MoO$_3$-SiO$_2$ as an efficient and reusable heterogeneous catalyst for the synthesis of 5-substituted 1*H*-tetrazoles

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Abstract

An efficient method for the preparation of 5-substituted 1*H*-tetrazole derivatives is reported using MoO$_3$-SiO$_2$ as an efficient heterogeneous catalyst. This method has the advantages of high yields, simple methodology and easy work-up. This catalyst could be recycled very easily, which makes this methodology environmentally benign.

Keywords: 5-substituted 1*H*-tetrazole, [2+3] cycloaddition, MoO$_3$-SiO$_2$, solid acid

1. Introduction

Despite the scarcity of tetrazoles in natural systems, the chemistry of this heterocycles has gained increasing attention since the early quickly 1980 (Bulter 1996). Tetrazoles have a wide range of applications in pharmaceuticals as lipophilic spacers and carboxylic acid surrogates, in materials as specialty explosives and information recording systems, in coordination chemistry as ligands and also as precursors to a variety of nitrogen-containing compounds (Bulter 1996; Herr 2002; Holland 1967; Figdor 1967; Rhonnstad 2002; Klapötke 2009; John 1989; Modarresi-Alam 2007). However, the utility of these compounds is limited due to their insufficient synthetic availability.

Tetrazoles are commonly formed from nitriles or cyanamides and an azide source via a 1,3-dipolar cycloaddition (Kadaba 1973; Curran 1999; Huff 1993; Modarresi-Alam 2009; Nasrollahzadeh 2009; Habibi 2010) Unfortunately, each of those protocols suffers from some disadvantages: the use of both toxic metals and expensive reagents, drastic reaction conditions, water sensitivity, and the presence of dangerous hydrazoic acid. The use of hydrazoic acid presents considerable experimental difficulties because of its toxicity and tendency to explode (Duncia 1991; Carini 1991; Wittenberger 1993). Due to safety considerations, we required a method that did not use of hydrazoic acid or an azide source that produced hydrazoic acid in situ because of the associated hazards. Therefore, it is desirable to develop a more efficient and convenient method for the synthesis of 5-substituted tetrazoles.

Recently, Sharpless and co-workers reported an innovative and safe procedure for the preparation of 5-substituted 1*H*-tetrazoles from the corresponding nitriles and NaN$_3$ in the presence of a stoichiometric amount or 50 mol % of Zn(II) salts (Demko 2001). As the catalytic load on these homogeneous catalysts is high, the separation of the products and recycling of catalyst becomes difficult, shifting our preference in favor of high efficient heterogeneous catalysts. Since then there have been reports of the use of various heterogeneous catalysts (Matthews 2000; Kantam 2006; Amantini 2004; Schmidt 2007; Kantam 2005; Kantam 2006), but most of these catalysts contain zinc or aluminium. The heterogeneous catalysts effective in the synthesis of tetrazoles were believed to be limited to the compounds containing zinc or aluminium. The development of a catalytic synthetic method for tetrazoles still remains an active research area.

In recent years heterogeneous catalysts have gained signiŁcant importance in organic syntheses because of economic and environmental considerations. These catalysts are generally less expensive, eco-friendly, high reactive, easy to handle and recoverable (Habibi 2010; Habibi 2011; Nasrollahzadeh 2009; Kantam 2006; Mohammadi 2010; Modarresi-Alam 2007; Modarresi-Alam 2008). Among various silica-based heterogeneous catalysts, MoO$_3$-SiO$_2$ has advantages of low cost, ease of preparation and can be recycled

(Dongare 2004; Maurya 2003; Umbarkar 2006). Molybdenum oxide supported on silica (MoO_3-SiO_2) has proved to be an efficient catalyst in promoting various organic reactions such as Beckmann rearrangement and nitration of aromatics. However, the utility of this catalyst for the synthesis of tetrazoles has not been explored before. We herein report a new protocol for preparation of 5-substituted 1*H*-tetrazoles derivatives from nitriles using MoO_3-SiO_2 as an efficient heterogeneous catalyst (Scheme 1).

2. Experimental

2.1. General

All reagents were purchased from Merck and Aldrich and used without further purification. ^{13}C NMR and ^{1}H NMR spectra were recorded on Brucker, 100 and 250 MHz using TMS as an internal standard. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. IR spectra were recorded on a Shimadzu 470 spectrophotometer. TLC was performed on Merck-precoated silica gel 60-F254 plates. Nano TiO_2 was prepared according to the literature (Hua 2007). Hua and co-workers studied the characterization of the Nano TiO_2 using powder XRD and TEM (Hua 2007).

2.2. General procedure for preparation of 5-substituted 1H-tetrazoles

20% MoO_3-SiO_2 was added to a mixture of nitrile (1.5 mmol), sodium azide (2.3 mmol) and distilled dimethylformamide (5 mL) and stirred at 120 ^{o}C for the appropriate time (Table 1). After completion of the reaction (as monitored by TLC), the catalyst was filtered and the filtrate was treated with ethyl acetate (35 mL) and 4N HCl (20 mL) and stirred vigorously. The resultant organic layer was separated and the aqueous layer was again extracted with ethyl acetate (25 mL). The combined organic layers were washed with water and concentrated to give the crude product. Column chromatography using silica gel gave pure product in high yield. All the products are known compounds and were characterized by comparing IR and ^{1}H NMR spectral data as well as melting points with those reported in the literature. All yields refer to isolated products.

5-Phenyl-1H-tetrazole (2a):

^{1}H NMR: δ 7.58-7.64 (m, 3H); 8.01-8.06 (m, 2H).

5-(4-Methylphenyl)-1H-tetrazole (2c):

^{1}H NMR: δ 2.47 (s, 3H); 7.49 (d, J = 8.0 Hz, 2H); 8.01 (d, J = 8.0 Hz, 2H).

5-(4-Nitrophenyl)-1H-tetrazole (2d):

^{1}H NMR: δ 8.30 (d, 2H); 8.45 (d, 2H).

5-(Naphthalen-2-yl)-1H-tetrazole (2f):

^{1}H NMR: δ 7.59-7.68 (m, 2 H); 7.98-8.18 (m, 4H); 8.65 (s, 1H).

3. Result and Discussion

The general synthetic method is depicted in Scheme 1. 5-Substituted 1*H*-tetrazoles were obtained from the reaction of nitrile with sodium azide in the presence of 20 % MoO_3-SiO_2 as an efficient heterogeneous catalyst as a solid acid catalyst at 120 ^{o}C for appropriate time in high yields.

To evaluate the scope and limitations of the methodology, reactions were carried out with various substituted benzonitriles including both electron-donating and electron-withdrawing substituents at *ortho*, *meta*, and *para* positions of the aromatic ring (Table 1). The results showed that there is no adverse effect of substituents, either electron-donating or electron-withdrawing, on the aromatic ring of benzonitriles on the product yield. All the products were characterized by comparing melting points with those of the reported compounds. The nature of the substituent on the benzonitrile did not affect the reaction time.

Interestingly 1,4-dicyanobenzene (Table 1, entry 8) afforded the mono-addition product, whereas in the reaction between sodium azide and 1,4-dicyanobenzene in the presence of Zn(II) salts the double-addition product was reported (Demko 2001). Reaction of the heteroaromatic nitrile, 3-pyridinecarbonitrile was complete at 120 ^{o}C after 6 h and gave the corresponding tetrazole in an excellent yield (Table 1, entry 9).

Because of environmental concerns, there is increasing need and interest in developing processes that minimize production of toxic hydrazoic acid. Here, because of direct use of sodium azide rather than hydrazoic acid in the synthesis of tetrazoles, a significant improvement in the synthesis is represented. Replacement of hydrazoic acid by inorganic azides, which are poorly soluble in organic solvents with low dielectric constants, causes an increase in reaction time and decrease in tetrazole yield (Herr 2002). Water was not a suitable solvent for this reaction. Not many organic solvents are stable at the high temperatures necessary for cycloaddition reactions (sometimes as high as 130 ^{o}C), and for this reason DMF is most commonly used for this purpose (Herr 2002; Kantam 2005; Kantam 2006).

Many solid acid catalysts have been used for the same transformation. Dongare and co-workers (Dongare 2004; Maurya 2003; Umbarkar 2006), have shown that 20% MoO_3-SiO_2 is very strong solid acid catalyst with acidity equivalent to 0.94 mmol NH_3 desorbed per gram of catalyst with 180m^2/g surface area and 71.64 Å average pore diameter. This catalyst contains molybdenum oxide nanoparticles of 1-2 nm dispersed on mesoporous silica. Fourier transform-infrared (FT-IR) spectra of adsorbed pyridine showed that the catalyst contains both Lewis as well as Brønsted acidity. Detailed Raman spectroscopic studies have shown the in situ formation of silicomolybdic acid on the catalyst surface in the presence of moisture. This in situ formed silicomolybdic acid imparts strong acidity to the catalyst which is responsible for very high catalytic activity. One of the main advantages of MoO_3-SiO_2 as catalyst was clean reactions without any side product. The MoO_3-SiO_2 catalyst could be recycled efficiently for three cycles without any appreciable loss in the yield. This reusability demonstrates the high stability and turnover of MoO_3-SiO_2 under operating condition. The reusability of the catalysts is one of the most important benefits and makes them useful for commercial applications.

The simplicity, together with the use of inexpensive, non-toxic and environmentally benign catalyst under thermal conditions is remarkable features of the procedure. The products were characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy and from melting points. The disappearance of one strong and sharp absorption band (CN stretching band), and the appearance of an NH stretching band in the IR spectra, were evidence for the formation of 5-substituted 1*H*-tetrazoles. ^{13}C NMR spectra display signals for tetrazole ring carbons of arylaminotetrazoles in the range of 154-157 ppm (depending on the nature of the substituents in the amino functionality) (Goljer 1983; Habibi 2010; Habibi 2011; Nasrollahzadeh 2009; Nasrollahzadeh 2010).

4. Conclusion

In conclusion, we have developed a novel and highly efficient method for the synthesis of 5-substituted 1*H*-tetrazoles by treatment of nitriles with sodium azide in the presence of MoO_3-SiO_2 as a reusable and efficient heterogeneous catalyst. The significant advantages of this methodology are high yields, elimination of dangerous and harmful hydrazoic acid and a simple work-up procedure. The catalyst can be recovered by simple filtration and reused without loss of activity. It also has excellent activity on an industrial scale and in most cases can be recovered from reaction mixtures and reused.

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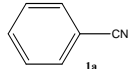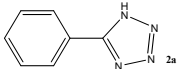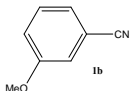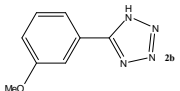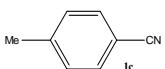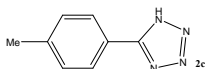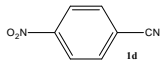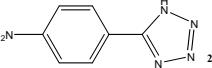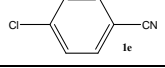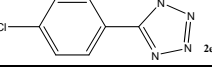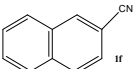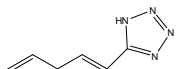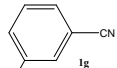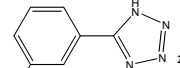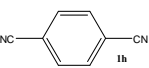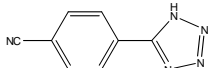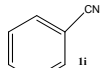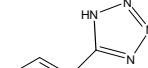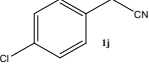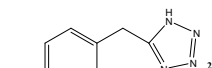
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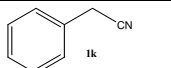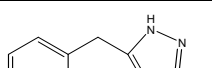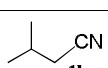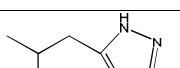
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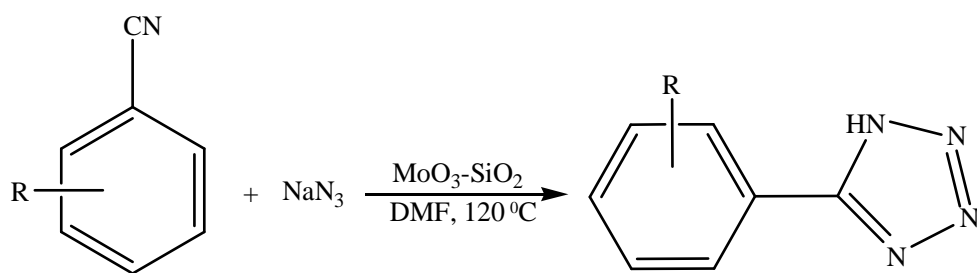
Scheme 1. Conversion of nitriles to the corresponding 5-substituted 1*H*-tetrazoles using MoO_3-SiO_2

Table 1. Synthesis of various 5-substituted 1H-tetrazoles in the presence of MoO$_3$-SiO$_2$ by reaction of sodium azide and nitriles at 120 ^{o}C

Entry	Substrate	Product	Time [h]	Yield [%][a]	Ref.
1			14	86	(Kantam 2005)
2			14	83	(Kantam 2005)
3			14	84	(Nasrollahzadeh 2009)
4			14	84	(Amantini 2004)
5			14	81	(Kantam 2005)
6			14	83	(Demko 2001)
7			14	83	(Nasrollahzadeh 2009)
8			22	84	(Nasrollahzadeh 2009)
9			6	84	(Kantam 2005)
10			24	77	(Kantam 2005)
11			24	78	(Kantam 2005)
12			30	65	(Mihina 1950)

[a]Yield refer to the pure isolated product.