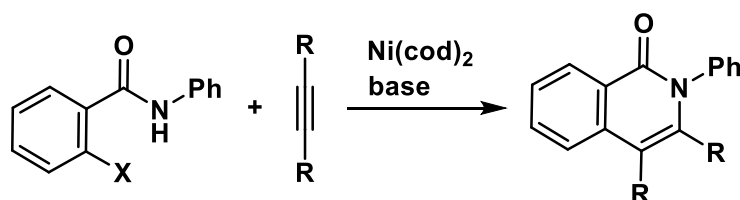


Nickel-Catalyzed C-O/N-H, C-S/N-H and C-CN/N-H Annulation of Aromatic Amides with Alkynes

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C-O bond activation reactions have been widely explored as an efficient tool for the transformation of phenol derivatives which are inexpensive and readily available.¹ The cleavage of the C-O bond required a high reaction temperature and the addition of a strong donor ligand. We recently reported the C-F/N-H annulation of aromatic amides with alkynes in the presence of a nickel catalyst, which gave isoquinolin-1(2*H*)-ones.² This reaction proceeded via the cleavage of the C-F bond without a ligand even at low temperature. A key to the success of the reaction is the addition of a base. The base abstracts a N-H proton from the substrate to generate the amide anion, which reacts with nickel to give catalytically active species. We hypothesized that C-O bond activation can be achieved by this methodology. After some examinations, it was found that benzamides bearing an alkoxy group at the *ortho* position reacts with alkynes to give the annulation product via the cleavage of the C-O bond.³ This reaction proceeded even in the absence of a ligand at low temperature, which tolerates various kinds of functional groups under the reaction conditions. This methodology is also applicable to the activation of other unreactive bonds, such as C-S and C-CN bonds.



(X = OPh, OCONR₂, SMe, CN)

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