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Efficient heterogeneous silver nanoparticles catalyzed one-pot synthesis of 5-substituted 1H-tetrazoles

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ABSTRACT

Silver nanoparticles (AgNPs), characterized by TEM, EDX and UV studies were used as an efficient heterogeneous catalyst for the synthesis of 5-substituted 1H-tetrazoles from various nitriles possessing different functional groups in excellent yields. All title compounds were characterized by spectroscopy (^{1}H NMR, ^{13}C NMR and IR) and crystallography.

1. Introduction

Tetrazoles are nitrogen containing heterocyclic compounds which are studied extensively due to their wide range of biological and commercial applications [1]. Tetrazoles have gained wide attention due to its use in drug design as an isosteric replacement for carboxylic acids [2]. Application of tetrazoles includes its use in pharmaceuticals, explosives and as precursors of a variety of nitrogen containing heterocyclic compounds like imidoylazides [3,4]. In addition, they have been successfully used in the field of material sciences and synthetic organic chemistry as analytical reagents and synthons [5,6]. Synthesis of tetrazole ring is a crucial step in organic, medicinal and synthetic chemistry. The various methods for synthesis of tetrazoles are well documented in literature. 5-Substituted 1H-tetrazoles are synthesized by reaction between hydrazoic acid and isocyanides, isocyanides and trimethysilyl azide, cyclization between primary amines/their salts with an orthocarboxylic acid ester and sodium azide [7–10].

Numerous catalysts used in the synthesis such as Lewis acids, $AgNO_3$ [11], $Fe(OAc)_2$ [12], $In(OTf)_3$ [13], PCl_5 [14], $Yb(OTf)_3$ [15], Cu_2O [16] and natrolite zeolite [17] are well documented. Sharpless and co-workers gave a simple and most efficient procedure for the synthesis of tetrazoles by the addition of sodium azide to nitriles using 50 mol% Zn(II) salts [18] which provided simple use of transition metal catalysts in the synthesis of various tetrazoles.

In the last one decade, the use of silver nanoparticles for catalysis have also gained wide attention due to its enhanced physical, chemical and biological properties as compared to their macro scaled counterparts [19]. AgNPs are synthesized by several physical, chemical and biological methods [20–22]. To the best of our knowledge, no report is available where the silver nanoparticles have been utilized for the synthesis of tetrazole analogs. This led us to investigate whether the silver nanoparticles could be useful for tetrazole synthesis.

Herein we report the utility of silver nanoparticles for one-pot synthesis of 5-substituted 1*H*-tetrazoles via (3 + 2) cycloaddition in high yields in continuation of our work on catalysis for the synthesis of various pharmacologically active compounds [11]. It is an extension of the ongoing research work in our laboratory on design and synthesis of antimicrobial agents [23], and X-ray analysis of small molecules [24].

2. Experimental

2.1. Materials

All nitriles were purchased from Alfa Aesar (A Johnson Matthey Company, Great Britain). Silver nitrate ($AgNO_3$ 99.8%), sodium borohydride ($NaBH_4$ 98%) and sodium azide were purchased from Sigma–Aldrich Chemicals and used as it is. Double-distilled water was used for the preparation of all aqueous solutions. All solvents and reagents were obtained commercially and used as received.

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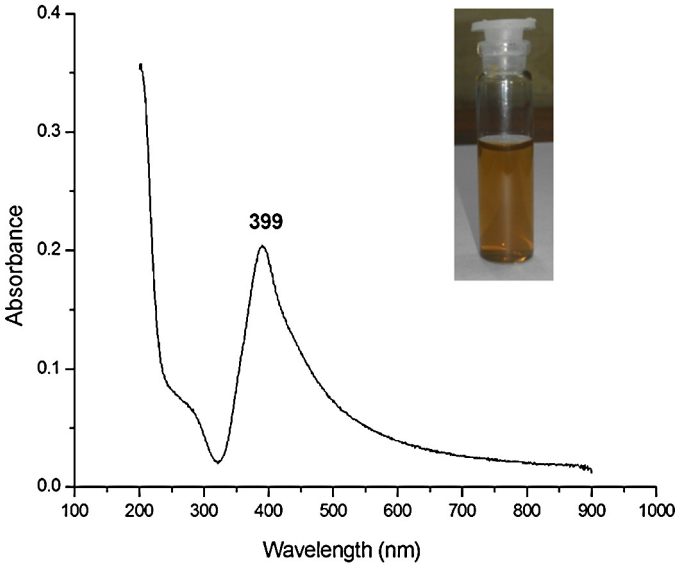


Fig. 1. UV–vis absorption spectrum of AgNPs.

2.2. Synthesis of catalyst

The catalyst AgNps was prepared according to the literature [23]. The aqueous solution of 10 ml of 0.001 M silver nitrate ($AgNO_3$) and 30 ml of 0.001 M sodium borohydride ($NaBH_4$) were prepared separately and ice-cooled. The $AgNO_3$ solution was added dropwise in $NaBH_4$ solution with vigorous stirring for 5 min. The mixture was left still for 1 h and then stirring continued again for 10 min. The yellow coloration of the solution confirms the formation of AgNps in the solution.

3. General procedure for preparation of 5-substituted 1H-tetrazole

Briefly, AgNPs (20 mol%) was added to the reaction mixture of the solution of benzonitrile (0.206 g, 2 mmol) in DMF (3 ml) and sodium azide (0.195 g, 3 mmol) with stirring for 8 h at 120 °C. The reaction was monitored by TLC and solvent removed in vacuo on completion of reaction. The crude product was then diluted by ice cooled water and centrifuged. The pH of the solution was adjusted to 2–3 by addition of 6 N HCl and extracted with ethylacetate. The resultant organic layer was separated and aqueous layer was extracted again with ethylacetate (3 × 20 mL). The combined organic layer was concentrated in vacuo to yield the crude white crystalline solid 5-phenyltetrazole in 82–93% yield. The crude tetrazole was then recrystallized by mixture of solvents (50% ethyl acetate in hexane) and subsequently characterized by ^{1}HNMR, ^{13}CNMR, IR and crystallography.

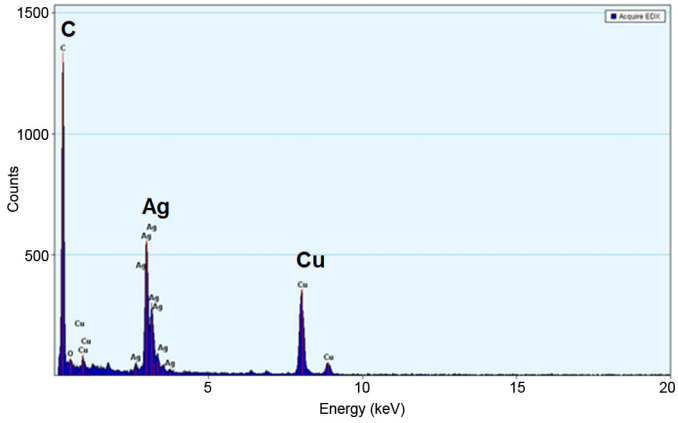


Fig. 3. Energy dispersive X-ray spectroscopy (EDX) of AgNPs.

4. Results and discussion

Silver nanoparticles were synthesized according to the reported procedure [25] and characterized using the surface plasmon resonance absorption in the UV–vis region. The UV–vis spectrum of AgNps shows characteristic absorption band at 399 nm for the yellow colored solution which is in agreement with the previous reports (Fig. 1) [26].

The morphological analysis of AgNps have been carried out using TEM, which suggests that the silver nanoparticles are not aggregated and the average size of the particle is estimated to be 40–42 nm (Fig. 2). High resolution transmission electron microscopy (HRTEM) image of AgNps as marked with the red frame (Fig. 2b) shows the interplanar spacing to be about 0.96 nm.

Moreover, Energy Dispersive X-Ray Spectroscopy (EDX) analysis (Fig. 3) shows a strong signal in the silver region which again confirms the formation of silver nanoparticles. In the present study, metallic AgNPs show typical optical absorption peak approximately at 3 keV due to surface plasmon resonance consistent with the literature value [25]. This analysis reveals that the nano-structures were formed solely of silver. The additional peaks in the EDX for

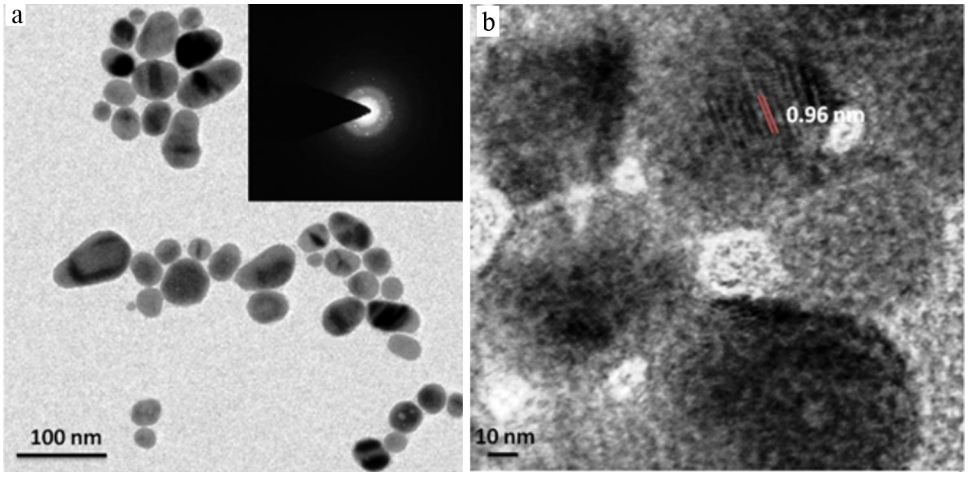


Fig. 2. Transmission electron microscopy (TEM) of AgNPs.

carbon and copper can be attributed due to the carbon coating on the copper grid.

The average size of AgNps is about 42 nm as calculated from DLS measurements using Zetasizer Nano-ZS90, Malvern Instruments at a scattering angle of 90° and constant temperature of 25 °C having a polydispersity index of ~0.2. Further, the zeta potential measurements reveal that the complex is negatively charged with a zeta potential of about −29.5 mV at the pH value of 4.0, indicating the stability of this composite at this pH (Fig. 4).

Subsequently, AgNPs were used for the synthesis of 5-substituted 1H-tetrazoles from various nitriles possessing a wide range of functional groups.

The reaction conditions were standardized and effect of solvents, temperature and catalyst loading were investigated to achieve best result for the formation of 5-substituted 1H-tetrazoles.

Experiments revealed that the nature of solvents play an important role. Reaction in polar protic solvents such as methanol and ethanol (Table 1, entries 9 and 10) results in only 27% and 22% product formation while acetonitrile (Table 1, entry 8) gave 36% product.

Table 1
Effect of catalyst and solvent on the formation of tetrazole **2a** from **1a**.

Sl no.	Catalyst	Solvent	Temp (°C)	Time (h)	% Yield
1.	AgNPs (10 mol%)	DMF	120	14	48
2.	AgNPs (10 mol%)	DMF	60	16	25
3.	AgNPs (20 mol%)	DMF	120	8	92
4.	AgNPs (20 mol%)	DMF	60	10	55
5.	AgNPs (30 mol%)	DMF	120	8	94
6.	AgNPs (30 mol%)	DMF	60	8	53
7.	AgNPs (20 mol%)	DMSO	120	8	57
8.	AgNPs (20 mol%)	CH_3CN	80	24	36
9.	AgNPs (20 mol%)	MeOH	63	24	27
10.	AgNPs (20 mol%)	EtOH	75	24	22
11.	AgNPs (20 mol%)	THF	65	24	-
12.	AgNPs (20 mol%)	$CHCl_3$	60	24	-
13.	AgNPs (20 mol%)	1,4-Dioxane	100	24	-
14.	AgNPs (20 mol%)	H_2O	100	24	-

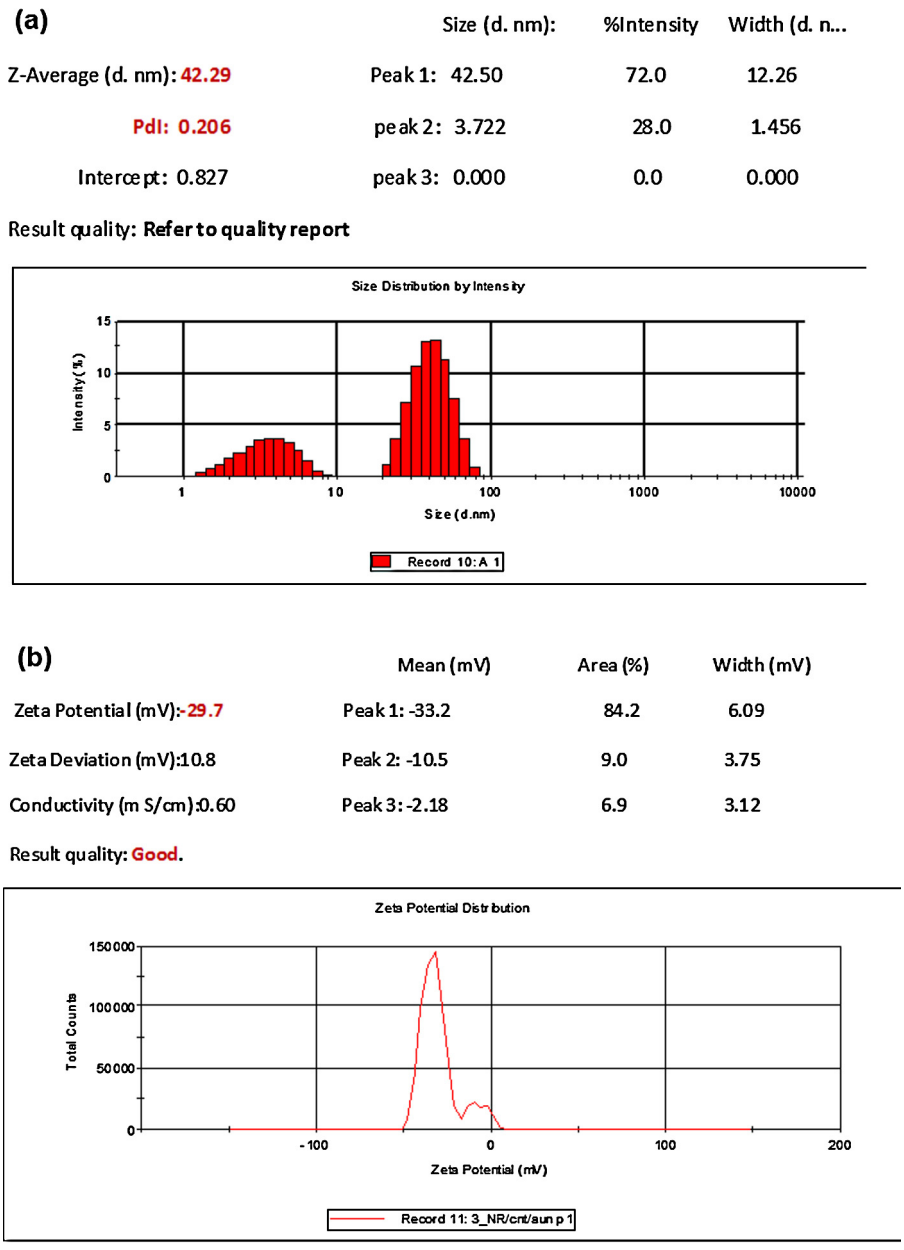


Fig. 4. (a) Size distributions of AgNPs with maximum intensity at 42 nm. (b) Stable AgNPs at −29.7 mV in Zeta potential analysis.

Other solvents such as THF, chloroform and 1,4-dioxane (Table 1, entries 11–13) also gave unsatisfactory results with no product formation even at elevated temperature after 24 h. The quest for green solvent motivated us to choose water as a reaction media but results were not encouraging (Table 1, entry 14). Interestingly, good yields were obtained with DMF (Table 1, entries 1–6) and DMSO (Table 1 entry 7). The higher yields of the products and comparative easier work up procedure led us to choose DMF over DMSO.

Further, the experiments on the effect of catalyst loading suggested 20 mol% catalyst is sufficient to perform (3 + 2) cycloaddition

Table 2
The synthesis of 5-substituted 1H-tetrazole with AgNPs under various substrates.[a]

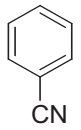
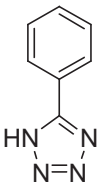
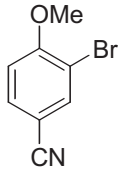
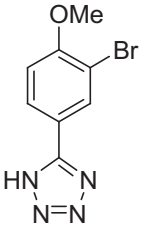
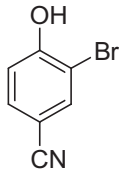
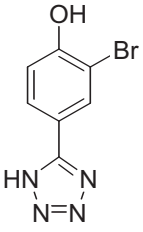
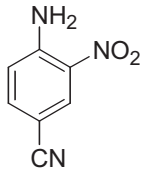
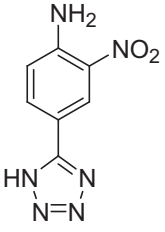
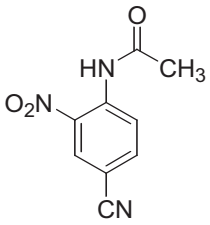
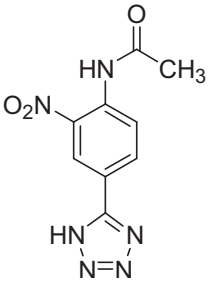
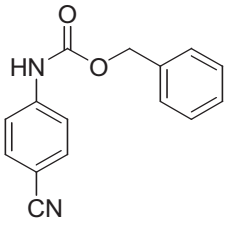
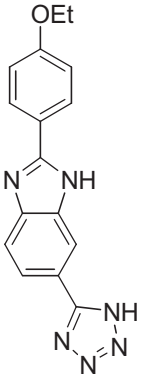
S no.	Substrate	1	Time (h)	Product	2	Yield[b] (%)
1		**1a**	8		**2a**	92
2		**1b**	8		**2b**	93
3		**1c**	8		**2c**[c]	86
4		**1d**	8		**2d**	87
5		**1e**	8		**2e**	82
6		**1f**	8		**2f**	85

Table 2 (*Continued*)

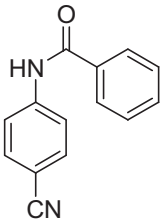
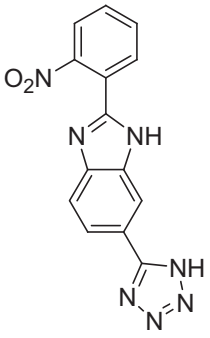
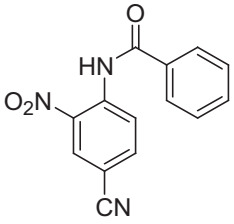
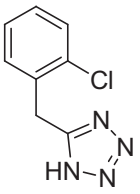
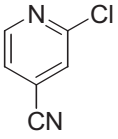
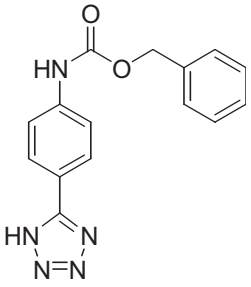
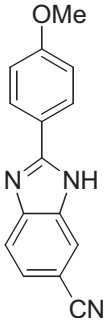
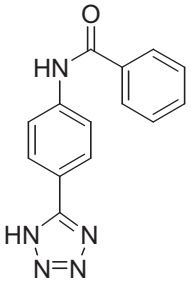
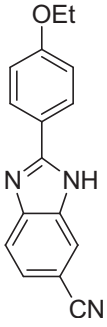
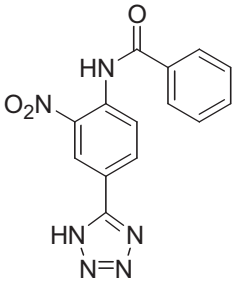
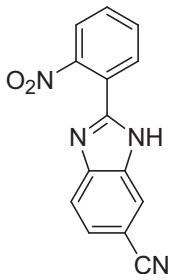
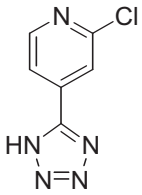
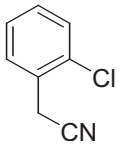
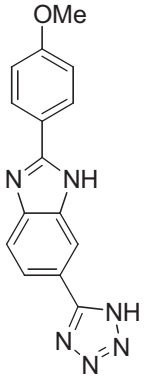
S no.	Substrate	**1**	Time (h)	Product	**2**	Yield[b] (%)
7		**1g**	8		**2g**	89
8		**1h**	8		**2h**	84
9		**1i**	8		**2i**	92
10		**1j**	8		**2j**	93
11		**1k**	8		**2k**	86

Table 2 (*Continued*)

S no.	Substrate	1	Time (h)	Product	2	Yield[b] (%)
12		**1l**	8		**2l**	89
13		**1m**	8		**2m**	83

[a] Reaction conditions: benzonitrile (2 mmol), NaN_3 (3 mmol), AgNPs (20 mol%), DMF (2–3 ml), reaction time 8 h, 120 °C.
[b] Experimental yield.
[c] Crystal structure.

in significantly higher yields (Table 1, entry 3). However, 10 mol% catalyst results in longer reaction time and lower yield (Table 1, entries 1 and 2). Finally, using 30 mol% catalyst we observed only a slight increase in the yield of product (Table 1, entries 5 and 6) at same temperature. The low temperature at the same catalyst loading also did not give better yield (Table 1, entries 2, 4 and 6). The optimized procedure followed for the synthesis of 5-substituted 1H-tetrazoles in the present study is: DMF as solvent and 20 mol% AgNPs as catalyst at 120 °C (Table 1, entry 3).

Substitution on aromatic ring produces difference in product formation, however the variation of yield in various substitutions is only ±5%. The effect of electron donating and withdrawing group is not clear in some cases, but in general, electron donating groups were found to give somewhat less yield in comparison to electron withdrawing group as is the case of (Table 2, entries 2–5, 10 and 11) methoxy, hydroxyl, amine, acetylated amine, methoxy and ethoxy group at para positions respectively. The methodology was also found applicable with benzimidazoles transformation bearing additional tetrazole moiety. Introduction of nitro group at meta position shows improved yield (Table 2, entry 8). Additionally, heterocyclic tetrazoles can also be prepared efficiently using AgNPs as catalyst (Table 2, entry 9). The protocol was also applied for the synthesis of aliphatic tetrazoles to get excellent yield (Table 2, entry 13). Hence, the above results show that the tetrazole formation via [3 + 2] cycloaddition reaction tolerates a wide range of substituents irrespective of their electronic behavior, positions and independent of the type of aromatic ring involved in conversion. Moreover, the authenticity of this approach was confirmed by X-rays analysis of compound **2c**. For the present study, X-ray quality single crystals of compound **2c** were grown in 50% ethyl acetate in hexane by slow evaporation solution growth method at room temperature. X-Rays structure revealed hydrated water molecule in 1:1 stoichiometric ratio in the crystal lattice of tetrazole (Fig. 5).

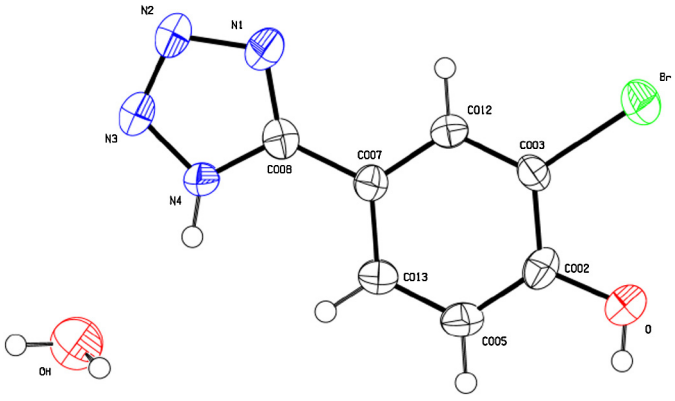


Fig. 5. ORTEP diagram of compound **2c**.

The tetrazole **2c** was crystallized in an orthorhombic cell and Pbca space group with the following lattice parameter: $a = 7.1637(8)$ Å, $b = 14.058(2)$ Å, $c = 18.350(2)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 3283.02(13)$ Å^3 and $\rho = 1.862$ g cm^{-3}.

The role of AgNPs as a catalyst in the synthesis of tetrazoles is shown in Fig. 6. Silver nanoparticles act as a Lewis acid activating the nitrile groups via complexation. Hence, it enhances the electrophilic character of cyanide group, which then reacts with sodium azide to form tetrazoles.

The recyclability of the catalyst was determined using the reaction and the conditions given in Scheme 1 (Fig. 7). The catalyst could be recovered easily by simple centrifugation and reused after washing with ethyl acetate and drying under vacuum. The recycled catalyst showed moderate to good catalytic activity for subsequent four catalytic cycles.

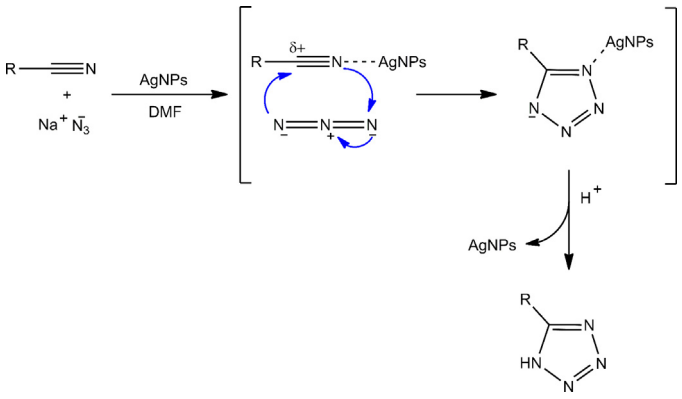
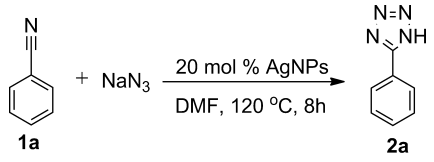


Fig. 6. Plausible mechanism for AgNPs catalyzed tetrazole synthesis.



Scheme 1. AgNPs catalyzed synthesis of 5-substituted 1H-tetrazoles.

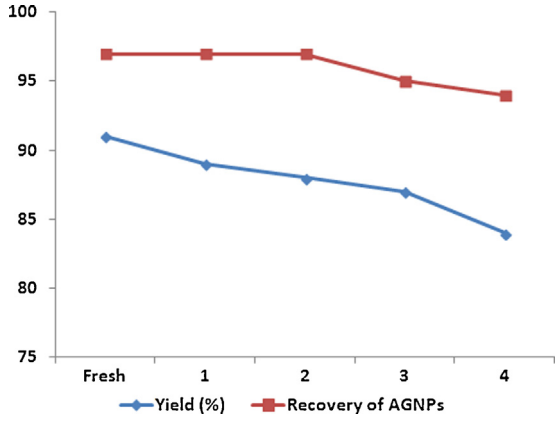


Fig. 7. Recyclability of the AgNp catalyst.

AgNps is thus an efficient and convenient reusable heterogenous catalyst for terazoles synthesis. The use of AgNPs as catalyst eliminates the formation of toxic waste and explosive by products. Further, the catalyst can be reused upto four cycles in our study with no significant loss of activity.

5. Conclusion

In conclusion, we report silver nanoparticles as an efficient and convenient catalyst for the one-pot synthesis of 5-substituted 1*H*-tetrazoles in various substituted nitriles and sodium azide in refluxing DMF in good to excellent yields. The easy availability of catalyst, a simple work-up procedure and better yields are significant advantages over other existing methods. Further studies in this area are in progress in our laboratory to broaden the scope of this and as well as other catalysts.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molcata.2014.05.008.

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