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# Rhodium(I) mediated arylation of aldehydes with arylboronic acids under base and water free conditions: A computational study☆

Alma Itzel Olivos Suarez, Joost N.H. Reek, Bas de Bruin*

*University of Amsterdam, Van't Hoff Institute for Molecular Sciences (HIMS), Homogeneous and Supramolecular Catalysis, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands*

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ABSTRACT

The mechanism for rhodium(I) mediated arylation of aromatic aldehydes by arylboronic acids under base and water free conditions was investigated with DFT methods. The detailed picture resulting from the calculations is that the reaction proceeds via an internal base mechanism, whereby the initially formed alcoholate (obtained by aryl migration to the aldehyde) attacks the electrophilic boron atom of the coordinated arylboronic acid substrate to facilitate the aryl transfer to the metal. Alternative pathways involving B–C oxidative addition or internal proton transfer followed by β-aryl transfer from thus resulting Rh–O–BPh(OH) moieties are kinetically disfavored. The rhodium atom does not change its oxidation state throughout this whole process, and all steps proceed smoothly within the coordination sphere of rhodium(I). Aldehyde migratory insertion into the $\mathrm{Rh^I}$-aryl bond appears to be the rate limiting step ($\Delta G^\dagger = +19.4\,\mathrm{kcal\,mol^{-1}}$) of the catalytic cycle. The subsequent elementary steps involved in the transmetallation process proceed with lower barriers ($<+16.3\,\mathrm{kcal\,mol^{-1}}$). The *cis*-$[\mathrm{Rh(OHCHPh_2)(OBOHPh)(PNH_2(OH)_2)_2}]$ species **R.S.** should be the resting state species under the catalytic conditions according to the DFT calculations.

## 1. Introduction

Aryl transfer from arylboronic acids to palladium is a key step in among others Susuki–Miyaura cross-coupling reactions [1,2]. These reactions generally require the presence of an external base and water. Formation of anionic borates $[\mathrm{B(Ar)(RO)(OH)_2}]^-$ under these conditions is thought to facilitate the transfer of the aryl group to the metal. Theoretical calculations on palladium model systems clearly confirmed this hypothesis [3–5].

The addition of arylboronic acids to aromatic aldehydes was first reported by Miyaura employing rhodium(I) catalysts [6,7], and several other interesting rhodium(I) catalysts have been studied since [8–10]. Most of these reactions deal with simple aromatic aldehydes (which are generally easier to arylate than other carbonyl compounds) and non-functionalized phenylboronic acid, but interesting other methods were also developed to achieve arylations of (1,2-di)ketones and (1,2-keto)esters [11–13], imines [14], cyanoformates [15] and α-ketoesters [16], or to use functionalized aldehydes and/or functionalized arylboronic acids [17,18]. Asymmetric versions of these interesting reactions have also been developed based on chiral phosphoramidites [19], phosphites [16] and chiral diene ligands [20,21]. Chiral $\mathrm{Rh^I}$(diene) complexes have also been applied in Rh-mediated enantioselective aryl transfer from arylboronic acids to α,β-unsaturated carbonyl compounds and imines [22]. The field is clearly dominated by rhodium(I) catalysis, although some recent reports focused on replacing rhodium by other (cheaper) transition metals such as ruthenium(II) [23], nickel [24], copper [25] and iron [26].

For most of the above reactions (aqueous) basic conditions are generally required/applied, presumably to promote aryl transfer from $[\mathrm{B(Ar)(OH)_2}]$ via $[\mathrm{(RO)(OH)_2B}]^-$ to the metal, as is the case in the palladium mediated Susuki–Miyaura cross-couplings. Experimental studies have shown that rhodium-hydroxo intermediates are important in the transmetallation steps of 1,4-addition of organoboronic acids to α,β-unsaturated carbonyl compounds [27], but the exact role of the base in the transmetallation steps of the rhodium(I) mediated systems remains somewhat elusive. To the best of our knowledge, there are no systematic computational studies available to explain the exact role or function of the base (and water) in the transmetallation steps of the rhodium(I) mediated systems. In this perspective, one of the experimental studies by Feringa, de Vries and Minnaard dealing with phosphoramidite rhodium(I) mediated (enantioselective) arylation of aldehydes is therefore particularly interesting, because this system does not strictly require the presence of an external base (nor water) for catalytic activity [19]. The main product obtained by aldehyde arylation is actually $[\mathrm{Ar}R\mathrm{CO{-}(B(OH)_2)}]^-$, which transforms into the

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* Corresponding author.
*E-mail address:* B.deBruin@uva.nl (B. de Bruin).

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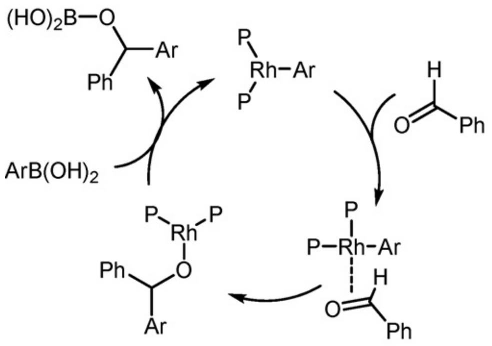
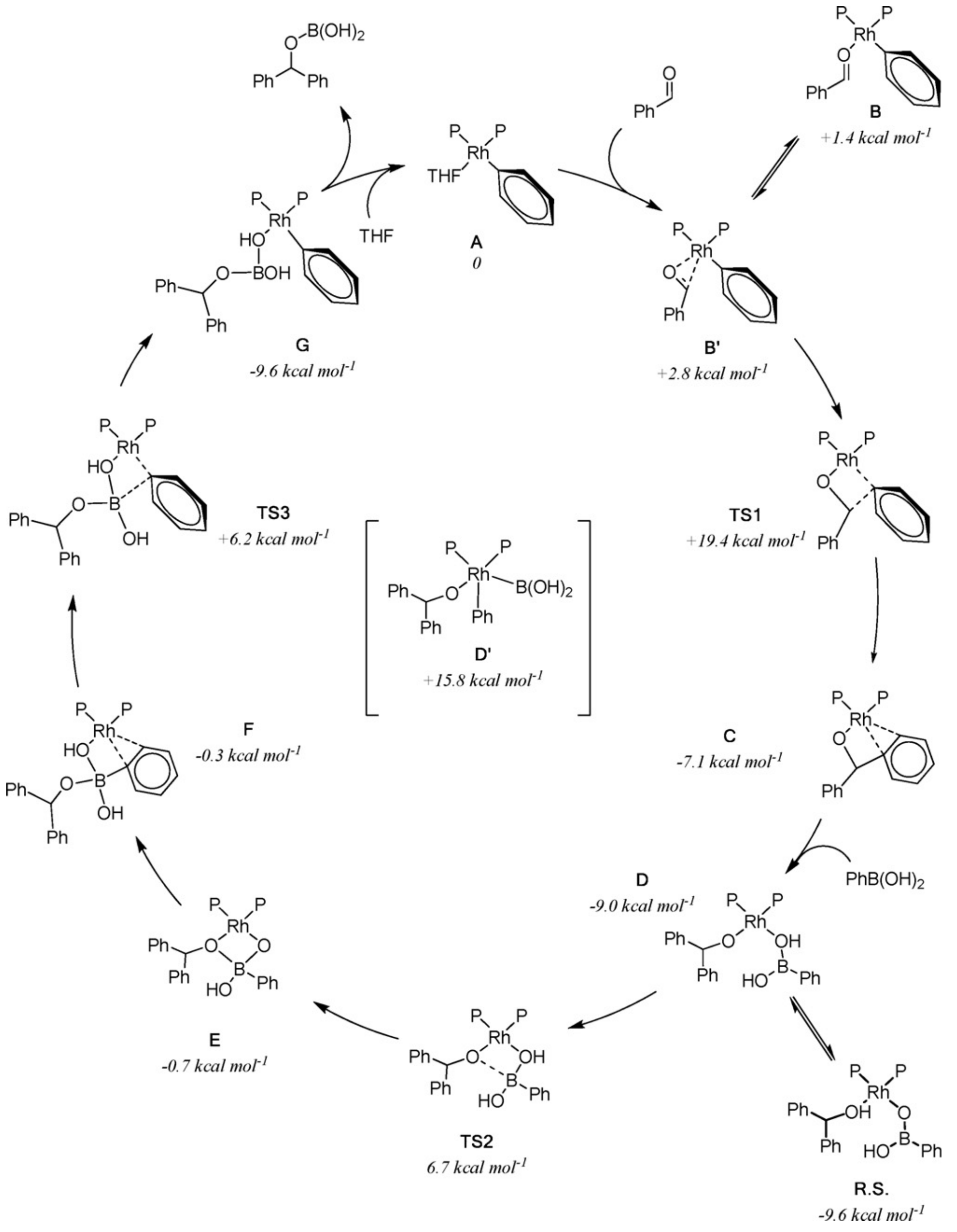
final alcohol products Ar*R*COH only after aqueous workup [19]. The general mechanism for these reactions, as proposed by Feringa, de Vries and Minnaard, is shown in Scheme 1.

As shown in Scheme 1, the rhodium-alcoholate intermediate (obtained by aldehyde insertion into the Rh-aryl bond) is proposed to be responsible for the direct aryl transfer from arylboronic acid to rhodium with liberation of $[\mathrm{Ar}R\mathrm{CO{-}(B(OH)_2)}]^-$. The basic mechanism in Scheme 1 does not give any insight into the proposed transmetallation process, and considering the importance of the reaction a detailed understanding of all elementary steps contributing to the mechanism is required to facilitate future developments by rational strategies. This triggered us to investigate the reaction mechanism of the rhodium mediated arylation of aldehydes in detail using DFT methods. Apart from an interest in the overall reaction mechanism, we were primarily interested in the question why no external base or water is required in the phosphoramidite based rhodium(I) mediated reactions. Since oxidative addition reactions are generally easier for rhodium(I) than for palladium(II), could B–C



**Scheme 1.** Proposed mechanism for phosphoramidite rhodium(I) mediated arylation of aldehydes.



**Scheme 2.** Summary of the DFT calculated reaction pathways for Rh-mediated arylation of aldehydes with aryl boronic acids (free energies $\Delta G^{\circ}_{298\,\mathrm{K}}$, in kcal mol$^{-1}$, included).