barium carbonate (2 g) and **36**[25b] (0.53 g) in 30 ml of dry carbon tetrachloride. After refluxing for 2 hr the suspension was filtered and the filtrate was processed to a colorless syrup, yield 0.68 g (quantitative), which was kept at 0°. Benzoylation of a portion at 0° in the usual way gave the product **37b** as a syrup showing a single spot on tlc with a higher mobility than **36** (chloroform–methanol, 100:1). Infrared data revealed some contamination with benzoic anhydride. A portion of this syrup was purified by preparative tlc to give the crystalline product **37b**, mp 95–96°.

Anal. Calcd for $C_{21}H_{21}BrO_6$: C, 56.13; H, 4.71; Br, 17.78. Found: C, 56.13; H, 4.64; Br, 17.98.

Methyl 4-*O*-Benzoyl-6-bromo-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (39).—Methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hexopyranoside (**38**)[43] was prepared by the catalytic hydrogenation of the corresponding 2,3-unsaturated glycoside.[48] To 1 g of **38** in 30 ml of carbon tetrachloride were added 0.8 g of NBS and 2 g of barium carbonate. The suspension was stirred under reflux for 2 hr. The reaction mixture was filtered, the filtrate was evaporated to a syrup which was dissolved in ether, and the solution was evaporated to a colorless syrup, yield 1.2 g (92%), which showed a major spot on tlc (chloroform–methanol, 100:0.5, medium); $[\alpha]_D$ 119° (*c* 1.946, chloroform); ir data (liquid film), 1724 cm^{-1} (ester); nmr data, τ 8.08 (C-2, C-3 protons, four-proton multiplet), 5.0 (C-4 proton, multiplet), 5.2 (C-1 proton, apparent doublet, J = 3.5 cps). A portion was purified by short-path distillation.

(48) E. Albano, D. Horton, and T. Tsuchiya, *Carbohydrate Res.*, **2**, 349 (1966), and references cited therein; R. U. Lemieux, E. Fraga, and K. A. Watanabe, *Can. J. Chem.*, **46**, 61 (1968).

Anal. Calcd for $C_{14}H_{17}BrO_4$: C, 51.07; H, 5.21; Br, 24.27. Found: C, 51.20; H, 5.21; Br, 24.67.

Methyl 4-*O*-Benzoyl-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (40).—Hydrogen was bubbled through a stirred methanolic suspension (80 ml) containing 0.3 g of **39**, 0.2 g of 20% palladium on charcoal, and 1 g of barium carbonate. After 6–7 hr, the suspension was filtered and the filtrate was processed to give the product as a colorless syrup, yield 0.175 g (78%), which showed a major spot on tlc (chloroform–methanol, 100:0.3, medium) in addition to traces of two slower moving spots. A portion was purified by preparative tlc to give the product as a pure syrup: $[\alpha]_D$ 182° (*c* 3.01, chloroform); nmr data, τ 8.78 (center of a doublet, C-6 protons), 8.10 (C-2, C-3 protons, four-proton multiplet).

Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 66.88; H, 7.26.

Registry No.—**3**, 18933-80-7; **4a**, 18933-81-8; **4b**, 18933-82-9; **6**, 4990-99-2; **7b**, 18933-84-1; **11**, 18933-85-2; **12**, 18933-86-3; **13**, 18933-87-4; **14**, 18933-88-5; **17a**, 18933-78-3; **17b**, 18933-79-4; **17c**, 18933-53-4; **18**, 18933-54-5; **19**, 18933-55-6; **21**, 10368-84-0; **22**, 10368-83-9; **23a**, 10427-79-9; **23b**, 18944-95-1; **26**, 18933-59-0; **27**, 18933-60-3; **28**, 18933-61-4; **30**, 18933-62-5; **32**, 18933-63-6; **34a**, 18933-64-7; **34b**, 18933-65-8; **35a**, 18944-96-2; **35b**, 18933-66-9; **37b**, 18933-67-0; **39**, 18933-68-1; **40**, 18933-69-2.

The Reaction of *O*-Benzylidene Sugars with *N*-Bromosuccinimide. IV. Neighboring-Group Effects and Rearrangements[1a]

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Reaction of various *O*-benzylidene acetals of sugars in which the acetal ring spans two secondary hydroxyl groups, with NBS, affords, in general, isomeric bromodeoxy sugar benzoates. In the presence of a nearby participating function (hydroxyl, ester) the acetal ring opening may be accompanied by rearrangement leading to the incorporation of bromine at a carbon atom other than those involved in the acetal ring.

We have shown in previous papers in this series[2,3] that 4,6-*O*-benzylidene acetals of various methyl hexopyranosides and disaccharides undergo smooth ring opening by the action of N-bromosuccinimide. With the exception[2] of methyl 4,6-*O*-benzylidene-β-D-galactopyranoside, the acetals under study gave the corresponding methyl 4-*O*-benzoyl-6-bromo-6-deoxyhexopyranosides as the preponderant, if not the exclusive, products. It was also demonstrated[1-3] that these products which possess the combined advantages of a displaceable group at C-6, as well as a selectively benzoylated site at C-4, are versatile synthetic intermediates in carbohydrate chemistry. The examples reported so far have dealt with acetals of the 2-aryl-1,3-dioxane type which are fused *cis* or *trans* to C-4 and C-6 of a hexopyranoside moiety. This paper describes the extension of the NBS reaction to other less common *O*-benzylidene sugars in which the acetal ring spans two *secondary* hydroxyl groups. In the simplest case of a 2-aryl-1,3-dioxolane type the reaction leads to isomeric bromo benzoate derivatives as a result of incorporation of a bromine atom at either carbon atom involved in the 1,3-dioxolane ring. When the molecule contains ester or hydroxyl functions which are in favorable spatial disposition with respect to the acetal ring, the reaction may lead to products other than those expected, due to rearrangements.

In a preceding paper[2] we elaborated on three possible mechanisms for the reaction of *O*-benzylidene sugars with NBS: a "radical-displacement"[4,5] type reaction, an initial hydrogen-abstraction step involving free radicals followed by an ionic termination reaction, and

(1) (a) Portions of this work were presented at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966, D29, and the 154th National Meeting, Chicago, Ill., Sept 1967, D16. For part I, see S. Hanessian, *Carbohydrate Res.*, **2**, 86 (1966). (b) To whom correspondence should be addressed at the Department of Chemistry, University of Montreal, Montreal 3, Quebec, Canada.

(2) S. Hanessian and N. R. Plessas, *J. Org. Chem.*, **34**, 1035 (1969), part II of this series.

(3) S. Hanessian and N. R. Plessas, *ibid.*, **34**, 1045 (1969), preceding paper (III) in this series.

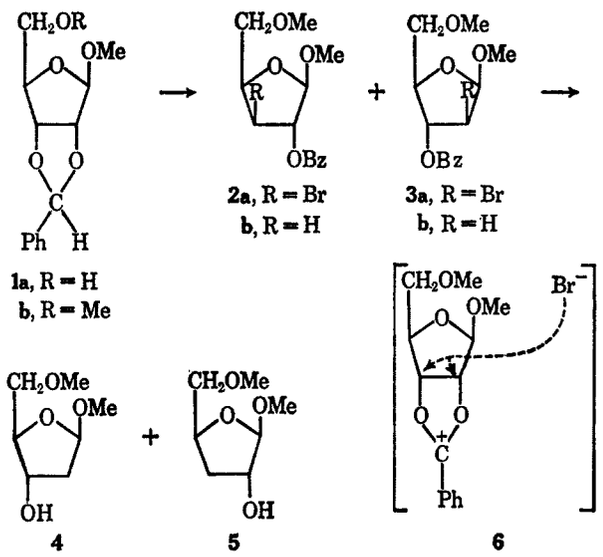
(4) D. L. Failla, T. L. Hullar, and S. B. Siskin, *Chem. Commun.*, 710 (1966).

(5) J. D. Prugh and W. C. McCarthy, *Tetrahedron Letters*, 1351 (1966).

finally a concerted-type mechanism proceeding through an intermediate 2-bromo-2-phenyl-1,3-dioxane derivative.[6]

In our first example we chose a substrate with a nearly symmetrically situated acetal function such as in compound **1b**[7] (Scheme I). Reaction of **1b** with NBS

SCHEME I



in the usual manner afforded a syrup in 85% yield which was relatively homogeneous by tlc. As in other NBS reactions,[1-3] the ring opening of the acetal was evident from an infrared spectrum of the product which exhibited strong ester absorption and from an nmr spectrum which lacked the benzylic proton. Vpc analysis as well as further transformations of the syrupy product indicated that two isomeric products **2a** and **3a** were formed in approximately equal amounts. Catalytic hydrogenation of the mixture gave the corresponding deoxypentosides **2b** and **3b** which exhibited the expected nmr spectral characteristics, but could not be resolved by chromatographic means. Catalytic debenzoylation of this mixture gave a syrup which showed two closely spaced components upon careful examination by tlc. These were separated by preparative tlc and were studied by nmr and mass spectroscopic[8] methods. The syrupy products were designated as methyl 2-deoxy-5-*O*-methyl-β-D-*erythro*-pentofuranoside (**4**) and methyl 3-deoxy-5-*O*-methyl-β-D-*erythro*-pentofuranoside (**5**). The mass spectral fragmentation patterns of **4** and **5**, which were quite similar, were corroborated by examination of the corresponding O-deuterated derivatives.[8]

The formation of **2a** and **3a** can be explained by attack of bromide ion (or radical) at C-2 and C-3 of the nearly symmetrical benzoxonium ion intermediate **6** (or its radical counterpart).[6] The proportion of the resulting products is presumably controlled by the relative accessibility of the attacking specie to C-2 and C-3, since both sites are of comparable reactivity and the products **2a** and **3a** should be more or less of equal thermodynamic stability. It can be concluded from the above transformations that when the benzylidene acetal involves two secondary hydroxyl groups having a similar steric environment in an appropriately substituted furanoid system, both possible ring-opening products can be formed.[9]

The formation of isomeric products in this and related examples imposes some limitation on the synthetic utility of the reaction for the large-scale preparation of only one of the expected products. On the other hand, the relative ease with which a net configurational inversion is effected from readily available intermediates leading to *trans*-orientated bromo benzoate derivatives is especially noteworthy in view of the limited methods available for such inversions in furanoid systems.[10] The stereospecific formation of vicinal bromo benzoates having a *trans* orientation from *cis*-acetals is also useful in the study of stable carboxonium salts and their reactions.[11]

Having thus investigated the ring-opening reactions of 2-phenyl-1,3-dioxolane rings which are *cis* fused to furanoid systems, it was of interest to extend the NBS reaction to such an acetal in a pyranoid system. In this case the nature of the products would be expected to be affected not only by steric and neighboring-group effects, but also by conformational factors.

Methyl 2-*O*-benzoyl-3,4-*O*-benzylidene-β-D-arabinopyranoside[12,13] (**8**) (Scheme II) was chosen for such a study because in addition to being one of the few crystalline representatives of this class of *O*-benzylidene derivatives, it possesses the participating C-2 benzoate function as a "built-in" feature. Compound **8** was prepared essentially as described in the literature[12] and could be separated into a pure diastereoisomer,[13] mp 119–120°, and a mixture of diastereoisomers, mp 96–100°, by fractional crystallization of the initial crude crystalline product. Reaction of **8** (pure or mixed diastereoisomers) with NBS in the usual manner afforded a colorless syrup in about 90% yield. This material was essentially homogeneous by tlc and exhibited the spectral properties expected of the product(s) resulting from ring opening of the acetal ring. Vpc analysis showed two major peaks in an approximate ratio of 1:2 which were assigned to

(6) With the available data, it is not possible to single out one particular mechanism. We shall therefore continue to adopt provisionally the second mechanism in our discussions, namely one which proceeds *via* aryloxonium ions.

(7) G. R. Barker, T. M. Noone, D. C. C. Smith, and J. W. Spoors, *J. Chem. Soc.*, 1327 (1955).

(8) D. C. DeJongh, J. D. Hribar, and S. Hanessian, Advances in Chemistry Series, No. 74, American Chemical Society, Washington, D. C., 1968, p 202.

(9) Some earlier observations[1] on the reaction of methyl 2,3-*O*-benzylidene-β-D-ribofuranoside derivatives with NBS indicated that a potential participating function (ester, hydroxyl) at C-5 could divert the reaction from its usual course. Preliminary experiments with the 5-*O*-benzoyl derivative of **1a** showed that one of the products was a methyl 2,3-di-*O*-benzoyl-5-bromo-5-deoxypentoside which was converted to the corresponding 5-deoxy derivative and its structure was ascertained by spectroscopic methods (nmr, mass[8]). The formation of the 5-bromodeoxy derivative can be explained by assuming a participation by the C-5 benzoate group to give an intermediate 3,5-benzoxonium ion, which is attacked by bromide ion preferentially at the primary carbon atom.

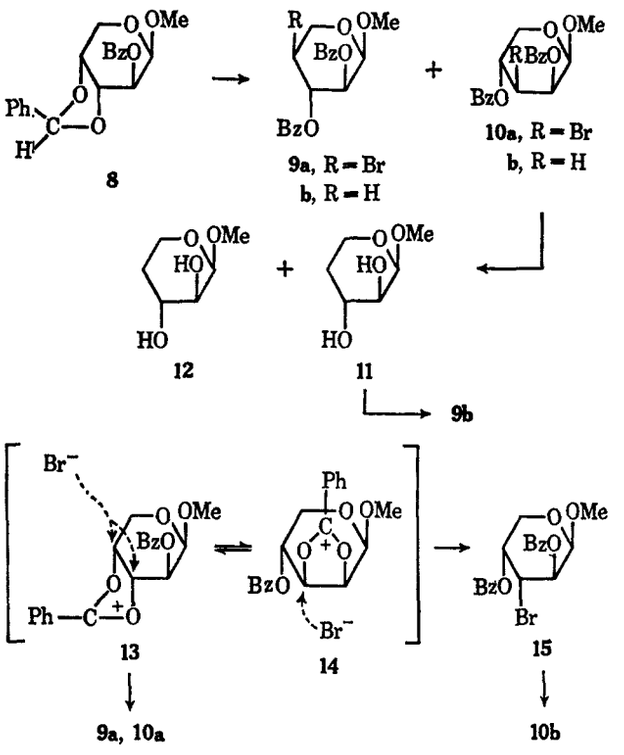
(10) For comments on the nucelophilic displacement reactions of sulfonate esters in furanoid systems see the following papers and references cited therein: B. R. Baker and A. H. Haines, *J. Org. Chem.*, **28**, 438 (1963); K. J. Ryan, H. Arzoumanian, E. M. Acton, and L. Goodman, *J. Am. Chem. Soc.*, **86**, 2497, 2503 (1964); N. A. Hughes and P. R. H. Speakman, *J. Chem. Soc.*, 2236 (1965); J. Cleophax, S. D. Gero, and J. Hildesheim, *Chem. Commun.*, 94 (1968).

(11) We have prepared carboxonium salts from appropriate halo ester intermediates in the presence of such reagents as silver fluoroborate or antimony pentachloride. These salts undergo ring-opening reactions with various nucleophiles (hydroxide, azide).[1] Details of this aspect of our work will be published in subsequent papers.

(12) M. A. Oldham and J. Honeyman, *J. Chem. Soc.*, 986 (1946).

(13) N. Baggett, K. W. Buck, A. B. Foster, and J. M. Webber, *ibid.*, 3401 (1965).

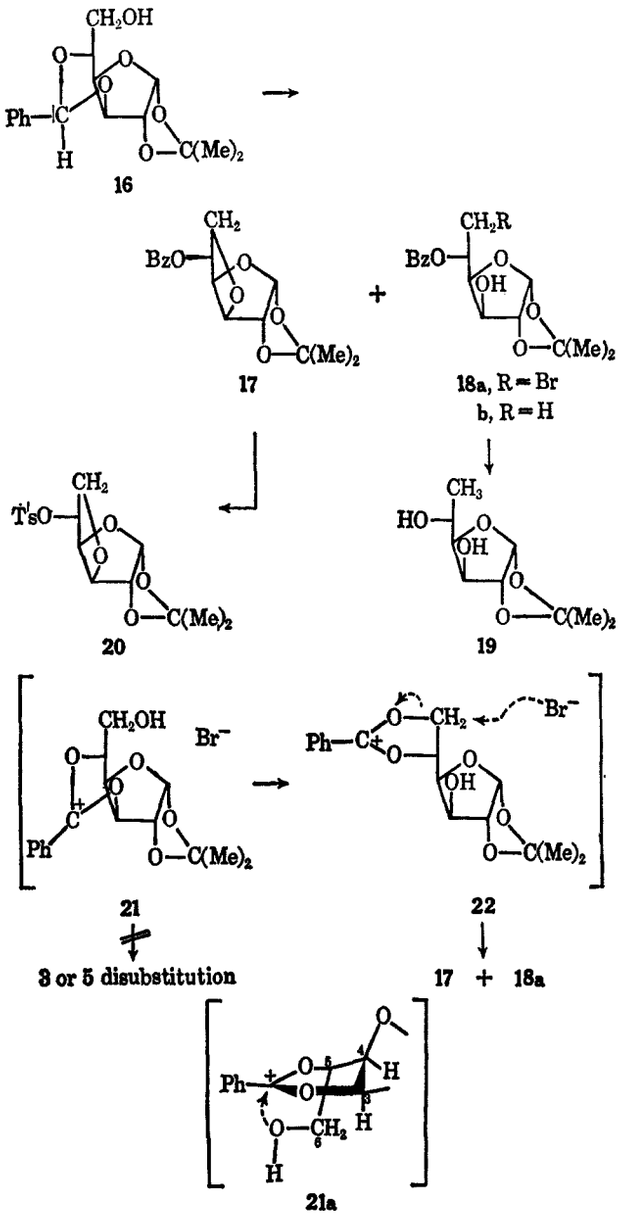
SCHEME II



methyl 2,3-di-*O*-benzoyl-4-bromo-4-deoxy-α-L-xylopyranoside (**9a**) and methyl 2,4-di-*O*-benzoyl-3-bromo-3-deoxy-β-D-lyxo(arabino?)pyranoside (**10a** and/or **15**), respectively. Reduction of the mixture gave a syrup which also showed two major peaks by vpc analysis. The positions of the bromine atoms in the original products were located by debenzoylation of the reduced syrupy mixture followed by careful separation of the resulting methyl 4-deoxy-β-D-*threo*-pentopyranoside (**11**) and methyl 3-deoxy-β-D-*threo*-pentopyranoside (**12**) by preparative tlc. The structures of these homogeneous syrupy substances were firmly established by spectroscopic (nmr, mass[8]) and chemical methods. Since only compound **11** was attacked by aqueous sodium periodate, the following series of steps were undertaken to establish the identity of the products of the NBS reactions. The mixture containing **11** and **12** was subjected to periodate oxidation and the degradation of **11** was monitored by tlc. Compound **12** which remained unaffected, was then isolated and benzoylated to give a homogeneous syrup which had the same retention time as the major peak observed in the vapor phase chromatogram of the original reduced mixture (**9b**, **10b**). It follows that the preponderant product in the reaction of **8** with NBS has the bromine atom at C-3. Attack of bromide ion at C-3 and C-4 in the benzoxonium ion[6] **13** is expected to be somewhat unfavored by 1,3 interactions with the C-2 axial benzoate group (*C*1 conformation) and the C-1 methoxyl group (1*C* conformation), respectively. Based on our experimental findings, however, it appears that C-4 is somewhat less favored to attack than C-3. It should be pointed out that the presence of the C-2 benzoate group in a conformationally flexible system such as **13** could lead to a rearranged benzoxonium ion[6] such as **14**. No trace of a 2-deoxypentose could be found when mixtures of **11** and **12** were subjected to appropriate colorimetric tests. If the intermediate **14** is indeed formed, then bromide ion will have to attack at C-3 stereoselectively to give **15** and hence **10b** after reduction.

A third type of *O*-benzylidene sugars is comprised of a select group where the acetal ring joins two secondary hydroxy groups, one being situated in a ring and another on an acyclic carbon atom as in 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-D-glucofuranose[14] (**16**)

SCHEME III



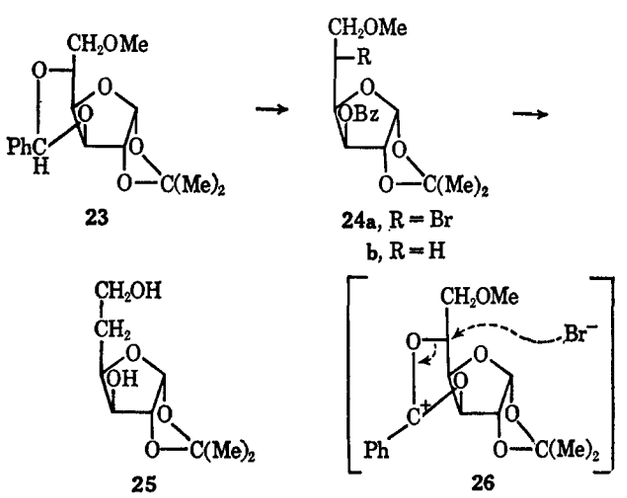
(Scheme III). This model was chosen to demonstrate the possible preference for attack of bromide ion at a secondary carbon (C-5) in an acyclic side chain rather than one in a furanose ring (C-3). Reaction of **16** with NBS afforded two products which were obtained as homogeneous syrups by column chromatography or preparative tlc; however, neither of the two were the expected ring-opening products. The component formed in smaller proportion contained no bromine and

(14) M. Brigl and H. Grüner, *Ber.*, **65**, 1428 (1932).

was identified as 3,6-anhydro-5-*O*-benzoyl-1,2-*O*-isopropylidene-D-glucofuranose (**17**) by its conversion into the known[15] crystalline 5-tosylate derivative **20**. The component formed in larger amount was identified as 5-*O*-benzoyl-6-bromo-6-deoxy-1,2-*O*-isopropylidene-D-glucofuranose (**18a**). Catalytic reduction of this product gave a chromatographically homogeneous syrup which was clearly the 6-deoxy analog **18b** as evidenced from its nmr spectrum. Catalytic debenzoylation afforded crystalline 6-deoxy-1,2-*O*-isopropylidene-D-glucofuranose[16,17] (**19**) which exhibited characteristic peaks in its mass spectrum.[8] Since none of the expected 3(5)-bromodeoxy-5(3)-benzoate derivatives resulting from an attack on the initially formed benzoxonium ion[6] **21** was obtained, it is evident that the observed products **17** and **18a** are formed by rearrangement of **21**. Inspection of molecular models reveals that the C-6 hydroxyl group is in favorable position for intramolecular attack (as in **21a**) to give an activated ortho ester or a rearranged benzoxonium ion[6] such as **22**. The latter now contains a 2-phenyl-1,3-dioxolenium ring involving primary (C-6) and secondary (C-5) carbon atoms and is attacked selectively at C-6 by bromide ion. The favored intramolecular attack by the C-3 hydroxyl group accounts for the formation of **17** in appreciable amount. In a simulated reaction in the presence of NBS and barium carbonate, compound **18a** remained uneffected and cannot be a precursor to **17**.

That the C-6 hydroxyl group in **16** had a profound influence on the nature of the products in NBS reaction was substantiated by the reaction of a derivative of **16** containing a nonparticipating function at C-6, such as the corresponding 6-*O*-methyl derivative **23** (Scheme IV). In this case, the NBS reaction afforded a single

SCHEME IV



product which was designated as 3-*O*-benzoyl-5-bromo-5-deoxy-1,2-*O*-isopropylidene-6-*O*-methyl-L-idofuranose (**24a**) on the basis of mechanistic considerations and further chemical transformations. Catalytic reduction of **24a** afforded syrupy 3-*O*-benzoyl-5-deoxy-6-*O*-methyl-1,2-*O*-isopropylidene-D-*xylo*-hexofuranose (**24b**) which exhibited the characteristic C-5 methylene splitting pattern in its nmr spectrum. Debenzoylation followed by treatment with boron trichloride in methylene chloride at −80° for a short period effected selective cleavage of the methyl group to give the known[18,19] 5-deoxy-1,2-*O*-isopropylidene-D-*xylo*-hexofuranose (**25**). Thus in the absence of a participating function at C-6 **23** is attacked preferentially at the less sterically hindered acyclic carbon (C-5) as depicted in Scheme IV (**26**).

The observations on the reaction of *O*-benzylidene sugars with NBS, which are recorded in this and previous papers in this series,[1-3] can be summarized[20,21] as follows. (1) Methyl 4,6-*O*-benzylidenehexopyranosides and their derivatives, including disaccharides, generally afford the corresponding 4-*O*-benzoyl-6-bromo-6-deoxy derivatives as the preponderant if not exclusive products. (2) Internal *O*-benzylidene acetals such as those joining vicinal *cis*-hydroxyl groups of a cyclic sugar derivative give isomeric *trans*-bromo benzoates. The relative proportions of these isomers seem to be dependent mainly on steric and conformational factors. (3) Benzylidene acetals involving a secondary hydroxyl group on a side chain and another on the ring in suitably protected sugars afford predominantly, if not exclusively, the isomer in which the bromine atom is attached to the side chain. (4) The presence of a participating group (ester, hydroxyl) near the acetal ring will often lead to rearranged benzoxonium ions,[6] which can be attacked intramolecularly or externally by a nucleophile (bromide, hydroxide). If the 2-aryl-1,3-dioxolenium ion in the rearranged specie involves primary and secondary carbon atoms of the sugar portion, then attack will usually occur at the primary carbon atom. The direction of acetal ring opening can thus be deliberately altered to varying extents, by placing the proper type of functional group in the molecule.

Experimental Section

Melting points are uncorrected. Nmr spectra were obtained in chloroform-*d*, unless otherwise stated, on a 60-Mc spectrometer using tetramethylsilane as reference. Optical rotations were measured with a Perkin-Elmer photoelectric polarimeter at 25°. Thin layer chromatography was performed on silica gel HF plates and the spots were detected with a spray containing 5% each of ammonium molybdate, sulfuric acid, and phosphoric acid after heating the plate for 10 min at 110°, and with a 1% potassium permanganate solution in 0.1 *N* sulfuric acid. Solvent systems and mobilities (slow, medium, fast) are given in the Experimental Section. Carbon tetrachloride and 1,1,2,2-tetrachloroethane were dried by passage over neutral alumina (Woelm) prior to use. Processed solutions of chloroform and ether were dried over anhydrous sodium sulfate. Vapor phase chromatography was done on columns containing 5% SE-30 (Analabs, Inc.) or 3% OV-17 (Applied Science Labs, Inc.) depending on the derivative. Mass spectra[8] were obtained by courtesy of Dr. D. C. DeJongh, Wayne State University.

Methyl 2,3-*O*-Benzylidene-β-D-ribofuranoside (1a).—A mixture of methyl β-D-ribofuranoside[22] (4.1 g) and 4 g of zinc

(15) H. Ohle, L. von Vargha and E. Erlbach, *Ber.*, **61**, 1211 (1928).
(16) A. S. Meyer and T. Reichstein, *Helv. Chim. Acta*, **29**, 152 (1946).
(17) E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **25**, 1753 (1958).
(18) E. J. Hedgley, O. Mérész, and W. G. Overend, *J. Chem. Soc.*, 888 (1967); E. J. Hedgley, O. Mérész, W. G. Overend, and R. Rennie, *Chem. Ind.* (London), 938 (1960).
(19) M. L. Wolfrom, K. Matsuda, F. Komitsky, Jr., and T. E. Whiteley, *J. Org. Chem.*, **28**, 3551 (1963).
(20) S. Hanessian, *Advan. Carbohydrate Chem.*, **21**, 143 (1966).
(21) S. Hanessian, ref 8, p 159.
(22) R. Barker and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 4605 (1961).

chloride in 20 ml of benzaldehyde was stirred at room temperature for 24 hr. The viscous mass was washed with small volumes of petroleum ether (bp 30–60°) then dissolved in chloroform and the resulting solution was washed successively with water, aqueous bicarbonate, and then water. Drying over sodium sulfate and evaporation afforded a colorless syrup which was steam distilled to remove excess benzaldehyde. Processing the residue gave a syrup which was relatively homogeneous by tlc (chloroform–2,2,4-trimethylpentane–methanol, 100:20:1, medium); yield 3.4 g. Purification was achieved by distillation, bp 142° (0.25 mm), yield 2.6 g of a colorless viscous syrup: $[\alpha]_D$ −59° (*c* 1.67, chloroform); nmr data, τ 4.80 (center of a doublet, J_{12} = 1.5 cps, C-1 proton), 6.51 (C-1 methoxyl protons, singlet), 4.15, 3.93 (benzylic protons, 1:1 ratio, diastereoisomers). The syrup solidified on standing at 0° and a portion was triturated with ether and petroleum ether and filtered; mp 40–41°; it was reported[7] as a syrup, bp 100° (bath), $[\alpha]_D$ −41° (chloroform).

Methyl 2,3-*O*-Benzylidene-5-*O*-methyl-β-D-ribofuranoside (1b).—To a refluxing solution of **1a** (1.5 g) in 45 ml of methyl iodide was added 3 g of silver oxide in portions over 2 hr. An additional 3 g of silver oxide was added during the next 24 hr. After refluxing 48 hr, an aliquot examined by tlc showed the absence of starting material. The mixture was filtered and the filtrate was evaporated to a colorless syrup which was homogeneous by tlc (chloroform–2,2,4-trimethylpentane–methanol, 100:20:0.2, medium); yield 1.63 g, 84%. A portion was distilled at 124–126° (0.125 mm); nmr data, τ 4.9 (center of a doublet, J_{12} = 2 cps, C-1 proton), 6.68, 6.65 (C-1 methoxyl and C-5 methoxyl protons, doublet), 4.22, 4.0 (benzylic protons, diastereoisomers).

Reaction of Methyl 2,3-*O*-Benzylidene-5-*O*-methyl-β-D-ribofuranoside with NBS.—To a suspension of 5 g of barium carbonate and 3 g of **1b** in 35 ml of carbon tetrachloride was added NBS (2.3 g). After refluxing for 2 hr, the mixture was filtered and the filtrate was evaporated to dryness. The syrup was dissolved in ether, and the latter solution was washed with water, dried, and evaporated to a colorless syrup which showed a major spot on tlc which was slightly faster than **1b**, in addition to minor slower moving spots; yield 3.3 g, 78%. This product which could be used for subsequent steps could be purified by column chromatography over alumina using chloroform as developer. A portion purified in this manner afforded an analytical sample. Further experiments demonstrated the product to be a mixture of **methyl 3-*O*-benzoyl-2-bromo-2-deoxy-5-*O*-methyl-β-D-arabinofuranoside (3a)** and **methyl 2-*O*-benzoyl-3-bromo-3-deoxy-5-*O*-methyl-β-D-xylofuranoside (2a)** in the approximate ratio of 1.5.1, respectively. Vpc analysis showed two major peaks in approximately the same ratio.

Anal. Calcd for $C_{14}H_{17}BrO_5$: C, 49.13; H, 4.13; Br, 23.35. Found: C, 48.66; H, 4.87; Br, 22.91.

Methyl 2-Deoxy-5-*O*-methyl-β-D-*erythro*-pentofuranoside (4) and Methyl 3-Deoxy-5-*O*-methyl-β-D-*erythro*-pentofuranoside (5).—To a solution of the aforementioned mixture of bromo benzoates (0.92 g) in 120 ml of methanol were added 0.4 g of palladium on charcoal (20%) and 1 g of barium carbonate. The mixture was hydrogenated at room temperature during 3–5 hr and processed as usual to give a colorless syrup which had a slightly slower chromatographic mobility than the starting material; yield 0.69 g, 98%. This syrupy mixture which contained **methyl 2-deoxy-5-*O*-methyl-β-D-*erythro*-pentofuranoside (3b)** and **methyl 3-deoxy-5-*O*-methyl-β-D-*erythro*-pentofuranoside (2b)** could not be resolved by vpc using a 3% OV-17 support and emerged as a single peak.

A portion of the syrup (0.12 g) was dissolved in 5 ml of methanol and a tiny piece of sodium was added to the resulting solution. After storage at room temperature overnight, the solution was neutralized with Dowex-50 (H^+), filtered, and evaporated to a pale yellow syrup which contained methyl benzoate. The syrup showed two major spots on tlc (chloroform–2,2,4-trimethylpentane–methanol, 100:20:5, medium). The two components were separated by preparative tlc and obtained as colorless syrups. The faster moving component (16 mg, 25%) was shown to be **4** while the slower component (30 mg, 50%) was **5**, based on differences in the splitting pattern of the C-1 proton; nmr data for **4**: τ 5.08 (C-1 proton, apparent doublet, J_{12} = 4.5 cps), 6.63 (C-5 methoxyl protons), 6.50 (C-1 methoxyl protons), 7.9–8.15 (C-2 protons, multiplet); nmr data for **5**: τ 5.17 (C-1 proton, singlet), 8–8.2 (C-3 protons, multiplet). The mass spectra[8] of **4** and **5** were quite similar, except for relative intensity differences. The mass spectra of the corresponding O-deuterated derivatives corroborated the assignments. Mass spectral data for **4** and **5** were no $M\cdot^+$, *m/e* 131 ($M - OCH_3$), *m/e* 117 ($M - CH_2{}^+OCH_3$, $M - 45$), *m/e* 45 ($CH_3{}^+O{=}CH_2$), etc.

Hydrolysis of small aliquots of **4** and **5** with 0.1 *N* hydrochloric acid overnight at room temperature afforded the syrupy free sugars which were homogeneous and had R_f 0.68 and 0.65, respectively, when chromatographed on paper in the solvent system butyl alcohol–ethanol–water (3:1:1).

Methyl 2-*O*-Benzoyl-3,4-*O*-benzylidene-β-D-arabinopyranoside (8).—A mixture of methyl β-D-arabinopyranoside (1.9 g) in 10 ml of benzaldehyde was heated at 135° for 3.5 hr with occasional evacuation of the flask to remove the water formed. Excess benzaldehyde was removed by steam distillation and the residual syrup was taken up in ether and filtered from some starting material (0.32 g). The filtrate was evaporated to a syrup which was dissolved in 4 ml of pyridine, cooled, and treated with 2 ml of benzoyl chloride. After standing at room temperature overnight, the mixture was poured into ice–water and the resulting mixture was extracted with chloroform and processed in the usual way. Evaporation of the solution afforded a syrup which crystallized from a mixture of ether–pentane containing a few drops of acetone to give 0.3 g of crystals: mp 96–100° (preliminary softening); nmr data, τ 3.70, 4.05 (benzylic protons, *ca.* 2:1 ratio). A second crop of crystals (0.1 g) from the mother liquors had mp 113–115°; nmr data, τ 4.0 (benzyl proton, singlet), 4.72 (C-2 proton, quartet), 4.9 (C-1 proton, doublet, J_{12} = 3 cps), 5.82 (C-5 protons), 6.56 (C-1 methoxyl protons). Recrystallization of material from the first crop from the same solvent mixture gave a product melting partially at 100° and ultimately at 114° which was still a mixture of diastereoisomers as evidenced by nmr. The mother liquors of recrystallization also contained both isomers. Recrystallization of material from the second crop gave crystals melting at 119–120°, lit.[13] (for **8**) mp 119–120°. Both products were homogeneous on tlc (benzene–2,2,4-trimethylpentane–methanol, 100:30:1, medium).

Reaction of Methyl 2-*O*-Benzoyl-3,4-*O*-benzylidene-β-D-arabinopyranoside with NBS.—To 1.18 g of **8** in 100 ml of carbon tetrachloride were added 0.7 g of NBS and 5 g of barium carbonate and the mixture was refluxed with stirring for 2 hr. Filtration and evaporation gave a colorless syrup which was dissolved in ether, the solution was washed with water, and the ethereal layer was processed as usual to give a syrup (1.28 g, 89%) showing essentially one spot on tlc (chloroform–2,2,4-trimethylpentane–methanol, 100:30:0.3, fast). A portion (0.14 g) was purified by preparative tlc for characterization purposes; nmr data, τ 4.2–4.5 (C-2, C-3, C-4, two-proton multiplet), 4,8 (center of a one-proton multiplet, C-1 proton), 6.53 (C-1 methoxyl proton, singlet). The product proved to be a mixture of **methyl 2,4-di-*O*-benzoyl-3-bromo-3-deoxy-β-D-lyxo(arabino?)pyranoside (10a, 15)**, and **methyl 2,3-di-*O*-benzoyl-4-bromo-4-deoxy-α-L-xylopyranoside (9a)**. Vpc analysis revealed two major peaks in the approximate ratio of 1:2, the preponderant product being **10a (15)**.

Anal. Calcd for $C_{20}H_{19}BrO_6$: C, 55.18; H, 4.39; Br, 18.36. Found: C, 55.01; H, 4.94; Br, 18.22.

The syrupy mixture (1.14 g) was dissolved in methanol (150 ml) and hydrogenated in the presence of 20% palladium on charcoal (0.7 g) and barium carbonate (5 g). After 6 hr the mixture was filtered and the filtrate was evaporated to a colorless syrup which had the same chromatographic mobility as the starting mixture of bromides; yield 0.74 g, 78%; nmr data, τ 7.4–7.75 (two-proton multiplet, C-3, C-4 protons). The syrup was a mixture of **methyl 2,4-di-*O*-benzoyl-3-deoxy-β-D-*threo*-pentopyranoside (10b) and methyl 2,3-di-*O*-benzoyl-4-deoxy-β-D-*threo*-pentopyranoside (9b)**. Vpc analysis now showed an approximate ratio of 3:1 of the respective products.

Catalytic debenzoylation of a portion (0.14 g) of the above mixture in the usual way gave a syrup. Careful examination of this product on tlc (benzene–methanol, 10:1, medium) revealed two very closely spaced components in addition to some minor faster moving components. Separation of an aliquot by preparative tlc gave the two products as homogeneous syrups. The faster moving component was oxidized in aqueous sodium periodate and is designated **methyl 4-deoxy-β-D-*threo*-pentopyranoside (11)**: $[\alpha]_D$ −151° (*c* 0.24, methanol); nmr data

(D_2O), τ 5.15 (center of a doublet, J_{12} = 4 cps, C-1 proton), 6.59 (C-1 methoxyl protons), 8.05–8.35 (C-4 protons, multiplet); mass spectral data,[8] no $M^{\cdot+}$, *m/e* 117 ($M - OCH_3$), *m/e* 104 ($M - 44$), *m/e* 88, *m/e* 70 (*m/e* 88 $- H_2O$), *m/e* 60 [$(CHOH-CHOH)^{\cdot+}$] (prominent). The mass spectrum of the O-deuterated analog of **11** corroborated these assignments.[8]

The slower moving component was unaffected by aqueous periodate and is designated **methyl 3-deoxy-β-D-*threo*-pentopyranoside (12)**: $[\alpha]D$ −176° (*c* 0.25, methanol); nmr data (D_2O), τ 5.24 (C-1 anomeric proton, partially obscured by HDO peak), 6.56 (C-1 methoxyl protons), 8–8.2 (C-3 protons, multiplet); mass spectral data,[8] $M^{\cdot+}$ 148, *m/e* 117 ($M - OCH_3$), *m/e* 104 ($M - 44$), *m/e* 44, etc. The mass spectrum of the O-deuterated analog of **12** corroborated these assignments.

The original NBS products **9a** and **10a** were identified in the following manner. An amount (0.3 g) of the reduced and debenzoylated syrupy mixture containing **11** and **12** was dissolved in water containing an excess of sodium metaperiodate and the solution was kept overnight at room temperature. Examination by tlc revealed that the isomer **11** was degraded. The solution was evaporated to dryness and the residue was extracted with ethanol and acetone. Evaporation gave a syrup (0.18 g) which consisted essentially of a major spot on tlc corresponding to **12**. A portion of this mixture was purified by preparative tlc and the eluted zone containing 40 mg of **12** was dissolved in pyridine (1.0 ml) and treated with 0.1 g of *p*-nitrobenzoyl chloride. After standing at room temperature the mixture was poured into ice–water and the solid that separated was washed with cold water, aqueous bicarbonate, and water and was finally dried; yield, 92 mg of **methyl 2,5-di-*O*-*p*-nitrobenzoyl-3-deoxy-β-D-*threo*-pentopyranoside** which showed a single spot on tlc (chloroform–2,2,4-trimethylpentane–methanol, 100:30:0.1, medium). The solid was dissolved in ethanol and evaporated to a syrup which solidified upon the addition of water. A portion was further purified for analytical purposes; $[\alpha]D$ −182° (*c* 0.5, chloroform).

Anal. Calcd for $C_{20}H_{18}N_2O_{10}$: C, 53.81; H, 4.06; N, 6.27. Found: C, 53.54; H, 4.07; N, 5.93.

The main portion of the diester was deacylated in methanol containing sodium methoxide, and the resulting syrup was benzoylated in the usual way. Isolation of the product and analysis by vpc afforded a single peak with the same retention time as the major peak in the original mixture containing **11** and **12**. It follows that the major peak with higher retention time in this mixture corresponds to the isomer **12** and the minor peak corresponds to the other isomer, **11**.

Reaction of 3,5-*O*-Benzylidene-1,2-*O*-isopropylidene-D-glucofuranose with NBS.—A suspension of **16** (0.5 g), NBS (0.314 g), and barium carbonate (1 g) in 25 ml of carbon tetrachloride was stirred under reflux for 2.5 hr. Filtration and evaporation gave a colorless syrup containing succinimide. The syrup was dissolved in ether and the solution was extracted with a small volume of water, dried, and evaporated to a syrup, yield 390 mg. This product exhibited two distinct spots on tlc (chloroform–2,2,4-trimethylpentane–methanol, 100:30:1, medium) in addition to some traces of much slower moving components. Separation of the two products was effected by preparative tlc or by column chromatography on alumina. A portion (0.3 g) resolved by the former technique gave 80 mg of the faster moving component which proved to be **3,6-anhydro-5-*O*-benzoyl-1,2-*O*-isopropylidene-D-glucofuranose (17)**: $[\alpha]D$ 29° (*c* 0.73, methanol); ir data, 1722 cm^{-1} (ester), no hydroxyl absorption; nmr data, τ 4.12 (C-1 proton, doublet, J_{12} = 3.5 cps), 4.80 (C-5 proton, multiplet); nmr data on **16**: τ 3.90 (C-1 proton, doublet, J_{12} = 3 cps), 4.09 (benzylic proton, singlet).

Anal. Calcd for $C_{15}H_{18}O_6$: C, 62.66; H, 6.50. Found: C, 62.60; H, 6.40.

A portion (32 mg) of **17** was debenzoylated in methanolic sodium methoxide and the resulting oily product was tosylated with tosyl chloride in pyridine in the usual way to give the corresponding 5-*O*-tosyl derivative **20**, yield 17 mg, mp 126–127°, lit.[15] mp 132°. This product was identical (ir, tlc, mixture melting point) with an authentic specimen.

The slower moving component from the preparative plates was isolated as a colorless syrup: yield 0.120 g; ir data (liquid film), 1710, 1726 cm^{-1} (ester); nmr data, τ 4.17 (C-1 proton), 4.80 (C-5 proton, multiplet). This product proved to be **5-*O*-benzoyl-6-bromo-6-deoxy-1,2-*O*-isopropylidene-D-glucofuranose (18a)**.

Anal. Calcd for $C_{16}H_{19}BrO_6$: C, 49.85; H, 4.70; Br, 20.06. Found: C, 50.09; H, 5.23; Br, 19.60.

A portion of **18a** (60 mg) was catalytically reduced in methanol in the presence of Raney nickel, triethylamine, and hydrogen. The reduced product **18b** was isolated as a chromatographically homogeneous syrup (35 mg): nmr data, τ 4.00 (C-1 proton), 4.72 (C-5 proton, multiplet), 8.35–8.65 (nine-proton multiplet, ketal and C-6 protons). The product **18b** was debenzoylated in the usual way to give crystalline **6-deoxy-1,2-*O*-isopropylidene-D-glucofuranose (19)**: mp 85–86°, lit.[16,17] mp 92°; mass spectral data,[8] no $M^{\cdot+}$, *m/e* 189 ($M - CH_3$), *m/e* 159 ($M - CH_3 \cdot CHOH$), *m/e* 160 (*m/e* 159, H), *m/e* 45 ($CH_3CH{=}^{+}OH$). The mass spectrum of the O-deuterated analog of **19** corroborated these assignments.[8]

3,5-*O*-Benzylidene-6-*O*-methyl-1,2-*O*-isopropylidene-D-glucofuranose (23).—Silver oxide (0.5 g) was added in portions to a refluxing solution of 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-D-glucofuranose (0.17 g) in 30 ml of methyl iodide. After refluxing overnight an additional 0.5 g of silver oxide was added. After refluxing for a total period of 36 hr the suspension was filtered and the filtrate was evaporated to dryness. The crystalline residue was crystallized from a mixture of ether and pentane to give the product in two crops: yield 153 mg (tlc, chloroform–2,2,4-trimethylpentane–methanol, 100:50:1, medium); mp 90–91°; $[\alpha]D$ 2.3° (*c* 0.22, chloroform); nmr data, τ 3.95 (two-proton multiplet, C-1 and benzylic protons), 6.60 (C-6 methoxyl protons).

Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.53; H, 6.58. Found: C, 63.85; H, 6.91.

Reaction of 3,5-*O*-Benzylidene-6-*O*-methyl-1,2-*O*-isopropylidene-D-glucofuranose with NBS.—To 0.1 g of **23** in 15 ml of carbon tetrachloride were added 62 mg of NBS and 0.2 g of barium carbonate. After refluxing for 2 hr the suspension was filtered and the filtrate was evaporated to a syrup which was dissolved in ether and the solution was washed with cold water. Processing the ethereal layer gave a chromatographically homogeneous colorless syrup; yield 0.12 g, 96%, which was designated **3-*O*-benzoyl-5-bromo-5-deoxy-6-*O*-methyl-1,2-*O*-isopropylidene-L-idofuranose (24a)**: ir data (liquid film), 1728 cm^{-1} (ester); tlc (chloroform–2,2,2-trimethylpentane–methanol, 100:30:0.5, medium), slightly faster than **23**. The syrup was further purified by preparative tlc for analytical purposes: yield 90 mg (72% over-all); $[\alpha]D$ 4.7° (*c* 4.15, chloroform); nmr data, τ 3.93 (C-1 proton, doublet, J_{12} = 3 cps), 4.42 (C-3 proton, doublet, J = 2.5 cps), 6.7 (C-6 methoxyl protons).

Anal. Calcd for $C_{17}H_{21}O_6Br$: Br, 19.41. Found: Br, 19.8.

A portion of the above product (63 mg) was dissolved in 50 ml of methanol and hydrogenated in the presence of 20% palladium on charcoal (0.1 g) during 3 hr. Filtration and evaporation gave **3-*O*-benzoyl-5-deoxy-6-*O*-methyl-1,2-*O*-isopropylidene-D-*xylo*-hexofuranose (24b)** (37 mg) as a colorless chromatographically homogeneous syrup: $[\alpha]D$ −20.7° (*c* 0.82, chloroform); vpc analysis indicated a purity of >98%; nmr data, τ 4.52 (C-1 proton, doublet, J_{12} = 3.5 cps), 3.95 (C-3 proton, apparent doublet, J = 4 cps), 6.66 (C-6 methoxyl protons), 8.00 (center of a two-proton quartet, C-5 protons).

Debenzoylation of **24b** in the usual way afforded a chromatographically homogeneous syrup which was dissolved in 10 ml of dichloromethane and saturated with boron trichloride at −80° during 3 hr. Evaporation of the solution afforded a syrup which consisted of some starting material and a second slower moving component on tlc. Isolation of this component by preparative tlc gave, after crystallization, **5-deoxy-1,2-*O*-isopropylidene-D-*xylo*-hexofuranose (25)** identical with an authentic specimen: nmr data, τ 4.03 (C-1 proton, doublet, J_{12} = 3.5 cps), 8.03 (center of a two-proton quartet, C-5 protons).

Registry No.—**1a**, 18929-99-2; **1b**, 18930-00-2; **3a**, 18930-01-3; **4**, 18930-02-4; **5**, 18930-03-5; methyl-2,5-di-*O*-*p*-nitrobenzoyl-3-deoxy-β-D-*threo*-pentopyranoside, 18991-68-9; **9a**, 18930-05-7; **9b**, 18930-06-8; **10a**, 18930-07-9; **10b**, 18930-08-0; **11**, 18930-09-1; **12**, 18930-10-4; **17**, 18930-11-5; **18a**, 18930-12-6; **23**, 18930-13-7; **24a**, 18930-14-8; **24b**, 18930-15-9; **25**, 7057-09-2.