Tetrahedron Letters,Vol.30,No.11,pp 1399-1400,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

AN EFFICIENT SYNTHESIS OF SUGAR PYRUVIC ACID ACETALS

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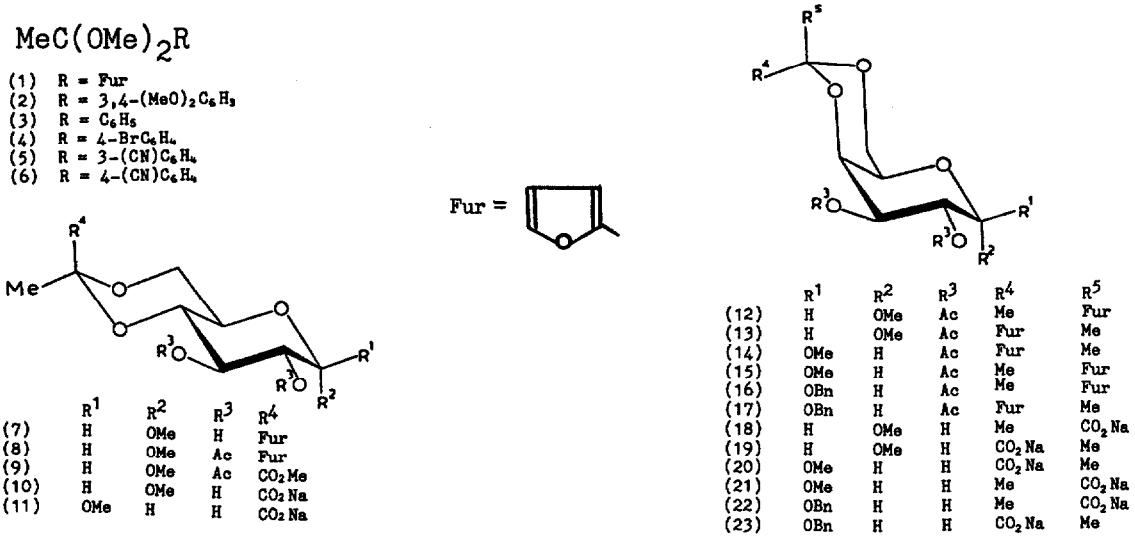
ABSTRACT - 4,6-O-(Carboxyethylidene)-glycopyranosides (e.g. 10) may be prepared by oxidation of the corresponding furan-2-ylethylidene derivatives (e.g. 7) which in turn are readily produced by acetal exchange between the 4,6-hydroxy groups of glycopyranosides.

Sugar pyruvate acetals are important[1] since they appear in many biologically significant polysaccharides and may constitute a vital part of the immunodominant region. Their preparation by the usual methods in which ketone carbonyls are condensed directly with the diols of sugars do not work, probably because the electron withdrawing carboxy group of the pyruvic acid derivative discourages ring closure onto the first formed hemiacetal. The modified reaction in which diols are exchanged with dimethyl acetals also terminates at the noncyclic mixed acetal stage. In Gorin's[2] pioneering work acetoxyacetone was condensed, albeit in very low yield, with the 4,6-diol of a sugar, with subsequent conversion of the acetoxymethyl group into a carboxylate. One new approach[3] to this problem has been to use silylated hydroxy compounds.

We on the other hand have investigated the use of methyl aryl and furan-2-yl ketone dimethyl acetals such as (1)-(6), which all exchange with pairs of sugar hydroxyls to give cyclic acetals that in principle may be oxidized with ruthenium tetraoxide[4] or ozone[5] to give pyruvic acid acetals. However, in model experiments with these acetals RuO_4 oxidation using the conditions described below only occurred at a useful rate with those derived from the first two, with the former appearing to be the most satisfactory. Oxidation with O_3 was less satisfactory, acetals derived from (1), for example, gave very complex mixtures of products. The general procedure is illustrated by the preparation of methyl 4,6-O-S-(1-carboxyethylidene)-α-D-glucopyranoside (10). Thus treatment[6] of methyl α-D-glucopyranoside with (1) gave the 2,3-dihydroxy 4,6-O-(furan-2-ylethylidene) S-isomer (7)[7] which, after chromatography, was acetylated at the 2,3-positions to give pure (8) in 70% overall yield. Oxidation of (8) (10 g), by a method similar to that of Sharpless,[4] followed by esterification gave, in 74% yield, the acetylated acetal ester (9) which was readily saponified to the sodium salt (10)[8] in 95% yield. The β-isomer (11)[9] was identically prepared in similar yield.



	R^1	R^2	R^3	R^4
(7)	H	OMe	H	Fur
(8)	H	OMe	Ac	Fur
(9)	H	OMe	Ac	CO_2Me
(10)	H	OMe	H	CO_2Na
(11)	OMe	H	H	CO_2Na

	R^1	R^2	R^3	R^4	R^5
(12)	H	OMe	Ac	Me	Fur
(13)	H	OMe	Ac	Fur	Me
(14)	OMe	H	Ac	Fur	Me
(15)	OMe	H	Ac	Me	Fur
(16)	OBn	H	Ac	Me	Fur
(17)	OBn	H	Ac	Fur	Me
(18)	H	OMe	H	Me	CO_2Na
(19)	H	OMe	H	CO_2Na	Me
(20)	OMe	H	H	CO_2Na	Me
(21)	OMe	H	H	Me	CO_2Na
(22)	OBn	H	H	Me	CO_2Na
(23)	OBn	H	H	CO_2Na	Me

To effect exclusive 4,6-acetalation with galactopyranosides their 2,3-diacetates were used in exchange reactions with (1). The 4,6-O-(furan-2-ylethylidene) 2,3-diacetates (12)-(17) were formed in good yield (75-90%) but as R-(equatorial Me) and S-stereoisomers in approximately a 2:1 ratio. Oxidation of the chromatographically pure R- and S- isomers of the methyl and benzyl 4,6-O-(furan-2-ylethylidene) galactosides (12-17) and subsequent methylation and saponification gave the sodium pyruvate acetals (18-20)[9] (21)[10] and (22 and 23)[10] in high yields.

Acknowledgement We thank the Wellcome Trust for generous support.

References and Notes

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(Received in UK 30 December 1988)