

Total and Formal Syntheses of Heterocyclic Natural Products and Drugs by MATSUDA-HECK-Reaction^[1]

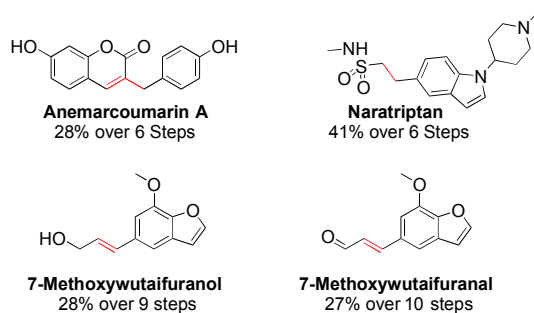
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The palladium catalysed MATSUDA-HECK-Reaction or arene diazonium salts is a powerful synthetic tool for the coupling of olefins and (heterocyclic) aryl compounds. Highlighted by mild reaction conditions, convenient synthesis^[2,3] of very reactive and extremely useful electrophiles, this C-C-bond forming reaction is a highly versatile and efficient reaction for the synthesis of complex structures^[4].

To the best of our knowledge, we report the first total syntheses of three known bioactive heterocyclic natural compounds^[5,6] and one formal synthesis^[7] of the anti-migraine drug Naratriptan, which are presented below. Furthermore, we developed new synthetic pathways for the novel olefins and arene diazonium tetrafluoroborates required, optimized the systems and implement the results in very efficient and atom economic routes.

Our reaction conditions are distinguished by low catalyst loading of inexpensive Pd(OAc)₂, short reaction times, excellent functional group tolerance, absence of bases and ligands, full stereoselectivity and good to excellent yields.



¹manuscripts in preparation; ²B. Schmidt, R. Berger, F. Hölter *Org. Biomol. Chem.* **2010**, *8*, 1406-1414.; ³B.Schmidt, R. Berger, F. Hölter *Adv. Synth. Catal.* **2010**, *352*, 2463-2473.; ⁴J. G. Taylor, A.V. Moro, C. R. D. Correia *Eur. J. Org. Chem.* **2011**, 1423-1428.; ⁵J. Y. Ui, S. L. Seul, J. Hana, E.-K. Seo, *J. Nat. Prod.* **2009**, *72*, 1895-1898.; ⁶H.Y. Huang, T. Ishiwaka, I.-S. Chen *J. Nat. Prod.* **2008**, *71*, 1146-1151.; ⁷B. Pete, G. Simig, L. Toeke *Heterocycles* **2003**, *60*, 2441-2455.