CHAPTER-III

Mesoporous titanosilicate Ti-TUD-1 catalyzed Knoevenagel condensation: An efficient green synthesis of trisubstituted electrophilic olefins at room temperature
> **INTRODUCTION**

A new, efficient and green methodology has been discussed in this section for the Knoevenagel condensation in the synthesis of trisubstituted electrophilic olefins using catalytic amount of mesoporous titanosilicate catalyst Ti-TUD-1, under mild conditions at room temperature.

![Trisubstituted electrophilic olefins](image)

**Trisubstituted electrophilic olefins** ($R, R' = \text{CN, CO}_2\text{Et, COCH}_3$)

> **Importance of Knoevenagel reaction**

In recent times much attention is being focused on the development of eco-friendly solid acid/base catalysts for organic synthesis. Therefore development of catalysts for C–C bond formation in organic synthesis following green approach always has become an important area for research. One such example is the versatile Knoevenagel condensation reaction,¹ a useful method for the synthesis of active dipolarophiles which finds application in 1, 3-cycloaddition reactions.² The reaction also has wide application in the synthesis of drugs,³ in polymer sciences,⁴ and in the synthesis of natural products.⁵ Great attention has been focused on this reaction for the production of a large number of important and useful fine chemicals in the synthesis of cosmetic, perfume, and pharmaceutical industry. Moreover, as an important precursor of potentially bioactive pyrimidine and chromene derivatives, the starting arylmethylenemalononitrile can also be produced by Knoevenagel reaction.
A brief review on the synthesis of electrophilic olefins

The classical Knoevenagel condensation involves the condensation of aldehydes and ketones with active methylene compounds in the presence of organic bases like pyridine, piperidine and ethylenediamine. Normally malononitrile, cyanoesters, β-ketoesters, malonic acids, malonates are used as the active methylene components containing two electron withdrawing groups (EWG). However the procedure results in a large amount of organic wastes due to polymerization and self condensation reactions. Hence, comes the necessity and importance of developing a clean and environment friendly catalytic methodology. Several methodologies have been developed for this synthesis. A brief review has been made on the classical Knoevenagel reaction.

Parida and his Rath⁶ reported the amine modified mesoporous silicate crystalline MCM-41 in the synthesis of cinnamic acid and its derivatives following classical Knoevenagel condensation (Scheme 1). Amine modification was done on MCM-41 in order to convert the catalyst to a solid base. A variety of amines loaded (wt %) over MCM 41 was used in the reaction using MeOH under reflux condition to generate high yield of the products.

A similar type of amine functionalized mesoporous silica based basic catalyst was prepared hydrothermally using Cetyl Triethyl Ammonium Bromide (CTAB) as surfactant by Bhaumik and hi co-workers⁷ and the catalyst was applied in the Knoevenagel reaction (Scheme 2). A variety of aromatic aldehydes were reacted with malononitrile to prepare α, β-unsaturated dicyanides in absolute ethanol at room temperature within 4-7 hours in good yields. The reaction was further extended to non-catalytic Diels Alder reaction.
The reaction was also studied applying various types of inorganic solid supports under different reaction conditions by Salem et al. They used alumina, KSF and K10 Montmorillonites as catalyst with substrates like different carbonyl compounds and variety of active methylene components (Scheme 3). A comparison study was shown with solvent free and aqueous condition.

Recently Xia and his co-workers reported the synthesis of basic ionic liquids functionalized hydroxyapatite-encapsulated γ-Fe₂O₃ magnetic nanoparticles and showed their application as an efficient and magnetically recyclable heterogeneous catalyst in Knoevenagel condensation reaction. Variety of aromatic and aliphatic carbonyl compounds was reacted with malononitrile or ethyl cyanoacetate under mild conditions in water to generate good yields of the products (Scheme 4).
The use of nanoparticles as catalysts in organic transformations has attracted considerable interest because of their high surface area-to-volume ratios. In the recent past, functionalized magnetic nanoparticles have been utilized as efficient recoverable catalyst for various organic transformations. Phukan et al.\textsuperscript{10} reported the bimetallic spinel \( \text{CoFe}_2\text{O}_4 \) as a magnetic nanoparticle in the Knoevenagel reaction in aqueous ethanolic medium (Scheme 5). The reaction was found to be highly efficient and completed in very short time.

![Scheme 4](image)

A novel protocol was reported by Khurana et al.\textsuperscript{11} wherein, polyethylene glycol (PEG) stabilized nickel nanoparticles have been used as a catalyst for chemoselective Knoevenagel condensation of aromatic aldehydes and Meldrum's acid to give 5-arylidene Meldrum's acid. The latter underwent tandem enol lactonization by Michael addition/cyclization sequence with active methylene compounds in the presence of Ni nanoparticles to give corresponding enol lactone derivatives in high yield (Scheme 6).

![Scheme 5](image)
A different approach was shown by Ghosh and his co-workers\textsuperscript{12} in the synthesis of 5-arylidene Meldrum's acid derivatives in the light induced uncatalyzed Knoevenagel condensation in aqueous ethanol. They also studied the effect of microwave condition over neutral alumina where a wide variety of aromatic aldehydes were reacted with Meldrum's acid to generate the product in excellent yields (Scheme 7).
Knoevenagel condensation of various aliphatic, aromatic and heterocyclic aldehydes with malononitrile was carried out in the solvent free condition in one step by employing a sulfate-ion promoted zirconia solid acid catalyst by Reddy and his group. This catalyst facilitates the reaction under solvent-free conditions at moderate temperatures providing excellent yields of the products (Scheme 8).

Shang et al carried out the Knoevenagel condensation of aromatic aldehydes with active methylene compound which proceeded efficiently in polyethylene glycol (PEG 400) at room temperature with L-proline as catalyst. The yield was high and the E-isomers were dominant products. Polyethylene glycol containing L-proline could be recycled and reused several times without noticeable decrease in the reactivity of the catalyst (Scheme 9).

A series of Hunig’s base tethered ammonium ionic liquids was used to catalyze the Knoevenagel condensation of aldehydes and ketones with malononitrile and ethyl cyanoacetate by Hardacre et al. The reactions were performed under homogeneous and under biphasic, liquid–liquid and liquid–silica supported ionic liquid conditions (Scheme 10).
Higher activity, in general, was found under homogeneous reaction conditions. However, the recyclability of the catalyst was improved by supporting the BIL (Basic Ionic Liquid) under biphasic conditions.

\[
\begin{align*}
\text{R}^1, \text{R}^2 &= \text{H, alkyl, aryl} \\
\text{Y} &= \text{CO}_2\text{H, CO}_3\text{R, COR, CN}
\end{align*}
\]

Scheme 10

A study involving the scope of substrate in the Knoevenagel reaction in an imidazolium ion based IL medium was conducted by Forbes et al. Reactivity trends favored formation of the product using electron deficient aryl aldehydes. However, use of electron rich aldehydes and ketones resulted in lower levels of conversion. A recycling study confirmed that the reaction medium could be used multiple times affording, with each run, the desired condensation product in excellent yield (Scheme 11).

\[
\begin{align*}
\text{R}^1, \text{R}^2 &= \text{H, alkyl, aryl} \\
\text{Y} &= \text{CO}_2\text{H, CO}_3\text{R, COR, CN}
\end{align*}
\]

Scheme 11

Knoevenagel condensation of various aromatic and heteroaromatic aldehydes with active methylene compounds like malononitrile, ethyl cyanoacetamide, ethyl cyanoacetate, barbituric acids, Meldrum’s acid, dimedone and pyrazolone was developed under catalyst free condition in aqueous media by Bhuyan and his group. The reactions proceeded
smoothly with stirring at room temperature and afforded excellent yields of the products in short time (Scheme 12).

Recently, Chowdhury and his co-workers\textsuperscript{18} used an acid-base bifunctional nanocrystalline Ce\textsubscript{x}Zr\textsubscript{1-x}O\textsubscript{2}, a mixed oxide solid solution with different C/Z ratio, in the classical Knoevenagel condensation to couple different aromatic aldehydes with malononitrile and ethyl cyanoacetate in ethanol under reflux conditions. Variety of aldehydes including heteroaromatics was used in this reaction generating high yield of the products (Scheme 13). The catalyst was recyclable three times without any significant change in activity.

\begin{scheme}
\begin{center}
\begin{tikzpicture}
\node at (0,0) {\text{H}};
\node at (1.5,0) {\text{O}};
\node at (3,0) {\text{X}};
\node at (3.5,0) {\text{Y}};
\node at (4,0) {\text{Z}};
\node at (4.5,0) {\text{R}};
\node at (0,0.5) {\text{R}};
\node at (0,-0.5) {\text{R}};
\node at (1.5,0.5) {\text{O}};
\node at (1.5,-0.5) {\text{O}};
\node at (3,0.5) {\text{X}};
\node at (3,-0.5) {\text{X}};
\node at (3.5,0.5) {\text{Y}};
\node at (3.5,-0.5) {\text{Y}};
\node at (4,0.5) {\text{Z}};
\node at (4,-0.5) {\text{Z}};
\node at (4.5,0.5) {\text{R}};
\node at (4.5,-0.5) {\text{R}};
\draw [->] (0,0) -- (1.5,0);
\draw [->] (1.5,0) -- (3,0);
\draw [->] (3,0) -- (3.5,0);
\draw [->] (3.5,0) -- (4,0);
\draw [->] (4,0) -- (4.5,0);
\draw [->] (0,0.5) -- (1.5,0.5);
\draw [->] (1.5,0.5) -- (3,0.5);
\draw [->] (3,0.5) -- (3.5,0.5);
\draw [->] (3.5,0.5) -- (4,0.5);
\draw [->] (4,0.5) -- (4.5,0.5);
\draw [->] (0,-0.5) -- (1.5,-0.5);
\draw [->] (1.5,-0.5) -- (3,-0.5);
\draw [->] (3,-0.5) -- (3.5,-0.5);
\draw [->] (3.5,-0.5) -- (4,-0.5);
\draw [->] (4,-0.5) -- (4.5,-0.5);
\node at (0,-1) {\text{water, rt, stirring}};
\node at (1.5,-1) {\text{NO catalyst}};
\end{tikzpicture}
\end{center}
\end{scheme}

\textbf{Scheme 12}

\textbf{Scheme 13}
“Mesoporous titanosilicate Ti-TUD-1 catalyzed Knoevenagel condensation: An efficient green synthesis of trisubstituted electrophilic olefins at room temperature”

> RESULTS AND DISCUSSION

Knoevenagel condensation reactions were studied by the candidate using variety of aromatic aldehydes and active methylene compounds in ethanol over Ti-TUD-1 at room temperature. The reactions were completed within short reaction time and predominantly $E$ selectivity was observed in the resulting products.

![Chemical reaction diagram]

> Advantage of the methodology

The classical Knoevenagel reaction has been carried out under basic conditions using bases like pyridine, piperidine, ethylenediamine and N-methylpiperazine. However, these procedures involve the production of organic wastes due to polymerization and self condensation reactions. Hence arises the necessity and importance of developing a clean and environment friendly catalytic methodology. Supported porous solid acid catalysts could be an effective solution to this problem. In the recent past, several mesoporous catalytic systems have been used. These involve the use of organic amine functionalized within the heterogeneous catalyst or mesoporous base catalyst. In our methodology mesoporous titanosilicate, Ti-TUD-1, a Lewis acid catalyst, has been used for the first time. The catalyst has high surface area and Ti, being in a highly dispersed state on the silica surface, is catalytically active. The high surface area helps in binding the substrate to the active site. Just 10 wt% of the catalyst was sufficient to catalyze the reaction. The catalytic system was so efficient that it could be reused five times without much reduction in its activity. Moreover, environmentally benign ethanol was being used as the reaction solvent and the reaction was
carried out at room temperature only. During the reaction there was no need for creating an inert atmosphere.

➢ Physical Characterization of mesoporous Ti-TUD-1

This has already been discussed in detail in chapter IIA (synthesis of bis(indolyl)methane catalyzed over Ti-TUD-1, vide page no. 43).

➢ Optimization of reaction conditions

Knoevenagel condensation reactions were studied using aromatic aldehydes and active methylene compounds over Ti-TUD-1. In order to show the efficacy of this catalyst, comparative studies were made with several catalysts along with the Ti-TUD-1 with different Ti loadings on mesoporous silica matrix. The results have been summarized in Table 1. In the model experiment benzaldehyde was treated with malononitrile in ethanol at room temperature. Mesoporous silica TUD-1 and bulk amorphous TiO₂ did not generate satisfactory yields even after long runs (entry 2 and 3, Table 1). The Ti-3-TUD-1 catalysts with Ti/Si molar ratio 0.03 furnished the best yield (entry 6). Higher loading in Ti-5-TUD-1 could not improve the result further (entry 7). This was possibly due to agglomeration of the active sites. This proved the active role of homogeneity of the catalyst where the 3 mol% loaded catalyst was most uniform. In the absence of any catalyst, the reaction provided negligible amount of product.

**Table 1.** Survey on the variation of catalysts in Knoevenagel Condensation*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>24 h</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>TUD-1</td>
<td>24 h</td>
<td>27</td>
</tr>
</tbody>
</table>
**Reaction conditions:** benzaldehyde (1 mmol), malononitrile (1.1 mmol), catalyst (10 wt%), Ethanol (5 mL), rt; isolated yield after purification.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>TiO₂</td>
<td>12</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>Ti-1-TUD-1</td>
<td>0.5</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>Ti-3-TUD-1</td>
<td>0.5</td>
<td>91</td>
</tr>
<tr>
<td>7</td>
<td>Ti-5-TUD-1</td>
<td>0.5</td>
<td>78</td>
</tr>
</tbody>
</table>

The optimization of the conditions was carried out using the best catalyst with different solvent variations. These have been recorded in Table 2. Ethanol yielded the best result in terms of time and yield (entry 4, Table 2) than the other conventional organic solvents, viz., toluene, dichloromethane, acetonitrile, tetrahydrofuran and dimethyl formamide being used. This was probably due to stabilization of the enolate of the active methylene compound and the polarized complex of aldehyde in ethanol due to solvation.

The reactivity of various active methylene compounds with benzaldehyde was also studied using the catalyst Ti-3-TUD-1 in ethanol and the results are shown in Table 3. Malononitrile was found to be the most effective among the all active methylene compounds due to better electron withdrawing effect which was evident from the reaction time and yield. Reactions with several other active methylene compounds were attempted but the products were not obtained in good yields. Possibly, the lower activation of the methylene group and hence the formation of less stable enolate with Ti appeared to be the cause.

On standardizing the condition a series of reactions were carried out using various aromatic aldehydes and malononitrile and the results have been recorded in Table 4. The reactions went smoothly with aromatic aldehydes substituted with different functionalities producing remarkably good yields (entries 1-8). Shorter reaction times were observed for strong electron-withdrawing groups (entries 2-3) compared to strong electron donating groups (entries 7, 8-12). Unsaturated aldehyde like *trans*-cinnamaldehyde (entry 13) and acid sensitive heterocycle like furfural (entry 14) furnished products in significantly good yield. In
all the cases, the reaction products showed exclusive $E$ selectivity as confirmed from NMR spectroscopy.

**Table 2. Solvent screening for the Knoevenagel Condensation***

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>24 h</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>Dichloromethane</td>
<td>12 h</td>
<td>47</td>
</tr>
<tr>
<td>3</td>
<td>Acetonitrile</td>
<td>2 h</td>
<td>73</td>
</tr>
<tr>
<td>4</td>
<td>Ethanol</td>
<td>0.5 h</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>Tetrahydrofuran</td>
<td>6 h</td>
<td>55</td>
</tr>
<tr>
<td>6</td>
<td>Dimethylformamide</td>
<td>6 h</td>
<td>64</td>
</tr>
</tbody>
</table>

♦Reaction conditions: benzaldehyde (1 mmol), malononitrile (1.1 mmol), Ti-TUD-1 catalyst (10 wt%), Ethanol (5 mL), rt; isolated yield after purification.

**Table 3. Variation of the active methylene components***

<table>
<thead>
<tr>
<th>Entry</th>
<th>Active methylene group</th>
<th>Time</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Malononitrile</td>
<td>0.5 h</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>Ethyl cyanoacetate</td>
<td>1.2 h</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>Acetylacetone</td>
<td>6 h</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>Ethyl acetoacetate</td>
<td>6 h</td>
<td>54</td>
</tr>
<tr>
<td>5</td>
<td>Diethyl malonate</td>
<td>6 h</td>
<td>trace</td>
</tr>
<tr>
<td>6</td>
<td>Acetoacetonilide</td>
<td>6 h</td>
<td>trace</td>
</tr>
</tbody>
</table>

♦Same reaction conditions; isolated yield.
Table 4. Knoevenagel Condensation between different aldehydes and malononitrile as active methylene compound*

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product 3</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆H₅</td>
<td>3a</td>
<td>30</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>4-NO₂-C₆H₄</td>
<td>3b</td>
<td>20</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>3-NO₂-C₆H₄</td>
<td>3c</td>
<td>20</td>
<td>88</td>
</tr>
<tr>
<td>4</td>
<td>4-CH₃-C₆H₄</td>
<td>3d</td>
<td>60</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>4-Cl-C₆H₄</td>
<td>3e</td>
<td>40</td>
<td>84</td>
</tr>
<tr>
<td>6</td>
<td>4-OH-C₆H₄</td>
<td>3f</td>
<td>90</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>4-NMe₂-C₆H₄</td>
<td>3g</td>
<td>120</td>
<td>77</td>
</tr>
<tr>
<td>8</td>
<td>4-OCH₃-C₆H₄</td>
<td>3h</td>
<td>90</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td>3-OCH₃-C₆H₄</td>
<td>3i</td>
<td>120</td>
<td>84</td>
</tr>
<tr>
<td>10</td>
<td>vanillyl</td>
<td>3j</td>
<td>75</td>
<td>81</td>
</tr>
<tr>
<td>11</td>
<td>3,4-di OMe-C₆H₃</td>
<td>3k</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>12</td>
<td>3,4,5-tri OMe-C₆H₂</td>
<td>3l</td>
<td>45</td>
<td>84</td>
</tr>
<tr>
<td>13</td>
<td>C₆H₄ CH=CH</td>
<td>3m</td>
<td>75</td>
<td>79</td>
</tr>
<tr>
<td>14</td>
<td>furfuryl</td>
<td>3n</td>
<td>30</td>
<td>94</td>
</tr>
</tbody>
</table>

*Reaction conditions: aldehyde (1 mmol), malononitrile (1.1 mmol), Ti-TUD-1 catalyst 10 wt%, Ethanol (5 mL), rt; isolated yield after purification.
Reusability study of the catalyst

From the context of green approach, reusability study of the catalyst was performed through condensation of benzaldehyde and malononitrile under the stabilized conditions. After completion of the reaction, the reaction mixture was centrifuged at 3000 rpm for 10 min and the supernatant layer was decanted. The deposited catalyst was collected after washing several times with ethanol to remove all the organic substances. It was then dried at 60 °C for 4h and was reused 5 consecutive times with a fresh batch of reactants following the same procedure. Almost reproducible results were obtained (Table 5). This proved the reusability of the catalyst. Atomic absorption spectroscopy was performed with the reaction filtrate to test whether Ti leached out from the catalyst surface. However, the assay did not show any trace of Ti atom in the solution which proved the efficacy of the catalyst in industry.

Table 5. Recycling of the catalyst*

<table>
<thead>
<tr>
<th>Cycles</th>
<th>Benzaldehyde (gm)</th>
<th>Catalyst (mg)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh</td>
<td>0.5</td>
<td>50</td>
<td>91</td>
</tr>
<tr>
<td>1</td>
<td>0.4</td>
<td>40</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>0.35</td>
<td>35</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>0.2</td>
<td>20</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>10</td>
<td>82</td>
</tr>
</tbody>
</table>

*Reaction conditions: benzaldehyde (1 mmol), malononitrile (1.1 mmol), Ti-TUD-1 catalyst 10 wt%, Ethanol (5 mL), rt; isolated yield after purification

Mechanism of the reaction

The high catalytic activity of Ti-TUD-1 is possibly due to the easy accessibility of the substrate molecules to the catalytic sites of the mesoporous system where Ti$^{4+}$ is in...
tetrahedral coordination and symmetrically dispersed over the three dimensional surface. Ti-TUD-1 performs a dual role, polarizing the aldehydes to increase carbonyl activity and also binds with the active methylene carbon to form a stable enolate complex. The latter then attacks the polarized carbonyl group and subsequently water elimination takes place to furnish the product. The plausible reaction pathway is summarized in Fig. 3.1.

![Diagram](image)

**Fig. 3.1. Probable mechanism of the Knoevenagel reaction over Ti-TUD-1.**

**EXPERIMENTAL**

- **General**

  The NMR spectra ($^1$H and $^{13}$C NMR) were recorded on a Bruker Avance 300 MHz spectrometer and TMS was used as the internal standard. Infrared spectra were recorded in KBr pellet in reflection mode with a Perkin Elmer RX-1 FT-IR spectrophotometer. X-Ray powder diffraction study was carried out on a Philips PW-1830 X-Ray diffractometer at a voltage of 35 kV and a current of 25 mA using CuKα radiation ($\lambda=154$ nm) at the scanning rate of 1°/minute in the 2θ range 0-5° and 10-70°. SEM was performed with a Hitachi-S 3400 N microscope at an operating voltage of 15 kV. The sample was coated with gold for effective imaging before being charged. TEM images were obtained from a JEOL JEM-2100
Transmission Electron Microscope at an operating voltage of 100 kV. The sample was prepared by placing one drop of the dispersed solution of the catalyst in acetone as solvent on a carbon coated copper grid followed by drying at room temperature. The emission fluorescence spectrum was recorded on a Perkin-Elmer spectrophotometer. Melting points (uncorrected) were determined on a Koffler Block apparatus. Synthetic grade chemicals from Acros and E-Merck were used for the preparation of the catalyst and from Spectrochem for carrying out the organic reactions. Analytical TLC was performed using E-Merck aluminium-backed silica gel plates coated with silica gel G. For column chromatography 60-120 mesh silica gel was used from Merck. All the solvents used in the reaction were distilled and dried over NaOH.

- **Representative procedure for the reaction**

The aldehyde (0.2 gm, 1.0 eq.) and active methylene compound (0.14 gm, 1.1 eq.) were taken in a 50 mL round bottom flask. 5 mL solvent was added and stirred at room temperature. Then the catalyst (0.02 gm) was added and stirring was continued under normal atmosphere till the starting materials were no longer present (monitored by TLC technique). The reaction mixture was separated from the catalyst by centrifugation. After drying under vacuum, the crude product was purified by column chromatography using 60-120 mesh silica gel and appropriate mixture of ethyl acetate/hexane as eluent. The purified products were characterized by IR spectroscopy, $^1$H NMR and $^{13}$C NMR spectrometry and elemental analysis.

- **Typical procedure for the synthesis of Mesoporous Ti-TUD-1.**

This part has been discussed in Chapter II (Synthesis of bis(indoly) methanes over Ti-TUD-1 catalyst, vide page no. 53).
CONCLUSION

A new inexpensive, reusable and environmentally benign catalytic process using mesoporous solid acid catalyst Ti-TUD-1 for the C=C bond formation in Knoevenagel condensation reaction under mild conditions with high selectivity and excellent yield has been developed. No side reactions like self condensation, dimerization and rearrangements were observed. The catalyst can be easily recovered from the reaction mixture by centrifugation and there was no trace of leaching of Ti in the filtrate.

PUBLICATION

"Mesoporous titanosilicate Ti-TUD-1 catalyzed Knoevenagel reaction: An efficient green synthesis of trisubstituted electrophilic olefins"
Bikash Karmakar, Biswajit Chowdhury, Julie Banerji*
SPECTROSCOPIC DATA OF SOME CHARACTERISTIC COMPOUNDS

Benzylidene malononitrile
Pale yellow crystalline solid; mp 84 °C; IR (KBr): 3431, 2981, 1723, 1604, 1257, 1200, 1088 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 7.27-7.58 (m, 1H, aromatic), 7.61-7.67 (m, 2H, aromatic), 7.79 (s, 1H, alkenic), 7.90 (d, \(J = 7.2\) Hz, 2H, aromatic); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 129.6 (CH), 130.7 (CH), 130.9 (C), 134.6 (CH), 159.9 (CH); Anal. calcd for C\(_{10}\)H\(_8\)Na: C, 77.92; H, 3.90; N, 18.18%. Found: C, 77.88; H, 3.95; N, 18.26%.

4-Nitrobenzylidene malononitrile
Yellow crystalline solid, mp 160 °C; IR (KBr): 3437, 3040, 2930, 2372, 2228, 1601, 1525, 1347, 1213, 1100, 824, 734 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 7.61 (s, 1H, alkenic), 8.01 (d, \(J = 9.3\) Hz, 2H, aromatic), 8.33 (d, \(J = 8.7\) Hz, 2H, aromatic); \(^{13}\)C-NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 87.6 (C), 111.6 (C), 112.6 (C), 124.6 (CH), 131.3 (CH), 135.8 (C), 150.4 (C), 156.8 (CH); Anal. calcd for C\(_{10}\)H\(_8\)NsO\(_2\): C, 60.30; H, 2.51; N, 21.10%. Found: C, 60.38; H, 2.55; N, 20.93%.

3-Nitrobenzylidene malononitrile
Yellow crystals; mp 137 °C; IR (KBr): 3755, 3436, 3040, 2930, 2372, 2228, 1601, 1525, 1347, 1213, 1100, 824, 734 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 7.73 (t, \(J = 8.1\) Hz, 1H), 7.82 (s, 1H, olefinic), 8.22 (d, \(J = 7.9\) Hz, 1H), 8.41 (d, \(J = 8.3\) Hz, 1H), 8.6 (s, 1H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)): \(\delta\) (ppm) = 86.9 (C), 111.6 (C), 112.6 (C), 125.6 (CH), 128.2 (CH), 131.0 (CH), 132.0 (C), 134.7 (CH), 148.7 (C), 156.9 (CH); Anal. calcd for C\(_{10}\)H\(_8\)NsO\(_2\): C, 60.30; H, 2.51; N, 21.10%. Found: C, 60.26; H, 2.59; N, 21.16%.
4-Methybenzyledene malononitrile

White crystalline solid, mp 129 °C; IR (KBr): 3436, 2929, 2220, 1586, 1413, 1184, 1036, 815 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 2.46 (s, 3H, tolyl), 7.34 (d, J = 8.1 Hz, 2H, aromatic), 7.72 (s, 1H, alkenic), 7.81 (d, J = 8.1 Hz, 2H, aromatic); ¹³C NMR (75.5 MHz, CDCl₃): δ (ppm) = 22.0 (CH₃), 81.2 (C), 112.8 (C), 114.0 (C), 128.5 (C), 130.4 (CH), 130.9 (CH), 146.4 (C), 159.7 (CH); Anal. calcd for C₁₁H₈N₂: C, 78.57; H, 4.76; N, 16.67%. Found: C, 78.64; H, 4.82; N, 16.59%.

4-Chlorobenzyledene malononitrile

White crystalline solid, mp 162 °C; IR (KBr): 3438, 2926, 2223, 1579, 1407, 1288, 1090, 1006, 824 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 7.53 (d, J = 8.7 Hz, 2H, aromatic), 7.73 (s, 1H, alkenic), 7.85 (d, J = 8.6 Hz, 2H, aromatic); ¹³C NMR (75.5 MHz, CDCl₃): δ (ppm) = 83.4 (C), 112.3 (C), 113.4 (C), 129.3 (C), 130.1 (CH), 131.8 (CH), 141.2 (C), 158.2 (CH); Anal. calcd for C₁₀H₅N₂Cl: C, 63.66; H, 2.65; N, 14.85%. Found: C, 63.59; H, 2.71; N, 14.92%.

4-Hydroxybenzyledene malononitrile

Yellow crystalline solid; mp 188 °C; IR (KBr): 3755, 3350, 3028, 2926, 2586, 2226, 1566, 1515, 1439, 1295, 1220, 938, 836 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.31 (s, 1H, OH), 6.85 (dd, J = 9.0 Hz, J = 2.4 Hz, 2H), 7.55 (s, 1H, olefinic); 7.72 (dd, J = 9.0 Hz, J = 2.1 Hz, 2H); ¹³C NMR (75.5 MHz, CDCl₃) δ 75.2 (C), 114.3 (C), 115.2 (C), 116.8 (CH), 122.9 (C), 134.0 (CH), 160.6 (CH), 164.1 (C); Anal. calcd for C₁₀H₇NO: C, 70.59; H, 3.53; N, 16.47%. Found: C, 70.65; H, 3.48; N, 16.54%.
4-N,N-dimethylaninobenzyledene malononitrile

Yellow crystals; mp 180 °C; IR (KBr): 3772, 3692, 3434, 1372, 2204, 1614, 1564, 1358, 1260, 1186, 814 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ (ppm) = 3.14 (s, 6H), 6.74 (d, J = 9.0 Hz, 2H), 7.47 (s, 1H, olefinic), 7.81 (d, J = 9.3 Hz, 2H); ¹³C NMR (75.5 MHz, CDCl₃) δ (ppm) = 40.3 (CH₃), 112.0 (CH), 112.1 (C), 114.8 (C), 115.8 (C), 133.7 (CH), 154.0 (C), 158.0 (CH); Anal. calcd for C₁₂H₁₁N₃: C, 77.83; H, 5.94; N, 22.70%. Found: C, 77.76; H, 5.88; N, 22.64%.

4-Methoxybenzyledene malononitrile

White crystalline solid; mp 116 °C; IR (KBr): 3754, 3449, 3028, 2948, 2850, 2550, 2038, 1605, 1509, 1445, 1369, 1319, 1182, 1020, 938 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 3.91 (s, 3H), 7.0 (d, J = 8.9 Hz, 2H), 7.65 (s, 1H, olefinic), 7.91 (d, J = 90. Hz, 2H); ¹³C NMR (75.5 MHz, CDCl₃) δ 55.8 (OCH₃), 78.7 (C), 113.3 (C), 114.4 (C), 115.2 (CH), 124.1 (CH), 133.4 (CH), 158.8 (C), 164.8 (C); Anal. calcd for C₁₁H₈N₂O: C, 71.74; H, 4.35; N, 15.22%. Found: C, 71.68; H, 4.40; N, 15.31%.

3-Methoxybenzyledene malononitrile

Pale Yellow solid; mp 116 °C; ¹H NMR (300 MHz, CDCl₃) δ 3.86 (s, 3H), 7.2 (m, 1H), 7.42-7.49 (m, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 55.5 (OCH₃), 83.0 (C), 112.6 (C), 113.6 (C), 114.1 (CH), 121.4 (CH), 123.9 (CH), 130.6 (CH), 132.0 (C), 159.9 (CH), 160.2 (C); Anal. calcd for C₁₁H₈N₂O: C, 71.74; H, 4.35; N, 15.22%. Found: C, 71.64; H, 4.27; N, 15.31%.
4-Hydroxy-3-methoxybenzyledene malononitrile

Yellow floppy solid; mp 129 °C; IR (KBr): 3338, 3015, 2964, 2507, 2224, 1465, 1431, 1390, 1025, 950, 725 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 3.98 (s, 3H), 6.38 (bs, 1H, OH), 7.02 (d, \(J = 7.3\) Hz, 1H), 7.31 (dd, \(J = 8.4\) Hz, \(J = 2.1\) Hz, 1H), 7.63 (s, 1H), 7.72 (s, 1H, olefinic); \(^13\)C NMR (75.5 MHz, CDCl\(_3\)) \(\delta\) (ppm) = 56.2 (OCH\(_3\)), 78.2 (C), 110.4 (CH), 113.6 (C), 114.4 (C), 124.0 (C), 129.0 (CH), 147.0 (C), 152.1 (C), 159.2 (CH); Anal. calcd for C\(_{11}\)H\(_8\)N\(_2\)O\(_2\): C, 66.0; H, 4.0; N, 14.0%. Found: C, 66.09; H, 4.1; N, 13.93%.

3,4-Dimethoxybenzyldene malononitrile

Bright yellow crystalline solid, mp 142 °C; IR (KBr): 3437.2, 2222.9, 1573.1, 1501.5, 1333.9, 1129.9 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)) \(\delta\) 3.77 (s, 3H), 3.84 (s, 3H), 7.17 (d, \(J = 8.4\) Hz, 1H), 7.56 (d, \(J = 8.6\) Hz, 1H), 7.6 (d, \(J = 2.1\) Hz, 1H), 8.30 (s, 1H, olefinic); \(^13\)C NMR (75.5 MHz, DMSO-d\(_6\)) \(\delta\) 55.6 (OCH\(_3\)), 56.2 (OCH\(_3\)), 76.8 (C), 112.08 (CH), 112.1 (CH), 114.2 (C), 114.9 (C), 124.25 (C), 127.4 (CH), 148.9 (C), 154.6 (C), 160.75 (C); Anal. calcd for C\(_{12}\)H\(_{10}\)N\(_2\)O\(_2\): C, 67.28; H, 4.71; N, 14.94%. Found: C, 67.31; H, 4.75; N, 14.88%.

3,4,5-Trimethoxybenzyldene malononitrile

Pale yellow crystalline solid, mp 140 °C; IR (KBr): 3436.0, 2216.6, 1570.6, 1507.0, 1269.5, 1141.9 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.77 (s, 6H), 3.78 (s, 3H), 7.33 (s, 2H), 8.34 (s, 1H, olefinic); \(^13\)C NMR (75.5 MHz, CDCl\(_3\)) \(\delta\) 48.7 (OCH\(_3\)), 56.2 (OCH\(_3\)), 60.9 (OCH\(_3\)), 79.6 (C), 108.6 (CH), 113.7 (C), 114.5 (C), 126.5 (C), 153.0 (C), 161.46 (C); Anal. calcd for C\(_{13}\)H\(_{12}\)N\(_2\)O\(_3\): C, 63.93; H, 4.95; N, 11.47%. Found: C, 63.96; H, 4.91; N, 11.49%. 
E-Cinnamyl malononitrile

Pale Yellow solid; mp 128 °C; IR (KBr): 3754, 3436, 3033, 2926, 2222, 1607, 1563, 1448, 1174, 978, 751 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)) \(\delta\) 7.22 (q, \(J = 8.8\) Hz, 1H, olefinic), 7.40-7.49 (m, 3H, aromatic), 7.57 (d, \(J = 15.0\)Hz, 1H, olefinic), 7.70-7.74 (m, 2H, aromatic), 8.23 (d, \(J = 10.8\) Hz, 1H, olefinic); \(^1^3\)C NMR (75.5 MHz, DMSO-d\(_6\)) \(\delta\) 81.1 (C), 112.3 (C), 114.3 (C), 123.01 (CH), 129.6 (CH), 129.8 (CH), 132.3 (CH), 134.23 (C), 151.24 (CH), 162.2 (CH); Anal. calcd for C\(_{12}\)H\(_9\)N\(_2\): C, 80.0; H, 4.44; N, 15.56%. Found: C, 80.11; H, 4.38; N, 15.51%.

Furfuryledene malononitrile

White crystalline solid, mp 70 °C; IR (KBr): 3437, 3017, 2220, 1681, 1602, 1415, 1218, 1062, 768 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDC\(_3\)): \(\delta\) (ppm) = 6.72 (q, \(J = 2.2\) Hz, 1H, aromatic), 7.36 (d, \(J = 3.7\) Hz, 1H, aromatic), 7.52 (s, 1H, alkenic), 7.81 (d, \(J = 1.6\) Hz, 1H, aromatic); \(^1^3\)C NMR (75.5 MHz, CDC\(_3\)): \(\delta\) (ppm) = 112.6 (C), 113.8 (C), 114.5 (CH), 123.4 (CH), 143.1 (CH), 148.1 (C), 149.6 (CH); Anal. calcd for C\(_6\)H\(_4\)N\(_2\)O: C, 66.66; H, 2.77; N, 19.44%. Found: C, 66.57; H, 2.68; N, 19.39%.
Fig. 3.2.1. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of benzylidene malononitrile
Fig. 3.2.2. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 4-nitrobenzyledeine malononitrile.
Fig. 3.2.3. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectra of 3-nitrobenzyledene malononitrile
Fig. 3.2.4. \(^1\)H NMR (A) (CDCl\(_3\)) and IR (B) (KBr) spectra of 4-methylbenzyledene malononitrile.
Fig. 3.2.5. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 4-chlorobenzylede malononitrile
Fig. 3.2.6. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 4-hydroxybenzyledenemalononitrile
Fig. 3.2.7. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 4-$N$, $N$-dimethylaminobenzyledene malononitrile
Fig. 3.2.8. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectra of 4-methoxybenzylidene malononitrile
Fig. 3.2.9. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 3-methoxybenzyledene malononitrile.
Fig. 3.2.10. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 4-hydroxy-3-methoxybenzyledene malononitrile
Fig. 3.2.11. $^1$H NMR (A) and $^{13}$C NMR (B) (d$_{6}$-DMSO) spectra of 3,4-dimethoxybenzyldene malononitrile
Fig. 3.2.12. $^1$H NMR (A) (d$_6$-DMSO) and IR (B) (KBr) spectra of 3,4,5-trimethoxybenzyledene malononitrile
Fig. 3.2.13. $^1$H NMR (A) and $^{13}$C NMR (B) ($d_6$-DMSO) spectra of cinnamyl malononitrile
Fig. 3.2.14. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectrum of furfuryledene malononitrile
Fig. 3.2.15. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl₃) spectrum of benzyledehethylcyanoacetate
References


