Directing Group Enhanced Carbonylative Ring Expansions of Amino Substituted Cyclopropanes

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Abstract

Our research programme is focussed upon the development of new catalysis platforms that enable direct access to medicinally valuable chiral scaffolds.1 Recently, we outlined a metal-catalysed (3+2+1) carbonylative cycloaddition strategy for the synthesis of complex nitrogen containing scaffolds (Scheme 1A).2 The key metallacyclic intermediates 1 are generated by Rh-catalysed carbonylative ring expansion of readily available amino-substituted cyclopropanes. To control the regioselectivity of this process we have developed a directing group based strategy, which takes advantage of the N-protecting group (Scheme 1B). This approach controls (a) the regioselectivity of oxidative addition (into the more hindered cyclopropane C-C bond) and (b) the regioselectivity of CO insertion. Mechanistic aspects of this process will be discussed. We will also outline a prototypical catalytic process that involves trapping of the metallacyclic intermediate with a tethered alkyne (Scheme 1C). Finally, a brief overview of current directions will be given.

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References