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Short Communication

Clean borrowing hydrogen methodology using hydrotalcite supported copper catalyst

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A B S T R A C T

The catalytic activity of Mg–Al hydrotalcite supported copper catalyst was investigated for clean C–C and C–N bond forming reactions using alcohols as alkylating agent (avoiding the use of traditional mutagenic halide reagents) has received much attraction as extremely atom efficient and greener process [1–8].

The borrowing hydrogen methodology (Scheme 1) involves the activation of an alcohol (I) by removal of hydrogen (H₂) to a carbonyl (II) for reaction with a nucleophile (carbanions of carbonyls/amines) to an unsaturated product (III), followed by hydrogenation using H₂ generated in dehydrogenation step to finally α-alkylated carbonyl or N-alkylated amine product (IV) [1–8]. A suitable catalyst is required for activation of the alcohols and to transfer hydrogen for reduction step. Several catalytic systems were developed to activate the alcohols for C- and N-alkylation reactions via borrowing hydrogen [11–32]. In spite of atom efficient feature of borrowing hydrogen method; this strategy could not offer 100% greener and industrially viable process for C- and N-alkylation reactions. The major constraints are the use of precious noble metal based catalyst along with ligands, metal salts or bases in high quantity as promoter, use of volatile and hazardous solvents under reflux condition, requirement of hydrogen acceptor in some cases, etc. The reported heterogeneous catalysts could also not show viability of this method due to very high temperature operation, side products formation and use of precious metals like Pd, excess amount of base as promoter, hydrogen acceptor, solvents, etc. [33–36]. The use of additives (base, salts, hydrogen acceptor, etc.) reduces the atom efficiency of the process. Williams stated that the development of more reactive catalysts, avoiding the use of noble metals, will be a welcome addition in this area [5]. Beller et al. mentioned that the development of less expensive bio-relevant metals such as iron or copper based catalyst will be one of the important goals to be achieved in this field [8].

Therefore, it is of great importance to develop an efficient, cheap and eco-friendly catalyst for activation of alcohols for borrowing hydrogen to have economically viable and environmentally more benign synthetic route for C–C and C–N coupling.

The copper catalysts, being less expensive metal based catalysts, have attracted much attention in heterogeneous catalysis, especially in alcohols activation [37–44]. The synergistic effect between the basicity of support and the hydrogen spillover of copper nanoparticle were reported to provide high activity in alcohols dehydrogenation and hydrogen transfer [42]. Recently we reported that the copper on Mg–Al hydrotalcite (Cu-HT) showed multifunctional activity in alcohol transformations [44]. It was of interest to combine the basic property of hydrotalcite with the catalytic property of copper to develop a supported copper catalyst for borrowing hydrogen. To the best of our knowledge, it is the first report of clean borrowing hydrogen methodology for activation of alcohols at comparatively low temperature with high selectivity using a purely heterogeneous catalyst.

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2. Experimental

2.1. General

All the chemicals used were of synthetic grade having purity >99% and were used without any further purification. The Mg–Al hydrotalcite (HT) sample with Mg/Al molar ratio of 2.0 was synthesized by co-precipitation method at constant pH [45]. The HT supported copper (Cu-HT) catalyst was prepared by wet impregnation of HT (4 g) with aqueous solution of copper acetate (0.025 M, 40 mL) under stirring for 24 h at room temperature, followed by filtration of solid and washing with distilled water (4×50 ml) and then drying at 70 °C for 12 h [44]. The Cu-HT was calcined at 520 °C for 4 h to obtain copper containing mixed oxides of MgO and Al₂O₃ (Cu-AHT). The catalysts were characterized by XRD, FT-IR, ICP, N₂ adsorption–desorption analysis, TGA, NH₃ & CO₂-TPD and H₂-TPR, and the details of catalyst characteristics have already been reported in our previous paper [44].

2.2. General procedure for C-alkylation of ketones and N-alkylation of amines using supported copper catalysts

A mixture of ketone/amine and alcohol in required molar ratio along with the catalyst was taken in a 50 mL reaction tube of reaction station at desired temperature under stirring for required reaction time. Afterwards the reaction mixture was cooled and diluted with dichloromethane (5 mL). The catalyst was filtered to recover it from the liquid phase. The reaction mixture was analyzed by gas chromatography (Agilent 5975) having a HP-5 (60 m) capillary column with a programmed oven temperature from 50 to 280 °C, a 0.5 cm³/min flow rate of N₂ as carrier gas and FID detector. The conversion of substrate (ketone/amine) was calculated on the basis of its weight percent. The products formed in the reactions were characterized by GC–MS analysis. The values in parenthesis given in all tables are selectivity.

3. Results and discussion

The Cu-HT and Cu-AHT catalysts possess finely dispersed copper species (3.0 and 3.5 wt.% copper, respectively) and multifunctional sites (acidic–basic sites and good surface reducibility) [44]. During the reaction, the catalysts showed high activity and selectivity for the targeted products.
dehydrogenation of cyclohexanol (1a) over Cu-HT (Scheme 2), in addition of cyclohexanol (1a′) significant amount of bi-cyclohexyl-2-one (1b′) and 2-cyclo-hexyl-cyclohexanol (1c′) were formed. The formation of 1a′ and 1c′ revealed the catalytic potential of Cu-HT for alcohols activation by borrowing hydrogen. The Cu-AHT did not show any activity in cyclohexanol dehydrogenation. The base catalyzed aldol condensation of cyclohexanone to α,β-unsaturated ketone intermediate (however, it was not detected in GC–MS analysis) followed by its hydrogenation with H2 produced in dehydrogenation step will give 1a′ and further hydrogenation will result to 1a″.

The catalytic property of both the catalysts (Cu-HT and Cu-AHT) was explored for C-alkylation of ketones and N-alkylation of amines using benzyl alcohol (1b) via borrowing hydrogen (Scheme 3a & 3b). For this, the deactivated substrates like acetophenone (2a) and aniline (3a) were selected. The results indicate that Cu-HT is highest in catalytic activity for C-alkylation and N-alkylation reactions giving 80% conversion of acetophenone with 60% selectivity of 2a′ and 99% conversion of aniline with 60% selectivity of 3a′, respectively. The higher basicity and relatively low temperature reducibility of intercalated copper species in Cu-HT (total basic sites: 12.76 mmol CO2/g) than Cu-AHT (total basic sites: 4.56 mmol CO2/g) may be desirable features for high activity in alcohol activation via borrowing hydrogen.

After optimizing the reaction conditions, the highest conversion of acetophenone (99.5%) and aniline (99%) with highest selectivity of respective alkylated products (96% of 2a′ and 98% of 3a′) were obtained at 180 °C, substrate/benzyl alcohol molar ratio of 2, after 15 h using catalytic amount of Cu-HT (see ESI). Both the alkylation reactions take place via borrowing hydrogen mechanism, in which 2a′ and 3a′ products are formed by nucleophilic reaction of 1b′ (produced in dehydrogenation of benzyl alcohol) with acetophenone and aniline, respectively. The 2a′ and 3a′ products are then reduced by H2, generated during dehydrogenation, to 2a and 3a′, respectively.

The C-alkylation of ketones and N-alkylation of amines with different alcohols was studied at optimized reaction condition (i.e., substrate/alcohol molar ratio of 2, 0.12 g Cu-HT catalyst, 180 °C, 15 h). The Cu-HT showed excellent activity for C-alkylation of acetophenone with different alcohols (1a-e) giving 71% to 99% conversion of acetophenone with 94% to 96% selectivity of corresponding alkylated products under similar reaction condition (Table 1). It indicates that the Cu-HT can be an efficient catalyst for selective α-alkylation of aromatic ketones with alcohols including primary, secondary and benzylic alcohols via borrowing hydrogen, which is of great interest in organic synthesis [17].

In C-alkylation of cyclohexanone (2b) with alcohols (1b-e), mono as well as dialkylated products were obtained with good conversion (77% to 87%) of cyclohexanone showing the potential of Cu-HT for α-alkylation of aliphatic ketones with alcohols (Table 2). The Cu-HT was also found to be active for N-alkylation of amines (3) with different alcohols giving conversion of amines in the range of 80% to 99% with significant selectivity to alkylated amines under same reaction condition (Table 3). However, unsaturated products were present in most of the alkylation reactions of cyclohexanone and amines, which may be due to incomplete reduction. The detail catalysis study on alkylation of acetophenone and aniline with benzyl alcohol revealed that alcohol/substrate molar ratio, catalyst amount, reaction time and temperature are the major reaction parameters influencing the conversion and product selectivity (see ESI). The complete conversion of unsaturated products (alkylated products) can be achieved by optimizing the above reaction parameters for individual substrates. Furthermore, the catalyst physico-chemical properties (like copper content, dispersion,

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<th>Entry</th>
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<th>Conv. (%)</th>
<th>Product (%)</th>
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<td>43</td>
<td>87</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
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<td>84</td>
</tr>
<tr>
<td>3</td>
<td>43</td>
<td>85</td>
<td>50</td>
</tr>
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</table>

Table 2
C-alkylation of cyclohexanone (2b) with alcohols (1).

<table>
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<tr>
<th>Entry</th>
<th>3</th>
<th>Conv. (%)</th>
<th>Product (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
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<td>80</td>
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<td>43</td>
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<td>(2b)</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>99</td>
<td>(2c)</td>
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Table 3
N-alkylation of amines (3) with alcohols (1).
support basicity, etc.) can also be tuned to have enhanced activity for these reactions. The high activity of Cu-HT for borrowing hydrogen is evident from its capability to activate the primary, secondary and benzylic alcohols for reaction with deactivated substrates (acetophenone and aniline).

4. Conclusion

The Cu-HT has great potential for catalysis of C- and N-alkylation reactions using alcohols as alkylating agent via borrowing hydrogen route, which can provide a very clean (solvent free, base free, ligands free and without hydrogen acceptor) process for synthesis of alkylated ketones and amines. The scope of Cu-HT could be as an efficient and cheap catalyst for α-alkylation of ketones, β-alkylation of alcohols, alkylation of amines and amides by borrowing hydrogen methodology.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.catcom.2012.12.027.

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