gel HF supports with benzene–methanol (99:1) as an irrigant for phenylhydrazones and chloroform–acetic acid (9:1) for furoic acid samples. Spots were visualized by uv light or by spraying with 10% ethanolic sulfuric acid followed by heating at 110° for 10 min.

Carbohydrates were commercially obtainable samples, with the exception of L-sorburonic acid, which was obtained from Northern Regional Research Laboratories, Peoria, Ill., as a gift.

Ultraviolet spectra were obtained on a recording Coleman Model 124 double beam grating spectrometer.

Preparation of 2-Furaldehyde.—Essentially the same procedure was followed for the preparation of 2-furaldehyde for all sugars tested. In a typical experiment 2.0 g of carbohydrate was placed in a 1-l. round-bottom flask containing 500 ml of 6 *N* sulfuric acid. The solution was brought to boiling, an operation which required about 30 min, and 250 ml of distillate was then collected over a 3-hr period. The 2-furaldehyde contained by the distillate was readily identified by its ultraviolet spectrum, which showed maxima at 227 and 278 mμ[13] and which was identical with the spectrum of an authentic sample. Yields of 2-furaldehyde in the distillate were estimated by a spectrophotometric measurement at 278 mμ based on a molar absorptivity of 2-furaldehyde of 18,000. The 2-furaldehyde was further identified by conversion to the phenylhydrazone and to 2-furoic acid in radiochemical experiments described below.

Reaction of 2-Amino-2-deoxy-D-glucose (12) in Borate Buffer.—The procedure of Zimmerman and Cosmatos[9] was repeated in this experiment. **12** (2.15 g), boric acid (9.27 g), and sodium hydroxide (6.0 g) were dissolved in 1 l. of water and held at 25° for 30 hr. The solution was then adjusted to pH 7 with concentrated hydrochloric acid and distilled as described above. The distillate contained a small amount of uv-absorbing material which showed maxima at 235 and 265 mμ. Assuming that all the absorbance at 265 mμ was due to 2-furaldehyde the total yield was 0.24%.

Preparation of 2-Furaldehyde-^{3}H Phenylhydrazone.—In a typical experiment, 2-furaldehyde was obtained from 3.0 g of D-xylose by distillation as described above with the exception that the solution contained 20 mCi of tritiated water. An equimolar amount of phenylhydrazine hydrochloride in 20 ml of water was added and the resulting precipitate was collected on a filter. This material was recrystallized from ethanol–water (1:1) to constant radiochemical activity. The 2-furaldehyde phenylhydrazone had mp 94° (lit.[14] mp 97°) and had a thin layer chromatographic flow rate identical with that of an authentic sample. Identical procedures were used in subsequent experiments using compound **8**, **9**, **10**, and **11**.

Preparation of 2-Furoic Acid-^{3}H.—A solution of 2-furaldehyde-^{3}H was obtained from D-xylose in tritiated water as described above. To the distillate was added 2.0 g of freshly prepared silver oxide and the pH was adjusted to 10 with sodium hydroxide solution. The suspension was stirred for 30 min with aeration and filtered, and the filtrate was passed through a column of Dowex 50 (hydrogen form). The eluate was evaporated to dryness and alternately sublimed at 110° (0.3 mm) and reevaporated from water until constant radiochemical activity was reached. The final product had mp 131° (lit.[15] mp 133°) and had a chromatographic mobility identical with that of an authentic specimen. Identical results were obtained using compounds **8**, **9**, **10**, and **11** as starting materials.

Preparation of Methyl 5-Nitro-2-furoate-^{3}H from 2-Furoic Acid-^{3}H.—A sample (12 mg) of 2-furoic acid-^{3}H derived from D-glucuronic acid as described above was diluted with inert material and recrystallized to give a sample having a specific activity of 0.357 μCi/mmol. This sample (936.8 mg) was esterified with diazomethane and the resulting ester was converted to methyl 5-nitro-2-furoate as described by Freure and Johnson.[16]

This compound after two recrystallizations from methanol and one from hexane had mp 79.5° (lit.[16] mp 81.6°) and ran as a single spot on thin layer chromatograms.

Anal. Calcd for $C_6H_5O_5N$: N, 8.18. Found: N, 7.90.

The specific activity of this derivative was 0.353 uCi/mmol and was not changed on further purification.

Registry No.—**7**, 58-86-6; **8**, 6556-12-3; **9**, 488-34-6; **10**, 50-81-7; **11**, 669-90-9; **12**, 3416-24-8; 2-furaldehyde, 98-01-1.

Acknowledgment.—This research was supported, in part, by a grant from the Corn Industries Research Foundation, a division of the Corn Refiners Association.

(13) A. P. Dunlop and F. Peters, "The Furans," Wiley, New York, N. Y., 1953, p 13.

(14) Reference 13, p 364.

(15) Reference 13, p 489.

(16) B. T. Freure and J. R. Johnson, *J. Amer. Chem. Soc.*, **53**, 1142 (1931).

New Route to Branched-Chain Sugars. Photoamidation and Photohydroxyalkylation of 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose

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The acetone-initiated photochemical addition of formamide to 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose (**1**) afforded trans 1:1 adducts, namely, 3-*C*-carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2**), 3-carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (**3**), and 3-deoxy-3-*C*-(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**4**) in 16, 15, and 7% yields (after chromatography), respectively. Irradiation of **1** in the presence of isopropyl alcohol and acetone gave the hydroxyisopropyl 1:1 adduct **4** in 31% yield and, in addition, a novel 1:2 adduct **6** which is tentatively assigned the structure of 3-deoxy-3,4-*C*-bis(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose in 8% yield. The proton magnetic resonance and high-resolution infrared spectra of these substances are described. Lithium aluminum hydride reduction of the carbamoyl sugar **3** afforded 3-*C*-aminomethyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose, isolated as its trifluoroacetamido derivative **7**.

In continuation of our studies on the chemistry of branched-chain sugars[1] we now wish to report a different approach to the synthesis of these novel sugars by photoaddition of formamide and of isopropyl alcohol to unsaturated carbohydrates.

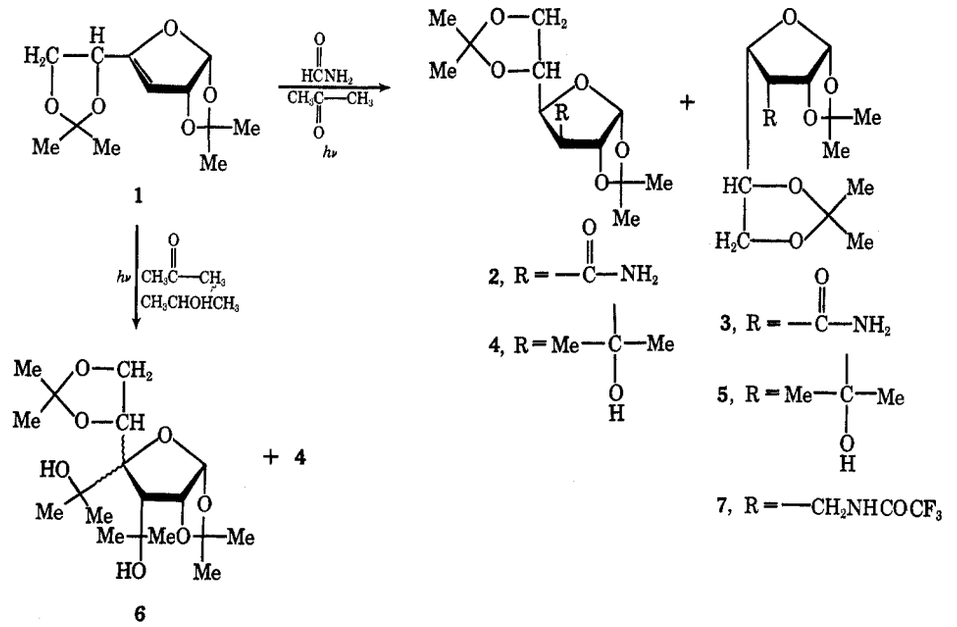
Formamide has been shown to undergo acetone-initiated photochemical addition to terminal[2] and nonterminal olefins[3] to yield 1:1 carbamoyl adducts. In the case of norbornene the reaction has been found to be stereospecific, leading exclusively to the exo isomer. This reaction, termed photoamidation, has also been

(1) (a) A. Rosenthal, *Advan. Carbohyd. Chem.*, **23**, 59 (1968); (b) A. Rosenthal and M. Sprinzl, *Carbohyd. Res.*, **16**, 337 (1971); (c) A. Rosenthal, K. S. Ong, and D. A. Baker, *ibid.*, **13**, 113 (1970); (d) A. Rosenthal and G. Schöllnhammer, *ibid.*, **15**, 421 (1970); (e) A. Rosenthal, and D. A. Baker, *Tetrahedron Lett.*, 397 (1969).

(2) (a) D. Elad and J. Rokach, *J. Org. Chem.*, **29**, 1855 (1964); (b) D. Elad and J. Rokach, *J. Chem. Soc.*, 800 (1965).

(3) D. Elad and J. Rokach, *J. Org. Chem.*, **30**, 3361 (1965).

SCHEME I



extended successfully to α,β-unsaturated esters.[4] The point of attachment of the carbamoyl [$\cdot C(=O)NH_2$] radical to the carbon–carbon double bond depends on the structure of the olefin. With terminal olefins, the 1:1 adduct was predominately the anti-Markovnikov one, but with nonterminal olefins mixtures of the two possible amides were obtained.

Because of the great importance of the amino sugars[5] as constituents of many antibiotics,[6] our laboratory has been interested in developing new general methods for the synthesis of analogues of the amino sugars which occur as moieties in some of the antibiotics. Photoamidation of unsaturated carbohydrates appeared to offer promise for the synthesis of carbohydrate carboxamides, structurally related to gougerotin.[7] Reduction of the blocked carbamoyl sugars might be expected to yield branched-chain amino sugars which would be homologues of the amino sugar moiety of puromycin.[7] An alternative approach to this synthesis, *via* the application of the nitromethane synthesis to a ketose, has been reported recently.[8]

When a solution of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose (**1**),[9] *tert*-butyl alcohol, formamide, and acetone was irradiated through a Pyrex filter for 22 hr, a mixture of three main products, **2**, **3**, and **4**, was formed (Scheme I). After work-up of the reaction mixture the chloroform-soluble components (part of the product was water soluble and not recovered) were separated by silica gel column chromatography using benzene–ethyl acetate as developer to afford two photoamidation adducts, **2** and **3**, in about equal yields (total yield ~31%) and a hydroxyisopropyl adduct, **4**, in ~7% yield. The structures of the photoproducts were readily deduced from an analysis of their infrared (ir) and proton magnetic resonance (pmr) spectra. The pmr spectra (see Figure 1 and Experimental Section) of all three compounds clearly showed a single H-3 methine hydrogen at τ 6.9–7.9, thus establishing that the carbamoyl and ketyl radical [$(CH_3)_2\cdot COH$] had added exclusively to C-3 of **1**. The C-2 hydrogen of both **2** (Figure 1A) and **4** gave doublets at τ 5.05 and 5.45, respectively ($J_{2,1}$ = 3.5 and 4.0 Hz), which collapsed to singlets on irradiation of the C-1 hydrogen. On the other hand, the C-2 hydrogen of **3** (Figure 1B) exhibited four peaks at τ 4.97 ($J_{2,1}$ = 4.0 and $J_{2,3}$ = 2.5 Hz) which collapsed to a doublet on irradiation of the C-3 hydrogen. Trans H_2–H_3 of the 1,2-*O*-isopropylidenefuranose sugars have small couplings of <0.5 Hz, whereas cis H_1–H_2 or H_2–H_3 have couplings of >2.5 Hz;[10] therefore the C-3 hydrogen of compounds **2** and **4** are trans to the C-2 hydrogen, whereas the C-3 hydrogen of **3** must be cis to the C-2 hydrogen. Similar consideration of the coupling constants of the C-3 hydrogen with the C-4 hydrogen must lead to the configuration of the C-4 of each of the compounds. Because the C-3 hydrogen of **2** gave a doublet at τ 6.87 ($J_{3,4}$ = 4.0 Hz), H-3 and H-4 must be cis oriented, and, because the C-3 hydrogen of **3** at a τ 6.96 exhibited four peaks with $J_{3,2}$ = 2.5 and $J_{3,4}$ = 7.0 Hz, H-3, H-4, and H-2 of the latter compound must also be cis oriented. Therefore, compounds **2** and **3** are undoubtedly 3-*C*-carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 3-*C*-carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose, respectively. Interestingly, the photoamidation products must have been formed *via* a trans addition of the carbamoyl and hydrogen radicals (hydrogen atom is abstracted from the formamide in the last step[2]) to the carbon–carbon double bond of **1**. Here the addition of the carbamoyl radical took place stereoselectively to C-3 and almost with equal

(4) J. Rokach and D. Elad, *J. Org. Chem.*, **31**, 4210 (1966).

(5) (a) A. B. Foster and M. Stacey, *Advan. Carbohyd. Chem.*, **7**, 247 (1952); (b) A. B. Foster and D. Horton, *ibid.*, **14**, 213 (1959); (c) A. B. Foster, and J. M. Webber, *ibid.*, **15**, 371 (1960).

(6) (a) J. D. Dutcher, *ibid.*, **18**, 259 (1963); (b) L. Hough and A. C. Richardson in "Rodd's Chemistry of Carbon Compounds," Vol. 1, Part F, S. Coffey, Ed., Elsevier, Amsterdam, 1967.

(7) J. J. Fox, K. A. Watanabe, and A. Bloch, *Progr. Nucleic Acid Res. Mol. Biol.*, **5**, 251 (1966).

(8) H. P. Albrecht and J. G. Moffatt, *Tetrahedron Lett.*, 1063 (1970).

(9) (a) F. Weygand and H. Wolz, *Chem. Ber.*, **85**, 256 (1952); (b) J. Prokop and D. H. Murray, *J. Pharm. Sci.*, **54**, 359 (1965).

(10) R. J. Abraham, L. D. Hall, L. Hough, and K. A. McLauchlin, *J. Chem. Soc.*, 3699 (1962).

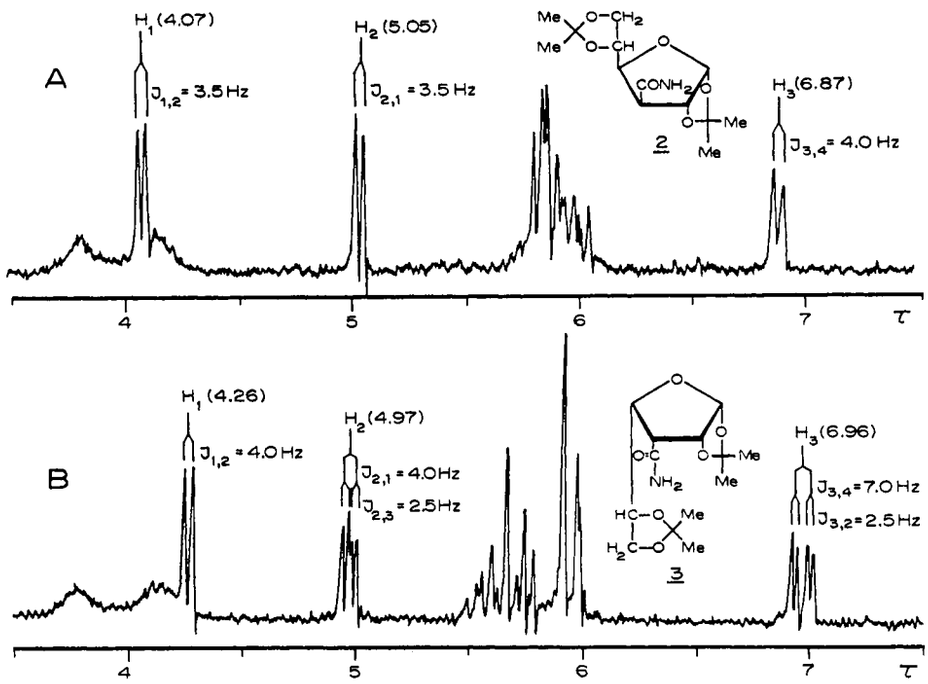


Figure 1.—Partial nmr spectra of (A) 3-*C*-carbamoyl-3-deoxy1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (2) and (B) 3-*C*-carbamoyl-3-deoxy-1.2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (3) in $CDCl_3$ at 100 MHz.

facility from both sides of the double bond as evidenced by the almost equal yield of **2** and **3**. The complete structure of the branched-chain hydroxyisopropyl sugar **4** was similarly deduced from its pmr spectrum (similar to that of **2**) and therefore it must be 3-deoxy-3-*C*-(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose. Presumably, **4** must have been formed *via* a trans addition of the ketyl group and hydrogen atom to **1**. In contrast to the photoamidation reaction the photohydroxyalkylation reaction was stereoselective since the ketyl group added stereoselectively to **1** to afford **4** only. Although 2-methylalkan-2-ols have been isolated from some reaction mixtures encountered in the light-induced amidation of terminal olefins,[2] the stereochemistry of these photoreactions has hitherto not been elaborated.

The second part of this investigation deals with the photoaddition of isopropyl alcohol to the same unsaturated sugar **1** to yield novel branched-chain hydroxyalkyl sugars. The light-induced addition of alcohols to olefins to afford homologous alcohols and telomers has been known for almost two decades.[11] When a solution of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enose (**1**) in isopropyl alcohol and acetone was irradiated for 26 hr through a Pyrex filter, the unsaturated sugar was converted mainly into a 1:1 and a 1:2 adduct to afford 3-deoxy-3-*C*-(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**4**) and an unexpected novel adduct **6** in 31 and 8% yields, respectively. In addition, pinacol was produced. These substances were separated by silica gel column chromatography using benzene–ethyl acetate as developer. The identity of pinacol was established by direct comparison with an authentic sample. The structure of **6** was deduced from its mass, pmr, and ir spectra. Its mass spectrum gave a peak at *m/e* 345 and a very small peak at *m/e* 360. Because isopropylidene derivatives of carbohydrates are known to lose a methyl group during their initial mass breakdown,[12] the molecular weight of **6** was 360. This molecular weight suggested strongly that compound **6** was an adduct of 1 mol of **1** and 2 mol of the ketyl group. Elemental analysis of **6** agreed with the molecular constitution $C_{18}H_{32}O_7$. The pmr spectrum of **6** in $CDCl_3$ clearly showed the presence of two hydroxyl peaks which disappeared on addition of D_2O and the presence of six high-field signals at τ 8.38–8.86 equal to eight methyl groups. These findings confirmed that two ketyl radicals must have added to the C_3–C_4 double bond of **1**. The configuration of C-3 of **6** was readily deduced from its pmr spectrum which showed a doublet at τ 4.09 (J = 4.5 Hz), four peaks at 5.01 ($J_{2,1}$ = 4.5 Hz and 7 Hz), and one doublet at 7.05 (J = 7 Hz). These signals were assigned to C-1, C-2, and C-3 hydrogens, respectively, because irradiation at τ 5.0 collapsed the doublets at 4.09 and 7.05 to singlets. Therefore, the C-3 hydrogen of compound **6** must be cis to the C-2 hydrogen. Because there is no hydrogen on C-4 of **6**, pmr could not be used to deduce the configuration of C-4. On the other hand, intramolecular hydrogen-bonding studies[13] carried out by high resolution ir spectroscopy on dilute carbon tetrachloride solutions and molecular model studies strongly suggested the configuration at C-4 of **6**. The broad intense peak at 3458 cm^{-1} indicated the presence of a hydroxyl group bonded to oxygen in a six-membered ring.[13] This obviously could arise from the bonding of the hydroxyl group on the C-3 hydroxyisopropyl group with the C-2 oxygen or from the bonding of the two hydroxyl groups if both

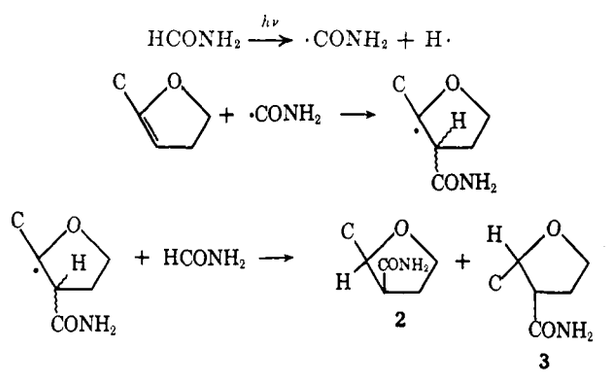
(11) (a) W. H. Urry, F. W. Stacey, O. O. Juveland, and C. H. McDonnell, *J. Amer. Chem. Soc.*, **75**, 250 (1953); (b) W. H. Urry, F. W. Stacey, E. S. Hayser, and O. O. Juveland, *ibid.*, **76**, 450 (1954).

(12) (a) D. C. De Jongh and K. Biemann, *ibid.*, **86**, 67 (1964); (b) N. K. Kochetkov and O. S. Chizhov, *Advan. Carbohyd. Chem.*, **21**, 39 (1966).

(13) (a) L. P. Kuhn, P. v. R. Schleyer, W. F. Batinger, Jr., and L. Eberson, *J. Amer. Chem. Soc.*, **86**, 650 (1964); (b) H. Spedding, *Advan. Carbohyd. Chem.*, **19**, 23 (1964); (c) K. N. Slessor and A. S. Tracey, *Can. J. Chem.*, **47**, 3989 (1969).

hydroxyisopropyl groups were cis oriented. However, the presence of a sharp intense peak at 3623 cm^{-1} indicated that one of the hydroxyisopropyl groups must be free, and furthermore, because the configuration of the C-3 hydroxyisopropyl group is known, the C-4 hydroxyisopropyl group must be trans to its C-3 counterpart; **6** is thus tentatively assigned as 3-deoxy-3,4-*C*-bis(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose.[14] From a stereochemical viewpoint, **6** might have been formed *via* a trans addition of the two ketyl groups to **1**. The omission of the hydrogen-abstraction step has been noted by other workers;[2] as an example, alkylated succinamides have been isolated in low yields from the photoamidation of terminal olefins. These trace compounds might have arisen from an addition of two carbamoyl free radicals to the olefin or else from a radical addition to formamide.

The course of the reaction for the photochemical synthesis of 1:1 adducts[2] of formamide and the unsaturated sugar **1** may be illustrated as follows.



The case of converting **3** into a branched-chain amino sugar having the L configuration by selective periodate degradation of the 5,6-diol of **3** followed by reduction of the aldehydo compound makes this synthesis potentially attractive.

Lithium aluminum hydride reduction of the carboxamide sugar **3** readily afforded a branched-chain amino sugar, namely 3-*C*-aminomethyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose. Quite unexpectedly, the corresponding branched-chain amino sugar from **2** proved to be unstable and could not be characterized.

Experimental Section

Irradiations were made with a 450-W Hanovia medium pressure mercury vapor lamp with Pyrex filter under oxygen-free nitrogen. The reaction mixture was cooled internally with running water. Agitation of the reaction mixture was achieved with magnetic stirring. Purified nitrogen was bubbled for 2 hr through the reaction mixture before irradiation. The progress of reactions and purity of products were checked by tlc on silica gel G. Grace silica gel and Woelm neutral alumina were used for column chromatography. Ir spectra were recorded in Nujol or in CCl_4 with a Perkin-Elmer Model 337 spectrometer, and pmr spectra were determined in deuteriochloroform solution with TMS as the internal standard using a Varian HA-100 spectrometer, ionizing potential 70 eV. Mass spectroscopy was obtained with a HMS-9 spectrometer. Optical rotations were measured at room temperature with a Perkin-Elmer Model 141 automatic polarimeter. Chemical analysis were performed by Mr. P. Borda of the Microanalytical Laboratory, University of British Columbia.

Photoamidation of 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enose (1)[9] to Yield Compounds 2, 3 and 4.—A solution of the unsaturated carbohydrate **1** (4.8 g) in anhydrous formamide (200 ml), *tert*-butyl alchohol (60 ml) and acetone (20 ml) was irradiated for 22 hr (or until all starting material was consumed as evidenced by tlc), after which the solution was diluted with 300 ml of saturated aqueous sodium chloride and then extracted with chloroform (3 × 200 ml). The combined chloroform extracts were washed with a saturated aqueous sodium chloride solution, dried over sodium sulfate, filtered, and concentrated to give a syrup (5.0 g). Investigation of the syrup by tlc (on silica gel using 1:1 benzene–ethyl acetate) showed three main products, corresponding to compounds **2**, **3**, and **4**, with R_f 0.65, 0.50, and 0.70, respectively. The syrup was applied to a silica gel column (700 g) and eluted with benzene–ethyl acetate (1:1 v/v). Progress was checked by tlc. About 70 l. of eluent was required. The fastest moving zone contained pure compound **4** (0.283 g) and the first part of the second zone (0.250 g) consisted of an almost equal mixture of compounds **4** and **2**. The main part of the second zone (0.673 g) consisted of pure **2**. The first part of the third zone consisted of an almost equal mixture (0.150 g) of compounds **2** and **3** and the principal portion of the third zone (0.747 g) contained pure compound **3**.

3-*C*-Carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (2).—The fraction containing pure **2** was recrystallized from hexane–benzene (2:1): mp 110–111.5°; $[\alpha]^{22}D$ −1.4° (*c* 4.7, chloroform); ir 1675 cm^{-1} (amide C=O); mass spectrum (70 eV) *m/e* 287 (calcd *m/e* 287); for τ^{CDCl_3} see Figure 1A (irradiation at τ 5.8 collapsed the doublet at 6.87 to a singlet and irradiation at τ 4.07 collapsed the doublet at 5.05 to a singlet; irradiation at τ 6.8 did not affect the doublet at τ 5.05).

Anal. Calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37; N, 4.88. Found: C, 54.31; H, 7.50; N, 4.68.

3-*C*-Carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (3).—The fraction containing pure compound **3** was recrystallized from carbon tetrachloride and from water: mp 152–154°; $[\alpha]^{22}D$ +19.0° (*c*, 1.8, chloroform); ir 1670 cm^{-1} (amide C=O); mass spectrum *m/e* 287 (calcd *m/e* 287); for τ^{CDCl_3} see Figure 1B (irradiation at τ 4.97 collapsed the signals at 6.96 to a doublet having J = 7 Hz and collapsed the doublet at τ 4.26 to a singlet; irradiation at τ 6.9 collapsed the signals at τ 4.97 to a doublet, J = 4 Hz).

Anal. Calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37; N, 4.88. Found: C, 54.21; H, 7.24; N, 4.64.

3-Deoxy-3-*C*-(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (4).—The first fraction containing **4** (homogeneous by tlc) was distilled at bp 110–120° (0.1 mm): $[\alpha]^{22}D$ −15.6° (*c* 1.8, chloroform); mass spectrum *m/e* 287 (M − CH_3) (calcd *m/e* 302); ir (0.005 and 0.001 *M* in CCl_4) 3700 (small peak), 3610 (strong peak), 3500 cm^{-1} (sh); τ^{CDCl_3} 4.28 (d, H-1, $J_{1,2}$ = 4.0 Hz), 5.45 (d, H-2, $J_{2,1}$ = 4.0 Hz), 5.56 (t, J = 7.5 Hz), 5.82 (q, H-4, $J_{4,3}$ = 3.0 Hz, $J_{4,5}$ = 7.5 Hz), 6.00 and 6.11 (m), 7.92 (d, H-3, $J_{3,4}$ = 3.0 Hz), 7.9–8.0 (OH peak, disappears on addition of D_2O), 8.40, 8.50, 8.58, 8.65, 8.67, 8.69 (6-Me) (irradiation of the doublet at τ 7.92 collapsed the quartet at 5.82 to a doublet; irradiation at τ 5.45 collapsed the doublet at 4.28 to a singlet).

Anal. Calcd for $C_{15}H_{26}O_6$: C, 59.58; H, 8.67. Found: C, 58.99; H, 8.88.

Reduction of 3-*C*-Carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (3) to Yield 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-trifluoroacetamidomethyl-α-D-gulofuranose (7).—The amide **3** (0.280 g) in anhydrous tetrahydrofuran (25 ml) was reduced with lithium aluminum hydride (0.370 g). After the reaction mixture was allowed to stand at room temperature for 1 hr, it was refluxed for 3 hr. Excess lithium aluminum hydride was then decomposed by dropwise addition of water. The solids were removed by filtration and washed with tetrahydrofuran. The combined filtrates were dried (Na_2SO_4) and evaporated under reduced pressure to yield a syrup which was treated with trifluoroacetic anhydride (1 ml) and pyridine (2 ml) at room temperature overnight. After evaporation of the acetylation mixture under reduced pressure, the syrup was partitioned between an equal volume mixture of dichloromethane–

(14) One referee has commented that, if the two –OH groups were H bonded together, one of the H atoms would still be free and would give rise to absorption at >3600 cm^{-1}. Furthermore, regardless of the stereochemistry at C-4, the –OH of the C-4 hydroxyisopropyl can bond in a six-membered ring to O-5. Thus, the C-3 hydroxyisopropyl group could be the free one (it is apparently free in compound **4**). Thus the complete structure of compound **6**, is not known.

water. The dichloromethane extract was dried over sodium sulfate, filtered, and evaporated to dryness. The residue was purified by chromatography on silica gel using benzene–ethyl acetate (1:1) as eluent. The main zone was crystallized from hexane: mp 131–132°; $[\alpha]^{22}D$ +8.8° (*c* 2.2, chloroform); τ^{CDCl_3} 4.28 (d, H-1, $J_{1,2}$ = 4.0 Hz), 5.5 (two d, H-2, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 1.5 Hz), 6.5 (2 H, CH_2N), 7.5 (m, H-3).

Anal. Calcd for $C_{15}H_{22}NO_6F_3$: C, 48.78; H, 5.97; N, 3.79. Found: C, 48.65; H, 6.09; N, 3.84.

Attempted Reduction of 3-*C*-Carbamoyl-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (2).—The amide **2** was subjected to lithium aluminum hydride reduction and the product was treated with trifluoroacetic anhydride and pyridine according to the same procedure as described above. Chromatographic (tlc) examination of the product showed a complex mixture of products which could not be separated. Pmr of the impure main fractions indicated that the sugar moiety had changed.

Photohydroxyalkylation of 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-erythro-hex-3-enose (1) to Yield Compounds 4 and 6.—A solution of **1** (4.0 g) in isopropyl alcohol (200 ml) and acetone (100 ml) was irradiated for 26 hr through a Pyrex filter. The product was worked up as described previously and then chromatographed on a silica gel comumn (1000 g) using benzene–ethyl acetate (1:3 to 2:1) as developer. The fastest moving zone **6** (0.500 g, 8%) was followed by a zone consisting of a mixture of compound **4** (1.59 g, 31%) and pinacol (1.0 g). The latter two compounds were separated by distillation at 0.1 mm and 100°. The pinacol was compared with an authentic sample of pinacol and shown to be identical (ir spectrum).

3-Deoxy-3,4-*C*-bis(1-hydroxy-1-methylethyl)-1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose (6).—Product **6** was recrystallized from benzene–hexane (1:9): mp 174–175° (crystal form changes at 147–149° from prisms to needles); $[\alpha]^{22}D$ +73° (*c* 1, chloroform); mass spectrum *m/e* 360 and 345 (M − CH_3) (calcd *m/e* 360); ir (0.005 and 0.001 *M* in CCl_4) 3623 (sharp intense peak due to free OH), 3458 cm^{-1} (intense broad peak); τ^{CDCl_3} 4.09 (d, H-1, $J_{1,2}$ = 4.5 Hz), 5.01 (two d, H-2, $J_{2,1}$ = 4.5 Hz, $J_{2,3}$ = 7.0 Hz), 5.62–6.1 (H-5 and H-6), 6.3–6.85 (broad OH peaks, disappear on addition of D_2O), 7.05 (d, H-3, $J_{3,2}$ = 7.0 Hz), 8.38, 8.46, and 8.50 (3-Me), 8.60 and 8.63 (4-Me), 8.86 (1-Me) (irradiation at τ 5.0 collapsed the doublets at 4.09 and 7.05 to singlets).

Anal. Calcd for $C_{18}H_{32}O_7$: C, 59.98; H, 8.95. Found: C, 59.68; H, 9.30.

Registry No.—**1**, 10368-85-1; **2**, 34289-95-7; **3**, 34289-96-8; **4**, 34297-59-1; **6**, 34289-97-9; **7**, 34289 98-0.

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Nucleosides. XIII.[1] Synthesis and Interconversions of *C*-Methyl-Branched 1-(3-Amino-3-deoxy-β-D-hexopyranosyl)uracils. An Empirical Method for Configurational Assignments at the Branch Point by Nuclear Magnetic Resonance[2]

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C-Methyl-branched 3′-nitrohexosyl uracils of gluco, galacto, manno, and allo configuration (**4–7**) were prepared from uridine by treatment with metaperiodate and subsequent base-catalyzed cyclization with nitroethane. Hydrogenation afforded the title compounds **12–15** which were further characterized as the *N*-acetyl (**20–22**) and the fully acetylated derivatives (**16–19**). While coupling patterns of the ring protons readily provided configurational proof for the arrangement of the hydroxyl groups at C-2′ and C-4′, the stereochemistry at the branch point was established chemically by conversion of the *gluco*-*N*-acetate **20** into derivatives of manno (**22**) and galacto configuration (**33**) in a series of reactions which involved as decisive steps a displacement *via* oxazolines of mesyl functions, introduced at C-2′ and C-4′, respectively. In the gluco → manno conversion, both intermediates possible, the O²,2′ cyclonucleoside **28** and the 2′,3′-oxazoline **29**, were isolated and their structures established by chemical and spectroscopical means. Tertiary acetoxy and acetamido resonances at a *C*-methyl branch, as compared to their secondary counterparts, are shifted toward higher field by about 0.1 ppm in $CDCl_3$ or in DMSO-d_6. This provides a facile and surprisingly accurate means for determining configurations at the tertiary center of *C*-methyl-branched cyclitol and pyranose peracetates.

Branched-chain sugar nucleosides, which were virtually unknown prior to 1966, have since attained considerable chemical interest,[3–10] no doubt mainly evoked by the cytotoxic and antiviral activities of some compounds of this type.[3] The prevailing synthetic route[3–10] consisted in linking nucleobase and branched-chain sugar *via* standard procedures of nucleoside synthesis, an approach which is encumbered by the still limited availability of branched-chain sugars and by certain unsuccessful attempts[11] to convert them into nucleosides. As an alternate approach toward the synthesis of branched-chain sugar nucleosides, we exploited the applicability of the dialdehyde–nitroalkane

(1) (a) For paper XII see J. Černá, F. W. Lichtenthaler, and I. Rychlík, *FEBS (Fed. Eur. Biochem. Soc.) Lett.*, **14**, 45 (1971). (b) Simultaneously taken as paper XVIII of the series "Nitromethane Condensations with Dialdehydes." Part XVII: F. W. Lichtenthaler and N. Majer, *Tetrahedron Lett.*, 411 (1969).

(2) Taken in part from the Doctoral Dissertation of H.Z., Technische Hochschule Darmstadt, June 1969. (b) Financial support of this work by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged. (c) A preliminary account of this work has appeared: F. W. Lichtenthaler and H. Zinke, *Angew. Chem.*, **78**, 774 (1966); *Angew. Chem., Int. Ed. Engl.*, **5**, 737 (1966).

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