36° ERSBQ - MG
ENCONTRO REGIONAL DA
DA SOCIEDADE BRASILEIRA DE QUÍMICA
A química atráves do tempo
reflexões sobre o passado, presente e futuro
da humanidade
22 a 24 de NOVEMBRO de 2024
DIAMANTINA - MG

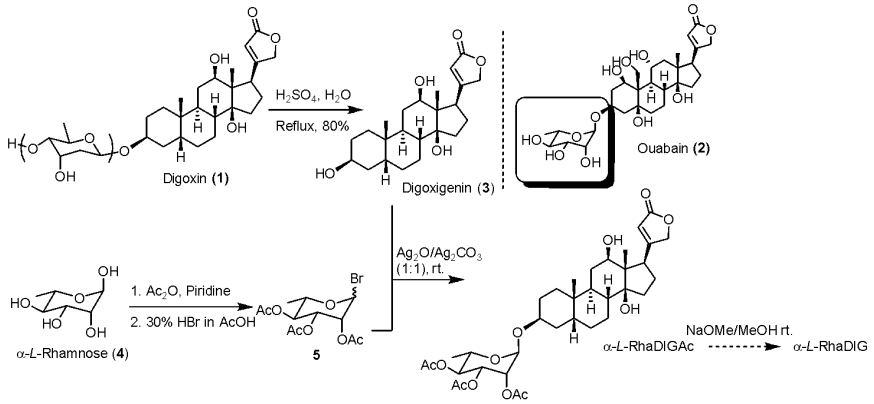
STUDY TOWARDS THE SYNTHESIS OF α-*L*-RHAMNOSE DIGOXIGENIN

Ericke C. Oliveira[1], Gustavo F. F. Lima[1], Jefferson L. Princival[2], Leandro A. O. Barbosa[3], José A. F. P. Villar[1*],

[1]Laboratório de Síntese Orgânica e Nanoestruturas, Universidade Federal de São João del Rei, campus CCO, Divinópolis, MG, CEP: 35.501-296.
[2] Laboratório de Catálise Orgânica, Universidade Federal de São João del Rei, campus CCO, Divinópolis, MG, CEP: 35.501-296.
[3] Laboratório de Bioquímica Celular, Universidade Federal de São João del Rei, campus CCO, Divinópolis, MG, CEP: 35.501-296.

e-mail: zevillar@ufsj.edu.br

Digoxin **1** is a cardiac glycoside derived from *Digitalis lanata* and is one of the oldest used medicaments in cardiology. It has been heavily employed when treating a number of heart problems, including congestive heart failure, atrial fibrillation or flutter, and certain cardiac arrhythmias[1]. The basic structure of cardiotonic steroids consists of a steroid backbone with a cis/trans/cis configuration and a lactone moiety at position 17β, also known as the aglycone. In addition, these compounds frequently have a sugar attached at position 3β of the steroidal nucleus[2]. On the other hand, Ouabain **2** is a cardiac glycoside isolated naturally from *Strophanthus gratus*. Compounds **1** and **2** inhibits the Na-K-ATPase membrane pump, resulting in an increase in intracellular sodium and calcium concentrations and the difference between **1** and **2** consisting of a glycosylated steroid core *L*-rhamnose (ouabain) or trisaccharide (digoxin)[3]. Thus, this work aims to develop a protocol for exchanging the sugar moiety from digoxin to *L*-rhamnose to further pharmacological and biochemical studies. In the first step, we remove the sugar from digoxin through acid hydrolysis, resulting in Digoxigenin (**3**) (yielding 80%). Simultaneously, we perform per-O-acetylation of α-*L*-rhamnose (**4**), followed by bromination (achieving 90% yield) in two steps. Subsequently, we synthesize the acetylated α-*L*-rhamnosyldigoxigenin derivative (α-*L*-RhaDIGAC) using selective Koenigs-Knorr reaction[4]. In conclusion, the α-*L*-RhaDIGAC was synthesized and characterized efficiently and currently we are optimizing this coupling reaction and planning for subsequent deacetylation of the acetyl groups to obtain final α-*L*-RhaDIG.



Scheme 1. Synthesis of α-*L*-Rhamnosyl digoxigenin (α-*L*-RhaDIG).

Acknowledgments: FAPEMIG, CAPES, CNPq, UFSJ, LCACCO-UFSJ.

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