

Highly Regioselective, Sequential and Multiple Palladium-Catalyzed Arylations of Vinyl Ethers Carrying a Coordinating Auxiliary. The First Example of a Heck Triarylation Process

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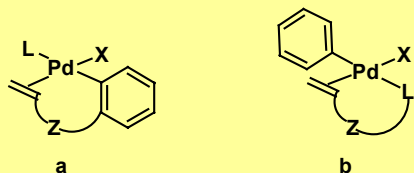


INTRODUCTION

The Heck reaction enjoys considerable popularity as a reliable and general method for carbon-carbon bond formation. Although the traditional intermolecular Heck arylation has found wide utility, the reaction is essentially limited to the monoarylations of olefins. An extension of the Heck methodology to include selective di- and triarylations appears attractive and should increase the preparative scope considerably.

The ability of intramolecular factors to overcome the reluctance of substituted alkenes to participate in the Heck insertion process allows the assembly of complex and sterically congested molecules. These synthetically valuable reactions rely upon the ready formation of a transient intramolecular π -complex (**a**). The observed increase in reaction rate using substrates with a coordinating, metal-directing auxiliary suggested that intermediate π -complexes of the type (**b**) might also facilitate sterically unfavourable intermolecular vinylic polysubstitutions.

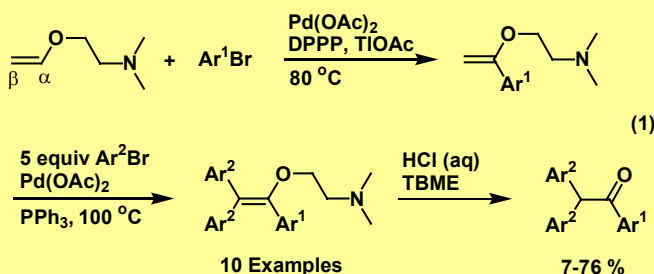
We hereby report multiple and selective vinylic substitution reactions involving non-substituted vinyl ethers carrying a palladium-coordinating nitrogen auxiliary. Traditional or microwave-assisted hydrolysis (SmithSynthesizer™) of the initially formed di- or triarylated products liberates the corresponding polyaromatic carbonyl compounds.



RESULTS

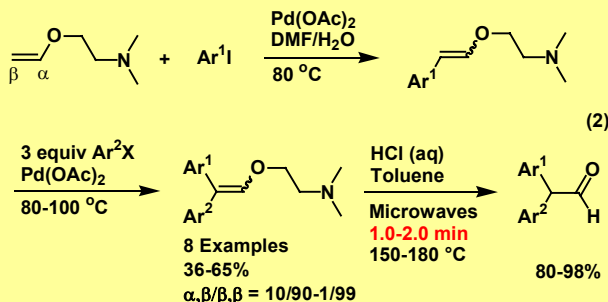
α,β,β -Triarylation experiments. Triarylated vinyl ethers were obtained when the mono α -arylated substrates were reacted with a five-fold excess of aryl bromide in the presence of the palladium catalyst for 48 h (Eq 1). The isolated yields in Eq 1 are cumulative and thus correspond to the four-step transformation of the starting aryl bromide into the carbonyl products.

With iodobenzene only a diarylated product, and no triarylation product (<1%), was detected and biphenyl formation was instead predominant.



RESULTS (continued)

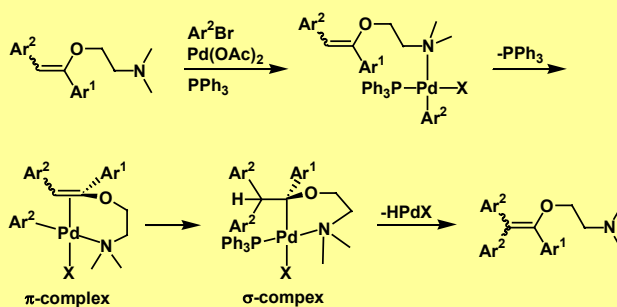
β,β -Diarylation experiments. The β,β -diaryl vinyl ethers could be prepared by a second chelation controlled β -arylation of monoarylated olefins using aryl iodides, or an electron-poor aryl bromide (Eq 2). It is notable that in most cases the second arylation occurred almost exclusively at the sterically hindered β -carbon, and only a small fraction, if any, of α,β -products were observed.



DISCUSSION

We propose that the chelation-accelerated α,β,β -triarylation proceeds as depicted in the Scheme. In this entropy-driven scenario, the oxidative addition complex is presented to the double bond after a nitrogen-palladium(II) pre-coordination. The subsequent nitrogen insertion via a six-membered palladacycle provides the chelated σ -alkyl palladium complex which subsequently undergoes β -elimination to deliver the tetra-substituted olefin and an unstable Pd(0) precursor.

Scheme



CONCLUSIONS

The principle of reactivity enhancement with Heck arylation reactions for substrates containing a palladium-coordinating group by a chelation effect has now been demonstrated. Heck triarylation reactions proceeded for the first time utilizing a catalyst-presenting auxiliary.

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