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ARTICLE TYPE

Wool-anchored Pd(OAc)$_2$ complex: a highly active and reusable catalyst for the desulfurative coupling reactions

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Abstract: A biomacromolecule-anchored palladium complex, wool-Pd(OAc)$_2$ complex, was prepared and characterized by IR, XPS, SEM and ICP. The new complex was used as a catalyst for the Liebeskind–Srogl desulfurative coupling reactions of pyrimidin-yl thioether derivatives with terminal alkynes and aryl boronic acids, respectively. Products were isolated in moderate to excellent yields. When 2-(phenylthio)-1,4-dihydropyrimidine derivatives were reacted with terminal alkynes and carboxyl acids, a domino reaction process was revealed. In these reactions, this novel and efficient catalyst was capable to be reused for at least nine rounds, and performed an endurable activity as well as the wide tolerance of the substrates.

Introduction

Pd-catalyzed cross-coupling reactions, versatile tool for the carbon-carbon bond construction, increasingly revealed its giant capacities in the organic synthesis.[1-6] Among them, the palladium catalyzed desulfurative cross-coupling reactions of diversified organosulfur compounds, well known as the "Liebeskind–Srogl cross coupling reaction", are widely used as a powerful tool in organic synthesis.[7-15] Inspirations from previous work continuously initiated the subsequential studies, with many progresses reported by Kappe[16-19] and others[20-24] in succession. Many organo-sulfur substrates were used under these modified Liebeskind–Srogl conditions, but thioethers were still one of the most widely available materials in organic synthesis and were therefore continued to be investigated.[7, 9-11, 25-30] Despite the low reactivity of simple aryl thioethers toward C-C coupling reactions,[9] plenty more efforts were made for the desulfurative cross coupling reactions of heteroaromatic thioether substrates with arylboronic acids,[9] organostannane reagents,[25-28] organoboranes,[29] and other nucleophiles.

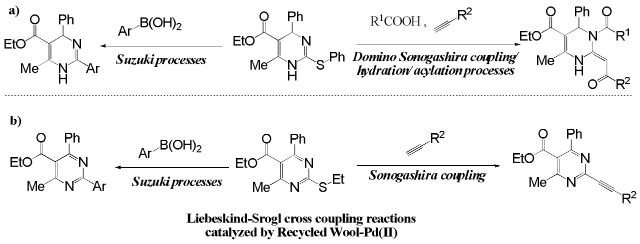
So far, as the powerful accelerant, palladium was the most widely used catalyst in the desulfurative cross-coupling reactions. However, it is beyond doubt the high price restricts the catalytic utility for wider applications of this luxury. And it is also crucial to reduce the wastes of reactions and to improve the processes of organic synthesis to be environmental-friendly. Many transition-metals have been tested for the desulfurative cross-coupling reactions and performed diversely. Inexpensive metals as copper and nickel were concerned for investigations besides palladium, ruthenium or rhodium in the cross-coupling reactions of thioethers or thioesters with arylboronic acids.[19] In 2007, Liebeskind and co-workers reported the cross coupling of thiol esters with boronic acids catalyzed by CuI-3-methylsalicylate (CuMeSal) instead of palladium,[12] and further techniques were continuously developed.[31-34] But still, palladium is nevertheless the most effective and steady catalyst, which participate an indispensible role in the desulfurative coupling reactions. Therefore it is significant to develop methods to save catalytic consumption or make the catalysts recycling.

In recent years, the application of polymer supported metal catalytic systems has been demonstrated as a fabulous solution for the catalysts recycling. It is also a new and nevertheless robust method of the transition-metal catalyzed synthesis in heterogeneous systems.[35-38] Plenty organic (mainly organic polymers), inorganic (such as silica, zeolites, metal oxides, etc.) and hybrid organic-inorganic (mainly grafted silica) supported transition-metal materials have been used in practice.[39-46] Studies upon transition-metal complexes achieved tremendous progress,[47-50] and also inspired our explorations.

Recently, natural biomacromolecule, such as chitosan, cellulose, wool, etc. were applied as the supporters for the palladium catalyzed processes.[51-53] In our previous studies, we have prepared the first generation biomacromolecule-PdCl$_2$ catalyst via simply method. It was used as a highly active and reusable heterogeneous catalyst for Suzuki, Heck, photocatalysis and photodegradation transformations.[54-58] As a supporter, wool is a natural biomacromolecule of the ordered amino acids that were cross-linked by S–S bonds. This feature supports a high dispersion of palladium particles and prevents the aggregation of Pd-black. 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, dihydropyrimidinthione (DHPM), can undergo a domino desulfurative coupling sequence with carboxylic acids and terminal alkynes. [59-60] In this paper, we introduce several desulfurative processes catalyzed by a wool-anchored palladium(II) acetate complex (Figure 1) under modified conditions (Scheme 1). Among these reactions, when the 2-(phenylthio)-1,4-dihydropyrimidines was reacted with terminal alkynes and carboxylic acids, a similar domino process was revealed. (Right, a, Scheme 1)

Notably, the wool-Pd(OAc)$_2$ complex as the catalyst is easy to separate from the reaction mixture by simple filtration, and retains good activity for at least nine successive runs without any additional activation treatment. Subsequent analysis suggested a negligible palladium leaching of the complex during the reaction process, indicating an amazing recycling catalytic capability.



Scheme 1. Desulfurative coupling reactions catalyzed by recycled wool-anchored palladium(II).

Results and Discussion

Preparation and Characterization of the catalysts

Figure 1. (a) Wool and (b) wool-Pd(OAc)$_2$ complex catalyst

The wool-anchored Pd(OAc)$_2$ was prepared via a simple method. 1.0 g the treated-wool pieces prepared in our laboratory[54-58] (Figure 1, a) and 0.2 g Pd(OAc)$_2$ were dipped in 30 mL of de-ionized water, the mixture was stirred at r.t. for 3 h until the white wool pieces became to brownish yellow. Then the biomacromolecule-Pd(OAc)$_2$ complex catalyst was filtered and washed with de-ionized water (3 × 20 mL) and acetone (3 × 20 mL), dried in a vacuum oven at 50 ^{o}C for 4 h (Figure, 1 b). 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).

The wool-Pd(OAc)$_2$ complex was characterized by fourier transform infrared spectroscopy (FTIR) measurements. (Figure 2). In Figure 2 (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 2 (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 2 (c), the –NH stretching vibration bands of –NH$_2$ has shifted to a higher wave number

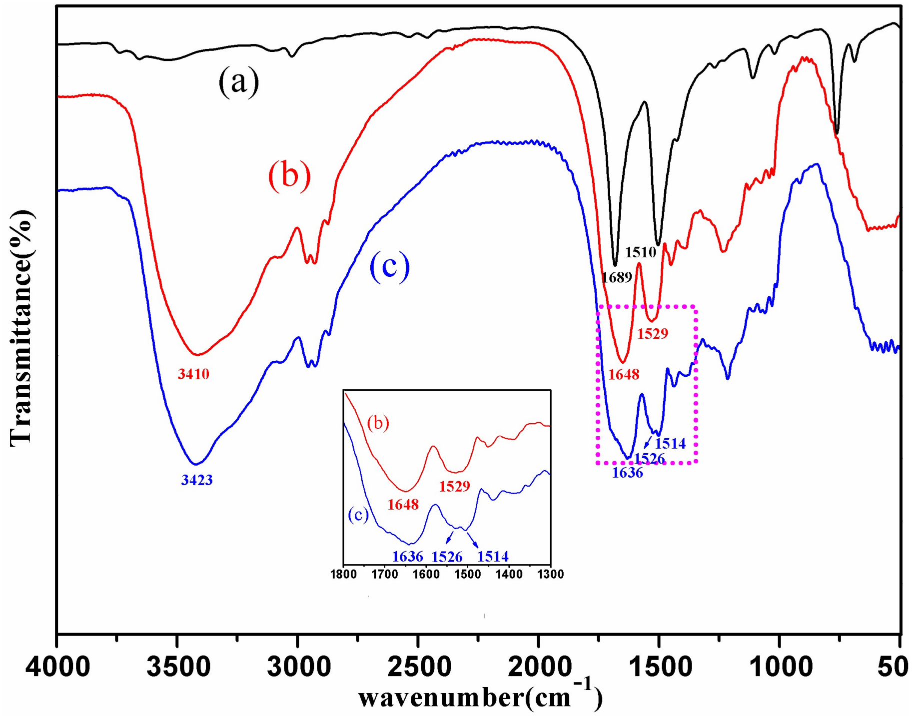


Figure 2. FTIR spectra of (a) Pd(OAc)$_2$, (b) wool, (c) wool-Pd(OAc)$_2$ complex

(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 (Table 1). 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 information reveals that coordination occurred between Pd(OAc)$_2$ and the wool fibre.

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

XPS Peaks		Binding energy (eV)			ΔE$_b$(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$_x$–		169.63	169.08	–0.55
			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 C$_{1s}$ = 284.80 eV.

In order to obtain a further insight of the changes from wool to wool-Pd(OAc)$_2$, X-ray photoelectron spectroscopy (XPS) measurement was used for analysis. [61-62] The binding energy of the sample was summarized in Table 1. It is realized that two components of the Pd$_{3d}$ peaks are consisted with the binding energy at 343.75 eV (Pd$_{3d3/2}$) and 338.38 eV (Pd$_{3d5/2}$) in Pd(OAc)$_2$, 343.08 eV (Pd$_{3d3/2}$) and 337.71 eV(Pd$_{3d5/2}$) in wool-Pd(OAc)$_2$ complex, which are originated from Pd$_{3d3/2}$ and Pd$_{3d5/2}$ of Pd^{II} (Figure 3). This binding energy of the Pd$_{3d\ 3/2}$ and Pd$_{3d\ 5/2}$ in the wool-Pd complex decreased 0.67 eV, respectively, which signify the increase of its electron density. Likewise, N$_{1s}$ binding energy change indicates electron density of the –NH$_2$ and –NH–CO– group in wool (Figure 4). The N$_{1s}$ binding energy, whose peak at 400.37 eV, was found to be 0.54 eV lower compared with that of wool. And the difference between –NH–CO– in wool and –NH–CO– in catalyst is 0.32 eV. There are three kinds of S containing groups: –SO$_x$–, –S–S– and –SH in wool, for which the S$_{2p}$ binding energies are different (Figure 5). The S$_{2p}$ binding energy change of –SO$_x$–in wool–Pd from that in wool are -0.55 eV and -0.22 eV, and that for –S–S– group is 0.72 eV minus, and –SH is -0.47 eV. The O$_{1s}$ binding energy change of wool–Pd from wool is 0.15 eV. These results further indicated that coordination or ionic bonds were formed by the connection of N atoms (in –NH$_2$ and –NH–CO–) and S atoms (in –SO$_x$–, –SH and –S–S–) with Pd atoms in the wool–Pd complex.

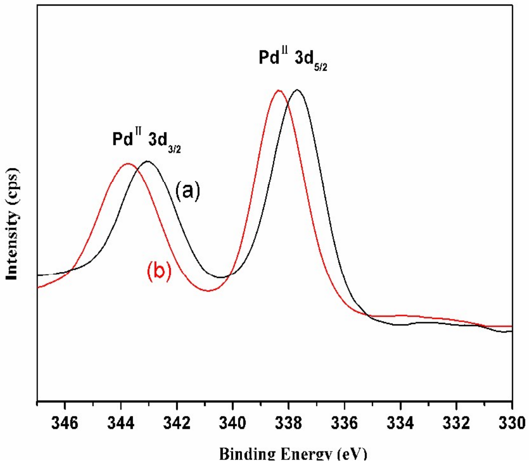


Figure 3. XPS spectra of (a) wool-Pd(OAc)$_2$ complex and (b) Pd(OAc)$_2$.

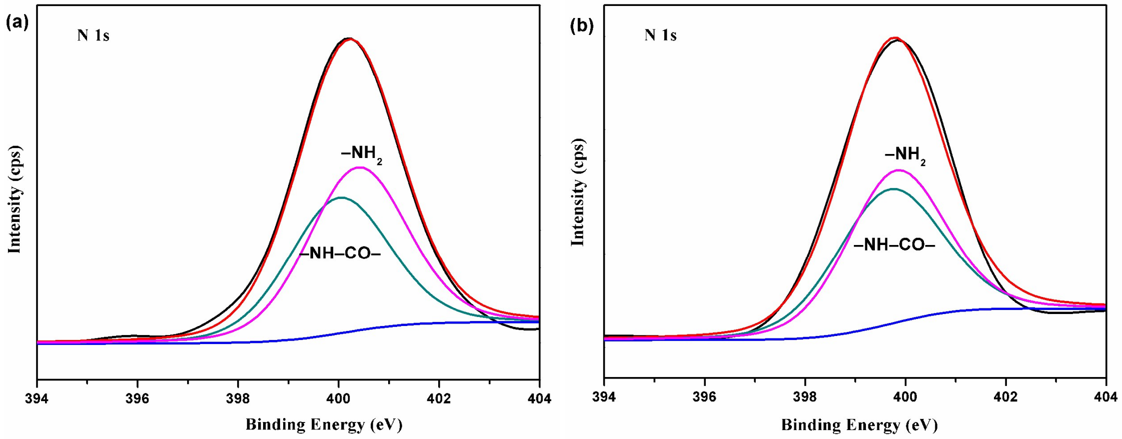


Figure 4. XPS spectra of N$_{1s}$: (a) wool, (b) wool-Pd(OAc)$_2$ complex.

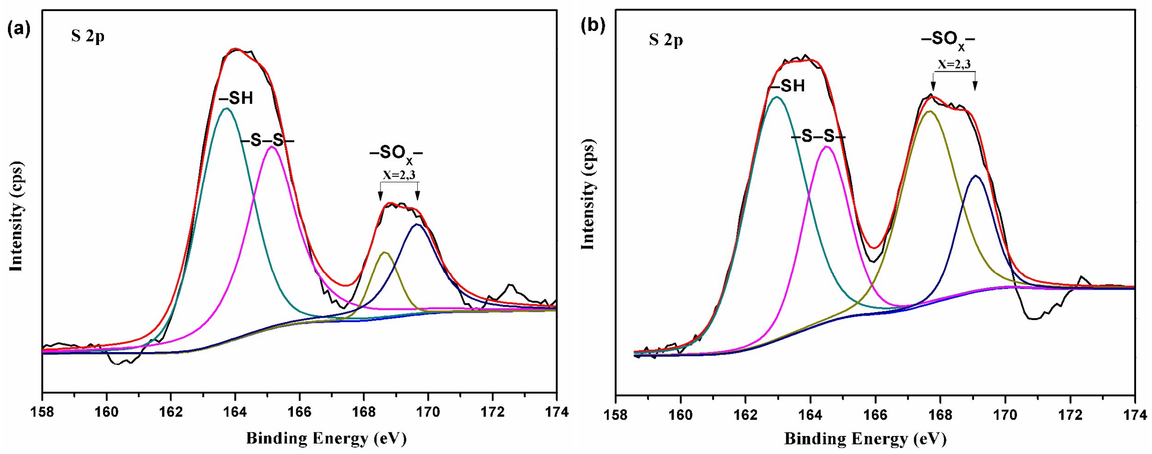


Figure 5. XPS spectra of S_{2p}: (a) wool, (b) wool-Pd$(OAc)_2$ complex.

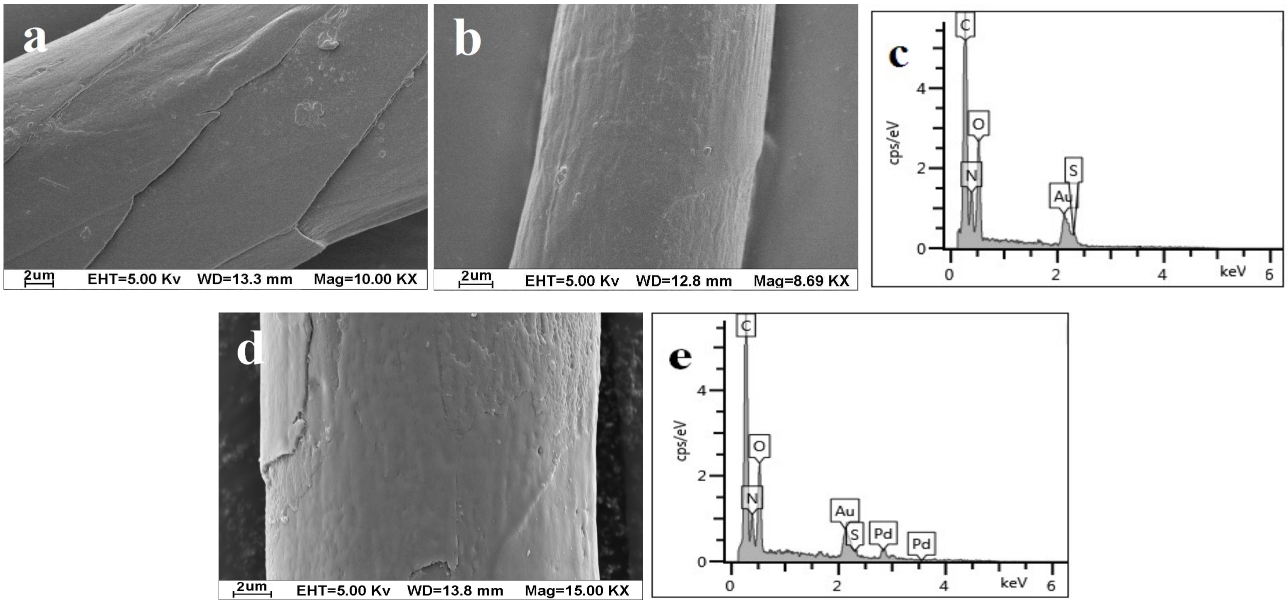


Figure 6. (a) SEM image of wool fibre, (b) SEM images of treated-wool fibre, (c) the corresponding EDX spectrum of the treated-wool fibre, (d) SEM images of Wool-Pd(II) complex, and (e) the corresponding EDX spectrum of catalyst.

The morphologies of the catalyst were followed by scanning electron microscopy (SEM) (Figure 6). As represented in the photographs, surface of the treated wool (Figure 6, b) was smoother; in contrary, the surface of the raw wool materials was covered with squamae (Figure 6, a). As displayed in Figure 4 (Figure 6, c), EDX spectrum suggested none of Pd and any other metal existed in the supporter except gold (samples were coated with gold using an Edwards S 150A sputter coat). And in the wool-Pd$(OAc)_2$ complex (Figure 6, d), there is no aggregation of palladium on the surface of wool fibre. And then the EDX spectrum (Figure 6, e) indicated that Pd was detected from the wool-Pd$(OAc)_2$ complex. The result indicated that palladium was dispersed uniformly onto the surface of wool fibre.

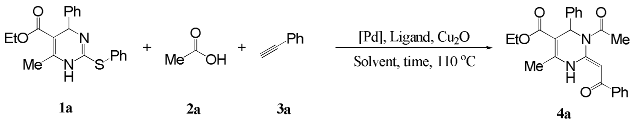
Desulfurative coupling reactions with terminal alkyne

As our initiative studies upon the desulfurative domio reactions among thioether, carboxylic acids and terminal alkynes, firstly, the reaction conditions were optimized. We use a 2-(phenylthio)-1,4-dihydropyrimidine derivative (**1a**) as substrate in the reactions with acetic acid (**2a**) and phenylacetylene (**3a**). (Table 2).

We tested the dosage of this wool-Pd$(OAc)_2$ catalyst (entry 1-4). The Pd content of the wool-Pd$(OAc)_2$ catalyst was measured to be 1.56 wt%. Obviously, 8 mg (0.4 mol%) wool-Pd$(OAc)_2$ catalyst (entry 2) can provide fine yields for the product **4a**, and dosage more than 10 mg didn't contribute distinct increase of the product yields (entry 4). Therefore in this condition, 10 mg (0.6 mol%) can be sufficient for catalysis. Time trials were taken out thereafter (entry 3, entry 5-7), and 48 hours' reaction can provide peak value of the yields (entry 3); prolonged reaction would not increase the yields (entry 7). Different solvents were used in the reactions (entry 3, 8, 9), and among them, dioxane was the best one. Different ligands were also tested (entry 3, entry 10-12), and DPE-Phos performed better. In order to estimate the superiority of wool-Pd$(OAc)_2$ complex compared to other palladium catalysts, palladium compounds as Pd$(OAc)_2$ (entry 13, 14),

$Pd(acac)_2$ (entry 15), $Pd_2(dba)_3$ (entry 16) and $PdCl_2(PPh_3)_2$ (entry 17) was tested for their catalytic capacities in this reaction. Although **4a** can be produced, but the yields were far lower than that wool-$Pd(OAc)_2$ catalyst does when the same amount (0.6 mol%) palladium was used. And only when more palladium was added (entry 13) can $Pd(OAc)_2$ afford a good yield level with that the wool-$Pd(OAc)_2$ catalyst did. Comparison between wool-$Pd(OAc)_2$ and wool-$PdCl_2$ (entry 18) indicated apparently that the former was more active within a shorter reaction time.

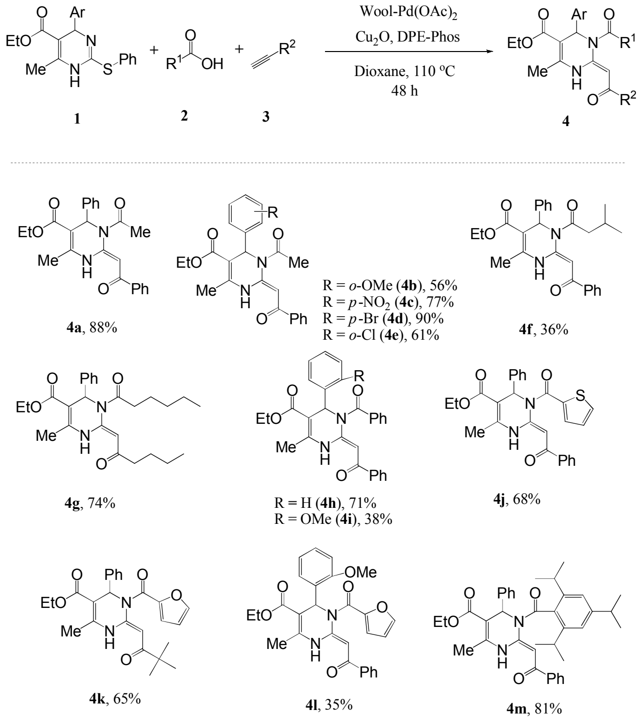
Table 2. Optimization of conditions [a]



Entry	Catalyst [b]	Ligand	Solvent	Time	Yields [c]
1	Wool-$Pd(OAc)_2$ (5 mg)	DPE-Phos	Dioxane	48 h	64%
2	Wool-$Pd(OAc)_2$ (8 mg)	DPE-Phos	Dioxane	48 h	79%
3	Wool-$Pd(OAc)_2$ (10 mg)	DPE-Phos	Dioxane	48 h	88% 150 [d]
4	Wool-$Pd(OAc)_2$ (15 mg)	DPE-Phos	Dioxane	48 h	91%
5	Wool-$Pd(OAc)_2$ (10 mg)	DPE-Phos	Dioxane	24 h	79%
6	Wool-$Pd(OAc)_2$ (10 mg)	DPE-Phos	Dioxane	36 h	85%
7	Wool-$Pd(OAc)_2$ (10 mg)	DPE-Phos	Dioxane	60 h	87%
8	Wool-$Pd(OAc)_2$ (10 mg)	DPE-Phos	Tolune	48 h	71%
9	Wool-$Pd(OAc)_2$ (10 mg)	DPE-Phos	Xylene	48 h	63%
10	Wool-$Pd(OAc)_2$ (10 mg)	PPh_3	Dioxane	48 h	65%
11	Wool-$Pd(OAc)_2$ (10 mg)	X-Phos	Dioxane	48 h	71%
12	Wool-$Pd(OAc)_2$ (10 mg)	-	Dioxane	48 h	36%
13	$Pd(OAc)_2$ (5 mol%)	DPE-Phos	Dioxane	48 h	86%
14	$Pd(OAc)_2$ (0.6 mol%)	DPE-Phos	Dioxane	48 h	46%
15	$Pd(acac)_2$ (0.6 mol%)	-	Dioxane	48 h	23%
16	$Pd_2(dba)_3$ (0.6 mol%)	-	Dioxane	48 h	28%
17	$PdCl_2(PPh_3)_2$ (0.6 mol%)	PPh_3	Dioxane	48 h	29%
18	Wool-$PdCl_2$ (10 mg)	DPE-Phos	Dioxane	48 h	56% 13 [d]

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.50 mmol), **3a** (0.38 mmol), Cu_2O (0.25 mmol), Ligand (2 mol %), solvent (2 mL); [b] Catalyst amount: 10 mg of Wool-$Pd(OAc)_2$ (Pd 1.56 wt %) equals to 0.6 mol%; [c] Isolated yield by column chromatography; [d] The TON value.

With the optimized reaction conditions, a series of 2-(phenylthio)-1,4-dihydropyrimidine derivatives were tested with various carboxylic acids and terminal alkynes (Scheme 2). In those reactions, the wool-$Pd(OAc)_2$ catalyzed domino desulfurative process can produce the desired product in moderate to excellent yields. Apparently, this complex can be an effective catalyst for the desulfurative coupling reaction. Different carboxylic acids including aliphatic, aromatic and heterocyclic acids were successfully reacted. Substituted group affect on the reaction slightly (**4b-4d**). Different terminal alkynes (**4e**, **4g**) can be tolerated well under these conditions leading to the desired products produced in good yields. The stereospecific blockaded example, the 2,4,6-triisopropylbenzoic acid, could also lead to the desired product (**4h**).

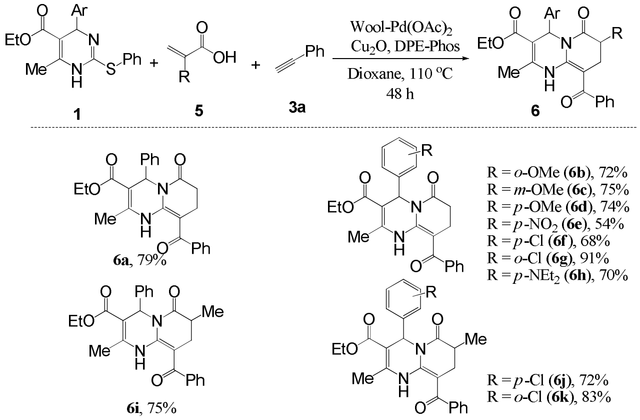


Scheme 2. Reaction conditions: **1** (0.25 mmol), **2** (0.50 mmol), **3** (0.38 mmol), Cu_2O (0.25 mmol), Wool-$Pd(OAc)_2$ (10 mg, Pd 1.56 wt %), DPE-Phos (2 mol%), dioxane (2 mL); Isolated yields of **4** by column chromatography.

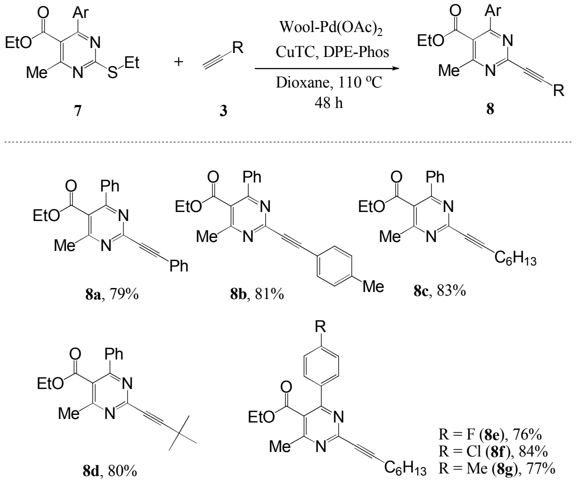
Then acrylic acids (**5**) was used as the carboxylic acid substrate to test the catalytic activity of this wool-$Pd(OAc)_2$ complex (Scheme 3). We are glad to see that wool-$Pd(OAc)_2$ catalyst can tolerate these substrates well with the bicycle products **6** produced in excellent yields. Substituent groups did not impact on the yields too much, except for the strong electric withdrawn groups like $-NO_2$ (**6e**). The Michael addition process[60] would not be affected when the acrylic acids got a α-substituent group (**6i-6k**). Compared with the acetic acid and other aliphatic acids, acrylic acids performed equally well with yields no less than the former examples (Scheme 3).

In the reactions with terminal alkynes under the catalytic system above, pyrimidine thioether derivatives performed different reactivities compared with the dihydropyrimidine thioether derivatives. When (ethylthio)pyrimidine derivatives (**7**) were examined in the same catalytic system, the domino process was hindered, with the sonogashira product **8** produced (Scheme 4).

A series of these 2-(ethylthio)pyrimidine derivatives (**7**) were exposed to the similar catalytic conditions we used above to react with varied terminal alkynes (**3**). Different alkynes were tolerated well, with the similar coupling products produced in excellent yields (**8a**-**8d**). Substitute groups on 2-(ethylthio)pyrimidines may slightly influence the conversion (**8e**-**8f**).



Scheme 3. Reaction conditions: **1** (0.25 mmol), **5** (0.50 mmol), **3a** (0.38 mmol), Cu$_2$O (0.25 mmol), Wool-Pd(OAc)$_2$ (10 mg, Pd 1.56 wt %), DPE-Phos (2 mol%), dioxane (2 mL); Isolated yields of **6** by column chromatography.



Scheme 4. Reaction conditions: **7** (0.25 mmol), **3** (0.50 mmol), CuTC (0.50 mmol), Wool-Pd(OAc)$_2$ (10 mg, Pd 1.56 wt %), DPE-Phos (2 mol%), dioxane (2 mL); Isolated yields of **8** by column chromatography.

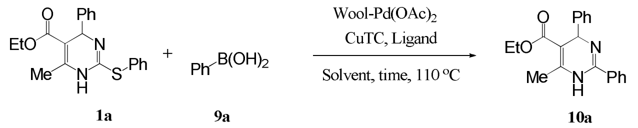
Desulfurative coupling reactions with aryl boronic acids

The wool-Pd(OAc)$_2$ can also be applicable in the desulfurative Suzuki coupling reactions. Therefore, the catalyst was also underwent the similar processes to catalyze the reactions between thioethers with aryl boric acids. We firstly optimized the reaction conditions. (Table 3)

Obviously, in this process, an appropriate ligand added could greatly accelerate the conversion (compare entry 9 with entry 1, 7, 8). And DPE-Phos was again adopted as a better choice. Different solvents were also tested, and dioxane perform the best (entry 1 compared with 5, 6). Finally, the time trials were carried out (entry 1-4), suggesting that 24 hours' reaction can afford the peak yield (entry 1), and prolonged reaction wouldn't increase the yields (entry 4). As the additive Cu(I), besides CuTC, other cuprous salts like CuOAc was also tested (entry 10), but was resulted with poor performance.

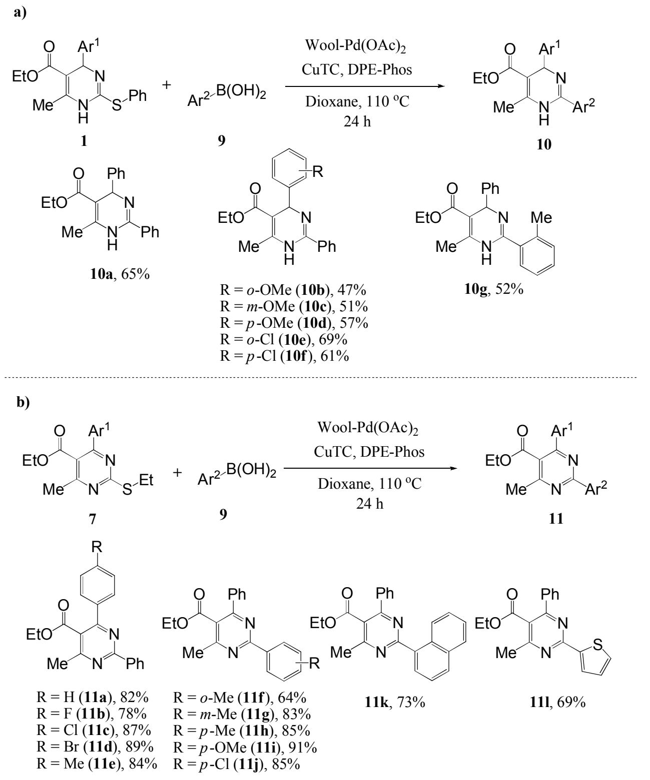
With the optimized reaction conditions (Table 3, entry 1), we investigated the reactivity of 2-(phenylthio)-1,4-dihydropyrimidine derivatives (**1**) (Scheme 5, a) and 2-(ethylthio)pyrimidine derivatives (**7**) (Scheme 5, b) with different aryl boronic acids, respectively.

Table 3. Optimization of conditions [a]



Entry	Ligand	Solvent	Time	Yields [b]
1	DPE-Phos	Dioxane	24 h	65%
2	DPE-Phos	Dioxane	12 h	44%
3	DPE-Phos	Dioxane	18 h	59%
4	DPE-Phos	Dioxane	36 h	64%
5	DPE-Phos	Tolune	24 h	43%
6	DPE-Phos	Xylene	24 h	49%
7	PPh$_3$	Dioxane	24 h	23%
8	X-Phos	Dioxane	24 h	31%
9	-	Dioxane	24 h	12%
10 [c]	DPE-Phos	Dioxane	24 h	54%

[a] Reaction conditions: **1a** (0.25 mmol), **9a** (0.5 mmol), CuTC (0.5 mmol), Wool-Pd(OAc)$_2$ (10 mg, Pd 1.56 wt %), Ligand (2 mol%), solvent (2 mL); [b] Isolated yield of **10a** by column chromatography. [c] CuOAc was used instead of CuTC.



Scheme 5. Reaction conditions: **1** or **7** (0.25 mmol), **8** (0.5 mmol), CuTC (0.5 mmol), Wool-Pd(OAc)$_2$ (10 mg, Pd 1.56 wt %), DPE-Phos (2 mol%), dioxane (2 mL); Isolated yields of **10** or **11** by column chromatography.

Apparently, this wool-anchored Pd can well tolerate both the dihydropyrimidine thioether derivatives (**1**) and the pyrimidine thioether derivatives (**7**), leading to the desired product **10** and **11** (Scheme 5). Different aryl boronic acids performed differently, as the substituent groups of boronic acids notably affected the yields of the product **10**. For example, *o*-tolyl boronic acid (**10g**) performed poorly under the same conditions compared with phenyl boronic acid (**10a**). The electron donating group on dihydropyrimidine also slightly declined the yields of the coupling product (**10b-10d**).

A series of 2-(ethylthio)pyrimidine derivatives (**7**) were tested with varied aryl boronic acids. The products can be isolated in higher yields (Products **11**). The substitute groups on **7** did not influence the yields of **11** much (**11a-11e**), but different aryl boronic acids yield the product quite differently (**11f-11l**). Heteroaryl boronic acid was also tested, but performed poorly (**11l**).

Recyclicity tests of the wool-Pd(OAc)$_2$ catalyst

The durability is one of the significant qualities of a heterogeneous catalyst compared with its homogenous counterpart. We carried out the experiments for the cyclicity of this wool-Pd(OAc)$_2$ complex through the reactions among **1a**, **2a** and **3a** under the optimized conditions as described above (Figure 7). The reaction was repeated for 9 cycles, in which the catalyst was recovered and reused for 8 times. During this test, the yields of the product only slightly declined.

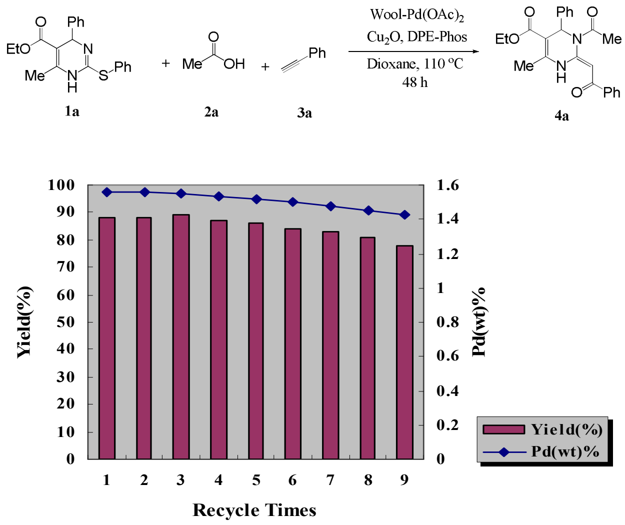


Figure 7. Endurance of the catalyst by the model reaction for synthesis of **4a**.

The catalyst was used repeatedly for nine times and then was examined by ICP-AES analysis within very narrow scope (1.56% to 1.43%) to observe its palladium content. The total TON value is 1320. Only 68 parts per billion palladium was detected in the reaction phase (by ICP-MS), indicating quite a slender metal leaching of the catalyst during the reactions. (Figure 7).

Hot Filtration Test

In order to illustrate the contributions made by the leached homogeneous palladium to the reactions, the hot filtration test[63-65] was also carried out for the reaction among **1a**, **2a** and **3a**. The reaction was operated under the standard conditions for 12 hours as it reached a conversion of 41%; then the mixture was filtered to remove the heterogeneous catalyst and further stirred under the preceding conditions for another 36 hours. But the conversion of the substrates remained at 41%. The yield of the product can reach 88% otherwise if the wool-Pd(OAc)$_2$ catalyst was not removed. These results suggested the indispensible role of the heterocatalyst for the reactions.

Characterization of the used catalysts after the reaction

XPS spectra analysis was implemented again after the wool-Pd(OAc)$_2$ complex was used. The binding energy of Pd was not changed after the wool-Pd(OAc)$_2$ complex was used. Measurements for the Pd$_{3d}$ peak were performed to illustrate the oxidation state of the palladium (Figure 8). 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 reaction, the Pd$_{3d}$ XPS spectra of the catalyst also showed two major peaks with binding energy at 337.71 eV and 343.07 eV, corresponding to the Pd(II) state. These results provided the direct evidences for the high recyclability and stability of this wool-Pd(OAc)$_2$ complex.

SEM images of the used wool-Pd(OAc)$_2$ catalyst indicated a very intrusting result (Figure 9). Catalyst sample that was reused for 9 times was analyzed. Rough surface was presented in the SEM image (Figure 9, a), and at a high magnification, a specified picture revealed the grains adsorbed on the wool fibre (Figure 9, b). EDX analysis informed the main element of the "grains" was the aggregation of copper, not palladium (Figure 9, c), and in the smooth surface (district "d" of (b)), the EDX analysis showed Cu and Pd were existed (Figure 9, d). In fact the used wool-Pd(OAc)$_2$ complex represented an attractive red color, which was quite similar with the copper red. For the Cu(I) additive we used in the desulfurative reactions, we consider that a measure of copper was aggregated on the surface of wool fibre. Further investigation upon this copper-adsorption has been carried out in our laboratory.

The above indicated that the catalyst is stable and recyclable.

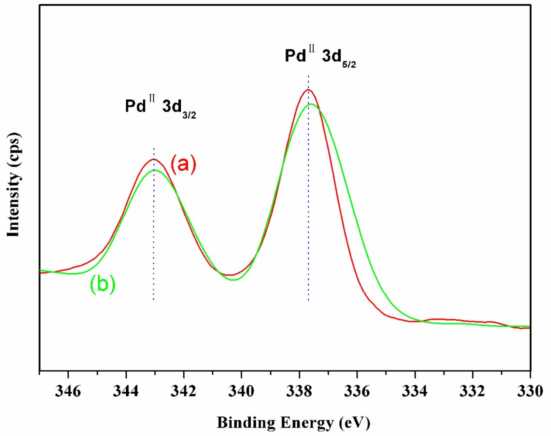


Figure 8. XPS spectra of (a) fresh and (b) reused catalyst.

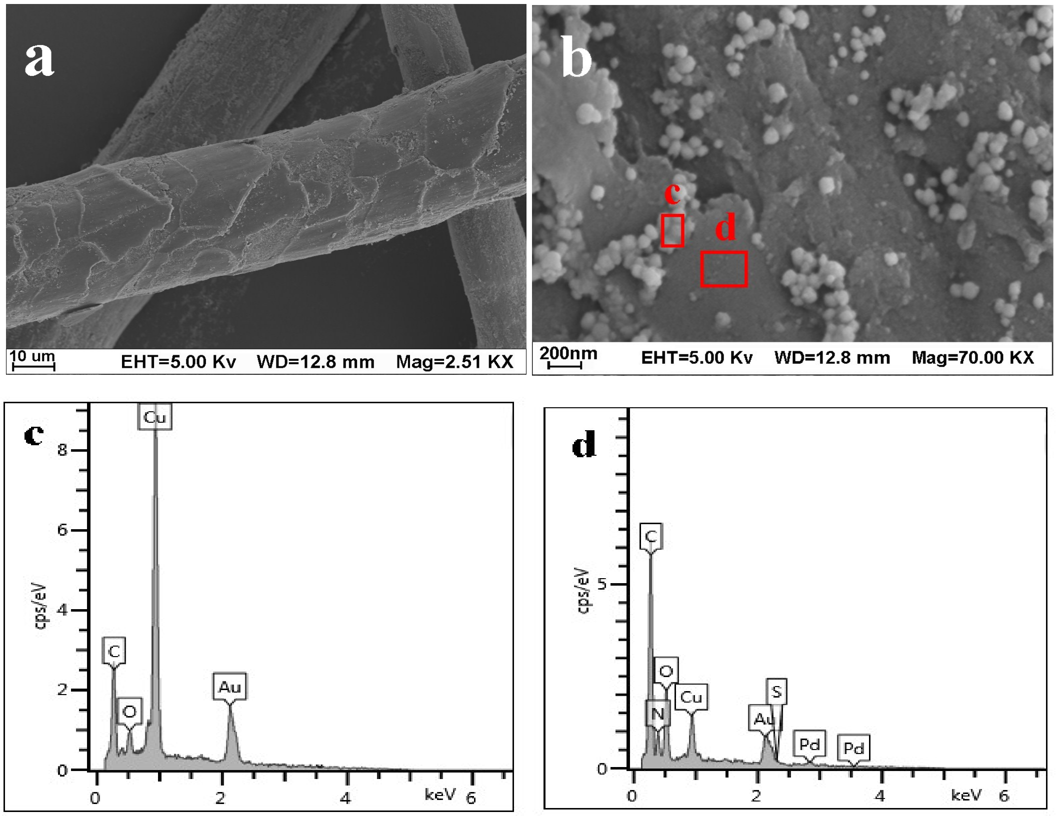


Figure 9. (a) SEM images of the reused catalyst, (b) SEM image of the reused catalyst at a high magnification, (c) EDX of the “grains”, (d) EDX of the surface without “grains”.

Conclusions

In conclusion, we have prepared and characterized the wool-anchored palladium acetate. This complex was applied in the desulfurative cross coupling reactions under the modified Liebeskind–Srogl conditions, in which the pyrimidine thioether derivatives were reacted differently with terminal alkynes and aryl boronic acids. Products were isolated in moderate to excellent yields. When 2-(phenylthio)-1,4-dihydropyrimidine derivatives were reacted with terminal alkynes and carboxyl acids, domino products were produced, whereas when aromatized heterocyclic sulfoethers brought the classical Sonogashira coupling products. The catalyst was also used to catalyze the desulfurative Suzuki coupling reactions between the pyrimidine thioether derivatives and aryl boronic acids. More importantly, the easy experimental handling catalyst is stable, shows negligible metal leaching, and can be reused for at least 9 successive runs. 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

2-(phenylthio)-1,4-dihydropyrimidine and 2-(ethylthio)-pyrimidines were prepared as the procedures in the *Supporting Informations*. All the other substrates and solvents were all purchased from J&K Scientific Ltd. All reagents were directly used from purchased without any further purification unless otherwise specified. Wool was provided by Gansu Jingyuan Woolen Mill (Jingyuan town, Gansu province, PR China).

All reactions were conducted under a nitrogen atmosphere with a dual-manifold Schlenk tube, unless otherwise mentioned, and in oven-dried glassware. All NMR spectra are recorded on MERCURY (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectrometers; chemical shifts are expressed in ppm (δ units) relative to TMS signal as internal reference in $CDCl_3$. Gas chromatography (GC) analysis was performed on a Shimadezu GC-2010 equipped with a 15 m × 0.53 mm × 1.5 μm RTX-1 capillary column and a oxyhydrogen flame detector. ICP-AES were measured on IRIS Advantage. XPS measurement was recorded on PHI5702 photoelectron spectrometer. Binding energy was referred to C_{1s} (284.80 eV). FTIR spectroscopy patterns were obtained on an FT/IR-660 Plus system (Jasco, Tokyo, Japan). The samples were mixed with KBr powders and pressed into a disk suitable for FTIR measurement. The morphologies of the catalyst were examined with field emission scanning electron microscopy (FE-SEM, Ultra Plus, Carl Zeiss). Elemental analysis of the photo catalyst was conducted by an energy-dispersive X-ray spectrometer (EDX) attached to the scanning electron microscope. Melting points were measured with an XT-4 apparatus. High-resolution mass spectra (HRMS) (ESI) were obtained with a Bruker Daltonics APEX II 47e and Orbitrap Elite mass spectrometer. Mass-spectra (EI) were recorded on a TRACE DSQ instrument. Column chromatography was generally performed on silica gel (200–300 mesh) and TLC analyses were conducted on silica gel GF254 plates.

General procedures for preparation of the treated-wool pieces [54-58]

Common commercial white wool was washed with distilled water and ethanol, and then cut to pieces. Subsequently, the wool pieces were treated by the mixture of $KMnO_4$ (3 g/L) and NaCl (25 g/L), and the pH was adjusted to 2.0, the mixture was stirred at 45 ^{o}C about 45 minutes, and then wool was turned to black-brown. Whereafter, the black-brown wool was dipped in the solution of Na_2SO_3 (20 g/L) and HAc (10 mol/L), stirred at 50 ^{o}C for 10minutes, after the wool was returned to white, washed with water several times, and then dried at 80 ^{o}C.

General procedures for operation the desulfurative coupling reactions

Under argon atmosphere, **1a** (0.25 mmol, 69 mg), wool-Pd(OAc)$_2$ (10 mg, Pd 1.56 wt %), Cu_2O (0.25 mmol, 36 mg), DPE-Phos (5 μmol, 2.5 mg, 2 mol%) were added into a Schlenk tube dried by Hot-gun. The tube was stopped and degassed with argon for three times. Then **2a** (0.50 mmol, 30 mg), **3a** (0.375 mmol, 38 mg) and dioxane (2 mL) were added by syringe. The mixture was stirred under argon atmosphere at 110°C for 48 h. Then the mixture was cooled down to room temperature with 2 mL saturated solution of NH_4Cl added to quench the reaction and 1 mL dilute solution of NaOH to neutralize the excess **2a**. Then, the organic components were extracted by acetic ether and evaporated in vacuum and further purified by column chromatography on silica gel with petroleum ether/ethanol (60:1) to give the product **4a** (89 mg, 88%) as yellow solid. Melting points were determined on an XT-4 electro thermal micro melting point apparatus and uncorrected. NMR spectra were recorded for ^{1}H NMR (400MHz) and ^{13}C NMR (100 MHz) on a Varian Mercuryplus-400 instrument, using TMS as internal standard. Mass spectra were recorded on a Bruker APEX II instrument. Elemental analyses were performed on a Carlo-Erba 1106 elemental analysis instrument. See *supporting information* for spectroscopic data of the products.

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Notes

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Wool-anchored $Pd(OAc)_2$ complex: a highly active and reusable catalyst for the desulfurative coupling reactions

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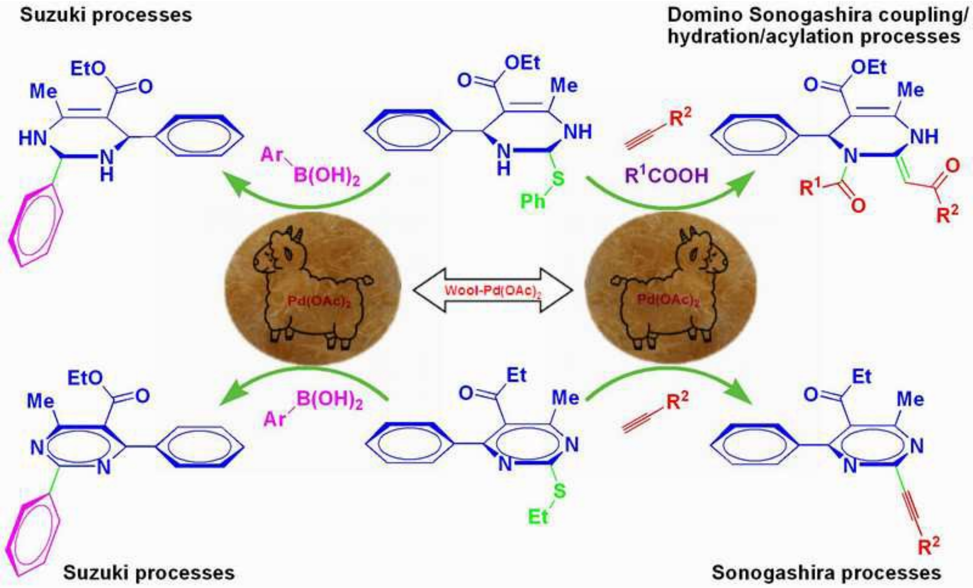

Abstract: A biomacromolecule-anchored palladium complex, wool-$Pd(OAc)_2$ complex, was used as a catalyst for the Liebeskind–Srogl desulfurative coupling reactions of pyrimidin-yl thioether derivatives with terminal alkynes and arylboronic acids, respectively. Products were isolated in moderate to excellent yields. Notably, when 2-(phenylthio)-1,4-dihydropyrimidine derivatives were reacted with terminal alkynes and carboxyl acids, a domino reaction process was revealed. In these reactions, this novel and efficient catalyst was capable to be reused for at least nine rounds, and performed an endurable activity as well as the wide tolerance of the substrates.

Keywords: Liebeskind–Srogl cross coupling, desulfurative coupling, Wool-anchored palladium, Heterogeneous catalyst, recycles