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Intramolecular Hydroamidation of *ortho*-Vinyl Benzamides Promoted by Potassium *tert*-Butoxide/*N*,*N*-Dimethylformamide

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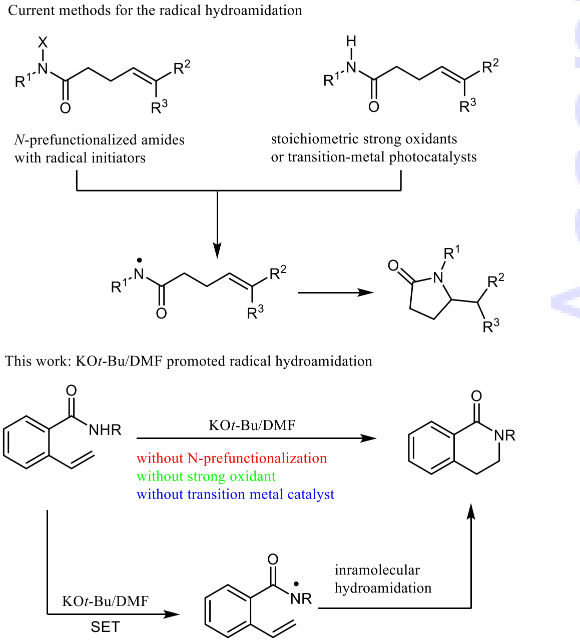
Abstract: An intramolecular hydroamidation of *ortho*-vinyl benzamides had been developed. The reaction was promoted efficiently by potassium *tert*-butoxide and *N*,*N*-dimethylformamide without the need for strong oxidants or transition-metal catalysts. A series of dihydroisoquinolinones and 3-benzylisoindolinones were prepared in good to excellent yields. The new method is operationally simple, scalable, and tolerant of various functional groups.

Keywords: hydroamidation; amidyl radical; potassium *tert*-butoxide; *N*,*N*-dimethylformamide; dihydroisoquinolinone; isoindolinone

Nitrogen-containing compounds are found widely in natural products, pharmaceuticals, agrochemicals, and materials.[1] The development of new methodologies for the selective formation of C-N bonds under mild conditions and in complex molecular settings is of great importance. The hydroamidation of olefins is a powerful approach to C−N bond construction.[2-3] Generally, these reactions were achieved in the presence of various transition-metal catalysts. An alternative strategy via amidyl radical intermediates has made limited progress.[4-5] Conventional methods for the generation of amidyl radicals require either prefunctionalized amides such as *N*-halo-, *N*-nitroso-, or *N*-phenylthioamide derivatives or the use of stoichiometric strong oxidants.[6-7] The direct activation of strong N–H bonds to generate the amidyl radical is more challenging (Scheme 1).[8] Knowles and co-workers recently reported a hydroamidation reaction of amides and olefins catalyzed by iridium photocatalysts via a proton-coupled electron transfer (PCET) pathway. In this process, a weak phosphate base and an iridium photocatalyst in the excited state jointly mediated the homolysis of the anilide N-H bond. The resulting amidyl radical added to the olefin to give the product.[8a-8d] Recently, Xu and co-workers developed an electrocatalytic method for the generation of amidyl radicals from *N*-aryl amides using the inexpensive ferrocene as the redox catalyst. This method was applied for the intramolecular hydroamidation of olefins with good functional group tolerance.[8e] Xiao and co-workers developed a photocatalytic intramolecular hydroamination of *β*,*γ*-unsaturated hydrazones via *N*-centered hydrazonyl radicals.[9] The radicals were suggested to be generated via the single-electron transfer of the anionic intermediates. Other catalytic activations of N-H bonds to generate nitrogen radicals were developed by the groups of Chiba[8f], Zheng[8g], and Li[8h]. These reactions require stoichiometric oxidants and/or expensive noble-metal catalysts. To overcome these limitations, green and sustainable hydroamidation reactions utilizing non-prefunctionalized amides under redox-neutral conditions are still desirable.

Recently, KO*t*-Bu/DMF has been used in a number of cross-coupling reactions with haloarenes via a single electron transfer pathway.[10] Our group has developed a series of radical reactions of amines, amides and diarylmethanes promoted by KO*t*-Bu/DMF.[11] The corresponding α-amino alkyl radicals, α-amido alkyl radicals and diarylmethyl radicals were proposed to be generated in these reactions. During the study of intramolecular C–N coupling of N′-aryl-2-halobenzohydrazides promoted by KO*t*-Bu, we proposed the generation of *N*-centered benzohydrazide radicals from 2-bromo and 2-iodo substrates.[11g] We speculate that the amidyl radical may be generated from amides promoted by KO*t*-Bu/DMF. The subsequent addition to olefins will give the valuable hydroamidation products (Scheme 1). Herein, we report an intramolecular hydroamidation reaction of *ortho*-vinyl benzamides promoted by KO*t*-Bu/DMF.



Scheme 1. Intramolecular radical hydroamidation of olefins.