Organic Process Research & Development **1997**, *1,* 325–327

Technical Notes

Highly Efficient Palladium-Catalyzed Coupling of Acetylene Gas with Aryl Iodides in Aqueous Medium

Chao-Jun Li,* Dong-Li Chen, and Christopher W. Costello

Department of Chemistry, Tulane University, New Orleans, Louisiana 70118

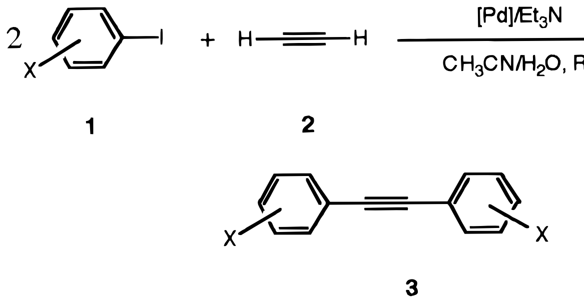
Abstract:

A mixture of acetonitrile and water was found to be a highly efficient medium for the palladium-catalyzed bis-coupling of acetylene gas with aryl iodides. Both water-soluble and -insoluble catalysts are effective. All couplings proceed in excellent yields at room temperature.

The coupling of aryl and vinyl halides with acetylene and acetylene derivatives is among the most important reactions in organic syntheses. These reactions include the coupling of aryl halides with copper(I) acetylides, the Castro reaction,[1] as well as the palladium-catalyzed reactions of aryl halides with (trialkylstannyl)acetylene, the Stille reaction,[2] with (trimethylsilyl)acetylene,[3] with alkynylzinc,[4] and with terminal alkynes.[5]

Recently, Casalnuovo,[6] Genet,[7] and Beletskaya[8] reported that the coupling of terminal acetylenes with aryl halides could proceed in aqueous media. However, the use of acetylene gas for aqueous coupling has not been reported and it usually requires the use of an amine as the solvent. On the other hand, Kundu[9] very recently reported that the bis-coupling of acetylene gas with aryl halides in dimethylformamide at 60 °C was highly moisture-sensitive. The presence of 5% of water completely derailed the process of the reaction, in which no product was obtained. Alternative approaches toward the coupling of an acetylene unit with two aryl halides use triethylamine as solvent for the coupling reaction, or use the Stille coupling with bis(tributylstannyl)acetylene in dioxin.[10] Synthetically, the use of acetylene gas is the most economical way of delivering an acetylene unit to organic substrates.

During our investigation of organic reactions in aqueous media,[11] we became interested in the results reported by Kundu[9] and were intrigued by the observed moisture-sensitivity of the acetylene reaction. We found that, instead of water impeding the reaction, the coupling of acetylene gas with aryl halides is highly efficient at room temperature in a mixture of acetonitrile and water (eq 1), contrary to the earlier report. The conditions are generally milder and the yields are better than previously reported results in organic solvents. A variety of aromatic halides are coupled to give the corresponding bis(aryl)acetylenes (Table 1). Both a water-soluble palladium catalyst [catalyst B, generated in situ from palladium acetate and 3,3′,3″-phosphinidynetris(benzenesulfonic acid) trisodium salt] and water-insoluble catalyst (catalyst A, generated in situ from palladium acetate and triphenylphosphine) can be used for the reaction. In the former case, the reaction had virtually the same result when water was the only solvent (compare entries 2 and 4). Even though the reaction was carried out in the presence of cuprous iodide as a cocatalyst, the reaction proceeded equally well without this cocatalyst (catalyst C, entry 3).



(1)

Both aromatic and heterocyclic iodides (entry 9) are highly effective for this reaction, and comparable yields are obtained in both cases, also differing from the previous report, which used dimethylformamide (where a much lower reactivity was observed for the latter compounds). On the other hand, a variety of aryl bromides have been tested and are not reactive enough under the present conditions (e.g., entry 5). Such a reactivity difference could impart selectivities. Substituents such as a nitro group (entries 6 and 7) and an ester group (entry 10) can tolerate the reaction; compounds bearing an active proton, such as phenol (entry

---

(1) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313.

(2) For reviews, see: Stille, J. F. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

(3) Brandsma, L.; Vanden Heuvel, H. G. M.; Verkruijsse, H. D. *Synth. Commun.* **1990**, *20*, 1889.

(4) (a) Neenan, T. X.; Whitesides, G. M. *J. Org. Chem.* **1988**, *53*, 2489. (b) King, A. O.; Negishi, E.; Villani, F. J., Jr., Silveira, A. *Ibid.* **1975**, *40*, 358.

(5) (a) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253. (b) Dieck, H. A.; Heck, F. R. *Ibid.* **1975**, *93*, 259. (c) Sonogashira, K.; Tohda, Y.; Hagira, N. *Tetrahedron Lett.* **1975**, 4467. (d) For a review, see: Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991.

(6) Calsalnuovo, A. L.; Calabreze, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 4324.

(7) Genet, J. P.; Blart, E.; Savignac, M. *Synlett* **1992**, 715.

(8) Davydov, D. V.; Beletskaya, I. P. *Russ. Chem. Bull.* **1995**, *44*, 965.

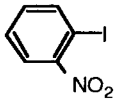
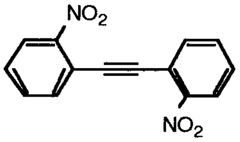
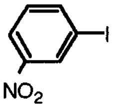
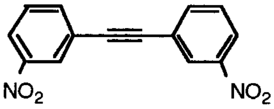
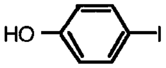
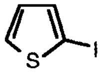
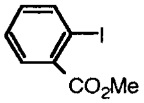
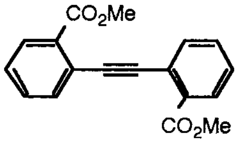
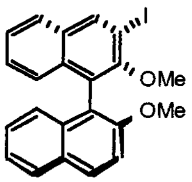
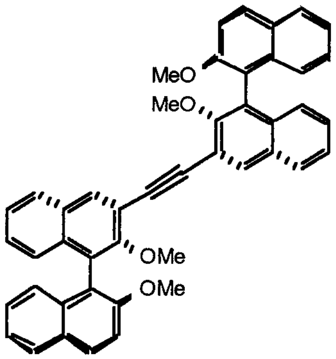
(9) Pal, M.; Kundu, N. G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 449.

(10) Cummins, C. H. *Tetrahedron Lett.* **1994**, *35*, 857.

(11) For general reviews, see: (a) Herman, W. A.; Kohlpaintner, C. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1524. (b) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023. (c) Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741.

S1083-6160(97)00208-9 CCC: $14.00

Table 1. Coupling of acetylene gas with aryl halides[a]

entry	substrate	catalyst	product	yield (%)
1	PhI	A	Ph—≡—Ph	90
2	PhI	B	Ph—≡—Ph	90
3	PhI	C	Ph—≡—Ph	89
4	PhI	B	Ph—≡—Ph	91[a]
5	PhBr	A	Ph—≡—Ph	0
6		A		90
7		A		91
8		A		79[b]
9		A		85
10		A		75
11		A		93

[a] Catalyst A: $Pd(OAc)_2/PPh_3/CuI$. Catalyst B: $Pd(OAc)_2/TPPTS/CuI$. Catalyst C: $Pd(OAc)_2/PPh_3$. Yields are referred to isolated ones after column chromatography. Notes on yield: (a) in water alone; (b) on standing, fast decompsoition of the compound was observed after purification.

8), can be used directly without (the usual) protection. Substrates without substituents and with electron-donating and electron-withdrawing groups gave comparable yields of the coupled products. Such a result is also different from the reaction in dimethylformamide, where the effect of substituents on the reaction is much more dramatic. The changing of the position of substitution (entry 6 vs entry 7) did not seem to have an effect on the outcome of the reaction. A binaphthol derivative was coupled to give bis(binaphthol) similarly (entry 11). The present study provides a simple and useful method for the coupling of aryl halides with acetylene gas.

In order to demonstrate the potential of the present method for practical applications, the coupling of iodobenzene with acetylene gas was carried out at a 51 g scale under the same reaction conditions. In this case, only 0.05 mol % of palladium and cuprous iodide catalysts was used, which is 100 times less than the small-scale reaction. The reaction was stopped after 10 h at room temperature. Gas chromatography analysis indicated 72% of the desired product. After workup, the diphenylacetylene was isolated in 59% yield through vacuum distillation. In principle, the yield of the product can be further increased by slightly increasing the amount of the catalysts being used.

General Experimental Procedure. A mixture of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), triphenylphosphine (13.1 mg, 0.05 mmol), and cuprous iodide (9.5 mg, 0.05 mmol) in acetonitrile/water (3:1) was stirred at room temperature for 20 min under nitrogen. To the mixture was added a solution of iodobenzene (204 mg, 1 mmol) and triethylamine (255 mg, 3 mmol) in acetonitrile. The nitrogen inlet was switched to an acetylene balloon. After a brief purging of the flask with acetylene, the reaction mixture was sealed and stirred overnight with the balloon on. Then, the reaction mixture was extracted with ether (3 × 20 mL), washed with water and brine, dried over magnesium sulfate, and concentrated. Column chromatography on silica gel (eluent: hexane/EtOAc = 20:1) gave diphenylacetylene (80 mg, yield 90%).

Received for review November 14, 1996.⊗

OP970208D

⊗ Abstract published in *Advance ACS Abstracts,* June 15, 1997.