Synthesis of fused tetrazolo iminosugars from azido monosaccharide derivatives

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Iminosugars, by virtue of their structural resemblance to monosaccharides, are among the most potent inhibitors of glycosidases, mimicking the transition states of the sugars involved in processes of inhibition. Due to this fact, 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 1 obtained from monosaccharides.\footnote{[1]} Now our attention is focused on the syntheses of novel bicyclic tetrazoles 7, by intramolecular cycloaddition, due to the possibility of combining azido and ciano groups in the same molecule. The tetrazole system is widely found in bioactive products but only a few examples of syntheses of fused pyrrolidines and piperidines with tetrazoles\footnote{[2,3]} have been reported to be evaluated as inhibitors.

With the aim of obtaining new and more potent analogues, we studied the formation of tetrazolic systems fused to different heterocycles formed from monosaccharide derivatives. Epoxyamides 1 were sequentially transformed into epoxyalcohols 2 and azido alcohols 3. Deprotection of the anomeric hydroxyl group after convenient functionalization gave 4. Conversion to azidoamides 5 and further transformation into azidonitriles 6 gave tetrazolobicycles 7 by cycloaddition.

(Chemical structures are not included here, but would typically be included in a scientific document.)

References