terium oxide solution at 60 Mc.p.s. with a sodium 2,2-dimethyl-2-silapentane 5-sulfonate internal reference standard,[31] included a singlet of the proper area at τ 8.60 attributable to the terminal deoxy group. The n.m.r. spectra of other terminal deoxy sugars have been shown[32] to possess similar high-field signals.

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.89; H, 7.37. Found: C, 44.15; H, 7.46.

Acknowledgment.—The authors are grateful to the late Dr. Alva Thompson and Mr. J. L. Minor of this laboratory for a supply of D-lyxono-1,4-lactone and to Mr. F. Komitsky, Jr., for obtaining and interpreting the n.m.r.

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Trifluoroacetyl as a Protecting Group for 1-Halo Sugars

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We would like to report the use of trifluoroacetyl as an effective blocking group of hydroxyl and amino substituents in the reactions of a 1-halo sugar.[2] The ease with which this group can be introduced, and, more importantly, the facility with which it can be removed, makes it a highly attractive protecting group especially for amino sugars which normally require quite vigorous conditions for N-deacylation.

Glycosidation of either cholesterol or cyclododecanol with 2-O-trifluoroacetyl-3-N-methyltrifluoroacetamido-3,4,6-trideoxyglucosyl bromide (I)[3] in 1,2-dichloroethane in the presence of mercuric cyanide[4] gave the corresponding cholesteryl and cyclododecyl glycosides II and III in good yield.

The facile removal of the trifluoroacetyl blocking group was demonstrated by converting III to its de-

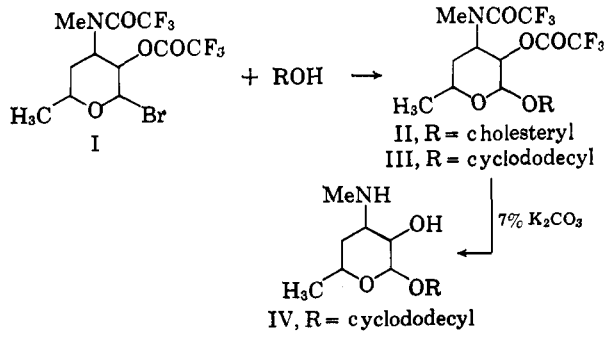
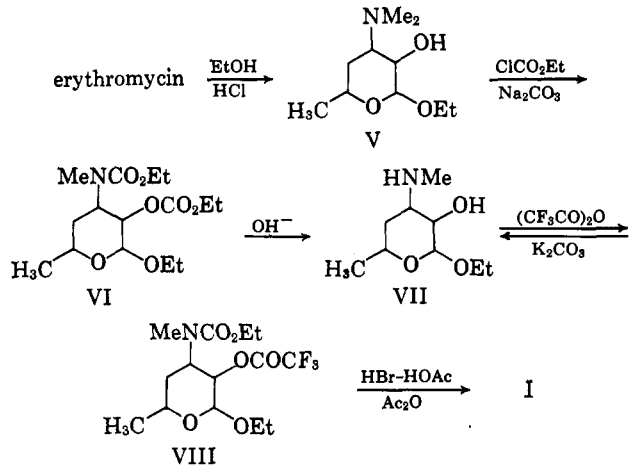


CHART I



acylated derivative IV in a 7% solution of potassium carbonate in aqueous methanol at room temperature for 4.5 hr.

The α-bromo-O,N-ditrifluoroacetylated sugar I was prepared according to the sequence outlined in Chart I. Erythromycin[5,6] was transglycosidated in refluxing ethanolic hydrogen chloride to ethyl desosaminide (V)[5] which was, in turn, converted to ethyl O,N-dicarbethoxydes-N-methyldesosaminide (VI) with ethyl chloroformate.[7] Hydrolysis to ethyl des-N-methyldesosaminide (VII) followed by trifluoroacetylation gave ethyl O,N-ditrifluoroacetyldes-N-methyldesosaminide (VIII) which was converted to I with hydrogen bromide in acetic acid. (Compound VIII could be hydrolyzed back to VII under the same conditions used to convert III to IV.)

Experimental[8]

Ethyl Desosaminide (V).—A solution of 135 g. (0.18 mole) of erythromycin[9] in 1.5–2 l. of absolute ethanol was heated under reflux for 2.5 hr. with hydrogen chloride bubbling through the solution. (The reaction mixture turned black almost immediately after refluxing began.) The ethanol was removed *in vacuo*, the black residue was dissolved in chloroform, and the chloroform solution was extracted twice with water. The combined aqueous extracts were washed with chloroform and made basic (pH *ca.* 12) with cold 10% sodium hydroxide, and the precipitated oily material was extracted into chloroform. The chloroform solution was dried and evaporated, and the orange liquid residue was distilled *in vacuo*. Ethyl desosaminide was obtained in 60% yield (22.4 g.): b.p. 73–80° (0.5 mm.), lit.[4] b.p. 65–67° (0.2 mm.); $[\alpha]^{25}D$ +116° (*c* 1.04, chloroform).

Ethyl O,N-Dicarboxydes-N-methyldesosaminide (VI).—A mixture of 1 g. (0.005 mole) of ethyl desosaminide and 2 g. of anhydrous sodium carbonate in 10 ml. (0.1 mole) of ethyl chloroformate was stirred at room temperature for 19 hr. The pale yellow reaction mixture was poured into chloroform, the chloroform solution was filtered to remove the suspended solid, and the filtrate was evaporated *in vacuo*. The evaporation was repeated twice more with fresh portions of chloroform to remove all the ethyl chloroformate. The pale yellow residue was dissolved in chloroform and the solution was washed with water, dried, and evaporated. The yellow residue was molecularly

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(2) The most commonly used protecting group is acetyl. For a comprehensive review of the preparation, properties, and reactions of 1-halo sugars, see L. J. Haynes and F. H. Newth, *Advan. Carbohydrate Chem.*, **10**, 207 (1955).

(3) Our interest in derivatives of the amino sugar desoamine derives from its being one of the more common sugar components of the macrolide antibiotics: A. B. Foster and D. Horton, *ibid.*, **14**, 213 (1959).

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(7) This reaction parallels the reported conversion of erythromycin to O,N-dicarbethoxydes-N-methylerythromycin.[5]

(8) Melting points are corrected. Microanalyses are by Galbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were taken as mulls in Nujol with a Perkin-Elmer Infracord spectrophotometer.

(9) We thank Abbott Laboratories for their generous gift of erythromycin.

distilled to yield 0.32 g. (30%) of a viscous, colorless liquid: b.p. 75–85° (heating block, 0.025 mm.); λ_{max}^{neat} (μ) 5.72 (carbonate) and 5.90 (urethan); $[\alpha]^{25}D$ +74° (*c* 1.00, chloroform).

Anal. Calcd. for $C_{15}H_{27}NO_7$: C, 54.04; H, 8.16; N, 4.20. Found: C, 54.09; H, 8.03; N, 4.27.

Ethyl Des-N-methyldesosaminide (VII).—To a solution of 1.3 g. (0.004 mole) of ethyl O,N-dicarbethoxydes-N-methyldesosaminide in 5 ml. of ethanol was added 6 ml. of 20% aqueous sodium hydroxide. The resulting two-phase system was heated under reflux for 5 hr., cooled, and poured into methylene chloride. More water was added and the aqueous phase thoroughly extracted with methylene chloride. The methylene chloride extracts were dried and evaporated yielding 0.6 g. (80%) of a colorless solid, m.p. 100–112°. The analytical sample was obtained by recrystallization from acetone: m.p. 119–120.5°; $[\alpha]^{25}D$ +191° (*c* 0.99, chloroform).

Anal. Calcd. for $C_9H_{19}NO_3$: C, 57.11; H, 10.12; N, 7.40. Found: C, 57.02; H, 10.63; N, 7.22.

Ethyl O,N-Ditrifluoroacetyldes-N-methyldesosaminide (VIII).—To a partial solution of 1 g. (0.005 mole) of ethyl des-N-methyldesosaminide in 15 ml. of anhydrous ether was added 6 g. (0.07 mole) of sodium carbonate. The mixture was cooled and vigorously stirred, and 8 ml. (0.057 mole) of trifluoroacetic anhydride was added at as rapid a rate as possible without the reaction getting out of control (*ca.* 5 min.). The cooling bath was removed and the vigorous stirring continued for 20 min. The reaction mixture was poured into chloroform, the excess anhydride was destroyed with ice, and the chloroform solution was washed with water, dried, and evaporated. The yellow liquid residue was distilled *in vacuo* to yield 1.5 g. (75%) of VIII as a colorless, fairly viscous liquid: b.p. 83–85° (0.15–0.2 mm.); $[\alpha]^{25}D$ +49.5° (*c* 1.00, chloroform); λ_{max}^{neat} (μ) 5.60 (ester) and 5.90 (amide).

Anal. Calcd. for $C_{13}H_{17}NO_5F_6$: F, 29.90; N, 3.67. Found: F, 29.61; N, 3.86.

2-O-Trifluoroacetyl-3-N-methyltrifluoroacetamido-3,4,6-trideoxyglucosyl Bromide (I).—A solution of 0.7 g. (0.0018 mole) of VIII in 2 ml. of 32% hydrogen bromide in acetic acid (Eastman) containing 0.25 cc. of acetic anhydride was kept at room temperature for 2 hr., then evaporated to dryness *in vacuo* at 25–40° (oil pump). The pasty solid residue was crystallized from boiling petroleum ether (b.p. 30–60°) and the hygroscopic white crystalline solid obtained was subjected to high vacuum pumping at room temperature over potassium hydroxide overnight: yield, 0.45 g. (59%); m.p. 73–77°; λ_{max}^{neat} (μ) 5.59 (ester) and 5.90 (amide). Because of its hygroscopic nature, the compound was not analyzed.

Cholesteryl Des-N-methyldesosaminide *via* the Ditrifluoroacetyl Derivative II.—To a solution of 1.9 g. (0.005 mole) of cholesterol (recrystallized from ethanol and dried at 100° *in vacuo* over P_2O_5 for 24 hr.) in 60 cc. of anhydrous 1,2-dichloroethane was added 1.3 g. of dried (P_2O_5, 56°, overnight *in vacuo*) mercuric cyanide and 2 g. of Drierite (the commercially available 8 mesh material was pulverized and dried *in vacuo* at 150° for 24 hr.). The suspension was stirred at room temperature for 1 hr., 2.1 g. (0.005 mole) of the bromo sugar I was added, and the mixture was stirred at room temperature for 23 hr. The insoluble salts were separated by filtration and the organic solution was washed with water, dried, and evaporated. The residue was twice taken up in petroleum ether and evaporated to yield 3.6 g. of an off-white solid, m.p. 147–152°, λ_{max}^{Nujol} (μ) 5.57 and 5.90, which was hydrolyzed directly by heating a suspension of the material in a mixture of 50 ml. of methanol and 50 ml. of 10% sodium hydroxide at reflux for 0.75 hr. The methanol was removed *in vacuo*, water was added, and the organic product was extracted with ether. The ether extracts were washed, dried, and evaporated, and the residue was washed with petroleum ether (b.p. 30–60°) (to remove unreacted cholesterol) to give 1.2 g. of a colorless solid, m.p. 146–152°. A suspension of this material in methanol was heated to boiling, cooled, and collected. Cholesteryl des-N-methyldesosaminide was thus obtained in 42% yield (1.1 g.) from the bromo sugar I: m.p. 151–156° (the cloudy melt cleared at 165°); $[\alpha]^{26}D$ +29° (*c* 1.01, chloroform).

Anal. Calcd. for $C_{34}H_{59}NO_3$: C, 77.07; H, 11.22; N, 2.64. Found: C, 77.09; H, 11.14; N, 2.66.

Cyclododecyl Des-N-methyldesosaminide *via* Its Ditrifluoroacetyl Derivative III.—To a solution of 0.184 g. (0.001 mole) of cyclododecanol in 50 ml. of anhydrous 1,2-dichloroethane was added 0.3 g. (0.0012 mole) of dried mercuric cyanide and 1 g. of pulverized predried Drierite. The suspension was stirred at room temperature for 1 hr., 0.42 g. (0.001 mole) of I was added, and the mixture was stirred at room temperature for 26 hr. The insoluble salts were removed by filtration, chloroform was added to the filtrate, and the organic solution was washed with water, dried, and evaporated to yield 0.55 g. of a green-yellow sirup, λ_{max}^{neat} (μ) 5.59 and 5.90, which was hydrolyzed directly by stirring in 14 ml. of a 7% solution of potassium carbonate in aqueous methanol (2:5, v./v.) at room temperature for 4.5 hr. The reaction mixture was poured into water and the organic product extracted with ether. The 0.3 g. of viscous yellow sirup obtained by drying and evaporating the ether absorbed in the 3-μ region in the infrared and showed no bands in the 5.5–6.0-μ region. Evaporative distillation of the crude product at *ca.* 110° (0.005 mm.) yielded 0.15 g. (46%) of a very viscous sirup (practically a glass), $[\alpha]^{25}D$ +76.5° (*c* 1.09, chloroform).

Anal. Calcd. for $C_{19}H_{37}NO_3$: C, 69.68; H, 11.39; N, 4.28. Found: C, 69.81; H, 11.27; N, 4.35.

Acknowledgment.—We thank Dr. G. Berkelhammer for his continued interest and Mr. William Fulmor and staff for the optical rotation data.

New Synthesis of L-Xylose-5-*t*

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L-Xylose labeled with high specific activity of tritium at the C-5 position was needed as an intermediate in the synthesis of L-ascorbic-6-*t* acid for use in biologic studies.

A survey of the literature showed that L-xylose has been obtained from D-glucose requiring four steps.[1,2] It is possible to introduce tritium at the first step if the sodium borohydride reduction of D-glucose to D-glucitol[3] is carried out with tritiated sodium borohydride. Since prolonged handling of radioisotopes is a distinct disadvantage, a different sequence of reactions was sought.

Following the general outline given by Heyns,[4] 1,2:3,5-di-O-cyclohexylidene-L-xylofuranose (I) was preferentially hydrolyzed to 1,2-mono-O-xylofuranose (II). Catalytic oxidation of II gave 1,2-mono-O-cyclohexylidene-L-xyluronic acid (III).

Several improvements were made in the preparation of III: (1) partial hydrolysis of 1,2:3,4-di-O-cyclohexylidene-L-xylofuranose (I) to the monocyclo compound II with 60% acetic acid, (2) construction of an efficient apparatus for catalytic oxidation, and (3) hydrolysis of the calcium salt of III to the acid. The methyl ester of 1,2-mono-O-cyclohexylidene-L-xyluronic acid (IV), not previously recorded in the literature, was prepared and the ester group was reduced with tritiated sodium borohydride. The purification of 1,2-mono-O-cyclohexylidene-L-xylofuranose-5-*t* after reduction was aided

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