Knoevenagel condensation and cyanosilylation reactions catalyzed by a MOF containing coordinatively unsaturated Zn(II) centers

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ABSTRACT

An aqueous solution of $Zn(NO_3)_2 \cdot 6H_2O$ reacts with tetraethylammonium salt of the tripodal ligand *tris*-(4-carboxy-2-phenoxyethyl)amine ($ptaH_3$) at room temperature, to form infinite interlinked 2D metallocycles. These 2D networks stack to form an overall 3D structure (**1**) where lattice water molecules occupy the metallocyclic cavities. On heating to 110 °C for 5 h under vacuum, **1** loses metal bound water molecules as well as lattice ones without framework collapse and leaves the metal ion coordinatively unsaturated. The coordination space in the structure (**1a**) can be utilized for Knoevenagel and cyanosilation reactions to give biologically important molecules. These reactions are catalyzed by Zn(II) centers which are coordinatively unsaturated. Larger carbonyl substrates cannot diffuse through the pores of **1a**, and afford poor yields of the desired products.

1. Introduction

The chemical industry represents a vital part of the economy of many countries. However, the manufacture of chemical products also leads to enormous quantities of environmentally harmful wastes. Heterogeneous catalysis is playing an increasingly important role [1,2] in smaller scale chemical manufacturing, often with the result of a major reduction in waste. Separation of the reaction products also becomes easier and the catalyst finds reusability due to less leaching problems unlike homogeneous catalysts. However, it is often found that catalytic activity of metal complexes immobilized on a solid support such as oxide and zeolite deteriorates [3,4] on exposure to moisture or heat leading to the loss of catalytic activity. The newly developed porous metal-organic framework (MOF) structures are promising as new generation heterogeneous catalytic materials [5–15] affording studies in the coordination space provided by the 3D structure of the MOF due to (1) well-ordered size and shape of the pores, (2) flexible and dynamic behavior in response to guest molecules, and (3) designable channel surface functionalities. These MOFs can be synthesized by applying mild synthetic conditions and importantly, each metal environment is identical due to the crystalline nature.

Porous MOFs can be rapidly built with multi-dentate ligands through self-assembly where the ligand topology, and coordina-

tion tendencies of the metal ion as well as synthetic conditions play crucial roles. For the optimal catalytic activity, two types of strategies are used: (i) introduction of organic groups to provide guest-accessible functional organic sites [16,17] and (ii) formation of coordinatively unsaturated metal sites [18–21]. If the metal is coordinatively saturated, the organic moiety incorporating functionality for non-covalent interactions can bind the reactant(s) through H-bonding, π–π stacking, etc., leading to their activation. In another case, metal ions bound to one or more solvent molecules can be heated to remove the solvent molecules exposing the metal ion to the reactants that can directly bind the metal ion and hence can be activated.

Recently, we have been focusing on the rational design strategies for MOFs using tripodal ligands and different transition metal ions to tune the micropores for selective sorption of small molecules as well as catalysis. The tripodal ligands are chosen because they form kinetically inert and thermodynamically stable complexes with metal ions. We had earlier designed and synthesized the tripodal ligand **L** (Scheme 1) bearing carboxylate functionality at each terminal and a long linker from the bridgehead nitrogen. The ligand topology favors formation, under hydrothermal conditions as well as ambient conditions, of highly porous structures occupied by supramolecularly bonded water molecules [22,23]. In a robust structure, these water molecules can be removed [24] without damaging the overall framework to afford cavities that can be used for potential applications.

The carboxylate donating ligand also favors formation of neutral MOFs, which is important for catalysis because the counter

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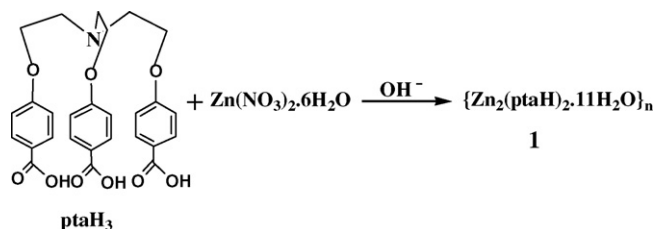
Scheme 1. Synthetic scheme for **1**.

anions often block the guest-accessible sites. Herein, we show that compound **1a** obtained by heating of **1**, catalyzes cyanosilylation of aromatic aldehydes, as well as more demanding Knoevenagel condensation reactions with size-selectivity that is consistent with the pore dimensions.

2. Experimental

2.1. Materials

Benzaldehyde, 4-methylbenzaldehyde, 4-nitrobenzaldehyde and 1-naphthaldehyde were procured from Aldrich and used as received. All the other chemicals and solvents were purchased from SD fine Chemicals (India) and solvents were purified before use.

2.2. Physical measurements

Spectroscopic data were collected as follows: IR (KBr disk, 400–4000 cm^{-1}) PerkinElmer Model 1320; X-ray powder pattern (Cu Kα radiation at a scan rate of 3 °C/min, 293 K) Siefert ISODEBYEFLEX-2002 X-ray generator; thermogravimetric analysis (heating rate of 5 °C/min) PerkinElmer model Pyris 6.

2.3. Synthesis of $\{Zn_2(ptaH)_2 \cdot 11H_2O\}_n$, ($\mathbf{1}$)

This compound is synthesized at room temperature by treating $Zn(NO_3)_2 \cdot 6H_2O$ with the tripodal ligand, **L** in THF as described earlier [23]. Synthesis of the ligand is described elsewhere [24]. On heating at 110 °C under vacuum for 5 h, crystals of **1** afford the de-solvated compound **1a** that is used as an active catalyst.

2.4. General procedure for Knoevenagel condensation reactions

A solution of an aromatic aldehyde (10.4 mmol) and malononitrile (10.4 mmol) in dichloromethane (20 mL) is stirred for 5 min at RT and then the catalyst **1a** (5 wt%) is added. The stirring continued at room temperature and progress of the reaction is monitored by TLC. Once the reaction is complete, the catalyst is removed by filtration, washed with DCM and recovered. This solid catalyst is reused

for the same reaction later. From the filtrate, solvent is removed under reduced pressure to form a solid that is recrystallised with EtOAc/hexane mixture.

2.5. General procedure for cyanosilylation reactions

A solution of an aromatic aldehyde (1.32 mmol) and trimethylsilyl cyanide (2.64 mmol) in benzene (10 mL) is stirred for 5 min and then catalyst **1a** (5 wt%) is added. The suspension is stirred under ice-cold condition for 45 min and progress of the reaction is monitored by TLC. Once the reaction is complete, the catalyst is removed by filtration, washed with benzene and recovered for reuse. After evaporation of solvent from the filtrate in a rotary evaporator, the crude solid obtained is recrystallised with EtOAc/hexane mixture.

3. Results and discussion

Once isolated, **1** is stable in air and insoluble in water as well as in common organic solvents. Thermal gravimetric analysis of **1** in air shows [26] that weight loss occurs in stages beginning at 80 °C and the loss of 14.57% corresponding to all of the water (calculated 14.74%) takes place just above 100 °C. Complete decomposition is achieved only at ~280 °C showing that the product is quite stable thermally.

Upon removal of all water molecules by heating crystals of **1** at 110 °C under vacuum for 5 h the de-solvated compound is obtained (**1a**). The FTIR spectrum of **1** shows a broad band around 3500 cm^{-1} attributable [23] to the presence of water molecules, which vanishes in **1a** [26]. Although X-ray powder patterns of **1** and **1a** show [26] marked changes with respect to position as well as intensity of the peaks, the de-solvated product (**1a**) is also crystalline and shows well-defined peaks. Hence, the pore structure of **1a** may be different from that of **1**.

3.1. Structural description

The Zn(II)-MOF reported earlier [23] showed the structure as an array of metallomacrocycles extending approximately along the crystallographic *b* axis (Fig. 1). Each Zn(II) ion exhibits tetrahedral coordination with ligation from three carboxylates from three different ligand units and one water O atom. The large voids in the structure contain an infinite chain of hydrogen-bonded water molecules through these macrocycles. The metallomacrocycles are stacked along the crystallographic *a* axis with an inter-planar spacing of approximately 6.3 Å in such a way that each Zn(II) ion of the metallocyclic array is present approximately in the middle of the oval shaped void of the next array (Fig. 2). The Zn(II) bound water molecules are oriented towards the center of the metallocyclic cavities. Compound **1** possesses an effective free volume of 14.5% as calculated with PLATON [25] after removing all the water
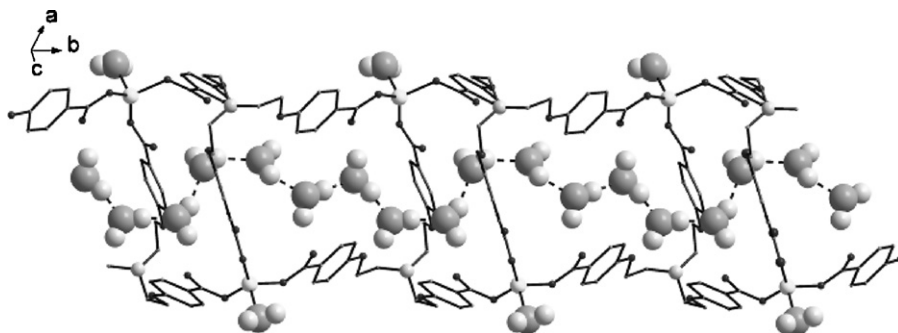

Fig. 1. A view of the interlinked metallomacrocycles extending along the crystallographic *b* axis illustrating the wave-like water chain inside the metallocyclic cavity.
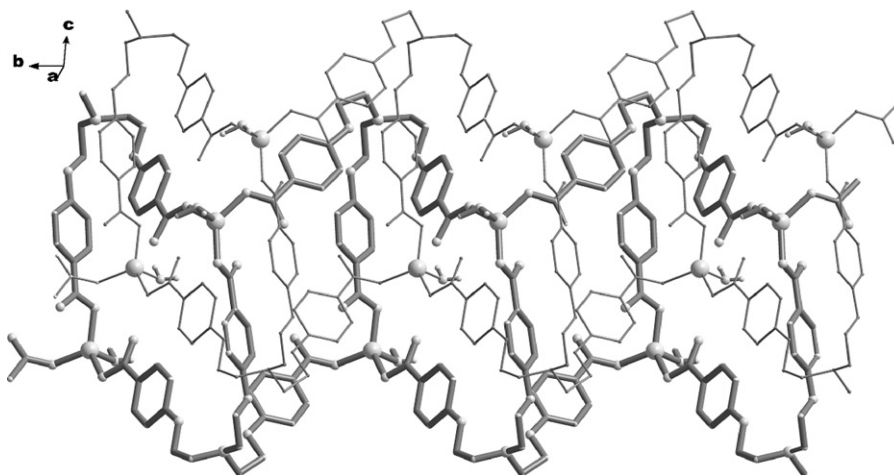
Fig. 2. Perspective view of the stacking of the two adjacent layers of **1** showing metal bound water molecule pointing towards the cavity.

molecules, which offers space for enclathration of a substrate for catalysis. The particular packing of the metallomacrocycles favors a substrate entering the void in one layer and accessing a metal ion in the next layer.

3.2. Knoevenagel condensation reactions

To probe the catalytic activity of **1a**, we have chosen Knoevenagel condensation reactions [27,28] to synthesize compounds (Table 1) derived from benzylidene malononitrile (BMN) because of their reported inhibitory activity [29] of the protein tyrosine kinase. For this, a number of aromatic aldehydes are allowed to react with malononitrile as the active methylene compound. The catalytic reactivity is also probed by using diethylmalonate in place of malononitrile. Results from these catalytic reactions are collected in Table 1.

Aromatic aldehydes are chosen as substrates due to their enclathration possibility via π–π stacking interactions inside the cavity of the MOF. We presume that the coordinatively unsaturated Zn(II) center interacts with these aldehydic O atom to selectively accommodate inside the metallocyclic cavity and activate activate the substrates leading to faster reaction rates. The enclatharated substrates are then allowed to react with each of the active methylene compounds in dichloromethane by stirring at room temperature.

In each case, about 5 wt% of **1a** (dehydrated **1**) is used as the catalyst. The reactions proceed at various rates depending upon the nature of the substrate (Table 1). Once the reaction is over as monitored by TLC, the catalyst is easily isolated from the reaction mixture and can be collected by filtration. No reaction occurs with $Zn(NO_3)_2{\cdot}6H_2O$ taken in the same solvent. Compound **1a** is stirred

separately in DCM/benzene for 2 days and the filtrate is collected. In none of the cases, the filtrate can catalyze any of the above reactions suggesting no leaching of Zn(II) from **1a**.

When compound **1** is used in place of **1a**, no catalytic activity can be observed presumably due to blockade of the cavity by lattice water molecules in addition to coordinatively saturated metal centers. Facile catalytic activity of **1a** points to the importance of coordinatively unsaturated metal centers as well as available void space in the compound.

To determine reusability of the catalyst, each reaction is carried out at least five times with the recovered catalyst without observing any loss of activity. The role of the catalyst **1a** towards the catalytic transformation is further established by the infrared spectra of 4-methylbenzaldehyde in the presence of **1a** which shows a doublet for the C=O stretching frequencies at 1704 and 1692 cm^{-1} (Fig. S5) corresponding to free and chemisorbed tolaldehyde, respectively. The red-shift of the C=O stretching frequency suggests that the carbonyl group binds the metal [30]. When substrates with increasing steric requirements are used, the reaction proceeds either very slowly or not at all (Table 1).

3.3. Cyanosilylation reactions

Encouraged by the positive results observed for the Knoevenagel condensation reactions, catalytic activity of **1a** towards cyanosilylation of carbonyl-functionalized organic substrates is carried out and the results are shown in Table 2. This reaction provides a convenient route to cyanohydrins, which are key derivatives in the synthesis of fine chemicals and pharmaceuticals. Like the Knoevenagel reac-

Table 1
Knoevenagel reactions catalyzed by **1a**

Entry	R	R_1	R_2	Time (min)	Yield (%)
1	4-NO_2Ph	CN	CN	180	80
2	4-NO_2Ph	CN	CO_2Et	120	85
3	4-NO_2Ph	CO_2Et	CO_2Et		0
4	4-BrPh	CN	CN	220	75
5	4-MePh	CN	CN	600	7

Table 2
Cyanosilylation reaction catalyses by **1a**
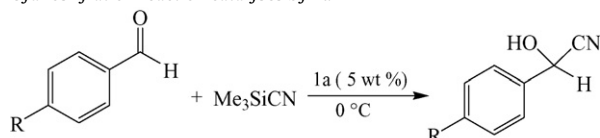
Entry	R	Solvent	Time (min)	Yield (%)[a]
1	H	DCM	120	32
2	H	C_6H_6	80	30
3	NO_2	DCM	90	92
4	NO_2	C_6H_6	45	92
5	Me	DCM	140	80
6	Me	C_6H_6	60	80

[a] isolated yield.

tions, the catalyst in these reactions can be reused without any loss of activity and the product formation depends upon the substrate structure.

In this case also, size of the substrate is important and thus, when 1-napthaldehyde is used as substrate, the reaction does not proceed at all. This suggests that the pore-size in **1a** is too small to readily accommodate the transition-state geometry required for driving the reaction to product.

4. Conclusion

This work describes construction of a porous MOF containing labile water molecules attached with the Zn(II) center and its activation on heating to produce coordinatively unsaturated metal center as guest interaction sites. The Knoevenagel condensation and cyanosilylation reactions performed with aromatic aldehydes with different steric requirements in the presence of de-solvated **1** produce the desired products. Compound **1a** displays a unique recoverable framework and the catalysis can be carried out at least five times with the recovered sample without any loss of activity. Presently we are working on other catalytic reactions with MOFs.

Supporting information available

TGA and FT-IR spectra for compound **1**, FT-IR spectra of 4-nitrobenzaldehyde and 4-methylbenzaldehyde in the presence of **1a**. PXRD curve for compound **1** and **1a**.

Acknowledgements

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2008.10.008.

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