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Pd-catalyzed oxidative homo-coupling of acrylates and aromatic alkenes for the conjugated diene synthesis

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ABSTRACT

We developed a bidentate monoanionic nitrogen ligand that was effective in the Pd-catalyzed oxidative homo-coupling reaction of acrylates and aromatic alkenes. In the presence of Pd(OAc)₂/ligand several conjugated dienes were obtained in good yields with high stereoselectivities.

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Conjugated Dienes

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Conjugated diene fragments are widely distributed in many natural compounds, optical materials and pharmaceuticals. Accordingly, diene syntheses attract considerable research interest. Pd-catalyzed C-H bond activation is a very powerful tools for C-C bond formation.² This method provides a straightforward and atom-economical strategy for synthesizing compounds. However, simple alkenes are not widely used to prepare dienes. Given the intrinsically poor activity of the ester group in coordinating with the metal center, the alkenvl C-H bond is difficult to activate.³ In 2004. Ishii et al. reported the first example of the oxidative cross-coupling reaction of acrylates with vinyl carboxylates under a Pd(OAc)₂/HPMoV/O₂ system (Scheme 1a).⁴ In 2009, Loh et al. developed an efficient method for the Pd-catalyzed oxidative cross-coupling reaction of simple olefins with acrylates (Scheme 1b).⁵ In 2015, Wen et al. reported the feasibility Pd-catalyzed homodehydrogenation coupling reaction of aromatic alkenes (Scheme 1c).⁶ However, in Loh and Wen's systems, the use of 20 mol% Pd(OAc)₂ catalyst achieves good yields, and decreased Pd(OAc)₂ amount to 10 mol%, leads to relatively low yield. Very recently, Lin and Feng et al. reported an elegant synthesis of 1,3-dienes from terminal alkenes via 1,4-palladium migration/Heck sequence.⁷

In a previous communication, we reported the palladium-

a) Ishii (2004) I% Pd(O/ Mo₁₁VO₄₀•nl NaOAc, O₂ (1atm) AcOH, 90 °C up to 76% yield b) Loh (2009) 20 mol% Pd(OAc)₂ Cu(OAc)₂, O₂ HOAc/DMSO, 60 °C up to 87% yield c) Wen (2015) 20 mol% Pd(OAc)₂ Cu(OAc)₂, O₂ R BnCl, DMF 110 °C up to 66% vield d) Lin and Feng (2018) 5 mol% Pd(OAc)₂ 10 mol% PAr₃ EWG CsOAc, THF 100 °C, 3 H up to 86% yield This wor nol% Pd(OAc)₂ 5 mol% L Ag₂CO₃ 1,4-dioxane 140 °C

Scheme 1. Pd-catalyzed simple alkenens to form conjugated dienes



catalyzed oxidative Heck reaction of simple arenes without directed groups.⁸ In such work, we found that a bidentate monoanionic nitrogen ligand 2-OH-1,10-phen/Pd(OAc)₂ more effectively catalyzed the oxidative Heck reaction of arenes than did 1,10-phen/Pd(OAc)₂. We believed that the complex of 2-OH-1,10-phen with Pd(OAc)₂ only contained one acetate anion on the Pd atom. Given that the binding ability of the acetic anion to Pd is not strong, a palladium intermediate with a vacant coordination site can be generated with relative ease and act as a catalyst for the C–H bond cleavage of simple arenes. On the basis of the design, we used bidentate monoanionic nitrogen ligands in the Pd-catalyzed oxidative homo-coupling reaction of acrylates and aromatic alkenes.

Table 1. Optimization of reaction conditions.

entry	ligand	oxidant	solvent	Т	yield ^b
		(equiv.)		(°C)	(%)
1	/	Ag_2CO_3 (1.0)	dioxane	140	n. p.°
2	L1	Ag ₂ CO ₃ (1.0)	dioxane	140	21
3	L2	Ag ₂ CO ₃ (1.0)	dioxane	140	n. p.
4	L3	Ag ₂ CO ₃ (1.0)	dioxane	140	14
5	L4	Ag ₂ CO ₃ (1.0)	dioxane	140	75 (72 ^d)
6	L5	Ag ₂ CO ₃ (1.0)	dioxane	140	n. p.
7	L6	Ag ₂ CO ₃ (1.0)	dioxane	140	n. p.
8	L7	Ag ₂ CO ₃ (1.0)	dioxane	140	n. p.
9	L4	AgOAc (1.0)	dioxane	140	60
10	L4	Ag ₂ CO ₃ (2.0)	dioxane	140	66
11	L4	Ag ₂ O (1.0)	dioxane	140	n. p.
12	L4	AgTFA (1.0)	dioxane	140	n. p.
13	L4	Cu ₂ CO ₃ (1.0)	dioxane	140	15
14	L4	Ag ₂ CO ₃ (1.0)	dioxane	150	55
15	L4	Ag ₂ CO ₃ (1.0)	dioxane	120	50
16	L4	Ag ₂ CO ₃ (1.0)	DME	140	35
17	L4	Ag ₂ CO ₃ (1.0)	CH ₃ CN	140	n. p.
18	L4	Ag ₂ CO ₃ (1.0)	DMF	140	9
19	L4	Ag ₂ CO ₃ (1.0)	DMA	140	27

^a All the reactions were conducted with 0.40 mmol of alkenes in 2.0 mL of solvent. ^b Yields were determined by ¹H NMR analysis of the crude product using CH_2Br_2 as the internal standard. ^c n. p. = no product. ^d Isolated yields.

To evaluate the feasibility of the homo-coupling reaction, we chose *n*-butyl acrylate as the substrate and 5 mol% of $Pd(OAc)_2$ as catalyst (Table 1). First, we used 1.0 equivalent Ag₂CO₃ as oxidant in 1,4-dioxane at 140 °C to conduct the reaction without the ligand, but no product was formed (entry 1). Adding 2-OH-1,10-phen (L1) led to a 21% product yield (entries 2). By contrast, the use of 1,10-phen (L2) totally inhibited the progress of reaction with no formation of the desired product (entry 3). The 2-OH-1,1'-bipyridine (L3) with a similar structure to that of L1 exhibited low catalytic activity (14% yield, entry 4). Interestingly, the use of 2-OH-4,4'-tBu-1,1'-bipyridine (L4) significantly increased the product yield to 72% (entry 5). We assumed that the presence of a t-butyl group in L4 can increase the solubility of the generated Pd/L4 complex relative to that of Pd/L1 in reaction. Other nitrogen ligands $(L5 \text{ to } L7)^9$ were also tested in reaction but did not attain improved results (entries 6-8). The survey of oxidants showed that silver salt was more

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effective than copper salt containing OAc^{-} or $CO_{3}^{2^{-}}$ (entries 9– 13). We also found that neither higher nor lower reaction temperatures were beneficial for the reaction yield (entries 14 and 15). Finally, various solvents, such as DME, CH₃CN, and DMF were screened (entries 16–19), but no further improvement was achieved.









^aAll the reactions were conducted with 0.40 mmol of alkenes in 2.0 mL of solvent. ^bIsolated yields.

Under the obtained optimized conditions, the scope of several acrylates was investigated (Table 2). Ethyl acrylate, methyl acrylate, and *n*-butyl acrylate provided the expected products in moderate to good yields. However, the reaction of buten-2-one led to 28% yield. We next examined the reaction of aromatic alkenes under the reaction conditions in Table 3. The reaction of styrene provided 51% of the desired product at 140 °C. Substituents at different positions on the benzene ring (para and meta positions) was also obtained in good yields. Styrene with electron-rich t-butyl groups provided the diene product in 73% yield. However, the arenes bearing electron-deficient substituents (Cl and F) attained moderate yields (48 and 52% yields). Moreover, a 1:1 mixture of styrene and n-butyl acrylate were examined under the reaction, three conjugated dienes were formed with the ration of 1:0.35:0.4 (determined by ¹H NMR, Scheme 2).

Table 3. Pd-catalyzed oxidative homo-coupling of aromatic alkenes.^{a,b}



 aAll the reactions were conducted with 0.40 mmol of alkenes in 2.0 mL of solvent. bIsolated yields. c140 °C.



Scheme 2. Experiments with the mixture of styrene and *n*-butyl acrylate



Scheme 3. Experiments with trans-Styrene-2-d

Mechanistically trans-styrene-2-*d* was prepared as described in literature¹⁰ and examined under the same reaction conditions (Scheme 3). Interestingly, only (1E,3E)-1,4-diphenyl-1,3-

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butadiene was obtained with no incorporation of the deuterium atom. Considering our preliminary mechanistic studies and previous literature, we proposed a possible mechanism (Scheme 3). Pd(OAc)₂ coordinated the ligand **L4** to form the active catalyst **A**. The terminal C–H bond of olefin was cleaved by the catalyst **A** to produce the intermediate **B**. Transmetallation of the alkenyl group of **B** into another **B** molecule then provided the intermediates **C** and **A**. Finally, reductive elimination formed the diene product and regenerated the active catalyst **A** in the presence of silver oxidant. Besides, the mechanism of intermediate **B** insertion into the vinyl bond of alkenes, followed by a β -H elimination step to generate the product, cannot be ruled out.

Scheme 3. Proposed catalytic cycle.

In summary, we have developed a bidentate monoanionic nitrogen ligand L4 and used it in the Pd-catalyzed oxidative homo-coupling reaction of acrylates and aromatic alkenes to attain moderate to good yields with high stereoselectivities. This method potentially enlarges the scope of oxidative coupling reactions and provides a new route for the synthesis of functional conjugated dienes.



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Supplementary Material

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Highlights

- A direct method for the preparation of • conjugated dienes is proposed.
- The reaction is proceeded via C-H bond • functionalization of alkenes.
- Acception The use of ligand L4 is essential for the •