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Tandem Diazotization Heck Reactions: A General Synthesis of Substituted Styrenes from Anilines[1)]*

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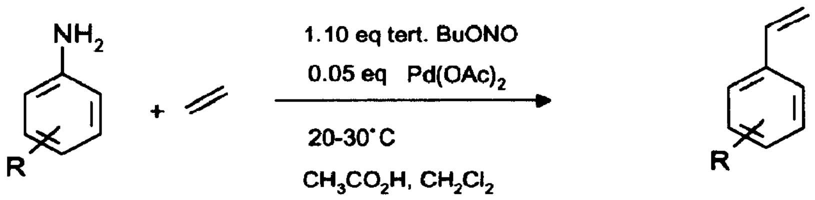
Abstract: *The palladium-catalyzed olefination of different anilines with ethylene is shown to proceed generally in good yields. The substituted styrenes were obtained highly selective in a direct tandem diazotization Heck reaction at room temperature under atmospheric pressure of ethylene without concomitant side reaction to stilbenes.*

The development of efficient methods for organic synthesis is a challenging endeavor in industrial chemistry. Tandem reactions, in particular, provide a very attractive tool to perform specific transformations in a simple and economic way.

Substituted styrenes are versatile building blocks and exhibit a broad range of technical applications, mostly monomers for the preparation of functional polymers.[2)] The resulting substituted polymers are useful in a wide variety of applications, e.g., in photoresists, in epoxy resins, as metal coatings, and the like.

Palladium catalyzed Heck reactions of aryl halogenides offer an easy and general entry to substituted styrenes.[3)] However, from an industrial point of view these syntheses have no considerable commercial interest, because of the rather expensive starting materials which have to be used, and sometimes the low selectivities, and because of further reactions to stilbenes.[4)] Compared to aryl iodides and aryl bromides anilines are an economically superior target for further functionalization. Previously, Heck reactions of diazonium salts have gained some interest,[5)] but to the best of our knowledge there has no direct synthesis of substituted styrenes starting from anilines been described. Thus, we thought it is worthwhile to investigate the palladium-catalyzed arylation of ethylene with anilines via diazonium intermediates.

As shown in scheme 1 after optimization of the conditions the tandem diazotization Heck reaction of anilines with ethylene proceeds best in the presence of palladium catalysts with tert. butyl nitrite as diazotization reagent in a mixture of acetic acid and organic solvents.[6)]



Scheme 1

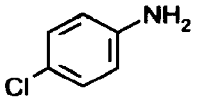
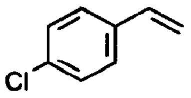
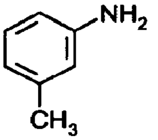
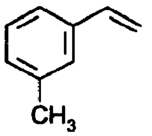
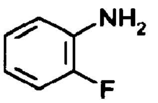
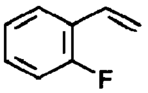
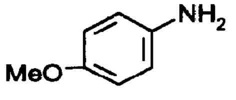
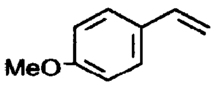
It is remarkable that the reaction takes place under very mild conditions. This is the first successful example for a Heck reaction with ethylene which already takes place even under atmospheric pressure of ethylene and at room temperature. Moreover, the method leads highly chemoselective to styrenes, although usually under low pressure of ethylene the formation of stilbenes is the prevailing reaction.[4)]

To investigate the scope of the reaction, a series of aniline substrates was subjected to our optimized conditions and the results are listed in Table 1.

Interestingly, the synthesis of styrenes is not very sensitive to the electronic nature of the aromatic substrate. This could be rationalized by the fact that oxidative addition of the palladium catalyst to the diazonium intermediate is not the rate determining step, in contrast to the generally accepted mechanism of Heck reactions of aryl bromides and aryl chlorides.[7)] As catalysts for the reaction palladium(II)salts performed best. It is very likely that they are reduced by the olefin in the first step of the reaction.[8)] In contrast, using palladium(0)phosphine systems or even adding phosphines to the reaction mixture decreased the yield of the desired products. This negative influence of the phosphine could be attributed to the observed reactions of phosphines with aryl diazonium salts.[9)]

The positive effect of the added organic solvent is not clear in total. Most likely, the increased solubility of ethylene in the mixed reaction media is responsible for higher yields. Advantageously, compared to classical Heck reactions of aryl halogenides or diazonium salts with ethylene no stoichiometric addition of base or salts is needed.[10)] Thus, the palladium catalyzed tandem diazotization Heck reaction appears to be an excellent method for the preparation of a wide variety of substituted styrenes. Future work is directed toward increasing turnovers and improving Heck reactions of anilines.

Table 1. Synthesis of Different Styrenes from Substituted Anilines[6)]

Substrate	Product	Yield[1)]
		72%
		66%
		70%
		64%

1) Yields were determined by GC. Isolated yields after destillation were usually 5-10% lower.

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References and Notes

* Dedicated to Professor Dr. Wolfgang Hilger on the occasion of his 65th birthday

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6. General procedure for the arylation of ethylene: A 250 ml three necked flask equipped with reflux condenser and a dropping funnel containing a Teflon-coated magnetic stirring bar was charged with 50 ml acetic acid. Subsequently, 40 mmol of the aniline derivative and 2.0 mmol palladium(II)acetate were added in a temperature range of 20-30°C. Ethylene was bubbled through this solution (20-30 ml/h). Then 45 mmol of tert-butyl nitrite was added at 15-25°C. After adding 50 ml dichloromethane, the reaction mixture was stirred at room temperature for 18 h. The yield was determined by GC.

   For isolation of the substituted styrenes (ten fold experiment), the solution was washed successively with water, 5% bicarbonate and again water. After separation the organic phase was dried with a mixture of potassium carbonate and sodium sulfate and after adding a small amount of 2,6-di-tert.-butyl-4-methylphenol as stabilizer distilled under reduced pressure.
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