Reactions of Relevance to the Chemistry of Aminoglycoside Antibiotics. Part 11.† Preparation of Olefins from Vicinal Diols

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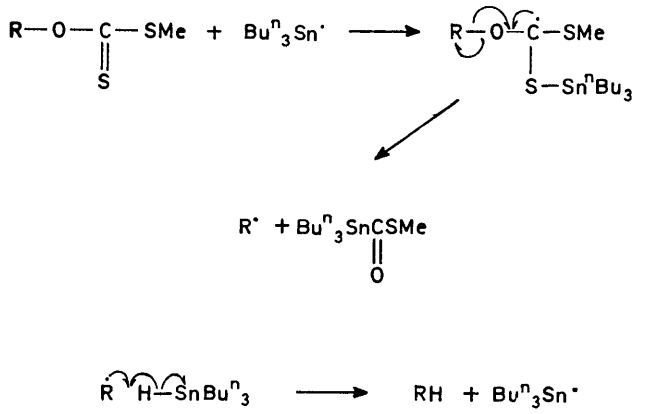
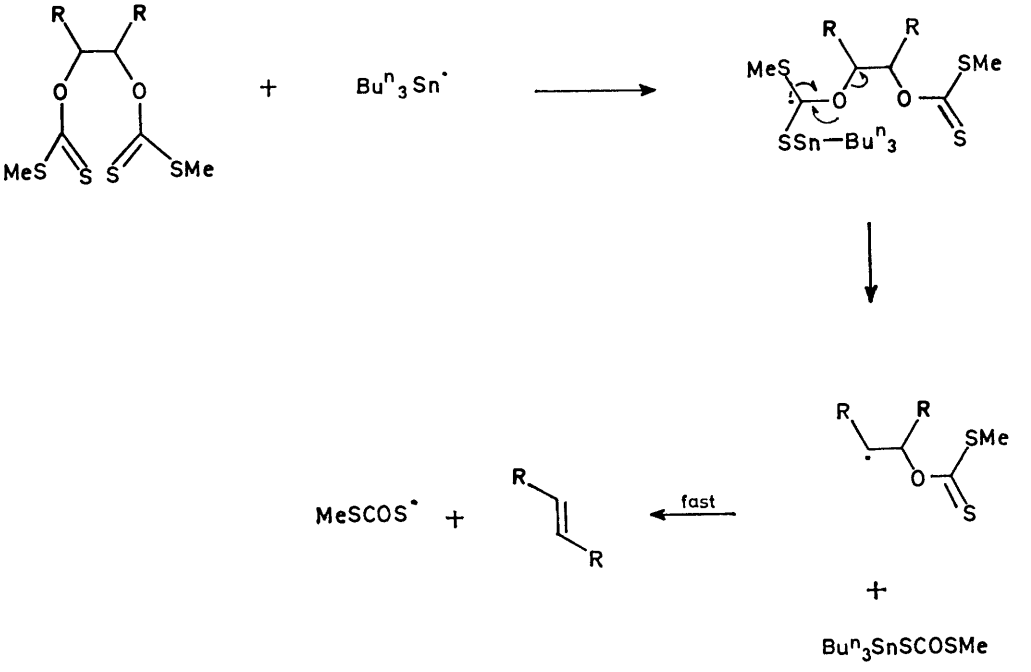
Vicinal diols are converted in high yield into olefins by reaction of the derived bisdithiocarbonates with tri-n-butylstannane in toluene or benzene. The stereochemistry of reaction is consistent with a stepwise radical fragmentation.

RECENTLY, carbohydrate esters containing the thiocarbonyl group have found application in novel mild procedures whereby hydroxy-functions may be selectively replaced by hydrogen[1] or halides.[2,3] For example, the reaction of *O*-alkyl-*S*-methyldithiocarbonates (xanthates) with methyl iodide gave the iodoalkane and di-*S*-methyldithiocarbonate *via* *S*-methylation followed by S_N2 displacement by iodide anion. Alternatively, reduction of xanthates with tri-n-butylstannane gave the deoxy-compound *via* a radical fragmentation (Scheme 1). Substitution in the β-position of the intermediate alkyl radical by a good radical leaving group should permit the synthesis of alkenes. Herein is described the conversion of vicinal diols into alkenes by the radical fragmentation of the derived bis-xanthates (Scheme 2).[4]



SCHEME 1

Attempts to prepare bisthioxobenzoates from vicinal diols using the Vilsmeier reagent ($Me_2\overset{+}{N}=CClPh\bar{C}l$) were unsuccessful due to formation of 1,2-chlorobenzoates *via* the cation (1) (Scheme 3).[5] Since the preparation of xanthates proceeds *via* anionic intermediates, species analogous with the cation (1) cannot be formed. Consistent with this and literature precedent,[3,6] a series of carbohydrate diols (2a), (3a), (5a), and (7a) were converted into the bis-xanthates (2b), (3b), (5b), and (7b), respectively, using sodium hydride (catalysed by imidazole), carbon disulphide, and methyl iodide in sequence in tetrahydrofuran (THF), as detailed previously[1] for monoxanthates. Formation of the bis-xanthates was consistent with spectra and microanalytical data. The D-glucose derivative (2b) had physical properties in agreement with literature values.[6]



SCHEME 2

† Part 10, D. H. R. Barton, G. Lamotte, W. B. Motherwell, and S. C. Narang, *J.C.S. Perkin I*, 1979, 2030.

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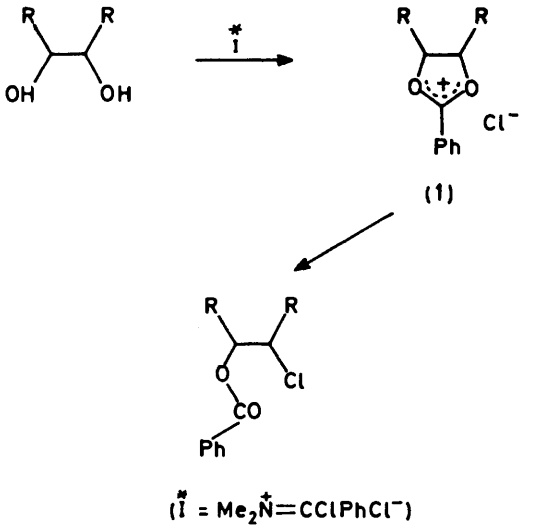
Reflux of each bis-xanthate with tri-n-butylstannane in toluene or benzene gave the corresponding olefin in good yield. Chromatography was necessary to remove tin compounds and minor by-products. The alkene (10) prepared by Bu^n_3SnH reduction of the known [3] bis-xanthate (9) required purification by chromatography on silica impregnated with silver nitrate. Structural assignments of all the alkenes [(4), (6), (8), and (10)]

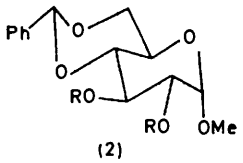


(1)

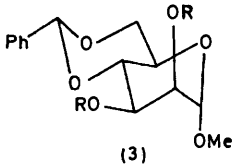
($\overset{*}{I}$ = $Me_2\overset{+}{N}$=CClPhCl$^-$)

SCHEME 3

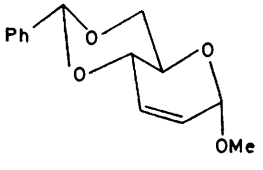
obtained were consistent with spectral and literature data (see Experimental section). The mannitol derivative (8) was obtained only as the *E*-isomer. In order to study further the stereochemistry of reduction, both



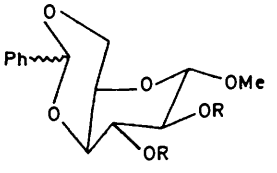
(2)
a; R = H
b; R = CS_2Me



(3)
a; R = H
b; R = CS_2Me

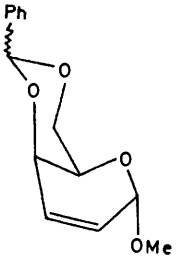


(4)

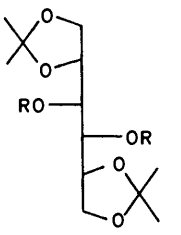


(5)
a; R = H
b; R = CS_2Me

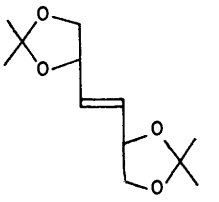
(*meso*)- and (±)-hydrobenzoin bis-xanthates (11b) and (12b) were prepared, fully characterised, and subjected to reduction with Bu^n_3SnH. In each case only (*E*)-stilbene was observed. Clearly, both the preference for *E*-stereochemistry and the formation of alkene (4) from both bis-xanthates (2b) and (3b) were consistent with the stepwise radical fragmentation (Scheme 2). The reaction has recently been applied to kanamycin- and butirosin-derived antibiotics.[7]



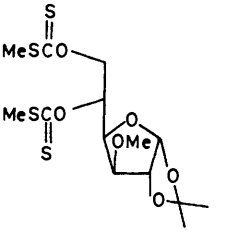
(6)



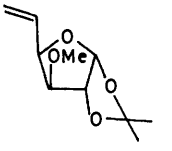
(7)
a; R = H
b; R = CS_2Me



(8)

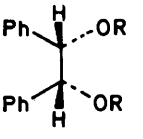


(9)

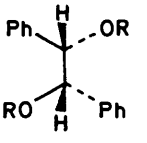


(10)

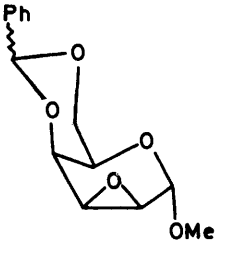
Alternative procedures exist for transformations of vicinal diols to alkenes. The classical Tipson–Cohen reaction [8] (NaI–Zn–DMF on diol bis-alkyl- or -aryl-sulphonates) is often unsuccessful. This is due to difficulty in the initial S_N2 displacement by iodide due to steric and stereoelectronic factors. The reaction is notably less suitable for the diols (2a) and (3a) than for the β-anomers.[9] The Corey–Winter reaction (trialkylphosphine on cyclic diol thioxocarbonate) requires prolonged reaction at high temperature (≥135 °C) but is stereospecific.[10] Biscyclo-octa-1,5-dienylnickel is an



(11)
a; R = H
b; R = CS_2Me



and enantiomer
(12)
a; R = H
b; R = CS_2Me



(13)

alternative reagent to the phosphine.[11] Electrophilic conditions (*e.g.* Ac_2O–heat on cyclic diol orthoesters or amides) reduce the synthetic usefulness of the Eastwood procedure.[12] Recently [13] Hanessian has improved this alkene preparation by treating 2-dimethylamino-1,3-dioxolans with methyl iodide. The use of n-butyllithium makes the Whitham [14] procedure (Bu^nLi on 2-phenyl-1,3-dioxolans) inapplicable to many substrates. Sharpless has deoxygenated vicinal diols *cis*-stereospecifically using potassium hexachlorotungstate(IV).[15] Recently Lythgoe has detailed the stereoselective synthesis of *E*-alkenes by reduction of β-acyloxysulphones with sodium amalgam.[16] β-(Methylthio)thiocarbonyloxysulphones and tri-n-butylstannane were reported to give *E*-alkenes; details are yet to be published. The bis-xanthate method herein described readily provides alkenes at low temperatures under mild neutral conditions using inexpensive reagents and, as such, should find application.

EXPERIMENTAL

General experimental conditions have been described previously.[1] Vicinal bisdithiocarbonates were prepared from the diol, sodium hydride, imidazole, carbon disulphide, and methyl iodide.[1] Data for compounds (2b) and (6) reported in our preliminary communication [4] have been corrected.

Methyl 4,6-O-*Benzylidene*-2,3-*di*-O-[(S-*methylthio*)*thiocarbonyl*]-α-D-*glucopyranoside* (2b).—This was obtained (yield 4.38 g, 95%) from the diol (2a) (2.82 g), m.p. 98—101° (from aqueous ethanol) (lit.,[6] 99—100.5°), $[\alpha]_D^{23}$ −19° (*c* 2.5) (lit.,[6] −18°).

Methyl 4,6-O-*Benzylidene*-2,3-*di*-O-[(S-*methylthio*)*thiocarbonyl*]-α-D-*mannopyranoside* (3b).—This was obtained (yield 435 mg, 94%) from the diol (3a) (282 mg), m.p. 167—169°, $[\alpha]_D^{23}$ −27° (*c* 1.0), $\nu_{max.}$ ($CHCl_3$) 1 370, 1 070, and 970 cm^{-1}, $\lambda_{max.}$ 280 nm (ε 14 800), τ(CCl_4) 2.72 (5 H, s, aryl-H), 3.7—4.02 (2 H, m, 2- and 3-H), 4.47 (1 H, s, PhC*H*), 5.21 (1 H, m, 1-H), 5.6—6.38 (4 H, m, 4-, 5-, 6-, and 6′-H), 6.56 (3 H, s, OMe), and 7.39 and 7.46 (6 H, 2s, SMe), *m/e* 370 (Found: C, 46.75; H, 4.8. $C_{18}H_{22}O_6S_4$ requires C, 46.7; H, 4.8%).

Methyl 4,6-O-*Benzylidene*-2,3-*di*-O-[(S-*methylthio*)*thiocarbonyl*]-α-D-*idopyranoside* (5b).—The diol (5a) (141 mg) [from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-talopyranoside (13) and alkali [17]] gave the *bisdithiocarbonate* (5b) (195 mg, 84%), m.p. 145—146.5° (from aqueous ethanol), $[\alpha]_D^{23}$ +154° (*c* 0.7), $\nu_{max.}$ ($CHCl_3$) 1 160, 1 135, 1 110, and 1 050 cm^{-1}, $\lambda_{max.}$ 283 nm (ε 22 300), τ($CDCl_3$) 2.58 (5 H, m, aryl-H), 4.0—4.5 (3 H, m, 2- and 3-H and PhCH), 5.04 (1 H, s), 5.6—6.16 (4 H, m), 6.6 (3 H, s, OMe), and 7.47 and 7.68 (6 H, 2s, SMe), *m/e* 355 (Found: C, 46.85; H, 4.8. $C_{18}H_{22}O_6S_4$ requires C, 46.7; H, 4.8%).

1,2;5,6-*Di*-O-*isopropylidene*-3,4-*di*-O-[(S-*methylthio*)*thiocarbonyl*]-D-*mannitol* (7b).—The diol (7a) (475 mg) gave the *bisdithiocarbonate* (7b) (721 mg, 90%), m.p. 82—84.5° (from aqueous ethanol), $[\alpha]_D^{23}$ +101° (*c* 2), $\nu_{max.}$ ($CHCl_3$), 1 420, 1 220, and 1 045 cm^{-1}, $\lambda_{max.}$ 280 nm (ε 23 300), τ(CCl_4) 3.75 (2 H, m, 3- and 4-H), 5.86 (2 H, m, 2- and 5-H), 6.01—6.21 (4 H, m, 1-, 1′-, 6-, and 6′-H), 7.4 (6 H, s, SMe), and 8.66 and 8.74 (12 H, 2 s, CMe_2), *m/e* 427 (Found: C, 43.5; H, 5.9. $C_{16}H_{26}O_6S_4$ requires C, 43.4; H, 5.9%).

(meso)-1,2-*Di*-[(S-*methylthio*)*thiocarbonyloxy*]-1,2-*diphenylethane* (11b).—(*meso*)-1,2-Diphenylethane-1,2-diol (11a) (315 mg) gave the *bisdithiocarbonate* (11b) (347 mg, 60%), m.p. 151—154° (from aqueous ethanol), $\nu_{max.}$ ($CHCl_3$) 1 420, 1 215, 1 050, and 925 cm^{-1}, $\lambda_{max.}$ 280 nm (ε 21 700), τ(CCl_4) 2.88 (10 H, m, aryl-H), 3.1 (2 H, s, CH), and 7.48 (6 H, s, SMe), *m/e* 287 (Found: C, 55.1; H, 4.6. $C_{18}H_{18}O_2S_4$ requires C, 54.75; H, 4.6%).

(±)-1,2-*Di*-[(S-*methylthio*)*thiocarbonyloxy*]-1,2-*diphenylethane* (12b).—(±)-1,2-Diphenylethane-1,2-diol (12a) (76 mg) gave bisdithiocarbonate (12b) (77 mg, 55%), m.p. 119—120°, $\nu_{max.}$ ($CHCl_3$) 1 420 1 200, 1 035, and 925 cm^{-1}, $\lambda_{max.}$ 280 nm (ε 19 400), τ(CCl_4) 2.86 (10 H, s, aryl-H), 3.08 (2 H, s, CH), and 7.46 (6 H, s, SMe), *m/e* 287 (Found: C, 54.6; H, 4.55%).

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranoside* (4).—Tri-n-butylstannane (1.2 g) and the bisdithiocarbonate (2b) (231 mg) in dry toluene (15 ml) were heated to reflux overnight, cooled, washed with aqueous potassium hydroxide, dried ($MgSO_4$), and evaporated. Chromatography on silica (diethyl ether–light petroleum gradient) and crystallisation from ethanol gave the alkene (4) (74 mg, 60%), m.p. 115—117° (lit.,[18] 112—120°), $[\alpha]_D$ +135° (*c* 1.0) (lit.,[18] 129°). The epimeric bisdithiocarbonate (3b) (128 mg) gave the same alkene (4) (54 mg, 79%), m.p. 115—117°, $[\alpha]_D$ +130°.

Methyl 4,6-O-*Benzylidene*-2,3-*dideoxy*-α-D-threo-*hex*-2-*enopyranoside* (6).—The bisdithiocarbonate (5b) (185 mg) and tri-n-butylstannane, treated as above, gave the alkene (6) (49 mg, 49%), m.p. 158—160° (from ethanol) (lit.,[19] 163—164°), $[\alpha]_D^{23}$ −105° (*c* 0.7) (lit.,[19] −130°).

1,2;5,6-*di*-O-*isopropylidenehex*-3-(E)-*enc*-D-threo-1,2,5,6-*tetraol* (8).—Reaction of the bisdithiocarbonate (7b) (265 mg) and tri-n-butylstannane in toluene gave the *E*-alkene (8) (89 mg, 65%), m.p. 78—80° (from aqueous ethanol) (lit.,[8] 80—82°), $[\alpha]_D^{23}$ +51° (*c* 0.7) (lit.,[8] 57.5°).

5,6-*Dideoxy*-1,2-O-*isopropylidene*-3-O-*methyl*-α-D-xylo-*hex*-5-*enofuranose* (10).—The bisdithiocarbonate (9) [3] (250 mg) and tri-n-nutylstannane (1.5 g) in benzene (15 ml) were heated to reflux for 60 h. Normal work-up and chromatography on silver nitrate–silica (1 : 19) (benzene–light petroleum gradient) gave the alkene (10) (75 mg, 62%), b.p. 101° at 5 mmHg (lit.,[20] 80° at 2 mmHg), $[\alpha]_D^{23}$ −44° (*c* 1.0 ethanol) (lit.,[20] −43°), identical with authentic material.[3]

(E)-*Stilbene*.—The (*meso*)-bisdithiocarbonate (11b) (394 mg) and tri-n-butylstannane in toluene gave (*E*)-stilbene (130 mg, 72%), m.p. 123—124° (from ethanol) (lit.,[21] 124°). The (±)-isomer (12b) also gave (*E*)-stilbene (77%), m.p. 123—124°. (*Z*)-Stilbene was not detected.

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REFERENCES

[1] D. H. R. Barton and S. W. McCombie, *J.C.S. Perkin I*, 1975, 1574.
[2] D. H. R. Barton and R. V. Stick, *J.C.S. Perkin I*, 1975, 1773.
[3] D. H. R. Barton, R. V. Stick, and R. Subramanian, *J.C.S. Perkin I*, 1976, 2112.
[4] A. G. M. Barrett, D. H. R. Barton, R. Bielski, and S. W. McCombie, *J.C.S. Chem. Comm.*, 1977, 866.
[5] T. G. Back, D. H. R. Barton, and B. L. Rao, *J.C.S. Perkin I*, 1977, 1715.
[6] A. K. Sanyal and C. B. Purves, *Canad. J. Chem.*, 1956, **34**, 426.

[7] T. Hayashi, T. Iwaoka, N. Takeda, and E. Ohki, *Chem. Pharm. Bull.*, 1978, **26**, 1786.
[8] H. L. Slates and N. L. Wendler, *J. Amer. Chem. Soc.*, 1956, **78**, 3749; R. S. Tipson and A. Cohen, *Carbohydrate Res.*, 1965, **1**, 338.
[9] T. Yamazaki, K. Matsuda, H. Sugiyama, S. Seto, and N. Yamaoka, *J.C.S. Perkin I*, 1977, 1981.
[10] E. J. Corey and R. A. E. Winter, *J. Amer. Chem. Soc.*, 1963, **85**, 2677.
[11] M. F. Semmelhack and R. D. Stauffer, *Tetrahedron Letters*, 1973, 2667.
[12] F. W. Eastwood, K. J. Harrington, J. S. Josan, and J. L. Pura, *Tetrahedron Letters*, 1970, 5223; J. S. Josan and F. W. Eastwood, *Austral. J. Chem.*, 1968, **21**, 2013; T. van Es, *Carbohydrate Res.*, 1967, **5**, 282.
[13] S. Hanessian, A. Bargiotti, and M. LaRue, *Tetrahedron Letters*, 1978, 737.
[14] J. N. Hines, M. J. Peagram, G. H. Whitham, and M. Wright, *Chem. Comm.*, 1968, 1593.
[15] K. B. Sharpless and T. C. Flood, *J.C.S. Chem. Comm.*, 1972, 370.
[16] P. J. Kocienski, B. Lythgoe, and S. Ruston, *J.C.S. Perkin I*, 1978, 829.
[17] E. Sorkin and T. Reichstein, *Helv. Chim. Acta*, 1945, **28**, 1; B. Capon, W. G. Overend, and M. Sobell, *Tetrahedron*, 1961, **16**, 106.
[18] F. H. Newth, *J. Chem. Soc.*, 1956, 471.
[19] R. U. Lemieux, E. Fraga, and K. A. Watanabe, *Canad. J. Chem.*, 1968, **46**, 61.
[20] J. S. Josan and F. W. Eastwood, *Carbohydrate Res.*, 1968, **7**, 161.
[21] 'I. Heilbron's Dictionary of Organic Compounds,' Volume 5, Eyre and Spottiswoode, London, 1965, p. 2919.