C-5 Bromination of Some Glucopyranuronic Acid Derivatives

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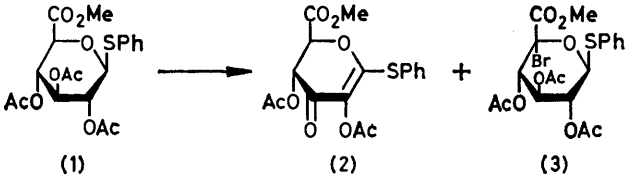
Treatment of methyl (phenyl tri-*O*-acetyl-1-thio-β-D-glucopyranosid)uronate with *N*-bromosuccinimide gave, as well as the expected hex-1-enopyranosid-3-ulose, the product of bromination at C-5. Methyl tetra-*O*-acetyl-β-D-glucopyranuronate on similar treatment gave a 5-*C*-bromo-derivative, in good yield. Methyl tri-*O*-acetyl-2,6-anhydro-L-gulonate afforded the 2-bromo-analogue which is the known glycosyl bromide of a derivative of L-*xylo*-hexulosonic acid and offers access to compounds in the L-ascorbic acid series and to the vitamin itself.

In the preceding paper [1] we report the light-promoted conversion of phenyl 1-thiohexopyranoside esters into phenyl 1-thiohex-1-enopyranosid-3-ulose esters by treatment with *N*-bromosuccinimide in refluxing carbon tetrachloride. During experiments designed to investigate the scope of this reaction a ring *C*-bromo-product was obtained; we now describe this novel compound and related bromo-derivatives, one of which can be converted into L-ascorbic acid.

Treatment of methyl (phenyl tri-*O*-acetyl-1-thio-β-D-glucopyranosid)uronate (1) with *N*-bromosuccinimide in refluxing carbon tetrachloride under a heat lamp gave two products (t.l.c.), which were isolated by preparative t.l.c. The major product, obtained in 43% yield as an oil, gave an n.m.r. spectrum consistent with that expected for the enone (2).[1] In particular, H-1, -2, and -3 of the precursor had been removed and H-4 of the product resonated as a doublet at the same field as the corresponding proton of the enone derived from the corresponding glucoside. The value of $J_{4,5}$ (5.5 Hz), however, was markedly less than that for the hexoside analogue (12 Hz); this is attributed to a conformational change, conceivably brought about by an attractive



interaction between the carbonyl oxygen atom bonded to C-6 and the carbonyl carbon atom at C-3. It is unlikely to be a result only of the change in electronegativity [2] of the substituents at C-5. The acetyl groups resonated at δ 2.08 and 2.18, indicating that the latter is part of a vinylic acetoxy-group.[1] Conceivably the sample contained small proportions of the 2-*O*-bromoacetyl analogue,[1] but this could not be confirmed

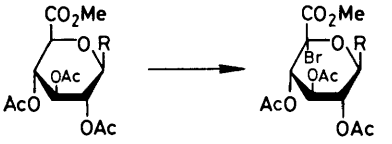
[1] R. J. Ferrier and R. H. Furneaux, preceding paper.
[2] K. L. Williamson, *J. Amer. Chem. Soc.*, 1963, **85**, 516; P. Laszlo and P. von R. Schleyer, *ibid.*, p. 2709.

by n.m.r. spectroscopy since the bromomethyl signal could have been masked by the methoxy-resonance. Integration of this resonance, however, showed that the bromoacetate was not present to an extent greater than 15%.

The second product (3) was isolated crystalline in 12% yield and was shown by elemental analysis to be a bromination product of the starting material. ^{1}H N.m.r. spectroscopy (60 MHz) confirmed this observation and indicated that substitution had occurred at C-5. The spectrum of the thioglycoside (1) was in keeping with those for related β-glucuronoside methyl esters:[3] the resonances for H-1—4 were unresolved within the range δ 4.6—5.4 (lit.,[3] 4.5—5.4), and H-5 resonated as an isolated doublet showing virtual coupling[3] at δ 4.10 ($J_{4,5}$ 10 Hz) (lit.,[3] 4.0—4.18; $J_{4,5}$ 10 Hz). In the spectrum of the bromo-derivative (3) the H-1—4 resonances were at δ 4.8—5.7, the CO_2Me resonance had also moved slightly downfield, from δ 3.73 to 3.80, and the OAc resonances were unaltered. The major feature was the absence of the H-5 resonance, and so structure (3) is assigned, the *R*-configuration following from optical rotational evidence discussed later.

When compound (1) was treated with *N*-bromosuccinimide in the dark no reaction occurred; therefore it appears that both the abstraction of H-1 which initiates the formation of the enone (2) and the abstraction of H-5 leading to the bromo-derivative (3) are homolytic processes with the methoxycarbonyl group providing stabilisation of a radical at C-5 competitively with the stabilisation provided at C-1 by the phenylthio-group.[1]

material (4) was fully resolved, showing doublets for H-1 (δ 5.90) and H-5 (4.31), triplets for H-3 and -4 (5.44 and 5.35, respectively) and a quartet for H-2 (5.24); ($J_{1,2}$ 8.2, $J_{2,3} = J_{3,4} = J_{4,5} = 9.7$ Hz). Likewise compounds (5) gave a fully resolves spectrum, but this was devoid of the resonance for H-5. The resonances for



(4) R = OAc (5) R = OAc
(7) R = H (8) R = H

H-1 and -4 were now doublets (δ 6.27 and 5.32, respectively) and those for H-2 and -3 triplets (5.22 and 5.53, respectively) ($J_{1,2}$ 9.0 Hz, $J_{2,3} = J_{3,4} = 10.0$ Hz). Since both an axial bromine atom and an axial methoxycarbonyl group at C-5 might be expected to deshield H-1 and -3,[5] the observed deshieldings of 0.37 and 0.09 p.p.m. cannot be used to assist with configurational assignment at C-5. H-2 and -4 are very slightly shielded (0.02 and 0.03 p.p.m.) following the bromination.

In the Table the ^{13}C chemical shifts are given for compounds (4) and (5), and are compared with those of penta-*O*-acetyl-β-D-glucopyranose.[6] Relative to the penta-acetate, the uronate derivative (4) shows a C-6 carbonyl resonance at 166.9 p.p.m. in place of the C-6 resonance at 61.6 p.p.m., and a methoxy-resonance at 52.9 p.p.m. in place of an acetyl resonance. Like that of the reference compound, C-1 of compound (4) resonated

^{13}C N.m.r. chemical shifts of compound (4), penta-*O*-acetyl-β-D-glucopyranose (PAG), and compound (5) (solvent $CDCl_3$; shifts downfield from internal tetramethylsilane)

Compound	C=O	C-1	C-2—5 [a]	C-6	OMe	CMe
(4)	169.8, 169.4, 169.1, 168.8	91.4	73.0, 71.8, 70.2, 69.0	166.9	52.9	20.7, 20.5
PAG [b]	170.1, 169.6, 169.2, 169.0, 168.7	91.6	70.3, 72.6, 67.9, 72.6	61.6		20.2, 20.1
(5)	169.5, 169.0, 168.9, 168.1	90.6	89.2, 70.8, 69.9, 69.3	164.2	54.1	20.5, 20.4

[a] Not individually assigned for compounds (4) and (5). [b] Converted from the CS_2 scale [$\Delta\delta$ ($Me_4Si - CS_2$) = 192.8 p.p.m.] (see ref. 7, page 23).

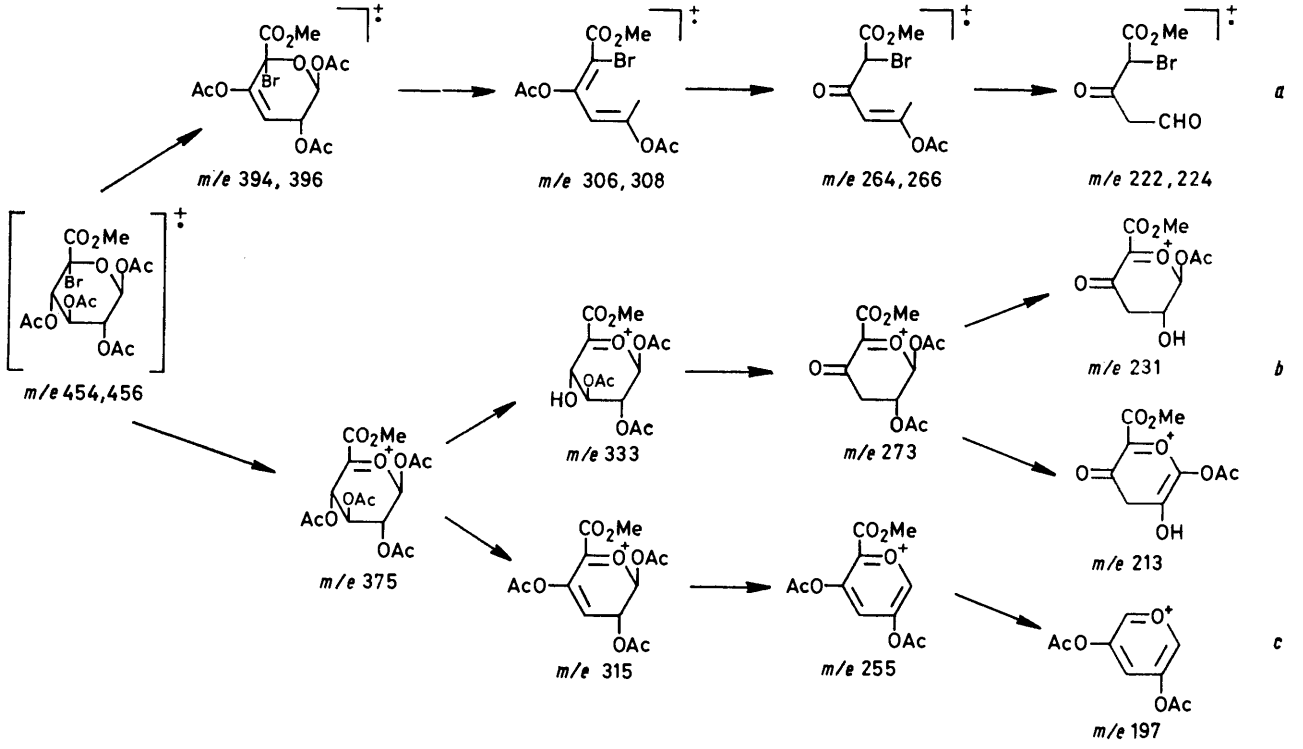
Radical brominations α to ester carbonyl groups are known with simple compounds,[4] and the ring oxygen atom in the glycoside (1) further assists the process observed at C-5 (as well as at C-1). It seemed probable that the C-5 bromination would be relatively favoured in uronate derivatives lacking a thio-substituent at C-1, and therefore methyl tetra-*O*-acetyl-β-D-glucopyranuronate (4) was tested. Again no reaction occurred when *N*-bromosuccinimide was used in the dark, but in the presence of benzoyl peroxide or bright light a single product (5) was readily formed and was isolated crystalline in 68% yield from the light-induced reaction. Analysis showed it to be a monobrominated compound and ^{1}H n.m.r. spectroscopy again revealed that H-5 had been replaced. The 270 MHz spectrum of the starting

about 20 p.p.m. downfield from the other ring carbon atoms, which gave four well resolved signals, almost equally spaced and with intensities almost equal to each other and to that of C-1. In the spectrum of the bromo-derivative (5) the one substantial change was a deshielding by about 20 p.p.m. of one of the four upfield ring carbon atoms, so that its signal became close to that of C-1, which was affected by only 0.8 p.p.m. When the ^{13}C n.m.r. experiment was repeated using single-frequency off-resonance decoupling rather than general proton decoupling, the carbon atom which had undergone deshielding on bromination gave an unaltered signal, confirming that it was the fully substituted C-5. Concurrently, the C-1—4 singlets became doublets and the

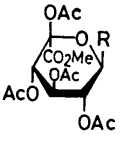
[3] M. Matsui and M. Okada, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 2129; 1972, **20**, 1033.
[4] N. P. Buu-Hoï and P. Demerseman, *J. Org. Chem.*, 1953, **18**, 649.
[5] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden–Day, San Francisco, 1964, p. 187.
[6] D. E. Dorman and J. D. Roberts, *J. Amer. Chem. Soc.*, 1971, **93**, 4463.

methoxy- and acetyl methyl resonances became quartets. In addition, the C-5 resonance of compound (5) was specifically reduced in intensity (by a factor of *ca.* 2), indicating that the atom involved is fully substituted and its resonance is subject to incomplete nuclear Overhauser enhancement.[7]

In the mass spectrometer (70 eV) compound (5) did not give a molecular ion, the ions of highest mass (and equal intensity) having *m/e* 394 and 396. This is consistent with loss of acetic acid from the molecular ion and the generation of an unsaturated species which underwent retrodienic cleavage to give an ion with *m/e* 306, 308 (Scheme, path *a*). This is one of the established main fragmentation pathways for pyranosyl acetates[8] and provides proof that the bromine atom is not bonded to C-1. The other pathways illustrated in the Scheme account for the generation of all the observed ions down to *m/e* 197 and largely parallel the fragmentations of hexopyranose penta-acetates. Although the step proposed for the generation of this last ion (loss of $CO_2 \cdot CH_2$) is unusual, loss of $CH_2 \cdot O_2C \cdot CH_2$ from some acetylated hexopyranosyl nucleoside derivatives has been reported.[9]



SCHEME



(6) R=OAc
(10) R=H

Compound (5) is remarkably stable, being readily sublimed even at atmospheric pressure, and can be recrystallised from alcohol. A pure sample is unchanged for many months at room temperature; impure samples decompose. Acetolysis with mercury(II) acetate in acetic acid gave a crystalline dextrotatory penta-acetate which is assigned structure (6) on the grounds of the rotational change encountered in its formation from the bromo-compound (5) ([*M*] −487 to +56°). Similar acetolysis of tetra-*O*-acetyl-α-L-glucopyranosyl bromide, which has related functionality and absolute stereochemistry in the vicinity of the reaction centre, would be expected to afford the product of inversion, penta-*O*-acetyl-β-L-glucopyranose, under these conditions[10] ([*M*] −820 to −16°).

As a further example of a uronate derivative with reduced radical-stabilising character at C-1, the 1-deoxy-analogue (7) (methyl tri-*O*-acetyl-2,6-anhydro-L-gulonate) was prepared for study by desulphurisation (with Raney nickel) of methyl (phenyl tri-*O*-acetyl-1-thio-β-D-glucopyranosid)uronate (1), which is readily available from the tetra-acetate (4).[11] Treated with *N*-bromosuccinimide under the lamp, compound (7) gave the

[7] G. C. Levy and G. L. Nelson, 'Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley–Interscience, New York, 1972, p. 30.

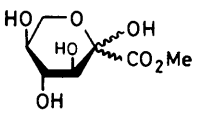
[8] K. Biemann, D. C. DeJongh, and H. K. Schnoes, *J. Amer. Chem. Soc.*, 1963, **85**, 1763.

[9] A. A. Magnin and A. M. Stephen, *Tetrahedron*, 1970, **26**, 4019.

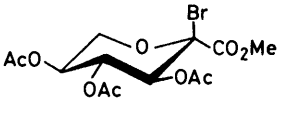
[10] R. S. Tipson, *J. Biol. Chem.*, 1939, **130**, 55; R. U. Lemieux, *Adv. Carbohydrate Chem.*, 1954, **9**, 1; B. Capon, *Chem. Rev.*, 1969, **69**, 407.

[11] R. J. Ferrier and R. H. Furneaux, *Carbohydrate Res.*, 1976, **52**, 63.

crystalline bromo-compound (8) (47% yield) which is the known acetylated glycosyl bromide of methyl L-*xylo*-hexulopyranosonate (9) and has been prepared



(9)



(8a)

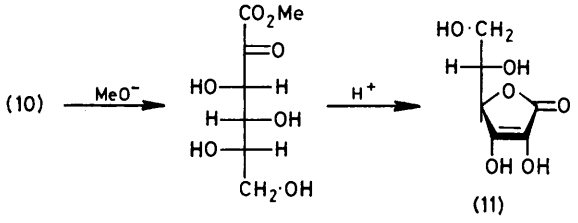
from it by treatment with phosphorus tribromide generated *in situ* in acetic anhydride containing perchloric acid.[12] The bromide obtained from compound (7) had m.p. and optical rotation in close agreement with those of the sample prepared from the ulosonic acid derivative (9),[12] and the former gave n.m.r. spectral data consistent with those published for the latter.[13]

Although the Japanese workers [12] represented their bromo-product as having the α-L-configuration, they apparently did not establish this point formally. It is here suggested that their method of synthesis establishes the correctness of their assignment since the strongly acidic conditions used would ensure that the thermodynamically favoured anomer would predominate, and this would be the α-L-pyranosyl compound which, in the $^1C_4$ conformation (8a), has the electronegative bromine and the electropositive methoxycarbonyl group axially and equatorially oriented, respectively, as required by electrostatic factors,[14] and all the other ring substituents equatorial. The configuration at the anomeric centre of compound (8) is thus *R* as illustrated, and substitution by the *N*-bromosuccinimide method had therefore occurred in compound (7) with retention of configuration.

Compound (8) ([*M*] −524°) is thus an α-L-glycosyl-bromide and as such would be expected to be,[15] and is, more laevorotatory than its β-anomer and its precursor (7) ([*M*] +124°).[16] Therefore the optical rotations of compounds (3) ([*M*] −409°) and (5) ([*M*] −487°), in relation to those of their respective precursors (1) ([*M*] −93°) and (4) ([*M*] +30°), can be taken as evidence of their having, like compound (8), the *R*-configuration at their tertiary centres.

The observed bromination at C-5 of the uronate derivatives (1), (4), and (7) appears to have few analogies, although several C-5 radicals of pyranose derivatives have been detected following irradiation of simple [17] and complex [18] carbohydrates. Bromination of tetra-*O*-acetyl-β-D-glucopyranosylbenzene was thought to occur at C-1 [19] and is perhaps the most similar reaction reported. Angyal's oxidation procedure by which acetylated methyl β-D-hexopyranosides are oxidised by chromium trioxide in acetic acid to methyl 5-hexulosonates [20] is apparently not related, since oxidation at C-5 follows that of C-1 and ring opening, but the unexpected finding that L-sorbose and D-fructose are converted into D-*threo*-hexo-2,5-diulose on treatment with bromine water in the presence of freshly precipitated strontium carbonate could be.[21]

Treatment of the bromide (8) with mercury(II) acetate in acetic acid gave a syrupy product which had ^{1}H n.m.r. characteristics consistent with its being the acetate (10), and a large rotational change during the reaction ([*M*] −524 to +191°) indicates that inversion occurs and that the product is the anomer of the known [13,22] methyl 2,3,4,5-tetra-*O*-acetyl-α-L-*xylo*-hex-2-ulopyranosonate ([*M*] −278°). Deacetylation of the acetate (10) with methanolic sodium methoxide according to the method of Ogawa *et al.*[23a] did not give L-ascorbic acid (11) as



these authors suggest, but this product was obtained by subsequent treatment with acid.[23b] Whereas the Japanese workers achieved base-catalysed ring closure during their deacetylation, we did not.

EXPERIMENTAL

Optical rotations were measured for solutions in chloroform in the concentration range 0.8—2% unless otherwise stated.

Reaction of Methyl (Phenyl Tri-O-acetyl-1-thio-β-D-glucopyranosid)uronate with N-Bromosuccinimide.—The phenyl thioglycoside [24] (1) (1 g), prepared directly from the corresponding β-glycosyl acetate,[11] and *N*-bromosuccinimide (2.1 g, 5.0 mol. equiv.) were heated under reflux and under a 250-W heat lamp in carbon tetrachloride (70 ml) for 0.5 h; the starting material had then been replaced by two compounds, one more and one less mobile on t.l.c. After cooling the solids and solvent were removed, the residual syrup was dissolved in chloroform, and the solution was washed with water, dried (Na_2SO_4), and evaporated. The residual yellow syrup was separated by preparative t.l.c.

The less mobile component (0.38 g, 43%) was an oil, δ (60 MHz; $CDCl_3$) 7.2—7.7 (5 H, m, Ph), 5.55 (1 H, d, $J_{4,5}$ 5.5 Hz, H-4), 4.97 (1 H, d, H-5), 3.71 (3 H, s, OMe),

[12] K. Goshima, N. Maezono, and K. Tokuyama, *Bull. Chem. Soc. Japan*, 1972, **45**, 3692.
[13] K. Goshima and K. Tokuyama, *Tetrahedron Letters*, 1969, 2383.
[14] R. U. Lemieux, *Pure Appl. Chem.*, 1971, **27**, 527.
[15] J. H. Brewster, *J. Amer. Chem. Soc.*, 1959, **81**, 5475, 5483.
[16] A. K. Bhattacharya, R. K. Ness, and H. G. Fletcher, *J. Org. Chem.*, 1963, **28**, 428.
[17] M. A. Collins, *Nature*, 1962, **193**, 1061.
[18] J. A. Arthur, T. Mares, and O. Hinojosa, *Textile J. Res.*, 1966, **36**, 630; P. J. Baugh, J. I. Goodall, G. O. Phillips, C. von Sonntag, and M. Dizdaroglu, *Carbohydrate Res.*, 1976, **49**, 315.
[19] J. N. BeMiller and H. L. Muenchow, *Carbohydrate Res.*, 1973, **28**, 253.
[20] S. J. Angyal and K. James, *Austral. J. Chem.*, 1970, **23**, 1209.
[21] G. C. Whiting and R. A. Coggins, *Chem. and Ind.*, 1963, 1925.
[22] K. Goshima, N. Maezono, and K. Tokuyama, *Carbohydrate Res.*, 1971, **17**, 245.
[23] (*a*) T. Ogawa, K. Taguchi, N. Takasaka, M. Mikata, and M. Matsui, *Carbohydrate Res.*, 1976, **51**, C1; (*b*) R. S. Ferrier, and R. H. Furneaux, *J.C.S. Chem. Comm.*, 1977, 332.
[24] B. Helferich, D. Turk, and F. Stoeber, *Chem. Ber.*, 1956, **89**, 2220.

2.08 and 2.18 (2 × 3 H, s, Ac), indicating that it was the enone (2). Crystallisation of the more mobile fraction (0.20 g, 17%) from ethanol gave *methyl* [*phenyl* (5R)-*tri*-O-*acetyl*-5-C-*bromo*-1-*thio*-β-D-*glucopyranosid*)*uronate* (3) (0.14 g, 12%), m.p. 107—108°, $[\alpha]_D$ −81° (Found: C, 45.5; H,4.5; Br, 15.9; S, 6.3. $C_{19}H_{21}BrO_9S$ requires C, 45.2; H, 4.2; Br, 15.8; S, 6.3%); δ 7.1—7.6 (5 H, m, Ph), 4.7—5.8 (4 H, m, H-1—4), 3.80 (3 H, s, OMe), 1.94 2.02, and 2.07 (3 × 3 H, s, Ac).

Methyl (5R)-*Tetra*-O-*acetyl*-5-C-*bromo*-β-D-*glucopyranuronate* (5).—Methyl tetra-*O*-acetyl-β-D-glucopyranuronate [25] (4) (5.0 g) and *N*-bromosuccinimide (2.8 g, 1.2 mol. equiv.) were heated in refluxing carbon tetrachloride (200 ml) and under the lamp for 1.75 h, after which a chromatographically more mobile product had replaced the starting material. Processing as above gave *methyl tetra*-O-*acetyl*-5-C-*bromo*-β-D-*glucopyranuronate* (4.1 g, 68%) (from ethanol). Recrystallised from this solvent it had m.p. 159—161°, $[\alpha]_D$ −107°, and after sublimation at 0.2 mmHg and 150 °C and further recrystallisation from ethanol it had m.p. 160—162°, $[\alpha]_D$ −107° (Found: C, 39.4; H, 4.1; Br, 17.8. $C_{15}H_{19}BrO_{11}$ requires C, 39.6; H, 4.2; Br, 17.6%); δ 6.25 (1 H, d, $J_{1,2}$ 7 Hz, H-1), 5.0—5.8 (3 H, m, H-2—4), 3.82 (3 H, s, OMe), and 2.01 2.04, 2.08, and 2.13 (4 × 3 H, s, CMe).

When the reaction was repeated with the acetylated uronate (1.0 g), *N*-bromosuccinimide (0.56 g, 1.2 mol. equiv.), and refluxing carbon tetrachloride (70 ml) for 3.5 h in the dark no reaction was detected by t.l.c. nor, after the usual processing, by n.m.r. When benzoyl peroxide (0.033 g) was added to an identical mixture slow reaction occurred to give the 5-*C*-bromo-derivative (t.l.c. evidence), which was the major carbohydrate component of the mixture after refluxing in the dark for 3.5 h.

Methyl (5S)-5-C-*Acetoxytetra*-O-*acetyl*-β-D-*glucopyranuronate* (6).—The bromo-compound (5) (4.5 g) and mercury(II) acetate (1.9 g, 0.6 mol. equiv.) were heated in dry acetic acid (20 ml) for 0.5 h at 70 °C. After removal of the solids and solvent the residue was extracted with chloroform–carbon tetrachloride (1 : 1; 80 ml) and the extract was washed with aqueous sodium iodide, then water, and dried. Removal of the solvent left a syrup which on trituration with ethanol gave the *penta-acetate* (3.1 g, 72%). Recrystallised from ethanol then methanol (× 2) it had m.p. 113—114°, $[\alpha]_D$ +13° (Found: C, 47.0; H, 5.2. $C_{17}H_{22}O_{13}$ requires C, 47.0; H, 5.1%); δ 6.30 (1 H, d, $J_{1,2}$ 5 Hz, H-1), 5.0—5.8 (3 H, m, H-2—4), 3.77 (3 H, s, OMe), 2.17 (3 H, s, OAc), and 2.04 (12 H, s, OAc).

Methyl Tri-O-*acetyl*-2,6-*anhydro*-L-*gulonate* (7).—Methyl (phenyl tri-*O*-acetyl-1-thio-β-D-glucopyranosid)uronate [24] (1) (9.0 g) was heated under reflux in ethanol (200 ml) in the presence of Raney nickel W7 (60 g). After 1 h, the solids and solvent were removed to afford a crystalline product, which on recrystallisation from ethanol gave the 2,6-*anhydride* (4.6 g, 68%), m.p. 116—117°, $[\alpha]_D$ +39° (Found: C, 49.0; H, 5.8. $C_{13}H_{18}O_9$ requires C, 49.1; 5.7%), δ 4.6—5.3 (3 H, m, H-3—5), 3.9—4.4 (2 H, m, H-2 and -6e), 3.70 (3 H, s, OMe), and 3.45 (1 H, q, $J_{5,6a}$ 7.5, $J_{6a,6e}$ 10.5 Hz, H-6a).

Methyl Tri-O-*acetyl*-α-L-xylo-*hexulopyranosylonate Bromide* (8).—Methyl tri-*O*-acetyl-2,6-anhydro-L-gulonate (2.0 g) and *N*-bromosuccinimide (2.24 g, 2.0 mol. equiv.) were heated under reflux, and under the lamp, in carbon tetrachloride (80 ml) for 50 min, after which the anhydride had been replaced by a major and a minor carbohydrate product. Processing as above gave a colourless syrup, which crystallised from ethanol to afford the *glycosyl bromide* (1.2 g, 47%). Recrystallised (× 2) from ethanol it had m.p. 103—107°, $[\alpha]_D$ −132° (Found: C, 39.3; H, 4.4; Br, 20.7. $C_{13}H_{17}BrO_9$ requires C, 39.3; H, 4.3; Br, 20.1%) (lit.,[12] m.p. 107—109°, $[\alpha]_D$ −135°); δ 5.41 (1 H, t, $J_{3,4} = J_{4,5} = 9$ Hz, H-4), 5.11 (1 H, d, H-3), 5.00 (1 H, h, $J_{5,6a}$ 9, $J_{5,6e}$ 5.5 Hz, H-5), 4.23 (1 H, q, $J_{6a,6e}$ 11 Hz, H-6e), 3.8 (1 H, q, H-6a), 3.78 (3 H, s, OMe), and 1.99, 2.01, and 2.03 (3 × 3 H, 3s, CMe) [lit.,[13] δ 5.53 (t, $J_{3,4} = J_{4,5} =$ 9 Hz, H-4), 5.20 (d, H-3). 5.09 (m, $J_{5,6a}$ 10.7, $J_{5,6e}$ 5.8 Hz, H-5), 4.25 (m, $J_{6a,6e}$ 11.3 Hz, H-6e), and 3.90 (m, H-6a)].

Methyl Tetra-O-*acetyl*-β-L-xylo-*hexulopyranosonate* (10).—The bromo-compound (8) (0.94 g) and mercury(II) acetate (0.49 g, 0.6 mol. equiv.) were heated in dry acetic acid (20 ml) for 0.5 h at 70 °C. The mixture was processed as for compound (6) to give a clear, colourless syrup (0.99 g, 105%), $[\alpha]_D$ +51°, δ 4.7—5.6 (3 H, m, H-3—5), 4.1 (2 H, m, H_2-6), 3.78 (3 H, s, OMe), and 2.13, 2.13, 2.11, and 2.06 (12 H, 3 s, OAc).

Ascorbic Acid (11).—The acetate (10) (0.82 g) was treated with methanolic 0.2M-sodium methoxide (14 ml) for 10 min at room temperature,[23a] and the solution was then neutralised carefully with methanolic hydrogen chloride and taken to dryness to give a pale yellow solid (0.53 g, 100% for methyl L-*xylo*-hexulosonate + NaCl), $\nu_{max.}$ 1 600 and 1 750 cm^{-1} (ascorbic acid 1 650 and 1 780 cm^{-1}). The product was dissolved in water–acetic acid (0.4 and 2.0 ml) and the undissolved salt (m.p. >250°) was removed by centrifugation. Removal of the solvent left a syrup which was redissolved in methanol (5 ml) and conc. hydrochloric acid (0.5 ml); evaporation then left a pale buff powder (0.36 g, 90%). Difficulty was found in recrystallising this material from aqueous acetic acid, but a sample recovered from the solvent and purified by washing with alcohol on a porous tile had m.p. 175—182° (lit., 189—191°); it and authentic L-ascorbic were identified by their *X*-ray powder diffraction patterns, i.r. spectra, c.d. spectra, and paper chromatographic mobilities (R_F 0.40) in butan-1-ol–acetic acid–water (250 : 60 : 250).[26] By iodimetric titration the synthetic sample was determined to be 89% pure; on paper chromatograms a trace of impurity (R_F 0.75) was observed. Unfractionated material obtained from the aqueous acetic acid by removal of the solvent contained appreciably more of this compound, which is conceivably an acid degradation product [12,13] rather than the oxidation product.[26] Aqueous acetic acid therefore is not satisfactory for purifying ascorbic acid although it appeared suitable in control experiments.

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