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INTRODUCTION OF ACID LABILE GROUPS AT GLYCOSIDIC CENTRES IN SUGARS AND STUDY OF THEIR MOBILITIES

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Allyl α-D-glucopyranoside prepared by the conventional method, was methylated and then the allyloxy group was isomerised into the prop-1-enyloxy group. Then by the mild acid hydrolysing conditions this group was converted into hydroxyl group.

Key words: Mobilities, Acid labile groups, Glycosides.

Introduction

In certain synthetic sequences in carbohydrate chemistry it is essential to block glycosidic centre temprorarily. For example in the synthesis of 1,4 oxathian derivatives alkyl groups were used to block C-2 in various sugars [1]. These substituents were readily removed by acid hydrolysis, but such treatment causes racemisation at sulphoxide centre. Similarly (+)-phenyl-*p*-tolyl sulphoxide was racemised by treatment with 12 *N*-hydrochloric acid in dioxan in 24 hrs at room temperature in an atmosphere of nitrogen [2]. To avoid racemisation, glycosidic hydroxyl group was blocked by a group which can be removed under very mild acid conditions.

In synthetic sequences allyl group was used to protect C-2, isomerised into prop-1-enyl group which can be removed under mild hydrolysing conditions. This type of isomerisation was observed in varity of compounds.

Safrole (1) was isomerised into *cis* and *trans* isosafrole (2), on treatment with tristriphenyl-phosphine-rhodium chloride in chloroform [3]. 2-Allyl-phenol (3a) and eugenol (3b) were converted into their corresponding (prop-1-enyl)-phenol (4a) and (4b) with dichlorobis-(benzanitrite) palladium (11) in refluxing benzene [4]. Isomerisation occurs readily when migrating double bond moves into conjugation with aromatic nucleas with $RhCl_3$. $3H_2O$ ethanol at 200° [5]. The rearrangement under vigrous basic conditions has been separated for a viscosity of compounds [6], but the rearrangement has been shown to accelerated under mild conditions by the use of potassium t-butoxide in dimethyl sulphoxide [7].

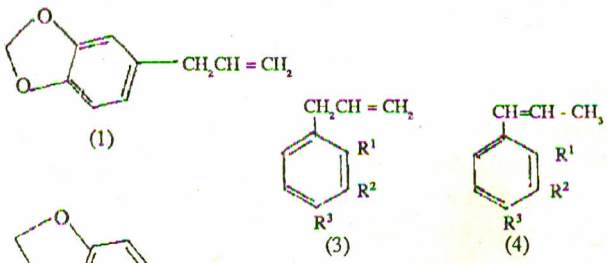
Due to the stability of allyl ethers and easy conversion into prop-1-enyl ethers it was decided to use the allyl group as a protecting group at C-2 in glycosides. The prop-1-enyl group can be conveniently removed by very mild acid hydrolysis conditions (e.g. with 0.1 *N* HCl, at 100° in 15 ,min. [7]. Gigg and Warren [8] have shown that the action of mercuric chloride in aqueous acetone, hydrolyses the prop-1-enyl group. The following equation was suggested for the hydrolysis of vinyl ether by mercuric chloride [8].

$$R\text{-}O\text{-}CH{=}R + HgCl_2 + H_2O \longrightarrow R\text{-}OH + OHC\text{-}CH(HgCl)R + HCl$$

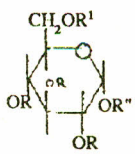
An alternative method for removing the prop-1-enyl group by oxidation with permanganate was also devised [7]. Thus 1,2: 5,6- di-O-isopropylidene-3-O-(prop-1-enyl)-D-glucofuranose was hydrolysed with 0.5 *N* methanolic sodium hydroxide and 4% aqueous potassium permangnate to give 1, 2: 5,6-di-O-isopropylidene-D- glucofuranose.

Experimental

Allyl α-1-glucopyranoside (5). A solution *D*-glucose (400 gm) in dry 1-propene-3-ol (800 ml) containing hydrogen chloride (24gm) was stored with vigrous stirred at 70° for 5 hrs. After cooling the mixture was neutralised with conc. ammonia and then treated with decolourising carbon, and evaporated. The syrupy residue (450 gm) was extracted with boiling acetone (5x1 L) and the concentrated extract was stored at 0° to give allyl- α-*D*- glucopyranoside (100 gm) m.p. 97-98°. $[\alpha]\ 26_D + 132°$ (c 4.2, water) Talley [9] reported m.p.



	R¹	R²	R³
a	OH	H	H
b	H	OCH_3	OH



(5) $RR^1 = H, R^{11} = CH_2 - CH = CH_2$
(6) $RR^1 = Me, R^{11} = CH_2 - CH = CH_2$
(7) $R\,R^1 = Me, R^{11} = CH = CH = CH_3$
(8) $R\,R^1 = Me, R^{11} = H$

100.5-101.5°, [α] 25_D + 115° (c 4.7 water) for this compound.

Allyl 2,3,4,6-tetra-O-methyl-α-D-glucopyranoside (1). Allyl α-*D*-glucopyranoside (5) 1gm was dissolved in *N, N*-dimethylformamide (20 ml). Sodium hydride (2.2gm, 20 mol) was added at room temperature and the suspension was shaken for 20 mins. Methyl iodide (9ml, 40 mol) was added dropwise with stirring and the mixture was kept at room temperature for 24 hrs. Methanol (60ml) was added, and when the effervescence had ceased the solution was concentrated under reduced pressure. Water (50 ml) was added to the residue and the mixture was extracted with chloroform (3 x 50 ml). The combined extract was washed with water (3 x 100 ml) dried ($MgSO_4$), and concentrated under reduced pressure to a syrup (1 gm) which was distilled to give the title compound, b.p. (100°/0.2 mm. [α]D^{25} + 160° (c i. o, chloroform) (found) C, 56.8; H 3.9 $C_{13}H_{24}O_4$ requries, C 56.5;H 8.7

The distilled glycoside (20 mg) was boiled under reflux with 2 N sulphuric acid (2 ml) for 2.5 hrs. After cooling, the mixture was neutralised to pH 7 with solid barium carbonate, and the filtered solution was extracted with chloroform (2 x 3 ml). The combined extract was dried ($MgSO_4$) and concentrated under reduced pressure to a syrup which was crystallised from diethyl ether light petroleum (b.p. 60-80°), to give 2,3,4,6-tetra-O-methyl D- glucopyranose m. p. 88°, identical with an authentic sample.

Isomerisation of allyl 2,3, 4,6-tetra-O-methyl- α - D-glucopyranoside. Allyl 2,3,4,6-tetra-*O*-methyl- α-*D*- glucopyranoside (6) 1 gm was dissolved in dry dimethyl sulphoxide (10 ml). Potassium-t-butoxide (0.5 gm) was added, and the mixture was heated for 15 mins. at 100°. The cooled mixture was then poured into water (50 ml) and extracted with chloroform (3 x 150 ml), dried with ($MgSO_4$), and concentrated under reduced pressure to a syrup (1 gms). The infrared spectrum of the syrup showed a strong absorption at *ca.* 1675cm^{-1} (prop-1-enyl) *cf. ca.* 1650 cm^{-1} for the allyl group.

The syrupy prop-1-enyl glycoside (7) 60 mg was dissolved in ethanol (1 ml), 0.1 N sulphuric acid (2 ml) was added, and the mixture was heated under reflux for 15 mins. The acid was neutralised with solid barium carbonate and the filtered solution was extracted with chloroform (3 x 3 ml). The combined extract was dried ($MgSO_4$) and concentrated to a syrup (40 mg). TLC (benzene-methanol, 9:1) showed mainly one component having the mobility of 2,3,4,6-tetra-O-methyl-D-glucopyranose. The syrup was crystallised from diethyl ether light petroleum (1:1) (b.p. 60- 80°) to give 2,3,4,6-tetra-O-methyl-D-glucopyranose (8) 20 mg, 40%, m.p. 88° that was identical with an authentic sample.

When allyl 2,3,4,6-tetra-*O*-methyl- α-*D*-glucopyranoside (6) was treated under these conditions (0.1 N H_2SO_4 for 15 mins), the starting material was recovered without any change as indicated by TLC, (silica gel, Merk Kieselgel G. used as absorbent, benzene-methanol 9:1 as solvent and vaniline sulphuric acid vapours used for detection).

Results and Discussion

Thus it was decided to investigate the use of allyl group for the protection of glycosidic centre. Firstly allyl glucopyranoside (5) was converted into allyl tetra-O-methyl–α-*D*-glucopyranoside (6) by the treatment with sodium hydride-methyl iodide in dimethyl formamide. The allyl group was then rearranged to the prop-1-enyl group (7) with potassium-t-butoxide in dimethyl sulphoxide. The reaction was complete (TLC) in 15 mins at 100° and the resulting compound was readily hydrolysed (0.1 *N* sulphuric acid at 100° for 15 mins) to give 2,3,4,6-tetra-O-methyl-*D*-glucose [(8), (Overall yield, 40%)]. These conditions of hydrolysis had no effect on the allyl glycoside before rearrangement. This shows that prop-1-enyl group is a suitable blocking group at C-2 in synthetic sequences.

NMR Spectra were recorded at 60 MHz, Varian A-60 instrument under normal working conditions for 5% solution in $CDCI_3$ with tetramethylsilane as internal reference. NMR Spectroscopy is useful in determining the extent of isomerisation. Thus a doublet centred at τ 8.5 appears in prop-1-enyl tetra-O-methyl- -D-glucopyranoside and this is characteristic for the terminal methyl group. Prop-1-enyl compounds were also characterised by the appearance of a sharp absorption at 1660cm^{-1} in the infrared spectrum.

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