
Olefination of sp^2 C-H Bonds by using Pd[II] / Pd[0] Catalysis

Introduction:

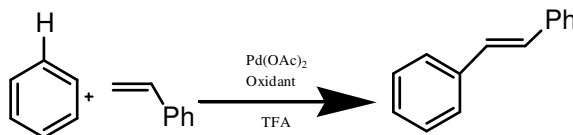
In the past decade, palladium-catalyzed C-H activation/C-C bond-forming reactions have emerged as promising new catalytic transformations; however, development in this field is still at an early stage compared to the state of the art in cross-coupling reactions using aryl and alkyl halides. This Review begins with a brief introduction of four extensively investigated modes of catalysis for forming C-C bonds from C-H bonds: PdII/Pd0, PdII/PdIV, Pd0/PdII/PdIV, and Pd0/PdII catalysis. A more detailed discussion is then directed towards the recent development of palladium(II)-catalyzed coupling of C-H bonds with organometallic reagents through a PdII/Pd0 catalytic cycle. Despite the progress made to date, improving the versatility and practicality of this new reaction remains a tremendous challenge. Among the myriad of important transition metal catalyzed synthetic transformations, palladium-catalyzed Heck coupling, cross-coupling (Kumada, Stille, Negishi, Suzuki–Miyaura, Hiyama), Tsuji–Trost allylation, and Buchwald–Hartwig amination reactions using organohalides and other surrogates are particularly valuable tools in synthetic chemistry. A common and critical feature of these catalytic processes is the formation of aryl or alkyl palladium(II) intermediates which can be subsequently functionalized to form carbon–carbon and carbon–heteroatom bonds.

Olefination of sp^2 C-H Bonds by using Pd[II]/Pd[0] Catalysis:-

The past five decades have witnessed noticeable progress in the development of palladium-catalyzed C-H activation and C-C bond-forming processes. Research in this field has largely focused on the discovery of new modes of catalysis and the expansion of substrate scope. One of

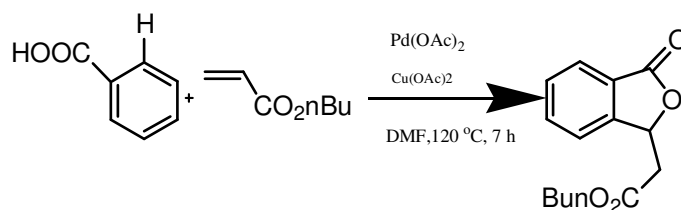
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the earliest examples concerns C-H activation of benzene by Pd(OAc)₂ and subsequent carbopalladation and b-hydride elimination to afford olefinated arenes (Scheme 1).[1]



Scheme 1 Palladium(II)-catalyzed olefination of arenes

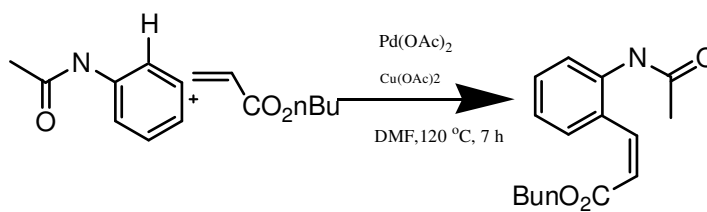
This early report by Moritani and Fujiwara demonstrated the impressive reactivity of palladium(II) in activating aryl C-H bonds; however, two major drawbacks largely hampered the application of this catalytic reaction.[1] First, a large excess of the arene was required (often used as the solvent). Second, there was a lack of control of the regioselectivity when monosubstituted benzene was used as the substrate. Addressing this latter shortcoming, an early attempt of using benzoic acid to achieve ortho selectivity represented an encouraging step forward (Scheme 2).[2]



Scheme 2 Directed ortho olefination of benzoic acid

In response to this regioselectivity problem, an instrumental development using a directing group was reported by de Vries and co-workers (Scheme 3).[3] The use of an anilide substrate afforded high ortho selectivity and allowed the

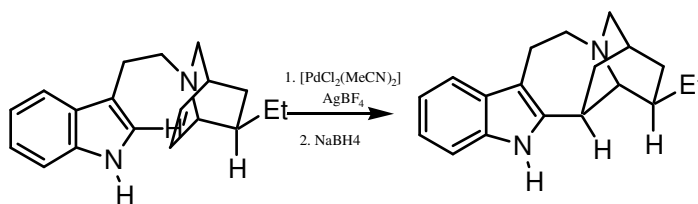
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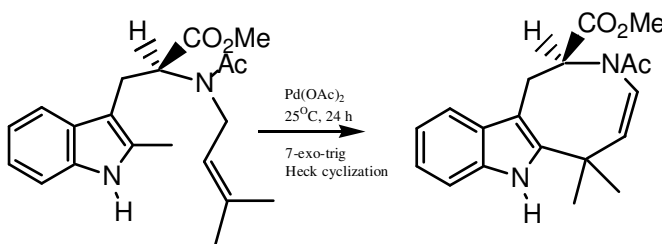
Scheme 3 Ortho-Selective olefination of arenes

arene to be used as the limiting reagent. In this reaction, benzoquinone is believed to be crucial for the C-C bondforming step, and the use of TsOH was also found to be beneficial.

Importantly, this study together with Fujiwara's early work has spurred recent studies on C-H activation/Heck coupling reactions using arenes possessing either high electron density or directing groups.[4] Notably, two elegant synthetic applications using an indole olefination have further inspired efforts towards improving this reaction (Scheme 7 and Scheme 8).[5] In the synthesis of ibogamine the carbon– palladium bond was reduced by NaBH₄ to give the desired product. An unexpected ring expansion of the alkylpalladium intermediate served extraordinarily well in the synthesis of (+)-austamide.



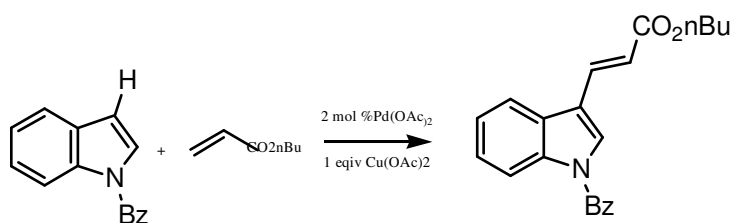
Scheme 4. Synthesis of ibogamine



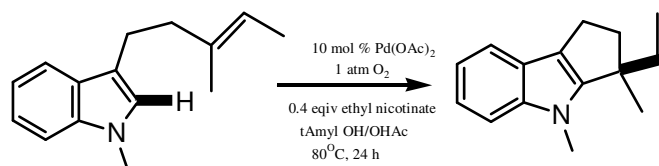
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Scheme 5. Synthesis of (+)-austamide

Although catalytic olefination of indoles using Pd(OAc)₂, and AgI and CuII salts as the reoxidants was reported as early as 1983 by Itahara et al. (Scheme 6).[6] several recent studies have greatly advanced this chemistry. Notably, the work of Ferreira and Stoltz, in which molecular oxygen is used as the reoxidant in the intramolecular olefination of indoles, was a significant development (Scheme 7).[7] In contrast, by using allylic acetates as the olefin partner, Ma and Yu cleverly avoided the need for an oxidant (Scheme 8).[8]



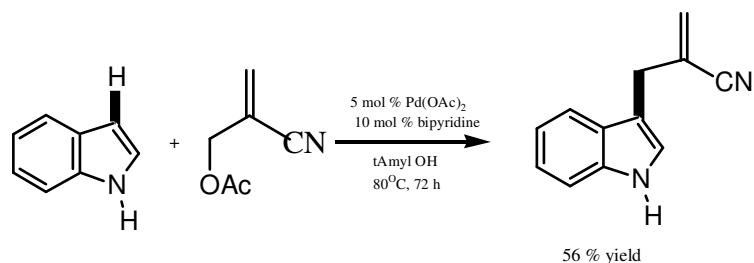
Scheme 6. Catalytic olefination of indoles by electrophilic palladation



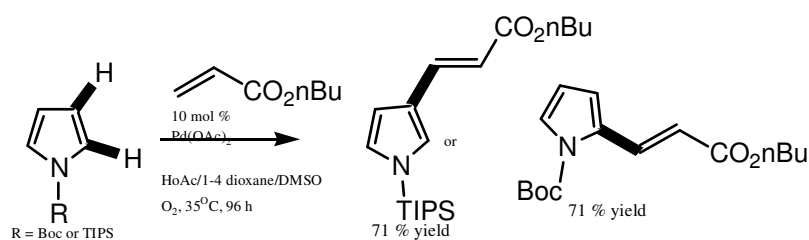
Scheme 7. Intramolecular olefination of indoles using O₂ as the oxidant

Achieving regioselective functionalization at either the 2-or 3-position of pyrroles through the use of different protecting groups is also synthetically useful (Scheme 9).[9] In this case, the agreement of the observed regioselectivity.

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Scheme 8. Oxidant-free olefination of indoles

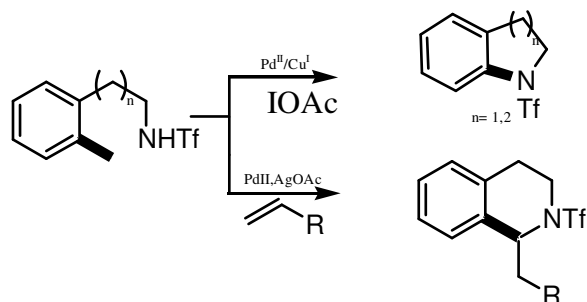


Scheme 9. Regioselective olefination of pyrroles.

with that of the electrophilic bromination reaction of protected pyrroles[10] lends valuable evidence to the hypothesis that an electrophilic palladation process is involved in these olefination reactions.

To expand the synthetic utility of directed C-H activation/ olefination, a concise and general route for the preparation of heterocyclic compounds from trifluoromethanesulfonyl-protected arylalkylamines has recently been developed using highly acidic triflamide groups to direct C-H activation (Scheme 10).[11]

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Scheme 10. Heterocycle synthesis by the olefination of arenes .

Conclusion:-

Recently, palladium-catalyzed C-H activation/C-C bondforming reactions have emerged as a promising set of synthetic transformation for the assembly of carbon-carbon bonds. Various catalytic cycles have been developed to accomplish the olefination, arylation, and alkylation of unactivated C-H bonds, including PdII/Pd0, PdII/PdIV, Pd0/ PdII/PdIV, and Pd0/PdII catalytic cycles. In many cases, C-H activation reactions with palladium require 5-10 mol% catalyst. Thus, from the standpoint of atom economy and overall cost, discovering more efficient catalytic systems with improved turnover is paramount. Regioselective arene C-H activation: The design of novel ligands to promote C-H activation of monosubstituted benzene regioselectively at the meta or para-positions would represent a new paradigm in reactivity and would greatly expand the scope of this new C-C bond-forming reaction.

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