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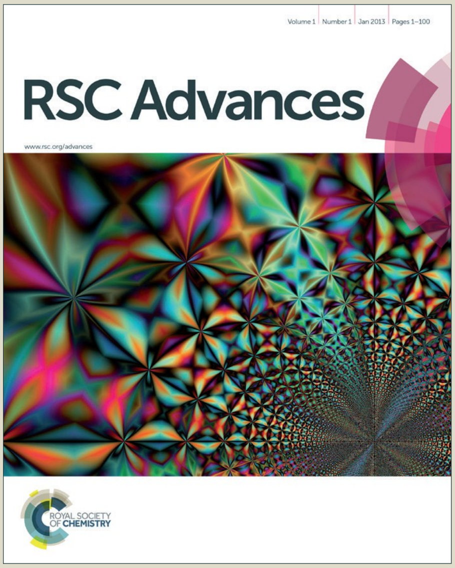

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Expanded perlite: an inexpensive natural efficient heterogeneous catalyst for the green and highly accelerated solvent-free synthesis of 5-substituted 1*H*-tetrazoles using [bmim]N_3 and nitriles

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Abstract: A versatile, green and highly accelerated protocol for preparing 5-substituted 1*H*-tetrazoles is reported. In this method, 5-substituted 1*H*-tetrazoles are synthesized from nitriles and [bmim]N_3, in the presence of the expanded perlite as an inexpensive natural efficient heterogeneous catalyst, under solvent-free condition. A wide variety of aryl nitriles underwent [3 + 2] cycloaddition to afford the desired tetrazoles in good to excellent yields, rapidly. This method has the advantages of high yields, short reaction times, simple methodology, and easy work-up. The catalyst can be recovered by simple filtration and reused delivering good yields.

Keywords: Expanded perlite, 5-Substituted 1*H*-tetrazoles, [3 + 2] Cycloaddition reaction, Heterogeneous catalyst, Solvent-free

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Introduction

Recently, considerable attention has been paid to the use of green methods in the synthesis of organic compounds. Catalysis organizes the foundation of chemical industry nowadays. Therefore, replacement of environmentally hazardous catalysts with non-toxic, effectual and reusable catalysts that have been associated with great reactivity, operational simplicity and non-corrosive nature is highly desired.[1-11] On the other hand removing solvent from the reaction medium is a safety subject, while solvents are potentially toxic. Hence, utilizing the solvent-free procedures is one of the proper options, particularly with respect to the E-factor.[12]

5-Substituted 1*H*-tetrazoles are an imperative class of heterocycles with an extensive range of applications in medicinal chemistry,[13,14] coordination chemistry,[15] agriculture,[16] photography,[17] speciality explosives in materials science[18] and information recording systems.[19] Furthermore, due to their similarity in acidity and planarity, they can function as lipophilic spacers and carboxylic acid substitutes[20] in pharmaceuticals. Synthesis of tetrazoles was first reported in 1901, *via* the reaction of hydrazoic acid with nitriles.[21] This approach had some drawbacks, such as high toxicity, explosive nature, and low boiling point (37 ˚C) of hydrazoic acid.[21] The most widely used method for the preparation of 5-substituted 1*H*-tetrazoles involves [3 + 2] cycloaddition of an azide anion with organic nitriles in the presence of different homogeneous and heterogeneous catalysts. [22,23] However, some of these methods suffer from disadvantages such as harsh reaction conditions, inferior yields of the desired product, long reaction times, formation of side products, stoichiometric amounts of the catalyst, water sensitivity, use of toxic solvents, use of organic azide complexes such as tin or silicon organic azides, and *in situ* generated hydrazoic acid.[24]

In continuation of our recent studies on the development of new methods for tetrazoles synthesis,[25-27] and according to the green chemistry legislations, herein, we are willing to

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report the superior activity of highly porous expanded perlite as a new green and efficient heterogeneous catalyst, to catalyze [3 + 2] cycloaddition reaction between organic nitriles and azide ion to corresponding 5-substituted 1*H*-tetrazoles, in high yields and purity (Scheme 1). The advantage of this method compared with previously published procedures, is in using 1-butyl-3-methylimidazolium azide [bmim]N_3 ionic liquid as azide source[28] (Scheme 1), in place of the highly toxic reagents such as NaN_3 or $TMSN_3$,[29-44] as well as using natural catalyst, in solvent-free conditions instead of the most commonly used toxic solvents in this context, such as DMF and DMSO.[31-37,39,41,45]

Results and Discussion

Perlite is a naturally glassy volcanic rock which contains usually 2-6 % water.[46] Unexpanded (raw) perlite, can expands up to 10-20 times of its initial volume, upon heating to elevated temperatures (700–1200 ˚C), which is then called "expanded perlite".[47] This phenomenon is due to the vaporization of the trapped water in the perlite structure. The resulting expanded material is a bright white, due to the reflectivity of trapped water bubbles. The bulk density of unexpanded perlite is around 1100 kg/m^3 (1.1 g/cm^3), while typical expanded perlite has a bulk density of about 30–150 kg/m^3 (0.03-0.150 g/cm^3).[48] Expanded perlite has several advantages such as light weight, high porosity along with strong adsorbability, natural abundance, admirable thermal and chemical stability, mechanical resistance, low cost, low toxicity, non-corrosiveness and ease of handling.[49-54] Production and consumption of perlite are very extensive.[55] United States, China, Greece, Japan, Hungary, Armenia, Italy, Mexico, Philippines and Turkey, are the leading countries in perlite production.[55] Furthermore, Iran is one of the best perlite suppliers in the Middle East that has several perlite resources specially in Mianeh, Semnan, Birjand, Ferdows, etc. Expanded perlite is widely used in many industries such as dyeing, food, drug, fuel oil, filter aid, filler in paint, enamels, glazes,

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plastics, and resins, etc.[56,57] The unique high-porous structure of expanded perlite makes it an excellent support for the preparation of heterogeneous catalysts.[58] Furthermore, expanded perlite has multi-catalytic active sites[59] which confirms that it is a potential candidate for heterogeneous catalyst in organic chemistry.[59, 60]

Characterization of expanded perlite

Expanded perlite was identified by X-ray fluorescence analysis (XRF), FT-IR spectroscopy, scanning electron microscopy and energy dispersive spectrometry (SEM-EDS).

XRF analysis of the catalyst

The chemical composition of the expanded perlite was determined by XRF (Table 1). As can be seen in Table 1, the principal compositions of the expanded perlite are SiO_2 and Al_2O_3. Accordingly, expanded perlite is considered to be a natural alumino-silicate.

Table 1: Chemical composition of expanded perlite

Constituent	SiO_2	Al_2O_3	K_2O	Fe_2O_3	Na_2O	CaO	MgO
Percentage	75.220	12.770	5.187	0.741	2.520	0.608	0.226
Constituent	BaO	SO_3	ZrO_2	TiO_2	Rb_2O	SrO	MnO
Percentage	0.087	0.060	0.014	0.110	0.012	0.008	0.066

FT-IR spectrum of the catalyst

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The FT-IR spectrum of expanded perlite was shown in Fig. 1a. There are five main absorption bands in the infrared spectrum of expanded perlite,[46] which were observed around 3439 cm^{-1}, 1625 cm^{-1} , 1044 cm^{-1} , 791 cm^{-1} and 463 cm^{-1} . The peaks at 3439 cm^{-1} and 1625 cm^{-1} are respectively assigned to the stretching and bending modes of the hydroxyl groups which are attached to the surface of expanded perlite (mainly Si-OH groups) and the adsorbed water molecules.[58b] The peaks positioned at 1044 cm^{-1} and 791 cm^{-1} are ascribed to Si–O stretching vibrations of Si-O-Si and Si-O-Al, respectively.[61] O–Si–O bending vibration was observed at about 463 cm^{-1}.[46]

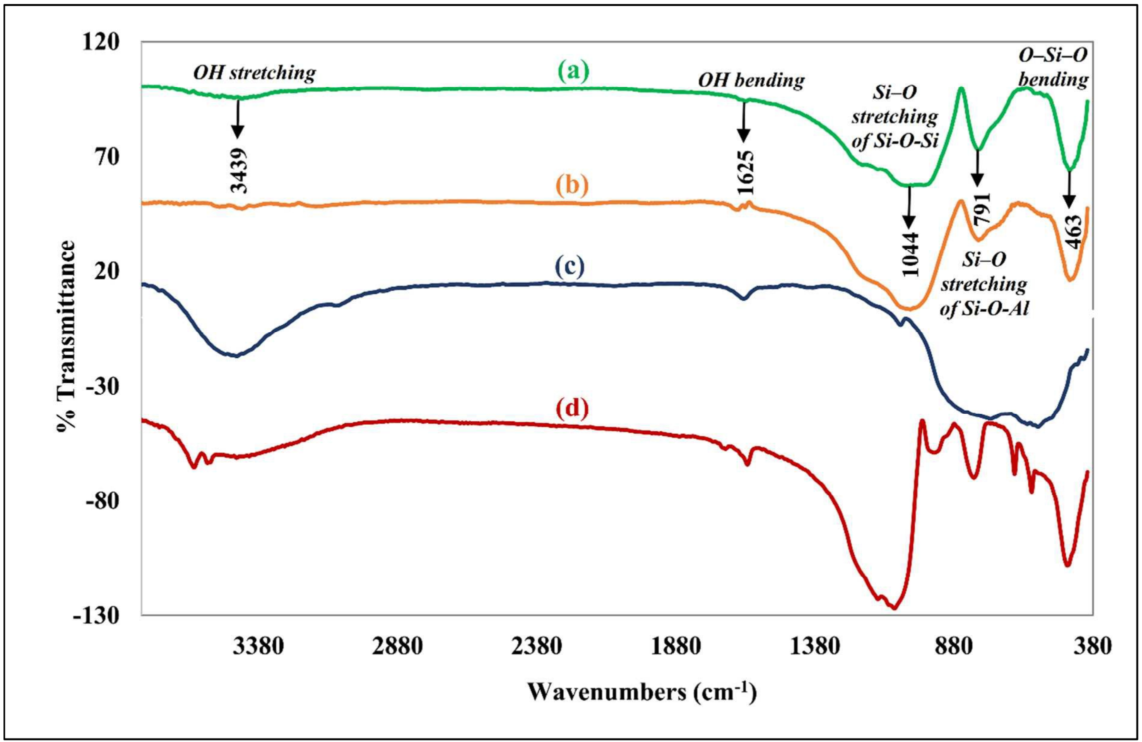

Fig. 1 FT-IR of (a) Fresh expanded perlite, (b) 6th Recovered expanded perlite, (c) Alumina, (d) Silica.

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SEM analysis of the catalyst

Fig. 2 illustrates the scanning electronic microscopy (SEM) of non-powdered expanded perlite (a-c) and finely powdered expanded perlite (d-f). It is clear that the morphology of the non-powdered expanded perlite is a layer structure with high porosity. The layer thickness size for non-powdered expanded perlite is around 844 nm – 1.794 μm. It is important to say that the layer structure of finely powdered expanded perlite was preserved whereas its porous nature was taken down upon powdering process.

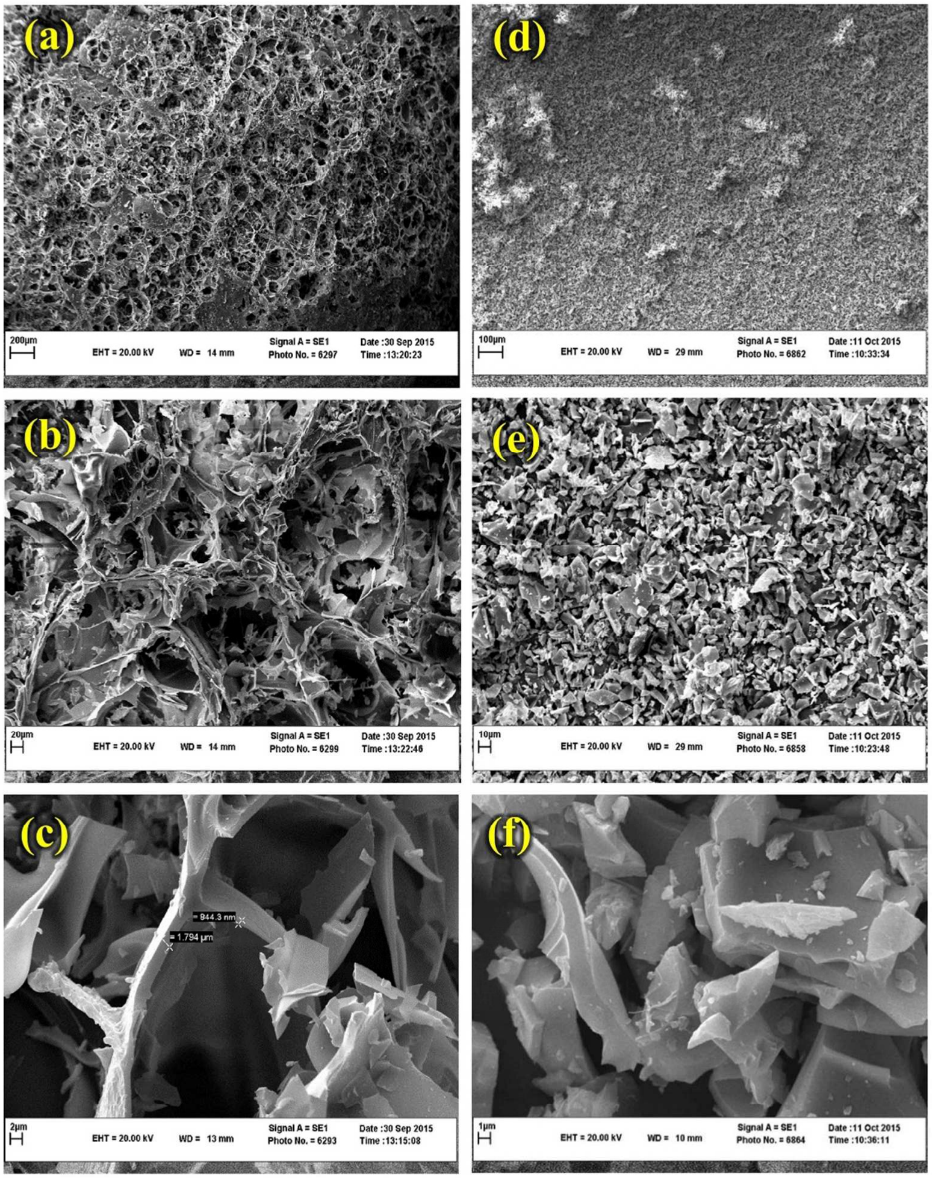

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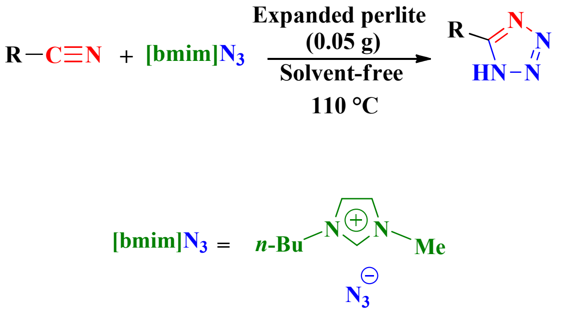
Fig. 2 SEM images of non-powdered expanded perlite (a-c) and finely powdered expanded perlite (d-f).

EDS analysis of the catalyst

The energy dispersive spectrum (EDS) of expanded perlite indicates the presence of Si, Al, O, Fe, K, Na as the main components of the expanded perlite (*see supporting information*) which is in a good agreement with the XRF results.

To benefit the unique properties of highly porous expanded perlite as an efficient natural green heterogeneous catalyst and to follow our interest in the synthesis of 5-substituted-1*H*-tetrazoles, we investigated the capability of expanded perlite to catalyze [3 + 2] cycloaddition reaction of nitriles with azide ion to achieve the desired 5-substituted-1*H*-tetrazoles (Scheme 1).



Scheme 1 Synthesis of different structurally 5-substituted-1*H*-tetrazoles in the presence of the expanded perlite under solvent-free conditions.

The reaction of benzonitrile and [bmim]N_3 was chosen as a model reaction for optimizing the reaction conditions (Table 2). When the model reaction was examined under solvent-free condition at 120 ºC in the absence of expanded perlite, very low yield of product was acquired, even after a prolonged reaction time (Table 2, entry 1). In contrast, by using the

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same reaction conditions, in the presence of the expanded perlite, the desired product was obtained in excellent yield after 10 min (Table 2, entry 2). This result implies to prominent role of highly porous expanded perlite in the synthesis of 5-phenyl-1*H*-tetrazole. As demonstrated in Table 2, at lower reaction temperature (110 ºC) the reaction progress was the same as at 120 ºC (Table 2, entry 3), whilst further decreasing the reaction temperature (100 ºC), leads to lower yield of product (Table 2, entry 4). So, temperature plays an important role in [3 + 2] cycloaddition reaction of nitriles with azide ion. Furthermore, the reaction was carried out in several solvents such as DMSO, DMF, CH_3CN, $CHCl_3$, toluene, CH_3NO_2, 1,4-dioxane, PEG and H_2O (Table 2, entries 5–13). On the basis of the data obtained from Table 1, the best result was obtained in solvent-free condition (Table 2, entry 3). To improve the yield of the reaction product, the effect of different molar ratios of reactants was examined (Table 2, entries 14, 15). According to this study, by decreasing the amount of azide ion to 1 mmol, lower yield of the product was obtained in longer reaction time (Table 2, entry 14), while additional amount of azide ion (2 mmol) was found to have no more effect on the product yield (Table 2, entry 15). To study the efficacy of catalyst amount, preparation of 5-phenyl-1*H*-tetrazole was performed under solvent-free condition at 110 ºC in the presence of 0.06 g and 0.04 g of catalyst. It is obvious from the results that the lower amount of catalyst resulted only 70% yield of the product even after long period of time (Table 2, entry 16) while further improvement of yield was not observed upon increasing the amount of catalyst (Table 2, entry 17). Hence 0.05 g of catalyst was considered as an optimum catalyst amount. To study the effect of the expanded perlite porosity (as corroborated by SEM images (Fig. 2)), on the [3 + 2] cycloaddition reaction of organic nitriles with azide ion, the model reaction was performed in the presence of non-powdered expanded perlite. Very low yield of the product was obtained in the presence of non-powdered expanded perlite (Table 2, entry 18). In continuing of our study, by considering the main components of the expanded perlite (*see*

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XRF results in Table 1), we decided to probe the reactivity of each segment. For this purpose, silica, alumina (neutral, acidic and basic) and mixture of 5.6:1 (w/w %) of silica : alumina were used as catalyst in [3 + 2] cycloaddition reaction of benzonitrile and azide ion, separately. As it is depicted in Table 2, neither these segments (silica and alumina), nor mixture of silica : alumina (5.6:1 w/w %) have the efficiency of expanded perlite for catalyzing this transformation (entries 19-23).

Table 2 Synthesis of 5-phenyl-1*H*-tetrazole under different reaction conditions.

Entry	Molar ratio Nitrile : Azide	Catalyst (g)	Temp (˚C)	Solvent	Time (h)	Isolated Yield (%)
1	1:1.5	-	120	-	15	30
2	1:1.5	0.05	120	-	10 min	95
3	**1:1.5**	**0.05**	**110**	-	**10 min**	**95**
4	1:1.5	0.05	100	-	1	90
5	1:1.5	0.05	110	DMSO	1	75
6	1:1.5	0.05	110	DMF	1	68
7	1:1.5	0.05	Reflux	CH_3CN	1	trace
8	1:1.5	0.05	Reflux	$CHCl_3$	1	-
9	1:1.5	0.05	Reflux	Toluene	1	trace
10	1:1.5	0.05	Reflux	CH_3NO_2	1	-
11	1:1.5	0.05	Reflux	1,4-Dioxane	1	-
12	1:1.5	0.05	110	PEG	35 min	69
13	1:1.5	-	Reflux	H_2O	24	10
14	1:1	0.05	110	-	30 min	80
15	1:2	0.05	110	-	10 min	95
16	1:1.5	0.04	110	-	1	70
17	1:1.5	0.06	110	-	10 min	95
18[a]	1:1.5	0.06	110	-	1	15
19[b]	1:1.5	0.06	110	-	1	25
20[c]	1:1.5	0.06	110	-	1	60
21[d]	1:1.5	0.06	110	-	1	10
22[e]	1:1.5	0.06	110	-	1	15

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23[f]	1:1.5	0.06	110	-	1	43

[a] Non-powdered expanded perlite was used as catalyst .

[b] Silica was used as catalyst.

[c] Neutral alumina was used as catalyst.

[d] Basic alumina was used as catalyst.

[e] Acidic alumina was used as catalyst.

[f] A mixture of 5.6:1 (w/w %) of silica : alumina was used as catalyst.

With the optimum reaction conditions in hand and aiming to extend the scope of our methodology, various structurally divergent nitriles possessing a wide range of functional groups (Scheme 1) were employed as substrates for this reaction. The results are summarized in Table 3. As the entries in Table 3 reveal, in spite of clear different effect of electrophilic nature of nitrile on the reaction times and product yields, the catalysis proceeded well for a wide variety of aryl nitriles, and provided the corresponding tetrazoles in high yields. Reactions of electron poor nitrile compounds were completed within a short reaction time, whereas electron rich nitriles required more reaction time to proceed properly, therefore it seems that the more electron-poor a nitrile, the faster it reacts. As it is depicted in Table 3, the reaction completion for aromatic nitriles with electron withdrawing substituents at *para* position took less time (10-25 min) for complete conversion of starting materials (Table 3, entries 2-5). Interestingly 1,4-dicyanobenzene (Table 3, entry 5) afforded the mono-addition product selectively, while in the reaction between sodium azide and 1,4-dicyanobenzene in the presence of Zn(II) salts the double addition product was reported.[62,22] 2-Amino-5-nitrobenzonitrile results the desired product in longer reaction time due to steric effect and electron donation of $-NH_2$ substitution at *ortho* position (Table 3, entry 6). Moreover, aromatic rings with electron donating groups gave the corresponding tetrazoles in high yields, although longer reaction times (20-60 min) were required (Table 3, entries 7-12). It is worth to note that, aryl nitrile containing a free hydroxyl group at *para* and *ortho* positions gave desired product in high yield after 30 and 20 min respectively (Table 3, entries 11 and 12).

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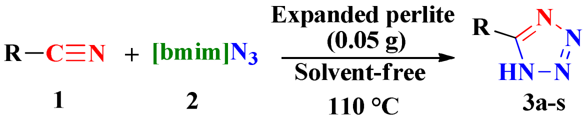
Hydroxyl group at *ortho* position render inductive effect which accelerates the cycloaddition reaction of 2-hydroxybenzonitrile. Phenanthrene-9-carbonitrile with steric hindrance at 9 position produced the corresponding tetrazole after 45 min (Table 3, entry 13). Similarly, heteroaryl nitriles were found to be extremely reactive substrate affording the relative tetrazole rapidly in the presence of expanded perlite (Table 3, entries 14-16). We next examined the cycloaddition of alkyl nitriles such as 2-phenylacetonitrile, 3-methylbutanenitrile and 4-methylpentanenitrile in the presence of the expanded perlite. It was found that alkyl nitriles in the presence of expanded perlite reacted smoothly to give the corresponding 5-substituted-1*H*-tetrazoles in excellent yields after 45-80 min (Table 3, entries 17-19). The results obtained from Table 3 indicate that [3 + 2] cycloaddition reaction of nitriles with azide ion in the presence of highly porous expanded perlite proceeds rapidly irrespective of the electronic nature of nitrile compounds.

Table 3. Synthesis of different structurally 5-substituted-1*H*-tetrazoles in the presence of the expanded perlite under solvent-free conditions.



Entry	R	Product	Time (min)	Isolated Yield (%)
1	C_6H_5	**3a**	10	95
2	4-ClC_6H_4	**3b**	15	94
3	4-BrC_6H_4	**3c**	25	90
4	4-$NO_2C_6H_4$	**3d**	10	91
5	4-CNC_6H_4	**3e**	10	96
6	2-NH_2 5-$NO_2C_6H_3$	**3f**	30	93
7	4-$EtOC_6H_4$	**3g**	35	90

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8	3,5-di-MeOC$_6$H$_4$	**3h**	60	92
9	4-MeC$_6$H$_4$	**3i**	57	94
10	3-MeC$_6$H$_4$	**3j**	50	94
11	4-OHC$_6$H$_4$	**3k**	30	85
12	2-OHC$_6$H$_4$	**3l**	20	93
13	9-phenanthrene	**3m**	45	84
14	4-pyridine	**3n**	20	95
15	2-pyridine	**3o**	35	91
16	2-thiophene	**3p**	20	89
17	C$_6$H$_5$CH$_2$	**3q**	45	95
18	(CH$_3$)$_2$CHCH$_2$	**3r**	80	90
19	(CH$_3$)$_2$CH(CH$_2$)$_2$	**3s**	65	91

All synthesized tetrazoles were known compounds and characterized by FT-IR spectroscopy, mass spectrometry and comparison of their melting points with known compounds. In addition, the structure of all products was certified by ^{1}H NMR and ^{13}C NMR spectroscopy. In all cases, formation of 5-substituted 1*H*-tetrazoles was confirmed by disappearance of the strong and sharp absorption band at about 2200 cm^{-1} (related to the CN stretching vibration), and the appearance of an absorption band at 3485-3329 cm^{-1} (related to the N-H stretching vibration). Moreover, the FT-IR spectra of all products reveal peaks at 1469-1430 cm^{-1} (due to scissoring bending C-H), 1293–1233 cm^{-1} (due to N–N=N–), 1189–1110 and 1106-1041 cm^{-1} (due to tetrazole ring). In ^{1}H NMR and ^{13}C NMR spectra, a signal at 10.98-7.80 and 164–151 ppm are correspond to the NH and quaternary carbon NH–C=N respectively.[25-27]

The plausible mechanism for the reaction pathway under current development is shown in Scheme 2. As mentioned before, only poor yield of product was obtained in the absence of expanded perlite even after a long reaction time (Table 2, entry 1). This fact, elucidated the superior catalytic activity of expanded perlite in [3 + 2] cycloaddition reactions of various

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organic nitriles with azide ion. Since the role of catalyst in [3 + 2] cycloaddition reaction is not apparent certainly, the next study was to understand which segment or feature of the expanded perlite has the essential effect on catalyzing process. Assuming that the reaction proceeds through hydrogen bonding of catalyst hydroxyls with nitrogen atom of nitrile, the model reaction was also carried out in the presence of silica, alumina and a mixture of silica : alumina (5.6:1 w/w %) (Table 2, entries 20-24). Although, the FT-IR spectra (Fig. 2) verified the existence of more OH groups in silica and alumina than expanded perlite, the reaction progress in the presence of each fundamental segments of perlite (silica, alumina and a mixture of silica : alumina (5.6:1 w/w %)) was not satisfying. These results led us to conclude that the hydroxyl groups of catalyst might affect the reaction progress but they had not the dominate role.

Then, to study the effect of the expanded perlite porosity (which corroborated by SEM images (Fig. 1)) on the [3 + 2] cycloaddition reaction of organic nitriles with azide ion, the model reaction was performed in the presence of finely powdered and non-powdered expanded perlite. Excellent yield of product was obtained in the presence of finely powdered expanded perlite, while 5-phenyl-1*H*tetrazole was obtained in 15 % yield in the presence of non-powdered perlite (Table 2, entry 19). Consequently, [3 + 2] cycloaddition reaction of organic nitriles with azide ion in the presence of expanded perlite was dependent on the physical form of the catalyst, strongly. Thus, the porosity of expanded perlite has not vital effect on the reaction rate.

The above findings instructed us to the presence of definite multi-catalytic active sites[59] on the surface of expanded perlite which presumably has the principal catalytic role in this transformation. By analogy with previous reports in the literature, as well as our recent studies,[25-27] it is assumed that a ternary complex **I** between nitrile compound, azide ion and expanded perlite would be formed in the transition state immediately as shown in Scheme 2.

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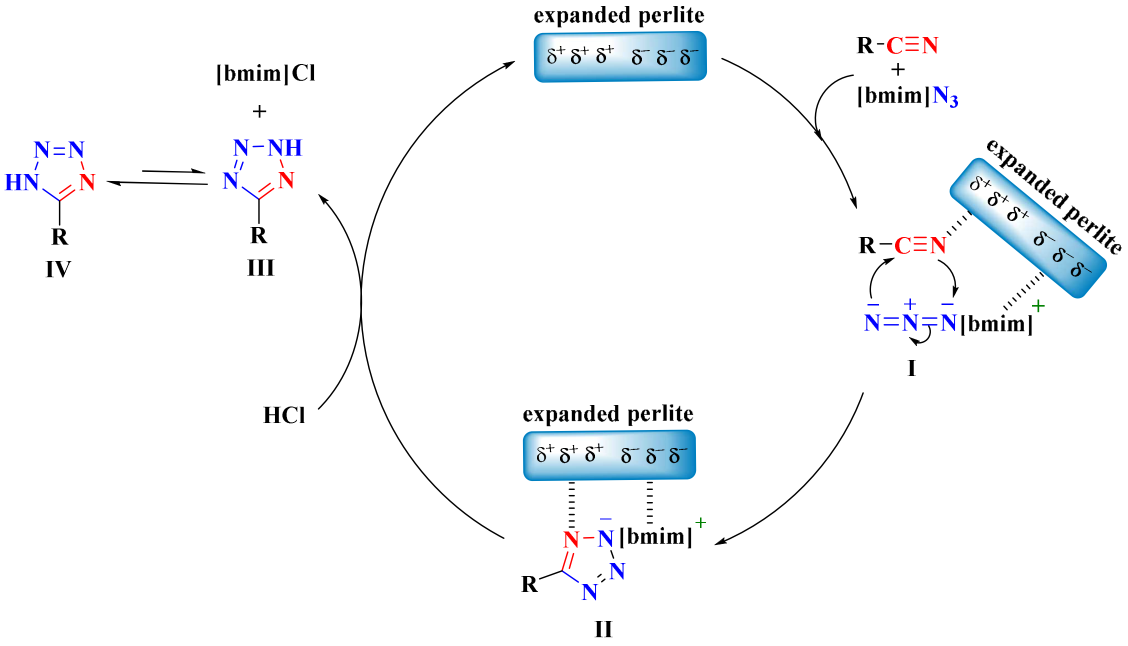
Subsequently, the nitrile functionality is activated through acidic sites of perlite surface which accelerates the cyclization step by increasing the electrophilicity of nitrile group. Then, the reaction proceeds *via* [3 + 2] cycloaddition between the C≡N bond of nitrile and azide ion to form the intermediate **II** which is followed by formation of complex **III** upon protonolysis by HCl (4 N). Complex **III** converted to more stable complex **IV** which is the desired 5-substituted 1*H*-tetrazole. Finally expanded perlite re-inters the catalytic cycle. It is worth to note that the expanded perlite was not destroyed in work-up procedure, since the expanded perlite offers very good chemical stability in acidic condition.[46] More investigation for the clarification of the mechanism and scope of this reaction are presently in progress in our laboratory.



Scheme 2 Proposed mechanism for the synthesis of 5-substituted-1*H*-tetrazoles in the presence of the expanded perlite.

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Heterogeneous catalysis is quite desirable due to ease of separation and probable reusability in further runs. Thus, the recyclability of expanded perlite was examined in the one-pot synthesis of 5-phenyl-1*H*-tetrazole **3a** under optimized conditions. After completion of [3 + 2] cycloaddition reaction of benzonitrile with azide anion, the reaction mixture was acidified and then the catalyst was separated by simple filtration from the reaction mixture. To remove all organic components, the catalyst was washed with distilled water, methanol and ethanol three times. The catalyst was dried at 100°C for 3 h. As it is illustrated in Fig. 3 no significant loss in catalytic activity and product yield was observed even after six runs.

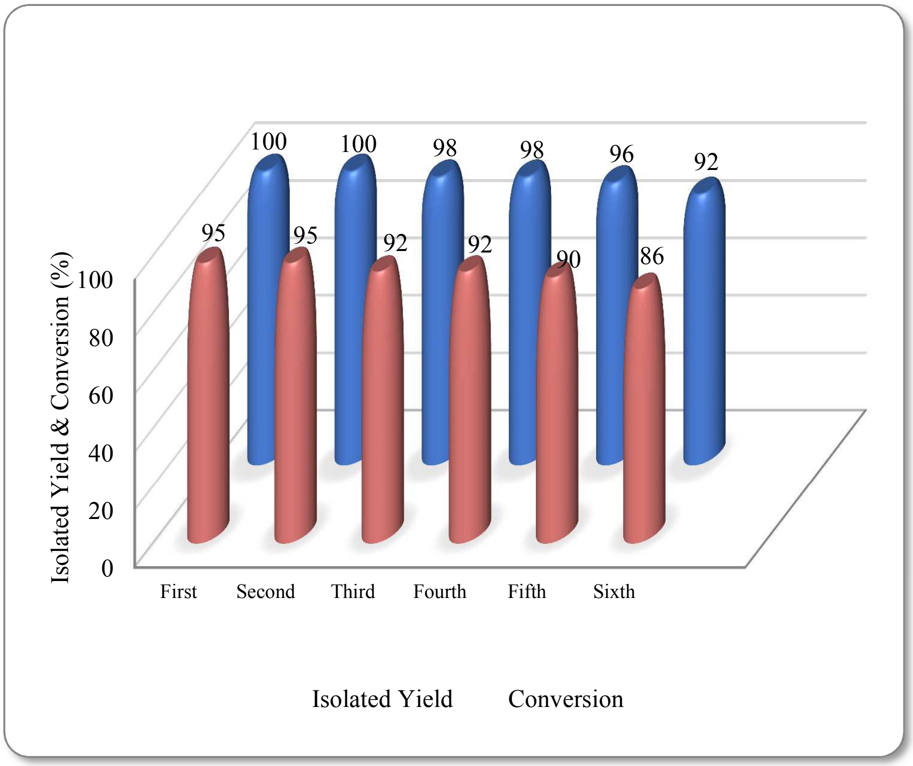

Fig. 3 [3 + 2] Cycloaddition reaction of benzonitrile with azide ion in the presence of reused expanded perlite.

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The FT-IR spectrum of the 6th recovered expanded perlite was shown in Fig. 1b. It is worth mentioning that the position, shape and relative intensity of all characteristic peaks are well maintained. The results suggest no significant changes were observed in the chemical structure of expanded perlite network even after six runs.

Experimental

General

The purity determinations of the products were accomplished by TLC on silica gel polygram STL G/UV 254 plates. The melting points of products were determined with an Electrothermal Type 9100 melting point apparatus. The FT-IR spectra were recorded on an Avatar 370 FT-IR Therma Nicolet spectrometer. The NMR spectra were provided on Brucker Avance 100, 300 and 400 MHz instruments in $CDCl_3$, DMSO-d_6 and CD_3CN. Mass spectra were recorded with Agilent Technologies (HP) 5973 Network Mass Selective Detector, Shimadzu GC-MS-QP5050 instruments and a CH7A Varianmat Bremem instrument (Germany) at 70 eV. Elemental compositions were determined with a Leo 1450 VP scanning electron microscope equipped with an SC7620 energy dispersive spectrometer (SEM-EDS) presenting a 133 eV resolution at 20 kV. The chemical compositions of the expanded perlite were specified with X-ray fluorescence spectroscopy (XRF), using BRUKER axs-S4 EXPLORER spectrometer. All of the products were known compounds and they were characterized by the FT-IR spectroscopy and comparison of their melting points with known compounds. The structure of all products was further confirmed by ^{1}H NMR, ^{13}C NMR spectroscopy, and mass spectrometry. Expanded perlite was obtained from Iran; Birjand resources.

Providing of neat expanded perlite powder

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Finely powdered expanded perlite (10 g) was added to 400 mL methanol and ethanol (1/1 v/v) and stirred at room temperature for 24 h. to remove organic components. The resulting suspension was filtered and washed by distilled water, methanol and ethanol three times respectively. The grey resulting expanded perlite powder was dried at 100 ºC for 3 h.

Preparation of 1-butyl-3-methylimidazolium chloride[63]

1-Chlorobutane (10.8 g, 0.8 mol) was added to 1-methyimidizole (8.2 g, 0.1 mol), in a round bottomed flask equipped with a reflux condenser. The mixture was stirred at 70 ºC for 48 h. After formation of two phases, the top layer which contains unreacted starting material was decanted. Then ethyl acetate (30 mL) was added with entire mixing followed by its decantation and this step was repeated three times. After the third decanting of ethyl acetate, remaining solvent was removed by heating at 70 ºC. The obtained pale yellow liquid was vacuum distilled and the resulting 1-butyl-3-methylimidazolium chloride was placed for vacuum drying at 80 ºC in a vacuum drying oven.

Preparation of 1-butyl-3-methylimidazolium azide[28]

Freshly prepared 1-butyl-3-methylimidazolium chloride (3.49 g, 20 mmol) and NaN_3 (1.30 g, 20 mmol) were added into 25 mL deionized water, and the mixture was stirred for 24 h at room temperature. The solvent was removed under reduced pressure at 50 ºC. To separate 1-butyl-3-methylimidazolium azide from the crude product (which contains azide ionic liquid and NaCl), the resulting was washed with acetonitrile (3×10 mL). The remaining acetonitrile was removed under high vacuum to yield yellow transparent liquid that became more viscous upon extensive drying. Isolated yield was 92 % (3.33 g).

Typical procedure for preparation of 5-phenyl-1*H*-tetrazole in the presence of expanded perlite

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Finely powdered expanded perlite (0.05 g) was added to a mixture of benzonitrile (0.103 g, 1 mmol) and [bmim]N_3 (0.271 g, 1.5 mmol).The resulting mixture was stirred at 110 ˚C. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled and treated with HCl (4 N, 10 mL) and ethyl acetate (2×10 mL). The catalyst was filtered and the resulting organic layer was washed with distilled water, dried over anhydrous sodium sulfate and concentrated to give the crude solid crystalline 5-phenyl-1*H*-tetrazole (**3a**). The crude product was recrystallized from *n*-hexane/ethylacetate (1:1) and 0.138 g of colourless crystals (95% Isolated Yield) was obtained.

Afterwards, to reuse the catalyst in the next runs, the separated catalyst from the reaction mixture was washed with distilled water, methanol and ethanol three times to remove all organic components and it was dried at 100°C for 3 h.

Conclusion

In conclusion, we have introduced highly porous expanded perlite as a green and high efficient heterogeneous catalyst which exhibited superior catalytic activity for the one-pot synthesis of 5-Substituted 1*H*-tetrazoles under solvent-free conditions. The essential catalytic role of expanded perlite in this transformation is activation of nitrile through its surface multi-catalytic active sites.[59] Stability, low-toxicity, low cost and recyclability are the significant properties of this catalyst. In comparison with previously published procedures, 1-butyl-3-methylimidazolium azide ([bmim]N_3) ionic liquid was used as an azide source, in place of the highly toxic reagents such as NaN_3 or $TMSN_3$. Various nitriles reacted with azide ion at 110 ºC to yield the corresponding 5-substituted-1*H*tetrazoles. The noteworthy advantages of this approach are excellent yields of products, short reaction times (in comparison with the previous existing methodologies), solvent-free conditions, simple work-up procedure, easy handling of the catalyst, elimination of hazardous and harmful hydrazoic acid as well as toxic

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solvents such as DMF and DMSO. These are also the predominant features supporting this method in a movement toward the green chemistry.

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Notes and references

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Graphical Abstract

Expanded perlite: an inexpensive natural efficient heterogeneous catalyst for the green and highly accelerated solvent-free synthesis of 5-substituted 1*H*-tetrazoles using [bmim]N_3 and nitriles

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A versatile, green and highly accelerated protocol for preparing 5-substituted 1*H*-tetrazoles is reported using expanded perlite as a heterogeneous catalyst.