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ScienceDirect
Tetrahedron 64 (2008) 339–344
Tetrahedron
www.elsevier.com/locate/tet

Ferric sulfate hydrate-catalyzed O-glycosylation using glycals with or without microwave irradiation

Guisheng Zhang*, Qingfeng Liu, Lei Shi, Jiuxia Wang

School of Chemical and Environmental Sciences, Henan Normal University, 46 East Construction Road, Xinxiang, Henan 453007, PR China

Received 24 August 2007; received in revised form 24 October 2007; accepted 26 October 2007
Available online 1 November 2007

Abstract

We have developed a novel glycal-based O-glycosylation reaction, in which the substrates are not only peracetyl glycals but also perbenzyl glucals to afford the corresponding 2,3-unsaturated-*O*-glycosides via Ferrier rearrangement. The reaction of the perbenzyl glucal with various alcohols catalyzed by ferric sulfate hydrate ($Fe_2(SO_4)_3 \cdot xH_2O$) was successfully carried out to give 2,3-unsaturated D-*O*-glucosides with exclusive α-selectivity and no formation of addition products 2-deoxy hexopyranosides was observed. It is the first report on peralkyl glycal efficiently undergoing Ferrier rearrangement instead of addition of alcohols catalyzed by Lewis acids. $Fe_2(SO_4)_3 \cdot xH_2O$ is an effective, convenient, and environmentally benign heterogeneous catalyst. It has low catalytic loading and recyclable without significant loss of activity.

Keywords: O-Glycosylation; Ferrier rearrangement; Ferric sulfate hydrate; Peracetyl or perbenzyl glucal; 2,3-Unsaturated *O*-glycosides

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1. Introduction

Ferrier rearrangement is an allylic rearrangement of glycal esters[1–3] in the presence of alcohols leading to 2,3-unsaturated glycosides. Since Ferrier rearrangement was discovered in 1969,[4] it has been routinely used in the area of carbohydrate chemistry. The unsaturated glycosides obtained through Ferrier rearrangement play an important role in the transformation of these compounds into other interesting carbohydrates.[5–7] 2,3-Unsaturated glycosides[8] have a unique place in carbohydrate chemistry, since they can be further functionalized and serve as chiral intermediate[8a,9] in the synthesis of biologically active compounds, such as glycopeptide blocks,[10] oligosaccharides,[11] and modified carbohydrates.[12] In addition, 2,3-unsaturated glycosides have also been employed in the synthesis of some important antibiotics,[13] nucleosides,[14] natural product-like compounds,[2b] and various natural products.[15]

The catalysts for the synthesis of 2,3-unsaturated glycosides via Ferrier rearrangement have continuously received extensive attention. A wide range of catalysts have been employed to form 2,3-unsaturated glycosides, such as $BF_3 \cdot OEt_2$,[16] $SnCl_4$,[17] $FeCl_3$,[18] $Sc(OTf)_3$,[19] $InCl_3$,[20] Montmorillonite K-10,[21] $BiCl_3$,[22] $Dy(OTf)_3$,[23] $CeCl_3 \cdot 7H_2O$,[24] $ZnCl_2$,[25] DDQ,[26] NIS,[27] $K_5CoW_{12}O_{40}$,[28] I_2,[29] CAN,[30] $HClO_4{-}SiO_2$,[31] $Bi(NO_3)_3 \cdot 5H_2O$,[32] $Fe(NO_3)_3 \cdot 9H_2O$,[32b] and $NbCl_5$.[33] These catalysts included Lewis acid catalysts and redox reagents. The acid catalysts, usually employed in sub-stoichiometric amount, generally provide good anomeric selectivity for the product under ambient conditions. However, they often suffer from the limited use of acid-labile glycal donors and acceptors. The oxidants are often required in stoichiometric amount, and long reaction time and/or high temperature are unavoidable. In addition, the reactions under these conditions usually give low anomeric selectivity for the product. Moreover, some of the catalysts are moisture sensitive and expensive. As a result, most of those methods do not satisfy the rule of green chemistry, and entail the problems of tedious work-up procedures and expensive reagents and equipment. Therefore, searching for environmentally benign and more economic synthetic methods with greater efficiency and more convenient procedures is still in strong demand.

In general, the substrates of Ferrier rearrangement are peracyl glycals or the glycals at least with 3-*O*-acyl group.

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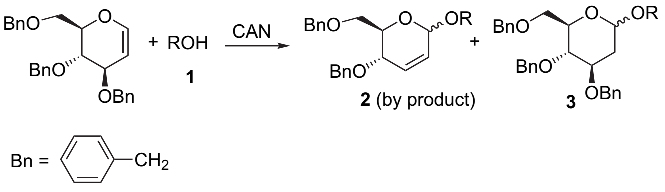
* Corresponding author. Tel./fax: +86 373 3325250.
E-mail address: zgs6668@yahoo.com (G. Zhang).

0040-4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.10.097

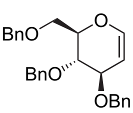
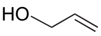
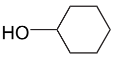
Perbenzyl glycals typically undergo addition reaction to form the corresponding addition products 2-deoxy *O*-glycosides instead of 2,3-unsaturated-*O*-glycosides. Benzyl is a very important protecting group in carbohydrate chemistry. To obtain benzyl-protected 2,3-unsaturated-*O*-glycosides via Ferrier reaction, 3-*O*-acyl-4,6-di-*O*-benzyl glycal was used as the Ferrier reaction substrate.[34] In this strategy, the hydroxy groups of the substrate should be protected selectively with benzyl and acyl groups. To date, convenient and effective approaches to benzyl-protected 2,3-unsaturated-*O*-glycosides directly from perbenzyl glycal have not been reported. CAN (ceric ammonium nitrate) was the only known reagent providing Ferrier rearrangement compounds as by-products from perbenzyl glycals. When CAN was applied, the reaction of perbenzyl glycal and alcohols led to the formation of 2-deoxy-glycoside (**3**) along with the Ferrier rearrangement product (**2**) due to the competition (Scheme 1).[30b] It was found that in the reaction of perbenzyl glucal with methanol, allyl alcohol, and cyclohexanol in the presence of 2 mol % of CAN, 2-deoxy products were formed as the major products along with the Ferrier products in the yields of 38%, 23%, and 18%, respectively (Table 1). Therefore, the development of a new glycal-based glycosylation method, in which the substrates include both peracyl and perbenzyl glucals, would represent an important advance.



Scheme 1. Reaction of perbenzyl glucal promoted by CAN.

In our efforts to develop highly efficient methods for functional group transformations, we found $Fe_2(SO_4)_3 \cdot xH_2O$ as an effective, reusable, operationally simple, and environmentally benign catalyst for tetrahydropyranylation[35] and preparation of acylals from aldehydes.[36] To further explore the potential of this reagent, we studied its behavior on both peracetyl glucal and perbenzyl glucal. The reaction of peracetyl glucal with alcohols catalyzed by $Fe_2(SO_4)_3 \cdot xH_2O$, as we anticipated, gave the Ferrier rearrangement products 2,3-unsaturated glucosides. However, this reaction was carried out with perbenzyl glucal, which, to our surprise, was also found to undergo Ferrier reaction instead of addition reaction. Both peracetyl and perbenzyl glucals reacted with alcohols catalyzed by $Fe_2(SO_4)_3 \cdot xH_2O$ to afford 2,3-unsaturated-*O*-glucosides in high yields with exclusive α-selectivity, no formation of 2-deoxy hexopyranosides (addition products) was observed. Encouraged by this result, we have explored $Fe_2(SO_4)_3 \cdot xH_2O$ as an efficient catalyst for Ferrier reaction of both peracetyl and perbenzyl glucals to synthesize the corresponding 2,3-unsaturated glucosides (Scheme 2).

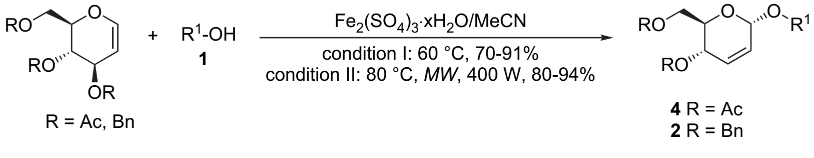
Table 1
Comparison of reaction results of $Fe_2(SO_4)_3 \cdot xH_2O$ with CAN

Glycal	Alcohol	Catalyst	Yields (%)	
			2 (α/β)	**3** (α/β)
	MeOH	$Fe_2(SO_4)_3 \cdot xH_2O$	81 (α only)	—
		CAN	38 (5:1)	56 (1.7:1)
		$Fe_2(SO_4)_3 \cdot xH_2O$	86 (α only)	—
		CAN	23 (4.7:1)	60 (1.1:1)
		$Fe_2(SO_4)_3 \cdot xH_2O$	82 (α only)	—
		CAN	18 (α only)	65 (11.5:1)

2. Results and discussion

To obtain some preliminary information on this synthetically useful reaction, initial experiments were performed with peracetyl glucal as the donor and ethanol as the acceptor. We first examined the reaction between glucal and ethanol in various solvent systems. Tri-*O*-acetyl-D-glucal (0.1360 g, 0.5 mmol) was treated with ethanol (1.5 mmol) and $Fe_2(SO_4)_3 \cdot xH_2O$ (0.025 g, 0.005 mmol)[37] in CH_2Cl_2, MeCN, DMF, $(CH_3)_2CO$, or THF at 60 °C to give ethyl 2,3-unsaturated glycopyranoside. Anhydrous acetonitrile was shown to be superior to the other solvents in terms of yields and reaction time. To study the effect of the catalyst, the reactions were carried out in acetonitrile in the presence of 10, 5, 2, 1, and 0.5 mol % of $Fe_2(SO_4)_3 \cdot xH_2O$. The results showed that 1 mol % of $Fe_2(SO_4)_3 \cdot xH_2O$ was enough for a fairly high yield. With 0.5 mol % of $Fe_2(SO_4)_3 \cdot xH_2O$, a lower yield was observed under same reaction period. Meanwhile, we also tested the effect of reaction temperature on the catalyzed reaction. When the reaction was carried out at room temperature, the reaction was sluggish. When it was carried out at 60 °C, the maximum yield was obtained in a short reaction period. This success encouraged us to study the scope of the reaction under the optimized condition: in the presence of 1 mol % of catalyst, anhydrous acetonitrile as reaction solvent, and at 60 °C. The results of using $Fe_2(SO_4)_3 \cdot xH_2O$ as a catalyst in the glycosylation are summarized in Table 2 (condition I).

Treatment of 3,4,6-tri-*O*-acetyl-D-glucal with various alcohols under the optimized conditions led to the corresponding 2,3-unsaturated alkyl glycosides (condition I, entries 1–9). The ^1H NMR data of the glycosides confirmed the α-configuration of the glycosyl products formed in the above reactions by comparison with the literature data. According to the published results, most of the Ferrier reactions of 3,4,6-tri-*O*-acetyl-D-



Scheme 2. Reactions of glucals catalyzed by $Fe_2(SO_4)_3 \cdot xH_2O$.