Pyridine-Functionalized MCM-41 as an Efficient and Recoverable Catalyst for the Synthesis of Pyran Annulated Heterocyclic Systems

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Pyridine-functionalized MCM-41 catalyzed reactions between tetracyanoethylene and various activated CH-acid compounds are described. These reactions afford the corresponding pyran annulated heterocyclic ring systems in high yields at room temperature within a few minutes. The work-up procedure is very simple and the products do not require further purification. The catalyst can be recycled and reused for several times without observable loss of performance.

Key words tetracyanoethylene; CH-acid; pyran; pyridine-functionalized MCM-41

Pyrans and their derivatives are of considerable interest because of their wide range of biological activities, such as spasmolytic, diuretic, anti-coagulant, anti-cancer, and anti-anaphylactic activity.[1—4] In addition, they can be used as cognitive enhancers, for the treatment of neurodegenerative disease, including Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease, Parkinson's disease, AIDS associated dementia and Down's syndrome as well as for the treatment of schizophrenia and myoclonus.[5] 4*H*-Pyrans also constitute the structural unit of a series of natural products.[6,7]

Tetracyanoethylene (TCNE) is the simplest of the per-cyanoalkenes (cyanocarbons). Due to four powerful electron-withdrawing cyano groups, the C–C double bond is highly electron-deficient and it is strongly electrophilic reagent. TCNE undergoes two principal types of reaction, namely, addition to its double bond and replacement of a cyano group. TCNE has received an extensive amount of study and the chemistry of this compound has been reviewed several times.[8—10]

The mesoporous molecular sieves such as MCM-41 which discovered by Mobil researchers in 1992, have large and uniform pore sizes, ultrahigh surface areas, large pore volume and rich silanol groups in the inner walls. The developments of mesoporous silicas such as MCM-41 have generated interest due to their potential applications such as catalysts, catalyst supports, separation media, and host materials for inclusion compounds.[11—13] Furthermore, because of special texture and properties of MCM-41, it has great potential as a matrix for immobilizing homogeneous catalysts. Other advantages for mesoporous are: (i) easy modification with organic groups and metal complexes, (ii) readily creating discrete and uniform active sites, (iii) easy access for substrates involving bulky molecule.[12,14]

Amorphous silica, alumina and other inorganic oxides have found widespread use as supports for the immobilization of catalytically active sites and photo- and electro-active species. These materials endowed with hydroxyl-rich surface which facilitate derivatization. In order to functionalize a silica surface, for example, a molecule containing a ligand group, or a group that may be readily converted to a ligand group, is reacted with the surface silanol groups. One approach is to use silane coupling agents.[15] Howell and co-workers used functional alkoxysilanes to anchor PPh_2, CN, NH_2, pyridine and cyclopentadiene ligands, amongst others.[16,17]

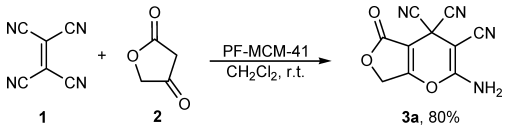
In continuation of our research interest to synthesis such as coumarins, pyrans, diazepines and quinolizines and also introduce new catalysts for organic reactions,[18—25] in this article we developed an efficient method for synthesis of pyran annulated heterocyclic ring systems in the presence of pyridine-functionalized MCM-41 (PF-MCM-41) as a recyclable catalysts, in high yield at room temperature (Chart 1).

Catalyst Preparation For the preparation of pyridine-functionalized MCM-41 a procedure similar to functionalizing by bipyridine was used.[26,27] A solution of 4-methyl-pyridine was added to a THF solution of lithium diisopropyl-amine. After 2 h the brown solution was cooled to −20 °C and then MCM-41 grafted with chloropropylsilyl groups was added. After 72 h, the reaction mixture was treated with the mix of ice and water. The solution was filtered off and the pale solid washed three times with 15 ml aliquots of ethanol, three times with 15 ml aliquots of diethyl ether, and dried under reduced pressure at room temperature for several hours (Chart 2).

The elemental analysis (CHN: C, 2.05; H, 0.30; N, 0.27) shows that substitution of the chlorine by the anion [4-CH_2-pyridine] gave a mesoporous silica containing *ca.* 0.2 mmol pyridyl groups per gram. IR (KBr, ν/cm^{-1}): 3440 s, 2925 m, 1640 m, 1596 m, 1554 m, 1071 *vs.*, 954 s, 866 m, 799 s, 459 s. The low angle powder XRD patterns of MCM-41 grafted with chloropropylsilyl (Fig. 1a) and pyridine (Fig. 1b) groups showed that the mesoporous structure of MCM-41 retained and high quality materials obtained.

Results and Discussion

In an initial experiment, the reaction of TCNE **1** with furan-2,4(3*H*,5*H*)-dione (tetronic acid) **2** in the presence of PF-MCM-41 (0.01 g) in CH_2Cl_2 afforded the 2-amino-5-oxo-



1 **2** **3a**, 80%

Chart 1. Reaction between TCNE and Tetronic Acid in the Presence of PF-MCM-41 as Catalyst

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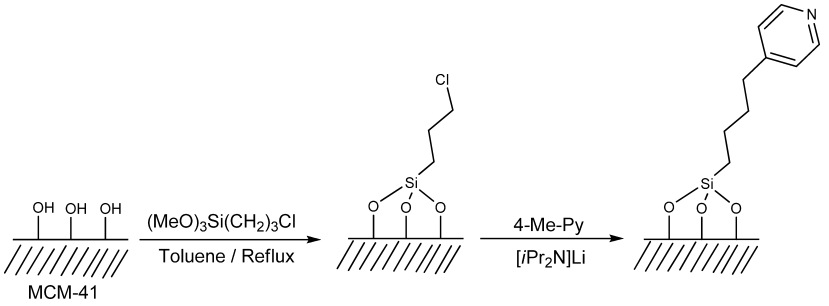


Chart 2. Preparation of Catalyst

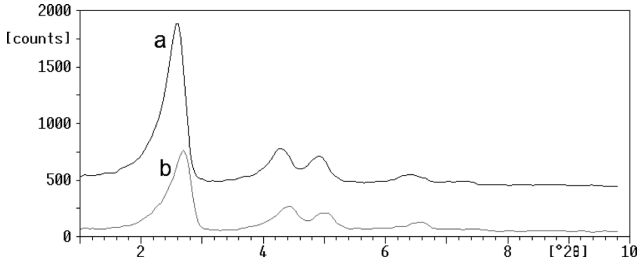
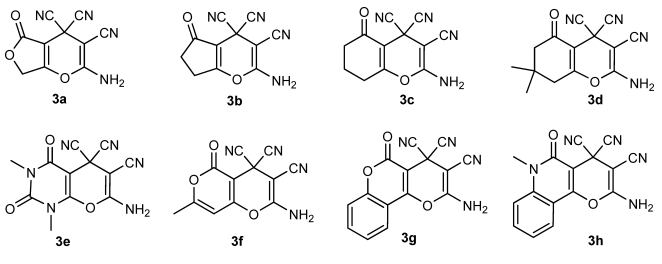


Fig. 1. XRD Patterns of Chloropropylsilyl (a) and Pyridine (b) Functionalized MCM-41



Product		3a	3b	3c	3d	3e	3f	3g	3h
Yield (%)		80	85	92	90	80	83	87	82
M. P. (°C)	Found	186-88	177-189	198-200	199-200	211-212	201-202	221-223	219-221
	Reported[a]	-	178-180	196-198	198-200	210	203	220	219

[a] Ref. 23

Fig. 2. Reaction of TCNE with Various β-Dicarbonyl Activated CH-Acids in the Presence of a Catalytic Amount of Pyridine-Functionalized MCM-41

5*H*-furo[3,4-*b*]pyran-3,4,4(7*H*)-tricarbonitrile **3a** in 80% yield. Similar reactivity was observed with other cyclic-1,3-dicarbonyl compounds such as cyclopentane-1,3-dione and cyclohexane-1,3-dione; results are summarized in Fig. 2.

In view of the success of the above mentioned reactions, we explored the use of 5,5-dimethylcyclohexane-1,3-dione (dimedone), 1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione, 4-hydroxy-6-methyl-2*H*-pyran-2-one, 4-hydroxy-2*H*-chromen-2-one and 4-hydroxy-1-methylquinolin-2(1*H*)-one as activated CH-acid. Treatment of 5,5-dimethylcyclohexane-1,3-dione, 1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione, 4-hydroxy-6-methyl-2*H*-pyran-2-one, 4-hydroxy-2*H*-chromen-2-one or 4-hydroxy-1-methylquinolin-2(1*H*)-one with TCNE **1** in the presence of PF-MCM-41 in CH_2Cl_2 at room temperature led to the formation of the corresponding pyran annulated heterocyclic systems in high yields (Fig. 2, products **3d**—**h**).

To illustrate the role of catalyst, the reaction of TCNE **1** with dimedone was studied in the absence of PF-MCM-41 catalyst. The yield of product under similar reaction conditions after 15 min was trace.

A mechanistic rationalization for the reaction is provided in Chart 3.

In order to obtain the best media, we have examined various solvents such as H_2O, EtOH, CH_3CN, $C_6H_5CH_3$, *n*-Hexan and CH_2Cl_2 in the presence of PF-MCM-41 catalyst. Test reaction was carried out by mixing tetracyanoethylen (0.13 g, 1 mmol) and dimedone (0.13 g, 1.10 mmol) in various solvents in the presence of 0.01 g of PF-MCM-41. As can be seen from Table 1, CH_2Cl_2 is the best solvent respect to yield and short reaction time. In the case of H_2O, the reaction time is long for the reasonable yield (Table 1, Entry 1).

Recyclability of the catalyst was examined too. For this reason, catalyst which was recovered from reaction between TCNE and tetronic acid by filtration was washed with 5 ml CH_2Cl_2; after drying the catalyst in oven (70 °C, 24 h), it was

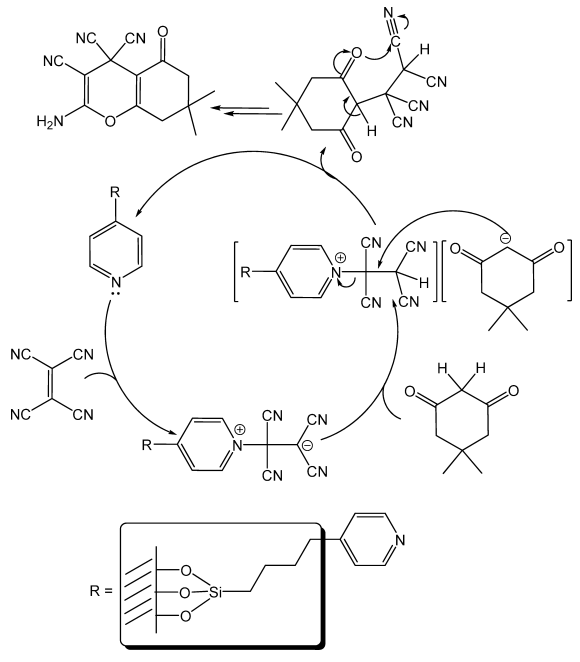
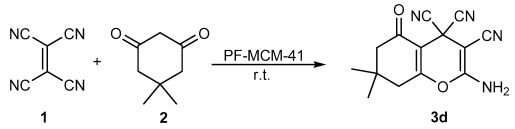


Chart 3. Proposed Pathway

used again. This procedure was carried out for four times. Results of these successive reactions are shown in Table 2. It is clear that by successive use of catalyst no decrease in reactivity or performance can be seen.

One of the aims of the present investigation is to solve the problems of using homogeneous catalyst such as separation and regeneration. Ease of separation is one of the most im-

Table 1. Effect of Solvent on the Reaction Times and Yields[a)]



Entry	Solvent	Time	Yield (%)
1	H_2O	16 h	70
2	EtOH	16 h	60
3	CH_3CN	16 h	55
4	$C_6H_5CH_3$	16 h	50
5	*n*-Hexan	16 h	40
6	CH_2Cl_2	15 min	90, 92, 90, 92, 94

a) Dimedone (1.1 mmol), tetracyanoethylen (1.0 mmol) in the presence of PF-MCM-41 (0.01 g) at room temperature in various solvents.

Table 2. Recycle of Catalyst[a)]

Cycle	PF-MCM-41 (g)	Yield (%)
1	0.019	93
2	0.018	91
3	0.018	92
4	0.014	92

a) Dimedone (1.1 mmol), tetracyanoethylen (1.0 mmol) in the presence of PF-MCM-41 (mentioned in table) at room temperature in CH_2Cl_2.

portant characteristics of heterogeneous catalysts. The separation of PF-MCM-41 from the reaction medium easily was carried out by filtration. After drying, it was reused for subsequent reactions (Table 2). Thus, this process could be also interesting for large-scale synthesis.

Conclusions

In conclusion, we have developed a rapid and very efficient pyridine-functionalized MCM-41-catalyzed approach for the synthesis of pyran annulated heterocyclic ring systems under mild reaction conditions with excellent yields. The present method has the advantages that not only the catalyst can be recycled and reused for several times without loss of performance, but also the substances can be mixed without any modification. The work-up procedure is very simple and the products do not require further purification. The simplicity of the present procedure makes it an interesting alternative to other approaches.

Experimental

Techniques and Materials Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.47 MHz. NMR spectra were obtained in DMSO-d_6. The chemicals used, were purchased from Merck and Fluka Chemical Companies.

Typical Experimental Procedure. Preparation of 2-Amino-5-*oxo*-5*H*-furo[3,4-*b*]pyran-3,4,4(7*H*)-tricarbonitrile (3a) To a magnetically stirred solution of tetracyanoethylene (0.13 g, 1.0 mmol) and PF-MCM-41 (0.01 g), in CH_2Cl_2 (15 ml), a solution of tetronic acid (0.10 g, 1.0 mmol) in CH_2Cl_2 (2 ml) was added drop wise at room temperature and the reaction mixture was stirred for 15 min. After completion of the reaction, solid catalyst was separated from reaction mixture by filtration. Then, solvent was removed under reduced pressure and the residue was crystallized from CH_2Cl_2/*n*-hexane 1 : 2 to yield 0.241 g of **3a** as a pink powder (90%). mp 198—200 °C. IR (KBr) (ν_{max}, cm^{-1}): 3424, 3338 (NH_2), 2210 (CN), 1741 (C=O). ^{1}H-NMR (300 MHz, DMSO-d_6) δ_H (ppm): 5.14 (2H, s, CH_2), 8.76 (2H, bs, NH_2). ^{13}C-NMR (75 MHz, DMSO-d_6) δ_C (ppm): 49.28, 67.30, 93.23 (C4, C3, C7), 112.61 (CN), 116.46 (CN), 141.20 (C5), 160.91, 167.01, 172.00(C6, C2, C9). MS, *m/z* (%): 228 (M$^+$, 20), 184 (40), 158 (100), 132 (55), 106 (30), 90 (35), 43 (60). *Anal.* Calcd for $C_{10}H_4N_4O_3$: C, 52.64; H, 1.77; N, 24.56. Found: C, 52.54; H, 1.73; N, 24.58.

Preparation of PF-MCM-41 A solution of 4-methyl-pyridine (8.0 mmol) in THF (40 ml) was added to a THF solution of lithium diisopropylamine (8.0 mmol). After 2 h the brown solution was cooled to −20 °C and then MCM-41 grafted with chloropropylsilyl groups was added (2.0 g). After 72 h, the reaction mixture was treated with the mix of ice and water. The solution was filtered off and the pale solid washed three times with 15 ml aliquots of ethanol, three times with 15 ml aliquots of diethyl ether, and dried under reduced pressure at room temperature for 48 h. Desired PF-MCM-41 was obtained quantitatively.

All of the products are known compounds (except product **3a**), which were characterized by IR, ^{1}H, ^{13}C-NMR, and mass spectra data. Their melting points were compared with literature reports, too.[23)]

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