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Palladium Complexes with Chelating Bis-NHC Ligands in the Mizoroki–Heck Reaction—Mechanism and Electronic Effects, a DFT Study

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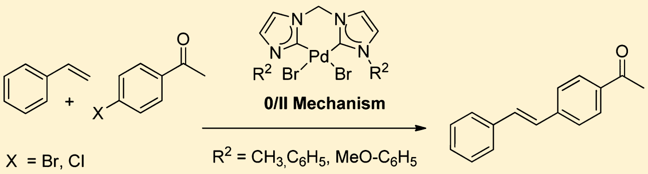
S Supporting Information

ABSTRACT: Experimental results have shown that palladium complexes with chelating aryl- and alkyl-substituted bis-NHC ligands, including $[(H_3C\text{-Im})_2CH_2]PdBr_2$, $[(C_6H_5\text{-Im})_2CH_2]PdBr_2$, and $[(H_3CO\text{-}C_6H_4\text{-Im})_2CH_2]PdBr_2$ are excellent catalysts for the Mizoroki–Heck reaction. To better understand and improve the catalysts, a density functional theory (DFT) study of the Heck reaction has been performed at the B3LYP/6-31G* level of theory, complemented by M06/def2-TZVP single-point calculations. Different mechanistic pathways have been investigated and compared to available experimental results. The most likely mechanism is a cationic catalytic cycle involving the palladium oxidation states 0 and +II. We also looked at other oxidation states, but on the basis of the calculated Gibbs free energy a +II/+IV mechanism can be excluded. Aryl substitution with electron-donating groups at the *para* position (e.g., the methoxy group in $[(H_3CO\text{-}C_6H_4\text{–Im})_2CH_2]PdBr_2$) was found to reduce the reaction barrier of the rate-determining step. This is in agreement with the experimental findings for the catalysts. The experimentally observed *cis* selectivity could also be explained by the DFT study.



INTRODUCTION

Since its discovery in 1972, the Mizoroki–Heck reaction has been widely used in organic synthesis.[1−7] It is also of considerable economic interest.[8,9] In 2010 the Nobel Prize Committee recognized the importance of this reaction by awarding the chemistry prize to Richard F. Heck together with Ei-ichi Negishi and Akira Suzuki *"for palladium-catalyzed cross couplings in organic synthesis"*.

During the last decades, various efficient homogeneous catalysts have been developed, e.g., Herrmann's palladacycle.[10,11] High turnover rates can be achieved for aryl bromides with standard protocols, and even the use of the less reactive aryl chlorides as substrates has become commonplace.[12,13]

Different palladium(II) complexes with bulky monodentate phosphines[14] as well as complexes of bidentate and pincer[15,16] ligands have been used, while since the discovery of stable N-heterocyclic carbenes (NHCs) by Arduengo[17,18] in 1991, there has been a growing interest in NHC ligands because of their high stability.[13,19−27] These ligands have also been found to be promising candidates for the development of catalysts for the Heck reaction.[13,28] Different groups have synthesized chelating NHC ligands that have been investigated in various catalytic reactions.[29−49]

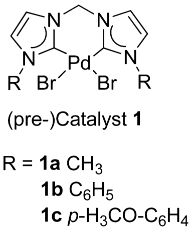


Figure 1. Palladium(II)–NHC complexes **1a**–**c**.

In 2007 we reported highly active palladium complexes with chelating NHC ligands bearing aromatic substituents (see Figure 1 and Table 1).[50] These chelated catalysts show considerable differences in reactivity with relatively minor modifications of the ligand. Because of their rigid geometries and small variations in steric bulk, they are ideal candidates for the examination of electronic effects on the reaction.

The well-known methyl-substituted complex **1a**, first reported by W. A. Herrmann in 1998, was chosen as the reference for this study.[51] The phenyl-substituted complex **1b**[52] allows an investigation of the electronic and steric effects of the aryl substitution, while the *p*-methoxyphenyl-substituted complex **1c**, which was experimentally shown to be a very active catalyst,[50] gives insight into the effects of electron-donating groups on the reaction barriers.

Experimental Data. A number of experimental results are available for these complexes.[50,53] We generally tested the activities of the different catalysts with a standard system in dimethylacetamide (DMAc) and therefore also selected these starting materials for the computational study. Styrene **2** and

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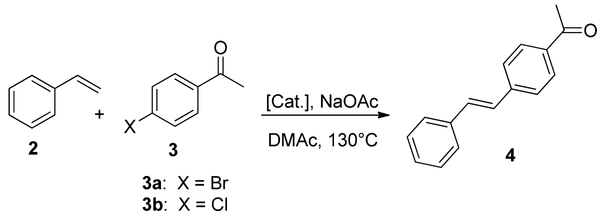
the aryl halogenides **3a** and **3b** were selected as substrates for this computational study in order to allow comparison with the experimental data from our previous investigations (see Table 1). As expected, *p*-chloroacetophenone (**3b**) is more difficult to activate than *p*-bromoacetophenone (**3a**). The experimental results show that complex **1c** is the most efficient catalyst for the reactions described above.

Table 1. Selected Experimental Results[50,53]

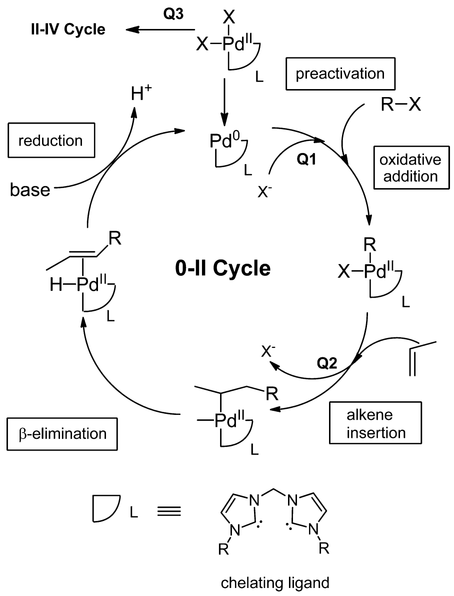


catalyst	cat. loading [mol %]	substrate	TON	TOF $[h^{-1}]$	conv. [%]
1a	0.5	**3a**	80	10	56
1a	0.5	**3b**	1	0	0.7
1b	0.5	**3a**	49	6	34
1b[a]	n/a	**3b**	n/a	n/a	n/a
1c	0.5	**3a**	141	47	99
1c	0.01	**3a**	7143	1191	100
1c	0.001	**3a**	29286	1126	41
1c	0.0001	**3a**	235714	8418	93
1c	0.5	**3b**	44	1.5	31
1c	0.01	**3b**	1143	38	16

[a] Because of the low conversion of substrate **3a**, no experiments with **3b** were conducted.

Mechanistic Studies. According to several mechanistic investigations of the Heck reaction, multiple competing mechanisms may be involved, depending on the nature of the catalyst, the substrates, and the reaction conditions.[54−67] Scheme 1 shows an overview of the mechanistic questions addressed in this paper based on a general catalytic cycle for the Heck reaction of palladium bis-NHC complexes. On the basis of the results of previous studies, we addressed the following questions: (a) Does the reaction proceed via an anionic cycle (Scheme 1, Q1)? On the basis of cyclic voltammetry (CV) studies of phosphine-based systems, it has been suggested that free halides might bind to the palladium center at different stages of the cycle.[67] (b) Does the reaction proceed via a cationic or a neutral pathway (Scheme 1, Q2)? Experimental (MS and CV)[68,69] as well as DFT[70−74] studies have shown that both pathways should be possible. The final question is (c) does the catalytic cycle involve the palladium oxidation states 0/+II or +II/+IV (Scheme 1, Q3)? While the Heck reaction is generally presumed to be catalyzed by palladium(0),[75] other proposals can be found in the literature.[56,76−78] In particular for chelated and pincer complexes there has been some controversy.[66,79−81]

Scheme 1. Calculated Catalytic Cycle for the Heck Reaction of Chelated Bis-NHC Palladium Complexes



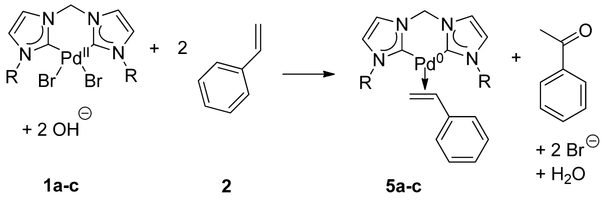
COMPUTATIONAL DETAILS

All of the calculations were performed with the Gaussian 03[82] and ORCA 3.0.2[83] program packages. Geometry optimization was carried out using Gaussian with the B3LYP hybrid density functional[84] and the 6-31G(d) basis set for all nonmetal atoms,[85,86] including bromine.[87] For palladium, a decontracted Hay−Wadt (N + 1) effective core potential and basis set were used.[88,89] All of the geometries were fully optimized without constraints. Harmonic force constants were calculated for all of the geometries in order to verify their identities as ground or transition states. All of the given transition states had only one imaginary frequency. In addition, intrinsic reaction coordinate calculations were carried out for selected transition states.[90−92] The uncorrected molecular electronic energies are given as ΔE(Gas). Gas-phase Gibbs free energies (ΔG(Gas)) and enthalpies (ΔH(Gas)) were calculated for an ideal gas under standard conditions (1 atm, 298 K) using the approach implemented in Gaussian 03.[93] To account for solvent effects, the conductor-based PCM method[94] as implemented by Barone and Cossi[95] was used for single-point calculations of gas-phase geometries using the united atom model with Kohn−Sham radii.[96,97] Gibbs free energies in solution were calculated by addition of the solvation free energy obtained from SCRF single-point calculations to the gas-phase Gibbs free energies[71,98] for the solvents dimethyl sulfoxide (DMSO), dimethylformamide (DMF), and DMAc. In order to test the accuracy of our results, we performed single-point calculations using the M06 functional,[99,100] which significantly enhances the description of dispersion. For these single-point calculations, we used the def2-TZVP basis set[101,102] for the nonmetal atoms and the LANLTZ basis set[103] with additional f polarization[104] for palladium, as provided by the ORCA package. We computed new Gibbs free energies in solution from these energies by adding the thermal corrections and DMAc solvation energies from the B3LYP/6-31G* results, as this approach ensured maximum comparability. In the further course of this article, we refer to this level of theory as M06/TZVP. For the sake of clarity, only DMAc Gibbs free energies (ΔG(DMAc)) are given; the other solvent energies are available in the Supporting Information. For DMAc a permittivity of 37.78 F/m was taken from the literature.[105] A Monte Carlo volume calculation of a DMAc molecule at the B3LYP/6-31G(d) level of theory led to a solvent radius of 3.089 Å, obtained using the molar volume. Parameters for DMF were taken from and used according to the literature.[106,107] Parameters for DMSO were used as included in Gaussian 03. When discussing parts of the catalytic cycle, we denote the Gibbs free energies of the respective reaction barriers defined in the text as $\Delta_{TS}G$ and the Gibbs free energies of the corresponding reactions as $\Delta_{R}G$. The same notation is used for enthalpies (ΔH) and electronic energies (ΔE).

RESULTS AND DISCUSSION

As the reaction is generally assumed to proceed via a Pd(0) active species, it is necessary to reduce **1a−c** to form this active species. This reduction step is not part of the catalytic cycle, and we consider it to be a preactivation step (see Scheme 2).

Scheme 2. Preactivation Reaction Using Styrene 2 as the Olefin and Hydroxide as the Base



The most probable active species was determined by DFT methods. It was interesting to note that recently Elsevier and co-workers succeeded in synthesizing palladium(0) maleic anhydride complexes with chelating bis-NHC ligands,[29] where only those with phenyl substituents were stable in solution. They showed that only the palladium(0) complexes were active in the semihydrogenation of 1-phenyl-1-propyne, while the corresponding palladium(II) allyl complexes did not show any activity.

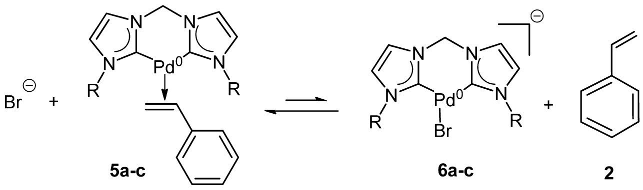
While for phosphine-based ligands there is a widely accepted consensus that palladium is reduced by oxidation of a phosphorus atom,[3,108] a corresponding mechanism for NHC-based ligands has never been proven experimentally. However, it has been well-known for a long time that olefins are able to reduce palladium(II).[109] The calculated reaction enthalpies and energies (see Table 2) and the absence of an induction period in the experimental kinetic study[50] indicate that the preactivation is fast.

Table 2. Reaction Energies for the Catalyst Preactivation (in kcal/mol)

complex	$\Delta_R E$(Gas)	$\Delta_R H$(Gas)	$\Delta_R G$(Gas)	$\Delta_R G$(DMAc)
1a	−172.4	−173.1	−163.8	−110.6
1b	−178.5	−174.1	−168.2	−168.4
1c	−177.5	−168.1	−167.3	−208.9

The Active Species. Whether the active species is charged is one of the important questions (Scheme 1, Q1). We therefore looked into the addition of a bromide ion to **5a−c** and the substitution of styrene in complexes **5a−c** by a bromide ion, leading to the anionic complexes **6a−c** (Scheme 3). When a bromide ion was coordinated to **5a−c**, the olefin dissociated during the geometry optimization. Furthermore, optimization of the anionic complex **6a** resulted in dissociation of the NHC ligand. The strongly donating nature of the bidentate NHC ligand seems to prevent an anionic mechanism. The substitution reaction in the case of **5b** and **5c** is endergonic with $\Delta_R G$(DMAc) > 20 kcal/mol.

Scheme 3. Stabilization of the Pd^0 Active Species by Counterions versus Styrene



The stabilizing effect of the coordination of olefinic substrates to palladium(0) compounds has been experimentally observed in the Heck reaction[110] and is supported by DFT results.[66] The lower relative concentration of catalyst versus olefin can therefore stabilize the active species, which might explain the experimental observation that lower catalyst loadings can lead to higher turnover numbers.[50] The π coordination of olefin **2** to the "naked" Pd(0) complex (see the Supporting Information) is highly exergonic.

Oxidative Addition. In this study, the oxidative addition reaction is preceded by the exchange of the olefin at **5a−c** against the aryl halogenides **3a** and **3b**, leading to the π-coordinated intermediates **7a−c** (see Figure 2). The oxidative addition then occurs as an intramolecular reaction. The corresponding nonplanar transition state (**TS 7**) has been previously described for other chelated systems.[66,111,112] The activation barrier is calculated to be the energy difference of **TS 7b** relative to the stabilized active species **5b**, including the dissociation of styrene and the association of **3a**/**3b**. Figure 2 describes the potential energy surface for intermediate **5b**, and the results for **5a** and **5c** are given in Table 3. The total Gibbs free energy of activation in these steps is strongly dependent on the aryl halogenide (see Figure 2).

With a $\Delta_{TS}G$(Gas) of 23.9 kcal/mol, the Gibbs free energy of the reaction barrier of **5b** is more than 5 kcal/mol higher for the chloride **3b** ($\Delta_{TS}G$(Gas) = 18.8 kcal/mol) than for the corresponding bromide **3a** (see Table 3). After solvent correction, the difference in Gibbs free energies, $\Delta\Delta_{TS}G$(DMAc), is 3.0 kcal/mol (see Figure 2). Using the M06 functional with its enhanced description of dispersion interactions leads to an energy difference of 3.4 kcal/mol. The Gibbs free energies including solvent correction indicate that the lowest reaction barriers of the three catalysts are calculated for **5a**. However, the difference in the gas-phase Gibbs free energies is less than 0.5 kcal/mol at the B3LYP/6-31G* level of theory. The M06/TZVP single-point calculations predict a higher energy barrier for **5a**, with a $\Delta\Delta_{TS}G$(M06) of about 1.5−2 kcal/mol with respect to the aryl substituted **5b** and **5c** (for the energies, see the Supporting Information). The triple-ζ M06 calculations (values given in parentheses) found lower activation barriers for the aryl-substituted complexes in the oxidative addition step.

It is difficult to assess the importance of π-donor effects of the ligands in this step. The B3LYP/6-31G* calculations indicate that they might be negligible; however, the M06/TZVP calculations show an influence of the donor ligand. Apart from **5a**, the two methods are in good agreement on the barrier heights, with the M06/TZVP energies higher by 1−2 kcal/mol.

Insertion. As explained above, an anionic intermediate could be excluded, and we next addressed the question of whether after the oxidative addition step the reaction proceeds via a neutral or cationic pathway (Scheme 1, Q2). A neutral pathway in this case would involve a pentacoordinated palladium intermediate (**8a−c**), as a halide and the olefin **2** have to be coordinated simultaneously. However, a systematic search did not lead to a corresponding minimum, in agreement with previous DFT studies.[112−114] Also, a full M06-D/TZVP optimization did not result in an energy minimum for a pentacoordinated palladium center. In the case of monodentate ligands, both neutral and cationic pathways are possible,[73] as one more coordination site is available compared with chelating ligands. In our case a ligand would have to dissociate, which seems unlikely given the thermal stability of the Pd(II)

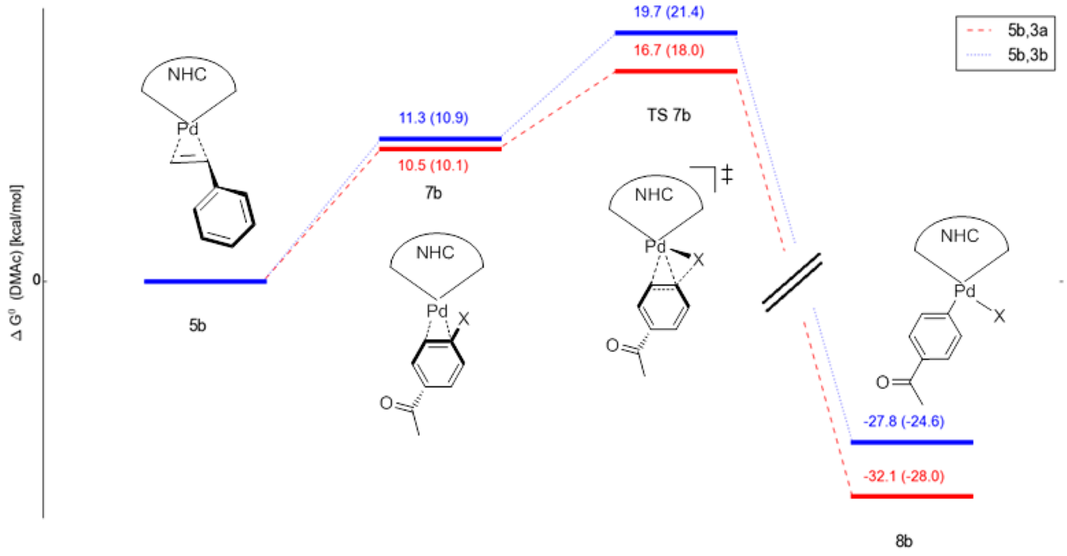


Figure 2. Oxidative addition of substrates **3a**/**3b** to **5b** (in kcal/mol; results for **5a** and **5c** are shown in Table 3; M06 energies are given in parentheses).

Table 3. Calculated Activation Energies ($\Delta_{TS}E$), Enthalpies ($\Delta_{TS}H$), and Gibbs Free Energies ($\Delta_{TS}G$) in the Gas Phase and Solution (DMAc) and M06/TZVP Energies for the Catalytic Systems (Catalyst, Substrate) in kcal/mol

system	$\Delta_{TS}E$(Gas)	$\Delta_{TS}H$(Gas)	$\Delta_{TS}G$(Gas)	$\Delta_{TS}G$(DMAc)	$\Delta_{TS}G$(M06)
5a, **3a**	18.7	18.1	18.4	14.6	19.3
5a, **3b**	24.5	23.8	24.0	18.6	23.3
5b, **3a**	19.6	18.8	18.8	16.7	18.0
5b, **3b**	24.8	24.0	23.9	19.7	21.4
5c, **3a**	19.5	18.8	18.8	16.3	17.2
5c, **3b**	24.8	23.9	24.2	20.3	21.8

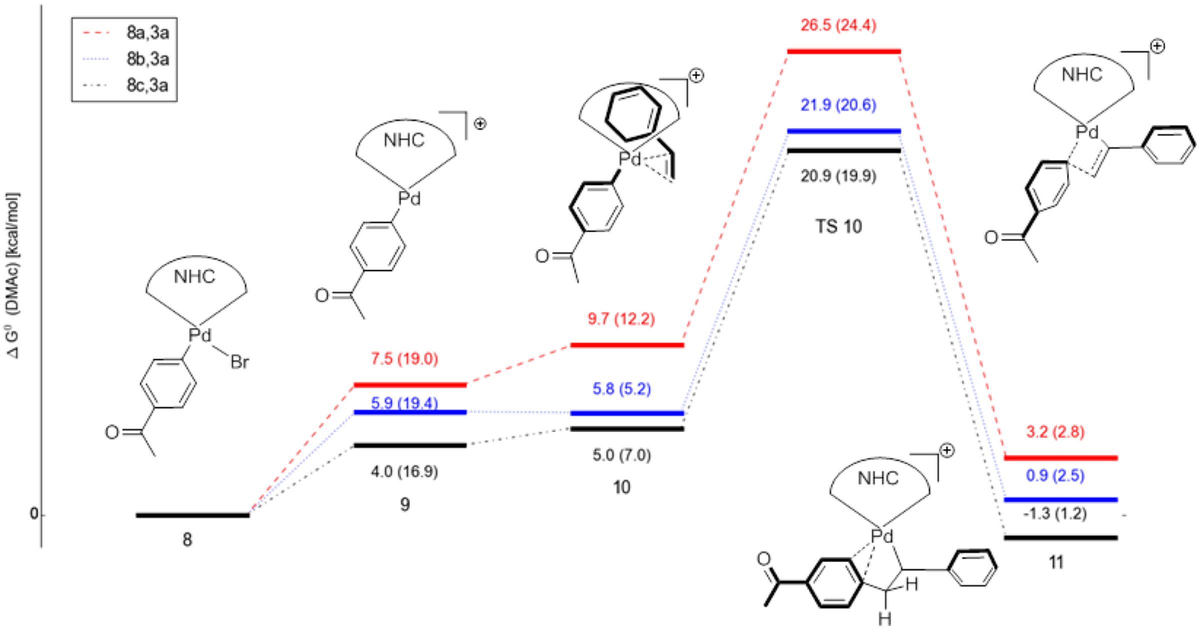


Figure 3. Insertion step of the cationic pathway with substrate **3b** (in kcal/mol; M06 energies are given in parentheses).

complexes.[33,41,50,53,115−121] We therefore can conclude that for our catalysts the most probable pathway is the cationic pathway. This sometimes leads to low selectivities, which are not observed for the neutral pathway.[122,123] Dissociation of the halide from the products of the oxidative addition **8a−c** leads to the cationic intermediates **9a−c**, and subsequent coordination of alkene **2** forms intermediates **10a−c**. From π complexes **10a−c**, insertion can occur via **TS 10a−c** (see Figure 3).

The given barrier for the insertion was calculated as the energy difference of transition state **TS 10a−c** relative to the product of the oxidative addition (**8a−c**). The reaction energy for the dissociation of the halogenido ligand (**8a−c** → **9a−c**) is

Table 4. Calculated Activation Energies ($\Delta_{TS}E$), Enthalpies ($\Delta_{TS}H$), and Gibbs Free Energies ($\Delta_{TS}G$) for the Insertion Step in the Gas Phase and Solution (DMAc) and M06/TZVP Energies for the Catalytic Systems (Catalyst, Substrate) in kcal/mol

system	$\Delta_{TS}E$(Gas)	$\Delta_{TS}H$(Gas)	$\Delta_{TS}G$(Gas)	$\Delta_{TS}G$(DMAc)	$\Delta_{TS}G$(M06)
8a, 3a	104.4	105.3	111.7	26.5	24.4
8a, 3b	113.4	110.2	120.1	32.7	24.2
8b, 3a	96.7	98.8	105.1	21.9	20.6
8b, 3b	105.3	106.3	113.6	24.8	21.2
8c, 3a	95.1	95.6	102.9	20.9	19.9
8c, 3b	103.6	104.5	111.3	24.1	21.3

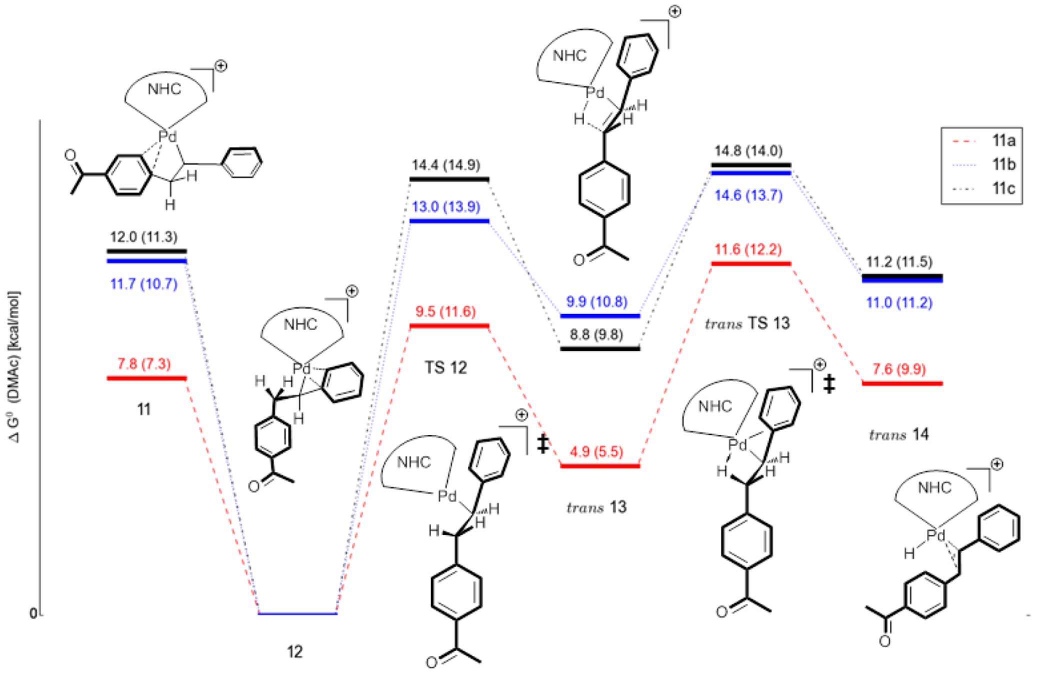


Figure 4. Intramolecular *β*-hydrogen elimination pathway for intermediates **11a–c** and substrate **3a** (in kcal/mol; M06 energies are given in parentheses).

therefore part of the effective reaction barrier for the insertion step and exerts an influence on this step. In a similar way, the energies of the insertion step would be influenced by different olefins. We therefore investigated the effect of the different aryl halogenides on the reaction energy of the dissociation step **8a–c** → **9a–c**, which is dependent on the halide coordinated to the metal center. Chloride dissociation is more endergonic than bromide dissociation by $\Delta\Delta_R G$(DMAc) = 3 kcal/mol in the case of **8b** and **8c** and 6 kcal/mol for **8a** when using B3LYP. With the M06 functional the difference in $\Delta\Delta_R G$(M06) is smaller, sometimes even less than 1 kcal/mol, because of a smaller $\Delta\Delta_R E$ of 2–3 kcal/mol with respect to B3LYP data in the gas phase. The dissociation energy is affected not only by the halide ion but also by the ability of the other ligand to stabilize the positive charge. The phenyl substituent in **8b** leads to a significant reduction in the dissociation energy with respect to **8a** (see Figure 3), and the donor effect of the *p*-methoxy group in the aromatic substituent in **8c** leads to a further decrease in energy, as the cationic charge is even more stabilized (see Figure 3). These energy differences are found in the gas phase as well as in calculations with different solvent models (see the Supporting Information) and are reflected in the total activation energies for the insertion step. Accordingly, for the reaction given in Figure 3 the activation energy $\Delta_{TS}G$(DMAc) for the insertion step is lowest for **8c** (20.9 kcal/mol), closely followed by **8b** (21.9 kcal/mol), and is significantly higher for **8a** (26.5 kcal/mol). The differences are more pronounced in the gas phase. Considering the total free energy, the transition states **TS 7** are calculated to have the highest energy in the cycle and thus should have the lowest probability at equilibrium. However, we are interested in the influence on the reaction rates. The oxidative addition step is irreversible, so no reverse reaction toward the reactants is possible. The insertion step also leads to a deep minimum (**12**; see below). This allows for the determination of the reaction kinetics of these steps from the size of the largest effective reaction barrier, which is also called the energetic span.[124]

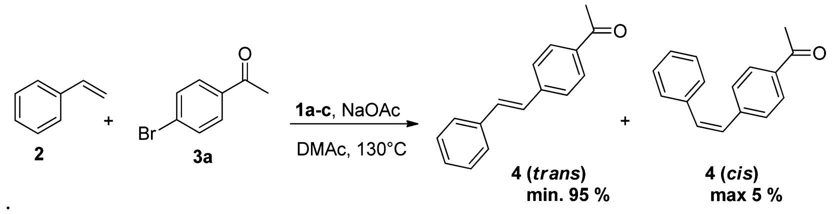
In all cases investigated at the B3LYP/6-31G* level of theory, the insertion step is calculated to have a higher reaction barrier than the oxidative addition step (see Tables 3 and 4). The calculations at the M06/TZVP level of theory agree well, as the insertion step also has the highest barrier, except that the oxidative addition for substrate **3b** and complexes **5b** and **5c** is calculated to have slightly higher barriers by <1 kcal/mol. Therefore, it is highly likely that the insertion is the rate-determining step, at least for the bromoaromatic **3a**. The catalyst efficiency therefore should be determined by the activation energy of intermediates **8a–c**, so *p*-methoxyphenyl substituted catalyst **1c** is generally predicted to be the most efficient catalyst, in agreement with the experimental results.

Using B3LYP, the barrier of the insertion step increases in the case of *p*-chloroacetophenone **3b**, the reaction of methyl-

Table 5. Selectivity of the *β*-Hydrogen Elimination in the Case of 12a (Energies in kcal/mol)

intermediate	Δ*E*(Gas)	Δ*H*(Gas)	Δ*G*(Gas)	Δ*G*(DMAc)	Δ*G*(M06)
12a	0.0	0.0	0.0	0.0	0.0
***cis* 13a**	8.6	7.8	7.3	7.6	7.8
***trans* 13a**	5.7	4.6	3.8	4.9	5.5
***cis* TS 13a**	16.6	13.5	13.2	13.4	13.2
***trans* TS 13a**	12.4	8.6	8.3	11.6	12.2

Scheme 4. Observed Selectivity in the Heck Reaction of 3a and 2 Catalyzed by 1a−c



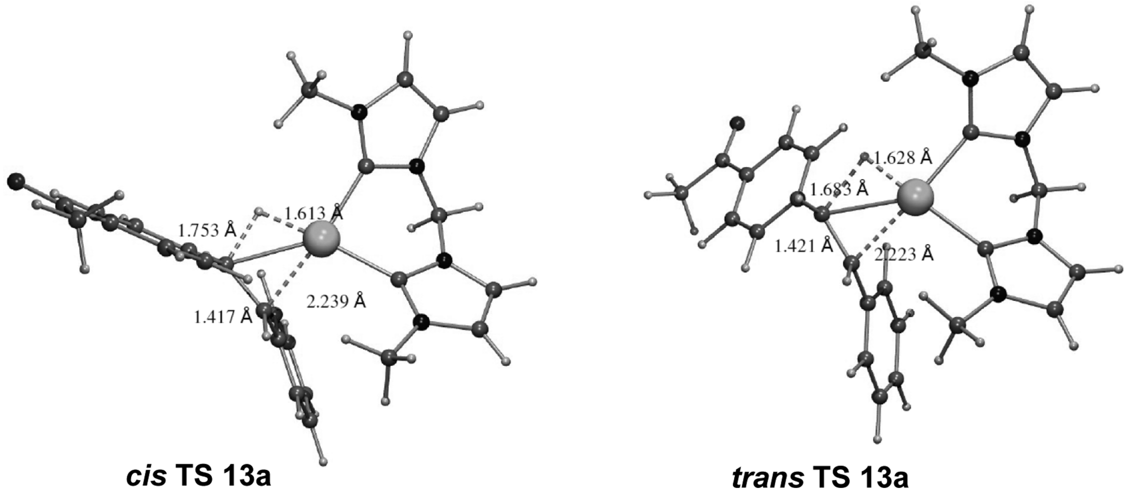


Figure 5. Transition states for *cis* and *trans β*-elimination.

substituted intermediate **8a** is calculated to be even less competitive against the aryl-substituted palladium species **8b** and **8c** (see Table 4). The latter result also agrees with the previously published experimental data, in which little turnover in the reaction of chloroarene **3b** and styrene **2** catalyzed by catalyst **1a** was observed.[50]

β-Hydrogen Elimination. To restore the double bond and release the product of the reaction, a proton has to be abstracted from the coupling products **11a−c**. This reaction step also determines which isomer (*cis*/*trans*) of the product **4** is formed. This *β*-hydrogen elimination may occur via different pathways: (a) it may occur directly by intermolecular deprotonation through a base; (b) it may be facilitated by prior formation of an agostic bond between the *β*-hydrogen and the palladium center (intermediates ***trans* 13a−c**);[125] (c) the reaction may proceed by intramolecular *β*-elimination of palladium from the agostic bond.

The main differences in Gibbs free energy between the catalysts can be found for the intermediates of the methyl-substituted complex **11a** and the aryl-substituted complexes **11b** and **11c**. In Figure 4, the preferred minima **12a−c** are plotted as the reference state. We investigated the reaction barriers for both the formation of the agostic bond and the intramolecular *β*-elimination. The formation of the agostic bond via ***trans* TS 12** is reversible, and therefore, the overall reaction barrier was calculated from the preferred minimum **12** to the transition state of the intramolecular *β*-elimination, ***trans* TS 13**. Overall, *β*-elimination was found not to be a rate-determining step ($\Delta_{TS}G$(DMAc) < 15 kcal/mol; Table 5). The M06/TZVP single-point calculations also agree well for this part of the mechanism.

We also investigated the *cis*/*trans* selectivity for **1a** in the reaction with **3a** (see Scheme 4). From our experimental data it is known that the *trans* product **4(*trans*)** is formed preferentially. The high *trans* selectivity in the reaction of olefin **2** with **3a** is observed for all three catalysts **1a−c.**[50] In the gas phase, *trans β*-elimination has a lower Gibbs free activation energy by $\Delta\Delta_{TS}G$(Gas) = 4.9 kcal/mol, predicting quantitative *trans* selectivity. The solvent-corrected $\Delta\Delta_{TS}G$(DMAc) value of 1.8 kcal/mol is smaller, explaining the observation of up to 5% *cis* product for the alkyl-substituted ligand[50] in the reaction with **3a**. When using M06 single-point calculations, $\Delta\Delta_{TS}G$ decreases further to about 1 kcal/mol. However, the selectivity is preserved.

From the transition states shown in Figure 5, it is obvious that the energy for the *cis* elimination is higher because of steric repulsion, as the aryl rings are forced into an eclipsed position. Also, the differences in bond lengths reflect the fact that ***trans* TS 13** is the earlier transition state, in line with the Hammond

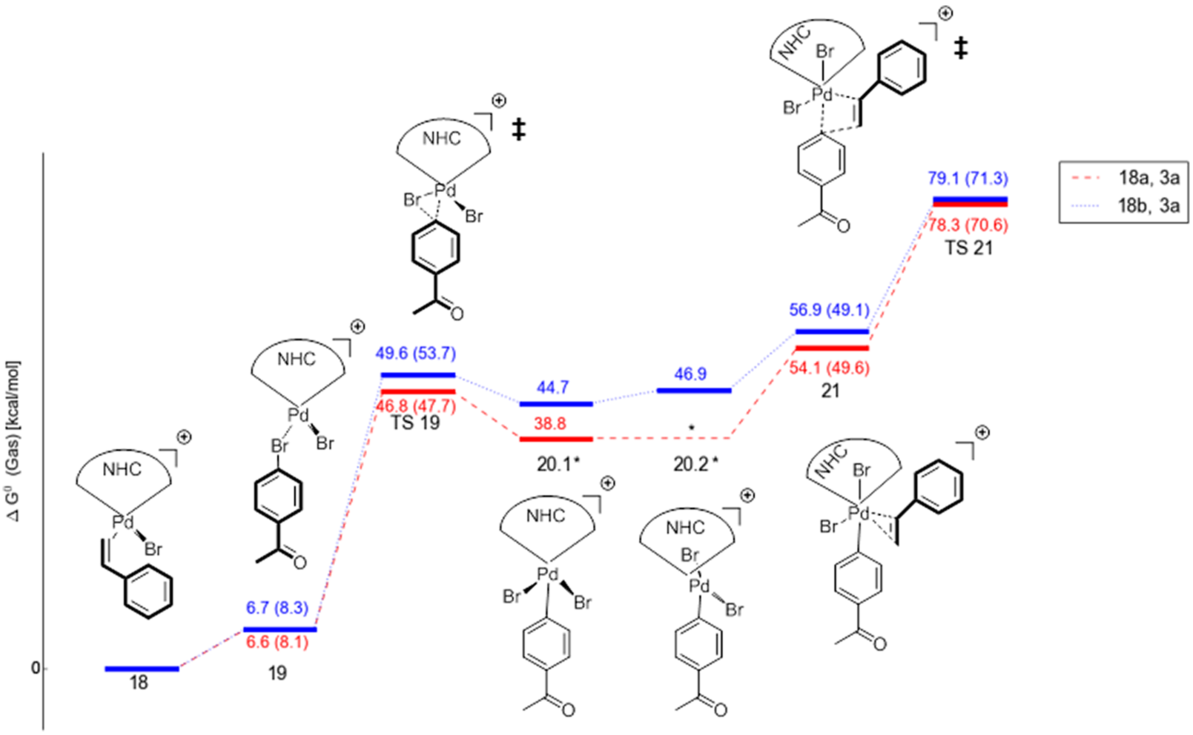


Figure 6. Oxidative addition and insertion for the complexes **18a** and **18b** in the +II/+IV mechanism. Energies are in kcal/mol, with M06 energies given in parentheses. *The calculations failed in some cases for the enantiomers **20.*x*** and therefore have not been included.

postulate (i.e., by the longer Pd−H bond and the shorter C−H$^{\beta}$ bond in Figure 5).

After intramolecular β-elimination, the substituted stilbene product **4** remains coordinated in the π complex **14**. The product **4** may then readily dissociate, forming the cationic palladium hydride **15**, which in turn can be coordinated by other π systems. Alternatively, it can be coordinated by an anion (e.g., bromide) to form the neutral palladium hydride **16**. The energies and geometries of these intermediates can be found in the Supporting Information. Any one of these intermediates is susceptible to reductive elimination by the base, thereby completing the catalytic cycle. According to reports in the literature, the reductive elimination in the Heck reaction is believed to be a fast step.[22,66,98] However, alternative elimination pathways with higher barriers have also been proposed.[74] A systematic study of these intermolecular proton transfer/elimination pathways is beyond the scope of this study and likely also not sufficiently accessible with our static DFT methodology.

Alternative Mechanisms. Apart from the cycle that involves the palladium oxidation states 0 and +II, other alternative mechanisms are also possible. As we recently showed for methane oxidation by this type of complex, catalytic cycles involving higher oxidation states cannot be excluded a priori (see Scheme 1, Q3).[119] Also, for the Heck reaction palladium(IV) complexes were recently shown to be accessible intermediates for PCP pincer complexes,[80,81] and the possibility of a mechanism via palladium(IV) intermediates has also been discussed in the literature.[79,126] Accordingly, the methyl- and phenyl-substituted complexes **1a** and **1b** were subjected to a study of different +II/+IV mechanisms in the gas phase using substrate **3a**. The mechanism with the lowest activation energies for the oxidative addition is presented here (Figure 6). As all of the other pathways lead to the same insertion step, we will not discuss them in detail, but further details are provided in the Supporting Information. Reaction energies were calculated relative to the cationic palladium(II) complexes **18a** and **18b** in order to make a solvent correction for the charge separation from **1a,b** + **2** → **18a,b** + Br^- unnecessary. From the π-coordinated complexes **18a** and **18b**, the σ-bromide complexes **19a** and **19b** can be formed by exchanging **2** with **3a**. In contrast to the 0/+II mechanism, no minimum for a π complex could be found. The reaction barrier $\Delta_{TS}G$(Gas) for the oxidative addition was calculated to be about 50 kcal/mol, independent of the functional used, and is about twice as high as that for the rate-determining step of the 0/+II mechanism (see Figure 3). It was also calculated to be so strongly endergonic that the reverse reaction has a $\Delta_{TS}G$(Gas) of less than 10 kcal/mol, implying that the oxidative addition step is reversible.

After oxidative addition, isomerization of **20.1** is necessary in order for styrene **2** to be coordinated at the *cis* position relative to the aryl ring as in **21**, as there is no transition state that directly connects **19** to an isomer of **20** that can coordinate styrene in the *cis* position relative to the aryl ring. These isomers would need the bromine to be in the Pd−C plane, but no minima for such isomers could be obtained. As the activation energies $\Delta_{TS}G$ for a +II/+IV mechanism are prohibitively high (greater than 70 kcal/mol, independent of the functional/basis set used), a 0/+II mechanism should be clearly preferred.

Figure 7 summarizes the calculated B3LYP energies for the most probable reaction mechanism established in this study, starting with the palladium(0) active species **5a−c** at the origin. The diagram clearly shows that the oxidative addition step and the insertion step are irreversible and that the reaction proceeds smoothly downhill.

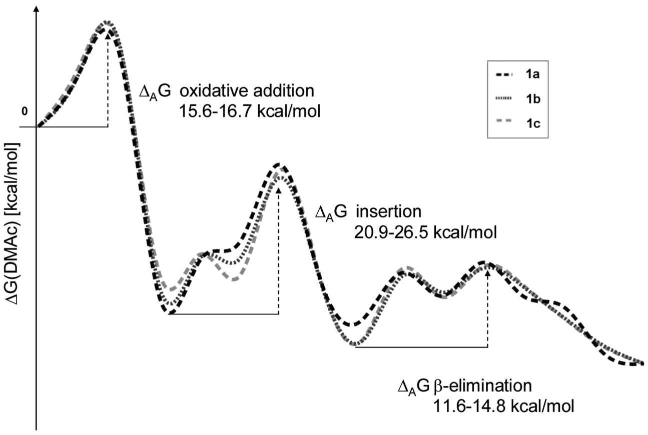


Figure 7. Overview of the complete Heck catalytic pathway for catalysts **1a**−**c** and substrate **3a**.

■ CONCLUSION

The mechanism of the Heck reaction catalyzed by chelated bis-NHC palladium complexes is predicted to follow a cationic mechanism between the palladium oxidation states 0/+II. The influence of the ligand on the oxidative addition step was found to be dependent on the level of theory. According to our results, olefin insertion is the rate-determining step. Our mechanism predicts *p*-chloroacetophenone to react more slowly than *p*-bromoacetophenone, in agreement with the experimental data. Furthermore, the observed *trans* selectivity of the reaction of *p*-bromoacetophenone with styrene can be explained by our DFT study. Possible mechanisms involving the palladium oxidation states +II and +IV are not competitive, considering the significantly higher barriers. According to our calculations, the main reason for the observed rate differences is the different stabilization of the positive charge in the insertion step, which explains the experimentally observed positive effect of π-donor-substituted aryl ligands on the reaction rate in the Heck reaction.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete ref 82 and Cartesian coordinates, energies, and additional data for solvent calculations (DMF and DMSO) and other functionals of intermediates and transition states. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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