Abstract

In this doctoral dissertation, we present new methodologies for the oxidation and functionalization of sulfur-containing functional groups with potential biological activity, with significant emphasis on environmentally benign aspects of green chemistry. The majority of the experimental work described in this thesis focuses on sulfoximines and their *N*-SCF_3 derivatives, which are bioisosteres of sulfonamides and sulfones and have already found applications in agrochemistry and the pharmaceutical industry. The first method presented is the selective oxidation of *N*-SCF_3 sulfoximines to the corresponding *N*-$SOCF_3$ and *N*-SO_2CF_3 derivatives. In most cases, the products could be isolated by simple extraction without the need for further purification. Most of the substrates were successfully oxidized at room temperature in environmentally benign, recyclable solvents, using a small excess of $NaOCl{\cdot}5H_2O$ as a green oxidant, which is converted to benign NaCl after the reaction. The method was also successfully scaled up, resulting in improved yields. Reactions performed on a larger scale were used to calculate various green chemistry metrics. All newly synthesized products were fully characterized and subsequently used as substrates in further transformations, such as Suzuki–Miyaura and Sonogashira coupling reactions. All the products were also tested for biological activity in collaboration with EU-OPENSCREEN. In addition to oxidation reactions, sulfoximines were also functionalized at the nitrogen atom with an interesting sulfonamide functional group, generated in situ via rearrangement of *N*-fluorobenzenesulfonamide. Through optimization of the reaction conditions, we were able to avoid the use of hazardous *n*-BuLi, very low temperatures, and strictly dry and inert conditions. This methodology enabled the preparation of a broad range of new products, some of which were further employed in subsequent transformations, including methylation of the sulfonamide group and various coupling reactions. The reaction was also investigated from a mechanistic perspective, and based on additional experiments and DFT calculations, a plausible reaction pathway was proposed. Similar sulfur-centered oxidations were also performed on sulfanilamides (R-$NHSCF_3$). Compared with the structurally related *N*-SCF_3 sulfoximines, sulfanilamides required different oxidation conditions. For the synthesis of sulfinamides ($NHSOCF_3$), *m*-CPBA in DCM was used, whereas H_2O_2 with Na_2WO_4 in AcOH was employed for the formation of sulfonamides ($NHSO_2CF_3$). In this way, 21 different products were prepared, some also on a larger scale. The sulfinamides were further evaluated as reagents for the transfer of the trifluoromethanesulfinate group (-$SOCF_3$) to various indoles.