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Synthesis, Biological Evaluation and Docking Studies of Casuarine Analogues: Effects of Structural Modifications at Ring B on Inhibitory Activity Towards Glucoamylase

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We report the total synthesis of a series of pyrrolizidine analogues of casuarine (**1**) and their 6-*O*-α-glucoside derivatives. The synthetic strategy is based on a totally regio- and stereoselective 1,3-dipolar cycloaddition of suitably substituted alkenes and a carbohydrate-based nitrone. We also report the evaluation of the biological activity of casuarine and its derivatives towards a wide range of glycosidases and a molecular modeling study focused on glucoamylase (GA) in which the binding modes of the newly synthesized compounds within the enzyme cavity are investigated. The results highlight the prominent structural features of casuarine and its derivatives that make them selective glucoamylase inhibitors.