Facile Conversion of 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranose into 1,3,4,5-Tetra-*O*-benzyl-L-sorbopyranose

Giovanni Casiraghi,[a]* Gloria Rassu,[b] Mara Cornia,[c] and Francesco Nicotra[d]

[a] *Dipartimento di Chimica dell'Università, I-07100 Sassari, Italy*
[b] *Istituto per l'Applicazione delle Tecniche Chimiche Avanzate ai Problemi Agrobiologici, CNR, I-07100 Sassari, Italy*
[c] *Istituto di Chimica Organica dell'Università, I-43100 Parma, Italy*
[d] *Dipartimento di Chimica Organica e Industriale dell'Università, I-20133 Milano, Italy*

The bromomagnesium salts of certain alcohols and phenols in dichloromethane cleanly promote the title transformation; the reaction proceeds *via* formal hydride transfer from C-5 to the anomeric carbon of the glucopyranose precursor.

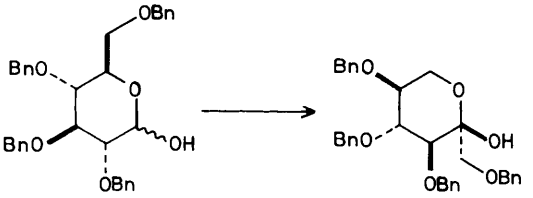
The synthesis of ketopyranoses from suitable aldose derivatives using a minimum number of synthetic manipulations remains a challenging problem in carbohydrate chemistry. Methods are available for this conversion including classical base-catalysed aldose–ketose rearrangements[1] and multi-step procedures involving C-1 reduction and subsequent C-5 oxidation.[2]

We now report the simple transformation of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**) into 1,3,4,5-tetra-*O*-benzyl-L-sorbopyranose (**2**) *via* an unprecedented one-step rearrange-

Table 1. Bromomagnesium salt-promoted rearrangement of aldopyranose (**1**) into ketopyranose (**2**).[a]

Entry	Promoter (equiv.)	Solvent	Yields of (**2**) (%)[b]	(**2**) : (**1**) ratio[c]
1	Bu^{t}OMgBr (0.1)	CH_2Cl_2	17	21 : 79
2	Bu^{t}OMgBr (0.5)	CH_2Cl_2	44	52 : 48
3	Bu^{t}OMgBr (1.0)	CH_2Cl_2	51	56 : 44
4	Bu^{t}OMgBr (5.0)	CH_2Cl_2	94	98 : 2
5	Bu^{t}OMgBr (5.0)	THF	36	51 : 49
6	Bu^{t}OMgBr (5.0)	C_6H_6	—	0 : 100
7	Bu^{t}OMgBr (5.0)	MeCN	—	0 : 100
8	Pr^{i}OMgBr (5.0)	CH_2Cl_2	90	96 : 4
9	MeOMgBr (5.0)	CH_2Cl_2	79	85 : 15
10	2,4,6-MePhOMgBr (5.0)	CH_2Cl_2	81	88 : 12
11	4-ClPhOMgBr (5.0)	CH_2Cl_2	86	95 : 5
12	PhOMgBr (5.0)	CH_2Cl_2	67	75 : 25

[a] All reactions were run under the conditions given for 4 h at 40 ± 2 °C. [b] In pure isolated compound. [c] Final composition by h.p.l.c. analysis; prolonged reaction times do not alter these values.



(**1**) (**2**)

(Bn = $PhCH_2$)

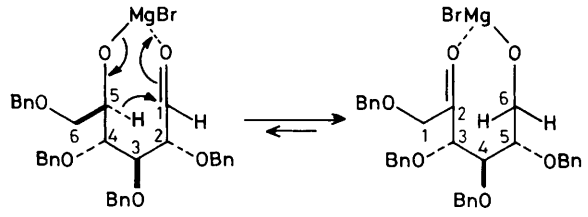
Scheme 1. *Reagents*: ROMgBr, CH_2Cl_2.

ment involving concomitant bromomagnesium alkoxide- or phenoxide-mediated C-1 reduction and C-5 oxidation.

The reaction (Scheme 1) proceeds cleanly under mild conditions producing L-α-(**2**) as the sole anomer, along with variable amounts of unconverted (**1**). Table 1 summarizes a number of experiments under various conditions.

The results show interesting aspects: firstly, the bromomagnesium salts of t-butyl alcohol, propan-2-ol, 2,4,6-trimethylphenol, and 4-chlorophenol, were the most efficient promoters, and among them alcoholates were preferable owing to easy removal of the parent alcohol during the reaction work-up; secondly, dichloromethane was the best choice of solvent, the reaction being sluggish and unselective in tetrahydrofuran (THF), and totally unproductive in hydrocarbon and polar solvents; thirdly, the final composition of the reaction mixture [(**2**) : (**1**) ratio] was critically dependent on the amount of bromomagnesium promoter, reaching a maximum value when a 5-fold excess was used.†

† Optimum experimental procedure was as follows; a solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (**1**) (1 mmol; *ca.* 85 : 15 α : β ratio) in dichloromethane (10 ml) was added dropwise over 5 min to a solution of t-butoxymagnesium bromide (5 mmol; from EtMgBr and Bu^{t}OH in Et_2O) in dichloromethane (10 ml) at room temp. under stirring, and the resulting solution was stirred at 40 °C for 4 h. Usual work-up gave crude 1,3,4,5-tetra-*O*-benzyl-α-L-sorbopyranose (**2**), contaminated by unchanged (**1**) (2%) and traces of Bu^{t}OH, which was then subjected to flash chromatography (silica gel; hexane–ethyl acetate 70 : 30) to furnish pure (**2**) (94%) as a colourless oil which slowly crystallized. White powder, m.p. 49—51 °C, $[\alpha]_D^{20}$ −12.94° (*c* 4, fresh solution in $CHCl_3$); lit.,[2] m.p. 48—51 °C, $[\alpha]_D^{20}$ −12.9 ± 0.3° (*c* 3.03, $CHCl_3$). ^{1}H n.m.r. ($CDCl_3$) δ 3.02 (br. s, 1 H, OH), 3.37 (ABq, 2 H, *J* 10.0 Hz, H-1), 3.49 (d, 1 H, $J_{3,4}$ 9.1 Hz, H-3), 3.6—3.8 (m, 3 H, H-5 and H-6), 3.95 (t, 1 H, $J_{4,5}$ 9.1 Hz, H-4), 4.4—5.0 (m, 8 H, 4 CH_2Ph), 7.0—7.6 (m, 20 H, 4 CH_2*Ph*); ^{13}C n.m.r. ($CDCl_3$) δ 61.03 (C-1), 71.91 (C-6), 73.24, 73.61, 75.42, 75.61 (4 CH_2Ph), 78.49 (C-4), 78.70 (C-5), 82.76 (C-3), 97.44 (C-2), 127.7—128.5 (20 $CH_{arom.}$), 137.44, 137.84, 138.32, and 138.71 (4 quaternary $C_{arom.}$).



(**3**) (**4**)

(Bn = $PhCH_2$)

Scheme 2

A mechanism to account for this transformation is outlined in Scheme 2. Most probably, in the first step, Lewis acidic bromomagnesium alkoxide (or phenoxide) promotes ring opening of glucopyranose (**1**) to give an aldehydo-sugar complex such as (**3**). In the key step, the reaction evolves through an internal hydride shift from C-5 (C-2 of the L-sorbose system) to the proximal C-1 (C-6 of the L-sorbose system) furnishing the keto-sugar complex (**4**) according to a Meerwein–Ponndorf–Verley-like reaction.[3] Sorbose-based complex (**4**) would be more stable than the glucose complex (**3**) and this difference might constitute one of the driving forces of this transformation.‡

In conclusion, the bromomagnesium salt-mediated rearrangement described here provides, by way of an unusual internal hydride-transfer process, a clean access to a protected ketopyranose starting from an equally protected aldopyranose. Studies directed towards synthetic applicability of this transformation as well as mechanistic investigations are planned.

Received, 15th February 1989; Com. 9/00701F

References

1 J. C. Speck, Jr., *Adv. Carbohydr. Chem.*, 1958, **13**, 63: J. E. Hodge, *ibid.*, 1955, **10**, 169.
2 Y. Rabinsohn and H. G. Fletcher, Jr., *J. Org. Chem.*, 1967, **32**, 3452.
3 A. L. Wilds, *Org. Reactions*, 1944, **2**, 178; W. von E. Doering and T. C. Aschner, *J. Am. Chem. Soc.*, 1953, **75**, 393; I. Watt, S. N. Whittleton, and S. M. Whitworth, *Tetrahedron*, 1986, **42**, 1047.

‡ The reverse transformation [(**2**) to (**1**)] under the conditions of entries 4 and 10 in Table 1 gave rise to the same final compositions of the forward processes.