Axial chirality, not only an academic curiosity
Towards atropopure biologically active molecules

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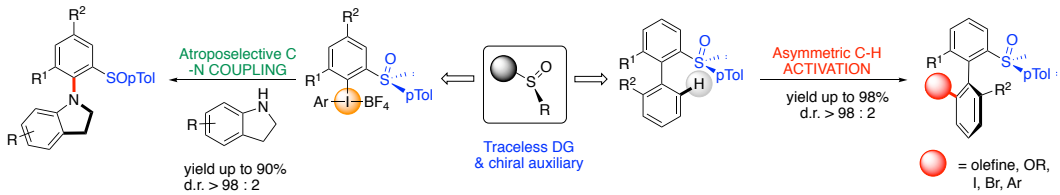
Atropisomerism is an important feature of numerous natural products and biologically active molecules. In particular over the last five years, axially chiral molecules has gained a growing importance in medicinal chemistry. Remarkably, 80% of FDA-approved kinase inhibitors contain an atropisomeric axis. Besides axially chiral ligands such as BINAP, BINOL and many others are clearly priviledged ligands in asymmetric catalysis. Nevertheless general strategies giving access to a large panel of axially chiral 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 targeted the first Cu-catalyzed atropoenantioselective N-arylation employing a chiral BOX ligand allowing the access to unprecedented C-N axially chiral compounds in good to excellent yields and stereoselectivities.[3]

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2) J. Rae, J. Frey, S. Choppin, J. Wencel-Delord, F. Colobert, *ACS Cat.* **2018**, *8*, 2805-2809.
3) Unpublished results