Merging C-H activation and sulfoxides to design new stereoselective scaffolds

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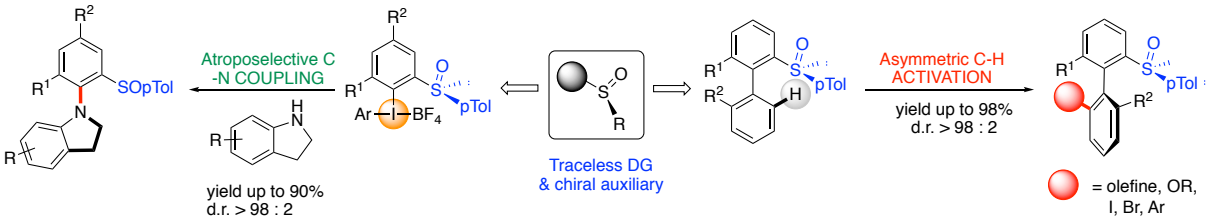
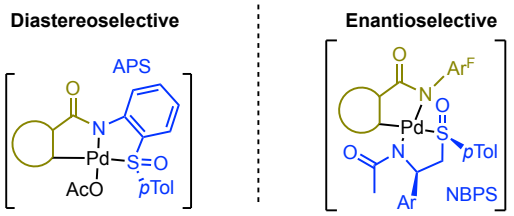
Over the decades, non-activated C-H bonds have been considered as dormant functionalities, hardly exploitable in the context of multistep synthesis of complex scaffolds. However, since few years, the C-H activation of arenes, and more recently alkanes, expanded tremendously. Nevertheless general strategies giving access to a large panel of stereogenic molecules are still missing. Following this objective we have recently developed an asymmetric C-H activation pathway to build up very efficiently an unlimited panel of atropisomerically pure biaryls. This concept involves direct, Pd-catalyzed functionalization of the biaryl precursors bearing a sulfoxide moiety. The stereogenic sulfoxide plays a role of both, directing group and chiral auxiliary, hence allowing the atroposelective C-H activation and subsequent functionalization with an array of coupling partners (C-C, C-O, C-X bond formation).[1] Recently we have also discovered that sulfoxide may be efficiently applied in the context of unprecedented atroposelective C-N couplings.[2] Furthermore, the traceless character of the sulfoxide moiety permits various post-modifications of the newly generated axially chiral compounds.



Then we endeavoured new strategies for the diastereoselective C(sp^3)-H functionalisation, using an original directing group, (*S*)-2-(*para*-tolylsulfinyl)aniline, allowing various transformations, such as arylation or challenging olefination. Afterwards, targeting enantioselective transformations, we developed a new ligand, *N*-((*S*)-1-(4-(*tert*-butyl)phenyl)-2-((*R*)-*para* tolylsulfinyl)ethyl)acetamide, that turned out to be a highly efficient chiral inductor for the direct functionalisation of cycloalkanes.[3]



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