

Synthesis of 5-substituted 1*H*-tetrazoles using natural and reusable Natrolite zeolite

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Abstract: During this study the application of Natrolite zeolite was investigated as a solid acid catalyst for efficient preparation of 5-substituted 1*H*-tetrazole derivatives. Excellent yields of products were obtained with a wide range of substrates. After completion of the reaction, the catalyst was recovered by filtration and reused several times with only a slight decrease of activity observed under the same reaction conditions.

Keywords: Natrolite zeolite, 5-substituted 1*H*-tetrazole, natural catalyst, heterogeneous catalyst, nitrile

INTRODUCTION

The importance of tetrazole chemistry during two decades ago, especially for their main applications in coordination chemistry, medicinal chemistry and materials applications caused to be considered by a lot of organic chemist researchers [1-9]. Tetrazoles can be used as isosteric replacements for carboxylic acids in drug design [2]. The preference of tetrazolic acids over carboxylic acids is their resistance against biological degradation in many metabolic [3,4]. Also tetrazoles can be used mainly for the preparation of imidoylazides [10].

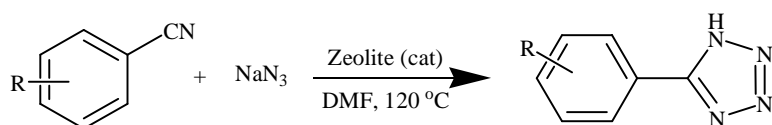
The conventional method of synthesizing tetrazoles is through the reaction of azide ions and organic nitriles or cyanamides [11-25]. There are several methods for the preparation of 5-substituted 1*H*-tetrazoles [14-17]. These methods suffer from one or more disadvantages, such as low yield, harsh reaction conditions, difficult to obtain and/or prepare starting materials, tedious work-up and use of expensive, toxic and explosive reagents such as hydrazoic acid. In an alternative way recently, Sharpless and co-workers reported an efficient synthesis of tetrazoles using sodium azide and nitriles with stoichiometric amounts (50 mol %) Zn (II) salts [18-20]. Despite the advantages of homogeneous metal catalysts, difficulties in recovering the Zn (II) salts from the reaction mixture severely inhibit their wide use in industry.

Zeolites are crystalline aluminosilicates with regular cages or ordered channels of molecular size that may be obtained either from natural sources (certain volcanic rocks) or manufactured synthetically. They are widely used in the fields such as adsorption, heterogeneous catalysis and ion-exchanging [26-28]. Among more than 150 known types of zeolites only 41 have natural analogues; others are fully synthetic. Due to their remarkable physical and chemical properties, zeolites have been used as heterogeneous catalysts in the various reactions.

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Among the natural zeolites, Natrolite zeolite, $\text{Na}_2[\text{Al}_2\text{Si}_3\text{O}_{10}] \cdot 2\text{H}_2\text{O}$, as natural catalyst is broadly used in the synthesis of specialty and fine chemicals [13,28]. Natrolite, space group *Fdd2*, is one of the fibrous zeolites with the framework constructed from the chains of corner-sharing Al and Si oxygen tetrahedral. The locations and strengths of acid sites are determined by the Al amounts and distributions in their frameworks.

In continuation of our recent work on the heterocycles [29] we herein report a new protocol for preparation of 5-substituted 1*H*-tetrazoles from a wide variety of nitriles using natural and reusable Natrolite zeolite (Scheme 1). Natural Natrolite zeolite was obtained from Hormak area, city of Zahedan, Sistan & Baluchestan province in Iran.



Scheme 1. Synthesis of 5-substituted 1*H*-tetrazoles.

RESULTS AND DISCUSSION

Initially, the amount of Natrolite zeolite catalyst required in the reaction between benzonitrile and sodium azide was optimized (Table 1).

Table 1. Preparation of 5-phenyltetrazole using different amounts of Natrolite zeolite at 120 °C^a.

Entry	Zeolite (g)	Solvent	Time (h)	Yield (%) ^b
1	0.15	DMF	12	80
2	0.14	DMF	12	80
3	0.13	DMF	12	80
4	0.10	DMSO	12	79
5	0.10	DMF	12	79
6	0.08	DMF	12	75
7	0.00	DMF	12	0.0

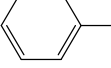
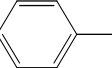
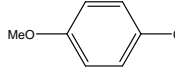
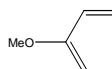
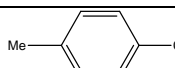
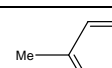

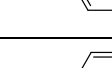
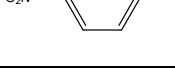
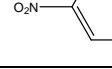
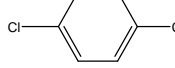
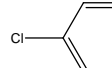
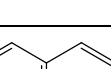
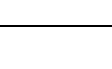
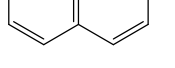
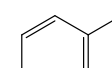
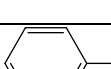
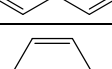
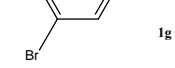
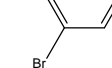
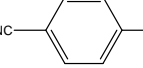

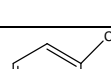

^a Reaction conditions: nitrile (2 mmol), sodium azide (3 mmol), Natrolite zeolite (0.1 g), DMF (6 mL), 12 h, 120 °C.

^b Isolated by column chromatography.

The results of optimization amount of Natrolite zeolite were found to be 0.1 g in the presence of nitrile (2 mmol) and sodium azide (3 mmol) in DMF (6 mL). At second step the effect of benzonitriles possessing a wide range of functional groups to understand the scope and generality of the Natrolite zeolite-promoted [2+3] cycloaddition reaction to form 5-substituted 1*H*-tetrazole was studied, (Table 2). Furthermore, the mono-addition product was obtained during the reaction of 1,4-dicyanobenzene and sodium azide (Table 2, entry 8), whereas in the presence of Zn(II) salts the double-addition product was reported [18-20].

Furthermore, a catalyst recycle experiment was carried out. The applied Natrolite zeolite is reusable catalyst which its activity remains intact even after five times application (Table 2, entry 8). This reusability demonstrates the high stability and turnover of the Natrolite zeolite under the operating condition.

Table 2. Synthesis of 5-substituted 1H-tetrazoles using Natrolite zeolite at 120 °C.

Entry	Substrate	Product	Time (h)	Yield (%) ^a	References
1			12	79	11, 18, 22, 25
2			12	79	22
3			12	77	11, 24
4			12	78	18, 22, 24
5			12	80	25
6			12	77	18, 24
7			12	78	17
8			18	82, 79 ^b	25
9			5	82	22
10			22	66	25
11			22	66	11, 22, 24
12			12	78	24

^a Isolated yield.

^b Yield after the five cycle.

The simplicity, together with the use of inexpensive, non-toxic and environmentally benign catalyst is remarkable features of the proposed procedure. The products were

identified using IR, ^1H NMR and ^{13}C NMR techniques and their melting points. The structures of the products were in agreement with their IR and NMR spectra. In the IR spectra of the 5-substituted 1*H*-tetrazoles, the CN peak had disappeared and a NH absorption band was detected.

CONCLUSION

In summary we have demonstrated the application of Natrolite zeolite for the synthesis of 5-substituted 1*H*-tetrazoles from nitriles under thermal conditions. The reaction was carried out in DMF which is a usable solvent. The significant advantages of this methodology are high yields, elimination of dangerous and harmful hydrazoic acid and a simple work-up procedure. Natrolite zeolite was demonstrated to be an efficient, thermally and chemically stable, environmental compatible and low cost catalyst that can be easily reused for many consecutive runs without a significant decrease in its catalytic reactivity. This methodology may find widespread use in organic synthesis for preparation of tetrazoles.

EXPERIMENTAL

All preliminary chemicals were purchased from Merck and Sigma-Aldrich. Natural Natrolite zeolite was obtained from Hormak area, city of Zahedan, Sistan & Baluchestan province in Iran. Reactions were followed by TLC using SILG/UV 254 silica gel plates. Melting points were measured using a BUCHI 510 apparatus in open capillaries and are uncorrected. IR spectra were obtained using a Shimadzu FT-IR-8300 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained using a Bruker Avance DPX 250 spectrometer operating at 250/62.5 MHz, respectively (δ in parts per million, J in hertz).

Catalyst characterization

The catalyst was characterized according to the literature [11h,13,28].

Typical procedure for the preparation of 5-substituted 1*H*-tetrazoles

A mixture of benzonitrile (2 mmol), sodium azide (3 mmol), and 0.1 g Natrolite zeolite in 6 mL distilled DMF was stirred at 120 °C for the appropriate time (Table 2) until TLC monitoring indicated no further progress in the conversion. The catalyst was filtered off, washed with water and ethanol and the filtrate was treated with EtOAc (35 mL) and 4*N* HCl (20 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic phase was washed with H_2O , dried (Na_2SO_4) and evaporated to yield a residue, which was purified by column chromatography to give the desired pure products. All products are known in the literature and were characterized by IR, NMR and melting points and their spectroscopic data identical to that reported in the literature [30].

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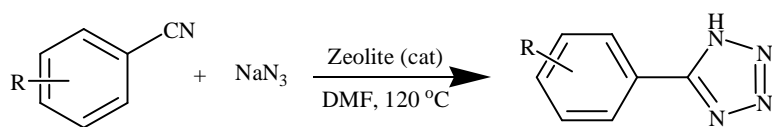
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