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Selective C-C bonds formation, *N*-alkylation and benzo[d]imidazoles synthesis by a recyclable zinc composite

Guanxin Zhu[a,b], Zheng-Chao Duan[a,c], Haiyan Zhu[a], Dongdong Ye[a], Dawei Wang[a,b,*]

[a] *The Key Laboratory of Synthetic and Biological Colloids, Ministry of Education, School of Chemical and Material Engineering, Jiangnan University, Wuxi 214122, China*
[b] *State Key Laboratory of Pulp and Paper Engineering, South China University of Technology, Guangzhou 510640, China*
[c] *School of Chemical and Environmental Engineering, Hubei Minzu University, Enshi 445000, China*

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ABSTRACT

Earth abundant metals are much less expensive, promising, valuable metals and could be served as catalysts for the borrowing hydrogen reaction, dehydrogenation and heterocycles synthesis, instead of noble metals. The uniformly dispersed zinc composites were designed, synthesized and carefully characterized by means of XPS, EDS, TEM and XRD. The resulting zinc composite showed good catalytic activity for the *N*-alkylation of amines with amines, ketones with alcohols in water under base-free conditions, while unsaturated carbonyl compounds could also be synthesized by tuning the reaction conditions. Importantly, it was the first time to realize the synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives by using this zinc composite under green conditions. Meanwhile, this zinc catalyst could be easily recovered and reused for at least five times.

Functionalized imines and amines are important intermediates for organic synthesis, biological, and pharmaceutical applications because they are widely used as pharmacophores in many biologically active compounds and agrochemicals [1,2]. Although the traditional methods of alkylation of primary amines with alkyl halides to functionalized amines are studied, great quantities of unexpected wastes create an undesirable ecological footprint. In addition, the reaction of amines with alkyl halides in the presence of large amounts of bases, which often suffers from overalkylation, and exhibits low selectivity for the desired products [3]. Hence, the development of efficient and sustainable methods is of infinite interest. To address these problems, borrowing hydrogen strategy is stand out from other methods [4]. *N*-Alkylation of amines and alcohols or two amines was documented for the preparation of imines or amines through the borrowing hydrogen strategy.

Earth abundant metals, like Mn, Fe, Co, Zn, Ni, are much economic, promising, valuable catalysts for borrowing hydrogen reaction, dehydrogenation and heterocycles synthesis. Kirchner *et al.* recently described an excellent example of cobalt-catalyzed borrowing hydrogen reaction and predicted that earth abundant metals are the most economic and promising catalysts for modern industry [5]. Therefore, the research on earth abundant metals for borrowing hydrogen reaction and dehydrogenation is highly interesting and desirable [6-10].

Recently, our group developed several triazole-skeleton ligand bridged transition-metal complexes, which showed good catalytic activities in dehydrogenation and borrowing hydrogen reactions [11-16]. However, most of the central metals are noble metals, low catalyst stability or catalysts are difficult to be recovered and reused [17-19]. Herein, we have described the synthesis of an unsymmetrical thienyl-pyrazoly-triazole ligand (TPT) and the corresponding heterogeneous zinc composite on molecular sieve (MS), which was carefully characterized by means of XPS, EDS, TEM and XRD (Scheme 1). The resulting zinc composite revealed good catalytic activity for borrowing hydrogen reaction of amines with amines in water under base-free conditions. Moreover, 2-aryl-1*H*-benzo[*d*]imidazole derivatives were synthesized with this zinc composite in water under base-free conditions.

The thienyl-pyrazoly-triazole ligand (TPT, 1) was synthesized in two steps with moderate yield (Scheme 2) and the detailed steps of TPT synthesis and purification were provided in Supporting information. TPT-Zn@MS was obtained through a one-pot method, as follows: A flame-dried flask was charged with TPT (1.0 equiv.) and freshly distilled THF under nitrogen at room temperature, then diethylzinc (1.0 mol/L in hexanes; 2.0 equiv.) was added drop-

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[*] Corresponding author at: The Key Laboratory of Synthetic and Biological Colloids, Ministry of Education, School of Chemical and Material Engineering, Jiangnan University, Wuxi 214122, China.

E-mail address: angdw@jiangnan.edu.cn (D. Wang).

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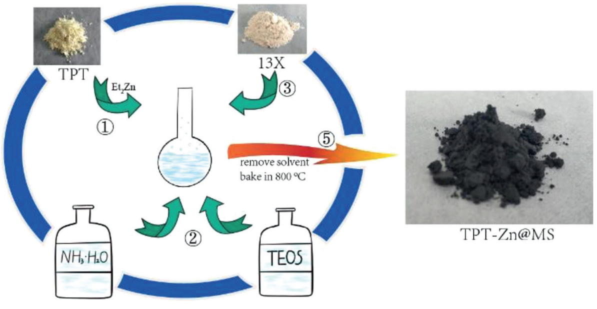
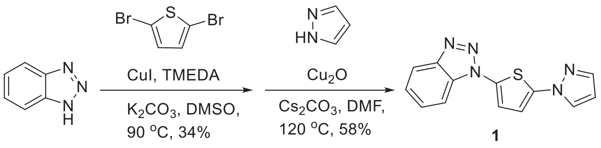


Scheme 1. The designed PPT-Zn@SBA-15.



Scheme 2. The synthesis of thienyl-pyrazoly-triazole.

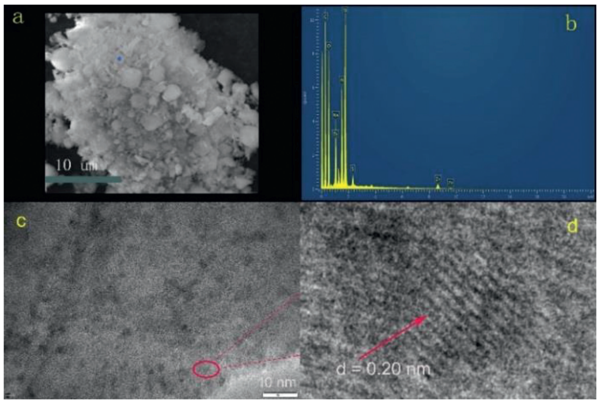


Fig. 1. SEM image (a), EDS pattern (b) and TEM images (c, d) of TPT-Zn@MS.

wise under vigorous stirring condition. The flask was removed after 30 min, then silica was introduced into the above flask by *in situ* hydrolysis of the added TEOS with ammonium hydroxide. After that the flask was heated to reflux at 65 °C for 5 h, the power of 13X molecular sieve (MS) was added to the solution and refluxed with vigorous stirring for another 5 h. The resulting mixture was grounded to a fine powder after removed the reaction solvent, and pyrolyzed at 800 °C with a constant argon flow for 2 h. Then the black power was cooled down to room temperature, and washed with HCl solution, water respectively. Finally, the resulting material (TPT-Zn@MS) was obtained for characterizations.

The prepared TPT-Zn@MS material was characterized by X-ray photoelectron spectrometry (XPS), scanning electron microscope (SEM), energy dispersive X-ray spectroscopy (EDS) and transmission electron microscopy (TEM).

The TEM images (Fig. 1) demonstrate the existence of crystal phases of zinc composite and the interplanar spacing of crystal phases is be afforded (Fig. 1d), which shows that the interplanar spacing of zinc composite is 0.205 nm. Furthermore, there are many crystal phases belong to 13X molecular sieve, suggesting the material remained active salts after firing and Zn was uniformly dispersed. Meanwhile, scanning electron microscope (SEM) and energy dispersive X-ray spectroscopy (EDS) were conducted to better characterize TPT-Zn@MS. As shown in Fig. 1a, this composite is amorphous, and we random sampled on five different areas to perform EDS test, the maximal element content of Zn is at 4.75 wt% and minimal element content is at 2.21 wt%, suggesting the distribution of Zn element was uniformly dispersed. Other element contents are as follows: Na (2.89 wt%), Al (2.331 wt%), Si (6.59 wt%), O (31.087 wt%), S (0.49 wt%).

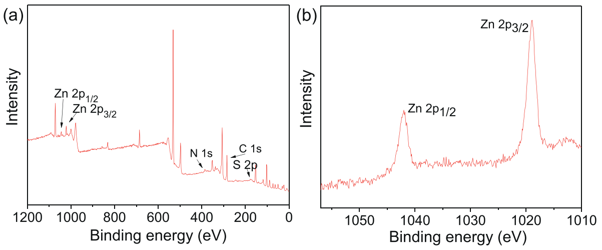


Fig. 2. (a) XPS spectra of TPT-Zn@MS, (b) narrow spectra of Zn.

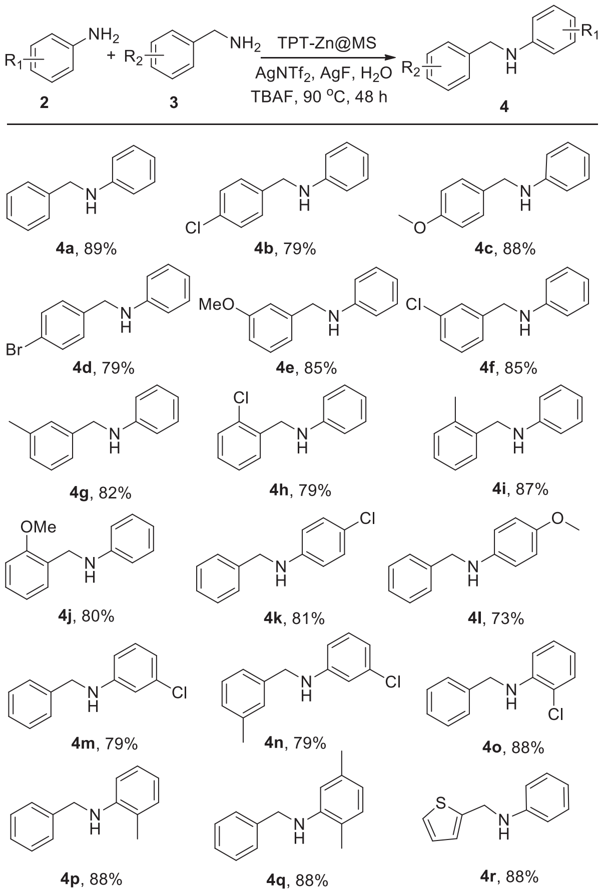
X-ray photoelectron spectroscopy (XPS) was subsequently performed to study the surface chemistry of TPT-Zn@MS. The Zn element content on the surface is 2.681 wt%, the result is achieved agreeable to the EDS results. In addition, low intensity of the N 1s and S 2p shows N and S elements maybe reacted with ultralow air, so that the content of N and S was under low level (Fig. 2).

With above encouraging zinc composite in hand, the catalytic activity of TPT-Zn@MS was next investigated. Initially, the challenging reaction involving *N*-alkylation of amines and amines was selected to test the catalyst activity of TPT-Zn@MS, especially in water. Compared to classical *N*-alkylation conditions, such as, strong base, organic solvents, sealed flask, this reaction was attempted in water under base-free conditions. After a series of conditions screening, it was disclosed that the reaction could occur in water under base-free conditions. For a higher yield, the additive experiments were carried out and the results showed that $AgNTf_2$/KF could produce a much higher yield. The introduction of phase transfer catalyst could further enhance the yield of desired product (Table 1, entry 11). It was observed that the reaction of amine and amine could not take place in the absence of catalyst (Table 1, entry 16). It should be noted that the reaction could take place under solvent-free conditions, however, only moderate yield was achieved (entry 21).

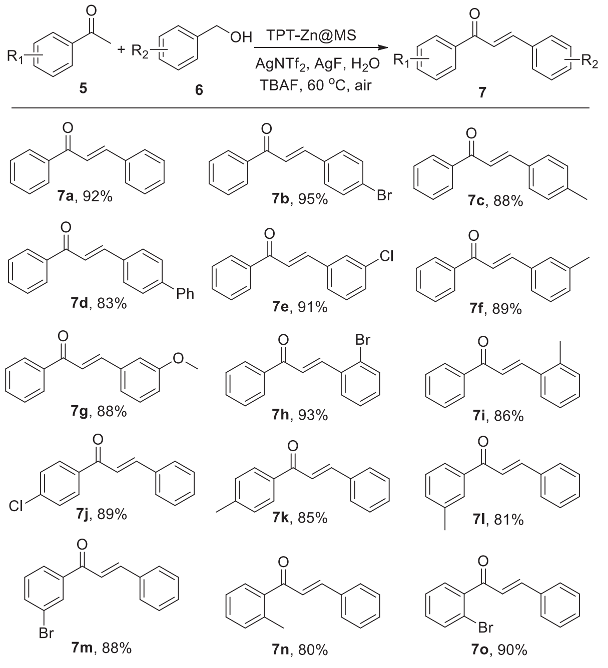
After establishing the optimal conditions, the substrate scope was then extended by utilizing a variety of substituted aromatic amines and various benzylamine derivatives. As showed in Scheme 3, all the amines were smoothly converted into the corresponding *N*-phenylbenzylamines and moderate to high isolated yields were obtained regardless of the electronic properties of starting materials.

It was confirmed that the substituent groups of aromatic amines and benzylamines, such as methoxyl, methyl and chloro, were smoothly reacted and it was noticed that the aromatic amines containing methoxyl or chloro groups produced much higher yields (**4c**, **4e**, **4f**). It was observed that benzylamines with electron-withdrawing group produced *N*-phenylbenzylamines in admirable yields (**4g**, **4i**, **4j**). In addition, 2-thiophenemethylamine could also react with aromatic amine and generated the desired product in moderate yield (**4l**).

Encouraged by such wonderful results, we further employed TPT-Zn@MS to ketones and various benzyl alcohols. After optimizing the condition of the reaction of ketones and various benzyl alcohols, it was demonstrated that the C-C bond formation could be smoothly transformed by this Zn composite, and then the substrate scope was explored and the results were summarized in Scheme 4. The experiments showed the products were obtained with good to excellent yields. It was noticed all combinations of ketones and benzyl alcohols provided high selectivity of the process on the formation of C=C bond. Under suitable conditions, both electron-rich and electron-deficient substrates could be reacted ef-

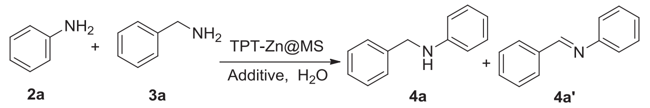


Scheme 3. Reaction of aromatic aimines and benzylamines. Reagents and conditions: **2** (1.0 mmol), **3** (1.2 mmol), TPT-Zn@MS (10 mg), $AgNTf_2$ (0.3 mmol), KF (0.3 mmol), TBAF (0.3 mmol), water (3.5 mL), 90 °C, 48 h, N_2. Isolated yields.



Scheme 4. Selective synthesis of unsaturated carbonyl compounds. Conditions: **5** (1.0 mmol), **6** (1.2 mmol), TPT-Zn@MS (10 mg), $AgNTf_2$ (0.3 mmol), KF (0.3 mmol), TBAF (0.3 mmol), water (3.5 mL), 60 °C, air, 12 h. Isolated yields.

Table 1
Optimization of reaction conditions.[a]



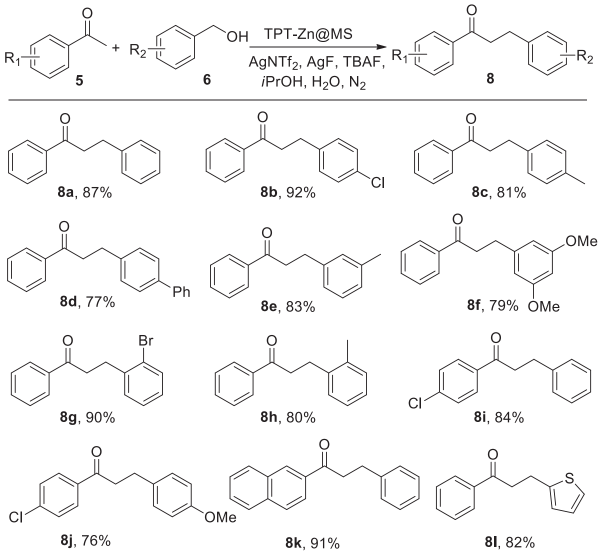
Entry	Cat.	Additive	Time (h)	Yield (**4a**) (%)[b]
1	TPT-Zn@MS	NaOH	24	<5
2	TPT-Zn@MS	Cs_2CO_3	24	<5
3	TPT-Zn@MS	K_2CO_3	24	<5
4	TPT-Zn@MS Cu@SiO_2	NEt_3	24	<5
5	TPT-Zn@MS	$AgNTf_2$	24	43
6	TPT-Zn@MS	AgOTf	24	31
7	TPT-Zn@MS	$AgBF_4$	24	12
8	TPT-Zn@MS	$AgSbF_6$	24	27
9	TPT-Zn@MS	$AgNTf_2$/AgF	24	62
10	TPT-Zn@MS	$AgNTf_2$/$AgNO_3$	24	17
11	TPT-Zn@MS	$AgNTf_2$/AgF/TBAF	24	86
12	-	$AgNTf_2$	24	<5
13	-	AgF	24	<5
14	-	TBAF	24	<5
15	-	-	24	<5
16	-	$AgNTf_2$/KF/TBAF	24	<5
17	TPT-Zn@MS	$AgNTf_2$/KF/TBAF	48	89
18	TPT-Zn@MS	$AgNTf_2$/KF/TBAF	12	81
19	TPT-Zn@MS	$AgNTf_2$/KF/TBAF	48	76[c]
20	TPT-Zn@MS	$AgNTf_2$/KF/TBAF	48	73[d]
21	TPT-Zn@MS	$AgNTf_2$/AgF/TBAF	48	46[e]
22	ZnO	$AgNTf_2$/AgF/TBAF	48	<5
23	$ZnCl_2$	$AgNTf_2$/AgF/TBAF	48	<5
24	$ZnCO_3$	$AgNTf_2$/AgF/TBAF	48	<5
25	TPT-Zn@MS	MS	48	<5
26	TPT-Zn@MS	TPT (1.5 equiv.)	48	<5

[a] Conditions: **2a** (1.0 mmol), **3a** (1.2 mmol), TPT-Zn@MS (10 mg), additive (0.3 mmol), H_2O (3.5 mL), 90 °C, N_2.
[b] Yields of isolated product.
[c] at 80 °C
[d] at 100 °C
[e] Solvent-free conditions.

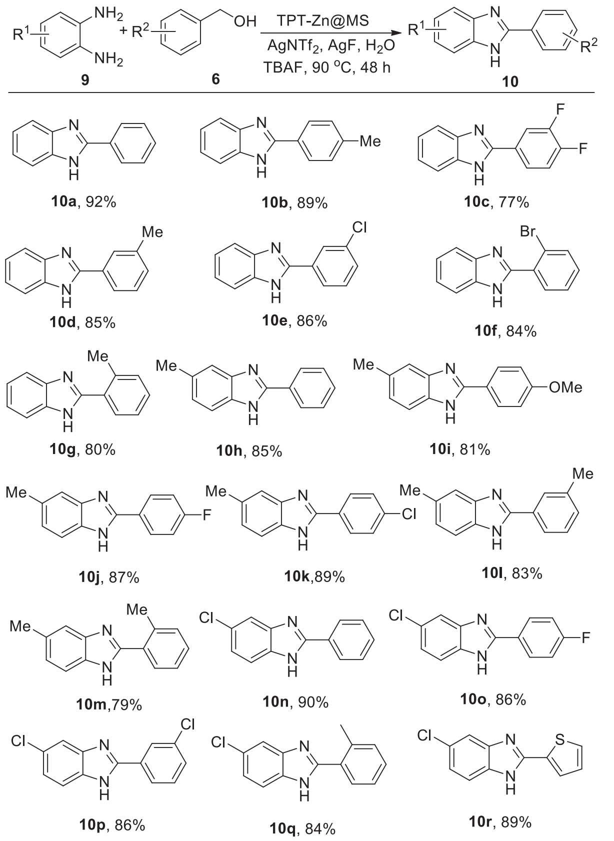
ficiently and the desired products were achieved with good yields (**7b**, **7e**, **7h**, **7k**, **7l**, **7n**). The electron-rich benzyl alcohols bearing methyl, methoxyl groups afforded the products in high yields (**7c**, **7d**, **7f**, **7g**, **7i**). The electron-efficient ketones bearing chloro, bromo groups were also suitable to this transformation in good yields (**7j**, **7m**, **7o**).

Interestingly, when we changed the conditions of the reaction of ketones and benzyl alcohols, an unexpected result was observed (Scheme 5). The 3-phenylpropiophenone as the main product was provided with the same TPT-Zn@MS catalytic system. We further demonstrated the C-C bond formation scope of ketones and benzyl alcohols with this reaction system, and the 3-phenylpropiophenone derivatives were provided in good to high yields. This system was able to tolerate the -Cl, -Me, -Ph and -OMe groups, even the strong electron-rich substrate like 3,5-dimethoxybenzyl alcohol was also reacted smoothly (**8f**). In addition, the 2-acetonaphthone and 2-thiophenemethanol were suitable to this transformation, leading to the corresponding products in 90% and 76% yields, respectively (**8k**, **8l**).

2-Aryl-1*H*-benzo[*d*]imidazole derivatives are an important and valuable natural products or intermediates and are found in natural alkaloids, pharmaceuticals and bioactive molecules [20]. Recently, we developed copper-catalyzed the synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives, however, strong base, organic solvents and the catalyst could not be recovered [21-23]. Therefore, we next utilized TPT-Zn@MS to catalyze the synthesis of 2-aryl-1*H*-benzo[*d*]imidazoles. The experiments revealed that lots of 2-aryl-1*H*-benzo[*d*]imidazole derivatives could be synthesized with TPT-Zn@MS as a catalyst in water under base-free conditions (Scheme 6).



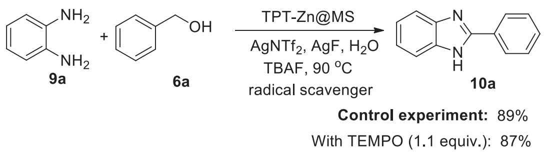
Scheme 5. Selective synthesis of phenylpropiophenones. Conditions: **5** (1.0 mmol), **6** (1.2 mmol), TPT-Zn@MS (10 mg), $AgNTf_2$ (0.3 mmol), KF (0.3 mmol), TBAF (0.3 mmol), *i*PrOH (3 mmol), water (3.5 mL), 90 °C, N_2, 48 h. Isolated yields.



Scheme 6. Substrate expansion of 2-phenylbenzimidazole. Conditions: **5** (1.0 mmol), **6** (1.2 mmol), TPT-Zn@MS (10 mg), $AgNTf_2$ (0.3 mmol), KF (0.3 mmol), TBAF (0.3 mmol), *i*PrOH (3 mmol), water (3.5 mL), 90 °C, N_2, 48 h. Isolated yields.

To better explore and understand what roles of TPT-Zn@MS and $AgNTf_2$ played in the synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives, the control experiments were introduced into this mechanism exploration and the results were listed in Table 1.

The experiments revealed that TPT-Zn@MS and additives played the important roles in 2-aryl-1*H*-benzo[*d*]imidazole synthesis process, which was not produced in the absence of TPT-Zn@MS. In addition, only TPT and MS could not catalyze this reaction. The control experiments were set up to exclude the possibility of a radical pathway including the single electron transfer process. The results showed that the yield of 2-aryl-1*H*-benzo[*d*]imidazole (**10a**) was almost the same by using TEMPO (1.1 equiv.) as a radical scavenger with TPT-Zn@MS as a catalyst (Scheme 7). As expected, the experiments disclosed that this process is not a single electron transfer one (SET).



Scheme 7. The control experiments.

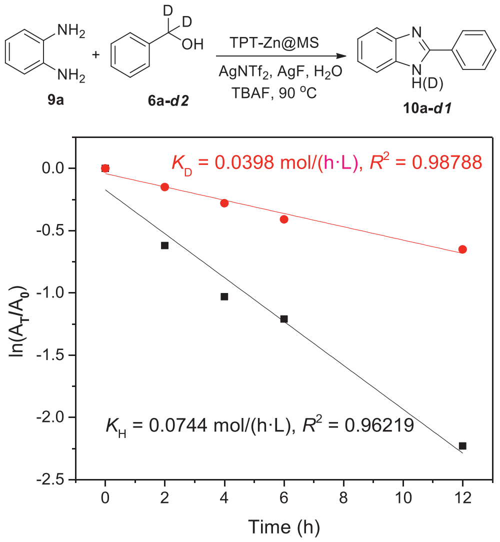
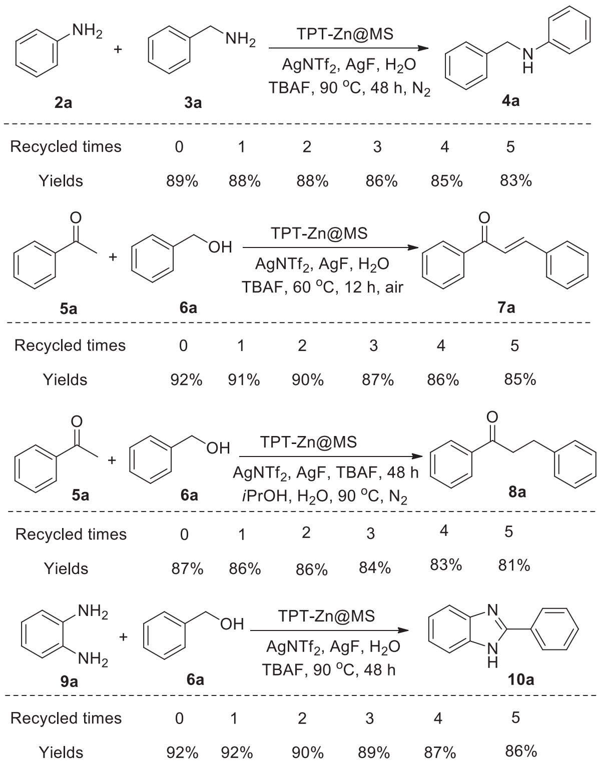


Fig. 3. Kinetic plot of 2-aryl-1*H*-benzo[*d*]imidazole. A_0: original concentration of substrate. A_t: concentration of substrate at time *t*. *K*: rate constant.

Hammett plot equation was investigated and the results were concluded in Supporting information Meanwhile, to clearly explain this reaction, kinetic isotope effect vale (KIE) was studied to explore the kinetically relevant elementary steps and the experiments revealed that KIE value (1.86) was achieved through the first order reaction plot between ln[**6a**] and ln[**6a-*d2***] (Fig. 3). This disclosed that the rate-determining step is the dehydrogenation of alcohol (**6a**) in the synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives.

TPT-Zn@MS was finally recovered and washed with water (10 mL × 3), ethanol (10 mL × 3) and water (10 mL × 3). After drying for 24 h, the recovered TPT-Zn@MS was reused to catalyze all the above four transformations and the recycled experiments were concluded in Scheme 8. It was demonstrated that yields of the desired products could be nearly maintained until the composite was recovered for even five times. In addition, the extent experiment of TPT-Zn@MS revealed that no copper was detected through ICP analysis, which exclude the effect of copper catalysis. Meanwhile, the ICP assessment of recovered TPT-Zn@MS showed that silver was not found.

Moreover, the summary of 2-aryl-1*H*-benzo[*d*]imidazole derivative derivatives synthesis [24-30] was listed in Table 2. It was observed that TPT-Zn@MS composite was a good catalytic system, which revealed a green method under base-free and water conditions with good recovery performance. This TPT-Zn@MS system offered an efficient methodology for the selective synthesis of saturated and unsaturated carbonyl compounds, 2-aryl-1*H*-



Recycled times	0	1	2	3	4	5
Yields	89%	88%	88%	86%	85%	83%

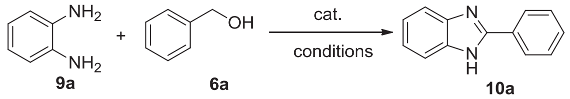
Recycled times	0	1	2	3	4	5
Yields	92%	91%	90%	87%	86%	85%

Recycled times	0	1	2	3	4	5
Yields	87%	86%	86%	84%	83%	81%

Recycled times	0	1	2	3	4	5
Yields	92%	92%	90%	89%	87%	86%

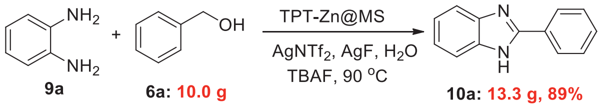
Scheme 8. Recycled experiments.

Table 2
The synthesis conditions of 2-aryl-1*H*-benzo[d]imidazole.



Catalyst	Conditions and yields	Solvent	Ref.
Co-PNNH pincer	$NaBEt_3H$, 4Å MS, 150 °C, 99%	Toluene	[16a]
Ir/TiO_2	100-120 °C, 96%	Mesitylene	[16b]
Ni/1,10-Phen	*t*-BuOK, 140 °C, 52%	Toluene	[16c]
Mn-NNS	140 °C, 20 h, 77%	Neat	[16d]
$Co(C_{10}H_{10}NO_2)_2$	Na_2CO_3, 92%	CH_3CN	[16e]
$Ru(PPh_3)_3$/Xantphos	$C_5H_{10}NH$, HOAc, reflux, 72%	Toluene	[16f]
Fe/dppf	150 °C, Ar, 24 h, 74%	Toluene	[16g]
TPT-Zn@MS[a]	90 °C, base-free, 92%	H_2O	this work

[a] Cycles number = 5.



Scheme 9. The synthesis of 1-benzyl-2-aryl-1*H*-benzo[*d*]imidazole in gram scale.

benzo[*d*]imidazole derivative derivatives with only water (or hydrogen gas) as by-products for the first time [31,32].

Finally, the gram-scale synthesis of 2-aryl-1*H*-benzo[*d*]imidazole from the reaction of phenylenediamine (**5a**) and benzyl alcohol (**2a**) was carried out. As expected, the result showed that the desired product (**10a**) was achieved smoothly in 89% yield (Scheme 9). This gram scale experiment disclosed that TPT-Zn@MS system could promote the synthesis 2-aryl-1*H*-benzo[*d*]imidazole derivatives under base-free conditions in water.

In conclusion, we developed a new type of heterogeneous TPT-Zn@MS catalyst, which was proved to be effective for selective borrowing hydrogen reaction of ketones and alcohols. TPT-Zn@MS was efficient for the *N*-alkylation of amines with amines, and the synthesis of synthesis of 2-aryl-1*H*-benzo[*d*]imidazole derivatives from diamines and alcohols. This provided an easy method the synthesis of substituted amines, 2-aryl-1*H*-benzo[*d*]imidazole derivatives with high yields in water.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgments

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2021.06.060.

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