L. Fiebig *et al.*, *Eur. J. Mass Spectrom.* **21,** 623–633 (2015)
Received: 8 December 2014 ■ *Revised: 6 February 2015* ■ *Accepted: 10 February 2015* ■ *Publication: 13 March 2015*

EJMS EUROPEAN JOURNAL OF MASS SPECTROMETRY
Special Issue Celebrating the 20th Anniversary of *EJMS—European Journal of Mass Spectrometry*

Individual steps of the Mizoroki–Heck reaction and intrinsic reactivity of intermediate organopalladium complexes studied in the gas phase

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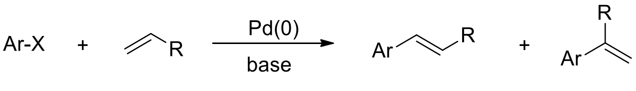
The mechanism of the Mizoroki–Heck reaction (MHR) was analyzed by collision-induced dissociation (CID) tandem-mass spectrometry and gas-phase ion/molecule reactions (IMRs) as well as by DFT computational analysis. The MHR was performed in the gas phase and the intrinsic reactivity of important intermediates was examined individually. Kinetics and substituent effects of cationic palladium-PCy_3-aryl complexes (Cy = cyclohexyl) with 2,3-dimethylbutadiene in the MHR were analyzed via IMRs and CID. The kinetics and ion structures of the species involved in the olefin insertion, i.e., the carbopalladation, were investigated. Moreover, linear free-energy correlations were applied and a concerted mechanism proceeding via a four-membered transition state for the carbopalladation step that exhibited only a minor charge separation was deduced.

Keywords: gas-phase Mizoroki-Heck reaction, ion molecule reactions, Hammett relation, reaction mechanism

Introduction

Palladium-catalyzed coupling reactions, such as the Mizoroki–Heck reaction (MHR) are extremely valuable synthetic tools in modern organic chemistry.[1] In the initial studies reported by Mizoroki, Heck, and co-workers, aryl triflates or aryl halogenides were coupled with olefins in the presence of a palladium(0) catalyst and a base (Scheme 1).[2–4]

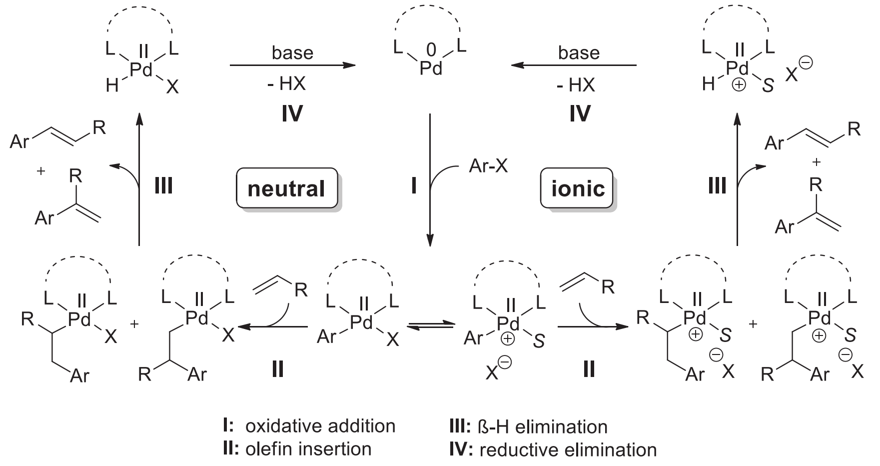
The elementary steps of the MHR are widely accepted and are similarly in both a neutral or an ionic catalytic cycle (Scheme 2).[5–9] Initially, the aryl substrate and an (*in situ* formed) Pd(0) species undergo an oxidative addition (step I) that yields an intermediate Pd(II) aryl complex of the type [Pd(phosphine)(Ar)(I)] and $[Pd(phosphine)(Ar)(S)]^+I^-$, respectively (S = solvent molecule). In the subsequent carbopalladation step, the Pd aryl complex reacts with the olefin in a *syn*-insertion leading to a σ-Pd-alkyl complex (step II). Subsequent β-Pd hydride elimination (step III) yields the linear or branched coupling product and a Pd–H complex that is finally transformed into the Pd(0) starting complex by a base-mediated reductive elimination (step IV).



Scheme 1. Pd(0)-catalyzed MHR.

Detailed kinetic analyses of the MHR revealed that the rate-determining step strongly depends on the electronic and steric properties of the reactants. However, many

ISSN: 1469-0667
doi: 10.1255/ejms.1310

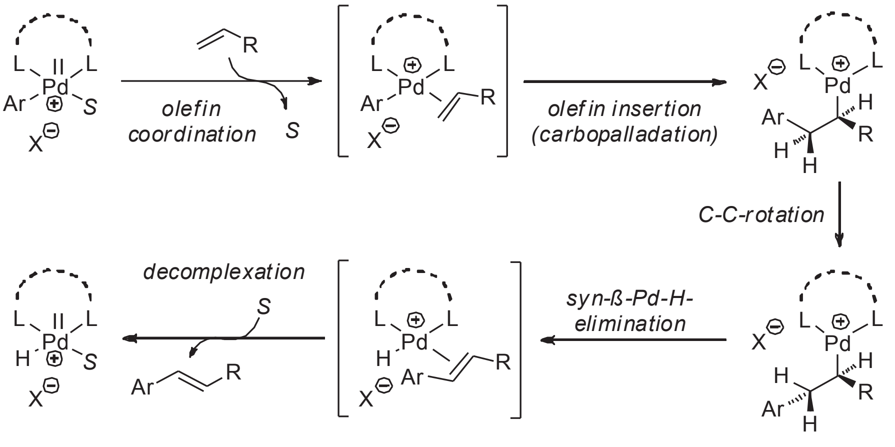


Scheme 2. Postulated neutral and ionic catalytic cycle of the MHR (*S* = solvent, Ar-X = aryl halide).[5–9]

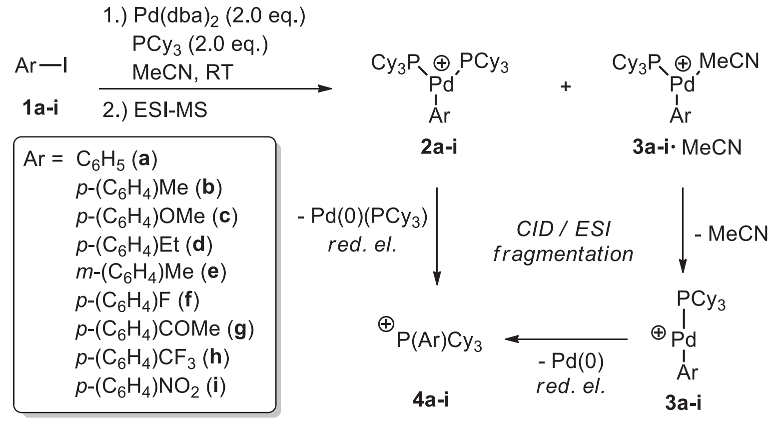
studies consistently found that the oxidative addition of aryl triflates and aryl iodides is usually fast and therefore not rate limiting.[8,10–13] Hence, in the MHR of these aryl substrates one of the subsequent steps is the slowest of the reaction, i.e. the kinetic bottleneck (Scheme 3). Extensive experimental investigations suggest that either the olefin coordination, the olefin insertion,[11,12,14,15] or even the β-hydride elimination[16,17] can determine the overall reaction rate. However, an individual examination of the carbopalladation or the β-hydride elimination remains difficult as these reaction steps follow the oxidative addition.

The elucidation of reaction mechanisms governed by homogeneous catalysts is a complex analytical problem, but electrospray ionization mass spectrometry (ESI-MS)[18–20] combined with tandem mass spectrometry (MS/MS)[21] proved to be a powerful and versatile approach to transfer even labile and reactive species from complex reaction solutions into the gas phase for further analysis. This strategy benefits from the facile coupling of a microreactor or a reflux apparatus to the mass spectrometer allowing a continuous infusion of the reaction solution into the ESI-MS instrument and thereby the monitoring and characterization of ionic reaction intermediates and products formed during the reaction.[22–25] Especially, the ionic catalytic cycle of the MHR is very suitable for an online-ESI-MS analysis, as a number of studies document. It was possible to study key intermediates of Mizoroki–Heck type reactions,[26] those of the Heck–Matsuda reactions (coupling of arene diazonium salts with olefins),[27,28] the tandem-Heck lactonizations,[29] oxyarylations (Oxa–Heck),[30] and the dehydrogenative MHR.[31]

Once transferred into the gas phase, collision-induced dissociation (CID) experiments of the reaction intermediates can afford characteristic fragmentation patterns that contain valuable pieces of information often enabling structural analysis. Furthermore, ion/molecule reactions (IMRs) between stored ions and neutral reagents infused into the buffer gas flow of the ion trap can be performed in an ion trap mass spectrometer.[32–34] In doing so, intrinsic structure–reactivity relationships of the ionic reaction intermediates can be studied *in vacuo* without the influence of solvent molecules



Scheme 3. Stepwise C(sp^2)-C(sp^2) coupling following the ionic MHR mechanism, including olefin coordination, olefin insertion, and syn-β-H-elimination (formation of the linear coupling product) (*S* = solvent, Ar = aryl moiety, X = halide).



Scheme 4. Oxidative addition of aryl iodides 1 **and Pd(0) and transfer of complex ions** 2 **and** 3**·MeCN into the gas phase via (+)ESI-MS. The complex ions [Pd(PCy$_3$)(Ar)]$^+$ (**3**) and [P(Ar)Cy$_3$]$^+$ (**4**) represent CID and ESI fragments of** 3**•MeCN and** 2**, respectively (see Figure S3, SI; Cy = cyclohexyl)).**

and counter ions, as numerous studies document.[32,35–37] This is particularly useful if the intermediates of interest tend to form complex equilibria and aggregates in solution, which is often the case in organometallic catalysis. Gas-phase IMRs, for instance, allow us to investigate the nature of the coordination sphere of organometallic complexes,[38–41] to screen the reactivity of potential catalysts in polymerization reactions,[42,43] or to examine complete transition-metal catalytic cycles.[44,45]

Herein, we report a stepwise examination of the MHR between aryl iodides and 2,3-dimethylbutadiene (DMB). After solution-phase *in situ* preparation, the intermediate Pd aryl complex ions [Pd(PCy$_3$)(Ar)]$^+$ were reacted with DMB under well-defined conditions in the gas phase (Cy = cyclohexyl). The use of the P(Cy$_3$) ligand and DMB in the gas phase allows us to investigate the kinetics and substituent effects of the carbopalladation and β-hydride elimination reaction steps. Especially, the selection of the P(Cy$_3$) ligand excludes aryl moiety scrambling processes in the respective [Pd(PCy$_3$)(Ar)]$^+$, which substantially complicate such experiments in the presence of triphenylphosphine ligands.[46] Additionally, the symmetric molecule DMB offers only olefinic protons on carbons 1 and 4 for the β-hydride elimination reaction, which exclusively leads to the linear MHR product with the formation of the branched regioisomer (see Schemes 1 and 5) excluded. The identity of IMR product ions as well as all other relevant ions is reliably confirmed by accurate mass measurements, MS/MS and density functional calculations.

Experimental section

Mass spectrometry

All MS^n experiments and gas-phase IMRs were performed on an LTQ Orbitrap hybrid instrument (Thermo Fisher, Bremen, Germany) equipped with a heated electrospray ionization source, linear ion trap, octapole collision cell, and an Orbitrap mass analyzer[47,48] capable of measurements with a high mass accuracy and an elevated resolving power. For (+)ESI-MS analysis, diluted solutions of the *in situ* formed aryl palladium complex ions **2** and **3**•MeCN were infused into the ion source *via* a syringe pump (flow rate 5 µL min^{-1}, ESI heater temperature 50°C, capillary temperature 275°C). Typical spray voltages were 3.0–3.5 kV. Stable spray conditions were achieved by the use of sheath and sweep gases (≥99.999% N$_2$).

MS^n experiments (collision gas helium, ≥99.999% He) were conducted in the linear ion trap with a collision energy adjusted to achieve extensive fragmentation.[49–51] Exact ion masses were measured in the Orbitrap analyzer [R_{FWHM} = 30.000 (FWHM = full width at half height)], which was externally calibrated with caffeine, trileucine, and thymopentin before and after each measurement. The sum formulas of all the presented ion structures were consistent with the experimentally determined ion masses ($\Delta m \leq 3$ ppm) and match the calculated isotope distributions (e.g., see Figure 1). Data acquisition was performed with the Thermo Fisher LTQ Tune Plus software. For data processing and analysis the Thermo Fisher software Xcalibur 2.1.0 was used.

Oxidative addition of iodides and Pd(0)

In a flame-dried and argon-flushed Schlenk flask the respective iodide **1** (0.02 mmol, 1.0 equiv.), bis(dibenzylideneacetone) palladium (23.0 mg, 0.04 mmol, 2.0 equiv.), and tricyclohexylphosphane (0.04 mmol, 11.2 mg, 2.0 equiv.) were suspended in dry acetonitrile (8 mL) under an argon atmosphere. The resulting solution was stirred at room temperature under an inert-gas atmosphere until oxidative addition, i.e. the formation of the complex ions **2**, **3**, and **3**•MeCN were observed in the (+)ESI mass spectrum (0.5–4 h).

IMRs and determination of second-order rate constants

IMRs were performed inside the LTQ part of the mass spectrometer. To this end, the helium buffer-gas supply of the LTQ was modified according to Gronert,[32,52] O'Hair and co-workers,[33,44] and Harman and Blanksby,[34] as described in detail elsewhere.[45,46] In brief, neutral reagents were injected

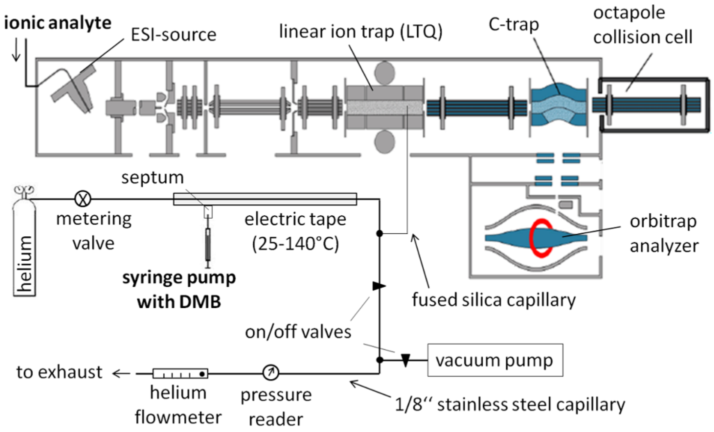


Figure 1. Schematic view of the modified helium buffer-gas supply to a LTQ Orbitrap hybrid mass spectrometer that allows the quantity-controlled introduction of neutral reagents into the linear ion trap. Illustration reproduced and modified with the kind permission of the manufacturer.[45,46]

into the LTQ helium flow via a septum using a pump-driven syringe (Figure 1). An open-split gas-flow divider that regulates the LTQ default pressure was replaced by a fused-silica restriction capillary (inner diameter 0.2 mm, length 25 cm) to prevent leakage of the gas mixture into the environment. As a consequence, the LTQ pressure was adjusted to the default trap pressure manually. Complete evaporation of the neutral reagents was assured by heating of the gas flow with an electric tape wrapped around the stainless steel helium capillary (ca. 130°C). To determine the molar neutral reagent/helium ratio, the flow rates of both the neutral reagent and the helium were measured, the latter using a Swagelok gas-flow meter. The experimental setup was validated using the gas-phase nucleophilic substitution of a bromide anion and methyl iodide and d_3-methyl iodide, respectively, as a test reaction.[34,44,53]

For the gas-phase carbopalladation reactions, DMB was introduced into the helium flow and reacted with Pd complex ions $[Pd(PCy_3)(Ar)]^+$ (**3**) isolated and stored in the ion trap (isolation width 8 Da). Kinetics of the olefin insertion were determined at reaction times of 0.03–20 ms. The reported rate constants are the averages of four independent measurements at different flow rates of DMB (0.5–1.0 µL min^{-1}) and of helium (195–215 sl h^{-1}). Prior to each experiment, a delay time, typically of 10–20 min, was kept to ensure constant-concentration conditions of neutral reagents inside the ion trap (i.e., no observable change of the precursor ion/product ion ratio at a specific reaction time). Further details regarding the determination of second-order rate constants are given in the Supplementary Information (Figures S1 and S2).

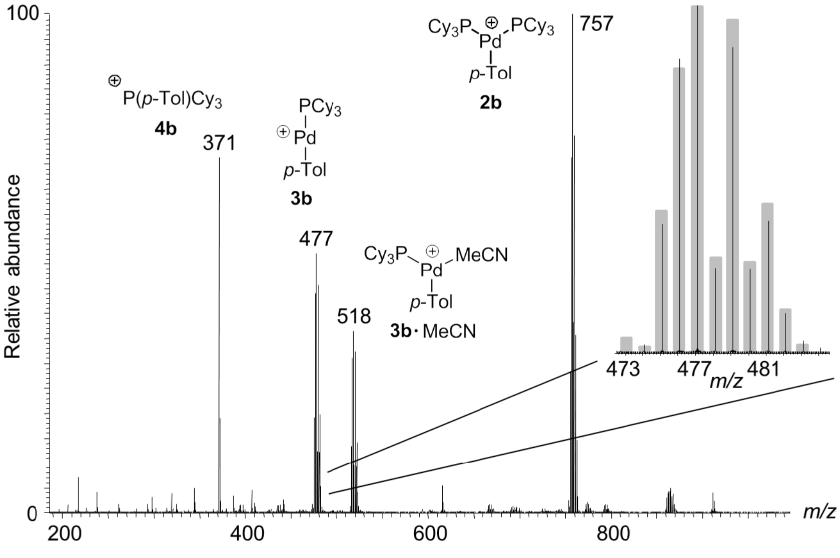


Figure 2. (+)ESI-MS spectrum of a reaction mixture of *p*-iodotoluene (1b, 1.0 equiv.), Pd(dba)$_2$ (2.0 equiv.), and PCy$_3$ (2.0 equiv.) in acetonitrile at room temperature under an inert gas atmosphere (inset: the theoretical isotopic distribution of $[Pd(PCy_3)(p\text{-}Tol)]^+$, 3b, is compared to the experimental isotopic pattern to document the consistency).

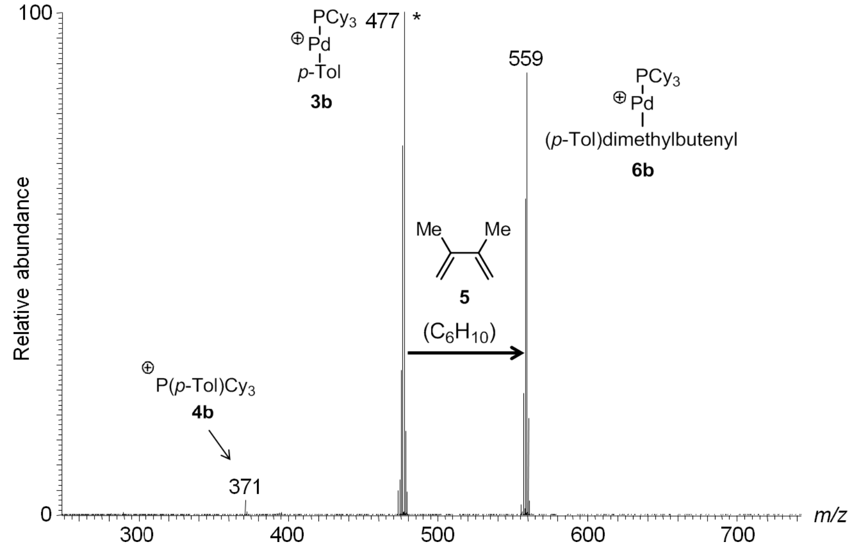


Figure 3. IMR of the Pd complex ion 3b **and DMB (**5**). The precursor ion is marked with an asterisk (isolation window 8 Da, ca. 10^{11} molecules DMB versus 10^4 ions in the LTQ).[32,45,46]**

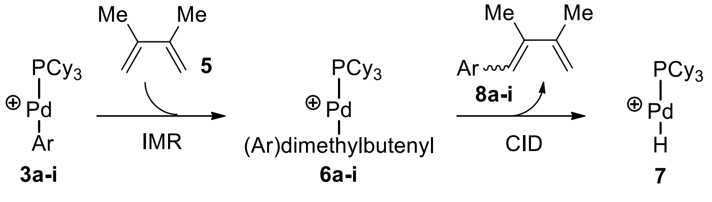
All IMRs were performed without the application of additional collision-activation energy. Experimental and theoretical data evidence that ions stored in quadrupole ion traps (QITs) were effectively thermalized by multiple collisions with the surrounding buffer-gas atoms. Therefore, the stored ions exhibited a Boltzmann energy distribution because the rapid energy exchange between the stored ions and the buffer gas outperformed the impact of the electric quadrupole field on the internal energy of the ions.[32,54] The effective temperatures of ions stored in QIT instruments at room temperature are in the range of 300–340K.[52,55] As a result, the ion trap environment is perfectly suitable for the investigation of quasi-thermal IMR.

Quantum chemical calculations

Theoretical calculations were carried out using the TURBOMOLE 6.6 program package.[56] For each of the ions **3a**•DMB, **6a**, and **7**•(Ph)DMB, a range of conformations was considered (data not shown). The most stable conformers we identified are shown in Figure 3. All the reported geometries were optimized at the DFT level of theory using the BP86 functional. The cc-pVTZ basis set was used for carbon, hydrogen, and phosphorus. The Stuttgart–Koeln MCDHF RSC ECP[57] basis set was used for palladium. To identify the optimized geometries as local minima of the potential energy surface (no imaginary frequencies), vibrational frequencies were calculated using the same functional and basis set as used for the geometry optimizations.

Results and discussion

To gain access to ionic Pd aryl complexes, the aryl iodides **1a** were reacted with Pd(dba)$_2$ (dba = dibenzylideneacetone) and PCy$_3$ in acetonitrile (Scheme 5). (+)ESI-MS analysis of the reaction mixture showed the ionic products of the oxidative addition, i.e. the complex ions **2**, **3**, and **3**•MeCN, after 2.5–4 h (Figure 1). According to the literature[58–60] and to previous studies in our group,[46] the Pd complexes [Pd(PCy$_3$)$_2$(Ar)]I und [Pd(PCy$_3$)(MeCN)(Ar)]I are formed in solution under these reaction conditions. During the ESI process, the loss of iodide yields the observed ionic complexes **2** and **3**·MeCN. The detected ions **3** and **4** represent *in-source* fragments of **3**•MeCN and **2**, respectively, and their formation is also observed in the CID spectra of **3**•MeCN and **2** (Figures S3). The product-ion spectrum of [Pd(PCy$_3$)(Ar)]$^+$ (**3**) is characterized by the extensive fragmentation of the phosphine ligand, including the neutral losses of cyclohexene (C$_6$H$_{10}$) and cyclohexane (C$_6$H$_{12}$), as well as the reductive elimination of Pd(0), to yield the phosphonium ion [P(Ar)Cy$_3$]$^+$ (**4**). The latter



Scheme 5. Gas-phase carbopalladation via IMR followed by β-hydride elimination induced upon CID. The corresponding MHR products are observed as neutral loss in the CID spectra of complex ions 6a–6i.

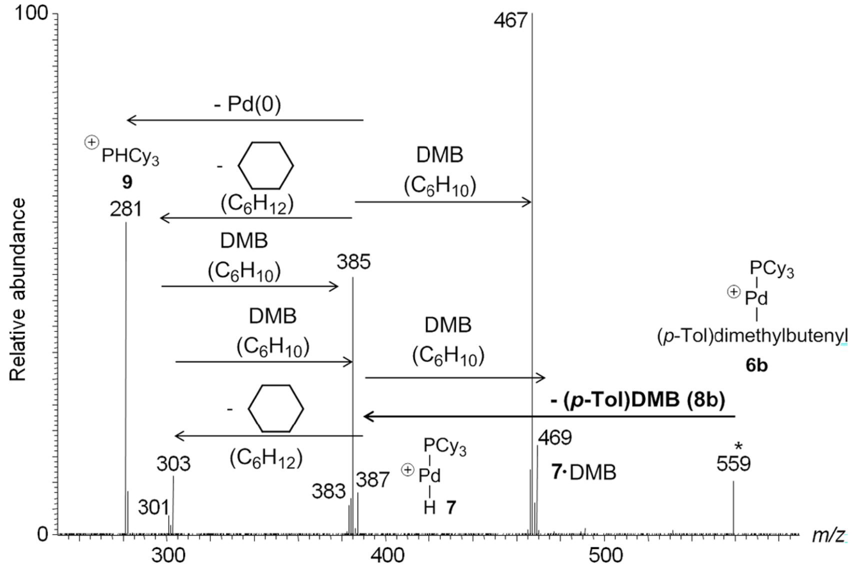


Figure 4. MS^3 product ion experiment of complex ion 6b. The precursor ion is marked with an asterisk and was isolated monoisotopically.

dissociates by subsequently losing three cyclohexene units (Figure S4).

The Pd complex ions **2**, **3**, and **3**•MeCN were isolated in the linear ion trap part of the instrument and were allowed to react with DMB (**5**) in the gas phase. However, only the complex ions $[Pd(PCy_3)(Ar)]^+$ (**3**) reacted with DMB under the formation of product ions **6**, as Figure 4 illustrates. This IMR proceeds with a mass increase of 82 Da (C_6H_{10}) relative to the corresponding precursor ion and is accompanied by a minor fragmentation reaction to the phosphonium ion **4** [Figure S4(a)].

Individual CID experiments of all nine IMR products **6a**–**6i** led to the formation of a common and characteristic product ion at *m*/*z* 387, matching the Pd hydrido complex $[Pd(PCy_3)(H)]^+$ (**7**). This ionic product indicates the release of the C–C coupling product; in the exemplary case shown in Figure 5, the *para*-tolyl-substituted DMB **8b** (see also Scheme 5). The

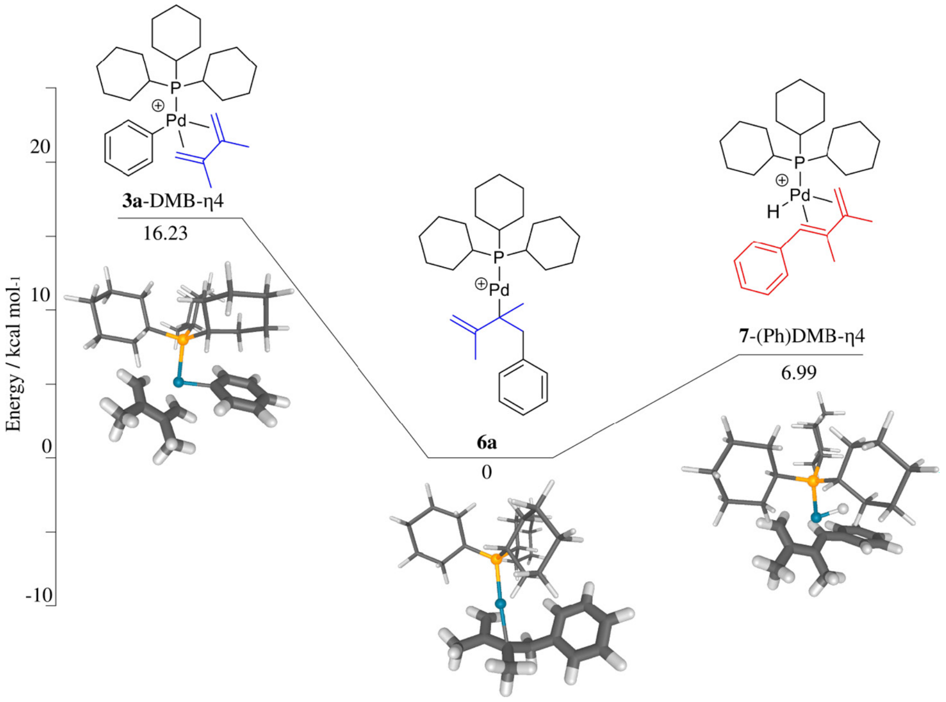
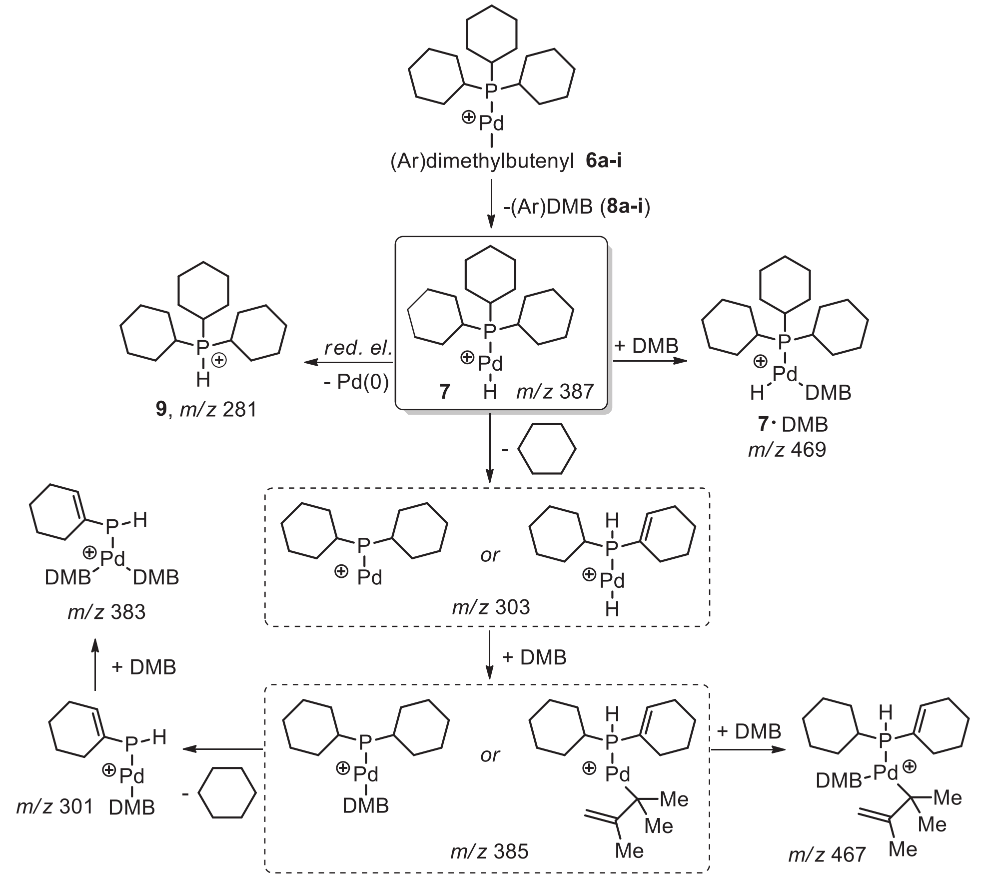


Figure 5. Calculated relative electronic energies for the stepwise carbopalladation and β-H elimination (DFT level of theory using the BP86 functional in a Stuttgart–Koeln MCDHF RSC ECP//cc-pVTZ basis).



Scheme 6. Supposed CID fragmentation pathway of complex ions 6 **based on the CID fragmentation pattern of complex ion** 7 **and of the fragment ions at *m/z* 281, *m/z* 385, and *m/z* 467. The elemental composition of the ions matches the respective accurate ion mass measured, but the depicted structures are not further verified and serve only to illustrate the proposed fragmentation pathway (*red. el.* = reductive elimination).**

identity of the Pd hydrido complex [Pd(PCy$_3$)(H)]$^+$ (**7**) ion was independently confirmed by an accurate ion-mass measurement and by careful evaluation of its experimental isotopic distribution (Figures 4 and S5). The reversed addition reaction, i.e. a neutral loss of DMB, was not observed in the CID experiments of the complex ions **6a**–**6i**. This observation, together with the formation of the hydrido complex ion **7**, evidences the completion of the gas-phase MHR between [Pd(PCy$_3$)(Ar)]$^+$ (**3**) and DMB. These experimental findings clearly document the gas-phase olefin insertion via IMRs and the ultimate formation of the σ-complex ions of the type [Pd(PCy$_3$)σ-(Ar-dimethylbutenyl)]$^+$ (**6**) which then undergo β-H elimination upon CID, generating the palladium hydrido species **7** and the MHR product, (Ar)DMB (**8**), as a respective neutral loss (Scheme 5). As the symmetric DMB molecule features olefinic protons for the β-hydride elimination reaction only on carbons 1 and 4, only the linear MHR product 1-(*para*-aryl)-2,3-dimethylbutadiene can be formed, with the formation of the branched regioisomer (see Schemes 1 and 5) excluded. However, the stereochemistry of the gas-phase MHR product cannot be addressed as the differentiation between the isobaric *E*-and Z-conformers is not possible by means of MS.

The MS^2-product ion spectra of all the σ-complex ions [Pd(PCy$_3$)σ-(Ar-dimethylbutenyl)]$^+$ (**6a**–**6i**) show the Pd hydrido complex **7**, aside from identical other fragment ions (Figure S5). Based on MS^4 product ion experiments of the fragment ions at *m/z* 281, *m/z* 385, and *m/z* 467 (Figure S6) as well as the observed fragmentation patterns of [Pd(PCy$_3$)(Ar)]$^+$ (**3**) and P(Ar)Cy$_3^+$ (**4**), these fragment ions are secondary fragmentation products of the initially formed Pd hydrido species **7** (Scheme 6).

Secondary fragmentation reactions are only observed in QIT CID product-ion experiments when broadband activation[61,62] or high activation energies are applied.[63,64] The secondary fragmentation processes observed in the present experiment performed at low activation energies near the threshold energy evidence the instability of the primarily formed product ion [Pd(PCy$_3$)(H)]$^+$ (**7**) (Figure 4). Since the Pd cation in the hydrido complex ion [Pd(PCy$_3$)(H)]$^+$ (**7**) receives only limited stabilization by the PCy$_3$-ligand and has a strong electron deficiency (only 12 valence electrons), it immediately attaches a DMB molecule still present in the gas phase of the QIT to gain further stabilization or it dissociates to form more-stable fragment ions, as shown in Figure 4. Thus, fragment ions **7**·DMB (*m/z* 469) and **9** (*m/z* 281) result from another IMR process with DMB still present in the QIT and reductive elimination of Pd(0), respectively. The fragment ions at *m/z* 301, 303, 383, 385, and 467 can be explained by a combination of cyclohexane neutral loss and adduct formation with DMB, as Scheme 6 illustrates. The identity of these ions was reliably confirmed by accurate mass measurements, ruling out the possibility that these signals represent Pd complex isotopologues.[1]

The MS/MS-based results provide essential pieces of information on the identity of complex ions **6a**–**6i**, but it is possible that during the IMR both olefin insertion and β-H elimination take place, leading to a complex ion $[Pd(PCy_3)(H)(Ar\text{-}DMB)]^{+\cdot}$, [**7**•(Ar)DMB], as the final IMR product. As it is impossible to distinguish between the isobaric species **6** and **7**•(Ar)DMB by means of MS, we performed a detailed computational analysis of all the Pd complex ions relevant for olefin coordination, carbopalladation, and β-H elimination in the gas phase (Figures 5 and S8). We report only the relative electronic energies because of the enormous complexity of the ions under investigation. For this reason we were unable to compute transition states, although this would be highly desirable. Figure 5 indicates that the DMB insertion, starting from the **3a**•DMB-η^4 adduct complex, is an exothermic process. The minimum enthalpy of association for a complex formed by an IMR association reaction under the given circumstances to be stable in a QIT has been roughly estimated to be about 25 kcal mol^{-1}.[45] These considerations and the fact that no loss of DMB was observed in the CID experiments of complex ions **6** hints toward the instantaneous carbopalladation after olefin complexation in the quasi-thermal conditions in the ion trap. On the contrary, the β-H elimination, i.e. the transformation from complex ion **6a** to **7**•(Ph)DMB-η^4, was found to be an endothermic reaction. The critical energy required for this transformation to proceed is probably not covered by the enthalpy of association. Hence, the DFT calculations suggest that the IMR of the Pd precursor ion **3** and DMB will lead to the σ-alkyl complex ion **6**. Only after the activation of this IMR product ion upon collision activation is the MHR product formed by β-H elimination and released as a neutral MHR product along with the complementary Pd hydrido complex ion **7**. Consistent with this detailed computational analysis of the IMR process between the precursor ions **3** and DMB, we were able to investigate the carbopalladation step individually.

For a kinetic analysis of the gas-phase carbopalladation, second-order rate constants of the IMR between $[Pd(PCy_3)(Ar)]^+$ (**3**) and DMB were determined at reaction times of 0.03–20 ms. The intensities of both the precursor ion **3** and of the low-abundance fragment ion $[P(Ar)Cy_3]^+$ (**4**) were summed to compensate for differences in the fragmentation extent of the precursor ions (see Figure 3). The determined second-order rate constants are listed in Table 1. Each value is the mean of four independent measurements using different olefin partial pressures in the ion trap. A detailed description of the experiments and the measurements is given in the Supplementary Information.[45] We found rate constants for the carbopalladation step of the gas-phase MHR of about 1–3 × 10^{-9}·cm^3·s^{-1}·molecule^{-1}. Since the differences in the *k* values for the set of aryl moieties lie in the range of the documented experimental error of the method (±20–30%)[37,49], it is reasonable to assume that the DMB insertion is not seemingly sensitive to the electronic effects of the aryl ligand. Consequently, the linear free energy correlation of the observed rate constants found for the different aryl moieties versus their respective Hammett parameter yields an indifferent result with a substantial dispersion of data points (Figure 6). A linear relationship is obviously absent, suggesting no substantial charge formation in the transition state of the particular reaction.

Table 1. Second-order rate constants of the IMR between $[Pd(PCy_3)(Ar)]^+$ (3a–3i) and DMB. The reported values are the averages of four independent measurements at different flow rates of olefin and helium. The presented error is the standard deviation.

Ar	*k* (10^{-9}·cm^3·s^{-1}·molecule^{-1})
C_6H_5 (6a)	3.1 ± 1.0
p-(C_6H_4)Me (6b)	1.8 ± 0.2
p-(C_6H_4)OMe (6c)	1.5 ± 0.1
p-(C_6H_4)Et (6d)	2.2 ± 0.1
m-(C_6H_4)Me (6e)	1.9 ± 0.2
p-(C_6H_4)F (6f)	1.5 ± 0.2
p-(C_6H_4)COMe (6g)	2.0 ± 0.4
p-(C_6H_4)CF_3 (6h)	1.6 ± 0.3
p-(C_6H_4)NO_2 (6i)	2.0 ± 0.2

Other studies have suggested that the olefin insertion reaction proceeds in a concerted manner via a four-membered transition state (Scheme 7a).[67–69] However, experimental findings have been reported that point toward a carbopalladation transition state with a positive charge concentration at the olefin (Scheme 7b).[70] In line with this result, Van Leeuwen and co-workers found a Hammett plot with a negative slope of the linear regression ($\rho = -1.5$) for the MHR of *para*-substituted iodobenzenes with styrene and the olefin coordination or insertion was determined to be the rate-limiting step in this case.[11] Our kinetic analysis of the gas-phase carbopalladation step suggests a DMB insertion proceeding through a transition state without substantial charge separation occurs (in accordance with Scheme 7a and Figure 6).

Conclusion

In the present study, a number of important individual steps of the palladium-catalyzed MHR between aryl iodides and DMB were investigated in the gas phase. The oxidative addition was

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[1] The kinetic examination of the β-hydride elimination combined with the release of the MHR reaction product (Ar)DMB (**8**) induced by CID indicates that the efficiency of these two steps does not depend on the electronic properties of the aryl ligand (see Figure S7 and further explanation in the Supplementary Information).

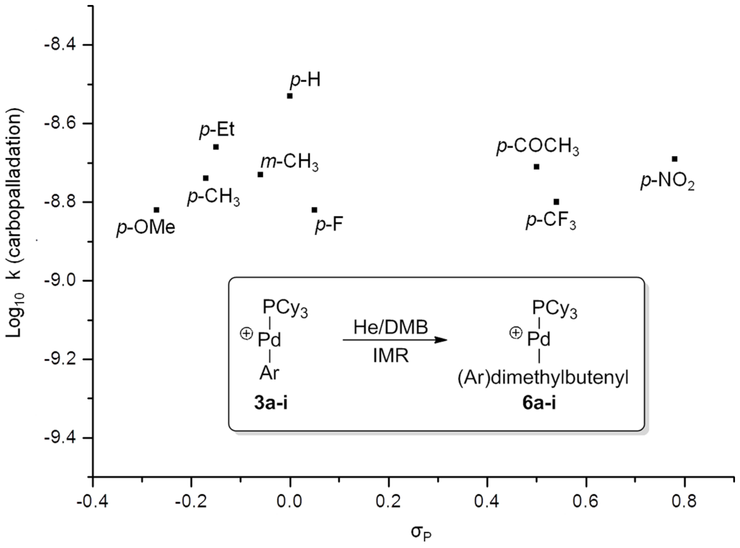
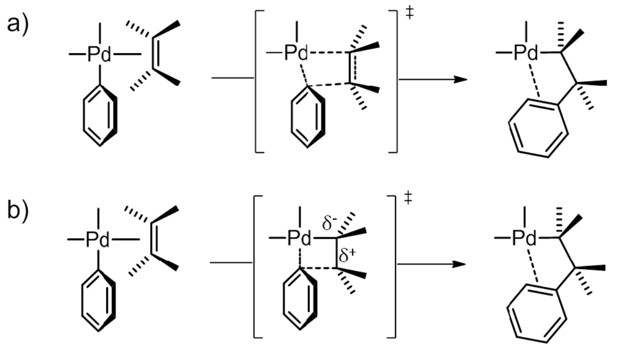


Figure 6. Log$_{10}$ plot of the carbopalladation rate constants as a function of the Hammett parameter σ_P.[65,66]

performed in solution prior to the electrospray phase transfer from solution to the gas phase, but both the carbopalladation and the β-hydride elimination were conducted in a controlled and defined manner in a linear QIT mass spectrometer. The experimental strategy allowed the direct and isolated examination of the C–C coupling step by the IMR between [Pd(PCy$_3$)(Ar)]$^+$ (**3**) and gaseous DMB and the collision-induced release of the neutral product (Ar)DMB (**8**) from the IMR product ion [Pd(PCy$_3$)σ-(Ar-dimethylbutenyl)]$^+$ (**6**), leading to the respective Pd hydrido complex ion (**7**). The identity and molecular structure of the [Pd(PCy$_3$)σ-(Ar-dimethylbutenyl)]$^+$ ion (**6**) was closely probed by extensive MS measurements (accurate ion mass, isotopic distribution), as well as by DFT calculations. Consistent with the experimental findings, theory indicated that the olefin insertion is exothermic whereas the β-hydride elimination is endothermic and therefore the rate-limiting step of the gas-phase MHR under investigation. These proposals are in agreement with the experimental findings that the carbopalladation via IMR takes place without further activation and the β-hydride elimination combined with the release of the reaction product (Ar)DMB (**8**) requires a substantial amount of activation energy to be fulfilled experimentally. The kinetic analysis of the carbopalladation step by IMR of the [Pd(PCy$_3$)(Ar)]$^+$ (**3**) complex ions with nine different aryl (Ar) substrates with DMB showed no trend and clearly evidenced that the reaction rate is independent of electronic effects of the aryl moiety.

This report underlines the great potential of gas-phase IMR in combination with theory and MS/MS techniques for the detailed reaction mechanism studies of transition-metal-mediated transformations, especially of those with homogeneous catalysts. The gas-phase strategy allows the selection and investigation of individual reaction steps as well as the intermediate species of a catalytic cycle, which is usually very difficult or even impossible because of their transient nature and instability in complex reaction solutions. The presented set of results encourages us to investigate further also the influence of subtle electronic and steric effects of the olefin on the outcome of MHR reactions in the gas phase.



Scheme 7. Carbopalladation *via* four-membered transition states with (a) little charge separation[67] and (b) polarization of the olefin C–C double bond.[70]

Supplementary information

Additional mass spectra of CID experiments, kinetic data of the gas-phase test reaction, and calculated complex ion structures are given in the Supplementary data associated with this article and can be found in the online version at http://dx.doi.org/10.1255/ejms.1310.

Acknowledgements

This work was generously supported by a doctoral fellowship of the 'Cusanuswerk' to L.F. J.H. thanks Prof. Dr Michael Dolg, Institute of Theoretical Chemistry, University Cologne for helpfull discussions.

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