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# Functionalization of the Imidazole Backbone by Means of a Tailored and Optimized Oxidative Heck Cross-Coupling

Davide Cirillo,[a] Francesco Angelucci,[a] and Hans-René Bjørsvik[a,*]

[a] Department of Chemistry, University of Bergen, Allégaten 41, N-5007 Bergen, Norway
telephone +47 55 58 34 52,
E-mail: hans.bjorsvik@kj.uib.no
Homepage: https://folk.uib.no/nkjhn/

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**Abstract:** A general and selective Pd-catalyzed cross-coupling of aromatic boronic acids with vinyl-imidazoles is disclosed. Unlike most cross-coupling reactions, this method operates well in absence of bases avoiding the formation of by-products. The reactivity is highly enhanced by the presence of nitrogen-based ligands, in particular bathocuproine. The method involves $MnO_2$ as oxidant for the oxidation Pd (0)→Pd (II), a much weaker oxidant than previously reported in the literature. This allows for the use of reactants that possess a multitude of functional groups. A scope and limitation study involving a series of 24 boronic acids, whereof 18 afforded TMs in yields in the range 41–95%. The disclosed method constitutes the first general method for the oxidative Heck cross-coupling on the imidazole scaffold, which moreover operates with a selection of other heterocycles.

**Keywords:** Synthetic method; Pd catalysis; Oxidative Heck cross-coupling; Imidazole; Boronic acid

## Introduction

Imidazole is an ubiquitous structural motif[1] that can be found in numerous naturally occurring biomolecules and man-made synthetic compounds. The imidazole ring is found on its own in the essential amino acid histidine and its hormone derivative histamine. Moreover, imidazole fused with a pyrimidine forms purine that ends up in a variety of molecules ranging from the nuclear bases adenine and guanine to the xanthines found in coffee, tea and cocoa. This preeminence can also be observed in medicinal chemistry, where the imidazole ring can be found in compounds that hold a multitude of biological activities[2] including cytotoxic,[3] antifungal,[4] and anti-histaminic.[5] Furthermore, imidazole-containing molecules have been designed to have transversal applications across different fields ranging from medical imaging, where 2-nitro-imidazoles are essential probes for PET imaging of hypoxia,[6] to the metalorganics, where NHC-ligands are widely employed for homogenous metal catalysis for example in olefin metathesis.[7]

Preparation of backbone substituted imidazoles has traditionally been realized through multi-component reactions.[8] However, during recent years functionalization of positions 4 and 5 of the imidazole have been explored, especially through Pd-catalyzed cross-coupling reactions.[9] In our research group, such chemistry has been implemented by means of mono- and di-halogenation of the imidazole backbone,[10] which then allowed for Suzuki,[11] Stille,[12] and Sonogashira[13] cross-coupling reactions.

The Heck cross-coupling reaction also allows the formation of a C–C bond. However, no organometallic species are required, since it only involves an aromatic halide and an olefin.[14] In spite of the greener approach and the great atom economy, the Heck cross-coupling normally requires high temperatures and long reaction times to reach full conversion; furthermore, the

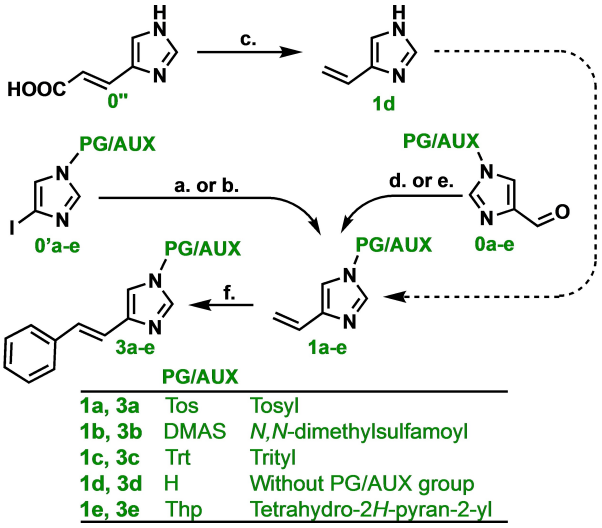
 

selectivity between the regioisomers 1,1 and 1,2 is often challenging to control.[15]

There have been several proposed improvements and innovations to the classical Heck cross-coupling, such as the decarbonylative approach[16] and the oxidative Heck cross-coupling.[17,18] The latter involves an organoboron reagent in place of the aromatic halide that is used in the classical Heck cross-coupling. This strategy replaces the first step of the catalytic cycle of the Heck cross-coupling, the oxidative addition, with a trans-metalation and it adds a new step in the catalytic cycle, which is the oxidation of the palladium (0) to a palladium (II) species. By avoiding the oxidative addition, considered the rate-determining step of the catalytic cycle, the oxidative Heck cross-coupling normally requires milder conditions to achieve a full conversion. In addition, by substantially lowering the reaction temperature, an improved regioselectivity is achieved.[19]

This strategy has been applied in our research group both for a medicinal chemistry project and for up-scaling,[20] proving the feasibility of the reaction also when a larger quantity of reagents is requested.

Since the Heck cross-coupling on the imidazole has been proven to be particularly challenging;[21,22] herein, we unveil an oxidative Heck cross-coupling method that allows formation of the 4-styryl-1*H*-imidazole scaffold using moderate conditions that afford excellent selectivity and high yield.




**Scheme 1.** Syntheses of 1-PG/AUX-4-vinyl-1*H*-imidazole (**1a**–**e**). (a) vinyl-Sn(Bu)$_3$, Pd(PPh$_3$)$_4$, DMF, 2 h, 100 °C. (b) vinyl-Bpin, Pd(PPh$_3$)$_4$, K$_2$CO$_3$, DMF, 18 h, 100 °C. (c) 220 °C, 18 h. (d) *t*-BuOK, Me–P(Ph)$_3$Br, THF, 3 h, 20 °C. (e) i) methyl acetohydrazonate, MgSO$_4$, MeOH, 60 °C; ii) Me$_3$S(O)I, *t*BuOK, MeCN, 20 °C, 2 h, then toluene, 90 °C, 16 h. (f) Oxidative Heck cross-coupling method disclosed herein, which makes use of Ph–B(OH)$_2$ **2** as reagent.

## Results and Discussion

### Synthesis of the Starting Material

The first step of our reaction pathway was to install a suitable unencumbered olefin on the imidazole backbone. Different strategies were evaluated, see Scheme 1. Initially we relied on a Stille coupling reaction previously developed in our research group to obtain target intermediate, pathway **a** of Scheme 1.

The Stille reaction afforded the highest yield (96%) when the experiment was carried out on a 0.3 mmol scale. Despite the excellent result, this approach was soon abandoned not only because the Stille cross-coupling presents toxicity issues regarding the organotin reagent and the side Sn-containing by-products, but also because the removal of organostannanes proved to be challenging.[23] Reducing the purification times and ruling out a possible interference by the tin halides was crucial as early in our development process we suspected their presence or absence might have a role in explaining our initial uneven results in the successive C–C bond forming step. This led us to investigate a second synthetic strategy, the Suzuki cross-coupling,[24,25] that involved the same starting material but with vinyl boronic acid pinacol ester as reagent. This strategy was also abandoned as it gave only poor yields (a maximum yield of 37% was attained). Moreover, this method possessed another burden, namely difficulties to separate starting material from target compound.

Synthesis of 4-vinylimidazole was reported as a thermal decarboxylation of urocanic acid,[26] pathway **c** of Scheme 1. This strategy provided pure target compound after distillation, but we were unable to reproduce the reported yield (we achieved a maximum yield of 9% only). A suitable compromise between the reaction outcome and required purity of target intermediate 4-vinyl-1*H*-imidazole was obtained by means of the Wittig reaction using 1*H*-imidazole-4-carbaldehyde as substrate, pathway **c** of Scheme 1, to obtain a yield of 52%. A similar strategy relying on carbonyl olefination via aziridination[27] was also tested; however, it proved to be much more laborious and failed to give any conversion.

### Early Screening

The procedure for the oxidative Heck cross-coupling was initially developed for a medicinal chemistry project in our group, which needed access to various molecules comprising a stilbene moiety.[20] These results spurred us to consider this method for the late stage functionalization of the imidazole backbone. Even if some of the initial experiments were encouraging (affording a yield of ≈40% conducted on 35 mg scale), attempts to replicate the experiments revealed

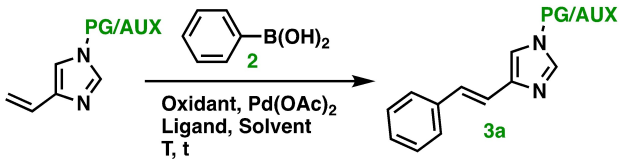
irreproducible results only. In some cases, we even observed zero conversion of the substrate, Table 1.

Experiments conducted at elevated temperature using microwave oven or with the presence of an inorganic base[28] failed as well.

Impurities present in the 4-vinyl-1*H*-imidazole substrate (from the previous synthetic step) appeared to be the cause of the varying success of the oxidative Heck cross-coupling reaction. This was particularly evident when the Stille cross-coupling was utilized in the forerunner step to produce the vinyl-1*H*-imidazole that served as substrate for the oxidative Heck cross-coupling.

The same problem was not equally present when the substrate 4-vinyl-1*H*-imidazole substrate was produced by means of the Wittig reaction, pathway **d** of Scheme 1, but a general difficulty in replicating the initial results remained. This spurred us to a more thorough screening (Table 1) of the reaction conditions. The first trials proved the importance of the oxidant for the success of the reaction. For example, target product was not achieved when benzoquinone was used as an oxidant, whereas a yield of ≈5% only was obtained when molecular oxygen and $Ag_2O$ were used.

**Table 1.** Early screening experiments tailoring the oxidative Heck cross-coupling to operate with imidazole as substrate.




| # | AUX | Oxidant | T[°C] | t[h] | L[f] | Yield-%[a] |
|---|---|---|---|---|---|---|
| 1 | Tos | $Cu(OAc)_2$ | 50 | 18 | **L4** | 44 |
| 2 | $CH_3$ | $Cu(OAc)_2$ | 50 | 18 | **L2** | 0 |
| 3 | Tos | $Cu(OAc)_2$ | 50 | 18 | **L2** | 0 |
| 4 | Tos | $Cu(OAc)_2$ | 50 | 18 | **L2** | 38 |
| 5 | Tos | $Cu(OAc)_2$ | 25 | 18 | **L4** | 0 |
| 6[b] | Tos | $Cu(OAc)_2$ | 25 | 18 | **L4** | 0 |
| 7 | Tos | $Cu(OAc)_2$ | 50 | 18 | **L4** | 0 |
| 8[c] | Tos | $Cu(OAc)_2$ | 50 | 4 | **L4** | 0 |
| 9 | Tos | $Cu(OAc)_2$ | 100 | 18 | **L4** | 0 |
| 10 | Tos | Benzoquinone | 60 | 18 | **L4** | 0 |
| 11[d] | Tos | $O_2$ | 80 | 18 | **L4** | 5 |
| 12[e] | Tos | $O_2$ | 100 | 18 | **L4** | 0 |
| 13 | Tos | $O_2$ | 60 | 4 | **L4** | 6 |
| 14 | Tos | $O_2$ | 60 | 4 | **L1** | 75 |

[a] LC.
[b] $Na_2CO_3$ used as an additive.
[c] Used microwave oven for heating.
[d] $Ag_2O$ used as an additive.
[e] $NaHCO_3$ used as an additive.
[f] **L1**, **L2**, and **L4** are described in Figure 1h.

Overall, side products comprising the imidazole scaffold were not observed (GC/LC–MS), but two different products derived from boronic acid were observed, namely the corresponding boroxine and the phenol produced due to the presence of the oxidant.[29] In contrast to observations in previous work,[18] homocoupling took place only to a minor extent, 1–2% (GC) only. From these initial promising screening results, various experimental parameters and reagents were explored with the ultimate goal of establishing a selective and high yielding method.

## Solvents

Previous reports disclosed that polar aprotic solvents are beneficial as reaction medium for the oxidative Heck cross-coupling reactions.[18,32] In our own solvent screening, Figure 1a, we reached a similar conclusion with acetonitrile and 1,4-dioxane both affording high conversions, followed by DMF.

The only outlier proved to be DMSO that afforded a yield of 6% only. Yields dramatically decreased when water was added to the mixture and similarly low results were obtained when a protic or an apolar solvent were used as reaction medium.

## Boronic Acid

Despite the excellent yields obtained when an excess (2 equiv.) of boronic acid was used in the initial test runs (Table 1), we wanted to investigate if such a high amount was truly necessary to achieve the full conversion and what was the minimum amount of reagent needed to obtain excellent yields during the reaction. Different experiments were carried out by using increasingly higher amounts of boronic acid. The results are shown in Figure 1b. High yields were achieved already when only 1 equiv. of boronic acid was employed; however, a slight excess (1.4 equiv.) of the reagent afforded an excellent yield of 98%.

## Catalyst

In our catalyst screening, Figure 1c, we decided to explore the most commonly used Pd catalysts that have been applied to the reaction. The catalyst that afforded the best conversion was $Pd(OAc)_2$, that afforded yields of 98% and became our catalyst of choice, which was consistent with previous findings.[20] Although other Pd(II) species afforded various levels of conversion, none gave comparable results in our setup. No conversion was observed when Pd(0), in the form of $Pd(PPh_3)_4$, was employed as catalyst. This was expected as the Pd would have been in the wrong oxidation state for the proposed reaction mechanism (Scheme 7).

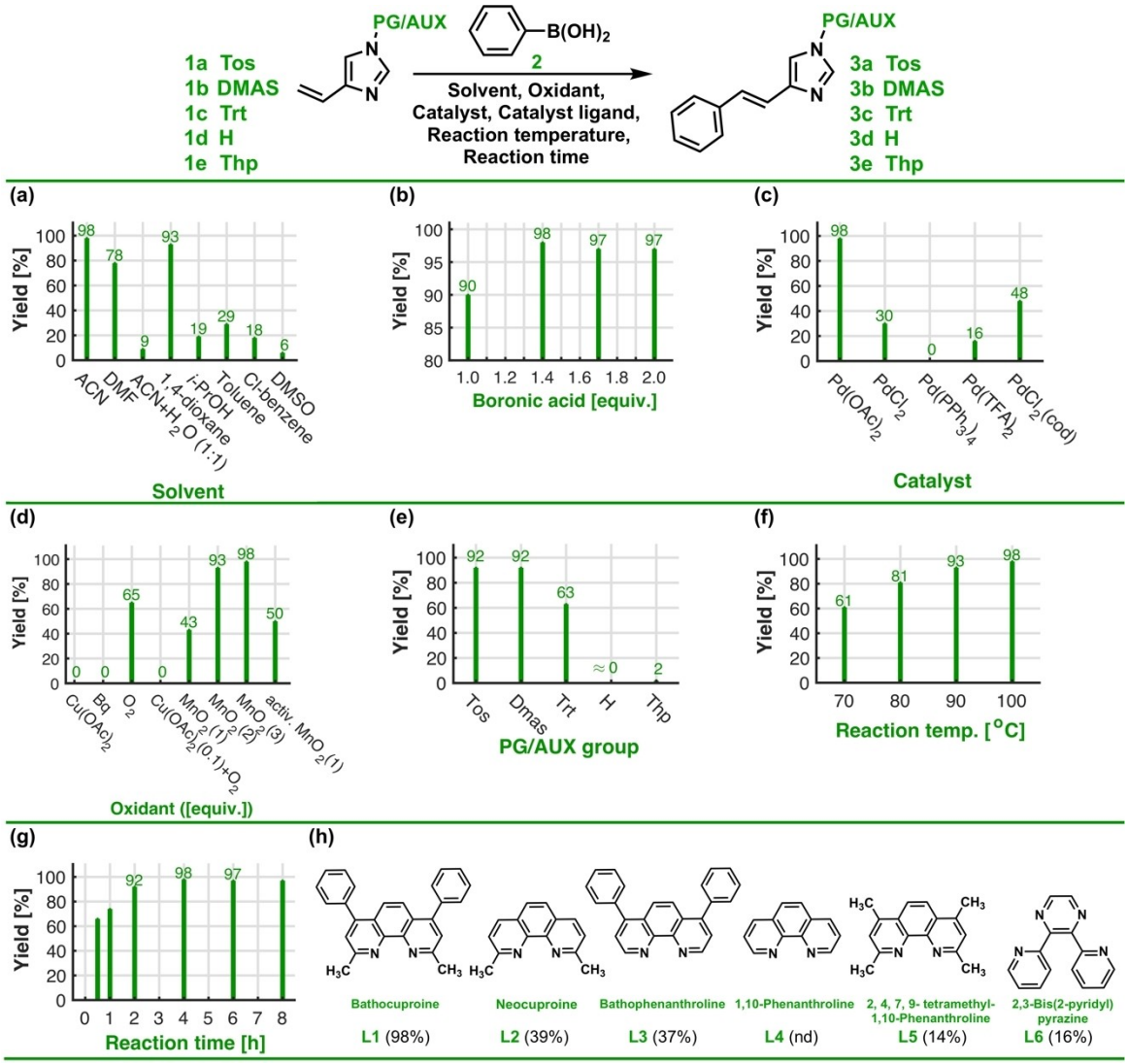



**Figure 1.** Screening of experimental variables: (a) type of solvent (select ACN), (b) quantity of boronic acid (utilize 1.4 equiv), (c) type of Pd-catalyst (select $Pd(OAc)_2$), (d) type and quantity of oxidant (utilize $MnO_2$, 3 equiv.). Activated manganese dioxide: $MnO_2$ was activated by heating at 150 °C for 18 h prior use, (e) type protective/auxiliary group (select Tos), Tos, DMAS, and Trt were isolated yields and H and Thp were measured by GC. (f) reaction temperature (utilize 100 °C), (g) reaction time (utilize 4 h), (h) type of ligand for catalyst (select Bathocuproine **L1**). General procedure: **1a** (221 μmol), phenyl boronic acid 2 (1.4 equiv.), $MnO_2$ (3 equiv.), Bathocuproine **L1** (5%), $Pd(OAc)_2$ (5%), solvent ACN (1 mL).

## Oxidant Screening

The nature of the oxidant is another crucial variable for the reaction as portrayed in Figure 1d. $Cu(OAc)_2$ that has been proven to operate outstandingly with other vinyl derivatives,[32] did not work in our setup, nor did Benzoquinone, another common oxidant.

Oxygen proved to be a valid alternative, but our screening confirmed $MnO_2$ as the best agent of the tested series. Its low cost, ease of removal, and the high yield afforded confirmed it as our chosen standard and led us to further investigations. In our proposed catalytic cycle (see Scheme 5) we conjectured that 2 equiv. of $MnO_2$ were necessary for the re-oxidation of Pd. This appears to be confirmed as only 43% conversion was observed when 1 equiv. was used, compared to 93% conversion when 2 were employed and 98% when a slight excess (3 equiv.) was utilized. We employed $MnO_2$ that the supplier marked as activated, however, it is known that the presence of moisture can affect its activity,[33] so we decided to test if running the reaction in anhydrous conditions with a $MnO_2$ that was activated through heating at 150 °C for 12 h would affect the yields.

Since the reaction already proceeded in near full conversion, we decided to test it on 1 equiv. of $MnO_2$, as this would make the changes in yield more apparent.

As expected, the yield increased from 43% (in normal conditions) to 50% (in anhydrous and activated conditions) corresponding to a quantitative conversion, highlighting how the presence of water can negatively influence the completion of the reaction.

### Auxiliary/Protective Group

The literature[30] and previous observations in our research group[12] suggested that the N–H bond of the imidazole ring might reduce the reactivity of the substrate in cross-coupling reactions. For this reason, various protective/auxiliary groups have been explored with the goal to steer clear of potential side-reactions and enhance the reactivity of the substrate.

The classes of commonly used protective groups for the N–H of imidazole comprises: *N*-Sulfonyl derivatives, *N*-alkyl/aryl derivatives, and carbamate derivatives.[31] From these classes we selected the most relevant examples: Tosyl (Tos), Trityl (Trt), DMAS, Thp, and non-protected (H). The protected substrate was in general synthetized by introducing the protective group first[12,13,32] on the 4-imidazolecarboxaldehyde followed by a Wittig reaction whereas 4-vinylimidazole was obtained by deprotection of the *N*-tosyl-4-vinylimidazole.[3] The results of the screening are shown in Figure 1e. As expected, almost no conversion was observed when the unprotected 4-vinylimidazole **1 d** was employed; however, various outcomes were observed when different protective groups were employed, suggesting that the group bound to the imidazole ring plays a role in enhancing or impeding the coupling reaction. In this regard, the protective groups act as, and should be more correctly termed, auxiliary groups. In our screening, we observed that when a sulphonamide auxiliary group like Tos or a sulfamide, like DMAS were used, the target molecules were obtained with excellent yields.

However, when the ring N is directly connected to a $sp^3$-hybridized carbon, a substantial decreases in outcomes were observed: 63% and 2% with Trt and Thp, respectively.

### Reaction Temperature

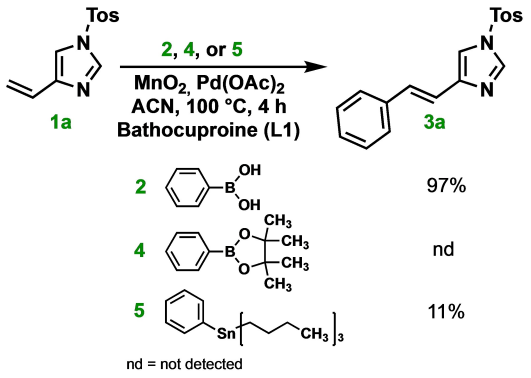
The outcome of the cross-coupling reaction was investigated at diverse reaction temperatures, Figure 1f. Reaction temperatures in the range (70–100 °C) were investigated. The cross-coupling reaction afforded yields in the range 61–98%, with the highest achieved yield at 100 °C.

### Reaction Time

A crucial experimental variable in organic synthesis is the reaction time. In our initial study of the oxidative Heck cross-coupling reaction, experiments were often left overnight (18 h) and worked-up the following morning, however once the reaction conditions were optimized in other regards, we observed that a good conversion to target molecule was already observable after only one hour. The cross-coupling reaction was thus further examined to reveal the conversion after various point of time, t∈[0 8] h, Figure 1g. This examination revealed that some experiments reach a yield of 66% already after only 30 min. and the yield continued to increase until t≈4 h. Decomposition of target molecule was not observed even at prolonged reaction time.

### Leaving Group of the Arene Moiety

Although, the reaction afforded excellent yields using a boronic acid as reagent, these are known to be unstable at higher temperatures and subject to several degradation pathways such as protodeboronation or homocoupling. Even though such side products were not observed in our investigation, we thought it would be useful for the general applicability of the method to investigate whether other leaving groups might be utilized. Boronic esters are often a more stable, but less reactive, alternative to boronic acids. In most cases, the ester is thought to have a "masking" function to the boronic acid and one of the most common examples is the pinacol ester.[38] Organotin compounds are a another alternative, as they still hold a prominent position in cross-coupling chemistry for their stability and tunability notwithstanding their toxicity.[23] Our screening of possible alternatives to boronic acids, Scheme 2, did not indicate that any improvements might be obtained. Full conversion was only achieved when the reactant was a boronic acid **2**, whilst no conversion was observed when the correspondent boronic ester **4** was employed. A yield of 11% was




**Scheme 2.** Screening experiments varying the leaving group of the arene moiety. Reaction conditions: **1 a** (221 µmol), a reagent (**2**, **4** or **5**) (1.4 equiv.), $MnO_2$ (3 equiv.), bathocuproine **L1** (5%), $Pd(OAc)_2$ (5%), ACN (1 mL).

obtained when the organotin reagent **5** was employed in the place of boronic acid.

## Ligand

The oxidative Heck cross-coupling has been carried out both in ligand-free[17,34,35] and in ligand-based reactions.[18,36] The addition of a Pd-chelating species rises from the need of a better regio- and stereoselectivity and of avoiding the accumulation of Pd(0) species that can agglomerate to form clusters of unreactive Pd that can slow the rate, or even block, the coupling reaction.

Traditionally, bidentate nitrogen ligands have been employed in oxidative Heck reactions due to low cost, greater stablility to air and moisture and because they facilitate the oxidation Pd(0)→Pd(II).[37] Since the 1, 10-phenanthroline family of ligands has already proven to be the suitable for this particular kind of cross-coupling, we limited our screening to the identification of which member of this family performed the best under our reaction conditions. The results of the screening are presented in Figure 1h.

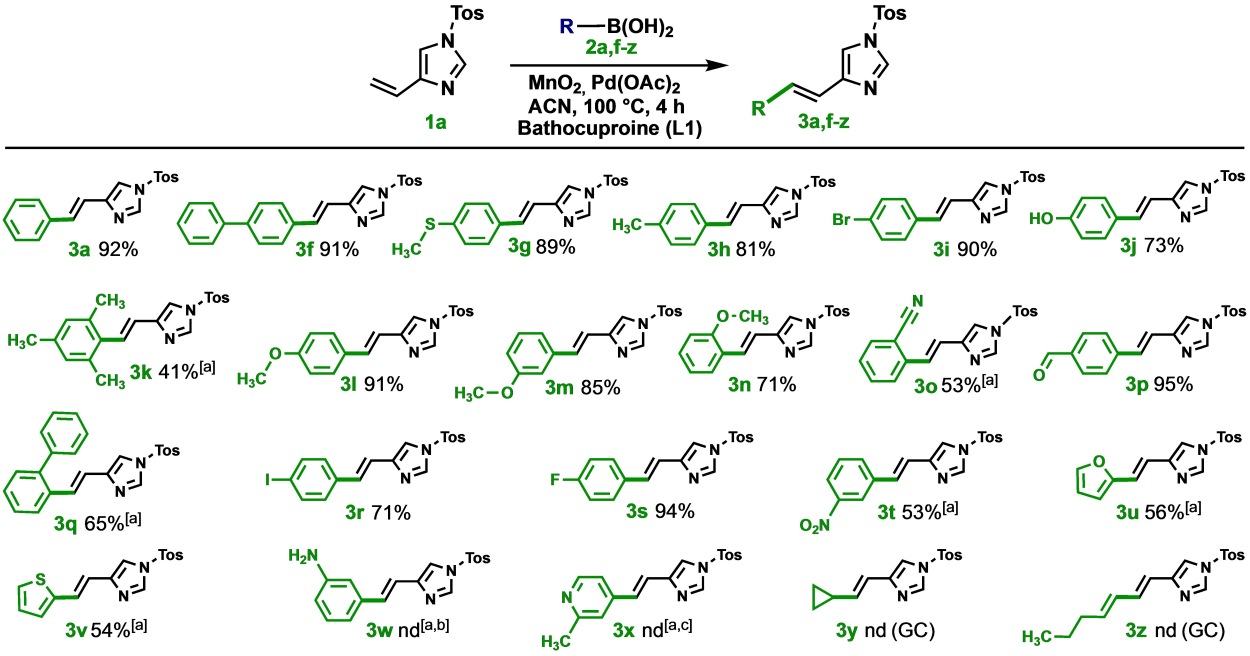
Initially the most promising ligands were neocuproine **L2** and bathophenanthroline **L3**. Nevertheless, the presence of both 2,9-dimethyl and 4,7-diphenyl substitutions proved to have a synergistic effect that increased substantially the yield when bathocuproine **L1** was used as a ligand. The combined action of bathocuproine **L1** and palladium in aerobic oxidations has previously been described.[40] Another previous report[41] also confirms the positive co-action of **L1** and Pd catalysts in an oxidative Heck approach.

## Other Additives

The use of various additives, such as a base or a silver species, has been previously discussed in the relevant literature.[39] Contrary to these insights, when the base $K_2CO_3$ was introduced as a part of the reaction mixture, the reaction was completely inhibited. $Ag_2O$ proved to be detrimental to the performance of the oxidative Heck coupling reaction, with an overall loss in yield $>20\%$ compared to the reaction run without it.

## Scope and Limitation of the Method

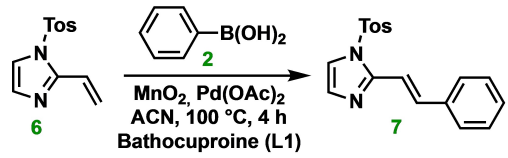
The developed oxidative Heck method was explored by utilizing *N*-tosyl-4-vinyl-1*H*-imidazole **1a** as substrate and a series of various boronic acids, see Scheme 3. The method proved to be a general, selective, and effective strategy to obtain 4-styryl-imidazoles that tolerate a huge variety of functional groups. Furthermore, the *Z*-isomer or the 1,1 substitution were not observed. Even though the reaction was carried out with a slight excess of the oxidant $MnO_2$



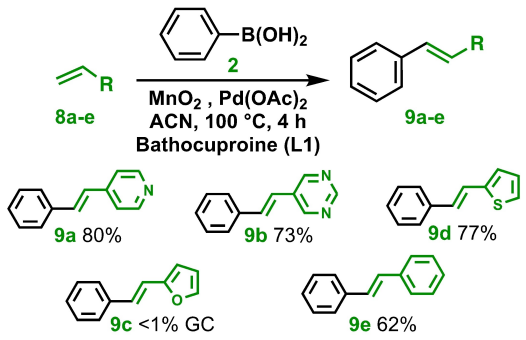

**Scheme 3.** Scope and limitation of the oxidative Heck cross-coupling reaction at optimized conditions. Reaction conditions: **1a** (221 µmol), boronic acid **3a**, **f–z** (1.4 equiv.), $MnO_2$ (3 equiv.), bathocuproine (5%), $Pd(OAc)_2$ (5%), ACN (1 mL). nd = not detected. [a] The reaction was carried out for 8 h with 2 equiv. of boronic acid. [b] The reaction afforded a yield of 39%, but TM appears to be unstable, since after the purification on HPLC, even more side products were observed. [c] The reaction was conducted in DMF because the boronic acid was not soluble in ACN or 1,4- dioxane. Traces of TM were detected using LC–MS.

we observed no oxidation of either the thioether group (**3 c**), the aldehyde (**3 l**), and the phenol (**3 f**). The oxidative Heck cross-coupling reaction proceeded also with both bromo- and iodo-arenes, in this context it is worth noting that no Suzuki cross-coupling reaction took place as a competing/parasite reaction.

The oxidative Heck cross-coupling reaction afforded high to excellent yields using 3- and 4-substitued phenylboronic acids as reagents, and proceeds with good yields also if functional groups were installed in the 2-position, even with cumbersome substituents (**3 m**). In general, electron-rich substituents on the phenyl boronic acid scaffold afforded higher conversion than the electron deficient ones. This trend was observed also with the good yields obtained if electron-rich heterocyclic boronic acids are employed compared to the lack of conversion when electron-poor heterocyclic boronic acids were used. Furthermore, the reaction only worked in the presence of arylboronic acids whereas no product was detected when aliphatic or alkenyl boronic acids were employed. In all unproductive reaction experiments only the substrate **1 a** was observed.




**Scheme 4.** Oxidative Heck cross-coupling on 1-tosyl-2-vinyl-1*H*-imidazole **6** using (221 µmol), phenyl boronic acid **2** (1.4 equiv.), $MnO_2$ (3 equiv.), bathocuproine (5%), $Pd(OAc)_2$ (5%), ACN (1 mL) to achieve (*E*)-2-styryl-1-tosyl-1*H*-imidazole **7**.

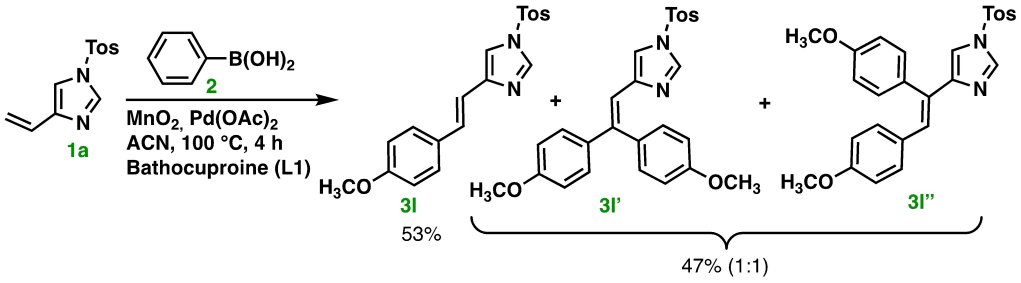



**Scheme 5.** Oxidative Heck cross-coupling with vinyl-*N*-heterocycles **8 a**–**e**. Reaction conditions: the vinyl-compound (2.2 mmol), phenyl boronic acid 2 (1.4 equiv.), $MnO_2$ (3 equiv.), bathocuproine (5%), $Pd(OAc)_2$ (5%), ACN (10 mL), and **8 a**–**e** (226 µmol), phenyl boronic acid (1.4 equiv.), $MnO_2$ (3 equiv.), bathocuproine (5%), $Pd(OAc)_2$ (5%), ACN (1 mL).

Our method for oxidative Heck cross-coupling was further explored with other vinyl-*N*-heterocycles as substrates, Scheme 5. The reaction was carried out both on micro-molar and milli-molar scale, which revealed that the method was scalable.

Overall, the results reveal a high functional group tolerance for the developed oxidative Heck cross-coupling method, which includes a mild oxidant ($MnO_2$), short reaction time, and without acid or base present.

The option of double substitution on the vinyl moiety by using an excess of the boronic acid was explored. The experiment portrayed in Scheme 6, afforded a product corresponding to either **3 l'** or **3 l**,**"** suggesting that a double arylation could be feasible when carried out with an excess of boronic acid and $MnO_2$. Indeed, when the reaction was performed with 10 equiv. of boronic acid and 6 equiv. of $MnO_2$, HPLC-MS and NMR analyses revealed three main products: the mono-substituted imidazole **3 l**, and the di-substituted imidazoles **3 l'** and **3 l.**" The formation of the 1:1 mixture of **3 l'** and **3 l"** reveals that the regio-selectivity is lost for the second cross-coupling.




**Scheme 6.** The oxidative Heck cross-coupling reaction in the using excess of both boronic acid **2** and oxidant $MnO_2$.

### Mechanism

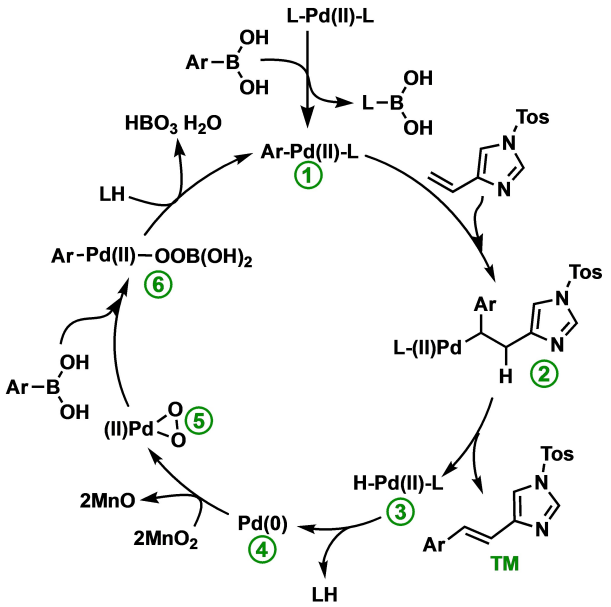
Based on the observed experimental results, a plausible reaction mechanism for the Pd catalytic cycle of the base-free boron oxidative Heck cross-coupling reaction was outlined, see Scheme 7.

The first step is a trans-metalation that produces the palladium (II) intermediate ①, which is in contrast with other coupling reactions where the boronic acid first is activated through the formation of an "ate" complex. The coordination of the alkene is followed by insertion ②, β-hydride- ③ and reductive eliminations producing target molecule **TM** and Pd (0) ④, respectively. Pd (0) is re-oxidized to Pd (II) by $MnO_2$. Notably 2 equiv. of the oxidant were needed to form the peroxopalladium complex ⑤, which is known to react with boronic acid[42] to produce complex ⑥.

## Conclusion

Functionalization of imidazoles is of great importance for applications in life science and industrial applications, in particular as NHC ligands for transition metal catalysis. Functionalization of the nitrogen atoms of the imidazole ring and the carbon in the 2-position can be performed relatively smoothly by means of existing methods in organic synthesis. However, functionalization of the backbone of imidazole is more challenging. Multicomponent reactions producing the imidazole ring with embedded functionality have been used, but such a strategy can also be challenging especially if sterically demanding groups are to be incorporated on the imidazole backbone (i.e. position 4 and 5).

In this study, the strategy of late stage functionalization has been used. Imidazole or a simple and readily available functionalized imidazole ring, such as imidazole carbaldehyde, can be used as the starting substrate. Hence, with imidazole carbaldehyde as the starting substrate, we have designed and developed a regioselective and high yielding method for oxidative Heck cross-coupling that provides (*E*)-4-styrylimidazole derivatives with broad functional group tolerability A method that, moreover revealed potential to be amended to fit other heterocycles. A substantial difference from previously disclosed oxidative Heck cross-coupling methods is that it involves $MnO_2$ as a terminal oxidant, which is cheap, easy to remove, and offers selectivity towards oxidation of Pd (0)→Pd (II). Several factors emerge to be crucial for the success of the method, amongst these the use of boronic acids in the place of boronic esters, the presence of the auxiliary group Tosyl and an adequate combination of Pd catalyst and ligand. Safe for a small number of exceptions, the disclosed method provided successful coupling products in yields ranging from a minimum of 41% up to 95%. We envision that the unveiled method will be useful for the construction of more complex heterocycle-centered frameworks, by either further functionalization of the olefin, of the functional groups located on the imidazole/heterocycle or on the newly bonded aromatic ring.




**Scheme 7.** Proposal for a reaction mechanism for the Pd catalysed base-free boron oxidative Heck cross-coupling reaction.

## Experimental Section

**General Experimental Information**. All reagents and solvents were purchased from commercial sources and used as received. Reagent-grade chemicals were purchased from commercial sources and used without further purification. All reaction mixtures and samples collected during column chromatography were monitored by means of TLC analysis (TLC plates Merck Kieselgel 60 F254). The TLC plates were observed under UV light at λ 254 nm and λ 365 nm. All final compounds were purified by either semi-preparative RP-HPLC or by autoflash chromatography. The HPLC eluting mixtures was of acetonitrile and $H_2O$ (both containing 0.1% Formic acid). Fractions of equal purity were pooled and dried under nitrogen flow overnight. $^{1}H$ and $^{13}C$ NMR spectra were recorded using a Bruker instruments AV 500 and Biospin 850SB. High-resolution mass spectra (HRMS) were performed with a Q-TOF Micro YA263 instrument.

### Experimental Procedures.

#### *General Procedures – Oxidative Heck Cross-Coupling*

***Method A:*** **1a** (55 mg, 221 μmol), bathocuproine (5%, 4 mg, 11 μmol), $Pd(OAc)_2$ (5%, 3 mg, 11 μmol), and the boronic acid (1.4 equiv., 310 μmol) that was dissolved in acetonitrile (1 mL)

was transferred to a pressure-resistant reaction tube (10 mL). $MnO_2$ (3 equiv., 58 mg, 665 µmol) was then added and the reactor tube that was sealed and heated for 4 h at 100 °C. After cooling, the solvent was evaporated under reduced pressure. The obtained crude was purified by mean of column chromatography packed with silica and an eluent composed of hexane and ethyl acetate. The highest intensity of UV-absorption is around 300 nm for all the products.

***Method B***: In a pressure-resistant reaction tube (10 mL), **1 a** (55 mg, 221 µmol), bathocuproine (5%, 4 mg, 11 µmol), Pd $(OAc)_2$ (5%, 3 mg, 11 µmol), the boronic acid (2.0 equiv., 442 µmol) was dissolved in acetonitrile (1 mL). To the mixture, $MnO_2$ (3 equiv., 58 mg, 665 µmol) was added and the vial was sealed and heated for 8 h at 100 °C. After cooling, the solvent was evaporated under reduced pressure and the crude was purified through HPLC (water:ACN + 0.1% HCOOH). The highest intensity of UV-absorption is around 300 nm for all the products.

**1-Tosyl-1*H*-imidazole-4-carbaldehyde**[13] **[37622-92-7] (0 a)**. 1*H*-imidazole-4-carbaldehyde (5.00 g, 52.0 mmol) and *p*-toluenesulfonyl chloride (1 equiv., 9.92 g, 52.0 mmol) were added to a Schlenk-tube under argon atmosphere. THF (dry, 40 mL) was then added to dissolve the solids and TEA (1 equiv., 7.26 mL, 5.27 g, 52.0 mmol) was added by a syringe. The reaction mixture was stirred under argon for 24 h at ambient temperature and checked through GC-MS. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The crude product was extracted from acid water with DCM (3 × 200 mL), the organic phases were combined and dried over $Na_2SO_4$ to afford the target compound in a yield of 98% (12.81 g, 51.2 mmol) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.07 (d, $J$ = 1.3 Hz, 1H), 7.94 (d, $J$ = 1.3 Hz, 1H), 7.89 (dt, $J$ = 8.1, 1.8 Hz, 2H), 7.41 (dt, $J$ = 8.1, 1.8 Hz, 2H), 2.47 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 185.59, 147.44, 142.89, 137.28, 133.82, 130.81, 127.77, 121.86, 21.81.

**1-Tosyl-4-vinyl-1*H*-imidazole [185850-13-9] (1 a)**. Under inert and anhydrous conditions, methyltriphenyl-phosphonium bromide (1.2 equiv., 8.56 g, 24.0 mmol) was placed in a three-necks flask and suspended in THF (dry, 30 mL). Then potassium *tert*-butoxide in THF (1 M, 1.1 equiv., 2.47 g, 22.0 mL, 22.0 mmol) was added by means of a syringe. The suspension turns into pale yellow color during the addition. After 30 min, **0 a** (5.0 g, 20.0 mmol) was added slowly (exothermic reaction) to the reaction mixture. The reaction mixture was stirred for 2 h at 20 °C and controlled by means of GC-MS. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The crude product was extracted from acidic water with DCM (3 × 200 mL), the organic phases were combined and dried over $Na_2SO_4$. Purification by means of column chromatography with silica gel and an eluent system composed of hexane:ethyl acetate = 82:18 provides target compound in a yield of 52% (2.51 g, 10.35 mmol) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.82 (dt, $J$ = 8.4, 1.5 Hz, 2H), 7.35 (dt, $J$ = 8.2, 1.5 Hz, 2H), 7.16 (s, $J$ = 0.7 Hz, 1H), 6.50 (dd, $J$ = 17.4, 11.0 Hz, 1H), 5.92 (dd, $J$ = 17.4, 1.4 Hz, 1H), 5.26 (dd, $J$ = 11.0, 1.4 Hz, 1H), 2.44 (s, 3H).$^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.33, 142.77, 136.74, 134.92, 130.45, 127.36, 126.93, 115.85, 113.79, 21.73.

**4-Formyl-*N*,*N*-dimethyl-1*H*-imidazole-1-sulfonamide [140174-48-7] (0 b)**.[13] 1*H*-imidazole-4-carbaldehyde (5.00 g, 52.0 mmol) and DMAS–Cl (1 equiv., 7.47 g, 5.59 mL, 52.0 mmol) were added to a Schlenk-tube under argon atmosphere. THF (dry, 30 mL) was then added to dissolve the mixture and TEA (1 equiv., 7.26 mL, 5.27 g, 52.0 mmol) was added by a syringe. The reaction mixture was stirred under argon for 24 h at 20 °C. Afterwards, the solvent was removed under reduced pressure. The crude product was extracted from acidic water with DCM (3 × 200 mL), the organic phases were combined and dried over $Na_2SO_4$ to afford target compound in a yield of 87% (9.21 g, 45.3 mmol) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.96 (d, $J$ = 1.2 Hz, 1H), 7.89 (d, $J$ = 1.3 Hz, 1H), 2.93 (s, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 185.55, 142.18, 137.58, 122.49, 39.54, 38.20.

***N*,*N*-Dimethyl-4-vinyl-1*H*-imidazole-1-sulfonamide [343880-85-3] (1 b)**. Methyltriphenylphosphonium bromide (1.2 equiv., 9.49 g, 26.6 mmol) was transferred to a three-necks round bottom flask (100 mL) under inert and anhydrous conditions. Then, was suspended in THF (dry, 30 mL), followed by the addition of potassium *tert*-butoxide in THF (1 M, 1.1 equiv., 2.73 g, 24.4 mL, 24.4 mmol) by a syringe (exothermic reaction). The suspension turned into a pale-yellow color. After 30 min, **0 b** (4.5 g, 22.1 mmol) was slowly added (exothermic reaction) to the mixture. The reaction mixture was stirred for 2 h at 20 °C and controlled by means of GC-MS. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The crude product was extracted from acidic water with DCM (3 × 200 mL), the organic phases were combined and dried over $Na_2SO_4$. Purification of isolated product by means of column chromatography packed with silica gel and an eluent system composed of hexane:ethyl acetate = 75:25 provides target compound in a yield of 62% (3.41 g, 13.7 mmol) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.07 (d, $J$ = 0.8 Hz, 1H), 6.50 (dd, $J$ = 17.4, 11.0 Hz, 1H), 5.90 (dd, $J$ = 17.4, 1.4 Hz, 1H), 5.23 (dd, $J$ = 11.0, 1.5 Hz, 1H), 2.80 (s, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 141.85, 136.82, 127.08, 115.54, 114.27, 38.19.

**1-Trityl-1*H*-imidazole-4-carbaldehyde [33016-47-6] (0 c).**[32] To a 250 mL round-bottomed flask 1*H*-imidazole-4-carbaldehyde (1.20 g, 12.5 mol), trityl chloride (1.1 equiv., 3.83 g, 13.7 mol) were dissolved in acetonitrile (40 mL) and stirred at 20 °C. Afterwards, triethylamine (1.72 equiv., 3.0 mL, 2.17 g, 21.5 mol) was added dropwise and the reaction was stirred 18 h. A mixture of hexane (4 mL) and deionized water (40 mL) was added and stirred for another 30 min. The slurry was filtered, and the filter cake was washed with water (2 × 10 mL) and dried under reduced pressure to afford target compound as a white solid in a yield of 84% (3.55 g, 10.5 mmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.61 (d, $J$ = 1.3 Hz, 1H), 7.53 (d, $J$ = 1.2 Hz, 1H), 7.41–7.33 (m, 9H), 7.15–7.08 (m, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 186.62, 141.55, 140.89, 140.62, 129.67, 128.55, 128.40, 126.76, 76.36.

**1-Trityl-4-vinyl-1*H*-imidazole [86803-29-4] (1 c)**. Under inert and anhydrous conditions, methyltriphenyl-phosphonium bromide (1.2 equiv., 4.43 g, 12.41 mmol) was transferred to a three-necks round bottom flask and suspended in THF (dry, 25 mL). Then, potassium *tert*-butoxide in THF (1 M, 1.1 equiv., 1.27 g, 11.4 mL, 11.4 mmol) was added by means of a syringe.

The mixture turned into a pale-yellow color. After 30 min, **0c** (3.5 g, 10.3 mmol) was slowly added (exothermic reaction) to the mixture. The reaction mixture was stirred for 2 h at 20 °C and monitored by means of GC-MS. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The crude product was extracted from acidic water with DCM (3 × 200 mL), the organic phases were combined and dried over $Na_2SO_4$. Purification of isolated product by means of column chromatography packed with silica gel and an eluent system composed of hexane:ethyl acetate = 88:12 provides target compound in a yield of 66% (2.30 g, 6.84 mmol) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, $J$ = 1.0 Hz, 1H), 7.28–7.22 (m, 9H), 7.10–7.04 (m, 6H), 6.69 (d, $J$ = 1.2 Hz, 1H), 6.47 (dd, $J$ = 17.4, 11.0 Hz, 1H), 5.75 (dd, $J$ = 17.4, 1.7 Hz, 1H), 5.03 (dd, $J$ = 11.0, 1.8 Hz, 1H).$^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.35, 139.57, 139.23, 129.79, 128.69, 128.10 (3 C + 1 C), 119.35, 112.15, 75.32.

**4-Vinyl-1*H*-imidazole [3718-04-5][3] (1d)**. 1-Tosyl-4-vinyl-1*H*-imidazole **1a** (1.0 g, 4.0 mmol) was transferred to a round-bottom flask (50 mL) and dissolved in MeOH (10 mL) whereupon HCl (37%, 2 mL) was added in one portion. The reaction mixture was refluxed for 2 h. MeOH was removed under reduced pressure and the crude was extracted with $Et_2O$ (2 × 100 mL) and HCl solution (1 M, 100 mL). The organic phases were discarded. The aqueous phase was made alkaline by slow addition of NaOH (exothermic) and extracted again with $Et_2O$ (3 × 100 mL). The organic phases were combined, dried over $Na_2SO_4$, to afford target compound in a yield of 85% (323 mg, 3.43 mmol) as a pale yellow solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 12.92 (s, 1H), 7.54 (s, 1H), 6.96 (s, 1H), 6.54 (dd, $J$ = 17.0, 11.2 Hz, 1H), 5.58 (d, $J$ = 17.4 Hz, 1H), 5.01 (d, $J$ = 10.6 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 135.87, 135.57, 126.63, 120.04, 112.11.

**1-(Tetrahydro-2*H*-pyran-2-yl)-4-vinyl-1*H*-imidazole [NEW] (1e)**. 4-Vinyl-1*H*-imidazole (500 mg, 5.31 mmol) was transferred to a round-bottomed flask (100 mL) and suspended in DMF (5 mL) at 20 °C. *p*TSA (5%, 67 mg, 0.265 mmol) and DHP (1.5 equiv., 670 mg, 0.73 mL, 7.97 mmol) were then added. The reaction was capped and heated at 100 °C for 18 h. The post-reaction mixture was cooled at 20 °C, whereupon the solvent was removed under reduced pressure. The crude mixture was extracted from basic water solution (NaOH 1 M, 200 mL) with DCM (2 × 200 mL). The organic phases were combined, dried over $Na_2SO_4$ and target product was obtained as a yellow oil in a yield of 92% (875 mg, 4.91 mmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.60 (s, $J$ = 0.8 Hz, 1H), 7.02 (d, $J$ = 0.8 Hz, 1H), 6.59 (dd, $J$ = 17.4, 11.0 Hz, 1H), 5.83 (dd, $J$ = 17.5, 1.7 Hz, 1H), 5.17 (dd, $J$ = 9.6, 2.4 Hz, 1H), 5.13 (dd, $J$ = 11.0, 1.7 Hz, 1H), 4.08–4.02 (m, 1H), 3.70–3.62 (m, 1H), 2.05–1.88 (m, 3H), 1.73–1.58 (m, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 140.90, 135.77, 128.56, 114.47, 112.31, 84.07, 67.72, 31.43, 24.80, 22.35.

**(*E*)-4-Styryl-1-tosyl-1*H*-imidazole [NEW] (3a)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: phenylboronic acid (38 mg). Eluent system composed of hexane:ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 92% (66 mg, 203 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, $J$ = 0.5 Hz, 1H), 7.84 (dt, $J$ = 8.5, 1.7 Hz, 2H), 7.47–7.43 (m, 2H), 7.39–7.29 (m, 5H), 7.26–7.21 (m, 2H), 6.87 (d, $J$ = 16.1 Hz, 1H), 2.44 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.36, 142.79, 136.95, 136.77, 134.92, 130.51, 130.48, 128.68, 127.88, 127.37, 126.55, 118.21, 113.93, 21.74. HRMS (ESI) m/z: [M + H] calcd for $C_{18}H_{17}N_2O_2S$ 325.10107; found 325.10131.

**(*E*)-*N*,*N*-Dimethyl-4-styryl-1*H*-imidazole-1-sulfonamide [NEW] (3b)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: *N*,*N*-dimethyl-4-vinyl-1*H*-imidazole-1-sulfonamide (55 mg, 273 µmol), phenyl-boronic acid (1.4 equiv., 47 mg, 383 µmol). Eluent system composed of hexane:ethyl acetate = 87:13. The title compound was isolated as a white solid in a yield of 92% (70 mg, 252 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.46–7.39 (m, 2H), 7.35–7.24 (m, 3H), 7.22 – 7.13 (m, 2H), 6.87 (d, $J$ = 16.1 Hz, 1H), 2.81 (s, $J$ = 6.0 Hz, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 141.85, 137.03, 136.87, 130.26, 128.71, 127.85, 126.55, 118.37, 114.48, 38.24. HRMS (ESI) m/z: [M + H] calcd for $C_{13}H_{16}N_3O_2S$ 278.09632; found 278.09742.

**(*E*)-4-Styryl-1-trityl-1*H*-imidazole [77705-84-1] (3c)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: 1-trityl-4-vinyl-1*H*-imidazole **1c** (56 mg, 166 µmol), phenylboronic acid (1.4 equiv., 28 mg, 233 µmol). Eluent system composed of hexane: ethyl acetate = 92:08. The title compound was isolated as a white solid in a yield of 63% (43 mg, 104 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, $J$ = 1.0 Hz, 1H), 7.44 (d, $J$ = 7.3 Hz, 2H), 7.38–7.27 (m, 12H), 7.25–7.13 (m, 7H), 6.93 (d, $J$ = 16.2 Hz, 1H), 6.87 (d, $J$ = 1.2 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.09, 139.28, 138.96, 137.50, 129.78, 128.57, 128.24, 128.20, 127.94, 127.76, 126.29, 119.87, 119.64, 75.68. HRMS (ESI) m/z: [M + H] calcd for $C_{30}H_{25}N_2$ 413.20177; found 413.20199.

**(*E*)-4-(2-([1,1′-Biphenyl]-4-yl)vinyl)-1-tosyl-1*H*-imidazole [NEW] (3f)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: [1,1′-biphenyl]-4-ylboronic acid (61 mg). Eluent system composed of hexane:ethyl acetate = 86:14. The title compound was isolated as a white solid in a yield of 91% (81 mg, 202 µmol).$^1$H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, $J$ = 0.4 Hz, 1H), 7.84 (d, $J$ = 8.4 Hz, 2H), 7.61–7.55 (m, 4H), 7.52 (d, $J$ = 8.3 Hz, 2H), 7.43 (t, $J$ = 7.7 Hz, 2H), 7.40–7.30 (m, 4H), 7.25 (d, $J$ = 1.3 Hz, 1H), 6.91 (d, $J$ = 16.1 Hz, 1H), 2.43 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.39, 142.82, 140.60, 136.99, 135.83, 134.92, 130.49, 130.01, 128.82, 127.39 (2 C + 2 C), 127.37 (2 C + 2 C), 127.00, 126.92, 118.26, 114.00, 21.75. HRMS (ESI) m/z: [M + H] calcd for $C_{24}H_{21}N_2O_2S$ 401.13237; found 401.13256.

**(*E*)-4-(4-(Methylthio)styryl)-1-tosyl-1*H*-imidazole [NEW] (3g)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-(methylthio) phenyl)boronic acid (52 mg). Eluent system composed of hexane: ethyl acetate = 87:13. The title compound was isolated as a white solid in a yield of 89% (67 mg, 180 µmol).$^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.83 (d, $J$ = 8.4 Hz, 2H), 7.36 (t, $J$ = 7.8 Hz, 4H), 7.29–7.18 (m, 4H), 6.82 (d, $J$ = 16.0 Hz, 1H), 2.48 (s, $J$ = 6.4 Hz, 3H), 2.43 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.36, 142.81, 138.25,

136.96, 134.91, 133.67, 130.47, 129.86, 127.36, 126.93, 126.58, 117.57, 113.80, 21.74, 15.71. HRMS (ESI) m/z: [M+H] calcd for $C_{19}H_{19}N_2O_2S_2$ 371.08879; found 371.08833.

**(*E*)-4-(4-Methylstyryl)-1-tosyl-1*H*-imidazole [NEW] (3h)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: *p*-tolylboronic acid (42 mg). Eluent system composed of hexane: ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 81% (61 mg, 180 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, $J$ = 0.5 Hz, 1H), 7.83 (dt, $J$ = 8.4, 1.7 Hz, 2H), 7.37–7.32 (m, 4H), 7.29 (d, $J$ = 16.1 Hz, 1H), 7.21 (d, $J$ = 1.0 Hz, 1H), 7.13 (d, $J$ = 8.0 Hz, 2H), 6.82 (d, $J$ = 16.1 Hz, 1H), 2.43 (s, 3H), 2.34 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.32, 142.97, 137.84, 136.91, 134.95, 133.99, 130.46 (2 C + 1 C), 129.40, 127.35, 126.48, 117.25, 113.61, 21.73, 21.27. HRMS (ESI) m/z: [M+H] calcd for $C_{19}H_{19}N_2O_2S$ 339.11672; found 339.11689.

**(*E*)-4-(4-Bromostyryl)-1-tosyl-1*H*-imidazole [NEW] (3i)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-bromophenyl) boronic acid (62 mg). Eluent system composed of hexane:ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 90% (80 mg, 198 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.84 (dt, $J$ = 8.6, 1.6 Hz, 2H), 7.44 (dt, $J$ = 8.6, 1.7 Hz, 2H), 7.36 (d, $J$ = 8.2 Hz, 2H), 7.31 (dt, $J$ = 8.5, 1.6 Hz, 2H), 7.27–7.22 (m, 2H), 6.85 (d, $J$ = 16.0 Hz, 1H), 2.44 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.43, 142.45, 137.03, 135.73, 134.86, 131.81, 130.49, 129.20, 128.00, 127.38, 121.62, 118.90, 114.27, 21.74. HRMS (ESI) m/z: [M+H] calcd for $C_{18}H_{16}BrN_2O_2S$ 405.00954; found 405.01439.

**(*E*)-4-(2-(1-Tosyl-1*H*-imidazol-4-yl)vinyl)phenol [NEW] (3j)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-hydroxyphenyl) boronic acid (43 mg). Eluent system composed of hexane:ethyl acetate = 75:25. The title compound was isolated as a white solid in a yield of 73% (55 mg, 162 µmol). $^1$H NMR (500 MHz, $CD_3CN$) δ 7.96 (s, 1H), 7.82 (d, $J$ = 8.4 Hz, 2H), 7.37 (d, $J$ = 8.1 Hz, 2H), 7.28 (d, $J$ = 8.4 Hz, 2H), 7.13 (d, $J$ = 16.1 Hz, 1H), 6.99 (s, 1H), 6.74–6.66 (m, 3H), 2.34 (s, 3H). $^{13}$C NMR (126 MHz, $CD_3CN$) δ 156.60, 146.59, 142.82, 136.95, 134.41, 130.22, 129.27, 128.56, 127.58, 126.95, 115.73, 115.14, 113.29, 20.39. HRMS (ESI) m/z: [M+H] calcd for $C_{18}H_{17}N_2O_3S$ 341.09740; found 341.09599.

**(*E*)-1-tosyl-4-(2,4,6-trimethylstyryl)-1*H*-imidazole [NEW] (3k)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: mesitylboronic acid (73 mg). The title compound was isolated as a yellow oil in a yield of 41% (33 mg, 90 µmol).$^1$H NMR (500 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.85 (d, $J$ = 8.4 Hz, 2H), 7.39–7.33 (m, 3H), 7.19 (s, 1H), 6.87 (s, 2H), 6.38 (d, $J$ = 16.4 Hz, 1H), 2.45 (s, 3H), 2.31 (s, 6H), 2.27 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.90, 141.76, 136.86, 136.51, 136.21, 131.97, 130.47, 128.78, 128.69, 127.44, 123.24, 117.26, 113.46, 21.75, 21.07, 20.94. HRMS (ESI) m/z: [M+H] calcd for $C_{21}H_{23}N_2O_2S$ 367.14802; found 367.14769.

**(*E*)-4-(4-Methoxystyryl)-1-tosyl-1*H*-imidazole [NEW] (3l)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-methoxyphenyl) boronic acid (47 mg). Eluent system composed of hexane:ethyl acetate = 87:13. The title compound was isolated as a white solid in a yield of 91% (72 mg, 203 µmol).$^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, $J$ = 0.6 Hz, 1H), 7.83 (dt, $J$ = 8.4, 1.9 Hz, 2H), 7.37 (ddd, $J$ = 16.0, 7.6, 4.9 Hz, 4H), 7.30–7.24 (m, 1H), 7.20 (d, $J$ = 0.9 Hz, 1H), 6.87 (dt, $J$ = 8.8, 1.9 Hz, 2H), 6.73 (d, $J$ = 16.1 Hz, 1H), 3.81 (s, 3H), 2.43 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 159.49, 146.29, 143.08, 134.97, 130.44, 130.08, 129.57, 127.80, 127.34, 116.13, 114.51, 114.13, 113.30, 55.31, 21.72. HRMS (ESI) m/z: [M+H] calcd for $C_{19}H_{19}N_2O_3S$ 355.11164; found 355.11280.

**(*E*)-4-(3-methoxystyryl)-1-tosyl-1*H*-imidazole [NEW] (3m)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (3-methoxyphenyl) boronic acid (47 mg). Eluent system composed of hexane:ethyl acetate = 87:13. The title compound was isolated as a white solid in a yield of 85% (67 mg, 189 µmol).$^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, $J$ = 0.6 Hz, 1H), 7.83 (dt, $J$ = 8.4, 1.7 Hz, 2H), 7.39–7.21 (m, 6H), 7.05 (d, $J$ = 7.7 Hz, 1H), 7.00–6.97 (m, 1H), 6.86 (d, $J$ = 16.0 Hz, 1H), 6.83–6.79 (m, 1H), 3.82 (s, 3H), 2.44 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 159.85, 146.38, 142.70, 138.22, 136.96, 134.91, 130.48, 130.40, 129.65, 127.37, 119.25, 118.56, 114.01, 113.55, 111.80, 55.22, 21.74. HRMS (ESI) m/z: [M+H] calcd for $C_{19}H_{19}N_2O_3S$ 355.11164; found 355.11180.

**(*E*)-4-(2-Methoxystyryl)-1-tosyl-1*H*-imidazole [NEW] (3n)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (2-methoxyphenyl) boronic acid (47 mg). Eluent system composed of hexane:ethyl acetate = 87:13.The title compound was isolated as a white solid in a yield of 71% (56 mg, 158 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, $J$ = 0.6 Hz, 1H), 7.83 (dt, $J$ = 8.4, 1.6 Hz, 2H), 7.60 (d, $J$ = 16.3 Hz, 1H), 7.47 (dd, $J$ = 7.6, 1.6 Hz, 1H), 7.35 (d, $J$ = 8.2 Hz, 2H), 7.25–7.20 (m, 2H), 6.97–6.91 (m, 2H), 6.88 (d, $J$ = 8.2 Hz, 1H), 3.86 (s, 3H), 2.44 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.22, 146.26, 143.49, 136.88, 135.01, 130.43, 128.87, 127.34, 127.11, 125.81, 125.78, 120.63, 119.08, 113.58, 110.92, 55.38, 21.72. HRMS (ESI) m/z: [M+H] calcd for $C_{19}H_{19}N_2O_3S$ 355.11164; found 355.11197.

**(*E*)-2-(2-(1-Tosyl-1*H*-imidazol-4-yl)vinyl)benzonitrile [NEW] (3o)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: (2-methoxyphenyl)boronic acid (65 mg). The title compound was isolated as a white solid in a yield of 53% (41 mg, 117 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, $J$ = 0.8 Hz, 1H), 7.86 (dt, $J$ = 8.5, 1.7 Hz, 2H), 7.66 (d, $J$ = 8.1 Hz, 1H), 7.64 (dd, $J$ = 7.8, 1.0 Hz, 1H), 7.59–7.52 (m, 2H), 7.38 (d, $J$ = 8.5 Hz, 3H), 7.32 (td, $J$ = 7.7, 1.1 Hz, 1H), 7.10 (d, $J$ = 16.0 Hz, 1H), 2.45 (s, 3H). $^{13}$C NMR (214 MHz, $CDCl_3$) δ 146.54, 141.90, 140.00, 137.08, 133.38, 132.74, 130.55, 130.03, 129.04, 127.71, 127.45, 125.95, 125.91, 123.48, 117.97, 115.19, 21.76. HRMS (ESI) m/z: [M+Na] calcd for $C_{19}H_{15}NaN_3O_2S$ 372.07827; found 372.07855.

**(*E*)-4-(2-(1-Tosyl-1*H*-imidazol-4-yl)vinyl)benzaldehyde [NEW] (3p)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-formyl-phenyl)boronic acid (46 mg). Eluent system composed of hexane:ethyl acetate = 87:13. The title

compound was isolated as a white solid in a yield of 95% (74 mg, 210 μmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.01 (s, 1H), 7.90–7.79 (m, 4H), 7.59 (d, $J$ = 8.2 Hz, 2H), 7.40–7.34 (m, 3H), 7.32 (s, 1H), 7.02 (d, $J$ = 16.0 Hz, 1H), 2.44 (s, 3H). $^{13}$C NMR (126 MHz, $CD_3CN$) δ 186.27, 141.24, 137.55, 136.82, 131.86, 130.17, 129.44, 125.23, 124.92, 123.74, 122.10, 121.63, 116.25, 109.87, 16.45. HRMS (ESI) m/z: [M + H] calcd for $C_{19}H_{17}N_2O_3S$ 353.09599; found 353.09772.

**(*E*)-4-(2-([1,1′-Biphenyl]-2-yl)vinyl)-1-tosyl-1*H*-imidazole [NEW] (3 q)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: [1,1′-biphenyl]-2-ylboronic acid (88 mg). The title compound was isolated as a white solid in a yield of 65% (58 mg, 145 μmol). $^1$H NMR (850 MHz, $CDCl_3$) δ 7.92 (d, $J$ = 0.8 Hz, 1H), 7.82 (dt, $J$ = 8.5, 1.8 Hz, 2H), 7.66 (dd, $J$ = 7.5, 1.0 Hz, 1H), 7.42–7.39 (m, 2H), 7.37–7.31 (m, 7H), 7.29 (d, $J$ = 16.0 Hz, 1H), 7.18 (d, $J$ = 1.2 Hz, 1H), 6.81 (d, $J$ = 16.0 Hz, 1H), 2.44 (s, 3H). $^{13}$C NMR (214 MHz, $CDCl_3$) δ 146.31, 142.99, 141.36, 140.73, 136.82, 134.91, 134.89, 130.45, 130.43, 129.78, 129.49, 128.18, 127.73, 127.50, 127.39, 127.19, 127.16, 125.87, 119.52, 113.70, 21.74. HRMS (ESI) m/z: [M + H] calcd for $C_{24}H_{22}N_2O_2S$ 401.13237; found 401.13287.

**(*E*)-4-(4-Iodostyryl)-1-tosyl-1*H*-imidazole [NEW] (3 r)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-Iodophenyl)boronic acid (77 mg). Eluent system composed of hexane:ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 71% (71 mg, 158 μmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.83 (dt, $J$ = 8.4, 1.7 Hz, 2H), 7.65 (dt, $J$ = 8.4, 1.8 Hz, 2H), 7.36 (d, $J$ = 8.5 Hz, 2H), 7.23 (d, $J$ = 16.3 Hz, 2H), 7.18 (dt, $J$ = 8.8, 1.9, 1.9 Hz, 2H), 6.86 (d, $J$ = 16.0 Hz, 1H), 2.44 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.44, 142.42, 137.77, 137.03, 136.30, 134.86, 130.49, 129.31, 128.22, 127.38, 118.99, 114.32, 93.12, 21.75. HRMS (ESI) m/z: [M + H] calcd for $C_{18}H_{16}IN_2O_2S$ 450.99772; found 450.99980.

**(*E*)-4-(4-Fluorostyryl)-1-tosyl-1*H*-imidazole [NEW] (3 s)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: (4-fluorophenyl) boronic acid (43 mg). Eluent system composed of hexane:ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 94% (71 mg, 207 μmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.86–7.81 (m, 2H), 7.44–7.38 (m, 2H), 7.36 (d, $J$ = 8.2 Hz, 2H), 7.28 (d, $J$ = 16.2 Hz, 1H), 7.23 (s, 1H), 7.05–6.98 (m, 2H), 6.78 (d, $J$ = 16.0 Hz, 1H), 2.43 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 162.46 (d, $J$ = 247.6 Hz), 146.39, 142.61, 136.96, 134.89, 132.97 (d, $J$ = 3.5 Hz), 130.48, 129.28, 128.06 (d, $J$ = 7.8 Hz), 127.36, 117.99 (d, $J$ = 2.0 Hz), 115.65 (d, $J$ = 21.6 Hz), 113.93, 21.74. HRMS (ESI) m/z: [M + H] calcd for $C_{18}H_{16}FN_2O_2S$ 343.09165; found 343.09199.

**(*E*)-4-(3-Nitrostyryl)-1-tosyl-1*H*-imidazole [NEW] (3 t)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: (3-nitrophenyl)boronic acid (74 mg). The title compound was isolated as a white solid in a yield of 53% (43 mg, 116 μmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.32 (t, $J$ = 1.9 Hz, 1H), 8.08 (ddd, $J$ = 8.2, 2.2, 0.9 Hz, 1H), 8.01 (s, 1H), 7.85 (dt, $J$ = 8.4, 1.8 Hz, 2H), 7.74–7.70 (m, 1H), 7.50 (t, $J$ = 8.0 Hz, 1H), 7.41–7.30 (m, 4H), 7.00 (d, $J$ = 16.0 Hz, 1H), 2.45 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.74, 146.57, 141.83, 138.64, 137.17, 134.76, 132.55, 130.55, 129.63, 127.85, 127.43, 122.25, 121.19, 120.65, 115.16, 21.76. HRMS (ESI) m/z: [M + H] calcd for $C_{18}H_{16}N_3O_4S$ 370.08615; found 370.08744.

**(*E*)-4-(2-(Furan-2-yl)vinyl)-1-tosyl-1*H*-imidazole [NEW] (3 u)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: Furan-2-ylboronic acid (50 mg). The title compound was isolated as a white solid in a yield of 56% (39 mg, 124 μmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.83 (dt, $J$ = 8.4, 1.8 Hz, 2H), 7.39–7.33 (m, 3H), 7.19 (d, $J$ = 1.0 Hz, 1H), 7.10 (d, $J$ = 15.8 Hz, 1H), 6.77 (d, $J$ = 15.8 Hz, 1H), 6.39 (dd, $J$ = 3.3, 1.8 Hz, 1H), 6.32 (d, $J$ = 3.3 Hz, 1H), 2.44 (s, 3H). The compound **19 a** decomposed and we were not able to record $^{13}$C NMR data and HRMS (ESI) for this compound.

**(*E*)-4-(2-(Thiophen-2-yl)vinyl)-1-tosyl-1*H*-imidazole [NEW] (3 v)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: Thiophen-2-ylboronic acid (57 mg). The title compound was isolated as a white solid in a yield of 54% (40 mg, 121 μmol). $^1$H NMR (850 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.85 (d, $J$ = 8.4 Hz, 2H), 7.46 (d, $J$ = 15.7 Hz, 1H), 7.39 (d, $J$ = 8.3 Hz, 2H), 7.22 (s, 1H), 7.20 (d, $J$ = 5.0 Hz, 1H), 7.06 (d, $J$ = 3.5 Hz, 1H), 7.00 (dd, $J$ = 5.0, 3.6 Hz, 1H), 6.70 (d, $J$ = 15.7 Hz, 1H), 2.47 (s, $J$ = 6.8 Hz, 3H). $^{13}$C NMR (214 MHz, $CDCl_3$) δ 146.36, 142.37, 142.21, 136.97, 134.89, 130.46, 127.65, 127.35, 126.69, 124.66, 123.66, 117.73, 113.77, 21.74. HRMS (ESI) m/z: [M + H] calcd for $C_{16}H_{15}N_2O_2S_2$ 331.05749; found 331.05888.

**1-Tosyl-1*H*-imidazole-2-carbaldehyde [155742-57-7]**.[13] 1*H*-imidazole-2-carbaldehyde (5.00 g, 52.0 mmol) and *p*-toluenesulfonyl chloride (1 eq., 9.92 g, 52.0 mmol) were added to a Schlenk-tube under argon atmosphere. THF (dry, 40 mL) was added to dissolve the solids. Then, TEA (1 equiv., 7.26 mL, 5.27 g, 52.0 mmol) was added by means of a syringe. The reaction mixture was stirred under argon for 24 h at ambient temperature and checked through GC-MS. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The crude product was extracted from acid water with DCM (3 × 200 mL), the organic phases were reunited and dried over $Na_2SO_4$ to afford the desired compound in a yield of 96% (12.45 g, 49.7 mmol) as a white solid. The NMR revealed an impure product with traces of *p*-toluenesulfonyl chloride present in the product. However, this impurity does not affect the following reaction and the isolated product was used in the following Wittig reaction step. NMR data of the compound was previously disclosed.[43]

**1-Tosyl-2-vinyl-1*H*-imidazole [NEW] (6)**. Methyl-triphenyl-phosphonium bromide (1.2 equiv., 8.56 g, 24.0 mmol) was transferred to a three-necks round bottom flask (100 mL) under inert and anhydrous conditions. Then, the solid was suspended in THF (dry, 30 mL). Potassium *tert*-butoxide in THF (1 M, 1.1 equiv., 2.47 g, 22.0 mL, 22.0 mmol) was added by means of a syringe (exothermic reaction). The reaction mixture turns into a pale-yellow color. After 30 min, **1 d** (5.0 g, 20.0 mmol) was slowly (exothermic reaction) added to the mixture and stirred for 2 h at 20 °C and monitored by means of GC-MS. Upon completion of the reaction, the solvent was evaporated under reduced pressure. The crude product was extracted from acid water with DCM (3 × 200 mL), the organic phases were

combined and dried over $Na_2SO_4$. Finally, purification by means of column chromatography packed with silica gel and an eluent system composed of hexane:ethyl acetate = 82:18 provides the target compound in a yield of 45% (2.24 g, 9.0 mmol) as a white solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.67 (dt, $J$ = 8.4, 1.8 Hz, 2H), 7.35 (d, $J$ = 1.6 Hz, 1H), 7.23 (d, $J$ = 8.4 Hz, 2H), 7.05 (dd, $J$ = 17.2, 11.1 Hz, 1H), 6.92 (d, $J$ = 1.6 Hz, 1H), 6.15 (dd, $J$ = 17.2, 1.6 Hz, 1H), 5.42 (dd, $J$ = 11.1, 1.5 Hz, 1H), 2.31 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.15, 145.91, 135.08, 130.30, 129.25, 127.23, 122.89, 122.06, 119.60, 21.66.

**(*E*)-2-Styryl-1-tosyl-1*H*-imidazole [NEW] (7)**. The title compound was synthesized according to the general procedure A using the following conditions and quantities: 1-tosyl-2-vinyl-1*H*-imidazole (55 mg, 221 µmol), phenyl-boronic acid (38 mg). Eluent system composed of hexane:ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 92% (66 mg, 203 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.78 (dt, $J$ = 8.4, 1.7 Hz, 2H), 7.63–7.50 (m, 4H), 7.46 (d, $J$ = 1.6 Hz, 1H), 7.42–7.37 (m, 2H), 7.36–7.29 (m, 3H), 7.06 (d, $J$ = 1.6 Hz, 1H), 2.40 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.52, 146.13, 136.38, 135.98, 135.23, 130.36, 129.59, 129.03, 128.86, 127.30, 127.23, 119.55, 113.47, 21.69. HRMS (ESI) m/z: [M + H] calcd for $C_{18}H_{17}N_2O_2S$ 325.10107; found 325.10133.

**(*E*)-4-Styrylpyridine [5097-93-8] (9a)**. The title compound was synthesized according to the general procedure A with some amendments for up-scaled use. In particular, the following conditions and quantities were used: a pressure-resistant reaction tube (20 mL) was charged with 4-vinylpyridine (231 mg, 2.20 mmol), bathocuproine (40 mg), $Pd(OAc)_2$ (25 mg), phenyl-boronic acid (375 mg), $MnO_2$ (535 mg), and ACN (10 mL). Eluent system composed of hexane:ethyl acetate = 90:10. The title compound was isolated as a white solid in a yield of 80% (317 mg, 1.75 mmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 8.56 (dd, $J$ = 4.5, 1.6 Hz, 2H), 7.71–7.64 (m, 2H), 7.60–7.53 (m, 3H), 7.47–7.40 (m, 2H), 7.35 (dt, $J$ = 7.3, 1.0, 1.0 Hz, 1H), 7.27 (d, $J$ = 16.5 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 150.01, 144.21, 136.13, 132.96, 128.80, 128.62, 127.04, 125.95, 120.84. HRMS (ESI) m/z: [M + H] calcd for $C_{13}H_{11}N$ 182.09697; found 182.09723.

**(*E*)-5-Styrylpyrimidine [35782-34-4] (9b)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: 5-vinylpyrimidine (24 mg, 226 µmol), phenyl-boronic acid (55 mg). The title compound was isolated as an off-white solid in a yield of 73% (66 mg, 203 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.87 (s, 2H), 7.54 (d, $J$ = 7.4 Hz, 2H), 7.40 (t, $J$ = 7.5 Hz, 2H), 7.37–7.31 (m, $J$ = 7.3 Hz, 1H), 7.24 (d, $J$ = 16.6 Hz, 1H), 7.00 (d, $J$ = 16.5 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.21, 154.27, 135.99, 132.87, 131.04, 128.92, 128.87, 126.88, 121.12.

**(*E*)-2-Styrylfuran [1202-49-9] (9c)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: 2-vinylfuran (50 mg, 531 µmol), bathocuproine (10 mg), $Pd(OAc)_2$ (6 mg) phenyl-boronic acid (130 mg), $MnO_2$ (139 mg), and ACN (2 mL). The title compound was observed in traces in GC-MS analysis but was not isolated (< 1% yield).

**(*E*)-2-Styrylthiophene [26708-50-9] (9d)**. The title compound was synthesized according to the general procedure B using the following conditions and quantities: 2-vinyltiophene (50 mg, 454 µmol), bathocuproine (8 mg), $Pd(OAc)_2$ (5 mg) phenyl-boronic acid (111 mg) $MnO_2$ (118 mg), and ACN (2 mL). The title compound was isolated as an off-white solid in a yield of yield 77% (65 mg, 349 µmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.41–7.37 (m, 2H), 7.29–7.24 (m, 2H), 7.19–7.10 (m, 3H), 6.99 (d, J = 3.6 Hz, 1H), 6.93 (dd, J = 5.1, 3.6 Hz, 1H), 6.86 (d, J = 16.1 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.90, 136.98, 128.71, 128.35, 127.61, 126.31, 126.11, 124.35, 121.80

**(*E*)-1,2-Diphenylethene [103-30-0] (9e)**. The title compound was synthesized according to the general procedure A with some amendments for up-scaled use. In particular, the following conditions and quantities were used: a pressure-resistant reaction tube (20 mL) was charged with styrene (208 mg, 2.00 mmol), bathocuproine (36 mg), $Pd(OAc)_2$ (22 mg), phenyl-boronic acid (341 mg), $MnO_2$ (521 mg), and ACN (10 mL). Eluent system composed of hexane:ethyl acetate = 90:10. White solid. Isolated yield 62% (224 mg, 1.24 mmol). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.54–7.50 (m, 4H), 7.36 (dd, $J$ = 8.5, 6.9 Hz, 4H), 7.28–7.23 (m, 2H), 7.11 (s, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 137.34, 128.70, 127.63, 126.53.

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