Mesoporous ZnS nanospheres: a high activity heterogeneous catalyst for synthesis of 5-substituted 1*H*-tetrazoles from nitriles and sodium azide[†]

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Mesoporous ZnS nanospheres is a novel heterogeneous catalyst for synthesis of 5-substituted 1H-tetrazoles from various nitriles and sodium azide with excellent catalytic performance.

Tetrazoles have been attracting increasing attention, due to their wide application,¹ such as in pharmaceuticals as lipophilic spacers and metabolically stable surrogates for carboxylic acid in medicinal chemistry, photography and information recording systems and special explosives in materials science, ligands in coordination chemistry, and valuable precursors to a variety of nitrogen-containing heterocycles in organic synthesis.

The most convenient route for the preparation of 5-substituted 1*H*-tetrazoles is via [3 + 2] cycloaddition of azide to the corresponding nitriles. Earlier synthetic methods suffered from some drawbacks including expensive and toxic metals, use of strong Lewis acids, and the presence of hydrazoic acid. In order to overcome these disadvantages, new pathways have been developed,² such as the catalytic method using a stoichiometric amount of inorganic salts^{3,4} and metal complex⁵ as a catalyst, and also using TMSN₃ and TBAF instead of metal salts under solvent-free conditions⁶ or in micellar media⁷ and ionic liquid.⁸ However, these homogeneous catalytic processes suffered from a serious troublesome problem, namely, the separation and recovery of the catalyst. Therefore, the heterogeneous alternatives are highly desirable and have already attracted much attention. Recently, several heterogeneous catalytic systems were reported using, for example, nanocrystalline ZnO,^{9a} Zn/Al hydrotalcite,^{9b} Zn hydroxyapatite^{9c} and Cu₂O¹⁰ as catalysts. Our group also prepared tetrazoles with high yield in a heterogeneous catalytic system using tungstate salts¹¹ or γ -Al₂O₃¹² as catalyst. In this communication, we report mesoporous ZnS nanospheres (MZNSS) as a new heterogeneous catalyst for synthesis of tetrazoles with super catalytic activity.

MZNSS were prepared according to a previously reported procedure with some modifications.¹³ Briefly, ZnS nanospheres were obtained by the pyrolysis of zinc acetate and thiourea in ethylene glycol containing PVP at 190 °C. The product was separated from the reaction mixture by centrifugation, washed several times with ethanol and treated with 0.1 M HNO₃. The size and morphology of the catalyst were

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Fig. 1 SEM (a,b), TEM (c,d) and HRTEM (e,f) images of MZNSS.

observed by scanning electron microscopy (SEM). Fig. 1a is the low-magnification SEM image of the MZNSS with average diameter about 70 nm. The enlarged SEM and TEM images (Fig. 1b and d) show that ZnS nanospheres have rough surfaces composed of nanoparticles with 3–5 nm diameters. The TEM image in Fig. 1d indicates the mesoporous structure of MZNSS. Fig. 1f is the HRTEM image of a ZnS nanosphere as marked with the black frame in Fig. 1e. The interplanar spacing is about 0.31 nm corresponding to the (002) lattice plane of hexagonal ZnS.

The XRD pattern of MZNSS (Fig. S1a[†]) is attributed to hexagonal ZnS phase (JCPDS card No. 75-1547). The energy dispersive spectrum (EDS) in Fig. S1b[†] shows that the catalyst only contains zinc and sulfur elements, demonstrating that the synthesized product is pure ZnS. Fig. S2[†] shows the N₂ adsorption/desorption isotherm and the pore-size distribution (inset) of MZNSS. The isotherm belongs to type IV with a hysteresis loop, demonstrating their mesoporous characteristics. The BET (Brunauer–Emmett–Teller) surface area and single point total pore volume are 223 m² g⁻¹ and 0.25 cm³ g⁻¹, respectively.

It is worth mentioning that ZnS, as a semiconductor material, is often used as a photocatalyst in degradation of contaminated water containing halobenzene derivatives, organic dyes and toxic metal ions, ^{13,14} but its use as a catalyst for synthesizing 5-substituted 1*H*-tetrazoles from nitriles and sodium azide has not been reported. The catalytic synthesis of 5-phenyltetrazole was completed and the results including yields and turnover numbers (TON) are summarized in Table 1. The ¹H NMR spectrum of as-synthesized product without purification (Fig. S3†) indicates that it is pure 5-substituted 1*H*-tetrazole without any by-products. The effect of reaction times and temperatures on the reaction was evaluated (Table 1, entries 1–6). The optimum reaction

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Table 1Catalytic performance of MZNSS under various reactionparameters^a

CN+ NaN ₃ (1) MZNSS, Solvent				
Entry	Time/h	$T/^{\circ}\mathrm{C}$	Yield of isolated product [%]	TON ^b
1	12	120	60	1.46
2	24	120	80	1.94
3	36	120	96	2.33
4	48	120	94	2.28
5	24	110	49	1.19
6	24	130	79	1.92
7^c	36	120	51	1.24
8^d	36	120	72	1.75
9^e	36	120	20	0.49
10 ^f	36	120	8	0.19
11^{g}	36	120	0	0
12	36	120	69^{h}	1.67
13	36	120	$> 65^{i}$	1.58

^{*a*} Reaction conditions: benzonitrile (2.5 mmol), NaN₃ (5.4 mmol), MZNSS (0.1 g) treated with 0.1 M HNO₃, DMF (5 ml). ^{*b*} The moles of tetrazole formed per mol catalyst. ^{*c*} In 7 ml DMF–H₂O (5/2). ^{*d*} In 5 ml DMSO. ^{*e*} In 5 ml THF. ^{*f*} In 5 ml H₂O. ^{*g*} Without catalyst. ^{*h*} Yield for the third cycle in DMF. ^{*i*} Yield for the sixth cycle in DMF.

conditions are 36 h and 120 °C. Further prolonging the reaction time or increasing the reaction temperature will not improve the yield of the reaction. The solvent has a prominent influence on the yield (Table 1, entries 3, 7-10). The experimental results show that DMF and DMSO are good solvents with 96% and 72% yields, respectively, whereas water and tetrahydrofuran (THF) are not suitable for the reaction. A control experiment showed that no reaction took place without MZNSS (Table 1, entry 11). Recyclability is important for industrial application of a catalyst. Therefore, the reuse performance of MZNSS was investigated (Table 1, entries 12, 13). The experimental results indicate that the performance of MZNSS shows some degradation after three times reuse, such as the yield of tetrazoles and specific surface area of MZNSS which decrease to 69% and 170 m² g⁻¹, respectively. But it is almost constant during another three cycles such that the yield is $\sim 65\%$. The reason for this might be that the mesoporous structure shows some variation after first time reaction.

For comparison, various catalysts were investigated for synthesis of tetrazoles under our experimental conditions. Although zinc salts exhibit high catalytic activity with yields of >90% (Table 2, entries 1–3) in our reaction system, the separation and reuse of the catalyst are troublesome problems due to dissolving in DMF completely. Therefore, MZNSS shows unique virtues, that is, not only is the catalytic performance comparable with homogeneous catalysts, but also the separation and reuse of the catalyst is easily achieved. As expected, commercial ZnO and ZnS show low catalytic activity (Table 2, entries 4, 5). ZnS and ZnWO₄ prepared by a precipitation method exhibit relatively high yields of 75% and 82% (Table 2, entries 6, 7), respectively. Our previous work¹¹ demonstrated that the catalytic active site was quite different and tungstates were the active sites in ZnWO₄ catalyst.

Table 2 Preparation of 5-substituted 1H-tetrazole with various catalysts^{*a*}

$ \begin{array}{ c c } \hline \\ \hline $				
Entry	Catalyst ^b	BET surface area/m ² g ⁻¹	Yield [%] ^c	TON ^d
	ZnCl ₂		93	2.26
2	$ZnBr_2$	_	96	2.33
;	$Zn(OAc)_2$	_	95	2.30
Ļ	commercial ZnO	35	61	1.48
5	commercial ZnS	29	51	1.24
5	ZnS^{e}	51	75	1.82
7	$ZnWO_4^e$	15	82	1.99
;	MZNSS	216	84	2.04
)	MZNSS ^g	223	96	2.33

^{*a*} Reaction conditions: benzonitrile (2.5 mmol), NaN₃ (5.4 mmol), DMF (5 ml), reaction time 36 h, 120 °C. ^{*b*} Amount of Zn²⁺ catalyst used is equivalent to that of 0.1 g MZNSS. ^{*c*} Isolated yields. ^{*d*} The moles of tetrazole formed per mol catalyst. ^{*e*} ZnS and ZnWO₄ prepared by precipitation method. ^{*f*} MZNSS untreated with 0.1 M HNO₃. ^{*g*} MZNSS treated with 0.1 M HNO₃.

More interestingly, experimental results reveal that the acid treatment has a significant influence on the catalytic performance of MZNSS. MZNSS treated with 0.1 M HNO₃ exhibits high catalytic activity with yield of 96% (Table 2, entry 9), while the untreated MZNSS shows lower activity with 84% yield (Table 2, entry 8). In order to get an insight into the role played by acid treatment, we first inspect which one is an active site: Zn^{II} or S^{II}. To this end, several control experiments were completed. The CdX, and ZnX (X = S, Se) were prepared by a precipitation method and the results of catalytic reaction (Table S1⁺) indicated that the catalytic performance of ZnX was much better than that of CdX and the anions (S and Se) have no obvious influence on their catalytic performance. It indicates that Zn^{II} is the catalytic active site. Secondly, as we well know, HNO3 can react with ZnS to produce H₂S, meantime some S vacancies remained, which made a coordination number of Zn^{II} unsaturation and resulted in more ZnII being exposed to reactants, therefore increasing the catalytic activity. On the other hand, H₂S in the solution or S^{II} in solid ZnS in air is easily oxidized by oxygen to form sulfur sol (in solution) or nanparticles (in air), which were deposited on the surface of ZnS to cover the catalytic active sites, thus degrading the catalytic activity of ZnS treated by acid. Whereas in the case of MZNSS, the situation is quite different, PVP playing an important role: in solution, PVP prevents sulfur sol particles from being deposited on the surface of ZnS, but reactant molecules (which are much smaller than sulfur sol particles) can pass through PVP to reach the catalytic active sites; in air, PVP protects ZnS from oxidation. So, acid treated MZNSS has a higher catalytic activity. Further evidence comes from the colour of the ZnS catalysts. All of as-prepared ZnS and MZNSS and acid treated MZNSS are white in colour, but acid treated ZnS prepared by a precipitation method and ZnS stored in air (including commercially available ZnS) are light yellow-brown, due to sulfur anion being oxidized to form sulfur. Also, the catalytic activity of the former is much higher than that of the latter.

Fable 3	The synthesis of	5-substituted	1H-tetrazoles	with	MZNSS ^a
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		(1) MZNSS, DMF		^N -N	
		(2) HCI	R	N-N	
Entry	Product	Yield $[\%]^b$	TON ^c	$TOF/10^{-3} h^{-1d}$	
1		96	2.33	64.7	
2		86	2.09	58.1	
3		99	2.40	66.7	
4		98	2.38	66.1	
5		93	2.26	62.8	
6		98	2.38	66.1	
7	H ₃ C-	99	2.40	66.7	
8	HN-N N	76	1.84	51.1	
9		95	2.30	63.9	
10		> 99	> 2.40	> 66.7	

^{*a*} Reaction conditions: benzonitrile (2.5 mmol), NaN₃ (5.4 mmol), MZNSS (0.1 g) treated with 0.1 M HNO₃, DMF (5 ml), reaction time 36 h, 120 °C. ^{*b*} Isolated yields. ^{*c*} The moles of tetrazoles formed per mol catalyst. ^{*d*} Rate of the formation of tetrazoles per mol catalyst per unit time.

In order to get an insight into the effect of starting materials on the yield of 5-substituted 1H-tetrazoles, various nitriles were used as the starting materials and the results are listed in Table 3. Most of the nitriles gave excellent yields over 90% and the highest yield >99% was obtained in the case of 4-cyanopyridine as a starting material (entry 10), while the relatively lower yield of 76% was obtained in the case of benzyl cyanide (entry 8). The influence of the site of substituents on the yield was inspected. When benzonitriles with 3-chloro and 4-chloro substituents were used as the starting materials, yields of >97% were achieved (entries 3, 4) whereas 86% yield was obtained when 2-chlorobenzonitrile was a starting reactant. Perhaps the chloro group in the ortho-position hampered the tetrazole formation. Not only the site of the substituents in benzonitrile, but also the electron-donating or electron-withdrawing properties of the substituents has a significant influence on the reaction yield. The experimental results show that reaction yield is higher with an electron-donating substituent than with an electronwithdrawing one (entries 4, 5, 7).

In conclusion, a simple and effective method for the synthesis of 5-substituted 1*H*-tetrazoles from nitriles and sodium azide has been developed using mesoporous ZnS nanospheres as a catalyst. The heterogeneous catalyst MZNSS with high surface area and fine mesoporous structure shows excellent catalytic performance for various nitriles, and also is easy to separate from the reaction mixture to be reused, the first time this has been reported. The MZNSS catalyst is a good candidate to substitute metal salts or other heterogeneous catalysts and has potential value for industrial applications.

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