Acta Chemica Scandinavica B 30 (1976) 777—780

Reaction of Sugar Esters with Hydrogen Fluoride. XV. Ring Contraction of some Hexopyranose Derivatives

KLAUS BOCK and CHRISTIAN PEDERSEN

Department of Organic Chemistry, Technical University of Denmark, DK-2800 Lyngby, Denmark

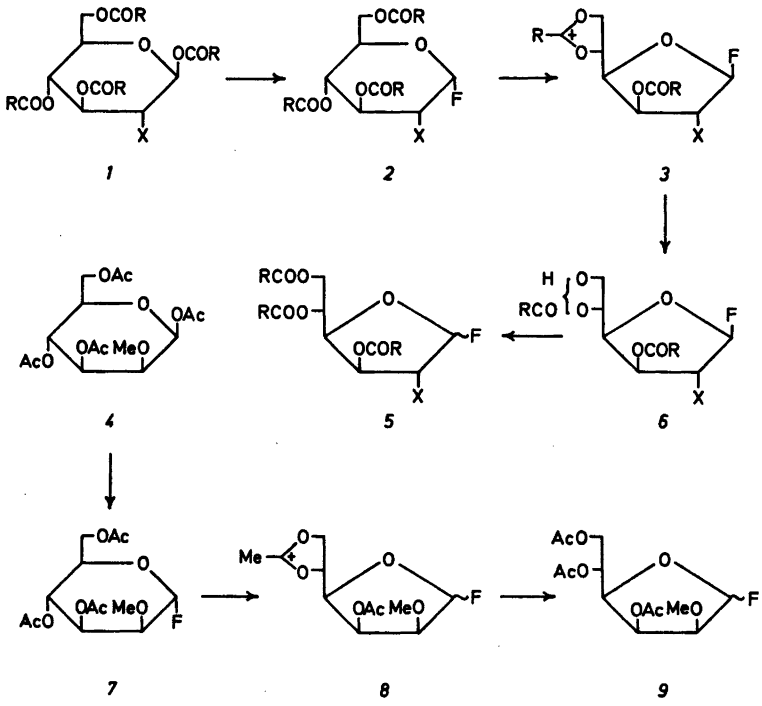
Prolonged treatment of 2-*O*-methyl-D-glucopyranose and -D-mannopyranose derivatives with anhydrous hydrogen fluoride leads to ring contraction and formation of the corresponding furanosyl fluorides. Similar results are obtained with 2-chloro- and 2-bromo-2-deoxy-D-glucopyranose derivatives.

Previously reported results on the treatment of tetra-*O*-benzoyl-2-*O*-methyl-β-D-glucopyranose (*1b*) with anhydrous hydrogen fluoride (HF) at room temperature showed that ring contraction to furanose derivatives took place to a certain extent.[1] Later experiments showed that acylated 2-*O*-methyl-D-xylose derivatives gave furanoses with HF whereas acylated 2-*O*-methyl-D-arabinose derivatives gave pyranoses.[2] In these two cases the nature of the final products is determined by the formation of stable dioxolanylium ions in HF solution.

In the previous study of the reaction of 2-*O*-methyl-glucose derivatives with HF the longest reaction time used was arbitrarily chosen to be 24 h.[1] However, when it was later found that ^{1}H NMR spectra could be measured on HF solutions the progress of the reaction of sugar esters with HF could be followed. It was then shown that dioxolanylium ions were the final products formed in anhydrous HF.[3,4] Using this technique the reaction of 2-*O*-methyl-D-glucose derivatives with HF has now been reinvestigated. Furthermore, the behaviour of 2-*O*-methyl-D-mannopyranose derivatives and of 2-chloro- and 2-bromo-2-deoxy-D-glucopyranose derivatives has also been studied.

When the reaction of tetra-*O*-benzoyl-2-*O*-methyl-β-D-glucopyranose (*1b*) with anhydrous HF was followed by ^{1}H NMR spectroscopy it was found that the fluoride (*2b*) was formed within *ca.* 20 min. On further reaction at room temperature (*2b*) slowly disappeared and a complex spectrum was observed. After 9 days no further changes were observed. Work up of the HF solution at this stage followed by benzoylation gave the anomeric furanosyl fluorides (α- and β-*5b*) in yields slightly higher than those obtained previously when 24 h reaction was used.[1] Only a few percent of the pyranosyl fluoride (*2b*) could be isolated.

Because of the slow reaction of (*1b*) the corresponding acetate (*1a*) was studied. Brief treatment of (*1a*) with anhydrous HF gave the α-pyranosyl fluoride (*2a*) in 80 % yield as previously reported.[5] On further reaction with HF the initially formed (*2a*) underwent ring concentration and after 48 h at room temperature NMR spectra of the HF solution showed that the dioxolanylium ion (*3a*) was present as virtually the only product. A 3 H signal at δ 2.86 shows that an acetoxonium ion is formed.[3,4] A 6 H signal at δ 2.56 arises from 2 equivalents of acetic acid and a 3 H signal at δ 2.32 from the 3-acetoxy group of (*3a*). A doublet centered at δ 6.18 with a splitting of 60 Hz (J_{1F}) and $J_{1,2} \simeq 0$ (H1-H2 *trans*) shows that the product is a β-furanosyl fluoride.[4] Further spectral data of (*3a*) are given in Table 1. Work up of the HF solution at this stage gave a mixture of partially acetylated furanoses (*6a*), which was immediately acetylated. Chromatography then yielded 63 % tri-*O*-acetyl-2-*O*-methyl-β-D-glucofuranosyl fluoride (β-*5a*) and 20 % of the corresponding α-anomer (α-*5a*). The latter was not observed in



a; R = CH_3, X = OMe c; R = CH_3, X = Br

b; R = C_6H_5, X = OMe d; R = CH_3, X = Cl

the NMR spectrum of the HF solution and is probably formed by anomerisation of (*β-5a*) during work up.

The structures of the acetylated furanosyl fluorides (α- and *β-5a*) are derived from their ^1H, ^{19}F, and ^{13}C NMR spectra (Table 1 and Ref. 6). The ^1H spectra are quite similar to those of the corresponding benzoates the structures of which were established by chemical means.[1]

Treatment of tetra-*O*-acetyl-2-*O*-methyl-*β*-D-mannopyranose (*4*) for 10 min with anhydrous HF at 0 °C gave a 63 % yield of tri-*O*-acetyl-2-*O*-methyl-α-D-mannopyranosyl fluoride (*7*).[5] On more prolonged reaction at room temperature (*7*) also underwent ring contraction, and after 48 h it was completely converted into the acetoxonium ion (*8*) as seen from the ^1H NMR spectrum in HF (Table 1). Work up and acetylation gave 40 % of tri-*O*-acetyl-2-*O*-methyl-*β*-D-mannofuranosyl fluoride (*β-9*) and 11 % of the corresponding α-anomer (*α-9*). The structures of these products were derived from their ^1H, ^{19}F, and ^{13}C NMR spectra (Table 1 and Ref. 6).

When gluco- or mannopyranose pentaacetates are treated with HF, they undergo inversion at C2 and C3 to give manno- and altropyranose derivatives.[7] Furanoses are formed to a minor extent only. In the absence of a 2-*O*-acyl group, as in the 2-*O*-methyl-pyranoses, inversion cannot take place and ring contraction therefore becomes predominating, leading to formation of the stable 5,6-dioxolanylium ions *3* and *8*. The pyranose derivatives might form 4,6-acetoxonium or benzoxonium ions; such ions have, however, not been observed in hydrogen fluoride solution. 4,6-Acetoxonium ions are formed when tetra-*O*-acetyl-*β*-D-glucopyranosyl chloride is treated with antimony pentachloride; with this reagent ring contraction does, on the other hand, not take place.[8]

Table 1. ^1H and ^{19}F chemical shifts and observed first order coupling constants of some hexofuranosyl fluorides and of dioxolanylium ions.

Compound, solvent	H1	H2	H3	H4	H5	H6	H6'	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	J_{1F}	J_{2F}	J_{4F}	Φ_F
α-*5a*, $CDCl_3$	5.88	3.89	5.46	4.59	5.24	4.54	4.12	3.8	3.5	5.0	9.0	2.5	5.2	−12.5	62.5	14.5	~1	−64.6
β-*5a*, $CDCl_3$	5.69	3.89	5.35	4.62	5.36	4.60	4.20	0	0	5.0	9.0	2.5	4.8	−12.5	62.0	5.0	6.0	−45.5
α-*5b*, $CDCl_3$	5.98	4.18	5.92	5.0	5.8	4.95	4.6	3.8	5.0	6.0	9.0	2.5	5.0	−12.5	62.5	16.5	~1	−63.3
β-*5b*, $CDCl_3$	5.83	4.10	5.74	5.07	5.88	5.08	4.75	0	0	5.5	9.0	2.5	4.5	−12.5	62.5	5.3	6.5	−45.3
α-*9*, $CDCl_3$	5.76	4.05	5.53	4.53	5.31	4.58	4.14	2.2	5.0	3.9	8.7	2.4	5.4	−12.2	64.7	16.1	2.0	−48.1
β-*9*, $CDCl_3$	5.72	3.82	5.72	4.44	5.36	4.61	4.24	3.4	5.2	4.8	9.5	2.3	4.7	−12.3	65.8	22.6	7.0	−53.8
β-*5c*, $CDCl_3$	5.96	4.28	5.56	4.85	5.41	4.70	4.24	0	0	4.5	9.0	2.5	4.7	−12.5	64.5	6.0	6.5	−25.5
3a, HF	6.18	4.43	6.1		5.2	——5.8		~0	~0						60	5.3		
3c, HF	6.13	4.43	6.08		5.4	——5.7		~0	~0						62	6.5		
3d, HF	6.12	4.52	6.0		5.3	——5.8		~0							56	~5		
8, HF	6.12	4.38	6.02		5.1	——5.7		3.5	5	~5						23		

Other acylated hexopyranoses without an *O*-acyl group at C2 would also be expected to undergo ring contraction on treatment with HF. To investigate this tetra-*O*-acetyl-2-bromo-2-deoxy-β-D-glucopyranose (*1c*) was reacted with HF. Brief treatment gave tri-*O*-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl fluoride (*2c*),[9] which slowly underwent further reactions in HF. After 2 weeks at +5 °C *1c* was completely converted into the acetoxonium ion (*3c*) as seen from the ^1H spectrum (Table 1). Work up and acetylation gave the 2-bromo-2-deoxy-furanosyl fluoride (β-*5c*).

The corresponding 2-chloro-2-deoxy compound (*1d*) behaved in the same way. After reaction with HF for 4 days at room temperature it was completely converted into the acetoxonium ion (*3d*) as seen from the ^1H NMR spectrum (Table 1). The HF solution was not worked up in this case.

Tetra-*O*-acetyl-2-chloro- or 2-bromo-2-deoxy-D-mannopyranose decomposed on prolonged treatment with anhydrous HF. This is probably analogous to the reaction of 2-chloro-2-deoxy-D-mannose derivatives with hydrochloric acid, which yields an unsaturated compound.[10] The latter would decompose on treatment with HF.[11]

It might be expected that acylated 2-deoxy-hexopyranoses, having no 2-*O*-acyl group, would behave analogously to the compounds described above. Previous work has, however, shown that tetra-*O*-benzoyl-2-deoxy-D-glucopyranose reacts in a completely different way when treated with anhydrous HF.[11]

The reaction of 3-*O*-methylated pyranoses with HF will be described in a forthcoming paper.

EXPERIMENTAL

^1H NMR spectra and thin layer chromatography was performed as described previously.[7] ^{19}F NMR spectra were measured at 94.10 MHz on a Varian HA-100 instrument. Positions of signals (ΦF) are given in ppm relative to internal methyl trifluoroacetate (5 %).

*Reaction of tetra-*O*-acetyl-2-*O*-methyl-β-D-glucopyranose (*1a*) with HF.* A solution of (*1a*)[12] (558 mg) in anhydrous HF (1 ml) was kept for 48 h at room temperature. It was then diluted with dichloromethane and poured on ice. The organic phase was washed twice with aqueous sodium hydrogen carbonate, dried

($MgSO_4$) and evaporated. The product (440 mg) was acetylated with acetic anhydride in pyridine to give 450 mg of a material which was separated into two fractions by preparative TLC using benzene-ether (1:1) as eluent. The fast-moving fraction gave 315 mg (63 %) of tri-*O*-acetyl-2-*O*-methyl-β-D-glucofuranosyl fluoride (*β-5a*) as a syrup, $[\alpha]_D^{20}$ −15.5° (*c* 4.9, $CHCl_3$). Anal. $C_{13}H_{19}FO_8$: C, H. The next fraction yielded 100 mg (20 %) of the syrupy α-anomer (*α-5a*), $[\alpha]_D^{20}$ +59.2° (*c* 0.9, $CHCl_3$). Anal. $C_{13}H_{19}FO_8$: C, H.

*Tetra-*O*-acetyl-2-*O*-methyl-β-*D*-mannopyranose (4) and HF.* Treatment of *4* [13] (583 mg) with anhydrous HF (1.5 ml) for 48 h at room temperature followed by work up and acetylation gave a crude product (350 mg) which was separated into two fractions by preparative TLC with ether-pentane (1:1) as eluent. The fast-moving fraction yielded 55 mg (11 %) of tri-*O*-acetyl-2-*O*-methyl-α-D-mannofuranosyl fluoride (*α-9*) as a syrup, $[\alpha]_D^{23}$ +45.7° (*c* 1.8, $CHCl_3$). Anal. $C_{13}H_{19}FO_8$: C, H. The slow-moving fraction gave 210 mg (40 %) of the corresponding β-anomer (*β-9*), which was crystallized from ether, m.p. 103–104 °C, $[\alpha]_D^{23}$ +11.1 (*c* 2.0, $CHCl_3$). Anal. $C_{13}H_{19}FO_8$: C, H.

*Reaction of tetra-*O*-acetyl-2-bromo-2-deoxy-β-D-glucopyranose* (1c) *with HF.* A solution of *1c* [14] (506 mg) in anhydrous HF (2 ml) was kept for 14 days at +5 °C. Work up and acetylation as described above gave 305 mg of crude product. Preparative TLC (ether-pentane 2:1) yielded 278 mg (61 %) of tri-*O*-acetyl-2-bromo-2-deoxy-β-D-glucofuranosyl fluoride (*β-5c*) as a syrup $[\alpha]_D^{20}$ +57.4° (*c* 2.8, $CHCl_3$). Anal. $C_{12}H_{16}BrFO_7$: C, H, Br.

Microanalyses were carried out by NOVO analytical laboratory.

REFERENCES

1. Pedersen, C. *Acta Chem. Scand. 20* (1966) 963.
2. Jacobsen, S., Jensen, R. S. and Pedersen, C. *Acta Chem. Scand. 26* (1972) 1561.
3. Pedersen, C. *Tetrahedron Lett.* (1967) 511.
4. Gregersen, N. and Pedersen, C. *Acta Chem. Scand. 22* (1968) 1307.
5. Foster, A. B., Hems, R., Westwood, J. H. and Hall, L. D. *Carbohydr. Res. 23* (1972) 316.
6. Bock, K. and Pedersen, C. *Acta Chem. Scand. B 29* (1975) 682.
7. Bock, K. and Pedersen, C. *Acta Chem. Scand. 27* (1973) 2701.
8. Paulsen, H. *Adv. Carbohydr. Chem. Biochem. 26* (1971) 127.
9. Hall, L. D. and Manville, J. F. *Can. J. Chem. 47* (1969) 361.
10. Adamson, J. and Foster, A. B. *Carbohydr. Res. 10* (1969) 517.
11. Lundt, I. and Pedersen, C. *Acta Chem. Scand. 25* (1971) 2749.
12. Hodge, J. E. and Rist, C. E. *J. Am. Chem. Soc. 74* (1952) 1498.
13. Deferrari, J. O., Gros, E. G. and Mastronardi, I. O. *Carbohydr. Res. 4* (1967) 432.
14. Hardegger, E. and Schüep, W. *Helv. Chim. Acta 53* (1970) 951.

Received March 19, 1976.