SYNTHESIS OF BENZISOTHIAZOLE DERIVATIVES AS POSSIBLE HIV-1 NUCLEOCAPSID PROTEIN-7 (NCp7) INHIBITORS

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HIV/AIDS continues to ravage Africa with about two thirds of the HIV-positive global population of 35 million currently residing in sub-Saharan Africa, and it is the fourth leading cause of death worldwide. Several clinically approved drugs have emerged since the 1980s for the treatment of HIV and the total number currently stand at around thirty. New anti-HIV drugs are required that are less toxic (reduced dosage) and which cope with the HIV mutations better. Hence, finding novel ways of blocking the virus are required, as well as the targeting of conserved targets. The HIV-1 nucleocapsid protein-7 (NCp7) is a small and highly basic zinc-binding protein that is strongly involved in many processes of the viral life cycle. This includes operating the strand transfer that promotes the activity of the reverse transcriptase (RT). NCp7 is therefore, considered as a promising target for the identification of new anti-HIV-1 therapeutic agents. The lead compound in this work is a benzoisothiazolone, which acts against the HIV zinc-finger protein NCp7. 2-(N-Boc)benzisothiazole was synthesized using sulfuryl chloride as the oxidizing agent to form sulfenyl chloride followed by reaction with the carbazate. The carbamate was deprotected using trifluoroacetic acid to form 2-aminobenzisothiazole. Reaction of sulfonyl chlorides bearing different alkyl, heteroaromatic and substituted heteroaromatic rings with 2-aminobenzisothiazole resulted in several substituted sulfonamides. Substituted benzisothiazolesulfonamides were synthesized starting from the readily available dithiodibenzoic acid. This work will highlight the synthesis of compounds that contain the benzoisothiazolone core.