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Palladium(II)-Catalyzed Decarboxylative Heck Arylations of Acyclic Electron-Rich Olefins with Internal Selectivity

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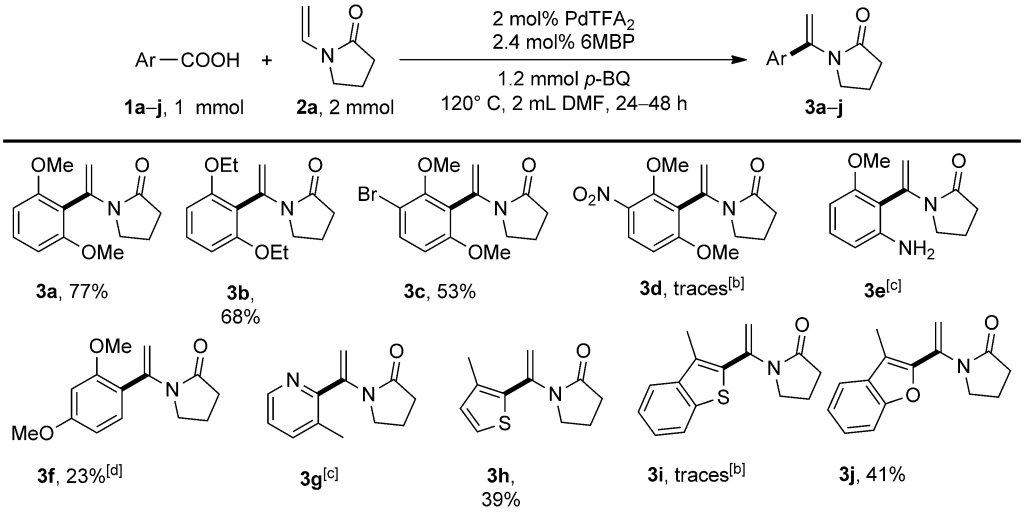
Abstract: Despite the recent emergence of decarboxylative C–C bond forming reactions, methodologies providing internally arylated electron-rich olefins are still lacking. We herein report on palladium(II)-catalyzed decarboxylative Heck arylations of linear electron-rich olefins with excellent selectivity for the internal position. The method allows a variety of electron-rich linear olefins to undergo arylation with *ortho*-functionalized aromatic carboxylic acids, including heterocycles. The reaction mechanism has been explored with ESI-MS studies to confirm previous findings, and to reveal the formation of a highly stable palladium complex as a result of the Heck product reacting with the catalyst.

Keywords: carboxylic acids; Heck reaction; mass spectrometry; olefination; palladium; reaction mechanisms

The Heck reaction and its spin-offs continue to serve chemists as a vital tool for the formation of C–C bonds between olefins and arenes.[1–9] While Mizoroki[1] and Heck[2] independently pioneered the palladium(0)-catalyzed arylation of an alkene with an organic halide, today known as the "classic Mizoroki–Heck reaction", Heck would also discover in 1975 an analogous palladium(II)-mediated vinylation of an olefin by employing a vinylboronic acid and stoichiometric loadings of palladium acetate.[10] Although reoxidizing agents had been reported to allow palladium(II)-catalyzed transformations already in 1968,[11] the so-called "oxidative Heck reactions" were not deemed feasible until Mori and co-workers demonstrated the use of $Cu(OAc)_2$ as a reoxidant of Pd(0) to Pd(II) in 2001,[12] followed by Jung and Larhed describing the use of molecular oxygen as a Pd(0) reoxidant.[13,14] Developments of both the classical Mizoroki–Heck reaction and its oxidative counterpart have provided for an impressive array of aryl-palladium precursors and olefinic substrates,[6,15,16] but there are shortcomings that justify further development. These include environmental hazards of aryl halides and their by-products, and limited commercial availability, laborious preparation, high cost and instability of some organometallic substrates.[6,15,16]

Metal-mediated decarboxylations of carboxylic acids were discovered in 1930,[17] and incremental developments followed,[18–24] but they were not exploited for C–C bond formations until recently. Pioneering work by Myers et al. showed that certain benzoic acids can undergo a palladium(II)-catalyzed process in which carbon dioxide is released to form the corresponding aryl-palladium complex, which in the presence of an oxidant (Ag_2CO_3) and alkenes yields vinylarenes.[25] As carboxylic acids are cheap, non-toxic, easy to prepare and widely available, the aforementioned drawbacks of traditional aryl-palladium precursors may thus be countered.[26,27] One major drawback of using palladium(II) catalysts for decarboxylation is the limitation to *ortho*-substituent bearing benzoic acids,[28–30] although Gooßen and co-workers have expanded the scope beyond this limitation for some non-oxidative cross-coupling reactions by employing bimetallic systems.[31–33] Several applications of palladium(II)-catalyzed decarboxylations have now been demonstrated, including Suzuki[34–36] and Sonogashira[37] cross-couplings, their oxidative counterparts,[38,39] as well as oxidative Heck-type reactions.[40–45] While successful efforts to promote internal selectivity in traditional Heck arylations of electron-rich olefins are manifold,[46] and its decarboxylative counterpart has been demonstrated for electron-rich cyclic olefins,[47] examples in the literature providing access to internally arylated acyclic electron-rich olefins *via* the decarboxylative pathway are lacking. Although oxidative decarboxylative arylations of indoles

Table 1. Scope of aromatic carboxylic acids.[a]



[a] Isolated yields. Regioselectivity confirmed by ^{1}H NMR.
[b] According to GC-MS.
[c] Not detected by GC-MS.
[d] Hydrolyzed and isolated as the corresponding ketone (see the Supporting Information).

have been demonstrated by Su and co-workers,[48] the only acyclic electron-rich olefin example reported is a low-yielding reaction with no substrate variability.[49]

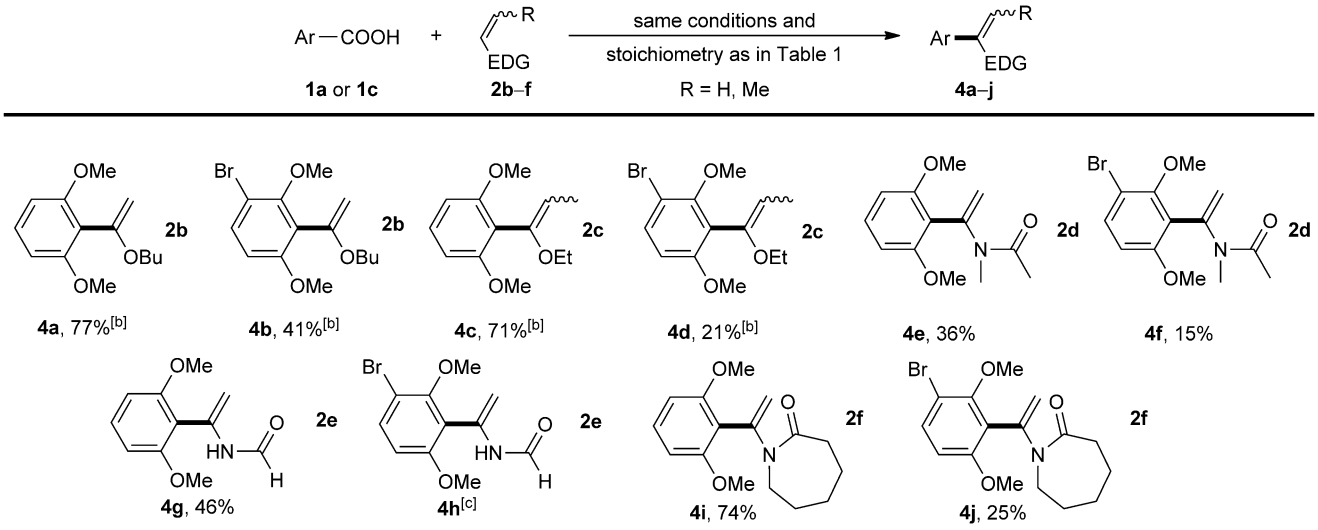
In 2010, our group reported a bidentate ligand-modulated palladium(II)-catalyzed decarboxylative method for the addition of benzoic acids to nitriles, promoting the formation of aryl ketones.[50,51] This inspired us to investigate whether a similar catalytic system might also promote decarboxylation and subsequent arylation of electron-rich olefins at the internal position. Rewardingly, reacting 2,6-dimethoxybenzoic acid (**1a**) with 1-vinylpyrrolidone (**2a**), using palladium(II) trifluoroacetate ($PdTFA_2$) and 6-methyl-2,2′-bipyridine (6-MBP) as the catalytic system and *para*-benzoquinone (*p*-BQ) as the reoxidant and DMF as the solvent, furnished the desired Heck product **3a** in 77% isolated yield after 24 h at 120 °C. Furthermore, no traces of terminally arylated Heck product, **1a**, or the protodecarboxylation by-product 1,3-dimethoxybenzene could be detected by ^{1}H NMR, GC-MS or LC-MS. To investigate the scope of the reaction, a variety of *ortho*-substituted aromatic carboxylic acids was tested (Table 1).

The di-*ortho*-substituted electron-rich carboxylic acids **1a** and **1b** provided the highest isolated yields (77% and 68%), whereas the less electron-rich bromo-bearing aromatic acid **1c** furnished a slightly lower yield of **3c** (53%). The nitro- and amino-substituted **1d** and **1e** yielded only traces of product, which is likely due to a significant drop in electron density and coordination of the amino group to palladium, respectively. The low yield of **3f** was expected with regards to the mono-*ortho*-substitution pattern of the carboxylic acid **1f**. The heterocyclic 3-methylpyridine-carboxylic acid **1g** was unable to produce **3g**, again likely due to sequestration of palladium by the pyridine nitrogen. Interestingly, the 3-methylthiophene-carboxylic acid **1h** furnished **3h** in 39% yield while its benzothiophene counterpart **1i** only produced traces of **3i**. The benzofuran analogue **1j** successfully reacted to yield 41% of **3j**, however. Despite the low to moderate range of yields, it is of crucial interest that all successful reactions demonstrated excellent regioselectivity with no detection of the corresponding terminal regioisomer.

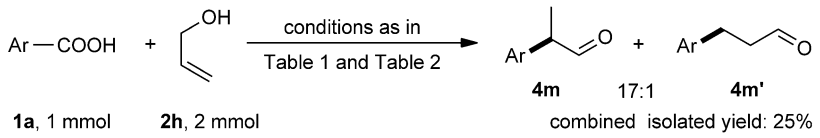
The scope of olefinic substrates was explored by reacting different terminal electron-rich olefins with **1a** and the less electron-rich **1c** (Table 2). The general pattern of reactivity was in agreement with previous studies,[29,30,41,52] namely that decreased electron density in the aromatic ring resulted in reduced reactivity. Nevertheless, all product-yielding reactions provided arylation exclusively at the internal vinylic position. Alkyl vinyl ethers **2b** and **2c** and enamide **2f** proved to be the most proactive olefinic substrates. While the outcome for *N*-vinylcaprolactam **2f** was more or less similar to that of enamide **2a**, one would expect the outcomes for enamide **2d** to be superior compared to **2e**. As the secondary amide nitrogen in **2e** is expected to coordinate the catalyst more strongly than the tertiary amide **2d**, it is interesting that **4e** was isolated in a lower yield than **4g**.

As the reaction exhibited unanimous preference for the internal position in the case of the electronically biased olefins, we were interested in the behavior of a less electron-rich olefin. Thus, allyl alcohol was

Table 2. Scope of electron-rich olefins.[a]



[a] Isolated yields. Regioselectivity confirmed by ^{1}H NMR.
[b] Hydrolyzed and isolated as the corresponding ketone (see the Supporting Information).
[c] Not detected by GC-MS.



Scheme 1. Regioselectivity of allyl alcohol.

chosen for investigation (Scheme 1). A regioselectivity of 17 to 1 was observed with allyl alcohol **2h** in favor of the internal position (determined by ^{1}H NMR) despite its electronically less biased nature, which is in accordance with a cationic pathway in the catalytic cycle.[53] Interestingly, both regioisomers **4m** and **4m′** were isolated as their corresponding saturated aldehydes. Although this *in situ* isomerization has been reported,[54] and the factors controlling it investigated,[55–57] high regioselectivities have only been obtained for the terminally arylated corresponding aldehydes. Whether this process is the result of a palladium hydride reverse addition–elimination remains to be investigated, but the high regioselectivity for the internally arylated product is noteworthy nevertheless.

The mechanistic framework of oxidative decarboxylative Heck reactions was elucidated by Myers and co-workers in 2005, with kinetic data and experiments with the captured Ar–Pd intermediate suggesting the extrusion of CO_2 to be the rate-determining step.[52] These findings have been supported by elaborate DFT studies performed by Zhang et al.[30] As our catalytic system employs a bidentate nitrogen-based ligand and the olefin is electron-rich, in contrast to the monodentate system employed by Myers et al. with electron-poor olefins, we were interested in investigating the cationic intermediates more in detail. Electrospray ionization mass spectroscopy (ESI-MS) has been successfully utilized in the elucidation of key intermediates in ongoing palladium-catalyzed transformations due to its soft method of ionization which yields few fragmentation products,[58–64] and was our tool of choice for further studies. The investigation was carried out by setting up an array of 10 identical reactions, in which **1a** reacted with **2a** as described in Table 1, and then sampling them at 10 different reaction times. Due to the build-up of pressure in the reaction, setting up ten identical reaction vessels allowed each vessel to be sampled once and then discarded. This eliminated the risk of interfering with the reaction due to a sudden drop in pressure, as opposed to sampling the same reaction vessel 10 times. After aliquots of each reaction were collected, an ESI-MS-(+) spectrum was recorded (within one hour after sampling) by scanning the last quadrupole (Q3) of a QTrap instrument in linear ion trap mode. The distributions of the detected organopalladium complexes (^{106}Pd and ^{108}Pd) at the 10 different reaction times are depicted in Table 3, and their structures are assigned based on MS/MS and given letters (**A–D** and **5**) based on their plausible role in the catalytic cycle.

Table 3. Detected organopalladium complexes at different heating times.[a]

Structures based on MS/MS[b]	*m/z*	[0	5	10	15	20	25	30	45	60	120][c]
[(N⌒N)-Pd-(TFA)]$^+$ (**A**)	389/391	●									
[(N⌒N)-Pd-(OOCAr)]$^+$ (**B**)	457/459	●									
[(N⌒N)-Pd-(OOCAr)(η^2-olefin)]$^+$ (**B'**)	568/570	●									
[(N⌒N)-Pd-(Ar)]$^+$ (**C**)	413/415	●	●	●	●						
[(N⌒N)-Pd-(Ar)(η^2-olefin)]$^+$ (**D**)	524/526	●	●	●							
[(N⌒N)-Pd-(σ-**3a**)]$^+$ (**5**)	522/524		●	●	●	●	●	●	●	●	●

[a] Gray shade intensity represents an approximation of relative abundance between the different complexes in the mother spectrum for each heating time. Unidentified complexes omitted for clarity.
[b] N⌒N, Ar, R = as in Figure 1.
[c] Heating time in minutes.

The highest prevalence of cationic organopalladium complexes with the characteristic isotopic pattern of palladium were observed prior to heating (Table 3 and Figure 1), which is surprising since product formation is not observable on GC-MS and LC-MS until at least 2 h of heating.

While the structural natures of the detected and identified complexes are consistent with previous findings,[29,30,52,65] three observations are noteworthy: (i) complex **B**, which precedes the decarboxylation step, is already formed at room temperature and diminished within 5 min of heating, indicating a fast decarboxylation step which contradicts previous findings;[30,52] (ii) the decarboxylated aryl-palladium species **C** and its olefin-coordinating counterpart **D**, which likely preludes the aryl-insertion step, are also formed at room temperature; (iii) an unexpected ionic species **5** begins to form after 5 min of heating and remains throughout the course of the reaction, indicating a highly stable complex that might present a dead end in the catalytic cycle. MS/MS for complex **5** revealed an aryl, olefin, palladium and ligand component, but not enough information to deduce the actual composition. In an attempt to isolate it, carboxylic acid **1a** and olefin **2a** were reacted according to Table 1 but with stoichiometric amounts of the palladium(II) catalyst instead of *p*-BQ and in a lower concentration [to avoid formation and precipitation of Pd(0)], in order to obtain complex **5** in isolable amounts (Scheme 2). To our delight, complex **5** was

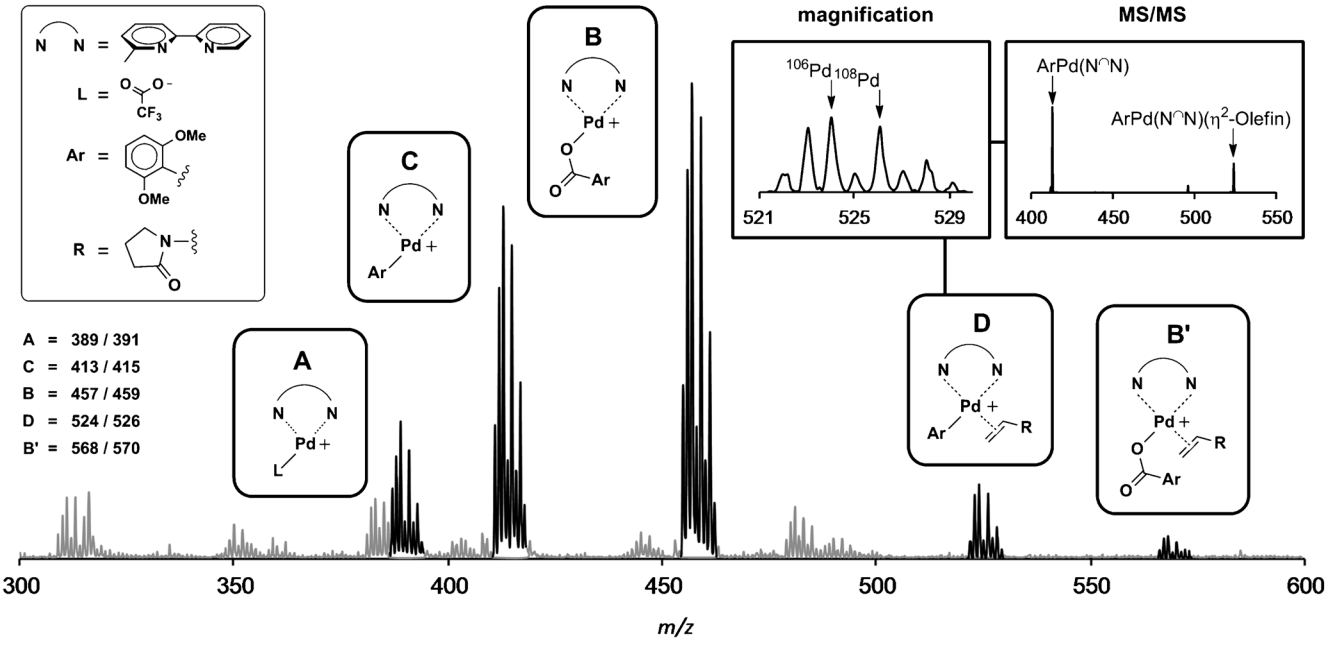
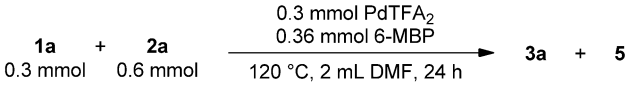
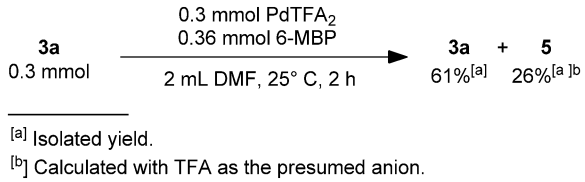


Figure 1. ESI-MS-(+) spectrum for the reaction of **1a** with **2a** as in Table 1 (prior to heating) with assigned Pd(II) complexes.



Scheme 2. Reaction with stoichiometric loading of palladium(II) at room temperature, according to LC-MS.



Scheme 3. Reaction of Heck product **3a** and catalyst.

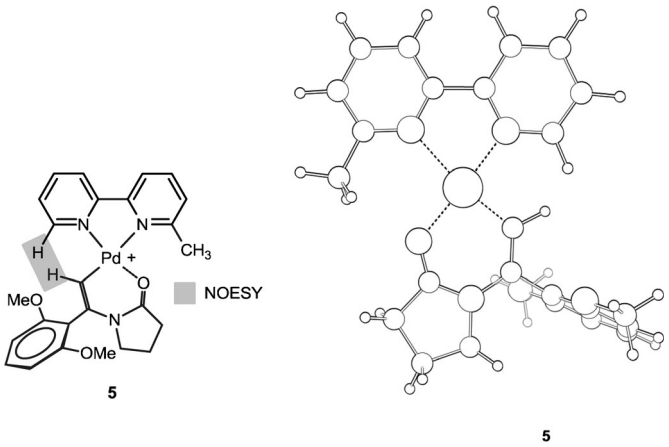


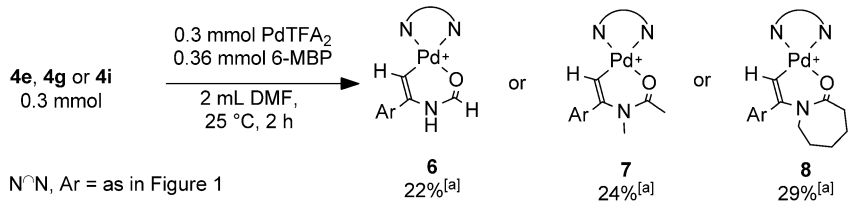
Figure 2. Proposed structure of complex **5** based on ESI-MS^n, HR-MS, ^{1}H NMR, ^{13}C NMR, HSQC, HMBC and NOESY (*left*), and lowest energy conformation according to DFT calculations (*right*) using Jaguar 7.9[68] employing the B3LYP hybrid functional[69–71] and LACVP** basis set, which uses an effective core potential for Pd and 6-31G** for elements H–Ar[72].

detected on LC-MS as a discrete compound along with Heck product **3a** (see the Supporting Information).

To establish if complex **5** is formed within the catalytic cycle or outside the cycle with the Heck product, **3a** was mixed with palladium and ligand in DMF (Scheme 3). Surprisingly, LC-MS revealed the formation of **5** within 30 min of stirring at room temperature, with **3a** still present in the solution. After 2 h of stirring at room temperature, a slight increase in the amount of complex **5** was observed according to LC-MS (Scheme 3), and the outcome remained unchanged after a total of 24 h of stirring at room temperature. Heating of complex **5** to 120 °C for 24 h did not indicate decomposition or significant changes in the ratio between **3a** and **5**. Addition of diethyl ether precipitated complex **5** to allow filtration and isolation, after which it was characterized experimentally (Figure 2, *left*). While fluorine was detected by ^{19}F NMR and the TFA anion was detected on TOF-MS in negative mode, the expected TFA anion could not be observed on ^{13}C NMR, thus rendering the anion of the complex currently uncharacterized. Attempts to obtain crystals for X-ray failed, despite trying various crystallization methods and exchanging $PdTFA_2$ to other palladium salts with anions such as Cl^- and BF_4^-. The experimental data were in accordance with the lowest energy conformation found for **5** according to DFT calculations (Figure 2, *right*), however. The nature of the transformation leading up to palladacycle **5** is unknown, but it may be similar to C–H activations of aromatic C–H bonds.[66,67]

As structure **5** is formed from the Heck product and catalyst at room temperature (Scheme 3), it is reasonable to assume that this also occurs during the decarboxylative Heck reaction. This means that the catalyst as well as Heck product **3a** are consumed to form species **5**, resulting in less catalytically active palladium being available for the Heck cycle thus reducing both the efficiency of the catalytic cycle and the yield of Heck product **3a**. These findings also indicate that decarboxylation may be the rate-determining step after all, despite the ESI-MS experiments suggesting otherwise: as catalytically active palladium continuously decreases, the concentration of active species in the catalytic cycle must decrease likewise. Hence, it is not correct to assume that complex **B** and the decarboxylation product **C** rapidly diminish exclusively as observed in the ESI-MS experiments (Table 3), but rather that all organopalladium species in the catalytic cycle decrease in concentration below the level of detection as palladacycle **5** accumulates to dominate the ESI-mass spectra.

Due to the similarities between olefin **2a** and olefins **2d–f** with regards to the enamide moiety, it seemed plausible that their corresponding Heck products are able to form homologues of complex **5**. Thus, Heck products **4e**, **4g** and **4i** were reacted with stoichiometric amounts of catalyst to indeed yield their corresponding homologous cationic species **6**–**8**, the structures of which could be characterized experimentally (Scheme 4). No crystals could be obtained for metallacycles **6**–**8**, nor could the expected TFA anion be detected on ^{13}C NMR despite the presence of fluorine on ^{19}F NMR, but the lowest energy conformations found using DFT calculations were in this case also in accordance with the experimental data (Figure 3). As for the true structures of **5**–**8** being formed in live decarboxylative Heck reactions, it is not unlikely for an equilibrium to be taking place between positively charged and neutral complexes, with the intramolecular carbonyl oxygen or an external trifluoroacetate anion, as well as an aryl carboxylate anion, coordinating the palladium center interchangeably. Performing the reaction with vinyl ether Heck



[a] Isolated yield, calculated with TFA as the presumed anion.

Scheme 4. Reactions of catalyst with Heck products from enamide-substituted olefins. Structures of **6–8** are based on ESI-MS^n, HR-MS, ^1H NMR, ^{13}C NMR, HSQC, HMBC, NOESY. $\widehat{NN}$, Ar, R = as in Figure 1.

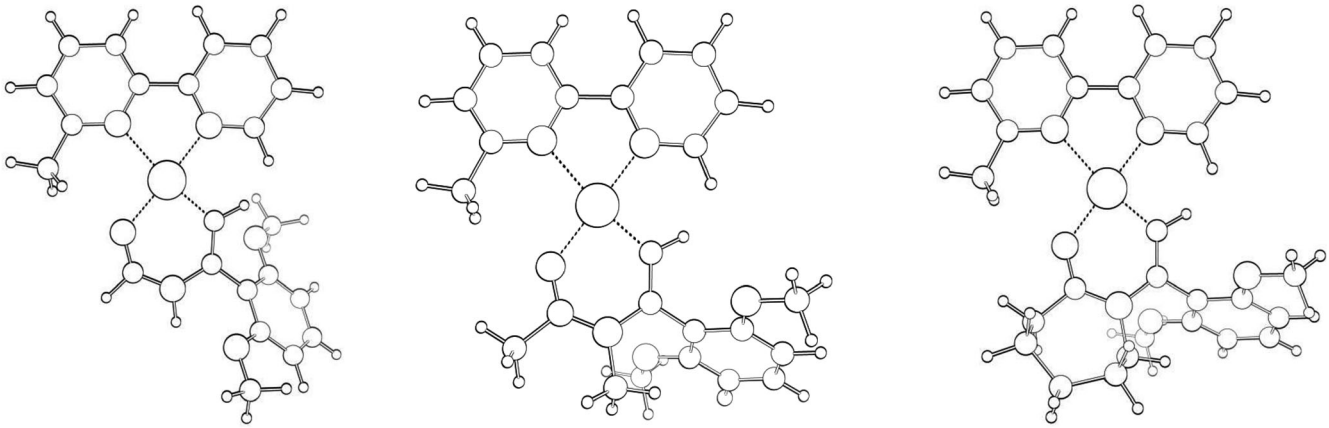


Figure 3. Lowest energy conformations of complexes **6–8** according to DFT calculations (performed with the same parameters as described in Figure 2).

product **4a**, which lacks the enamide moiety, did not produce a corresponding palladium complex.

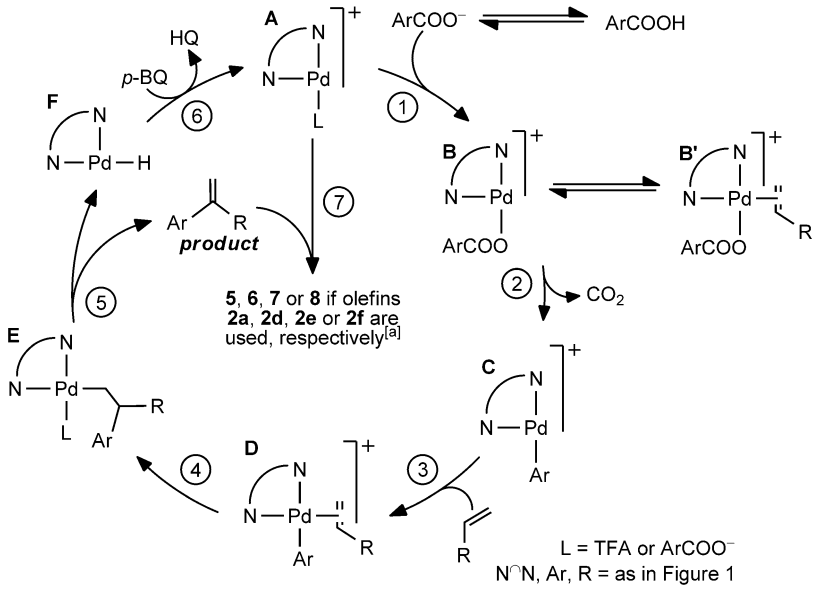
A plausible reaction route, derived from complexes **A**–**D** and **5**, is proposed in Scheme 5 and involves the following key steps: (i) carboxyl ligand exchange of intermediate **A** with the carboxylic acid to form complex **B** (which is in equilibrium with species **B′** given the excess of olefin); (ii) decarboxylation of the palladium(II)-carboxylate to generate the aryl-palladium intermediate **C**; (iii) coordination of the olefin double bond to give complex **D**; (iv) aryl-insertion followed by internal rotation to produce structure **E**; (v) β-hydride elimination and release of product to form complex **F**; (vi) reoxidation of Pd(0) to Pd(II) by *p*-BQ to generate bidentate coordinated catalyst **A** which either reinitiates the catalytic cycle, or (vii) in the case of olefins **2a** and **2d–f** undergoes a reaction with their corresponding Heck products to yield **5**–**8**, respectively.

In conclusion, we have developed an oxidative palladium(II)-catalyzed Heck method that gives access to internally arylated electron-rich olefins with excellent regioselectivity, compatible with a wide variety of linear electron-rich olefins and various *ortho*-functionalized benzoic acids, including heterocycles. ESI-MS and MS/MS analyses of ongoing reactions detected key intermediates in the catalytic cycle which confirms previous findings regarding the mechanism. It was also found that the catalyst is intercepted by some Heck products to form a highly stable complex that presumably reduces both the yield and the efficiency of the catalytic cycle. Ongoing efforts in our laboratory are aimed at expanding the scope of this reaction, while providing further insight into the reaction mechanism by DFT calculations.

Experimental Section

General Information

Reactions were performed in Teflon-coated stir-bar-containing Biotage 2–5 mL process vials. Analytical TLC was performed using Merck aluminium-backed 0.2 mm silica gel 60 F-254 plates. Visualization was done with UV light. Silica gel 60 was purchased from Merck. Aluminum oxide (activated, neutral, Brockmann I, STD grade, approx. 150 mesh, 58 Å) was purchased from Sigma–Aldrich. NMR spectra were recorded on a Varian Mercury plus at 25 °C for ^1H at 400 MHz, for ^{13}C NMR at 100 MHz. Chemical shifts (δ) are reported in ppm and referenced indirectly to TMS *via* the



[a] Complexes **5**–**8** may exist as positively charged complexes or neutral complexes with $ArCOO^-$ or TFA as ligand.

Scheme 5. Proposed reaction route supported by MS-detected organopalladium complexes.

solvent (or residual solvent) signals. Low-resolution mass spectra were recorded on a GC-MS instrument equipped with a CP-Sil 8 CB capillary column (30 m × 0.25 mm, 0.25 μm) operating at an ionization energy of 70 eV. The oven temperature (GC) was 70–300 °C. Analytical UHPLC-MS was performed on a Dionex UltiMate 3000 with a Bruker amaZon iontrap mass spectrometer using a Phenomenex Kinetex core-shell C18, 2.6 μm, 4.6 × 50 mm column with MeCN in 0.05% aqueous HCOOH as mobile phase at a flow rate of 2 mL min^{-1}. All solvents, starting materials, and reagents are commercially available and were used as received.

General Procedure for Decarboxylative Heck Arylations (Table 1 and 2) Exemplified in the Synthesis of 3a

A 2–5 mL process vial was charged with 2,6-dimethoxybenzoic acid **1a** (182 mg, 1 mmol), 1-vinylpyrrolidine-2-one (111 mg, 2 mmol), $Pd(O_2CCF_3)_2$ (6.7 mg, 0.02 mmol), 6-methyl-2,2′-bipyridine (4.1 mg, 0.024 mmol), *para*-benzoquinone (130 mg, 1.2 mmol) and DMF (2 mL). The vial was thereafter capped under air and heated in a metal block preheated to 120 °C for 24 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (5 mL) and filtered through an aluminum oxide plug using a 78:20:2 mixture of ethyl acetate:*i*-hexane:Et_3N (15 mL). The filtrate was washed with brine (2 × 20 mL) and the combined aqueous phases were extracted with ethyl acetate (2 × 20 mL). The washed filtrate and the organic portions were combined, dried through a 1PS phase separator filter and concentrated under reduced pressure, followed by purification on by silica column chromatography (*i*-hexane:ethyl acetate:Et_3N) to furnish the product **3a** as a pale green oil; yield 190 mg (77%); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.22$ (t, $J = 8.5$ Hz, 1H), 6.54 (d, $J = 8.5$ Hz, 2H), 5.67 (s, 1H), 4.81 (s, 1H), 3.77 (s, 6H), 3.36 (t, $J = 7.0$ Hz, 2H), 2.43 (t, $J = 8.0$ Hz, 2H), 1.99–1.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 173.86$, 158.11, 135.62, 129.55, 115.45, 106.41, 103.87, 56.04, 48.33, 32.59, 17.89; HR-MS (ESI$^+$):: $m/z =$ 248.1284, calcd. for $C_{14}H_{17}NO_3$ $[M+H]^+$: 248.1287.

Procedure for ESI-MS-(+) Experiments

This study used a 3200 QTrap mass spectrometer manufactured by AB Sciex (Concord, ON, Canada). A 100 μL aliquot was collected from each reaction mixture, diluted 10 times with acetonitrile, and introduced by continuous infusion with the aid of a syringe pump at a flow-rate of 5 μL min^{-1} through a fused silica capillary (with a 50 μm inner and a 184 μm outer diameter). The ion source used was a Turbo V source in positive ESI mode. The following MS conditions were used: temperature (TEM) ambient, curtain gas (CUR) 15 psi, ion source gas 1 (GS1) 10 psi, ion source gas 2 (GS2) 10 psi, ion spray voltage (IS) 5500 V, the declustering potential (DP) was 40 V and entrance potential (EP) 10 V for all measurements. MS data were collected in enhanced MS mode (EMS) and MS/MS data were collected in enhanced product ion mode (EPI). The collision gas parameter (CAD) was set to an arbitrary number, 11, for EMS (linear ion trap MS scan) and high for the EPI, which corresponds to a pressure reading of 4.0×10^{-5} Torr. The collision energy (CE) was 25 eV for all experiments aside from the EMS where it was set to 10 eV. Acquisition and processing of the MS data was performed with Analyst 1.4.2 (AB Sciex).

General Procedure for Palladium Complex Synthesis Exemplified in the Synthesis of 5

Heck product **3a** (74 mg, 0.3 mmol) was dissolved in DMF (1 mL) in a glass vial and stirred to homogeneity. $Pd(O_2CCF_3)_2$ (99.5 mg, 0.3 mmol) and 6-methyl-2,2′-bipyridine (61 mg, 0.36 mmol) were dissolved in DMF (1 mL) in another glass vial and stirred to homogeneity. The two solutions were then mixed to give 2 mL of reaction mixture, which was stirred at room temperature for 2 h. The reaction mixture was filtered with a syringe filter to remove small particles (only visible using a magnifying glass), after which diethyl ether was added to precipitate **5**. The precipitate was filtered off to give palladium complex **5** as a yellow solid; yield 50 mg (26%); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.68$ (dd, $J = 5.8$, 1.7 Hz, 1H), 8.37–8.32 (m, 1H), 8.19–8.13 (m, 2H), 7.94–7.88 (m, 1H), 7.56–7.52 (m, 1H), 7.41–7.36 (m, 2H), 6.65 (d, $J = 8.5$ Hz, 2H), 5.51 (s, 1H), 3.70 (s, 6H), 3.49 (t, $J = 7.3$ Hz, 2H), 2.72–2.67 (m, 2H), 2.54–2.52 (m, 3H), 2.14–2.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.34$, 162.36, 162.07, 161.77, 158.17, 157.72, 153.15, 149.21, 140.44, 139.73, 130.59, 128.82, 126.45, 126.37, 125.51, 124.32, 120.51, 117.32, 111.69, 104.16, 55.40, 50.44, 34.70, 31.46, 29.47, 22.82, 18.36; HR-MS (ESI$^+$): $m/z = 522.1017$, calcd. for $C_{25}H_{26}N_3O_3Pd^+$ $[M]^+$: 522.1009.

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