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Research paper

Conversion of Zeolite-X into Various Ion Exchanged Forms and Investigation of their Catalytic Efficiency for the Synthesis of 5- Substituted 1H-tetrazole Derivatives

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ABSTRACT

We have developed lucid protocol for the synthesis of 5- substituted 1H-tetrazole derivatives under various aromatic aldehydes in presence of catalyst Zeolite H- X under solvent free condition. In this method reaction times decreases with many more advantages (like low costs, quantitative yields, without using any organic solvent). We also found derivatives of 5-substituted 1H- tetrazole with good to impressive yields (90–97%). In the present experimentation synthesized zeolite is characterized by using techniques like X-ray diffraction (XRD), scanning electronic microscopy (SEM), and Fourier transform-infrared (FT-IR spectroscopy) and catalyst is separated by simple filtration and washed with appropriate solvents without loss of any catalytic activity.

1. Introduction

In medicinal chemistry, material science and catalysis, there is a great applicability of nitrogen- containing heterocyclic compounds among which Tetrazoles form a major category (Bai et al., 2011; Damavarapu et al., 2010). Tetrazoles are significantly used as a non-classical bio-isosteres to carboxylic acids and they help in imparting high lipophilicity, better absorption and show resistance to metabolism (Herr, 2002). Tetrazoles are contained in Sartans like candesartan- an anti-hypertensive, to melukast- an anti-asthmatic, pemirolast- an anti- allergic, valsartan and Iosartan (Alonen et al., 2008). It also finds its applicability in a number of biological phenomena where it acts as an anti-inflammatory, anti-fungal, anti-viral, anti-diabetics, anti-tubercular, anti-cancer, so on and so forth (Karabanovich et al., 2015; Ostrovskii et al., 2012; Sangal and Kumar 1986; Wood et al., 2001: Crossby et al., 2010). The synthesis of various

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tetrazole-based structures is a process of continuous exploration because of its wide usage universally. In their synthesis, one-pot strategy is beneficial because the isolation of intermediate products is avoided (Wittenberger et al., 1994; Duncia, 1991). Many homogenous catalysts which contain metals such as Fe(OA2c), copper acetate, Bronsted and Lewis acids and zinc(II) salts (Demko and Sharpless, 2001; Bonnamour and Bolm, 2009; Heravi et al., 2012) were used in carrying out some of the above reactions but the methods mentioned above also have some de-merits which include the use of toxic nitriles as a starting material, excessive reagents and use of strong Lewis acids. Aluminium azides and tin were used as the source of azide in some reactions but these are toxic organo- metallic reactants and have no convenience while separating the metal residue (Aureggi et al., 2007). In comparison to nitriles, aldehydes are easily accessible, are less toxic and are easy enough to be handled. In the process of synthesis of tetrazoles from aldehydes, very few methods have been witnessed. i.e. $ZnBr_2$, Cu-MCM- 41, P_2O_5, ZSM-5, Magnetized water, Cu $(OAc)_2$ and 1, 3 dipolar cycloaddition (Sridhar et al., 2013; Khan et al., 2016; Ghodse et al., 2018; Bakherad., 2017: Tisseh et al., 2012). Some other disadvantages of such methods of synthesis also include long reaction time, un-easy reaction condition and highly toxic substance is generated.

In our analysis we report herein silica supported Zeolite H-X as a catalyst for the synthesis of 5-substituted 1H-tetrazoles between sodium azide, malononitrile and various aromatic aldehydes.

2. Methodology

2.1 Synthesis of Zeolite-X

For Synthesis of Zeolite-X 50g of Sodium Hydroxide is dissolved in 50 ml of distilled water. To it 48.5 g of Alumina Trihydrate is added and stirred at 100 °C until dissolved as per the method of Wang and Zhou (2013).

2.2 Conversion of Zeolite-X

The schematic representation of conversion of Zeolite material into ion exchanged forms is shown below in Fig. 1.

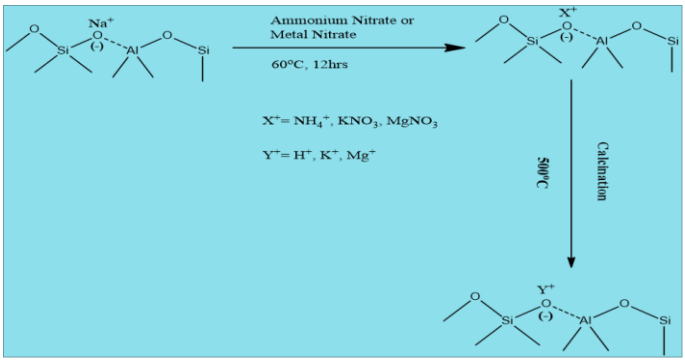

Fig. 1 Schematic representation of conversion of Zeolite- X into ion exchanged forms

2.3 Synthesis of 5-substituted 1H-tetrazoles

A mixture of aldehyde (1.0 mmol), malononitrile (1.0 mmol), sodium azide (1.0 mmol) and catalyst Zeolite H-X (0.05g) are added to a 10-mL round-bottomed flask. The reaction combination is stirred at 60^0C, and the reaction evolution is monitored by TLC using ethyl acetate as the eluent. After achievement of the reaction, the impetuous formed is filtered and purified by recrystallization from chloroform to give the preferred product (Fig. 2).

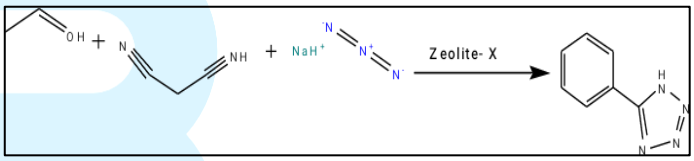

Fig. 2 Synthesis of 5-substituted 1H-tetrazoles

2.4 Spectral Data

Spectral data obtained was as per reported by Bai et al. (2011).

3. Characterization

3.1 X-ray Diffraction

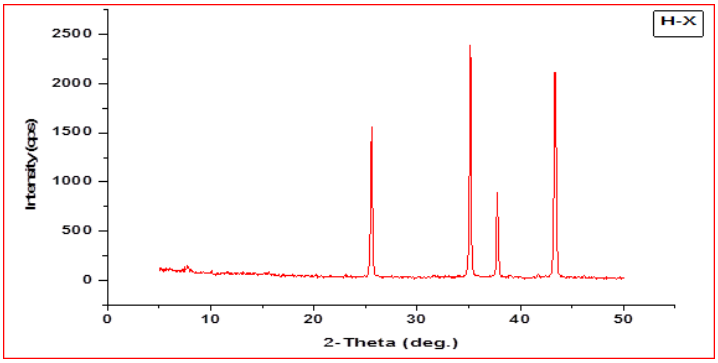

Fig. 3(a) XRD spectrum of Zeolite Na-X

For X-ray diffraction, the samples are sieved in an ABNT number 200 (0.074mm) sieve and then placed in an aluminum sample holder for X-ray diffraction assays, using Shimadzu XRD 6000 equipment.

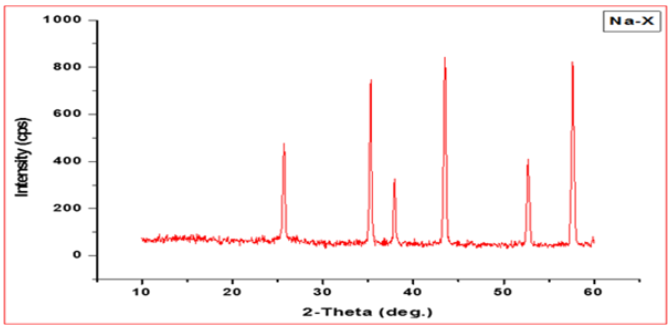

Fig. 3(b) XRD spectrum of Zeolite H-X

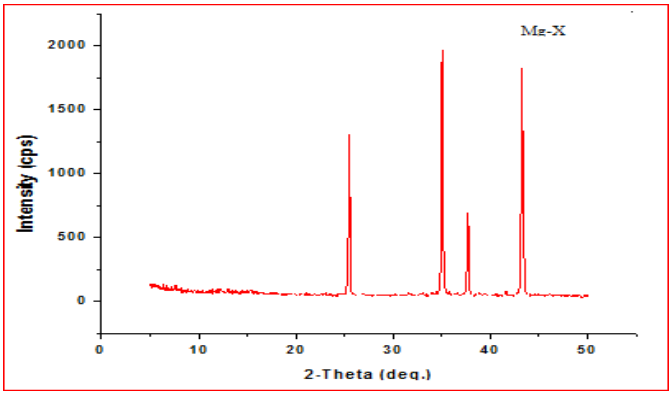

Fig. 3(c) XRD spectrum of Zeolite Mg-X

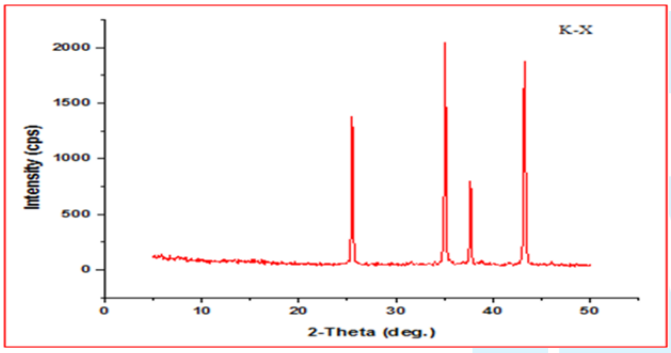

Fig. 3(d) XRD spectrum of Zeolite K-X

Powder X-ray diffraction pattern of calcined Zeolite-X, H-X-form and metal ion exchanged forms (Mg+ zeolite- X, K+ zeolite- X) are shown in Figs. 3 (a-d). In all these cases the degree of crystallinity is very high and the materials are crystalline in nature without any amorphous phase. Zeolite-X has maximum peak intensity for the major diffraction peaks. Also change in the diffraction patterns among the three forms can be attributed to perturbations in the framework structure, crystal morphology, phase purity and crystal size. From the diffraction signals, the sharp peak at 2 value corresponding to 16.5 for zeolite-X is clearly observed. Further it is observed that the X-ray diffraction pattern of H –X form and various metal ion exchanged forms (Mg+ zeolite- X, K+ zeolite- X) are similar to the diffraction patterns of their parent zeolite. These observations indicate that zeolite framework has not undergone any significant structural change during the incorporation of metal ion, thus only slight changes in the intensity of the bands were observed. Slight change in the intensities of the peaks suggested that the super cage of zeolites were able to store metal ions without any strain.

3.2 Fourier Transform-Infrared spectroscopy (FT-IR)

FTIR spectroscopy is used to identify the structural features and adsorption sites in the Zeolite materials. For FTIR analysis, samples are subjected to physical treatment in accordance with KBr method, which consists of mixing 0.007 g of the sample and 0.1 g of KBr, grinding and pressing the solid mixture to 5 ton for 30 s in order to form a pellet that allows the passage of the light. In the present studies, FT- IR spectra are obtained using the Perkin Elmer Spectrum two FTIR Spectrometer in the wavelength range from 4000 cm^{-1} to 500 cm^{-1}.

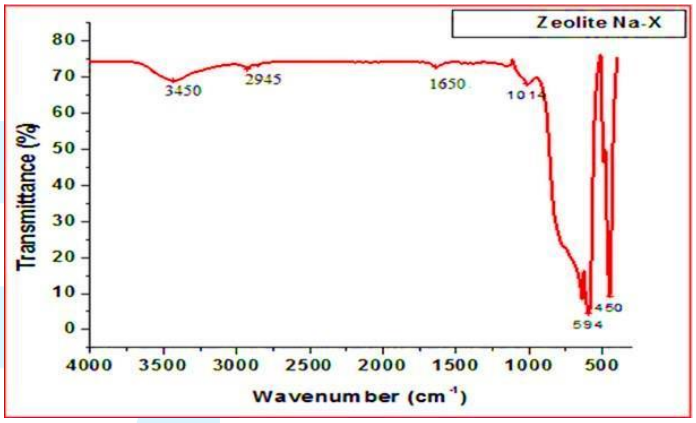

Fig. 4(a) FTIR spectra of Zeolite Na-X

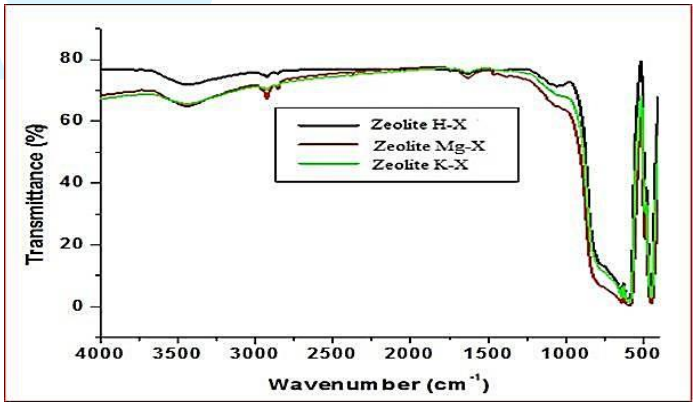

Fig. 4(b) FTIR spectra of various forms of Zeolite

Fig. 4(a) represents the FTIR spectrum of the Zeolite Na-X. The absorption band at around 450cm^{-1} is attributed to Si, Al-O bond and those at 1014 cm^{-1} and 594 cm^{-1} respectively are attributed to asymmetric and symmetric stretches of the Zeolite framework. A band for OH group observed at 3450 cm^{-1}. Fig. 4(b) represents the FTIR spectra of the various ion exchanged forms of the Zeolite -X, it is obviously observed that spectra of various ion exchanged forms

of Zeolite -X are similar to their individual parent Zeolite materials.

3.3 Scanning Electron Microscopy (SEM)

Surface micrographs of calcined Zeolite-X , its H forms and metal ion exchanged forms (Mg^+ zeolite-X, K^+ zeolite-X) are obtained by SEM (JEOL-JSM 5800, SEM) instrument. Scanning electron micrographs (SEM) of zeolites are taken at 10,000X magnifications for understanding crystal morphology of these samples is shown in Fig. 5.

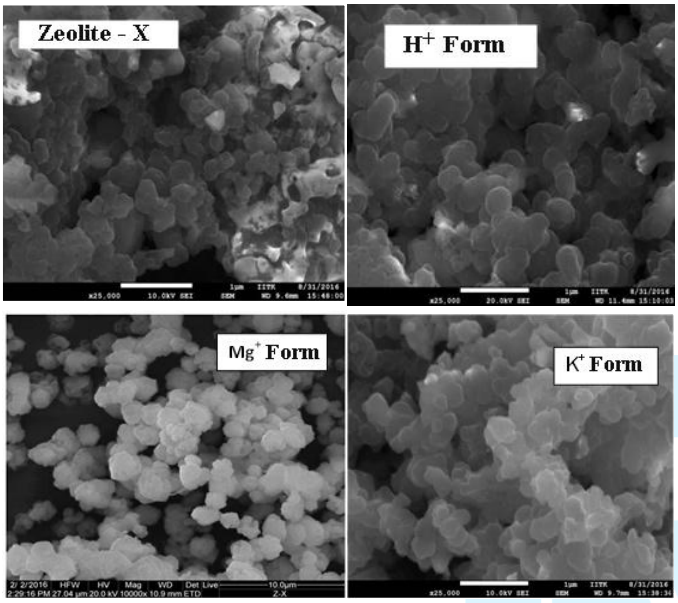

Fig. 5 SEM Images of various forms of Zeolite-X

From Fig. 5 Zeolite-X particles mostly appears as thin polyhedrons having particle size in 1-3µm range. Further it is clearly observed that surface micrographs of H form and various metal ion exchanged forms of zeolite- X are similar to the surface micrographs of their parent zeolite- X which shows that they possess the same morphology. However small variation in the surface micrographs of some forms is observed and this may be due to impurity deposition on zeolite surface by organic part of ammonium salt and metal salt used during the formation of H form and various metal ion exchanged forms which could not have been removed properly during calcination process.

4. Result and Discussion

Zeolite-X, their H- form and metal ion-exchanged forms (H^+ zeolite- X, Mg^+ zeolite- X, K^+ zeolite-X) are synthesized and their catalytic is studied for the synthesis of 5- substituted 1H-tetrazoles. Catalytic activity of H- form Zeolite- X and metal ion-exchanged forms (Mg^+ zeolite- X, K^+ zeolite- X) are used as catalyst to test the catalytic efficiency for the Synthesis 5-substituted 1H-tetrazoles by varying:

4.1 Effect of catalyst

Activity of different forms of (H+ zeolite- X, Mg+ zeolite- X, K+ zeolite- X) for the synthesis of tetrazole derivatives are investigated by using reactants benzaldehyde, malononitrile and sodium azide in the molar ratio of 1:1:1 and catalyst amount 500 mg without solvent reflux condition for 12 minutes at 60 ^oC. Fig. 6 shows %e yield of tetrazoles over various zeolite – X forms and it is found that the activity decreases in the order H^+-form > K^+ - form. >Mg^+-form This is because of the higher surface area and active sites present in H^+-form than other forms which decreases in the above order (Table 1 & Fig. 6).

Table 1 Effect of catalyst on % yield of tetrazoles

[a]Catalytic forms	[b]Zeolite- X
H^+ Form	97
K^+ Form	91
Mg^+ Form	85

[a]Reaction conditions: Benzaldehyde: malononitrile: sodiumazide: 1:1:1, Time 12 min, Temperature 60 ^oC; [b]Isolated yields

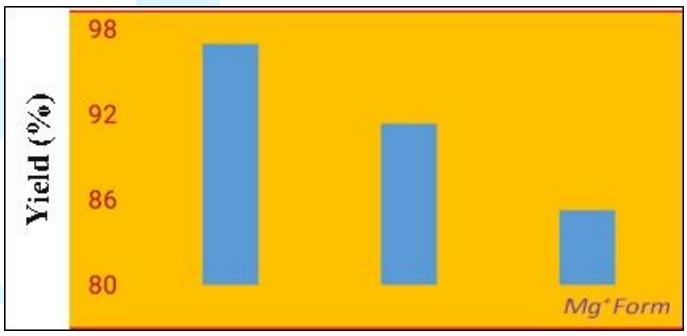

Fig. 6 Effect of catalyst on % yield of tetrazoles over various zeolite-X forms

4.2 Effect of Reaction Time

Effect of reaction time on the synthesis of tetrazoles over various catalytic forms of zeolites-X (H^+ zeolite-X, Mg_+ zeolite- X, K^+ zeolite- X) is studied by using reactants benzaldehyde, malononitrile and sodium azide in the molar ratio of 1:1:1 at 60 ^oC. Fig. 7 shows % yield of tetrazoles over various catalytic forms of zeolite- X at various time intervals. It is observed that %e yield increases with time up to certain optimum reaction time (12 minutes) after which it increases slightly rather remains almost constant. The reason for this increase may be attributed to increase in contact time between reactants and catalyst which is responsible for their conversion into final products. After optimum time no further increase in yield is

observed because reaction gets almost completed within this period (Table 2 & Fig. 7).

Table 2 Effect of reaction time on % yield of tetrazoles over various catalytic Forms of Zeolite- X

[a]Time (min)	[b]H+ zeolite-X	[b]K+ zeolite-X	[b]Mg+ zeolite-X
3	63	60	56
6	75	71	67
9	86	82	76
12	97	84	81
15	97	89	85
18	97	94	91

[a]Reaction conditions: Benzaldehyde: malononitrile: sodium azide: 1: 1:1, Temperature 60 °C [b]Isolated yields

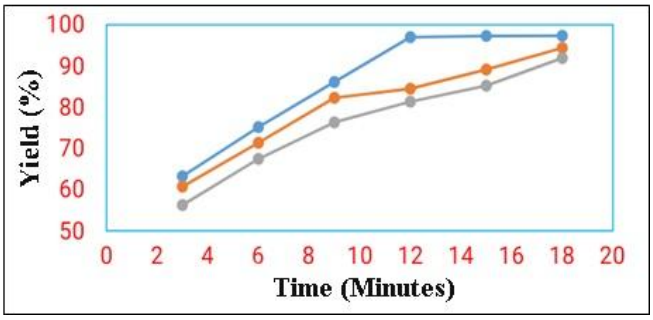

Fig. 7 Effect of reaction time on % yield of tetrazoles over various catalytic Forms of Zeolite- X

4.3 *Effect of amount of catalyst*

The effect of amount of catalyst on the synthesis of tetrazoles over various catalytic forms of zeolite- X (H^+ zeolite-X, Mg^+ zeolite- X, K^+ zeolite-X,) is investigated over a range of 100-600 mg at 60°C keeping all other parameters constant. Fig. 8 shows %e yield of tetrazoles over various catalytic forms of zeolite-X at different amounts. It is observed that yield of tetrazoles increases with increasing the amount of catalyst in the range of 200 – 600 mg after that it remains constant. The reason for this increasing up to 500 mg may be attributed to increase in availability of active sites with increase in amount of catalyst. These active sites bind to reactants and convert them into their final products. Thus the weight of above used catalyst equal to 500 mg is the maximum catalyst loading for the synthesis of tetrazole derivatives (Table 3 & Fig. 8).

Table 3 Effect of amount of catalyst on % yield of tetrazoles over various Catalytic forms of Zeolite- X

[a]Catalyst weight (mg)	[b]H+ zeolite-X	[b]K+ Zeolite-X	[b]Mg+ Zeolite-X
200	70	65	60
300	78	75	71
400	86	81	77
500	97	88	82
600	97	88	82

[a]Reaction conditions: Benzaldehyde: malononitrile: sodiumazide: 1:1:1, Temperature 60 °C, Time: 6 minutes; [b]Isolated yields

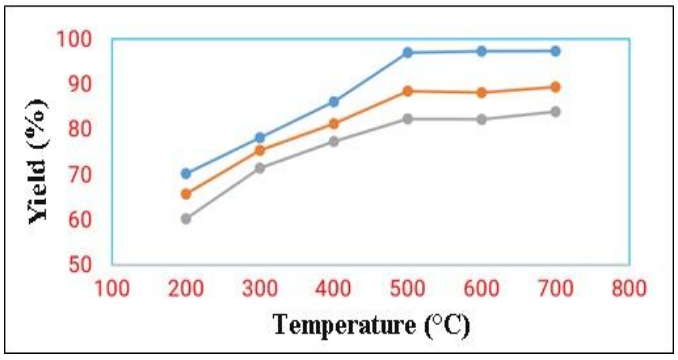

Fig. 8 Effect of weight of catalyst on %e yield of tetrazoles over various Catalytic forms of Zeolite- X

4.4 *Effect of reaction temperature*

Effect of reaction temperature on the synthesis of tetrazoles over various catalytic forms of zeolite- X (H^+ zeolite-X, Mg^+ zeolite-X, K^+ zeolite-X) is studied by taking reactants benzaldehyde, malononitrile and sodium azide at varying temperature from 15 °C to 75 °C. Fig. 9 shows %e yield of tetrazoles over various catalytic forms of zeolite- X at different amounts. It is observed that yield of tetrazoles increases with increasing temperature up to 60°C after which it remains constant. Yield increases because increase in temperature activates the reactants by providing them necessary activation energy for their conversion into products. After 60°C there is almost no further increase in yield because at this temperature the reactants have attained sufficient energy equal to required activation energy and further increase in energy has no impact on reaction (Table 4 & Fig. 9).

Table 4 Effect of reaction temperature on %e yield of tetrazoles over various Catalytic forms of Zeolite-X

[a]Reaction Temperature (° C)	[b]H+ zeolite- X	[b]K+ zeolite-X	[b]Mg+ zeolite-X
20	76	68	63
40	86	81	75
60	97	92	85
80	97	92	85

[a]Reaction conditions : Benzaldehyde: malononitrile: sodium azide: 1: 1:1, Time: 12 min; [b]Isolated yields

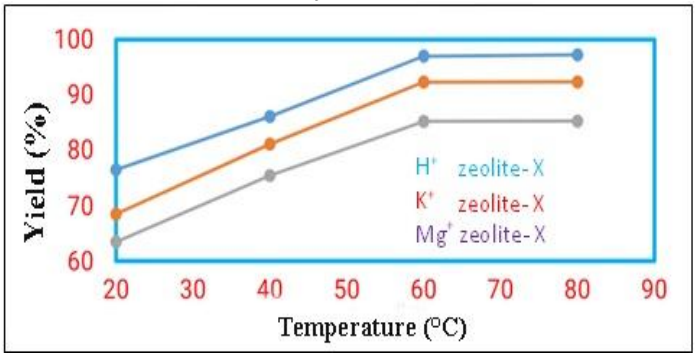

Fig. 9 Effect of reaction temperature on %e yield of tetrazoles over various Catalytic forms of Zeolite-X

4.5 Catalyst Recycling

Effect of catalyst recycling on the synthesis of tetrazoles over various catalytic forms of zeolite- X (H^+ zeolite- X, Mg^+ zeolite- X, K^+ zeolite- X) is studied by recycling above catalyst thrice and re-using them in the same reaction at 60°C keeping the other parameters constant. Fig. 10 shows %e yield of tetrazoles over various catalytic forms of zeolite- X. Recycling experiments are conducted to find out the stability of the catalyst after the reaction. Using the fresh H+ Zeolite- X as catalyst (500 mg) the yield of product is 97 % while the recovered catalyst in the three subsequent runs gave the of 95.20%, 93.41% and 90.17% respectively (Table 5 & Fig. 10).

Table 5 Effect of catalyst recycling on %e yield of xanthenes over various Catalytic forms of Zeolite-X

[a]Runs	[b]H^+ zeolite-X	[b]K^+ Zeolite-X	[b]Mg^+ Zeolite-X
1st run	97	95	93
2nd run	95	92	90
3rd run	93	90	87
4th run	90	88	83

[a]Reaction conditions: Benzaldehyde: malononitrile: sodium azide: 1: 1:1, Time: 12 min, Temperature: 60 °C; [b]Isolated yields

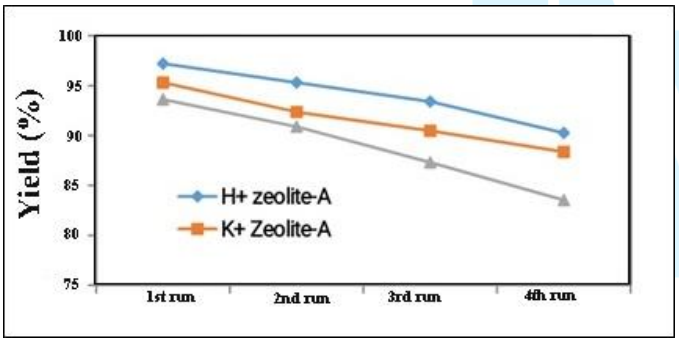

Fig. 10 Effect of catalyst recycling on % yield of tetrazoles over various Catalytic forms of Zeolite- X

Initially the focus is on the synthesis of 5-substituted 1H-tetrazole derivatives and reaction is carried out using various forms of zeolite- X through a simple condensation reaction between malononitrile (1.0 mmol), sodium azide (1.0 mmol) and aldehyde (1.0 mmol) under solvent free condition. It is shown that no product is observed under reflux conditions in the absence of a catalyst. However, when the reaction is carried out using zeolites as catalyst under reflux condition, the product with a yield of 97% (for H+ zeolite-X) is achieved within 12 minutes. Several aromatic aldehydes under the optimized reaction conditions are studied. This condensation reaction occurs smoothly under solvent free condition and reaction is almost completed within 12 minutes. Several aromatic aldehydes smoothly converts to afford a wide range of tetrazoles. The reaction is also carried out using various forms of zeolite- X as catalyst under reflux condition. Several examples illustrating this general method for the synthesis of tetrazoles over H+ zeolite are summarized in Table 6.

Table 6 Synthesis of 5-substituted 1H-tetrazole derivatives

Entry	Ar	Product	[a]Time (min)	[b]Yield (%)
1	Ph	3a	12	97
2	4-Me-C_6H_4	3b	12	97
3	4-Me_2N-C_6H_4	3c	12	94
4	2,4-$Cl_2C_6H_3$	3d	10	90
5	2-NO_2-C_6H_4	3e	10	90
6	4-Cl-C_7H_5	3f	10	87
7	4-OH-C_6H_4	3g	10	84
8	4-NO_2-C6H_4	3h	9	80

[a]Reaction condition: malononitrile (1.0 mmol), sodium azide (1.0 mmol) and aldehyde (1.0 mmol), catalyst, H-Zeolite-X, Temperature: 60 °C; [b]Isolated yields

5. Conclusion

In conclusion, we developed a quick, consistent, brilliant and environmentally benign method for the synthesis of 5-substituted 1H-tetrazoles from malononitrile, sodium azide and various aromatic aldehydes. After conclusion of the reaction, the catalyst is separated by simple filtration and washed with appropriate solvents via chloroform and ethyl acetate and recycled 2-4 times without loss of any catalytic activity. The main reward of this process is short reaction time, high admirable yield, no solvent and low catalyst loading. Further, Zeolites are extremely useful as catalysts for several important reactions such as cracking, isomerisation and hydrocarbon synthesis. Zeolites can also promote a diverse range of catalytic reactions including acid-base and metal induced reactions

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Declaration of Conflict

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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