

NUCLEOPHILIC DISPLACEMENT OF CARBOHYDRATE
PRIMARY HALIDES WITH LITHIO-1, 3-DITHIANE

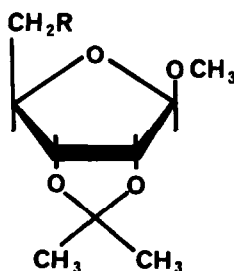
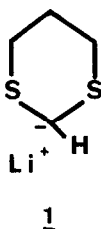
A.M. SEPULCHRE, G. VASS and S.D. GERO


Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif-sur-Yvette, France

(Received in UK 16 July 1973; accepted for publication 3 August 1973)

The use of 2-lithio-1,3-dithianes for the synthesis of branched- and extended-chain carbohydrate derivatives has been recently reported¹. A new procedure, based on nucleophilic displacement reactions of primary halogeno groups with 2-lithio-1,3-dithiane - leading to deoxy-extended-chain monosaccharides - is the subject of this communication. We describe herein the preparation of methyl 5-deoxy-5-C-(1',3'-dithianyl)-2,3-O-isopropylidene-β-D-ribofuranoside **4** and the derivatives of 1-deoxy-1-C-(1',3'-dithianyl)-D-erythritol **9-11**.

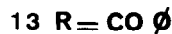
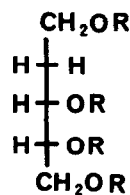
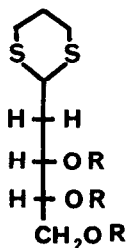
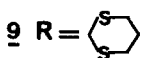
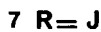
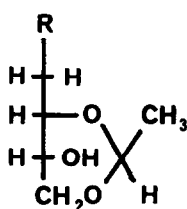
Treatment of methyl 5-deoxy-5-iodo-2,3-O-isopropylidene-β-D-ribofuranoside **2** with an equimolar quantity of 2-lithio-1,3-dithiane **1** in hexamethylphosphoramide (HMPA) at -20° for 16 hours afforded the highly crystalline methyl 5-deoxy-5-C-(1',3'-dithianyl)-2,3-O-isopropylidene-β-D-ribofuranoside **4** in 43 % yield, m.p. 75-76°C, $[\alpha]_D^{26} -20^\circ$ (c 0.96 in CHCl₃). The structure of **4** was established from mass and NMR spectral data. Treatment of **4** with ceric ammonium nitrate in aqueous acetonitril³ at room temperature gave the syrupy C-formyl derivative (78 %) **5** which was reduced *in situ* with sodium borohydride to the known methyl 5-deoxy-2,3-O-isopropylidene-β-D-ribo-hexofuranoside **6** (homoribose), $[\alpha]_D^{25} -53^\circ$ (c 2.81 in CH₃OH), [lit.⁴, $[\alpha]_D^{23} -54.6^\circ$ (c 2.3 in CH₃OH)]. Methyl 5-deoxy-5-C-(1',3'-dithianyl)-2,3-O-isopropylidene-β-D-ribofuranoside **4** could also be obtained from methyl 2,3-O-isopropylidene-5-O-toluene-p-sulphonyl-β-D-ribofuranoside **3** in a similar displacement reaction, albeit in low yield (5 %).



- 2** R = J
3 R = OTs
4 R = 
5 R = CHO
6 R = CH₂OH

The synthesis of 1-deoxy-1-C-(1', 3'-dithianyl)-D-erythritol started from 1-deoxy-2, 4-O-ethylidene-1-halogeno-erythritol **7** and **8**. Reaction of **7** with an equimolar quantity of 2-lithio-1, 3-dithiane in HMPA at -20° for 16 hours afforded the syrupy 1-deoxy-1-C-(1', 3'-dithianyl)-2, 4-O-ethylidene-D-erythritol **9** in 51 % yield, $[\alpha]_D^{25} -36^{\circ}$ (c 1.9 in CHCl_3). Acidic hydrolysis of the latter led to the crystalline 1-deoxy-1-C-(1', 3'-dithianyl)-D-erythritol **10**, m.p. $123-124^{\circ}$, $[\alpha]_D^{26} -35^{\circ}$ (c 1.1 in MeOH). Peracetylation of **10** furnished the oily 2, 3, 4-tri-O-acetyl-1-deoxy-1-C-(1', 3'-dithianyl)-D-erythritol **11**, $[\alpha]_D^{25} + 6.3^{\circ}$ (c 6.35 in CHCl_3). **11** was desulphurised and the resultant syrupy 3, 4, 5-tri-O-acetyl-2-deoxy-D-erythro-pentose was reduced *in situ* with sodium borohydride to 2-deoxy-D-erythro-pentitol **12**, readily characterised as its crystalline perbenzoate **13**, m.p. $129-130^{\circ}$, $[\alpha]_D^{28} - 15^{\circ}$ (c 0.81 in CHCl_3) [lit. ⁶ m.p. 129°C , $[\alpha]_D -14^{\circ}$ (c 1.0 in CHCl_3)]. The preparation of **9** can also be achieved in 28 % yield from 1-deoxy-1-chloro-2, 4-O-ethylidene-D-erythritol **8**, readily obtained by heating 2, 4-O-ethylidene-O-toluene-p-sulphonyl-D-erythritol with lithium chloride in HMPA-toluene⁷. **8** has melting point $107-108^{\circ}$, and $[\alpha]_D^{25} - 40^{\circ}$ (c 1.05 in CHCl_3).

The examples described above show that the nucleophilic displacement of primary halides with lithio-1, 3-dithiane is a very convenient alternative procedure ^{4, 5, 8} for an one carbon chain-extension in carbohydrate chemistry.



Acknowledgment : The authors wish to express their sincere gratitude to Professor E. Lederer for constant encouragement. This work was supported by a research grant from the D.G.R.S.T.

REFERENCES

1. A.M. Sepulchre, G. Lukacs, G. Vass et S.D. Gero, Bull. Soc. Chim. France, 4000, 1972 ; A.M. Sepulchre, G. Vass et S.D. Gero, C.R. Acad. Sc. Paris (C), 274, 1077, 1972 ; A.M. Sepulchre, A. Gateau-Olesker, G. Lukacs, G. Vass, S.D. Gero and W. Voelter, Tetrahedron Letters, 3945, 1972 ; H. Paulsen, V. Sinnwell and P. Stadler, Chem. Ber., 105, 1978, 1972.
2. H.M. Kissman and B.R. Baker, J. Amer. Chem. Soc., 79, 5534, 1957.
3. Tsé-Lok Ho, Honor C. Ho and C.M. Wong, J. C.S., Chem. Comm., 791, 1972.
4. J.A. Montgomery and K. Hewson, J. Org. Chem., 29, 3436, 1964.
5. I. Ziderman and E. Dimant, J. Org. Chem., 32, 1267, 1967.
6. E. Hardegger, H. Gempeler and A. Züst, Helv. Chim. Acta, 40, 1819, 1957.
7. H.B. Sinclair, Carbohyd. Res., 15, 147, 1970.
8. H. Arzoumanian, E.M. Acton and L. Goodman, J. Amer. Chem. Soc., 86, 74, 1964.