohols with benzyl alcohols required a slightly longer time and 2 equivalent secondary alcohol to afford high conversion and selectivity (Table 4, entry 11–13).

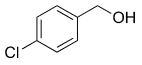
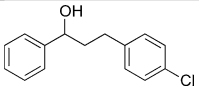
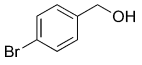
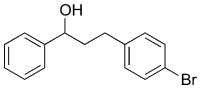
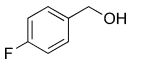
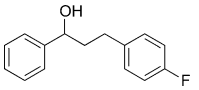
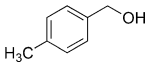
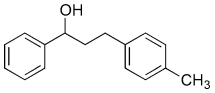
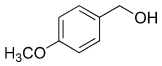
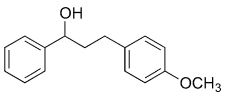
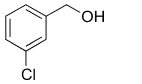
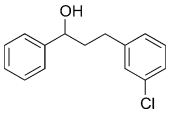
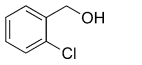
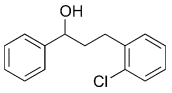
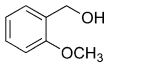
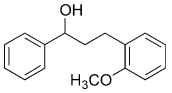
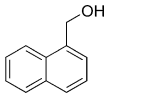
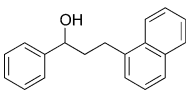
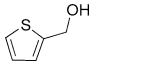
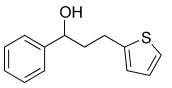
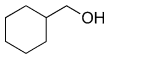
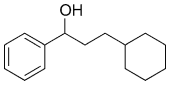
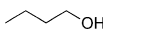
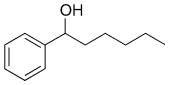
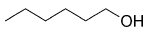
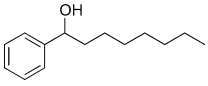
Reaction mechanism

A plausible mechanism for this tandem β-alkylation of secondary alcohols with primary alcohols is shown in Scheme 3. A similar mechanism was proposed by Fujita, Yamaguchi and Li with (DHBP)Ir complexes for the dehydrogenation alcohols and α-alkylation of ketones, respectively.[19,24] Initially, the precatalyst **3a** was transformed to active catalyst **P** bearing a bipyridonate ligand by extrusion of one molecule of HCl in the presence of KO*t*Bu. Next, complex **P** promoted oxidation of the secondary and primary alcohols by accepting the alcoholic proton with its bipyridonate ligand moiety to afford an alkoxy ruthenium species **Q**. Then, β-hydride elimination from complex **Q** would generate a dihydride Ru^{II} species **R** and corresponding carbonyl compounds. Subsequently, base catalysed cross-aldol condensation between the ketones and aldehydes afforded the α,β-unsaturated ketones. Finally, the cooperation of the Ru-hydride and the ligand hydroxyl proton facilitated the hydrogenation of the C=C bond of the α,β-unsaturated ketones to generate the ketone **B** and the regenerated complex **P**. Following similar cooperative catalysis, ketone **B** was then hydrogenated to afford the corresponding alcohol **A**.

To obtain more information about this proposed mechanism, some test reactions were carried out. In order to find out which unsaturated bond in the α,β-unsaturated ketone (C=C or C=O) would be hydrogenated first, two control experiments

Table 3. β-Alkylation of 1-phenylethanol with diverse substituted benzyl alcohol.[a]

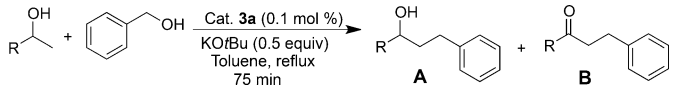


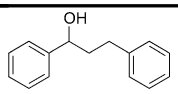
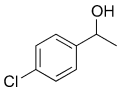
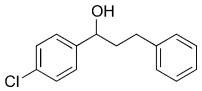
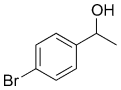
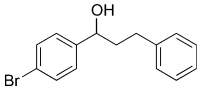
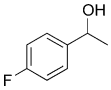
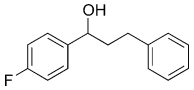
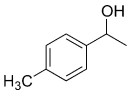
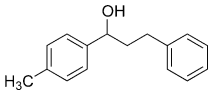
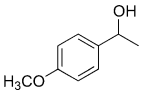
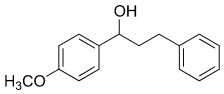
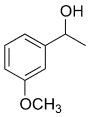
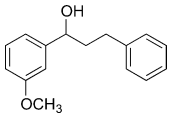
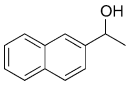
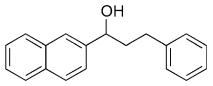
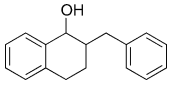
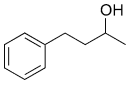
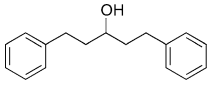
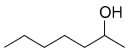
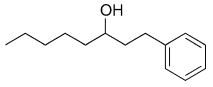
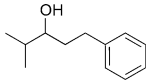
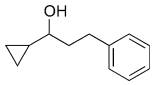
Entry	Primary alcohol	Product	Conv.[b] [%]	A/B ratio[b]
1			100	91:9
2			100	90:10
3			100	89:11
4			78	89:11
5			98	98:2
6			96	91:9
7			52	94:6
8			71	89:11
9[c]			99	92:8
10[d]			55	99:1
11[e]			93	89:11
12[d]			84	98:2
13[d]			83	96:4

[a] Reaction condition: catalyst **3a** (0.1 mol%), secondary alcohol (1.25 mmol), benzyl alcohol (1.25 mmol) and KO*t*Bu (0.625 mmol) in reflux condition in toluene for 75 min. [b] Determined by ^{1}H NMR spectroscopy with respect to the secondary alcohol. [c] 3 h reflux. [d] 4 h reflux. [e] 6 h reflux.

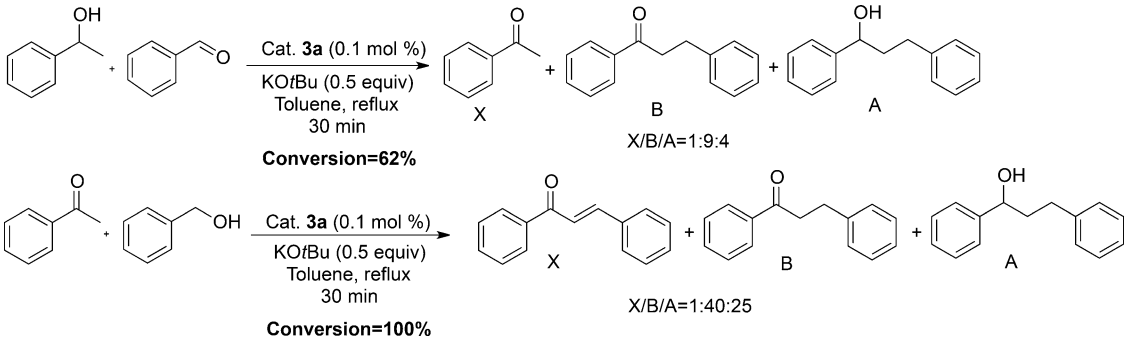
were carried out following the standard catalytic condition. The reaction of 1-phenylethanol with benzaldehyde in the presence of **3a** showed 62% conversion of 1-phenylethanol after 30 min and produced acetophenone, 1,3-diphenylpropan-1-one (**B**) and 1,3-diphenyl-2-propan-1-ol (**A**) in a 1:9:4 ratio. After the reaction no unreacted benzaldehyde was detected as it was converted to benzyl alcohol and benzoic acids by base-promoted Cannizzaro reaction. Under similar conditions, reaction of acetophenone with benzyl alcohol afforded chalcone, compound **B** and compound **A** in 1:40:25 ratio (100% conversion of acetophenone). In both reactions, selective C=C bond hydrogenated product of chalcone that is, compound **B** was identified as the major and 1,3-diphenylpropan-1-ol (**A**) as minor product. Importantly, in both cases, only the C=O bond hydrogenated product of chalcone, that is, 1,3-diphenylprop-2-en-1-ol was not observed. These results indicate that the re-

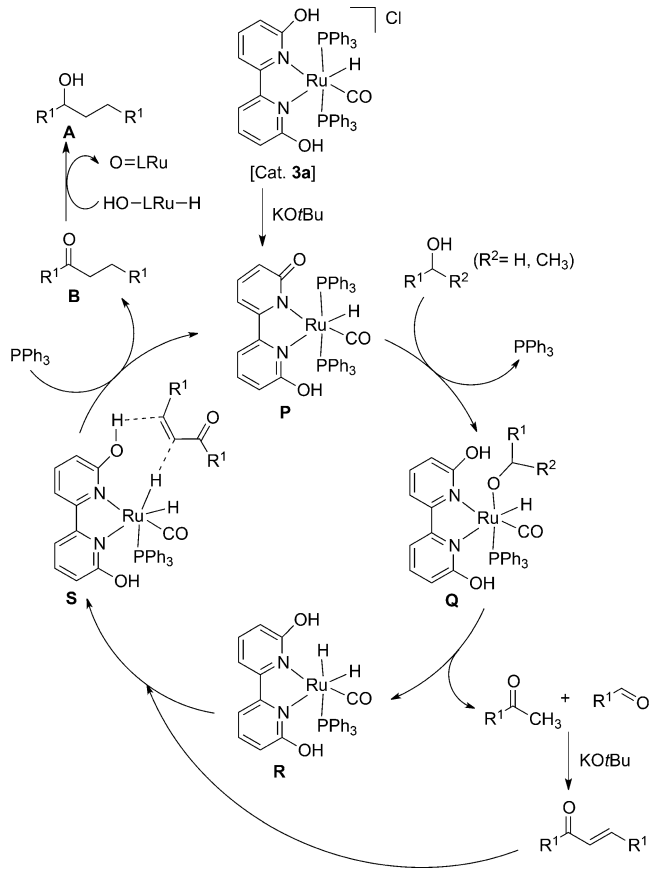
Table 4. β-Alkylation of 1-phenylethanol with different substituted benzyl alcohol.[a]



Entry	Secondary alcohol	Product	Conv.[b] [%]	A/B ratio[b]
1			99.7	93:7
2			100	90:10
3			91	93:7
4			86	81:19
5			97	96:4
6			95	85:15
7			98	91:9
8			95	93:7
9			65	72:28
10[c]			61	99:1
11[c,d]			54	99:1
12[c,d]			99	99:1
13[c,d]			99	99:1

[a] Reaction condition: catalyst **3a** (0.1 mol%), secondary alcohol (1.25 mmol), benzyl alcohol (1.25 mmol) and KO*t*Bu (0.625 mmol) in reflux condition in toluene for 75 min. [b] Determined by ^{1}H NMR spectroscopy with respect to the secondary alcohol. [c] 4 h reflux. [d] 2.5 mmol secondary alcohol and 1.25 mmol benzyl alcohol was used and conversion was determined with respect to benzyl alcohol.





Scheme 3. Proposed reaction mechanism.

duction of the C=C bond of the α,β-unsaturated ketone is much faster than the reduction of the C=O bond, which is consistent with prior reports.[13c, 14, 28]

We also studied complex **3a**-catalysed time-dependent product distribution of β-alkylation of 1-phenylethanol with benzyl alcohol (Figure 3). The selectivity for the 1,3-diphenylpropan-1-ol (**A**) gradually increased with time and reached maximum at the end of the reaction. However, the concentration of 1,3-diphenylpropan-1-one (**B**) was nominal and did not change significantly during the course of the reaction.

Dissociation of PPh_3 might be involved in two separate steps of the proposed catalytic cycle: in the oxidative addition

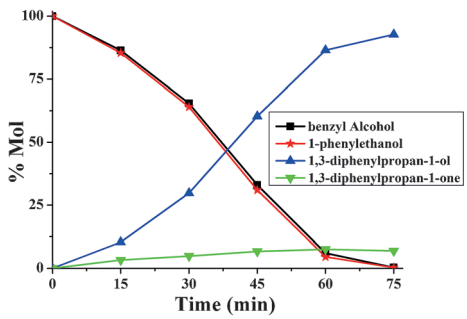


Figure 3. Time-dependence product distribution of β-alkylation of 1-phenylethanol with benzyl alcohol catalysed by catalyst **3a**.

of alcohols (**P** to **Q**) and in the β-hydride elimination from the alkoxy ruthenium species (**Q** to **R**), as both of these intermediates are six-coordinated 18-electron species. In order to examine the importance of PPh_3 dissociation, β-alkylation of 1-phenylethanol with benzyl alcohol was carried out in the presence of excess PPh_3 (2–8 equiv), which is shown in Figure 4. Conversion of 1-phenylethanol decreased significantly when excess of PPh_3 was added to the reaction mixture. This suggests that in the catalytic cycle, elimination of PPh_3 from the active complex was essential. However, based on this observation we cannot conclude whether in the rate-determining step dissociation of PPh_3 was involved or not. To isolate the proposed intermediates mentioned in the catalytic cycle, we treated complex **3a** with various bases such as KO*t*Bu, KOH, K_2CO_3 and Cs_2CO_3 in DCM in the presence and absence of 1-phenylethanol. However, all these attempts to isolate the intermediates were unsuccessful.[29] The homogeneous nature of this catalytic system was proved by the Hg-poisoning test.

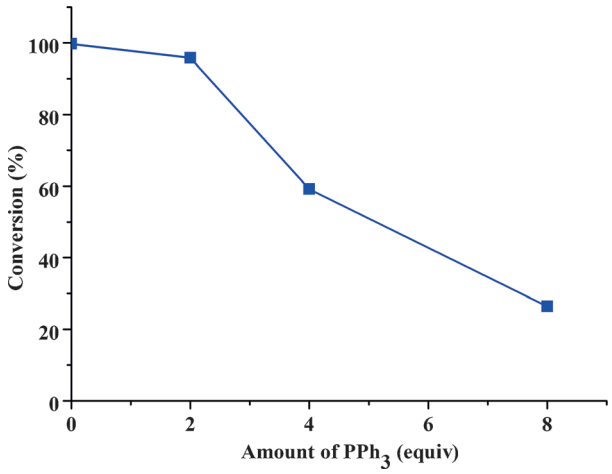


Figure 4. Effect of externally added PPh_3 on catalyst **3a** in β-alkylation of 1-phenylethanol with benzyl alcohol.

Conclusions

In summary, employing a series of Ru^{II} complexes bearing bipyridine-based functional ligands, β-alkylation of secondary alcohols using primary alcohols was investigated. Complex **3a** having 6,6′-dihydroxy-2,2′-bipyridine ligand was found to be a highly effective and versatile precatalyst which displayed the highest reactivity among all the complexes. The present protocol provides efficient, atom economical and a greener strategy for the synthesis of a variety of β-alkylated secondary alcohols with high selectivity. Control experiments suggested that this system preferentially reduced the C=C bond of the α,β-unsaturated ketone over the C=O bond. Notably, this is a rare example of an effective and versatile bifunctional Ru^{II} catalysed tandem β-alkylation reaction of secondary alcohols under mild conditions. Importantly, compared to all the previously reported catalysts, complex **3a** exhibited the highest reactivity and this study revealed the unique potential of this system in C–C

bond forming reactions by utilising alcohols as alkylating agents.

Experimental Section

General procedures and materials

All reactions were carried out under an inert atmosphere by using standard Schlenk-line techniques. Glassware was dried in a 100 °C oven, overnight, before use. Solvents were dried by distillation under argon according to standard literature methods and deoxygenated prior to use. $RuCl_3 \cdot n H_2O$ (39% Ru) was purchased from Arora Matthey, India. All the chemicals were purchased from Sigma–Aldrich, Alfa Aesar, SD Fine and Spectrochem. 6,6′-dihydroxy-2,2′-bipyridine,[26] 6,6′-dimethoxy-2,2′-bipyridine,[26] [RuHCl(CO)(PPh_3)$_3$],[30] [$RuCl_2$(PPh_3)$_3$],[31] [(2,2′-bipyridine)Ru(H)(CO)(PPh_3)$_2$]Cl (**1a**)[32] and [(2,2′-bipyridine)$RuCl_2$(PPh_3)$_2$] (**2a**)[33] were synthesised according to previously reported literature procedures. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on Jeol 400 and 500 MHz spectrometer. Elemental analysis was performed on a Thermoquest EA1110 CHN analyser. The crystallised compounds were powdered, washed several times with dry diethyl ether and dried under vacuum for at least 48 h prior to elemental analyses. ESI-MS were recorded on a Waters Micromass Quattro Micro triple-quadrupole mass spectrometer. All the GC analysis were carried out by using a Perkein Elmer Clarus 600 gas chromatograph and GC-MS were taken by using an Agilent 7890 A gas chromatograph equipped with Agilent 5890 triple-quadrupole mass system.

General procedure for β-alkylation of secondary alcohols with primary alcohol

The catalytic β-alkylation of secondary alcohol reaction was carried out in Schlenk tube under closed argon conditions. Initially catalyst **3a** (0.1 mol%) and KO*t*Bu (0.5 equiv) were taken as solid and then under argon conditions secondary alcohol (1 equiv), primary alcohol (1 equiv) and toluene (2 mL) were added and the resulting mixture was heated at 130 °C (oil bath temperature) for 75 min. After it cooled to room temperature, the toluene was evaporated under reduced pressure and the resulting mixture was purified by silica gel column chromatography using ethyl acetate and hexane as eluent to afford the desire product.

Synthesis of [(6,6′-dimethoxy-2,2′-bipyridine)Ru(H)(CO)(PPh_3)$_2$]Cl (2a)

A mixture of 6,6′-dimethoxy-2,2′-bipyridine (15 mg, 0.069 mmol), [Ru(H)(CO)(Cl)(PPh_3)$_3$] (66.1 mg, 0.069 mmol) and DCM (6 mL) was stirred at room temperature under argon condition for 12 h. Then diethyl ether was added to precipitate the product and resulting bright yellow solid was washed carefully with diethyl ether and hexane to remove free triphenylphosphine. Yield: 40 mg (64%). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.22$ (d, $J = 7.65$ Hz, 1H, bpy-H), 8.15 (d, $J = 7.65$ Hz, 1H, bpy-H), 7.94 (t, $J = 9.2$ Hz, 1H, bpy-H), 7.73 (t, $J = 7.65$ Hz, 1H, bpy-H), 7.32–7.00 (m, 30H, Ph-H), 6.63 (d, $J = 7.65$ Hz, 1H, bpy-H), 5.91 (d, $J = 9.15$ Hz, 1H, bpy-H), 3.73 (s, 3H, -CH_3), 3.08 (s, 3H, -CH_3), −11.11 ppm (t, $J = 19.9$ Hz, 1H, Ru-H). ^{13}C NMR (125 MHz, CD_2Cl_2): $\delta = 206.31$ (t, $^3Jcp = 14.3$ Hz, CO), 164.64 (s, bpy-C), 163.93 (s, bpy-C), 154.90 (s, bpy-C), 153.81 (s, bpy-C), 142.06 (s, bpy-C), 141.52 (s, bpy-C), 133.17 (Ph-C), 128.08 (s, Ph-C), 117.90 (s, Ph-C), 117.90 (s, bpy-C), 117.66 (s, bpy-C), 107.59 (s, bpy-C), 107.39 (s, bpy-C), 55.83 (s, CH_3), 55.58 ppm (s, CH_3). ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): $\delta = 46.64$ ppm. ESI-MS: *m/z* 871.1793 ([*M*−Cl]$^+$, predicted: 871.1792). Elemental analysis calcd (%) for $C_{49}H_{43}ClN_2O_3P_2Ru$: C 64.93, H 4.78, N 3.09; found C 64.68, H 4.56, N 2.87.

Synthesis of [(6,6′-dimethoxy-2,2′-bipyridine)$RuCl_2$(PPh_3)$_2$] (2b)

A mixture of 6,6′-dimethoxy-2,2′-bipyridine (20 mg, 0.092 mmol), [$RuCl_2$(PPh_3)$_3$] (88.7 mg, 0.092 mmol) and DCM (6 mL) was stirred at room temperature under argon for 12 h. Work-up procedure was similar to **2a**. Yield: 52.6 mg (63%). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 8.00 (d, $J = 7.45$ Hz, 2H), 7.69–7.65 (m, 14H), 7.56–7.52(m, 6H), 7.47–7.44 (m, 12H), 6.74 (d, $J = 8.15$ Hz, 2H), 4.03 ppm (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 163.49$, 153.52, 139.33, 133.05, 132.15, 128.63, 113.71, 110.98, 53.30 ppm. ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): $\delta = 29.79$ ppm. Elemental analysis calcd (%) for $C_{48}H_{42}Cl_2N_2O_2P_2Ru$: C 63.16, H 4.64, N 3.07; found: C 62.91, H 4.42, N 2.88.

Synthesis of [(6,6′-dihydroxy-2,2′-bipyridine)Ru(H)(CO)(PPh_3)$_2$]Cl (3a)

A mixture of 6,6′-dihydroxy-2,2′-bipyridine (100 mg, 0.053 mmol) and [Ru(H)(CO)(Cl)(PPh_3)$_3$] (506.1 mg, 0.053 mmol) was heated at 60 °C for 24 h in 6 mL dry DMF under argon. After cooling the solution slowly, the pale yellow precipitate was filtrated off and washed with ether and hexane. Yield: 380 mg (81%). ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.02$ (t, $J = 6.65$ Hz, 2H, bpy-H), 6.90 (d, $J =$ 8.85 Hz, 2H, bpy-H), 6.86–6.74 (m, 30H, Ph-H), 6.46 (d, $J = 6.65$ Hz, 1H, bpy-H), 5.66 (d, $J = 8.9$ Hz, 1H, bpy-H), −13.19 ppm (t, $J =$ 15.55 Hz, 1H). ^{31}P{^{1}H} NMR (202 MHz, [D_6]DMSO): $\delta = 46.59$ ppm. ESI-MS: *m/z* 843.1479 ([*M*−Cl]$^+$, predicted: 843.1479). Elemental analysis calcd (%) for $C_{47}H_{39}ClN_2O_3P_2Ru$: C 64.27, H 4.48, N 3.19; found: C 63.98, H 4.31, N 2.96.

Synthesis of [(6,6′-dihydroxy-2,2′-bipyridine)$RuCl_2$(PPh_3)$_2$] (3b)

A mixture of 6,6′-dihydroxy-2,2′-bipyridine (85 mg, 0.045 mmol) and [$RuCl_2$(PPh_3)$_3$] (433 mg, 0.045 mmol) was heated at 60 °C for 24 h in 6 mL dry DMF under argon. After cooling the solution slowly, the bright yellow precipitate was filtrated off and washed with ether and hexane to remove free triphenylphosphine. Yield: 280 mg (70%). Due to very poor solubility in any common solvent such as DCM, DMSO, DMF and MeOH etc., ^{1}H and ^{13}C NMR spectra could not be recorded for this complex. Elemental analysis calcd (%) for $C_{46}H_{38}Cl_2N_2O_2P_2Ru$: C 62.45, H 4.33, N 3.17; found: C 62.38, H 4.18, N 2.98.

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FULL PAPER

Catalysis

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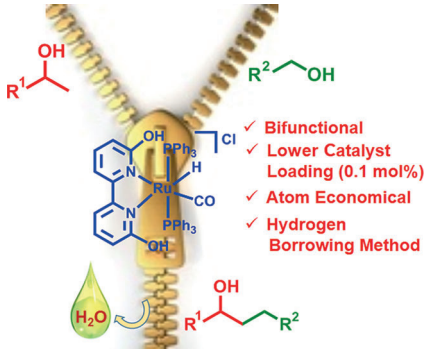
■■ – ■■

Bifunctional Ru^{II}-Complex-Catalysed Tandem C–C Bond Formation: Efficient and Atom Economical Strategy for the Utilisation of Alcohols as Alkylating Agents



Alcohols as alkylating agents: A rare example of highly efficient, atom economical and a greener strategy for the synthesis of a variety of β-alkylated secondary alcohols with high selectivity is presented.