Selective mono-methylation of phenylacetonitrile to 2-phenyl propionitrile over 3-aminopropylsilyl functionalized MCM-41

C. Venkatesan and A.P. Singh *

Catalysis Division, National Chemical Laboratory, Pune 411 008, India

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Selective mono-methylation of phenylacetonitrile to 2-phenylpropionitrile by dimethyl carbonate as an alkylating agent was studied for the first time using alkali-ion-exchanged and organic base functionalized MCM-41 as catalyst. 3-Aminopropylsilyl functionalized NH_2-Na-Al-MCM-41 is found to be the superior catalyst among a series of alkali-ion-exchanged MCM-41 and microporous basic zeolite catalysts giving 98.4 wt% conversion of phenylacetonitrile and >92 wt% selectivity to 2-phenylpropionitrile.

KEY WORDS: methylation; phenylacetonitrile; 2-phenylpropionitrile; NH_2-Na-Al-MCM-41.

1. Introduction

Since mono-methylated arylacetonitriles are important precursors of 2-arylpropionic acids, the well-known anti-inflammatory drugs [1], the alkylation of phenylacetonitrile (PAN) under safe conditions and with non-toxic alkylating agents instead of toxic and corrosive alkylating agents such as phosgene, dimethylsulfate and methyl iodide is of interest. Direct base-promoted mono-alkylation of methylene-active compounds is not easy in industry because of the relevant quantity of dimethyl derivatives obtained with the usual methylating agents [2,3]. Since the reaction usually proceeds to dialkylation, even under phase transfer catalysis conditions, the direct mono-methylation of PAN was less selective [4,5]. Tundo *et al.* [6,7] observed very high selectivity for the mono-methylation of PAN when dimethyl carbonate (DMC) was used as an alkylating agent under gas–liquid phase-transfer catalyst conditions. Under vapor phase and methanol as alkylating agent, basic zeolites were also examined [8]. Alkali metal carbonates and organic bases have been studied in the selective mono-methylation of aryl acetonitrile and methyl aryl acetates in detail under batchwise conditions [9]. Many solid bases have recently been found useful in the production of fine chemicals [10–13]. Recent advances in the area of mesoporous silica materials mean that the organic functionalized and alkali-ion-exchanged MCM-41 with higher surface area may be prepared by careful control of the synthesis conditions [14,15]. They can also be synthesized over a large range of framework Si/Al ratios and could be developed as basic catalysts [16,17], particularly for those who are dealing with large molecules as in fine chemistry and pharmaceutical production, and overcome the steric limitations presented by microporous molecular sieves. Basicity would be favored by larger aluminum content in the structure and the electropositive nature of the charge-compensating cations. To our knowledge there is no report using amine-functionalized and alkali-ion-exchanged mesoporous materials for the mono-methylation reaction of PAN with DMC. In this paper we report for the first time our studies on the catalytic activity of aminopropyl silyl functionalized MCM-41 catalyst in the selective mono-methylation of PAN with DMC (scheme 1, see table 1). The influence of reaction temperature was also examined on the conversion of PAN, rate of PAN conversion and selectivity for 2-phenylpropionitrile (2-PPN) using NH_2-Na-Al-MCM-41. The result obtained over NH_2-Na-Al-MCM-41 is compared with that over the conventional base, K_2CO_3.

2. Experimental

Fumed silica (Sigma), 3-aminopropyltriethoxysilane (3-APTS, Lancaster), sodium aluminate (28.4% Na_2O, 46.8% Al_2O_3, 24.8% H_2O), cetyltrimethylammonium bromide (CTMAB, Loba), tetramethylammonium hydroxide (TMAOH 25% solution in water, Loba), potassium nitrate and deionized water were used as the reagents for the synthesis of catalysts. The Na-Al-MCM-41 and NH_2-Na-Al-MCM-41 materials were synthesized by a modified refluxing method [18]. Typically, the molar composition of the synthesis mixture was as follows:

SiO_2	0.018
Al_2O_3	0.24
CTMAB	0.3
TMAOH	0.018
Na_2O	120
H_2O	

* To whom correspondence should be addressed.
E-mail: apsingh@cata.ncl.res.in

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For the synthesis of NH_2-Na-Al-MCM, tetraethyl orthosilicate (TEOS) and 3-aminopropyltriethoxysilane (3-APTS) in methanol were taken in the molar ratio of 0.8 : 0.2, respectively. The synthesis mixture was stirred for 3 h and refluxed at 373 K for 48 h. The final products (NH_2-Na-Al-MCM-41 and Na-Al-MCM-41) were obtained as reported in reference [19]. K-Na-MCM-41 was obtained by the ion exchange of Na-Al-MCM-41 with 1 M KNO_3 solution at 353 K for 6 h. Supported K/Na-MCM-41 was obtained by the incipient wetness method using KNO_3 and then calcined at 813 K for 6 h [13]. KL was synthesized according to the literature [20]. The samples were analyzed for Si/Al ratio and cations by wet chemical analysis and atomic absorption spectroscopy (AAS). All the synthesized samples were characterized by X-ray diffractograms (Rigaku D MAX III VC with Cu K_α radiation, $\lambda = 1.5418$ Å). The catalysts were further characterized by N_2 adsorption (BET) techniques for surface area. The selective mono-alkylation of phenyl acetonitrile with DMC as alkylating agent was carried out in a 250 ml stainless Parr autoclave equipped with stirrer and temperature controllable sensor. All the catalysts were activated at 473 K for 3 h and stored in a desiccator for a few minutes before the reaction. In a typical run freshly activated catalyst (0.5 g) was added to the phenyl acetonitrile (15 mmol) and DMC (300 mmol) mixture in the stainless steel autoclave and flushed with nitrogen before heating to the required temperature. The products were analyzed by a gas chromatograph (HP 6890) equipped with an FID detector and capillary column (50 m × 0.2 mm) of methyl silicone gum. The products were also identified by GC-MS and compared with authentic samples. The rate of PAN conversion is calculated in terms of turnover frequency (TOF), *i.e.* number of moles of PAN converted per hour per mole of Al.

3. Results and discussion

The Si/Al ratio and surface areas of the samples decrease drastically when alkali metals (Na, K) are loaded over Na-Al-MCM-41, which is attributed to the dissolution of surface by the alkali and results in the formation of potassium silicate and potassium aluminate [13]. A similar effect is also confirmed in an XRD pattern as shown in figure 1, where the intense basic hexagonal peak (100) decreases when alkali metal is exchanged or loaded over Na-Al-MCM-41. The physicochemical and catalytic activities of various basic catalysts such as Na-Al-MCM-41, K-Na-Al-MCM-41, K/Na-Al-MCM-41, NH_2-Na-Al-MCM-41 and microporous zeolite KL in the selective mono-methylation of PAN with DMC in batchwise conditions at 473 K for 10 h are presented in table 1. The results obtained over various heterogeneous solid base catalysts are compared under identical reaction conditions with the conventional catalyst, K_2CO_3. The main product, 2-PPN, results from the selective side-chain mono-methylation of PAN. Disubstituted products are also detected, which are formed by the consecutive reactions, while trace amounts of others (ring-substituted products) are obtained by the parallel reactions. Na-Al-MCM-41 gave lower activity

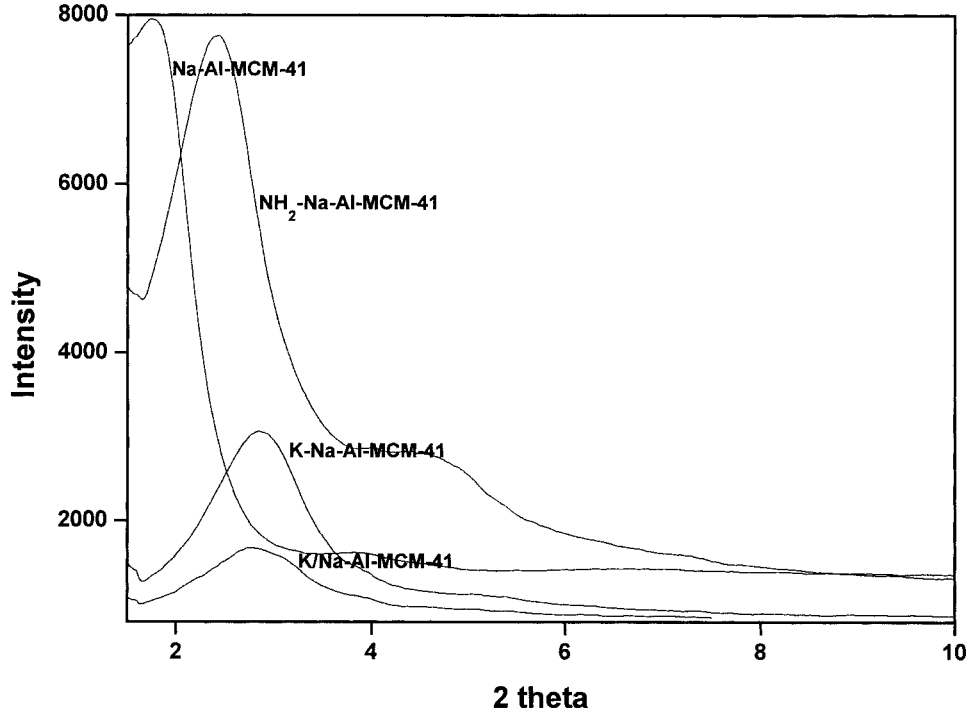


Figure 1. X-ray diffractograms for various MCM-41 catalysts.

for PAN conversion (11.1 wt%) and selectivity to 2-PPN (31 wt%) whereas microporous KL zeolite has moderate activity for PAN conversion (55.5 wt%) and selectivity (53 wt%). The K-exchanged Na-Al-MCM-41 gave a conversion of PAN of 56.2 wt% and a selectivity for 2-PPN of 70 wt%, while the KNO_3 loaded (2.07 mmol/gm) over Na-Al-MCM-41 (K/Na-Al-MCM-41, obtained by the incipient wetness method) increases the catalytic activity higher, 89.4 wt% PAN conversion and 89 wt% selectivity for 2-PPN, which may be attributed to the formation of K_2O species (produced during calcination at 813 K) on the surface which provides higher basicity to the catalyst. The one-step pot synthesized NH_2-Na-Al-MCM-41 shows superior activity and selectivity compared with the other catalysts. Under identical reaction conditions, NH_2-Na-Al-MCM-41 shows 98.5 wt% conversion of PAN and 91 wt% 2-PPN selectivity. 3-Aminopropylsilyl groups anchored on the walls of mesoporous walls show a remarkable activity for the methylation of PAN and selectivity to 2-PPN. The TOF of PAN conversion over Na-Al-MCM-41, K-Na-Al-MCM-41, K/Na-Al-MCM-41, NH_2-Na-Al-MCM-41 and zeolite KL is found to be 15.4, 33.5, 33.2, 1372.5, and $42.5 \times 10^{-2}\,h^{-1}\,mol^{-1}$ Al, respectively. The catalyst (NH_2-Na-Al-MCM-41) polarizes the DMC into an electrophile (CH_3^+), which in turn reacts with active methylene carbon of PAN, resulting in the formation of 2-PPN. Under identical reaction conditions, the K_2CO_3 gave comparable conversion of PAN (100 wt%) but selectivity is found to be poor, 80 wt% compared with the mesoporous KNO_3 loaded K/Na-Al-MCM-41 and NH_2-Na-Al-MCM-41 catalysts.

The influence of temperature on the selective mono-methylation of PAN with NH_2-Na-Al-MCM-41 catalyst at a constant catalyst/PAN ratio of 0.28 was studied with different temperature ranges, *i.e.* 423–473 K. The variation of conversion of PAN, rate of PAN conversion and product distribution as a function of reaction temperature is given in figure 2. A significant increase in the conversion of PAN is achieved with increase in the reaction temperature. At lower temperature (423 K) the conversion of PAN, rate of PAN conversion and selectivity for 2-PPN are 13.9 wt%, $1.94\,h^{-1}\,mol^{-1}$ Al (TOF) and 22 wt%, respectively. The lower selectivity for 2-PPN at lower temperature may be attributed to the formation of reaction intermediates as evidenced by Tundo *et al.* [6]. The conversion of PAN and selectivity to 2-PPN increases from 13.9 to 36.9 wt% and 28 to 66 wt%, respectively, when the temperature is increased from 423 K to 433 K. While the activity is less, the selectivity is higher as compared with the reported K_2CO_3 catalyzed reaction at the same reaction conditions [6]. Again, when the temperature increased from 433 K to 443 K, the conversion of PAN, rate of PAN conversion and selectivity for 2-PPN increased to a higher level, *i.e.* 89.7 wt%, $12.5\,h^{-1}\,mol^{-1}$ Al (TOF) and 91 wt%, respectively. Further increase in the reaction temperature (453 K) gave a marginal increase in the PAN conversion (98.4 wt%), rate of PAN conversion ($13.73\,h^{-1}\,mol^{-1}$ Al) and selectivity for 2-PPN (92 wt%). Selectivity for 2-PPN starts decreasing slowly at higher temperature above the optimum level (>453 K), indicating the formation of di-alkylated product. The reasons for the higher conversions at higher temperature may be attributed to the effective polarization of DMC into an electrophile (CH_3^+) and activation of active methylene group of PAN. The calculated apparent activation energy for the mono-methylation of PAN is 108 kJ/mol.

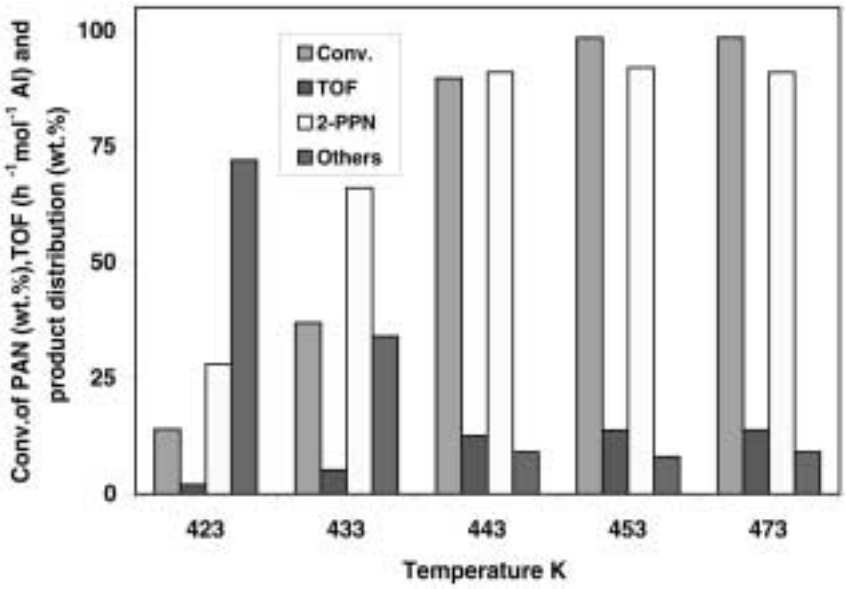
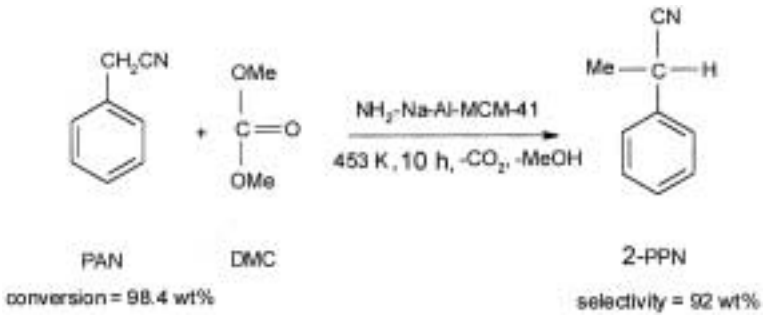


Figure 2. Influence of reaction temperature on the conversion of PAN (wt%), TOF ($h^{-1}\,mol^{-1}$ Al) and product distribution. Reaction conditions: see the footnotes to table 1.

Table 1
Activities of different catalysts in the mono-methylation of PAN



Scheme 1

Catalyst	SiO_2/Al_2O_3 (molar ratio)	Cations (%) [a]		Surface area [b] (m^2/g)	Conv. of PAN (wt%) [c]	TOF ($10^{-2}\,h^{-1}$ mol^{-1} Al)	Product selectivity (wt%) [d]	
		Na	K				2-PPN	Others
Na-Al-MCM-41	33	98.2	1.8	1243	11.1	15.4	31	69
K-Na-Al-MCM-41	14	25.1	74.9	540	56.2	33.5	70	30
K/Na-Al-MCM-41 [e]	9	20.3	79.7	91	89.4	33.2	89	11
NH_2-Na-Al-MCM-41 [f]	33	98.2	1.8	558	98.5	1373	91	9
K-L	6.8	2	98	215	55.5	42.5	53	47
K_2CO_3	–	–	100	–	100	–	80	20

[a] Chemical analysis by atomic absorption spectroscopy.
[b] Measured by N_2 adsorption (BET method).
[c] Reaction conditions: PAN = 0.015 mol; DMC = 0.3 mol; catalyst = 0.5 g; reaction temperature = 473 K; reaction time = 10 h.
[d] 2-PPN = 2-phenyl propionitrile; others = dimethylated and ring products.
[e] KNO_3 loaded on Na-Al-MCM-41.
[f] Elemental analysis (Perkin-Elmer CHN analysis); C = 6.68, H = 2.71, N = 2.65%.

4. Conclusions

In summary, NH_2-Na-Al-MCM-41 catalyzes the mono-methylation of PAN with DMC efficiently, which leads to the formation of 2-PPN in high selectivity (92 wt%). Under identical reaction conditions the activity (conversion of PAN) trend after 10 h reaction time is as follows: $K_2CO_3 > NH_2$-Na-Al-MCM-41 > K/Na-Al-MCM-41 > K-Na-Al-MCM-41 > KL > Na-Al-MCM-41. It is concluded that the presence of strong basic sites in the catalysts seems to be the important factor for the polarization of substrates and also for the formation of 2-PPN. A higher yield of the products can be achieved by increasing the reaction temperature up to an optimum reaction temperature (453 K).

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