

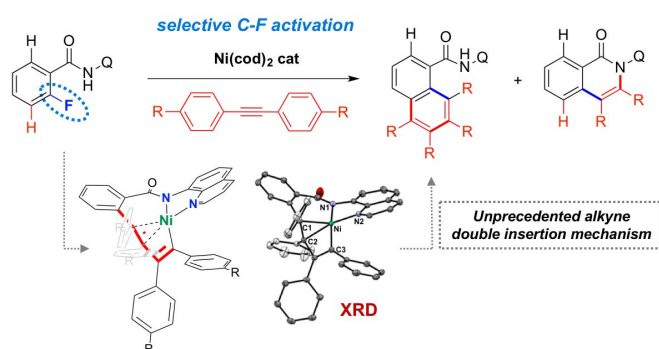
CHEMO-DIVERGENT NICKEL(0)-CATALYZED ARENE C-F ACTIVATION WITH ALKYNES: UNPRECEDENTED DOUBLE-INSERTION

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Fluorinated compounds are key structural moieties in numerous areas of chemistry, with applications to catalysis, medicine and material sciences.[1] The introduction of fluorinated motifs changes properties of a given molecule, and in the pharmaceutical industry context, improves the stability and lifetime of F-containing pharmaceuticals. However, the stability is often too pronounced and the lead compound is frequently poorly biodegradable. Therefore, it is furthermore desirable to develop new sustainable methods for the functionalization of aromatic C-F bonds, as a useful strategy to establish novel chemical transformation of aryl fluorides. Transition metal-catalyzed Ar-F functionalization is considerably more challenging than classical Ar-H or Ar-Hal (Hal = I, Br, Cl) activation, generally showing low selectivities and requiring electronically biased polyfluorinated substrates.[2] In particular, C-C formation reaction via C-F cleavage of fluoroarenes using nickel catalyst has been reported using activated aryl nucleophiles, such as highly reactive Grignard reagents, zincates and boronic acids as the coupling partner for C-C formation via transmetalation [3]. Herein we show Nickel-catalyzed C-F activations enabled chemo-divergent C-C formation with alkynes by chelation assistance. The judicious choice of the alkynes electronic properties thus allowed the selective synthesis of alkyne mono-annulation or double-insertion aromatic homologation products. A key unprecedented 9-membered nickelocyclic intermediate species was isolated and crystalized, unravelling the mechanistic pathway to the aromatic homologation product by challenging double C-F/C-H activation.



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