
화학과 대학원 세미나

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Palladium–Catalyzed Deprotonative Arylation of Azaarylmethyl Derivatives

Aryl(azaaryl)methyl derivatives are prominent in biologically active small molecules, exhibiting antitumor, antiviral, anti-HIV, and antihistamine activities. In considering the synthesis of a family of drug-like molecules based on the aryl(pyridinyl)methane cores, we envisioned a united approach to access these important structural motifs based on a non-traditional umpolung approach. Our strategy entailed a palladium-catalyzed deprotonative cross-coupling process (DCCP) with pyridylmethyl ethers and aryl bromides by a noble Palladium–NIXANTPHOS catalyst to generate arylated secondary ethers, while the tertiary alcohols would be accessed via a tandem DCCP/[1,2]–Wittig rearrangement. The method has extended pertinent examples of such reactions with N–Boc benzylalkylamines, azaarylmethylamines, Isoindolinones, Benzoxazoles and diaryl(heteroaryl)methanes. A cheap nickel catalyst allows the less reactive but inexpensive aryl chlorides.

김병선 교수

경상대학교 화학교육과