Tetrahedron Letters No.3, pp. 266, 1971. Pergamon Press. Printed in Great Britain.

A NEW SYNTHESIS OF D-RIBOSE FROM L-GLUTAMIC ACID[1]

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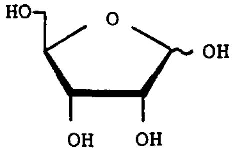
(Received in Japan 4 December 1970; received in UK for publication 18 December 1970)

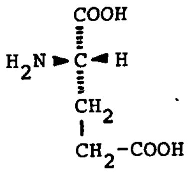
Synthesis in the carbohydrate field is concerned mainly with chemical transformations of monosaccharides that are either naturally-occurring or readily obtainable.[2] Total synthesis of some monosaccharides and related compounds starting from simple non-carbohydrate substances[2,3] has also been reported. Mention should be made, however, that resolution is usually inevitable at some stage of the synthetic route to obtain optically active objectives in the latter case. This communication describes a new synthesis of D-ribose (I) from L-glutamic acid (II) without resolution, making use of the asymmetric center of II as that at C_4 of I.

Nitrous acid deamination of II in aqueous solution gave a lactone acid (III), which was esterified to the corresponding lactone ester[4] (IV), $[\alpha]^{32}_{D}$ +11.5°(EtOH), ir(film) 1783, 1745 cm^{-1}, in 76% yield from II. This deamination reaction is considered to proceed with full retention of configuration due to the participation of the neighboring carboxylate group.[5] Reduction of IV with $NaBH_4$ in EtOH afforded the lactone alcohol (V) in 65% yield, $[\alpha]^{26}_{D}$ +31.3°(EtOH), ir(film) 3400, 1762 cm^{-1}, which gave a benzoate (VI), mp 59-60.5°, ir($CHCl_3$) 1777, 1730 cm^{-1}. This reduction may be analogous to examples in which α-hydroxy, α-halo, and α-amino esters are reduced much more easily with $NaBH_4$ than are α-unsubstituted esters.[6] Treatment of V with benzyl bromide and silver oxide in the usual manner afforded the corresponding benzyl ether (VII), bp 160° (0.02mm), $[\alpha]^{15}_{D}$ +18.1°(EtOH), ir(film) 1776, 740, 701 cm^{-1}, in 79% yield. This benzyl ether (VII) was treated with sodium and ethyl formate in Et_2O. The resulting sodium salt (VIII) was heated in acidic aqueous dioxane to give 5-O-benzyl-2,3-dideoxy-D-pentofuranose (IX) by the sequence of reactions involving hydrolysis of the lactone ring, decarboxylation and subsequent ring re-closure.[7] IX gave the corresponding 2,4-dinitrophenylhydrazone, mp 97-98.5°, ir(KBr) 3370, 3290, 1620, 1591, 1517 cm^{-1}. Methyl glycoside (X), bp 120°(2mm), was obtained in 65% yield from VII and was shown to be an anomeric mixture based on glc as well as nmr(CCl_4), τ 6.76, 6.80 (OCH_3, s). The reaction of X with bromine in Et_2O in the presence of $CaCO_3$ followed by heating of the product in MeOH afforded the monobromo derivative (XI), bp 138°(1mm), in 88% yield, as a mixture of diastereomers, nmr(CCl_4) τ 4.95, 5.00 (C_1-H, s), 5.7-6.1 (C_2-H, C_4-H, m), 6.72, 6.77 (OCH_3, s). Dehydrobromination of XI with MeONa in MeOH gave the unsaturated pentose derivative (XII) in 89% yield, also as an anomeric mixture, ir(film) 1628 cm^{-1}, nmr($CDCl_3$) τ 3.9 (C_2-H, m), 4.1-4.4 (C_1-H, C_3-H, m), 6.66, 6.68 (OCH_3, s). It is noteworthy that XII easily decomposes to furfurylalcohol benzyl ether, especially with acidic substances.

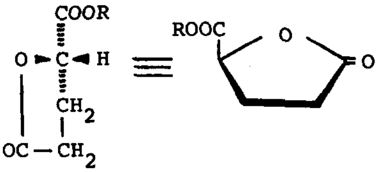
Oxidation of XII with $KMnO_4$ in aqueous acetone[8] gave a syrup (XIII), which was treated with acetone in the presence of HCl to give a mixture of acetonides, bp 145°(2mm), in 43% yield. Separation by silica gel column chromatography afforded two acetonides: XIVa, bp 145°(2mm), $[\alpha]_D^{21}$ -52.3°(benzene), nmr(CCl_4) τ 5.20 (C_1-H, s), 5.40 (C_3-H, d), 5.61 (C_2-H, d), 5.75 (C_4-H, quar.) and XIVb, $[\alpha]_D^{21}$ +32.1°(benzene), nmr(CCl_4) τ 5.25 (C_1-H, s), 5.40 (C_3-H, quar.), 5.60 (C_2-H, d), 5.9-6.2 (C_4-H, m). Nmr coupling constants of XIVa ($J_{12}<0.5$, $J_{23}=6.2$, $J_{34}<0.5$ Hz) and XIVb ($J_{12}<0.5$, $J_{23}=5.8$, $J_{34}=3.3$ Hz) suggest[9] that XIVa and XIVb are methyl 5-O-benzyl-2,3-O-isopropylidene-β-D-ribofuranoside[9a,10] and methyl 5-O-benzyl-2,3-O-isopropylidene-α-D-lyxofuranoside, respectively. The acetonide mixture before separation consists of XIVa and XIVb in a ratio of 2.7 : 1 based on glc analysis. This result was at variance with our expectation that dihydroxylation would occur stereoselectively to the ribose configuration regardless of the configuration at C_1.[8] Acetylation of XIII with acetic anhydride and pyridine also gave a mixture of diacetates (XV), which was separated to methyl 5-O-benzyl-2,3-di-O-acetyl-β-D-ribofuranoside (XVa), bp 175°(0.1mm), $[\alpha]_D^{24}$ -26.8°(benzene) and methyl 5-O-benzyl-2,3-di-O-acetyl-α-D-lyxofuranoside (XVb), bp 165°(0.05mm), $[\alpha]_D^{24}$ +73.8°(benzene). The ratio of XVa and XVb in the acetylation product was similar to that for acetonides based on



(I)

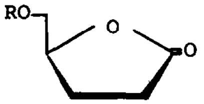


(II)



(III): R=H

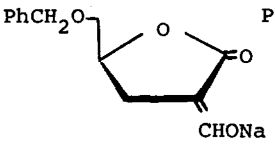
(IV) : R=C_2H_5



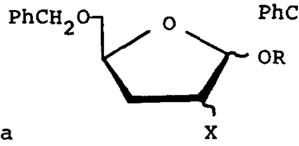
(V) : R=H

(VI) : R=PhCO

(VII): R=$PhCH_2$



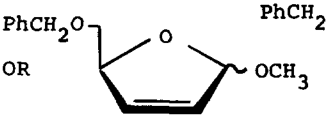
(VIII)



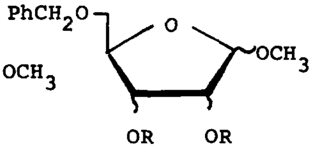
(IX): R=H, X=H

(X) : R=CH_3, X=H

(XI): R=CH_3, X=Br

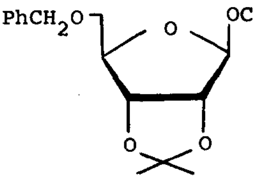


(XII)

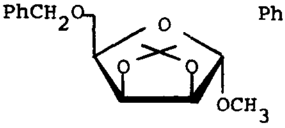


(XIII): R=H

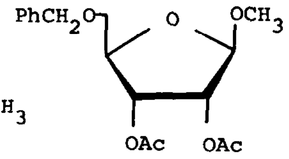
(XV) : R=Ac



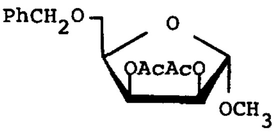
(XIVa)



(XIVb)



(XVa)



(XVb)

glc analysis. Oxidation of XII with OsO_4 followed by treatment with alkali-mannitol and acetylation of the product gave the same result as $KMnO_4$ oxidation but in a higher yield of 67%.

On the other hand, XIII was hydrogenated with Pd-charcoal in MeOH at the atmospheric pressure of hydrogen and its product was treated with 1/10 N H_2SO_4. The syrup obtained, which would be a mixture of D-ribose and D-lyxose, was treated with aniline according to the reported procedure.11) Recrystallizations from ethyl acetate-hexane afforded an anilide, mp 119-122°, $[\alpha]_D^{23}$ +59.0° (pyridine), ir(KBr) 3335, 1608, 1512 cm^{-1}, which was identical with authentic D-ribose anilide, mp 119-122°, $[\alpha]_D^{23}$ +60.2°(pyridine), prepared from commercial D-ribose, based on mixed fusion and ir spectral comparison.

Experiments on the reactions of the unsaturated pentose derivative (XII) leading to other sugars, amino and thio sugars are now in progress.

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