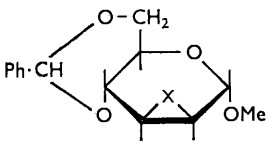
1237. 2,3-*Dideoxy*-2,3-*epithio*-*glycosides* [1]

By R. D. Guthrie and D. Murphy

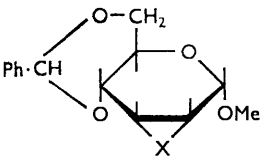
The reaction of simple acylic and alicyclic epoxides with alkali-metal thiocyanates to give the corresponding episulphides is well known.[2-6] Treatment of cyclopentene oxide or cyclohexene oxide [5] with the potassium salt gave the corresponding episulphide together with polymeric material. Similar treatment of cyclopentene oxide [6] with the ammonium salt gave predominantly the *trans*-thiocyanohydrin with some episulphide. The difference in products from the potassium and ammonium salts was attributed to the difference in basicity of the two reagents.[6]

Christensen and Goodman [7] reported that methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (I) reacted with ammonium thiocyanate to give the methyl 4,6-*O*-benzylidene-3-deoxy-3-thiocyano-α-D-altroside.* No methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-epithio-α-D-alloside (IV) was formed directly; it was obtained from the thiocyanohydrin in two further steps in an overall yield of 28% from the *manno*-epoxide (based on the corrected yields). The lack of direct formation of the episulphide was attributed to the rigidity of the pyranose ring due to the benzylidene group.

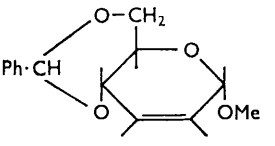
This view has been criticised on two counts,[1] the main one being that conformational mobility is possible in such systems (cf. ref. 8), and it was further shown that direct conversion of the *manno*-epoxide (I) into the *allo*-episulphide (IV) was possible, using potassium thiocyanate, in 20% yield (see ref. 1 and Experimental section). Reaction of the *allo*-epoxide (III) with potassium thiocyanate failed to yield any of the *manno*-episulphide (II).



(I : X = O) (II : X = S)



(III : X = O) (IV : X = S)



(V)

In the steroid series it has since been shown that epoxides can be converted directly into episulphides by potassium thiocyanate, albeit in low yield,[9] and that a vicinal diaxial thiocyanato-ol (which would be the first product in the epoxide reaction) can be converted directly into an episulphide.[10]

An alternative one-step route from epoxides to episulphides is the reaction with

* It should be noted that, assuming that the weights of products are given correctly, some yields in the paper describing this work have been calculated incorrectly.

[1] Preliminary report of part of this work, R. D. Guthrie, *Chem. and Ind.*, 1962, 2121.
[2] M. G. Ettlinger, *J. Amer. Chem. Soc.*, 1950, **72**, 4792.
[3] C. C. Culvenor, W. Davies, and K. H. Pausacher, *J.*, 1946, 1050.
[4] A. Synder, J. M. Stewart, and J. B. Ziegler, *J. Amer. Chem. Soc.*, 1947, **69**, 2672.
[5] E. E. van Tamelen, *J. Amer. Chem. Soc.*, 1951, **73**, 3444.
[6] L. Goodman and B. R. Baker, *J. Amer. Chem. Soc.*, 1959, **81**, 4924.
[7] J. E. Christensen and L. Goodman, *J. Amer. Chem. Soc.*, 1961, **83**, 3827.
[8] F. H. Newth, *Quart. Rev.*, 1959, **13**, 30, and references therein.
[9] D. A. Lightner and C. Djerassi, *Tetrahedron*, 1965, **21**, 583.
[10] K. Takeda, T. Komeno, J. Kawanami, S. Ishihara, H. Kadokawa, H. Tokura, and H. Itani, *Tetrahedron*, 1965, **21**, 329.

thiourea.[3,11,12] Extension of this reaction to methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside (I) gave the epithio-alloside (IV) in 29% yield. Reaction with the corresponding *allo*-epoxide (III) gave the hitherto unknown epithio-mannoside (II) (63%) together with methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-didehydro-α-D-*erythro*-hexopyranoside (V) (20%). This latter product, whose formation was surprising, must arise from elimination from the thiouronium intermediate and not from the episulphide, since prolonged treatment of the epithio-mannoside with thiourea gave only unchanged starting compound.

Thus, the best route for the formation of these two epithio-sugar derivatives is the thiourea method rather than through thiocyanohydrins. Neither of the epithio-sugars gave a yellow colour with concentrated sulphuric acid, as did some 5,6-epithio-sugars.[12]

It has been shown that aliphatic and steroid episulphides have an ultraviolet absorption band at about 260 mμ (ε 50—200),[13,14] due to an optically active transition.[14] The ultraviolet spectra of the epithio-sugars (II) and (IV) (dioxan solution) did not show this band at all clearly as it was masked by the complex absorption due to the phenyl ring of the benzylidene group. (The spectra were essentially the same as those of the corresponding epoxides.) The optical rotatory dispersion curves of the *allo*-episulphide showed a positive Cotton effect, and the *manno*-isomer a very weak positive effect, both around 258 mμ, showing that these sugar episulphides do have an ultraviolet absorption band in that region.

The proton magnetic resonance spectrum of the epithiomannoside (II), in chloroform, has the features predictable from the observations of Hough and his co-workers.[15] The phenyl, benzylidene-methine, and methoxyl protons occurred at τ 2·63, 4·41, and 6·61, respectively. The anomeric proton (H-1) gave a singlet (τ 5·14) showing zero coupling between H-1 and H-2, as found for the other *manno*-epi-derivatives.[15] The signals due to H-2 and H-3 occurred in the 6·5—6·9 region and were partly hidden under the methoxyl signal.

Experimental.—Rotations were measured for chloroform solutions. Where possible compounds were identified by mixed m. p., and by infrared spectroscopy.

Preparation of methyl 4,6-O-*benzylidene*-2,3-*dideoxy*-2,3-*epithio*-α-D-*alloside* (IV). (a) *With potassium thiocyanate.* The 2,3-anhydro-mannoside (I) (0·5 g.), and potassium thiocyanate (1·0 g.) in 2-methoxyethanol (10 ml.) and water (1 ml.) were boiled under reflux for 4·5 hr. The solution was poured into water (30 ml.), and the white solid product twice recrystallised from propan-2-ol to give the epithio-alloside (IV) (10%), m. p. 165—170°, $[\alpha]_D^{18}$ +195° (*c* 1·0) (lit.,[7] m. p. 166—167°, $[\alpha]_D^{28}$ +192°), $[\phi]_{400}$ +1180, $[\phi]_{300}$ +3060, $[\phi]_{265}$ +5380 pk., $[\phi]_{251}$ +3350 tr., $[\phi]_{227}$ +7300 (dioxan).

(b) *With potassium thiocyanate and ammonium chloride.* The 2,3-anhydro-mannoside (I) (0·5 g.), potassium thiocyanate (1·0 g.), and ammonium chloride (0·075 g.) in 2-methoxyethanol (10 ml.) and water (1 ml.) were boiled under reflux for 4·5 hr. The mixture was poured into water (30 ml.), and the white solid product (no SCN at about 2160 $cm.^{-1}$) collected and dried (0·41 g.), m. p. 98—130°, $[\alpha]_D^{18}$ +165° (*c* 1·0). The solid was twice recrystallised from propan-2-ol, to give the 2,3-epithio-alloside (IV) (20%), m. p. 167—169°, $[\alpha]_D^{18}$ +195° (*c* 1·0).

(c) *With thiourea.* The 2,3-anhydro-mannoside (I) (2·6 g.) and thiourea (3·0 g.) in ethanol (100 ml.) were boiled under reflux for 16 hr. The solution was evaporated, and the crystalline residue extracted with chloroform (50 ml.); evaporation gave the 2,3-epithio-alloside (IV) (36%), m. p. 160—164°, $[\alpha]_D$ +192° (*c* 1·2). Recrystallisation from propan-2-ol gave the product (29%), m. p. 164—166°.

Methyl 4,6-O-*benzylidene*-2,3-*dideoxy*-2,3-*epithio*-α-D-*mannoside.* Methyl 2,3-anhydro-4,6-

[11] C. C. Culvenor, W. Davies, and N. S. Heath, *J.*, 1949, 278; F. G. Bordwell and H. M. Anderson, *J. Amer. Chem. Soc.*, 1953, **75**, 4959.
[12] L. D. Hall, L. Hough, and R. A. Pritchard, *J.*, 1961, 1537.
[13] R. E. Davis, *J. Org. Chem.*, 1958, **23**, 216; A. M. Creighton and L. N. Owen, *J.*, 1960, 1524.
[14] C. Djerassi, H. Wolff, D. A. Lightner, E. Bunnenburg, K. Takeda, T. Komeno, and K. Kuriyama, *Tetrahedron*, 1963, **19**, 1547.
[15] D. H. Buss, L. Hough, L. D. Hall, and J. F. Manville, *Tetrahedron*, 1965, **21**, 69.

O-benzylidene-α-D-alloside (III) (2 g.) and thiourea (2·2 g.) in propan-2-ol (30 ml.) were boiled under reflux for 48 hr. Pouring into water gave a white solid product. Careful recrystallisation of the solid from propan-2-ol gave two solids, each recrystallised from the same solvent, to give *methyl* 4,6-O-*benzylidene*-2,3-*dideoxy*-2,3-*epithio*-α-D-*mannoside* (II) (63%), m. p. 173—174°, $[\alpha]_D^{22}$ +130° (*c* 0·65), $[\phi]_{400}$ +830, $[\phi]_{300}$ +1870, $[\phi]_{265}$ +2330 pk., $[\phi]_{248}$ +1830 tr., $[\phi]_{227}$ +3120 (dioxan) (Found: C, 59·8; H, 5·7; S, 11·4. $C_{14}H_{16}O_4S$ requires C, 60·0; H, 5·8; S, 11·4%), and methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-didehydro-α-D-*erythro*-hexopyranoside (V) (20%), m. p. 111—112°.

A similar experiment, using the 2,3-anhydro-alloside (III) (20 g.), gave the same products (58 and 18%).

The 2,3-epithio-mannoside (II) and thiourea were boiled under reflux in propan-2-ol for 40 hr. Pouring into water, and recrystallisation of the solid product, gave only unchanged epithio-mannoside (82%).

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