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STEREOCHEMICAL STUDIES—XXX[1]
STEREOSELECTIVE SYNTHESIS OF D-RIBOSE FROM L-GLUTAMIC ACID[2]

M. TANIGUCHI, K. KOGA and S. YAMADA*
Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Tokyo-113, Japan

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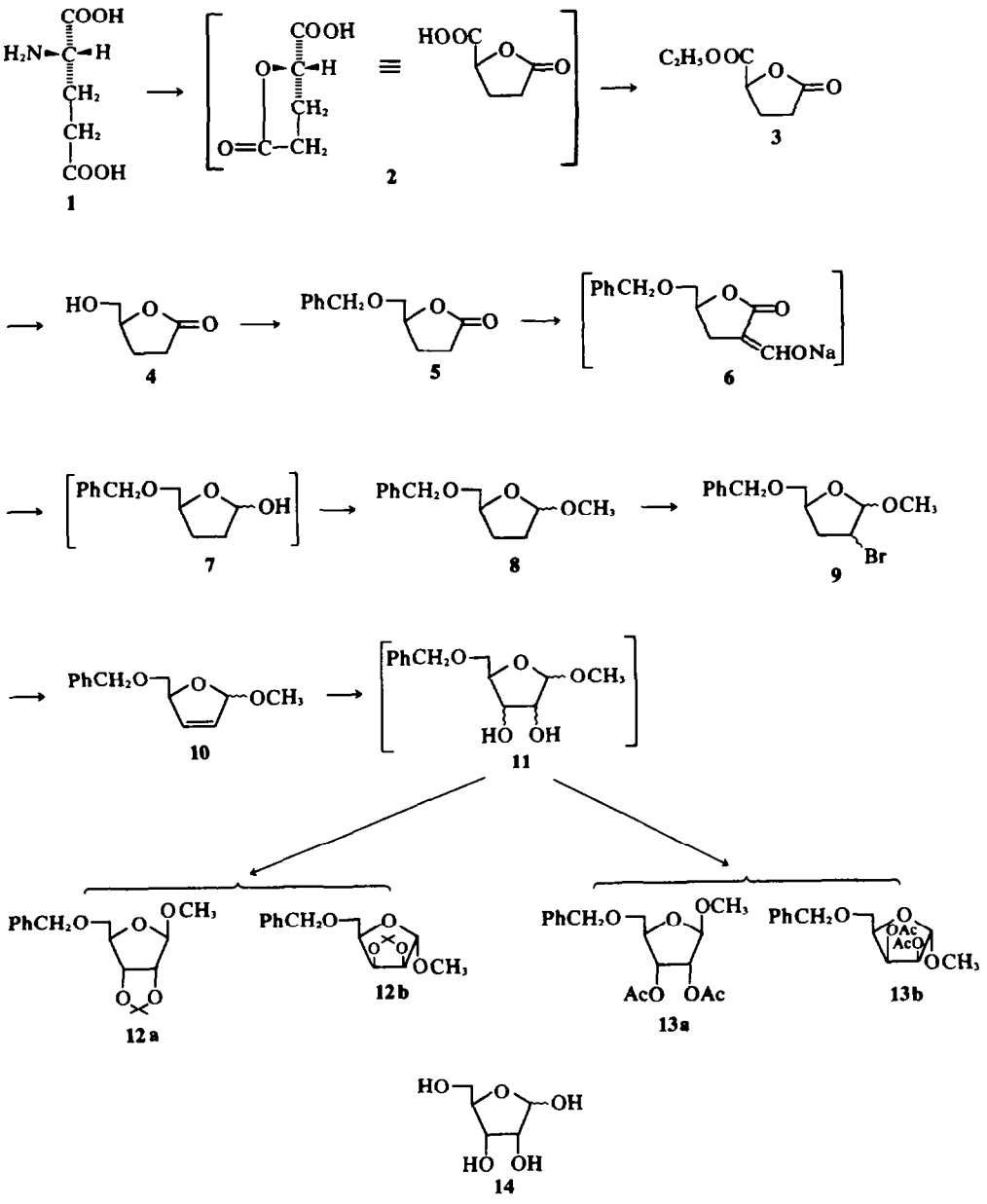
Abstract—A new stereoselective synthesis of D-ribose (**14**) starting from L-glutamic acid (**1**) is described, by making use of the chiral center of **1** as that at C-4 of **14**. Oxidation of methyl 5-O-benzyl-2,3-dideoxy-D-pent-2-enofuranoside (**10**) with potassium permanganate or osmium tetroxide was shown to occur preferentially from the rear side of the OMe group at C-1.

The synthesis in the carbohydrate field is concerned mainly with chemical modification of naturally occurring monosaccharides.[3] Total synthesis of some monosaccharides and related compounds starting from non-carbohydrates has also been reported.[4] In the latter case, however, it should be mentioned that optical resolution is inevitably required at some stage of the synthetic route to obtain optically active objectives from achiral or racemic starting materials. It is highly desirable, therefore, to use a suitably constructed and optically active compound as a starting material to avoid a resolution step in the synthesis.

The present paper describes a new synthesis of D-ribose (**14**) from L-glutamic acid (**1**) without a resolution step as shown in the Scheme by making use of the chiral center of **1** as that at C-4 of **14**. The reason why we chose **1** as the starting material is as follows: (1) Nitrous acid deamination of **1** is reported[5] to give only the substitution product, i.e., (*S*)-γ-carboxy-γ-butyrolactone (2). This reaction is expected[5,6] to proceed with full retention of configuration due to the participation of the neighboring α-carboxylate group. (2) Selective reduction of the ester group in (*S*)-γ-ethoxy*carbonyl*-γ-butyrolactone (3) to (*S*)-γ-hydroxy*methyl*-γ-butyrolactone (4) is expected to be realizable from our earlier findings[7] that α-hydroxy esters are reduced to α-hydroxy alcohols (1,2-diols) with sodium borohydride much more rapidly than the corresponding α-unsubstituted esters are. This means that **1** is an ideal starting material for **4**, a compound having the parent skeleton of D-pentose. (3) **1** is one of the most inexpensive optically active compounds and is now commercially produced in quantity. On the other hand, we insisted on getting 2,3-unsaturated derivative, i.e., methyl 5-O-benzyl-2,3-dideoxy-D-pent-2-enofuranoside (**10**) as a key compound in the synthesis, because it should be a desirable intermediate for various kinds of D-pentoses including deoxy-, amino-, thio- and halo-derivatives, and also because there has been an example[8] that the reaction to the double bond in this type had occurred stereoselectively trans to the substituent at C-4, regardless of the substituent at C-1.

Nitrous acid deamination of **1** in aqueous solution gave a lactone acid (**2**), which was converted to the corresponding lactone ester (**3**) in 76% yield from **1**. Purification of **2** by vacuum distillation caused partial racemization probably due to its high boiling point. Reduction of **3** with sodium borohydride in ethanol at room temperature afforded the lactone alcohol (**4**) in 64% yield, whose IR absorption at 3400 and 1762 cm^{-1} indicated the presence of hydroxy and γ-lactone functions. Treatment of **4** with benzyl bromide and silver oxide in dimethyl formamide at room temperature gave the corresponding benzyl ether (**5**) in 79% yield. Benzyl group was employed as hydroxy brocking because of its stability under acidic and alkaline conditions. This benzyl ether (**5**) was treated with sodium and ethyl formate in ether under the Claisen reaction condition. The resulting yellow precipitates (presumably **6**) was heated in acidic aqueous dioxane to give 5-O-benzyl-2,3-dideoxy-D-pentofuranose (**7**) by the sequence of reactions involving hydrolysis of the lactone ring, decarboxylation and subsequent ring re-closure.[9] As **7** was unstable, it was treated immediately with methanolic hydrogen chloride to give the corresponding methyl furanoside (**8**) in 65% yield from **5**. **8** was found to be a mixture of diastereomers showing two peaks in GLC analysis as well as two methoxy singlet signals (δ, 3·20 and 3·24) in NMR spectrum. The reaction of **8** with bromine in ether in the presence of calcium carbonate followed by heating of the product in methanol afforded a diastereomeric mixture of monobromo derivatives (**9**) in 88% yield. Treatment of **9** with excess sodium



methoxide in methanol under reflux gave the unsaturated compound (**10**) in 89% yield, whose IR absorption at 1628 cm^{-1} indicated the presence of a double bond. **10** was also found to be a mixture of diastereomers based on two methoxy singlet signals (δ, 3·32 and 3·34) in NMR spectrum. The isolation of α- and β-anomer, however, was not successful, since **10** easily decomposes to furfuryl alcohol benzyl ether on extended heating or on acidic treatment, as does methyl 5-O-benzoyl-2,3-dideoxy-β-D-pent-2-enofuranoside.[10]

Oxidation of **10** with potassium permanganate in aqueous acetone[8] gave a syrup (**11**), which was treated with acetone in the presence of hydrogen chloride to give a mixture of isopropylidene derivatives in 43% yield. GLC analysis of this mixture showed it to be composed of two isopropylidene derivatives (**12a** and **12b**) in a ratio of 2·7:1, which were isolated by silica gel column chromatography. NMR spectrum of **12a** exhibited $J_{1,2}$ and $J_{3,4}$ (< 0·5 and < 0·5 Hz, respectively) similar in magnitude to those[11] of both H-1–H-2 and H-3–H-4 trans protons, while that of **12b** exhibited $J_{1,2}$ and $J_{3,4}$ (< 0·5 and 3·3 Hz, respectively) similar to those[12] of H-1–H-2 trans and H-3–H-4 cis protons. These data shows that **12a** is methyl 5 - O - benzyl -

2,3 - O - isopropylidene - β - D - ribofuranoside and **12b** is methyl 5 - O - benzyl - 2,3 - O - isopropylidene - α - D - lyxofuranoside. Two other possible isopropylidene derivatives, i.e., α-D-ribofuranoside and β-D-lyxofuranoside, were not detected in the reaction product by GLC analysis. Acetylation of **11** with acetic anhydride in pyridine also afforded two acetates (**13a** and **13b**) in a ratio of 2·7:1, which were isolated again by silica gel column chromatography. Judging from NMR coupling constants, they were found to be methyl 5 - O - benzyl - 2,3 - di - O - acetyl - β - D - ribofuranoside (**13a**) ($J_{1,2} < 0·5$, $J_{2,3} = 4·5$ and $J_{3,4} = 9·0$ Hz) and methyl 5 - O - benzyl - 2,3 - di - O - acetyl - α - D - lyxofuranoside (**13b**) ($J_{1,2} = 2·5$, $J_{2,3} = 4·5$ and $J_{3,4} = 4·5$ Hz). These values are similar to those[13] of 1,3,5 - tri - O - benzoyl - 2 - O - methanesulfonyl - β - D - ribofuranose ($J_{1,2} < 0·5$, $J_{2,3} = 4·6$ and $J_{3,4} = 7·0$ Hz) and 1,2,3,5 - tetra - O - benzoyl - α - D - lyxofuranose ($J_{1,2} = 1·5$, $J_{2,3} = 5·2$ and $J_{3,4} = 5·4$ Hz), respectively. Oxidation of **10** with osmium tetroxide, followed by alkali-manitol treatment and acetylation, gave the same result as that obtained by the oxidation with potassium permanganate in a higher yield of 67%. Contrary to our initial expectation that oxidation would occur to afford the products of the *ribo* configuration regardless of the configuration at C-1, these results clearly indicate that the reaction occurred completely from the rear side of the methoxy group at C-1.

On the other hand, **11** was subjected to hydrogenolysis with palladium-charcoal in methanol containing hydrogen chloride under the atmospheric pressure of hydrogen. The product was hydrolyzed with dilute sulfuric acid to give an oil, which was treated with aniline according to the reported method.[14] Recrystallization of the product afforded an anilide of m.p. 119–122°, $[\alpha]_D^{23} + 59·0°$ (pyridine), which was shown to be identical with the authentic D-ribose anilide of m.p. 119–122°, $[\alpha]_D^{23} + 60·2°$ (pyridine), prepared from commercial D-ribose in the same way. D-Ribose anilide has been known to be hydrolyzed to D-ribose.[14]

Unsaturated compound (**10**) prepared in the present synthesis is considered to be an important intermediate leading to various kinds of other D-pentoses, which is the subject of the next report.[15]

EXPERIMENTAL

All m.ps and b.ps are uncorrected. IR spectra were measured with a JASCO DS-402G spectrometer. NMR spectra were measured with a JEOL JNM-3H-60 spectrometer (60 MHz) or a Varian HA-100 spectrometer (100 MHz) using tetramethylsilane as an internal standard. Optical rotations were measured with a Yanaco OR-50 automatic polarimeter. Microanalyses were performed by the members of the Central Analysis Room of our faculty.

(S)-(+)-γ-Ethoxycarbonyl-γ-butyrolactone (**3**)[16]

To a suspension of **1** (90 g, 0·612 mole) in H_2O (240 ml) and conc HCl aq (126 ml) was added a soln of $NaNO_2$ (63 g, 0·912 mole) in H_2O (135 ml) during 4 h under vigorous stirring at −5°–0°, and then the resulting clear soln was allowed standing at room temp overnight. The solvent was evaporated *in vacuo* to dryness below 50° to give a residue, which was shaken with EtOAc (300 ml). The insoluble material was filtered off and washed with EtOAc. The filtrate and washings were combined, and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* afforded (*S*) - γ - carboxy - γ - butyrolactone as a pale yellow syrup. A soln of this syrup and *p*-toluenesulfonic acid (2 g) in EtOH (130 ml) and benzene (300 ml) was refluxed for 5 h, and then was distilled off under atmospheric pressure until the b.p. raised to 79°. Benzene (1 l.) was added to the residue, and the whole was washed with H_2O, 10% Na_2CO_3 aq, H_2O, and dried over Na_2SO_4. Evaporation of the solvent and distillation of the residue gave **3** as a colorless liquid (73·5 g, 76% yield based on **1**) of b.p. 135–140°/10 mm; $[\alpha]_D^{32} + 11·5°$ (*c* = 2·93, EtOH); IR ν_{max}^{film} cm^{-1}: 1783 (lactone), 1745 (ester); NMR (CCl_4) δ: 1·32 (3H, t, J = 7 Hz, $-CH_2-CH_3$), 2·1–2·9 (4H, m, $-CH_2-CH_2-$), 4·23 (2H, q, J = 7 Hz, $-O-CH_2-CH_3$), 4·85 (1H, m, $-CH_2-CH-O-$).

(S)-(+)-γ-Hydroxymethyl-γ-butyrolactone (**4**)

To a stirred suspension of $NaBH_4$ (10·5 g, 0·277 mole) in EtOH (200 ml) was added a soln of **3** (67·5 g, 0·427 mole) in EtOH (330 ml) at 20–25°, and the whole was stirred at room temp for 1 h. The mixture was adjusted to pH 3 with 10% HCl aq, the resulting ppt was filtered off, and the filtrate was evaporated *in vacuo*. MeOH was added to the residue and then evaporated *in vacuo*. This process of MeOH addition and evaporation was repeated 4 times, and then the residue was purified by column chromatography on silica gel (250 g) with 7% EtOH–$CHCl_3$ as eluting solvent to give an orange-colored oil. Repeated distillations of this oil gave **4** as a colorless liquid (32 g, 65% yield) of b.p. 131–147°/7 mm; $[\alpha]_D^{26} + 31·3°$ (*c* = 2·92, EtOH); IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1762 (lactone); NMR ($CDCl_3$) δ: 2·0–2·8 (4H, m, $-CH_2-CH_2-$), 3·6–4·0 (3H, m, $-OH$, $-CH_2-O-$), 4·65 (1H, m, $-CH_2-CH-O-$). (Found: C, 51·57; H, 7·11. $C_5H_8O_3$ requires: C, 51·72; H, 6·94%).

O-Benzoate of **4**. A soln of **4** (1·8 g, 15·5 mmoles) and benzoyl chloride (3·0 g, 21·3 mmoles) in pyridine (30 ml) was refluxed for 1·5 h, and then was evaporated *in vacuo* to dryness. The residue was shaken with H_2O and benzene, and the organic layer was separated, washed successively with 10% Na_2CO_3 aq, H_2O, 10% HCl aq, H_2O, and dried over Na_2SO_4. Evaporation of the solvent afforded a pale yellow solid (3·3 g, 97% yield). Recrystallizations from benzene–hexane gave white needles of m.p. 59–60·5°; $[\alpha]_D^{26} + 48·2°$ (*c* = 1·03, EtOH); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1777 (lactone), 1730 (benzoate); NMR ($CDCl_3$) δ: 2·0–2·8 (4H, m, $-CH_2-CH_2-$), 4·45 (2H, m, $-CH_2-O-$), 4·85 (1H, m, $-CH_2-CH-O-$), 7·5–8·0 (5H, m, C_6H_5-). (Found: C, 65·71; H, 5·35. $C_{12}H_{12}O_4$ requires: C, 65·44; H, 5·49%).

(S)-(+)-γ-Benzyloxymethyl-γ-butyrolactone (**5**)

A suspension of **4** (25 g, 0·216 mole), benzyl bromide (85 g, 0·497 mole) and silver oxide (40 g, 0·172 mole) in DMF (170 ml) was vigorously stirred with protection from light at room temp for 48 h, and then the insoluble material was filtered off and washed with $CHCl_3$ (1 l.). The filtrate and washings were combined and allowed to stand overnight in the refrigerator, and then the resulting ppt was filtered off. Pyridine (100 ml) was added to the filtrate, and the whole was washed successively with H_2O, 10%

HCl aq, H_2O, 10% Na_2CO_3 aq, H_2O, and dried over Na_2SO_4. Evaporation of the solvent and distillation of the residue gave **5** (35 g, 79% yield) as a pale yellow liquid of b.p. 160–164°/0·02 mm; $[\alpha]_D^{15}$ + 18·1° (c = 2·70, EtOH); NMR (CCl_4) δ: 1·8–2·5 (4H, m, $-CH_2-CH_2-$), 3·47 (2H, m, $-CH-CH_2-O-$), 4·45 (1H, m, $-CH-CH_2-O-$), 4·45 (2H, s, $C_6H_5-CH_2-O-$), 7·17 (5H, s, C_6H_5-). (Found: C, 69·61; H, 6·84. $C_{12}H_{14}O_3$ requires: C, 69·88; H, 6·84%).

Methyl 5-O-*Benzyl*-2,3-*dideoxy*-D-*pentofuranoside* (**8**)

EtOH (0·4 ml) was added to a suspension of powdered Na (4·0 g, 0·174 atom) in dry ether (70 ml), and the mixture was stirred at room temp for 2 h.[9] To this suspension was added under stirring a soln of **5** (29·0 g, 0·141 mole) and ethyl formate (14·0 g, 0·189 mole) in dry ether (85 ml) at such a rate that moderate refluxing was maintained, and then the whole was stirred at room temp overnight. After cooling in ice-bath for 3 h, the yellow ppt was filtered, washed with dry ether, and dried in the desiccator. To a soln of this hygroscopic material in H_2O (140 ml) and dioxane (200 ml) was added 10% HCl aq (55 ml), and the mixture was refluxed for 72 h, during which the generation of CO_2 gas was recognized. After cooling, the soln was extracted with EtOAc, and the organic layer was washed with sat $NaHCO_3$ aq, sat NaCl aq, and dried over Na_2SO_4 for only 30 min. Evaporation of the solvent *in vacuo* to dryness afforded a syrup (**7**) showing a positive Benedict test, which was soon dissolved in 0·5% HCl–MeOH (170 ml), and the soln was refluxed for 5 h. 5% KOH–MeOH was added to neutralize the mixture and the solvent was evaporated *in vacuo*. Benzene was added to the residue and the insoluble materials were filtered off. Evaporation of the filtrate afforded an orange-colored oil. Distillation of this oil gave **8** (20 g, 65% yield based on **5**) as a colorless liquid of b.p. 120–128°/2 mm; $[\alpha]_D^{15}$ + 23·8° (c = 5·60, MeOH); NMR (CCl_4) δ: 1·80 (4H, m, $-CH_2-CH_2-$), 3·20, 3·24 (total 3H, two s, $-O-CH_3$), 3·40 (2H, m, $-O-CH_2-CH-$), 4·18 (1H, m, $-O-CH_2-CH-$), 4·47, 4·49 (total 2H, $C_6H_5-CH_2-O-$), 4·87 (1H, m, $CH_3-O-CH-$), 7·18 (5H, s, C_6H_5-). (Found: C, 70·39; H, 8·12. $C_{13}H_{18}O_3$ requires: C, 70·24; H, 8·16%). GLC analysis (15% Carbowax 20M, 2m, at 200°) showed two peaks at retention times of 12·5 and 13·0 min.

2,4-*Dinitrophenylhydrazone of* **7**. A soln of **7** (0·2 g) and 2,4-dinitrophenylhydrazine (0·2 g) in EtOH (2 ml) was refluxed for 3·5 h, and then the insoluble materials were filtered off. Ether was added to the residue obtained on evaporation of the filtrate *in vacuo*, and the whole was triturated. The resulting yellow ppt was obtained by filtration and recrystallized from EtOH–H_2O to give yellow needles of m.p. 97–98·5°; IR ν_{max}^{KBr} cm^{-1}: 3370, 3290, 1620, 1591 (hydrazone), 1517, 1323 (nitro). (Found: C, 55·51; H, 5·14; N, 14·28. $C_{18}H_{20}O_6N_4$ requires: C, 55·66; H, 5·19; N, 14·43%).

Methyl 5-O-*benzyl*-2-*bromo*-2,3-*dideoxy*-D-*pentofuranoside* (**9**)

Br_2 (12 g, 75 mmoles) was added under vigorous stirring to a soln of **8** (16·0 g, 72·1 mmoles) in dry ether (150 ml) in the presence of $CaCO_3$ (8·8 g, 88·0 mmoles), and then the mixture was refluxed for 1 h. After cooling, the insoluble materials were filtered off and washed with ether. The filtrate and washings were combined and evaporated *in vacuo* to afford a yellow oil, which was dissolved in MeOH (200 ml) and the whole was refluxed for 2 h. 5% KOH–MeOH was added to neutralize the mixture, and the solvent was evaporated *in vacuo*. Benzene was added and the insoluble materials were filtered off. Evaporation of the filtrate left an orange-colored oil. Distillation gave a colorless liquid (19·0 g, 88% yield) of b.p. 150–164°/3 mm; $[\alpha]_D^{18}$ + 15·8° (c = 2·16, MeOH); NMR (CCl_4) δ: 2·1–2·6 (2H, m, $-CH_2-CHBr-$), 3·23, 3·28 (total 3H, two s, CH_3-O-), 3·50 (2H, m, $-O-CH_2-CH-$), 3·9–4·3 (2H, m, $-CHBr-$, $-O-CH_2-CH-$), 4·52 (2H, s, $C_6H_5-CH_2-O-$), 5·0 (1H, two signals of different intensity, $CH_3-O-CH-$), 7·23 (5H, s, C_6H_5-). (Found: C, 52·09; H, 5·71; Br, 26·48. $C_{13}H_{17}O_3Br$ requires: C, 51·84; H, 5·69; Br, 26·53%).

Methyl 5-O-*benzyl*-2,3-*dideoxy*-D-*pent*-2-*enofuranoside* (**10**)

To a soln of NaOMe (prepared from Na (4·7 g, 0·204 atom)) in MeOH (100 ml) was added **9** (7·7 g, 25·7 mmoles) and the whole was refluxed for 20 h. The solvent was evaporated *in vacuo* to dryness to give a residue, which was mixed with benzene. The insoluble materials were filtered off and washed with benzene. The filtrate and washings were combined and evaporated to dryness *in vacuo*. Distillation of the residue gave a colorless liquid (4·9 g, 89% yield) of b.p. 123–126°/2 mm; $[\alpha]_D^{13}$ – 73·5° (c = 2·29, MeOH); IR ν_{max}^{film} cm^{-1}: 1628 (double bond); NMR ($CDCl_3$) δ: 3·32, 3·34 (total 3H, two s, CH_3-O-), 3·45 (2H, m, $-O-CH_2-CH-$), 4·80 (1H, m, $-O-CH_2-CH-$), 5·5–5·9 (2H, m, $CH_3-O-CH-$, $-CH=CH-CH-CH_2-$), 6·10 (1H, m, $CH_3-O-CH-CH=CH-$), 7·22 (5H, s, C_6H_5-). This compound easily decomposes to furfuryl alcohol benzyl ether.

Methyl 5-O-*Benzyl*-2,3-O-*isopropylidene*-β-D-*ribofuranoside* (**12a**) *and methyl* 5-O-*Benzyl*-2,3-O-*isopropylidene*-α-D-*lyxofuranoside* (**12b**)

To a soln of **10** (7·6 g, 34·5 mmoles) in acetone (60 ml) and H_2O (25 ml) under ice-cooling was added in portions $KMnO_4$ (7·0 g, 44·3 mmoles) under stirring at −15–−10° for 2·5 h, and then the mixture was allowed standing at room temp overnight. The ppt was filtered off and washed with CH_2Cl_2, and the filtrate was extracted with CH_2Cl_2. The combined CH_2Cl_2 layer was dried over Na_2SO_4 and evaporated to dryness *in vacuo* to afford a syrup (5·5 g). This syrup (1·0 g) was dissolved in acetone (30 ml) containing conc HCl aq (1 drop), and the mixture was stirred at room temp for 2 h. Evaporation of the solvent *in vacuo* gave a residue, which was mixed with benzene. Evaporation of the benzene *in vacuo* to dryness afforded a yellow oil (1·0 g), which was purified by column chromatography on silica gel to give a mixture of **12a** and **12b** (0·80 g, 43% yield based on **10**). Distillation gave a colorless liquid of b.p. 145°/2 mm. (Found: C, 65·43; H, 7·58. $C_{16}H_{22}O_5$ requires: C, 65·29; H, 7·53%). This sample showed two peaks on GLC analysis (15% Carbowax 20M, 2m, at 220°) at retention times of 12 and 14·5 min in an area ratio of 1:2·7. The corresponding two isomers were isolated as pure forms by column chromatography on silica gel with benzene as eluting solvent. **12a** (retention time 14·5 min) was obtained as a colorless liquid of b.p. 145°/2 mm; $[\alpha]_D^{21}$ – 52·3° (c = 1·59, benzene); NMR (CCl_4) δ: 1·26, 1·42 (6H, two s, CH_3-C-CH_3), 3·20 (3H, s, CH_3-O-), 3·35 (2H, m, $-O-CH_2-CH-$), 4·25 (1H, q, $-O-CH_2-CH-$), 4·39 (1H, d, $J_{2,3}$ = 6·2 Hz,

CH_3–O–CH–CH_2–), 4·46 (2H, s, C_6H_5–CH_2–O–), 4·60 (1H, d, $J_{2,3}$ = 6·2 Hz, CH_3–O–CH–CH–CH_2–), 4·80 (1H, s, CH_3–O–CH–), 7·23 (5H, s, C_6H_5–). (Found: C, 65·47; H, 6·72%). **12b** (retention time 12 min) was obtained as a colorless liquid of b.p. 140°/2 mm; $[\alpha]_D^{21}$ + 32·1° (*c* = 1·25, benzene); NMR (CCl_4) δ: 1·25, 1·37 (6H, two s, CH_3–C–CH_3), 3·25 (3H, s, CH_3–O–), 3·4–3·7 (2H, m, –O–CH_2–CH–), 3·8–4·1 (1H, m, –O–CH_2–CH–), 4·40 (1H, d, $J_{2,3}$ = 5·8 Hz, CH_3–O–CH–CH–), 4·49 (2H, s, C_6H_5–CH_2–O–), 4·60 (1H, d–d, $J_{2,3}$ = 5·8 and $J_{3,4}$ = 3·3 Hz, CH_3–O–CH–CH–CH–), 4·75 (1H, s, CH_3–O–CH–), 7·22 (5H, s, C_6H_5–). (Found: C, 65·25; H, 7·50%).

Methyl 5 - O - *Benzyl* - 2,3 - *di* - O - *acetyl* - β - D - *ribofuranoside* (**13a**) *and methyl* 5 - O - *Benzyl* - 2,3 - *di* - O - *acetyl* - α - D - *lyxofuranoside* (**13b**)

(a) $KMnO_4$ *Oxidation.* The crude product **11** (2·2 g) obtained from **10** (3·8 g) according to the procedure as described above, and Ac_2O (3·5 g, 34·3 mmoles) in pyridine (20 ml) were mixed and allowed standing at room temp for 4 h. The mixture was poured into 5% $NaHCO_3$ aq (20 ml) under ice-cooling, and the whole was extracted with EtOAc. The combined organic layer was dried over Na_2SO_4. Evaporation of the solvent gave a brown oil (3·0 g), which showed two peaks on GLC analysis (15% Carbowax 20M, 2m, at 240°) at retention times of 16 and 18 min in an area ratio of 2·7 : 1. The corresponding two diacetates were isolated as pure forms by column chromatography on silica gel with CH_2Cl_2-benzene as eluting solvent followed by distillation. **13a** (retention time 16 min) was obtained as a colorless liquid of b.p. 175°/0·1 mm; $[\alpha]_D^{24}$ – 26·8° (*c* = 2·03, benzene); IR ν_{max}^{film} cm^{-1}: 1755, 1242 (acetate); NMR (CCl_4) δ: 1·98, 2·06 (6H, two s, –OCOCH_3), 3·30 (3H, s, CH_3–O–), 3·51 (2H, d, $J_{4,5}$ = 5·5 Hz, –O–CH_2–CH–), 4·15 (1H, m, –O–CH_2–CH–), 4·50 (2H, s, C_6H_5–CH_2–O–), 4·78 (1H, s, CH_3–O–CH–), 5·08 (1H, d, $J_{2,3}$ = 4·5 Hz, CH_3–O–CH–CH–), 5·22 (1H, d-d, $J_{2,3}$ = 4·5 Hz and $J_{3,4}$ = 9·0 Hz, CH_3–O–CH–CH–CH–), 7·22 (5H, s, C_6H_5–). (Found: C, 60·44; H, 6·52. $C_{17}H_{22}O_7$ requires: C, 60·34; H, 6·55%). **13b** (retention time 18 min) was obtained as a colorless liquid of b.p. 165°/0·05 mm; $[\alpha]_D^{24}$ + 73·8° (*c* = 2·09, benzene); IR ν_{max}^{film} cm^{-1}: 1755, 1242 (acetate); NMR (CCl_4) δ: 1·90, 1·95 (6H, two s, –OCOCH_3), 3·34 (3H, s, CH_3–O–), 4·52 (2H, d, $J_{4,5}$ = 6·0 Hz, –O–CH_2–CH–), 4·2–4·5 (1H, m, –O–CH_2–CH–), 4·43 (2H, s, C_6H_5–CH_2–O–), 5·07 (1H, d-d, $J_{1,2}$ = 2·5 and $J_{2,3}$ = 4·5 Hz, CH_3–O–CH–CH–), 5·42 (1H, t, $J_{2,3}$ = 4·5 and $J_{3,4}$ = 4·5 Hz, CH_3–O–CH–CH–CH–), 7·22 (5H, s, C_6H_5–). (Found: C, 60·58; H, 6·62%.)

(b) OsO_4 *Oxidation.* To a stirred soln of **10** (0·45 g, 2·05 mmoles) in dry ether (20 ml) was added a soln of OsO_4 (0·52 g, 2·05 mmoles) in dry ether (20 ml) at room temp, and then pyridine (0·33 g, 4·17 mmoles) in dry ether (15 ml) was added. A brown tar was separated, and the whole was allowed standing at room temp overnight, and then the residue obtained by decantation was dissolved in CH_2Cl_2 (30 ml). Mannitol (4 g) in 1% KOH aq (40 ml) was added and the whole was stirred vigorously at room temp for 5·5 h. The organic layer was separated, washed with sat NaCl aq, and dried over Na_2SO_4. Evaporation of the solvent gave a brown oil (0·44 g). A soln of this oil and Ac_2O (0·70 g, 6·83 mmoles) in pyridine was allowed standing at room temp for 3 h. The mixture was poured into 5% $NaHCO_3$ aq (15 ml) under ice-cooling, and the whole was extracted with EtOAc. The combined organic layer was washed with sat NaCl aq, and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* to dryness left an oil, which was purified by column chromatography on silica gel to give a pale yellow oil (0·46 g, 67% yield based on **10**). This sample was shown to be composed of **13a** and **13b** in a ratio of 2·7 : 1 based on GLC analysis.

D-*Ribose anilide*

A mixture of **11** (1·9 g, 7·42 mmoles) and 5% Pd–C (0·3 g) in MeOH (100 ml) and sat HCl–MeOH (1 drop) was shaken vigorously under the atmospheric pressure of H_2 until the absorption of H_2 ceased. The catalyst was filtered off, and the filtrate was evaporated *in vacuo* to dryness to give a syrup (1·1 g, 90% yield). A soln of this syrup (1·0 g, 6·02 mmoles) in 0·1 N H_2SO_4 aq (100 ml) was refluxed for 2·5 h. The soln was cooled to room temp and neutralized with $BaCO_3$. After filtration, the aqueous soln was evaporated *in vacuo* to dryness, and the residue was extracted with EtOH (4 ml). Evaporation to dryness gave a yellow oil (0·9 g), which was dissolved in H_2O (10 ml), and then the soln was adjusted to pH 4 with 3N H_2SO_4 aq. To this soln was added a soln of aniline (0·4 ml) in EtOH (4 ml) under ice-cooling, and the mixture was allowed standing in a refrigerator overnight. The resulting ppt was obtained by filtration, and recrystallized from EtOAc-hexane to give colorless platelets of m.p. 119–122°; $[\alpha]_D^{23}$ + 59·0° (*c* = 0·90, pyridine). (Found: C, 56·65; H, 6·92; N, 5·81. $C_{11}H_{15}O_4N \cdot \frac{1}{2}H_2O$ requires: C, 56·40; H, 6·89; N, 5·98%). This sample was shown to be identical with the authentic sample (m.p. 119–122°; $[\alpha]_D^{23}$ + 60·2° (*c* = 0·81, pyridine)) prepared from commercial D-ribose in a manner described in a literature[14] by mixed m.p. test and IR spectral comparison.

REFERENCES

[1]Part XXIX: M. Kitamoto, K. Hiroi, S. Terashima and S. Yamada, *Chem. Pharm. Bull. Tokyo* **22**, 459 (1974)

[2]Preliminary communication: K. Koga, M. Taniguchi and S. Yamada, *Tetrahedron Letters* 263 (1971)

[3a]L. Hough and A. C. Richardson, *Rodd's Chemistry of Carbon Compounds* (Edited by S. Coffey), Vol. IF, p. 198, Elsevier, Amsterdam (1967); [b]L. Hough and A. C. Richardson, *The Carbohydrates* (Edited by W. Pigman and D. Horton), Vol. IA, p. 114, Academic Press, New York (1972)

[4]J. K. N. Jones and W. A. Szarek, *The Total Synthesis of Natural Products* (Edited by J. Apsimon), Vol. 1, p. 1, Wiley-Interscience, New York (1973)

[5]A. T. Austin and J. Howard, *J. Chem. Soc.* 3278, 3284, 3593 (1961)

[6a]P. Brewster, F. Hiron, E. D. Hughes, C. K. Ingold and P. A. D. S. Rao, *Nature*, **166**, 179 (1950); [b]S. Yamada, M. Taniguchi and K. Koga, *Tetrahedron Letters* 25 (1969); [c]M. Taniguchi, K. Koga and S. Yamada, *Chem. Pharm. Bull. Tokyo*, **20**, 1438 (1972)

[7]H. Seki, K. Koga and S. Yamada, *Ibid.* **15**, 1948 (1967)

[8]I. Iwai, T. Iwashige, J. Asai, K. Tomita, T. Hiraoka and J. Ide, *Ibid.* **11**, 188 (1963)

[9]F. Korte and K. H. Buchel, *Chem. Ber.* **92**, 877 (1959)

[10]R. J. Ferrier, *Advances in Carbohyd. Chem.* **24**, 229 (1969)

[11]N. J. Leonard and K. L. Carraway, *J. Heterocycl. Chem.* **3**, 485 (1966)

[12]S. J. Angyal, V. A. Pickles and A. Ahluwalia, *Carbohyd. Res.* **3**, 300 (1967)

[13]J. D. Stevens and H. G. Fletcher, Jr., *J. Org. Chem.* **33**, 1799 (1968)
[14a]R. L. Whistler and J. N. BeMiller, *Methods in Carbohyd. Chem.* **1**, 81 (1961); [b]G. A. Howard, G. W. Kenner, B. Lythgoe and A. R. Todd, *J. Chem. Soc.* 855 (1946)
[15]M. Taniguchi, K. Koga and S. Yamada, *Chem. Pharm. Bull. Tokyo*, in press
[16]H. Plieninger, G. Ege, R. Fischer and W. Hoffmann, *Chem. Ber.* **94**, 2106 (1961)
[17]N. J. Leonard, F. C. Sciavolino and V. Nair, *J. Org. Chem.* **33**, 3169 (1968)