Selective Pd-catalysed C(sp^3)–H functionalization of 2-aminocyclobutane-1-carboxylique acids (ACBCs)

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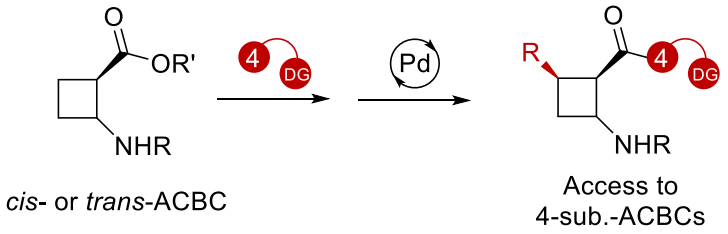

In the area of foldamer science, *cis*- and *trans*-cyclobutane β-amino acid derivatives (ACBCs)[1] are building blocks particularly attractive as monomer units for the preparation of peptidomimetic architectures due to their resistance to proteolysis and displaying structural mimicry.[2,3] Although there is an increasing demand for their synthetic access, the development of efficient, selective, and step and atom economical approach to functionalize the *cis*- and *trans*-ACBC at the peripheral sites remains a challenge.[4] In addition, selective Pd-catalyzed auxiliary-directed C(sp^2) / C(sp^3)–H functionalization to derivatize amino acids (AAs) side-chains has emerged as an efficient and straightforward route to further extend the range of non-proteinogenic AAs available as means to increase the structural diversity of the peptides.[5] Surprisingly, β-AAs have received very scant attention and, as far as we know, ***no example has been reported for the Pd-catalysed C(sp^3)–H functionalization of cyclobutane β-AAs***.[6] Herein, during this talk, I will present you our recent research and development on the regio- and stereoselective Pd-catalyzed *syn* vicinal direct C(sp^3)–H functionalization of *cis*- and *trans*-ACBCs. A large scope of substituted cyclobutane β-amino acid derivatives (arylated, alkynylated, alkenylated and alkylated) at the peripheral C$_4$ position as well as the late stage C(sp^3)-H functionalization of hybrid peptides containing ACBCs will be thus presented.

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