

Microwave-promoted palladium catalysed Heck cross coupling reaction in water[†]

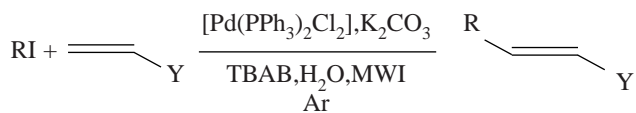
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Palladium-catalysed vinylation of aryl halides in water without organic cosolvent via microwave irradiation under phase transfer conditions to give the *trans*-stilbenes and substituted *trans*-cinnamic acid in good to high yield.

Palladium-catalysed reactions of organic halides with alkenes (Heck type reaction) are known to be a very convenient method for forming carbon–carbon bonds at unsubstituted vinylic positions.¹ This reaction is greatly facilitated when performed under phase transfer conditions using a tetraalkylammonium salt in conjunction with an inorganic base,² also this reaction can even be realised in water using the Pd/M₂CO₃/QX (QX is quaternary ammonium salt) catalyst system.³ Recently, the use of additives such as silver(I)⁴ or thallium(I) salts,⁵ organotrifluoromethanesulfonates,⁶ tetraphenylphosphonium salts^{1e,7} or Ph₄PX/ clay⁸ and perfluorinated phosphines⁹ have provided marked improvements in Heck-type reactions. However, most substrates for coupling require reaction times ranging from hours to days for full conversion. In 1996, Hallberg reported the first palladium-catalysed carbon–carbon formation promoted by microwaves.¹⁰ A series of fast Heck-reactions were completed in a few minutes by the flash heating methodology.¹¹

Microwaves are known to accelerate many organic reactions in polar solvents or in absence of solvent and some important reviews have been published.¹² Recently, we have also reported the synthesis of chiral glycerol selenide ethers¹³ and glycerol sulfide ethers¹⁴ under microwave irradiation conditions. Several microwave-assisted palladium-catalyzed reactions have been recently reported.^{10,11,15} Aqueous reaction conditions offer a safe, economic and environmental friendly alternative in organic synthesis. We herein report palladium-catalysed Heck coupling reactions in water in absence of any organic solvents and in good yields were obtained using microwave technology. The arylation reaction of alkenes with aryl iodides proceeded smoothly under microwave irradiation to give the desired *trans*-products exclusively. The reaction is shown in Scheme 1 and results are summarized in Table 1.



	1	2		3a–g
	R	Y	R	Y
3a	Ph	Ph	3e	2-O ₂ NC ₆ H ₄
3b	Ph	COOH	3f	4-CH ₃ C ₆ H ₄
3c	4-HO ₂ CC ₆ H ₄	COOMe	3g	4-CH ₃ C ₆ H ₄
3d	4-O ₂ NC ₆ H ₄	Ph		COOH

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[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Fast palladium-catalysed coupling reaction of aryl iodides with alkenes under microwave irradiation^a

Product ^b	R	Y	Yield(%) ^c	M.p./ °C	Lit. m.p. ^d
3a	Ph	Ph	91	122–124	124
3b	Ph	COOH	88	132–133	133
3c	<i>p</i> -HO ₂ CC ₆ H ₄	COOMe	92	236–238	238
3d	<i>p</i> -O ₂ NC ₆ H ₄	Ph	89	152–154	155
3e	<i>o</i> -O ₂ NC ₆ H ₄	Ph	86	70–72	72
3f	<i>p</i> -CH ₃ C ₆ H ₄	Ph	89	119–120	120
3g	<i>p</i> -CH ₃ C ₆ H ₄	COOH	93	197–198	198

^aAll product gave satisfactory IR, ¹H NMR, and MS. ^bUnless indicated otherwise the reactions were carried out in the presence of K₂CO₃ using [Pd(PPh₃)₂Cl₂]-TBAB as catalyst in H₂O at 375 W for 10 min under argon. ^cIsolated yield. ^d*Dictionary of Organic Compounds*, ed. J. Buckingham and F. Macdonald, Chapman and Hall, London, 6th edn., 1996.

We investigated the effect of different mole ratios on the reaction of styrene with iodoarenes under microwave irradiation. The results show the best mole ratio is PhI:PhCH=CH₂:K₂CO₃:[Pd(PPh₃)₂Cl₂]:TBAB = 1:1.5:3.0:0.05:0.06. We have also investigated the effect of different phase-transfer catalysts on the reaction of styrene with iodoarenes. It was found that the activities of catalysts are in the following sequence :TBAB>TBAl>TBAC>PEG-400. We have also investigated the effects of irradiation power and time on the reaction. It was found that the highest yields of compounds **3a–g** are obtained at a power level of 375 W for 10 min continuous irradiation.

The effectiveness of the microwave irradiation and conventional heating for the formation of compounds **3a–g** has been compared and results are summarized in Table 2 and Table 3. The results showed that the synthesis of compounds **3a–g** under microwave irradiation were 18–42 times faster than under conventional heating and yields of compounds **3a–g** are very low for 10 minutes under conventional reflux. This ratio between the reaction time using conventional reflux and microwave irradiation (*t_c* / *t_{mw}*) under same conditions, quantifies the microwave heating effect.

In conclusion, we have described a microwave-promoted Heck reaction in water. Using this method, we can largely decrease the reaction cost and avoid the use of organic solvents. The results show that the microwave irradiation provides the same selectivity, with respect to halide displacement as compared to the original reaction.

Experimental

Microwave irradiation was carried out with a commercial microwave oven GlanzWP 750B at 2450 Hz. ¹H NMR spectra were recorded in CDCl₃ on a BRUKER PT 80A Spectrometer using tetramethylsilane as internal standard. Chemical shifts were reported as δ in ppm. IR spectra were measured with an Alpha centauri FI-IR spectrometer as KBr discs. Mass spectra were recorded on a QP-1000A GC-MS using

Table 2 Comparison of time and yields on the formation of compounds **3a-g** using microwave and conventional heating^a

Product	Conventional heating ^b		Microwave heating			
	t / min	Yield(%)	Power/W	t / min	Yield (%) ^c	t _c / t _{mw}
3a	420	85	375	10	91	42
3b	180	88	375	10	88	18
3c	420	90	375	10	92	42
3d	180	80	375	10	89	18
3e	180	80	375	10	86	18
3f	420	84	375	10	89	42
3g	300	54	375	10	93	30

^aThe reactions were carried out in the presence of K₂CO₃ using [Pd(PPh₃)₂Cl₂]- TBAB as catalyst in H₂O under argon. ^bReflux temperature (95 °C). ^cIsolated yield.

Table 3 Comparison of yields on the formation of compounds **3a-g** using microwave and conventional reflux^a

Product	Conventional heating ^b		Microwave heating		
	t / min	Yield (%) ^c	Power/W	t / min	Yield (%) ^c
3a	10	10	375	10	91
3b	10	15	375	10	88
3c	10	5	375	10	92
3d	10	12	375	10	89
3e	10	12	375	10	86
3f	10	8	375	10	89
3g	10	11	375	10	93

^a The reactions were carried out in the presence of K₂CO₃ using [Pd(PPh₃)₂Cl₂]- TBAB as catalyst in H₂O under argon. ^bReflux temperature (95 °C). ^cIsolated yield.

the electron impact mode (70eV). Melting points were determined with an Electrothermal micromelting point apparatus and were uncorrected. All solvents were used without further purification. [Pd(PPh₃)₂Cl₂] was prepared according to ref. 18. The remaining chemicals were obtained from commercial sources. All reactions were conducted under an argon atmosphere.

Preparation of compounds 3a-g: A mixture of styrene (7.5 mmol), aryl iodides (5 mmol), K₂CO₃ (2.07g, 15 mmol), [Pd(PPh₃)₂Cl₂] (0.17g, 0.25 mmol), tetrabutylamine bromide (0.1g, 0.3 mmol) and H₂O (10 ml) was irradiated at 375W for 10 minutes by microwaves under argon. The mixture was cooled and acidified with dilute HCl, then extracted with Et₂O (20 ml × 3). The organic phase was dried over magnesium sulfate. The dried ethereal solution was concentrated. The product was purified by column chromatography on silica gel using petroleum/ethyl acetate (V/V 16:1) as the eluent or recrystallized.

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