Comprehensive Organic Chemistry Experiments for the Laboratory Classroom

Edited by Carlos A M Afonso, Nuno R Candeias,
Dulce Pereira Simão, Alexandre F Trindade,
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7.4. Sonogashira Coupling Reaction of Aryl Derivatives: A Versatile Method for Acetylide Building Blocks

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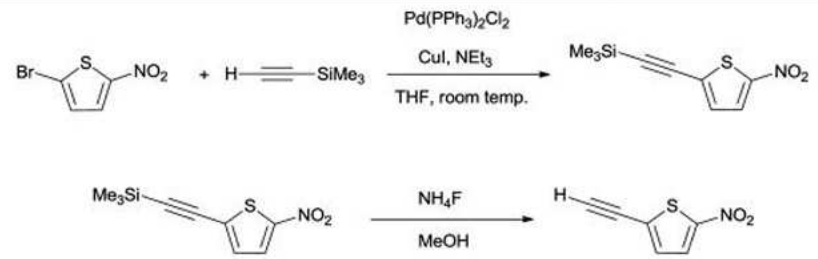

Number of sessions (duration of each session)	Hazard level	Difficulty level	Level of study
2 (5 h + 3 h)	Moderate	High	Intermediate
Class names Aryl halides, terminal alkynes, alkylsilanes			
Concepts involved Palladium catalysis, cross coupling reaction, deprotection of alkynylsilanes			
Chemicals needed 5-Bromo-2-nitrothiophene, triethylamine, copper(I) iodide, ammonium fluoride, bis(triphenylphosphine)palladium(II) dichloride, ethynyl(trimethyl)silane, tetrahydrofuran, *n*-hexane, diethyl ether, methanol, silica gel, anhydrous sodium sulfate, saturated sodium bicarbonate solution, 5% hydrochloric acid solution			
Equipment and experimental techniques involved Liquid–liquid extraction, column chromatography, NMR, heating plate with magnetic stirring, vacuum/nitrogen line, rotatory evaporation apparatus			
Keywords Chromatography, cross coupling, heterocyclic chemistry, NMR, palladium catalysis, terminal alkynes			

Background

The coupling of aryl or vinyl halides with terminal alkynes catalysed by palladium, commonly known as the Sonogashira[1] cross-coupling reaction, is one of the most important and widely used sp^2–sp carbon–carbon bond formation reactions in organic synthesis. The obtained products have frequently found applicability in several areas of chemistry, such as natural products, biologically active molecules, dyes, molecular electronics, dendrimers and conjugated polymers. The reaction name arises from the discovery in 1975 by Sonogashira *et al.* that this process could be performed easily at room temperature using a palladium catalyst, combined with a co-catalytic amount of CuI in an amine as solvent (Scheme 7.4.1).[1]

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