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Catalytic Coupling of Terminal Acetylenes with Iodoarenes and Diaryliodonium Salts in Water

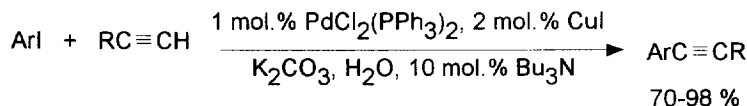
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Abstract: The catalytic coupling of terminal acetylenes with iodoarenes and diaryliodonium salts are shown to occur in aqueous K_2CO_3 in the presence of 10 mol.% Bu_3N under very mild conditions using $PdCl_2(PPh_3)_2$ and CuI as catalyst precursor to give substituted tolans in high yields.

The palladium-catalyzed coupling of terminal acetylenes with organic halides is a widely used reaction in organic synthesis. The most effectively this reaction proceeds in the presence of catalytic amounts of palladium complex and cuprous iodide.¹ Usually the reaction is carried out in anhydrous organic solvent.² A few examples of this reaction in aqueous medium have been reported.^{3,4} The palladium complexes containing water soluble phosphine ligands were used in this cases.³

We now report that the reaction of terminal acetylenes with iodoarenes catalyzed by $PdCl_2(PPh_3)_2$ - CuI can be easily carried out in neat water in the presence of small amount Bu_3N and K_2CO_3 as a base (see Table 1).



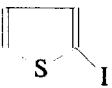
This result is in good agreement with recent experiments showing water to be highly effective medium for palladium-catalyzed reactions, for example: carbonylation of iodoarenes,⁵ cross-coupling of aryl halides with boronic acids,⁶ arylation of olefins.⁷

The reaction of terminal acetylenes with iodoarenes, bearing various functionalities at ambient temperature in aqueous K_2CO_3 was complete in 1-6 h giving excellent yields of substituted tolans (Table 1).

The most reactive of alkynes studied has proved to be phenyl acetylene. Both water soluble and insoluble iodoarenes enter the reaction. There is no noticeable difference in reaction time between iodoarenes containing electron-withdrawing and electron-donating groups. In contrast, when the reaction catalyzed by $PdCl_2(PPh_3)_2$ - CuI was performed in organic solvent in the presence of Et_3N (1,5-2 equiv.) the reaction time depends upon substituent of iodoarene.⁸

The investigation of the reaction of *p*-iodonitrobenzene with phenyl acetylene in aqueous organic solvents (Table 2) has shown that the DMF-H₂O (9:1) is the best as a solvent and K₂CO₃ as a base. The reaction time is increased when the reaction is carried out in 50% aqueous DMF because of poor solubility of reagents. However, the most effectively the reaction proceeds in water without organic solvent in presence of K₂CO₃ and 10 mol.% Bu₃N.

Table 1. Reaction of ArI with RC≡CH, PdCl₂(PPh₃)₂ (1 mol%), CuI (2 mol%), K₂CO₃, H₂O, 10 mol.% Bu₃N, 20°C, Argon.⁹

Entry	ArI	RC≡CH	t, h	Yield ^a of RC≡CAr, %
1	<i>p</i> -O ₂ NC ₆ H ₄ I	PhC≡CH	1	98
2	<i>p</i> -O ₂ NC ₆ H ₄ I	<i>n</i> -C ₅ H ₁₁ C≡CH	4	95
3	<i>p</i> -O ₂ NC ₆ H ₄ I	<i>p</i> -(<i>n</i> -C ₉ H ₁₉)C ₆ H ₄ C≡CH	6	88
4	<i>m</i> -NO ₂ NC ₆ H ₄ I	PhC≡CH	1	97
5	<i>o</i> -O ₂ NC ₆ H ₄ I	PhC≡CH	1,5	95
6	<i>p</i> -NCC ₆ H ₄ I	PhC≡CH	1,5	96
7	<i>p</i> -NCC ₆ H ₄ I	<i>p</i> -(<i>n</i> -C ₉ H ₁₉)C ₆ H ₄ C≡CH	6	70
8	<i>p</i> -HOCC ₆ H ₄ I	PhC≡CH	1	89
9	<i>p</i> -AcC ₆ H ₄ I	PhC≡CH	1,5	96
10	<i>p</i> -ClC ₆ H ₄ I	PhC≡CH	0,5	95
11	C ₆ H ₅ I	PhC≡CH	2	92
12	<i>p</i> -MeOC ₆ H ₄ I	PhC≡CH	2	98
13		PhC≡CH	40min	80
14b	<i>p</i> -IC ₆ H ₄ I	<i>n</i> -C ₅ H ₁₁ C≡CH	1	85
15c	<i>o</i> -O ₂ NC ₆ H ₄ Br	PhC≡CH	1,5	90
16d	<i>p</i> -O ₂ NC ₆ H ₄ I	PhC≡CH	4	93

a) Isolated yields based on ArI. Products were characterized by UV, ¹H, ¹³C NMR spectroscopy and elemental analysis.

b) Both iodine atoms were displaced.

c) 60°C.

d) without CuI, 60°C.

In contrast the usual palladium-catalyzed cross-coupling reaction, in this case the organometallic compound **1** appears to be generated in situ in catalytic quantities from acetylene under action of the base and CuI (Scheme 1, ligands on the scheme are omitted). Then high reactive **1** enters reaction of cross-coupling with iodoarene. The process includes a step of oxidative addition (a), followed by an alkylation of adduct **2** (b) to give aryl alkynyl derivative of palladium **3**, which easily regenerates the Pd(0) through the reductive elimination

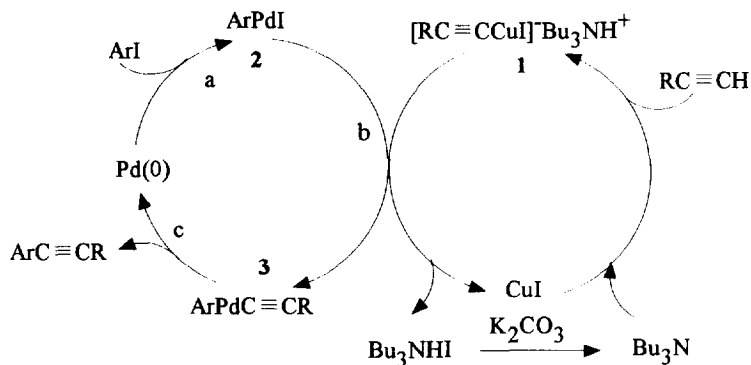
(c) of substitution product. The role of cuprous iodide is important to facilitate the reaction. For example, in the absence of CuI the reaction of *p*-iodonitrobenzene with phenyl acetylene proceeds at 60°C (Table 1, entry 16).

Table 2. Influence of solvent and base on coupling of *p*-O₂NC₆H₄I (1 mmol) with phenyl acetylene (1,3 mmol) (K₂CO₃, H₂O, 1 mol.% PdCl₂(PPh₃)₂, 2 mol.% CuI, 10 mol.% Bu₃N), 20°C, Argon

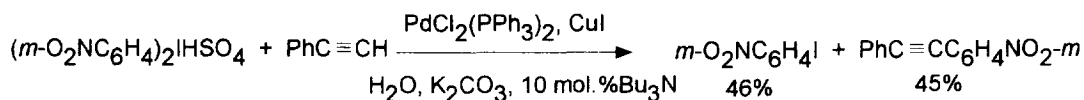
Entry	Solvent	Base	t, h	Yield ^a , %
1	DMF:H ₂ O, 9:1	K ₂ CO ₃	1	98
2	DMF:H ₂ O, 9:1	Na ₂ CO ₃	2	90
3	DMF:H ₂ O, 1:1	K ₂ CO ₃	2	65
4	H ₂ O	K ₂ CO ₃ + 10mol.% Bu ₃ N	0,75	98
5	MeCN:H ₂ O, 9:1	K ₂ CO ₃	2	20
6	dioxane:H ₂ O, 9:1	K ₂ CO ₃	2	trace

a) Isolated yield

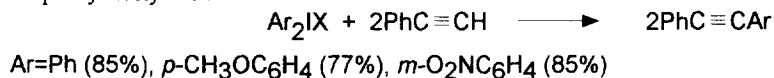
Scheme 1.



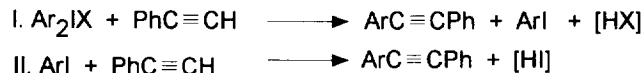
More reactive diaryliodonium salts can easily react with terminal acetylenes under these conditions. The reaction of bis(*m*-nitrophenyl)iodonium sulfate was complete at ambient temperature in 10 min to give *m*-nitrotolan and *m*-iodonitrobenzene:



Both aryl groups of diaryliodonium salts are consumed if the reaction proceeds in the presence of 2 mol. equiv. of phenyl acetylene :



The reaction proceeds in two steps:



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- In a typical experiment the mixture of 0,249 g (1 mmol) *p*-iodonitrobenzene, 0,133 g (1,3 mmol) phenyl acetylene, 0,007 g (0,01 mmol) PdCl₂(PPh₃)₂, 0,0038 g (0,02 mmol) CuI, 0,0185 gl (0,1 mmol) Bu₃N and 2 ml (2 mmol) 1M aq. K₂CO₃ was stirred for 1 h at ambient temperature under argon. The product was extracted with ether and recrystallized from MeOH to give pure sample of 4-nitrotolan.

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