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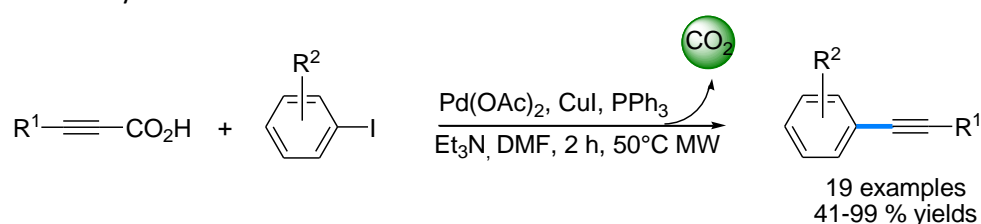
Palladium and Copper Catalyzed Sonogashira Decarboxylative Coupling of Aryl Iodides and Alkynyl Carboxylic Acids

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Abstract

A mild procedure of palladium and copper catalyzed decarboxylative cross-coupling reaction of aryl halides and alkynyl carboxylic acids has been developed. Low molecular weight acids, to introduce small building blocks, were specifically used. This methodology is easy to implement and uses common reactants and catalysts.



1. Introduction

The Sonogashira cross-coupling reaction is the most useful tool for the formation of the C(sp²) – C(sp) bond¹ and it is used as a key step in total synthesis.² This reaction proceeds *via* palladium catalyzed coupling between aryl halides and terminal alkynes in the presence of copper salts as co-catalysts. One limitation of this coupling is the alkyne source, in particular the use of volatile terminal alkynes. The decarboxylative Sonogashira reaction between aryl halides and alkynyl carboxylic acids has emerged as an alternative to the Sonogashira reaction,³ and terminal alkynes are replaced by the corresponding alkynyl carboxylic acids that are easily available and stable for handling and storage. Lee and co. reported the first decarboxylative coupling of alkynyl carboxylic acids and aryl halides in 2008:⁴ unsymmetrically substituted diaryl alkynes were synthesised from propiolic acid *via* the consecutive reactions of the Sonogashira reaction and the decarboxylative coupling (DCC) reaction using palladium salts in the presence of a phosphine ligand and a base to catalyze the two couplings. This methodology has been developed for the preparation of unsymmetrical diaryl alkynes, one pot⁵ or in continuous flow reaction systems,⁶ and also for the preparation of symmetrical diaryl alkynes from aryl bromides⁷ or aryl chlorides.⁸ In 2011, Kim and co. described Sonogashira – homocoupling sequence from propiolic acid.⁹ After the coupling between propiolic acid and aryl iodides under Sonogashira conditions, addition of silver carbonate provided a homocoupling reaction for the formation of corresponding diynes. Lee and co. extended palladium-catalyzed DCC reactions between phenylpropiolic acid or oct-2-ynoic acid with aryl halides in the presence of a phosphine ligand and tetrabutylammonium fluoride as the base at 90°C.¹⁰ Coupling between aryl chlorides and various alkynyl carboxylic acids has been catalyzed by cyclopalladated ferrocenyimine in the presence of phosphine ligand.¹¹ The use of palladium nanoparticles as catalysts combined with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) provided ligand-free decarboxylative coupling.¹² Development of this methodology achieved a palladium-free DCC reaction with copper (I) as the catalyst. Using this approach, Xue and co. reported the coupling between aryl halides and alkynyl carboxylic acids catalyzed by copper iodide in the presence of 1,10-phenanthroline as the ligand, cesium carbonate as the base, and *N,N*-dimethylformamide as solvent at 130 °C.¹³ Another example was reported by Mao and co. The reaction

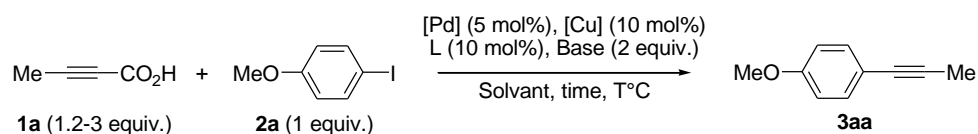
was performed by copper iodide in the presence of triphenylphosphine as the ligand, potassium carbonate as the base, and dimethylsulfoxide or water as the solvent at 100 °C.¹⁴ Muthusubramanian and co. also developed a DCC reaction followed by cyclization in order to form heterocycles.¹⁵ This strategy was used with aryl alkynyl carboxylic acids and substituted 2-iodotrifluoroacetanilide in the presence of copper (I)/L-proline as the catalytic system. Moreover, a decarboxylative coupling reaction was developed with various substrates such as benzyl halides,¹⁶ 1,1,1-trifluoro-2-iodoethane,¹⁷ boronic acids¹⁸ or arene diazoniums¹⁹ instead of classical aryl halides. Stereospecific decarboxylative coupling of benzyl esters of propiolic acids has recently been reported.²⁰ Mainly aryl alkynyl carboxylic acids are used, though some methodologies have been extended to alkyl alkynyl carboxylic acids.^{10,11,13,14b,21}

We focused on using alkynyl carboxylic acids, in particular the alkynyl alkyl acids, in the decarboxylative Sonogashira reaction. But-2-ynoic acid and pent-2-ynoic acid were of particular interest since they allow the introduction of propyne and butyne that are more difficult to handle under the usual Sonogashira cross-coupling conditions. We present here a new methodology for the alkynylation of aryl halides under microwave conditions.

2. Results and discussion

In order to optimize the reaction protocol, we examined a range of palladium and copper catalysts, ligands, bases and solvents, using the coupling of but-2-ynoic acid **1a** with 1-iodo-4-methoxybenzene **2a** as the test reaction (Table 1). It should be noted that the conversion must be complete as the starting material **2a** and product **3aa** cannot be separated by chromatography on silica gel. The reaction was performed initially at room temperature to determine the most appropriate catalysts and reagents (entries 1–22). A range of palladium catalysts (entries 1–6), copper catalysts (entries 8–11) and ligands (12–14) were examined. The use of palladium and copper seemed to be essential to carry out the coupling reaction (entries 1 and 8). The use of palladium (II) acetate, copper iodide and triphenylphosphine as the catalytic system provided the most effective reaction (entries 6 and 7). Various organic and inorganic bases (entries 15–18) and solvents (entries 19–22) were then tested. Triethylamine and *N,N*-dimethylformamide (DMF) were the most efficient base and solvent respectively (entry 7). In order to obtain a total conversion, the reaction was performed under conventional heating or under microwave irradiation (entries 23–27). Conversion was only 60 % at 50 °C for one day (entry 23). Heating at 100 °C under microwave irradiation led to degradation of the product (entry 24).

However, similar conversion was achieved by conventional heating at 50°C for one day and under at 50°C under microwave irradiation for 2 hours (entries 23 and 27). Finally, the amount of acid **2a** was increased to 3 equivalents to obtain total conversion at 50°C MW for 2 hours (entry 29) or at room temperature for two days (entry 30). The time saved obtained under microwave irradiation encouraged us to develop this reaction under these conditions.

Table 1. Optimization of reaction conditions

Entry	[Pd]	[Cu]	Ligand	Alkyne (equiv.)	Base	Solvent	Temp (°C)	Time (h)	Conv. (%) ^a
1	-	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	48 h	0
2	PdCl ₂ (PPh ₃) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	16 h	15
3	PdCl ₂ (MeCN) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	16 h	15
4	Pd(PPh ₃) ₄	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	16 h	20
5	Pd ₂ dba ₃	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	16 h	36
6	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	16 h	50
7	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	rt	48 h	85
8	Pd(OAc) ₂	-	PPh ₃	1.2	Et ₃ N	DMF	rt	48 h	0
9	Pd(OAc) ₂	(CF ₃ SO ₃) ₂ Cu	PPh ₃	1.2	Et ₃ N	DMF	rt	48 h	4
10	Pd(OAc) ₂	CuSO ₄ ·5H ₂ O	PPh ₃	1.2	Et ₃ N	DMF	rt	48 h	10
11	Pd(OAc) ₂	CuBr	PPh ₃	1.2	Et ₃ N	DMF	rt	48 h	37
12	Pd(OAc) ₂	CuI	-	1.2	Et ₃ N	DMF	rt	72 h	0
13	Pd(OAc) ₂	CuI	Phenanthroline	1.2	Et ₃ N	DMF	rt	72 h	0
14	Pd(OAc) ₂	CuI	L-Proline	1.2	Et ₃ N	DMF	rt	72 h	14
15	Pd(OAc) ₂	CuI	PPh ₃	1.2	<i>i</i> -Pr ₂ NH	DMF	rt	48 h	11
16	Pd(OAc) ₂	CuI	PPh ₃	1.2	K ₂ CO ₃	DMF	rt	48 h	29
17	Pd(OAc) ₂	CuI	PPh ₃	1.2	DBU	DMF	rt	48 h	5
18	Pd(OAc) ₂	CuI	PPh ₃	1.2	-	DMF	rt	48 h	0
19	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	<i>i</i> -PrOH	rt	48 h	0
20	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	H ₂ O	rt	48 h	0
21	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	THF	rt	48 h	14
22	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	MeCN	rt	48 h	52
23	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	50°C	24 h	60
24	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	MW 100 °C	0.5 h	- ^b
25	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	MW 50 °C	0.5 h	38
26	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	MW 50 °C	1 h	55
27	Pd(OAc) ₂	CuI	PPh ₃	1.2	Et ₃ N	DMF	MW 50 °C	2 h	65
28	Pd(OAc) ₂	CuI	PPh ₃	2	Et ₃ N	DMF	MW 50 °C	2 h	85
29	Pd(OAc) ₂	CuI	PPh ₃	3	Et ₃ N	DMF	MW 50 °C	2 h	100
30	Pd(OAc) ₂	CuI	PPh ₃	3	Et ₃ N	DMF	rt	48 h	100

^a Determined by ¹H NMR; only decarboxylative coupling products were observed. ^b Degradation of the product was observed.

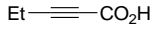

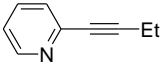
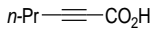
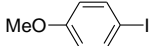
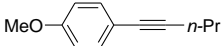
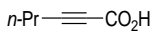

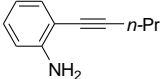
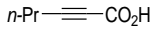
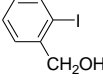
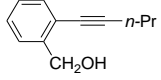
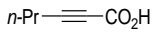
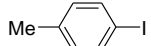
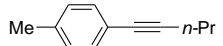
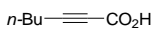
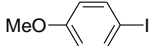
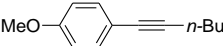
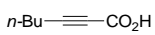
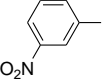
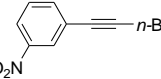
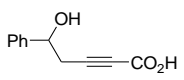
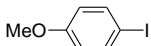
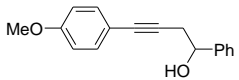
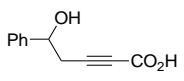
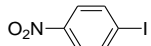
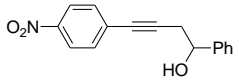
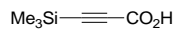
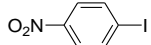
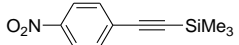
Various available aryl halides and alkyl alkynyl carboxylic acids were used to investigate the scope of the decarboxylative Sonogashira reaction and the results are summarized in Table 2. First the reaction was developed with but-2-ynoic acid **1a** and *ortho*-, *meta*- or *para*-substituted aryl iodides **2** (entries 1, 2, 4 and 5). The corresponding decarboxylative coupling product was isolated in modest to good yields. With pent-2-ynoic acid **1b** (entries 6–11), hex-2-ynoic acid **1c** (entries 13–16), hept-2-ynoic **1d** (entries 17 and 18), or 5-hydroxy-5-phenylpent-2-ynoic acid **1e** (entries 19 and 20), only two equivalents of these acids were required to obtain total conversion. Coupling of these acids with various aryl iodides provided the expected product in good yields. In the case of *o*-iodoaniline **2d** (entries 5, 10, 14), some amidation of the amine group (5 to 10 %) were observed in the crude but this by-product was easily eliminated during the purification. Aryl bromide **2'b** was used in DCC reaction with acids **1a**, **1b**, instead of aryl iodide **2b** (entries 3 and 8): the coupling products **3ab** and **3bb** were obtained in lower yields. No conversion was achieved with aryl chlorides. The use of 2-iodopyridine **2f**

in the coupling with 2-pentynoic acid **1b** yielded 68 % of the product although the conversion was not total (conv = 72 %, entry 13). The coupling of 3-(trimethylsilyl)propionic acid **1f** and aryl iodide **2b** did not lead to total conversion (conv = 57 %) but in this case the coupling product **3fb** could be isolated in 43 % yield (entry 22).

Table 2. Decarboxylative cross-coupling between alkynyl acids **1** and aryl halides **2**

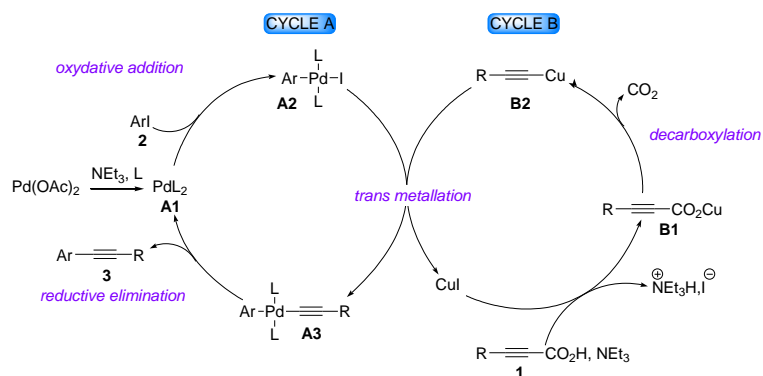
$R^1-C\equiv C-CO_2H$ (1, 2-3 equiv.) + $Ar-X$ (2, 1 equiv.) $\xrightarrow[DMF, 2\text{ h}, 50^\circ C\text{ MW}]{Pd(OAc)_2 (5\text{ mol}\%), CuI (10\text{ mol}\%), PPh_3 (10\text{ mol}\%), Et_3N (2-3\text{ equiv.})}$ $Ar-C\equiv C-R^1$ (3)

Entry	Alkynyl carboxylic acids	Aryl halides	Product	Yield (%) ^a
1	1a	2a	3aa	41
2	1a	2b	3ab	99
3	1a	2'b	3ab	58
4	1a	2c	3ac	86
5	1a	2d	3ad	44 ^b
6	1b	2a	3ba	85
7	1b	2b	3bb	99
8	1b	2'b	3bb	69
9	1b	2c	3bc	83
10	1b	2d	3bd	79
11	1b	2e	3be	66

12	 1b	 2f	 3bf	68
13	 1c	 2a	 3ca	75
14	 1c	 2d	 3cd	71
15	 1c	 2e	 3ce	70
16	 1c	 2g	 3cg	67
17	 1d	 2a	 3da	83
18	 1d	 2c	 3dc	97
19	 1e	 2a	 3ea	68
20	 1e	 2b	 3eb	74
21	 1f	 2b	 3fb	43

^a Isolated yield. ^b Degradation of the product after 24h.

On the basis of our results and of the literature, the mechanism reaction shown in Scheme 1 was proposed. The requirement of palladium and copper salts suggests that each has a distinct function. We therefore proposed a mechanism based on two catalytic cycles: one for the C-C bond coupling involved the palladium salts (Cycle A), the other one for the decarboxylation of alkynyl carboxylic acid catalyzed by copper salts (Cycle B). In the presence of base and copper (I), alkynyl carboxylic acid **1** led to the formation of copper carboxylate **B1** which was subjected to decarboxylation.^{14b,22} The alkynyl copper **B2** formed is a well-known intermediate in Sonogashira reaction.¹ Palladium salts allowed the formation of C-C bond *via* a classic mechanism: first an oxidative addition leading to intermediate **A2** followed by a *trans*-metallation with alkynyl copper **B2** which resulted in complex **A3**. Eventually, a reductive elimination provided the expected compound **3** and regenerated palladium (0) **A1**.



Scheme 1. Plausible mechanism of decarboxylative Sonogashira reaction

3. Conclusion

To conclude, we have developed an efficient method for the Sonogashira decarboxylative cross-coupling reaction between aryl halides and alkynyl carboxylic acids. This reaction is easy to implement and uses common reactants and catalysts. It can be performed either at room temperature or under microwave conditions, the latter requiring shorter reaction times. A range of aryl alkynyl compounds and aryl halides were prepared in modest to good yields.

References and notes

- Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874–922.
- Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489.
- Park, K.; Lee, S. *RCS Adv.* **2013**, *3*, 14165–14182.
- Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett.* **2008**, *10*, 945–948.
- Tartaggia, S.; De Lucchi, O.; Gossen, L. J.; *Eur. J. Org. Chem.* **2012**, 1431–1438.
- Lee, H. J.; Park, K.; Bae, G.; Choe, J.; Song, K. H.; Lee, S.; *Tetrahedron Lett.* **2011**, *52*, 5064–5067. (b) Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2010**, *75*, 6244–6251.
- (a) Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2010**, *75*, 6244–6251; (b) Park, K.; Bae, G.; Park, A.; Kim, Y.; Choe, J.; Song, K. H.; Lee, S. *Tetrahedron Lett.* **2011**, *52*, 576–580.
- Li, X.; Yang, F.; Wu, Y.; *RCS Adv.* **2014**, *4*, 13738–13741.
- Park, J.; Park, E.; Kim, A.; Park, S.-A.; Lee, Y.; Chi, K.-W.; Jung, Y. H.; Kim, I. S. *J. Org. Chem.* **2011**, *76*, 2214–2219.
- Moon, J.; Jang, M.; Lee, S. *J. Org. Chem.* **2009**, *74*, 1403–1406.
- Li, X.; Yang, F.; Wu, Y. *J. Org. Chem.* **2013**, *78*, 4543–4550.
- Pyo, A.; Kim, J. D.; Choi, H. C.; Lee, S. *J. Organomet. Chem.* **2013**, *724*, 271–274.
- Zhao, D.; Gao, C.; Su, X.; He, Y.; You, J.; Xue, Y. *Chem. Commun.* **2010**, *46*, 9049–9051.
- (a) Qu, X.; Li, T.; Sun, P.; Zhu, Y.; Yang, H.; Mao, J. *Org. Bio. Mol. Chem.* **2011**, *9*, 6938–6942; (b) Li, T.; Sun, P.; Yang, H.; Zhu, Y.; Yan, H.; Lu, L.; Mao, J. *Tetrahedron* **2012**, *68*, 6413–6419.
- Ponpandian, T.; Muthusubramanian, S. *Tetrahedron Lett.* **2012**, *53*, 4248–4252.
- Zhang, W.-W.; Zhang, X.-G.; Li, J.-H. *J. Org. Chem.* **2010**, *75*, 5259–5264.
- Hwang, J.; Park, K.; Choe, J.; Min, H.; Song, K. H.; Lee, S. *J. Org. Chem.* **2014**, *79*, 3267–3271.
- (a) Feng, C.; Loh, T.-P. *Chem. Commun.* **2010**, *46*, 4779–4781; (b) Shi, L.; Jia, W.; Li, X.; Jiao, N. *Tetrahedron Lett.* **2013**, *54*, 1951–1955.
- Jadhav, V. G.; Sarode, S. A.; Nagarkar, J. M.; *Tetrahedron Lett.* **2015**, *56*, 1771–1774.
- a) Mendis, S. N.; Tunge, J. A. *Org. Lett.* **2015**, *17*, 5164–5167; b) Tomita, R.; Koike, T.; Akita, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 12923–12927.
- Caporale, A.; Tartaggia, S.; Castellin, A.; De Lucchi, O. *Beilstein J. Org. Chem.* **2014**, *10*, 384–393.
- Jia, W.; Jiao, N. *Org. Lett.* **2010**, *12*, 2000–2003.