Intramolecular [3+2] cycloaddition of azido-unsaturated esters derived of monosaccharides

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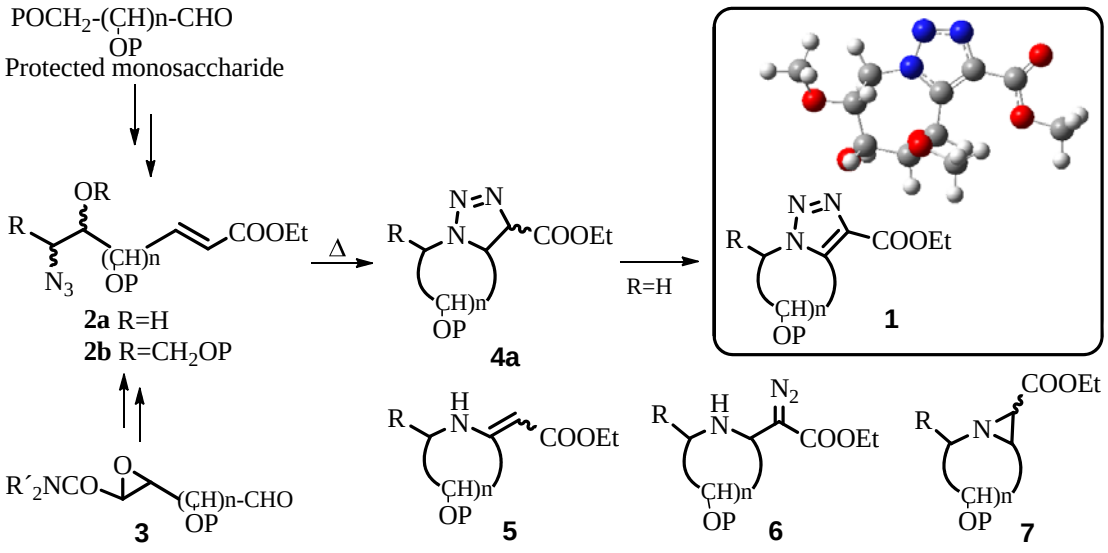
Iminosugars[1] have been shown to be very potent inhibitors of glycosidases and glycolsyltransferases. Due to their ability to resemble the transition states of the sugars involved in these processes, a variety of monocyclic and bicyclic iminosugars have been synthesized or isolated from natural sources over the years. As part of our ongoing work on the preparation of glycosidase inhibitors, we developed stereoselective methods for synthesizing iminosugars from 2,3-epoxyamides obtained from monosaccharides.[2]

Now, we are interested in the syntheses of novel bicyclic triazoles **1**, by intramolecular cycloaddition, due to the possibility of combining azido group and unsaturated esters in the same molecule. The triazole system is broadly considered in syntheses of bioactive products and the option of fused iminosugar with triazole has been evaluated.[3] Firstly, we started with a less complex azido derivative **2a** to continue with azido compounds **2b** obtained from our 2,3-epoxyamides **3**, by regioselective introduction of an azido group. The fused triazolines **4a** were formed by heating of **2a**. Aromatization of **4a** afforded byciclic triazoles **1**. There are several possibilities in the cyclization process depending on the reaction conditions and products **5, 6** and **7** can be formed. Moreover, we conducted a theoretical DFT based study of the cycloaddition to value the probability of formation of the triazoline **4a** and subsequent aromatization to triazole **1**, *versus* elimination to the unsaturated ester **5**.



References

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