Syntheses of Anomeric Glucopyranosylidene Diazides

J.-P. Praly, Z. El Kharraf, and G. Descotes

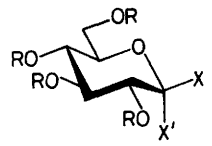
Laboratoire de Chimie Organique II, U.A. CNRS 463, ESCIL, 43, Boulevard du 11 Novembre 1918, 69622 Villeurbanne, France

Protected glucopyranosylidene diazides have been obtained in good yields by two routes which involve nucleophilic substitutions at the anomeric position of either 2,3,4,6-tetra-*O*-acetyl-1-bromo-β-D-glucopyranosyl chloride or 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone, in the presence of silver azide or trimethylsilyl azide, respectively.

The recently reported photobromination of peracetylated glycopyranosyl-β-chlorides (**1**) offers an opportunity for chemo- and stereo-selective substitutions at the anomeric centre of C-1 *gem*-bromochlorosugars. Such transformations were achieved by the treatment of (**1**) and (**2**) (gluco and manno configuration) with silver fluoride[1] or hydroxy nucleophiles[2,3] (alcohols, glycols, catechol) in association with activators [CF_3SO_3Ag-*syn*-collidine, $Hg(CN)_2$]. We now report the nucleophilic attack of azide anions to yield the novel sugar diazides (**4**) and (**8**).

Our first experiments involving prolonged stirring of (**1**) in various solvents [$MeCOMe–H_2O$, $MeNO_2$, dimethylformamide (DMF)] with sodium or lithium azides at temperatures ranging from 20 to 60 °C resulted mainly in the recovery of the starting material whereas use of hexamethylphosphoramide (HMPA) as the solvent led to the corresponding C-1 chlorinated glucal.[1] However, we have now found that the new compound (**4**) was obtained when (**1**) (0.45 mmol) was treated with silver azide† (0.9 mmol) in dry nitromethane (5 ml) at room temperature (24 h). The ^{13}C NMR spectrum ($CDCl_3$) of the reaction products indicated the presence of a major (70% ratio) new compound [δ 99.9 (C-1)]. The minor compound (~30%) was identified unambiguously as being the C-1 *gem*-dichloride (**5**) [δ 111.9 (C-1)].[1] Since both compounds have identical chromatographic mobilities, the reaction mixture was treated with silver triflate (0.45 mmol) in the presence of *syn*-collidine (0.45 mmol) and methanol in excess, to selectively derivatize (**5**), thus permitting a more conve-

† Caution: silver azide is a powerful explosive.



R	X	X'	Compound
Ac	Cl	Br	(**1**) (2 manno)
Ac	N_3	Cl	(**3**)
Ac	N_3	N_3	(**4**)
Ac	Cl	Cl	(**5**)
Ac	OMe	OMe	(**6**)
Bn	=O		(**7**)
Bn	N_3	N_3	(**8**)

Bn = $PhCH_2$

nient chromatographic separation. Under these conditions, (**5**) was quantitatively converted into the more polar anomeric orthoester (**6**),[3] easily separated (silica gel, ethyl acetate–n-hexane 1—3 v/v) from the unaffected diazide (**4**) (60% yield), syrup;‡ IR (CCl_4), ν 2125 cm^{-1}(N_3); UV $\lambda_{max.}$ (ethanol), (ε): 264 (22), 218 (180) nm; $[\alpha]_D^{24}$ + 120°, (*c* 1.3 in dichloromethane).

The easy conversion of sugar lactones in the presence of hydroxy nucleophiles[4] (*e.g.*, ethylene glycol) and Lewis acids into anomeric spiro orthoesters by nucleophilic attack at the anomeric position might suggest that other nucleophiles might react similarly. The availability of sugar lactones and the possible use of the safe, commercially available trimethylsilyl azide offers an attractive method for the large scale preparations of sugar diazides. This was confirmed as follows: a solution of the benzylated lactone (**7**) (0.5 mmol) and trimethylsilyl azide (2.5 mmol) in dry dichloromethane (5 ml) was stirred for 8 h, at room temperature after dropwise addition of boron trifluoride–etherate (0.5 mmol). After aqueous work-up and separation of a more polar compound by column chromatography, the benzylated *gem*-diazide (**8**) was obtained (45%) as an oil.‡ ^{13}C NMR ($CDCl_3$) δ 101.6 (C-1); IR (CCl_4), ν 2130, 2110 cm^{-1} (N_3); $[\alpha]_D^{26}$ +167° (*c* 1.1 in chloroform).

These preliminary results indicate that the new glucopyranosylidene diazides are readily accessible using mild conditions from two types of precursors, namely sugar anomeric dihalides or lactones. The failure to detect the formation of the monoazide (**3**) from (**1**) contrast with our previous observations recorded with fluoride anions. The transformation of sugar lactones seems a more convenient way to prepare such diazides with respect to better substrate availability and safety. The synthetic applications of this new class of compounds, mainly as anomeric carbene precursors,[5] are under investigation.

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‡ The elemental analysis gave satisfactory results.

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