

A Convenient Catalytic Route to Symmetrical Functionalized Bithiophenes

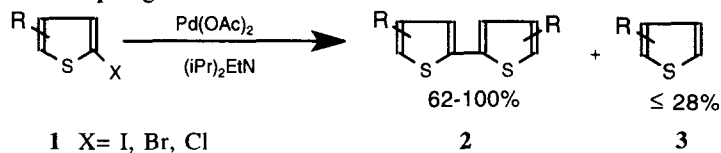
Jwanro Hassan, Laurence Lavenot, Christel Gozzi and Marc Lemaire*.

Institut de Recherches sur la Catalyse et Laboratoire de Catalyse et Synthèse Organique, CNRS, Université C. Bernard. CPE, Bât.308, 43 bd. du 11 nov. 1918, 69622 Villeurbanne, France

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Abstract: A series of symmetrical functionalized bithiophenes has been synthesized in good to excellent yields via homocoupling of thiophene halides in the presence of Pd(OAc)₂ as a catalyst. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Bithiophenes and their derivatives are important compounds, in view of their numerous potential applications [1]. The literature offers several methods for the synthesis of bis-heteroaromatics, Ullmann reaction [2] is the main way to prepare symmetrical biaryls but this method requires a stoichiometric amount of copper. Recently, other methods have been developed; the chelated (triphenylphosphine or 2,2'-bipyridine) nickel (0) complex reducing agents [3] were used to synthesize a number of nitrogen, sulfur or oxygen containing bis-aromatic derivatives. This method requires however stoichiometric amount of Ni(OAc)₂ and an excess of NaH, triphenylphosphine or 2,2'-bipyridine. Recently, we showed the efficiency of Pd(OAc)₂/nBu₄NBr as a catalyst for the direct arylation of activated thiophenes by iodoaryl [4] in a Heck type reaction. Otherwise, this catalyst has been proved to be efficient for the synthesis of symmetrical biaryls via homocoupling of arylhalides [5,6]. We present here the results obtained for the direct synthesis of symmetrical bithiophenes by using Pd(OAc)₂ as catalyst (scheme 1 table 1). Thiophene halides bearing various activating groups are successfully coupled in good to excellent yields. In all cases, diisopropylethylamine appears to be the most efficient and selective base. Toluene is used in order to avoid the carbon halogen bond reduction. In general, the use of tetraalkylammonium salt accelerates the reaction rate and increases yields (method A). However, in the case of 2-bromo-5-nitrothiophene (entry 4 method B) the use of quaternary ammonium salt was avoided because of the difficulty to purify coupling product. Otherwise, in the case of 2-iodo-3-methylthiophene (entry 7 method B), the quaternary ammonium salt does increase neither rate nor yield of the coupling reaction.



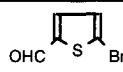
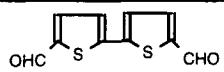
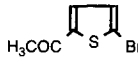
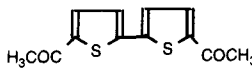
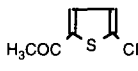
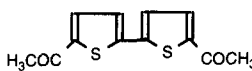
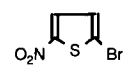
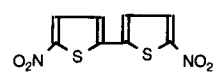
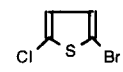
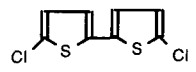

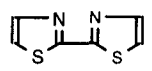

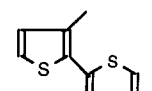
Scheme 1: Homocoupling of thiophene halides catalyzed by palladium.

Fax: 04-72-43-14-08

E-mail: Marc.Lemaire@univ-lyon1.fr

In summary, by using the Pd(OAc)₂ as a catalyst with diisopropylethylamine as base, we have developed an easier and new method for homocoupling reaction of 3 or 5 substituted thiophene halides. Part of the mechanism (i.e the nature of the reducing agent) is still unknown and further work is under progress and will be reported in due course.

Table 1: Homocoupling reaction of functionalized thiophenes halides^a

Entry	Substrate 1	Reaction Condition	Time (h)	Product 2	Ref ^b	Reduction yield 3 GC (%)	Yield (%) ^c
1		A	4		[3]	17	71 (83)
2		A	4		[3]	7	80 (82)
3		A	106		[3]	10	73 (83)
4		B	5		[7]	28	58 (62)
5		A	24		[7]	3	68 (73)
6		A	23		[8]	-	86 (92)
7		B	4		[9]	0	92 (100)

a)- All Homocoupling reactions were carried out at 105°C in Toluene (3 ml) with $8 \cdot 10^{-3}$ mol of thiophene halide, $0,4 \cdot 10^{-3}$ mol of Pd(OAc)₂ and $8 \cdot 10^{-3}$ mol of diisopropylethylamine. Procedure A: $4 \cdot 10^{-3}$ mol of nBu₄NBr. Procedure B: Without quaternary ammonium salt. b)- All products 2 have been fully characterized and comparison with already published data are in agreement. c)- Isolated yield, the value in parentheses indicates GC yield..

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