Microwave Assisted Copper-Free Sonogashira Coupling with a Polystyrene Bound Phosphine Ligand

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Summary

Sonogashira coupling reactions of monosubstituted alkynes and aryl halides were performed with palladium acetate as catalyst and resin bound PS-Triphenylphosphine as ligand. No added copper salt was needed. Diethylamine or pyrrolidine was used as base and THF as solvent. The reactions were heated by microwaves to 130°C or 150°C for 15 minutes using Initiator™ Sixty. The observed conversions, measured by LC-MS, were typically 81-97 % for aryl bromides and aryl iodides and lower, 15-75 %, for aryl chlorides. Only traces of triphenylphosphine oxide could be detected after the reaction was completed.



Background

The Sonogashira reaction¹ consists in its classical form of the palladium catalyzed coupling of monosubstituted copper alkynes and aryl halides, in the presence of a yield phosphine-ligand, to disubstituted alkynes. The reaction is one of the most important routes to alkenyl- and arylsubstituted alkynes. An important recent improvement reaction of the is the variants.² development copper-free of Moreover, the use of a phosphine-ligand in the protocol, results in contamination of the reaction mixture with the corresponding phosphine oxide, which generally is difficult to remove. By applying an immobilized ligand,³ the removing of phosphine oxide is strongly facilitated.

Experimental Procedure

To a 0.5-2 mL microwave reaction vial containing 0.4 mmol aryl halide, 0.48 mmol (1.2 equiv.) monosubstituted alkyne and 0.08 mmol PS-Triphenylphosphine³ (2.15)mmol/g, 20 mol %) was added 0.75 mL base, pyrrolidine or diethylamine, 0.25 mL THF and palladium acetate (0.02 mmol, 5 mol %). The vial was capped and heated with microwaves for 15 minutes using Initiator[™] Sixty at the temperature stated in the Table. After cooling, the vial was decapped, the mixture was filtered and the remaining solids were washed with THF. The combined solutions were analyzed by LC-MS at an appropriate wavelength.



Entry	Ar-X	HR	Base	T °C	Conv. %, LC-MS	Entry	Ar-X	HR	Base	T °C	Conv. %, LC-MS
1	⟨Br	н	A	130	96	8		н	в	150	95
2	Br N	н	В	150	97	9	° → NH Br	н	А	130	93
3	⟨Br	нОн	А	130	96	10	O Br	н	В	150	81
4	N Br	н-=-	В	150	94	11	O Br	нОн	А	130	85
5	N Br	нОн	А	130	92	12	CI N	н	в	150	78
6		н	В	150	92	13		н	А	150	15
7		н	A	130	92	14	N CI	н	в	150	27

A= Pyrrolidine B= Diethylamine

Table

References

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- 2. Gelman, D.; Buchwald, S.L. Angew.Chem., 2003, 115, 6176
- 3. PS-Triphenylphosphine, Synthesis and Purification Catalog, 2007, Biotage, pages 103-107

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