

Radical Dideoxygenation Reaction of a 1,4-Bis-dithiocarbonate: A Strategy for the Synthesis of Chiral Polyhydroxylated Thiolane Derivatives

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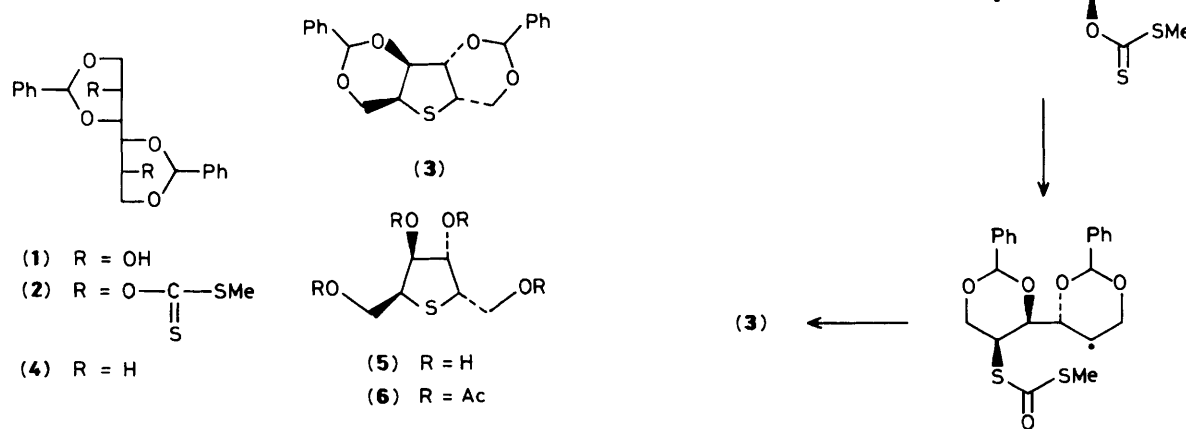
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The radical deoxygenation reaction of 2,5-bis(*S*-methylthiocarbonyl)-*D*-mannitol derivative (2) to form an unusual thiolane derivative (3) has been achieved.

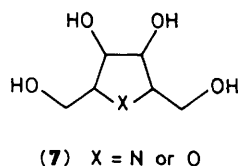
Polyether natural products¹ having a bis-tetrahydrofuran skeleton have received much attention during the last few years, primarily owing to various biological activities associated with them. In connection with our programme² on bis-tetrahydrofuran molecules,³ we required the optically active intermediate *syn*-vicinal diol derivative (4), and realised that simultaneous dideoxygenation of *D*-mannitol (C_2 symmetry) was the most logical strategy.

The readily obtainable⁴ 1,3,4,6-di-*O*-benzylidene-*D*-mannitol (1) was converted into the 2,5-bis-dithiocarbonate derivative (2) (83%) {m.p. 210 °C, $[\alpha]_D -43^\circ$ ($CHCl_3$)} by sequential reaction with sodium hydride, carbon disulphide, and methyl iodide in tetrahydrofuran. Subsequent reaction of (2) with freshly distilled tri-*n*-butyltin hydride in refluxing toluene containing a catalytic amount of α,α -azoisobutyro-

nitrile for 18 h gave a single product {m.p. 209 °C, $[\alpha]_D -103^\circ$ ($CHCl_3$)} which undoubtedly was not the required 2,5-dideoxy compound (4). However, on the basis of ¹H n.m.r. and mass spectral studies, the structure of the product was assigned as (2*S*,3*S*,4*S*,5*S*)-di-*O*-benzylidene-3,4-bis-hydroxy-2,5-bis-hydroxymethylthiolane (3) (80%). For instance the ¹H n.m.r. spectrum revealed resonances due to half the molecule, suggesting C_2 symmetry. Moreover, the characteristic⁵ coupling between H-2/H-3† or H-4/H-5 indicated the stereochemistry at both C-2 and C-5 to be *S*. (Scheme 1).



Scheme 1



† The characteristic coupling constants for (3) were obtained by spectral analysis and phase sensitive COSY experiments ($J_{1,2}$ 1.4, $J_{1,2}$ 2.6, $J_{2,3}$ 2.4, and $J_{3,4}$ 2.0 Hz]. In addition a difference nuclear Overhauser enhanced (n.O.e.) experiment revealed the expected enhancement for ring protons.

The formation of (3) was rather surprising and to the best of our knowledge⁶ the incorporation of a sulphur atom during Barton-McCombie radical deoxygenation⁷ has not previously been reported. A possible mechanistic pathway is suggested in Scheme 1.

Reductive desulphurisation of (3) in the presence of Raney nickel in refluxing ethanol afforded the required compound (4) (92%) $\{[\alpha]_{\text{D}} - 28^{\circ} (\text{CHCl}_3)\}$. Compound (3) was also transformed into the tetrol (5) and the tetra-acetate derivative (6) by conventional reactions.

In view of the fact that polyhydroxylated ring heterocyclic compound (7; X=N or O) are valuable^{8,9} building blocks in natural product synthesis, the corresponding thiolane precursor (3) may find added advantage as a chiral template because the simple reductive desulphurisation would provide easy access to an acyclic system.

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