The Facile Bromination by N-Bromosuccinimide of Benzylidene Acetals of Carbohydrates. Application to the Synthesis of 2,6-Imino Carbohydrates (Substituted 2,5-Oxazabicyclo[2.2.2]octanes)[1a,b]

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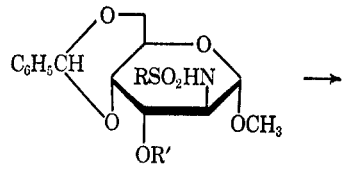
N-Bromosuccinimide (NBS) reacts very selectively with highly substituted benzylidene acetals to give ω-bromo benzoates in which the bromine occupies the least substituted carbon. Thus, NBS reacted with methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**6**), methyl 2-benzenesulfonamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (**1**), and methyl 4,6-*O*-benzylidene-2-deoxy-2-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (**10**) to give high yields of the respective 4-*O*-benzoyl-6-bromo-6-deoxy derivatives **7**, **2**, and **11**. In methanolic sodium methoxide, **2** was smoothly converted to the substituted 2,5-oxazabicyclo-[2.2.2]octane, methyl *N*-benzenesulfonyl-2,6-dideoxy-2,6-imino-α-D-altropyranoside (**3**), whereas **11** was rapidly converted to the substituted 3,7-oxazabicyclo[4.1.0]heptane (**15**). The reaction of benzylidene acetals with NBS therefore offers a convenient entry into 2,6-imino sugar derivatives, provided a good leaving group is not *trans*-vicinal to the nitrogen function.

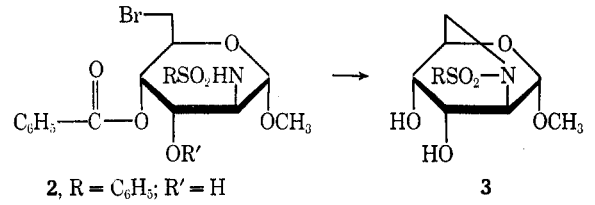
The 6-deoxy-6-halo substituted sugars are important synthetic intermediates,[2] but their preparation is often an involved process. This paper describes the facile formation of 4-*O*-benzoyl-6-bromo-6-deoxy substituted sugars by bromination–oxidation of 4,6-*O*-benzylidene substituted sugars with N-bromosuccinimide (NBS).[1,3-8] The utility of this reaction is demonstrated by convenient conversion of methyl 2-benzenesulfonamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (**1**) into the bicyclic sugar, methyl *N*-benzenesulfonyl-2,6-dideoxy-2,6-imino-α-D-altropyranoside (**3**) *via* the intermediate methyl 2-benzenesulfonamido-4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-D-altropyranoside (**2**).[9]

Oxidation by N-Bromosuccinimide.—During the course of other work it became necessary to study the effect of NBS on 2-(2-methylphenyl)dioxolane (**4**).

SCHEME I

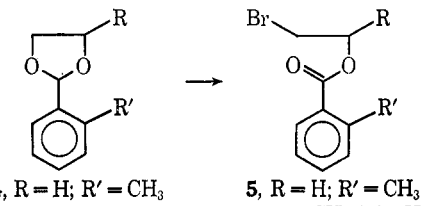


1, R = C_6H_5; R′ = H
10, R = 4-$CH_3C_6H_5$; R′ = Ts



2, R = C_6H_5; R′ = H
11, R = 4-$CH_3C_6H_5$; R′ = Ts

3



4, R = H; R′ = CH_3
8, R = CH_3; R′ = H

5, R = H; R′ = CH_3
9, R = CH_3; R′ = H

The acetal **4** was smoothly converted by NBS in refluxing benzene into the 2-bromo ester **5**.[4b] The structure of **5** was confirmed by its nmr spectrum and by its independent synthesis from *o*-toluic acid.[10a]

To explore the scope[10b] of this facile reaction, the highly substituted 2-phenyl-1,3-dioxane, methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**6**), when treated with NBS using benzoyl peroxide as catalyst, smoothly furnished the known[11] methyl 2,3,4-tri-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (**7**) in 70% yield. No evidence for alternative 4-bromo-6-benzoyl isomer (**7a**) was obtained. This marked preference for benzylidene cleavage to introduce the bromo group at the least substituted carbon is fortified by

(1) (a) A preliminary report of part of this work has appeared [D. L. Failla, T. L. Hullar, and S. B. Siskin, *Chem. Commun.*, 716 (1966)]. (b) This work was supported in part by Grant AM 10234, National Institutes of Health. (c) To whom all correspondence should be addressed. (d) Undergraduate Research Participant.

(2) For reviews of halodeoxy sugars see (a) S. Hanessian, *Advan. Carbohydrate Chem.*, **21**, 143 (1966); (b) J. E. G. Barnett, *ibid.*, **22**, 177 (1967); (c) S. Hanessian, Advances in Chemistry Series, No. 74, American Chemical Society, Washington, D. C., 1968, p 159.

(3) See also (a) S. Hanessian, *Carbohyd. Res.*, **2**, 86 (1966); (b) S. Hanessian and N. R. Plessas, *J. Org. Chem.*, **34**, 1035, 1045, 1053 (1969).

(4) (a) J. D. Prugh and W. C. McCarthy, *Tetrahedron Lett.*, 1351 (1966). (b) In analogous reactions, alkyl acetals of aromatic (ref 5) and alkyl aldehydes (ref 6) react with NBS (or bromine) to give alkyl esters and the corresponding bromide. The reaction of acetals with peroxides (ref 7) and of benzylic ethers with NBS or bromine (ref 8) are also analogous.

(5) (a) E. N. Marvell and M. J. Joncich, *J. Amer. Chem. Soc.*, **73**, 973 (1951); (b) D. G. Markees, *J. Org. Chem.*, **23**, 1490 (1958); (c) S. O. Lawesson and T. Busch, *Ark. Kemi*, **17**, 421 (1961); (d) A. Rieche, E. Schmitz, W. Schade, and E. Beyer, *Chem. Ber.*, **94**, 2926 (1961). The reaction of 2-phenyldithiolane with bromine to give a bromine-containing product may be analogous [H. Fassbender, *Ber.*, **20**, 460 (1887)].

(6) (a) J. B. Wright, *J. Amer. Chem. Soc.*, **77**, 4883 (1955); U. S. Patent 2,751,343 (1956), cited in *Chem. Abstr.*, **51**, 2039c (1957); (b) L. A. Cort and R. G. Pearson, *J. Chem. Soc.*, 1682 (1960).

(7) (a) L. P. Kuhn and C. Wellman, *J. Org. Chem.*, **22**, 774 (1957); (b) E. S. Huyser, *ibid.*, **25**, 1820 (1960); (c) see ref 5c; (d) E. S. Huyser and Z. Garcia, *J. Org. Chem.*, **27**, 2716 (1962).

(8) (a) M. Okawara, H. Sato, and E. Imoto, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **58**, 924 (1955); *Chem. Abstr.*, **50**, 12878 (1956); (b) J. Blair, W. R. Logan, and G. T. Newbold, *J. Chem. Soc.*, 2443 (1956) and ref cited therein; (c) see ref 5b; (d) L. L. Braun and J. H. Looker, *ibid.*, **26**, 574 (1961); (e) R. E. Lovins, L. J. Andrews, and R. M. Keefer, *ibid.*, **30**, 4150 (1965) and earlier papers; (f) G. A. Russell and Y. R. Vinson, *ibid.*, **31**, 1994 (1966); (g) for the selective removal by bromine of benzyl ethers on carbohydrates, see J. N. BeMiller, R. E. Wing, and C. Y. Meyers, *ibid.*, **33**, 4292 (1968).

(9) The facile conversion of **1** into **3** by this method may be contrasted to a previous synthesis [W. Meyer zu Reckendorf, *Chem. Ber.*, **98**, 93 (1965)] in which the 2,6-iminoaltroside, methyl *N*-benzoyl-2,6-dideoxy-2,6-imino-α-D-altropyranoside, was prepared in four steps from methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside in about 27% overall yield.

(10) (a) The experiments on dioxolane **4** were conducted by D. L. Failla, State University of New York at Buffalo, 1965. (b) Initial studies were directed at the reaction of 2-methoxytetrahydropyran and methyl 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranoside with NBS. Although reaction occurred, more than one major product appeared to result, and thus the study of benzylidene sugars was undertaken.

(11) B. Helferich, W. Klein, and W. Schafter, *Ann. Chem.*, **447**, 19 (1926).

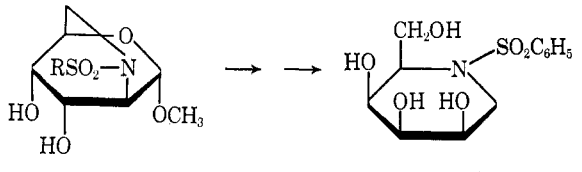
the observation that 2-phenyl-4-methyldioxolane (**8**) is oxidized by NBS to give 1-methyl-2-bromoethyl benzoate (**9**) in 77% yield[4a] and that other 4,6-*O*-benzylidene sugars also give 6-bromo-6-deoxy derivatives.[3]

The reaction is most readily rationalized by postulating initial formation of a 2-bromo-2-phenyldioxane (dioxolane)[12] which then ionizes to the oxonium ion[3,13] **7b**; attack on **7b** by the liberated bromide is supported by the observation that NBS bromination of *O,O'*-benzylidenecyclohexane-*cis*-1,2-diol gave the product of SN2 attack, *trans*-2-bromocyclohexyl benzoate, in 82% yield.[5d]

To provide the requisite derivatives for synthesis of bicyclic sugars, **1** was oxidized with NBS, using barium carbonate as acid acceptor,[3] to give **2** in 96% yield. Similarly, the *N,O*-ditosyl derivative (**10**) was cleaved by NBS, using benzoyl peroxide as catalyst, to give **11** in at least 70% yield.

Even though the amides **1** and **10** contain four functional groups (OH, NH, anomeric H, and $ArCH_3$) which can react with NBS, the oxidation occurs preferentially at the benzylic carbon with concomitant bromination at the primary carbon of the sugar. This is demonstrated by the good yields of isolable product and the minimal amounts of by-products as shown by examination (tlc) of the crude reaction mixtures. This selectivity of reaction strongly suggests that the NBS oxidation–bromination of benzylidene acetals may be of value in the generation of ω-bromo benzoates and the nonacidic cleavage of benzylidene acetals in complex systems.

Cyclizations.—The 2,6-imino sugars are relatively rare but offer a convenient entry into the 1-deoxy-*piperidino* type of sugar derivatives (eq 1).[14] The



(1)

2,6-imino sugars and the analogous 2,6-anhydro sugars can be constructed in three ways; (a) ring closure between a C-6 aldehyde and a C-2 nitrogen (or hydroxyl) function, in a manner analogous to the recent syntheses of *pyrrolidino* and *piperidino* sugars,[15] followed by reduction to the anhydro sugar, (b) displacement of a tosylate at C-2 by a C-6 nitrogen[16] or hydroxyl[14] group, and (c) displacement of a leaving group at C-6 by a nitrogen[9] or oxygen[17] nucleophile at C-2.

Method c now becomes an attractive route to 2,6 (and 3,6-) bicyclic sugars because of the facile bromination–oxidation of 4,6-*O*-benzylidene acetals by NBS to give the requisite 6-bromo substituted sugar. Thus, blockage by 4,6-*O*-benzylidene can be maintained during construction of the appropriate C-2, C-3 substitution and then in one step the C-6 bromide can be obtained in excellent yield.

Treatment of bromo ester **2** with methanolic sodium methoxide at room temperature gave **12** in 70% yield, whereas methoxide treatment at 65° gave the desired cyclized product (**3**) in 78% yield.

To facilitate further chemistry of **3** it was desired to retain the 4-*O*-benzoyl group during the cyclization. Treatment of **2** with sodium hydride in dimethoxyethane furnished a syrupy product which was likely a mixture of the 3-*O*- and 4-*O*-benzoates (**13**). Methanolysis of **13** gave diol **3**. No attempt was made to separate the mixture of benzoates and no further studies were conducted.

The bromo ester **11** can conceivably cyclize to give the 6-membered ring derivative (**14**) or the 3-membered ring derivative (**15**) (Chart I). Treatment of **11** with methanolic sodium methoxide at *room temperature* gave the aziridine **15**, *not* the piperidine **14**. This cyclization undoubtedly proceeded under such mild conditions because the attacking sulfonamido anion and the leaving sulfonate ion are in the *trans*-diaxial orientation.[18] This facile cyclization therefore obviates the use of starting materials which have good leaving groups *trans*-vicinal to the sulfonamide function.

To study the chemistry of the C-3, C-4-vicinal glycol system of **3**, preliminary studies directed at the synthesis of the olefinic sugar **16** were done. The syrupy 3,4-di-*O*-tosylate **17**, readily derived from diol **3**, resisted reaction with sodium iodide in 2,4-pentanedione and with sodium iodide–zinc dust in N,N-dimethylformamide.[19] For an alternative route to **16**, diol **3** was smoothly converted[20a] into the thionocarbonate **18**. Treatment of **18** with trimethyl or triethyl phosphite[20b] at *ca.* 150° gave decomposition of **18** into a mixture of products. The mixture is presently under study and the results will be reported later.

Experimental Section[21]

Methyl 2-Benzenesulfonamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (1).—To a stirred suspension of methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside[22] (12.60 g, 45 mmol) in pyridine (50 ml) and dichloromethane[23] (50 ml), maintained at 25–40°, was added benzenesulfonyl chloride (7.20

(12) Such α-haloacetals have been postulated previously in the reaction of diethyl benzylidene acetal with NBS to give ethyl benzoate (ref 5a).

(13) (a) For a general discussion see S. Hunig, *Angew. Chem. Intern. Ed. Engl.*, **3**, 548 (1964); (b) S. Hunig, personal communication.

(14) A similar scheme has recently been used to furnish a derivative of 1,5-anhydro-D-mannitol [E. D. M. Eades, D. H. Ball, and L. Long, Jr., *J. Org. Chem.*, **30**, 3949 (1965)].

(15) For a review see H. Paulsen, *Angew. Chem. Intern. Ed. Engl.*, **5**, 495 (1966).

(16) Treatment of methyl 3,4-*O*-isopropylidene-2,6-di-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside with hydrazine followed by hydrogenation over Raney nickel gave the 2,6-imino derivative in 76% yield [A. Zobáčová and J. Jary, *Collect. Czech. Chem. Commun.*, **29**, 2042 (1964)].

(17) D. A. Rosenfeld, N. K. Richtmeyer, and C. S. Hudson, *J. Amer. Chem. Soc.*, **70**, 2201 (1948).

(18) B. R. Baker and T. L. Hullar, *J. Org. Chem.*, **30**, 4049 (1965), and preceding papers.

(19) R. S. Tipson and A. Cohen, *Carbohyd. Res.*, **1**, 338 (1965).

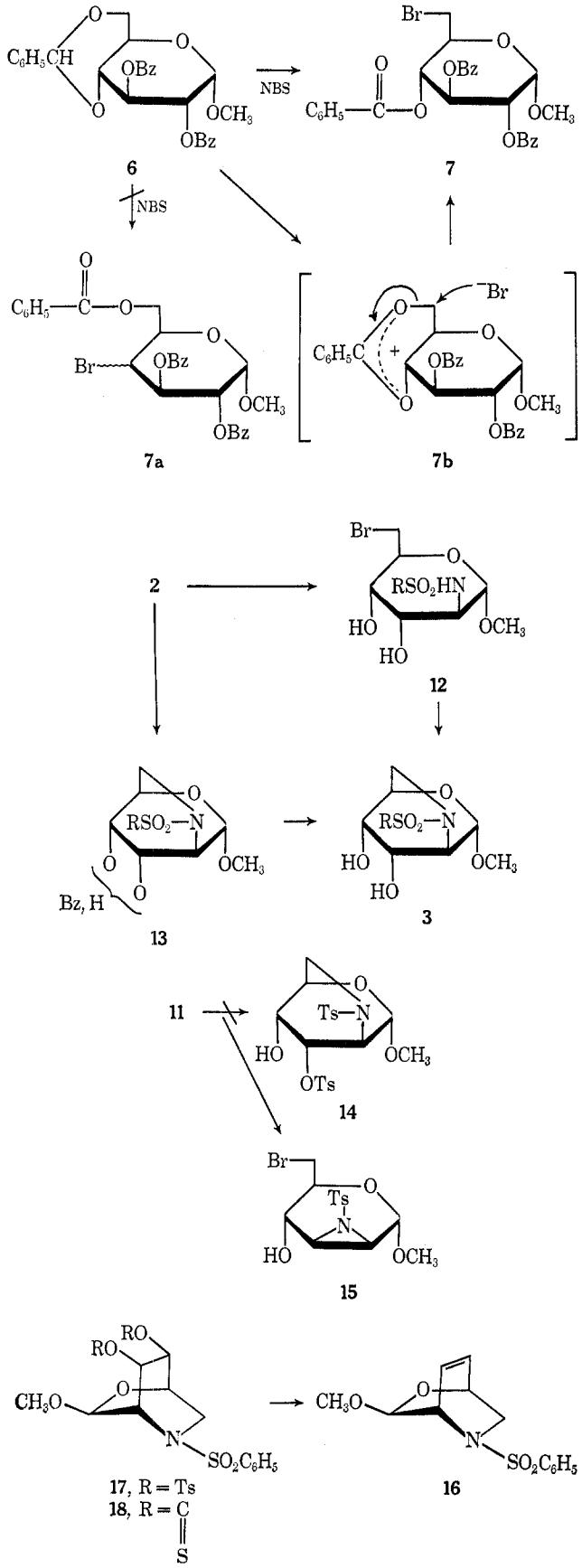
(20) (a) D. Horton and W. N. Turner, *ibid.*, **1**, 444 (1966); (b) E. J. Corey and R. A. E. Winter, *J. Amer. Chem. Soc.*, **85**, 2677 (1963).

(21) Melting points were taken with a Fisher–Johns melting block and are corrected. Infrared spectra were determined in KBr disks, unless otherwise indicated, with a Perkin-Elmer Model 237 spectrophotometer; only some of the more characteristic strong bands are noted. Nmr spectra were determined in $CDCl_3$ solution on a Varian A-60 spectrometer; δ values are reported in parts per million downfield from the tetramethylsilane internal standard. Elemental analyses were performed by A. Bernhardt, Mülheim, West Germany. Petroleum ether used throughout was a fraction of bp 30–60°. Thin layer chromatography (tlc) was done with silica gel G using chloroform–acetone (4:1 volume) as the solvent system unless otherwise indicated. The compounds were detected by exposing the plates to iodine vapor; the relative proportions of the components were estimated visually. Chloroform extracts were dried over anhydrous magnesium sulfate. All solutions were concentrated by spin evaporation at 60–70° under reduced pressure (aspirator) unless otherwise indicated. Whenever pyridine was employed in a reaction, the residual pyridine in the chloroform extract was always removed by repeated spin evaporation of toluene until the odor of pyridine was absent.

(22) B. R. Baker and T. L. Hullar, *J. Org. Chem.*, **30**, 4038 (1965), and ref 8 and 9a contained therein.

(23) Using 50 ml of pyridine alone gave a very heavy suspension which prevented efficient stirring; consequently a cosolvent was added.

CHART I



ml, 56 mmol). During the addition the mixture was kept at 25–40° by occasional cooling in ice–water. The resulting solution was kept at room temp for 30 min, then poured into ice–water (100 ml), and the mixture stirred 15 min. The layers were separated, and the aqueous layer was extracted with chloroform (three 20-ml portions).

To dissolve suspended product, chloroform was added (approximately 20 ml). The combined chloroform solutions were washed with water (15 ml), dried, and concentrated to a heavy suspension. The crude product was decolorized in hot ethyl acetate (300 ml), the charcoal being washed by additional hot ethyl acetate (150 ml). Concentration gave a near-white product (*ca.* 19 g)[24] which was recrystallized by dissolving the solid in warm ethyl acetate (125 ml), cooling to room temp, and slowly adding petroleum ether (300 ml).[25] Crystallization occurred on addition of the petroleum ether and was complete in 15–30 min. The mixture was filtered and the product was washed with the solvent of crystallization (50 ml) followed by petroleum ether to give 16.23 g (86%) of air-dried **1**, mp 173–174°. Recrystallization twice from ethanol (2 volumes)–petroleum ether (3 volumes) gave pure **1**: mp 175–176°; ν_{max} 3490, 3300, 1340, and 1040 cm^{-1}.

Anal. Calcd for $C_{20}H_{23}NO_7S$ (421.5): C, 56.98; H, 5.50; N, 3.32; S, 7.61. Found: C, 56.93; H, 5.88; N, 3.52; S, 7.86.

Methyl 2-Benzenesulfonamido-4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-D-altropyranoside (2). A.—To a suspension of **1** (1.00 g, 2.37 mmol) in dry CCl_4 (50 ml) was added NBS (0.465 g, 2.61 mmol) and $BaCO_3$[3] (1.4 g, 7.11 mmol). The mixture was heated to reflux and turned orange 7 min after refluxing began. After refluxing 1 hr the mixture was cooled to room temperature, concentrated, and chloroform (50 ml) was added. The chloroform solution was stirred 15 min, filtered, and the precipitate rinsed with $CHCl_3$ (10 ml). The filtrate was rinsed with water (three 50-ml portions), dried, and concentrated to a slightly yellow glass. Crystallization from EtOAc–petroleum ether very readily gave **2** (1.137 g, 96%), mp 160–162°. Recrystallization from EtOH–petroleum ether gave the analytical sample: mp 165–168°; ν_{max} 3490, 3210, 1725, and 1265 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}BrNO_7S$ (500.4): C, 48.00; H, 4.43; Br, 15.95; N, 2.80. S, 6.40. Found: C, 48.20; H, 4.39; Br, 15.95; N, 2.96; S, 6.26.

B.—To a suspension of **1** (0.500 g, 1.19 mmol) in CCl_4 (30 ml) was added NBS (0.212 g, 1.10 mmol) and benzoyl peroxide (*ca.* 10 granules). The mixture was heated to reflux, turned red 90 sec after refluxing began, then became cloudy and pale yellow. After refluxing 90 min the mixture was cooled to room temperature, filtered, and the precipitate rinsed with a small amount of CCl_4. The precipitate weighed 0.521 g. The filtrate was washed with a 1:1 solution (10 ml) of aqueous $NaHCO_3$ and 0.1 *M* thiosulfate, rinsed with H_2O until neutral, dried, and concentrated to a glass (0.113 g, 19%). Crystallization from EtOH–petroleum ether gave **2**, mp 159–164°. The product was recrystallized from EtOH–petroleum ether to give 0.301 g of **2**, mp 165–166° (51%; total yield of 70%).[26]

Methyl *N*-Benzenesulfonyl-2,6-dideoxy-2,6-imino-α-D-altropyranoside (3). A.—To a suspension of **2** (1.00 g, 2 mmol) in MeOH (12 ml) at room temperature was added 1 *N* methanolic sodium methoxide (10 ml). The suspended **2** immediately dissolved to give a yellow solution. The solution was refluxed 2 hr, cooled to room temperature, neutralized with CO_2, and diluted with H_2O (25 ml). The aqueous solution was extracted with $CHCl_3$ (three 25-ml portions), and the combined $CHCl_3$ extracts were rinsed with H_2O (25 ml), dried, and concentrated to a yellow syrup. Decolorization of the syrup in EtOH followed by crystallization from EtOH–petroleum ether gave **3** (0.490 g, 78%), mp 112–113°. Recrystallization from the same solvents gave the analytical sample: mp 125–126°, ν_{max} 3510, 1460, 1345, and 1160 cm^{-1}.

Anal. Calcd for $C_{13}H_{17}NO_6S$ (315.4): C, 49.51; H, 5.41; N, 4.44; S, 10.17. Found: C, 49.65; H, 5.40; N, 4.55; S, 10.24.

B.—A solution of **2** (0.150 g, 0.3 mmol) in 1,2-dimethoxyethane (10 ml) containing NaH (9.6 mg, 0.4 mmol) was refluxed 5 hr, cooled, CO_2 and H_2O added, and extracted with $CHCl_3$ (three

(24) Decolorization in hot ethanol gave a yellow crude product which crystallized in only 70–75% yield to give a yellow product. Further decolorization in ethanol gave no improvement in appearance of the product. Decolorization in ethyl acetate gave a nearly white product which crystallized very readily and in 85–90% yield. Thus, ethyl acetate is clearly the solvent of choice for the decolorization.

(25) Using less ethyl acetate resulted in very rapid crystallization and insufficient solvent volume to get satisfactory crystallization. Ethanol gave a too rapid crystallization, and large volumes were required.

(26) This procedure is satisfactory for small scale. However, on a larger scale, the bromine released from the NBS caused poor yield and made isolation of the product difficult.

5-ml portions). The combined $CHCl_3$ extracts were washed with H_2O (5 ml), dried, and concentrated to a syrup (0.134 g). The syrup showed carbonyl absorption (1720 cm^{-1}), by tlc was demonstrably different from **2** and **3**, and thus appeared to be **13**. Methanolysis of the syrup as described for the preparation of **12** gave **3**, mp 124–125°, and thus supports the formulation of **13**.

2-Bromoethyl 2-Methylbenzoate[10] **(5). A. Reaction of 2-(2-Methylphenyl)dioxolane (4) with *N*-Bromosuccinimide.**—A solution of dioxolane **4** (0.328 g, 2 mmol) in CCl_4 (5 ml) was refluxed 12 hr with NBS (0.356 g, 2 mmol). The mixture was cooled to room temperature and filtered to remove succinimide. The filtrate was diluted with CCl_4 (15 ml), cooled to 0°, and washed successively with ice-cold 1 *N* NaOH (20 ml) and H_2O (10 ml). Spin evaporation of the combined dried organic layers gave a colorless liquid (0.384 g, 79%), homogeneous by tlc (benzene–isohexane, 3:2 v/v): $\nu_{max}^{CHCl_3}$ 1710, 1250, and 735 cm^{-1}; nmr absorption at δ 2.60 (3 H, s; $ArCH_3$), 3.55 (2 H, t; J = 6.0 Hz; OCH_2CH_2Br), 4.55 (2 H, t, J = 6.0 Hz; OCH_2CH_2Br), and 7.25 (4 H; ArH).

B. From 2-Methylbenzoic Acid.—A solution of 2-methylbenzoic acid (13.62 g, 0.1 mol) and 2-bromoethanol (12.50 g 0.1 mol) in C_6H_6 (100 ml) containing concentrated H_2SO_4 (0.5 ml) was refluxed 12 hr using a Dean–Stark trap. After usual work-up the ester was distilled and a center cut taken, to give pure **5**, bp 82–83° (0.05 Torr). This product had ir absorption identical to that of the product obtained above in **A**.

Anal. Calcd for $C_{10}H_{11}BrO_2$ (243.1): C, 49.40; H, 4.56; Br, 32.88. Found: C, 49.59; H, 4.69; Br, 32.71.

Methyl 2,3,4-Tri-*O*-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside (7).—To a solution of **6**[27] (0.500 g, 1.02 mmol) in C_6H_6 (3 ml) was added NBS (0.182 g, 1.02 mmol) and benzoyl peroxide (*ca.* 0.002 g). The solution was refluxed for 1 hr at which time all the succinimide had settled to the bottom. The solution turned red when refluxing began, then later became clear and colorless. The mixture was cooled to room temperature, filtered, and the precipitate washed with benzene (5 ml). The filtrate was washed with a 1:1 solution (*ca.* 10 ml) of saturated aqueous $NaHCO_3$ and aqueous 0.1 *M* sodium thiosulfate, rinsed with water until neutral, dried, and concentrated to a syrup (0.557 g, 95%). Tlc (C_6H_6) showed the syrup to contain a small amount of succinimide. Crystallization from hot MeOH gave **7** (70%): mp 125–126° (lit.[11] mp 122°); ν_{max} 1720 and 1260 cm^{-1}.

Methyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-2-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (11).—To a suspension of **10**[28] (2.50 g, 4.26 mmol) in benzene (100 ml)[29,30] was added NBS (0.758 g, 4.26 mmol) and benzoyl peroxide (0.011 g, 0.0426 mmol). The mixture was refluxed 45 min. The reaction mixture turned red 2 min after refluxing began and became pale yellow 30 min later. The mixture was cooled to room temperature, filtered, and the precipitate was rinsed with C_6H_6 (20 ml). The filtrate was washed with a 1:1 solution (*ca.* 100 ml) of aqueous $NaHCO_3$ and 0.1 *M* sodium thiosulfate. The filtrate was rinsed with H_2O until neutral, dried, and concentrated to a glass (1.729 g. 46%). The precipitate was extracted with $CHCl_3$ (three 25-ml portions). The combined $CHCl_3$ extracts were rinsed with H_2O (25 ml), dried, and concentrated (1.098 g, 74% total). Tlc showed one major spot and three minor ones. The material extracted from the precipitate and the glass were dissolved in alcohol, combined, and decolorized (2.268 g). Crystallization from benzene[31,32] (35 ml)–petroleum ether (70 ml) gave crude **11** (2.185 g, 57%), mp 129–132°. Tlc showed one spot. Recrystallization in the same manner gave the analytical sample: mp 157–158°; ν_{max} 3240, 3000, 2890, 1740, 1180, and 1090 cm^{-1}.

Anal. Calcd for $C_{28}H_{32}BrNO_9S$ (668.6): C, 50.11; H, 4.53; Br, 12.05; S, 9.70. Found: C, 49.66; H, 5.04; Br, 12.15; S, 10.00.

Methyl 2-Benzenesulfonamido-6-bromo-2,6-dideoxy-α-D-altropyranoside (12).—To a suspension of **2** (0.100 g, 0.20 mmol) in MeOH (1.2 ml) at room temperature was added 1 *N* methanolic sodium methoxide (1 ml). The solution was kept 1 hr at room temperature, then neutralized by addition of CO_2, diluted with H_2O (5 ml), and extracted with $CHCl_3$ (three 5-ml portions). The combined $CHCl_3$ extracts were washed with H_2O (5 ml), dried, and concentrated to a glass (0.069 g, 87%). Tlc of crude material showed one spot. The glass (0.050 g) crystallized from EtOH (1 ml)–isohexane (2.5 ml) to give **12** (0.041 g), mp 149–160°. Recrystallization from EtOAc (1 ml)–isohexane (4 ml) gave the analytical sample: mp 175°; ν_{max} 3490, 3440, 3320, 1315, 1160, and 1070 cm^{-1}.

Anal. Calcd for $C_{13}H_{18}BrNO_6S$ (396.3): C, 39.40; H, 4.58; Br, 20.17; N, 3.54; S, 8.09. Found: C, 39.55; H, 4.87; Br, 20.08; N, 3.60; S, 7.98.

Methyl 6-Bromo-2,3-imino-*N*-(*p*-tolylsulfonyl)-2,3,6-trideoxy-α-D-altropyranoside (15).—To a solution of **11** (1.00 g, 1.5 mmol) in MeOH (9 ml) at room temp was added 1 *N* methanolic sodium methoxide (7.5 ml). The solution was allowed to stand overnight, neutralized with CO_2, and diluted with H_2O (10 ml). The resulting solution was extracted with $CHCl_3$ (three 10-ml portions). The combined $CHCl_3$ extracts were washed with H_2O (10 ml), dried, and concentrated *in vacuo* (to free of methyl benzoate) to give a white solid which was crystallized from EtOH–petroleum ether at 5° to give **15** (0.541 g, 92%), mp 143–145°. Repeated recrystallization from the same solvents gave the analytical sample: mp 157–158°; ν_{max} 3470, 1330, and 1160 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}BrNO_5S$ (392.3): C, 42.85; H, 4.63; Br, 20.37; N, 3.75; S, 8.17. Found: C, 42.33; H, 4.82; Br, 19.78; N, 3.53; S, 8.02.

Methyl *N*-Benzenesulfonyl-3,4-di-*O*-(*p*-tolylsulfonyl)-2,6-dideoxy-2,6-imino-α-D-altropyranoside (17).—To a solution of **3** (0.200 g, 0.63 mmol) in pyridine (20 ml) at room temperature was added *p*-toluenesulfonyl chloride (1.22 g, 6.34 mmol). The solution was kept 44 hr at 50°, protected from moisture, cooled to room temperature, poured onto ice (20 g), and stirred 5 min. The aqueous mixture was extracted with $CHCl_3$ (three 10-ml portions). The combined chloroform extracts were rinsed with water (10 ml), dried, and concentrated to give a yellow syrup. The syrup was dissolved in $CHCl_3$ and concentrated to give a yellow glass (0.370 g, 86%); ν_{max} 1600, 1350, and 1175 cm^{-1}. Tlc showed no starting material in the glass, and a small amount of material at the origin.

Anal. Calcd for $C_{27}H_{25}NO_{10}S_3$ (623.7): C, 51.99; H, 4.68; N, 2.25; S, 15.43. Found: C, 50.74; H, 4.75; N, 2.14; S, 14.88.

A solution of **17** in 2,4-pentandione containing NaI (2 mol equiv) was refluxed 24 hr. Tlc and ir analysis revealed the syrupy product to be essentially **17**. Similar results were obtained when a solution of **17** in diglyme was refluxed with NaI (10 mol equiv) and Zn dust (10 mol equiv)[19] for 5 hr.

Methyl *N*-Benzenesulfonyl-2,6-dideoxy-2,6-imino-α-D-altropyranoside 3,4-Thionocarbonate (18).—A solution of **3** (1.2 g, 3.81 mmol) in warm acetone (20 ml) was added to 0.815 g (4.57 mmol) of *N,N'*-thiocarbonyldiimidazole[33] (prepared[34a] from trimethylsilylimidazole[34b] and thiophosgene), and the mixture was boiled 1 hr under nitrogen. The solution was cooled to room temperature and evaporated to give a yellow solid (2.092 g). The solid was extracted with warm MeOH (45°) and the yellow methanolic solution decanted from the white solid product (1.03 g, 76%). Crystallization of the solid from *N,N*-dimethylformamide–ether gave **18**: mp 223–224°; ν_{max} 1360, 1310, 1060, 1025, 960, 745, and 680 cm^{-1}. Refrigeration of the yellow methanolic solution gave more crystalline product (total of 1.08 g, 79% yield).

Anal. Calcd for $C_{14}H_{15}NO_6S_2$ (257.4): C, 47.05; H, 4.23; N, 3.92; S, 17.94. Found: C, 46.96; H, 4.23; N, 3.97; S, 17.85.

Registry No.—NBS, 128-08-5; **1**, 21727-71-9; **2**, 14168-92-4; **3**, 21727-73-1; **5**, 6639-16-3; **11**, 14168-93-5; **12**, 21727-75-3; **15**, 21727-76-4; **17**, 21727-77-5; **18**, 21727-78-6.

(27) P. A. Levene and G. M. Myer, *J. Biol. Chem.*, **76**, 513 (1928).

(28) B. R. Baker and T. L. Hullar, *J. Org. Chem.*, **30**, 4049 (1965).

(29) When the reaction was done in carbon tetrachloride, the mixture turned cloudy after 40 min and gave a green gummy precipitate which was dissolved in chloroform during the filtration step. After several recrystallizations, tlc showed only one spot.

(30) Insufficient benzene was used as solvent, causing approximately half of the product to precipitate. About 300 ml benzene should have been used.

(31) When recrystallized from ethanol–isohexane, the product sometimes oiled out before crystallizing. After several recrystallizations this did not occur.

(32) Crystallization required a minimum of 6 hours at 5°.

(33) H. A. Staab and G. Walther, *Ann. Chem.*, **657**, 98 (1962).

(34) (a) T. J. Pullirkat and G. Urry, *Tetrahedron Lett.*, 1953 (1967); this method was found considerably more satisfactory in our hands than the original (ref 33) or a modified method (ref 20a). (b) L. Birkhofer and A. Ritter, *Angew. Chem. Intern. Ed. Engl.*, **4**, 427 (1965).