Carbohydrate Research, 147 (1986) C1–C2
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Preliminary communication

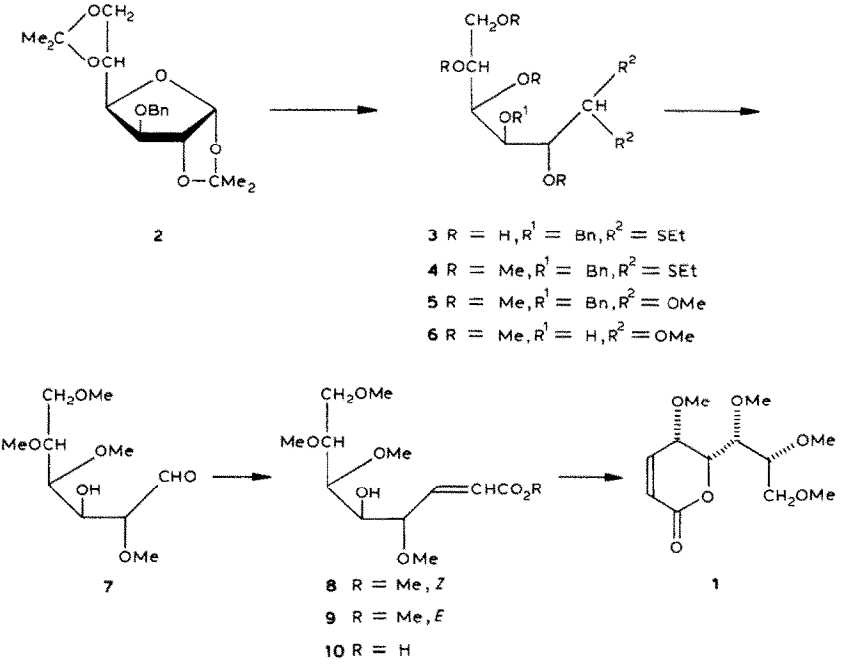
Higher-carbon sugars: a novel approach

SERAFIN VALVERDE, SILVESTRE GARCIA-OCHOA, and MANUEL MARTÍN-LOMAS
Instituto de Quimica Organica, C.S.I.C., Juan de la Cierva 3, 28006 Madrid (Spain)

(Received October 14th, 1985; accepted for publication, November 20th, 1985)

As a result of our interest in the enantiospecific synthesis of natural compounds containing α,β-unsaturated δ-lactones[1,2], the preparation of these fragments, using carbohydrate precursors, has been considered. Such syntheses require chiral synthons having the L configuration, and we have prepared[3] 2,3-dideoxy-L-*threo*-hex-2-enono-1,5-lactone from L-tartaric acid. A recent publication[4] suggested the extension of this reaction to other hexoses, to give extended-chain lactones of the D or L series, and we now report preliminary results.

The synthesis of 2,3-dideoxy-4,6,7,8-tetra-*O*-methyl-D-*gluco*-oct-2-enono-1,5-lactone (**1**) was carried out as shown in the annexed Scheme.



0008-6215/86/$03.50

Treatment of 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[5,6] (**2**) with ethanethiol–hydrochloric acid (2 h, room temp.) gave, after column chromatography, 3-*O*-benzyl-D-glucose diethyl dithioacetal (**3**, 73%), $[\alpha]_D$ +22° (*c* 0.1, chloroform). Methylation (NaH, MeI, tetrahydrofuran, 0°) of **3** afforded 3-*O*-benzyl-2,4,5,6-tetra-*O*-methyl-D-glucose diethyl dithioacetal (**4**, 77%). Transacetalation of **4**, using HgO–$HgCl_2$ in anhydrous methanol, gave the dimethyl acetal **5** (91%), $[\alpha]_D$ +18° (*c* 0.1, chloroform). Catalytic hydrogenolysis (Pd/C, methanol) of **5** and treatment of the resulting acetal **6** with aqueous 10% oxalic acid absorbed on silica gel[7] yielded 2,4,5,6-tetra-*O*-methyl-*aldehydo*-D-glucose (**7**, 82%), $[\alpha]_D$ −7.8° (*c* 0.2, chloroform), the ^{1}H-n.m.r. spectrum of which contained a singlet at δ 9.8 for an aldehyde proton.

The Wittig reaction of **7** with methoxycarbonylmethylenetriphenylphosphorane in methanol at 0° afforded a mixture (77%) of the isomeric α,β-unsaturated esters **8** and **9** (*Z*,*E*-ratio 3:1) based on ^{1}H-n.m.r. data. Lactonisation of the mixture of esters in benzene solution containing a catalytic amount of toluene-*p*-sulphonic acid gave, after column chromatography, **1** (60%), $[\alpha]_D$ +64° (*c* 0.15, chloroform). N.m.r. data ($CDCl_3$): ^{1}H, δ 6.8 (dd, 1 H, *J* 5 and 10 Hz, H-3), 6.1 (d, 1 H, *J* 10 Hz, H-2), 4.7 (t, 1 H, *J* 5 Hz, H-5), 4.2 (t, 1 H, *J* 5 Hz, H-4), plus signals for the side chain and the methoxyl groups; ^{13}C, 162.7 (C-1), 141.9 (C-3), 122.9 (C-2), 79.2, 78.3, 77.7 (C-5, C-6, C-7), 69.7 (C-8), and 69.5 p.p.m. (C-4).

Lactonisation was also accomplished by heating 2,3-dideoxy-4,6,7,8-tetra-*O*-methyl-D-*gluco*-oct-2-enonic acid (**10**) in toluene solution. The acid **10** was prepared (90%) by hydrolysis of the mixture **8** + **9** with 2M lithium hydroxide in tetrahydrofuran.

Extension of the above sequences for the preparation of other lactones having extended chains is being studied.

ACKNOWLEDGMENTS

We thank Dr. Gabor Lukacs (C.N.R.S., Gif-sur-Yvette) for helpful discussions, and CSIC and CAICYT for financial support.

REFERENCES

1 A. Alemany, C. Pascual, C. Marquez, S. Valverde, A. Perales, J. Fayos, and M. Martinez-Ripoll, *Tetrahedron Lett.*, (1979) 3579–3582; 3583–3586.
2 R. M. Rabanal, J. Escudero, M. Martin-Lomas, S. Valverde, A. Perales, and J. Fayos, *Carbohydr. Res.*, 141 (1985) 49–56.
3 S. Valverde, B. Herradon, and M. Martin-Lomas, *Tetrahedron Lett.*, 26 (1985) 3731–3734.
4 R. W. Franck, C. S. Subramanian, and T. V. John, *Tetrahedron Lett.*, 25 (1984) 2349–2442.
5 Y. Oikawa, T. Nishi, and O. Ymemitsu, *J. Chem. Soc., Perkin Trans. 1*, (1985) 19–26.
6 R. L. Whistler and W. C. Lake, *Methods Carbohydr. Chem.*, 6 (1972) 228.
7 F. Huet, A. Lechevalier, M. Pellet and J. M. Conia, *Synthesis*, (1978) 63–65.