Carbohydrate Research, 235 (1992) 163–178
Elsevier Science Publishers B.V., Amsterdam

Synthesis, crystalline structure, conformational analysis, and azidolysis of methyl 2,3-anhydro-α-D-manno- and -allo-pyranoside *p*-bromobenzyl ethers *

Xinfu Wu [a], Fanzuo Kong [a], Depei Lu [a] and Genpei Li [b]

[a] *Research Center for Eco-Environmental Sciences, Academia Sinica, P.O. Box 934, Beijing (China)*
[b] *Insitute of Physical Chemistry, Peking University, Beijing (China)*

(Received May 20th, 1991; accepted in revised form May 13th, 1992)

ABSTRACT

Methyl 2,3-anhydro-4,6-di-*O*-*p*-bromobenzyl-α-D-allopyranoside (**6**) was synthesized from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**1**) via the intermediate methyl 4,6-di-*O*-*p*-bromobenzyl-2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside. Treatment of **6** with sodium azide selectively afforded methyl 3-azido-4,6-di-*O*-*p*-bromobenzyl-3-deoxy-α-D-glucopyranoside in 70% yield. Methyl 2,3-anhydro-4,6-di-*O*-*p*-bromobenzyl-(**17**) and methyl 2,3-anhydro-4,6-di-*O*-benzyl-α-D-mannopyranoside (**18**) were obtained from **1** via the intermediates methyl 4,6-di-*O*-*p*-bromobenzyl- and methyl 4,6-di-*O*-benzyl-2-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside. Azidolysis of **17** and **18** with sodium azide in the presence of tetraethylammonium chloride in *N*,*N*-dimethylformamide gave the respective 3-azidoaltropyransides, in yields of 80%, by exclusive 3-attack. The crystal structure of compound **6** is orthorhombic with a space group of $P2_12_12_1$, and the 2,3-anhydropyranose moiety is in an almost ideal $^0H_5$ half-chair conformation. The crystals of **17** are also orthorhombic, belonging to space group $P2_12_12_1$, but the conformation is a hybrid of the $^0H_5$ half-chair and the ^0E sofa. Analysis by NMR spectroscopy suggests that in solution in $CDCl_3$ the conformation of **17** remains the same as, and that of **6** undergoes a change from, the respective solid-state conformations.

INTRODUCTION

Oxirane derivatives are widely employed as intermediates in a variety of chemical modifications of monosaccharides[1–3] and in the synthesis of oligosaccharides[4,5]. A large number of these derivatives have been examined by NMR spectroscopy, mainly to determine their configurational and conformational characteristics[5–9]. An X-ray study[10] of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside revealed an asymmetry in the deviations of C-5 and O-5 from the C-1–C-2–C-3–C-4 plane and the values were −0.645 and −0.147 Å, respectively,

Correspondence to: Dr. F. Kong, Research Center for Eco-Environmental Sciences, Academia Sinica, P.O. Box 934, Beijing, China.

* Project supported by the National Natural Science Foundation of China.

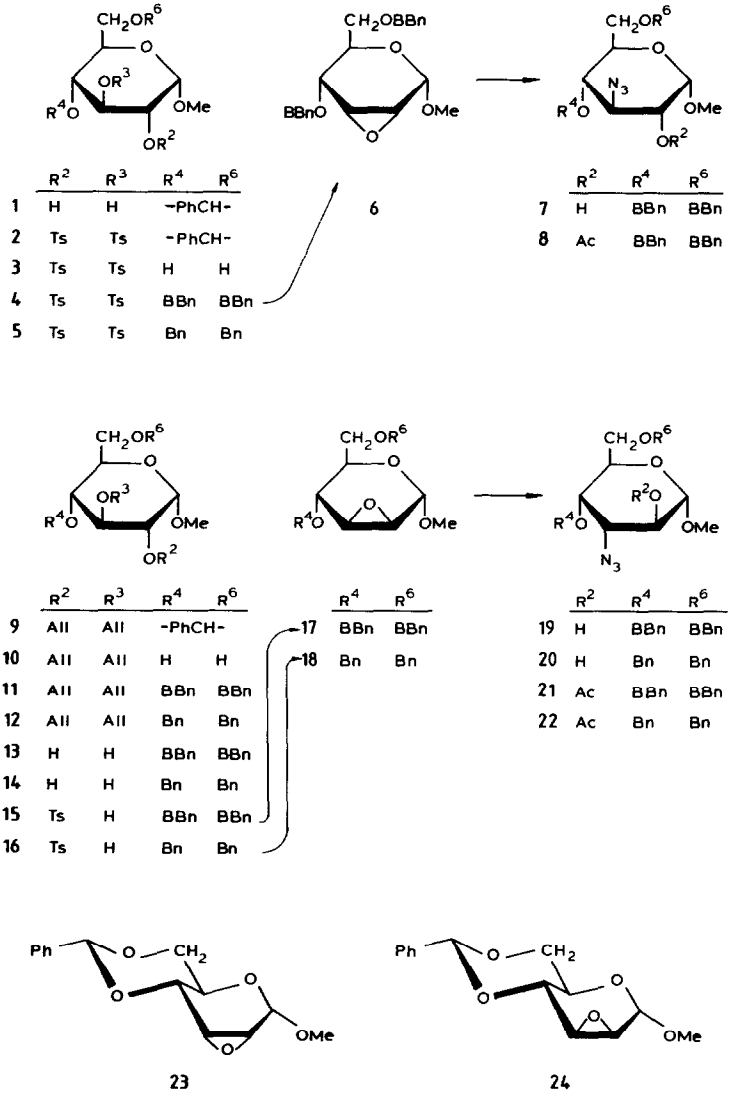
which suggested a hybrid of the $^{O}H_5$ half-chair and E_5 sofa conformations for the anhydropyranose moiety. Similarly, a crystal structure determination[11] on methyl 2,3-anhydro-6-bromo-6-deoxy-4-*O*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-α-D-allopyranoside showed a hybrid, $^{O}H_5 + E_5$ conformation (C-5 and O-5 of the 2,3-anhydropyranose moiety deviated from the C-1–C-2–C-3–C-4 plane by −0.666 and −0.112 Å, respectively). Other examples of this hybrid were found by Krajewski et al.[12–14], who investigated the crystal structures of several 2,3-anhydro-4-deoxy-L-sugar derivatives. Thus, there are many cases of molecules that do not conform to the conventionally accepted, ideal $^{O}H_5$ conformation[1,15]. In this connection it was of interest to investigate the crystal structure of methyl 2,3-anhydro-4,6-di-*O*-*p*-bromobenzyl-α-D-allopyranoside (**6**) and -α-D-mannopyranoside (**17**). We also found that the ring opening of **6** with sodium azide gave the 3-azido product selectively, while the ring opening of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside gave[16,17] primarily the 2-azido product. In contrast, the azidolysis of **17** showed the same regiospecificity (3-azido product) as the related 4,6-*O*-benzylidene derivative. Herein we report the conformational analysis of **6** and **17** in the solid state and in solution, and describe their selective azidolysis.

RESULTS AND DISCUSSION

Methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (**2**), prepared by the conventional method[18], was hydrolytically debenzylidenated[19] to give methyl 2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (**3**). The treatment of compound **3** with sodium hydride and benzyl bromide in oxolane gave a complex mixture which was difficult to resolve. In contrast, *p*-bromobenzylation and benzylation of compound **3** under phase transfer conditions furnished compounds **4** and **5** in quantitative and 80% yields, respectively. These results demonstrate the merit of the phase transfer conditions, which are easily controlled and give an easily processed mixture in contrast to the method using benzyl trichloroacetimidate[20].

Ring closure of compound **4** carried out in the conventional way[21] furnished crystalline compound **6** in 80% yield.

Methyl 2,3-anhydro-4,6-di-*O*-*p*-bromobenzyl- (**17**) and methyl 2,3-anhydro-4,6-di-*O*-benzyl-α-D-mannopyranoside (**18**) were similarly synthesized from **1**. First, methyl 2,3-di-*O*-allyl-4,6-*O*-benzylidene-α-D-glucopyranoside[22] (**9**), prepared from **1** by allylation in the presence of sodium hydride, was converted into **10** by hydrolytic debenzylidenation in aqueous 60% acetic acid. Compound **10** was then converted into **11** and **12** by *p*-bromobenzylation and benzylation, respectively, in the conventional way. After rearrangement of the allyl groups to 1-propenyl with potassium *tert*-butoxide in toluene under reflux, the products were treated with mild acid to give compounds **13** and **14** as white crystals. *p*-Toluenesulfonylation of **13** and **14** under phase transfer conditions afforded exclusively the 2-toluenesulfonate derivatives **15** and **16**, in yields of 91 and 90%, respectively. Treatment of



15 and **16** with sodium methoxide under reflux for 20 min gave **17** and **18** in yields of 83 and 85%, respectively.

In the azidolysis of compound **6** an appropriate solvent system was required for good selectivity and high yield of product. Reaction in 4:1 ethanol–water with sodium azide and ammonium chloride as reagents gave the 3-azido product **7** (70%), while in 2-methoxyethanol–water, hexamethylphosphoramide–water, or *N*,*N*-dimethylformamide–water, mixtures of 3-azido and 2-azido derivatives were

obtained, perhaps because of the elevated reflux temperatures of these solvents. The IR spectrum of compound **7** showed a strong absorption at 2120 cm^{-1} due to the azido group.

To confirm its configuration, compound **7** was converted into **8** by acetylation. The ^1H NMR spectrum of compound **8** was assigned by the use of single frequency decoupling. Irradiation of the H-1 doublet at δ 4.89 simplified the signal at δ 4.72 from a doublet of doublets to a doublet having $J_{2,3} = 10.2$ Hz. This signal was thus assigned to H-2. Irradiation of the upfield triplet signal of H-3 at δ 3.50 simplified that of H-2 to a doublet and that of H-4 to a doublet from a triplet at δ 3.94 with $J_{3,4}$ and $J_{4,5}$ of 10.6 Hz. The large coupling constants for H-2–H-3, H-3–H-4, and H-4–H-5 unambiguously verified the glucose configuration of **8**.

The azidolysis of compounds **17** and **18** was conducted in *N*,*N*-dimethylformamide in the presence of tetrabutylammonium chloride at 90° for 4–7 days *. Only one product was detected on TLC in each case, and purification of the products by column chromatography afforded compounds **19** and **20** in yields of 80 and 81%, respectively. The IR spectra showed strong absorptions at 2140 cm^{-1} due to the azido group. Portions of compounds **19** and **20** were converted into **21** and **22** by acetylation in the conventional way to facilitate their configurational assignment, again achieved by single frequency decoupling. The downfield position of the H-2 signal as a broad doublet at δ 4.912 with $J_{2,3} = 3.8$ Hz, and the resonance of H-3 as a broad triplet at δ 3.853 with $J_{2,3}$ and $J_{3,4} \sim 3.5$ Hz, clearly indicated the altropyranose configuration.

Molecular conformations of compounds **6** *and* **17**.—Perspective views of **6** and **17** derived from the X-ray structure determination are shown with atom numbering, in Figs. 1 and 2, respectively.

The crystal data are as follows: Compound **6**, $C_{21}H_{22}Br_2O_5$; MW = 514.19; orthorhombic, space group $P2_12_12_1$: $a = 9.150(7)$, $b = 30.371(8)$, $c = 7.703(1)$ Å; $V = 2136.4(8)$ Å^3, $F(000) = 1032$ e; $D_c = 1.607$ g cm^{-3} for $z = 4$; $\mu(Cu K\alpha) = 5.18$ mm^{-1}. Compound **17**, $C_{21}H_{22}Br_2O_5$, MW = 514.19; orthorhombic, space group $P2_12_12_1$; $a = 9.3592(7)$, $b = 29.479(4)$, $c = 7.6124(5)$ Å; 2099.9(3) Å^3; $F(000) = 1032$ e, $D_c = 1.607$ g cm^{-3} for $z = 4$; $\mu(Cu K\alpha) = 5.18$ mm^{-1}.

For compound **6**, the E-map calculated with the MULTAN 87 program showed a good coincidence with the interpretation of the Patterson map. A Fourier synthesis based on the phases of the Br atoms revealed the remaining C and O atoms of the molecule. The anisotropic refinement gave the final R as 0.07 for 1374 observed [$|F_o| \leqslant 3\sigma(F_o)$] reflections. In the refinement the unit weight was used for all reflections, of which 66 were considered to be affected by extinction and thus excluded at the final stage. The R factor [$R = \Sigma(|R_o| - |F_c|)/\Sigma(|F_o|)$] finally converged to 0.07. The final atomic coordinates and equivalent temperature

* The use of ammonium chloride as a co-reagent did not give satisfactory results.

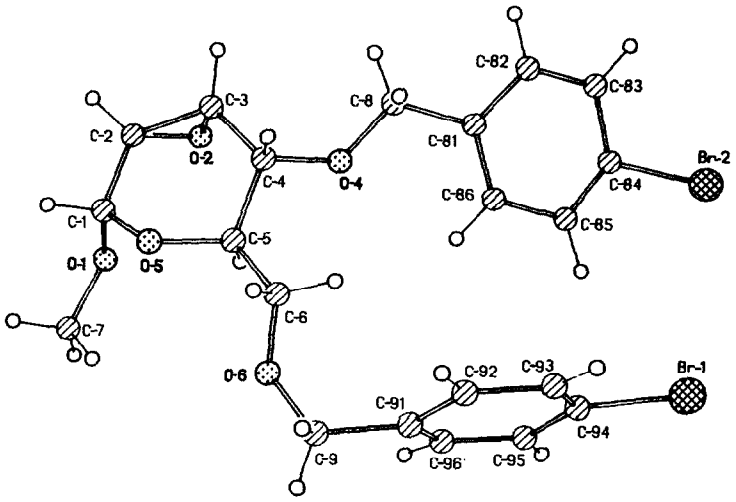


Fig. 1. Perspective view of compound **6**.

factors are given in Table I *. For compound **17**, initial position parameters of the Br atoms were determined by a three-dimensional Patterson function with the aid of the direct method (SHELEX 87). The remaining nonhydrogen atoms (C and O) were located on a subsequent Fourier map, and the structure then refined. The

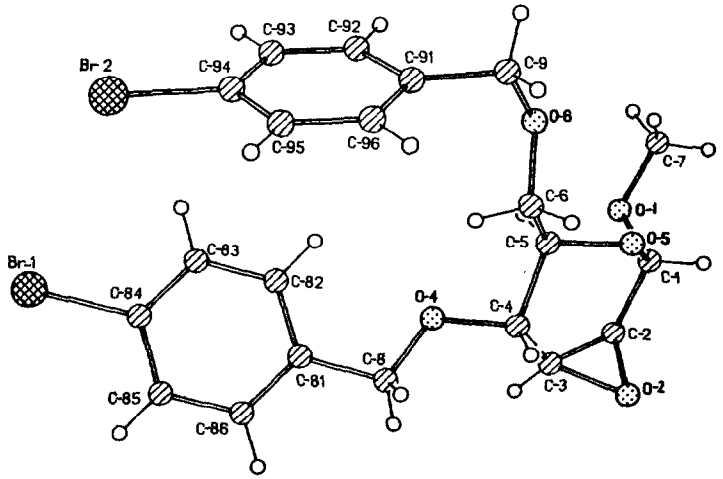


Fig. 2. Perspective view of compound **17**.

* Tables of observed and calculated structure factors, bond lengths, bond angles, and related data have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, Netherlands. Reference should be made to No. BBA/DD/510/*Carbohydr. Res.*, 235 (1992) 163–178.

TABLE I

Fractional coordinates and equivalent temperature factors for the nonhydrogen atoms of compound **6**

Atom	x/a [a]	y/b	z/c	U_{eq} (Å^2) [b]
Br-1	0.1157(3)	−0.0047(1)	−0.5143(5)	0.519(5)
Br-2	0.1161(2)	−0.0812(1)	0.0004(4)	0.113(4)
O-5	−0.7477(11)	−0.2076(3)	−0.3377(13)	0.081(7)
O-1	−0.7095(12)	−0.2563(3)	−0.5636(13)	0.094(8)
O-2	−0.6789(14)	−0.1739(4)	−0.7222(13)	0.111(8)
O-4	−0.5210(10)	−0.1188(3)	−0.4793(18)	0.091(8)
O-6	−0.4777(11)	−0.2158(4)	−0.1416(16)	0.091(8)
C-1	−0.7992(16)	−0.2241(5)	−0.5004(27)	0.095(9)
C-2	−0.8110(19)	−0.1889(6)	−0.6397(25)	0.091(8)
C-3	−0.7427(19)	−0.1445(6)	−0.6039(25)	0.083(7)
C-4	−0.6549(16)	−0.1392(5)	−0.4381(22)	0.081(9)
C-5	−0.6209(17)	−0.1820(4)	−0.3524(22)	0.074(9)
C-6	−0.5566(14)	−0.1775(5)	−0.1792(22)	0.074(9)
C-7	−0.7044(17)	−0.2955(5)	−0.4671(32)	0.110(13)
C-8	−0.5210(10)	−0.0730(4)	−0.4857(32)	0.101(12)
C-81	−0.3610(16)	−0.0574(4)	−0.5020(26)	0.077(10)
C-82	−0.3281(20)	−0.0167(5)	−0.5714(29)	0.098(12)
C-83	−0.1914(21)	−0.0010(4)	−0.5804(29)	0.110(14)
C-84	−0.0838(17)	−0.0284(5)	−0.5101(26)	0.116(13)
C-85	−0.1079(18)	−0.0672(4)	−0.4250(21)	0.081(12)
C-86	−0.2508(16)	−0.0822(4)	−0.4279(22)	0.076(11)
C-9	−0.4052(15)	−0.2121(4)	0.0231(26)	0.088(10)
C-91	−0.2776(18)	−0.1798(5)	0.0230(16)	0.073(7)
C-92	−0.2875(16)	−0.1399(5)	0.0992(22)	0.073(8)
C-93	−0.1698(24)	−0.1098(6)	0.1036(24)	0.109(12)
C-94	−0.0430(12)	−0.1212(4)	0.0111(28)	0.080(8)
C-95	−0.0261(16)	−0.1608(5)	0.0710(18)	0.078(7)
C-96	−0.1493(18)	−0.1889(6)	−0.0720(22)	0.070(8)

[a] Standard deviations are shown in parentheses. [b] $U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3}$

final R factor was 0.078 for 1808 reflections. The final atomic positional and equivalent thermal parameters are listed in Table II. Some torsion angles for **6** and **17** are indicated in Table III.

The mean Csp^3–Csp^3 bond length, 1.516 Å, and the mean Csp^3–O distance. 1.428 Å, are in the normal range for carbohydrates. The mean Br–Csp^2 bond length, 1.885 Å, and the mean Csp^3–Csp^2 distance, 1.444 Å, are in agreement with the values found in many previous investigations of mono- and di-saccharides. As in other 2,3-anhydropyranoside derivatives[10–14], a shortening of the C-2–C-3 bond, to 1.443 Å, was observed in **17**. The pyranose endocyclic valence angles at C-2 and C-3 had values of 120.8 and 120.2°, respectively, thus making the C-2–C-3 bond similar to a double bond. In contrast, an abnormal C-2–C-3 bond length was observed in **6**, although the pyranose endocyclic valence angles at C-2 and C-3 had values of 117.6 and 118.1°. In **6** and **17**, C-1–O-1 is shorter than O-1–C-7 by 0.03 and 0.024 Å, respectively.

TABLE II

Fractional coordinates and equivalent temperature factors for the nonhydrogen atoms of compound **17**

Atom	x/a [a]	y/b	z/c	U_{eq} (Å^2) [b]
Br-1	−0.6270(1)	−0.5044(1)	0.4835(3)	0.102(1)
Br-2	−0.6143(1)	−0.5834(1)	−0.0117(2)	0.075(1)
O-5	0.2437(8)	−0.7048(2)	0.3301(10)	0.046(4)
O-1	0.1893(9)	−0.7507(2)	0.5710(11)	0.054(5)
O-2	0.3853(9)	−0.6449(2)	0.5648(13)	0.069(5)
O-4	0.0084(7)	−0.6151(2)	0.4701(13)	0.052(4)
O-6	−0.0125(10)	−0.7131(3)	0.1045(13)	0.066(6)
C-1	0.2892(13)	−0.7215(3)	0.5018(20)	0.057(7)
C-2	0.3048(14)	−0.6821(4)	0.6258(19)	0.057(8)
C-3	0.2328(13)	−0.6397(4)	0.5920(19)	0.058(8)
C-4	0.1464(12)	−0.6335(3)	0.4258(17)	0.050(7)
C-5	0.1142(13)	−0.6791(3)	0.3375(15)	0.046(6)
C-7	0.1827(14)	−0.7930(3)	0.4843(23)	0.069(8)
C-8	−0.0013(12)	−0.5667(3)	0.4669(22)	0.055(7)
C-81	−0.1542(12)	−0.5531(3)	0.4771(18)	0.048(6)
C-82	−0.2611(13)	−0.5801(4)	0.4125(17)	0.050(7)
C-83	−0.4012(15)	−0.5663(4)	0.4192(17)	0.057(8)
C-84	−0.4359(13)	−0.5249(4)	0.4828(21)	0.060(8)
C-85	−0.3307(15)	−0.4959(4)	0.5431(18)	0.064(8)
C-86	−0.1890(14)	−0.5113(4)	0.5454(17)	0.053(7)
C-6	0.0586(14)	−0.6724(4)	0.1546(17)	0.054(7)
C-9	−0.0862(16)	−0.7076(5)	−0.0618(19)	0.069(9)
C-91	−0.2124(14)	−0.6765(4)	−0.0483(16)	0.054(7)
C-92	−0.3337(15)	−0.6891(4)	0.0517(18)	0.059(8)
C-93	−0.4516(15)	−0.6620(4)	0.0628(18)	0.060(8)
C-94	−0.4525(13)	−0.6211(4)	−0.0270(18)	0.055(7)
C-95	−0.3356(15)	−0.6079(4)	−0.1242(18)	0.057(8)
C-96	−0.2170(15)	−0.6350(4)	−0.1341(17)	0.054(7)

[a] Standard deviations are shown in parentheses. [b] $U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3}$

TABLE III

Some torsion angles in compounds **6** and **17**

Bonds	Angle (°)	
	6	**17**
Pyranose ring		
O-5–C-1–C-2–C-3	11.9	21.1
C-1–C-2–C-3–C-4	5.0	−3.2
C-2–C-3–C-4–C-5	13.3	15.8
C-3–C-4–C-5–O-5	−49.1	−47.3
C-4–C-5–O-5–C-1	70.2	71.5
C-5–O-5–C-1–C-2	−50.5	−56.5
2,3-Anhydro ring		
O-5–C-1–C-2–O-2	77.3	−49.6
C-1–C-2–O-2–C-3	−106.5	112.2
C-2–O-2–C-3–C-4	109.8	−111.4
O-2–C-3–C-4–C-5	52.7	82.0

TABLE IV

^1H and ^{13}C NMR data for the 2,3-anhydrides **6**, **17**, **22**, and **24** and the 3-azido derivatives **8** and **21**

Compound	^1H Chemical shifts (δ)							
	H-1	H-2	H-3	H-4	H-5	H-6	H-6′	CH_3O
6	4.91	3.51	3.45	3.96	3.92	3.67	3.63	3.45
17	4.93	3.11 [a]	3.35 [a]	3.63	3.72	3.69	3.55	3.47
23	4.36	2.88	3.06	3.44	4.29	4.05	3.40	3.12
24	4.61	2.86	3.25	3.56	3.72	4.04	3.42	3.00
8	4.89	4.72	3.50	3.94	3.74	3.68	3.61	3.38
21	4.59	4.91	3.85	3.99	4.13	3.80	3.70	3.40
	$^3J_{H,H}$ *values (Hz)*							
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	
6	3.3	3.4	~0.8	9.2	3.6	2.0	−11.3	
17	0	3.9	0	9.1	2.4	4.9	−10.1	
23	2.8	4.3	1.6	9.1	5.1	10.5	−10.1	
24	0.6	3.6	0	9.4	4.4	10.1	−10.1	
8	3.8	10.1	10.3	10.6	2.6	1.2	−10.3	
21	0	~3.8	3.5	9.9	5.0	1.9	−10.9	
	^{13}C *Chemical shifts* ($^1J_{C,H}$ *values*)							
	C-1	C-2	C-3	C-4	C-5	C-6		CH_3O
6	94.86	54.74	51.46	72.05	66.65	68.64		55.89
	(166.0)	(183.0)	(180.5)	(150.4)	(143.2)	(148.0, 140.6)		(142.8)
17	96.16	49.75 [b]	53.25 [b]	69.10	67.13	69.10		55.70
	(168.4)	(181.4)	(178.8)	(147.1)	(149.0)	(141.9, 138.3)		(142.7)
23	95.7	53.0	50.4	78.4	60.5	69.1		55.3
	(165.0)	(181.0)	(184.0)	(140.0)	(152.0)	(151.5, 140.5)		
24	97.2	50.6	53.9	75.2	62.2	69.4		55.2
	(169.0)	(181.5)	(183.0)	(146.0)	(146.0)	(149.0, 139.5)		

[a,b] These values may be interchanged.

A small value of the asymmetry parameter[23] [$\Delta C_2(2-3) = 1.4°$] for **6** indicated an $^0H_5$ half-chair conformation for the 2,3-anhydropyranose ring (puckering parameters: $Q = 0.539$ Å, $\theta = 58.7°$, and $\phi = 340°$). The sequence C-1–C-2–C-3–C-4 forms a four-atom plane within 0.03 Å, characteristic for a half-chair conformation; C-5 and O-5 deviate from this plane by −0.404 and 0.356 Å, respectively.

A similar analysis for **17** also identified a four-atom plane (C-1, C-2, C-3, and C-4) with C-5 and O-5 deviations of −0.330 and 0.444 Å, respectively. A larger value of the asymmetry parameter[23] [$\Delta C_2(2-3) = 7.5°$] implied a hybrid $^0H_5 + {}^0E$ conformation (puckering parameters[24] $Q = 0.550$ Å, $\theta = 51.7°$, and $\phi = 347°$). Comparison of the X-ray data for **6**, **17**, and **24** (ref. 10) showed that the conformation of the pyranose ring probably depends not only on the magnitudes and directions of the interaction of O-2 and O-1, but also on those of O-2 and O-4 or O-6 or both.

The angles between the normals to the benzene rings for **6** and **17** are 59.4 and 60°, respectively. The molecular packing in the crystals of **6** and **17** is normal Van

der Waals packing, because there is no inter- or intra-molecular hydrogen bonding interaction.

The conformations of **6** and **17** in solution were established from their ^{1}H NMR spectra. Chemical shifts and coupling constants assigned by single frequency decoupling are given in Table IV. As in the corresponding 4,6-*O*-benzylidene compounds **23** and **24**, the ^{1}H and ^{13}C nuclei of the oxirane rings in **6** and **17** are the most strongly shielded, although the H-2 and H-3 signals of **6** appear downfield of those of **23**, with $\Delta\delta = 0.65$ and 0.20, respectively. The H-2 signal is always upfield of the H-3 signal in the spectra of the 4,6-*O*-benzylidene derivatives, but downfield of the H-3 signal for compound **6**. This may be attributed to the interaction of the oxirane ring oxygen with both the methoxy and the 4-*p*-bromobenzyloxy groups. For **17**, the H-2 and H-3 signals are also downfield, compared to those of compound **24**. The couplings between H-1 and H-2, H-2 and H-3, and H-3 and H-4 are similar for **6** and **23**, and for **17** and **24**. Closer comparison of **6** and **23** shows **6** having a larger value of $J_{1,2}$ (3.4 Hz, vs. 2.8 Hz for **23**), and smaller values of $J_{2,3}$ (3.4 Hz, vs. 4.3 Hz for **23**) and $J_{3,4}$ (0.8 Hz, vs. 1.6 Hz for **23**). The differences imply a smaller dihedral angle between H-1 and H-2, and a larger dihedral angle between H-3 and H-4, for **6** compared to **23**.

From the ^3J values it is possible to calculate dihedral angles with the aid of the modified Karplus equation[25]. The calculated angles, together with those obtained from X-ray data, are listed in Table V. The fact that the calculated values for **17** are in good agreement with the X-ray values indicates that compound **17** has the same conformation in the solid state and in solution. However, for compound **6**, differences between the calculated values and the X-ray values were observed for the dihedral angles between H-1 and H-2, and H-3 and H-4, perhaps revealing the conformation of **6** in solution is different from that in the crystal.

Assignment of the ^{13}C NMR spectra of **6** and **17** was accomplished by a two-dimensional heterocorrelation technique, and from fully ^{1}H–^{13}C coupled spectra. The chemical shifts and $^1J_{C,H}$ values (in parentheses) are shown in Table IV. The chemical shifts of C-2 and C-3 in **6**, and the difference of chemical shifts

TABLE V

H–H Torsion angles in **6** and **17**. Comparison of crystal structure and NMR values

Bonds	Angle (°)			
	6		**17**	
	Crystal	NMR	Crystal	NMR
H-1–C-1–C-2–H-2	−22.5	−56	−76.6	−82
H-2–C-2–C-3–H-3	1.4		−0.1	
H-3–C-3–C-4–H-4	42.1	68	108.5	99
H-4–C-4–C-5–H-5	−169.6	−164	−167.1	−162
H-5–C-5–C-6–H-6	81.6		79.8	
H-5–C-5–C-6–H-6′	−159.8		−159.7	

between C-2 and C-3 are similar to those in **23**, while C-4 appears relatively upfield and C-5 downfield in the spectra of **6** and **17** compared to those of their analogues **23** and **24**, respectively. The coupling between C-2 and H-2 is 2.5 Hz larger than that of C-3 and H-3 in **6**, while in **23** and **24** the differences were −0.3 Hz.

As judged from the coupling constants shown in Table IV, the conformation of compound **17** in solution is similar to that of its analogue **24**, although there are some differences in the solid state. Compounds **17** and **24** may have the same conformation in their transition states, so that both undergo the same *trans*-diaxial ring opening by nucleophiles. The presence of an α-methoxy group at C-1 is an important factor in the high selectivity of the ring opening because it strongly inhibits nucleophilic attack at C-2, as described by a report on the ring opening of methyl 2,3-anhydro-4,6-di-*O*-methyl-β-D-mannopyranoside[26]. The very slow rate of azidolysis of **17** also indicates retardation by the 1-methoxy group.

In contrast, *trans*-diequatorial ring opening occurred in the azidolysis of **6**. The selectivity difference between **6** and **23** is perhaps caused by a difference in ring flexibility; compound **6** is more flexible than **23**, which has a rigid, *trans*-fused ring system. Thus, compound **6** may adopt a different conformation in its transition state from that of **23**, allowing the inductive effect of the anomeric center to play a predominant role in directing attack at position 3. A similar selective 3-attack on some 2,3-anhydro-6-deoxyallopyranoside derivatives was observed[27] by others.

EXPERIMENTAL

General methods.—Optical rotations were determined at 20° with a Perkin–Elmer Model 241-MC automatic polarimeter. Melting points were determined with a "Mel-Temp" apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer 125 spectrometer. ^1H And ^{13}C NMR spectra were recorded with Varian XL-400, Varian XL-200, and Bruker 90 MHz spectrometers, for solutions in $CDCl_3$. Chemical shifts are given in ppm downfield from internal Me_4Si. For conformational analyses, ^1H NMR spectra were measured in the pulsed Fourier-transform mode at 20°C. Mass spectra were recorded with a JMS-D3005 mass spectrometer, using a direct sample introduction technique. Analytical LC was carried out in stainless-steel columns packed with silica gel (10 × 150 mm or 4.6 × 250 mm) or Lichrosorb-NH_2 (4.6 × 250 mm), with peak detection by a differential refractometer (Model 1107L, made by LDC, Division of Milton Roy Company, Riviera Beach, FL, USA). Ethyl acetate–petroleum ether (bp 60–90°) was used as the eluent, at a flow rate of 1 to 4 mL min^{-1}. TLC was performed on Silica Gel G and HF, detection being effected either by charring with 30% (v/v) H_2SO_4 in MeOH or by UV light. Preparative chromatography was performed on columns (16 × 240, 18 × 300, and 35 × 400 mm) of silica gel (120–200 mesh).

For X-ray diffraction investigations, recrystallization of compounds **6** and **17** from hexanes afforded transparent, colorless crystals. Single crystals of **6** measuring 0.2 × 0.3 × 0.8 mm and of **17** measuring 0.2 × 0.25 × 0.7 mm were used for the

X-ray study. The unit-cell dimensions of both crystals were determined by a least-squares refinement, using the 2θ values of 25 strong reflections measured on a Rigaku AFC-5R diffractometer with nickel-filtered Cu$K\alpha$ radiation. Intensity data were measured by the 2θ-ω scan technique ($2\theta \leqslant 120$) on the same diffractometer. The scan rate and scan width were 8°/min and $\Delta 2\theta = (1.2 + 0.3 \text{ tg } \theta)°$, respectively. Background (scanning time 5 s) was measured before and after each scan. The intensities of three reflections were measured after every 100 reflections. The corrections for usual Lorentz and polarization factors were applied for both crystals but those for absorption and extinction were ignored. Of the 2344 unique reflections measured for **6** only 1390 had nonzero intensities [$|F_o| > 3\sigma(F_o)$], and for compound **17** there were 1808 nonzero reflections out of 2072.

Both structures were solved by the direct method (MULTAN 87 and SHELEX 88) and refined by the block-diagonal least-squares procedure, minimizing $\Sigma W(\delta F_o)^2$. In the subsequent refinement anisotropic temperature factors were adopted for nonhydrogen atoms and isotropic ones for hydrogen atoms. The maximum residual electron density is ~ 0.4 e Å^{-3} at both final difference Fourier maps (δF map). The neutral atomic scattering factors were taken from the International Tables for X-ray Crystallography III (1974). All the computations were performed on a Micro-VAX II or Panafacom U-1500 computer at the Institute of Physical Chemistry, Peking University.

*Methyl 4,6-di-*O-p-*bromobenzyl-2,3-di-*O-p-*tolylsulfonyl-α-*D-*glucopyranoside* (**4**). —A suspension of methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (**2**) (mp 150–152°, 16 g, 27 mmol, prepared by the conventional method[21] from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside) in 80% acetic acid (50 mL) was heated on a steam bath for 0.5 h. Acetone (10 mL) was added, and TLC showed the disappearance of the starting material when the mixture was heated for 1 h more. After removal of the acid with sequential additions and evaporations of water and EtOH, the syrupy residue was treated for 30 min on a steam bath with 12:5:3 MeOH–water–triethylamine (40 mL)[19]. The solvents were evaporated, water was added, and the byproduct was removed by extraction with petroleum ether. Compound **3** was obtained as a syrup by continuous extraction of the aqueous solution with methylene chloride and subsequent evaporation of the solvent (12.85 g, 94%).

To a solution of **3** (12.85 g, 25.4 mmol) in methylene chloride (50 mL) were added tetrabutylammonium hydrogensulfate, *p*-bromobenzyl bromide (16.7 g, 66.5 mmol), and NaOH (5%, 50 mL), and the reaction mixture was heated for 72 h under reflux with vigorous stirring. TLC indicated that the 4,6-di-*O*-*p*-bromobenzylated derivative was the only product. The reaction mixture was diluted with methylene chloride, and the organic layer was separated, washed with 0.2 M HCl, water, satd aq $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated to dryness. Crystallization from methylene chloride yielded 21.5 g (100%) of compound **4**; mp 126–127°; $[\alpha]_D^{20} + 47.5°$ (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.78–7.97 (m, 16 H, arom H), 5.13 (t, 1 H, $J_{2,3}$ and $J_{3,4}$ 9.4 Hz, H-3), 4.79 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1),

4.62, 4.51, 4.31, 4.17 (4 d as 2 q_{AB}, 4 H, ^2J 11.0 and 12.0 Hz, 2 CH_2Ph), 4.27 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.4 Hz, H-2), 3.75–3.53 (m, 4 H, H-4,5,6), 3.25 (s, 3 H, OCH_3), 2.43, and 2.36 (2 s, 6 H, 2PhCH_3).

Anal. Calcd for $C_{35}H_{36}Br_2O_{10}S_2$ (840.56): C, 50.00; H, 4.32; Br, 19.01. Found: C, 50.16; H, 4.36; Br, 18.43.

*Methyl 4,6-di-*O*-benzyl-2,3-di-*O*-p-tolylsulfonyl-α-*D*-glucopyranoside* (**5**).—Compound **3** (510 mg, 1 mmol) was converted into compound **5** by the same procedure as used for the conversion of **3** into **4**. Column chromatography with 1:3 EtOAc–petroleum ether afforded pure **5** as a syrup, yield 550 mg (80%); $[\alpha]_D^{20}$ + 111.4° (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.80–7.10 (m, 18 H, arom H), 5.14 (t, 1 H, $J_{1,2}$ and $J_{3,4}$ 9.4 Hz, H-3), 4.78 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.66, 4.54, 4.42, 4.25 (4 d as 2 q_{AB}, ^2J 10.4 and 12.2 Hz, 2 CH_2Ph), 4.26 (dd, 1 H, $J_{1,2}$ 3.4, $J_{2,3}$ 9.4 Hz, H-2), 3.75–3.55 (m, 4 H, H-4,5,6), 3.23 (s, 3 H, OCH_3), 2.42, and 2.34 (2 s, 6 H, PhCH_3); MS: *m/z* 681 (M^+).

*Methyl 2,3-anhydro-4,6-di-*O*-p-bromobenzyl-α-*D*-allopyranoside* (**6**).—Compound **4** (420 mg, 0.5 mmol) was dissolved in dry methylene chloride (5 mL), the solution was stirred and cooled to −15° in an ice–salt bath, and NaOMe in MeOH (M, 1 mL) was added dropwise. The reaction mixture was stirred for 1 h at room temperature, and kept for 48 h in the refrigerator at 0°, and for 24 h at ambient temperature. TLC indicated that the reaction was complete. The mixture was diluted with methylene chloride, and sodium *p*-toluenesulfonate was filtered off. The filtrate was washed with water, dried (Na_2SO_4), and evaporated, and the product was purified by recrystallization from methylene chloride–petroleum ether to furnish compound **6** as white crystals, yield 180 mg (70%); mp 85–86°; $[\alpha]_D^{20}$ + 54.0° (*c* 1, $CHCl_3$); ^{1}H NMR data are given in Table IV.

Anal. Calcd for $C_{21}H_{22}Br_2O_5$ (514.19): C, 49.05; H, 4.31; Br, 31.07. Found: C, 49.08; H, 4.33; Br, 31.01.

*Methyl 3-azido-4,6-di-*O*-p-bromobenzyl-3-deoxy-α-*D*-glucopyranoside* (**7**).—A suspension of **6** (400 mg, 0.78 mmol) in EtOH (15 mL) was mixed with a solution of sodium azide (1 g, 15 mmol) and ammonium chloride (1 g, 19 mmol) in water (4 mL), and the mixture was heated, with vigorous stirring, for 24 h under reflux, when TLC (benzene–acetone) indicated the starting material had been converted into a major product. The reaction mixture was cooled and poured with stirring into ice–water to give the product **7** as an amorphous solid. Recrystallization from diethyl ether yielded **7** (300 mg, 70%) mp 86°; $[\alpha]_D^{20}$ + 179° (*c* 0.1, $CHCl_3$); IR: 2120 cm^{-1} (N_3); ^{1}H NMR ($CDCl_3$): δ 7.49–7.05 (m, 8 H, arom H), 4.78 (d, 1 H, $J_{1,2}$ 4.8 Hz, H-1), 4.75, 4.58, 4.43, 4.39 (4 d as 2 q_{AB}, ^2J 11.0 and 12.1 Hz, 2 CH_2Ph), 3.72–3.60 (m, 5 H, H-2,4,5,6), 3.44 (t, 1 H, $J_{2,3}$ and $J_{3,4}$ ~ 10 Hz, H-3), and 3.43 (s, 3 H, OCH_3).

Anal. Calcd for $C_{21}H_{23}Br_2N_3O_5$ (557.22): C, 45.26; H, 4.16. Found: C, 45.13; H, 4.09.

*Methyl 2-*O*-acetyl-3-azido-4,6-di-*O*-p-bromobenzyl-3-deoxy-α-*D*-glucopyranoside* (**8**).—To a solution of **7** (100 mg, 0.18 mmol) in pyridine (1 mL) was added acetic

anhydride (0.5 mL), and the mixture was kept overnight at room temperature. After conventional processing, compound **8** was obtained as white plates in quantitative yield; mp 78–79°; $[\alpha]_D^{20}$ + 104° (*c* 0.4, $CHCl_3$); ^1H NMR data are given in Table IV.

Anal. Calcd for $C_{23}H_{25}Br_2N_3O_6$ (599.26): C, 46.09; H, 4.20. Found: C, 46.32; H, 4.29.

Methyl 2,3-di-O-allyl-α-D-glucopyranoside (**10**).—Methyl 2,3-di-*O*-allyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**9**) was prepared from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside by the conventional method with NaH and allyl bromide in oxolane, yield 100%; mp 61–64° (lit.[22] 66–67°); ^1H NMR ($CDCl_3$): δ 7.69–7.33 (m, 5 H, arom H), 6.20–5.77 (m, 2 H, 2 CH_2=C*H*), 5.56 (s, 1 H, PhC*H*), 5.40–5.11 (m, 4 H, 2 CH_2=CH), 4.80 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.55–3.41 (m, 9 H, 2 CH_2=CHCH_2, H-2,3,4,5,6), and 3.47 (s, 3 H, OCH_3).

A suspension of **9** (3.62 g, 10 mmol) in acetic acid (60%, 50 mL) was heated for 5–6 h on a steam bath, after which time the acid was removed by sequential additions and evaporations of water and EtOH. The syrupy residue was treated for 30 min on a steam bath with 12:5:2 MeOH–water–triethylamine (20 mL). Upon recovery by evaporation of its solution the crude product was washed with petroleum ether several times to remove part of the starting material and byproducts. Column chromatography gave compound **10** as a syrup, yield 2.08 g (76%); ^1H NMR ($CDCl_3$): δ 6.16–5.68 (m, 2 H, 2 CH_2=C*H*), 5.32–5.09 (m, 4 H, 2 CH_2=CH), 4.80 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.36–4.09 (m, 4 H, 2 CH_2=CHCH_2), 3.82–3.46 (m, 5 H, H-2,3,4,5,6), 3.42 (s, 3 H, OCH_3), and 3.17 (br s, 2 H, O*H*).

Methyl 2,3-di-O-allyl-4,6-di-O-p-bromobenzyl-α-D-glucopyranoside (**11**).—Compound **10** (5.5 g, 20 mmol) was dissolved in dry oxolane (dried over CaH_2, 300 mL), the solution was cooled in an ice bath, and NaH (in oil, 80%, 390 mg, 13 mmol) and *p*-bromobenzyl bromide (13.7 g, 55 mmol) were added. TLC indicated that the starting material disappeared when the mixture was refluxed with vigorous stirring for 5–6 h. The precipitate was filtered off, the filtrate was evaporated, and the residue was then subjected to steam distillation to remove excess *p*-bromobenzyl bromide. Compound **11** was obtained as a syrup by conventional processing, yield 11.5 g (94%); $[\alpha]_D^{20}$ + 63.0° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.44, 7.42, 7.19, 7.04 (4 d, 8 H, *J* 8.1, 8.5 Hz, arom H), 5.98–5.88 (m, 2 H, 2 CH_2=C*H*), 5.30–5.13 (m, 4 H, 2 CH_2=CH), 4.78, 4.57, 4.40, 4.39 (4 d as 2 q_{AB}, 4 H, ^2J 10.6 and 12.2 Hz, 2 CH_2Ph), 4.79 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.37–4.14 (m, 4 H, 2 CH_2=CHCH_2), 3.76 (t, 1 H, $J_{2,3}$ and $J_{3,4}$ 9.6 Hz, H-3), 3.70–3.58 (m, 3 H, H-5 and 2 H-6), 3.52 (t, 1 H, $J_{3,4}$ and $J_{4,5}$ 9.6 Hz, H-4), 3.43 (dd, $J_{1,2}$ 3.7, $J_{2,3}$ 9.6 Hz, H-2), and 3.39 (s, 3 H, OCH_3).

Anal. Calcd for $C_{27}H_{23}Br_2O_6$ (612.33): C, 52.95; H, 5.26. Found: C, 52.91; H, 5.09.

Methyl 4,6-di-O-p-bromobenzyl-α-D-glucopyranoside (**13**).—To a solution of **11** (10 g, 16.3 mmol) in dry benzene (250 mL) was added potassium *tert*-butoxide (2.74 g, 24.5 mmol). After allowing the reaction to proceed for 3 h under reflux with

vigorous stirring, more potassium *tert*-butoxide (2.24, 20 mmol) was added, and the mixture was kept for an additional 8 h. The suspension was then cooled and the precipitate filtered off, and the filtrate was washed with water, dried (Na_2SO_4), and concentrated to a syrup. To the residue was added acetic acid (60%, 50 mL), and the mixture was refluxed for 2 h. The solution was evaporated to give a syrup that was purified by column chromatography (1 : 3 to 1 : 1 EtOAc–petroleum ether) to afford **13**, yield 6.2 g (71%); ^{1}H NMR ($CDCl_3$): δ 7.73–7.07 (m, 8 H, arom H), 4.89–4.45 (m, 5 H, H-1 and 2 CH_2Ph), 4.00–3.47 (m, 6 H, H-2,3,4,5,6), 3.44 (s, 3 H, OCH_3), and 2.09 (br s, 2 H, 2 OH).

Anal. Calcd for $C_{21}H_{24}Br_2O_6$ (532.20): C, 47.38; H, 4.54. Found: C, 47.52; H, 4.36.

Methyl 4,6-di-O-p-*bromobenzyl-2*-O-p-*tolylsulfonyl-α*-D-*glucopyranoside* (**15**).—To a solution of **13** (2.13 g, 4.0 mmol) in methylene chloride (30 mL) were added tetrabutylammonium hydrogensulfate (100 mg), *p*-toluenesulfonyl chloride (880 mg, 4.6 mmol), and aq NaOH (5%, 5.4 mmol), and the mixture was vigorously stirred overnight at ambient temperature. On conventional processing followed by column chromatography, compound **15** was obtained as crystals, yield 2.50 g (91%); mp 109–110°; $[\alpha]_D^{20}$ + 62.3° (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.89–6.93 (m, 12 H, arom H), 3.29 (s, 3 H, OCH_3), and 2.46 (s, 3 H, PhCH_3).

Anal. Calcd for $C_{28}H_{30}Br_2O_8S$ (686.38): C, 48.99; H, 4.40. Found: C, 48.76; H, 4.52.

Methyl 4,6-di-O-*benzyl-2*-O-p-*tolylsulfonyl-α*-D-*glucopyranoside* (**16**).—Methyl 4,6-di-*O*-benzyl-α-D-glucopyranoside (**14**) was prepared conventionally from methyl 2,3-di-*O*-allyl-α-D-glucopyranoside (**10**) by benzylation (→ **12**) and the deallylation of the product. Compound **14** was obtained in an overall yield of 68%; mp 105–106°; $[\alpha]_D^{20}$ + 114° (*c* 0.4, $CHCl_3$) (lit.[22] mp 76–78°, $[\alpha]_D^{20}$ + 119.1°); ^{1}H NMR ($CDCl_3$): δ 7.33 (m, 10 H, arom H), 4.82 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.81, 4.51 (2 d as q_{AB}, 2 H, ^2J 11.7 Hz, CH_2Ph), 4.62 (s, 2 H, CH_2Ph), 3.95–3.49 (m, 6 H, H-2,3,4,5,6), 3.46 (s, 3 H, OCH_3), and 2.11 (br s, 2 H, 2 OH).

To a solution of **14** (1.5 g, 4.0 mmol) in methylene chloride (30 mL) were added NaOH (5%, 6.5 mL), tetrabutylammonium hydrogensulfate (100 mg), and *p*-toluenesulfonyl chloride (1 g, 5.3 mmol), and the mixture was vigorously stirred overnight at ambient temperature. Compound **16** was obtained as white needles by the same procedure as described for conversion of **13** into **15**, yield 1.98 g (90%); mp 83–84°; $[\alpha]_D^{20}$ + 106.0° (*c* 0.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.87–7.07 (m, 15 H, arom H), 4.69 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 3.27 (s, 3 H, OCH_3), and 2.44 (s, 3 H, PhCH_3).

Anal. Calcd for $C_{28}H_{23}O_8S$ (528.60): C, 63.61; H, 6.10. Found: C, 63.55; H, 6.48.

Methyl 2,3-anhydro-4,6-di-O-p-*bromobenzyl-α*-D-*mannopyranoside* (**17**).—To a solution of **15** (1.15 g, 1.67 mmol) in dry methylene chloride (10 mL) was added NaOMe in MeOH (3 M, 4 mL). TLC (1 : 3 EtOAc–petroleum ether) showed that the reacton was complete when the mixture was refluxed for 20 min under an N_2 atmosphere. Then the precipitated sodium *p*-toluenesulfonate was filtered off, the

filtrate was concentrated, and the residue was purified by column chromatography to afford **17** as white needles, yield 800 mg (83%); mp 108–109°; $[\alpha]_D^{20}$ + 93.3° (*c* 0.5, $CHCl_3$); ^1H NMR data are given in Table IV.

Anal. Calcd for $C_{21}H_{22}Br_2O_5$ (514.19): C, 49.05; H, 4.31; Br, 31.07. Found: C, 48.93; H, 4.10; Br, 31.03.

Methyl 2,3-anhydro-4,6-di-O-benzyl-α-D-mannopyranoside (**18**).—To a solution of **16** (1.5 g, 2.8 mmol) in dry methylene chloride (15 mL) was added a solution of NaOMe in MeOH (3 M, 7 mL). TLC (1:3 EtOAc–petroleum ether) showed that the reaction was complete after 20 min at reflux under an N_2 atmosphere. The reaction mixture was processed and purified by the same procedure as used for conversion of **15** into **17**, and **18** was obtained as a syrup (850 mg, 85%); $[\alpha]_D^{20}$ + 121° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.33 (m, 10 H, arom H), 4.93 (s, 1 H, H-1), 4.74, 4.60, 4.50, 4.46 (4 d as 2 q_{AB}, 4 H ^2J 11.0 and 13.2 Hz, CH_2Ph), 3.75–3.55 (m, 4 H, H-4,5,6), 3.49 (s, 3 H, OCH_3), 3.34, and 3.09 (2 d, 2 H, $J_{2,3}$ 3.6 Hz, H-2,3).

Anal. Calcd for $C_{21}H_{24}O_5$ (356.40): C, 70.76; H, 6.78. Found: C, 71.01; H, 7.08.

Methyl 3-azido-4,6-di-O-p-bromobenzyl-3-deoxy-α-D-altropyranoside (**19**).—To a solution of **17** (300 mg, 0.58 mmol) in *N*,*N*-dimethylformamide (5 mL) were added sodium azide (380 mg, 5.58 mmol) and tetraethylammonium chloride (60% in water, 800 mg, 2.9 mmol), and the mixture was vigorously stirred for 4 days at 90° under an N_2 atmosphere. The suspension was poured into ice–water with stirring. Most of the product separated as a syrup, and another portion was obtained by repeated extraction of the aqueous phase with petroleum ether. Column chromatography of the crude product gave syrupy compound **19**, yield 260 mg (80%); $[\alpha]_D^{20}$ + 89° (*c* 0.7, $CHCl_3$); IR: 2140 cm^{-1} (N_3); ^1H NMR ($CDCl_3$): δ 7.44–7.10 (m, 8 H, arom H), 4.57 (br s, 1 H, H-1), 4.58, 4.54, 4.41 (3 d incl 1 q_{AB}, 4 H, ^2J 11.6 Hz, 2 CH_2Ph), 4.08–4.05 (m, 1 H, H-5), 3.95 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 9.5 Hz, H-4), 3.91 (br t, $J_{2,3}$ and $J_{3,4}$ 3.5 Hz, H-3), 3.88 (br d, $J_{2,3}$ 3.5 Hz, H-2), 3.68 (dd, 1 H, $J_{5,6}$ 4.4 $J_{6,6'}$ 10.3 Hz, H-6), 3.62 (dd, 1 H, $J_{5,6'}$ 1.8 Hz, H-6'), and 3.39 (s, 3 H, OCH_3).

Anal. Calcd for $C_{21}H_{23}Br_2N_3O_5$ (557.33): C, 45.26; H, 4.16; N, 7.54. Found: C, 45.04; H, 4.07; N, 7.45.

Methyl 2-O-acetyl-3-azido-4,6-di-O-p-bromobenyl-3-deoxy-α-D-altropyranoside (**21**).—Compound **19** (200 mg, 0.36 mmol) was acetylated in pyridine with acetic anhydride by a conventional method to give a theoretical yield of **21**; ^1H NMR data are given in Table IV.

Anal. Calcd for $C_{21}H_{22}Br_2N_3O_5$ (599.26): C, 46.09; H, 4.20; N, 7.01. Found: C, 46.34; H, 4.27; N, 7.14.

Methyl 2-O-acetyl-3-azido-4,6-di-O-benzyl-3-deoxy-α-D-altropyranoside (**22**).—To a solution of compound **18** (800 mg, 2.25 mmol) in *N*,*N*-dimethylformamide (10 mL) were added sodium azide (1.46 g, 22.5 mmol) and tetraethylammonium chloride (60% in water, 3.04 g, 11 mmol). The mixture was vigorously stirred for 7 days at 95° under an N_2 atmosphere. The suspension was then processed and purified as for the conversion of **17** into **19**. Compound **20**, obtained in 81% yield

(730 mg), was acetylated by a conventional method to give compound **22** (100%); IR: 2140 cm^{-1} (N_3); ^1H NMR ($CDCl_3$): δ 7.50–7.24 (m, 10 H, arom H), 4.90 (br d, $J_{2,3} \sim 3.6$ Hz, H-2), 4.68, 4.62, 4.59, 4.52 (4 d, 4 H, J 12.1 and 13.0 Hz, 2 CH_2Ph), 4.58 (br s, 1 H, H-1), 4.12 (m, 1 H, H-5), 3.97 (dd, 1 H, $J_{3,4}$ 3.6, $J_{4,5}$ 8.6 Hz, H-4), 3.84 (br t, 1 H, $J_{2,3}$ and $J_{3,4}$ 3.6 Hz, H-3), 3.79 (dd, 1 H, $J_{5,6}$ 3.6, $J_{6,6'}$ 10.9 Hz, H-6), 3.69 (dd, $J_{5,6'}$ 1.1 Hz, H-6'), 3.38 (s, 3 H, OCH_3), and 2.07 (s, 3 H, CH_3CO).

REFERENCES

1 N.R. Williams, *Adv. Carbohydr. Chem. Biochem.*, 25 (1970) 109–179.
2 M. Černý and J. Staněk, Jr., *Adv. Carbohydr. Chem. Biochem.*, 34 (1977) 107–146.
3 H. Paulsen and W. Stenzel, *Chem. Ber.*, 111 (1978) 2334–2347.
4 R.L. Halcomb and S.J. Danishefsky, *J. Am. Chem. Soc.*, 111 (1989) 6661–6666.
5 M.M. Abdel-Malik, Q. Peng, and A.S. Perlin, *Carbohydr. Res.*, 159 (1987) 11–23.
6 A.M. Bionucci, G. Catelani, F. Colonna, and L. Monti, *Carbohydr. Res.*, 140 (1985) 144–150.
7 G. Catelani, L. Monti, and P. Tognetti, *Carbohydr. Res.*, 97 (1981) 189–197.
8 K.S. Kim, D.M. Vyas, and W.A. Szarek, *Carbohydr. Res.*, 72 (1979) 25–33.
9 M. Chmielewski, J. Mieczkowski, W. Priebe, A. Zamojski, and H. Adamowicz, *Tetrahedron*, 34 (1978) 3325–3330.
10 A.M. Pilotti and B. Stensland, *Acta Crystallogr., Sect. B.*, 28 (1972) 2821–2825.
11 J. Thiem, J. Schwentner, E. Schuttpelz, and J. Kopf, *Chem. Ber.*, 112 (1979) 1023–1034.
12 J.W. Krajewski, P. Gluziński, Z. Urbańczyk-Lipkowska, A. Banaszek, L. Párkányi, and A. Kálmán, *Carbohydr. Res.*, 144 (1985) 13–22.
13 J.W. Krajewski, P. Gluziński, A. Banaszek, G. Argay, and A. Kálmán, *Carbohydr. Res.*, 166 (1987) 19–25.
14 J.W. Krajewski, Z. Urbańczyk-Lipkowska, P. Gluziński, and A. Banaszek, *Carbohydr. Res.*, 194 (1989) 31–36.
15 E.L. Eliel, N.L. Allinger, S.J. Angyal, and G.A. Morrison, *Conformational Analysis*, Interscience, New York, 1965, pp 42, 356, and 371.
16 A.C. Richardson, *Methods Carbohydr. Chem.*, 6 (1972) 218–224.
17 R.D. Guthrie and D. Murphy, *J. Chem. Soc., Perkin Trans. 1*, (1963) 5288–5294.
18 R.S. Tipson, *Methods Carbohydr. Chem.*, 2 (1963) 246–250.
19 H.H. Baer, and B. Radatus, *Carbohydr. Res.*, 157 (1986) 65–81.
20 K. Ok, Y. Takagi, T. Tsuchiya, S. Umezawa, and H. Umezawa, *Carbohydr. Res.*, 169 (1987) 69–81.
21 L.F. Wiggins, *Methods Carbohydr. Chem.*, 2 (1963) 188–191.
22 J.W. Van Cleve and C.R. Russell, *Carbohydr. Res.*, 25 (1972) 465–473.
23 W.L. Duax, C.M. Weeks, and D.C. Rohrer, *Top. Stereochem.*, 9 (1976) 271–383.
24 D. Cremer and J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.
25 C.A.G. Haasnoot, F.A.A.W. De Leeuw, and C. Altona, *Bull. Soc. Chim. Belg.*, 89 (1980) 125–131.
26 W.H.G. Lake and S. Peat, *J. Chem. Soc.*, (1938) 1417–1421.
27 R.I. Hollingsworth, E.M. Hrabak, and F.B. Dazzo, *Carbohydr. Res.*, 154 (1986) 103–113.