

SYNTHESIS OF 2-DEOXY- β -C-PYRANOSIDES BY DIASTEREOSELECTIVE HYDROGEN ATOM TRANSFER

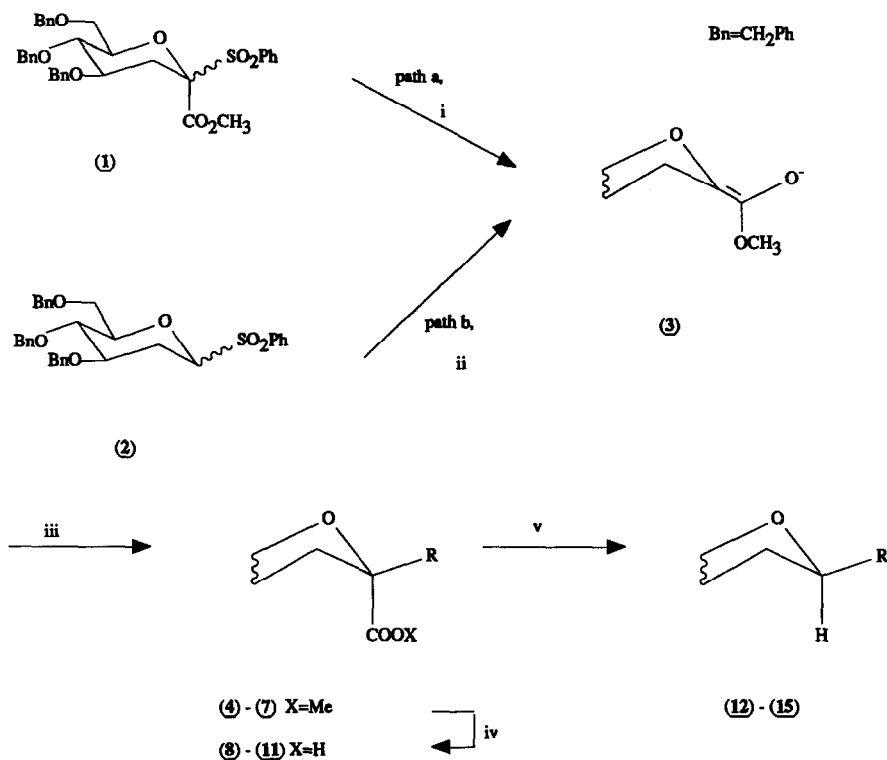
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Abstract: 2-Deoxy- β -C-pyranosides are synthesized by sequential treatment of methyl 3-deoxy-2-phenylsulphonyl-4,5,7-tri-O-benzyl-D-arabino-heptulosonate with lithium naphthalenide and an alkyl halide followed by saponification and reductive decarboxylation.

The synthesis of C-glycopyranosides by carbon-carbon bond formation at the anomeric centre of variously activated pyranosides has attracted much attention in recent years resulting in the description of several diverse and elegant solutions.¹ We present here an extension of our earlier work on the synthesis of 2-deoxy- β -glycosides² to the synthesis of 2-deoxy- β -C-glycosides in which the stereochemistry at the "anomeric" centre is determined by diastereoselective hydrogen atom transfer to a glycosyl radical.

The overall process, presented in the scheme and summarized in the table, involves formation of the key carbon-carbon bond at C-1 by alkylation of the ester enolate (**3**) with an alkyl halide. The enolate (**3**) is generated either from the 3-deoxy-2-phenylsulphonyl heptulosonate (**1**)² with lithium naphthalenide (LN) (path a) or *in situ* from the sulphone (**2**)² by deprotonation with lithium diisopropylamide, quenching with dimethyl carbonate and desulphonylation with lithium naphthalenide (path b). The so-formed heptulosonate C-glycosides (**4**)-(7) are then saponified to the corresponding acids (**8**)-(11) which are subject to reductive decarboxylation according to the Barton protocol³ by reaction of their triethylammonium salts with the heterocycle (**16**) followed by tungsten photolysis of the intermediate O-acyl thiohydroxamates in the presence of a tertiary mercaptan giving ultimately the β -C-glycosides (**12**)-(15).



(4), (8), (12) R=CH₂CH=CH₂; (5), (9), (13) R=CH₂Ph; (6), (10), (14) R=Me;

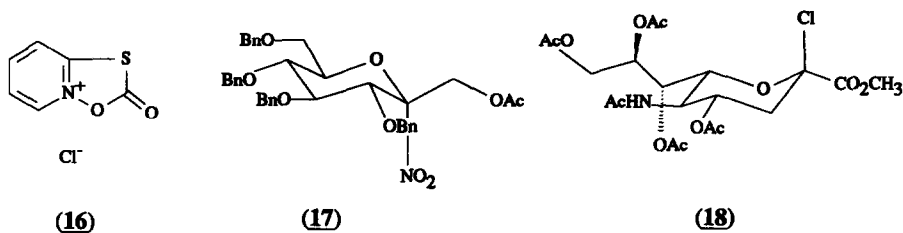
(7), (11), (15) R=CH₂OCH₂CH₂SiMe₃

i) LN; ii) LDA, MeOCOOME, LN; iii) R-X; iv) KOH; v) Et₃N;

(16) R'SH, hv

Scheme

In each example the key reductive decarboxylation step was carried out at 0°C in dichloromethane and resulted in the formation of a single diastereoisomer (within the limits of n.m.r. detection), assigned as the "β-anomer". This selectivity is in accordance both with the reduction of the related compounds (17) and (18) with tin hydrides in which, it is reported, the intermediate C-1 radicals are quenched exclusively from the axial direction⁴ and with the N-bromosuccinimide mediated bromination of various pyranoses and uronate and ulosonate esters in which bromine is introduced at an axial position.⁵

Table⁶

RX	Method	Ester	(% Yield)	Acid	(% Yield)	C-Glycosides	(% Yield)
CH ₂ =CHCH ₂ Br	B	(4)	(44)	(8)	(77)	(12)	(73)
PhCH ₂ Br	B	(5)	(56)	(9)	(72)	(13)	(92)
CH ₃ I	A	(6)	(50)	(10)	(88)	(14)	(56)
Me ₃ SiCH ₂ CH ₂ OCH ₂ Cl ⁷	A	(7)	(70)	(11)	(82)	(15)	(58)

A = path a ; B = path b

Obvious extensions to this facile, highly stereoselective, methodology include the formation of spirocyclic C-glycosides and spiroketals.

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