



Highly efficient mesoporous base catalyzed Knoevenagel condensation of different aromatic aldehydes with malononitrile and subsequent noncatalytic Diels–Alder reactions

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ABSTRACT

Knoevenagel condensation and [4 + 2] cycloaddition reactions are very important class of reactions in synthetic organic chemistry. We have prepared amino-functionalized mesoporous silica through co-condensation of 3-aminopropyltriethoxy-silane (APTES) along with tetraethylorthosilicate (TEOS) in presence of a cationic surfactant CTAB hydrothermally. Small angle powder XRD, HR TEM, FE SEM, N₂ sorption and FT IR spectroscopic tools are used to characterize the 2D-hexagonal mesostructure and to identify the presence of surface –NH₂ groups in amino-functionalized mesoporous silica material. Our experimental results reveal that amino-functionalized mesoporous silica is an efficient base catalyst for the Knoevenagel condensation of different aromatic aldehydes with malononitrile to α,β -unsaturated dicyanides under very mild reaction condition and in the presence of ethanol solvent. The isolated α,β -unsaturated dicyanides obtained through the condensation reaction further react very efficiently with cyclopentadiene to form a series of Diels–Alder cycloaddition products in excellent yields in the absence of any catalyst.

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1. Introduction

Ordered mesoporous materials having exceptionally high surface areas and tunable pores of nano-scale dimensions gained increasing interests over the years and found numerous potential applications in different frontier areas like adsorption [1], metal ion uptake [2], catalysis [3,4], sensing [5] and so on. In order to functionalize the surface of mesoporous silica and thus to explore their applications in different catalytic transformations a large number of organosilanes have been used as precursors during synthesis or post-synthesis functionalization for the preparations of organically modified mesoporous materials [6–8]. Thus, organic–inorganic hybrid mesoporous materials containing active functional groups grafted at the surface of the mesopores can be designed based on the particular requirement of the active sites in a catalytic reaction.

Knoevenagel reaction is the condensation of an aromatic aldehyde and a compound containing active methylene group, which proceeds in the presence of a catalytic amount of strong base [9]. Srasra et al. [10] has incorporated nitrogen species in microporous zeolites through ammonia treatment and observed their

high catalytic activity in base catalyzed Knoevenagel condensation. Mesoporous zeolitic structures [11] or surface modification in the presence of alkali metal cation [12], oxinitride [13], tetraalkylammonium cation [14], N,N-dimethyldecylamine [15], etc. has been found an alternative strategy of generating a highly active catalytic site necessary for base catalyzed Knoevenagel condensation. Amino-functionalized mesoporous silica synthesized through co-condensation of 3-aminopropyltriethoxysilane and tetraethylorthosilicate has been utilized in base catalyzed Knoevenagel condensation for the synthesis of α,β -unsaturated carboxylic acids in recent times [16–22]. These organically functionalized mesoporous silicas are particularly effective when the reactions are carried out in polar solvents like ethanol or DMF. Parinda and Rath [23] have prepared amino-functionalized mesoporous silica by co-condensation method, which showed high malonic ester conversion and selectivity for cinnamic acid. However, diethylmalonate (DEM) or ethyl cyanoacetate (ECA) are mostly used as active methylene compounds in the previous reports of Knoevenagel reactions over functionalized mesoporous silicas, which leads to corresponding unsaturated carboxylic acid or α -cyanocarboxylate as the products. Decarboxylation occurs in the former case is undesirable as it reduces the fruitful utilization of the carbon atoms. Thus further functionalization of the Knoevenagel reaction product through Diels–Alder [4 + 2] cycloaddition reaction [24,25] can provide a new strategy in designing novel target molecules.

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In this context it is pertinent to mention that for the Knoevenagel condensation reactions with high catalytic activities are mostly observed over a large number of organic solvents, like DMSO, which is toxic and environmentally hazardous for disposal. Whereas, ethanol is a common organic solvent and it can be easily disposable. Herein, we describe a new route to synthesize α,β -unsaturated dicyano compounds via Knoevenagel condensation of aromatic aldehydes and malononitrile catalyzed by amino-functionalized mesoporous material in presence of ethanol solvent. α,β -Unsaturated dicyano compounds formed in the initial condensation step can act as a good dienophile in Diels–Alder cycloaddition reaction with cyclopentadiene, which can be used as a building block for designing novel target molecules.

2. Experimental

2.1. Synthesis of amino-functionalized mesoporous silica

Organosilane precursor 3-aminopropyltriethoxy-silane (APTES, Aldrich) along with tetraethylorthosilicate (TEOS, Aldrich) in 1:5 molar ratio were used for the synthesis of amino-functionalized mesoporous silica. In a typical synthesis procedure cetyltrimethylammonium bromide (CTAB, Loba Chemie, 0.0075 mol 2.73 g) was dissolved in an aqueous solution of tartaric acid (0.6 g in 30 g H₂O) under vigorous stirring condition. The resulting mixture was stirred for about 30 min to obtain a clear solution. Then 1.105 g APTES (0.005 mol) was added into the solution. After 30 min of stirring 5.245 g TEOS (0.025 mol) was added in the reaction mixture and it was stirred for about 2 h to obtain a gel. After 2 h stirring 2 M NaOH solution was added dropwise into the gel until the pH reached *ca.* 12.0. The gel was aged overnight with continuous stirring. Then the gel was heated in a closed stainless steel autoclave at 373 K for 48 h. After the hydrothermal treatment the slurry was filtered and washed several times with water and dried under vacuum. The template CTAB was removed from as-synthesized sample by extracting solid material three times with ammonium acetate–ethanol solution.

2.2. Characterization techniques

Powder X-ray diffraction patterns were recorded on a Bruker D-8 Advance SWAX diffractometer operated at 40 kV voltage and 40 mA current. The instrument has been calibrated with a standard silicon sample, using Ni-filtered Cu K α ($\lambda = 0.15406$ nm) radiation. Nitrogen adsorption/desorption isotherms were obtained by using a Bel Japan Inc. Belsorp-HP at 77 K. Prior to gas adsorption, sample was degassed for 4 h at 393 K under high vacuum conditions. A JEOL JEM 6700F field emission scanning electron microscope was used for the determination of morphology of the particles. FT IR spectra of the samples were recorded using a Nicolet MAGNA-FT IR 750 Spectrometer Series II.

2.3. Knoevenagel condensation and Diels–Alder cycloaddition reactions

In a typical synthesis procedure for Knoevenagel condensation 1 mmol aromatic aldehyde was mixed with the 1 mmol malononitrile in 5 ml absolute ethanol taken in a round bottom flask. Then 20 mg template-free amino-functionalized mesoporous silica catalyst was added in it and the reaction mixture was stirred at room temperature for *ca.* 5–7 h. After that reaction mixture was filtered and the solid was washed with the ethanol and dried. The solvent was removed by a rotary evaporator to obtain the solid product residue. Then it was crystallized from absolute ethanol. For the Diels–Alder cycloaddition reaction 1 mmol of α,β -unsaturated

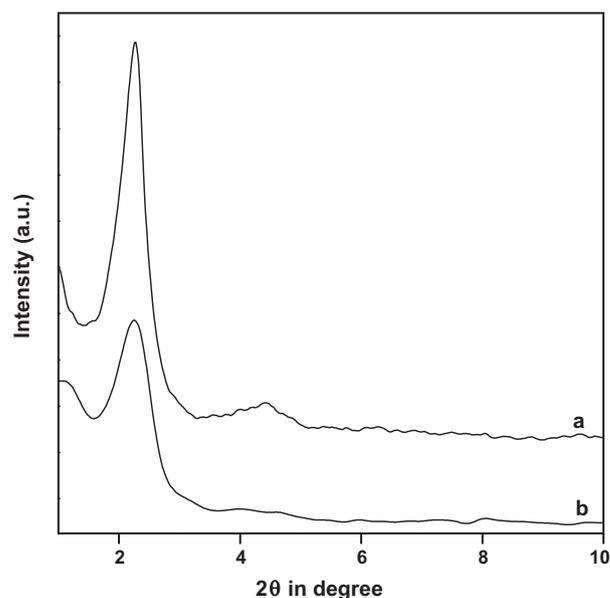


Fig. 1. XRD patterns of as-synthesized (a) and template-free (b) amino-functionalized mesoporous silica.

dicyanides was mixed with the 2 ml freshly distilled cyclopentadiene taken in 5 ml dry THF in a round bottom flask. The mixture was cooled to 273 K and then a pinch of hydroquinone was added and the reaction mixture was stirred vigorously for 4–7 h at 273 K. After the reaction was completed, solvent THF has been removed by the rotary evaporator and the solid product was dried in the air. The condensation as well as cycloaddition products were characterized by the ¹H and ¹³C NMR spectroscopy.

3. Results and discussion

3.1. Characterizations of the catalyst

The powder XRD patterns of the as-synthesized and template-free amino-functionalized mesoporous silica are shown in Fig. 1. As

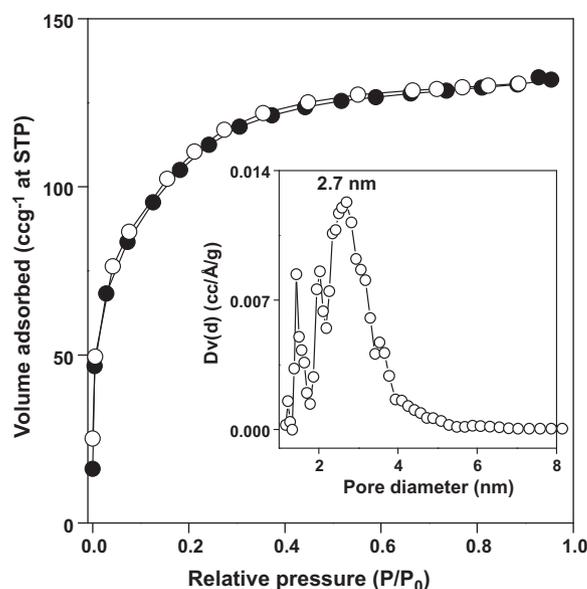


Fig. 2. N₂ adsorption/desorption isotherms of amino-functionalized mesoporous silica. Adsorption points are marked by filled circles and those of the desorption are by open circles. BJH pore size distribution is shown in the inset.

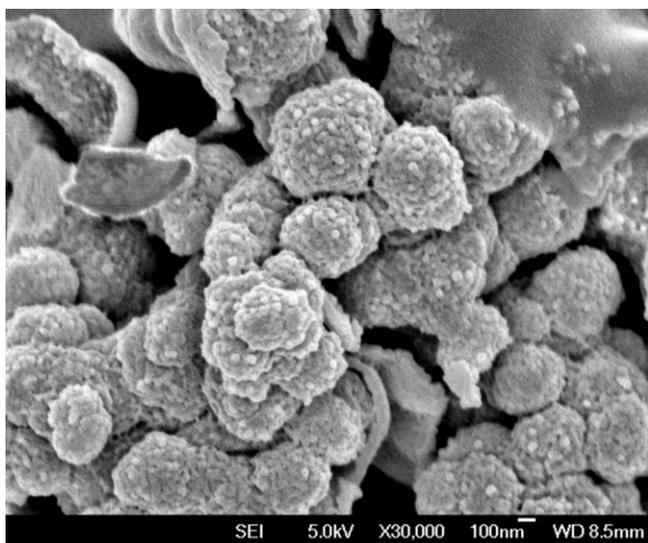


Fig. 3. FE SEM image of amino-functionalized mesoporous silica.

seen from the patterns that the as-synthesized material is mesoscopically ordered, showing three diffractions for the 100, 110, 200 planes corresponding to 2D-hexagonal mesophase, whereas in the template-free sample 110 and 200 peak intensities are considerably reduced. The N_2 sorption isotherms of template-free amino-functionalized mesoporous silica are shown in Fig. 2. These isotherms can be classified as type IV characteristic of small mesopores with no sharp capillary condensation step [26,27]. Pore size distribution of this sample estimated by employing the NLDFT method is shown in the inset of Fig. 2, suggesting the existence of mesopores having dimension of ca. 2.7 nm in this material. The BET surface area and pore volume of this material are $392 \text{ m}^2 \text{ g}^{-1}$ and 0.2 ml g^{-1} , respectively. Estimated peak pore width of ca. 2.7 nm is good for carrying out the Knoevenagel condensation reaction of the bulky organic aldehydes with malononitrile inside the nano-channels. FE SEM image of the amino-functionalized mesoporous silica sample is shown in Fig. 3. As seen from the figure that this material is composed of very tiny spherical nanoparticles of ca. 25–40 nm in diameter. These small nanoparticles are self-aggregated to form uniform large spherical particles of dimension

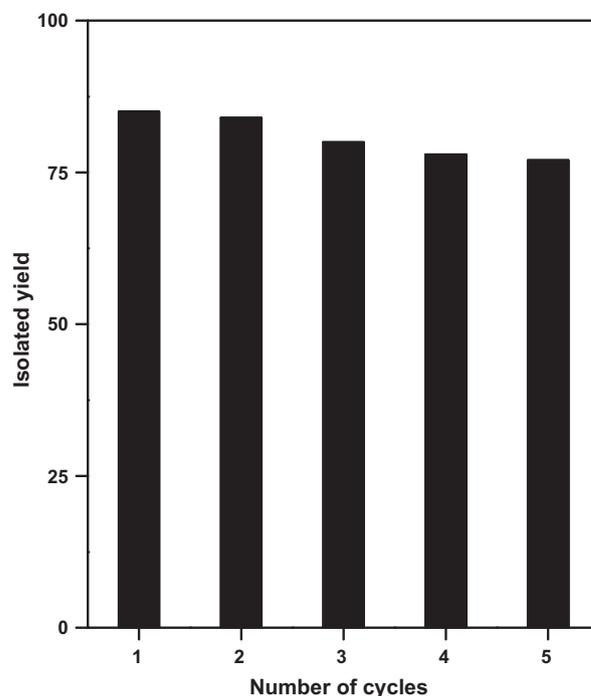


Fig. 5. Recycling efficiency of amino-functionalized mesoporous silica catalyst.

ca. 300–500 nm in size. CHN chemical analysis results revealed the loading of $-\text{NH}_2$ groups for this amino-functionalized mesoporous material is 3.09 mmol g^{-1} , which is considerably good to carry out the base catalyzed reactions. Further, the presence of N–H bending vibration at 690 cm^{-1} and $-\text{NH}_2$ symmetric bending vibration at 1557 cm^{-1} , in the FT IR spectrum suggested successful grafting of 3-aminopropyl group onto the surface of the amino-functionalized mesoporous materials [23].

3.2. Catalysis

The amino-functionalized mesoporous material is used as catalyst in the liquid phase Knoevenagel condensation reaction (Fig. 4) over various electron-withdrawing and electron-donating aromatic aldehydes. Yields of various α,β -unsaturated dicyano products obtained in this reaction are given in Table 1. As seen from the table that reaction proceeds almost exclusively at room temperature (298 K). For all the substrates, very high yields of the condensation products are obtained within 4–7 h reaction time. We have tested the catalytic efficiency of amino-functionalized mesoporous material in five repetitive reaction cycles for the reaction between benzaldehyde and malononitrile. We have plotted the recycling efficiency of the catalyst for these five consecutive catalytic cycles for the condensation reaction between benzaldehyde and malononitrile (Fig. 5). It was found that the catalyst can be efficiently recycled and reused for five repeating cycles without much loss of efficiency. This indicates that our amino-functionalized mesoporous silica is a very efficient catalyst for Knoevenagel condensation. Electron withdrawing group present in the *para* position of the aromatic ring increases the yield (Fig. 1) by activating the aldehyde group due to $-I$ effect. When $-\text{NO}_2$ group is present in the *ortho* position of the aromatic ring the yield of the product has been minimized. This could be attributed to the steric hindrance at the reaction site. On the other hand the yield for the $-\text{OH}$ group containing substrate decreases a little bit due to the $+R$ effect of the $-\text{OH}$ group present in the ring. Further, we have carried out Knoevenagel condensation over a well known solid base catalyst Mg–Al–hydrotalcite [28] for the

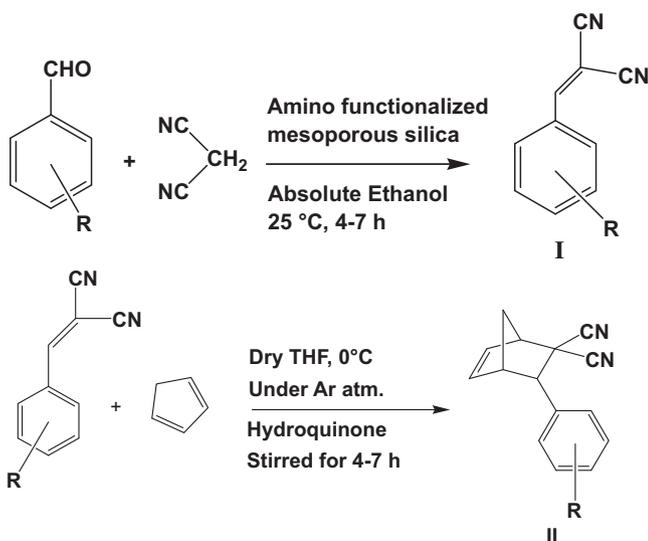
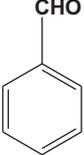
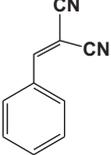
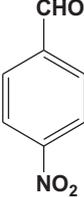
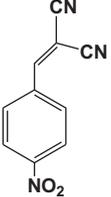
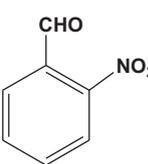
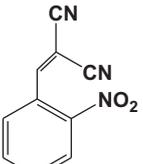
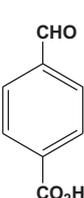
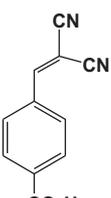
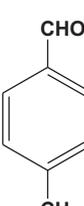
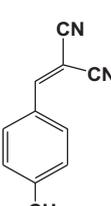
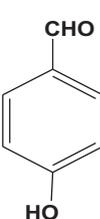
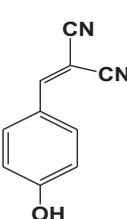
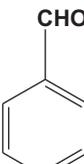
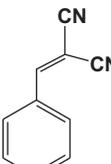


Fig. 4. Reaction pathway for the Knoevenagel condensation reactions over amino-functionalized mesoporous silica.

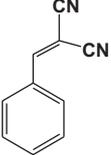
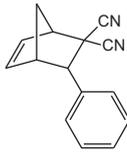
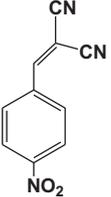
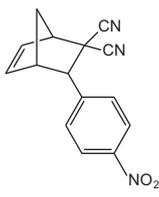
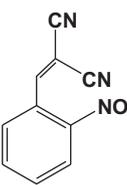
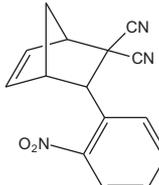
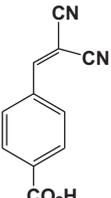
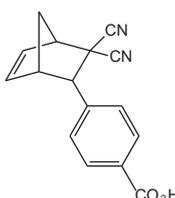
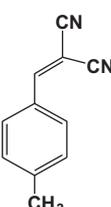
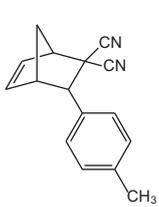
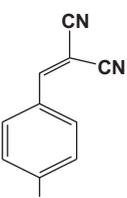
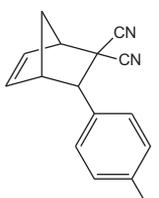
Table 1
Knoevenagel condensation of different aldehydes with malononitrile over amino-functionalized mesoporous silica.^a

| Entry | Aldehyde | Time (h) | Yield (%) | Product | TOF ^b (h ⁻¹) |
|-------|---|----------|-----------|---|-------------------------------------|
| 1 |  | 6 | 90 |  | 5.23 |
| 2 |  | 5 | 95 |  | 4.53 |
| 3 |  | 6 | 80 |  | 4.04 |
| 4 |  | 6 | 84 |  | 4.31 |
| 5 |  | 5 | 82 |  | 5.56 |
| 6 |  | 7 | 80 |  | 3.68 |
| 7 |  | 6 | 65 |  | 0.68 |

^a ¹H and ¹³C NMR chemical shifts are given in supporting materials.

^b TOF=turn over frequency=moles of substrate converted per mole of -NH₂ group (loading of -NH₂ groups in amino functionalized mesoporous silica = 3.09 mmol g⁻¹).

Table 2
Diels-Alder [4+2] cycloaddition reactions of dicyano derivatives with cyclopentadiene.

| Entry | Dicyano compound | Time (h) | Yield (%) | Product |
|-------|--|----------|-----------|---|
| 1 |  | 5 | 75 |  |
| 2 |  | 4 | 80 |  |
| 3 |  | 4 | 82 |  |
| 4 |  | 6 | 75 |  |
| 5 |  | 7 | 70 |  |
| 6 |  | 7 | 70 |  |

reaction between benzaldehyde and malononitrile for comparison. The yield of the condensation product was 65%. However, for our amino-functionalized mesoporous material the yield was 90%. From this data it is clear that mesoporosity in our amino-functionalized mesoporous material facilitates this condensation reaction. Moreover, when the reaction between benzaldehyde and malononitrile is carried out in absence of catalyst no condensation product formed. This result suggests that Knoevenagel condensation reactions described herein are purely catalytic in nature.

3.3. Mechanism of condensation

In Fig. 6 we have shown a plausible mechanism for the base catalyzed Knoevenagel condensation of different aromatic

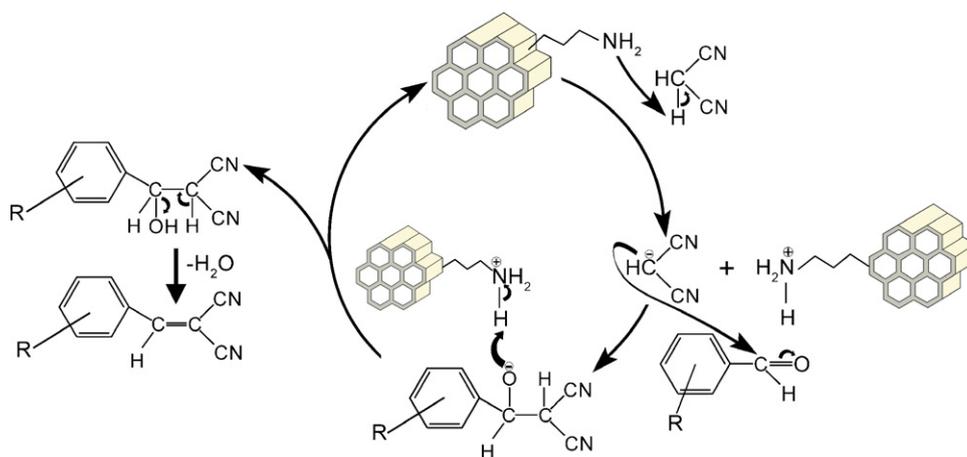


Fig. 6. Proposed mechanism for the Knoevenagel condensation over amino-functionalized mesoporous silica.

aldehydes with malononitrile. Here the -NH_2 group of amino-functionalized mesoporous silica picks up one proton from the active methylene group of malononitrile, which is acidic in nature due to presence of two strong electron withdrawing cyano groups. The conjugate base generated here is stable due to conjugation with the cyano groups. Now, this anion makes nucleophilic attack to the carbonyl carbon atom of the substituted aromatic aldehydes. The β -hydroxyl compound (carbon atom attached with the cyano group designated as α) is generated when -ve charge over oxygen takes up one proton from the catalyst and the catalyst is regenerated. The β -hydroxyl compound leads to the formation of α,β -unsaturated dicyano compounds via the elimination of one molecule of water.

3.4. Diels–Alder cycloaddition reaction

The α,β -unsaturated dicyano compounds obtained herein, can behave as a good dienophile for [4+2] Diels–Alder cycloaddition reaction [29,30] due to presence of two cyano groups, by which a cyclic bridge headed compound can be obtained on reaction with a conjugated diene (Fig. 4). When the α,β -unsaturated dicyano compound **I** (Fig. 4) reacts with cyclopentadiene observed yield of the cyclic bridge headed compound **II** is 87%. For other aldehydes the [4+2] Diels–Alder cycloaddition product yield varies from 76 to 85%. It is interesting to note that the products of Knoevenagel condensation catalyzed by amino-functionalized mesoporous material are unsaturated dicyano compounds. These compounds undergo facile [4+2] cycloaddition reaction with cyclopentadiene within a few hours to generate 3-phenylsubstituted bicyclo [2.2.1] hept-5-ene-2,2-carbonitrile derivatives (Table 2). It is pertinent to mention that these types of bicyclic compounds are very rarely mentioned in the literature. Only one synthetic methodology has been reported, which is connected with hydroquinone derivative [31]. However, it took very long time for the completion of reaction and crystallization involved carcinogenic benzene solvent. Similar analogous bicyclo [2.2.1] hept-5-ene derivatives are also synthesized in benzene solvent [32]. Similar reaction has also been carried out under ultrasound condition for 24 h for the completion of reaction [33]. Alternatively, the reaction can be performed in the presence of catalytic amount of CuSO_4 and ZnI_2 [34]. But in our case no such organic solvent or catalyst was needed and bicyclic compound was obtained from only the removal of THF solvent. Further, the reaction takes 4–7 h for the completion under noncatalytic conditions. In this reaction hydroquinone acts as an anti-oxidant. It protects the dienophiles to undergo rapid polymerization under the reaction conditions. Thus our synthetic procedure is more efficient than the

previously reported methods for the preparation of bicyclo [2.2.1] hept-5-ene compounds.

These results suggest that strategy described herein can be utilized for the synthesis of new bridge headed compound, which can be further reacted to form desired target molecule. Moreover, reduction of the cyano group leads to the formation of primary amine group that can be easily condensed with any aldehydes and generates the imine bond, which has a wide application in biological chemistry as an antioxidant. For the reaction between DEM and benzaldehyde over amino-functionalized mesoporous silica [23] the product ester hydrolyzed and decarboxylate instantly. But here as we have used malononitrile as active methylene compound, only dicyano compounds are formed. Thus the catalytic reaction described here provides the homologation of carbon, which is very important in organic synthesis.

4. Conclusions

From the above experimental results we can conclude that amino-functionalized mesoporous silica synthesized through co-condensation of APTES and TEOS is an efficient base catalyst in the Knoevenagel condensation of different aromatic aldehydes with malononitrile for the synthesis of α,β -unsaturated dicyanides in very good yields. α,β -Unsaturated dicyano compounds obtained herein, behaves excellent dienophile for the Diels–Alder cycloaddition reaction with cyclopentadiene under noncatalytic conditions, which can be an efficient target strategy for the synthesis of a bridge headed functionalized target molecules.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2010.11.039.

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