Synthesis of *C*-Glycosyl Compounds. Part 2.[1,2] Reactions of Aldonic Acid Lactones with Ethyl Isocyanoacetate

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2,3 : 5,6-Di-*O*-isopropylidene-D-mannono-1,4-lactone reacted with ethyl isocyanoacetate and 1,5-diazabicyclo-[4.3.0]non-5-ene (DBN) to give ethyl 5-[(1*S*)-1,2 : 4,5-di-*O*-isopropylidene-D-arabinitol-1-yl]oxazole-4-carboxylate (1), in contrast with the products, (*E*)- and (*Z*)-ethyl 3,6-anhydro-2-deoxy-2-formylamino-4,5 : 7,8-di-*O*-isopropylidene-D-*manno*-oct-2-enonate, obtained when potassium hydride was used as the base. Similarly, 2,3 : 5,6-di-*O*-isopropylidene-D-allono-1,4-lactone gave the oxazole (9) and the oct-2-enonates [(15) and (16)], respectively, when DBN and potassium hydride were used as the base. With DBN as the base, 2,3-*O*-isopropylidene-4-*O*-methyl-L-rhamnono-1,5-lactone (20) gave the oxazole (21) in low yield, and with potassium hydride as the base both the oxazole (21) and an oct-2-enonate (23) were obtained in low yield. The reaction with 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone and with potassium hydride as the base gave the oxazole (27) as the major product but no oct-2-enonates. With DBN as the base, elimination occurred and only the unsaturated lactone (24) was identified. Similarly, 5,6-di-*O*-isopropylidene-2,3-di-*O*-methyl-L-*erythro*-hex-2-enono-1,4-lactone gave only elimination products, the lactones (33) and (34), when either of the two bases was used. The oxazoles (1), (9), (21), and (27) were converted into a series of derivatives by a sequence of acetylation, hydrolysis, and hydrogenolysis experiments. The reaction mechanism whereby the oxazoles and oct-2-enonates are produced is discussed briefly.

In Part 1 [1] we described the preparation of (*E*)- and (*Z*)-ethyl 3,6-anhydro-2-deoxy-2-formylamino-4,5 : 7,8-di-*O*-isopropylidene-D-*manno*-oct-2-enonate from 2,3 : 5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone by formylaminomethylenation [3] with ethyl isocyanoacetate (EIA) and potassium hydride in tetrahydrofuran. As the reaction represents a route to *C*-glycosyl compounds,[4] we wished to explore its scope, and now report [2] on the effect of changes, similar to those described [5] for aldehydes and ketones, in the reaction conditions; the reactions of EIA with other aldonic acid lactone derivatives have also been studied.

A comparison of yields in a series of formylaminomethylenation reactions of the mannono-lactone and EIA using a variety of strong bases (butyl-lithium,[5a] potassium t-butoxide,[5a] sodium hydride,[5a,b] and potassium hydride [1,5c]) showed that potassium hydride was the most suitable. The use of sodium ethoxide in ethanol [5a,c] was not examined in detail when a small-scale experiment showed (t.l.c.) that ethyl (ethyl 2-deoxy-2-formylamino-4,5 : 7,8-di-*O*-isopropylidene-α-D-*manno*-D-*glycero*-oct-3-ulo-3,6-furanosid)onate and its D-*manno*-L-*glycero*-epimer were the major products, as expected.[1] With sodium cyanide in ethanol,[5d,e] the lactone was consumed and very polar material (t.l.c.) was obtained. An attempt to acetylate this material gave unchanged lactone in *ca.* 80% yield; consequently, the reaction was not investigated further.

When the lactone was treated with equivalent amounts of EIA and 1,5-diazabicyclo[4,3,0]non-5-ene (DBN) in tetrahydrofuran,[6] either by the low temperature procedure [1] or at 25 °C, a product which was less polar than the formylaminomethylenation products [1] and formed a monoacetate on acetylation was isolated in moderate yield. Its mass spectrum and an accurate mass determination ($M^+ - CH_3$) indicated that the compound was isomeric with the oct-2-enonates [1] and this was confirmed by the mass spectral and analytical data of its monoacetate. The presence of a free hydroxy-group was shown by i.r. spectroscopy, and the presence of an oxazole ring in the compound and its monoacetate was evident [7] from their n.m.r., i.r., and u.v. spectra. These data established that the product was the oxazole (1), which gave the monoacetate (2).

To confirm the structure (1) the oxazole was partially hydrolysed; the products were acetylated to give three compounds which were separated by chromatography. The penta-acetate (5) was readily identified by the usual spectral and analytical techniques and the other two compounds were shown, by their n.m.r. and mass spectral and analytical data, to be isomeric triacetates, each containing one isopropylidene group. However, it could not be assumed that they were simply the 1,2-*O*-isopropylidene- and the 4,5-*O*-isopropylidene-triacetates because acid-catalysed migrations of isopropylidene groups can take place during acid hydrolysis; moreover, it is unusual for a terminal acetal group in such acyclic

[1] Part 1, R. H. Hall, K. Bischofberger, S. J. Eitelman, and A. Jordaan, *J.C.S. Perkin I*, 1977, 743.

[2] Preliminary publication, S. J. Eitelman, R. H. Hall, and A. Jordaan, *J.C.S. Chem. Comm.*, 1976, 923.

[3] D. Hoppe, *Angew. Chem. Internat. Edn.*, 1974, **13**, 789; U. Schöllkopf, *ibid.*, 1970, **9**, 763.

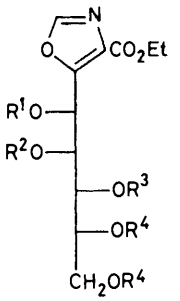
[4] For recent examples, see L. Kalvoda, *J. Carbohydrates Nucleosides Nucleotides*, 1976, **3**, 47; C. M. Gupta, G. H. Jones, and J. G. Moffatt, *J. Org. Chem.*, 1976, **41**, 3000; T. Huynh-Dinh, J. Igolen, J.-P. Marquet, E. Bisagni, and J.-M. Lhoste, *ibid.*, p. 3124; G. Just and S. Kim, *Canad. J. Chem.*, 1976, **54**, 2935; U. Reichman, C. K. Chu, I. Wempen, K. A. Watanabe, and J. J. Fox, *J. Heterocyclic Chem.*, 1976, **13**, 933; K. Arakawa, T. Miyasaka, and N. Hamamichi, *Chem. Letters*, 1976, 1119.

[5] (*a*) U. Schöllkopf, F. Gerhart, R. Schröder, and D. Hoppe, *Annalen*, 1972, **766**, 116; (*b*) A. J. Brink and A. Jordaan, *Carbohydrate Res.*, 1974, **34**, 1; (*c*) K. Bischofberger, A. J. Brink, O. G. de Villiers, R. H. Hall, and A. Jordaan, *J.C.S. Perkin I*, 1977, 1472; (*d*) D. Hoppe and U. Schöllkopf, *Annalen*, 1972, **763**, 1; (*e*) J. C. A. Boeyens, A. J. Brink, R. H. Hall, A. Jordaan, and J. A. Pretorius, *Acta Cryst. B*, in the press.

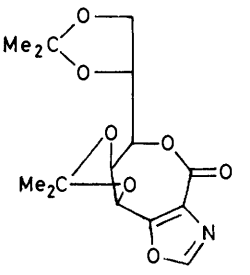
[6] *Cf.* M. Suzuki, M. Miyoshi, and K. Matsumoto, *J. Org. Chem.*, 1974, **39**, 1980.

[7] (*a*) I. J. Turchi and M. J. S. Dewar, *Chem. Rev.*, 1975, **75**, 389; (*b*) R. Schröder, U. Schöllkopf, E. Blume, and I. Hoppe, *Annalen*, 1975, 533.

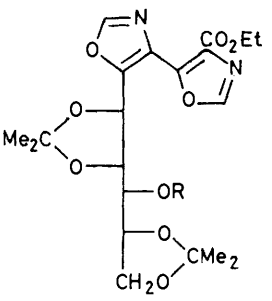
compounds to be retained at the expense of a non-terminal acetal group, under the conditions used.[8] The n.m.r. spectra of compounds (1), (2), and (5) showed H-1 signals at τ 4.05, 4.08, and 3.48 respectively. The corresponding H-1 doublets of the two triacetates occurred at τ 4.06 and 3.31, indicating that the compound with the H-1 doublet at τ 4.06 had retained the 1,2-*O*-isopropylidene group and was the triacetate (3), and that the other compound contained a 1-*O*-acetyl group. Similarly, the 4-protons of compounds (1) and (2) resonated above τ 5.80, whereas those of compounds (3) and (5) and the second triacetate resonated below τ 5.00, indicating that the second triacetate was the 2,3-*O*-isopropylidene compound (4). Further first-order analysis of the n.m.r. spectra of compounds (1)—(5) confirmed that the triacetates were compounds (3) and (4).



(1) $R^1R^2=R^4R^4=CMe_2$, $R^3=H$
(2) $R^1R^2=R^4R^4=CMe_2$, $R^3=Ac$
(3) $R^1R^2=CMe_2$, $R^3=R^4=Ac$
(4) $R^1=R^4=Ac$, $R^2R^3=CMe_2$
(5) $R^1=R^2=R^3=R^4=Ac$

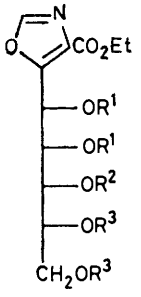


(6)

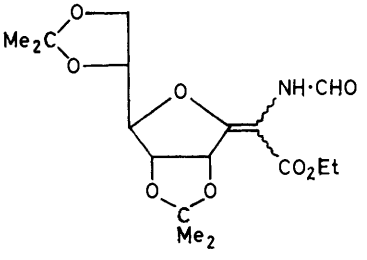


(7) R=H
(8) R=Ac

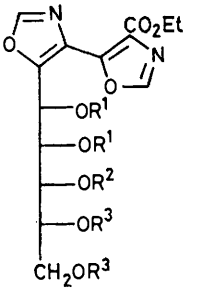
Compound (1) was converted into the lactone (6) by heating a solution in DBN, with simultaneous removal of ethanol and DNB (150 °C; 0.1 mmHg). N.m.r. spectroscopy revealed the absence of the ethoxy-group and the structure was confirmed by the usual analytical and spectral methods. Further, compound (6) was reconverted quantitatively into compound (1) on treatment with sodium ethoxide in ethanol. The reaction of the lactone (6) with equivalent amounts of EIA and DBN gave the double oxazole (7), which yielded the monoacetate (8) on acetylation. The double oxazoles (7) and (8) were readily identified by their two low-field singlets (H-2 of the oxazole rings, τ *ca.* 2.0).



(9) $R^1R^1=R^3R^3=CMe_2$, $R^2=H$
(10) $R^1R^1=R^3R^3=CMe_2$, $R^2=Ac$
(11) $R^1R^1=CMe_2$, $R^2=R^3=H$
(12) $R^1R^1=CMe_2$, $R^2=R^3=Ac$
(13) $R^1=R^2=R^3=H$
(14) $R^1=R^2=R^3=Ac$



(15), (16)



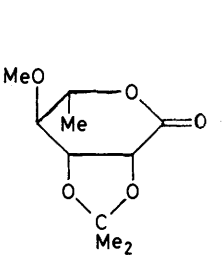
(17) $R^1R^1=R^3R^3=CMe_2$, $R^2=H$
(18) $R^1R^1=R^3R^3=CMe_2$, $R^2=Ac$
(19) $R^1=R^2=R^3=Ac$

The reaction of 2,3 : 5,6-di-*O*-isopropylidene-D-allono-1,4-lactone [9] with EIA and DBN (25 °C) gave the oxazole (9) in 56% yield, which was converted by a series of acetylations and hydrolyses into compounds (10)—(14). Formylaminomethylenation of the lactone by the method described [1] for its mannono-isomer gave the expected oct-2-enonates (15) and (16) in 59 and 2% yield, and the oxazole (9) (0.5%) and the double oxazole (17) (10%) as

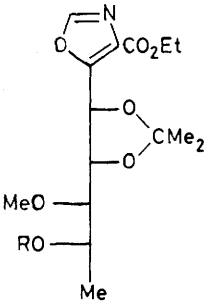
[8] H. Zinner, G. Rembarz, and H. P. Klocking, *Chem. Ber.*, 1957, **90**, 2688; U. Lerch, M. G. Burdon, and J. G. Moffatt, *J. Org. Chem.*, 1971, **36**, 1507.

[9] J. M. Ballard and B. E. Stacey, *Carbohydrate Res.*, 1970, **12**, 37; M. Haga, M. Takano, and S. Tejima, *ibid.*, 1970, **14**, 237.

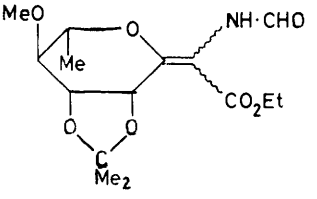
by-products. (By-products similar to those obtained [1] from the formylaminomethylenation of the mannono-lactone were not observed.) Presumably the double oxazole (17) was obtained either by reaction of the allono-lactone with the self-condensation product of EIA,[1,7b] or by a route involving a lactone similar to compound (6). Compound (17) was further characterized as the monoacetate (18) and the penta-acetate (19).



(20)



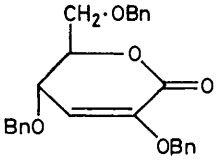
(21) R = H
(22) R = Ac



(23)

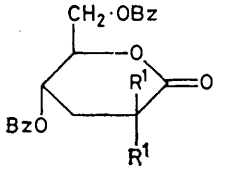
As an example of a 1,5-lactone, 2,3-*O*-isopropylidene-4-*O*-methyl-L-rhamno-1,5-lactone (20) was prepared by oxidation of 2,3-*O*-isopropylidene-4-*O*-methyl-α-L-rhamnose.[10] Reaction of the lactone with EIA and DBN was slow; after 4 days 60% of the lactone was recovered and only 13% of the expected oxazole (21) was obtained. With EIA and potassium hydride, the lactone was consumed in *ca.* 1 h but only low yields of an oct-2-enonate (23) (13%) and the oxazole (21) (19%) were isolated from the complex mixture of products. The oxazole (21) was further characterized as its monoacetate (22).

2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone [11] with EIA and DBN gave the unsaturated lactone (24) and not the expected oxazole (27). The same product was obtained in the absence of EIA. The structure (24) was established by conversion into the known [12] 2,4,6-tri-*O*-benzoyl-3-deoxy-D-*arabino*-hexono-1,5-lactone (25); simultaneous hydrogenation and hydrogenolysis of compound (24) and benzoylation of the products obtained, gave a mixture of (25) and its C-2 epimer (26). With EIA and potassium hydride the glucono-lactone gave the oxazole (27) in 43% yield. The oxazole (30), which must have been obtained by transesterification, and compound (24) were isolated as by-products, but the expected oct-2-enates were not detected in the complex mixture. The oxazoles (27) and (30) were converted into compounds (28), (29), and (31) by a series of acetylations and hydrogenolyses.

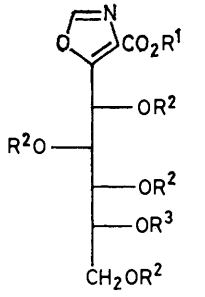


(24)

Bn = CH_2Ph, Bz = COPh



(25) R^1 = OBz, R^2 = H
(26) R^1 = H, R^2 = OBz



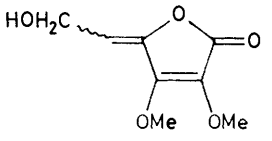
(27) R^1 = Et, R^2 = Bn, R^3 = H
(28) R^1 = Et, R^2 = Bn, R^3 = Ac
(29) R^1 = Et, R^2 = R^3 = Ac
(30) R^1 = R^2 = Bn, R^3 = H
(31) R^1 = R^2 = Bn, R^3 = Ac

5,6-*O*-Isopropylidene-2,3-di-*O*-methyl-L-*erythro*-hex-2-enono-1,4-lactone [13] and EIA with DBN or potassium hydride as base gave only the isomeric unsaturated lactones (32) and (33); these lactones were also formed on treatment of the lactone with DBN only.

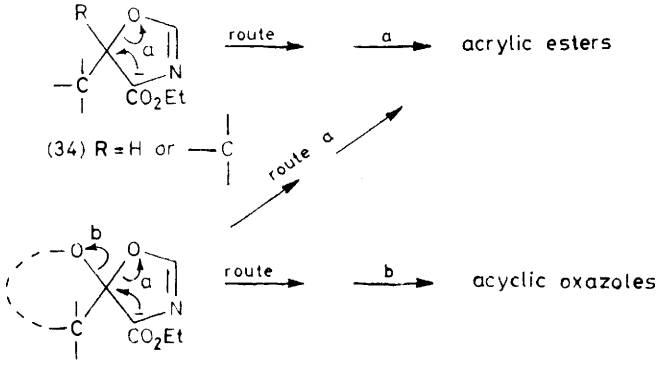
The reaction of carbonyl compounds with EIA in basic and aprotic medium involves [3,5a] an oxazolide

[10] S. J. Angyal, V. A. Pickles, and R. Ahluwalia, *Carbohydrate Res.*, 1967, **3**, 300.
[11] H. Kuzuhara and H. G. Fletcher, *J. Org. Chem.*, 1967, **32**, 2531.
[12] R. M. de Lederkremer, M. I. Litter, and L. F. Sala, *Carbohydrate Res.*, 1974, **36**, 185.
[13] J. S. Brimacombe, A. W. Murray, and Z. U. Hague, *Carbohydrate Res.*, 1975, **45**, 45.

anion, with the negative charge at C-4. With aldehydes and ketones the intermediate (34) can undergo only one type of ring fission, to give a ' pentadienide anion,' which

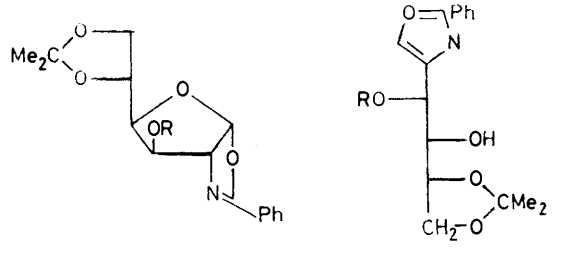


(32), (33)



(35)

on protonation gives an acrylic ester (route a). However, with lactones a spiro-intermediate (35) is formed and ring fission of what was originally the lactone ring is also possible. This leads to an alkoxide, which on protonation gives an acyclic oxazole (route b). A similar mechanism has been proposed [14] to explain the base-catalysed conversion of the oxazoline (36) into the oxazole (37).



(36) (37)

R = CH_2·CH : CH_2

Clearly, where base-catalysed elimination reactions can be suppressed, the size of the lactone ring and the nature of the base employed influence the course of the reaction; oxazole formation (route b) is favoured by the 1,5-lactones and by the use of the large, hindered organic base DBN.

EXPERIMENTAL

General experimental procedures were as described in Part 1,[1] with the following additions. The compounds all exhibited unexceptional i.r. spectra and details are given only for compounds (1), (15), (16), and (20), which are representative examples of the oxazoles, lactones, and oct-2-enonates. Similarly, the compounds all exhibited unexceptional n.m.r. spectra and details are only given for selected, typical compounds [(1), (6), (15), (16), (20), (23), (24), and (32)]. U.v. spectra were recorded for solutions in ethanol (99.9%), unless otherwise stated. Where possible, samples of oils were distilled under high vacuum (kugelröhre) for microanalysis. Syrups which could not be distilled were chromatographed until homogeneous by t.l.c. in several solvent systems and until their n.m.r. and i.r. spectra exhibited no extraneous peaks; accurate mass determinations of molecular ions or of suitable fragment ions were then obtained by high resolution mass spectrometry.

Ethyl 5-[(1S)-1,2 : 4,5-*Di*-O-*isopropylidene*-D-*arabinitol*-1-*yl*]*oxazole*-4-*carboxylate* (1).—A solution of 2,3 : 5,6-di-O-isopropylidene-D-mannono-1,4-lactone (2.58 g, 10 mmol), EIA (1.13 g, 10 mmol), and DBN (1.24 g, 10 mmol) in dry tetrahydrofuran (25 ml) was stirred for 3 days at 25 °C; the solvent was then evaporated off *in vacuo* (<40 °C) and the residue was chromatographed with ethyl acetate–benzene (1 : 1) as eluant to give the *oxazole* (1) as an oil (1.82 g, 49%), $[\alpha]_D^{20}$ −49°, $\nu_{max.}$ 3 545 (OH), 3 140 (H–C=N), 1 705 (CO), 1 605 (C=C), and 1 360 cm^{-1} (CMe_2), $\lambda_{max.}$ 228 nm (log ε 3.90), M^+ 371, τ 2.16 (1 H, s, H-2 of oxazole), 4.05 (1 H, d, $J_{1,2}$ 7 Hz, H-1), 5.25 (1 H, dd, $J_{2,1}$ 7, $J_{2,3}$ 2 Hz, H-2), 5.62 (2 H, q, O·CH_2·CH_3), *ca.* 5.80—6.11 (3 H, m, H-4, -5a, -5b), 6.66br (1 H, m, simplifies with D_2O, H-3), 7.95br (1 H, d, $J_{OH,3}$ 8 Hz. disappears on addition of D_2O, OH), 8.32, 8.48, and 8.66 (12 H, 3 s, 4 CH_3), and 8.51 (3 H, t, O·CH_2·CH_3) (Found: *m/e*, 356.135. $C_{16}H_{22}NO_8$ requires $M^+ - CH_3$, 356.135).

Acetylation with acetic anhydride in pyridine, followed by chromatography with ethyl acetate–benzene (1 : 1) as eluant, gave the *monoacetate* (2) as an oil (89%), $[\alpha]_D^{19}$ −62°, $\lambda_{max.}$ 228 nm, (log ε 3.88), M^+ 413 (Found: C, 55.2; H, 6.5; N, 3.2. $C_{19}H_{27}NO_9$ requires C, 55.2; H, 6.5; N, 3.3%).

Ethyl 5-[(1S)-1,4,5-*Tri*-O-*acetyl*-2,3-O-*isopropylidene*-D-*arabinitol*-1-*yl*]*oxazole*-4-*carboxylate* (4), *its Penta*-O-*acetyl Analogue* (5), *and its* 3,4,5-*Tri*-O-*acetyl*-1,2-O-*isopropylidene Analogue* (3).—Compound (1) (230 mg, 0.6 mmol) in aqueous acetic acid (30%; 5 ml) was heated at 75 °C for 10 min, the solvents were evaporated off *in vacuo*, and the residue was acetylated with acetic anhydride in pyridine. Work up in the usual manner followed by chromatography with benzene–acetone (9 : 1) as eluant gave first a mixture of two compounds (*ca.* 190 mg), as shown by n.m.r. spectroscopy, and then the *triacetate* (3) as an oil (45 mg, 16%), $[\alpha]_D^{20}$ −36°, $\lambda_{max.}$ 208 and 224 nm (log ε 4.32 and 4.10), *m/e* 442 ($M^+ - CH_3$) (Found: *m/e* 442.135. $C_{19}H_{24}NO_{11}$ requires $M^+ - CH_3$, 442.135).

The mixture first eluted was rechromatographed with hexane–acetone (3 : 1) as eluant to give the *triacetate* (4) as an oil (50 mg, 17%), $[\alpha]_D^{21}$ +21°, $\lambda_{max.}$ 208 and 223 nm (log ε 4.13 and 4.09), *m/e* 442 ($M^+ - CH_3$) (Found: *m/e*, 442.135. $C_{19}H_{24}NO_{11}$ requires $M^+ - CH_3$, 442.135). Further elution gave the *penta-acetate* (5) as an oil (98 mg, 31%), $[\alpha]_D^{21}$ +32°, $\lambda_{max.}$ 215 nm (log ε 3.92), M^+ 501 (Found: *m/e* 441.126. $C_{19}H_{23}NO_{11}$ requires $M^+ - CH_3CO_2H$ 441.127).

5-[(1S)-1,2 : 4,5-*Di*-O-*isopropylidene*-D-*arabinitol*-1-*yl*]-*oxazole*-4-*carboxylic Acid Lactone* (6).—2,3 : 5,6-Di-O-isopropylidene-D-mannono-1,4-lactone was treated as described for the preparation of compound (1). After removal of the tetrahydrofuran, the DBN was evaporated off at 150 °C (0.1 mmHg) to leave a residue which, on chromatography with benzene–acetone (3 : 1) as eluant, gave a solid.

[14] R. Gigg and C. D. Warren, *J. Chem. Soc.* (*C*), 1968, 1903.

Recrystallization from acetone–hexane gave the *lactone* (6) (48%), m.p. 186—188 °C, $[\alpha]_D^{19}$ −45°, $\lambda_{max.}$ 208 and 220 nm (log ε 3.63 and 3.58), M^+ 325, τ 1.02 (1 H, s, H-2 of oxazole), 4.53 (1 H, d, $J_{1.2}$ 8 Hz, H-1), 5.06 (1 H, d, $J_{2.1}$ 8 Hz, H-2), 5.45—6.14 (4 H, m, H-3, -4, -5a, -5b), and 8.56, 8.57, 8.63, and 8.65 (12 H, 4 s, 4 CH_3) (Found: C, 55.4; H, 5.8; N, 4.3. $C_{15}H_{19}NO_7$ requires C, 55.4; H, 5.9; N, 4.3%).

Reconversion of the Lactone (6) *into Compound* (1).—A solution of the lactone (6) (0.25 g, 0.8 mmol) in ethanol (99.9%, 15 ml) containing sodium ethoxide (*ca.* 20 mg) was stirred at 25 °C for 2 h; t.l.c. indicated that the starting material had reacted completely. Acetic acid (5 drops) was added to the solution and the solvents were evaporated off *in vacuo* to give compound (1) (0.28 g; contaminated with sodium acetate), identical (i.r., mass, and n.m.r. spectra) with compound (1) prepared previously.

5-[(1S)-1,2 : 4,5-*Di*-O-*isopropylidene*-D-*arabinitol*-1-*yl*]-4-(4-*ethoxycarbonyloxazol*-5-*yl*)*oxazole* (7).—The lactone (6) (0.25 g, 0.08 mmol) was treated with EIA and DBN as described for the preparation of compound (1). Similar work-up and chromatography with benzene–acetone (3 : 1) as eluant gave starting material (6) (59 mg, 23%) and then *compound* (7) as an oil (75 mg, 25%), $[\alpha]_D^{21}$ +3°, $\lambda_{max.}$ 218 nm (log ε 3.94), M^+ 438 (Found: *m/e*, 423.140. $C_{19}H_{23}N_2O_9$ requires $M^+ - CH_3$, 423.140).

Acetylation, followed by chromatography with ethyl acetate–benzene (1 : 1) as eluant, gave the *monoacetate* (8) as an oil (94%), $[\alpha]_D^{20}$ +49°, $\lambda_{max.}$ 221 nm (log ε 4.40), M^+ 480 (Found: *m/e* 465.152. $C_{22}H_{25}N_2O_{10}$ requires $M^+ - CH_3$, 465.151).

Ethyl 5-[(1R)-1,2 : 4,5-*Di*-O-*iospropylidene*-D-*ribitol*-1-*yl*]-*oxazole*-4-*carboxylate* (9).—2,3 : 4,5-Di-*O*-isopropylidene-D-allono-1,4-lactone [9] (2.58 g, 10 mmol) was treated with EIA and DBN as described for the preparation of compound (1). Work-up and chromatography with ethyl acetate–benzene (3 : 2) as eluant gave the *oxazole* (9) as an oil (2.04 g, 55%), $[\alpha]_D^{20}$ +48°, $\lambda_{max.}$ 227 nm (log ε 3.87), M^+ 371 (Found: C, 55.3; H, 7.0; N, 3.6. $C_{17}H_{25}NO_8$ requires C, 55.0; H, 6.7; N, 3.8%).

Acetylation gave the *monoacetate* (10) (80%), m.p. 109—111 °C (from hexane), $[\alpha]_D^{20}$ +40°, $\lambda_{max.}$ 227 nm (log ε 3.93), *m/e* ($M^+ - CH_3$) 398 (Found: C, 55.2; H, 6.5; N, 3.3. $C_{19}H_{27}NO_9$ requires C, 55.4, H, 6.7, N, 3.4%).

Ethyl 5-[(1R)-1,2-O-*Isopropylidene*-D-*ribitol*-1-*yl*]*oxazole*-4-*carboxylate* (11) *and Ethyl* 5-[(1R)-D-*Ribitol*-1-*yl*]*oxazole*-4-*carboxylate* (13).—Compound (9) was hydrolysed as described for compound (1). Work-up and chromatography with ethyl acetate–methanol (7 : 2) as eluant gave *compound* (11) as an oil (175 mg, 22%), $[\alpha]_D^{20}$ +43°, $\lambda_{max.}$ 228 nm (log ε 3.76), M^+ 331 (Found: *m/e*, 316.102. $C_{13}H_{18}NO_8$ requires $M^+ - CH_3$, 316.103). Further elution gave *compound* (13) (350 mg, 48%), m.p. 112—114 °C (from ethanol–hexane), $[\alpha]_D^{20}$ +42° (H_2O), $\lambda_{max.}$ 221 nm (log ε 3.95) (Found: C, 45.1, H, 6.2; N, 4.7. $C_{11}H_{17}NO_8$ requires C, 45.3; H, 5.9; N, 4.8%).

Acetylation of compound (11) gave the *triacetate* (12) as an oil (76%), $[\alpha]_D^{20}$ +57°, $\lambda_{max.}$ 225 nm (log ε 3.72), *m/e* ($M^+ - CH_3$) 442 (Found: *m/e*, 442.135. $C_{19}H_{24}NO_{11}$ requires $M^+ - CH_3$, 442.135). Acetylation of compound (13) gave the *penta-acetate* (14) as an oil (89%), $[\alpha]_D^{20}$ +49°, $\lambda_{max.}$ 220 (log ε 3.93), M^+ 501 (Found: C, 50.0; H, 5.3; N, 2.8. $C_{21}H_{27}NO_{12}$ requires C, 50.3; H, 5.4; N, 2.8%).

Formylaminomethylenation of 2,3 : 5,6-*Di*-O-*Isopropylidene*-D-*allono*-1,4-*lactone with EIA*.—2,3 : 5,6-Di-*O*-isopropylidene-D-allono-1,4-lactone [9] (8.0 g, 31 mmol) was treated with EIA and potassium hydride as described [1] for its D-mannono-isomer; similar work-up gave an oil (*ca.* 8.7 g). Chromatography with benzene–ethyl acetate (3 : 2) as eluant gave the oxazole (9) (58 mg, 0.5%), identical (i.r., u.v., mass, and n.m.r. spectra) with compound (9), prepared previously.

Further elution gave (E)- or (Z)-*ethyl* 3,6-*anhydro*-2-*deoxy*-2-*formylamino*-4,5 : 7,8-*di*-O-*isopropylidene*-D-*allo*-*oct*-2-*enonate* (15) as an oil (230 mg, 2%), $[\alpha]_D^{20}$ −224°, $\nu_{max.}$ 3 300 (NH), 1 690 (CO), and 1 380 cm^{-1} (CMe_2), $\lambda_{max.}$ 208 and 250 nm (log ε 3.89 and 4.03), M^+ 371, τ 1.69 and 1.88 (1 H, s, and d, $J_{CHO.NH}$ 11 Hz, simplifies on addition of D_2O, CHO), 3.24br (1 H, d, $J_{NH.CHO}$ 11 Hz, disappears on addition of D_2O, NH), 4.25 (1 H, d, $J_{4.5}$ 6.5 Hz, H-4), 5.12—6.20 (7 H, m, H-5, -6, -7, -8a, -8b, O·CH_2·CH_3), and 8.56—8.76 (15 H, m, 4 CH_3, O·CH_2·CH_3) (Found: C, 55.2; H, 6.9; N, 3.6. $C_{17}H_{25}NO_8$ requires C, 55.0; H, 6.7; N, 3.8%).

Next eluted was the *oct*-2-*enonate* (16) as an oil (6.8 g, 59%), $[\alpha]_D^{20}$ −241°, $\nu_{max.}$ 3 400 (NH), 1 690 (CO), and 1 380 cm^{-1} (CMe_2), $\lambda_{max.}$ 207 and 248 nm (log ε 3.62 and 3.98), M^+ 371, τ 1.83 and 1.99 (1 H, 2d, $J_{CHO.NH}$ 2 and 11 Hz, simplifies on addition of D_2O, CHO), 2.89 and 3.16br (1 H, s, and d, $J_{NH.CHO}$ 11 Hz, disappears on addition of D_2O, NH), 4.68 and 4.71 (1 H, 2d, $J_{4,5}$ 6 Hz, H-4), 5.22—5.44 and 5.70—6.19 (7 H, m, H-5, -6, -7, -8a, -8b, O·CH_2·CH_3), and 8.49—8.80 (15 H, m, 4 CH_3, O·CH_2·CH_3) (Found: C, 55.3; H, 7.0; N, 3.6. $C_{17}H_{25}NO_8$ requires C, 55.0; H, 6.7; N. 3.8%).

Further elution gave 5-[(1R)-1,2 : 4,5-*di*-O-*isopropylidene*-D-*ribitol*-1-*yl*]-4-(4-*ethoxycarbonyloxazol*-5-*yl*)*oxazole* (17) (1.36 g, 10%), $[\alpha]_D^{20}$ +51°, $\lambda_{max.}$ 213 and 261 nm (log ε 3.94 and 3.86), M^+ 438 (Found: C, 54.8; H, 6.1; N, 6.2. $C_{20}H_{26}N_2O_9$ requires C, 54.8; H, 5.9; N, 6.4%); the *monoacetate* (18) was an oil (91%), $[\alpha]_D^{20}$ +49°, $\lambda_{max.}$ 213 and 260 nm (log ε 3.94 and 3.91), M^+ 480 (Found: C, 55.0; H, 6.0; N, 5.6. $C_{22}H_{28}N_2O_{10}$ requires C, 55.0; H, 5.8; N, 5.8%).

4-[4-*Ethoxycarbonyloxazol*-5-*yl*]-5-[(1R)-*penta*-O-*acetyl*-D-*ribitol*-1-*yl*]*oxazole* (19).—Compound (17) was hydrolysed with aqueous acetic acid (30%; 20 ml) at 80 °C for 1.5 h. Removal of the solvents left a syrup which was acetylated. Work-up gave a syrup which was chromatographed with ethyl acetate–benzene (1 : 1) as eluant to give the *penta-acetate* (19) as an oil (254 mg, 20%), $[\alpha]_D^{20}$ +48°, $\lambda_{max.}$ 209 and 254 nm (log ε 3.96 and 3.70), *m/e* ($M^+ - CH_2CO$) 526 (Found: *m/e*, 466.122. $C_{20}H_{22}N_2O_{11}$ requires $M^+ - CH_2CO - CH_3CO_2H$, 466.122).

2,3-O-*Isopropylidene*-4-O-*methyl*-L-*rhamnono*-1,5-*lactone* (20).—2,3-*O*-Isopropylidene-4-*O*-methyl-α-L-rhamnose [10] (2.18 g, 10 mmol) was oxidized with acetic anhydride and dimethyl sulphoxide, as described [9] for a similar compound, to give a solid which on recrystallization from ethyl acetate–hexane afforded the *lactone* (20) (1.88 g, 87%), m.p. 90—91 °C, $[\alpha]_D^{20}$ −137°, $\nu_{max.}$ 1 760 (CO) and 1 380 cm^{-1} (CMe_2), *m/e* ($M^+ - CH_3$) 201, τ 5.32 and 5.54 (2 H, 2 d, $J_{2.3} = J_{3,2} = 8$ Hz, H-2, -3), 5.76 (1 H, dq, $J_{5.4}$ 9.5, $J_{5.CH_3}$ 6.5 Hz, H-5), 6.50 (3 H, s, OCH_3), 6.80 (1 H, dd, $J_{4.5}$ 9.5, $J_{4.3}$ 5 Hz, H-4), 8.50 and 8.59 (6 H, 2s, $2CH_3$), and 8.58 (3 H, d, $J_{CH_3.5}$ 6.5 Hz, CH_3) (Found: C, 55.4; H, 7.3. $C_{10}H_{16}O_5$ requires C, 55.5; H, 7.5%).

Ethyl 5-[(1R)-5-*Deoxy*-1,2-O-*isopropylidene*-3-O-*methyl*-L-*arabinitol*-1-*yl*]*oxazole*-4-*carboxylate* (21).—Compound (20) (216 mg, 1 mmol), EIA, and DBN were treated as described for the preparation of compound (1). After 4 days the mixture was worked up and the residue chromatographed with benzene–acetone (3 : 1) as eluant to give starting

material (130 mg, 60%). Further elution gave *compound* (21) as an oil (28 mg, 13%), $[\alpha]_D^{18}$ +43°, $\lambda_{max.}$ 225 nm (log ε 3.92), M^+ 329 (Found: *m/e*, 314.124. $C_{14}H_{20}NO_7$ requires $M^+ - CH_3$, 314.124); the *monoacetate* (22) was an oil (90%), $[\alpha]_D^{18}$ +15°, $\lambda_{max.}$ 208 and 225 nm (log ε 3.91 and 3.86), M^+ 371 (Found: *m/e*, 314.124. $C_{14}H_{20}NO_7$ requires $M^+ - CH_3 - CH_2CO$, 314.124).

(E)- *or* (Z)-*Ethyl* 3,7-*Anhydro*-2-*deoxy*-2-*formylamino*-4,5-O-*isopropylidene*-6-O-*methyl*-L-rhamno-*oct*-2-*enonate* (23).—Compound (20) (1.4 g, 6.5 mmol), EIA, and potassium hydride, treated as described [1] for a similar compound, gave a syrup. Chromatography, and rechromatography of mixed fractions, with benzene–acetone (3 : 1) as eluant, gave a solid which, on recrystallization from acetone–hexane, yielded *compound* (23) (270 mg, 13%), m.p. 157—159 °C, $[\alpha]_D^{18}$ −290°, $\lambda_{max.}$ 207 and 250 nm (log ε 4.02 and 3.52), M^+ 329, τ 1.80 and 1.98 (1 H, 2d, $J_{CHO.NH}$ < 1 and 11 Hz, simplifies on addition of D_2O, CHO), 2.78 and 3.10br (1 H, s and d, $J_{NH.CHO}$ 11 Hz, disappears on addition of D_2O, NH), 5.12 and 5.14 (1 H, 2d, $J_{4.5}$ 7.5 Hz, H-4), 5.74 and 5.76 (2 H, 2q, O·CH_2·CH_3), *ca.* 6.24 (2 H, m, H-5, -6), 6.46 (3 H, s, OCH_3), *ca.* 6.84 (1 H, m, H-7), and 8.40—8.88 (12 H, m, 3 CH_3, O·CH_2·CH_3) (Found: C, 54.7; H, 6.9; N, 4.3. $C_{15}H_{23}NO_7$ requires C, 54.7; H, 7.0; N, 4.2%).

Further elution gave compound (21) (400 mg, 19%), identical (i.r., u.v., mass, and n.m.r. spectra) with that prepared previously.

2,4,6-*Tri*-O-*benzyl*-3-*deoxy*-D-erythro-*hex*-2-*enono*-1,5-*lactone* (24).—2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone [11] (1.1 g, 2 mmol), EIA, and DBN, treated as described for the preparation of compound (1), gave a syrup. Chromatography with benzene–diethyl ether (19 : 1) as eluant gave a solid which, on recrystallization from ethanol, afforded *compound* (24) (128 mg, 20%), m.p. 93—94 °C, $[\alpha]_D^{19}$ +52°, $\lambda_{max.}$ (MeOH) 215 and 240 nm (log ε 5.17 and 4.97), *m/e* 339 ($M^+ - CH_2Ph$), τ *ca.* 2.75 (15 H, m, 3 Ph), 4.38 (1 H, d, $J_{3.4}$ 4 Hz, H-3), 5.22 (2 H, s, O·CH_2Ph), *ca.* 5.56 (6 H, m, H-4, -5, 2 O·CH_2Ph), and *ca.* 6.40 (2 H, m, H-6a, -6b) (Found: C, 75.3; H, 6.3. $C_{27}H_{26}O_5$ requires C, 75.4; H, 6.0%).

On treating the lactone with 1 equiv. of DBN, compound (24) was obtained in 62% yield.

2,3,6-*Tri*-O-*benzoyl*-3-*deoxy*-D-arabino-*hexono*-1,5-*lactone* (25) *and its* D-ribo-*Analogue* (26).—Compound (24) (250 mg, 0.6 mmol) was hydrogenated over palladium (25 °C; 24 h; 50 lb in^{-2}) in aqueous tetrahydrofuran (10%; 15 ml). The mixture was then filtered and the solvents were removed *in vacuo* to give a syrup which was benzoylated in the usual manner. The residue so obtained was chromatographed with benzene–acetone (8 : 1) as eluant to give compound (25) (55 mg, 20%), m.p. 157 °C (lit.,[12] 158—160 °C), $[\alpha]_D^{20}$ +31° [aqueous acetone (90%)] {lit.,[12] +27° [aqueous acetone (90%)]}.

Further elution gave the *isomer* (26) (57 mg, 21%), m.p. 115—117 °C, $[\alpha]_D^{20}$ −10° [aqueous acetone (90%)], *m/e* (M^+ − COPh) 369 (Found: C, 68.2; H, 5.0. $C_{27}H_{22}O_8$ requires C, 68.3; H, 4.7%).

Formylaminomethylenation of 2,3,4,6-*Tetra*-O-*benzyl*-D-*glucono*-1,5-*lactone with EIA*.—2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone (10 g, 18 mmol), EIA, and potassium hydride, treated as described [1] for a similar compound, gave a syrup which was chromatographed; mixed fractions were rechromatographed with benzene–acetone (4 : 1) as eluant to give compound (24) (206 mg, 2.5%), identical with that prepared previously.

Further elution gave *benzyl* 5-[(1R)-1,2,3,5-*tetra*-O-*benzyl*-D-*arabinitol*-1-*yl*]*oxazole*-4-*carboxylate* (30) as an oil (580 mg, 4%), $[\alpha]_D^{20}$ +21°, $\lambda_{max.}$ 209 and 232 nm (log ε 4.44 and 3.81), M^+ 713 (Found: C, 73.8; H, 6.0; N, 1.9. $C_{44}H_{43}NO_8$ requires C, 74.0; H, 6.0; N, 2.0%); the *monoacetate* (31) was an oil (65%), $[\alpha]_D^{20}$ +25°, $\lambda_{max.}$ 209 and 230 nm (log ε 4.53 and 3.90), *m/e* ($M^+ - CH_2Ph$) 664 (Found: C, 72.8; H, 6.1; N, 1.8. $C_{46}H_{45}NO_9$ requires C, 73.1; H, 5.9; N, 1.8%).

Next eluted was *ethyl* 5-[(1R)-1,2,3,5-*tetra*-O-*benzyl*-D-*arabinitol*-1-*yl*]*oxazole*-4-*carboxylate* (27), as an oil (5.2 g, 43%), $[\alpha]_D^{20}$ +28°, $\lambda_{max.}$ 216 and 331 nm (log ε 4.83 and 4.57) (Found: *m/e*, 560.228. $C_{32}H_{34}NO_8$ requires $M^+ - CH_2Ph$, 560.228); the *monoacetate* (28) was an oil (84%), $[\alpha]_D^{20}$ +37°, $\lambda_{max.}$ 216 and 231 nm (log ε 4.16 and 3.89), M^+ 693 (Found: C, 71.0; H, 1.9; N, 6.4. $C_{41}H_{43}NO_9$ requires C, 71.0; H, 2.0; N, 6.2%).

Ethyl 5-[(1R)-*Penta*-O-*acetyl*-D-*arabinitol*-1-*yl*]*oxazole*-4-*carboxylate* (29).—Compound (27) (490 mg, 0.7 mmol) was debenzylated as described for compound (24) and the product was acetylated in the usual manner to give a syrup. Chromatography with ethyl acetate–benzene (1 : 1) as eluant gave a solid. Recrystallization from ethyl acetate–hexane gave the *penta-acetate* (29) (190 mg, 57%), m.p. 130—131 °C, $[\alpha]_D^{20}$ +64°, $\lambda_{max.}$ 227 nm (log ε 4.87), M^+ 501 (Found: C, 50.4; H, 5.3; N, 2.7. $C_{21}H_{27}NO_{13}$ requires C, 50.3; H, 5.4; N, 2.8%).

(E)- *and* (Z)-2,3-*Dimethoxy*-6-*hydroxyhexa*-2,4-*dien*-4-*olides* (32) *and* (33).—5,6-*O*-Isopropylidene-2,3-di-*O*-methyl-L-*erythro*-hex-2-enono-1,4-lactone [13] (210 mg, 0.85 mmol), EIA, and DBN, treated as described for the preparation of compound (1), gave an oil. Chromatography with benzene–ethyl acetate (4 : 1) as eluant gave a solid which on recrystallization from ethyl acetate–hexane yielded the *isomer* (32) (100 mg, 69%), m.p. 80—81 °C, $[\alpha]_D^{19}$ 0°, $\lambda_{max.}$ 208 and 258 nm (log ε 3.92 and 3.90), M^+ 186, τ 4.50 (1 H, t, $J_{5.6}$ 7 Hz, H-5), 5.61br (2 H, d, $J_{6.5}$ 7 Hz, sharpens on addition of D_2O, H-6a, -6b), and 5.86 and 6.08 (6 H, 2 s, 2 OCH_3) (Found: C, 51.6; H, 5.4. $C_8H_{10}O_5$ requires C, 51.6, H, 5.5%).

Further elution gave the *isomer* (33) (10 mg, 7%), m.p. 36—38 °C (from hexane) $[\alpha]_D^{19}$ 0°, $\lambda_{max.}$ 205 and 260 nm (log ε 3.93 and 4.22), M^+ 186 (Found: C, 51.6; H, 5.7. $C_8H_{10}O_5$ requires C, 51.6, H, 5.5%).

With potassium hydride as the base the isomers (32) and (33) were obtained in *ca.* 30% yield, with only DBN present they were obtained in *ca.* 80% yield.

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