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INTRODUCTION OF ALKALI LABILE GROUPS AT GLYCOSIDIC CENTRES IN VARIOUS SUGARS AND STUDY OF THEIR RATES OF HYDROLYSIS

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P-Nitrophenyl L-rhamnophyranoside (2) and *p*-nitrophenyl-α-D-mannopyranoside (4) were prepared and each was subjected to alkaline hydrolysis. After 96 hrs, 80% hydrolysis was observed for rhamnopyranoside whereas 65% was observed for the mannopyranoside.

Key words: Hydrolysis of *p*-nitro phenyl,Glycosides.

Introduction

In many synthetic sequences in carbohydrate chemistry, certain acid labile substituents were used for temporary blocking of C-2 hydroxyl group and after the completion of syntheses these were removed under acid hydrolysing conditions. In the stereo- specific synthesis of 1,4 oxathian-S-oxides such treatment causes racemisation at sulphoxide centre [1]. To overcame this difficulty alkali labile substi-tuents were used for temporary blocking of C-2 hydroxyl group.

The sensitivity of phenyl glycosides to alkali has been evident for over a century. Bouchardat [2] described the alkaline decomposition of salicin, a glucoside occuring in leaves and bark of the willow *(Salix helix)* [2]. Salicin [2] populin [3] and benzohelicin [4] were hydrolysed with aqueous barium hydroxide. It was found [4] that phenyl β-D-glu- copyranoside and β-D-galactopyranoside were easily hydrolysed by aqueous alkali (1.3 N KOH at ca. 100°) to give the 1,6-anhydro sugars. However, phenyl α-D-glucopyranoside was uneffected and phenyl α-D- galactopyranoside was attacked very slowly. It has therefore been suggested [5] that the hydrolysis is facilitated by anchimeric assistance of the *trans* hydroxyl group at position 2. Hydrolysis is also facilitated by electron attracting substituents in the phenyl ring [6]. For example p-nitrophenyl α-D-glucopyranoside was hydrolysed by 1.3 *N*-potassium hydroxide at Ca. 100°, while the corresponding phenyl derivative shows extreme resistance [6,7] towards hydrolysis. Similarly, treatment of *p*-nitro- phenyl-2-deoxy-α-D-glucopyranoside with 0.1 *N* sodium hydroxide at 100° results in rapid hydrolysis whereas the corresponding phenyl derivative remains unchanged [7]. It was therefore decided to examine the possible use of *p*-nitrophenyl group, for temporarily blocking the glycoside centre in rhamnose and mannose.

Experimental

p-Nitrophenyl 2,3,4-tri-O-acetyl-rhamnopyranoside;(1). This compound was prepared according to the general method of Shafizadeh and Stacey [7].

L-rhamnose monohydrae (m.p.92°) was dehydrated by storage at 80°/12 mm/Hg. Dehydrated L-rhamnose (7 gm) was dissolved in dry pyridine (28 ml), freshly distilled acetic anhydride (25 ml) was added and the solution was stored at room temperature for 24 hrs. The solution was poured into ice-water (500 ml) and extracted with chloroform (3 x 500 ml). The combined extract was washed with aqueous sulphuric acid (1%) until the aqueous layer remained acidic, and was then further washed with aqueous sodium hydrogen carbonate and finally with water. The dried ($MgSO_4$) extract was concentrated under diminished pressure to give crude 1,2,3,4-tetra-*O*-acetyl-L-rhamnopyranose as a syrup (13.2gm) that was used without further purificiation.

The crude 1,2,3,4-tetra-*O*-acetyl-L-rhamnopyranose (8.5gm), *p*- nitrophenol (8gm), and anhydrous zinc chloride (1.6gm) were kept with constant stirring at 80° for 2 hrs. At 20 mins intervals, the acetic acid produced was removed under diminished pressure. The black solid mass was extracted with benzene (3 x 200 ml). The combined extract was washed three times with aqueous sodium hydroxide (5%) and then three times with water, dried with $MgSO_4$ and concentrated to a syrup by evaporation under diminished pressure. The syrup was triturated with ethanol and then recrystallised from ethanol to give the acetyl derivative, a crystalline solid (1), 7gm, m.p. 145-146° $[\alpha]28_D$ + 113° (c 1.0, methanol) (Found C, 52.65; H, 5.0; N, 3.4. $C_{18}H_{21}NO_{10}$ requires C, 52.55 H, 5.15; N, 3.4%).

p-Nitrophenyl L-*rhamnopyranoside (2).* This compound was prepared according to the general method of Shafizadeh and Stacey [7].

p-Nitrophenyl 2,3,4-tri-*O*-acetyl-L-rhamnopyranoside (1)6 gm was dissolved in dry methanol (375 ml). Sodium (300 mg) was added, and the solution was kept at room temperature for 24 hrs with constant stirring. One drop of water was then added and the solution was treated with carbon dioxide gas for 3 hrs. The mixture was evaporated to dryness under diminished pressure. The solid residue was extracted with boiling ethyl acetate (3 x 150 ml) and the extract was

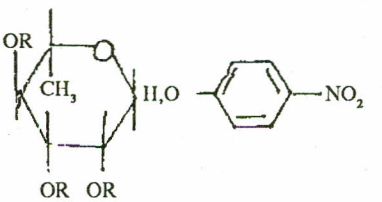
evaporated to dryness. The residue was crystallised from ethyl acetate light petroleum (b.p. 80-100°) to give *p*-nitrophenyl L-rhamnopyranoside (4gm), m.p. 165°. [α] 28_D + 120° (c 0.8, water) (found C, 50.7; 5.3; N, 4.7. $C_{12}H_{15}NO_5$ requires 0.50.5; H.5.3; N, 4.9%).

p-Nitrophenyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside (3). *D*-Mannose (7 gm) was dissolved in dry pyridine (25 ml), acetic anhydride (30 ml) was added, and the solution was stored at 37° for 8 hrs and then poured into icewater (300 ml). The mixture was extracted with chloroform (3 x 300 ml). The combined extract was repeatedly washed with aqueous sulphuric acid (1%) until the aqueous layer remained acidic, and then washed with aqueous sodium hydrogen carbonate and water. The dried ($MgSO_4$) extract was concentrated under reduced pressure to a syrup, and crystallisation of the syrup with ethanol gave 1,2,3,4,6-penta-*O*- acetyl-α-D-mannopyranose, m.p. 110°; Conchie and Levvy [8] recorded m.p. 117° for the α-D-anomer. The crude product was used for the next stage.

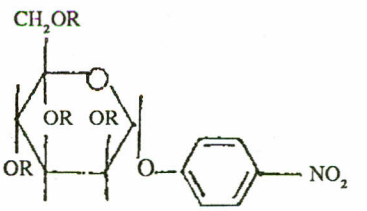
The crude penta-acetate (8.5 gm), *p*-nitrophenol (8 gm) and anhydrous zinc chloride (1.6 gm) were mixed and stored at 80° for 2 hrs. At short intervals (about 15 mins), the generated acetic acid was removed under diminished pressure. The black solid mass was cooled and then extracted with benzene (3 x 150 ml). The combined extract was washed repeatedly with aqueous sodium hydroxide (5%) and water, dried ($MgSO_4$), and concentrated under reduced pressure to a syrup. Crystallisation of syrup from ethanol gave glycoside (4 gm), m.p. 155°, [α] D^{21} + 96° (c 1.0, methanol) (Found C, 51.4; H, 5.05; N, 3.2. $C_{20}H_{28}NO_{12}$ requires C.51.2; H, 4.9; N, 3.0%), Conchie and Levvy [8] recorded m.p. 156-157°, $[\alpha]_D$ + 105° (chloroform) for this compound.

p-Nitrophenyl-α-D-mannopyranoside (4). p-Nitrophenyl 2,3,4,6- tetra-*O*-acetyl-α-D-mannopyranoside (6 gm) was dissolved in dry methanol (375 ml), sodium metal (300 mg) was added and the solution was stored at room temperature with constant stirring for 18 hrs. A drop of water was then added and the solution was treated with carbon dioxide (gas) for 3 hrs. The mixture was concentrated to a syrup that was then extracted with boiling ethyl acetate (3 x 150 ml). The combined extract was concentrated to a syrup under reduced pressure. Crystallisation of the syrup from ethanol gave the glycoside (3 gm), m.p. 177-180°, [α]D^{22} + 144° (c 1.1, water) (Found C, 47.7; H, 5.1; N, 4.1. $C_{12}H_{15}NO_8$ requires C, 47.8; H, 5.0; N, 4.7%). Conchie and Levvy [8] recorded m.p. 183- 184°, [α]D + 145° in water, for this compound.

Alkaline hydrolysis of p-nitrophenyl L-rhamnopyranoside (2), and p-nitrophenyl –α-D-mannopyranoside (4). Portions (20 mg) of glycoside were separately dissolved in potassium hydroxide solution (ca. 0.5 M water-ethanol 3:2; 25 ml) and the solutions were kept at room temperature (22°) with constant stirring. After suitable intervals, portions (1 ml) were with drawn and diluted with water (50 ml) and the absorbance at 400 μm as then determined on a Unicam SP-500 spectrophotometer. The amount of *p*-nitrophenol formed was determined from a graph prepared by using standard solutions of *p*-nitrophenol, and the results are shown in the Table 1.



(1) R = Ac
(2) R = H



(3) R= Ac
(4) R= H

Table 1.

Time (hrs)	Rhamnopyranoside (2) Absorbance	Amount of *p*-nitrophenol(mg)	% Hydrolysis	Mannopyranoside (4) Absorbance	Amount of *p*-nitrophenol (mg)	% Hydrolysis
5	0.1625	1.4	14	0.09	0.90	9
24	0.50	4.4	44	0.28	2.50	25
48	0.77	6.6	66	0.51	4.50	45
76	0.88	7.7	77	0.68	6.0	60
96	0.90	8.0	80	0.73	6.50	65
120	0.93	8.1	81	0.83	7.20	72
144	0.93	8.1	81	0.84	7.25	72
168	1.0	8.8	88	0.87	7.60	76
192	1.0	8.8	88	0.92	8.15	81
216	1.0	8.8	88	0.92	8.25	81
264	1.0	8.8	88	0.96	8.40	84

Results and Discussion

p-Nitrophenyl L-rhamnopyranoside was prepared by the treatment of 1,2,3,4 tetra-*O*-acetyl-L-rhamnopyranose with *p*- nitrophenol and zinc chloride followed by de-acetylation with methanolic sodium methoxide to afford *p*-nitrophenyl

L- rhamnopyranoside (2). *p*-Nitrophenyl-α-D-mannopyranoside (4), was also prepared by a similar method. Although the anomeric configuration of *p*-nitrophenyl L-rhamnoside has not yet been determined, the specific rotation ($[\alpha]_D$ + 120° in water) and that of the triacetate ($[\alpha]_D$ + 113° in methanol) are suggestive of the-β-L-α-configuration cf $[\alpha]_D$ + 145° in water for *p*-nitrophenyl α-D- mannopyranoside and + 96° in methanol for its tetraacetate.

p-Nitrophenyl-L-rhamnopyranoside (2) and p-nitrophenyl α-D- mannopyranoside (4) were subjected to alkaline hydrolysis, (ca 0.5 M.KOH water ethanol 3:2, 25 ml at 22°). After intervals the percentage of hydrolysis was determined by the measurement of the amount of *p*-nitrophenol produced, on Unicam SP-500 spectrometer. In 24 hrs, 44% hydrolysis was observed in the rhamnopyranoside whereas 25% in mannopyranoside. *p*-Nitro mannopyranoside was 81% hydrolysed in 192 hrs. Due to slow hydrolysing rate in mannopyranoside, it was suggested that rhamnopyranoside is a better sugar for above synthetic sequences.

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