Carbohydrate Research, 228 (1992) 81–93
Elsevier Science Publishers B.V., Amsterdam

Selective protections on 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-D-glucopyranose*

Abderrahime Bouali, Paul Boullanger†, Dominique Lafont,
Laboratoire Chimie Organique II, U.R.A. C.N.R.S. 463. Université Claude Bernard Lyon I, E.S.C.I.L., 43 Bd. du 11 Novembre 1918, F-69622 Villeurbanne (France)

and Bernard Fenet
Centre Commun de Résonance Magnétique Nucléaire, Université Claude Bernard Lyon I, Bât. 721, 43 Bd. du 11 Novembre 1918, F-69622 Villeurbanne (France)

(Received February 8th, 1991; accepted June 10th, 1991)

ABSTRACT

Regioselective monoacetylation of 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-D-glucopyranose (**1**) gave a mixture of 3-*O*-acetyl and 4-*O*-acetyl derivatives, the structures of which were established by two-dimensional, phase-sensitive NOESY and confirmed by chemical proofs. The benzylation of **1**, on the other hand, led to 2-allyloxycarbonylamino-1,6-anhydro-3,4-di- (**5**) or 2-allyloxycarbonylamino-1,6-anhydro-2 -*N*-benzyl-3,4-di-*O*-benzyl-2-deoxy-β-D-glucopyranose (**10**). The regioselective cleavage of **5** with titanium tetrachloride gave the expected 3-*O*-benzyl derivative, the structure of which was ascertained by chemical proofs; the same reaction performed on **10** led to the opening of the anhydro ring to afford 3-benzyl-[3,4-di-*O*-benzyl-1,2-dideoxy-α-D-glucopyrano]-[2,1-d]-2-oxazolidone.

INTRODUCTION

1,6-Anhydro derivatives of carbohydrates are useful acceptors in glycosylation reactions[1]. The anhydro ring provides simultaneous protections of both OH-1 and OH-6, and the $^1C_4$ conformation introduces drastic changes in the hydroxyl group reactivities, as compared with the more common $^4C_1$ derivatives. Confirming this current interest, recent studies were published concerning the preparation of protected 1,6-anhydro-β-D-glucopyranose derivatives[2] or the opening of the anhydro ring of mono- or oligo-saccharides in order to obtain glycosylation donors[3].

In a continuation of our study of the synthesis of oligosaccharides related to glycoproteins[4,5], we recently described a new method for the preparation of 1,6-anhydro derivatives of pyranoses[6]. When applied to 2-amino-2-deoxy sugars, this method allows the preparation of glycosyl acceptors, thus providing a convenient access to (1→3)- and (1→4)-linked residues in oligosaccharides having a 2-amino-2-deoxy sugar as the reducing unit. The aforementioned linkages are of importance in, for example, chitobiose [β-D-GlcNAc-(1→4)-D-GlcNAc], *N*-acetyllactosamine [β-D-Gal-(1→4)-D-

* Dedicated to Professor Serge David on the occasion of his 70th birthday.
† To whom correspondence should be addressed.

0008-6215/92/$ 05.00

GlcNAc], and lacto-*N*-biose [β-D-Gal-(1→3)-D-GlcNAc]. Such examples represent important building blocks of glycosaminoglycans and other oligo- or poly-saccharides of biological interest.

As reported earlier by our laboratory[7,8], the protection by an allyloxycarbonyl group of the amino group fulfills most of the requirements in carbohydrate chemistry (*e.g.*, ease of chemoselective protection, stability in most of the usual reaction conditions, and ease of chemoselective deprotection). Since 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-D-glucopyranose (**1**) was easily prepared[6] from 2-amino-2-deoxy-D-glucose, we found it of interest to prepare various glycosylation acceptors from this starting material by regioselective protection of OH-3 or OH-4.

RESULTS AND DISCUSSION

The regioselective protection of 1,6-anhydro-β-D-glucopyranose derivatives has always represented a challenge in carbohydrate chemistry due to the presence of three axial hydroxyl groups in a molecule having the $^1C_4$ conformation. It was early recognized[9] that OH-3 of such derivatives is less reactive than OH-2 and OH-4, but attempts at direct regioselective protection (benzoylation or benzylation) have previously resulted in complex mixtures and low yields[9–13]. The same problems were observed recently for the partial methanolysis and hydrazinolysis of fully acylated 1,6-anhydro-β-D-glucopyranose derivatives[14]. More recently, the use of 2,4-dibutylstannylene acetals of 1,6-anhydro-β-D-glucopyranose was reported in the regioselective synthesis of 4-OH protected 1,6-anhydro-β-D-glucopyranose derivatives (4-*O*-benzoyl, 4-*O*-tosyl, or 4-*O*-benzyl) by treatment with an appropriate electrophile[15,16]. This procedure could not be applied to the 2-amino-2-deoxy derivatives of 1,6-anhydro-β-D-glucopyranose because of the presence of a protected amino function at C-2. In this series, the aforementioned better reactivity of OH-4 over OH-3 was not observed[17], and more complicated syntheses were designed to obtain partly protected derivatives of 2-amino-1,6-anhydro-2-deoxy-β-D-glucopyranose. Thus Schmitt and Sinaÿ[17] reported the regioselective opening of an anhydride[18] previously protected at OH-4; Dasgupta and Garegg[19], and Kloosterman *et al.*[20] have reported nucleophilic substitutions of 2-trifluoromethanesulfonates in the D-*manno* configuration.

In order to obtain further information on the *N*-allyloxycarbonyl group in carbohydrate chemistry, mainly in glycosylation reactions, we attempted the direct regioselective protection of 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-D-glucopyranose (**1**)[6]. Acetylation was performed either at low temperature in dichloromethane with acetyl chloride and an excess of pyridine, or at room temperature in pyridine with acetic anhydride. The former conditions yielded the diacetylated derivative **4** (12%), a monoacetylated derivative (28%) and its corresponding positional isomer (22%), and some unreacted starting material **1** (20%). In the latter acetylation using the same conditions previously reported for the acetylation of 2-acetamido-1,6-anhydro-2-deoxy-β-D-glucopyranose[17], the respective yields were 29, 37, 4, and 2%. Since no reference compound has been described in this series, the identification of both mono-

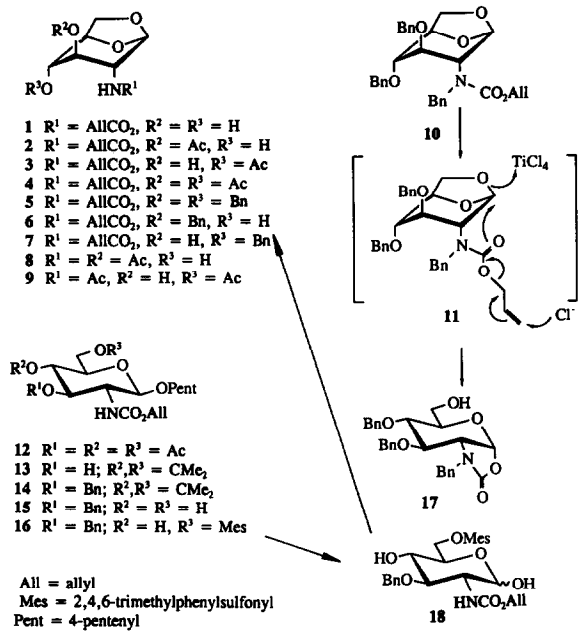

TABLE I

^{13}C-N.m.r. spectra of compounds **1–6**, **10**, and **12–18**[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*NCH_2Ph*
1[b]	101.32	54.52	73.32	71.33	77.14	65.83	
2	101.43	52.17	73.62	69.22	76.93	65.89	
3	102.26	55.19	70.61	74.30	74.95	65.85	
4	101.62	52.61	71.12	70.96	74.45	65.97	
5	101.44	51.26	77.50	76.65	74.33	65.73	
6	101.75	51.24	80.68	69.90	77.09	65.68	
10	102.34	59.33	79.40	76.89	74.86	65.66	48.73
12	101.93	56.84	73.67	69.96	72.32	62.96	
13	103.00	59.44	72.51	67.98	75.26	62.68	
14	102.96	58.04	80.06	67.74	75.71	62.76	
15	102.41	57.79	83.82	72.20	74.85	62.88	
16	102.03	57.48	83.23	71.09	74.28	69.60	
17	94.91	54.07	75.32	72.68	72.68	63.45	46.41
18	92.75	55.94	80.80	70.43	71.59	69.85	

[a]Recorded for solutions in CD_3COCD_3 with Me_4Si as internal standard. The spectra contained additional signals corresponding to the allyloxycarbonyl group (except for **17**), OCH_2–$CH=CH_2$, at δ 65.7 ± 0.3, 134.3 ± 0.3, 1176.3 ± 0.3, respectively. Every compound also showed the complementary signals corresponding to the other protecting groups.[b] Ref. 6.

acetylated isomers **2** and **3** was achieved by high resolution n.m.r. spectrometry. Most of the ^1H and ^{13}C signals (Table I) could be assigned on the basis of ^1H–^{13}C 2D experiments, except those corresponding to the C-3, H-3 and C-4, H-4 positions. Owing to the arrangement of substituents in the 1,6-anhydro derivatives in the D-*gluco* configuration, most of the vicinal and long-range coupling constants were of the same order of

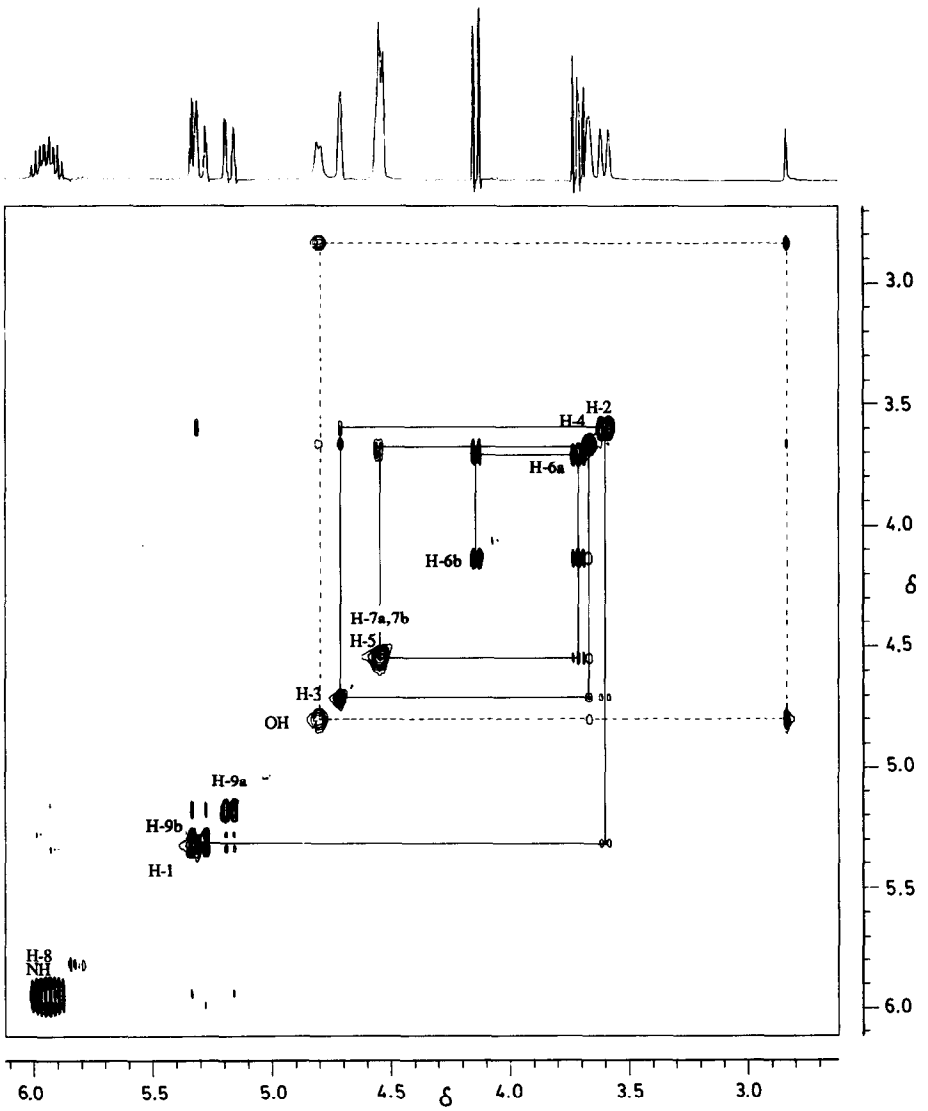

Fig. 1. Phase-sensitive NOESY spectrum of compound **2**. The spectrum was recorded overnight on a solution of product (10 mg) in CD_3COCD_3 (0.5 mL) at 22°. Acquisition time, AQ, 1.08 s; S12, 4096; τ_m 3 s; NE, 512; NS, 8 for **2** and 32 for **3**. All off-diagonal cross correlation peaks (indicated in italics) were negative, except those coming from the slow exchange process between OH and the residual water of acetone; H-7a, 7b are allylic protons; H-8 and H-9a,9b are vinylic protons.

magnitude[15,21], and three different methods were used successively for the unambiguous interpretation of ^{1}H-n.m.r. spectra of these derivatives. Selective decoupling and two-dimensionnal, double-quantum filtered COSY experiments (DQF–COSY) were unsuccessful in the complete assigment of all n.m.r. signals, since the long-range coupling constants did not allow a sequential information to be obtained. The third n.m.r. approach (two-dimensional, phase sensitive NOESY), based on the dipolar interactions between protons in close spacial proximity, confirmed the assignments. As the n.O.e. effect is related to the internuclear distance ($1/r^6$), correlation peaks may be expected between neighboring protons only, thus enabling the sequential assignment of the sugar-ring protons.

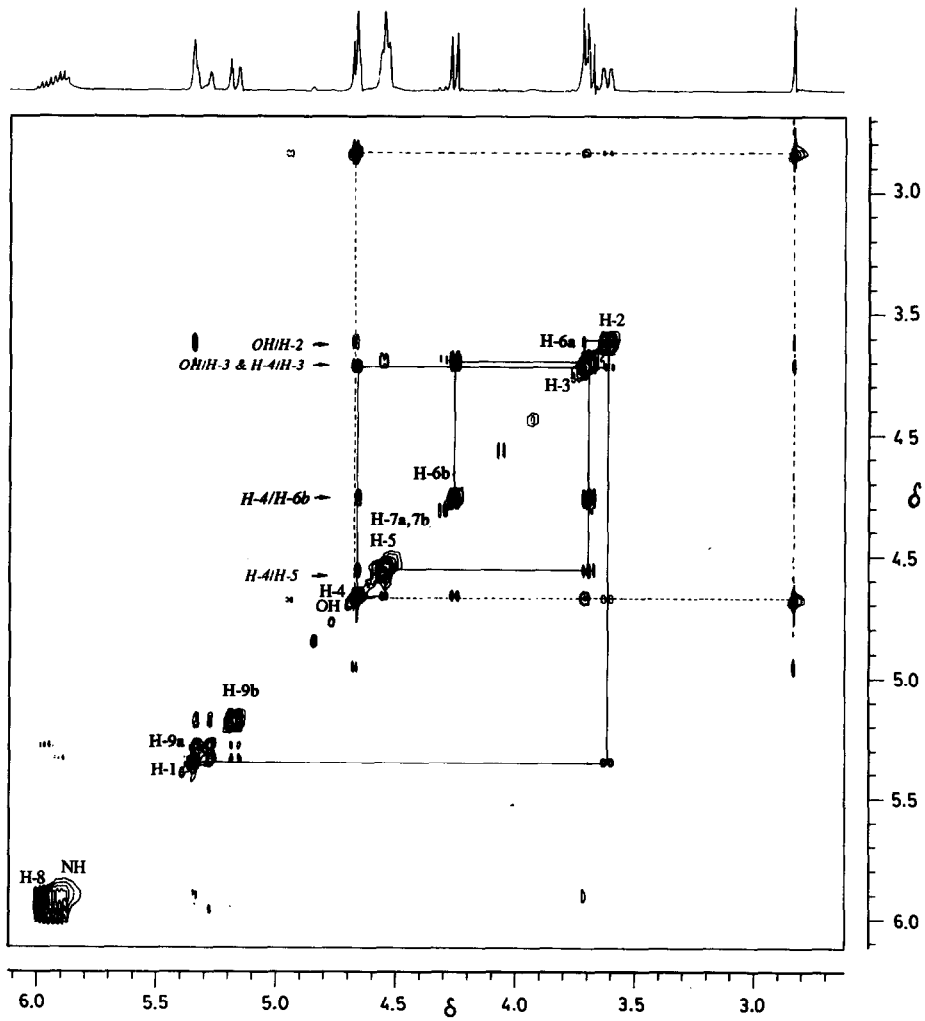

Fig. 2. Phase-sensitive NOESY spectrum of compound 3. For experimental details, see legend to Fig. 1.

The motion of small molecules, such as **2** and **3**, is characterized by short correlation times; longitudinal relaxation times (T_1) of protons, dominated by dipolar interactions, were rather long (2.4 s), and the n.O.e effects were therefore negative. By adjusting the mixing time τ_m of the NOESY sequence as $\tau_m = T_{1av}$, a very good 2D matrix was obtained in an overnight experiment, in which all the expected proximity data were present. The equatorial orientations of the ring protons allowed a sequential assignment from H-1 to H-5. The chemical shift of H-3 (Fig. 1), together with the crosscorrelation peaks between OH and H-4, identified **2** as the 3-*O*-acetyl derivative. The signals of OH and H-4 for **3** (Fig. 2) were very close, but the large coupling constant exibited by OH, in contrast to that obtained for H-4, allowed discrimination. In this isomer, the OH proton gave an n.O.e. correlation with both H-2 and H-3, and an exchange peak with the residual water of acetone. The present study showed that the 2D phase-sensitive NOESY method (more often used for macromolecules) allows the assignment of all signals of a small carbohydrate molecule, as long as the n.O.e. effect is kept growing during the mixing-time corresponding to T_1 of the observed protons.

The structural characterisation by n.m.r. of **2** and **3** was further confirmed by chemical proofs. Isomers **2** and **3** were separately *N*-deallyloxycarbonylated with tetrakis(triphenylphosphine)palladium, and then the amino group was selectively reacetylated to afford **8** (78%) and **9** (84%), respectively. Their physical constants were then compared with those reported earlier[17] and were in complete agreement with the proposed structures.

Owing to the poor regioselectivity of the acetylation reactions, the regioselective benzylation of **1** was studied. Monobenzylation using 1 equiv. of benzyl chloride or bromide under the usual conditions did not lead to the expected derivatives **6** and **7** in good yields; the reaction was very sluggish and showed poor regioselectivity. In contrast, the dibenzylation of **1** gave a reasonable yield. It is noteworthy that the choice of the benzylating agent and the choice of the base were of crucial importance. The reaction performed with 3 equiv. of benzyl chloride in oxolane with sodium hydride as the base had to be carefully monitored to afford the dibenzyl compound **5** in 91% yield. The addition of tetrabutylammonium iodide to increase the reaction rate[22] led to the tribenzyl derivative **10** in 87% yield. It should be mentionned that **5** was obtained more easily (75% yield) from **1** with benzyl bromide and barium oxide–barium hydroxide in *N,N*-dimethylformamide as the benzylating agent.

The regioselective debenzylation of the 1,6-anhydro-2-azido-3,4-di-*O*-benzyl-2-deoxy-β-D-glucopyranose with various Lewis acids to afford 1,6-anhydro-2-azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranose in a very regioselective manner was recently reported[23]. In order to extend this reaction to the 2-allyloxycarbonylamino derivatives **5** and **10**, various Lewis acids were tested under the same conditions as those reported[23]. The best results, in terms of yields and purity of the reaction mixtures, were obtained with titanium tetrachloride. Thus, when the dibenzyl compound **5** was treated with 1.2 equiv. of titanium tetrachloride at 0° for 15 h, the major derivative **6** was formed in 70% yield, and the alternative positional isomer **7**, formed in low yield, could be characterized by ^{1}H-n.m.r. spectroscopy only. The regioselective deprotection of **5** could be attributed to

the favored complexation of titanium tetrachloride with three suitably arranged nucleophilic atoms (N-2, O-4, and O-5). On the other hand, treatment of the tribenzyl derivative **10** at room temperature under the same condition, afforded the *N*-benzyloxazolidinone **17** *via* the simultaneous opening of the anhydro ring and the removal of the allyl group. This removal is probably due to a nucleophilic attack (**11**) of a halide ion, as previously reported[7] for a bromide ion during the glycosylation reactions using a glycosyl bromide as the starting material.

The structure of compound **6** was further confirmed by an alternative procedure in which the 3-*O*-benzyl protective group was unambigously introduced at an early stage of the synthesis. 1,3,4,6-Tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose[7] was glucosylated with 4-pentenol to give **12** from which the aglycon group might be selectively removed[24]. After *O*-deacetylation, **12** was treated with 2,2-dimethoxypropane and a catalytic amount of camphosulfonic acid to afford **13**, which was then benzylated with benzyl bromide and barium hydroxide–barium oxide to give **14**. After removal of the isopropylidene group to give diol **15** and treatment with 2-mesitylenesulfonyl chloride in pyridine, the resulting intermediate **16** was deprotected at O-1 with (dicollidine)iodonium perchlorate[25] to afford **18**. The cyclisation of this latter derivative was effected in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in ethanol[6] and the 1,6-anhydro derivative obtained was found to be identical with **6**, thereby confirming the n.m.r. characterization. The structures of all compounds were ascertained by ^{1}H- and ^{13}C-n.m.r. spectroscopy.

In conclusion, the regioselective esterifications of 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-D-glucopyranose (**1**) were shown to be less selective than with the 2-acetamido intermediates. The monobenzylations, on the other hand, did not lead to the expected high-yield, stereoselective formation of derivatives. Nevertheless, the regioselective deprotection of 2-allyloxycarbonylamino-1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy-β-D-glucopyranose (**5**) afforded the expected 3-*O*-monobenzyl isomer is good yield. This method, although very sensitive to the purity of the Lewis acid, allowed the preparation of the glycosyl acceptor **6** by a shorter route than, and in a yield higher than that of the usual reaction pathway in which the 3-*O*-benzyl protective group is introduced at an early stage. Finally, the n.m.r. technique (two dimensional, phase-sensitive NOESY) used in this work allowed the unambiguous identification of the structure of the mono protected derivatives of 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-D-glucopyranose.

EXPERIMENTAL

General methods. — Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were measured at 21° with a Perkin–Elmer 241 polarimeter for solutions in a 1-dm cell. ^{1}H- (300 MHz) and ^{13}C-n.m.r. (75.5 MHz) spectra (internal standard, Me_4Si) were recorded with a Bruker AM 300 spectrometer. For NOESY spectra[26] recorded in the phase-sensitive mode[27], the standard Bruker sequence using TPPI for quadrature detection in F_1 dimension was utilized. Prior to

starting NOESY experiments, a T_1 measurement was performed. The mixing time τ_m and the relaxation delay D_1 were choosen as a function of the average T_1 and fixed respectively to T_1 and 3 × T_1. Prior to 2D F.t. and to attenuate the effect of signal truncation, the data were multiplied by a square-shifted sine-bell ($\pi/2$) in F_2 and F_1 dimensions[28]. In the ^{1}H-n.m.r. spectra of **2** and **3**, all coupling constants were not determined unambiguously and some of them are only cited as they were deducted from NOESY correlations. Column chromatography was performed on Matrex™ Silica Gel Amicon (230–400 mesh). Elemental analyses were performed at the Laboratoire Central d'Analyses du C.N.R.S. (Solaize, France).

*Acetylation of 2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-*D*-glucopyranose* (**1**). — To a solution of **1** (ref. 6; 0.461 g, 1.88 mmol) in dichloromethane (4 mL) and pyridine (1.5 mL), cooled to −38°, was added acetyl chloride (150 μL, 2.11 mmol) dropwise over 2 h. After 2 more hours at −38°, the reaction was quenched by addition of methanol (5 mL), and the mixture was diluted with chloroform (50 mL), and washed once with water. The base was neutralized with dilute HCl, and the solution washed again with water and dried ($CaCl_2$) before concentration to dryness. The syrupy residue was chromatographed on silica gel (3:1, ethyl acetate–hexane) and the following compounds were successively eluted before the unreacted starting material **1** (48 mg, 20%):

*3,4-Di-*O*-acetyl-2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-*D*-glucopyranose* (**4**). Colorless syrup (76 mg, 12%). $[\alpha]_D$ −63° (*c* 3.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 6.10 (br. d, 1 H, NH), 5.95 (m, 1 H, $OCH_2CH=CH_2$), 5.39 (br. s, 1 H, H-1), 5.31 and 5.17 (2 m, 2 H, $OCH_2CH=CH_2$), 4.75 (m, 1 H, $J_{3,4}$ 1.9, $J_{4,5}$ 3.5, $J_{2,4}$ 1.6 Hz, H-4), 4.69 (m, 1 H, $J_{2,3}$ 2.8, $J_{3,5}$ 1.4 Hz, H-3), 4.61 (m, 1 H, $J_{5,6a}$ 6.0, $J_{5,6b}$ 0.9 Hz, H-5), 4.53 (m, 2 H, $OCH_2CH=CH_2$), 4.23 (dd, 1 H, $J_{6a,6b}$ 7.8 Hz, H-6b), 3.76 (m, 1 H, H-6a), 3.62 (m, 1 H, $J_{1,2}$ 1.1, $J_{2,NH}$ 9.2 Hz, H-2), 2.10 and 2.13 (2 s, 6 H, 2 $COCH_3$); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{14}H_{19}NO_8$: C, 51.06; H, 5.82; N, 4.25. Found: C, 51.00; H, 5.83; N, 4.09.

*4-*O*-Acetyl-2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-*D*-glucopyranose* (**3**). — Colorless syrup (149 mg, 28%), $[\alpha]_D$ −28° (*c* 7.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 5.93 (br. m, 1 H, NH), 5.93 (m, 1 H, $OCH_2CH=CH_2$), 5.33 (br. s, 1 H, $J_{1,2}$, $J_{1,3}$, H-1), 5.31 and 5.18 (2 m, 2 H, $OCH_2CH=CH_2$), 4.65 (br. m, 2 H, $J_{2,4}$, $J_{3,4}$, $J_{4,5}$, H-4, OH), 4.57 (m, 1 H, $J_{5,6a}$ 5.8, $J_{5,6b}$ 1.0 Hz, H-5), 4.53 (m, 2 H, $OCH_2CH=CH_2$), 4.13 (dd, 1 H, $J_{6a,6b}$ 7.2 Hz, H-6b), 3.71 (m, 1 H, $J_{2,3}$, H-3), 3.69 (m, 1 H, H-6), 3.61 (m, 1 H, H-2), and 2.12 (s, 3 H, $COCH_3$); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{12}H_{17}NO_7$: C, 50.17; H, 5.97; N, 4.88. Found: C, 49.84; H, 5.95; N, 4.72.

*3-*O*-Acetyl-2-allyloxycarbonylamino-1,6-anhydro-2-deoxy-β-*D*-glucopyranose* (**2**). — Colorless syrup (117 mg, 22%), $[\alpha]_D$ −23° (*c* 5.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 5.90 (br. d, 1 H, $J_{2,NH}$ 10 Hz, NH), 5.93 (m, 1 H, $OCH_2CH=CH_2$), 5.32 (br. s, 1 H, $J_{1,2}$, $J_{1,3}$, H-1), 5.31 and 5.17 (2 m, 2 H, $OCH_2CH=CH_2$), 4.84 (br. d, 1 H, OH), 4.70 (m, 1 H, $J_{2,3}$, $J_{3,4}$, $J_{3,5}$, H-3), 4.57 (m, 1 H, $J_{4,5}$, $J_{5,6}$ 5.8, $J_{5,6b}$ 1.0 Hz, H-5), 4.54 (m,

2 H, $OCH_2CH=CH_2$), 4.13 (dd, 1 H, $J_{6a,6b}$ 7.8 Hz, H-6b), 3.71 (m, 1 H, $J_{4,6a}$ 0.6 Hz, H-6a), 3.67 (m, 1 H, $J_{2,4}$, H-4), 3.60 (m, 1 H, H-2), and 2.10 (s, 3 H, $COCH_3$); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{12}H_{17}NO_7$: C, 50.17; H, 5.97; N, 4.88. Found: C, 50.38; H, 6.12; N, 4.70.

*2-Allyloxycarbonylamino-1,6-anhydro-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranose* (**5**). — To a solution of **1** (1.0 g, 4.08 mmol) in dry oxolane (10 mL) was added NaH (0.340 g, 14.2 mmol), and the mixture was kept under N_2 before addition of benzyl chloride (2.3 mL, 20.0 mmol). The reaction was monitored by t.l.c. and stopped after 15 h at room temperature. After evaporation of the mixture, the residual material was redissolved in chloroform and the organic solution was washed with water, dried ($CaCl_2$), and concentrated before chromatography (1:2 ethyl acetate–chloroform). Compound **5** (1.58 g, 91%) was recovered as an oil that crystallized on standing, m.p. 62° (hexane), $[\alpha]_D$ −57° (*c* 1.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 7.37–7.28 (m, 5 H, Ph), 5.93 (m, 1 H, $OCH_2CH=CH_2$), 5.70 (d, 1 H, $J_{2,NH}$ 9.8 Hz, NH), 5.35 (br. s, 1 H, H-1), 5.29–5.17 (m, 2 H, $OCH_2CH=CH_2$), 4.73 (m, 1 H, H-5), 4.69–4.57 (m, 4 H, 2 CH_2Ph), 4.55–4.53 (m, 2 H, $OCH_2CH=CH_2$), 4.16 (dd, 1 H, $J_{5,6a}$ 0.8, $J_{6a,6b}$ 7.1 Hz, H-6a), 3.78 (m, 1 H, H-2), 3.68 (dd, 1 H, $J_{5,6b}$ 5.9 Hz, H-6b), and 3.61–3.59 (m, 2 H, H-3,4); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40; N, 3.29. Found: C, 67.66; H, 6.31; N, 3.24.

*2-Allyloxycarbonylamino-1,6-anhydro-2-*N*-benzyl-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranose* (**10**). — To a solution of **1** (1.0 g, 4.08 mmol) in dry oxolane (10 mL) was added NaH (0.340 g, 14.2 mmol), and the mixture was kept under N_2 before addition of tetrabutylammonium iodide (0.147 g, 0.4 mmol) and benzyl chloride (2.4 mL, 20.9 mmol). The reaction was monitored by t.l.c. and stopped after 1 h at room temperature. After concentration of the mixture, the residual material was dissolved in chloroform and the organic solution was washed with water, dried ($CaCl_2$), and concentrated before chromatography (1:2 ethyl acetate–chloroform). Compound **10** (1.69 g, 87%) was recovered as an oil, $[\alpha]_D$ −27° (*c* 1.0, chloroform); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{31}H_{33}NO_6$: C, 72.21; H, 6.45; N, 2.72. Found: C, 72.16; H, 6.52; N, 2.76.

Regioselective debenzylations using $TiCl_4$. General procedure. — To a solution of the benzyl ether (1.4 mmol) in dichloromethane (10 mL) was added a freshly prepared M solution of $TiCl_4$ in the same solvent (1.7 mL). After disappearence of the starting material (t.l.c.), the mixture was poured into a saturated aqueous solution of $NaHCO_3$; the aqueous layer was extracted twice with dichloromethane, and the combined organic extracts were dried ($MgSO_4$) before evaporation of the solvent. The residual oil was chromatographed on silica gel (2:1 ethyl acetate–hexane).

*2-Allyloxycarbonylamino-1,6-anhydro-3-*O*-benzyl-2-deoxy-β-*D*-glucopyranose* (**6**). — This derivative was obtained as a white crystalline material (70% yield) from **5** by use of the aforementioned general procedure (15 h at 0°); m.p. 127–128° (acetone–hexane), $[\alpha]_D$ +63° (*c* 1.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 7.40–7.25 (m, 5 H,

Ph), 6.00–5.86 (m, 2 H, N*H*, $OCH_2CH=CH_2$), 5.33 (br. s, 1 H, H-1), 5.30 and 5.16 (2 m, 2 H, $OCH_2CH=CH_2$), 4.72–4.60 (m, 3 H, H-5, CH_2Ph), 4.54 (m, 2 H, $OCH_2CH=CH_2$), 4.18 (dd, 1 H, $J_{5,6}$ 1.0, $J_{6a,6b}$ 7.0 Hz, H-6a), 3.80–3.77 (m, 2 H, H-2, 4), 3.66 (dd, 1 H, $J_{5,6b}$ 6.0 Hz, H-6b), and 3.48 (m, 1 H, H-3); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{17}H_{21}NO_6$: C, 60.88; H, 6.31; N, 4.18. Found: C, 60,57; H, 6.26; N, 4.00.

*3-Benzyl-[3,4-di-*O*-benzyl-1,2-dideoxy-α-*D*-glucopyrano]-[2,1-*d*]-2-oxazolidone* (**17**). — This derivative was obtained as an oil (82% yield) from **10** by the aforementioned general procedure (16 h, room temperature), $[\alpha]_D$ +20° (*c* 1.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 7.38–7.18 (m, 15 H, 3 Ph), 5.86 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 4.78 (d, 1 H, *J* 15.3 Hz, 0.5 NCH_2Ph), 4.60 and 4.51 (2 q, 4 H, 2 OCH_2Ph), 4.01 (d, 1 H, 0.5 NCH_2Ph), 4.08–3.92 (m, 3 H, H-3,4, OH), 3.88 (m, 1 H, $J_{4,5}$ 2.9, $J_{5,6a}$ 1.5, $J_{5,6b}$ 7.1 Hz, H-5), and 3.80–3.60 (m, 3 H, H-2,6a,6b); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{28}H_{29}NO_6$: C, 70.72; H, 6.15; N, 2.96. Found: C, 70,57; H, 6.17; N, 2.86.

*4-Pentenyl 3,4,6-tri-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-*D*-glucopyranoside* (**12**). — 1,3,4,6-Tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose[29] (20 g, 46.4 mmol) and 4-pentenol (4.45 mL, 53.4 mmol) were dissolved in dry, alcohol-free dichloromethane (200 mL). The mixture was flushed with N_2 and cooled to −30° before addition of trimethylsilyl trifluoromethanesulfonate (9.8 mL, 54.0 mmol). The mixture was stirred for 24 h at −30°, and then the reaction quenched with triethylamine (11.4 mL). The solution was allowed to reach 0° before being washed with a dilute solution of aqueous $NaHCO_3$ and then water. After drying (Na_2SO_4) and evaporation, a crystalline material was recovered, which was recrystallized twice from ethanol (57% yield). After evaporation, the mother liquors were chromatographed on silica gel (1:1 ethyl acetate–hexane) to provide a second crop (23% yield), m.p. 114°, $[\alpha]_D$ +0.4° (*c* 5.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 6.47 (d, 1 H, $J_{2,NH}$ 8.6 Hz, NH), 5.97–5.75 (m, 2 H, $CH=CH_2$, allyl and pentenyl), 5.28–5.12 (m, 3 H, H-3, $CH=CH_2$, allyl), 5.03 and 4.93 (2 m, 2 H, $CH=CH_2$, pentenyl), 4.97 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 9.7 Hz, H-4), 4.76 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.58–4.44 (m, 2 H, CH_2–$CH=CH_2$, allyl), 4.26 (dd, 1 H, $J_{5,6a}$ 5.0 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.09 (dd, 1 H, $J_{5,6b}$ 2.4 Hz, H-6b), 3.85 and 3.56 (2 m, 2 H, OCH_2, pentenyl), 3.81 (m, 1 H, H-5), 3.64 (m, 1 H, $J_{2,3}$ 10.8 Hz, H-2), 2.09 (m, 2 H, CH_2, pentenyl), 2.02, 1.98, 1.94 (3 s, 9 H, 3 CH_3CO), and 1.64 (m, 2 H, CH_2, pentenyl); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{21}H_{31}NO_{10}$: C, 55.13; H, 6.83; N, 3.06. Found: C, 54.99; H, 6.95; N, 3.05.

*4-Pentenyl 2-allyloxycarbonylamino-2-deoxy-4,6-*O*-isopropylidene)-β-*D*-glucopyranoside* (**13**). — A solution of **12** (8.0 g, 17.5 mmol) in methanol (100 mL) was treated overnight with a catalytic amount of sodium methoxide. After neutralization with a cation-exchange resin (Amberlite IR-120, H^+) and filtration, the solution was concentrated to dryness and the residue treated overnight with 2,2-dimethoxypropane in the presence of a catalytic amount of camphosulfonic acid. After neutralization ($NaHCO_3$) and evaporation, the residue was dissolved in dichloromethane (150 mL) and the

solution washed once with water, dried (Na_2SO_4), concentrated, and chromatographed on silica gel (3:1 ethyl acetate–hexane) to afford **13**, white crystals (83% yield), m.p. 114° (hexane), $[\alpha]_D$ − 47° (*c* 2.2, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 6.40 (d, 1 H, $J_{2,NH}$ 9.1 Hz, NH), 5.96–5.71 (m, 2 H, C*H* = CH_2, allyl and pentenyl), 5.26 and 5.11 (2 m, 2 H, CH = C*H*$_2$, allyl), 4.98 and 4.90 (2 m, 2 H, CH = C*H*$_2$, pentenyl), 4.52–4.47 (m, 3 H, H-1, C*H*$_2$–CH = CH_2, allyl), 4.36 (d, 1 H, $J_{3,OH}$, 4.8 Hz, OH), 3.82–3.74 (m, 2 H, H-6a, 0.5 CH_2, pentenyl) 3.71 (dd, 1 H, $J_{5,6b}$ 9.6, $J_{6a,6b}$ 10.0 Hz, H-6b), 3.66 (d, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 9.0 Hz, H-3), 3.51 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 3.44 (m, 1 H, 0.5 CH_2 pentenyl), 3.42 (m, 1 H, $J_{1,2}$ 8.3 Hz, H-2), 3.18 (m, 1 H, $J_{5,6a}$ 5.6 Hz, H-5), 2.06, 1.57 (2 m, 4 H, 2 CH_2, pentenyl), 1.46 and 1.30 [2 s, 6 H, C(CH_3)$_2$]; ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{18}H_{29}NO_7$: C, 58.20; H, 7.87; N, 3.77. Found: C, 58.14; H, 7.81; N, 3.74.

*4-Pentenyl 2-allyloxycarbonylamino-3-*O*-benzyl-2-deoxy-4,6-*O*-(isopropylidene)-β-*D*-glucopyranoside* (**14**). — A solution of **13** (1.86 g, 5 mmol) in dry *N,N*-dimethylformamide (20 mL) was stirred overnight at room temperature in the presence of $Ba(OH)_2$ (0.79 g, 2.5 mmol), BaO (3.06 g, 20 mmol), and benzyl bromide (0.75 mL, 6.3 mmol). The reaction was then quenched with methanol (2 mL) and the mixture was diluted with chloroform (100 mL), prior to filtration and evaporation to dryness. The residue was dissolved in dichloromethane (100 mL) and the solution was washed with water, dried ($CaCl_2$), and concentrated. The residue was purified by column chromatography (2:5 ethyl acetate–hexane) to afford **14**, white crystals (81% yield), m.p. 96° (hexane), $[\alpha]_D$ + 15° (*c* 1.0, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 7.33–7.20 (m, 5 H, Ph), 6.49 (m, 1 H, NH), 5.96–5.75 (m, 2 H, C*H* = CH_2, allyl and pentenyl), 5.27 and 5.13 (2 m, 2 H, CH = C*H*$_2$, allyl), 5.00 and 4.92 (2 m, 2 H, CH = C*H*$_2$, pentenyl), 4.82–4.65 (2 d, 2 H, *J* 11.9 Hz, C*H*$_2$-Ph), 4.58 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.55–4.50 (m, 2 H, C*H*$_2$–CH = CH_2, allyl), 3.84 (dd, 1 H, $J_{5,6a}$ 5.6, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.83–3.70 (m, 4 H, H-3,4,6b, 0.5 C*H*$_2$, pentenyl), 3.56 (m, 1 H, $J_{2,3}$ 9.5, $J_{2,NH}$ 8.0 Hz, H-2), 3.47 (m, 1 H, 0.5 C*H*$_2$, pentenyl), 3.25 (m, 1 H, $J_{4,5} = J_{5,6b}$ 9.5 Hz, H-5), 2.09, 1.61 (2 m, 4 H, 2 CH_2, pentenyl), 1.51 and 1.37 [2 s, 6 H, C(CH_3)$_2$]; ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{25}H_{35}NO_7$: C, 65.05; H, 7.64; N, 3.03. Found: C, 64.94; H, 7.56; N, 3.01.

*4-Pentenyl 2-allyloxycarbonylamino-3-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**15**). — Compound **14** (1.85 g, 4 mmol) was heated for 0.5 h in 50% aqueous acetic acid (20 mL) before evaporation to dryness and coevaporation of the residual solvent twice with toluene. The resulting material crystallized from hexane (1.40 g, 83% yield), m.p. 119°, $[\alpha]_D$ + 5.6° (*c* 1.0, chloroform); ^{13}C-m.n.r., see Table I.

Anal. Calc. for $C_{22}H_{31}NO_7$: C, 62.69; H, 7.41; N, 3.32. Found: C, 62.31; H, 7.35; N, 3.72.

*4-Pentenyl 2-allyloxycarbonylamino-3-*O*-benzyl-2-deoxy-6-*O*-(2,4,6-trimethylphenylsulfonyl)-β-*D*-glucopyranoside* (**16**). — A solution of mesitylenesulfonyl chloride (0.825 g, 3.77 mmol) in pyridine (10 mL) was added dropwise to a solution of **15** (1.06 g, 2.5 mmol) in pyridine (10 mL) cooled to − 10°. The mixture was allowed to warm to room temperature and was stirred for 6 h. The reaction was then quenched with

methanol (0.5 mL) and the solvent evaporated. The residue was purified by column chromatography (4:5 ethyl acetate–hexane) to afford **16**, white crystals (79% yield), m.p. 97° (hexane), $[\alpha]_D$ +8.3° (*c* 1.2, chloroform); ^{1}H-n.m.r. (CD_3COCD_3): δ 7.33–7.06 (m, 7 H, C_6H_5 and C_6H_2), 6.51 (d, 1 H, $J_{2,NH}$ 7.5 Hz, NH), 5.95–5.74 (m, 2 H, -C*H* = CH_2, allyl and pentenyl), 5.28–4.92 (m, 4 H, CH = CH_2, allyl and pentenyl), 4.85 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 4.84 and 4.71 (2 d, 2 H, *J* 11.3 Hz, CH_2-Ph), 4.55–4.44 (m, 2 H, CH_2–CH = CH_2, allyl), 4.34 (d, 1 H, $J_{3,OH}$ 10.3 Hz, OH), 4.08 (dd, 1 H, $J_{5,6a}$ 5.4, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.73 (m, 1 H, 0.5 CH_2, pentenyl), 3.70–3.48 (m, 5 H, H-2,3,4,5, 6b), 3.40 (m, 1 H, 0.5 CH_2, pentenyl), 2.63 [s, 6 H, (CH_3)$_2C_6H_2$], 2.30 (s, 3 H, $CH_3C_6H_2$), 2.07, and 1.60 (2 m, 4 H, 2 CH_2, pentenyl); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{31}H_{41}NO_9S$: C, 61.67; H, 6.85; N, 2.32. Found: C, 61.73; H, 6.62; N, 2.32.

*2-Allyloxycarbonylamino-3-*O*-benzyl-2-deoxy-6-*O*-(2,4,6-trimethylphenylsulfonyl)-*D*-glucopyranose* (**18**). — A solution of **16** (0.489 g, 0.81 mmol) in diethyl ether (6.8 mL) and dichloromethane (1.7 mL) was stirred with (dicollidine)iodonium perchlorate (0.420 g) and water (29.2 μL) for 6 h before a new addition of (dicollidine)iodonium perchlorate (0.344 g). After 18 h at room temperature, the mixture was filtered on Celite, and the filtrate was diluted with dichloromethane, washed with a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) and water, and dried (Na_2SO_4). After evaporation, the mixture was purified by column chromatography (8:9 ethyl acetate–hexane) to afford first the unreacted starting material **16** (14%) and then **17** as a syrup (56% yield); ^{1}H-n.m.r. (α-D anomer; CD_3COCD_3): δ 7.35–7.07 (m, 7 H, C_6H_5 and C_6H_2), 6.12 (d, 1 H, $J_{2,NH}$ 8.2 Hz, NH), 5.95–5.83 (m, 2 H, C*H* = CH_2, OH-1), 5.27 and 5.13 (m, 2 H, CH = CH_2), 5.10 (m, 1 H, H-1), 4.88 and 4.76 (2 d, 2 H, *J* 11.4 Hz, CH_2-Ph), 4.79 (d, 1 H, $J_{4,OH}$ 5.8 Hz, OH-4), 4.57–4.46 (m, 2 H, CH_2–CH = CH_2), 4.24 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 10.4 Hz, H-6a), 4.14 (dd, 1 H, $J_{5,6b}$ 5.7 Hz, H-6b), 4.04 (m, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 3.75–3.68 (m, 2 H, H-3,4), 3.52 (m, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 9.8 Hz, H-2), 2.61 (s, 6 H, (CH_3)$_2C_6H_2$), and 2.30 (s, 3 H, $CH_3C_6H_2$); ^{13}C-n.m.r., see Table I.

Anal. Calc. for $C_{26}H_{33}NO_9S$: C, 58.30; H, 6.21; N, 2.62. Found: C, 58.10; H, 6.14; N, 2.70.

Cyclization of compound **18** *into 1,6-anhydro derivative* **6**. — The reducing sugar **18** (0.242 g, 0.45 mmol) in absolute ethanol (10 mL) was treated at room temperature for 10 h with 1,8-diazabicyclo[5.4.0]undec-7-ene (0.137 g, 0.9 mmol). After evaporation to dryness, the residue was chromatographed on silica gel (2:1 ethyl acetate–hexane) to afford **6** (0.113 g, 75%), the physical constants of which were identical with those reported earlier in this paper.

ACKNOWLEDGMENTS

The authors thank the C.N.R.S. and the Université Claude Bernard for financial help and Doctor Grahame MacKenzie for fruitful discussions.

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