

Stereoselective Synthesis of 2,3-unsaturated-*O*-Glycosides promoted by TeBr₄

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O uso de uma quantidade catalítica de tetrabrometo de telúrio(IV) para promover a *O*-glicosilação de glicais e levar aos *O*-glicosídeos insaturados correspondentes é descrita. Os compostos desejados foram obtidos em bons rendimentos e em elevada seletividade α .

The use of a catalytic amount of tellurium(IV) tetrabromide to promote the *O*-glycosylation of glycols to yield 2,3-unsaturated-*O*-glycosides is described. The desired compounds were obtained in good yields and high α -selectivity.

Keywords: *O*-glycosylation, tellurium tetrabromide, 2,3-unsaturated-*O*-glycosides

Introduction

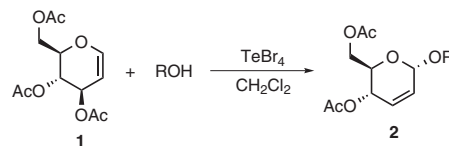
The development of synthetic methodologies for the efficient and stereoselective synthesis of glycosides is one of the main interests in carbohydrate chemistry. In this context, the synthesis of 2,3-unsaturated-*O*-glycosides have attracted considerable attention in this field due to their importance as intermediates in the synthesis of several compounds.¹

One of the important-*O*-glycosylation method for producing 2,3-unsaturated-*O*-glycosides, is the Ferrier rearrangement, originally promoted by BF₃·Et₂O, which involves a nucleophilic substitution reaction combined with an allylic shift in a glycal.² The orientation of the formed glycoside bond, α or β , depends on some combination of control elements, being the most important the 'kinetic anomeric effect'.³

A number of other Lewis acids such as InCl₃,⁴ montmorillonite-K10,⁵ SnCl₄,⁶ BiCl₃,⁷ FeCl₃,⁸ Sc(OTf)₃,⁹ ZnCl₂,¹⁰ LiBF₄,¹¹ Dy(OTf)₃,¹² AuCl₃,¹³ CeCl₃,¹⁴ and ZrCl₄¹⁵ can be used in the reaction. In addition, oxidizing agents such as DDQ,¹⁶ NIS,¹⁷ iodine,¹⁸ I(Coll)₂ClO₄,¹⁹ CAN²⁰ and HClO₄ on silica gel²¹ can promote the reaction. Most of the methods require a large excess of alcohol leading in some cases to an extensive work up. In addition, some have drawbacks in generality, yields and diastereoselectivity.

Tellurium tetrahalides (TeCl₄, TeBr₄ and TeI₄) have seen considerable research activity because of their structural versatility and potential utility as *synthons* in many chemical reactions.²² They can react with both Lewis bases and Lewis acids.²³ This amphoteric behavior can be understood in terms of the partially ionic Te-X bonding.

In this way, tellurium(IV) tetrabromide could be the Lewis acid choice to promote the *O*-glycosylation of glycols **1** to yield 2,3-unsaturated-*O*-glycosides **2** (Scheme 1).

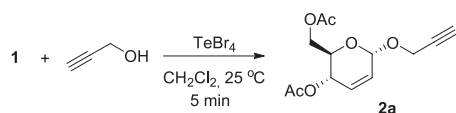


Results and Discussion

Our initial studies have focused on the development of an optimum set of reaction conditions. In this way, a solution of glycal **1** (1.0 mmol) and propargyl alcohol (1.2 mmol) in CH₂Cl₂ (10 mL) were treated at room temperature with different amounts of TeBr₄ and the progress of the reaction was monitored by TLC. The results are depicted in Table 1.

In all cases the reaction proceeded smoothly leading to the complete conversion into the 2,3-unsaturated-*O*-glycoside **2a** in high yield and with almost exclusive α -selectivity (Table 1, entries 1-5). It is also interesting

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Table 1. Influence of the amount of TeBr₄ in the synthesis of 2,3-unsaturated-*O*-glycoside, **2a**

entry	TeBr ₄ (equiv.)	Ratio α:β ^a	Yield (%) ^b
1	0.5	89:11	90
2	0.3	91:9	91
3	0.1	93:7	92
4	0.05	87:13	92
5	0.01	50:50	60

^aThe anomeric ratios were obtained by ¹H NMR and confirmed by gas chromatography for all reactions; ^bIsolated yield.

to note that when the amount of TeBr₄ was reduced to 0.01 equiv., a significant decrease in the yield and anomeric selectivity was observed (Table 1, entry 6).

Next, we explored the scope of the reaction for the synthesis of 2,3-unsaturated-*O*-glycosides using glycol **1** and various alcohols (Table 2).²⁷ In the majority of the studied examples, the reaction was faster and more diastereoselective when compared to other literature described catalysts.⁴⁻²¹

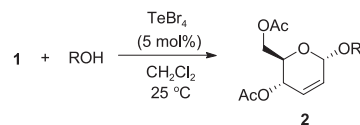
As shown in Table 2, reactions with aliphatic and alicyclic alcohols required longer reaction times (entries 6-12). This effect was observed before for other catalytic systems.²¹

The reaction of glycol **1** with *t*-BuOH is described to be difficult to proceed,²¹ but in our case the reaction gave a clean product in high yield and excellent anomeric selectivity (Table 2, entry 10). More reactive alcohols such as allylic, benzylic and propargylic gave better yields and shorter reaction times if compared with aliphatic and alicyclic alcohols (Table 2, entries 1, 2, 3 and 5). The reaction time increased when a homoallylic alcohol was used (Table 2, entry 4). A lower yield was observed when phenol was used as the nucleophile (Table 2, entry 13). This effect was also observed before for other catalytic systems.^{4,21}

We have also examined the influence of the temperature in the reaction. When the reaction was heated under reflux, shorter reaction times were observed if compared with Table 2, without any loss of diastereoselectivity (Table 3).

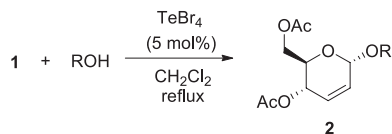
Conclusions

In summary, we have demonstrated that the TeBr₄ is useful to carrying out the synthesis of 2,3-unsaturated-*O*-glycosides under mild conditions, excellent yield

Table 2. TeBr₄ promoted synthesis of 2,3-unsaturated-*O*-glycosides **2**

entry	ROH	Product	time (h)	Ratio α:β ^a	Yield (%) ^b
1			0.1	89:11	92
2			0.1	88:12	94
3			0.25	88:12	86
4			1.0	89:11	87
5			0.25	86:14	85
6	MeOH		1.5	78:22	86
7	EtOH		5.0	83:17	84
8	<i>n</i> -PrOH		2.5	88:12	85
9	<i>i</i> -PrOH		1.5	90:10	92
10	<i>t</i> -BuOH		2.0	93:7	86
11			1.0	91:9	90
12			1.0	89:11	85
13	PhOH		0.1	88:12	70

^aThe anomeric ratios were obtained by ¹H NMR and confirmed by gas chromatography for all reactions. ^bIsolated yield.

Table 3. TeBr₄ promoted synthesis of 2,3-unsaturated-*O*-glycosides, **2**

entry	Product	time (h)	$\alpha:\beta^a$	Yield (%) ^b
1	2d	0.1	90:10	80
2	2f	0.1	86:14	84
3	2g	0.3	89:11	91
4	2h	0.3	90:10	87
5	2i	0.3	90:10	90
6	2j	0.3	88:12	89
7	2l	0.25	91:9	91
8	2m	0.25	87:13	86

^aThe anomeric ratios were obtained by ¹H NMR and confirmed by gas chromatography for all reactions. ^bIsolated yield.

and good α -anomeric selectivity. The methodology is synthetically useful and could be applied for the synthesis of more complex glycosides.

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27. Representative procedure for the synthesis of prop-2-ynyl-4,6-di-*O*-acetyl-2,3-dideoxy- α -D-erythro-hex-2-enopyranoside (**2a**): To a 25 mL round bottomed flask containing a solution of glucal **1** (272 mg, 1.0 mmol) and the appropriate alcohol (1.2 mmol) in dichloromethane (10 mL) at 0 °C was added TeBr₄ (Aldrich) (22.4 mg, 5 mol%). The ice bath was removed and the mixture was stirred for the time indicated on Table 2 (or refluxed for the time indicated on Table 3). Brine (5.0 mL) was then added and the

mixture was stirred until the yellow color disappear. The mixture was extracted with EtOAc (210.0 mL) and the organic phase dried over MgSO₄. The solvents were removed under reduced pressure followed by purification by flash chromatography column [hexanes:EtOAc (95:5)] to yield 246 mg (92%) of the title compound as a white solid. mp: 58-59 °C (lit.²⁴ 59 °C). ¹H NMR (300 MHz, CDCl₃): δ 2.07 (s, 3H, -OCOCH₃), 2.09 (s, 3H, -OCOCH₃), 2.45 (t, *J* 2,4 Hz, -C≡CH), 4.04-4.10 (m, 1H, H-5), 4.20 (dd, *J* 11.2 and 5.1 Hz, 2H, H_a-6, H_b-6), 4.29 (d, *J* 2,4 Hz, -CH₂C≡C), 5.22 (br s, 1H, H-1), 5.30-5.34 (m, 1H, H-4),

5.80-5.85 (m, 1H, H-2), 5.91 (br d, *J* 10,2 Hz, 1H, H-3); ¹³C NMR (75 MHz, CDCl₃): δ 170.7, 170.2, 129.7, 127.1, 92.7, 79.0, 74.8, 67.1, 65.0, 62.7, 55.0, 20.9, 20.7; LMRS (EI) *m/z*: 268(1), 213(9), 166(23), 153(16), 124(99), 111(25), 95(9), 85(69), 81(11), 67(5), 57(12), 55(10), 43(100). The spectroscopic data of all synthesized compounds match with the reported values: **2f**, **2g**;²⁴ **2b**, **2c**, **2e**, **2i**;¹³ **2d**, **2h**;²⁵ **2j**, **2m**; **2l**,²⁶ and **2n**.⁴

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