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C-C/C-N Cross-Coupling Reactions of Aryl Sulfonates Catalyzed by an Eco-Friendly and Reusable Heterogeneous Catalyst: Wool-Pd Complex

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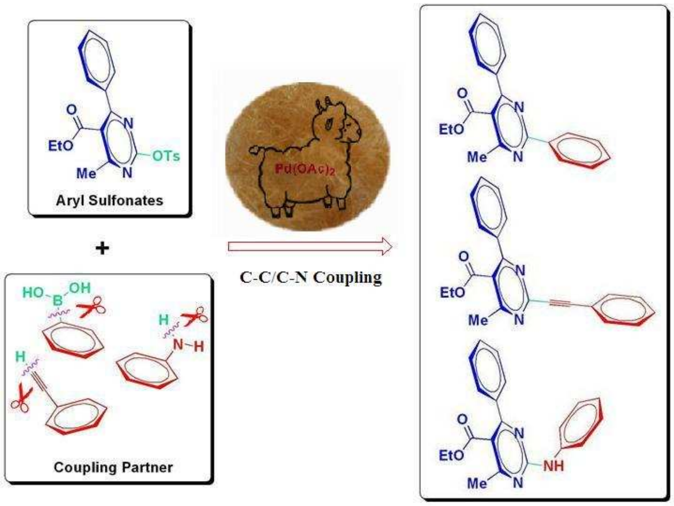

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Keywords: C-C/C-N coupling, Aryl sulfonates, Wool-$Pd(OAc)_2$ complex, Heterogeneous catalyst

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ARTICLE TYPE

C-C/C-N Cross-Coupling Reactions of Aryl Sulfonates Catalyzed by a Reusable Heterogeneous Catalyst: Wool-Pd Complex

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Abstract: A well-defined heterogeneous palladium catalyst, supported on biomacromolecule, natural wool fibre, was found to be an effective catalyst for the C-C/C-N coupling of pyrimidin-2-yl sulfonates with arylboronic acids, terminal alkynes or anilines, giving the desired coupling products in good to high yields. The catalyst was characterized by XPS, IR, SEM and ICP. More importantly, the easy experimental handling catalyst is stable, shows negligible metal leaching, and can be reused for at least 10 successive runs. Undoubtedly, a wide scope of reactant, insensitive to the electron effects and the excellent coupling yields make these catalyst systems potentially useful in organic synthesis.

Introduction

Heteroaromatic systems are important constituents of a wide range of natural products, pharmaceuticals, and fine chemicals, hence methods for their functionalization are of high interest.[1, 2] Currently, Pd-catalyzed cross-coupling reactions are the most efficient method for the construction of aromatic C-C and C–N bonds both in industrial and academic settings. [3, 4] Among the electrophiles used in the Pd-catalyzed C-C/C-N coupling reactions, aryl sulfonates, which readily accessible from cheap, commercially available phenols and sulfonyl chlorides, are a class of interesting coupling partners to aryl halides and triflates.[5] While aryl sulfonates have not been considered as a general partner for such cross-coupling reactions due to their low reactivity.

In recent years, a few examples of the Pd-catalyzed C-C coupling reaction of halo-substituted pyrimidines were reported.[6, 7] We have recently developed the palladium- or copper-catalyzed cross-coupling reactions of aryl boronic acids, alkynes or amines with 4-aryl-pyrimidin-2-yl sulfonates as electrophiles to generate the C-C and C-N bonds.[8-11] Despite the attractive properties of many homogeneous catalysts in terms of activity and selectivity, they suffer from a number of drawbacks which lie in the removal and the reuse of the catalyst, for the recycling of catalysts is also a task of great economic and environmental importance in the industry. In this context, heterogeneous catalysts are desired because of easy separation, recycling, and leaving products virtually free of palladium residues. A number of organic (mainly organic polymers and carbon material), inorganic (silica, zeolites, metal oxides, etc.) and hybrid organic-inorganic supports (mainly grafted silica) for palladium nanoparticles have been used.[12-18] Nevertheless, problems still existed. For instance, the requirements of several steps to synthesize supporter itself with appropriate bore diameter, cross-linking degrees, the lower loading of palladium and severe catalyst leaching. This would be due to the size of palladium, and the inactive large particles (even bulk Pd) were formed during the reaction.[19]

Recently, natural biomacromolecule, such as chitosan,[20-21] cellulose, [22] wool, [23-25] etc. were applied in the supporters for the palladium catalyzed several important processes. Among them, for the supporter, wool is a natural biomacromolecule of ordered amino acids cross-linked by S–S bonds, and there are many hybrid pores on the surface of wool fibre. The feature supports a high dispersion of palladium particles and prevents the aggregation of Pd-black. Our research in the field of biopolymer-based materials prompted us to investigate the use of wool as a green support material for palladium. Due to their biodegradability, biocompatibility, ready availability, cheap and green, wool is attracting growing interest as environment friendly substitutes for classical organic inorganic and polymer supports. In our previous studies, we have prepared the first generation of biomacromolecule-$PdCl_2$ complex catalyst via simply method. It was used as a highly active and reusable heterogeneous catalyst for Suzuki, Heck, photocatalysis and photodegradation transformations.[26-30]

In the context, we became interested in applying the biomacromolecule-$PdCl_2$ catalyst in the cross-coupling reaction of 4-aryl-pyrimidin-2-yl sulfonates and boronic acids, alkynes or amines. Unfortunately, these reactions did not work well under these conditions, only giving low yields.

Herein, we report our work on a readily available, wool-$Pd(OAc)_2$ complex catalyst, remains practically unexplored, could serve as an excellent catalyst in the C-C and C-N cross-coupling reactions of pyrimidin-2-yl sulfonates with arylboronic acids, terminal alkynes and amines. In particular, the heterogeneous catalyst was prepared via simple method, displayed higher activities (the total TONs is 853) and stability, which shows negligible metal leaching and can be reused for more than 10 times without any additional activation treatment.

Results and Discussion

Synthesis and Characterization of the catalyst

The mixture of 1.0 g the treated-wool pieces[26-30] (a, Figure 1) and 0.2 g $Pd(OAc)_2$ in 30 mL of de-ionized water was stirred at r.t. for 3 h until the white wool pieces become to brownish yellow. Then the mixture was filtered and washed with de-ionized water (3 × 20 mL) and acetone (3 × 20 mL), dried in a vacuum oven at 50 °C for 4 h (b, Figure 1). The palladium content in Wool-Pd(II) complex was determined by means of inductively coupled plasma equipped with atomic emission spectrometry (ICP-AES) and amounted to be 1.56 wt % (0.15 mmol/g).

Figure 1. (a) Fresh wool and (b) wool supported with $Pd(OAc)_2$.

The detailed electronic configurations of wool-$Pd(OAc)_2$ complex were examined by X-ray photoelectron spectroscopy (XPS) measurements. The data was shown in Table 1. It can be seen that Pd_{3d} peaks are consisted of two components with binding energy at 343.75 eV ($Pd_{3d3/2}$) and 338.38 eV ($Pd_{3d5/2}$) in $Pd(OAc)_2$, 343.08eV ($Pd_{3d3/2}$) and 337.71eV ($Pd_{3d5/2}$) in wool-

Table 1. XPS date of the $Pd(OAc)_2$, wool and wool-$Pd(OAc)_2$ complex[a]

XPS Peaks		Binding energy (eV)			$\triangle E_b$ (eV)
		$Pd(OAc)_2$	Wool	Wool-Pd complex	
Pd_{3d}	$Pd_{3d\ 3/2}$	343.75		343.08	−0.67
	$Pd_{3d\ 5/2}$	338.38		337.71	−0.67
N_{1s}	$-NH_2$		400.37	399.83	−0.54
	–NH–CO–		400.05	399.73	−0.32
S_{2p}	$-SO_3H$		168.18	167.96	−0.22
	–S–S–		165.05	164.33	−0.72
	–SH		163.8	163.33	−0.47
O_{1s}			531.93	532.08	0.15

[a] The binding energy is referred to C1s = 284.80 eV.

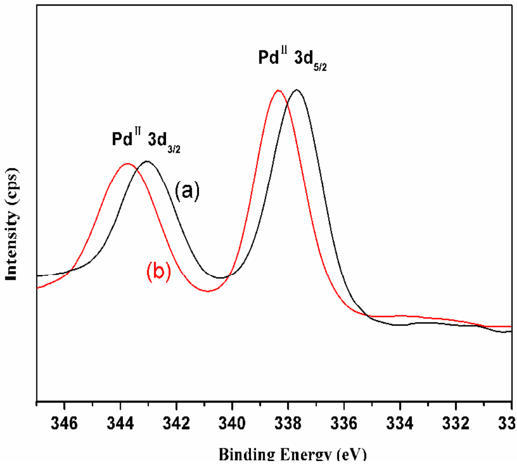


Figure 2. XPS spectra of (a) $Pd(OAc)_2$ and (b) wool-$Pd(OAc)_2$ complex.

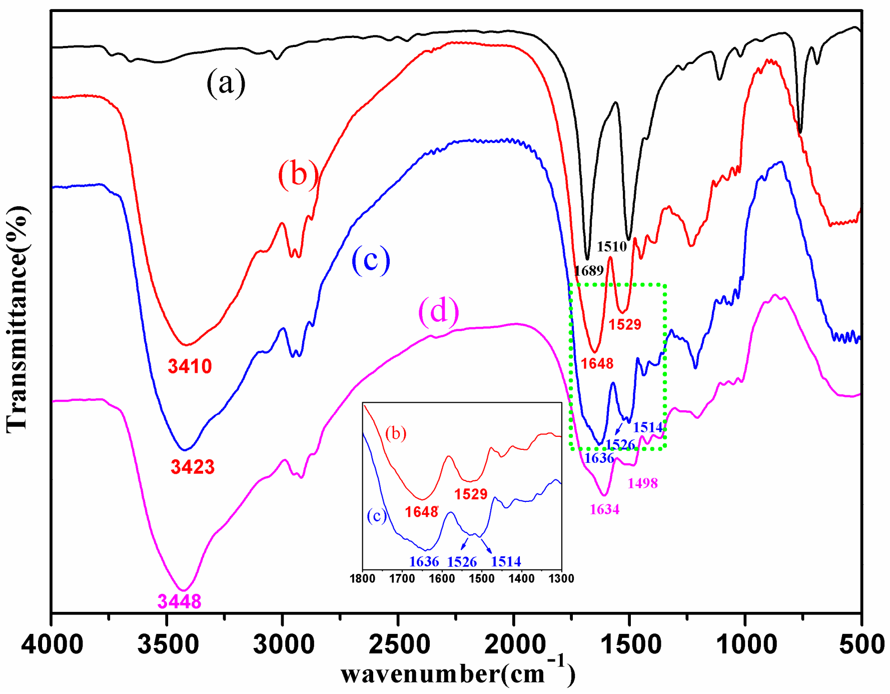


Figure 3. FTIR spectra of (a) $Pd(OAc)_2$, (b) wool, (c) wool-$Pd(OAc)_2$ complex, (d) the reused catalyst.

$Pd(OAc)_2$ complex respectively, which are originated from $Pd_{3d3/2}$ and $Pd_{3d5/2}$ of Pd^{II}. The difference of Pd_{3d} binding energy means the electron density increase as Pd 3d binding energy changes (Figure 2). Similarly, the peak at 400.37 eV is assigned to the binding energy of $–NH_2$ (N_{1s}) in wool, it was found to 0.54 eV higher than that in wool-$Pd(OAc)_2$. And the difference between –NH–CO– in wool and –NH–CO– in catalyst is 0.32 eV. Furthermore, there are major peaks with binding energies at 168.18 eV, 165.05 eV, and 163.80 eV in wool, corresponding to $–SO_3H$, –S–S–, and –SH respectively. The difference of S_{2p} binding energy between –S–S– in wool and wool–$Pd(OAc)_2$ complex catalyst is 0.72 eV, and that between –SH in wool and wool–$Pd(OAc)_2$ complex catalyst is 0.47 eV. The change of $–SO_3H$ binding energy in wool and catalyst is only 0.22 eV. Likewise, little change of the binding energy of the O_{1s} was observed. The results show $–SO_3H$ and O are unreactive, the coordination or ionic bonds are formed in $Pd(OAc)_2$ with $–NH_2$, –NH–CO–, –S–S– and –SH groups.

For further investigation of the chemical structural changes from wool to wool-$Pd(OAc)_2$, we performed Fourier transform infrared spectroscopy (FTIR) measurements. In Figure 3 (a), the absorption bands at 1689 and 1510 cm^{-1} are attributed to C=O stretching and $-CH_3$ bending vibration of $Pd(OAc)_2$, respectively. From the Figure 3 (b), in the wool, the peak at 3410 cm^{-1} can be assigned to the characteristic –NH stretching vibration bands of $–NH_2$, and the band at 1529 cm^{-1} and 1648 cm^{-1} can be attributed to the –NH and C=O bending vibration of –NH–CO–. And in Figure 3 (c), wool-$Pd(OAc)_2$, the –NH stretching vibration bands of $–NH_2$ has shifted to a higher wave number (3423 cm^{-1}), indicating a decrease in the $–NH_2$ group fraction. It can be confirmed that coordination or ionic bonds were formed by the connection of N atoms (in $–NH_2$) with Pd atoms in the wool-$Pd(OAc)_2$ complex. This is relatively consistent with the XPS data. Furthermore, in comparison with the wool, in catalyst, the peak of C=O stretching vibration were broadening and moved to 1636 cm^{-1}. This was due to the fact that the C=O stretching vibration of $Pd(OAc)_2$ was close to the C=O bending vibration of the wool, it was resulted that the peak of the $Pd(OAc)_2$ was wrapped, and the C=O bending vibration of wool-$Pd(OAc)_2$ was broadening. On the other hand, in wool-$Pd(OAc)_2$, the characteristic $-CH_3$ bending vibration of $Pd(OAc)_2$ can be observed at 1514 cm^{-1}. The above is further indicated that the coordination was formed between $Pd(OAc)_2$ and the wool. For Figure 4 (d), compared with the fresh catalyst, there is no obvious change for the reused. Therefore, the wool-$Pd(OAc)_2$ complex is stable and recyclable.

The morphologies of the catalyst were found out by scanning electron microscopy (SEM) (Figure 4). In Figure 4, (a) was the photographs of raw wool, on the surface, the wool fibre was close covered with squamae, and the surface of treated-wool (b) was smooth. As displayed in Figure 4 (c), EDX spectrum suggested none of Pd and any other metal existed in the supporter except gold (samples were coated with gold using Q150R sputter coat). In the wool-Pd complex catalyst (d), no obvious Pd particle on the surface of supporter was observed, even at a high magnification. Furthermore, the EDX measurement of the catalyst (f) showed that the presence of Pd on the surface of fibre, and then the elemental mapping images (e) revealed that a homogeneous distribution of Pd on the surface of the fiber. The result indicated that palladium was dispersed uniformly onto the surface of wool fibre.

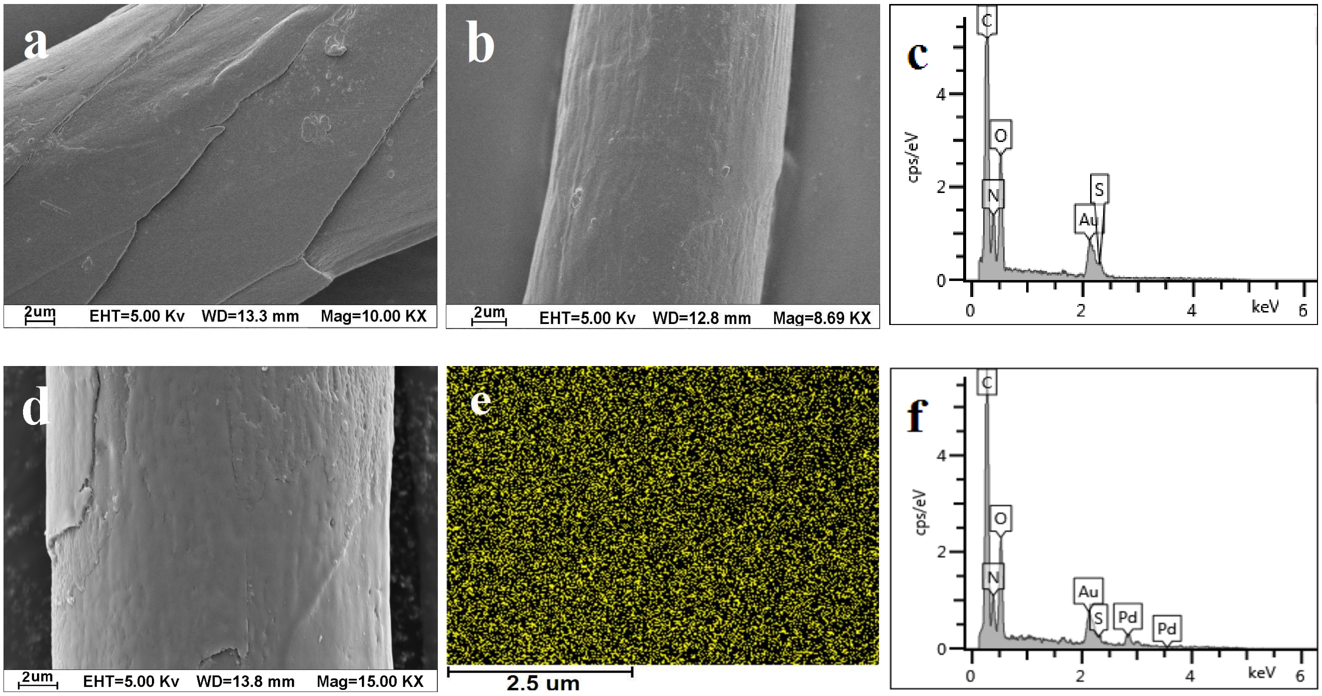


Figure 4. (a) SEM image of wool fibre, (b) SEM images of treated-wool fibre, (c) the corresponding EDX spectrum of the treated-wool fibre, (d) SEM images of Wool-Pd(II) complex, and (e) the corresponding EDS mapping of Pd, (f) the corresponding EDX spectrum of catalyst.

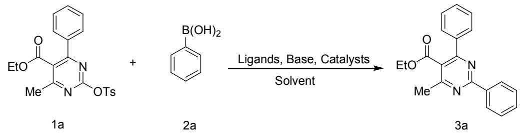
Wool-Pd(OAc)$_2$-catalyzed Coupling Reaction of Pyrimidin-2-yl Sulfonates with Arylboronic Acid

Initial examinations were carried out using pyrimidin-2-yl sulfonate **1a** (0.25 mmol) and phenylboronic acid **2a** (0.375 mmol) as the model substrates in the presence of wool-Pd(OAc)$_2$ complex catalyst (Pd 1.56 wt %) at 110 °C for 24 h to find the most efficient base, ligand and solvent. The representative results are shown in Table 2. It can be seen that the choice of ligand and base was an important factor. 2,2'-Oxybis(2,1-phenylene)bis-(diphenylphosphane) (DPE-Phos) was the suitable ligand, affording excellent yield (Table 2, entry 5), however, PPh$_3$ or 2-(dicyclohexylphosphino)-2',4',6'-triisopropylbiphenyl (X-Phos) provided moderate transformation (Table 2, entries 1-2). We then observed the amount of the catalyst (entry 3-6) to confirm the optimized amount as 20 mg (1.2 mol%). With regard to the base, K$_3$PO$_4$ was a prerequisite for obtaining high activity (in 93% yield). Only a trace to poor conversion of product **3a** was observed with the other bases, such as NaOAc, CsCO$_3$, K$_2$CO$_3$, NaF, DBU and DIPEA (Table 2, entries 7-12). Finally, a variety of solvents were tested and it was found that 1,4-dioxane gave the best yield, and in other solvents lower yields were obtained (Table 2, entries 13-15). Comparison between wool-Pd(OAc)$_2$ and wool-PdCl$_2$ (entry 16) indicated apparently that the former was more active within a shorter reaction time. Thus, K$_3$PO$_4$ (2.0 equiv.) and DPE-Phos (6 mol %) in 1,4-dioxane with wool-Pd(OAc)$_2$ (Pd 1.56 wt %) at 110 ^{o}C were selected as the optimized conditions for high cross-coupling conversion. As expected, we did not observe any product in the presence of wool only or in the absence of a catalyst. The absence of a ligand also resulted in a poor product yield (entries 17-19).

With these successful reaction conditions in hand, we set out to test the wool-Pd(OAc)$_2$ complex catalyst system for Suzuki coupling reaction, employing a variety of substituted pyrimidin-2-yl sulfonates **1** with different arylboronic acids **2** as depicted in Table 3. Functional groups of arylboronic acids, such as Me, MeO, F, and Cl, are well tolerated under the applied conditions (Table 3, entries 2-7). Most of them proceeded well to give the desired products **3** in good to high yields except for the special case of ortho-methylphenylboronic acid **2d** (Table 3, entry 4). Due to steric hindrance, the yield of starting from ortho-methylphenylboronic acid was 68%, lower than para- and meta-methylphenylboronic acids (up to 81%) (Table 3, entries 2-4). On the other hand, for the activated arylboronic acid, 1-naphthylboronic acid **2h** was also a suitable reaction partner (Table 3, entry 8).

Subsequently, a wide range of pyrimidin-2-yl sulfonates were examined. To our delight, both electron-rich and electron-poor pyrimidin-2-yl sulfonates took place smoothly to give the desired coupling products **3h-m** in good to high yields (Table 3, entries 9-13). In addition, halogenated pyrimidin-2-yl sulfonates were highly tolerated, fluoro, chloro and bromo derivatives performed well (Table 3, entries 11-13), and satisfactory yields were obtained: 92%, 89% and 88%. Exciting, the formed products are only halogenated compound, since the halogen functionalities were inert in the cross-coupling progress.

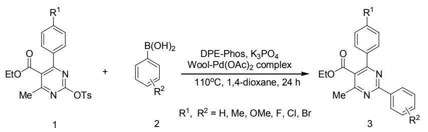
Table 2. Optimization for the Catalytic System. [a]

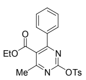
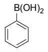
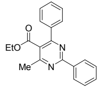
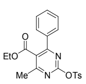
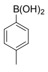
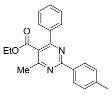
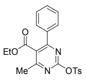
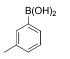
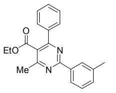
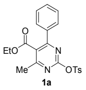
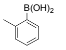
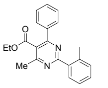
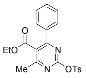
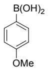
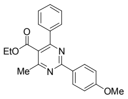
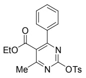
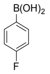
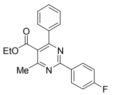
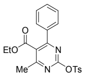
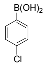
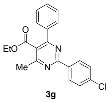
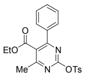
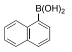
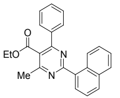
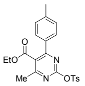
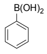
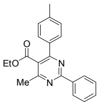
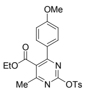
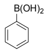
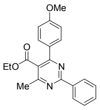
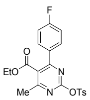
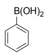
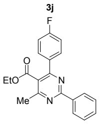
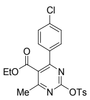
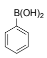
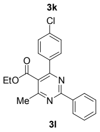
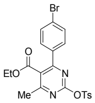
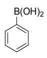
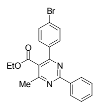


Entry	Catalysts	Catalysts amount	Base	Ligands	Solvent	Yield[c]
1	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	PPh$_3$	dioxane	56%
2	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	X-Phos	dioxane	41%
3	Wool-Pd(OAc)$_2$	10 mg	K$_3$PO$_4$	DPE-Phos	dioxane	65%
4	Wool-Pd(OAc)$_2$	15 mg	K$_3$PO$_4$	DPE-Phos	dioxane	81%
5	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	DPE-Phos	dioxane	93%
6	Wool-Pd(OAc)$_2$	30 mg	K$_3$PO$_4$	DPE-Phos	dioxane	95%
7	Wool-Pd(OAc)$_2$	20 mg	NaOAc	DPE-Phos	dioxane	16%
8	Wool-Pd(OAc)$_2$	20 mg	CsCO$_3$	DPE-Phos	dioxane	trace
9	Wool-Pd(OAc)$_2$	20 mg	K$_2$CO$_3$	DPE-Phos	dioxane	0%
10	Wool-Pd(OAc)$_2$	20 mg	NaF	DPE-Phos	dioxane	0%
11	Wool-Pd(OAc)$_2$	20 mg	DBU	DPE-Phos	dioxane	0%
12	Wool-Pd(OAc)$_2$	20 mg	DIPEA	DPE-Phos	dioxane	11%
13	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	DPE-Phos	toluene	12%
14	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	DPE-Phos	Xylene	23%
15	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	DPE-Phos	CH$_3$CN	trace
16[b]	Wool-PdCl$_2$	20 mg	K$_3$PO$_4$	DPE-Phos	dioxane	51%
17	Wool	20 mg	K$_3$PO$_4$	DPE-Phos	dioxane	0%
18	-	-	K$_3$PO$_4$	DPE-Phos	dioxane	0%
19	Wool-Pd(OAc)$_2$	20 mg	K$_3$PO$_4$	-	dioxane	10%

[a] Reaction condition: **1a** (0.25 mmol), **2a** (0.375 mmol), ligands (20 mol % or 6 mol %), base (2.0 equiv.), catalyst (Pd 1.56 wt %), solvent (5 mL), 110 ^{o}C, 24 h. [b] wool-PdCl$_2$ as catalysts, in 48 h. [c] Isolated yield of **3a** by column chromatography.

Table 3. Suzuki coupling of pyrimidin-2-yl sulfonates with arylboronic acids.[a]

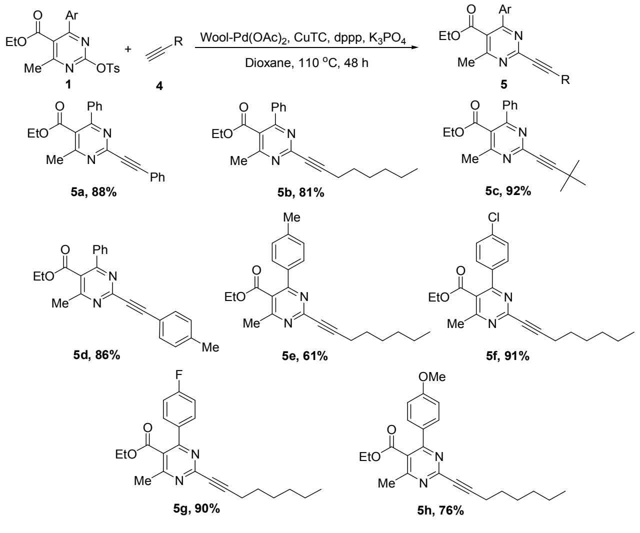


Entry	Sulfonate	Arylboronic acid	Product	Yield (%) [b]
1	 1a	 2a	 3a	93 51 [c]
2	 1a	 2b	 3b	81 38 [c]
3	 1a	 2c	 3c	86
4	 1a	 2d	 3d	68
5	 1a	 2e	 3e	88
6	 1a	 2f	 3f	92
7	 1a	 2g	 3g	94
8	 1a	 2h	 3h	96
9	 1b	 2a	 3i	89 43 [c]
10	 1c	 2a	 3j	88
11	 1d	 2a	 3k	92
12	 1e	 2a	 3l	89
13	 1f	 2a	 3m	88

[a] Reaction conditions: Reaction conditions: 1 (0.25 mmol), 2 (0.375 mmol), DPE-Phos (6 mol %), wool-Pd(OAc)$_2$ (20 mg, Pd 1.2 mol %), K$_3$PO$_4$ (2.0 equiv.), stirred in 5 mL 1,4-dioxane at 110 °C, 24 h. [b] Yield of isolated product. [c] Wool-PdCl$_2$ (20 mg, Pd 11.7 wt %) was used instead of wool-Pd(OAc)$_2$, in 48 h.

Wool-Pd(OAc)$_2$-catalyzed Coupling Reaction of Pyrimidin-2-yl Sulfonates with Terminal Alkynes

The Sonogashira reaction is one of the most widely used synthetic protocols for carbon-carbon bond formations. And the promising result encouraged us to explore terminal alkynes as new partner of coupling reaction with pyrimidin-2-yl sulfonates using the wool-Pd(OAc)$_2$ complex as catalyst. Firstly, we screened typical reaction parameters including different copper salts, ligands, bases as well as different solvents. When CuI was used as copper additive, poor yield of product **5a** was obtained. When the copper (I) thiophenecarboxylate (CuTC) was adopted instead of CuI, the yield was slowly increased to 53%. Strikingly, the ligand was critical to the feasibility of the reaction, and a range of different ligands were more or less active. 1,3-bis(diphenyphosphino)propane (dppp) afforded the higher yields in 88%, while the PPh$_3$, 2,2'-oxybis(2,1-phenylene)bis-(diphenylphosphane) (DPE-Phos) and 2-(dicyclohexylphosphino)-2',4',6'-triisopropylbiphenyl (X-Phos) afforded **5a** in a yield of trace, 38% and 72%, respectively. Similarly with the Suzuki reaction, the best base and solvent for the reaction were found to be K$_3$PO$_4$ and 1,4-dioxane.



Scheme 1. Sonogashira coupling of pyrimidin-2-yl sulfonates with alkynes.

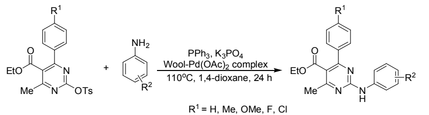
Following, with the optimal conditions in hand, various pyrimidin-2-yl sulfonates and alkynes with electron withdrawing and donating groups were also examined (Scheme 1). In general, it can be seen that there was no significant difference in reactivity for the studied reactants with different electronic properties. The result was similar to Suzuki reactions.

Wool-Pd(OAc)$_2$-catalyzed C-N Coupling Reaction of Pyrimidin-2-yl Sulfonates with Anilines

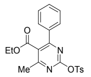
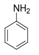
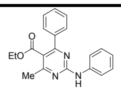
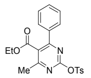
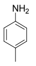
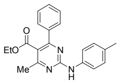
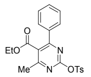
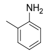
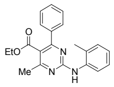
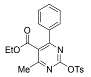
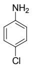
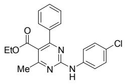
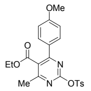
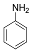
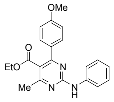
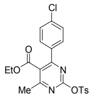
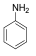
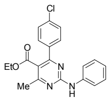
In addition, we further applied the catalytic system in C-N coupling of pyrimidin-2-yl sulfonates **1** with anilines **6**. To investigate the optimized conditions, in a model reaction, pyrimidin-2-yl sulfonate (**1a**) and aniline (**6a**) were used as starting materials in 1,4-dioxane. The reaction was examined with respect to base and ligand. And the influence of various bases and ligands demonstrated that the combination of K_3PO_4 (as base) and PPh_3 (as a ligand) gave the best results with the N-arylation product **7a** (83% yield in 24 h).

To extend the scope of C-N coupling reaction, a variety of aryl sulfonates with anilines were examined and excellent yields were observed for the substrates tested (Table 4). It can be seen from the Table 4 that there was not obvious trend or difference in reactivity between the systems of various electrical properties. Both electron-deficient and electron-rich anilines as reactants generated good to excellent yields(Table 4, entries 2-4), but the yield decreased when **6c** was used as reactant (Entry 3). Notably, sterically hindered substituents on the aryl tosylates have some effect on the reaction, and *o*-toluidine provided **7c** only in 43% yield. To our delight, **1e** was converted to desired halogenated N-arylation products in good to high yields (Table 4, entry 6).

Table 4. C-N coupling of pyrimidin-2-yl sulfonates with anilines. [a]



1 6 7

Entry	Sulfonate	Arylboronic acid	Product	Yield (%) [b]
1	 1a	 6a	 7a	83
2	 1a	 6b	 7b	76
3	 1a	 6c	 7c	43
4	 1a	 6d	 7d	79
5	 1c	 6a	 7e	61
6	 1e	 6a	 7f	85

[a] Reaction conditions: Reaction conditions: 1 (0.25 mmol), 6 (0.375 mmol), PPh_3 (20 mol %), catalyst (20 mg, Pd 1.2 mol %), K_3PO_4 (2.0 equiv.), stirred in 5 mL 1,4-dioxane at 110 °C, 24 h. [b] Yield of isolated product.

Recycling of the Catalyst

The lifetime of a heterogeneous catalyst play a key role in the catalytic reaction for practical applications, which is superior to a homogenous one. Recyclability of the catalyst was studied for the Suzuki coupling reaction, with **1a** and **2a** as model, giving the product under the optimization conditions as described above. The wool-$Pd(OAc)_2$ complex could be easily recovered through by filtration, washed with de-ionized water (3 × 10 mL) and acetone (3 × 10 mL), dryed in a vacuum oven at 50 °C. Then the used catalyst and new substrates were added for the next cycle.

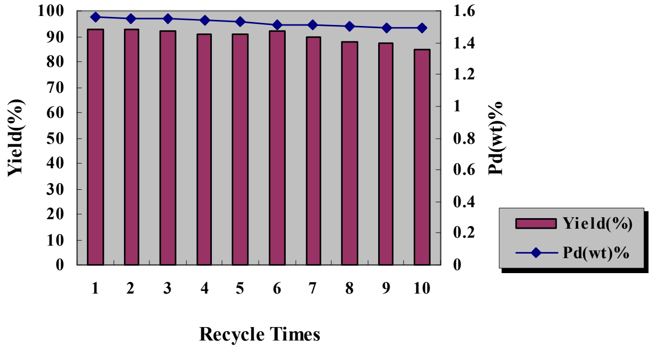


Figure 5. The recycling of catalyst in the Suzuki reaction.

Figure 5 showed no obvious decreases in yields after 10 cycles, and the total TON value of wool-$Pd(OAc)_2$ is 853, higher than the wool-$PdCl_2$ (the total TON value is 435). At the end of the reaction, the Pd content of the catalyst was examined by ICP-AES analysis within very narrow scope (1.56% to 1.49%), as little as 31 parts per billion Pd are observed in solution, suggesting that metal leaching is not significant during the reaction. The contamination of palladium residues for the products also could be suppressed.

After the reaction, the catalyst was again examined by SEM, EDS mapping and EDX. The image indicates that the surface morphology of the used catalyst has little change, and no accumulation of palladium nanoparticles was formed on wool-$Pd(OAc)_2$ complex, as indicated in Figure 6. The EDS mapping images (b) reveal that palladium was still dispersed uniformly onto the surface of wool fibre. Thereby, the catalyst retained good catalytic activity during the recycling tests.

To further investigate the reused catalyst, XPS measurements for the Pd $_{3d}$ peak were also performed to elucidate the oxidation state of the Pd (Figure 7). XPS spectra demonstrate that the Pd species in fresh catalyst were presented in the Pd^{II}, as evidenced by the binding energies of Pd $_{3d5/2}$ and Pd $_{3d3/2}$ electrons at 337.71 eV and 343.08 eV, respectively. After the Suzuki reaction, the Pd $_{3d}$ XPS spectra also showed two major peaks with binding energy at 337.70 eV and 343.06 eV, corresponding to the Pd^{II} state. The XPS results indicated that the oxidation state of the Pd was Pd^{II}, both in the fresh and reuse catalyst. This provided the direct evidences for the high recyclability and stability of the new catalyst.

We also carried out the experiments of recycling towards the C-N coupling reactions (Figure 8). The reactions between **1a** and **6a** were studied as model. We tested the catalyst in the reaction system for 8 times, and also, there was no obvious decrease in the product yield. The Pd content of the catalyst was also examined by ICP-AES analysis (1.56% to 1.51%). Only 24 parts per billion Pd was observed in solution. The results indicated a fine recycle performance of the catalyst in the C-N coupling reactions.

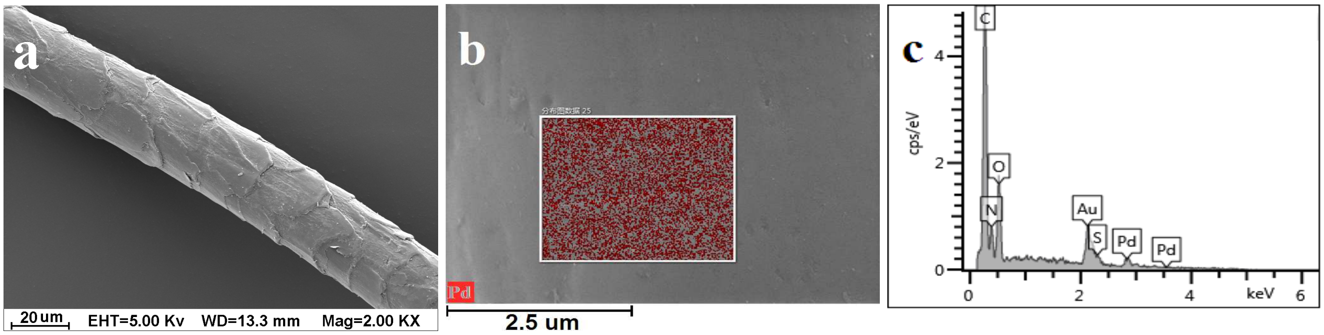


Figure 6. (a) SEM image of the reused catalyst (after the Suzuki reaction), (b) SEM image and the corresponding EDS mapping of Pd of the reused catalyst at a high magnification, (c) the corresponding EDX spectrum.

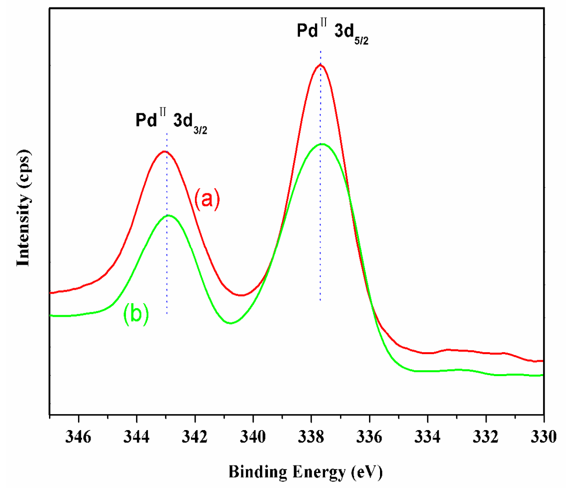


Figure 7. XPS spectra of (a) fresh and (b) reused catalyst.

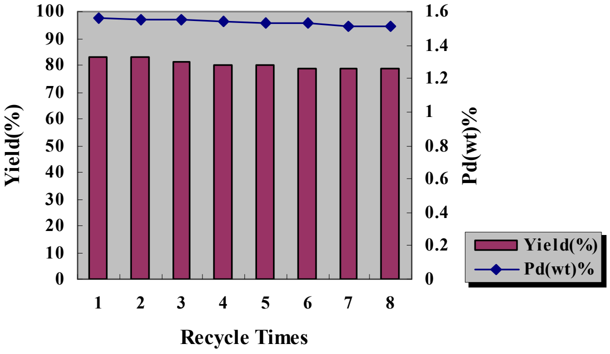


Figure 8. The recycling of catalyst in the C-N coupling reactions.

Hot Filtration Test

A hot filtration technique is preferred to check if the leached metal species are responsible for the catalytic activity. In order to evaluate the catalytic contributions of the leached palladium from the wool-Pd(OAc)$_2$ complex, we carried out the hot filtration tests upon the C-C and C-N coupling reactions, respectively. For the C-C coupling reaction, the test was operated between the reaction of **1a** and **2a**, whose reaction mixture was stirred for 8 hours and filtered to remove the heterogeneous catalyst, and then the mixture was stirred for another 20 hours. As a result, no further reaction was detected.

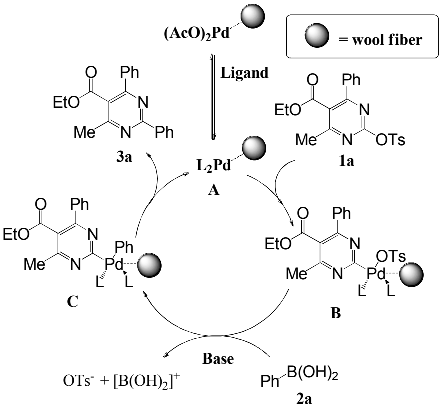
Similarly, the hot filtration test was also applied to the C-N coupling reactions between **1a** and **6a**. The mixture was reacted under the standard conditions for 8 hours, and then was filtered to remove the wool-Pd(OAc)$_2$ complex. Then the mixture was continued to be stirred, but no reaction was detected for another 20 hours.

The above suggested that leaching of palladium was not a effective active species, and the true indispensible catalyst was wool-Pd(OAc)$_2$ complex.

Proposed mechanism for the Suzuki reaction

On the basis of the above results, and also in accordance with previous literature reports, [31] a plausible reaction pathway for the Suzuki coupling reaction is proposed as shown in Scheme 2.

Firstly, palladium atom of wool-Pd(OAc)$_2$ complex coordinated with ligand, and then the reaction was catalyzed through the usual addition step of Pd into the C-O bond of the substrate **1a**, with an intermediate generated as complex **B**. Then, complex **B** was coupled with phenel boronic acid **2a** in the presence of base to produce the intermediate **C**. Finally, the product **3a** was provided through the elimination of Pd, which continued catalyzing the coupling reaction or break away from ligand and return to the original Pd(OAc)$_2$ supported on wool.



Scheme 2. Proposed mechanism for Suzuki reaction.

Conclusions

In summary, to the best of our knowledge, the result reported in this paper was the first example of practical and easily available wool-Pd(OAc)$_2$ complex which can catalyze the C-C and C-N coupling of pyrimidin-2-yl sulfonates with arylboronic acids, terminal alkynes and anilines smoothly. Remarkably, the catalytic systems offers numerous advantages: 1) the catalyst was prepared *via* simply produce, 2) the catalyst was environmentally-friendly, easy removal from the reaction mixture, high stability and reusability, 3) the reactions can tolerate a broad scope of substituted pyrimidin-2-yl sulfonates with corresponding coupling partners. Further investigations to understand the detailed mechanism and extend the application of the system to other transformations are currently ongoing in our laboratory.

Experimental Section

General Experimental Procedure for Suzuki Coupling Reaction of Pyrimidin-2-yl Sulfonates with Arylboronic acids

Pyrimidin-2-yl sulfonate **1** (0.25 mmol), arylboronic acid **2** (0.375 mmol), K_3PO_4 (2.0 equiv.), DPE-Phos (6 mol %), wool-Pd(OAc)$_2$ complex catalyst (20 mg, Pd 1.56 wt %) were added to 5 mL 1,4-dioxane in a 15 mL sealed tube, and then it was evacuated and purged with nitrogen gas four times sequentially, the mixture was stirred at 110 ^{o}C for 24 h. After completion, the mixture was cooled to room temperature, quenched by addition of saturated aqueous NH_4Cl (3 mL), and extracted with ethyl acetate (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with a mixture of ethyl acetate and petroleum ether (1:60) as eluent. The product was analyzed by GC-MS or NMR analysis. The conversion and selectivity were determined using GC analysis. All the prepared compounds are known and were compared with authentic samples.

General Experimental Procedure for Sonogashira Coupling Reactions of Pyrimidin-2-yl Sulfonates with Terminal Alkynes

A sealed tube, containing the mixture of reaction was evacuated and purged with nitrogen gas four times. Pyrimidin-2-yl sulfonate **1** (0.25 mmol), terminal alkyne **4** (0.375 mmol), K_3PO_4 (2.0 equiv.), dppp (6 mol %), wool-Pd(OAc)$_2$ complex catalyst (20 mg, Pd 1.56 wt %) and CuTC (10 mol %) were added to 5 mL 1,4-dioxane and the reaction mixture was stirred at 110 °C for 48 h. After completion, the mixture was cooled to room temperature, quenched by addition of saturated aqueous NH_4Cl (3 mL), and extracted with ethyl acetate (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with a mixture of ethyl acetate and petroleum ether as eluent (1:40). All the prepared compounds are known and were compared with authentic samples.

General Experimental Procedure for C-N Coupling Reaction of Pyrimidin-2-yl Sulfonates with Anilines

All reactions were conducted under nitrogen atmosphere in a dual-manifold Schlenk tube. Pyrimidin-2-yl sulfonate **1** (0.25 mmol), anilines **6** (0.375 mmol), K_3PO_4 (2.0 equiv.), PPh_3 (20 mol %), 20 mg of wool-Pd(OAc)$_2$ complex catalyst (Pd1.56 wt %) were added to 5 mL 1,4-dioxane in a 15 mL sealed tube, and then it was evacuated and purged with nitrogen gas four times sequentially, the mixture was stirred at 110 ^{o}C for 24 h until the reaction was completed. After cooling the mixture to room temperature, it was quenched with saturated NH_4Cl aqueous solution (3 mL), and extracted with ethyl acetate (3 × 5 mL). The organic solvents were combined and washed with aqueous NaOH (2 mmol/mL, 2 mL), brine, and then dried with anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography, eluting with a mixture of ethyl acetate and petroleum ether (1:30). All the prepared compounds are known and were compared with authentic samples.

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Notes

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