Tetrahedron 68 (2012) 544–551

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Carbohydrate-derived PSE acetals: controlled base-induced ring cleavage

Florence Chéry [a], Elena Cabianca [a,b], Arnaud Tatibouët [a,*], Ottorino De Lucchi [b], Patrick Rollin [a,*]

[a] Institut de Chimie Organique et Analytique, UMR 6005, Université d'Orléans, B.P. 6759, F-45067 Orléans, France
[b] Dipartimento di Chimica, Università Ca' Foscari di Venezia, Dorsoduro 2137, I-30123 Venezia, Italy

ARTICLE INFO

Article history:
Received 30 June 2011
Received in revised form 2 November 2011
Accepted 4 November 2011
Available online 11 November 2011

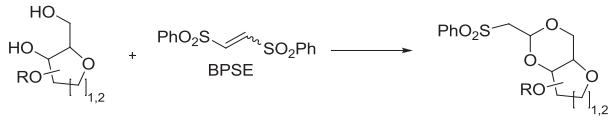
Keywords:
Acetal
Phenylsulfonylethylidene
Alkoxyvinyl sulfones
Protecting group
Carbohydrate

ABSTRACT

Retro-Michael type reactions applied to PSE acetals protecting monosaccharides led either to complete removal or to ring-cleavage. In protic medium, application of standard basic conditions resulted in acetal deprotection, while the use of butyl lithium in aprotic medium allowed controlled ring-cleavage. A regio- and stereoselective C- over O-alkylation was observed during the process. Furthermore, depending on the substrates and the reaction conditions involved, new carbohydrate-derived β-alkoxyvinyl sulfones were obtained with varying regioselectivity.

1. Introduction

We have introduced in the carbohydrate field phenylsulfonylethylidene (PSE) acetals,[1] which can readily be prepared through a Michael-type reaction of the corresponding diols with 1,2-bis(phenylsulfonyl)ethylene (BPSE) (Scheme 1).



Scheme 1. Synthesis of carbohydrate-derived PSE acetals.

Our previous studies have disclosed that those atypical PSE acetals show striking properties[2] compared to standard acetal protective groups—notably a strong reluctance to acid-catalyzed hydrolysis. A major part of sulfone chemistry is dedicated to the formation and reactivity of the derived stabilized carbanions.[3] In particular, simple α-sulfonyl carbanions have been used in alkylation[4] or in acylation[5] reactions, in aldol-type reactions[6] as well as in Michael additions on α,β-unsaturated acceptors.[7] Whereas anions derived from γ-sulfonylated acetals have been studied extensively,[8] the reactivity of β-acetalic sulfones in basic media was scarcely investigated.[9,10] On the other hand, elimination of a sulfone group through reductive cleavage of a C–S bond is a standard reaction.[11] In the present work, we report on the behaviour of previously described carbohydrate-derived PSE acetals[1b,2] under strongly basic conditions to explore *the selective ring cleavage and deprotection* conditions.

2. Results and discussion

2.1. Retro-Michael reaction for PSE acetal removal

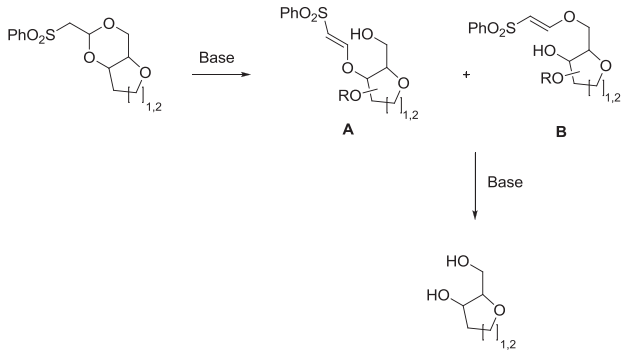
From earlier results, it is known that PSE acetals are not affected under acidic conditions;[1b,2c] contrastingly, they can undergo cleavage under strongly reductive conditions (e.g., $LiAlH_4$[1b]) or under strongly basic conditions ($LiNH_2$ in liquid ammonia[12]). PSE acetal removal should follow two consecutive retro-Michael type reactions involving two possible isomeric intermediates **A** and **B** (Scheme 2).

Taking into consideration that the previously reported conditions to effect PSE acetal cleavage are particularly harsh and should be modified, we have performed a preliminary study (Table 1) on the reactivity of our standard[1b,2a] model substrate—methyl 2,3-di-*O*-benzyl-4,6-*O*-(2-phenylsulfonyl)ethylidene-α-D-glucopyranoside **1** and other selected pyrano- and furano-type PSE acetals (Scheme 3).

Deprotections under various protic conditions were first tested on PSE acetal **1**. This exploration (Table 1, entries 1–7) showed that KOH or $CsCO_3$ in refluxing EtOH effected total cleavage of the acetal with reasonably good yields. In one case (entry 5) direct acetylation of the crude mixture afforded the 4,6-di-*O*-acetyl derivative in 86%

* Corresponding authors. Tel.: +33 (0)238 41 73 70; fax: +33 (0)238 41 72 81; e-mail address: arnaud.tatibouet@univ-orleans.fr (A. Tatibouët).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.11.009

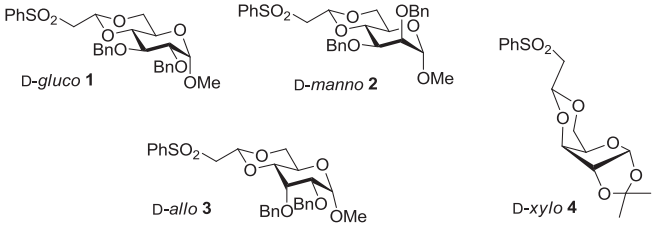


Scheme 2. Suggested double retro-Michael mechanism for the cleavage of carbohydrate-derived PSE acetals.

Table 1
Base-induced cleavage of PSE acetals in protic solvents

Entry	PSE acetal	Base [c]	Solvent	Temperature	Time	Yield
1	**1**	LiCl	MeOH/H_2O (1:1)	rt	24 h	No reaction
2	**1**	NaOH [1 M]	MeOH/H_2O (1:1)	rt	24 h	No reaction
3	**1**	K_2CO_3 [0.35 M]	EtOH/H_2O (1:1)	Reflux	16 h	No reaction
4	**1**	KOH [0.5 M]	EtOH	Reflux	3 h	51%
5	**1**	KOH [0.5 M]	EtOH	Reflux	5 h	86%[a]
6	**1**	$CsCO_3$ [0.4 M]	EtOH	Reflux	5 h	70%
7	**1**	$CsCO_3$ [0.5 M]	EtOH	Reflux	3 h	69%
8	**2**	KOH [1.5 M]	EtOH/H_2O (1:1)	Reflux	16 h	63%
9	**2**	KOH [0.5 M]	EtOH	Reflux	16 h	65%
10	**3**	KOH [0.5 M]	EtOH	Reflux	16 h	80%
11	**4**	KOH [0.6 M]	EtOH	Reflux	3 h	82%

[a] Per-O-acetylation was realized to optimize purification of the compound.



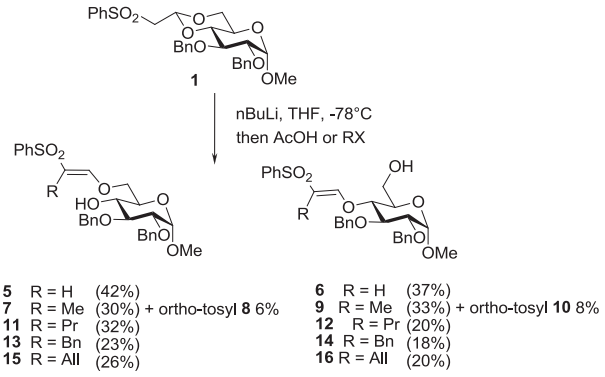
Scheme 3. PSE acetals examined in the base-induced deprotection assays.

yield. Application of the KOH/EtOH procedure to the D-mannopyranoside **2**,[1b] the D-allopyranoside **3**,[2a] and the D-xylofuranose **4**[1b] led to similar deprotection yields, which compared favourably with the results previously reported by us: using the $LiAlH_4/Et_2O$ procedure, PSE acetal cleavage of **1** and **4** was effected in 77% and 78% yields, respectively.[1b] Therefore it comes out that the above protic conditions can advantageously be used for the deprotection of PSE acetals.

2.2. Retro-Michael reaction in controlled ring opening of PSE acetals

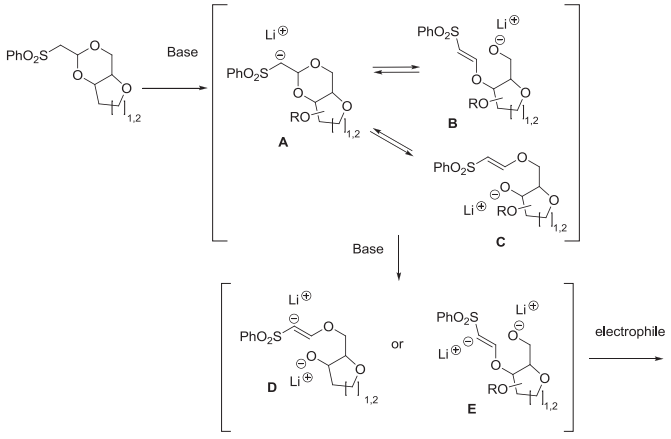
The retro-Michael process outlined in Scheme 2 allows to predict a possible controlled ring opening to produce synthetically useful alkoxyvinyl sulfones:[12] applying a strong base in aprotic conditions would cleave the PSE acetal ring to form isomeric intermediates **A** and **B** (Scheme 2).

Our model PSE acetal **1** was subjected to the conditions previously set up by Simpkins to convert PSE acetals into alkoxyvinyl sulfones,[9] using *n*-BuLi (2 equiv) in THF at −78 °C, then quenching the reaction with electrophilic species—namely a protic acid or an alkyl halide (Scheme 4). Proton-quenching by acetic acid resulted in a ca. 1:1 mixture of regioisomeric alkoxyvinyl sulfones **5** and **6** in which the double bond was shown to be exclusively *E*-configurated. Alkyl halide quenching led in moderate yields to regioisomeric pairs of *C*-alkylated β-alkoxyvinyl sulfones **7**, **9** and **11**–**16**. Additionally, minor C-methylation of the phenyl group was detected in the sole case of **8**/**10**.



Scheme 4. Base-induced ring cleavage of PSE acetal **1** and C-alkylation.

The poor regioselectivity observed between the primary (*O*-6) and the secondary (*O*-4) positions on the carbohydrate template might result from an equilibrium established in such conditions between the cyclic acetal and open-chain anionic species (Scheme 5). The first equivalent of *n*-BuLi is used to extrude the proton α to the sulfonyl group; elimination then occurs with cleavage of the cyclic acetal **A** to produce a vinyl sulfone **B** or **C**. The second equivalent of *n*-BuLi extrudes the most reactive α-vinylic proton to form the stabilized carbanion **D** or **E**, which finally attacks the electrophilic species to stereoselectively afford the *E*-alkoxyvinyl sulfone.[13]



Scheme 5. Intermediates in base-induced ring cleavage of a PSE acetal.

The retro-Michael O-regioselection outcome of the cleavage is indeed disappointing. On the contrary, the regio- and stereoselectivities of the alkylation are far more satisfactory. No O-alkylation was detected whatever excess of electrophile used and a selective C-alkylation in α position of the β-alkoxyvinyl sulfones was observed. Eisch et al. have shown α-metallation of vinyl