Nanocrystalline ZnO as an Efficient Heterogeneous Catalyst for the Synthesis of 5-Substituted 1*H*-Tetrazoles

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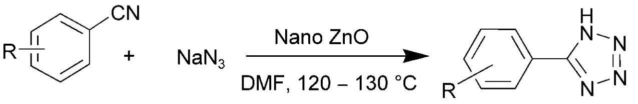
Abstract: Nanocrystalline ZnO is an effective heterogeneous catalyst for the [2+3]-cycloaddition of sodium azide with nitriles to afford 5-substituted 1*H*-tetrazoles in good yields.

Keywords: [2+3]-cycloaddition; heterogeneous catalyst; nano ZnO; 5-substituted 1*H*-tetrazoles

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 heterocycles.[1] Generally, 5-substituted 1*H*-tetrazoles are prepared by the addition of azides to nitriles.[2] The earlier reported methods suffer from some disadvantages like use of strong Lewis acids, expensive and toxic metals and the *in situ* generated hydrazoic acid is highly toxic and explosive. Later, Sharpless and co-workers reported an innovative and safe procedure for the synthesis of tetrazoles by the addition of sodium azide to nitriles using stoichiometric amounts of Zn(II) salts in water.[3] Very recently, Pizzo and co-workers efficiently synthesized tetrazoles by the addition of $TMSN_3$ to organic nitriles using 10 mol % TBAF as catalyst.[4]

In recent years, there has been increasing emphasis on the use and design of environmentally friendly solid catalysts to reduce the amount of toxic waste. Nanocrystalline metal oxides[5] have been efficiently used as absorbents for gases and destruction of hazardous chemicals and as catalysts for organic transformations such as epoxidation,[6] benzylation,[7] etc. These high reactivities are due to high surface areas combined with unusually reactive morphologies.

ZnO is an important semiconductor material and has been used widely in pigments, cosmetics, chemical sensors, solar cells and optoelectronics.[8] Recently, efficient Friedel–Crafts acylation as well as Beckmann rearrangement reactions and a facile synthesis of cyclic ureas from diamines have been reported using ZnO catalyst.[9]



Scheme 1. Nano ZnO-catalyzed synthesis of 5-substituted 1*H*-tetrazoles.

Herein, we report the synthesis of 5-substituted 1*H*-tetrazoles from a wide variety of organic nitriles with sodium azide using nano ZnO catalyst (Scheme 1).

In an effort to develop a better catalytic system, various reaction parameters were studied for the preparation of 5-phenyltetrazole by the reaction of benzonitrile with sodium azide and the results are summarized in Table 1. The solvent has a pronounced effect in these reac-

Table 1. Screening of reaction parameters for the formation 5-phenyltetrazole.[a]

Entry	Solvent	Azide	Catalyst	Yield [%][b]
1	Water	NaN_3	Nano ZnO	10
2	DMSO	NaN_3	Nano ZnO	42
3	NMP	NaN_3	Nano ZnO	70
4	DMF	NaN_3	Nano ZnO	72, 66[c]
5	DMF	$TMSN_3$	Nano ZnO	68
6	DMF	NaN_3	ZnO (Commercial)	58
7	DMF	NaN_3	$Zn(acac)_2$	69[d]
8	DMF	NaN_3	$ZnBr_2$	70[d]
9	[bmim][BF_4]	NaN_3	Nano ZnO	32
10	[bmim][BF_4]	NaN_3	$Zn(acac)_2$	20[e]
11	[bmim][BF_4]	NaN_3	----	0

[a] Reaction conditions: nitrile (2.5 mmol), NaN_3 (2.75 mmol), nano ZnO (0.1 g), DMF (5 mL), reaction time (14 h), 120–130 °C.
[b] Yield of isolated products.
[c] Yield after third cycle.
[d] Stoichiometric amounts of Zn salts were used.
[e] $Zn(acac)_2$, 10 mol %.

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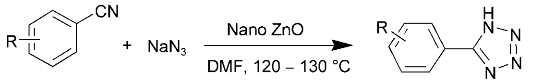
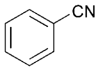
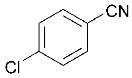
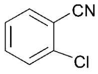
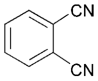
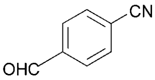
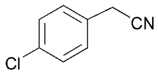
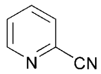
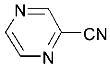
Table 2. Nano ZnO-mediated preparation of 5-substituted 1*H*-tetrazoles.[a]



Entry	Substrate	Temp [°C]	Time [h]	Yield [%][b]
1		120	14	72
2		130	14	74
3		130	14	70
4		130	24	81
5		120	14	69
6		120	24	71
7		120	6	79
8		120	5	82

[a] Reaction conditions: nitrile (2.5 mmol), NaN_3 (2.75 mmol), nano ZnO (0.1 g), DMF (5 mL), 120–130 °C.

[b] Isolated yields.

tions (Table 1, entries 1–4), in which DMF and NMP provided better yields. $TMSN_3$ was also used in the reaction with benzonitrile in DMF at 120 °C (Table 1, entry 5). Various catalysts were screened and it was found that Nano ZnO is an effective catalyst (Table 1, entries 4, 6–8). A control reaction conducted under identical conditions but devoid of nano ZnO gave no addition product, despite prolonged reaction times. Nano ZnO was recovered quantitatively by simple centrifugation and reused for three cycles with minimal loss of activity (Table 1, entry 4).

We chose a variety of structurally divergent benzonitriles possessing a wide range of functional groups to understand the scope and the generality of the nano ZnO promoted [2+3]-cycloaddition reaction to form 5-substituted 1*H*-tetrazoles and the results are summarized in Table 2. Among the various nitriles tested, benzonitriles gave moderate to good yields (Table 2, entries 1–5). 2-Chloro- and 4-chlorobenzonitriles reacted similarly to provide the corresponding tetrazoles which shows that there is no effect of the substitution on benzonitrile (Table 2, entries 2 and 3). Interestingly, phthalonitrile afforded the monoaddition product (Table 2, entry 4), whereas with Zn(II) salts the diaddition product is reported[3] in the literature. 4-Formylbenzonitrile gave only the 1*H*-tetrazole with the carbonyl (aldehyde) functionality remaining untouched (Table 2, entry 5). 4-Chlorophenylacetonitrile provided good yields with a long reaction time (Table 2, entry 6). Heteroaromatic nitriles such as 2-pyridinecarbonitrile and cyanopyrazine gave the corresponding tetrazoles in shorter reaction times with excellent yields (Table 2, entries 7 and 8).

In conclusion, we have developed a simple and efficient method for the preparation of 5-substituted 1*H*-tetrazoles *via* [2+3]-cycloaddition using nano ZnO as a heterogeneous catalyst. Various nitriles reacted with NaN_3 at 120–130 °C to yield the corresponding 5-substituted 1*H*-tetrazoles with moderate to good yields (69–82%). The catalyst can be readily recovered and reused. This methodology may find widespread use in organic synthesis for the preparation of 5-substituted 1*H*-tetrazoles.

Experimental Section

Typical Procedure for the Preparation of 5-Substituted 1*H*-Tetrazoles

Nano ZnO (0.1 g) was added to a mixture of benzonitrile (0.257 g, 2.5 mmol) and sodium azide (0.178 g, 2.75 mmol) in DMF (5 mL) and stirred the mixture was at 120 °C for 14 h. After completion of reaction (as monitored by TLC), the catalyst was centrifuged, washed with ethyl acetate and the centrifugate was treated with ethyl acetate (30 mL) and 5 N HCl (20 mL) and stirred vigorously. The resultant organic layer was separated and the aqueous layer was again extracted with ethyl acetate (20 mL). The combined organic layers were washed with water and concentrated to give the crude solid crystalline 5-phenyltetrazole. Column chromatography was performed using silica gel (100–200 mesh) to afford pure 5-phenyltetrazole; yield: 0.277 g (72%). ^1H NMR (200 MHz, $CDCl_3$/DMSO): $\delta = 8.04$ (m, 2H), 7.61 (m, 3H); MS (70 eV): *m/z* (%) = 146 (M^+, 12.65%), 118 (100%), 103 (13.94%), 91 (36.70%), 77 (30.37%), 63 (26.58%), 39 (17.72%).

Acknowledgements

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