

An efficient synthesis of arylaminotetrazoles as via [2+3] cycloaddition of nitriles and sodium azide via solid acid catalysis

Abbas Teimouri^{*a}, Alireza Najafi Chermahini^b

^aPayame Noor University (PNU), Isfahan, Iran, Tel. 0311-7380003; fax: 0311-7381002; E-mail: a_teimouri@pnu.iut.ac.ir

^bDepartment of Chemistry, Yasouj University, Yasouj, Iran

Abstract: The [3+2] cycloaddition between various nitriles and sodium azide proceeds smoothly in the presence of zeolite and sulfated Zirconia as effective catalyst and in the water and DMF/MeOH, to give the corresponding arylaminotetrazoles in good to high yields. The reaction most probably precedes through the in situ formation of a catalyst azide species, followed by a successive [3+2] cycloaddition with the nitriles. This method has the advantages of high yields, simple methodology, and easy work-up. The catalyst can be recovered by simple filtration and reused in good yields.

Keywords: Zeolite, Sulfated Zirconia, Green synthesis, arylaminotetrazoles

INTRODUCTION

Tetrazoles are a class of heterocyclic compounds that contain nitrogen and are currently under intensive focus due to their wide range of applications [1], mainly as a result of the roles played by tetrazoles in coordination chemistry, material sciences, pharmaceuticals, explosives, and photography.[1–7]

Among them, 5-substituted tetrazoles have received much attention recently, and new preparative methods have appeared [12]. Therefore, it is desirable to develop a more efficient and convenient method for the synthesis of 5-substituted tetrazoles. The acid-catalyzed cycloaddition between hydrazoic acid and nitriles has long been one of the main routes to 5-substituted tetrazoles. However, this standard procedure needs the direct addition of large excess amounts of dangerous and harmful hydrazoic acid [9]. The conventional method of synthesizing tetrazoles is by addition of azide ions to organic nitriles or cyanamides. [10]. Earlier reported methods for the synthesis of 5-substituted tetrazoles suffer from drawbacks such as the use of strong Lewis acids, or expensive and toxic metals, and the in situ-generated hydrazoic acid which is highly toxic and explosive [11, 12]. Several syntheses of 5-substituted tetrazoles have been reported through the [2+3] cycloaddition of nitriles using azides in the presence of catalysts. [13] The development of a catalytic synthetic method for the tetrazoles still remains an active research area. An important objective of chemistry is to adapt classical

processes so that pollution effects are kept to a minimum, with both reduction in energy and consumption of raw materials. Solid acid catalysts play a prominent role in organic synthesis under heterogeneous conditions.

Nowadays, more and more heterogeneous Bronsted acids, e.g., zeolites are preferred from an economical perspective as well as from an ecological viewpoint. Due to its high protonic acidity and unique shape-selective behavior, HZSM-5, HY, and H-beta have been shown to be a highly active and stable catalyst for reactions [14]. Zirconia is attracting considerable interest on account of its potential use as a catalyst support. Among various solid acid catalysts investigated in recent times, the sulfation promoted zirconia has received much attention due to its strong acidity, high thermal stability, large specific surface area, and ability to perform organic reactions at much lower temperatures. Recent investigations reveal that promoted zirconia is an exceptionally good solid acid catalyst for various organic synthesis and transformation reactions having enormous industrial applications [15].

In continuation of our interest in the development of efficient and environmentally friendly methods for the catalytic synthesis of heterocycles, and application of heterogeneous reagents for development of the useful synthetic methodologies [16], we report herein the synthesis of arylaminotetrazoles using the zeolite and sulfated Zirconia-catalyzed [3+2] cycloaddition between a wide variety of nitriles and sodium azide in water and DMF/MeOH (Scheme 1).

EXPERIMENTAL

Instruments and characterization

All reagents were purchased from Merck and Aldrich and used without further purification. Products were characterized by spectroscopy data (IR, FTIR, ^1H NMR and ^{13}C NMR spectra), elemental analysis (CHN) and melting points. A JASCO FT/IR-680 PLUS spectrometer was used to record IR spectra using KBr pellets. NMR spectra were recorded on a Bruker 400 Ultrashield NMR and DMSO- d_6 was used as solvent. Melting points reported were determined by open capillary method using a Galen Kamp melting point apparatus and are uncorrected. Mass Spectra were recorded on a Shimadzu Gas Chromatograph Mass Spectrometer GCMS-QP5050A/Q P5000 apparatus.

Catalyst preparation

2.2.1. Synthesis of ZSM-5 and HZSM-5

For synthesis of ZSM-5, hydrated aluminum sulfate and sodium silicate solution were the sources of aluminum and silicon, respectively. The tetrapropylammonium bromide was used as the structure-directing template [17]. ZSM-5 Zeolite was synthesized according to the procedure described earlier

[13]. The solid phase obtained was filtered, washed with distilled water several times, dried at 120 °C for 12 hours and then calcined at 550 °C for 6 hours. And followed by ion exchange with NH_4NO_3 solution (three times), The acid hydrogen form of the compound is prepared by transferring the oven-dried compound to a tube furnace. Heat the ammonium zeolite for 3 hours to ensure the thermal decomposition of NH_4^+ ions. Over the course of this process, zeolite should turn from a white to brown/black color [17].

Synthesis of Sulfated Zirconia

Amorphous hydrated zirconia synthesized by hydrolysis of ZrCl_4 with a concentrated (25%) solution of ammonia according to the procedure described earlier [18]. The obtained hydrous zirconia sample was dried at 120 °C for 12 h. Sulfated Zirconia (SZ) was prepared by suspending ZrO_2 in a solution of 0.5M H_2SO_4 . After 90 min stirring the mixture was filtered and washed with 0.05M H_2SO_4 . The precipitate was dried at 120 °C and calcined for 2 h at 600 °C with subsequent cooling in either a desiccator or under ambient conditions. [18].

General procedure for the synthesis of tetrazoles

The procedure for the synthesis of the tetrazole **3** (Scheme 1) is representative. In a round bottom flask phenylcyanamide (0.24 g, 2 mmol), sodium azide (0.4 g, 6mmol), Catalyst (50 mg) and DMF or water (20 ml) were charged. Then the reaction mixture stirred at in distilled dimethylformamide (DMF) at 110–120 °C, DMF/MeOH at 80 °C and refluxed in water for 24 h. The progress of reaction (after 2, 4, 6, 12, 18 and 24 h.) was followed by HPLC and TLC (75:25 ethylacetat:n-hexane). After the completion of the reaction, the catalyst was separated by centrifugation, washed with doubly distilled water and acetone, and the centrifugate was treated with 6M HCl (20 mL) and while being stirred vigorously. The aqueous solution finally obtained was extracted twice with ethyl acetate; the combined organic phase was washed with water and concentrated to precipitate the crude solid crystalline.

5-Phenylamino-1H-tetrazole (3a)

Mp 214– 216 °C; (lit.19 215–217 °C); ^1H NMR (DMSO- d_6 , 300 MHz): δ =6.91 (t, J=7.3 Hz, 1H), 7.30 (t, J=7.9 Hz, 2H), 7.47 (d, J=8.2 Hz, 2H), 9.71 (s, 1H), 15.32 (s, br, 1H); ^{13}C NMR (DMSO- d_6 , 300 MHz): δ =116.5, 121.2, 127.7, 141.5, 155.6; IR (KBr) 3326, 3218, 1625, 1579, 1536, 1494, 1050, 781, 744, 688, 660 cm^{-1} ; MS; EI: m/z = 161 (M^+).

5-(4-Nitrophenyl)amino-1H-tetrazole (3b)

Mp 216–218 °C; (lit.20 218–220 °C); IR (KBr): ν 3556, 3229, 3106, 1632, 1575, 1488, 1336, 1295, 1052, 839, 741 cm^{-1} ; ^1H NMR (300 MHz, DMSO- d_6): δ =7.75 (d, J =7.3 Hz, 2H), 8.23 (d, J =9.3 Hz, 2H), 10.92 (br s, 1H); ^{13}C NMR (300 MHz, DMSO- d_6): δ =155.6, 146.6, 140.6, 124.2, 114.8; MS; EI: m/z = 206 (M^+).

1-(4-Chlorophenyl)-5-amino-1H-tetrazole (3c)

Mp 214–216 °C (lit.19 215–217 °C); ^1H NMR (DMSO- d_6 , 300 MHz): δ =6.93 (s, 2H), 7.62 (d, J =8.6 Hz, 2H), 7.66 (d, J =8.6 Hz, 2H); ^{13}C NMR (DMSO- d_6 , 300 MHz): δ =126.4, 130.2, 133.2, 134.4, 155.1; FTIR (KBr) 3340, 3136, 1648, 1583, 1577, 1491, 1450, 1324, 1144, 1076, 1012, 838, 735, 630 cm^{-1} . MS; EI: m/z = 195 (M^+).

1-(4-Bromophenyl)-5-amino-1H-tetrazole (3d)

Mp 236–238 °C; (lit.20 245–247 °C); ^1H NMR (DMSO- d_6 , 300 MHz): δ =6.95 (s, 2H), 7.52 (d, J =8.1 Hz, 2H), 7.76 (d, J =8.1 Hz, 2H); ^{13}C NMR (DMSO- d_6 , 300 MHz): δ =123.2, 126.4, 132.6, 134.1, 155.8; IR (KBr) 3340, 3140, 1647, 1581, 1570, 1489, 1420, 1322, 1139, 1108, 1092, 836, 816 cm^{-1} ; MS; EI: m/z = 240 (M^+).

1-(4-Methylphenyl)-5-amino-1H-tetrazole (3e)

Mp 176–178 °C (lit.20 202–204 °C); ^1H NMR (DMSO- d_6 , 300 MHz): δ =2.36 (s, 3H), 6.84 (s, 2H), 7.37 (d, J =7.8 Hz, 2H), 7.41 (d, J =8.3 Hz, 2H); ^{13}C NMR (DMSO- d_6 , 300 MHz): δ =21.8, 125.8, 131.6, 132.4, 139.2, 155.6; FTIR (KBr) 3316, 3147, 1650, 1593, 1571, 1463, 1320, 1140, 1090, 834, 818, 610 cm^{-1} . MS; EI: m/z = 175 (M^+).

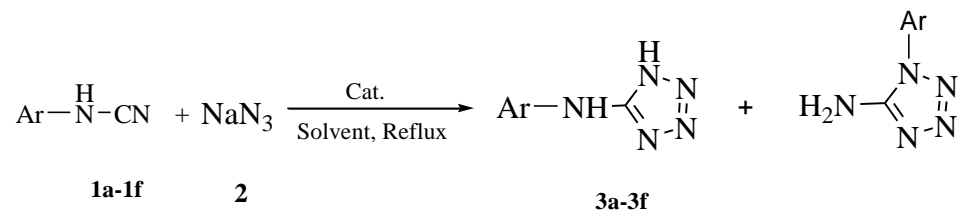
1-(4-Methoxyphenyl)-5-amino-1H-tetrazole (3f)

Mp 212–214 °C; (lit.20 200–202 °C); IR (KBr): ν 3307, 3126, 2977, 1651, 1583, 1456, 1440, 1379, 1186, 1165, 1136, 1084, 841, 620 cm^{-1} ; ^1H NMR (300 MHz, acetone- d_6): δ =3.87 (s, 3H), 6.14 (s, 2H), 7.16 (d, J =8.9 Hz, 2H), 7.47 (d, J =8.9 Hz, 2H); ^{13}C NMR (300 MHz, acetone- d_6): δ =56.23, 115.87, 127.5, 128.1, 156.4, 161.5; MS; EI: m/z = 191 (M^+).

RESULTS AND DISCUSSION

In continuation of our recent work on applications of heterogeneous reagents for the development of synthetic methodologies, we report a new protocol for the preparation of amino tetrazoles from a wide variety of nitriles using zeolite and sulfated Zirconia as a solid acid catalyst (Scheme 1).

In the reaction between phenylcyanamides **1a-f** and sodium azide **2** we investigate effect of phenylcyanamide: sodium azide ratio and catalyst (Table 1). Attempts to carry out these reactions in the absence of catalyst in the water, DMF and MeOH did not yield the products indicating that the clay is acting as a catalyst (Table 1, entry 1 and 2). First, we optimized the amount of catalyst required in the reaction between benzonitrile and sodium azide. The different amounts of zeolite as the catalyst (20 mg, 50 mg, and 100 mg) were tried and it was found that 50 mg of catalyst gave the maximum yield of the products. An increase in the amount of catalyst did not improve the result to any great extent. However with using 20 mg of catalyst the reaction was completed after 76 h. In addition the amount of sulfated zirconia was optimized using different amounts (10, 20 and 50 mg) of catalyst. It was observed that 20 mg of catalyst has the best results. Again an increase in the value of catalyst was not improve the yield and with values lower than 20 mg the reaction was completed in the long times (72 h).



Catalyst= Zeolite and Zirconia

Scheme 1.

One of the most important advantages of heterogeneous catalysis over the homogeneous counterpart is the possibility of reusing the catalyst by simple filtration, without loss of activity. In a typical experiment, after the reaction was completed, the catalysts were recovered from the reaction mixtures by simple filtration and were purified by washing the solid residues with deionized water and acetone followed by drying in an oven at 100 °C for 40 min. From each experiment, more than 98% of the catalyst was recovered. The recovered catalyst was reused three times without any loss of activity (Table 1, entry 16-17) (See Figure 1).

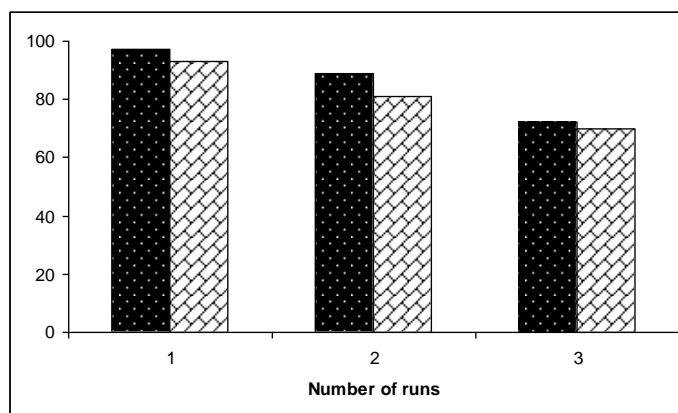


Fig. 1 The results obtained from catalyst reuse Zeolite (black bars) and Sulfated zirconia (white bars) in the tetrazole formation

We next examine the effect of solvent. In the present study we used DMF-Methanol and water as the solvent. Not many organic solvents are stable at the high temperatures necessary for cycloaddition reactions (sometimes as high as 130 °C), and for this reason DMF is most commonly used for this purpose [3]. However the use of water as a clean, inexpensive, and universal solvent combines features of both economic and environmental advantages.

Table 1 Effect of catalysts and solvents on the formation of tetrazole.

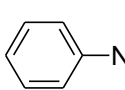
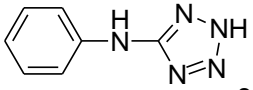
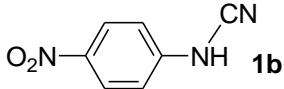
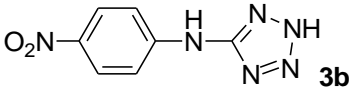
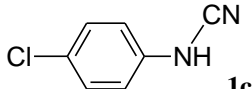
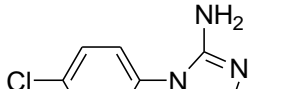
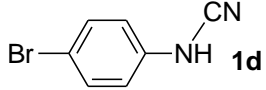
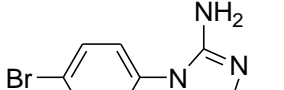
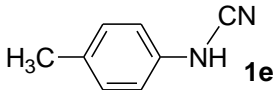
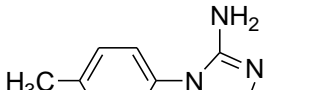
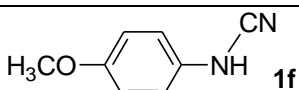
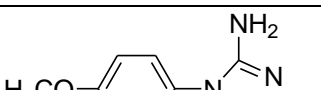
Entry	Solvent	Phenyl cyanamide: sodium azide	Zeolite	% Conversion ^a	Sulfated Zirconia	% Conversion
1	H ₂ O	1:3	-	-	-	-
2	DMF	1:3	-	-	-	-
3	DMF/MeOH (9/1)		-	-	-	-
4	H ₂ O	1:1	50	92	50	90
5	DMF	1:1	50	90	50	86
6	DMF/MeOH (9/1)	1:1	50		50	
7	H ₂ O	1:3	50	94	50	92
8	DMF	1:3	50	94	50	90
9	DMF/MeOH (9/1)	1:3	50		50	
10	H ₂ O	1:3	100		100	
11	DMF	1:3	100		100	
12	DMF/MeOH (9/1)	1:3	100		100	
13	H ₂ O	1:1	20	30	20	35
14	DMF	1:1	20	20	20	25
15	H ₂ O	1:3	50	76	50	60
16	DMF	1:3	50	54	50	40
17	DMF/MeOH (9/1)	1:3	50		50	

Conversion, followed by HPLC

Several substituted nitriles reacted with sodium azide to give the corresponding tetrazoles in good yields. The nature of the substituents on the nitriles had a significant effect on the tetrazole formation reaction (Table 2). Reactions of electron poor aromatic and heteroaromatic nitriles such as 2, 3, 4-

cyanopyridines and 4-nitrobenzotrile were completed within a few hours (Table 2, entries 3, 4, 5 and 6). Some electron rich nitriles required higher temperature, therefore, it seems that the more electron-poor a nitrile, the faster it reacts. Interestingly, the best percent conversions were observed for nitriles with electron withdrawing substituents. However electron donating groups (e.g.OH and NH₂) were the least reactive ones. With acetylation of 4-hydroxy benzonitrile better yields was obtained but for 4-amino benzonitrile and 2-amino benzonitrile even heating till 72 hours no product was formed.

Table 2 Preparation of arylaminotetrazoles in the presence of catalyst by reaction between sodium azide and nitriles^{a,b}

Entry	Substrate	Product	Yields ^c				Ref.
			Zeolite		Sulfated Zirconia		
			H ₂ O	DMF	H ₂ O	DMF	
1	 1a	 3a	75	90	80	90	19
2	 1b	 3b	84	94	80	90	20
3	 1c	 3c	70	86	72	90	19
4	 1d	 3d	85	95	72	94	20
5	 1e	 3e	90	92	80	90	20
6	 1f	 3f	74	90	90	95	20

^a The products were characterized by IR, ¹H-NMR, ¹³C-NMR and mass spectroscopy.

^b Reaction times (24 h)

^c Isolated yields after recrystallization

^e The product did not isolated

CONCLUSION

In conclusion, we have developed a simple, ecofriendly and efficient method for the preparation of aryl aminotetrazoles using zeolite and sulfated Zircona as effective and reusable catalyst. Various cyanamides reacted with NaN_3 in the water and DMF/MeOH to yield the corresponding arylaminotetrazoles.

The significant advantages of this methodology are high yields, simple methodology, easy work-up and elimination of dangerous and harmful hydrazoic acid, a simple work-up procedure, and easy preparation and handling of the catalyst. The catalyst can be recovered by filtration and reused.

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