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Mesoporous $AlPO_4$: A Highly Efficient Heterogeneous Catalyst for Synthesis of 5-Substituted 1*H*-Tetrazoles from Nitriles and Sodium Azide via [3 + 2] Cycloaddition

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The mesoporous $AlPO_4$ with high surface area and fine mesoporous structure was prepared by a soft template method and showed excellent catalytic performance for synthesis of 5-substituted 1*H*-tetrazoles from various nitriles and sodium azide with excellent yields (91%–98%). The heterogeneous $AlPO_4$ catalyst is a good candidate to substitute metal salts or other heterogeneous catalyst and has potential value for industry application.

In the nearest decades, research on tetrazoles has been attracting great attention, due to its wide applications,[1] such as metabolically stable surrogates for carboxylic acid,[2] lipophilic spacers in pharmaceuticals, as well as special explosive and information recording systems in material science.[3]

The most conventional way to synthesize 5-substituted 1*H*-tetrazoles is via [3 + 2] cycloaddition of nitriles and sodium azides.[4] However new challenges have arisen since the use of strong Lewis acids or expensive and toxic metals may lead to the production of hydrazoic acid.[5] Recently, several new catalytic systems have been developed to overcome these disadvantages. Jursic and his colleagues have effectively synthesized 5-substituted 1*H*-tetrazoles with $TMSN_3$ and TBAF instead of metal salts in micellar media.[6] The same method was also carrid out by Pizzo and co-workers under solvent-free conditions.[7a] Sharpless and co-workers reported a safer and more convenient method for this reaction using a stoichiometric amount of Zn(II) salts in water.[7b,7c]

Although those homogeneous catalysts exhibit excellent activity in the reaction, the separation and recovery of the catalyst is still a big challenge. In this concern, novel heterogeneous catalysts are urgently needed. Currently several heterogeneous catalysts were reported for the synthesis of 5-substituted 1*H*-tetrazoles in DMF, including Zn/Al hydrotalcite,[8a] nanocrystalline ZnO,[8b] or Cu_2O.[8c] In recent years, great interest has been focused on the study of novel heterogeneous catalysts in our group. Previously, we have synthesized the tetrazoles with high yields in heterogeneous catalytic systems using tungstate salts[9a] and mesoporous ZnS[9b] as catalyst. In this paper, mesoporous $AlPO_4$ (MA) was reported as a new heterogeneous catalyst with large surface area for the synthesis of 5-substituted 1*H*-tetrazoles from nitriles and sodium azide in DMF.

The mesoporous $AlPO_4$ was prepared by a soft template method in ethanol solution containing P123, H_3PO_4, and $AlCl_3$, following aging and calcination (see SI).[10] XRD (Figure S1)[10] of MA shows diffraction peaks and their relative intensities are in good agreement with the standard XRD pattern of $AlPO_4$ (JCPDS: 760234), which shows that the synthesized product is high purity $AlPO_4$. TEM images of the MA (Figures 1a and 1b) indicated that the catalyst exhibited worm-like mesoporous structures, which well agreed with the XRD at small angle (Figure 1c). As we all know, the surface area and pore structure of a catalyst are important for catalytic activity. The mesoporous structure can provide larger BET surface area and more active sites, which can improve the catalytic activity. N_2 adsorption–desorption isotherms showed that $AlPO_4$ presented large BET surface area ($370\,m^2\,g^{-1}$) (Figure 1d). The pore size distribution (inset of Figure 1d) showed the evidence of narrow uniform pore with about 10 nm pore diameter.

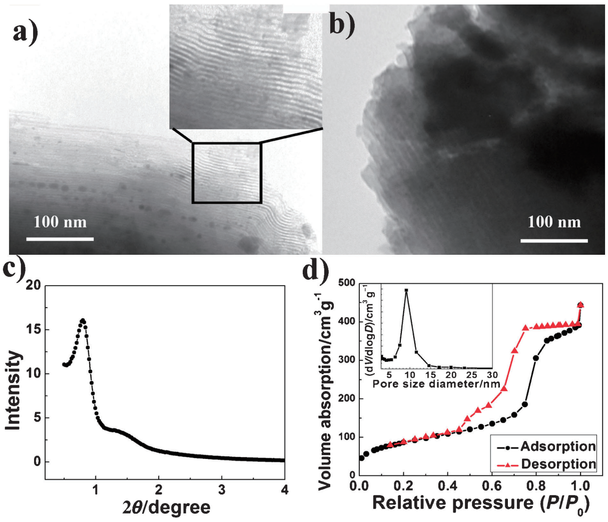


Figure 1. (a), (b) TEM images of mesoporous $AlPO_4$. (c) XRD pattern in small-angle region and (d) N_2 adsorption–desorption isotherms at 77 K, the inset is the pore size distribution of mesoporous $AlPO_4$.

In order to get optimum conditions for the reaction, the amount of MA catalyst, the reaction temperature and time, and the solvent were evaluated. The results are summarized in Table 1, including yields, turnover numbers (TON), and turnover frequency (TOF). Entry 1 in Table 1 shows that no reaction occurred without MA catalyst while 5-phenyltetrazole can be obtained in 92% yield when 0.1 g of MA was added as catalyst (Table 1, Entry 2). Further increasing the amount of MA

Table 1. Catalytic performance of MA under various reaction parameters[a]

Entry	Catal. /g	t /h	T /°C	Solvent	Yield /%[b]	TON /mol mol^{-1}	TOF /10^{-3} × h^{-1}
1	0	12	120	DMF	0	0	0
2	0.1	12	120	DMF	92	2.806	234
3	0.2	12	120	DMF	95	1.449	121
4	0.05	12	120	DMF	76	4.636	386
5[c]	1.0	12	120	DMF	90	2.745	229
6	0.1	24	120	DMF	94	2.867	143
7	0.1	48	120	DMF	96	2.928	61
8	0.1	12	100	DMF	65	1.983	165
9	0.1	12	140	DMF	82	2.501	208
10	0.1	12	120	DMSO	87	2.653	221
11	0.1	12	120	NMP	81	2.471	206
12	0.1	12	120	H_2O	Trace		
13	0.1	12	120	DMF	85[d]	2.59	216

[a]Reaction conditions: benzonitrile (2.5 mmol), MA (0.1 g), and NaN_3 (2.6 mmol) were stirred in 5 mL of DMF for 12 h at 120 °C. [b]Isolated yield (average of two runs). [c]Reaction conditions: benzonitrile (25 mmol), MA (1.0 g), and NaN_3 (26 mmol) were stirred in 50 mL of DMF for 12 h at 120 °C. [d]Yield for the third time use.

(Table 1, Entry 3) or amplifying 10 times the amount of the raw materials (Table 1, Entry 5), has no significant change for the yield of 5-phenyltetrazole, whereas decreasing the amount of MA leads to decrease the yield a lot (Table 1, Entry 4). Entries 2, 6, and 7 in Table 1 show the optimum reaction time for the reaction is 12 h, further extended reaction time has little effect on the reaction yield. The optimum reaction temperature is 120 °C, either decreasing or increasing the reaction temperature has an unfavorable influence on the reaction (Table 1, Entries 2, 8, and 9). In addition, the solvent also played a remarkable role (Table 1, Entries 2 and 10–12). The experimental results show that DMF, DMSO, and NMP are good solvent with 92%, 87%, and 81% yields, respectively, under the optimum conditions. Among them, DMF is more preferable, whereas water is not suitable for the reaction (Table 1, Entry 12). Comprehensively, the optimum reaction conditions for synthesis of 5-phenyltetrazole are as follows: 0.1 g of MA as catalyst, reacting for 12 h, reaction temperature 120 °C, and DMF as solvent. The recycle experiments show that the MA exhibits a good reused performance and reaction yield still remain 85% after reuse for the third time (Table 1, Entry 13). It indicates that the prepared MA is quite stable in the reaction process with good recyclability which is crucial for industrial application.

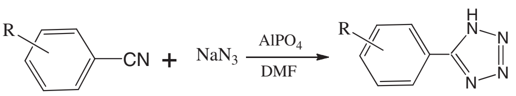
In order to evaluate the catalytic performance of the MA, a series of aluminum salts and oxide and various benzonitrile derivatives as the starting materials were tested under the optimum reaction conditions. The results are listed in Table 2. Compared with the MA, $AlPO_4$ prepared by precipitation with low BET surface area (21 m^2 g^{-1}, Figure S2)[10] exhibits relatively low catalytic activity (Table 2, Entry 1). $AlCl_3$ and $Al_2(SO_4)_3$ exhibited moderate catalytic performance (Table 2, Entries 2 and 3), while $Al(OH)_3$ and γ-Al_2O_3 showed lower catalytic capability than $AlPO_4$ (Table 2, Entries 4 and 5). Using Na_3PO_4 as a catalyst, no detectable reaction takes place, indicating that

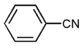
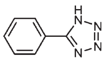
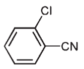
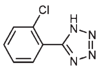
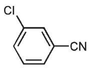
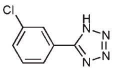
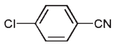
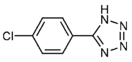
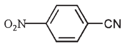
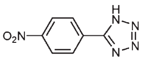
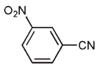
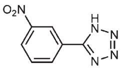
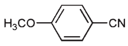
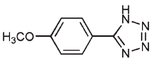
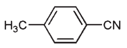
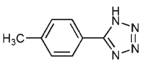
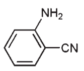
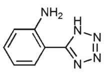
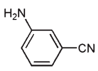
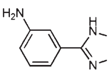
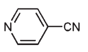
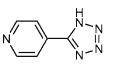
Table 2. Preparation of 5-substituted 1*H*-tetrazoles with various aluminum catalysts[a]

Entry	Catalyst[b]	Yield /%[c]	TON /mol mol^{-1}	TOF /10^{-3} × h^{-1}
1	$AlPO_4$[d]	77	2.349	196
2	$AlCl_3$	78	2.379	198
3	$Al_2(SO_4)_3$	82	2.501	208
4	$Al(OH)_3$	35	1.068	88.9
5	γ-Al_2O_3	7.8	0.2379	19.8
6	Na_3PO_4	0	0	0
7	Al	0	0	0

[a]Reaction conditions: benzonitrile (2.5 mmol), NaN_3 (2.6 mmol), DMF (5 mL), reaction time 12 h, 120 °C. [b]Amount of Al^{3+} used is equivalent to that of 0.1 g of $AlPO_4$. [c]Isolated yields (average of two runs). [d]Prepared by precipitation method.

Table 3. The synthesis of 5-substituted 1*H*-tetrazole with $AlPO_4$ under various substrates[a]



Entry	Starting material	Product	Yield /%[b]	TON /mol mol^{-1}	TOF /10^{-3} × h^{-1}
1			92	2.806	234
2			82	2.501	208
3			93	2.836	237
4			90	2.745	229
5			75	2.288	191
6			88	2.684	221
7			87	2.654	221
8			90	2.745	229
9			91	2.776	231
10			89	2.715	226
11			98	2.989	249

[a]Reaction conditions: benzonitrile derivative (2.5 mmol), NaN_3 (2.6 mmol), $AlPO_4$ (0.1 g), DMF (5 mL), reaction time 12 h, 120 °C. [b]Isolated yields (average of two runs).

the catalytic active component of $AlPO_4$ is Al^{3+} rather than PO_4^{3-} (Table 2, Entry 6). Using aluminum metal as a catalyst, also no catalytic reaction can be observed, which further indicates that the catalytic active species is Al^{3+} but not the neutral aluminum atom (Table 2, Entry 7). All these results indicate that the MA is a promising highly active catalyst, which not only exhibits unique catalytic performance, but also is easily separated and reused.

Furthermore, various benzonitrile derivatives were used as the starting materials and the results are listed in Table 3. Although the reaction yields for various benzonitrile derivatives are all over 75%, the substituent effect still can be seen on the reaction. As shown in Table 3, the electron-donating substituent is of great advantage to the reaction and the pyridol nitrile is most favorable one, while the NO_2-group is harmful for the reaction.

In summary, we demonstrated that the mesoporous $AlPO_4$ with high surface area and fine mesoporous structure exhibits excellent catalytic performance for the synthesis of 5-substituted 1*H*-tetrazoles. Also as a heterogeneous catalyst, the mesoporous $AlPO_4$ exhibits an excellent recoverability and ease of reusage which is crucial for industrial application.

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