Carbohydrate Research, 33 (1974) 287–295

THE INTERCONVERSION OF MONOSACCHARIDE CONFIGURATIONS ARABINOSE TO LYXOSE

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(Received September 10th, 1973, accepted in revised form, November 29th, 1973)

ABSTRACT

Selective oxidation of the primary hydroxyl group of 1,3-*O*-benzylidene-D-arabinitol (**1**) with methyl sulfoxide–*N*,*N*′-dicyclohexylcarbodiimide–pyridinium trifluoroacetate (Pfitzner–Moffatt reagent), followed by debenzylidenation, provided a route for configurational conversion of D-arabinose into D-lyxose (**4**) The same reaction-sequence was then used for the synthesis of the L enantiomers The sugars prepared were purified by ion-exchange column chromatography and characterized by o r d., n m r, t l c, and g l c.

INTRODUCTION

The configurations of various diastereoisomeric sugars are related through a common alditol, for example, D-arabinose, D-arabinitol, and D-lyxose This relationship offers, in principle, a simple route for the synthesis of uncommon and labeled aldoses from common ones Although Fischer's proof of the D-glucose structure provides a classical example of this type of interconversion of configuration, his synthesis of L-gulose is neither direct nor practical, because it involves too many intermediate steps Previous attempts to oxidize alditols directly to the aldoses resulted in poor yields, and mixtures of products of higher oxidation-states[1,2]

The advent of the Pfitzner–Moffatt oxidation technique suggested the use of this method for a facile configurational interconversion of the type described This method efficiently oxidizes isolated primary and secondary hydroxyl groups to the corresponding aldehydes or ketones, under very mild conditions[3]. This report deals with the use of the Pfitzner–Moffatt oxidant, dimethyl sulfoxide (Me_2SO)–*N*,*N*′-dicyclohexylcarbodiimide (DCC)–pyridinium trifluoroacetate, for the conversion of 1,3-*O*-benzylidine-D-arabinitol (**1**) into D-lyxose (**4**) Once the reaction conditions had been established, a similar synthetic sequence allowed the preparation of L-lyxose, starting from 1,3-*O*-benzylidene-L-arabinitol.

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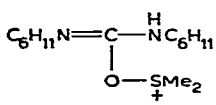
Preparation of the aldehyde by Pfitzner–Moffatt oxidation of the isolated primary alcohol group of **1** was technically difficult On the preparative scale, column chromatography of the final reaction-product was required to give the pure syrupy sugar, free from side products Similar difficulties undoubtedly impeded purification of 3′-*O*-acetylthymidine-5′-aldehyde, the product of Pfitzner and Moffatt's first report[3] Explicit purification procedures were described in the synthesis of 1,2 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose by oxidation of a C-6 primary hydroxyl group[4] (compare ref 5) In the present report, intermediates and final products were obtained in adequate yields and were characterized by g l c , t l c , formation of derivatives, n m r spectroscopy, and comparison of optical rotatory data This new technique could be used for the interconversion of other saccharides, between D-glucose and L-gulose for example and it could also facilitate the preparation of uncommon, radioactive sugars

RESULTS AND DISCUSSION

The success of this synthesis depends on two factors (*a*) the oxidation must be limited to the aldehyde stage, (*b*) the oxidation should be selective for primary alcohol groups The first point was convincingly established by Pfitzner and Moffatt when they showed that their oxidation leads, even over prolonged reaction-periods[3], exclusively to aldehydes or ketones without any traces of the corresponding acids However, competitive studies between the different classes of alcohols have not been reported, and prior to this investigation the question of selectivity toward the primary alcohol function of a sugar remained in doubt.

The available literature suggests that the rate-limiting step of the Me_2SO–DCC oxidation may be the nucleophilic attack of an alcohol (ROH) on the ionic Me_2SO–DCC intermediate **5** leading to the formation of the alkoxysulfonium salt **6**, if this is correct, the reaction should be susceptible to the steric requirements of the attacking nucleophile, in this case the protected alditol Support for this view is provided by the degree of steric preference shown by this reagent in the oxidation of 11α-hydroxyprogesterone and 11β-hydroxyprogesterone The equatorially oriented 11α-hydroxyl group is readily oxidized in the presence of either anhydrous phosphoric acid or trifluoroacetic acid as the proton source, the 11β-hydroxyl group remained completely unreacted under similar reaction-conditions[6]



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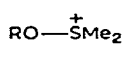

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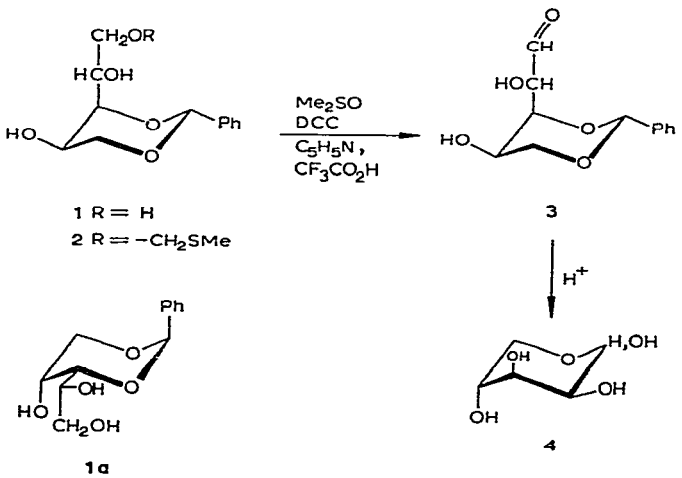
Considering these results, it seemed reasonable to expect some degree of steric preference in the proposed oxidation This report demonstrates the feasibility of the conversion of D-arabinose via D-arabinitol into D-lyxose and also provides evidence

for at lease partial selectivity of the Me_2SO–DCC oxidant toward the primary alcohol groups of certain monosaccharides

The 1,3-benzylidene acetal (**1**) of D-arabinitol was prepared by a literature method[7], with modification of the isolation procedure The melting point of the product agreed with the reported value, and the specific rotation ($[\alpha]_{589}^{25}$ +11 0°) accorded with the value reported by Fluharty[8] but differed from that of Haskins *et al* [7] who reported $[\alpha]_D^{20}$ −7 6° (*c* 2 0, pyridine) G l c of the per(trimethylsilylated) derivative revealed a homogenous product, and a similar result was obtained by t l c Both procedures would have detected any unreacted alditol The yield of compound **1** was low, and variations in the reaction conditions failed to increase it Use of zinc chloride as the Lewis-acid catalyst led to the dibenzylidene acetal Other investigators[10] have also recorded low yields for the monobenzylidenation of L-arabinitol, in contrast to the original report[7]

The purified product gave characteristic hydroxyl and phenyl absorption bands in the i r and the n m r spectrum of a lyophilized solution in D_2O revealed a singlet (benzylic proton) shifted to lower fields (δ 5 75) than observed[9] in the analogous 2-phenyl-1,3-dioxane structure (δ 5 20) The deshielding of this acetal-ring proton may be attributed to the presence of the axially oriented dihydroxyethyl group in compound **1** A similar shift to lower field is observed for the benzyl proton of the 2,4-cyclic acetal ring in 1,3 2,4-di-*O*-benzylidene-L-arabinitol[10] The available data suggests that the chair conformation of **1**, having an equatorially oriented phenyl substituent and an axially oriented dihydroxethyl group, is favored over the alternative chair conformation **1a**



The mild, ambient-temperature reaction conditions and the essentially neutral medium of the Me_2SO–DCC oxidation are ideally suited for retention of the acid-sensitive benzylidene protecting group present in the conversion **2**→**3** In our experience, pyridinium trifluoroacetate is the most convenient proton source in the oxidation

of **1** The stoichiometry reflects the commonly employed ratios of reactants, and the excess of DCC employed is converted into the insoluble *N,N'*-dicyclohexylurea by addition of oxalic acid, the latter is concomitantly converted to carbon dioxide and carbon monoxide[11] Although the oxidation step proceeded smoothly, isolation and purification of the resultant 3,5-*O*-benzylidene-D-lyxose (**3**) proved considerably more difficult As this product is partially water-soluble, extraction of **3** into an organic phase could not be accomplished efficiently, and thus residual amounts of water-soluble side products and Me_2SO were not removed by partitioning at this stage Evaporation of the ether phase gave a small amount (0 2 g) of a solid that was not *N,N'*-dicyclohexylurea, it showed a negative Schiff test, and it may have been the (methylthio)methyl ether derivative **2**

The crude, syrupy aldehyde **3** displayed in its i r spectrum a strong carbonyl band and absorptions due to the phenyl C-H out of-plane bending modes T l c indicated the presence of one major reducing component and a trace of a periodate–benzidine-positive product indicated by chromatography to be lyxose The latter evidently arose from partial, but slight, hydrolysis of the acetal, either during the oxidation or during isolation D-Arabinose might have been formed by migration of the acetal group during the oxidation, but this sugar was not present in the product It is also possible that ketones could be formed by oxidation of the secondary hydroxyl groups, but such products were not detected by chromatography.

Pure compound **3** was obtained by column chromatography on silica gel, it failed to crystallize but it was homogeneous by t l c Debenzylidenation of **3** gave homogeneous D-lyxose (**4**) The n m r spectrum of D_2O-exchanged, chromatographically pure **3**, in chloroform-*d*, revealed a characteristic aldehyde-proton signal (δ 9 65) and a deshielded benzylic proton (δ 5 55) It is expected on conformational grounds and by analogy with compound **1** that the favored conformation of **3** is the one depicted

Acid-catalyzed hydrolysis of **3** gave crude D-lyxose (**4**) that by t l c and g l c contained a small proportion of D-arabinitol As the starting material (**1**) used was devoid of the free alditol, the occurrence of the latter in the final product must have been due to incomplete reaction at the oxidation step Both benzylidene derivatives, **1** and **3**, possessed similar but not identical mobilities on t l c, and were not unequivocally resolved during routine t l c analysis of crude **3** Efforts to crystallize **4** from the crude reaction product failed, and column chromatography on silica gel did not afford completely pure product However, ion-exchange chromatography of the borate complex of the product, according to a modified literature method, afforded homogeneous **4**, the alditol was apparently retained on the resin column[18]

The final product **4** was characterized extensively by physical methods, in particular by n m r and o r d data The chromatographic analyses, particularly g l c, also support the identification The n m r spectra of each of the four common pentoses in D_2O are quite characteristic, particularly the $J_{1,2}$ values and the chemical shifts of the anomeric protons The observed pair of doublets at δ 5 01 and 4 87 for **4**, corresponding to H-1α and H-1β respectively, identify it as α,β-lyxopyranose The

measured anomeric-proton ratio of H-1 α 70% is in good agreement with the reported value in the same solvent, and further supports the configurational assignment[13]

Earlier we postulated the possible formation of D-arabinose in this synthesis, however, the n m r spectrum of **4** prior to, and after column chromatography, did not show signals at δ 5 25 (H-1 β) and 4 51 (H-1 α) (lit values δ 5 34, and 4 60, respectively)[13] that would have corresponded to the anomeric-proton doublets of an equilibrated D_2O solution of a known sample of D-arabinose under similar conditions The only significant difference between the n m r spectrum of **4** prior to chromatography, and the spectrum of the chromatographed product, was a higher proton count for the former sample and additional bands in the δ 4 1–4 region This result is consistent with the presence of some D-arabinitol in the crude product The variance in the anomeric assignment given to the low-field doublets in the spectra of the respective sugars, namely δ 5 08 (H-1 α) for D-lyxose *vs* δ 5 34 (H-1 β) for D-arabinose, was established[13] by equilibrating the sugars in D_2O Lemieux and Stevens[13] rationalized the n m r parameters for D-lyxose in D_2O by assuming that it exists equally in both the **1***C* and *C***1** chair conformations Crystalline β-D-arabinose is known from X-ray analysis, to exist as the pyranose in the **1***C* conformation[14], during mutarotation in D_2O the δ 4 51 (lit δ 4 60)[13] doublet is produced and is assigned as H-1 α, and no other signals arise in the region δ 5 5–4 5 (except the HOD signal) The n m r data for **4** thus firmly establish the lyxopyranose configuration

As expected[15], no Cotton effect was observed between 200 and 600 nm in the o r d spectrum of a mutarotated solution of **4** The plain dispersion-curve observed is readily distinguished by its rotational magnitude from the similar curve for a mutarotated solution of D-arabinose The specific rotation, $[\alpha]_{589}^{25}$ −13 8°, for compound **4** is in good agreement with reported values In the 205–190-nm region, the curve for D-lyxose appeared to reach a maximum, however, this result is not reliable because the absorption occurs very near the limit of the instrument's range The o r d data presented establishes the D enantiomeric configuration of the lyxopyranose structure

Both crystalline and syrupy **4** were homogeneous by t l c , neither D-arabinose nor D-arabinitol R_F 0 26 (*A*) were detected The compounds in question are resolved by t l c , but the difference in the respective mobilities is not large and reliance on this single criterion could be misleading The g l c separation of the per(trimethylsilyl) ethers provides a better criterion for the identification and the purity of compound **4** The mutarotated syrup isolated by column chromatography, and also the crystalline product were examined, and they showed a characteristic reversal of α β anomeric ratio[16]. The former product showed a doublet, the major peak R_M 0 41 corresponding to the derivative of the α anomer, integration of peak areas gave an α β ratio of ~7 3, This value is in good agreement with the n m r. result obtained for the mutarotated product The freshly prepared *O*-trimethylsilyl derivative of the crystallized **4** exhibited an anomeric ratio of ~1 9 and identical retention-times. The crystalline product thus consists almost entirely of the β anomer, this conclusion is also supported by the fact that the α anomer has a lower m p The possible side products D-arabinitol (R_M 0 51)

and D-arabinose [R_M 0 49 (β) and R_M 0 68 (α)] were not detected in the final product

The combined evidence firmly establishes that not conversion of D-arabinose to D-lyxose was achieved The yield (71% overall) obtained from the conversion steps was adequate and can probably be improved The synthesis of L-lyxose paralleled the one described for the D enantiomer in all major details As expected, the o r d spectrum mirrored the one obtained for the D isomer The preferential oxidation of a primary alcohol group, in the presence of a free secondary hydroxyl group, has been demonstrated, and further investigations to fully quantitate this aspect of the synthesis are in progress The method described may find useful applications in the study of carbohydrate metabolism

EXPERIMENTAL

General methods. — Melting points were determined on a Reichert micro melting point stage and are uncorrected I r spectra were recorded with a Perkin–Elmer 237B Spectrophotometer for 1% dispersions in potassium bromide (disc) Specific rotations and o r.d spectra were measured on a Cary-60 spectrophotometer thermostated at 25 0 $\pm$0 1° N m r spectra were obtained at ~30° with either a Varian T-60 or an HA-100 spectrometer Unless otherwise stated, spectra were obtained for equilibrated ~30% solutions in D_2O a 10% concentration of sodium 4,4-dimethyl-4-silapentanoate-*2,2,3,3-d*$_4$ (TSP deuterated) (Merck) was employed as the internal standard (δ 0 00) and lock signal T l c was effected on glass plates coated with a 250-μm layer of Silica Gel G (Brinkman), the developing systems employed were (*A*) 4 5 1 butyl alcohol–acetic acid–water, and (*B*) 4 6 3 pyridine–butyl alcohol–water Visualization was achieved with either sulfuric acid, iodine vapor, Schiff, or periodate–benzidine sprays G l c was carried out with a Hewlett–Packard model 5750B gas chromatograph equipped with a thermal-conductivity detector, disc integrator and a column (243 8 × 0 635 cm) packed with 10% (*w/w*) Carbowax 1540, supported on 80–100 mesh, acid-washed DMCS-treated Chromsorb W Operation was isothermal at 130°, unless otherwise stated Helium was the carrier gas at the flow rate of ~60 ml/min at 40 lb in $^{-2}$ pressure All of the carbohydrates were chromatographed as their trimethylsilyl ethers, prepared according to a standard procedure[17] or by using TRI-SIL reagent (Pierce). The retention times reported are relative to that of the per(trimethylsilyl) ether of D-mannitol (R_M 1 0) used as the internal standard Dimethyl sulfoxide was dried by distillation under diminished pressure and stored over activated Linde Molecular Sieve, Type 4A Elemental analyses were performed by Galbraith Labs , Knoxville, Tenn

*Preparation of 1,3-O-benzylidene-*D*-arabinitol* (**1**) — A slow stream of dry hydrogen chloride gas was passed into a suspension of D-arabinitol (40 0 g, 0 263 moles) in distilled benzaldehyde (33 ml) for approximately 3 h, and then the mixture was allowed to solidify Following to the literature method[7], trituration in the cold with dilute sodium hydrogencarbonate and then water gave a white solid (15 8 g). Concentration of the aqueous phases under diminished pressure yielded an

additional 8 7 g of crystalline solid The combined crops were dried *in vacuo* over phosphorus pentaoxide, and extracted with ethyl acetate in a Soxhlet apparatus The cooled extract gave the product as a crystalline mass of needles, yield 24 2 g (38%), m p 149 5–150 5° (lit m p 151–152°)[7], λ_{max}^{KBr} 3400–3200 broad (OH), 1080 (Ph–O), 740, 680 cm^{-1} (Ph), C=O absent, n m r data δ 7 55 (5-proton singlet), 5 75 (1-proton singlet), 4 29 (2-proton doublet), 4 00 (3-proton multiplet), and 3 80 (2-proton doublet)

Anal Calc for $C_{12}H_{16}O_5$ C, 59 99, H, 6 71 Found C, 59 85, H, 6 65

The high yields (>80%) claimed in the literature were not achieved The specific rotation, $[\alpha]_{589}^{25}$ +11 0° (*c* 1 3, abs ethanol) was in agreement with the data of Fluharty[8], but differed from that recorded in pyridine by Haskins *et al* [7] The compound was chromatographically homogeneous by t l c, R_F 0 57 (*A*), iodine and periodate–benzidine positive, by comparison D-arabinitol had R_F 0 26 (*A*) and D-arabinose R_F 0 22 (*A*) The per(trimethylsilyl) ether showed a single component (R_M 1 19) by g l c, the D-arabinitol derivative gave R_M 0 51

3,5-O-Benzylidene-D-lyxose (**3**) — To a stirred solution of 1,3-*O*-benzylidene-D-arabinitol (**1**, 1 5 g, 6 4 mmole) in anhydrous dimethyl sulfoxide (30 ml) containing *N,N'*-dicyclohexylcarbodiimide (5 13 g, 24 9 mmole), was added anhydrous pyridine (0 5 ml) and trifluoroacetic acid (0 24 ml, 3 23 mmole) The mixture was stirred for a total of 18 h at ~25°, and then filtered The filtrate was diluted with anhydrous ethyl ether (30 ml), treated with a solution of oxalic acid (1 6 g) in anhydrous methanol (5 ml), and stirred for 1 h until evolution of carbon dioxide ceased The resultant suspension was filtered and the solid residue was identified as *N,N'*-dicyclohexylurea (5 5 g) by its i r spectrum, and m p (225–226°)

The filtrate was diluted with an equal volume of water and a small residue of *N,N'*-dicyclohexylurea was filtered off Following partitioning of the phases, the ether layer was discarded (negative Schiff test) and the aqueous layer (pH ~5, positive Schiff test) was concentrated under diminished pressure at 25° to a clear syrup of the crude aldehyde **3**, which was subsequently dried *in vacuo* over phosphorus pentaoxide, yield 1 3 g (85%), λ_{max}^{KBr} 3350 (–OH), 2870 (–CHO), 1725 (C=O), 800 cm^{-1} (Ph) T l c showed one major component (Schiff and iodine positive) R_F 0 54 (*A*), R_F 0 65 (*B*), and a trace of a slower (Schiff and periodate–benzidine positive) component, R_F 0 31 (*A*), R_F 0 42 (*B*), migrating as lyxose by chromatography, a control sample of D-arabinose had R_F 0 22 (*A*), R_F 0 31 (*B*)

Chromatographic purification of 3,5-O-benzylidene-D-lyxose (**3**) — A solution of crude **3** (0.25 g) in 2 ml of chloroform was applied to a silica gel (EM-PF254) column (35 × 1 cm) which was eluted with 49.1 chloroform–isopropyl alcohol by using a high pressure (Milton Roy) mini-pump, and fractions were assayed by t l c (solvent *B*), Schiff and sulfuric acid reagents) The fractions containing **3** were pooled to give 0 20 g of a clear syrup (80% recovery), n m r data (chloroform-*d*, D_2O exchanged) δ 9 65 (1-proton doublet), 7 50 (5-proton singlet), 5 55 (1-proton singlet), 4 30 (2-proton doublet), and 4 00 (3-proton multiplet)

D-*Lyxose* (**4**) — A solution of crude **3** (1 0 g, 4 2 mmole) in 0 05M sulfuric acid

(30 ml) was kept for 5 h at 35°. The hydrolyzate was brought to pH 5 5 by the addition of AG-1-X8 (HCO_3^-) resin The resin was removed by filtration, and the filtrate was concentrated to a low volume under diminished pressure and extracted three times with ether. Further evaporation afforded crude **4** as a light yellow syrup, which was dried over phosphorus pentaoxide, yield 0 56 g (3 73 mmole, 88%) G l c indicated the presence of approximately 1% of arabinitol (R_M 0 51) T l c gave a similar result; the major component **4** had R_F 0 31 (*A*), R_F 0 42 (*B*), and gave positive periodate–benzidine and Schiff tests, and a trace contaminant had R_F 0 25 (*A*), R_F 0 31 (*B*), and was periodate–benzidine positive, Schiff negative.

Chromatography and analysis of D-*lyxose* (**4**) — A solution of the crude, syrupy **4** (0 250 g) in 2 ml 0 1M boric acid was applied to a column (1 5×40 cm) of AG-1-X8 (borate) resin (Bio-Rad) according to the method of Zill[18] Elution was performed with a Holter (model RL-175) pump and a solution of changing borate concentration, giving a linear pH gradient between 7 5 and 9 0 Fractions (8 ml) were collected automatically and monitored for reducing saccharide by the Park colorimetric assay[19] Positive fractions (40–55) were pooled, concentrated *in vacuo* at 25°, neutralized with Dowex-50 X8 (H^+) resin, filtered, and evaporated *in vacuo* to dryness Methanol (20 ml) was added and evaporated off *in vacuo*, and the procedure was repeated 3 times The resultant light-colored syrup (0 21 g, 84%) was dried over phosphorus pentaoxide, dissolved in hot ethanol (3 ml), seeded, and kept at 4° Gradual crystallization occurred After 24 h, an equal volume of isopropyl alcohol was added and the mixture was again kept at 4° for ~1 week The crystalline **4** had m p 115–116° (lit 117–118° for the β anomer)[20,21] The i r spectrum was identical with that of a known sample The product was homogeneous by t l c (solvent systems *A* and *B*) G l c of the per(trimethylsilyl) derivative of crystalline **4** gave R_M 0 41 (α) small, 0 57 (β) large, α β ratio 0 6 9 5, the mutarotated syrup gave R_M 0 41 (α) large, 0 57 (β) small, α β ratio 6 5 3 3 The o r d. spectrum of the mutarotated syrup showed a plain dispersion curve to 200 nm, $[\alpha]_{589}^{25}$ −13 8°, $[\alpha]_{300}^{25}$ −82 5° (equil , *c* 1 65, water), lit $[\alpha]_D^{24}$ −14 0° (*c* 7 7, water)[20] A control of D-arabinose had $[\alpha]_{589}^{25}$ −105°, $[\alpha]_{300}^{25}$ −550° (equil , *c* 1 0, water), plain dispersion curve The n m r spectrum of **4** (line positions established relative to calibration side-bands) gave δ 5 01 (1-proton doublet, $J_{1,2}$ 4 0 Hz, H-1α, 70%), 4 87 (1-proton doublet, $J_{1,2}$ 1 4 Hz, H-1β, 30%), and other signals in a narrow band at δ 3 5–4 1

A solution of crystalline **4** (0 1 g) in 1 ml of water was treated with 2,4-dinitrophenylhydrazine (0 13 g) in 5 ml of abs ethanol according to a conventional procedure[22] Recrystallization of the orange-colored solid from 85% ethanol–water afforded a crystalline product m p 170–171°, after drying at 80° over phosphorus pentaoxide.

Anal. Calc for $C_{11}H_{14}N_4O_8$ C, 40.01, H, 4 27, N, 16 96 Found C, 40 20, H, 4 49, N, 17.11.

L-*Lyxose* — The enantiomeric 3,5-*O*-benzylidene-L-arabinitol, prepared from L-arabinitol, showed a specific rotation $[\alpha]_{589}^{25}$ −11 1° (*c* 1 0, abs. ethanol) and m p. 148–149° It was treated with the Me_2SO–*N*,*N*′-dicyclohexylcarbodiimide

reagent in a manner analogous to that for the D enantiomer and isolated in like manner All of the physical parameters, and the i r and n m r spectra, were identical, except for the positive plain o r d curve observed, $[\alpha]_{589}^{25}$ +14 0°, $[\alpha]_{300}^{25}$ +83° (equil , *c* 1 60, water)

ACKNOWLEDGMENTS

The authors acknowledge the support received from the Department of Chemistry, Texas A & M University

REFERENCES

1 R BOGNÁR AND L SOMOGYI, *Acta Chim Acad Sci Hung*, 14 (1958) 407
2 K HEYNS AND H PAULSEN, *Angew Chem*, 69 (1957) 600
3 K E PFITZNER AND J G MOFFATT, *J Amer Chem Soc*, 87 (1965) 5661
4 D HORTON, M NAKADATE, AND J M J TRONCHET, *Carbohyd Res*, 7 (1968) 56
5 G B HOWARTH, W A SZAREK, AND J K N JONES, *J Chem Soc*, (*C*) (1970) 2218
6 K E PFITZNER AND J G MOFFATT, *J Amer Chem Soc*, 87 (1965) 5670
7 W T HASKINS, R M HANN, AND C S HUDSON, *J Amer Chem Soc*, 65 (1943) 1663
8 A L FLUHARTY, Dissertation, University of California, Berkeley, *Diss Abst*, 20 (1959–1960) 28
9 N BAGGETT, K. W BUCK, A B FOSTER, M H RANDALL, AND J M WEBBER, *Proc Chem Soc*, (1964) 118
10 A B FOSTER, A H HAINES, T D INCH, M H RANDALL, AND J M WEBBER, *Carbohyd Res*, 1 (1965) 145
11 F ZETZSCHE, AND H LINDLER, *Ber*, 71B (1938) 2095
12 R F BUTTERWORTH AND S HANESSIAN, *Can J Chem*, 49 (1971) 2755
13 R U LEMIEUX AND J D STEVENS, *Can J Chem*, 44 (1966) 249
14 H HORDVIK, *Acta Chem Scand*, 15 (1961) 16
15 R G NELSON AND W C JOHNSON, JR , *J Amer Chem Soc*, 94 (1972) 3343
16 R J FERRIER, *Tetrahedron*, 18 (1962) 1149
17 C C SWEELEY, R BENTLEY, M MAKITA, AND W W WELLS, *J Amer Chem Soc*, 85 (1963) 2497
18 J X KHYM AND L P ZILL, *J Amer Chem Soc*, 74 (1952) 2090
19 J T. PARK AND M J JOHNSON, *J Biol Chem*, 181 (1949) 149
20 W. N HAWORTH AND E L HIRST, *J Chem Soc*, (1928) 1221
21 H S ISBELL AND W W PIGMAN, *J Org Chem*, 1 (1937) 505
22 H G FLETCHER, JR , *Methods Carbohyd Chem*, 1 (1962) 78