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Indium trichloride catalyzed glycosidation. An expeditious synthesis of 2,3-unsaturated glycopyranosides[†]

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Abstract

Treatment of tri-*O*-acetyl-D-glucal **1** with various alcohols and phenols in the presence of $\text{InCl}_3/\text{CH}_2\text{Cl}_2$ at ambient temperature gave the corresponding alkyl and aryl 2,3-unsaturated glycopyranosides in excellent yields with short reaction times and good anomeric selectivity. © 2000 Elsevier Science Ltd. All rights reserved.

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Indium trichloride, which is a relatively strong Lewis acid, has been used as a catalyst for a wide variety of organic reactions viz., transmetallation with organotin compounds,¹ Mukaiyama aldol reactions,² imino Diels–Alder reactions³ and Barbier reactions involving addition of allyltin reagents to aldehydes or aldoses to give adducts with high diastereoselectivity.⁴

Herein, we present our preliminary results on the interesting utility of InCl_3 as an efficient catalyst for the synthesis of alkyl and aryl 2,3-unsaturated glycopyranosides **2–11** via the Ferrier rearrangement.

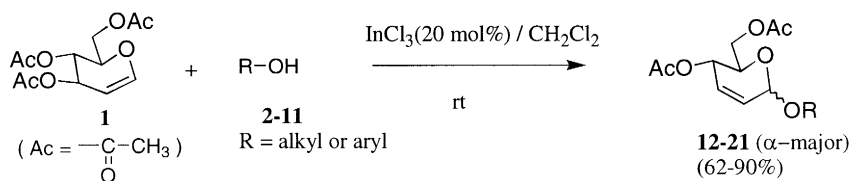
When 1 equiv. of tri-*O*-acetyl-D-glucal **1** was treated with 1.2 equiv. of benzyl alcohol **5** and anhydrous InCl_3 in CH_2Cl_2 for 10 min at ambient temperature, benzyl 2,3-unsaturated glycopyranoside **15** was obtained in 86% yield with the α -anomer as the major product. Likewise, other alcohols led to facile glycosidation upon reaction with **1** in $\text{InCl}_3/\text{CH}_2\text{Cl}_2$ affording the corresponding alkyl 2,3-unsaturated glycopyranosides **12–17** in excellent yields (Scheme 1).

The reaction was extended to phenols which furnished the corresponding 2,3-unsaturated aryl glycopyranosides **18–20** in moderate yields with the α -anomer as the major product. Extension of this reaction to *o*-iodobenzyl alcohol **6** gave the corresponding α -glycoside **16** which is a potential precursor for chiral isochroman type compounds (Table 1).

In the case of methyl 2,3,4-tri-*O*-methyl- α -D-glucofuranoside **11**, within 1 h, the disaccharide **21** was formed in 80% yield with the α -anomer (α : β 9:1) as the major product (Scheme 2).

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[†] Dedicated to Professor T. R. Govindachari, Advisor, Centre for Natural Products, SPIC Science Foundation, Chennai, India, on the occasion of his 85th birthday.

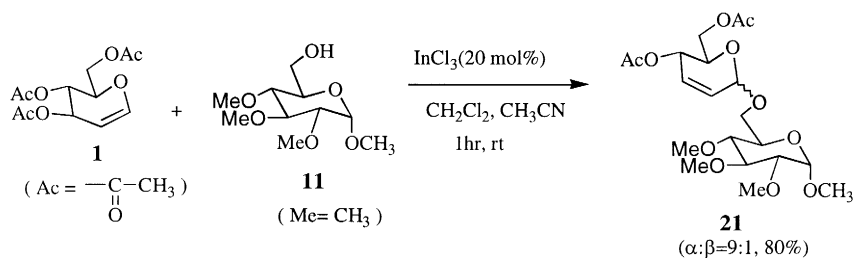


Scheme 1.

 Table 1
 InCl₃ mediated glycosidation of alcohols and phenols with **1**

R- OH (R=)	Product	Time (min)	Yield (%)	$\alpha:\beta$ *
methyl	12	10	90	7:1
propargyl	13	10	90	9:1
cyclohexyl	14	30	90	9:1
benzyl	15	10	86	6.3:1
<i>o</i> -iodobenzyl	16	15	87	9:1
<i>o</i> -nitrobenzyl	17	10	80	7:1
<i>p</i> -methylphenyl	18	10	60	8:1
<i>p</i> -methoxyphenyl	19	10	65	7.5:1
<i>p</i> -chlorophenyl	20	15	62	9:1

*Anomeric ratios were determined by ¹H NMR (200/400 MHz) spectroscopy.



Scheme 2.

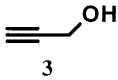
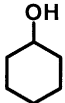
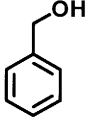
To the best of our knowledge, this is the first report on InCl₃ mediated Ferrier rearrangements. Several Lewis acids have been employed to bring about the Ferrier rearrangement.⁵ Other reagents such as, the environmentally more acceptable clay catalyst⁶ montmorillonite K-10, DDQ,⁷ (enabling neutral conditions) and *N*-iodosuccinimide,⁸ (providing a non-acidic medium to effect Ferrier rearrangement on 4-*n*-pentenoyl esters of glycals) are also known to bring about the Ferrier rearrangement under mild conditions.

The efficacy of a few other catalysts viz., LiClO₄, LiBF₄, BF₃·Et₂O and SnCl₄ was examined for the Ferrier rearrangement of **1** with selected alcohols. It was observed that among these catalysts, InCl₃ is found to be the best (Table 2).

In all the cases studied, the reaction was fast with InCl₃ as compared to other catalysts. Besides the diastereoselectivity, the yield is greatest with InCl₃. We have also examined a few other catalysts such as TaCl₅, PsCl₃, LnCl₃ in dichloromethane. However, none of these Lewis acids was found to catalyze the Ferrier rearrangement.

In summary, we have observed that anhydrous InCl₃ in CH₂Cl₂ is a useful catalyst for the rapid synthesis of alkyl and aryl 2,3-unsaturated glycopyranosides in excellent yields with good anomeric

Table 2
Study of various acid catalysts in the Ferrier rearrangement of **1** with alcohols

Alcohol	Lewis acid Catalyst (temp.)	Time	Glycoside Yield (α : β)*
 3	LiClO ₄ / Et ₂ O (27°C)	18hrs	13 90% (6:1)
	LiBF ₄ / CH ₃ CN (27°C)	4hrs	86% (8:1)
	BF ₃ .Et ₂ O (0°C to 27°C)	30min	82% (6.3:1)
	SnCl ₄ /CH ₂ Cl ₂ (0°C to 27°C)	45min	80% (9:1)
	Montmorillonite K-10 / CH ₂ Cl ₂ (40°C) ^{6a}	1 hr	97% (6.4:1)
	InCl ₃ / CH ₂ Cl ₂ (27°C)	10min	92% (9:1)
 4	LiClO ₄ / Et ₂ O (27°C)	18hrs	14 90% (6:1)
	LiBF ₄ / CH ₃ CN (27°C)	4hrs	86% (8:1)
	BF ₃ .Et ₂ O (0°C to 27°C)	45min	70% (9:1)
	SnCl ₄ /CH ₂ Cl ₂ (0°C to 27°C)	1hr	80% (6.5:1)
	Montmorillonite K-10 / CH ₂ Cl ₂ (40°C) ^{6a}	1hr	93% (7.3:1)
	InCl ₃ / CH ₂ Cl ₂ (27°C)	10min	90% (9:1)
 5	LiClO ₄ / Et ₂ O (27°C)	16hrs	15 85% (5:1)
	LiBF ₄ / CH ₃ CN (27°C)	4hrs	86% (4:1)
	BF ₃ .Et ₂ O (0°C to 27°C)	45min	80% (4:1)
	SnCl ₄ /CH ₂ Cl ₂ (0°C to 27°C)	45min	85% (4.6:1)
	Montmorillonite K-10		(see ref. 9)
	InCl ₃ / CH ₂ Cl ₂ (27°C)	10min	91% (6.3:1)

*Anomeric ratios were determined by ¹H NMR (200/400 MHz) spectroscopy.

selectivity. Tandem 'O' to 'C' rearrangement of aryl 2,3-unsaturated glycopyranosides to form the 2,3-unsaturated C-aryl glycosides is currently under investigation.

Typical experimental procedure: To a mixture of tri-*O*-acetyl-D-glucal **1** (1 mmol) and the aglycone (1.1 mmol), was added anhydrous InCl₃ (0.2 mmol; 20 mol%) in dry CH₂Cl₂ (1–2 mL) at ambient temperature. The contents were stirred for the required time (Table 1) and the reaction monitored by TLC. The reaction mixture was quenched by the addition of aqueous sodium hydrogen carbonate (10%, 25 mL), extracted with dichloromethane (3×25 mL), dried over anhydrous sodium sulphate, filtered and concentrated. The residue was purified by flash column chromatography on silica gel to obtain the products.

Acknowledgements

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