Preparation of Analogues of the Carbohydrate Moiety of the Polyoxins

By **Karl Bischofberger, Abraham J. Brink,* Olof G. de Villiers, Richard H. Hall,** and **Amor Jordaan,** National Chemical Research Laboratory, South African Council for Scientific and Industrial Research, Pretoria 0001, Republic of South Africa

Syntheses of 2-*C*-[ethoxycarbonyl(formylamino)methylene] carbohydrate derivates by formylaminomethylenation of two pentofuranosulosides and a pentopyranosuloside are described. Hydrogenation of the unsaturated branched-chain compounds gave glycosides bearing protected amino-acid moieties as substituents at C-2. Hydrolysis and reduction experiments that establish the structures of the branched-chain compounds are described.

THE discovery of the naturally occurring polyoxins [1] has led to considerable interest in carbon–carbon linked sugar α-amino-acids, and a number of such compounds with the α-carbon atom of an α-amino-acid moiety attached to C-1,[2] C-3,[3] or C-4 [4] of furanose sugars have been prepared. We now report the preparation of furanose and pyranose derivatives which have α-amino-acid chains at C-2.

For these syntheses, suitable protected glycosulosides were required as starting materials. Oxidation of methyl 3,5-*O*-isopropylidene-β-D-xylofuranoside [5] and its α-anomer [5] with ruthenium tetraoxide gave the ulosides (1) and (2), respectively, as syrups. The pentopyranosuloside (20) was prepared from L-arabinose by a route similar to that described [6] for its enantiomer. As all these ulosides were unstable to some degree, each batch was used as soon as possible after preparation. The uloside (2) could be stored for longer periods as its crystalline hydrate.

Reaction of compound (1) with ethyl isocyano(potassio)acetate in an aprotic solvent,[7] gave as expected a *ca.* 1 : 1 mixture of the isomeric formylaminomethylenated sugars (3) and (5) in 65% yield. Attempts to separate the components by chromatography failed, and the mixture was therefore hydrogenated over Raney nickel in ethanol to give a mixture of compounds (7) and (9). These derivatives also could not be separated by chromatography, but fractional crystallization afforded pure compound (7). As hydrogenation of the mixture of compounds (3) and (5) gave two and not four products, it was concluded that hydrogenation had occurred only from the less hindered α-face of these molecules. This conclusion could not be substantiated by the n.m.r spectrum of compound (7): the $J_{2,3}$ value (5 Hz) precluded [8] an assignment of a *cis*- or *trans*-relationship to the protons on C-2 and -3. The stereochemical relationship of these two protons was, however, determined through hydrolysis of compound (7) to give the lactone (11), which was characterized as the acetate (12). Previous work has shown [9] that a lactone could only have been formed had the two participating substituents been *cis*-oriented. Compounds (7), (11), and (12) therefore all have the D-*lyxo*-configuration.

Mild acidic hydrolysis of compound (7) or (12) under conditions which are known not to cause epimerization [2c] gave a ninhydrin-positive lactone (15) which had a positive Cotton effect at 216 nm in its c.d. spectrum. As all L-amino-acids except the cyclic amino-acid proline give positive Cotton-effect curves,[10] it followed that the side-chain in compound (15), and consequently the side-chains in compounds (7) and (12), have the absolute *S*-configuration.

To establish the structure of compound (9), which we were unable to obtain pure, a mixture of compounds (7) and (9) was also hydrolysed under mild acidic conditions and the product mixture was acetylated with sodium acetate and acetic anhydride to give the lactone (12) and compound (16) as the only products.

The i.r. spectrum of compound (16) showed that it did not contain a lactone group and that a free hydroxy-group was present. It seemed unlikely that the reason for the lack of a lactone ring in compound (16) was a *trans*-disposition of the hydroxy- and the ester groups; such a disposition would imply that some hydrogenation of the mixture of compounds (3) and (5) to give compounds (7)

[1] R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley–Interscience, New York, 1970, p. 218.

[2] (*a*) K. Bishofberger, R. H. Hall, and A. Jordaan, *J.C.S. Chem. Comm.*, 1975, 806; (*b*) S. J. Eitelman, R. H. Hall, and A. Jordaan, *ibid.*, 1976, 923; (*c*) R. H. Hall, K. Bischofberger, S. J. Eitelman, and A. Jordaan, *J.C.S. Perkin I*, 1977, 743; (*d*) A. J. Brink and A. Rosenthal, *J. Carbohydrates Nucleosides Nucleotides*, 1975, **2**, 243.

[3] A. J. Brink, J. Coetzer, O. G. de Villiers, R. H. Hall, A. Jordaan, and G. J. Kruger, *Tetrahedron*, 1976, **32**, 965, and previous publications; A. Rosenthal and B. Cliff, *J. Carbohydrates Nucleosides Nucleotides*, 1975, **2**, 263, and previous publications.

[4] N. P. Damodaran, G. H. Jones, and J. G. Moffatt, *J. Amer. Chem. Soc.*, 1971, **93**, 3812; T. Naka, T. Hashizume, and M. Nishimura, *Tetrahedron Letters*, 1971, 95; H. Ohrui, H. Kuzuhara, and S. Emoto, *ibid.*, p. 4267; S. Ohdan, T. Okamoto, S. Maeda, T. Ichikawa, Y. Araki, and Y. Ishido, *Bull. Chem. Soc. Japan*, 1973, **46**, 981; H. Paulsen and E. Mäckel, *Chem. Ber.*, 1973, **106**, 1525; K. Ochi and K. Okui, *Chem. and Pharm. Bull. (Japan)*, 1974, **22**, 2223.

[5] B. R. Baker, R. E. Schaub, and J. H. Williams, *J. Amer. Chem. Soc.*, 1955, **77**, 7.

[6] The α-D-enantiomer has been described: H. Hollmann and H. P. C. Hogenkamp, *J. Amer. Chem. Soc.*, 1970, **92**, 671; T. Takamoto, M. Ohki, R. Sudoh, and T. Nakagawa, *Bull. Chem. Soc. Japan*, 1973, **46**, 670.

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

[8] J. D. Stevens and H. G. Fletcher, jun., *J. Org. Chem.*, 1968, **33**, 1799.

[9] A. J. Brink and A. Jordaan, *Carbohydrate Res.*, 1975, **41**, 355.

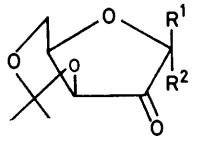
[10] W. Klyne and P. M. Scopes, in 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry,' ed. G. Snatzke, Heyden, London, 1967, p. 200.

and (9) had taken place from the very hindered β-sides of the molecules. The fact that compound (16) contained a free hydroxy-group which could not be readily acetylated also indicated that some form of steric restraint other than a *trans*-disposition of the substituents on C-2 and C-3 was present. Dreiding models of compounds (12) and (16) showed that there was no hindrance to the formation of a lactone ring in compound (12), where the amino-acid side-chain had the *S*-configuration, but that when the amino-acid moiety had the *R*-configuration, the formation of a lactone was seriously impeded by the proximity of the β-oriented methoxy-group to the *N*-formyl group. In addition, the bulky substituents on C-1′ of the D-amino-acid derivative (16) would also prevent ready acetylation of the hydroxy-group at C-3.

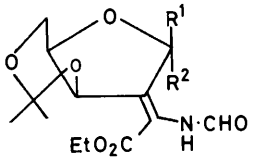
To verify these stereochemical arguments, compound (16) was hydrolysed to compound (19), which showed the negative Cotton effect of a D-amino-acid derivative at 214 nm in its c.d. spectrum and also contained a lactone group as shown by its i.r. spectrum. Clearly lactone formation between the *cis*-substituents on C-2 and -3 had been made possible by hydrolysis of the bulky anomeric β-methoxy-group.

During the assignment of structures to compounds (3) and (5) and their derivatives, it was assumed that no anomerization under the basic reaction conditions had taken place. This assumption was supported by previously reported [11] work, where anomerization did not take place during base-catalysed reactions of similar compounds. The failure of compound (16) to undergo lactonization could also only be explained by the supposition that there was steric hindrance by an anomeric β-methoxy-group.

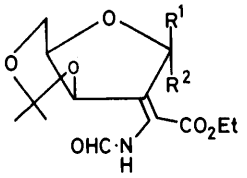
The $J_{1,2}$ values of the compounds derived from both compounds (3) and (5) were such (*ca.* 5 Hz) that we were unable to confirm the configurations at the anomeric positions of these derivatives.[8] Conclusive evidence that no anomerization had occurred during the preparation of compounds (3) and (5) was however obtained by



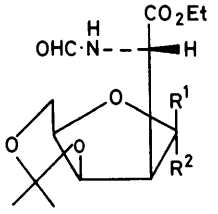
(1) R^1=OMe, R^2=H
(2) R^1=H, R^2=OMe



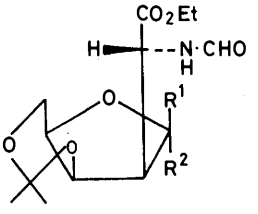
(3) R^1=OMe, R^2=H
(4) R^1=H, R^2=OMe



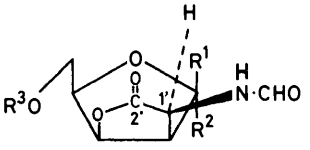
(5) R^1=OMe, R^2=H
(6) R^1=H, R^2=OMe



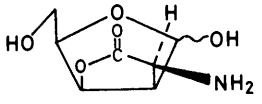
(7) R^1=OMe, R^2=H
(8) R^1=H, R^2=OMe



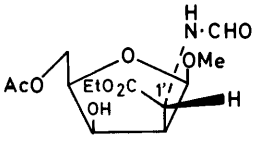
(9) R^1=OMe, R^2=H
(10) R^1=H, R^2=OMe



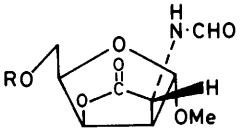
(11) R^1=OMe, R^2=R^3=H
(12) R^1=OMe, R^2=H, R^3=Ac
(13) R^1=H, R^2=OMe, R^3=H
(14) R^1=H, R^2=OMe, R^3=Ac



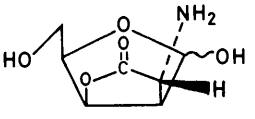
(15)



(16)



(17) R=H
(18) R=Ac



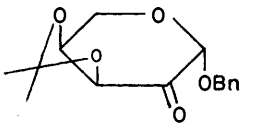
(19)

[11] S. W. Gunner, R. D. King, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), 1970, 1954; A. Rosenthal, M. Sprinzl, and D. A. Baker, *Tetrahedron Letters*, 1970, 4233.

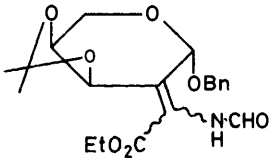
the formylaminomethylenation of the α-anomer of compound (1), the uloside (2). A mixture of the *Z*- and *E*-isomers (4) and (6) in the ratio 3 : 1 (n.m.r. evidence) was obtained in *ca.* 70% yield. Pure compound (4) was obtained by fractional crystallization but compound (6) could not be purified.

As in the case of compounds (3) and (5), catalytic hydrogenation of compound (4) to give the product (10), and of a mixture of compounds (4) and (6) to give a mixture of compounds (8) and (10), took place only from the α-face of the molecules. The direction of the hydrogenation of the double bonds in compounds (4) and (6) therefore seemed to be determined entirely by the presence of the 3,5-*O*-isopropylidene group and not by that of the anomeric α-methoxy-group.

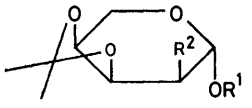
Compounds (8) and (10) were separated by column



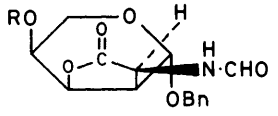
(20)



(21)



(22) R^1 = Bn, R^2 = CH(NH·CHO)·CO_2Et(*R*)
(23) R^1 = H, R^2 = CH(NH·CHO)·CO_2Et(*R*)
(24) R^1 = Ac, R^2 = CH(NH·CHO)·CO_2Et(*R*)
(25) R^1 = Bn, R^2 = CH(NH·CHO)·CO_2Et(*S*)
(26) R^1 = H, R^2 = CH(NH·CHO)·CO_2Et(*S*)
(27) R^1 = Ac, R^2 = CH(NH·CHO)·CO_2Et(*S*)
(28) R^1 = Bn, R^2 = CH(NH·Me)·CO_2Et(*R*)
(29) R^1 = Bn, R^2 = CH(NH·Me)·CO_2Et(*S*)



(30) R = H
(31) R = Ac

Bn = Benzyl

chromatography, but an assignment of the relative stereochemistry of the substituents on C-2 and -3 by n.m.r. spectroscopy was not possible ($J_{2,3}$ 5.5 Hz). The *cis*-relationship between H-2 and -3 of both compounds (8) and (10) was again determined by mild acidic hydrolysis which gave the lactones (13) and (17), respectively, characterized as their acetates [(14) and (18)].

Acidic hydrolysis of compound (8) under more forcing conditions gave a ninhydrin-positive compound which had c.d. and i.r. spectra identical with those of compound (15). Similarly, compound (10) was hydrolysed to compound (19). The side-chain of compound (8) therefore has the *S*-configuration and that of compound (10) the *R*-configuration.

Since the hydrogenation of compounds (4) and (6) occurred stereospecificially from the α-side of the molecules, the above results established that compound (4) had *Z*-stereochemistry and compound (6) *E*-stereochemistry.

Since it was then established from n.m.r. data that the α-methyl uloside (2) gave a pair of unsaturated derivatives (4) and (6) different from the pair of derivatives (3) and (5) obtained from the β-methyl uloside (1), the assumption that no anomerization took place during formylaminomethylenation seemed to be well founded. Also, it followed that compounds (7) and (8) as well as compounds (12) and (14) were anomeric pairs. Application of Hudson's isorotation rules bore out the fact that compounds (7) and (12) were the β-anomers and compounds (8) and (14) the α-anomers.

The reaction of a representative pyranosuloside, 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosuloside (20),[6] with ethyl isocyano(potassio)acetate gave a mixture (21) which decomposed when chromatographic separation was attempted and it was therefore hydrogenated over Raney nickel in ethanol without prior purification to give a mixture of the protected α-amino-acid derivatives (22) and (25). Pure compounds (22) and (25) were obtained by chromatography and both showed $J_{2,3}$ *ca.* 2.5 Hz, and large $J_{1,2}$ values (*ca.* 8 Hz); therefore both compounds were β-L-*ribo*-derivatives.[12] These assignments were confirmed by hydrolysis of compound (25) to the lactone (30), which was characterized as its acetate (31).

The *N*-formyl groups in compounds (22) and (25) were reduced by diborane in tetrahydrofuran to give the *N*-methyl derivatives [(28) and (29)]. From the signs of the Cotton-effects exhibited by the c.d. spectra of compounds (28) and (29), the *R*-configuration was assigned to the side-chain of compound (28) and the *S*-configuration to that of compound (29).

Both compounds (22) and (25) could be debenzylated by hydrogenolysis over palladium–charcoal to give compounds (23) and (26), respectively. Acetylation then gave compounds (24) and (27).

The use of compounds (24) and (27) as well as derivatives of compounds (5) and (6) for nucleoside synthesis is under investigation and the results will be reported elsewhere.

EXPERIMENTAL

For general experimental procedures, see ref. 2*c*.

All new crystalline compounds gave acceptable elemental analytical figures. Accurate mass measurements were made on the highest *m/e* peaks of those homogeneous syrups that could not be purified for analysis by high vacuum distillation. New compounds all exhibited unexceptional n.m.r. and i.r. spectra, although the n.m.r. spectra of compounds containing the NH·CO group were complicated by

[12] R. J. Ferrier, *Progr. Stereochem.*, 1969, **4**, 43.

the partial double bond character of the amide group.[13] Full details of analytical and spectroscopic data are available as Supplementary Publication No. SUP 22040 (15 pp.).*

Methyl 3,5-O-*Isopropylidene*-β-D-threo-*pentofuranosuloside* (1).—To a solution of methyl 3,5-*O*-isopropylidene-β-D-xylofuranoside (10 g) in carbon tetrachloride (100 ml), saturated aqueous sodium hydrogen carbonate (25 ml) and ruthenium dioxide hydrate (500 mg) were added, and the solution was stirred vigorously. Aqueous 5% sodium periodate was then added dropwise until no more starting material could be detected by t.l.c. Excess of periodate was destroyed with a few drops of propan-2-ol and the mixture was filtered. The organic layer was separated and the aqueous layer lyophilized. The residue was stirred with chloroform (200 ml) for 5 min, the mixture filtered, and the filtrate combined with the organic phase. Removal of solvent gave the *uloside* (1) (9.05 g, 90%) as an oil, $[\alpha]_D^{20}$ −36°, *m/e* 187 (M^+ − 15).

Methyl 3,5-O-*Isopropylidene*-α-D-threo-*pentofuranosuloside* (2).—Methyl 3,5-*O*-isopropylidene-α-D-xylofuranoside (12.5 g) was oxidized with ruthenium dioxide as in the preparation of compound (1). The aqueous layer of the reaction mixture was thoroughly extracted with chloroform (10 × 200 ml) to give *compound* (2) as an oil (9.6 g, 76%), which crystallized from ether–hexane as its hydrate, m.p. 69—70 °C. Anhydrous compound (2) had $[\alpha]_D^{22}$ +111°, *m/e* 187 (M^+ − OCH_3).

Benzyl 3,4-O-*Isopropylidene*-β-L-erythro-*pentopyranosuloside* (20).—L-Arabinose was converted into benzyl 3,4-*O*-isopropylidene-α-L-arabinose, which was oxidized (RuO_2) as described for the preparation of compounds (1) and (2) to give the *uloside* (20).[6]

Methyl 2-*Deoxy*-2-C-[(E)- *and* (Z)-*ethoxycarbonyl*(*formylamino*)*methylene*]-3,5-O-*isopropylidene*-β-D-threo-*pentofuranoside*, (3) *and* (5).—To a suspension of potassium hydride (600 mg; 50% suspension in oil), in dry tetrahydrofuran (THF) (60 ml) stirred at −78 °C, a solution of the uloside (1) (3.03 g) and ethyl isocyanoacetate (1.7 g) in dry THF (20 ml) was added dropwise. The temperature of the mixture was allowed to rise to *ca.* −20 °C, and hydrogen evolution then began. The temperature was kept at *ca.* 10 °C until evolution of hydrogen had ceased, and the solution was then stirred at ambient temperature for 2 h. The solvent was removed, water (100 ml) was added, and the pH of the mixture was adjusted to *ca.* 6 with 0.1N hydrochloric acid. The mixture was extracted with chloroform (3 × 100 ml) and the combined extracts were washed with saturated aqueous sodium hydrogen carbonate (100 ml). Removal of the solvent gave an inseparable mixture of compounds (3) and (5) (2.949 g, 63%).

Methyl 2-*Deoxy*-2-C-[(Z)- *and* (E)-*ethoxycarbonyl*(*formylamino*)*methylene*]-3,5-O-*isopropylidene*-α-D-threo-*pentofuranoside*, (4) *and* (6).—Compound (2) (1.986 g) was treated with equimolar amounts of ethyl isocyanoacetate and potassium hydride in dry THF as in the preparation of compound (3), to give a mixture of compounds (4) and (6) (2.233 g, 71%). Fractional crystallization from acetone–hexane gave pure compound (4), m.p. 107—108 °C, $[\alpha]_D^{21}$ +250°, *m/e* 315 (M^+).

Benzyl 2-*Deoxy*-2-C-[(R)-*ethoxycarbonyl*(*formylamino*)*methyl*]-3,4-O-*isopropylidene*-β-L-*ribopyranoside* (22) *and its Epimer* (25).—The uloside (20) (6.5 g) was treated with equimolar amounts of ethyl isocyanoacetate and potassium hydride in dry THF (12 ml) as in the preparation of compound (3) to give a mixture of benzyl (*E*)- and (*Z*)-2-deoxy-2-*C*-[ethoxycarbonyl(formylamino)methylene]-3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosides (21) (8 g) as an oil which decomposed when chromatographic separation was attempted. The mixture was hydrogenated in absolute ethanol (150 ml) over Raney nickel (25 °C; 50 lb in^{-2}; 3 days); filtration and evaporation left a pale yellow oil (*ca.* 8 g). Chromatography with chloroform–ethyl acetate (1 : 1) as eluant gave an oil which slowly crystallized. Recrystallization from ethyl acetate–hexane gave the (R)-*epimer* (22) (1.35 g, 15%), m.p. 75—77 °C, $[\alpha]_D^{20}$ +111°, *m/e* 378 (M^+ − 15).

Further elution gave an oil which crystallized. Recrystallization gave the (S)-*epimer* (25) (4.51 g, 49%), m.p. 116—117 °C, $[\alpha]_D^{20}$ +109°, *m/e* 378 (M^+ − 15).

Methyl 2-*Deoxy*-2-C-[(S)- *and* (R)-*ethoxycarbonyl*(*formylamino*)*methyl*]-3,5-O-*isopropylidene*-β-L-*lyxofuranoside*, (7) *and* (9).—A mixture of compounds (3) and (5) (6.0 g) was dissolved in ethanol (50 ml) and hydrogenated at atmospheric pressure over a catalytic amount of Raney nickel until uptake had ceased. Filtration and evaporation gave a mixture of compounds (7) and (9) (5.4 g, 90%) as an oil which crystallized. Repeated fractional crystallization from hexane–acetone afforded compound (7), m.p. 154—155 °C, $[\alpha]_D^{20}$ −106°, *m/e* 302 (M^+ − 15).

Methyl 2-*Deoxy*-2-C-[(R)-*ethoxycarbonyl*(*formylamino*)*methyl*]-3,5-O-*isopropylidene*-α-D-*lyxofuranoside* (10).—Compound (4) (3 g) in ethanol (50 ml) was hydrogenated at atmospheric pressure over a catalytic amount of Raney nickel until uptake had ceased, to give compound (10) (2.89 g, 96%) as an oil, $[\alpha]_D^{21}$ +80°, *m/e* 302 (M^+ − 15).

Methyl 2-*Deoxy*-2-C-[(S)-*ethoxycarbonyl*(*formylamino*)*methyl*]-3,5-O-*isopropylidene*-α-D-*lyxofuranoside* (8).—A mixture of compounds (4) and (6) was hydrogenated as in the preparation of compound (10) to give a mixture of compounds (8) and (10) in quantitative yield. Chromatography with chloroform–methanol (17 : 3) as eluant gave compound (10) and then *compound* (8), which crystallized from acetone–hexane as needles, m.p. 87—88 °C, $[\alpha]_D^{21}$ +34°, *m/e* 316 (M^+ − 1).

Methyl 5-O-*Acetyl*-2-C-[(S)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-β-D-*lyxofuranoside* 2′,3-*Lactone* (12).—Compound (7) (228 mg) was dissolved in 70% acetic acid (20 ml) and the mixture was kept at 20 °C for 24 h. The solvent was removed and the residue was chromatographed with chloroform–methanol (17 : 3) as eluant to give *methyl* 2-C-[(S)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-2-β-D-*lyxofuranoside* 2′,3-*lactone* (11) as an oil (160 mg, 95%), $[\alpha]_D^{21}$ −185°, *m/e* 200 (M^+ − OCH_3),

Compound (11) (100 mg) was dissolved in acetic anhydride (10 ml), anhydrous sodium acetate (100 mg) was added, and the mixture was stirred at 20 °C for 20 h. The acetic anhydride was removed *in vacuo*, chloroform (50 ml) was added, the mixture was filtered, and the solvent was removed to give crystalline material (105 mg). Recrystallization from acetone–hexane gave *compound* (12) (95 mg, 80%), m.p. 123 °C, $[\alpha]_D^{21}$ −134°, *m/e* 242 (M^+ − OCH_3),

Methyl 5-O-*Acetyl*-2-C-[(S)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-α-D-*lyxofuranoside* 2′,3-*Lactone* (14).—Compound (8) (130 mg) was hydrolysed with 70% acetic acid as described for the preparation of compound (11) to give *methyl* 2-C-[(S)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-α-D-*lyxofurano*-

* For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

[13] A. J. Brink and A. Jordaan, *Carbohydrate Res.*, 1974, **34**, 1.

side 2′,3-*lactone* (13) (85 mg, 90%) as an oil, $[\alpha]_D^{21}$ −15° (methanol), *m/e* 200 ($M^+ - OCH_3$).

Compound (13) (600 mg) was acetylated with sodium acetate in acetic anhydride as described for the preparation of compound (12) to give *compound* (14) (565 mg, 80%) as an oil, $[\alpha]_D^{21}$ +27°, *m/e* 242 ($M^+ - OCH_3$).

Benzyl 5-O-*Acetyl*-2-C-[(S)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-β-L-*ribopyranoside* 2′,3-*Lactone* (31).—Compound (25) (553 mg) was treated with 70% acetic acid (50 ml) as described for the preparation of compound (12) to give *benzyl* 2-C-[(S)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-α-L-*ribopyranoside* 2′,3-*lactone* (30) (316 mg, 91%) as an oil, $[\alpha]_D^{19}$ +113°, *m/e* 307 (M^+). Acetylation of compound (28) (250 mg) with sodium acetate and acetic anhydride, as for the preparation of compound (12), gave *compound* (31) (228 mg, 80%) which crystallized from acetone–hexane; m.p. 207—208 °C, $[\alpha]_D^{19}$ +94°, *m/e* 258 ($M^+ - C_7H_7$).

Acidic Hydrolysis of Compound (12).—Compound (12) (21 mg) was added to 0.5M-hydrochloric acid (5 ml) and the mixture was heated on a water-bath for 4 h. The solvent was removed, distilled water (10 ml) was added, and the the solution was lyophilized. The *amino-lactone* (15) (16.5 mg, 95%) was obtained as a glass, c.d. (*c* 2.235 × 10^{-3} in water), $[\theta]_{250}$ 0, $[\theta]_{240}$ +18°, $[\theta]_{230}$ +215°, $[\theta]_{220}$ +425°, $[\theta]_{216}$ +448°, $[\theta]_{210}$ +367°, $[\theta]_{200}$ +179°.

Methyl 5-O-*Acetyl*-2-*deoxy*-2-C-[(R)-*ethoxycarbonyl*(*formylamino*)*methyl*]-β-D-*lyxofuranoside* (16).—A mixture of compounds (7) and (9) (1.402 g) was hydrolysed with 70% acetic acid and the product was acetylated with sodium acetate and acetic anhydride as in the preparation of compound (12). Chromatography of the product mixture with chloroform–methanol (9 : 1) as eluant gave compound (12) (294 mg, 24%) and *compound* (16) (1.012 5 g, 72%) as needles from acetone–hexane, m.p. 125—126 °C, $[\alpha]_D^{21}$ −23°, *m/e* 288 ($M^+ - OCH_3$).

Acidic Hydrolysis of Compound (16).—Compound (16) (35 mg) was hydrolysed with 0.5M-hydrochloric acid as described for the hydrolysis of compound (12) to give *compound* (19) (24 mg, 97%) as a hygroscopic glass, c.d. (*c* 2.06 × 10^{-3} in water) $[\theta]_{250}$ 0, $[\theta]_{240}$ −19.5°, $[\theta]_{230}$ −176°, $[\theta]_{220}$ −487°, $[\theta]_{214}$ −575°, $[\theta]_{210}$ −536°, $[\theta]_{200}$ −234°.

Acidic Hydrolysis of Compounds (8) *and* (10).—Hydrolysis of each of compounds (8) and (10) (20 mg each) as described for hydrolysis of compound (12), gave products which had c.d. and i.r. spectra identical with those of compounds (15) and (19), respectively.

Methyl 5-O-*Acetyl*-2-C-[(R)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-α-D-*lyxofuranoside* 2′,3-*Lactone* (18).—Compound (10) (670 mg) was hydrolysed with 70% acetic acid as for the preparation of compound (11) to give *methyl* 2-C-[(R)-*carboxy*(*formylamino*)*methyl*]-2-*deoxy*-α-D-*lyxofuranoside* 2′,3-*lactone* (17) (510 mg, 98%), which crystallized from acetone–hexane; m.p. 156—157 °C, $[\alpha]_D^{20}$ −70°, *m/e* 200 ($M^+ - OCH_3$).

Compound (17) (350 mg) was acetylated with sodium acetate in acetic anhydride as for the preparation of compound (12) to give *compound* (18) (380 mg, 92%), which crystallized from acetone–hexane; m.p. 149—150 °C, $[\alpha]_D^{20}$ −80°, *m/e* 242 ($M^+ - OCH_3$).

2-*Deoxy*-2-C-[(R)-*ethoxycarbonyl*(*formylamino*)*methyl*]-3,4-O-*isopropylidene*-β-L-*ribopyranoside* (23) *and its Epimer* (26).—Compound (22) (500 mg), was hydrogenated in ethanol (99.9%, 40 ml) over palladium–charcoal (10%) (25 °C; 50 lb in^{-2}; 40 h) to give *compound* (23) (99%) as a glass, *m/e* 288 ($M^+ - 15$). The *S*-epimer (25) was hydrogenated as described for the preparation of compound (23) to give *compound* (26) as a glass, *m/e* 288 ($M^+ - CH_3$).

1-O-*Acetyl*-2-*deoxy*-2-C-[(R)-*ethoxycarbonyl*(*formylamino*)*methyl*]-3,4-O-*isopropylidene*-β-L-*ribopyranose* (24) *and its Epimer* (27).—Compound (23) (310 mg) was acetylated with pyridine (3 ml) and acetic anhydride (5 ml). The mixture was left for 20 °C for 20 h and then poured into ice–water (100 ml). The mixture was extracted with chloroform (3 × 10 ml) and the combined extracts were washed with cold saturated aqueous sodium hydrogen carbonate (2 × 50 ml). Removal of solvent gave *compound* (24) (328 mg, 93%) as an oil, $[\alpha]_D^{22}$ +55°, *m/e* 330 ($M^+ - 15$).

Compound (26) on acetylation similarly gave *compound* (27) as an oil, $[\alpha]_D^{22}$ +107°, *m/e* 330 ($M^+ - 15$).

Benzyl 2-*Deoxy*-2C-[(R)-*ethoxycarbonyl*(*methylamino*)*methyl*]-3,4-O-*isopropylidene*-β-L-*ribopyranoside* (28) *and its Epimer* (29).—A solution of diborane in tetrahydrofuran (2.5 ml; 1M) was added to a solution of compound (22) (197 mg), in THF (2.5 ml) at 0 °C. The solution was stirred with the exclusion of moisture for 18 h (25 °C) and treated as described [2c] for similar compounds. Work-up gave a syrup which was chromatographed with chloroform–ethyl acetate (1 : 1) as eluant to yield a solid which crystallized. Recrystallization from ethyl acetate–hexane gave *compound* (28) (75 mg, 40%), m.p. 111—112 °C, $[\alpha]_D^{20}$ +84°, *m/e* 364 ($M^+ - 15$); c.d. (*c* 8.7 × 10^{-4} in methanol) $[\theta]_{215}$ −2 020°, $[\theta]_{220}$ −3 580°, $[\theta]_{223}$ −3 720°, $[\theta]_{230}$ −3 230°, $[\theta]_{240}$ −1 670°, $[\theta]_{250}$ −370°, $[\theta]_{260}$ 0.

[6/2207 *Received*, 2nd *December*, 1976]