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### **Graphical Abstract**





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## Manganese-Catalyzed Sonogashira Coupling of Aryl Iodides

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### ARTICLE INFO

ABSTRACT

Article history: Received Received in revised form Accepted Available online An interesting manganese-catalyzed Sonogashira coupling reaction of aryl iodides has been developed. With PEG-400 as the green solvent and under mild reaction conditions, a variety of diarylacetylenes were obtained in moderate to good yields.

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Transition metal-catalyzed cross-coupling reactions are found to be extremely powerful in constructing new carboncarbon bonds.<sup>1</sup> In all the known name reactions, Sonogashira coupling reaction,<sup>2</sup> which was discovered in the early 1970s has been emerged as one of the most potent transformations.<sup>3</sup> The corresponding acetylenic products are important synthetic units in preparation of natural products and biologically active molecules as well.<sup>4</sup> Concerning the importance of this reaction, tremendous efforts have been put in developing new catalyst systems during the past decades. In addition to the wellestablished palladium-catalyzed systems,<sup>5</sup> many other nonexpensive metal catalysts have also been explored and applied include Cu,<sup>6</sup> Fe,<sup>7</sup> and Ni catalysts<sup>8</sup>. However, to our surprise, manganese as an abundant and toxicologically benign catalyst was not reported in Sonogashira coupling.9 On the other hand, poly(ethylene glycol)s (PEGs) have recently drawn much attention for their applications as green solvents in oxidation, reduction, substitution, and organometallic reactions.<sup>10</sup> As environmental benign and readily available compounds, PEGs can substitute volatile or halogenated organic solvents and even give a better catalytic reactivity than the traditional organic solvents. Under this background, taking the advantages of manganese catalysts and PEG solvent into consideration and the interesting of Sonogashira coupling, we become interested in filling this missed gap. Herein, we wish to report our recent developed manganese-catalyzed Sonogashira coupling reaction with PEG-400 as the solvent. To the best of our knowledge, we here report the first example of manganese-catalyzed Sonogashira reaction.

Initially, this Sonogashira coupling reaction was carried out with iodobenzene and phenyl acetylene as the model substrates using Mn(OAc)<sub>2</sub><sup>2</sup>H<sub>2</sub>O as the catalyst in PEG-400 at 70°C with Et<sub>3</sub>N as the base (Table 1, entry 1). To our delight, 11% yield of the desired diphenylacetylene was obtained. Then, different bases were examined (Table 1, entries 2-5). Notably, DABCO gave the best result among the tested bases (Table 1, entry 3). The yield of the desired product can be further improved by increasing the amount of DABCO to 2.5 equivalents (Table 1, entry 6). While no better results could be obtained by continuing to increase the loading of DABCO to 3 equivalents. Subsequently, some other commonly applied manganese catalysts were tested. Among them,  $Mn(OAc)_2$  afforded the corresponding product in 28% yields (Table 1, entry 7). No product could be observed neither with MnF<sub>3</sub>, MnBr<sub>2</sub>, MnCl<sub>2</sub>, Mn(acac)<sub>2</sub>, nor Mn<sub>2</sub>(CO)<sub>10</sub> as the catalyst in PEG (Table 1, entries 8-12) Finally, the effects of organic solvents including CH<sub>3</sub>CN, DMF, 1,4-dioxane, and C<sub>2</sub>H<sub>5</sub>OH were also tested and no better results can be obtained compared with PEG-400 (Table 1, entries 13-16). Remarkably, both air and moisture are tolerable by this new developed manganese based catalytic system. The same results can be obtained as well when the reaction was performed under nitrogen atmosphere.

Table 1. Scre	ening of rea	ction conditions. <sup>a</sup>
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Entry	Catalyst	Base	Solvent	Yield $(\%)^b$
$1^c$	Mn(OAc) <sub>3</sub>	Et <sub>3</sub> N	PEG-400	11
2 <sup>c</sup>	Mn(OAc) <sub>3</sub>	DBU	PEG-400	1
3 <sup>c</sup>	Mn(OAc) <sub>3</sub>	DABCO	PEG-400	59
4 <sup>c</sup>	Mn(OAc) <sub>3</sub>	NaOAc	PEG-400	22
5 <sup>c</sup>	Mn(OAc) <sub>3</sub>	KOH	PEG-400	1
6	Mn(OAc) <sub>3</sub>	DABCO	PEG-400	66
7	Mn(OAc) <sub>2</sub>	DABCO	PEG-400	28
8	$MnF_3$	DABCO	PEG-400	0
9	$MnBr_2$	DABCO	PEG-400	0
10	MnCl <sub>2</sub>	DABCO	PEG-400	0
11	Mn(acac) <sub>2</sub>	DABCO	PEG-400	0
12	$Mn_2(CO)_{10}$	DABCO	PEG-400	0

uron						
13	Mn(OAc)3	DABCO	CH <sub>3</sub> CN	0		
14	$Mn(OAc)_3$	DABCO	DMF	14		
15	Mn(OAc) <sub>3</sub>	DABCO	1,4-dioxane	8		
16	$Mn(OAc)_3$	DABCO	EtOH	14		
<sup><i>a</i></sup> Reaction conditions: iodobenzene (1.0 mmol), phenylacetylene (1.0 mmol),						
Catal. (10 mol%), base (2.5 equiv.), solvent (2 mL), 24 h. <sup>b</sup> GC yield, with						
dodecane as the internal standard. <sup>c</sup> base (2 equiv.).						

With the optimized reaction conditions in hand,<sup>11</sup> we then performed the generality and limitation testing (Table 2). Firstly, a variety of aryl iodides were examined (Table 2, entries 1-18). Substrates with methyl group substituted at meta-, and paraposition provided the desired products in higher yield while methyl substituted ortho- at the position gave 31% yield which due to the steric hindrance (Table 2, entries 2, 4 vs. 3). Ethyl substitution gave similar yield as the methyl group (Table 2, entry 5). Electron-deficient groups such as ketone, ester, nitro, nitrile, and trifluoromethyl groups furnished the corresponding products in high to excellent yields (Table 2, entries 7-11). Polysubstituted fluoro group also worked well and gave the desired diarylacetylene product in 82% yield (Table 2, entry 12). Halosubstitutions were investigated as well, 78% and 68% yield were obtained with para-fluoro and ortho-chloro groups while the para-bromo group gave 20% yield which might due to the activation of the C-Br bond by the manganese catalyst (Table 2, entries 13-15). We found that heteroaryl group like pyridyl can also be tolerated well; the desired product was isolated in moderate to good yields (Table 2, entries 16 and 17). Furthermore, biphenyl and naphthyl substitutions can also be applied as the substrates and achieve the desired diaryl alkynes in 53% and 58% isolated yields (Table 2, entries 18-19). Encouraged by these results, we went on our study with various aryl alkynes (Table 2, entries 20-22). Good yields can be obtained with both methyl- or chlorosubstituted phenylacetylenes. 1-Ethynylcyclohex-1-ene was tested instead of phenyl acetylene and gave the corresponding (cyclohex-1-en-1ylethynyl)benzene in 35% yield (Table 2, entry 23). However, propargylic substrates failed under our conditions.

Table 2. Sonogashira coupling reaction of aryl iodides and terminal aryl alkynes.<sup>a</sup>





Mn(OAc)<sub>3</sub>.2H<sub>2</sub>O (10 mol%), DABCO (2.5 equiv.), PEG-400 (2 mL), 70 °C, 19-24 h.<sup>b</sup> Isolated yield.

In conclusion, we have developed the first manganesecatalyzed Sonogashira coupling reaction. Compared with the traditional Sonogashira reaction conditions, this strategy utilized a cheap and environmental benign manganese catalyst, and the reaction was performed with PEG-400 as the green solvent at the open air under mild reaction conditions. Catalyzed by the in situ formed manganese nanoparticles, various of substituted diphenylacetylenes were obtained in moderate to good yields under standard conditions.

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- 11. General procedure: In a 25 mL reaction tube, Mn(OAc)<sub>3</sub>.2H<sub>2</sub>O (10 mol%), DABCO (2.5 equiv.) and a stirring bar were added. Then iodobenzene (1 mmol), phenylacetylene (1 mmol) and PEG-400 (2 mL) were injected by syringe. The reaction tube was closed and transferred to a 70 °C oil bath for 19-24 hours. After the reaction completed, the reaction mixture was cooled down to room temperature. Water (2 mL) was added and the reaction mixture was extracted with ethyl acetate and then concentrated and purified by column chromatography.

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- 1. Manganese-Catalyzed Sonogashira Coupling
- 2. With PEG-400 as the green solvent
- 3. Good functional group tolerance and good yields

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