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MICROWAVE-INDUCED IODINE-CATALYZED GLYCOSYLATION OF ALCOHOLS WITH GLYCALS

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Abstract:
Microwave-induced iodine-catalyzed glycosylation of alcohols with glycals derived from galactose and glucose was conducted. The reaction produced a mixture of α-and β-glycosides in good yields.

Key Words:
Iodine, Glycal, Ferrier rearrangement, Stereoselectivity.

Introduction:

Ferrier rearrangement is an important reaction for the synthesis of 2,3-unstaturated oxygen-glycosides [I]. This method describes a reaction of glycal with alcohol in the presence of an acid to prepare 2,3-unsaturated sugars[II]. A various amounts of hydrochloric acid, sulfuric acid, $BF_3 \cdot Et_2O$, $SnBr_4$, $EtAlCl_2$ are used for this purpose (III-VI]. In general, a mixture of isomers are formed in this reaction. We describe here a microwave-assisted iodine-catalyzed Ferrier rearrangement of alcohols with glycals obtained from galactose and glucose. Several catalysts or acidic reagents do not yield products with galactose glycal and low stereoselectivities are observed in some examples with glucose glycal [VII-XI]. We report here a simple microwave-induced iodine-catalyzed reaction of diverse alcohols with galactose and glucose glycals in a good yield.

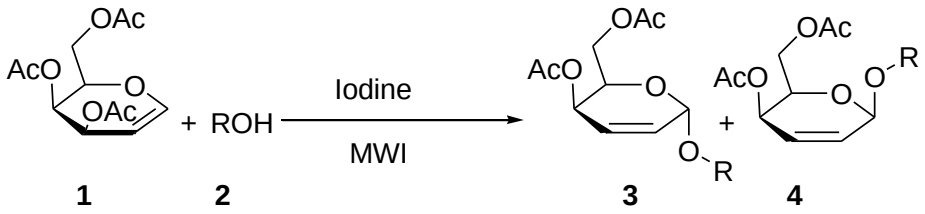
Results and Discussions:

Galactose glycal **1** on reaction with alcohol **2** in the presence of iodine as catalyst resulted a mixture of α-and β-glycosides in good yields using Microwave irradiation (**3** and **4**, **Scheme 1**). The reaction was exceptionally fast and the axially-oriented product **3** became the major isomer. A parallel reaction with glucose glycal **5** with alcohol **2** afforded **5** and **6** (**Scheme 3**).

Microwave method is attractive to prepare highly functionalized glycoside derivatives. Importantly, unsaturated alcohols are used effectively. The mechanism of this process is not established. The mild acidity of the iodine is responsible for the success of this reaction. The formation of the two isomers is possible because of an isomerization of the glycal to 2, 3-didehydro structure [XII-XIII].

The α-glycosides are formed because of an axial approach to the anomeric center of the allylic carbocation of the glycal by the alcoholic group (**Scheme 1**).

SCHEME 1: Iodine catalysed microwave induced
Glycosylation of the 3,4,6-Tri-O-acetyl-D-glactal with alcohol



1 **2** **3** **4**

Table 1:

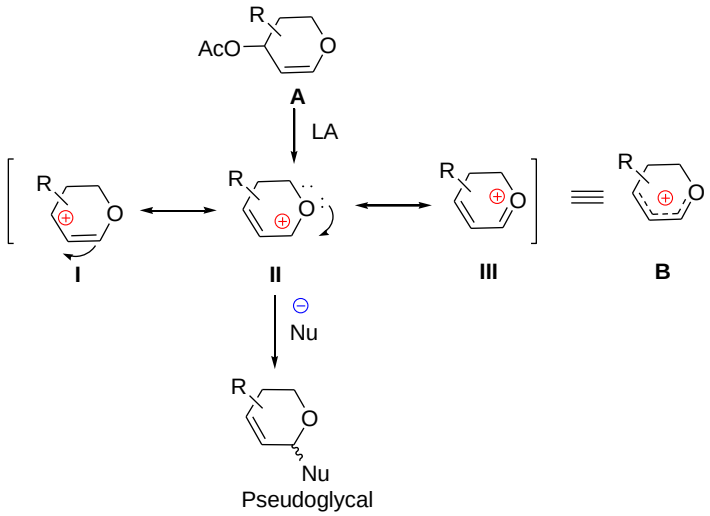
Entry	**2** (R)	Diasteromeric ratio[a] **3** (α) + **4** (β)	Time (min)	Yield[b] (%)
1	Me	**3a** (α) + **4a** (β) [9:1]	2	90
2	Et	**3b** (α) + **4b** (β) [9:1]	2	85
3	Bn	**3c** (α) + **4c** (β) [8:2]	2	90
4	Cy	**3d** (α) + **4d** (β) [7:3]	2	65
5	Cp	**3e** (α) + **4e** (β) [7:3]	2	65
6	All	**3f** (α) + **4f** (β) [9:1]	2	75
7	Propargyl	**3g** (α) + **4g** (β) [9:1]	2	70

a : Diastereomeric ration were determined by ^{1}H NMR of crude crude mixture.

b: isolated yield after column chromatography.

An equatorial attack may produce the β-glycoside. The nature of the product confirms that the equatorial attack is not possible due to the nonbonding electronic repulsion between the oxygen of the pyranoside ring and the lone pair of electrons present in the oxygen atom of the β-isomeric product **(Scheme 2)**. The cabocation reacts with alcohol from the axial side and therefore, α-glycosides become the major product. An equatorial attack produces β-isomeric compounds [XIV-XV].

SCHEME 2: General mechanism of o-glycosylation



SCHEME 3: Iodine catalysed microwave induced Glycosylation of the 3,4,6-Tri-O-acetyl-D-glucal with alcohol

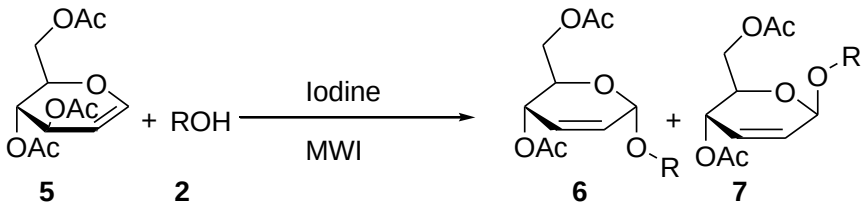


Table 1:

Entry		Diasteromeric ratio[a] **6** (α) + **7** (β)	Time (min)	Yield[b] (%)
1	Me	**6a** (α) + **7a** (β) [9:1]	2	90
2	Et	**6b** (α) + **7b** (β) [9:1]	2	85
3	Bn	**6c** (α) + **6c** (β) [8:2]	2	90
4	Cy	**6d** (α) + **7d** (β) [7:3]	2	65
5	Cp	**6e** (α) + **7e** (β) [7:3]	2	65
6	All	**6f** (α) + **6f** (β) [9:1]	2	75
7	Propargyl	**6g** (α) + **7g** (β) [9:1]	2	70

a : Diastereomeric ration were determined by ^{1}H NMR of crude crude mixture.

b: isolated yield after column chromatography.

Glycosylation with galactose glycal is difficult because of the stereochemistry of the C-4 carbon center. This does not assist in the neighboring group participation. It may be possible to couple the glycal derivatives with complex hydroxyl compounds using microwave method.

Experimental Section:

General procedure for the glycosylation of alcohols:

To a solution of the alcohol (1 mmol) was added tri-O-acetyl-D-glucal (1.5 mmol) followed by iodine (20 mg) in 1, 2-dichloroethane (2 mL) at room temperature. The mixture was irradiated at domestic microwave oven, cooled and washed with dichloromethane. The organic part was collected and evaporated. The crude NMR spectra was taken and it showed the presence of two glycosides in unequal proportions.

Conclusions:

Hydroxy compounds on reaction with various 3-acetoxyglycals in presence of iodine as a catalyst using microwave-technique produced diastereomeric α-and β-glycosides. The stereochemistry and nature of the groups in glycals are vital role for the success of this reaction.

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