Alkaloids as Chiral Building Blocks, Auxiliaries, Ligands, and Molecular Diversity

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Among c. 20 000 of known alkaloids isolated from natural sources and their numerous derivatives, few belong to privileged chiral molecules that shaped the stereochemistry and enantioselective synthesis since their birth. Alkaloids, initially used as efficient resolving agents, currently provide a rich portfolio of powerful chiral ligands, organocatalysts, and to lesser extent auxiliaries dedicated to C□C and C–heteroatom bond formation. These include ephedra, lupine, and Cinchona alkaloids and their derivatives. The biological activity of alkaloids makes them suitable to target biologically relevant chemical space by providing chiral, medicinally favored scaffolds for preparation of diversity-oriented libraries. Recently, even structurally complex alkaloids have been demonstrated to be a valuable source for generating chiral molecular diversity by ring-distortion approach. Alkaloids with a combination of novel synthetic tools comprising cross-coupling chemistry, CH-heteroarene functionalization, or click chemistry provide an access to libraries for catalytic and biological screening. Problems with availability of the alkaloids as well as restriction regarding the use of many of them make the development of alkaloid chemistry slower than it deserves.

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