(final, 2.5 hr) (c 1.0, H_2O). The material also traveled as a single spot on paper chromatography using 2-propanol–water–ammonia (7:2:1) and 1-butanol–water–ammonia (7:2:1) systems.

Anal. Calcd for $C_8H_{18}ClNO_4$: C, 42.19; H, 7.97; N, 6.15. Found: C, 42.18; H, 8.03; N, 6.40.

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Registry No.—**1**, 53951-08-9; **2**, 55570-34-8; **3**, 55570-35-9; **4**, 53928-92-0; **5**, 55570-36-0; **6**, 55570-37-1; **7**, 55570-38-2; **8**, 55637-43-9; **9**, 51255-06-2; **10**, 51209-16-0; **11**, 55570-39-3; **11** HCl, 55605-89-5; **11** methiodide, 55605-90-8; **12**, 55570-40-6; **12** HCl, 55570-41-7; **13**, 55570-42-8; sodium benzoate, 532-32-1; methanesulfonyl chloride, 124-63-0; acetic acid, 64-19-7.

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Synthesis and Reactions of Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-α-D-*threo*-hex-4-enopyranoside[1]

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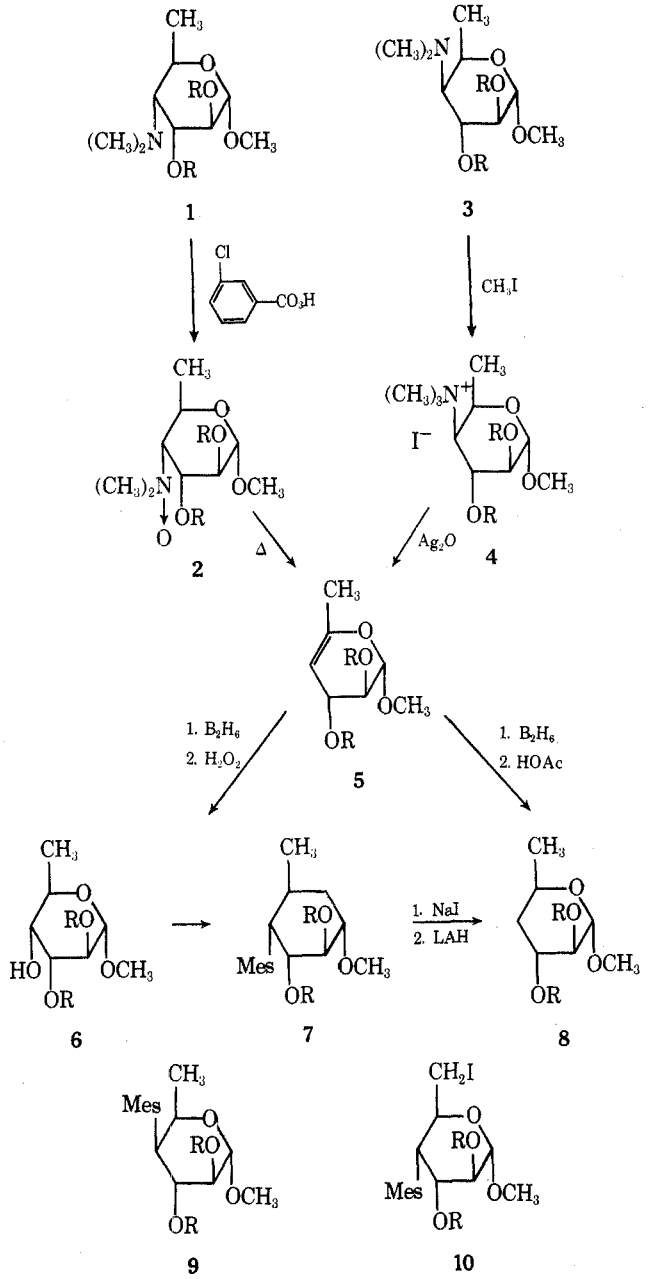
The syntheses of a 4,6-unsaturated sugar derivative, methyl 2,3-di-*O*-benzyl-4,6-dideoxy-α-D-*threo*-hex-4-enopyranoside (**5**), by a Cope elimination of methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-(*N*,*N*-dimethylamino)-*N*-oxo-α-D-altropyranoside (**2**) and by a Hofmann elimination of methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-(*N*,*N*-dimethylamino)-α-D-idopyranoside methiodide (**4**) are described. Hydroboration of **5** and subsequent oxidation with hydrogen peroxide yielded methyl 6-deoxy-2,3-di-*O*-benzyl-α-D-altropyranoside (**7**), whereas hydroboration of **5** followed by hydrolysis with acetic acid provided methyl 2,3-di-*O*-benzyl-4,6-dideoxy-α-D-*arabino*-hexopyranoside (**8**).

Unsaturated sugars, although neglected for a long time, are gaining importance recently because of their potential value in synthetic carbohydrate chemistry.[3] In addition, it has been suggested that some unsaturated sugars play significant biological roles in metabolic pathways.[4,5] Unsaturated sugars also occur naturally, for example, ascorbic acid and the nucleoside antibiotic, blasticidin S.[6] We now describe the synthesis of a 4,5-unsaturated hexose derivative and its hydroboration reactions under oxidative and nonoxidative conditions.

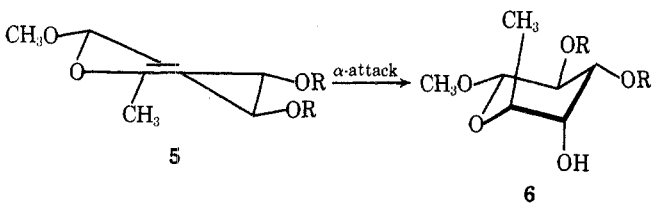
Treatment of methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-(*N*,*N*-dimethylamino)-α-D-altropyranoside[7] (**1**) with freshly purified *m*-chloroperbenzoic acid[8] afforded the *N*-oxide **2**, which was characterized as its crystalline hydrochloride. Pyrolysis of **2** at 98–100° under reduced pressure (Cope elimination) gave the unsaturated sugar, 2,3-di-*O*-benzyl-4,6-dideoxy-α-D-*threo*-hex-4-enopyranoside (**5**), in 72% yield. Compound **5** was also prepared by a Hofmann elimination reaction as follows. Conversion of methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-(*N*,*N*-dimethylamino)-α-D-idopyranoside[9] (**3**) to the quaternary ammonium iodide (**4**) followed by treatment of **4** with silver oxide in methanol provided **5** in 52% yield. The structure of **5** was established by its analysis and spectral data.

Attempted synthesis of **5** by base-catalyzed elimination of methyl 2,3-di-*O*-benzyl-6-deoxy-4-*O*-methylsulfonyl-α-D-idopyranoside[7,9] (**9**) and from methyl 2,3-di-*O*-benzyl-6-deoxy-6-iodo-4-*O*-methylsulfonyl-α-D-altropyranoside[7] (**10**) according to the procedure of Helferich and Himmen[10] were unsuccessful.

Hydroboration of **5** with a mixture of sodium borohydride and boron trifluoride etherate and subsequent treatment with hydrogen peroxide provided methyl 6-deoxy-2,3-di-*O*-benzyl-α-D-altropyranoside (**6**) in 72% yield. The structure of **6** was confirmed by its conversion to the crystalline methylsulfonate **7** and its identification with an authentic sample.[7] The formation of **6** as the major product in this reaction suggests that the addition of diborane takes



place almost exclusively from the bottom side of the molecule (α-attack) as shown below. No other product was detected in the reaction mixture.



Hydroboration of **5** followed by hydrolysis with acetic acid gave methyl 2,3-di-O-benzyl-4,6-dideoxy-α-D-*arabino*-hexopyranoside (**8**). The structure of **8** was established as follows. Treatment of **7** with sodium iodide to form a mixture of epimeric 4-iodo derivatives[11] and subsequent reduction of this mixture with lithium aluminum hydride provided **8** which was shown to be identical with the hydroboration product of **5** by ir, GC, and optical rotation.

Attempted hydrogenation of **5** under a variety of conditions was unsuccessful. Thus, **5** appeared to decompose (by TLC) during hydrogenation using methanol, ethanol, dioxane, and acetic acid as solvents and platinum and Pd/C as catalysts.

Experimental Section

Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Thin layer chromatography was carried out using silica gel H from Brinkmann Instruments on 5 × 20 glass plates. A solvent system consisting of diethyl ketone, diisopropyl ketone, and ligroin (6:3:1) was used unless otherwise mentioned. The NMR spectra were taken on a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Infrared spectra were recorded on a Perkin-Elmer Infracord instrument. Specific rotations were measured using a Perkin-Elmer 141 polarimeter. Gas chromatographic analyses were performed on a F & M Model 810 instrument fitted with a dual ionization detector. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-4-(*N,N*-dimethylamino)-*N*-oxo-α-D-altropyranoside (2). A solution of 128 mg (0.33 mmol) of the dimethylamino sugar[7] **1** in 50 ml of ether and 64 mg (0.36 mmol) of 99.9% pure *m*-chloroperbenzoic acid[8] was stirred at room temperature for 24 hr. An additional 10 mg of the peracid was added and stirring was continued for 1 more hr. The acid was neutralized by stirring with 60 mg of $NaHCO_3$ for 1 hr. The inorganics were filtered and the filtrate was washed with water. The ether extract was dried ($MgSO_4$) and evaporated to dryness to give 104.3 mg (76.8%) of **2** as a colorless gum. A solution of this material was treated with HCl in 2-propanol and the hydrochloride was recrystallized from 2-propanol–ether, 92 mg (81%), mp 171–172°, $[\alpha]^{25}D$ +81.8° (*c* 0.9, MeOH).

Anal. Calcd for $C_{22}H_{32}ClNO_5$: C, 63.07; H, 7.36; Cl, 8.09; N, 3.20. Found: C, 63.04; H, 7.49; Cl, 8.10; N, 3.22.

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-4-(*N,N*-dimethylamino)-α-D-idopyranoside Methiodide (4). A solution of 148 mg (0.38 mmol) of methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-(*N,N*-dimethylamino)-α-D-idopyranoside[9] (**3**) in 10 ml of CH_3OH and 5 ml of CH_3I was heated under reflux on a steam bath for 2.5 hr. Evaporation of the solvents in vacuo followed by trituration with ether yielded 147 mg (73%) of **4**, mp 159–162°. Recrystallization from methanol–ether gave pure **4**, mp 162–163°, $[\alpha]^{25}D$ +12.6° (*c* 0.8, CH_3OH).

Anal. Calcd for $C_{24}H_{34}INO_4$: C, 54.65; H, 6.49; I, 24.07; N, 2.66. Found: C, 54.45; H, 6.47; I, 24.16; N, 2.73.

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-α-D-*threo*-hex-4-enopyranoside (5). A. By Cope Elimination of 2. A solution of 100 mg (0.24 mmol) of the hydrochloride salt of **2** was passed over a column of Dowex-1 (HCO_3^- form) and eluted with methanol. Evaporation of the solution in vacuo yielded 83.4 mg (91%) of **2** as a gum. This material was taken up in a sublimation apparatus, degassed with N_2, and pyrolyzed at 100° (0.1 mmHg). The product was recrystallized from methanol–water to give 50 mg (71%) of **5**: mp 62–62.5°; ir ($CHCl_3$) 1675 cm^{-1} (double bond); NMR ($CDCl_3$) τ 2.61 (s, 10, aromatic), 5.15–5.43 (complex m, 6, CH_2, H-2, H-3), 5.95 (broad s, 1, H-4), 6.27 (d, $J_{1,2}$ = 3 Hz, 1, H-1), 6.49 (s, 3, OCH_3), 8.21 (s, 3, C-CH_3); $[\alpha]^{23}D$ −20.1° (*c* 1.0, CH_3OH).

Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.04; H, 7.25.

B. By Hofmann Elimination of 4. A mixture of 96 mg (0.18 mmol) of **3** in 25 ml of CH_3OH and 10 ml of water and silver oxide (freshly prepared from 52.3 mg of $AgNO_3$) was heated on an oil bath at 60–65° for 20 min. The solvents were removed under vacuum and the residue was diluted with 10 ml of water and extracted with ether. The ether extract was dried ($MgSO_4$) and evaporated to dryness to give 32.2 mg (52.5%) of **5**, mp 59–61°. It was recrystallized from methanol–water, mp 62–62.5°, $[\alpha]^{24}D$ −20° (*c* 1.0, CH_3OH). A mixture melting point with the analyzed sample from A above was unchanged.

Methyl 6-Deoxy-2,3-di-*O*-benzyl-α-D-altropyranoside (6). A solution of 340 mg (1 mmol) of **5** and 17 mg (0.5 mmol) of $NaBH_4$ in 1 ml of diglyme (distilled over $LiAlH_4$ under reduced pressure) was stirred at 20° in a cold water bath. A solution of 140 mg (1 mmol) of boron trifluoride etherate in 0.5 ml of diglyme was added dropwise to the stirred mixture in about 20 min. After stirring for an additional 1 hr, the reaction mixture was cooled in an ice bath and 1 ml of water was added followed by 0.5 ml of 2 *N* NaOH solution and 0.5 ml of 30% H_2O_2. Care was taken to maintain the solution slightly basic, around pH 8. After stirring for 1 hr, the solution was poured onto water and extracted thoroughly with ether. The combined ether extracts were washed with $NaHCO_3$ solution,

dried ($MgSO_4$), and concentrated under vacuum to give 274 mg (77%) of **6** as an oil. Column chromatography over Woelm grade I neutral alumina gave 241 mg (67.3%) of **6**, homogeneous in several TLC systems, $[\alpha]^{26}D$ +44.7° (*c* 1.1, CH_3OH).

Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.48; H, 7.31. Found: C, 70.71; H, 7.19.

Methyl 6-Deoxy-2,3-di-*O*-benzyl-4-*O*-methylsulfonyl-α-D-altropyranoside (7). A solution of 72 mg (0.2 mmol) of **6** in pyridine was treated with 460 mg of methanesulfonyl chloride at 0° for 2 days. The mixture was poured onto ice–water, and the solid was filtered and recrystallized from 2-propanol to give 72 mg (82%) of **7**, mp 85–86°, $[\alpha]^{24}D$ +54.0° (*c* 0.9, $CHCl_3$) [lit.[9] mp 85–86°, $[\alpha]^{25}D$ +53.9° (*c* 1.0, $CHCl_3$)].

Methyl 2,3-Di-*O*-benzyl-4,6-dideoxy-α-D-*arabino*-hexopyranoside (8). A. By Hydroboration of 5. Compound **5** (170 mg, 0.5 mmol) was subjected to hydroboration as described under the preparation of **6** using $NaBH_4$ and boron trifluoride etherate in diglyme. The reaction mixture was decomposed with 45 mg (0.75 mmol) of glacial acetic acid and the solution was boiled for 2 hr. The solvents were evaporated in vacuo and the product was extracted with ether, washed with $NaHCO_3$, dried ($MgSO_4$), and concentrated under vacuum to give 131 mg (76.6%) of an oil. This material was purified by column chromatography on Florisil to yield 112 mg of **8** as an oil, $n^{24}D$ 1.5325, $[\alpha]^{23}D$ +74.3° (*c* 0.9, $CHCl_3$), homogeneous on TLC.

Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.78; H, 7.79.

B. From Compound 7. A solution of 150 mg (0.34 mmol) of **7** in 30 ml of acetonylacetone and 240 mg (1.6 mmol) of sodium iodide was heated at 125° for 3.5 hr with mechanical stirring. The mixture was cooled, diluted with 5 ml of water, and extracted thoroughly with petroleum ether (bp 50–70°). The petroleum ether extract was washed with sodium thiosulfate solution followed by water, dried ($MgSO_4$), and evaporated to dryness to give 123 mg of a pale yellow oil showing two major spots on TLC, probably corresponding to methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-iodo-α-D-altropyranoside and methyl 2,3-di-*O*-benzyl-4,6-dideoxy-4-iodo-α-D-idopyranoside. This material was further purified by column chromatography over Woelm grade I alumina to yield 87 mg of a mixture of the two iodo derivatives. A solution of 85 mg (0.18 mmol) of this mixture in 20 ml of anhydrous ether was treated with 130 mg of lithium aluminum hydride. The excess hydride was destroyed by the careful addition of water. The inorganic salts were removed by filtration, the filtrate was washed with water, dried ($MgSO_4$), and concentrated under vacuum, and the residue (48 mg, 76%) was evaporatively distilled to yield 31 mg of **8**, $n^{24}D$ 1.5316, $[\alpha]^{24}D$ +76.4° (*c* 1.4, CH_3OH). This material was identical with the sample prepared by the hydroboration of **5** as shown by its ir spectrum, TLC, and GC using a 5-ft 6% ethylene glycol succinate column.

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Registry No.—**1**, 55570-39-3; **2** HCl, 55570-70-2; **3**, 55570-20-2; **4**, 55570-71-3; **5**, 55570-72-4; **6**, 33159-49-8; **7**, 55570-73-5; **8**, 55570-74-6; iodomethane, 74-88-4; methanesulfonyl chloride, 124-63-0.

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Bicyclic Nucleosides Related to Pyrimidine Nucleosides. IV. Synthesis of 4- and 6-Ribofuranosylthiazolo[5,4-*d*]pyrimidines and 4-Arabinofuranosylthiazolo[5,4-*d*]pyrimidines[1]

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Ribosylation of the bis(trimethylsilyl) derivative of thiazolo[5,4-*d*]pyrimidine-5,7-dione has afforded a mixture of α- and β-4-(2,3,5-tri-*O*-benzoyl-D-ribofuranosyl)thiazolo[5,4-*d*]pyrimidine-5,7-dione. Thiation of the β anomer was followed by methylation to afford 7-methylthio-4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)thiazolo[5,4-*d*]pyrimidin-5-one, which on treatment with methanolic ammonia was converted to 7-amino-4-(β-D-ribofuranosyl)thiazolo[5,4-*d*]pyrimidin-5-one, a cytidine analog. An alternate ribosylation using a Friedel–Crafts catalyst afforded the 6-ribosyl derivative. Thiation of thiazolo[5,4-*d*]pyrimidine-5,7-dione afforded thiazolo[5,4-*d*]pyrimidin-5-one-7-thione, which was condensed with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose to afford the 4,6-diribosyl derivative.

In recent years there has been an increasing interest in the synthesis of bicyclic nucleosides with a ribofuranosyl moiety residing in the pyrimidine ring. This interest has been generated to a large extent by the isolation and identification of 3-ribosyluric acid from beef blood.[2] This interest has been directed to a large extent toward 3-ribosyl purines[3–5] but other ring systems have also been investigated.[6,7] These systems have generally afforded, in addition to the desired isomer, substantial amounts of other products. This has been found to be especially true in the case of the purines.[5] In an effort to improve the selectivity of the ribosylation reaction we have investigated and reported on the use of a bulky 8 substituent in the purine series to direct the site of ribosylation to the 3 position.[8–10] This prompted us to investigate an alternate approach to the synthesis of this type of pyrimidine analog. We have now investigated the use of the thiazolo[5,4-*d*]pyrimidine ring system in which ribosylation of the thiazole ring would result in the loss of aromaticity in that ring and should, therefore, be inhibited.[11] Using this approach, the uridine