Tetrahedron Letters,Vol.23,No.4,pp 405-408,1982 0040-4039/82/040405-04$03.00/0
Printed in Great Britain

α- and β-D-GLUCOPYRANOSYL PHOSPHATES from O-α-D-GLUCOPYRANOSYL TRICHLOROACETIMIDATES [1]

Richard R. Schmidt [+], Michael Stumpp and Josef Michel
Fakultät Chemie, Universität Konstanz
7750 Konstanz (Germany)

Abstract: *β-D-Glucopyranosylphosphates were obtained in high yields from O-α-D-glucopyranosyl trichloroacetimidates 2a-c and phosphoric acid monoesters and diesters 5-10. Some β-phosphates were transformed into the corresponding α-derivatives by acid catalysis.*

Glycosyl phosphates are of importance as cell wall materials and as intermediates in the biological glycosyl transfer [2]. Methods for the synthesis of glycosyl phosphates from 1-O unprotected glycoses or 1-O-acyl glycopyranoses are available, however, low yields or low α,β-selectivities are often observed [3]; improvements were partially reached with halogenoses [4], 1.2-ortho esters [5], 1.2-oxazolines [6], and 1-O-thallium(I) salts [7].

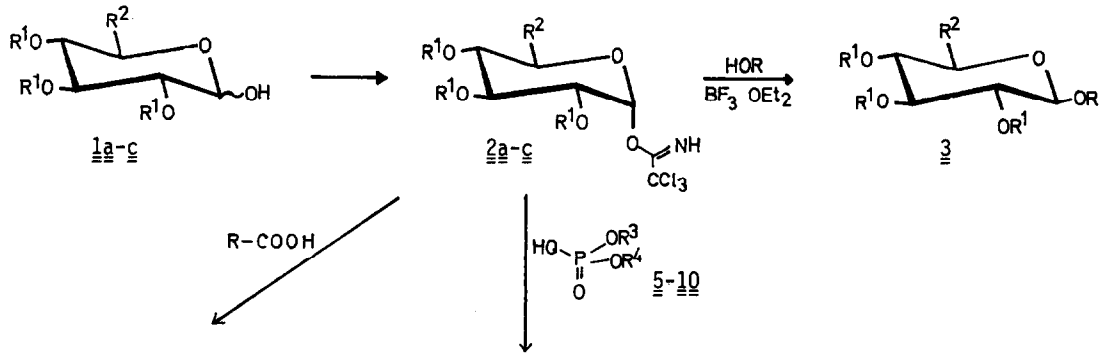
A convenient synthesis of glucopyranosyl phosphates should be possible from O-α-D-glucopyranosyl trichloroacetimidates 2a-c, which are directly accessible from 1-O-unprotected glucose derivatives in quantitative yield [8-10]: Alcohols and 2a-c give β-D-glucopyranosides 3 under mild acid catalysis; however, carboxylic acids and 2a-c yield 1-O-acyl β-D-glucopyranoses 4 without any further acidic catalyst [8-11]; therefore phosphoric acid monoesters and diesters 5-10 and 2a-c should afford directly the corresponding β-D-glucopyranosyl phosphates [12] (Table 1).

As expected, the β-D-glucopyranosyl phosphate 11a-β was obtained exclusively from benzyl protected O-α-D-glucopyranosyl trichloroacetimidate 2a and pure dibenzyl phosphate (5). Similarly, the β-D-glucopyranosyl phosphates 12a-β, 13a-β, 11b-β [13]-13b-β, and 11c-β, 12c-β were synthesized in high yields from 2a and di-n-butyl phosphate (6) or cetyl phosphate (7), from acylated glucopyranosyl trichloroacetimidate 2b and 5-7, and from benzylated glucopyranosyluronate trichloroacetimidate 2c and 5 or 6.

However, use of commercially available 5 led, presumably due to contamination with traces of strong acid, via 11a-β directly and exclusively to the α-phosphate 11a-α. The same effect was reached by the addition of acid to the reaction mixture of 2a and 5: With boron trifluoride etherate a slow 11a-β to 11a-α rearrangement was observed; however, addition of hydrogen chlor-

ide resulted in instantaneous and almost complete 11a-α formation [14]. As shown for 13a-β the conversion to 13a-α is also initiated by prolonged reaction times; this phenomenon is perhaps due to autocatalysis [15]. According to these results the immediate formation of the α-D-glucopyranosyl phosphates 14a-α - 16a-α from 2a and oleyl phosphate 8, glyceryl phosphate 9, or the chiral (S)-bisnaphthyl phosphate 10 is due to the presence of strong acid.

The structural assignments are based on ^{1}H-NMR data (Table 2). As shown for the transformation 11b-β to 17 acyl deprotection is an almost quantitative reaction under mild alkaline conditions.



a : R^1 = Benzyl; R^2 = CH_2OR^1 5 : R^3 = R^4 = Benzyl 8 : R^3 = H; R^4 = Oleyl

b : R^1 = Acetyl; R^2 = CH_2OR^1 6 : R^3 = R^4 = n-Butyl 9 : R^3 = H; R^4 = $CH(-CH_2-O-C_6H_4-CH_3)_2$

c : R^1 = Benzyl; R^2 = COOMe 7 : R^3 = H, R^4 = n-Cetyl 10 : R^3, R^4 =

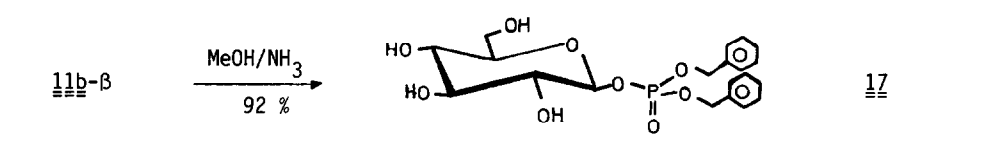
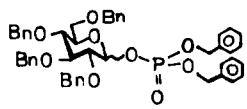
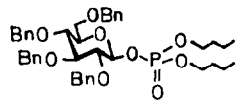
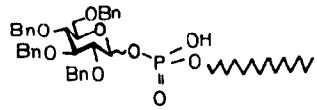
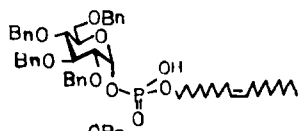
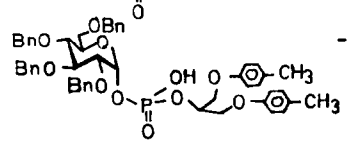
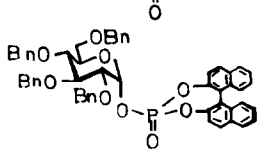
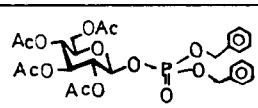
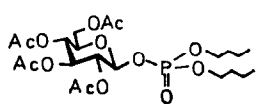
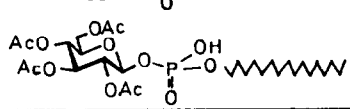
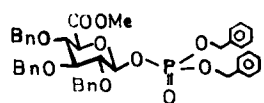
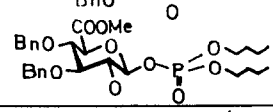


Table 1: Reactions of 2a-c with 5-10: Results [a]

Substrates	Reaction Time [h] [b]	Products	β	α	Yield [%] [c]
2a + 5	1		11a-β	-	93
2a + 5 [d]	1		-	11a-α	60
2a + 6	1		12a-β	-	92
2a + 7	0.5		13a-β	-	83
2a + 7	30		13a-β +	13a-α	81 (α:β=2:5)
2a + 8	1		-	14a-α	71
2a + 9	1		-	15a-α	65
2a + 10	3		-	16a-α	59
2b + 5	1		11b-β	-	80
2b + 6	3		12b-β	-	69
2b + 7	3		13b-β	-	30
2c + 5	3		11c-β	-	82
2c + 6	3		12c-β	-	80

[a] Abbreviations: Bn = Benzyl; Ac = Acetyl; Me = Methyl. [b] All reactions were carried out in CH_2Cl_2 at r.t. without any additional catalyst. [c] Isolated yields; all compounds gave correct elemental analyses. [d] Use of commercially available 5 as substrate.

Table 2: Optical Rotations [a] and ^{1}H-NMR-Data [b]

Compounds	$[\alpha]_{578}^{20}$	δ	1-H $J_{1,2}$[Hz]	$J_{1,p}$[Hz]
11a-β	+25,7° (c = 0.1)	5.25 (dd)	7.0	7.0
12a-β	+22° (c = 0.1)	6.32 (dd)	7.0	7.0
13a-β	+16.7° (c = 0.1)	5.20 (dd)	7.0	7.0
11b-β[c]	+ 3,5° (c = 0.1)	5.45 (dd)	7.0	7.0
12b-β	+ 3° (c = 0.1)	5.32 (dd)	7.0	7.0
13b-β	+ 5.3° (c = 0.1)	5.31 (dd)	7.0	7.0
11c-β	+12.8° (c = 0.1)	5.35 (dd)	7.0	7.0
12c-β	[d]	5.25 (dd)	7.0	7.0
17	+ 2.3° (c = 0.1)	5.00 (dd)	7.0	7.0
11a-α	+57° (c = 0.1)	6.01 (dd)	3.0	7.0
13a-α	+48° (c = 0.1)	5.95 (dd)	3.0	8.0
14a-α	+20.3° (c = 0.1)	6.10 (dd)	3.0	7.0
15a-α	+31.5° (c = 0.1)	5.95 (dd)	3.0	7.0
16a-α	+123.0° (c = 0.1)	6.35 (dd)	3.0	7.0

[a] In $CDCl_3$. [b] 80 MHz-spectra in $CDCl_3$, internal TMS, [c] see ref. 14. [d] Not determined, mp. 68°C

1) Glycosylimidates, Part 4. This work was supported by the DEUTSCHE FORSCHUNGSGEMEINSCHAFT and the FONDS DER CHEMISCHEN INDUSTRIE - Part 3: see ref. 10.

2) N. Sharon and H. Lis, Chem.Eng.News. 59 (13), 21 (1981); M.R. Rosner and H.G. Khorana, J. Biol.Chem. 254, 5918 (1978) and ref.

3) L.L. Danilov, M. Troitzki, N.S. Utkina, V.N. Shibaev, and N.K. Kochetkov, Carbohydr.Res. 87, 141 (1980) and ref.

4) C.F. Cori, S.P. Colowich, and G.T. Cori, J.Biol.Chem. 121, 465 (1937); M.L. Wolfron and D.E. Pletcher, J.Am.Chem.Soc. 63, 1050 (1941).

5) a) L.V. Volkova, L.L. Danilov, and R.P. Eystigneeva, Carbohydr.Res. 52, 165 (1974); b) V.L. Sebjakin, L.V. Volkova, E.E. Rusanova, and R.P. Evstigneeva, J.Org.Chem. USSR 1980, 2021; c) M.A. Salan and E.J. Behrman, Carbohydr.Res. 90, 83 (1981); and ref.

6) C. Augé, C.D. Warren and R.W. Jeanloz, Carbohydr.Res. 82, 85 (1980) and ref.

7) A. Granata and A.S. Perlin, Carbohydr.Res. 94, 165 (1981).

8) R.R. Schmidt and J. Michel, Angew.Chem. 92, 763 (1980), Angew.Chem.Int.Ed.Engl. 19, 731 (1980)

9) R.R. Schmidt and G. Grundler, Synthesis 1981, in print.

10) R.R. Schmidt and J. Michel, Angew.Chem., submitted for publication.

11) Similar reactions were reported with the corresponding trichloroacetimidates of mannopyranose, mannofuranose, galactopyranose, xylopyranose, and some oligosaccharides: R.R. Schmidt, Lecture, IX° Journees sur la Chimie et la Biochimie des Glucides, Aussois, January 1981; Lecture, 1st European Symposium on Carbohydrates and Glycoconjugates, Vienna, September 1981.

12) Phosphates of other carbohydrates were synthesized by the same procedure: M. Stumpp, Diplomarbeit, University of Konstanz, 1981.

13) 11b-β was synthesized independently, see ref. 5a; the ^{1}H-NMR-spectral assignments are not in accordance.

14) About 5 % α-halogenose was obtained.

15) Solutions or oils of other β-phosphates were also converted to the corresponding α-derivatives upon standing.

(Received in Germany 23 October 1981)