ABSTRACT

SYNTHETIC AND MECHANISTIC STUDIES OF RUTHENIUM CATALYSED C–N AND C–H BOND ACTIVATION REACTIONS

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Transition metal catalyzed C–H and C–N functionalization methods have emerged as an innovative tool for designing efficient synthesis of fine chemicals by using readily available starting materials without the formation of wasteful byproducts. One of the paramount challenges in C–H functionalization research field has been to promote regio- and stereoselective C–H bond activation on saturated hydrocarbon substrates. While much progress has been achieved on promoting selective sp^2 C–H activation reactions on unsaturated hydrocarbon substrates in the past decades, catalytic sp^3 C–H bond and functionalization methods on saturates hydrocarbon substrates remain as the frontier topic of C–H functionalization research.

The well-defined cationic Ru–H complex with a benzoquinone ligand was found to be an effective catalytic system for the dehydrative sp^3 C–H coupling reaction of indoles with enones to form 3,5-disubstituted carbazole products. The analogous coupling of 2-alkylindoles with linear enones bearing cyclic olefinic group afforded tetracyclic carbazole products. The combined experimental and DFT calculations uncovered a mechanism of the coupling reaction via an initial coupling of indole and enone substrates, the rate-limiting heterolytic sp^3 C–H activation step, and the subsequent cyclization and dehydration steps. We devised a Ru-catalyzed deaminative coupling method for 2-aminoaryl aldehydes and ketones with readily available branched amine substrates, which efficiently leads to a regioselective synthesis of 2-substituted and 2,4-disubstituted quinoline derivatives. We have been able to synthesize a number of biologically active quinoline derivatives, including graveolinine and a triplex DNA intercalator by using the catalytic method. The preliminary kinetic and mechanistic studies indicate that the reaction proceeds via the coupling between initially formed imine and 2-aminoarylimine substrates, in which the C–N bond cleavage is the rate-determining step of the coupling reaction. We also developed a catalytic synthesis of 3-substituted flavanone and 3,3-disubstituted quinazolinone derivatives from the deaminative coupling reaction of 2-hydroxyaryl ketones and 2′-aminobenzamides with simple amines. The kinetic data supported a reaction mechanism via an intramolecular [1,3]-carbon migration of the initially formed imine followed by the imine-to-allylamine isomerization and the cyclization (C–O bond formation) steps.