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Efficient Synthesis Of Alkyl And Aryl 2,3-Unsaturated Glycopyranosides *via* Ferrier Rearrangement

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ABSTRACT

The reactions of 3,4,6-tri-*O*-acetyl-D-glucal with phenolic and aliphatic alcohol in various Lewis acid catalysts (namely $La(NO_3)_3.6H_2O$, $InCl_3$, $ZnCl_2$ and BF_3•OEt_2) have furnished the corresponding alkyl and aryl 2,3-unsaturated glycopyranosides *via* Ferrier rearrangement. BF_3•OEt_2 showed the best Lewis acids catalysts with excellent yields and minimum reaction times. The reactions performed in CH_3CN gave better yields and shorter reaction times compared to CH_2Cl_2. The electron withdrawing properties of aromatic ring resulting lower yields of aryl 2,3-unsaturated glycopyranosides compared to alkyl 2,3-unsaturated glycopyranosides under this condition. This study is significant in the preparation of *O*-glycosides *via* Ferrier rearrangement.

| Ferrier rearrangement | Lewis acids | alcohols | glycosides |

1. INTRODUCTION

Ferrier rearrangement is an attractive methodology for the synthesis of glycoside derivatives with various alcohols. It is an efficient reaction for the substitution at the anomeric position with allylic rearrangement [1,2]. The Ferrier rearrangement involves the addition of nucleophile onto the intermediate allylic axycarbenium ion, preferentially in a quasi-axial orientation [1]. This rearrangement leads to the formation of alkyl and aryl 2,3-unsaturated-*O*-glycosides, which are versatile chiral intermediates in the synthesis of several biologically active natural products [1,2]. 2,3-unsaturated-*O*-glycosides are also important building blocks in the synthesis of some antibiotics [1].

A variety of reagents, Lewis acids and oxidants were reported to undergo Ferrier rearrangement [3]. $SnCl_4$, $LiClO_4$, $LiBF_4$ and $FeCl_3$ are common Lewis acid used to allow this rearrangement [1,2,4-6]. The requirement of an acid catalyst to bring about the Ferrier rearrangement precludes its applicability to substrates that are sensitive to acidic conditions [4]. The use of strongly acidic conditions frequently leads to the formation of undesirable side products competing with the main reaction [2]. Some of these acidic methods involve stoichiometric amounts of catalysts, strongly acidic conditions, long reaction times, unsatisfactory yields and low diastereoselectivity [3].

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This has led to the development of essentially neutral, mild and non-acidic alternative catalysts such as 2,3-dichloro-5,6-dicyano-*p*-bezoquinone (DDQ), N-iodosuccinimide (NIS), I_2, acidic Montmorillonite-K10, cerium ammonium nitrate (CAN), lanthanum (III) nitrate hexahydrate ($La(NO_3)_3.6H_2O$) and $InCl_3$ under different conditions [1-4, 7-10].

In this paper, we report Lewis acid-promoted allylic rearrangement of 3,4,6-tri-*O*-acetyl-D-glucal with 4-hydroxybenzaldehyde and aliphatic alcohols with different type of catalysts at different solvents. This study was used as model studies for the synthesis of glycosides bearing chalcone derivatives *via* Claisen-Schmidt condensation of aldehyde and acetophenone [11].

2. EXPERIMENTAL

2.1 Materials, method and instruments

Solvents were dried using standard method. All chemicals were used as received. All reactions were performed under nitrogen atmosphere. ^{1}H NMR spectra were recorded on a JEOL 500 MHz instrument using TMS as an internal standard. The IR spectra were obtained on a Perkin Elmer Instruments Spectrum Gx1v5.0 using NaCl disc. Reactions were monitored by thin-layer chromatography carried out on 0.2 mm Merck pre-coated silica gel plates (60 F_{254}).