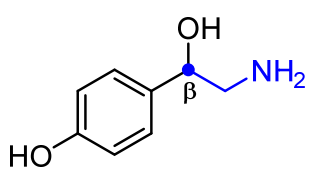
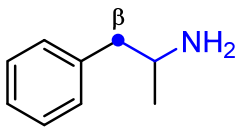
Chemical synthesis of new compounds is always a challenge. Simple structural core molecules often require a complex multi-step preparation. Every single synthetic step may need many reagents, significant amounts of solvents, energy, human resources and time. It is also worth to mention wastes that are generated in huge amount. There are by-products, unreacted reagents, and solvents used in the synthesis and purification of the product that stay after organic synthesis. Minimization of steps number of any organic synthesis is an important task for economic reasons and environmental protection. For complex organic molecules that contain many C-H bonds, the direct functionalization is the shortest way of their modification. From that perspective, replacement of many classical cross-coupling reactions by C-H bonds functionalization seems to be a natural evolution in organic synthesis.

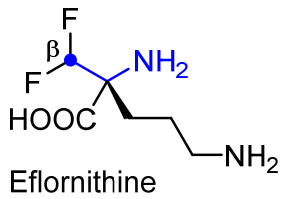
Site-selectivity is an important issue for organic compounds that contain many positions that might be modified by C-H activation chemistry. It can be controlled by specially designed directing group (DG) using pre-coordination approach. Particularly interesting is a selective and general method of *beta* functionalization of aliphatic amines. Structural motifs containing functional group in that position (e.g., phenyl, hydroxyl) are key structural components in medicines and natural products. The important point is that such structures can be obtained from simple aliphatic amines using C-H functionalization approach. For example ephedrine and amphetamine from isopropylamine, salbutamol, and synephrine from ethylamine.



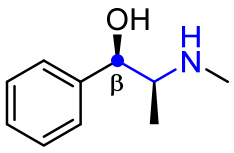
Synephrine



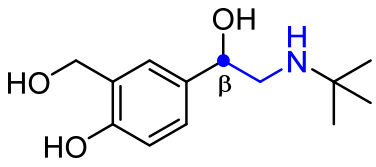
Amphetamine



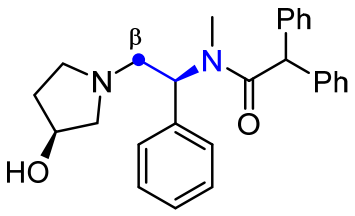
Eflornithine



Ephedrine

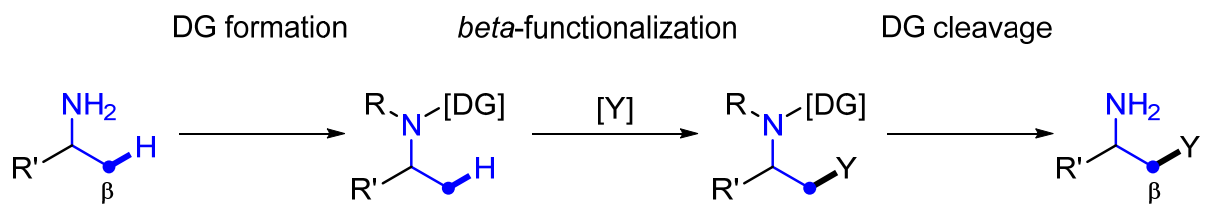


Salbutamol



Asimadoline

The project is intended to solve the problem of *beta* C-H bonds functionalization of primary aliphatic amines using directing group (DG). In the initial phase, such element will be attached to the molecule. The fundamental step is transition metal catalyzed C-H bond functionalization. During that process, DG will direct transformation in the correct position. Finally, the amine with functionality in *beta* position will be recovered by directing group cleavage.



We would like to develop a general method for directed *beta* functionalization of primary aliphatic amine. The methodology is not designed to replace traditional synthetic methods that are used for the preparation of known pharmaceuticals. Successful completion of the project will open a unique synthetic route leading to numerous new compounds with structural core diversification and a huge application potential. The results may be relevant for drug design and modification of known bioactive molecules.