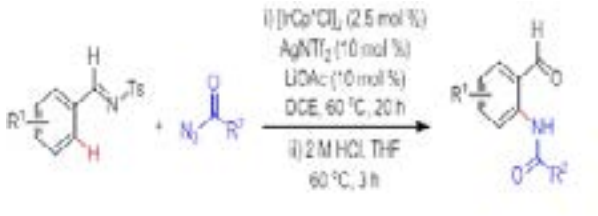
Saegun Kim, Organic Chem Curr Res 2018, Volume:7
DOI: 10.4172/2161-0401-C1-023

Synthesis and anti-inflammatory evaluation of 2-aminobenzaldehydes via Ir(III)-catalyzed C-H amidation

Saegun Kim
Sungkyunkwan University, South Korea

Transition-metal-catalyzed C-N bond formation reactions via C-H bond activation have been of great interest in organic and medicinal chemistry due to the prevalence of bioactive nitrogen-containing heterocycles. In this area, various N-amidation surrogates, such as N-carboxylates, N-tosylates, organic azides and dioxazolones, have been investigated as relevant sources for the C-H amidation reactions. Particularly, N-acyl azides have been intensively studied in the direct C–N amidation reactions of sp^2 C-H bonds, although N-acyl azides can be readily converted to aryl isocyanates through the Curtius rearrangement under thermal and photochemical conditions. 2-Aminobenzaldehydes have been utilized as ubiquitous precursors for the construction of various heterocycles such as quinolines, acridines, quinolinones, dibenzonaphthyridines, benzoxazin-4-ones and natural neocryptolepine. Furthermore, N-substituted ortho-aminobenzaldehydes have been employed for the formation of pharmaceutically relevant indoles. Due to the weak coordinating ability of aldehydes to transition metals, aldimines have been recently applied as alternative directing groups to afford ortho-functionalized benzaldehydes. In shrap contrast, aldimines were also used as electrophilic coupling partners in C-H activation event leading to the corresponding secondary amine adducts. In continuation of our recent works on site-selective C-H amidation of (hetero)arenes, we herein report the Cp*Ir(III)-catalyzed direct amidation of aldimines with N-acyl azides followed by *in-situ* acidic hydrolysis affording ortho-amidobenzaldehydes. It is noted that the resulting ortho-amidated benzaldehydes are readily converted to various biologically relevant heterocycles such as 4H-1,3-benzoxazin-4-ones, quinazoline and 1,2-dihydroquinoline. Additionally, synthesized ortho-amidated benzaldehydes and 4H-1,3-benzoxazin-4-ones were evaluated for anti-inflammatory activity against interleukin-1β (IL-1β) and tumor necrosis factor alpha (TNF-α) with lipopolysaccharide-induced RAW264.7 cells, and were found to display promising anti-inflammatory activity competitive with dexamethasone as a positive control.



jameskim1991@naver.com