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$InCl_3$-induced C-glycosylation of per-*O*-acetylglycals with allyltrimethylsilane

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Abstract

$InCl_3$ has been used for the first time as a mediator for the C-glycosylation of per-*O*-acetylglycals with allyltrimethylsilane, and the reactions proceeded to give products in good-to-excellent yield and in high diastereoselectivity. The 1,5-anti diastereoselectivity in the allylation of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol and 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol and the 1,4-anti diastereoselectivity with 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*erythro*-pent-1-enitol are in the range 80–90%, whereas 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol furnished exclusively the corresponding *C*-α-D-galactopyranosyl compound.

Keywords: $InCl_3$; C-Glycosylation; Allyltrimethylsilane; Glycal

C-Glycosylation is a key reaction for the introduction of a carbon chain into sugars. Due to the importance [1] of *C*-glycosylic compounds (often termed '*C*-glycosides'), the present subject has received considerable attention in recent years [2]. Allyl *C*-glycosides are particularly attractive due to the presence of the terminal double bond that is amenable to easy functionalisation leading to other chiral molecules [3], as well as to carbon analogues of synthetic carbohydrate vaccines.

Previous reports on allyl 2,3-unsaturated per-*O*-acetyl *C*-glycosides include synthesis via carbon–Ferrier rearrangement [4a,b] from substituted D-glycals [5a,b,c] or from unprotected glycals [5d] and allyltrimethylsilane at low temperatures (-50 to -78 °C) in the presence of $BF_3{\cdot}OEt_2$, $TiCl_4$, TiF_4, SnF_4 and Me_3SiOTf. Although $InCl_3$ has been extensively investigated for a number of C–C bond formation reactions, such as the coupling of allylstannanes [6a,b] and aldehydes, Diels–Alder reactions [6c,d], water-mediated Mukaiyama aldol reactions [6e–h], Michael reactions [6i,j], aldol-type Mannich reactions [6k] etc., to the best of our knowledge its use as a mediator in allylsilane reactions, particularly in the carbohydrate field, has not been reported. This fact gave us impetus to study the carbon–Ferrier rearrangement of per-*O*-acetylglycals with allyltrimethylsilane utilising $InCl_3$ as the mediator (Scheme 1).

Our general reaction conditions involve the addition of allyltrimethylsilane (2 equivalents) to a stirred suspension of per-*O*-acetylglycal (1 equivalent) and $InCl_3$ (1.5–2 equivalents) in

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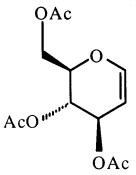
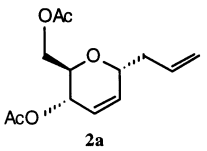
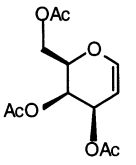
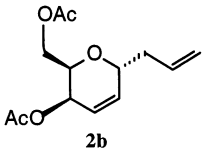
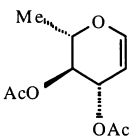
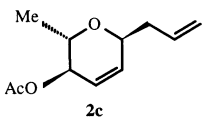
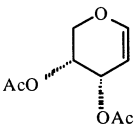
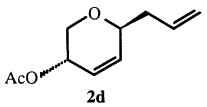
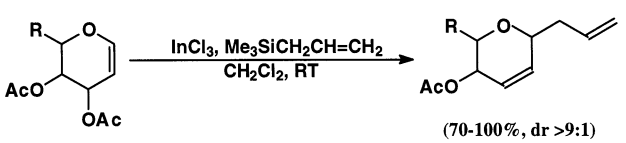
Table 1
$InCl_3$-induced C-glycosylation of per-*O*-acetylglycals with allyltrimethylsilane

Substrate	Product [a,b]	Time (h)	Yield (α/β)
 **1a**	 **2a**	1.5	95% (9:1)
 **1b**	 **2b**	24	78% (100:0)
 **1c**	 **2c**	1.5	100% (18:1)
 **1d**	 **2d**	2	70% (9.5:1)

[a] For characterisation data for **2a**, **2b**, and **2d**, see Ref. [8].
[b] ^1H NMR data ($CDCl_3$) for compound **2c**: δ 1.24 (d, 3 H, *J* 6.5 Hz, CH_3), 2.08 (s, 3 H, $OCOCH_3$), 2.33 (m, 1 H, $CH_2CH{=}CH_2$), 2.44 (m, 1 H, $CH_2CH{=}CH_2$), 3.90–3.94 (dq, 1 H, *J* 6.5 Hz, 4.7 Hz, H-5′), 4.17–4.23 (m, 1 H), 4.81–4.90 (m, 1 H), 5.08–5.16 (m, 2 H), 5.75–5.95 (m, 3 H).

dichloromethane at room temperature (20–30 °C). After completion of the reaction as determined by thin-layer chromatography (TLC), the reaction was quenched with saturated aqueous sodium bicarbonate, diluted with dichloromethane, and worked up in the usual manner. The crude product was purified by chromatography on silica gel to afford the allyl 2,3-unsaturated acetyl *C*-glycoside in high yield and with high α-diastereoselectivity (see Table 1). All products were characterised by ^1H and ^{13}C NMR spectroscopy (at 300 and 75 MHz, respectively), by elemental analysis,



Scheme 1.

and by comparing the $[\alpha]_D$ values with those in the literature. The α:β ratios were determined by GLC.

The yield and 1,5-anti diastereoselectivity in the allylation of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**1a**) (95%, α:β 9:1) and 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol (**1c**) (100%, α:β 18:1) are quite high. The 1,4-anti diastereoselectivity with 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*erythro*-pent-1-enitol (**1d**) followed the same trend as also observed earlier by Hosokawa et al. [7] in the C-glycosylation of allyltrimethylsilane and silyl acetylenes with acetylated pentopyranoglycals induced by other Lewis acids. 3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol (**1b**), however, gave exclusively the corresponding *C*-α-galactoside, i.e., 3-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl)-1-pro-

pene (**2b**) (no β compound could be detected either by GLC or by NMR spectroscopy). Repeating the reactions with a catalytic amount of $InCl_3$ furnished unchanged starting per-*O*-acetylglycals in all the above-mentioned cases.

It may be mentioned that reactions of **1a** with trimethylphenylsilane and ethynyltrimethylsilane in the presence of $InCl_3$ (even with >2 equivalents) failed to give the desired *C*-glycoside product, as was noted earlier by Isobe and co-workers [5a] on similar reactions induced by $BF_3{\cdot}OEt_2$.

In conclusion, the present method of $InCl_3$-induced C–C bond formation provides a highly efficient alternative to the existing methodologies for the synthesis of allyl 2,3-unsaturated-*C*-α-glycosides. The process has several notable advantages, such as operational simplicity and mild reaction conditions that make use of a reagent of relatively low toxicity. Moreover, this is the first demonstration of $InCl_3$-mediated reaction of allylsilane with glycals.

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