Synthesis of selenium linked steroidal glycoconjugates

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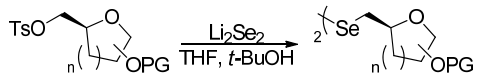
INTRODUCTION

Steroidal glycosides derivatives are found in several natural products and shows cardiotonic and anticancer activity, such as diosgine and digitoxin.[1] On the other hand, selenoglycosides have been explored as potential anti-HIV, anticancer and antioxidants.[2] We have recently described the synthesis of selenium linked carbohydrate and amino acid glycoconjugates.[3] In this work we synthesized cholesterol Se-glycoconjugates by selective ring opening of cholesterol epoxide.

RESULTS AND DISCUSSION

Initially were obtained glycosyl diselenides **2** from *D*-galactose, *D*-ribose and *D*-xylose in 3 steps in 82-90% yield, by reacting sugar-protected tosylates **1** with Li_2Se_2 (figure 1). The cholesterol epoxides **3** were obtained by a previously optimized methodology involving asymmetric epoxidation of a double bound.[4]



1 **2**

Figure 1. Synthesis of carbohydrate diselenides

We then explored the selenium linkage of the two structures with reductive cleavage of the diselenide derived from *D*-galactose to provide the nucleophilic cholesterol epoxide opening. After the *in situ* formation of the nucleophilic selenocarbohydrate specie by reaction with a suitable reductant agent in inert atmosphere it was added a solution of the cholesterol. The best yields were obtained after 48h in THF/EtOH or DMF (Table 1, entries 2 and 3). Changing the reducing agent furnished lower yields as well as addition of $ZnCl_2$ catalyst (entries 8-10).

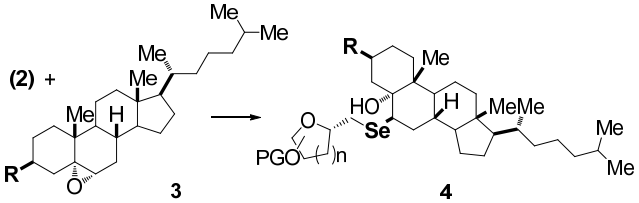


Figure 2. Synthesis of steroidal selenoglycoconjugates

Table 1. Reaction between 1:1.8 eqv. of **2** and **3**

#	R	Reducing agent	Solvent	T (°C)	t (h)	Yield (%)
1	OH	$NaBH_4$	THF/EtOH	66	24	37
2	OH	$NaBH_4$	THF/EtOH	66	48	65
3	OH	$NaBH_4$	DMF	80	48	60*
4	OH	$NaBH_4$	DMF	120	48	53
5	OH	$NaBH_4$	EtOH	76	48	50
6	OMe	$NaBH_4$	DMF	80	48	45
8	OH	$NaBH_4$	THF/EtOH	66	48	5%**
9	OH	$LiAlH_4$	THF/EtOH	80	48	5%
10	OH	$LiEt_3BH$	THF	66	48	50%

*1:1 diselenide:epoxide; **1 eqv. of $ZnCl_2$

We choose to explore the scope of the reaction with equimolar mixture of the diselenide and the epoxide in DMF at 80º for 48h with $NaBH_4$ changing the sugar from *D*-galactose to *D*-ribose diselenide, were similar yields were obtained (figure 3).

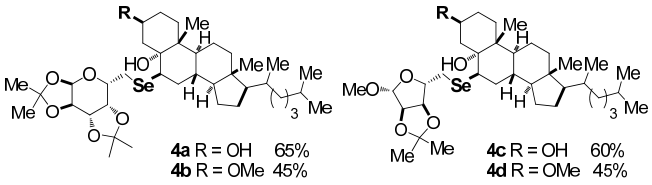


Figure 3. Steroidal selenoglycoconjugates.

CONCLUSION

It was successfully achieved steroidal selenoglycoconjugates in a convergent and stereoselective synthesis and modification of both sugar and cholesterol units are under investigation. The new compounds posses high molecular complexity and potential biological activity.

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