

## Nano TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> as an efficient and recycable catalyst for the synthesis of 5-substituted-1*H*-tetrazoles

Fatemeh Abrishami<sup>a,\*</sup>, Maryam Ebrahimikia<sup>a</sup>, Fatemeh Rafiee<sup>b</sup>

<sup>a</sup>Faculty of Chemistry and Chemical Engineering, Malek-Ashtar University of Technology, Tehran, Iran.

<sup>b</sup>Department of Chemistry, Alzahra University, Vanak, Tehran, Iran.

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### ABSTRACT

An efficient method for the synthesis of 5-substituted-1*H*-tetrazoles through the reaction of nitriles with sodium azide using titanium oxide-supported boric acid (TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub>) catalyst was reported. The reactions were carried out at 120 °C and provided the corresponding tetrazoles in good to excellent yields. This method displayed significant advantages such as stability of the catalyst, high product yield, simple methodology, and easy work up. Also, this catalyst can be reused several times without loss of its catalytic activity. The aromatic nitriles with electron-donating and electron-withdrawing groups could be accomplished. The structural characteristics of the catalyst were identified by FT-IR, powder X-ray diffraction (XRD), scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX) and inductively coupled plasma (ICP) analyses.

**Keywords:** [3+2] Cycloaddition, Heterogeneous catalyst, 5-Substituted-1*H*-tetrazoles, Titanium oxide-boric acid, Recyclable.

### 1. Introduction

Tetrazoles are an important class of heterocycles with a wide range of applications. In particular, they have shown strong medicinal activities such as sedatives [1], antinociceptive [2], anticonvulsant [3], anticancer [4], antidiabetic [5], antihypertensive [6], herbicides [7], diuretics [8], hormonal [9], antimicrobial [10], antifungal [11], anti-inflammatory [12], antiallergic [13], and antibacterial [14] activities. Furthermore, these nitrogen-rich rings have found applications as synthons in synthetic organic chemistry [15,16].

Because of their potent usefulness, the synthesis of tetrazole nucleus has received much attention recently. Among the various methodologies that have been developed for the synthesis of 5-substituted-1*H*-tetrazoles, the most common method is the 1,3-dipolar cycloaddition of nitriles and organic/inorganic azide, first reported by Hantzsch and Vagt [17]. Earlier work suffered from drawbacks including use of expensive and toxic metal organic azide complexes such as tin or silicon, highly moisture-sensitive reaction conditions, use of amine salts, strong Lewis acid, and hydrazoic acid which are extremely toxic, explosive, and volatile

[18,19]. In 2001, Demko and Sharpless reported an innovative, safe and environmentally friendly procedure in water with stoichiometric amounts of Zn(II) salts as catalyst [20,21]. This procedure has shown a good level of generality but in the case of sterically hindered aromatic or alkyl inactivated nitriles, it required high temperatures (140-170 °C) [22].

The various homogeneous and heterogeneous catalytic systems were reported for the synthesis of 5-substituted-1*H*-tetrazoles such as Cu<sub>2</sub>O [23], modified montmorillonite K-10 [24], copper(II) supported on superparamagnetic Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub> [25], nickel zirconium phosphate [26], ZnO/Co<sub>3</sub>O<sub>4</sub> [27], Pd(PPh<sub>3</sub>)<sub>4</sub> [28], mesoporous ZnS nanospheres [29], nano CuFe<sub>2</sub>O<sub>4</sub> [30], Fe(OAc)<sub>2</sub> [31], triethylammonium chloride [32], and 4'-phenyl-2,2':6',2''-terpyridine copper(II) complex immobilized onto activated multi-walled carbon nanotubes [33]. However, a drawback of the homogeneous catalytic processes is difficulty in separation and recovery of the catalysts. Therefore, heterogeneous alternatives are highly desirable and have attracted increasing attention [34].

Titanium dioxide is a well-studied material with a wide range of applications. For example, it is used as catalysis, photoelectrode in dye-sensitized solar cells, in photochromic devices, in lithium batteries,

\*Corresponding author email: fatemeabrishami@yahoo.com  
Tel.: +98 21 2297 0168; Fax: +98 21 2296 2257

photocatalysts, white pigments and corrosion-protective coatings [35]. TiO<sub>2</sub> combines good electrical properties with high catalytic activity and excellent stability in many solvents over a wide pH range [36].

Although there are different kinds of catalysts for the synthesis of 5-substituted-1*H*-tetrazoles in the literatures, their harsh reaction conditions and approximately low yields are big problems in this area. So, effort to find a catalytic system, which is capable to facilitate the reaction conditions and afford the higher yields in short reaction time is of great importance.

In continuation of our research in the development of novel and efficient synthetic method, we report a remarkable activity of the boron-modified nano titanium dioxide (rutile) (TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub>) to catalyze [3+2] cycloaddition reaction between organic nitriles and sodium azide to afford corresponding 5-substituted-1*H*-tetrazoles in high yields and purity.

## 2. Experimental

All reagents and solvents of this study, are commercially available and were purchased from commercial suppliers (Acros, Merck and Aldrich) and used without further purification. Yields refer to isolated products. The thermal stability of the prepared catalyst was evaluated using a Mettler Toledo thermogravimetric analyzer under nitrogen purge with a heating rate of 10 °C/ min. The elemental analysis of the catalysts was carried out by inductively coupled plasma (ICP-Perkin Elmer 5300DV). Energy dispersive X-ray spectroscopy (EDX) analysis was studied by SiriusSD-silicon drift detector. The purity determination of the substrate and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates.

All melting points were determined on a Gallenkamp apparatus and are uncorrected. The FT-IR adsorption spectra were run on a spectrophotometer (Nicolet 800) as KBr disks. Vibrational transition frequencies were reported in wave number (cm<sup>-1</sup>). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker (Avance DRX-500) spectrometer at 500 and 125 MHz, respectively. Chemical shifts (δ) are given in ppm from tetramethylsilane as internal standard, and the spectra were recorded in DMSO-*d*<sub>6</sub> as solvent at room temperature. X-ray diffraction (XRD) patterns of the catalyst were recorded with a PW 3710 Philips X-ray diffractometer at room temperature using monochromatic Cu K<sub>α</sub> radiation with wavelength of λ = 0.15418 nm. The peak position and intensity were obtained between 0° and 50° with a rate of 0.04°s<sup>-1</sup>. The morphology of the catalyst was observed using a TSCAN scanning electron microscope (SEM).

### 2.1. Preparation of titanium oxide-supported boric acid (TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub>) [37]

A round-bottomed flask containing 30 mL water and boric acid (32 mmol, 2g) was heated to 60–80 °C. While the mixture was stirring, titanium oxide (60–120 mesh, 18 g) was added gradually with constant stirring and refluxed for 5 h. The slurry of TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> was then filtered and washed with water. The residue was dried at 100 °C for 24 h.

### 2.2. General procedure for the synthesis of 5-substituted-1*H*-tetrazole

A mixture of nitrile (1 mmol), sodium azide (1.3 mmol), ammonium acetate (1 mmol), TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> (20 mg) and 1 mL DMSO was added in a 25 mL round bottomed flask and heated at 120 °C under air atmosphere. The mixture was vigorously stirred under these reaction conditions and its completion was monitored by thin layer chromatography (TLC) (EtOAc:*n*-hexane, 75:25). After completion of reaction, the catalyst was separated from the reaction mixture by simple filtration. The filtrate was treated with ethyl acetate (10 mL) and 5 N HCl (5 mL) and stirred vigorously. The resultant organic layer was separated, and the aqueous layer was again extracted with ethyl acetate (10 mL). The combined organic layers were washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure using a rotary evaporator to give the crude solid crystalline 5-substituted-1*H*-tetrazole. The crude solid product was purified by silica gel column chromatography (EtOAc:*n*-hexane, 75:25).

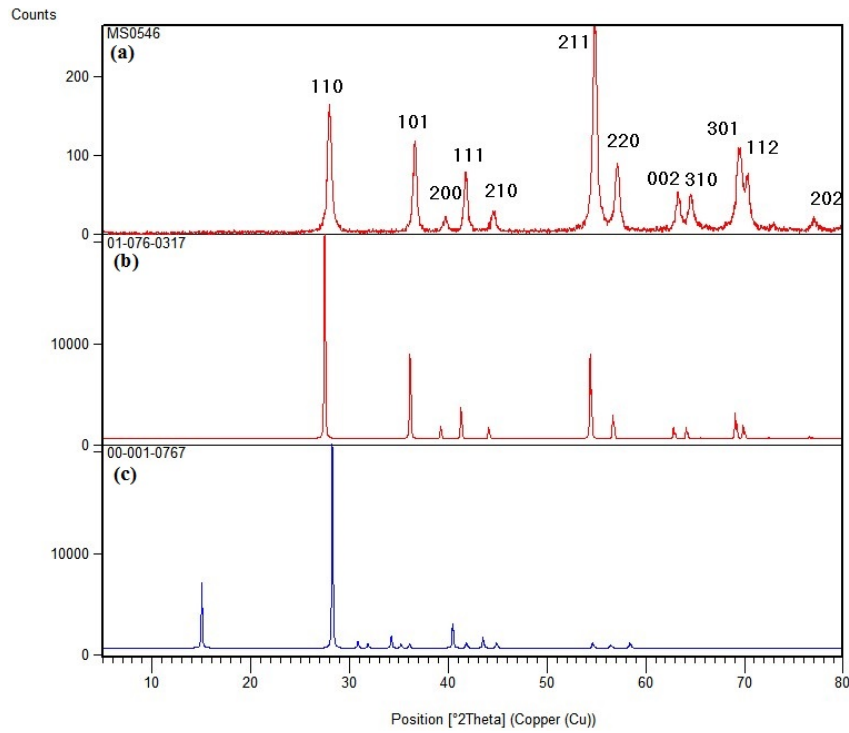
### 2.3. Procedure for catalyst recycling

After filtration, the catalyst was washed with dichloromethane (5 ml × 3) to remove any organic impurities. Then it was dried in oven at 100 °C for 5 h and used for the next cycle under optimized conditions.

## 3. Results and Discussion

### 3.1. Characterization of the catalyst

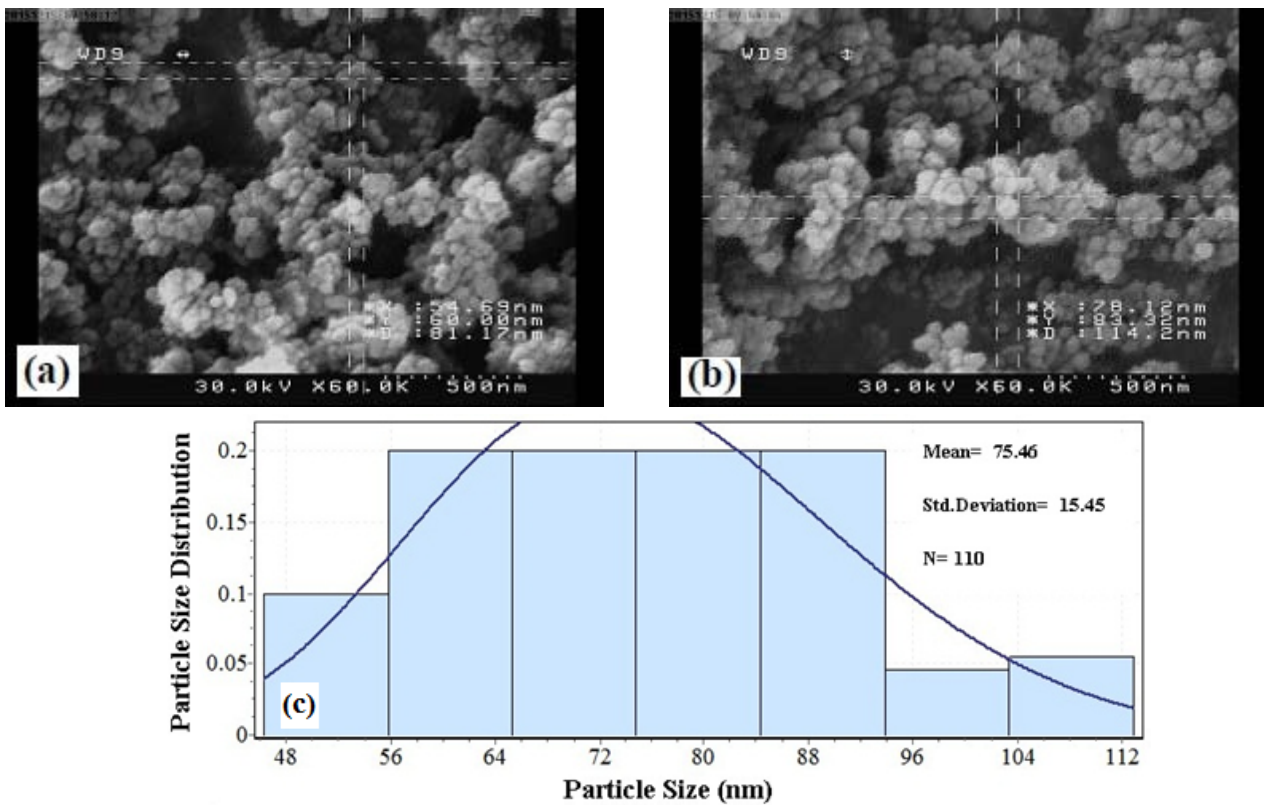
The structure of TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> as a novel nano catalyst was identified by FT-IR, XRD and SEM analysis. The diffraction peaks of TiO<sub>2</sub> were observed at 2θ = 27.4°, 36.1°, 39.2°, 41.2°, 44.0°, 54.3°, 56.6°, 62.8°, 64.1°, 69.0° and 69.8° corresponding to the planes of (110), (101), (200), (111), (210), (211), (220), (002), (310), (301) and (112) respectively, they well matched with the diffraction peaks of rutile TiO<sub>2</sub> phase (Fig. 1). The XRD pattern of TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> remained almost unchanged compared to rutile TiO<sub>2</sub> pattern which indicated that the unit cell parameters of TiO<sub>2</sub> phases were not substantially modified.



**Fig. 1.** a) XRD pattern of TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> nanoparticles, b) standard diffraction data of TiO<sub>2</sub>, c) standard diffraction data of H<sub>3</sub>BO<sub>3</sub>.

The surface morphology, orientation and particle sizes of the boron-modified TiO<sub>2</sub> were determined using SEM (Fig. 2). The SEM image shows that the phase consists

of spherical shape particles. The mean particles size of H<sub>3</sub>BO<sub>3</sub>-TiO<sub>2</sub> is ~75 nm. In figure 2c, particles size distribution is discernible.



**Fig. 2.** SEM images of a) nano TiO<sub>2</sub>, b) TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> nanoparticles and c) Particle size distribution of TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> nanoparticles.

An energy dispersive X-Ray analyzer (EDX) was also used to check the elemental identification and quantitative compositional information of  $\text{TiO}_2\text{-H}_3\text{BO}_3$  nanoparticles (Fig. 3). The EDX analysis revealed the presence of Ti, O, and B in the sample. The presence of Ti  $L_{\alpha}$  peak at 0.452 keV, Ti  $K_{\alpha}$  peak at 4.508 keV, B  $K_{\alpha}$  peak at 0.183 keV and O  $K_{\alpha}$  peak at 0.525 keV is observed. Boron gives a very weak signal in EDX spectra due to its low atomic number. Furthermore, the boron amount of the catalyst was 3 wt%, which was determined by ICP analysis.

Fig. 4 shows representative FTIR spectra of  $\text{TiO}_2$ ,  $\text{H}_3\text{BO}_3$  and  $\text{TiO}_2\text{-H}_3\text{BO}_3$  catalysts. In figure 4b, the broad band centered at  $500\text{-}600\text{ cm}^{-1}$  is likely due to the vibration of the Ti–O bonds in the  $\text{TiO}_2$  lattice. The peaks at  $1620\text{-}1630\text{ cm}^{-1}$  and the broad peaks appearing at  $\sim 3422\text{ cm}^{-1}$  are assigned to vibrations of hydroxyl groups [40]. The spectrum of boric acid is included in figure 4c, showing bands at  $812.0$ ,  $883.0$ ,  $1194.5$ ,  $1438.9$ , and  $3209.4\text{ cm}^{-1}$ . There are two peaks at  $812.0$  and  $883.0\text{ cm}^{-1}$  that arise from the B–O–H bending vibration out of plane, and these vibrations overlap with some of the other B–O stretching vibrations. The peaks located at  $1438.9\text{ cm}^{-1}$  and  $1194.5\text{ cm}^{-1}$  can be assigned to the asymmetric B–O stretching vibration and in-plane B–O–H bending vibration, respectively. The strong IR absorption peaks at  $3209.4\text{ cm}^{-1}$  should be attributed to the O–H vibration. FTIR spectrum of the  $\text{TiO}_2$  sample modified with boric acid (Fig. 4a) can be interpreted as a mixture of features from both  $\text{TiO}_2$  and boric acid. However, the vibration of Ti–O–B did not appear; this indicated that there is no binding between  $\text{TiO}_2$  and  $\text{H}_3\text{BO}_3$ , and  $\text{H}_3\text{BO}_3$  was only physically absorbed on the surface of titan.

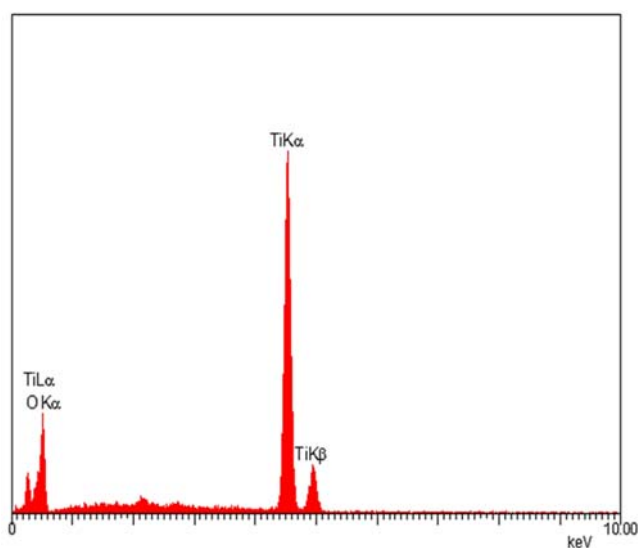


Fig. 3. EDX analysis of  $\text{TiO}_2\text{-H}_3\text{BO}_3$ .

Fig. 5 shows the TGA curve of  $\text{TiO}_2\text{-H}_3\text{BO}_3$  catalyst. The TGA was performed at nitrogen atmosphere to indicate the decomposition temperature of catalyst. As seen from the TGA plot of catalyst, the catalyst shows two weight losses at lower temperature ( $<170\text{ }^\circ\text{C}$ ) due to the release of physisorbed on the surface. Therefore, it can be used at the reaction condition.

### 3.2. Catalytic activity

After confirming the exact characteristics of the catalyst, 5-substituted-1*H*-tetrazoles were synthesized using an environmentally benign heterogeneous catalyst ( $\text{TiO}_2\text{-H}_3\text{BO}_3$ ). The influence of experimental parameters such as solvent, temperature, and amount of catalyst were investigated on the [3+2] cycloaddition reaction of nitriles with sodium azide (Table 1).

Thus, benzonitrile (1.0 mmol) was treated with sodium azide (1.3 mmol) and ammonium acetate (1 mmol) in toluene, tetrahydrofuran (THF), dimethylsulfoxide (DMSO), and *N,N*-dimethylformamide (DMF) and water. Among the tested solvents (using 14 mol% of  $\text{TiO}_2\text{-H}_3\text{BO}_3$ ), THF gave a low yield of 5-phenyl-1*H*-tetrazole whereas the yield was dramatically improved using DMSO (Table 1, entries 1 and 2).

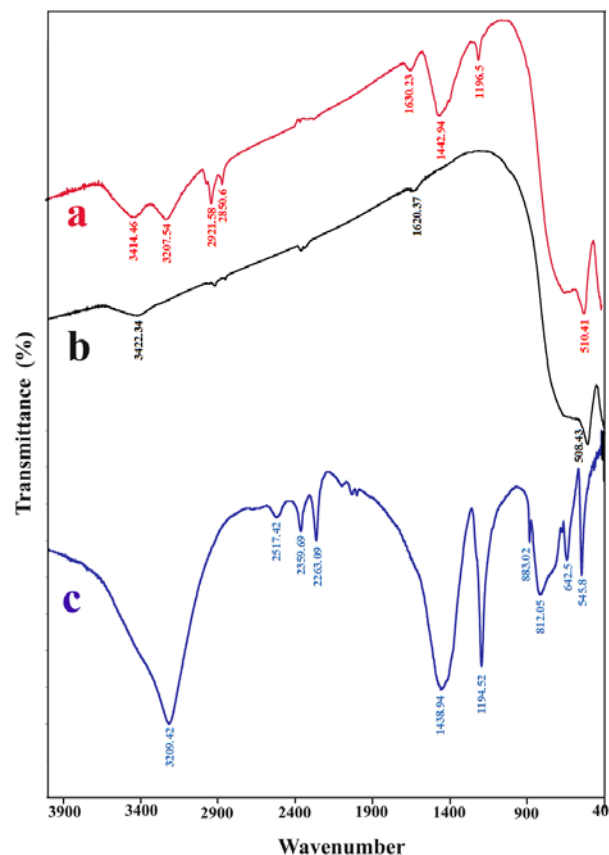


Fig. 4. FTIR spectra of a)  $\text{TiO}_2\text{-H}_3\text{BO}_3$  nanoparticles, b) titanium dioxide and c) boric acid.

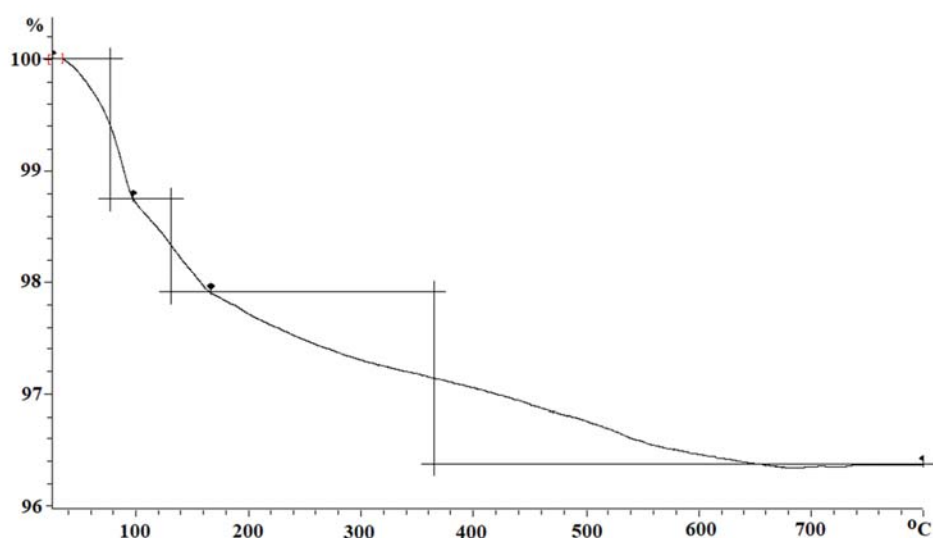
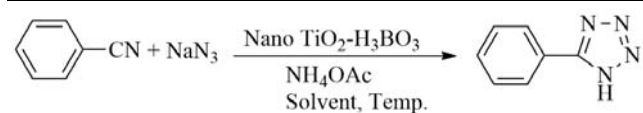


Fig. 5. TGA curve of  $\text{TiO}_2\text{-H}_3\text{BO}_3$ .

Table 1. Optimization of various reaction parameters for the preparation of 5-substituted-1*H*-tetrazole.



Entry	Solvent	Catalyst (mg)	Condition	Time (min)	Yield <sup>b</sup> (%)
1	THF	20	Reflux	140	20
2	DMSO	20	120 °C	70	97
3	DMF	20	120 °C	90	80
4	Toluene	20	Reflux	120	30
5	H <sub>2</sub> O	20	Reflux	140	40
6	DMSO	20	RT	180	20
7	DMSO	20	60 °C	120	30
8	DMSO	20	80 °C	100	70
9	DMSO	20	100 °C	70	86
10	DMSO	-	120 °C	360	0
11	DMSO	10	120 °C	120	80
12 <sup>c</sup>	DMSO	20	120 °C	120	60
13	DMSO	30	120 °C	70	96
14 <sup>d</sup>	DMSO	20	120 °C	160	81
15 <sup>e</sup>	DMSO	20	120 °C	120	86

<sup>a</sup>Reactions conditions: benzonitrile (1 mmol), NaN<sub>3</sub> (1.3 mmol), ammonium acetate (1 mmol), solvent (1 mL).

<sup>b</sup>Yield of isolated product.

<sup>c</sup>In the absence of ammonium acetate.

<sup>d</sup>In the presence of TiO<sub>2</sub> as a catalyst.

<sup>e</sup>In the presence of H<sub>3</sub>BO<sub>3</sub> as a catalyst.

To improve the efficiency of the reaction, the effect of temperature was studied by carrying out the model reaction at different temperatures (room temperature, 60 °C, 80 °C, 100 °C and 120 °C) and the best results were obtained at 120 °C (Table 1, entries 2, 6-9).

The scope and generality of this catalytic system for the [3+2] cycloaddition reaction of various aryl/heteroaryl cyanides with sodium azide were investigated and the results are summarized in Table 2.

It is obvious that this method is more suitable for nitriles with electron-withdrawing groups. For example, the reaction of 1,4-dicyanobenzene provided the corresponding product in 91% yield after 40 min (Table 2, entry 9), while the reaction of 4-methylbenzonitrile took a longer time giving an 81% isolated yield (Table 2, entry 3). Heteroaromatic nitriles such as 4-pyridinecarbonitrile and 3-pyridinecarbonitrile provided the corresponding tetrazoles in good yields after short reaction times (Table 2, entries 6 and

7). The reaction of sterically hindered *ortho*-substituted aryl nitrile afforded the desired tetrazole in 60% yield, although a prolonged reaction time was required (Table 2, entry 2).

Dicyanobenzene is an interesting substrate for study of mono-addition or di-addition reactions. It has been reported that the di-addition product is obtained using soluble Zn (II) salts as catalysts, whereas the mono-addition product is obtained with the use of solid zinc oxide catalyst. He and co-workers found that mono- and di-addition products could be selectively synthesized by simply adjusting the molar ratio of NaN<sub>3</sub> to nitriles and the rate of addition of NaN<sub>3</sub> to the reaction solution [50].

The di-addition product was obtained when the molar ratio of NaN<sub>3</sub> to nitrile was about 2, whereas when the molar ratio was about 1, the methodology of adding NaN<sub>3</sub> to the reaction solution had a crucial influence on the formation of mono- and di-addition products.

**Table 2.** TiO<sub>2</sub>-H<sub>3</sub>BO<sub>3</sub> catalyzed synthesis of 5-substituted-1*H*-tetrazole.

Entry	R	Time (min)	Yield <sup>b</sup> (%)	TON <sup>c</sup>	TOF <sup>d</sup>	m.p. (°C) <sup>e</sup>		Ref.
						Found	Reported	
1	C <sub>6</sub> H <sub>5</sub> -	70	98	17818.2	15229.2	215–217	215–216	[34]
2	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	180	75	13636.4	4545.5	151–152	152–153	[48]
3	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	120	81	14727.3	7363.6	247–249	248–250	[41]
4	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> -	100	87	15818.2	9472	266–268	268–269	[41]
5	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> -	90	91	16545.4	11030.3	260–261	261–263	[34]
6	4-Pyridinyl-	60	78	14181.8	14181.8	250–252	251–253	[34]
7	3-Pyridinyl-	90	79	14363.6	9575.7	225–226	224–225	[45]
8	<i>o</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> -	120	60	10909.1	5454.5	142–145	143–144	[49]
9 <sup>f</sup>	<i>p</i> -CNC <sub>6</sub> H <sub>4</sub> -	40	91	16545.4	24694.6	257–258	258–260	[45]
10 <sup>f</sup>	<i>m</i> -CNC <sub>6</sub> H <sub>4</sub> -	60	83	15090.9	15090.9	213–215	214–216	[45]
11 <sup>f</sup>	CNCH <sub>2</sub> -	80	94	17090.9	12850.3	115–117	116–118	[34]
12	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> -	240	90	16363.6	4090.9	159–161	160–161	[41]
13	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> -	90	73	13272.7	8848.5	123–125	123–124	[34]
14	<i>p</i> -OHCC <sub>6</sub> H <sub>4</sub> -	80	79	14363.6	10799.7	180–181	180–182	[45]

<sup>a</sup>Reactions conditions: Nitrile (1 mmol), sodium azide (1.3 mmol), ammonium acetate (1 mmol), catalyst (20 mg), DMSO (1 mL) at 120 °C.

<sup>b</sup>Yield of isolated product.

<sup>c</sup>Moles of tetrazole formed per mole of catalyst.

<sup>d</sup>Turn over number per time unit.

<sup>e</sup>Literature values in parentheses.

<sup>f</sup>Reaction carried with 2.6 mmol of NaN<sub>3</sub>.

If  $\text{NaN}_3$  is completely added into the reaction solution before the chemical reaction, both adducts are formed with similar yields (61:24). This indicates that the substrate and mono-addition products show similar reaction with  $\text{NaN}_3$ . On the other hand, if  $\text{NaN}_3$  is added gradually over a period of 6 h, the dominant product is the mono-addition one [51]. It is noteworthy that dicyanobenzenes only give mono-adduct even when using a 1:2 molar ratio of dicyanobenzenes to sodium azide and 20 mg of  $\text{TiO}_2\text{-H}_3\text{BO}_3$ . The efficiency of this catalyst in comparison with other heterogeneous catalytic systems was determined and it gave a better yield in a shorter time (Table 3).

Due to the environmental concerns, their costs and toxicities, recycling of the catalyst is of high importance. In order to recover the catalyst nanoparticles, after completion of the reaction of benzonitrile with sodium azide, the catalyst was separated from the reaction mixture through centrifuging the reaction mixture. The collected catalyst was washed with 5 mL of ethanol followed by doubly distilled water several times, and dried in an oven at  $100^\circ\text{C}$  for 2-3 h. The recovered catalyst can be reused over five consecutive runs. The catalytic activity of the catalyst decreased only after the fourth cycle and before that, it remains effective. The yields of these five consecutive runs were 98, 98, 95, 93 and 91 % respectively. Furthermore, ICP analysis of the fresh and 5<sup>th</sup> recovered catalyst showed that after five recycles the boron amount of the catalyst was changed from 3 wt% to 2.8 wt%; this proved the stability and recyclability of the catalyst.

A plausible mechanism for this reaction is shown in Scheme 1. There may be many Lewis acid sites on the surface of  $\text{TiO}_2\text{-H}_3\text{BO}_3$ . Coordination between Lewis acid sites of this catalyst and the nitrile is the dominant factor influencing [3+2] cycloaddition. The [3+2] cycloaddition between the  $\text{C}\equiv\text{N}$  bond of nitrile compound and azide ion takes place readily to form the intermediate **I**. Protonolysis of the intermediate could be done using  $\text{H}^+$  of  $\text{NH}_4\text{OAc}$  or acidic extraction with  $\text{HCl}$ , resulting in the formation of 5-substituted-1*H*-tetrazole and  $\text{TiO}_2\text{-H}_3\text{BO}_3$ . Ammonium acetate may produce ammonium azide in situ by reaction of ammonium acetate and sodium azide making availability of azide ion for [3+2] cycloaddition with nitrile easily and also ammonium acetate is used as a proton source to provide the desired tetrazoles.

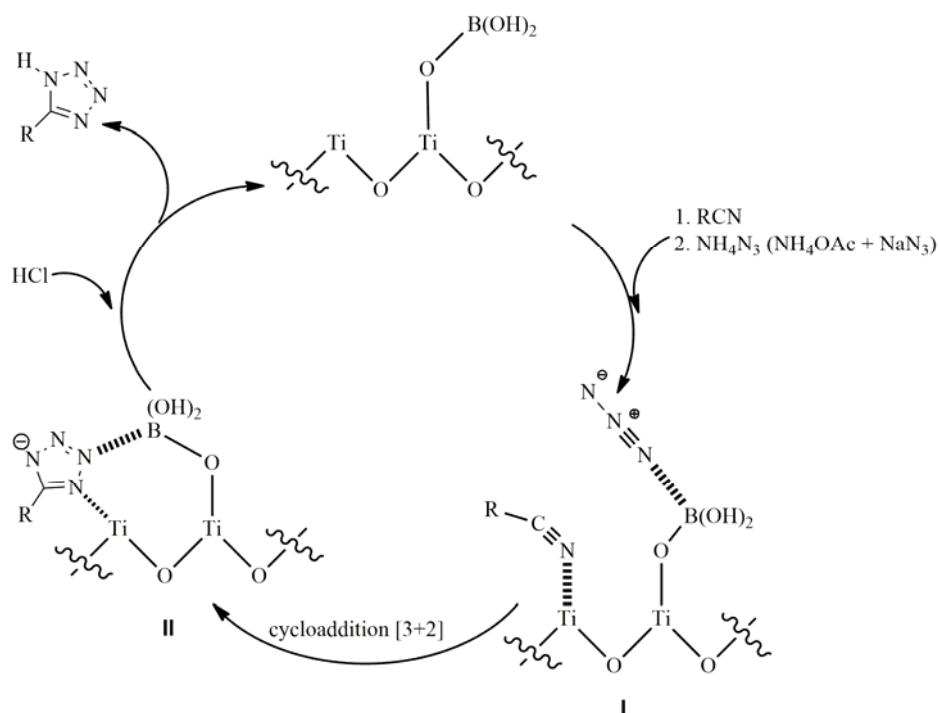
#### 4. Conclusions

In conclusion, we developed a simple and efficient method for the synthesis of 5-substituted-1*H*-tetrazoles via the [3+2] cycloaddition reaction of nitriles with sodium azide in the presence of 14 mol% of  $\text{TiO}_2\text{-H}_3\text{BO}_3$  as a recyclable catalyst. The use of inexpensive and easily available catalyst, clean reaction with good to high yields and a relatively short reaction time are the attractive advantages of this method. This methodology may find widespread use in organic synthesis for the preparation of 5-substituted-1*H*-tetrazoles. Considering easy preparation and good efficiency of the proposed catalytic system, this catalyst has the high potential to be tested for its catalytic performance and in other types of organic transformations required for Lewis acid catalytic centers such as Mukaiyama aldol reaction.

**Table 3.**  $\text{TiO}_2\text{-H}_3\text{BO}_3$  catalyzed synthesis of 5-substituted-1*H*-tetrazole.

Entry	Catalyst	Temp. ( $^\circ\text{C}$ )	Time (h)	Yield (%)	Ref.
1	Zn/Al hydrotalcite	120	12	84	[27]
2	Nano ZnO	120	14	72	[41]
3	Graphene	120	36	63	[42]
4	CoY Zeolite	120	14	90	[34]
5	Zinc hydroxyapatite	120	12	78	[43]
6	$\text{CuFe}_2\text{O}_4$	120	12	82	[30]
7	$\text{FeCl}_3\cdot\text{SiO}_2$	120	36	81	[44]
8	Sulfated zirconia	120	24	90	[45]
9	$\text{B}(\text{C}_6\text{F}_5)_3$	120	8	94	[46]
10	nano $\text{TiO}_2/\text{SO}_4^{2-}$	120	1.30	97	[47]
11	$\text{TiO}_2\text{-H}_3\text{BO}_3$	120	1.2	98	This work





**Scheme 1.** A plausible mechanism for the synthesis of 5-substituted-1H-tetrazoles.

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