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Syntheses of L-Sorbosylthymines and Related Compounds[1)]

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1, 3, 4, 5-Tetra-*O*-acetylsorbopyranosylureas were prepared from sorbopyranosyl chloride via 1, 3, 4, 5-tetra-*O*-acetylsorbopyranosylisocyanates. 1-Ureido- and 6-ureidosorbofuranoses were obtained from the corresponding aminosorboses. The transformations of the ureas thus obtained into *N*-(sorbose)thymines were achieved, although with difficulty, by the direct condensation of halogeno- or tosylsorboses with metal salts of thymine.

A variety of nucleosides have received considerable interest in connection with their potential biochemical activities. However, synthetic studies have dealt almost exclusively with the preparation of aldose derivatives, such as ribosylpyrimidines or glucosylpurines. This paper will discuss the introduction of the thymine group into sorboses at the C-1, C-2, and C-6 positions through urea derivatives.

1) Sorboses. Part VIII. For Part VII, see K. Tokuyama, M. Kiyokawa and M. Katsuhara, *J. Org. Chem.*, **30**, 4057 (1965).

Mercuric salts of thymine or theophylline in inert solvents are generally employed for nucleoside synthesis.[2-5] The condensation of the salts with 1, 3, 4, 5-tetra-*O*-acetyl-α-L-sorbopyranosyl chloride (I)[6] in xylene did not give any of the expected nucleoside; instead, a colorless sirup with no chlorine and nitrogen was obtained. It showed a positive resorcin test (Seliwanoff test),[7] a strong band due to an enol acetate, a weak band due to a double bond in the infrared, and an ultraviolet maximum at 210 mμ. These facts suggested that the structure of the product was 2-deoxy-1, 3, 4, 5-tetra-*O*-acetyl-L-sorbopyranos-2, 3-ene (II) or -1, 2-ene. The NMR spectrum, showing a singlet (two protons) at τ 5.24 due to the $-CH_2-$ at the C-1 position and no signals at a lower field, was consistent with the structure of II. The condensation reaction in such a polar solvent as *N*, *N*-dimethylformamide (DMF) or nitromethane in the presence of mercuric cyanide[8,9] gave the same results. The formation of II was observed even in the absence of the salt to a small extent. Therefore, this type of reaction was thought to be not suitable for sorbose nucleoside synthesis.

Another promising route to sorbosylthymine utilizes urea derivatives[10-14] (for the scheme, see Charts 1 and 2). Thus I was treated with silver isocyanate in anhydrous toluene under heating. The sirup produced showed a strong band at 2245 cm^{-1} characteristic of the N=C=O stretching vibration.[15] Thin-layer chromatography revealed that the sirup was a mixture of the major α, β-anomers (III and IV) and the minor II.

The ammonolysis of the sirup mixture of the III and IV isocyanates was performed by adding methanolic ammonia at 0°C; the subsequent fractional recrystallization furnished *N*-(1, 3, 4, 5-tetra-*O*-acetyl-α-L-sorbopyranosyl)urea (V) and the β-anomer of V (VI). The ureas, V and VI, gave satisfactory analyses and revealed absorptions at 1659 and 1530 cm^{-1} characteristic of the –CO–NH– group. From the optical rotations, V was determined to have the α-configuration, and VI, the β-configuration.

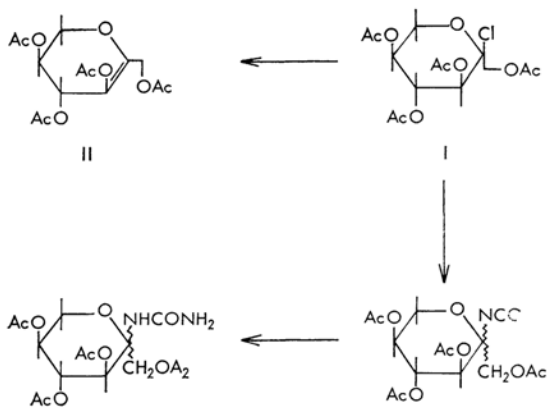
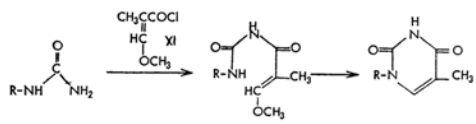


Chart 1

The α-urea V was condensed with 2-methyl-3-methoxyacryloyl chloride (XI) in pyridine.[12,16] After the reaction product had been purified by silica gel-column chromatography, 1-(1, 3, 4, 5-tetra-*O*-acetyl-α-L-sorbopyranosyl)-3-(2-methyl-3-methoxyacryloyl)urea (VII) was obtained as a colorless powder. This showed an ultraviolet absorption at 255 mμ. The ring closure and simultaneous deacetylation of this compound by



V	(R=R_1)	VII	(R=R_1)	VIII	(R=R_1')
VI	(R=R_2)	IX	(R=R_2)	X	(R=R_2')
XXIII	(R=R_3)	XXV	(R=R_3)	XXVII	(R=R_3)
XXIV	(R=R_4)	XXVI	(R=R_4)	XXVIII	(R=R_4)

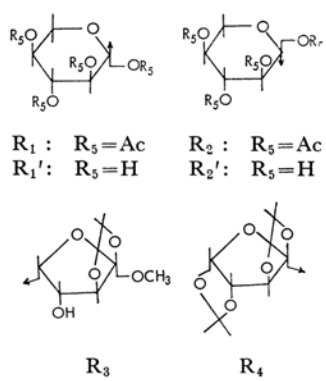


Chart 2

2) N. Yung and J. J. Fox, *Methods Carbohydrate Chem.*, **2**, 108 (1963).
3) E. Fischer and B. Helferich, *Ber.*, **47**, 210 (1914).
4) J. Daroll and B. A. Lowky, *J. Am. Chem. Soc.*, **73**, 1650 (1951).
5) H. M. Kissman, C. Pidacks and B. R. Baker, ibid., **77**, 18 (1955).
6) H. H. Schlubach and G. Graefe, *Ann.*, **532**, 211 (1937).
7) A. Atake and N. Seno, "Jikken Kagaku Koza," Bd. 23, Ed. by Chem. Soc. of Japan, Publisher, Maruzen, Tokyo (1957), p. 374.
8) B. Coxon and H. G. Fletcher, *J. Am. Chem. Soc.*, **85**, 2637 (1963).
9) N. Yamaoka, K. Aso and K. Matsuda, *J. Org. Chem.*, **30**, 149 (1965).
10) M. N. Schrool, *Rec. Trav. Chim.*, **22**, 1 (1903).
11) A. Hynd, *Biochem. J.*, **20**, 195 (1926).
12) B. Helferich and W. Kosche, *Ber.*, **59**, 69 (1926).
13) T. Naito and T. Kawakami, *Chem. Pharm. Bull.*, **10**, 627 (1962).
14) T. Ukita, R. Hamada and M. Yoshida, ibid., **12**, 454 (1964).
15) H. Hoyer, *Chem. Ber.*, **89**, 2677 (1962).
16) T. Naito and M. Sano, *Chem. Pharm. Bull.*, **9**, 709 (1961).

treament with monomethylamine, followed by the purification of the reaction product by cellulose column chromatography, afforded a brown sirup (VIII). The sirup VIII showed analytical data corresponding to those of L-sorbosylthymine, a positive resorcin test, and the ultraviolet maximum at 303 mμ characteristic of thymine. Similarly, β-L-sorbopyranosylthymine (X), λ_{max}^{UV} 285 mμ, was prepared from the β-urea VI via 1-(1, 3, 4, 5-tetra-*O*-acetyl-β-L-sorbopyranosyl)-3-(2-methyl-3-methoxyacryloyl)urea (IX). The sorbopyranosylthymines thus obtained, VIII and X, were unstable; e. g., they released the thymine moiety upon mild acetylation.

The introduction of thymine into the C-1 and C-6 positions of L-sorbose was also studied. Previously we observed that the condensation of 1-*O*-tosyl-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XII) with 2-thiouracil in DMF gave *S*-substituted (XIII) and *O*, *S*-disubstituted thiouracil (XIV).[1] The analogous condensation of XII with the sodium salt of thymine was attempted. However, the product formed was 1-deoxy-1-dimethylamino-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XV), which was identified by comparison with an authentic sample prepared by the reaction of XII with dimethylamine. The formation of XV in this reaction is interesting, but we have no reasonable explanation for this finding at the present time. On the other hand, the treatment of XII with the sodium salt of theophylline in DMF gave the expected compound (XVI), which showed a band characteristic of theophylline in the infrared spectrum. Therefore, the introduction of the thymine group into the C-1 and C-6 positions of sorbose was carried out through ureidosorbose in a way similar to that used with VIII and X.

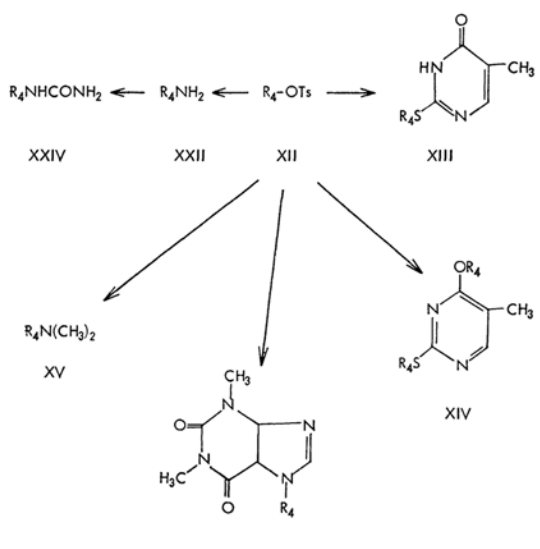


Chart 3

2, 3 : 4, 6-Di-*O*-isopropylidene-α-L-sorbofuranose (XVII)[17] was converted into 1-*O*-methyl-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XVIII) with methyl iodide in the presence of sodium ethoxide in liquid ammonia. In the methylation of XVII, methyl iodide and sodium alkoxide in liquid ammonia were more satisfactorilly used than dimethylsulfate in an alkaline medium[18] or methyl iodide and potassium in liquid ammonia and an inert solvent.[19] The partial deacetonation of XVIII gave a monoacetonated compound (XIX), which was then converted into 6-tosylate (XX) on tosylation under cooling. The heating of XX with liquid ammonia led to 1-*O*-methyl-6-deoxy-6-amino-2, 3-*O*-isopropylidene-α-L-sorbofuranose (XXI).

When XXI (or the 1-deoxy-1-amino-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XXII) previously reported[20]) in dilute alcohol was treated with potassium cyanate in the presence of one equivalent of acetic acid, the crystalline urea derivative XXIII (or XXIV), was obtained. This product XXIII (or XXIV) was then condensed with XI by a procedure similar to that used for V (see Chart 2); this produced an unstable intermediate XXV (or XXVI) which showed an ultraviolet absorption at 250 mμ. Without purification, XXV (or XXVI) was immediately treated with aqueous ammonia. There was thus isolated by thin-layer chromatography the desired thymine derivative XXVII (or XXVIII). The product XXVII (or XXVIII) gave analytical data corresponding to the structure and showed a positive resorcin test and the ultraviolet absorption at 270 mμ characteristic of thymine.

The thymine derivatives of L-sorbose obtained above, VIII, X, XXVII and XXVIII, were found to be unstable, and they were slowly converted into sorbose or aminosorboses at room temperature. The conversion was found to be more rapid in an aqueous solution.

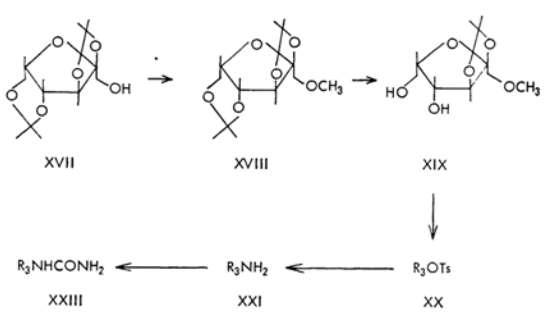


Chart 4

17) T. Reichstein, *Helv. Chim. Acta*, **17**, 311 (1934).
18) E. L. Hirst and E. Percival, *Methods Carbohydrate Chem.*, **2**, 145 (1963).
19) R. S. Tipson, ibid., **2**, 150 (1963).
20) K. Tokuyama, This Bulletin, **37**, 1133 (1964).

Experimental[21]

1, 3, 4, 5-Tetra-*O*-acetyl-α-L-sorbopyranosyl Chloride (I).—A mixture of 1, 3, 4, 5-tetra-*O*-acetyl-α-L-sorbopyranose (6 g.)[6,22] and aluminum chloride (15.5 g.) in chloroform (90 ml.) was stirred at room temperature for 1 hr. The precipitates were removed by filtration and washed with ether (400 ml.), and the washings were combined with the filtrate. The combined solution was then washed with cold water, cold aqueous sodium bicarbonate, and cold water successively. The dried solution was evaporated under reduced pressure to leave a yellow sirup which was purified by silica gel-column chromatography with benzene and ether (9 : 1 v/v). The recrystallization of the thus-purified sirup from ether and petroleum ether gave needles (1.8 g.); m. p. 62—64°C, $[\alpha]_D^{25}$ −83.2 (*c* 1.027, chloroform).[6]

Found: C, 45.85; H, 5.22; Cl, 9.67. Calcd. for $C_{14}H_{19}O_9Cl$: C, 45.92; H, 5.32; Cl, 9.23%.

The Reaction of Mercuric Salt of Thymine with I.—To a suspension of mercuric salt of thymine (2.1 g.)[2] in dry xylene (150 ml.), there was added a dry xylene solution (25 ml.) of I (1.8 g.). Traces of water were removed by azeotropic distillation with xylene (50 ml.). After it had been refluxed for 1.5 hr., the solution was concentrated to a sirup which showed, on thin-layer chromatography, no spot with a positive resorcin test and ultraviolet absroption. The purification of the sirup on an alumina column (neutral) (25 g.) with benzene gave a colorless sirup (II) (220 mg.); $[\alpha]_D^{22}$ +217.6 (*c* 1.032, chloroform).

Found: C, 51.06; H, 5.81. Calcd. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49%.

1, 3, 4, 5-Tetra-*O*-acetyl-L-sorbopyranosyl Isocyanate (III and IV).—A solution of I (0.6 g.) in anhydrous toluene (6 ml.) was added to a suspension of silver isocyanate (0.45 g.)[23] in anhydrous xylene (10 ml.), and the mixture was heated at 100—110°C for 2.5 hr. under stirring. After it had been cooled, the precipitates (silver chloride and unreacted silver isocyanate) formed were removed by filtration and washed with toluene, and the washings were combined with the filtrate. The combined solution was then concentrated to about 1—2 ml. under reduced pressure, and to the residue there was added 10—20 ml. of petroleum ether (20 ml.). The upper organic layer was separated by decantation from a small amount of the yellow sirup precipitated. A yellow sirup (0.54 g.) was obtained on the removal of the solvent. IR cm^{-1} $\nu_{N=C=O}$ 2245 (liquid film). The thin-layer chromatogram (silica gel) showed two major spots (III and IV) and one minor spot (II).

***N*-(1, 3, 4, 5-Tetra-*O*-acetyl-L-sorbopyranosyl)urea (V and VI).**—Silver chloride was removed by filtration from a reaction mixture of I (9.4 g.) and silver isocyanate (7.2 g.) by a similar procedure to those used above for III and IV. When ammonia was bubbled into the filtrate under stirring at 0°C, crystals appeared immediately. After 5 min., the crystals (5.98 g.) were filtered, washed with ether, and dissolved in chloroform and methanol (20 : 1 v/v); petroleum ether was then added to the solution until crystals appeared again. The recrystallization of the resultant crystals from methanol gave colorless needles (VI) (1.53 g.); m. p. 194—195°C, $[\alpha]_D^{24.5}$ +65.1 (*c* 1.049, methanol).

Found: C, 46.05; H, 5.85; N, 7.40. Calcd. for $C_{15}H_{22}N_2O_{10}$: C, 46.15; H, 5.68; N, 7.18%.

From the mother liquor (chloroform - methanol - petroleum ether), the α-anomer (V) (1.49 g.) was obtained; this was recrystallized from methanol, m. p. 217—219°C, $[\alpha]_D^{23.5}$ −34.4 (*c* 0.973, chloroform).

Found: C, 46.35; H, 5.79; N, 7.34. Calcd. for $C_{15}H_{22}N_2O_{10}$: C, 46.15; H, 5.68; N, 7.18%.

1-(1, 3, 4, 5-Tetra-*O*-acetyl-α-L-sorbopyranosyl)-3-(2-methyl-3-methoxyacryloyl)urea (VII).—To a suspension of V (2.0 g.) in chloroform (20 ml.), XI (1.5 g.)[24] and pyridine (0.8 ml.) were added. The mixture was stirred for 2 days at room temperature. After the precipitates had been removed by filtration, the solvent was removed under reduced pressure and the residue was dissolved in chloroform (20 ml.), and washed with 5% sodium bisulfite, 5% sodium bicarbonate, and water successively. The dried solution was then evaporated under reduced pressure to leave a yellow sirup. This sirup was washed with petroleum ether. A plae yellow powder (2.05 g.) was thus obtained. λ_{max}^{UV} 255 mμ (ethanol).

Found: C, 49.39; H, 5.85; N, 5.66. Calcd. for $C_{20}H_{28}N_2O_{12}$: C, 49.18; H, 5.78; N, 5.74%.

***N*-(α-L-Sorbopyranosyl)thymine (VIII).**—To a solution of VII (2 g.) in hot ethanol (10 ml.), 40% aqueous monomethylamine (12 ml.) was added in several portions within 4 hr. at 80—85°C. The mixture was concentrated under reduced pressure, and the residue was washed with chloroform, dissolved in ethanol (8 ml.), and subjected to column chromatography on cellulose (2.4×52 cm.). The column was eluted with *n*-butanol - ethanol - water (4-1-5, v/v), and 5 ml. portion of each of the effluents was taken. The fractions (tubes Nos. 43—47) which showed ultraviolet absorption were combined, and the solvent was evaporated to give a hygroscopic brown sirup (40 mg.). $[\alpha]_D^{23}$ −25.1 (*c* 0.987, water), λ_{max}^{UV} 303 mμ (water).

Found: C, 42.70; H, 6.42; N, 9.09. Calcd. for $C_{11}H_{16}N_2O_7 \cdot H_2O$: C, 42.99; H, 6.23; N, 9.12%.

1-(1, 3, 4, 5-Tetra-*O*-acetyl-β-L-sorbopyranosyl)-3-(2-methyl-3-methoxyacryloyl)urea (IX).—A suspension of VI (1.3 g.) in chloroform (12 ml.) was mixed with XI (1.0 g.) and pyridine (0.6 ml.), and then treated by a procedure similar to that used for VII. A pale yellow powder (1.33 g.) was obtained; λ_{max}^{UV} 255 mμ (ethanol).

Found: C, 49.13; H, 5.98; N, 5.42. Calcd. for $C_{20}H_{28}N_2O_{12}$: C, 49.18; H, 5.78; N, 5.74%.

***N*-(β-L-Sorbopyranosyl)thymine (X).**—IX (1.33 g.) was treated by a procedure similar to that used for VIII. Crude X was then purified from this by cellulose-column chromatography using *n*-butanol-ethanol-water in a way similar to that described above. The fractions (tubes Nos. 45—46) that showed ultraviolet absorption were combined and concentrated to dryness

21) Melting points were determined on a Kofler block. The NMR spectra were measured on a Varian A-60 spectrometer at 60 Mc. in deuteriochloroform at room temperature, using tetramethylsilane as an internal standard.

22) Y. Khouvine and M. G. Arragon, *Bull. soc. chim. France*, **1938**, 1404.

23) G. Dean, *J. Chem. Soc.*, **1904**, 1371.

24) G. Shaw and R. N. Warrener, ibid., **1958**, 153.

under reduced pressure. A brown sirup (0.05 g.) was thus obtained. $[\alpha]_D^{24}$ −9.6 (*c* 0.660, water), λ_{max}^{UV} 285 mμ (water).

Found: C, 41.57; H, 6.28; N, 8.15. Calcd. for $C_{11}H_{16}N_2O_7 \cdot 2H_2O$: C, 40.74; H, 6.22; N, 8.64%.

1-Deoxy-1-ureido-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XXIV).—To a hot solution of XXII (3.8 g.) in ethanol (20 ml.) there was added a solution of potassium cyanate (1.6 g.) in water (20 ml.) and then glacial acetic acid (1.1 ml.). After it had been heated on a boiling water bath for 25 min., the solution was concentrated under reduced pressure. The recrystallization of the residual sirup from methanol and *n*-hexane gave colorless needles (2.4 g.); m. p. 180°C (decomp.), $[\alpha]_D^{28}$ −29.7 (*c* 1.060, chloroform).

Found: C, 51.20; H, 7.52; N, 9.51. Calcd. for $C_{13}H_{22}N_2O_6$: C, 51.64; H, 7.34; N, 9.27%.

***N*-(1-Deoxy-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose-1)thymine (XXVIII).**—The treatment of XXIV (1.51 g.) in chloroform (15 ml.) and pyridine (0.5 ml.) with XI (1.0 g.) in a way similar to that used for VIII gave an intermediate (XXVI) [1.67 g., λ_{max}^{UV} 250 mμ (ethanol)] as a yellow sirup. To a solution of XXVI (1.47 g.) in hot ethanol (4 ml.), aqueous ammonia was then added in several portions within 6 hr. at 80—90°C. After the solvent had been removed, a yellow powder was obtained; this was purified into a colorless powder by alumina thin-layer chromatography with chloroform and acetone (1 : 1, v/v). $[\alpha]_D^{24}$ −8.5 (*c* 1.017, chloroform), λ_{max}^{UV} 270 mμ (water).

Found: C, 55.52; H, 6.81; N, 7.51. Calcd. for $C_{17}H_{24}O_7N_2$: C, 55.43; H, 6.56; N, 7.61%.

1-*O*-Methyl-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XVIII).—Small pieces of sodium (12.8 g.) were slowly added to a solution of XVII (135 g.) in liquid ammonia (300 ml.) at about −40°C. To the solution, ethanol (about 40 ml.) was added to discharge the blue color of sodium, and then methyl iodide (77 g.) was then added over a 1 hr. period. After 2 hrs.' stirring, the ammonia was allowed to evaporate, and the solution was extracted with benzene. The benzene solution was washed with water and dried, and the solvent was removed. The distillation of the residual sirupy crystals gave XVIII (165 g.); b. p. 111°C/2 mmHg; m. p. 53°C, $[\alpha]_D^{23}$ −11.1 (*c* 1.075, acetone).

Found: C, 57.09; H, 7.67. Calcd. for $C_{13}H_{22}O_6$: C, 56.95; H, 8.03%.

1-*O*-Methyl-2, 3-*O*-isopropylidene-α-L-sorbofuranose (XIX).—A solution of XVIII (41.8 g.) in 60% acetic acid (100 ml.) was warmed at 80°C for 1 hr. The reaction mixture was then cooled, made alkaline with sodium hydroxide, and extracted with chloroform. After the solvent had been removed, the residue was distilled to give a colorless sirup (25.35 g.); b. p. 140°C/2 mmHg, $[\alpha]_D^{23}$ +33.3 (*c* 1.191, chloroform).

Found: C, 51.58; H, 7.83. Calcd. for $C_{10}H_{18}O_6$: C, 51.28; H, 7.69%.

1-*O*-Methyl-6-*O*-tosyl-2, 3-*O*-isopropylidene-α-L-sorbofuranose (XX).—Into a solution of XIX (5.4 g.) in pyridine (15 ml.), tosyl chloride (3.76 g.) was stirred in small portions under cooling. After having been stirred at 0—−5°C for 7 hr., the reaction mixture was poured into a saturated sodium carbonate solution (100 ml.) and extracted with chloroform, which had previously been washed with water and dried; the solvent was then evaporated under reduced pressure. The recrystallization of the residue from benzene and *n*-hexane gave colorless needles; m. p. 37°C, $[\alpha]_D^{23}$ +21.4 (*c* 1.129, chloroform).

Found: C, 52.21; H, 5.73; S, 8.61. Calcd. for $C_{17}H_{24}O_8S$: C, 52.58; H, 6.19; S, 8.24%.

1-*O*-Methyl-6-deoxy-6-amino-2, 3-*O*-isopropylidene-α-L-sorbofuranose (XXI).—A solution of XX (150 g.) and liquid ammonia (150 ml.) in an autoclave was heated on a boiling-water bath for 20 hr. After the liquid ammonia had been removed, the residue was extracted with chloroform and the solvent removed. The distillation of the residue gave a colorless sirup (32 g.); b. p. 125°C/3 mmHg, m.p. 55°C, $[\alpha]_D^{24.5}$ +8.3 (*c* 1.074, methanol).

Found: C, 51.46; H, 8.32; N, 5.82; CH_3O, 13.11. Calcd. for $C_{10}H_{19}NO_5$: C, 51.50; H, 8.15; N, 6.01; CH_3O, 13.30%.

1-*O*-Methyl-6-deoxy-6-ureido-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XXIII).—To a hot solution of XXI (1.8 g.) in ethanol (7 ml.), there was added a solution of potassium cyanate (0.8 g.) in water (7 ml.), and then glacial acetic acid (0.6 ml.). After being heated on a boiling water bath for 3 hr., the solution was concentrated and extracted with ethyl acetate, and the solvent was removed. The recrystallization of the residue from ethanol and *n*-hexane gave colorless rods; m. p. 184°C (decomp.), $[\alpha]_D^{25}$ −22.4 (*c* 1.006, ethanol).

Found: C, 47.58; H, 7.29; N, 9.89. Calcd. for $C_{11}H_{20}O_6$: C, 47.83; H, 7.25; N, 10.14%.

***N*-(6-Deoxy-1-*O*-methyl-2, 3-*O*-isopropylidene-α-L-sorbofuranose-6)thymine (XXVII).**—The treatment of XXIII (0.95 g.) in chloroform (10 ml.) and pyridine (0.6 ml.) with XI (0.6 g.) in a way similar to that used for VII gave an intermediate (XXV) [1.1 g., λ_{max}^{UV} 250 mμ (ethanol)]. The compound XXV thus obtained was treated by the procedure used for XXVIII. The crude product was purified by silica-gel thin layer chromatography. XXVII (0.049 g.) was obtained as a colorless sirup; $[\alpha]_D^{25}$ −34.9 (*c* 0.988, ethanol), λ_{max}^{UV} 270 mμ (water).

Found: C, 49.71; H, 6.66; N, 7.56. Calcd. for $C_{15}H_{22}N_2O_7 \cdot H_2O$: C, 49.99; H, 6.71; N, 7.77%.

7-(1-Deoxy-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose-1)theophylline (XVI).—Theophylline (1.8 g.) was dissolved in hot water (ca. 100 ml.) containing potassium carbonate (0.7 g.), and the water was removed under reduced pressure. The residue was well dried in a desiccator. The potassium salt of theophylline thus obtained was added to DMF (40 ml.) containing XII (3 g.). The solution was refluxed for 10 hr. After it had cooled, the solution was filtered, the filtrate was evaporated to dryness under reduced pressure, and the residue was extracted with chloroform. The solvent was removed, and the residue was recrystallized from ether to give colorless needles of XVI (0.62 g.); m. p. 181—183°C; $[\alpha]_D^{24}$ −2.7 (*c* 1.033, chloroform).

Found: C, 54.01; H, 6.35; N, 13.39. Calcd. for $C_{19}H_{26}N_4O_7$: C, 54.02; H, 6.20; N, 13.26%.

1-Deoxy-1-dimethylamino-2, 3 : 4, 6-di-*O*-isopropylidene-α-L-sorbofuranose (XV).—A mixture of XII (5 g.), 40% aqueous dimethylamine (25 ml.), and methanol (25 ml.) in an autoclave was heated on

a boiling water bath for 30 hr. After cooling, the solution was evaporated and extracted with chloroform, which had previously been washed with water and dried, and then evaporated. The distillation of the residue gave a colorless sirup (2.4 g.); b. p. 105—107°C/5 mmHg, $[\alpha]_D^{24}$ −1.5 (*c* 1.105, chloroform).

Found: C, 58.38; H, 8.89; N, 4.89. Calcd. for $C_{14}H_{25}NO_5$: C, 58.51; H, 8.77; N, 4.87%.

A mixture of the potassium salt of thymine (1 g.) and XII (3 g.) in DMF (50 ml.) was refluxed for 20 hr. After it had cooled, the solution was filtered, and the filtrate was evaporated under reduced pressure. The distillation of the residue gave XV (0.8 g.).

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