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Note

Silver tetrafluoroborate as an effective catalyst for the anomerisation of glycosyl fluorides

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Although anomerisation reactions have received considerable attention in carbohydrate chemistry, the anomerisation of glycosyl fluorides has not been reported hitherto. It is well known that treatment of acylated sugars with liquid hydrogen fluoride[1] gives the thermodynamically stable α-acylglycosyl fluorides. Under the strongly acidic conditions employed, epimerisation of the neighbouring substituents often takes place[2]. We now report on the anomerisation of glycopyranosyl fluorides under mild conditions.

In contrast to the easy S_N2 anomerisation of glycosyl chlorides and bromides in the presence of the corresponding tetrabutylammonium halides[3], treatment of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl fluoride (**1**α) with tetrabutylammonium fluoride did not give the α-anomer (**1**β), whereas the reaction of **1**α with classic anomerising agents ($TiCl_4$, $SnCl_4$, $BF_3 \cdot Et_2O$) resulted in the rapid formation of a mixture of D-glucose tetra-acetates. However, by using g.l.c. and t.l.c., it was possible to detect, in the former experiment, traces of **1**β, evidently arising from cations **5** and **6** (S_N1), but variations of solvent, temperature, and concentration of Lewis acid did not increase the yield of **1**β.

An increase in the concentration of F^- in the reaction mixture would be expected to shift the equilibrium towards **1**β. Recently[4], it has been shown that, in reactions with acylglycosyl chlorides, $AgBF_4$ can be used as an organic solvent-soluble F^- donor. When solutions of **1**α and $AgBF_4$ in aromatic solvents were boiled under reflux, 63% of **1**β was obtained. The reaction proceeded smoothly, but there was a considerable induction period which could be attributed to the need for the formation ($AgBF_4 \rightleftarrows AgF + BF_3$) of microquantities of BF_3 to initiate anomerisation.

The conversion of **1**α into **1**β took place easily at room temperature (50% yield) if traces of anhydrous HCl or $BF_3 \cdot Et_2O$ were added to a solution of **1**α and $AgBF_4$ in benzene, which confirms the mechanism mentioned above. The reaction rate depends on the concentration of BF_3 and solvation decreases it considerably.

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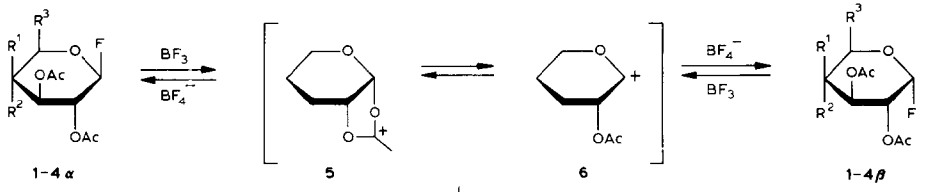

1 R^1 = H, R^2 = OAc, R = CH_2OAc
2 R^1 = OAc, R^2 = H, R^3 = CH_2OAc
3 R^1 = OAc, R^2 = R^3 = H
4 R^1 = R^3 = H, R^2 = OAc

Thus, the reaction of **1α** (0.57 mmol), $AgBF_4$ (0.26 mmol), and $BF_3 \cdot Et_2O$ (0.24 mmol) was complete in 10 min in nitromethane, in 24 h in acetonitrile, and in 3 weeks in ether. A highly active system, apparently containing free BF_3, was formed by refluxing a solution of $AgBF_4$ in dichloromethane for ~5 min. If, after cooling the mixture to 10°, glycosyl fluoride was added, anomerisation was complete in 5–30 min.

The foregoing method was applied to the glycosyl fluorides **1–4α**. Prolonged contact of the product with the catalyst resulted in a decrease in yield and, in each of these reactions, the formation of ~5% of fully acetylated sugar was detected; at equilibrium, the mixtures from **3** (*arabino*) and **4** (*xylo*) contained ~10% of the starting fluoride. Blank experiments with thermodynamically stable 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and -D-manno-pyranosyl fluoride and 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl fluoride showed that they were degraded slowly (~24 h) and afforded a mixture of partially hydrolysed and peracetylated compounds (*cf.* ref. 4), which accords with the proposed mechanism.

Other possible catalysts were investigated. Although pyridinium tetrafluoroborate did not cause anomerisation, dissolution of **1α** at room temperature in dichloromethane containing $Py \cdot HBF_4$ and $BF_3 \cdot Et_2O$ (molar ratios 30:10:1) gave 57% of **1β**. The strong polarisation of the B–F bond in the $Py \cdot BF_3$ complex could result in the complex being an F^- donor in the presence of excess of $BF_3 \cdot Et_2O$, thereby causing anomerisation (method *C*). Good yields of the more stable anomers could be obtained only at low concentrations of BF_3 (Py–$BF_3 \cdot Et_2O$ ratio 1:1.5). For ratios of **1α**–catalyst of 1:3 and 1:0.12, the yields of **1β** were 30% and 73%, respectively. This explains why only traces of **1β** were formed when **1α** was treated with pure $BF_3 \cdot Et_2O$.

Thus, for the anomerisation of glycosyl fluorides, simultaneous action of microquantities of Lewis acid (BF_3) and excess of F^- donor is necessary, and the use of silver tetrafluoroborate as a catalyst offers such a combination.

EXPERIMENTAL

All melting points are uncorrected. Optical rotations were measured with an

A-1 EPO automatic polarimeter (U.S.S.R.) for solutions in $CHCl_3$. Preparative column chromatography was performed on Silpearl spherical silica gel (Č.S.S.R.) with benzene–ether mixtures, and t.l.c. was performed on Silufol (Č.S.S.R.) with detection by gradual heating. G.l.c. was carried out using a Tsvet-104 instrument (U.S.S.R.), equipped with a glass column (1.5 m × 3 mm) containing 3% of EGSP-Z on Inerton Super (0.125–0.16 mm) (Č.S.S.R.), at 200°. All reactions were performed in Me_2SiCl_2/MeOH silylated glassware, using solvents freshly distilled from CaH_2.

Anomerisation. — *Method* A. A mixture of β-fluoride **1α** or **2α** (1 mmol) and $AgBF_4$ (0.25 mmol) in benzene (3 mL) was boiled under reflux until starting material had disappeared (t.l.c.). The mixture was then washed twice with cold, saturated, aqueous $NaHCO_3$ and then water, dried (Na_2SO_4), and concentrated *in vacuo,* and the residue was subjected to chromatography. After recrystallisation from ether–heptane, the following α-glycosyl fluorides were obtained: **1β** (63%), m.p. 107.5–108°, $[\alpha]_D$ +90° (lit.[1] m.p. 108°, $[\alpha]_D$ +90.1°); **2β** (73%), m.p. 67–68°, $[\alpha]_D$ +96.5° (lit.[5] syrup, $[\alpha]_D$ +106.6°).

Method B. Compounds **1–4α** (1 mmol) were each added to a solution of $AgBF_4$ (25 μmol) in CH_2Cl_2 (2 mL) preheated until distinctly turbid and then cooled to 10°. After anomerisation was complete, work-up as in method *A* gave **1β** (94%); **2β** (62%); **3β** (72%), m.p. 117°, $[\alpha]_D$ +136° (lit.[1] m.p. 117–118°, $[\alpha]_D$ +138.2°); and **4β** (45%), m.p. 87°, $[\alpha]_D$ +66.5° (lit.[1] m.p. 87°, $[\alpha]_D$ +67.2°).

Method C. Fluoride **1α** or **4α** (1 mmol) was added to a stirred solution of pyridine (0.12 mmol) and $BF_3 \cdot Et_2O$ (0.18 mmol) in CH_2Cl_2 (2 mL) at 10°. After 30 min, the mixture was washed twice with water and worked-up as in method *A*. The yields of **1β** and **4β** were 73% and 43%, respectively.

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