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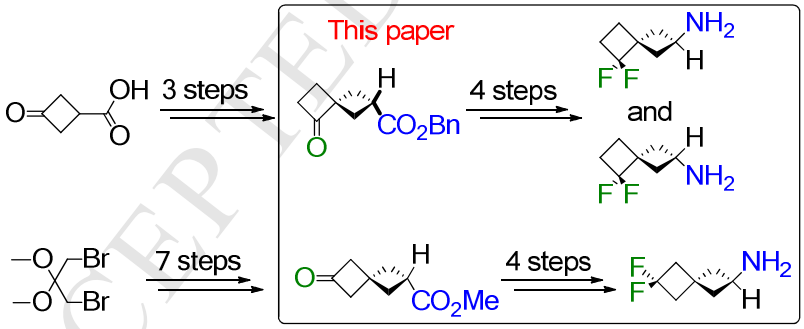
Abstract

New non-flattened amino group-containing building blocks and fluorinated analogs based on the spiro[3.3]heptane motif were synthesized. The syntheses included a challenging deoxofluorination of sterically hindered carbonyl groups *via* an intermediate carbocation. The synthesized compounds could be useful in medicinal chemistry due to their three-dimensional shape, and a different pattern of the fluorine substitution.



Keywords: fluorine, conformational restriction, non-flattened building blocks, spiro compounds

Introduction

Since the first fluorine-containing drug fludrocortisone was introduced, the use of fluorine substitution became a common practice in drug design. Today, around 25% of marketed drugs contain fluorine. Amongst these are the extremely popular atorvastatin (Lipitor®), fluoxetine (Prozak®), escitalopram (Lexapro®). The introduction of fluorine into lead molecules during their optimization often significantly improves the pharmacokinetic and pharmacodynamic properties of drug candidates.