

## A Facile Tandem Protocol for the Crossed Aldol Condensation in SiO<sub>2</sub>.OSO<sub>3</sub>H Ionic Liquid under Solventless Condition

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Research Article

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### ABSTRACT

**Objectives:** Removing organic solvents in chemical synthesis is important in the drive towards benign chemical technologies. Organic solvents are high on the list of toxic compounds due to the problems in containing volatile compounds and the sheer large volume of them used in industry. Some advantages of utilizing solventless reactions are that the compounds are often sufficiently pure to avoid extensive purification using chromatography, the reactions can be rapid, and often reaching substantial completion in several minutes compared to hours in organic solvents, and the energy usage can be much lower. Among organic reactions, aldol condensations are important and excellent tools in organic synthesis, providing a good way to form carbon-carbon bonds. The main objectives of this paper are to carry out crossed - aldol condensation reactions with dicyclohexylketones with different aromatics aldehydes in the presence of silica sulphuric acid [SiO<sub>2</sub>.OSO<sub>3</sub>H] as an ionic liquid catalyst under solvent free condition to afford the corresponding  $\alpha$ ,  $\beta$  - unsaturated crossed - aldol products in excellent yields and to recover and reuse the catalyst for subsequent use.

**Study design:** Green chemical reaction using silica-sulphuric acid as a catalyst under solventless condition.

**Place and Duration of Study:** Department of Chemistry, Sir Theagaraya College, Chennai-21, Tamilnadu, India, between June 2009 and July 2010.

**Methodology:** The ionic liquid SiO<sub>2</sub>.OSO<sub>3</sub>H was prepared according to the reported procedure in an eco-friendly way by the reaction of silica gel and chlorosulphonic acid. It is interesting to note that the reaction is easy, clean and not requiring any work-up procedure. Using this ionic liquid, crossed-aldol condensation of dicyclohexyl ketones with aromatic aldehydes were carried out. After complete conversion of the ketones as indicated by the TLC, the mixture was cooled to room temperature. Dichloromethane (20 - 30 ml) was

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added and heated for a few minutes, the reagent was concentrated and the solid residue was recrystallized from ethanol to afford the pure product. The catalyst was recycled by washing the solid reagent remained on the filter by EtOAc (20 ml) followed by drying in an oven (50°C) for 2hr. Products were characterized by spectral analyses such as UV-Visible, FT-IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR.

**Results:** The reactions were completed with excellent yields (90 - 95%) within 2 - 5 hr at the temperature range of 80-85°C. The reaction does not require any additional catalyst because the ionic liquid itself acts as a catalyst and solvent as well in these experiments, the products were isolated and the remaining catalyst was washed and reloaded with fresh substrates benzaldehyde and dicyclohexyl ketones. Under these conditions, no self-condition of the starting materials was observed. When similar reactions were carried out in sulphuric acid (conventional acid catalyst), a mixture of products was obtained in poor yields. One of the greatest advantages of the reagent SiO<sub>2</sub>.OSO<sub>3</sub>H is that it is recoverable and reusable for several times without potential loss in its catalytic activity.

**Conclusion:** The conventional esterification reactions (without ionic liquids) suffer from many problems like poor efficiency, side reactions, consumption of huge environmentally hazardous chemicals, etc., The use of ionic liquids for these reactions eradicate the aforementioned problems encountered in the conventional procedures.

*Keywords: Green synthesis; ionic liquid; silica sulphuric acid; crossed-aldol condensation; dicyclohexylketones; solvent less reaction;*

## 1. INTRODUCTION

The development of environmentally improved new synthetic routes, which are as much direct as possible and resort to the use of safe and non-toxic starting materials, is a major target of modern chemistry of organic synthesis (Rajendran, 2010). In recent years, the interest in room temperature ionic liquids (RTILs) is increasing as green reaction media for synthetic organic chemistry. Researchers have recently found that such ionic liquids are very useful as solvents as well as catalysts for several organic and inorganic syntheses (Kumar, 2009). Ionic liquids are good candidates for replacement of toxic and volatile organic compounds because of their lower vapor pressures and lack of flammability (Ahluwalia, Aggarwal, 2006). The synthesis of these ionic liquids (ILs), their characterization and possible applications have been developing progressively as the properties of this class of organic salts with melting points below the boiling point of water have gained intensive attention in nearly all fields of chemistry (Zhang et al., 2005). Furthermore, through the incorporation of functional groups, the synthesis of task specific ionic liquids (TSILs) has been a focus of research, leading to tailor-made substances for desired applications. Traditional chemical synthesis focused on optimizing yields, with little regard to a chemical's impact on the environment and its long term viability. There is now a realization that more benign chemical synthesis is required, as an integral part of developing sustainable technologies (Rajendran, 2010). Optimizing the yield is important but other issues need to be addressed, including minimizing the number of steps, simplicity, waste, atom efficiency, energy usage, safety and whether the chemistry is environmentally acceptable (Dailei Song et al., 2009). In the present work, crossed aldol reactions were carried out in the presence of silica-sulphuric acid as the ionic liquid catalyst to afford the corresponding  $\alpha$ ,  $\beta$  - unsaturated crossed - aldol products in excellent yields and to recover and reuse the catalyst for subsequent use.

Generally the equilibrium constants for esterification with most of the primary alcohols are near unity. For an instance, the equilibrium constant for the esterification of acetic acid with ethyl alcohol is 3.38. The reaction is driven to completion by using the reactant alcohol as the solvent. Because the alcohol is present in large excess, the equilibrium is driven toward the ester product. This is an example of Le Chatelier's principle.

Recently there has been a paradigm shift away from using solvents in organic synthesis as solventless reactions can lead to improved outcomes, and more benign synthetic procedures, in for example an aldol condensation reaction as shown above. Sustainability is increasingly an important issue in broader context when you are talking about health, energy, and the sciences.

Ionic liquids (ILs), especially room temperature ionic liquids (RTILs) have attracted extensive research interest in recent years as environmentally benign solvents due to their favorable properties like non-inflammability, negligible vapor pressure, reusability and high thermal stability (Zhang et al., 2005). They have also been referred to as 'designer solvents' as their physical and chemical properties could be adjusted by a careful choice of cation and anion. Apart from this they exhibit acidic properties. Combining these unique properties of ionic liquids, they are emerging as a green reaction media (catalyst + solvent) in organic synthesis. The use of ionic liquids as reaction medium may offer a convenient solution to both the solvent emission and catalytic recycling problem.

Crossed-aldol reaction is an excellent tool for the formation of C-C bond in many classes of carbonyl compounds (Smith and March, 2001). Due to the importance of methylene structured unit which is found in many naturally occurring compounds and antibiotics, condensation of cycloalkanones with aromatic aldehydes and ketones is of special interest and crossed aldol condensation is an effective pathway for these preparations (Shelton et al., 2009). However traditional acid-or base-catalyzed reactions suffer from the reverse reaction and self condensation of starting materials. In several industrially important processes (e.g., nitration, esterification, sulphonation, etc.,) a large excess of sulphuric acid is required because, the water by-product slows the reaction down by diluting the acid. At the end of these processes, a large amount of 'spent acid' is obtained which in batch reactions, is neutralized and disposed of, while in continuous processes, it has to be recycled by complex techniques (Wang et al., 2006). Also, the separation of the products from the acid is often a difficult and energy consuming process that habitually implies a basic aqueous work-up. Moreover, sulphuric acid is corrosive and is dangerous to transport and handle. Consequently any reduction in the amount of sulphuric acid needed dangerous and / or any simplification in handling procedures would be highly convenient in terms of risks reduction, economic advantages and environment protection (Larock, 1999). On the other hand, there is an intense current research and general interest in heterogeneous system because of the perceived opportunities (Shelke et al., 2009). In continuation of our studies on the application of  $\text{SiO}_2 \cdot \text{OSO}_3\text{H}$  as a versatile and stable solid acid catalyst in organic synthesis, we wish to report an efficient and selective method for condensation of dicyclohexyl ketones with various aromatic aldehydes under solvent free conditions (Ganeshpure et al., 2006).

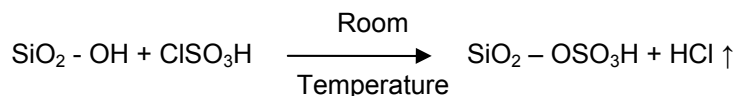
## 2. EXPERIMENTAL DETAILS

### 2.1 Materials and Reagents

All chemicals (AR grade) were commercially available and used without further purification unless otherwise stated. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. UV-VIS spectra were recorded in double beam Uv-vis spectrophotometer (Lambda series model, Shimadzu make), IR spectra were recorded on Perkin-Elmer FT-IR spectrophotometer in KBr disc.  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectra were recorded on a high resolution 400 MHz NMR spectrophotometer (Bruckner model) in  $\text{CDCl}_3$  /  $\text{DMSO-D}_6$  as a solvent and chemical shift values are recorded in  $\delta$  units (ppm) relative to TMS as an internal standard.

### 2.2 Preparation of Silica Sulphuric Acid Ionic Liquid

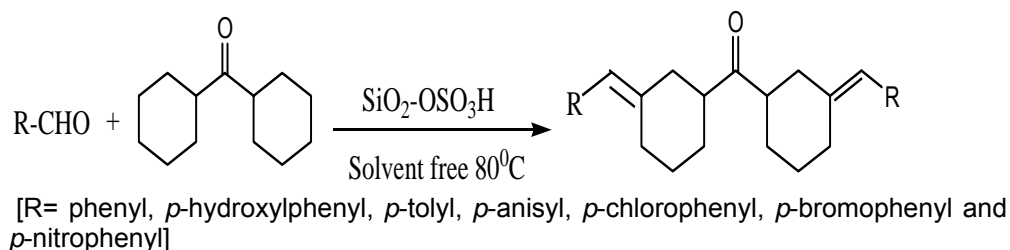
The ionic liquid  $\text{SiO}_2\cdot\text{OSO}_3\text{H}$  was prepared according to the reported procedure in an eco-friendly way by the reaction of silica gel and chlorosulphonic acid (Ganeshpure et al., 2007; Sahoo et al., 2006). It is interesting to note that the reaction is easy, clean and not requiring any work-up procedure. A 500ml suction flask was used. It was equipped with a constant-pressure dropping funnel containing chlorosulphonic acid (23.3 g, 0.2mol) and a gas inlet tube for conducting HCl gas over an absorbing solution (water). It was charged with silica gel (60.0 g) and chlorosulphonic acid was added drop wise over a period of 30 minutes at room temperature. After the addition was completed the mixture was shaken well for 30 minutes, a white solid of silica sulphuric acid (76.0 g) was obtained (Scheme 1).



**Scheme 1. Synthesis of ionic liquid [silica-sulphuric acid]**

### 2.3 General Procedure for Crossed-Aldol Condensation of Dicyclohexyl Ketones with Aromatic Aldehydes with Aromatic Aldehydes

Dicyclohexyl ketones (2mmol), aromatic aldehydes (4.2mmol) and silica sulphuric acid (1.5g, equal to 4mmol of  $\text{H}^+$ ) were mixed thoroughly, placed in a glass tube and capped. The mixture was heated in an oven at 80-85°C for 2 – 5 hr (Table 1). After complete conversion of the ketones as indicated by the TLC, the mixture was cooled to room temperature (Dailei Song et al., 2009). Dichloromethane (20 - 30 ml) was added and heated for a few minutes, the reagent was concentrated and the solid residue was recrystallized from ethanol to afford the pure product. The catalyst was recycled by washing the solid reagent remained on the filter by EtOAc (20 ml) followed by drying in an oven (50°C) for 2h (Scheme 2).



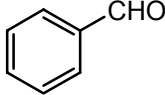
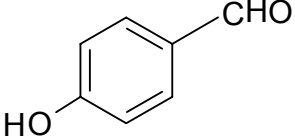
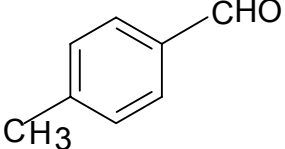
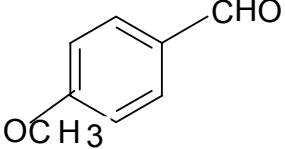
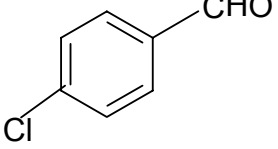
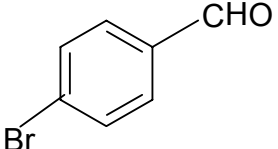
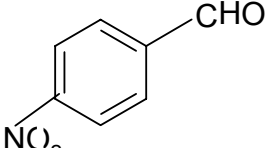
**Scheme 2. Condensation reactions of various aldehydes with dicyclohexyl ketones**

### 3. RESULTS AND DISCUSSION

In continuation of our research work on crossed-aldol condensation reaction and development of novel synthetic methodologies (Rajendran, 2010). Herein, we would like to report a simple, efficient and rapid method for the crossed-aldol reaction of dicyclohexyl ketones with different aromatic aldehydes using silica-sulphuric acid a solid ionic liquid as an efficient catalyst under solvent free conditions. The results are summarized in the Table 1.

The reactions were completed within 2.5 - 5 hr and excellent yields (90 - 95%) were noted. The reaction does not require any additional catalyst because the ionic liquid itself acts as a catalyst and solvent as well in these experiments, the products were isolated and the remaining catalyst was washed and reloaded with fresh substrates benzaldehyde and dicyclohexyl ketones (Table 2). Under these conditions, no self-condition of the starting materials was observed. When similar reactions were carried out in sulphuric acid (conventional acid catalyst), a mixture of products was obtained in poor yields (Table 1). This is attributed to the self condensation of aromatic aldehydes (Ahluwalia and Aggarwal, 2006). It was found that there is no considerable change in the reaction time and temperature, demonstrating that silica sulphuric acid can be reused in crossed-alcohol condensation without any environmental discharge (Trost and Flemming, 1991). The products obtained in all these reactions were characterized by spectral techniques (Uv-vis spectra were recorded in double beam Uv-vis spectrophotometer (Lambda series model, Shimadzu make), IR spectra were recorded on Perkin-Elmer FT-IR spectrophotometer in KBr disc. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded on a high resolution 400 MHz NMR spectrophotometer (Bruckner model) in CDCl<sub>3</sub> / DMSO-D<sub>6</sub> as a solvent and chemical shift values are recorded in δ units (ppm) relative to TMS as an internal standard (Ahluwalia and Aggarwal, 2006).

**Table 1. Effect of silica sulphuric acid on crossed aldol condensation reaction of dicyclohexyl ketones with various aldehydes**

Entry	Aldehyde	Time (hr)	Temp (°C)	Yield (%) <sup>a</sup>
1		2.5 3.0 <sup>b</sup>	80 80 <sup>b</sup>	91 85 <sup>b</sup>
2		4.0 5.0 <sup>b</sup>	82 90 <sup>b</sup>	90 90 <sup>b</sup>
3		4.5 5.0 <sup>b</sup>	85 98 <sup>b</sup>	90 82 <sup>b</sup>
4		5.0 7.0 <sup>b</sup>	82 95 <sup>b</sup>	92 85 <sup>b</sup>
5		3.0 4.5 <sup>b</sup>	80 93 <sup>b</sup>	93 86 <sup>b</sup>
6		3.0 4.5 <sup>b</sup>	81 92 <sup>b</sup>	92 85 <sup>b</sup>
7		2.0 3.0 <sup>b</sup>	75 87 <sup>b</sup>	95 92 <sup>b</sup>

<sup>a</sup>Isolated yield based upon the starting aldehyde<sup>b</sup>Effect of sulphuric acid (conventional catalyst) on crossed aldol condensation reaction of dicyclohexyl ketones with various aldehydes.

**Table 2. Reuse of SiO<sub>2</sub>.OSO<sub>3</sub>H in the condensation reaction between Benzaldehyde and dicyclohexyl ketones**

Run	Time (hr.)	Temp (°C)	Yield (%) <sup>a</sup>
1	2.5	80	91
2	2.5	80	90
3	2.5	80	91
4	2.5	80	91
5	2.5	80	90

<sup>a</sup>Isolated yield based upon the starting aldehyde

#### 4. CONCLUSION

In conclusion we have described a simple, efficient and a facile tandem protocol for the crossed-aldol condensation reaction of different aromatic aldehydes with dicyclohexyl ketones at 80 - 85°C to give 90 - 91% yield. The major advantages of the present method are much faster reaction, easy work up procedure and good to excellent yields and avoiding the usage of hazardous organic solvent and toxic catalyst. In addition to this, the SiO<sub>2</sub>.OSO<sub>3</sub>H was successfully reused for four runs without potential loss of activity. This proves that this method is much more convenient than those with conventional catalysts.

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