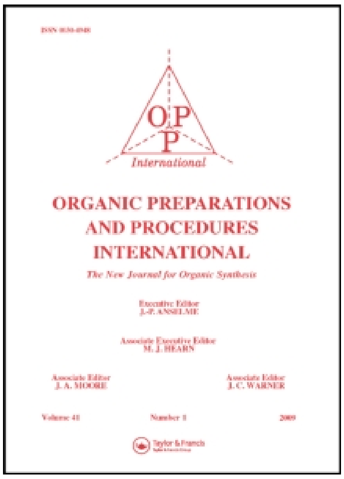

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Herczegh, Pal , Bognar, Rezso and Timar, Erzsebet(1978) 'SYNTHESIS OF 2-DEOXYALDONONITRILES BY CHAIN ELONGATION OF MONOSACCHARIDE DIETHYL DITHIOACETALS', Organic Preparations and Procedures International, 10: 5, 211 — 214

To link to this Article: DOI: 10.1080/00304947809355041

URL: http://dx.doi.org/10.1080/00304947809355041

ORGANIC PREPARATIONS AND PROCEDURES INT. 10(5), 211-214 (1978)

SYNTHESIS OF 2-DEOXYALDONONITRILES BY CHAIN ELONGATION OF MONOSACCHARIDE DIETHYL DITHIOACETALS

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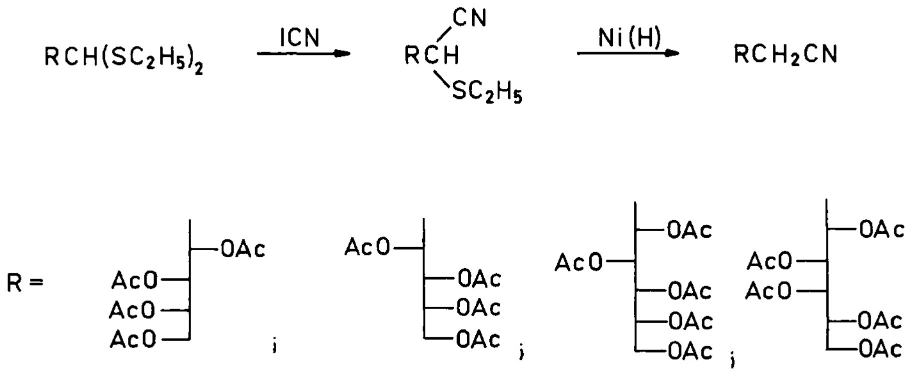
2-Deoxyaldononitriles can be useful intermediates in the synthesis of open-chain heterocyclic derivatives of sugars[1] and they can be transformed into 2-deoxyaldoses as in the Kiliani-Fischer method. Recently Pochat and Levas[2] prepared 2-ethylthiocarboxylic acid nitriles by the reaction of aliphatic and aromatic diethyl dithioacetals with equimolar quantity of cyanogen iodide generated *in situ* from mercuric cyanide and iodine.

We attempted to use this reaction for the appropriate transformation of aldose diethylmercaptal per-O-acetates. In our case, aldose diethyl dithioacetals with a solution of 2.5 equivalents of cyanogen iodide in acetonitrile gave the epimeric mixtures of 2-ethylthio-aldononitriles, the chains of which were longer by one carbon than that of the starting aldose.



The products showed a characteristic nitrile absorption at 2240 cm^{-1} and only one ethyl group in the NMR spectra. The 4:1 epimeric ratio in the crude reaction product prepared from D-glucose diethyl dithioacetal penta-O-acetate, shows the great stereoselectivity of the reaction. We could isolate one of the two diastereomers in every case but it was impossible to determine the configuration of the newly generated asymmetric center because of free rotation in the open chain.

Assuming that the reaction proceeds according to the Maltby rule,[3] we can postulate that in the reaction of D-glucose, D-galactose, D- and L-arabinose mercaptals, the preponderant products were the D-glycero-D-gulo, the D-glycero-L-manno-, the D-manno- and L-manno isomer respectively. We did not attempt to isolate the minor isomers because the diastereometric mixtures were desulfurized in the next step, giving 2-deoxy-aldonitrile per-O-acetates and eliminating the C-2 asymmetric center. The desulfurization was performed in acetone because other solvents such as benzene, ethanol, methanol, formic acid, ethyl acetate and acetonitrile caused major side-reactions. The structures of 2-deoxyaldononitriles were established by IR and NMR.

EXPERIMENTAL

Melting points are uncorrected and were determined on a Kofler block. IR spectra were obtained with a Unicam SP 200 spectrophotometer as KBr discs. NMR spectra were recorded with a JEOL MH-100 instrument in CDCl$_3$ solutions using TMS as internal standard. Optical rotations were determined with a Bendix automatic polarimeter.

Reaction of D-Glucose Diethyl Dithioacetal Penta-O-acetate with Cyanogen Iodide. Typical Procedure.- Dry mercuric cyanide (2.56 g, 10 mM) and iodine (5.12 g, 20 mM) were stirred in acetonitrile (7.0 ml) for 1 hr. at room temperature. The precipitated mercuric iodide was filtered. To the filtrate was added 2.0 g (4.2 mM) of penta-O-acetyl-D-glucose diethyl dithioacetal. The mixture was stirred for 1 hr. at 25°, then evaporated and the remaining syrup was extracted with chloroform. This solution was extracted with sodium thiosulfate and sodium bisulfite solutions and dried with magnesium sulfate. Evaporation gave 1.77 g (96%) of a syrupy mixture of the two epimeric 2-ethylthio-3,4,5,6,7-penta-O-acetyl-D-*gluco*-heptononitriles. IR: 2240 cm^{-1} (CN). NMR: δ 1.30, 1.32 ppm (two triplets, in a 1:4 4atio, 3 H). Treatment of this mixture with *n*-butanol resulted in the crystallization of one of the two epimers, yield: 53%, mp. 58-59°; $[\alpha]_D^{23}$ = -11° (c 1.3, $CHCl_3$).

Anal. Calcd. for $C_{19}H_{27}NO_{10}S$: N, 3.03, S, 6.94.
Found: N, 3.03, S, 7.01.

2-Ethylthio-3,4,5,6,7-penta-O-acetyl-D-galacto-heptononitrile.- From D-galactose diethyl dithioacetal penta-O-acetate. The epimeric mixture was crystallized from *n*-butanol to give 62% of a pure epimer, mp. 130.5-131.5°. $[\alpha]_D^{23}$ = -5° (c 1.4, $CHCl_3$). IR: 2240 cm^{-1} (CN). NMR: δ 1.3 (triplet, 3 H, ethyl CH_3, 2.68 quartet, 2 H, $-CH_2-$).

Anal. Calcd. for $C_{19}H_{27}NO_{10}S$: N, 3.03, S, 6.94.
Found: N, 3.03, S, 6.81.

2-Ethylthio-3,4,5,6-tetra-O-acetyl-D-arabino-hexononitrile.- From D-arabinose diethyl dithioacetal tetra-O-acetate. 55% of a pure epimer from *n*-butanol, mp. 58-59°, $[\alpha]_D^{23}$ = 57° (c 1.2, $CHCl_3$). IR: 2240 cm^{-1} (CN).

Anal. Calcd. for $C_{16}H_{23}NO_8S$: N, 3.59, S, 8.23.
Found: N, 3.59, S, 8.20.

2-Ethylthio-3,4,5,6-tetra-O-acetyl-L-arabino-hexononitrile.- From L-arabinose diethyl dithioacetal tetra-O-acetate. 54% of a pure isomer was obtained from *n*-butanol, mp. 58-59°; $[\alpha]_D^{23}$ = -57°. The IR and NMR spectra were identical with that of the D-*arabino* derivative, i.e. the two compound were enantiomers. *Anal*. Found: N, 3.58, S, 8.11.

2-Deoxy-D-gluco-heptononitrile penta-O-acetate. Typical Procedure.- 2-Ethylthio-D-*gluco*-heptononitrile (1.0 g) was refluxed with Raney-nickel (15 g) in acetone (20 ml) for 5 hrs. at 70°. The nickel was filtered and the solvent evaporated. The remaining material was crystallized from ethanol to give 0.3 g (34%) of the title compound, mp. 73°, $[\alpha]_D^{23}$= 43° (c 1.7, $CHCl_3$). IR: 2250 cm^{-1} (CN). NMR: 2.3 (multiplet, 2 H, 2-CH_2, no ethyl group).

Anal. Calcd. for $C_{17}H_{23}NO_{10}$: N, 3.49.
Found: N, 3.54.

2-Deoxy-D-galacto-heptononitrile penta-O-acetate.- Yield: 23% (EtOH), mp. 164-165°; $[\alpha]_D^{23}$= 41° (c 0.68, $CHCl_3$). IR: 2250 cm^{-1} (CN). NMR: δ 2.6 (multiplet, 2 H, 2-CH_2).

Anal. Calcd. for $C_{17}H_{23}NO_{10}$: N, 3.49.
Found: N, 3.51.

2-Deoxy-D-arabino-hexononitrile tetra-O-acetate.- Yield: 13%, mp. 122-124°. $[\alpha]_D^{23}$= 16°; IR: 2250 cm^{-1} (CN). NMR: 2.65 (multiplet, 2 H, 2-CH_2).

Anal. Calcd. for $C_{14}H_{19}NO_8$: N, 4.25.
Found: N, 4.52.

2-Deoxy-L-arabino-hexononitrile tetra-O-acetate.- Yield: 13%, mp. 122-124°; $[\alpha]_D^{23}$ = -16°. IR: 2250 cm^{-1} (CN).

Anal. Calcd. for $C_{14}H_{19}NO_8$: N, 4.25.
Found: N. 4.30.

Acknowledgements. Thanks are due to Dr. I. Farkas for his advice and to Dr. L. Szilagyi for the NMR spectra. The Hungarian Academy of Sciences is acknowledged for financial support.

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(Received September 23, 1978; in revised form June 14, 1978)