

O-Sulfated Derivatives of Glucuronic Acid

Mariano J. L. Castro, Natalia Salmaso, José Kovensky and Alicia Fernández Cirelli

Centro de Investigaciones en Hidratos de Carbono (CIHIDECAR, CONICET), Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, Pab. II, 3er. Piso, 1428 Buenos Aires, Argentina

E-mail: mcastro@qo.fcen.uba.ar, jose@qo.fcen.uba.ar, afc@rec.uba.ar

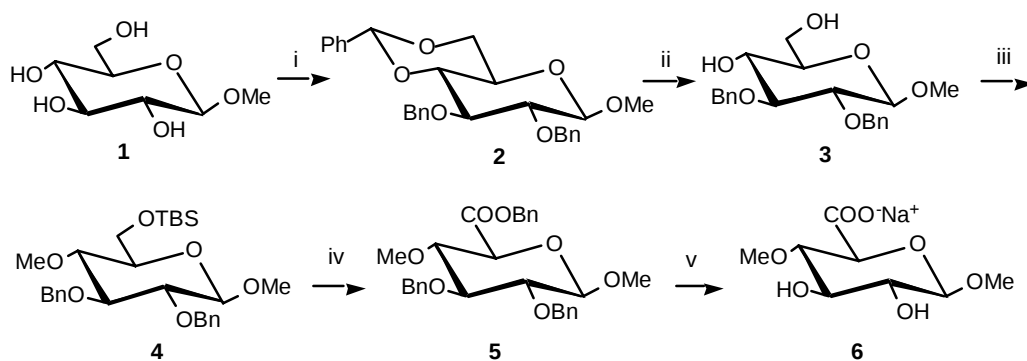
Abstract: 4-O-Substituted D-glucuronic acid derivatives were synthesized from D-glucose in order to study the regioselectivity of sulfation.

Introduction

Glycosaminoglycans, as heparin and heparan sulfate, interact with various proteins, and their binding properties are related to the glycosidic sequence and the number and position of sulfate groups. In our laboratory, we performed a variety of chemical modifications of the polysaccharide chain. On sulfation of heparan sulfate, the regioselective sulfation of glucuronic acid units in O-2 has been observed.¹ This result is interesting due to biological properties of heparan sulfate.

Experimental

The synthesis of derivatives of glucuronic acid was performed as shown in Fig. 1.



i. Ph(OMe)₂, PTSA; NaH, BnBr. ii. MeOH, H⁺. iii. TBSCl, Et₃N, DMAP; MeOTf.
iv. H₂SO₄, CrO₃, acetone. v. H₂, Pd-C.

Figure 1.

Sulfation of **6** was accomplished with $\text{SO}_3\cdot\text{Et}_3\text{N}$ in DMF in the reaction conditions employed for heparan sulfate. The products were purified by chromatography and characterized by NMR (^1H and ^{13}C).

Results and Discussion

Sulfation of methyl 4,6-*O*-benzylidene D-glucopyranoside, and methyl 4-*O*-benzoyl-D-glucopyranosiduronate showed no selectivity 2- and 3-*O*-sulfated derivatives. This result is in accordance with previous reports on similar reactivity of HO-2 and HO-3 in acylation reactions of compounds of D-*gluco* configuration.

The selectivity observed in heparan sulfate would therefore be related to the structure of the glycosidic chain. In this polysaccharide, the regular sequence is composed by a β -D-glucuronic acid unit linked to HO-4 of *N*-acetyl or *N*-sulfate-D-glucosamine residue. The linking of the glucosamine to the next glucuronate is α , giving an alternating sequence. This anomeric configuration would allow the formation of hydrogen bonds between both residues, involving the HO-3 of glucuronic acid units, preventing their sulfation. Oligosaccharide models needed to study this hypothesis can be prepared from compound **3**.

Acknowledgements: The authors are indebted to the Universidad de Buenos Aires (UBA) and the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) for financial support. A.F.C. and J.K. are Research Members of the CONICET.

References and Notes

1. Kovensky, J.; Fernández Cirelli, A. *Carbohydr. Res.* **1997**, *303*, 119.