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

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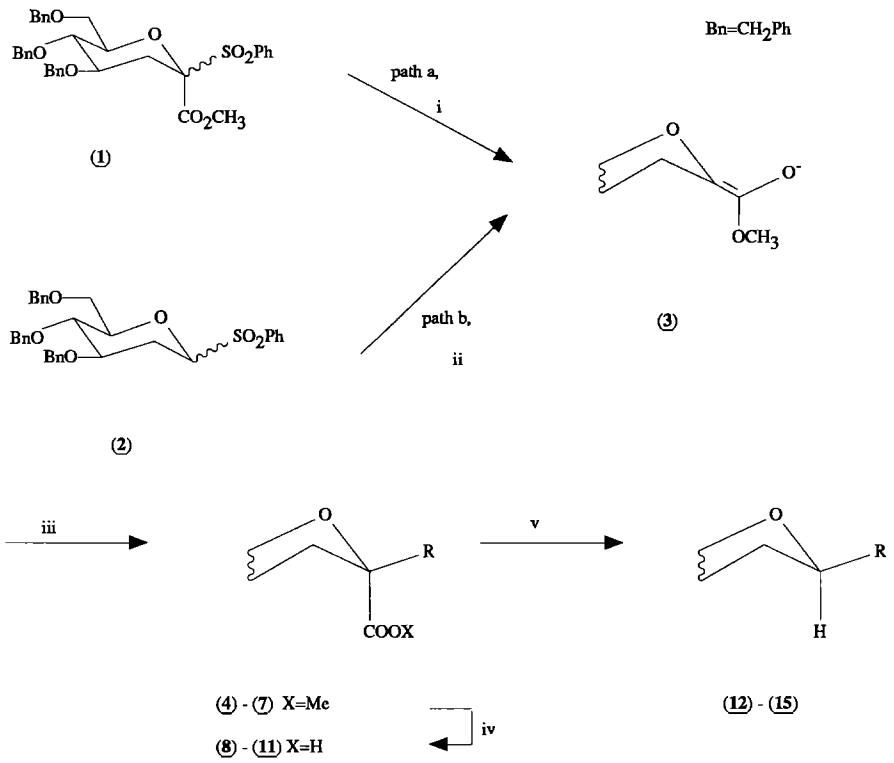
Abstract: 2-Deoxy-β-C-pyranosides are synthesized by sequential treatment of methyl 3-deoxy-2-phenylsulphonyl-4,5,7-tri-O-benzyl-D-arabino-heptulosonate with lithium naphthalenide and an alkyl halide followed by saponification and reductive decarboxylation.

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-glycosides[2] 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 protocol[3] 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=$CH_2CH=CH_2$; (5), (9), (13) R=CH_2Ph ; (6), (10), (14) R=Me ;

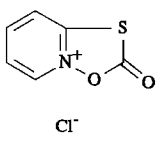
(7), (11), (15) R=$CH_2OCH_2CH_2SiMe_3$

i) LN ; ii) LDA, MeOCOOMe, LN ; iii) R-X ; iv) KOH ; v) Et_3N ;

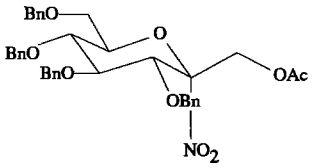
(16) R'SH, hυ

Scheme

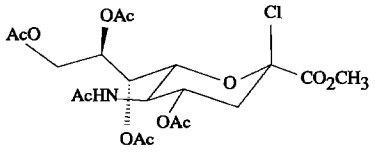
In each example the key reductive decarboxylation step was carried out at 0°C in dichloromethane and resulted in the formation of a single diastereoisomer (within the limits of n.m.r. detection), assigned as the "β-anomer". This selectivity is in accordance both with the reduction of the related compounds (17) and (18) with tin hydrides in which, it is reported, the intermediate C-1 radicals are quenched exclusively from the axial direction[4] 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]



(16)



(17)



(18)

Table[6]

RX	Method	Ester (% Yield)	Acid (% Yield)	C-Glycosides (% Yield)
CH_2=$CHCH_2Br$	B	(4) (44)	(8) (77)	(12) (73)
$PhCH_2Br$	B	(5) (56)	(9) (72)	(13) (92)
CH_3I	A	(6) (50)	(10) (88)	(14) (56)
$Me_3SiCH_2CH_2OCH_2Cl$[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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