Reactions of Relevance to the Chemistry of Aminoglycoside Antibiotics. Part 7.† Conversion of Thiocarbonates into Deoxy-sugars

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Radical-initiated reduction of five- or six-membered ring thiocarbonates, followed by alkaline hydrolysis, affords a convenient synthesis of 2-, 3-, 4-, and 5-deoxy-sugars. For 5,6- and 4,6-thiocarbonates the regiospecificity of the reaction complements the recently developed synthesis of 6-deoxy-sugars by ring opening of the same thiocarbonates with methyl iodide. Applications in the synthesis of 2-deoxy-D-ribose and 2'-deoxyadenosine are described.

We recently reported [1] that the thiocarbonate ring in compounds like (1) was smoothly opened [2] by treatment with methyl iodide to furnish a 6-deoxy-6-iodo-sugar. Reduction of the latter, suitably with the Cr^{2+}–thiol reagent, followed by alkaline hydrolysis, gave a high yield of the 6-deoxy-sugar (2).

We also recently developed [3] the reduction of thiocarbonyl derivatives of secondary, but not primary, alcohols with tributyltin hydride to give smoothly the corresponding hydrocarbon. This reduction has a radical mechanism. The failure of the primary derivatives to fragment is due to the lesser stability of primary relative to secondary carbon radicals.[4]

With these conclusions in mind it is clear that the reduction of a thiocarbonate such as (1) by tributyltin hydride (see Scheme) should provide a convenient route to 5-deoxy-sugars. In the present paper [5] we show that

† Part 6, T. G. Back, D. H. R. Barton, and B. L. Rao, preceding paper.

[1] D. H. R. Barton and R. V. Stick, *J.C.S. Perkin I*, 1975, 177.

[2] See also F. N. Jones and S. Andreades, *J. Org. Chem.*, 1969, **34**, 3011; E. Vedejs and E. S. C. Wu, *ibid.*, 1974, **39**, 3641.

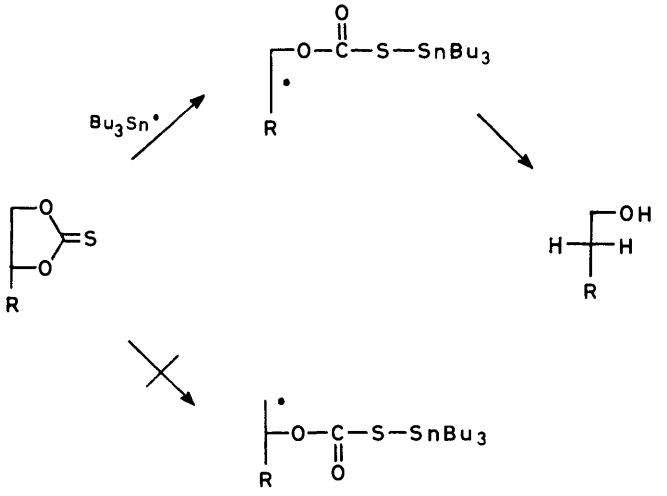
[3] D. H. R. Barton and S. W. McCombie, *J.C.S. Perkin I*, 1975, 1574.

[4] C. Walling, ' Free Radicals in Solution,' Wiley, New York, 1957; K. U. Ingold and B. P. Roberts, ' Free-radical Substitution Reactions,' Wiley–Interscience, New York, 1971.

[5] Preliminary communication, D. H. R. Barton, and R. Subramanian, *J.C.S. Chem. Comm.*, 1976, 867.

this is indeed the case. The reaction complements well the ring-opening reactions with methyl iodide.

Reaction of the thiocarbonate (1) with tributyltin hydride in toluene under reflux with addition of αα′-azoisobutyronitrile as initiator gave, after alkaline hydrolysis, the 5-deoxy-sugar (4) (67%). None of the isomeric 6-deoxy-sugar (2) was detected. An authentic sample of (4) was synthesised by a well established route.[6] The two sugars (2) and (4) were characterised as their crystalline 3,5-dinitrobenzoates [(3) and (5), respectively]. Unlike the other thiocarbonyl systems that we have studied [3] an initiator was needed for thiocarbonate reductions.



SCHEME

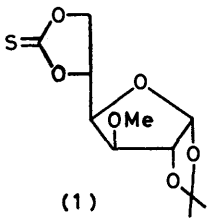
Similarly the known [7] 4,6-thiocarbonate (6) gave the 4-deoxy-sugar (7) (61%), characterised as the toluene-*p*-sulphonate [8] and also by oxidation with platinum oxide–oxygen to the acid (9). The latter was methylated with diazomethane to give the methyl ester (10).

Treatment of the thiocarbonate (6) with methyl iodide gave the known [1] 6-deoxy-6-iodo-compound (11), which on reduction by the Cr^{2+}–thiol procedure followed by alkaline hydrolysis gave in 90% yield the 6-deoxy-sugar (12).

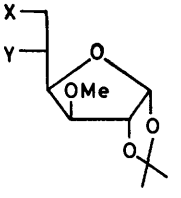
In both the foregoing examples of thiocarbonate reduction the thiocarbonate is formed from a glycol with one primary and one secondary hydroxy-group. As already discussed, the regioselectivity of the reaction is predictable. The same remark cannot be made about the reduction of a thiocarbonate based on two secondary hydroxy-groups. We examined, therefore, the reduction of the known [9] thiocarbonate (13). By the usual procedure this afforded the 3-deoxy-sugar (14a) [3] (60%) and the 2-deoxy-sugar (15a) [10] (30%) in high overall yield. These compounds were characterised as their acetates [11] (14b) and (15b), respectively.

Benzoylation of the deoxy-sugar (15a) gave the benzoate (15c). An authentic specimen of the latter was synthesised as follows. The benzylidene derivative (14c) was selectively benzoylated to give the monobenzoate (14d).[12] The latter was converted into its dithiocarbonate (14e) and reduced by the standard procedure [3] to give the authentic benzoate (15c) in high yield.

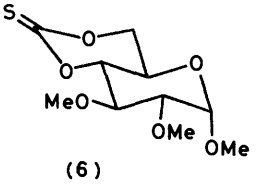
Alternatively, the diol thiocarbonate (13) was treated with methyl iodide to give a mixture of the iodo-derivatives (16) and (17) in high yield. Reduction with the Cr^{2+}–thiol reagent followed by alkaline hydrolysis gave



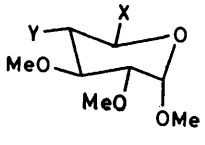
(1)



(2) X = H, Y = OH
(3) X = H, Y = 3,5-$(NO_2)_2C_6H_3\cdot CO_2$
(4) X = OH, Y = H
(5) X = 3,5-$(NO_2)_2C_6H_3\cdot CO_2$, Y = H



(6)



(7) X = $CH_2\cdot OH$, Y = H
(8) X = $CH_2\cdot OTs$, Y = H
(9) X = CO_2H, Y = H
(10) X = CO_2Me, Y = H
(11) X = CH_2I, Y = $MeS\cdot CO_2$
(12) X = Me, Y = OH

the mixture of deoxy-sugars (14a) and (15a) in the same high overall yield and in the same ratio as for the reduction with tributyltin hydride.

The benzylidene group was readily removed from the deoxy-sugar (15a) by mild acidic hydrolysis to give the triol (18).[13]

[6] E. J. Hedgley, O. Meresz, and W. G. Overend, *J. Chem. Soc.*, (*C*) 1967, 888; A. Zobacova, V. Hermankova, Z. Kejurtova, and J. Jary, *Coll. Czech. Chem. Comm.*, 1975, **40**, 3505.
[7] D. Trimmell, W. M. Doane, C. R. Russell, and C. E. Rist, *Carbohydrate Res.*, 1971, **17**, 319.
[8] N. K. Kochetkov and A. I. Usov, *Tetrahedron*, 1963, **19**, 973.
[9] E. I. Stout, W. M. Doane, B. S. Shasha, C. R. Russell, and C. E. Rist, *Carbohydrate Res.*, 1966, **3**, 354; E. I. Stout, W. M. Doane, and C. R. Russell, *ibid.*, 1972, **22**, 351.
[10] B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), 1966, 398.
[11] B. Coxon, *Tetrahedron*, 1965, **21**, 3481.
[12] R. W. Jeanloz and D. A. Jeanloz, *J. Amer. Chem. Soc.*, 1957, **79**, 2579.
[13] R. U. Lemieux and S. Levine, *Canad. J. Chem.*, 1962, **40**, 1926.

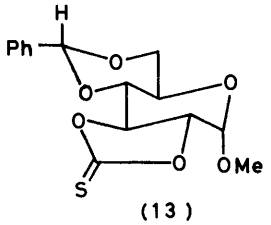
We then turned our attention to the synthesis of 2-deoxy-D-ribose from D-ribose itself. The known methyl β-D-ribofuranoside (19) was converted into the non-crystalline thiocarbonate (20a) in the usual way. Acetylation gave the crystalline acetate (20b). Reduction of the acetate in the usual way [3] followed by alkaline hydrolysis and reacetylation gave the known [14] 2-deoxy-derivative (24) (55% isolated) and 3-deoxy-derivative (23) (25% isolated). The mixed deoxy-derivatives were in the ratio 60 : 40 ($[\alpha]_D$).

Alternatively, the thiocarbonate (20b) was treated with methyl iodide to give a mixture of the iodides (21) and (22). Without separation the mixture was reduced with the Cr^{2+}–thiol reagent to give, after alkaline hydrolysis and reacetylation, the deoxy-sugars (23) and (24) in essentially the same yields as above.

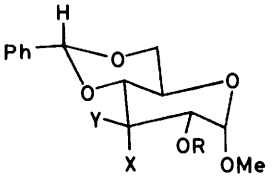
We have also examined the applicability of thiocarbonates in the synthesis of 2′- and 3′-deoxyadenosine. The known [15] thiocarbonate (26a) was prepared from adenosine (25). Acetylation gave the diacetate (26b), which on reduction with tributyltin hydride in dimethylacetamide followed by alkaline hydrolysis and reacetylation afforded the triacetate (27) [16] (60%) and the isomeric triacetate (28) (29%). Mild acidic hydrolysis afforded 2′-deoxyadenosine [16,17] (29) and 3′-deoxyadenosine [18] (30).

In the course of this work we also examined the isomerisation of the *OO*-thiocarbonates (1) and (6) to the *OS*-thiocarbonates (31) and (32), respectively. The latter reaction was already known.[7]

The regiospecificity observed in the radical opening of 5,6- and 4,6-thiocarbonate rings is in agreement with the view [19] that the radical bromination of benzylidene acetals affords first a bromo-derivative, which then undergoes ionic ring opening by bromide anion displacement at C-6.

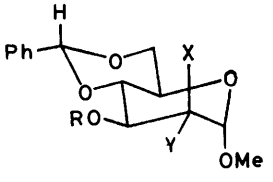


(13)



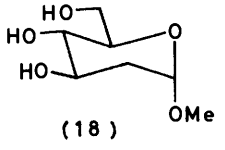
(14) a; R = X = Y = H
b; R = Ac, X = Y = H
c; R = X = H, Y = OH
d; R = X = H, Y = CO_2Ph
e; R = CS_2Me, X = H, Y = CO_2Ph

(16) R = COSMe, X = I, Y = H

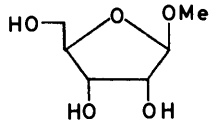


(15) a; R = X = Y = H
b; R = Ac, X = Y = H
c; R = COPh, X = Y = H

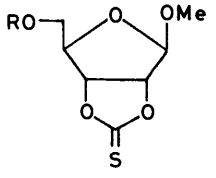
(17) R = COSMe X = I, Y = H



(18)



(19)



(20) a; R = H
b; R = Ac

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. ^1H N.m.r. spectra were recorded for solutions in $CDCl_3$ (unless otherwise stated) with tetramethylsilane as internal standard on a Varian T-60 or HA-100 instrument. U.v. spectra were determined for ethanolic solutions, and optical rotations for solutions in chloroform unless otherwise stated. All solvents were purified by standard techniques.

The phrase ' normal work-up ' refers to dilution with water, extraction with dichloromethane or diethyl ether, washing with dilute acid or base, water, drying (over sodium or magnesium sulphate), and evaporation under reduced pressure. Column chromatography was performed on silica (eluant light petroleum–diethyl ether). Light petroleum refers to the redistilled fraction with b.p. 40—60 °C.

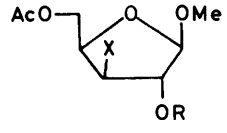
Tributyltin hydride was made by reducing tributyltin chloride with lithium aluminium hydride in ether.[20]

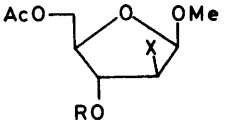
5-Deoxy-1,2-O-isopropylidene-3-O-methyl-D-xylohexofuranose (4).—The thiocarbonate [1] (1) (0.276 g), tributyltin hydride (0.583 g), and αα′-azoisobutyronitrile (0.015 g) in

[14] C. D. Anderson, L. Goodman, and B. R. Baker, *J. Amer. Chem. Soc.*, 1959, **81**, 898.
[15] G. L. Tong, W. W. Lee, and L. Goodman, *J. Org. Chem.*, 1965, **30**, 2854.
[16] M. J. Robins and R. K. Robins, *J. Amer. Chem. Soc.*, 1965, **87**, 4934.
[17] R. H. Iwamato, E. M. Acton, and L. Goodman, *J. Org. Chem.*, 1962, **27**, 3949.
[18] D. H. Murray and J. Prokop, *J. Pharm. Sci.*, 1965, **54**, 1468.
[19] S. Hanessian and N. R. Plessas, *J. Org. Chem.*, 1969, **34**, 1035, 1045, 1053.
[20] H. G. Kuivila and O. F. Beumel, *J. Amer. Chem. Soc.*, 1961, **83**, 1246.

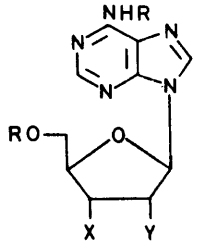
dry toluene (15 ml) were added dropwise to refluxing toluene (20 ml) under argon, during 45 min. Subsequent additions of the tin hydride (2 × 0.292 g) together with the radical initiator (2 × 0.01 g) after 2 and 4 was necessary. The reaction was complete in 6 h. The solution was treated with aqueous sodium hydroxide (10%; 10 ml) at *ca.* 40 °C for 12 h. The organic layer was separated and the aqueous layer re-extracted with ether. The combined organic extract was washed repeatedly with water until free of base and dried (Na_2SO_4). Concentration to a syrup, followed by chromatographic elution through silica gel with light petroleum–ether mixtures of increasing polarity, gave *compound* (4) (0.124 g, 57%) as an oil, $[\alpha]_D^{22}$ −49° (*c* 2.1), $\nu_{max.}$ (Nujol) 3 590, 1 380, 1 370, 1 240, and 900 cm^{-1} (Found: C, 55.2; H, 8.15. $C_{10}H_{18}O_5$ requires C, 55.0; H, 8.25%).

5-*Deoxy*-6-O-(3,5-*dinitrobenzoyl*)-1,2-O-*isopropylidene*-3-O-*methyl*-α-D-*xylohexofuranose* (5).—The 5-deoxy-sugar (2)

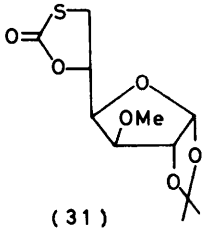




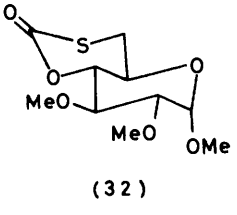
(21) R = COSMe, X = I (22) R = COSMe, X = I
(23) R = Ac, X = H (24) R = Ac, X = H



(25) R = H, X = Y = OH
(26) a; R = H, XY = C:S
b; R = Ac, XY = C:S
(27) R = Ac, X = OAc, Y = H
(28) R = Ac, X = H, Y = OAc
(29) R = H, X = OH, Y = H
(30) R = X = H, Y = OH



(31)



(32)

(0.08 g) in dry pyridine (5 ml) was heated under reflux with 3,5-dinitrobenzoyl chloride (0.20 g) for 12 h. The solvents were removed *in vacuo*. Chromatographic elution, through silica, with dichloromethane–methanol (2 : 1), gave the crystalline 3,5-*dinitrobenzoate* (5) (0.093 g, 60%), m.p. 81—83° (from dichloromethane–methanol), $[\alpha]_D^{22}$ −12° (*c* 0.9 in MeOH), $\nu_{max.}$ (Nujol) 1 550, 1 265, and 790 cm^{-1} (Found: C, 49.5; H, 4.7; N, 6.55. $C_{17}H_{20}N_2O_{10}$ requires C, 49.5; H, 4.85; N, 6.8%).

The 6-deoxy-sugar (2) [1] (0.104 g) similarly gave 6-*deoxy*-5-O-(3,5-*dinitrobenzoyl*)-1,2-O-*isopropylidene*-3-O-*methyl*-α-D-*xylohexofuranose* (3) (0.123, 58%), m.p. 71—73° (from methanol–ether), $[\alpha]_D^{22}$ −19° (*c* 1.1 in MeOH), $\nu_{max.}$ (Nujol) 1 570, 1 240, 1 100, and 765 cm^{-1} (Found: C, 49.4; H, 4.65; N, 6.5. $C_{17}H_{20}N_2O_{10}$ requires C, 49.5; H, 4.85; N, 6.8%). Mixed m.p.s of the above two derivatives were depressed.

Methyl 4-*Deoxy*-2,3-*di*-O-*methyl*-α-D-*glucopyranoside* (7).—Methyl 2,3-di-*O*-methyl-α-D-glucopyranoside 4,6-thiocarbonate (6) [7] (0.264 g), tributyltin hydride (0.582 g), and αα′-azoisobutyronitrile (0.015 g), in dry toluene (20 ml), were added dropwise to refluxing toluene (20 ml) under argon during 45 min. Subsequent additions of the tin hydride (2 × 0.292 g) together with the azoisobutyronitrile (2 × 0.01 g) after 2 and 4 h was necessary. The reaction was complete in 6 h. The solution was hydrolysed and worked up as for compound (4) to give *compound* (7) (0.125 g, 61%) as an oil, $[\alpha]_D^{22}$ +70° (*c* 1.0 in MeOH), $\nu_{max.}$ (Nujol) 3 605 cm^{-1} (OH) (Found: C, 52.2; H, 8.45. $C_9H_{18}O_5$ requires C, 52.4; H, 8.75%).

The 4-deoxy-sugar (7) (0.10 g) was dissolved in dry pyridine (3 ml) and treated with toluene-*p*-sulphonyl chloride (0.05 g) at room temperature for 8 h. Normal work-up and chromatography on silica gel gave the known toluene-*p*-sulphonate (8) (0.123 g, 70%), $[\alpha]_D^{22}$ +94.5° (*c* 0.9 in $CHCl_3$) (lit.,[8] $[\alpha]_D$ +93°).

Methyl Ester (10) *of the* 4-*Deoxy-sugar* (7).—The 4-deoxy-sugar (7) (0.10 g) and platinum oxide (0.02 g) in dichloromethane (10 ml) were stirred vigorously while oxygen was bubbled in. After 12 h, the mixture was filtered and washed with methanol–water (1 : 1). The combined filtrate, on concentration, gave the crude acid (9). This in dry ether (25 ml) was treated with an excess of diazomethane. Work-up, followed by chromatography, gave the *methyl ester* (10) (0.046 g, 40%), $[\alpha]_D^{22}$ +59° (*c* 1.07), $\nu_{max.}$ (Nujol) 1 775 and 1 260 cm^{-1} (Found: C, 51.0; H, 7.4. $C_{10}H_{18}O_6$ requires C, 51.3; H, 7.65%).

Methyl 6-*Deoxy*-2,3-*di*-O-*methyl*-α-D-*glucopyranoside* (12).—The deoxy-iodo-derivative (11) [1] (0.110 g) in dry dimethylformamide (1 ml) and butane-1-thiol (0.15 ml) with chromium(II) acetate [21] (0.15 g) added was stirred (12 h; 60 °C) under nitrogen. The mixture was evaporated and the residue triturated with ether. Evaporation left an oil which in methanol (2 ml) was treated with sodium methoxide (0.03 g) in methanol (2 ml) and left at room temperature (12 h). Acetic acid was added to neutrality. Extraction into ether, concentration, and chromatography gave *compound* (12) (0.04 g, 90%), $[\alpha]_D^{22}$ +119° (*c* 1.2), $\nu_{max.}$ (Nujol) 3 600 cm^{-1} (OH) (Found: C, 52.25; H, 8.35. $C_9H_{18}O_5$ requires C, 52.4; H, 8.75%).

Methyl 4,6-O-*Benzylidene*-3- *and* 2-*deoxy*-α-D-*glucopyranosides* (14a) *and* (15a) *by Reduction of the* 2,3-*Thiocarbonate* (13).—Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-thiocarbonate (13) [9] (0.325 g), tributyltin hydride (0.582 g), and azoisobutyronitrile (0.015 g), in dry toluene (15 ml), were added dropwise during 45 min to refluxing toluene (20 ml) under argon. Subsequent additions of tin hydride (2 × 0.291 g) together with azoisobutyronitrile (2 × 0.01 g) after every 2 and 4 h were required to complete the reaction (7 h). Work-up as for compound (2), followed by chromatography, gave the 3-deoxy-sugar (14a) (0.159 g, 60%), m.p. 181—183°, $[\alpha]_D^{22}$ +122° (*c* 1.0 in MeOH) (lit.,[3] m.p. 184—185°, $[\alpha]_D$ +123°); and the 2-deoxy-sugar (15a) (0.079 g, 30%), m.p. 159—160° (from light petroleum–ethyl acetate); $[\alpha]_D^{22}$ +82° (*c* 1.0 in Me_2CO) {lit.,[10] m.p. 151—152°, $[\alpha]_D$ +90° (*c* 1.0 in Me_2CO)}.

Methyl 2-O-*Acetyl*-3-*deoxy- and* 3-O-*Acetyl*-2-*deoxy*-4,6-O-*benzylidene*-α-D-*glucopyranosides* (14b) *and* (15b).—The

[21] D. H. R. Barton and N. K. Basu, *Tetrahedron Letters*, 1964, 3151; D. H. R. Barton, N. K. Basu, R. H. Hesse, F. S. Morehouse, and M. M. Pechet, *J. Amer. Chem. Soc.*, 1966, **88**, 3016.

mixture (see above) of 3-deoxy- and 2-deoxy-sugars (14a and b) (0.266 g; *ca.* 60% of 3- and 40% of 2-deoxy) in dry pyridine (5 ml) and an excess of acetic anhydride (2 ml) was stirred at room temperature for 8 h. Dilution with cold water and normal work-up followed by chromatography on silica, gave the *3-deoxy-2-acetate* (14b) (0.175 g, 65%), m.p. 134—136° (from dichloromethane–methanol), $[\alpha]_D^{22}$ +69.0° (*c* 1.3), $\nu_{max.}$ (CCl_4) 1 370 and 1 230 cm^{-1} (Found: C, 62.8; H, 6.25. $C_{16}H_{20}O_6$ requires C, 62.6; H, 6.5%); and the 2-deoxy-3-acetate (15b) [11] (0.098 g, 30%), m.p. 124—125°, $[\alpha]_D^{22}$ +75° (*c* 1.1) {lit.,[11] m.p. 130—131°, $[\alpha]_D^{25}$ +79.1° (*c* 1.28)}.

Methyl 3-O-*Benzoyl*-4,6-O-*benzylidene*-2-O-[(*methylthio*)*thiocarbonyl*]-α-D-*glucopyranoside* (14e).—The known [12] 3-benzoate (14d) (2.0 g), imidazole (0.01 g), and sodium hydride (0.120 g) in dry tetrahydrofuran (50 ml) were stirred for 6 h at room temperature. Carbon disulphide (3 ml) and methyl iodide (2 ml) were added successively at intervals of 30 min. The mixture was worked up in the usual way. Elution with dichloromethane on a silica column gave the 2-(*methyl dithiocarbonate*) (14e) (1.8 g). The product was crystallised from light petroleum; m.p. 173—176°, $[\alpha]_D^{21}$ +68° (*c* 1.09), $\lambda_{max.}$ 280 (ε 3 220) and 220 nm (204) (Found: C, 58.1; H, 5.25; S, 13.1. $C_{23}H_{24}O_7S_2$ requires C, 57.9; H, 5.05; S, 13.45%).

Methyl 3-O-*Benzoyl*-4,6-O-*benzylidene*-2-*deoxy*-α-D-*glucopyranoside* (15c).—The 2-(methyl dithiocarbonate) (14e) (0.460 g), tributyltin hydride (0.582 g), and azoisobutyronitrile (0.01 g) in dry toluene (15 ml) were added dropwise to refluxing toluene (20 ml) under argon during 45 min. Addition of the tin hydride (0.291 g) and the radical initiator (0.01 g) after 2 h was necessary. The reaction, which was complete in 5 h, was worked up in the usual way. Chromatography on silica (elution with light petroleum) gave the *2-deoxy-3-benzoate* (15c) (0.330 g), m.p. 92—96°, $[\alpha]_D^{22}$ +8° (*c* 0.06) (Found: C, 68.0; H, 5.8. $C_{21}H_{22}O_6$ requires C, 68.1; H, 5.95%).

The 2-deoxy-sugar (15a) (0.100 g), obtained by reduction of the thiocarbonate (13), in dry pyridine (1 ml) and benzoyl chloride (0.4 ml) was kept at 5 °C overnight. Work-up in the usual way gave the 2-deoxy-sugar benzoate (15c), identical with the benzoate described above.

Methyl 4,6-O-*Benzylidene*-3- *and* 2-*deoxy*-α-D-*glucopyranosides* (14a) *and* (15a) *by Reaction of Methyl Iodide with the* 2,3-*Thiocarbonate* (13).—The 2,3-thiocarbonate (13) [9] (0.324 g) was dissolved in methyl iodide (1.5 ml) and heated (80 °C) in a sealed tube for 2 h. Normal work-up, washing with thiosulphate, *etc.*, gave a mixture of the deoxy-iodo-derivatives (16) and (17) (0.300 g). This mixture in dimethyl formamide (4 ml) and butane-1-thiol (0.4 ml) with added chromium(II) acetate (0.5 g) was stirred (12 h; 70 °C) under nitrogen and evaporated; the residue was triturated with ether. Evaporation left a solid residue which in methanol (5 ml) was treated with sodium methoxide (0.2 g) in methanol (5 ml) at room temperature for 12 h. Acetic acid was added to neutrality and the product was extracted into ether. Evaporation gave a mixture of 3- and 2-deoxy-derivatives (14a) and (15a), which were separated as their acetates (14b) (50%) and (15b) (23%), characterised earlier.

The *2-Deoxy-glycoside* (18).—Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (15a) (0.2 g) in acetone (10 ml) was stirred with sulphuric acid (4N; 6 ml) at room temperature, until starting material had disappeared (48 h). The mixture was neutralised with aqueous sodium hydrogen carbonate and filtered. The filtrate was evaporated *in vacuo* and the residue crystallised from methanol–water to give the 2-deoxy-glycoside (18) (0.08, 60%), m.p. 90—91°, $[\alpha]_D^{22}$ +140° (*c* 1.0 in MeOH) {lit.,[13] m.p. 93.5—94.5, $[\alpha]_D$ +143° (*c* 0.9 in MeOH)}.

Methyl 5-O-*Acetyl*-β-D-*ribofuranoside* 2,3-*Thiocarbonate* (20b).—Methyl β-D-ribofuranoside (19) [22] (0.75 g) in dry tetrahydrofuran (10 ml) and thiocarbonyldi-imidazole [23] (0.690 g) in dry tetrahydrofuran (10 ml) were mixed and stirred (60 °C; 4 h). Normal work-up gave a syrup (20a) which exhibited strong u.v. absorption at 264 nm (C:S). This syrup (0.70 g) in dry pyridine (5 ml) was treated with acetic anhydride (0.3 ml) at room temperature for 12 h. The mixture was poured into crushed ice and extracted with ether. The ether layer was washed with water, dried (Na_2SO_4), concentrated and passed through a column of silica gel. Elution with light petroleum–ether (1 : 1) gave compound (20b) (0.510 g, 51%), m.p. 104—106° (from ethyl acetate–light petroleum), $[\alpha]_D^{22}$ −60° (*c* 0.59), M^+ 248, $\nu_{max.}$ (CCl_4) 1 250 cm^{-1} (C:S), $\lambda_{max.}$ 239 nm (ε 16 600), δ ($CDCl_3$) 2.05 (3 H, s, OAc), 3.20 (3 H, s, OMe), and 5.15—5.25 (1 H, d, H-1).

Methyl 2,5-*Di*-O-*acetyl*-3-*deoxy- and* 3,5-*Di*-O-*acetyl*-2-*deoxy*-β-D-*ribofuranosides* (23) *and* (24) *by Reduction of the Thiocarbonate* (20b).—The thiocarbonate (20b) (0.248 g), tributyltin hydride (0.600 g), and azoisobutyronitrile (0.012 g) in dry toluene (10 ml) were added dropwise to refluxing toluene (20 ml) under argon, druing 40 min. Additions of the tin hydride (2 × 0.292 g) together with the radical initiator (2 × 0.01 g) after 2 and 4 h were necessary. The reaction was complete in 6.5 h, after which the product was hydrolysed and worked up as for the product(5). The crude product (0.230 g) in pyridine (5 ml) and acetic anhydride (1.2 ml) was left for 12 h at room temperature. Normal work-up followed by chromatography on silica gel (elution with hexane–ether mixtures of increasing polarity) gave the 2,5-di-*O*-acetyl-3-deoxyribofuranoside (23) (0.058 g, 25%), b.p. 58—64° at 0.2 mmHg $[\alpha]_D^{22}$ −34° (*c* 1.1 in $CHCl_3$) {lit.,[14] b.p. 50—60° at 2.0 mmHg, $[\alpha]_D$ −37° (*c* 2.0 in $CHCl_3$)} and the 3,5-di-*O*-acetyl-2-deoxy-ribofuranoside (24) (0.138 g, 55%), b.p. 55—61° at 0.15 mmHg, $[\alpha]_D^{22}$ −54° (*c* 1.0) {lit.,[14] b.p. 60—70° at 2 × 10^{-3} mmHg, $[\alpha]_D$ −55° (*c* 1.0 in $CHCl_3$)}.

Methyl 2,5-*Di*-O-3-*deoxy- and* 3,5-*Di*-O-*acetyl*-2-*deoxy*-β-D-*ribofuranosides* (23) *and* (24) *by Reaction of Methyl Iodide with the Thiocarbonate* (20b).—The thiocarbonate (20b) (0.248 g) in acetonitrile (10 ml) and methyl iodide (3 ml) was stirred (80 °C) for 12 h. Normal work-up, thiosulphate washings, *etc.* gave a mixture of the deoxy-iodides (21) and (22) (0.310 g), $\lambda_{max.}$ 210 (ε 4 700) and 252 nm (625), $\nu_{max.}$ (Nujol) 1 715 cm^{-1} (C:O).

To the deoxy-iodo-derivatives (21) and (22) (0.300 g) in dry dimethylformamide (2 ml) and butane-1-thiol (0.2 ml) was added chromium(II) acetate (0.350 g). The mixture was stirred (12 h; 70 °C) under nitrogen and evaporated, and the residue was triturated with ether. Concentration of the ether layer gave an oil (0.265 g) which in methanol (2 ml) was treated with sodium methoxide (0.150 g) in methanol (1 ml) at room temperature (20 h). Normal work-up gave an oil which, in dry pyridine (1.5 ml) and acetic anhydride (0.6 ml), was left at room temperature (12 h). Subsequent work-up, followed by chromatography, gave the 2,5-di-*O*-acetyl-3-deoxy-compound (23) (0.06 g,

[22] R. Baker and H. G. Fletcher, jun. *J. Org. Chem.*, 1961, **26**, 4605.

[23] T. J. Pullukat and G. Urry, *Tetrahedron Letters*, 1967, 1953.

24%) and the 3,5-di-*O*-acetyl-2-deoxy-compound (24) (0.116 g, 49%), identical with those obtained earlier.

6-*Acetamido*-9-(5-0-*acetyl*-β-D-*ribofuranosyl*)*purine* (26b). —Adenosine (25) was converted into the thiocarbonate (26a).[15] The thiocarbonate (26a) (0.4 g) in dry pyridine (15 ml) and acetic anhydride (0.6 ml) was maintained at 40 °C for 8 h. The solvent was removed *in vacuo* at 60 °C (bath temperature). The resulting amorphous solid was triturated with ether and extracted into ether. The ether layer was washed with water, dried (Na_2SO_4) and concentrated to dryness. The resulting oil crystallised from ethyl acetate to give *compound* (26b) (0.42 g, 80%), m.p. 140—143°, $[\alpha]_D^{22}$ −27.5° (*c* 0.8 in MeOH), $\lambda_{max.}$ 243 nm (ε 16 350) (Found: C, 45.6; H, 3.9; N, 17.7; S, 8.5. $C_{15}H_{15}N_5O_6S$ requires C, 45.8; H, 3.8; N, 17.8; S, 8.15%).

6-*Acetamido*-9-(3,5-*di*-O-*acetyl*-2-*deoxy*-β-D-*ribofuranosyl*)-*purine* (27) *and* 6-*Acetamido*-9-(2,5-*di*-O-*acetyl*-3-*deoxy*-β-D-*ribofuranosyl*)*purine* (28).—The thiocarbonate (26b) (0.393 g), tributyltin hydride (0.600 g), and azoisobutyronitrile (0.02 g) in dry dimethylacetamide (20 ml) were added dropwise during 45 min to refluxing dimethylacetamide (10 ml) under argon. Further additions of the tin hydride (2 × 0.291 g) together with azoisobutyronitrile (2 × 0.01 g) after 2 and 4 h was necessary to complete the reaction. The solvents were removed *in vacuo* after a total of 6 h and the crude product was treated with methanolic sodium hydroxide (10%; 10 ml) at 40 °C for 12 h. The solution was neutralised by careful addition of N-hydrochloric acid (to pH 7) and the solvent removed *in vacuo*. The solid residue (0.330 g) was dissolved in dry pyridine (10 ml), an excess of acetic anhydride (1.5 ml) was added, and the mixture was left at 30—40 °C for 12 h. Normal work-up followed by elution with dichloromethane–methanol mixtures of increasing polarity on a silica column gave the 2′-deoxy-compound (27) (0.191 g, 60%), m.p. 123—127° (from ethyl acetate) (lit.,[16] 125—127°) and the 3′-*deoxy-compound* (28) (0.095 g, 29%), m.p. 116—119° (from ethyl acetate), $[\alpha]_D^{22}$ −18° (*c* 0.6 in MeOH), $\nu_{max.}$ (Nujol) 1 710, 1 540, 1 210, and 780 cm^{-1} (Found: C, 50.7; H, 5.0; N, 18.7. $C_{16}H_{19}N_5O_6$ requires C, 50.95; H, 5.05; N, 18.55%).

2′- *and* 3′-*Deoxyadenosines* (29) *and* (30).—The 2′-deoxy-triacetate (27) (0.200 g) in methanol (15 ml) was treated with N-hydrochloric acid (10 ml) for 24 h at room temperature. The solution was neutralised with sodium hydrogen carbonate (2% solution), filtered, and concentrated *in vacuo*. The residue was recrystallised from methanol–water to give 2′-deoxyadenosine (29) (0.121 g, 80%), m.p. 183—188°, $[\alpha]_D^{22}$ −25° (*c* 0.4 in H_2O) (lit.,[16] m.p. 187—188°, $[\alpha]_D$ −25°). Similarly, the 3′-deoxy-triacetate (28) (0.200 g) gave 3′-deoxyadenosine (30) (0.128 g), m.p. 223—229°, $[\alpha]_D^{22}$ −43° (*c* 0.7 in H_2O) (lit.,[18] m.p. 222—226°, $[\alpha]_D$ −47°).

Isomerisation of the OO-*Thiocarbonate* (1) *to the* OS-*Thiocarbonate* (31) *by Potassium Iodide*.—The 5,6-thiocarbonate (1) (0.138 g) in acetonitrile (10 ml) was refluxed with potassium iodide (0.400 g) for 16 h. The mixture was filtered, the filtrate concentrated to dryness, and the residue chromatographed on silica. Elution with light petroleum–ether (1 : 2) gave the OS-*thiocarbonate* (31) in almost quantitative yield, m.p. 97—98° (from dichloromethane–methanol), $\nu_{max.}$ (Nujol) 1 780 cm^{-1} (Found: C, 47.65; H, 5.8; S, 11.7. $C_{11}H_{16}O_6S$ requires C, 47.8; H, 5.85; S, 11.6%).

Isomerisation of the OO-*Thiocarbonate* (6) *to the* OS-*Thiocarbonate* (32) *by Potassium Iodide*.—Methyl 2,3-di-*O*-methyl-α-D-glucopyranoside 4,6-thiocarbonate (6) (0.132 g) in acetonitrile (10 ml) was refluxed with potassium iodide (0.415 g) for 12 h. Work-up as above gave the *OS*-thiocarbonate (32) in quantitative yield, m.p. 126—128°, $[\alpha]_D^{22}$ +26° (lit.,[7] m.p. 127—128°, $[\alpha]_D$ +26.8°). Use of tetrabutylammonium iodide instead of potassium iodide gave the same result.

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