Iodine as a Reagent for the Ready Hydrolysis of Prop-1-enyl Glycosides, or their Conversion into Oxazolines

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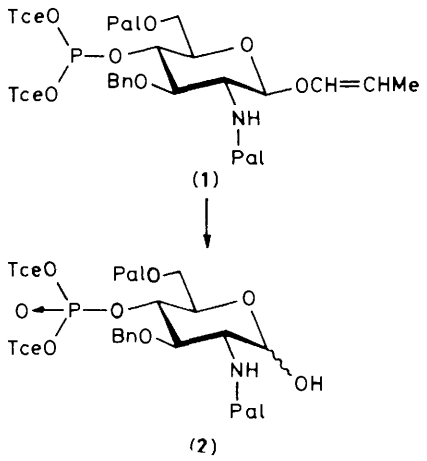
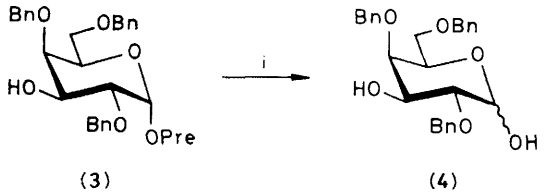
Iodine in oxolan with suitable additives rapidly effects the hydrolysis of prop-1-enyl glycosides to free sugars, and the cyclization of prop-1-enyl β-glycosides of *N*-acylglucosamines to oxazolines.

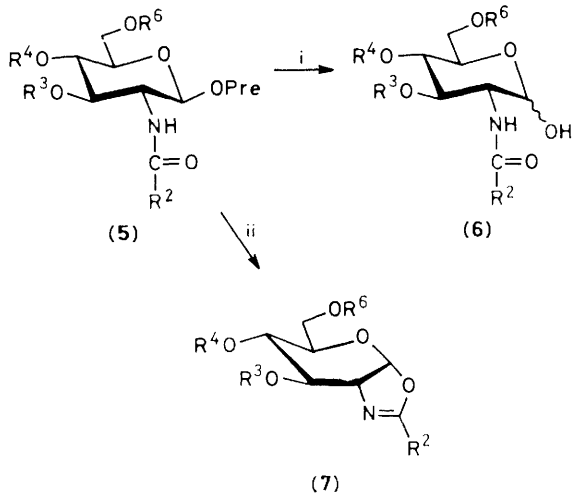
Prop-1-enyl glycosides are frequently encountered in work on the synthesis of oligosaccharides and related compounds, as a result of the use of the allyl group to stabilize the anomeric centres of sugars while protecting groups are being attached.[1–3] When the anomeric centre is to be unmasked, the allyl glycoside is isomerized to the prop-1-enyl glycoside.[4] The latter can be hydrolysed to the free sugar in mildly acidic milieux,[4] or under neutral conditions in the presence of mercury(II) salts.[3] Alternatively the prop-1-enyl β-glycosides of substituted *N*-acyl-glucosamines and -galactosamines may



Bn = benzyl, Pal = palmitoyl, Tce = 2,2,2-trichloroethyl.



Bn = benzyl, Pre = prop-1-enyl. i, I_2, H_2O in oxolan.



	R^6	R^4	R^3	R^2
a	Bn	Bn	Ac	Me
b	Bn	Ac	Bn	Me
c	Ac	Ac	Ac	Me
d	Pal	H	Bn	C_{15}
e	Bn	Bn	H	Me
f	Bn	Bn	Thp	Me
g	H	H	Bn	C_{15}
h	H	H	Pal	C_{15}

Bn = benzyl, C_{15} = n-pentadecyl, Pal = palmitoyl, Pre = prop-1-enyl, Thp = tetrahydropyran-2-yl. i, I_2, H_2O in oxolan; ii, I_2, DBU in oxolan.

be cyclized to 1,2-oxazolines (**7a**—**e**) by treatment with mercury(II) chloride–mercury(II) oxide in an anhydrous medium.[5] The oxazolines are useful as glycosylating agents.[6]

Recently we undertook the conversion of the phosphite ester[7] (**1**) of the propenyl glycoside (**5d**) into the corresponding phosphate, and on oxidation of the compound with iodine in oxolan-2,6-dimethylpyridine–water observed a concomitant loss of the prop-1-enyl group to give (**2**). Further investigation established iodine as a convenient reagent for the hydrolysis or cyclization of prop-1-enyl glycosides. The compounds examined were (**3**),[2] (**5a**),[5] (**5b**),[5] (**5c**),[5] (**5d**),[8] (**5e**),[5] (**5g**),[9] and (**5h**).[9] In addition, prop-1-enyl 2-acetamido-4,6-di-*O*-benzyl-2-deoxy-3-*O*-(tetrahydro-2-pyranyl)-β-D-glucopyranoside (**5f**), was prepared by the treatment of (**5e**) with dihydropyran and toluene-*p*-sulphonic acid; ^{1}H n.m.r. ($CDCl_3$) δ 6.19 (m, OC*H*=) and 1.93—1.37 (m, protons on C-3—C-5 of the tetrahydro-2-pyranyl group).

Hydrolysis was accomplished by dissolving the glycoside (1 mmol) in oxolan–water 4:1 (v/v) (10 ml), then adding iodine (500 mg, 2 mmol) and stirring the mixture for 5 min at room temperature. When an acid-labile protecting group was present [tetrahydro-2-pyranyl for (**5f**)], pyridine (0.32 ml, 4 mmol) was added immediately after the iodine. The products were recovered by diluting the reaction mixtures with water and extracting with chloroform. Excess iodine was destroyed by washing the chloroform extracts twice with freshly prepared, 5% aqueous sodium bisulphite. In every case t.l.c. showed the quantitative conversion of the glycoside into a slower moving product having the same R_f value as the free sugar (1-hydroxy compound) obtained by mercury-catalysed hydrolysis. The crystalline product from the α-galactoside (**3**) was further identified as 2,4,6-tri-*O*-benzyl-α,β-D-galactopyranose (**4**); m.p. 125 °C, $[\alpha]_D$ +41.2 → +37° in $CHCl_3$; lit.[10] m.p. 123—4 °C, $[\alpha]_D$ +40.4 → +36.7°; the ^{1}H n.m.r. spectrum was as expected.

When propenyl glycosides (**5a**—**e**) were dissolved in dry oxolan (molecular sieves) and treated with iodine (1.5 mol. equiv.) and 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU, 2 mol. equiv.) for *ca.* 5 min they again underwent complete reaction. The products, isolated as just described for the free sugars (**4**) and (**6a**—**h**), were identified by t.l.c. and n.m.r. spectroscopy as the oxazolines (**7a**—**e**). Each of the compounds co-chromatographed with an authentic sample prepared by the procedure of Nashed *et al.*[5] ($HgCl_2$–HgO in acetonitrile), and their anomeric (H-1) protons gave signals having the δ and *J* values characteristic of oxazoline derivatives of glucosamine[5] [(**4d**) 5.97 and 7.4 Hz; (**4e**) 6.03 and 7.4 Hz]. In addition, (**7a**) on treatment with allyl alcohol and toluene-*p*-sulphonic acid gave a glycoside, the previously unknown allyl 2-acetamido-3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside; ^{1}H n.m.r. ($CDCl_3$) δ 7.41—7.07 (m, Ph-H), 5.94 (d, N*H*), 5.94—5.77 (m, -C*H*=), 4.44 (d, *J* 8.0 Hz, H-1), and 2.00 and 1.94 (2 s, $COCH_3$). The yields of isolated products were: (**7a**), >95%; (**7b**), >90%; (**7c**), >80%; (**7d**), *ca.* 85%; (**7e**), 85%.

The reactions we observed can be rationalized in terms of an electrophilic attack by iodine on the double bond of the propenyl group, making C-1 of this group electron deficient. In analogy to the well known iodomethoxylation reaction, water then attacks C-1 to give a hemiacetal, which decomposes to the free sugar and (presumably) 2-iodopropanal. In the special case where a carbonyl oxygen of a neighbouring, *trans*-disposed *N*-acyl group is present, this can attack C-1 of the sugar and displace the entire anomeric substituent as 2-iodopropanal.

Owing to their simplicity and rapidity, the procedures described here for the transformation of prop-1-enyl glycosides are markedly superior to methods employing mercury(II) salts, particularly for the preparation of oxazolines. The

hydrolytic procedure should serve equally well for the cleavage of prop-1-enyl ethers but we have not tested this.

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