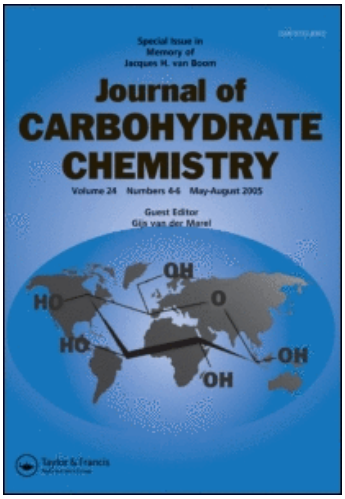

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

A Novel Stereoselective Route to Alkyl 2-Deoxy-β-D-glucosides via S-(2-Deoxy-α-glucosyl) Phosphorodithioates

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To cite this Article Michalska, Maria and Borowiecka, Joanna(1983) 'A Novel Stereoselective Route to Alkyl 2-Deoxy-β-D-glucosides via S-(2-Deoxy-α-glucosyl) Phosphorodithioates', Journal of Carbohydrate Chemistry, 2: 1, 99 — 103
To link to this Article: DOI: 10.1080/07328308308058811
URL: http://dx.doi.org/10.1080/07328308308058811

J. CARBOHYDRATE CHEMISTRY, 2(1), 99-103 (1983)

Communication

A NOVEL STEREOSELECTIVE ROUTE TO ALKYL 2-DEOXY-β-D-GLUCOSIDES VIA S-(2-DEOXY-α-GLUCOSYL) PHOSPHORODITHIOATES

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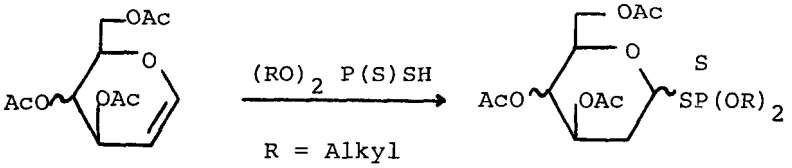
Received March 18, 1983

Intense interest in sugar components of anthracycline antibiotics and antitumor drugs generated a need for stereoselective methods of synthesis of 2-deoxy sugar glycosides. Although several efficient procedures leading to 2-deoxy-α-glycosides were elaborated, there is no satisfactory general procedure leading to the β-anomers. The methods described are not stereoselective and involve separation of anomeric intermediates of glycosides.[2]

In the recent studies from this laboratory it was shown that O,O-dialkylphosphorodithioic acids (2) add quantitatively and regiospecifically to the acetylated glycals (1) to give the phosphorodithioates (3).[3] The stereoselectivity of the addition depends on the



1 2 3

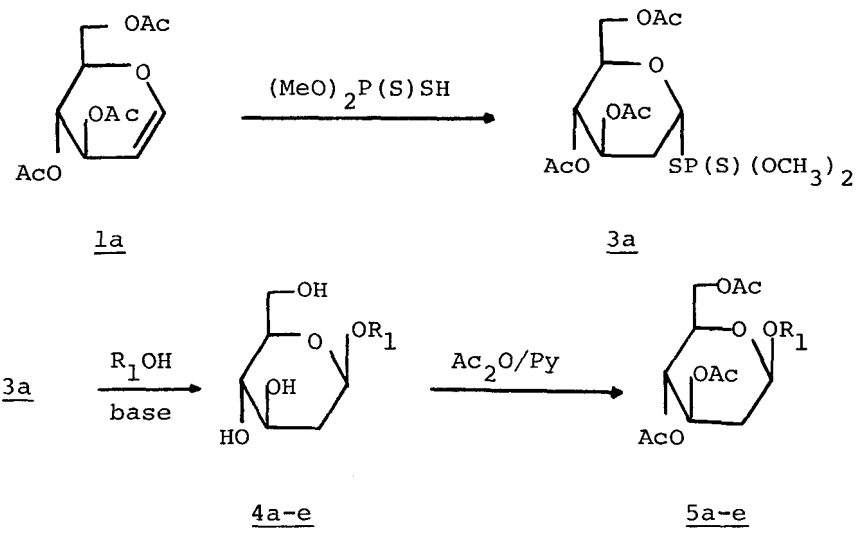
SCHEME 1

 0732-8303/83/0201-0099$3.50/0

substituents at the phosphorus atom. The addition of commercially available O,O-dimethylphosphorodithioic acid proceeds in fully stereoselective manner leading exclusively to the α-anomers.

We now report a novel approach to the synthesis of alkyl 2-deoxy-β-D-glucosides starting from D-glucal via the adduct (3). Our synthetic procedure is based on the nucleophilic displacement of the dialkyldithiophosphoryl group of (3) by alcohols in the presence of bases which proceeds with full inversion of configuration at the anomeric center. Interestingly, the rate of this displacement is considerably higher than that at the phosphorus atom and according to the ^{31}P NMR evidence there is no indication of sulphur-phosphorus bond cleavage. In the case of peracetylated sugars this synthesis is accompanied by deacetylation and leads directly to the unprotected 2-deoxy-β-D-glycosides.

The synthesis of alkyl 2-deoxy-β-glycosides is exemplified by the sequence of reactions starting from 3,4,6-tri-O-acetyl-D-glucal (1a).



For R_1, see Table 1.

SCHEME 2

The formation of the β-glucosides was quantitative according to the ^{31}P NMR data;[4] however, in order to verify the actual yields of isolated products, the glucosides (4a - e) were reacetylated. In all cases the yield of analytically pure acetylated alkyl 2-deoxy-β-D-glucosides (5a - e) exceeded 85%. The β-configuration of the glucosides obtained is evident from their ^{1}H NMR spectra and other properties, including the specific rotation values (Table 1).

In a typical procedure performed on a mmole scale stoichiometric amounts of freshly distilled O,O-dimethylphosphorodithioic acid and 3,4,6-tri-O-acetyl-D-glucal are dissolved in ca. 5 mL of dry benzene. The addition is completed within 48 hrs at room temperature. The reaction mixture is concentrated to a small volume, a twofold excess of the appropriate alcohol containing 1.1 equivalent of sodium is added and the mixture kept at room temperature for ca. 2 hrs. Evaporation of the solvents in vacuo affords the semi-crystalline residue which is then acetylated by acetic anhydride/pyridine according to standard procedure, and the peracetylated alkyl 2-deoxy-β-D-arabinohexoside is isolated in the usual way.[6]

Further application of this method to the synthesis of oligo-2-deoxysaccharides, 2-deoxy-N-glycosides and 2-deoxy-2-oximino-β-D-glycosides are under way and will be reported in due course.

ACKNOWLEDGMENTS

This work was supported by the grant from the Polish Academy of Sciences (MR-I-12).

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TABLE 1 : Physical and NMR Data for alkyl 3, 4, 6-tri-O-acetyl-2-deoxy-β-D-glucopyranosides 5 (a-e) [a]

Compound	R_1	M. p [b] (°C)	$[\alpha]_D^{18}$ [c]		^{1}H NMR [d] δ (ppm)
5a	CH_3 [e]	96 - 97	- 22	H-1	4.48 ($J_{1,2a}$ = 9.5 Hz, $J_{1,2e}$ = 2 Hz)
5b	C_2H_5	80 - 81	- 28	H-1	4.58 ($J_{1,2a}$ = 9.5 Hz, $J_{1,2e}$ = 2Hz)
5c	n-C_3H_7	55 - 57	- 31	H-1	4.57 ($J_{1,2a}$ = 9.5 Hz, $J_{1,2e}$ = 2Hz)
5d	i-C_3H_7 [f]	64 - 66	- 34	H-1	4.65 ($J_{1,2a}$ = 9.5 Hz, $J_{1,2e}$ = 2Hz)
5e	i-C_4H_9	67 - 68	- 50 [g]	H-1	4.52 ($J_{1,2a}$ = 10 Hz, $J_{1,2e}$ = 2.5Hz)

[a] For compounds 5 (a-e) satisfactory elemental analyses were obtained. [b] From diethyl ether. [c] In chloroform . [d] ^{1}H NMR spectra were recorded with a Varian 60 MHz apparatus, $CDCl_3$ as solvent . [e] Ref. 2b and 2f. [f] Ref. 5. [g] $[\alpha]_{578}^{20}$.

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