Organic Letters

Letter

pubs.acs.org/OrgLett

Thiophene-Alkyne-Based CMPs as Highly Selective Regulators for Oxidative Heck Reaction

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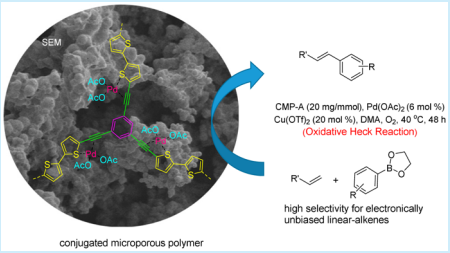
Supporting Information

ABSTRACT: Thiophenes containing an adjacent C≡C group as ligands for Pd^{II}-promoted organic reactions are reported for the first time. These ligands were utilized as catalytic sites and integrated into the skeleton of conjugated microporous polymers. By employing these CMP materials as selective regulators, oxidative Heck reactions between arylboronic esters and electronically unbiased alkenes provide highly selective linear products.



The Heck–Mizoroki reaction provides a versatile strategy to convert vinylic C–H bonds into C–C bonds.[1] However, olefins that lack directing groups or electronic biased groups gave a mixture of Heck isomers with low selectivity. Most precedents achieve regioselectivity by using substrates that have an intrinsic electronic bias. Electron-rich vinyl ethers and vinyl amides favor coupling adjacent to the heteroatom to give the branched products,[2] while electron-poor olefins, such as acrylates and styrenes, favor coupling at the terminal position to give the linear products (Figure 1).[3] The scope of these reactions is severely limited, however, by challenges in controlling the product regioselectivities.

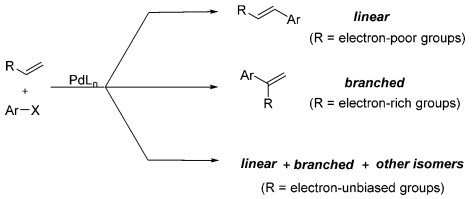
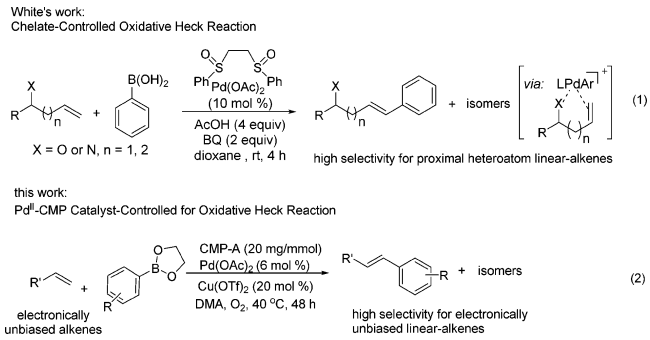


Figure 1. Different products of the Heck reaction.

Recent developments have begun to address these limitations through the identification of catalyst systems. For example, Zhou and co-workers developed Pd-catalyzed branched-selective Heck reaction of electronically unbiased alkenes with bulky bisphosphine.[4] Jamison's group reported Heck-coupling reactions between benzyl chlorides and electronically unbiased alkenes using $[Ni(cod)_2]$ and PCy_2Ph, providing a regioselective access to branched products.[5] The Stahl group also demonstrated high regioselectivity in the Heck-type synthesis of branched conjugated dienes using the catalyst derived from palladium and phenanthroline-type ligands.[6]

As noted above, linear-selective Heck coupling typically requires electron-poor substrates. However, Sigman and co-workers demonstrated that high linear selectivity could be achieved by submitting electronically unbiased alkene substrates to a catalytic system incorporating a carbene ligand.[7] White's group reported a chelate-controlled intermolecular oxidative Heck reaction catalyzed by a versatile $Pd(OAc)_2$/sulfoxide catalyst that proceeds with excellent selectivities for a wide range of non-resonance-biased α-olefins with proximal oxygen and nitrogen functionality (Scheme 1, eq 1).[8] However, electronically nonbiased aliphatic alkenes yielded very poor selectivity.

Scheme 1. Pd^{II}/Sulfur-Containing Catalyst for Oxidative Heck Reaction



Received: June 21, 2017

DOI: 10.1021/acs.orglett.7b01858
Org. Lett. XXXX, XXX, XXX–XXX

Conjugated microporous polymers (CMPs) are a novel class of porous materials with an extended π-conjugation in an amorphous organic framework.[9] Owing to the wide-ranging flexibility in the choice and design of functional units, the available control of pore parameters, and the advantage of easy separation, these polymers can be tailored for use in various applications, such as gas adsorption,[10] energy storage,[11] sensing,[12] light emitting,[13] and light harvesting.[14] More recently, specific functionalities were achieved by the introduction of designed catalytic sites into CMPs, particularly for heterogeneous catalysis, because these material are synthetically versatile and have good thermal stability and excellent chemical robustness to acids, bases, and organic solvent. For example, Cooper and co-workers have shown that CMP-CpIr-3 is a highly active catalyst for reductive amination[15a] and RP-CMP1 is an effective noble-metal-free photocatalyst for heterogeneous photocatalytic aza-Henry reactions.[15b] Recently, our group also reported a privileged pyridine-alkyne-based CMPs as a heterogeneous catalytic ligand for the Pd^{II}-catalyzed oxidative Heck reaction with high linear selectivity.[16] The rigid porous structures of CMPs have a positive effect on controlling the regioselectivity of organic reactions.

In the past few years, the Pd^{II}/sulfur-containing catalyst system has been reported. Stahl demonstrated that $Pd(OAc)_2$/DMSO is an effective catalyst for the aerobic oxidation of alcohols and other organic substrates.[17] Shi and co-workers have shown a $Pd(OAc)_2/iPr_2S$-catalyzed oxidative cross-coupling of electron-deficient polyfluoroarenes with completely unactivated aromatics.[18] Diisopropyl sulfide was indispensable for promoting the efficacy. The famous White reagent was also used in chelate-controlled intermolecular oxidative Heck reaction.[8] Thiophene as polymer unit is the hotspot in material chemistry.[19] However, thiophene−Pd complex catalyzed organic reactions have not been reported. Interestingly, we found that ligands of thiophene containing an adjacent C≡C group promote organic reactions. Herein, we develop a method for oxidative Heck reaction using novel thiophene−alkyne-based CMPs as highly selective regulators (Scheme 1, eq 2). Not only can these units provide catalytic sites, but they also serve as building blocks in the CMP skeleton.

Aliphatic olefins with electronical unbiasedness are challenging substrates for selective oxidative Heck reaction.[7,8] Therefore, in our initial screening experiments, 1-hendecene was investigated by different thiophene-type ligands (Figure 2). $Pd(OAc)_2$ in the absence of an ancillary ligand led to low selectivity despite higher conversions. Thiophene (Figure 2, L1) and bithiophene (Figure 2, L2) inhibit Pd^{II} activity leading to low yield and selectivity. In comparison with thiophene and bithiophene, the thiophene containing adjacent C≡C groups as ligands (Figure 2, L3−L6) showed higher yields and regioisomeric ratios. The yield was obviously decreased when a thiophene-type ligand L7 in which the C≡C bond is too far from the S sites to coordinate to the palladium center was used. The ligand 2,5-diphenylthiophene (Figure 2, L8) led to a lower regioisomeric ratio of linear product compared with L6. Based on above results, we selected L4 (a bifunctional ligand consists of C≡C and thiophene-S sites with proper coordination geometric angle) as a functional unit and further integrated into the skeleton of CMP to serve as a heterogeneous catalytic ligand.

CMP-A and CMP-B were synthesized by sonogashira coupling in the presence of $PdCl_2(PPh_3)_2$ and CuI. In comparison, the thiophene-containing polymer POL-A without C≡C bond was also synthesized by free radical polymerization (see the Supporting Information, Scheme S1). In the presence of CMP-B or POL-A, moderate yields and regioisomeric ratios were obtained. Excitedly, the use of CMP-A as a heterogeneous ligand gave the product in 73% yield, excellent ratio of ln/br (ln/br = 30:1) and good selectivity of linear product (rr = 3.5:1, rr = linear/all other isomers), which was much better than white's catalyst (ln/br = 8:1, rr < 1:1).[8] In controlling the regioselectivity, porous polymers (CMP-A, CMP-B) are better than monomeric thiophene-type ligands (L3, L6), which could be largely attributed to the confinement effect of the porous structure of CMP materials.

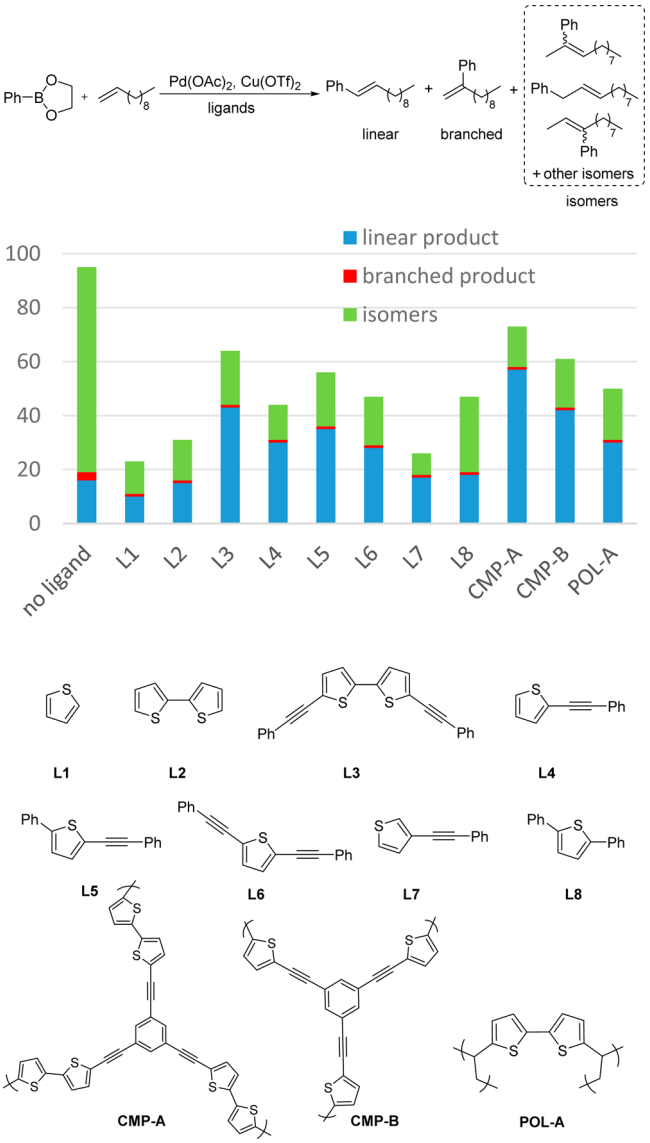


Figure 2. Effect of ligands on the formation of different products of the model reaction. In addition to the formation of the linear product (blue bars), branched product (red bars) and other isomers (green bars) was also observed. Ratio of linear/branched/other isomers as determined by GC analysis. The model reaction: 1-hendecene (0.5 mmol), phenylboronic ester (1.0 mmol), $Pd(OAc)_2$ (6 mol %), $Cu(OTf)_2$ (20 mol %), L1-L8 (20 mol %), CMP-A, CMP-B or POL-A (10 mg), DMA (3 mL), 40 °C, O_2 (1 atm), 48 h.

DOI: 10.1021/acs.orglett.7b01858
Org. Lett. XXXX, XXX, XXX−XXX

To explore the structure–activity relationship, CMP-A and related prepared $Pd(OAc)_2$/CMP-A were characterized by thermogravimetry (TG), N_2 adsorption–desorption analysis, scanning electron micrograph (SEM), transmission electron micrograph (TEM) and X-ray photoelectron spectroscopy (XPS). The TG shows that CMP-A remains intact at temperatures up to 400 °C, even with only about 8% weight loss at 800 °C, indicating its good thermal stability (Figure S1). Nitrogen adsorption–desorption analysis demonstrates that CMP-A possesses hierarchical porosity, which is further confirmed by SEM (Figure 3A) and TEM (Figure S2) images.

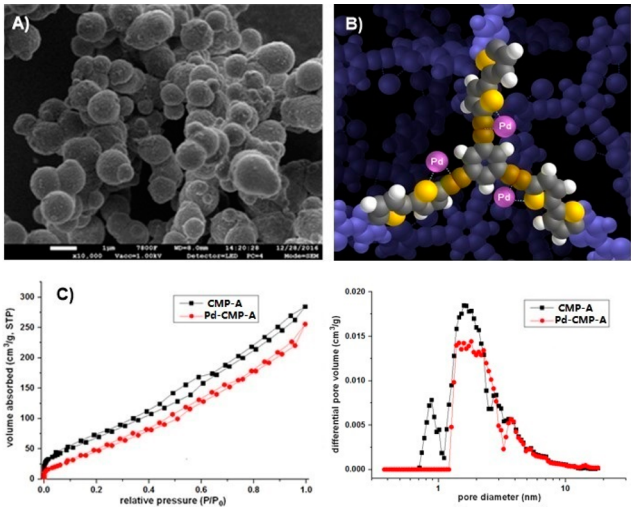
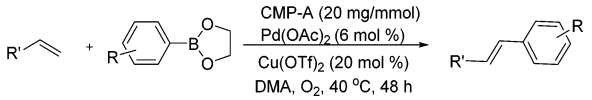


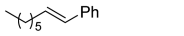
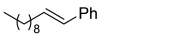
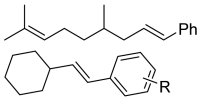
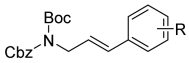
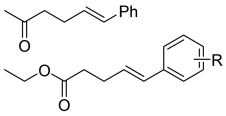
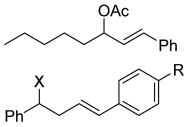
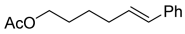
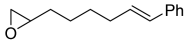
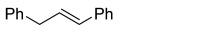
Figure 3. (A) Scanning electron microscopy (SEM) of CMP-A. (B) Node–strut topology for simulated network fragment for Pd^{II}/CMP-A. Key: H (white ball), C of benzene and thiophene (gray ball), C of alkyne (dark yellow ball), S (yellow ball), Pd (violet ball), C) N_2 adsorption–desorption isotherms. (D) Pore size distribution curves.

The BET surface areas and total pore volumes of CMP-A are up to 269.8 m^2/g and 0.441 cm^3/g, respectively. The pore sizes of CMP-A are mainly distributed between 1 and 4 nm which was calculated from the method of nonlocal density functional theory (NLDFT), indicating that the hierarchical porous CMP-A mainly consists of micropores and mesopores. The confinement effect of these porous space play an important role in controlling the regioselectivity for the Heck reaction. No obvious change in the pore size distribution emerged between CMP-A and $Pd(OAc)_2$/CMP-A (Figure 3D). Despite the slight decrease in specific surface area, $Pd(OAc)_2$/CMP-A is still significantly microporous (Figure 3C). Furthermore, XPS confirmed the coordination of palladium with sulfur of thiophene (Figure S3). The network fragments of Pd^{II}/CMP-A have been simulated by node–strut topology (Figure 3B). In addition, the elemental distribution in the $Pd(OAc)_2$/CMP-A was determined by using the energy-dispersive X-ray spectroscopy (EDX) mapping technique in scanning electron microscopy. The highly dispersed character of all functional elements (C, S and Pd) demonstrates the excellent integration of homogeneously distributed active functional sites (Figure S4).

The $Pd(OAc)_2$/CMP-A system was evaluated by using a variety of electronically unbiased alkenes and arylboronic esters, which displayed excellent selectivity toward a broad range of alkenes. Of note, in the presence of CMP-A, aliphatic olefins were converted smoothly to the (*E*)-linear products in good yields with excellent ln/br selectivity (>15:1 ratio in most cases) (Table 1, entries 1–8). The straight-chain olefins (Table 1, entries 1–2) and branched-chain olefin (Table 1, entry 3) all proceed with good yields and regioselectivities. Vinylcyclohexane yielded excellent regioselectivity with a range of arylboronic esters (Table 1, entries 4–8). In addition, this oxidative Heck reaction favors formation of the (*E*)-linear products and tolerant various functional groups. The catalyst $Pd(OAc)_2$/CMP-A promoted the cross-coupling of a doubly protected allylic amine with a range of arylboronic esters to afford the linear products with good yields and high selectivities (Table 1, entries 9–11). The olefins bearing a ketone (Table 1, entry 12) or ester (Table 1, entries 13 and 14) all proceeded with good yields and excellent regioselectivity. It should be pointed out that good yields and excellent selectivities were observed for an allyl ester, a type of substrate that is prone to undergo oxidative

Table 1. Substrate Scope of Oxidative Heck Reaction[a]



entry	product	yield/%[b] (yield/%[c])	linear:branched[d]
1		78[e] (16)	33:1
2		73[e] (20)	30:1
3		60[f](21)	16:1
4	R = H	65 (21)	19:1
5	R = *p*-^{n}Bu	75	12:1
6	R = *p*-CHO	81	24:1
7	R = *p*-CN	92	24:1
8	R = *m*-F	72	16:1
			
9	R = *p*-CHO	80[g]	>100:1
10	R = *p*-Br	79[g]	>100:1
11	R = 2,5-dichlor	72[g]	>100:1
12		60 (28)	>100:1
13	R= 3,4,5-methoxy	52[h] (29)	50:1
14	R = H	61 (27)	30:1
15		65 (18)	>100:1
16	X = OAc, R = H	54 (29)	100:1
17	X = OAc, R = OMe	62 (18)	100:1
18	X = OTBS, R = H	41 (32)	>100:1
19		74[f] (14)	24:1
20		60 (24)	20:1
21		68 (28)	50:1

[a]Reaction conditions: olefins (0.5 mmol), arylboronic esters (1.0 mmol), $Pd(OAc)_2$ (6 mol %), $Cu(OTf)_2$ (20 mol %), CMP-A (10 mg), DMA (3 mL), 40 °C, O_2 (1 atm), 48 h. The selectivity for product (rr = linear/all other isomers) was >10:1 unless otherwise noted. [b]Isolated yield. [c]Recovered starting material. [d]Determined by ^{1}H NMR spectroscopy. [e]rr = 3.5:1. [f]rr = 8:1. [g]CMP-A (5 mg). [h]60 °C

DOI: 10.1021/acs.orglett.7b01858
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addition in the presence of a palladium catalyst (Table 1, entry 15).[20] Substrates containing an acetyl- or TBS-protected homoallylic alcohol also afforded high selectivities and moderate to good yields with a range of arylboronic esters (Table 1, entries 16−19). Alkenyl epoxides usually suffered from nucleophilic attack by organoboron compounds.[21] However, the alkene containing a oxirane group was a suitable substrate for the oxidative Heck reaction in the presence of $Pd(OAc)_2$/CMP-A, delivering the desired product with good yield and selectivity (Table 1, entry 20).

In conclusion, we have reported thiophenes containing an adjacent C≡C group as ligands with Pd^{II} promoting an organic reaction for the first time. These ligands were utilized as catalytic sites and integrated into the skeleton of conjugated microporous polymers. The CMP material with bifunctional ligand feature (C≡C and thiophene) and porous structure could achieve excellent linear-selectivity with electronically unbiased alkenes in oxidative Heck reaction. This work developed a way to use CMP as highly selective catalyst in controlling the regioselectivity of organic reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b01858.

Experimental details (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the National Natural Science Foundation of China (No. 21272190), the Strategic priority research program of the Chinese Academy of Sciences (Grant No. XDB17020400), and NFFTBS (No. J1310024).

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DOI: 10.1021/acs.orglett.7b01858
Org. Lett. XXXX, XXX, XXX−XXX