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Syntheses and Properties of some Acetylated Alkyl Glucosides

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In connection with an investigation of the action of strong acids on acetylated glucosides, it was necessary to prepare a number of acetylated alkyl glucosides. This paper deals with the syntheses and properties of these substances. Most of them are already known but have in some cases been prepared by new methods. All specific rotations have been measured in chloroform solution (2 %), because this seems to be the solvent most generally used. The specific rotations of many of the previously known substances had been measured in other solvents.

The molecular rotations (Tables 1 and 2) show certain regularities. Methanol is a »super» primary alcohol and its glucosides stand in a class by themselves, but for the four other primary alkyl β-glucosides the molecular rotation is remarkably constant. Also the secondary alkyl β-glucosides have about the same molecular rotations with one exception, cyclopentyl β-glucoside. This is not unexpected. One must assume that the cyclopentane ring, with its rigid, planar configuration, will deviate considerably from open, aliphatic chains in its light absorbing properties. The molecular rotations of the other cycloalkyl β-glucosides are also somewhat different from those with open chains but here the deviations are much smaller, being surprisingly small for cyclobutyl β-glucoside. The β-glucosides of the two optically active butanols can not be compared directly with the other ones, but the mean value of their molecular rotations (— 9,800°) agrees well with the rest of the series studied.

For the β-glucosides in which the alkyl group contains chlorine, hydroxyl, alkoxyl or acetoxyl groups, the molecular rotation is higher than for the unsubstituted alkyl β-glucosides.

Rather few alkyl α-glucosides have been prepared. The transformation of the β-glucosides into the α-form is not particularly diffitl,cu but the acetylated

Table 1. Tetraacetyl-β-alkyl glucosides.

Alkyl group	M.p. °C *	$[\alpha]_D^{20}$	$[M]_D^{20}$
Methyl	104—105	— 18.7°	— 6,800°
Ethyl	106—107	— 22.7	— 8,500
Propyl	102—103	— 20.6	— 8,000
n-Butyl	65.5—66.5	— 20.2	— 8,200
iso-Butyl	120—121	— 19.8	— 8,000
iso-Propyl	136—137	— 24.4	— 9,500
l-sec. Butyl	125—126	— 34.4	— 13,900
d-sec. Butyl	101—103	— 14.2	— 5,700
Pentyl (3-)	109.5—110.5	— 21.5	— 9,000
Cyclobutyl **	124—126	— 26	— 10,500
Cyclopentyl **	134.5—135.5	— 33.6	— 14,000
Cyclohexyl	120—121	— 23.8	— 10,200
Cycloheptyl **	108.5—109	— 22.0	— 9,800
tert. Butyl	144—144.5	— 11.6	— 4,700
Allyl	89.5—90	— 24.2	— 9,400
Benzyl	96—97	— 53.2	— 23,300
$ClCH_2CH_2$-	117.5—118	— 13.8	— 5,600
$HOCH_2CH_2$-	103—103.5	— 7.6	— 3,000
$AcOCH_2CH_2$- **	53.5—54.5	— 14.4	— 6,200
$H_5C_2OCH_2CH_2$-	65—66	— 19.5	— 8,200
$HOCH_2CH_2CH_2$-	97—98	— 17.0	— 6,900

Table 2. Tetraacetyl-α-alkyl glucosides.

Alkyl group	M.p. °C *	$[\alpha]_D^{20}$	$[M]_D^{20}$
Methyl	100—101	+ 131°	+ 47,400
Ethyl	60.5—61.5	+ 132	+ 49,700
iso-Propyl	85.5—86.5	+ 143	+ 55,800
Cyclopentyl **	46—47	+ 140	+ 58,200
Cyclohexyl	40—41	+ 122	+ 52,300
tert. Butyl	69—70	+ 129 ***	+ 52,100***
Allyl	51—52	+ 130	+ 50,400
Benzyl	109.5—110.5	+ 142.5	+ 62,400

* All melting points uncorrected.
** These substances are new.
*** The values reported in a previous communication [10] are erroneous.

α-glucosides of this type have low melting points and it is often very difficult to obtain them in crystalline form. This is unfortunate, because when both the α- and β-glucosides are known, one can determine the Hudson values, which are more informative than the molecular rotations.

The 2B values (Table 3) are, in correspondance with the theory, rather constant. Their mean value is about 43,000. The 2A value shows much greater variation. It increases in the series methyl < ethyl < *iso*propyl. For cyclohexyl it is about the same as for *iso*propyl, while the value for cyclopentyl is much higher. The low value for tertiary butyl is unexpected; from the series above one would expect a higher value. The benzyl glucosides have the highest 2A value, but also here the 2B value is quite normal.

Table 3. Hudson values for tetraacetyl alkyl glucosides.

Alkyl group	2A	2B
Methyl	54,200	40,600
Ethyl	58,200	41,200
iso-Propyl	65,300	46,300
Cyclopentyl	72,200	44,200
Cyclohexyl	62,500	42,100
tert. Butyl	56,800 ***	47,400 ***
Allyl	59,800	41,000
Benzyl	85,700	39,100

EXPERIMENTAL PART

The mercuric acetate method

Some tetraacetyl-β-alkyl glucosides were prepared by a modification of the method of Zemplén [1] for alkyl cellobiosides.

Acetobromoglucose (8.22 g, 20 mmole) was dissolved in absolute benzene (40 ml). The anhydrous alcohol in question (16 ml) and mercuric acetate (3.03 g, 9.5 mmole) were added and the mixture was boiled for 15 minutes on the steam bath. When cold the solution was washed with water, dried over calcium chloride and concentrated under reduced pressure. The residue was recrystallized from ethanol-water, 1 : 1.

The glucosides prepared by this method are listed in Table 4.

From Table 4 it is evident that the mercuric acetate method is satisfactory for the preparation of tetraacetyl-β-alkyl glucosides. The yields are rather good, 50 % or better, and it is quicker than the method of Koenigs and Knorr. The reaction time is much shorter and commercially available mercuric acetate is used instead of the silver oxide or carbonate which must be freshly prepared. When, however, the alcohol is expensive,

Table 4. Glucosides prepared by the mercuric acetate method.

Alkyl group	M.p. °C	Yield %	Previous preparation Reference	Yield %
Methyl	104—105	57	2	51
Ethyl	106—107	56	2	70
n-Propyl	102—103	63	3	76
iso-Propyl	136—137	66	3	57
n-Butyl	65.5—66.5	51	4	71
sec.-Butyl	Mixture of d- and l-forms	56	4	—
iso-Butyl	120—121	59	4	53
tert. Butyl	144—144.5	45	4	39
Allyl	89.5—90	69	5	80
$ClCH_2CH_2$-	117.5—118	59	6	50
$H_5C_2OCH_2CH_2$-	65—66	50	9	82

the method is out of the question. In this case the method of Koenigs and Knorr, improved by Helferich and Goerdeler [5], is to be preferred.

The characteristic data of the substances prepared by this method correspond well with those of other authors. The only exception is tetraacetyl-β-(β-chlorethyl) glucoside. Coles, Dodds and Bergeim [6] report that their substance melted at 114° and contained 8.36 % of chlorine. The substance prepared in this laboratory melted at 117.5—118°.

$C_8H_{11}O_6Cl\,(OCCH_3)_4$ (410.7) Calc. Cl 8.63 Acetyl 41.9
Found » 8.69 » 41.9

The yield of *tert.* butyl glucoside was raised from 29 to 45 % when the reaction was carried out in tertiary butanol without any benzene.

The crude mixture of the tetraacetyl-β-butyl (2-) glucosides was fractionated by recrystallization from ethanol-water. The pure *l*-derivative (configuration determined by Veibel and Lillielund [4]) melted at 125—126° and had a specific rotation of — 34.4°. The corresponding data for the *d*-derivative were: M.p. 101—103° $[\alpha]_D^{20}$ — 14.2°.

Tetraacetyl-β-cyclopentyl glucoside

Tetraacetyl-β-cyclohexyl glucoside and tetraacetyl-β-benzyl glucoside were prepared by the method of Fischer and Helferich [7]. Tetraacetyl-β-cyclopentyl glucoside was prepared analogously.

Acetobromoglucose (30 g) was dissolved in a mixture of absolute ether (400 ml) and absolute cyclopentanol (100 g) and freshly prepared silver oxide (15 g) was added. The mixture was shaken for 5 hours and then centrifuged, filtered and concentrated under reduced pressure to a sirup which was submitted to steam distillation. When most of the

cyclopentanol had been removed, the steam distillation was discontinued. The glucoside, a slight yellow sirup, soon crystallized. It was recrystallized from ethanol.

Yield 21 g (69 %) M.p. 134.5—135.5°. $[\alpha]_D^{20}$ — 33.6°.

$C_{11}H_{16}O_6(OCCH_3)_4$ (416.2) Calc. Acetyl 41.3 Found Acetyl 41.5

Tetraacetyl-α-cyclopentyl glucoside

Tetraacetyl-α-cyclohexyl glucoside was prepared by the method of Pacsu [8]. Tetraacetyl-α-cyclopentyl glucoside was prepared analogously. Titanium tetrachloride (4.5 g) in absolute chloroform (30 ml) was added to a solution of tetraacetyl-β-cyclopentyl glucoside (10 g) in absolute chloroform (100 ml). The mixture was boiled under reflux in the absence of moisture for 75 minutes. It was then allowed to cool and poured into ice-water. The colorless chloroform solution was washed with aqueous potassium bicarbonate and with water, dried over calcium chloride and concentrated under reduced pressure. The residue was dissolved in light petroleum. After several weeks in the refrigerator the substance crystallized. Yield 7.5 g. M.p. 46—47°. $[\alpha]_D^{20}$ + 140°.

$C_{11}H_{16}O_6(OCCH_3)_4$ (416.2) Calc. Acetyl 41.3 Found Acetyl 41.4.

Tetraacetyl-β-cycloheptyl glucoside

Tetraacetyl-β-cycloheptyl glucoside was prepared by the method of Helferich and Goerdeler [5].

Acetobromoglucose (7.5 g) was dissolved in a mixture of cycloheptanol (6 ml) and absolute chloroform (100 ml). Drierite (7 g) was added and the mixture was shaken for 30 minutes. Then, freshly prepared silver oxide (4 g) was added and the shaking continued for 10 hours. The mixture was worked up in the same way as for the β-cyclopentyl glucoside.

Yield 6.4 g. (79 %) M.p. 108.5—109.5°. $[\alpha]_D^{20}$ — 22°.

$C_{13}H_{20}O_6(OCCH_3)_4$ (444.2) Calc. Acetyl 38.9 Found Acetyl 38.9

By the same method the β-glucosides of cyclobutanol and pentanol (3-) were prepared.

Tetraacetyl-β-cyclobutyl glucoside

No yield can be specified because one of the starting materials, cyclobutanol, was not pure and the amount available was too small to permit any purification. The resulting glucoside was recrystallized from ethanol until the melting point and the specific rotation were constant. M.p. 124—126°. $[\alpha]_D^{20}$ — 26°.

$C_{10}H_{14}O_6(OCCH_3)$ (402.2) Calc. Acetyl 42.8 Found Acetyl 43.0

Tetraacetyl-β-pentyl(3-) glucoside

Previously prepared by Veibel. [11]. Yield 75 %. M.p. 83—85°. $[\alpha]_D^{20}$ — 21.5°

$C_{11}H_{18}O_6(OCCH_3)$ (418.2) Calc. Acetyl 41.1 Found Acetyl 41.0

Pentaacetyl-β-glycol glucoside

Tetraacetyl-β-glycol glucoside was prepared according to Karjala and Link [9]. Pentaacetyl-β-glycol glucoside was prepared by acetylation of the tetraacetyl derivative with acetic anhydride in pyridine. Yield 100 %. The substance was recrystallized from ether — light petroleum. M.p. 53.5—54.5°. $[\alpha]_D^{20}$ — 14.4°.

Tetraacetyl-β-trimethyleneglycol glucoside was prepared by the method of Karjala and Link [9].

The syntheses of the α-glucosides of methyl-, ethyl-, *iso*propyl-, *tert.* butyl-, allyl- and benzyl-alcohol have been described in earlier papers [10].

SUMMARY

A number of acetylated alkyl glucosides, five of which are new, have been prepared. Eleven glucosides have been prepared by the mercuric acetate method, which was found to be a satisfactory method. The molecular rotation of the substances is discussed.

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