SYNTHESIS OF OPTICALLY PURE POLYFLUOROBENZO[d]SULTAMS: AN EVIDENT EXAMPLE OF SELF-INDUCTION OF CHIRALITY

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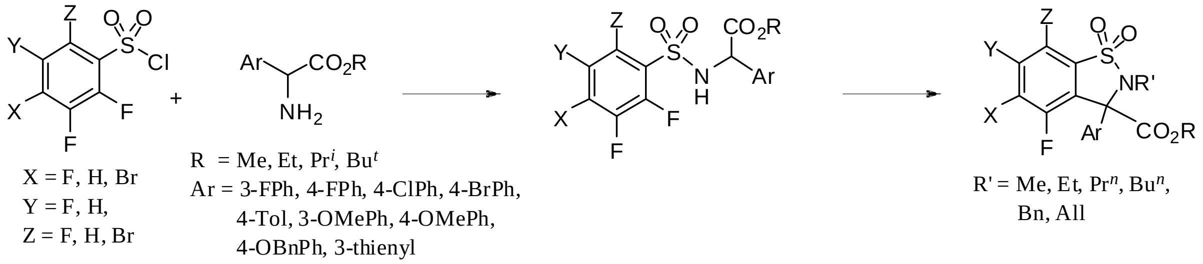
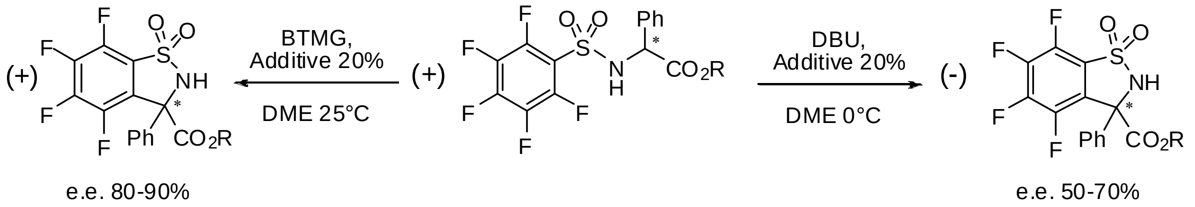
Cyclic sulfonamides (sultams), analogously to open chain sulfonamides, find important applications in human therapeutics.[1] In particular, as a result of their biological activity[2] and low toxicity, they have been employed in several fields of medicine, as drugs or as functional moiety of more complex molecules.

Furthermore Oppolzer's sultam[3] and saccharin derived 3-alkyl benzosultams[4] are relevant in asymmetric synthesis as chiral auxiliaries in many stereoselective transformations. In contrast to the large number of sultam containing structures reported, few examples of 3-carboxy substituted benzosultams are known.

In this communication we describe the preparation of 3-aryl polyfluorobenzo[d]sultams, obtained from the cyclization of the corresponding (polyfluorobenzene)sulfonamides, through two different and complementary synthetic pathways: "one-pot" *N*-alkylation of open-chain sulfonamides, then cyclization under solid-liquid phase transfer catalysis (SL-PTC) conditions, and homogeneous ring closure, using DBU as organic-soluble base. Our methodologies have been succesfully applied to a large series of (polyhalobenzene)sulfonamides obtaining the corresponding sultams in good to excelent yields.



Preliminary experiments performed on the non-racemic N-(pentafluorbenzene)sulfonamido L-phenylglycine, methyl ester, gave an unexpected 15% e.e. of tetrafluorobenzo[d]sultam, indicating the starting sulfonamide as the source of the stereochemical information; several basic conditions were tested to improve the product e.e. and the couple DBU/*t*-Bu-tetramethyl guanidine (BTMG) was found to be the most effective basic system, furnishing the sultam in 50-70% e.e.; a quite fascinating result, was obtained using BTMG as the sole base: in fact, not only the highest e.e. (80-90%) were reached, but the desired product was found to have opposite configuration to that obtained under the other basic conditions employed so far.



Almost all N-alkylated compound were obtained in > 95% e.e. after one or more crystallization.

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