Reactions of Glycosyl Fluorides. Synthesis of *C*-Glycosides

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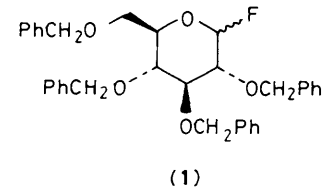
Glycosyl fluorides were found to react with a number of nucleophilic reagents with or without catalysis leading to a variety of *C*-glycosides and related compounds.

Whereas glycosyl bromides and chlorides have been extensively utilized in organic synthesis, particularly in glycosidation reactions,[1] the corresponding fluorides have received relatively little attention. Recent developments in these[2] and other laboratories[3,4] rendering these carbohydrate intermediates readily available have now made it possible to explore their chemistry. In this communication we report preliminary results indicating the versatility of glycosyl fluorides in organic synthesis and in particular their use in the construction of *C*-glycosides,[5] and in the following communication we describe the utilization of these intermediates in the synthesis of some novel hetero-glycosides.[6]

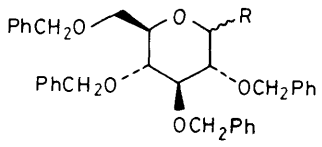
Table 1. Synthesis of *C*-glycosides and related compounds from glycosyl fluorides.

Entry	Reagents (equiv.) and conditions	R	Yield (ratio α:β)[h]
Substrate (**1**)[a,b,c] → product (**2**).[b]			
1	$Me_3SiCH_2CH{=}CH_2$ (2), $BF_3{\cdot}Et_2O$ (0.2)[e]	$CH_2CH{=}CH_2$	95 (>20 : 1)
2	$AlMe_3$(1.2), PhMe, 0 °C	Me	95 (>20 : 1)
3	$AlMe_2CN$ (1.2), PhMe, 0 °C	CN	96 (*ca.* 10 : 1)
4	Me_3SiCN (2), $BF_3{\cdot}Et_2O$ (0.2)[e]	CN	90 (*ca.* 3 : 1)
5	AlH_3 (1), Et_2O, 0 °C	H	90
6	$MgBr_2{\cdot}Et_2O$ (10), CH_2Cl_2, 25 °C	Br	90 (>20 : 1)
7	Me_3SiCH_2CN (2), $BF_3{\cdot}Et_2O$ (0.2)[e]	CH_2CN	85 (*ca.* 3 : 1)
8	$CH_2{=}CHCH$ (10), MgBr·Et_2O (5), $Bu^n{}_3SnH$ (2), AIBN[f] (0.1), PhMe, 80 °C	CH_2CH_2CN	61 (>10 : 1)
9	$PhC(OSiMe_3){=}CH_2$ (2), $BF_3{\cdot}Et_2O$ (0.2)[e]	CH_2COPh	95 (*ca.* 2 : 1)
10	$\overline{CH_2[CH_2]_2CH{=}COSiMe_3}$ (2), $BF_3{\cdot}Et_2O$(0.2)[e]	$\overline{CH[CH_2]_3C{=}O}$	89[g]
Substrate (**3**)[a,b,d] → product (**4**).[b]			
11	$Me_3SiCH_2CH{=}CH_2$ (2), $BF_3{\cdot}Et_2O$ (0.2)[e]	$CH_2CH{=}CH_2$	59[g]
12	$\overline{CH_2[CH_2]_2CH{=}COSiMe_3}$ (2), $BF_3{\cdot}Et_2O$ (0.2)[e]	$\overline{CH[CH]_3C{=}O}$	90[g]
13	$MgBr_2{\cdot}Et_2O$ (10), CH_2Cl_2, 25 °C	Br	95 (>20 : 1)

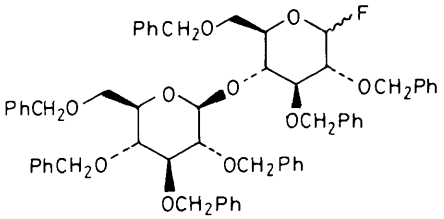
[a] Prepared from the corresponding phenylthioglycoside and *N*-bromosuccinimide–diethylamino sulphur trifluoride (ref. 2); [b] structure determined by spectroscopic methods; [c] α : β mixture *ca.* 1 : 1; [d] α : β mixture *ca.* 3 : 2; [e] CH_2Cl_2, 0 °C; [f] AIBN = azoisobutyronitrile; [g] ratio not determined; [h] ratio determined by ^1H n.m.r.



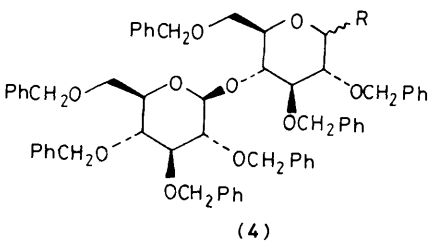
(**1**)



(**2**)



(**3**)



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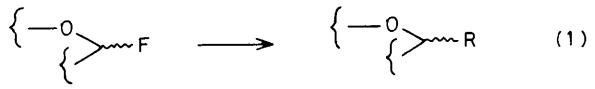

(1)

Typically, the *C*-glycosidation reactions were performed according to equation (1) in the presence of a Lewis acid (0.2 equiv.) as catalyst. Table 1 exhibits a number of examples from the monosaccharide and disaccharide series.†‡ In the case of specially activated nucleophiles (entries 2,3,5) no catalyst was necessary. Noteworthy is the beneficial action of $MgBr_2{\cdot}Et_2O$ on the free radical coupling of glycosyl fluorides to Michael acceptors (entry 8) which presumably proceeds *via* the corresponding bromides as demonstrated by entries 6 and 13. Finally, glycosyl fluorides are easily converted into the parent tetrahydropyran systems in excellent yields as indicated by entry 5.

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† New compounds exhibited satisfactory spectroscopic and analytical data. Yields refer to pure isolated (flash column chromatography–silica) products.

‡ ^1H N.m.r. data (250 MHz, $CDCl_3$, Me_4Si): (**2**; R = CH_2CN) δ 7.48—7.08 (m, 20H, aromatic), 4.98—4.29 (m, 9H, benzylic, anomeric), 3.85—3.42 (m, 6H, CHO), 2.86—2.47 (m, 2H, CH_2CN); (**4**; R = $CH_2CH{=}CH_2$) δ 7.6—7.1 (m, 35H, aromatic), 5.82 (m, 1H, olefinic), 5.2—3.2 (m, 30H, benzylic, anomeric, olefinic), 2.49 (m, 2H, allylic).