Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2019, **29**, 378–379

Mendeleev Communications

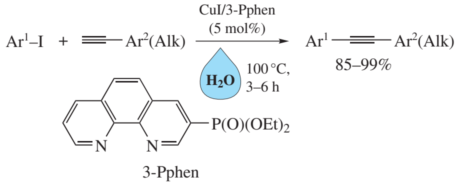
Enhanced catalytic activity of CuI/diethoxyphosphoryl-1,10-phenanthrolines in ‘on water’ Cu-catalyzed Sonogashira reaction

Alexander Yu. Mitrofanov* and Irina P. Beletskaya*

Department of Chemistry, M. V. Lomonosov Moscow State University, 119991 Moscow, Russian Federation.
Fax: +7 495 939 1139; e-mail: mitrofanov@org.chem.msu.ru, beletska@org.chem.msu.ru

DOI: 10.1016/j.mencom.2019.07.005

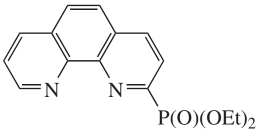
The use of CuI/diethoxyphosphoryl-1,10-phenanthrolines and ‘on water’ conditions in the Cu-catalyzed Sonogashira reaction of aryl iodides with terminal alkynes significantly increases the reaction rate as compared to that in organic solvents.



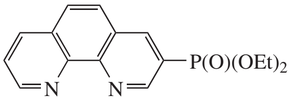
Replacement of palladium by cheaper and more available copper in various cross-coupling reactions is one of the main trends in modern catalysis. At present, many reactions of C–C or C–heteroatom bonds formation, catalyzed by palladium complexes, can be carried out in the presence of salts, complexes or copper nanoparticles.[1–7] For example, one of the most important reactions of C–C bond formation, the cross-coupling of aryl halides with terminal alkynes (the Sonogashira reaction), was usually performed simultaneously in the presence of palladium and copper compounds.[8,9] However, in recent decades, a fairly large number of examples of such reaction comprise only copper catalysis.[1–7,10–11] As a rule, in those cases various toxic organic solvents were employed, whereas the use of water, an affordable and environmentally friendly solvent, was rare[12–15] despite its active usage in palladium-catalyzed reactions.[16–18]

Also, considerable interest in using water as a reaction medium is caused by the fact that water can significantly accelerate organic reactions carried out under ‘on water’ conditions. This phenomenon was systematically studied by the Sharpless group on the example of the Diels–Alder reactions, the Claisen rearrangements, and some others.[19] Later the acceleration was observed in the reactions catalyzed by transition metals, which opened the way for the development of new efficient transition metal-based catalytic systems.[20,21]

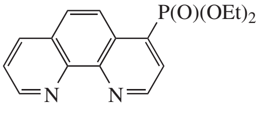
Recently, in the context of our work on organic-inorganic hybrid materials[22] for catalysis we obtained a series of mono- and diphosphorylated 1,10-phenanthrolines and their copper complexes.[23,24] For the purpose to immobilize copper complexes with 2-, 3- and 4-diethoxyphosphoryl-1,10-phenanthrolines (2-Pphen, 3-Pphen and 4-Pphen, respectively) on TiO_2 and to prepare heterogeneous catalysts, we evaluated their activity in the Sonogashira reaction. Their catalytic activity in the coupling of 4-iodoanisole with phenylacetylene in toluene was relatively low and comparable to that of the copper complex with unsubstituted phen.[25] Here we investigated activity of Pphens in the Cu-catalyzed Sonogashira reaction carried out in water and showed that the use of water as a solvent significantly accelerates the reaction of various aryl iodides with terminal alkynes.



2-Pphen



3-Pphen



4-Pphen

We chose the coupling of phenylacetylene **1a** with 4-iodoanisole **2a** as a model reaction to determine the optimal reaction conditions. First, we tested the catalytic system $CuSO_4 \cdot 5H_2O$/3-Pphen (10 mol%) as a precatalyst because of its solubility in water with K_2CO_3 as a base at 100 °C for 3 h. The target product **3a** was obtained in 44% yield (Scheme 1, Table 1, entry 1). Addition of PEG-400 (20 mol%) allowed us to increase the yield up to

Table 1 Optimization of conditions for the model reaction between phenylacetylene **1a** and 4-iodoanisole **2a**.[a]

Entry	Catalyst	Ligand	Solvent	Base	*t*/h	NMR yield of **3a** (%)
1[b]	$CuSO_4 \cdot 5H_2O$	3-Pphen	H_2O	K_2CO_3	3	44
2	$CuSO_4 \cdot 5H_2O$	3-Pphen	H_2O	K_2CO_3	3	68
3	$CuSO_4 \cdot 5H_2O$	3-Pphen	H_2O	K_3PO_4	3	35
4	$CuSO_4 \cdot 5H_2O$	3-Pphen	H_2O	KOAc	3	6
5	$CuSO_4 \cdot 5H_2O$	3-Pphen	H_2O	KOH	3	18
6	CuI	3-Pphen	H_2O	K_2CO_3	1	99
7	CuI	3-Pphen	toluene	K_2CO_3	48	60
8	CuI	3-Pphen	–	K_2CO_3	48	12
9	CuI	3-Pphen	1,4-dioxane	K_2CO_3	24	66
10	CuI	3-Pphen	EtOH	K_2CO_3	24	45
11	CuI	phen	H_2O	K_2CO_3	3	traces
12	CuI	2-Pphen	H_2O	K_2CO_3	3	34
13	CuI	4-Pphen	H_2O	K_2CO_3	3	80
14[c]	CuI	3-Pphen	H_2O	K_2CO_3	3	96

[a] Reaction conditions: copper salt (0.025 mmol, 10 mol%), ligand (0.025 mmol, 10 mol%), PhC≡CH (33 μl, 0.3 mmol), $4\text{-}MeOC_6H_4I$ (58.5 mg, 0.25 mmol), base (0.5 mmol), PEG-400 (20 mg, 20 mol%) in solvent (1 ml) at 100 °C. [b] In the absence of PEG-400. [c] With 5 mol% CuI/Pphen.

$$\mathrm{R{-}C{\equiv}CH} \quad + \quad \mathrm{ArI} \xrightarrow{\text{i}} \mathrm{R{-}C{\equiv}C{-}Ar}$$

1a R = Ph
1b R = 4-MeC_6H_4
1c R = 4-ClC_6H_4
1d R = 4-NCC_6H_4
1e R = *n*-C_6H_{13}
1f R = Cy

2a Ar = 4-$MeOC_6H_4$
2b Ar = 4-MeC_6H_4
2c Ar = 3,5-$Me_2C_6H_3$
2d Ar = 4-$F_3CC_6H_4$
2e Ar = 4-NCC_6H_4
2f Ar = 4-$O_2NC_6H_4$
2g Ar = 4-$MeO_2CC_6H_4$
2h Ar = 2-$O_2NC_6H_4$

3a–m

3	R	Ar	Yield of **3** (%)
a	Ph	4-$MeOC_6H_4$	94
b	Ph	4-MeC_6H_4	90
c	Ph	3,5-$Me_2C_6H_3$	89
d	Ph	4-$F_3CC_6H_4$	94
e	Ph	4-NCC_6H_4	92
f	Ph	4-$O_2NC_6H_4$	97
g	Ph	4-$MeO_2CC_6H_4$	93
h	Ph	2-$O_2NC_6H_4$	91
i	4-MeC_6H_4	4-$MeOC_6H_4$	99
j	4-ClC_6H_4	4-$MeOC_6H_4$	99
k	4-NCC_6H_4	4-$MeOC_6H_4$	96
l	*n*-C_6H_{13}	4-$MeOC_6H_4$	85
m	Cy	4-$MeOC_6H_4$	87

Scheme 1 *Reagents and conditions*: i, CuI (2.4 mg, 5 mol%), 3-Pphen (3.9 mg, 5 mol%), ArI (0.25 mmol), alkyne (0.3 mmol), PEG-400 (20 mg, 20 mol%), H_2O (1 ml), 100 °C, 3 h (or 6 h for **2b**,**c**). Yields after chromatographic isolation.

68% (entry 2). Among several bases in the reaction performed using $CuSO_4{\cdot}5H_2O$/3-Pphen (10 mol%) in the presence of PEG-400 (20 mol%) (entries 3–5), K_2CO_3 was found to be most effective, whereas CuI/3-Pphen system showed higher catalytic activity, and in this case the reaction was completed in 1 h (entry 6). Meantime, only a trace of product **3a** was obtained with unsubstituted phenanthroline (entry 11) in contrast to the previously published results.[14] Isomeric diethoxyphosphoryl-1,10-phenanthrolines, 2-Pphen and 4-Pphen, were less effective ligands than 3-Pphen (entries 12, 13). It is important to note that CuI/3-Pphen has significantly improved catalytic activity under ‘on water’ conditions in comparison with the reaction in organic solvents (entries 7, 9, 10) or under neat conditions (entry 8). The use of smaller amounts of CuI and 3-Pphen (5 mol%) required prolonged time, but also provided a high yield of the product (entry 14). Thus, the optimized reaction conditions involve CuI (5 mol%), 3-Pphen (5 mol%), and K_2CO_3 (2 equiv.) in water at 100 °C.

To examine the scope and limitations for the the found catalytic system, a variety of aryl iodides and terminal alkynes were tested under the optimized conditions[†] (see Scheme 1). Electron-rich, electron-neutral and electron-deficient aryl iodides **2a–g** reacted with phenylacetylene **1a** to afford the corresponding diarylacetylenes **3a–g** in excellent yields. *ortho*-Substituted aryl iodide, 1-iodo-2-nitrobenzene **2h**, reacted with **1a** to give the desired product **3h** in 91% yield. Excellent yields of products **3i–m** were achieved for other alkynes **1b–f** and 4-iodoanisole **2a**. Unfortunately, aryl bromides were essentially unreactive (9% of product was obtained from 4-bromoanisole).

This work was supported by the Russian Foundation for Basic Research (grant no. 16-33-60207).

References

1 I. P. Beletskaya and A. V. Cheprakov, *Organometallics*, 2012, **31**, 7753.
2 I. P. Beletskaya and A. V. Cheprakov, *Coord. Chem. Rev.*, 2004, **248**, 2337.
3 *Copper-Mediated Cross-Coupling Reactions*, eds. G. Evano and N. Blanchard, John Wiley & Sons, Hoboken, 2014.
4 C. Maaliki, E. Thiery and J. Thibonnet, *Eur. J. Org. Chem.*, 2017, 209.
5 F. Monnier and M. Taillefer, *Angew. Chem., Int. Ed.*, 2009, **48**, 6954.
6 L. Penn and D. Gelman, in *PATAI'S Chemistry of Functional Groups*, John Wiley & Sons, Ltd., 2011.
7 H. Rao and H. Fu, *Synlett*, 2011, 745.
8 K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, 1975, **16**, 4467.
9 A. V. Rassolov, G. N. Baeva, I. S. Mashkovsky and A. Yu. Stakheev, *Mendeleev Commun.*, 2018, **28**, 538.
10 M. B. Gawande, A. Goswami, F.-X. Felpin, T. Asefa, X. Huang, R. Silva, X. Zou, R. Zboril and R. S. Varma, *Chem. Rev.*, 2016, **116**, 3722.
11 A. Yu. Mitrofanov, A. V. Murashkina, I. Martín-García, F. Alonso and I. P. Beletskaya, *Catal. Sci. Technol.*, 2017, **7**, 4401.
12 G. Chen, X. Zhu, J. Cai and Y. Wan, *Synth. Commun.*, 2007, **37**, 1355.
13 J. T. Guan, G.-A. Yu, L. Chen, T. Q. Weng, J. J. Yuan and S. H. Liu, *Appl. Organomet. Chem.*, 2009, **23**, 75.
14 Y. Liu, V. Blanchard, G. Danoun, Z. Zhang, A. Tlili, W. Zhang, F. Monnier, A. Van Der Lee, J. Mao and M. Taillefer, *ChemistrySelect*, 2017, **2**, 11599.
15 D. Yang, B. Li, H. Yang, H. Fu and L. Hu, *Synlett*, 2011, **2011**, 702.
16 I. P. Beletskaya and A. V. Cheprakov, in *Organic Synthesis in Water*, ed. P. A. Grieco, Springer, Dordrecht, 1998, pp. 141–222.
17 D. Sinou, in *Modern Solvents in Organic Synthesis*, ed. P. Knochel, Springer, Berlin, 1999, pp. 41–59.
18 T. Kitanosono, K. Masuda, P. Xu and S. Kobayashi, *Chem. Rev.*, 2018, **118**, 679.
19 S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2005, **44**, 3275.
20 A. Chanda and V. V. Fokin, *Chem. Rev.*, 2009, **109**, 725.
21 R. N. Butler and A. G. Coyne, *Org. Biomol. Chem.*, 2016, **14**, 9945.
22 A. Mitrofanov, S. Brandès, F. Herbst, S. Rigolet, A. Bessmertnykh-Lemeune and I. Beletskaya, *J. Mater. Chem. A*, 2017, **5**, 12216.
23 A. Mitrofanov, A. Bessmertnykh-Lemeune, C. Stern, R. Guilard, N. Gulyukina and I. Beletskaya, *Synthesis*, 2012, **44**, 3805.
24 A. Mitrofanov, M. Manowong, Y. Rousselin, S. Brandès, R. Guilard, A. Bessmertnykh-Lemeune, P. Chen, K. M. Kadish, N. Goulioukina and I. Beletskaya, *Eur. J. Inorg. Chem.*, 2014, 3370.
25 A. Y. Mitrofanov, A. G. Bessmertnykh-Lemeune and I. P. Beletskaya, *Inorg. Chim. Acta*, 2015, **431**, 297.

Received: 9th January 2019; Com. 19/5798

[†] All reactions were carried out under argon atmosphere. All halides and alkynes were purchased from Aldrich and Alfa. Copper(I) iodide (98%) was purchased from Alfa. NMR spectra were measured in $CDCl_3$ on a Bruker Avance-400 spectrometer with TMS as an internal standard. Diethoxyphosphoryl-1,10-phenanthrolines were obtained according to the published method.[23]

General procedure of cross-coupling of aryliodides with alkynes. An 8 ml glass vial was charged with the alkyne (0.3 mmol), aryl iodide (0.25 mmol), K_2CO_3 (79 mg, 0.5 mmol), CuI (2.4 mg, 5 mol%), 3-Pphen (3.9 mg, 5 mol%), PEG-400 (20 mg, 20 mol%) and water (1 ml) under argon. The vial was closed with a Teflon cap and the heterogeneous reaction mixture was stirred at 100 °C for 3 or 6 h (see Scheme 1). After cooling, the mixture was extracted with EtOAc, the extract was dried over $MgSO_4$. After evaporation, the residue was purified by flash chromatography on silica gel with light petroleum as the eluent. ^1H and ^{13}C NMR spectroscopic data of products were consistent with those described previously.[13]