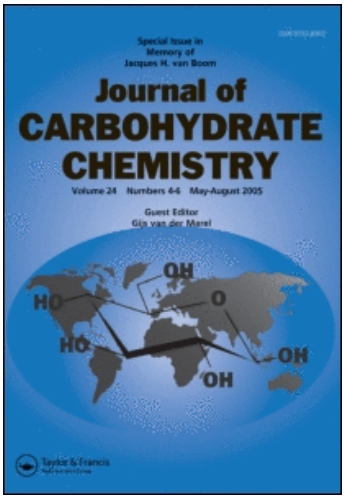


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Syntheses of *N*-Acyl and *N*-Alkoxycarbonyl Derivatives of 2-Alkoxycarbonylamino-2-deoxy-D-glucose

Dominique Lafont[a]; Paul Boullanger[a]
[a] Laboratoire de Chimie Organique II, URA CNRS 463, Université LYON I, ESCIL, Villeurbanne, Cedex, France

To cite this Article Lafont, Dominique and Boullanger, Paul(1992) 'Syntheses of *N*-Acyl and *N*-Alkoxycarbonyl Derivatives of 2-Alkoxycarbonylamino-2-deoxy-D-glucose', Journal of Carbohydrate Chemistry, 11: 5, 567 — 586
To link to this Article: DOI: 10.1080/07328309208016149
URL: http://dx.doi.org/10.1080/07328309208016149

J. CARBOHYDRATE CHEMISTRY, 11(5), 567-586 (1992)

SYNTHESES OF *N*-ACYL AND *N*-ALKOXYCARBONYL DERIVATIVES OF 2-ALKOXYCARBONYLAMINO-2-DEOXY-D-GLUCOSE

Dominique LAFONT* and Paul BOULLANGER

Laboratoire de Chimie Organique II, URA CNRS 463
Université LYON I, ESCIL, 43 Bd du 11 Novembre 1918
69622 VILLEURBANNE Cedex - FRANCE

Received November 19, 1991 - Final Form March 4, 1992

ABSTRACT

N-Acyl and *N*-alkoxycarbonyl derivatives of 1,3,4,6-tetra-*O*-acetyl-2-alkoxycarbonylamino-2-deoxy-β-D-glucopyranose have been synthesized using mixed anhydrides and symmetrical or disymetrical pyrocarbonates.These derivatives have been used as donors in 1,2-*trans*-glycosylation reactions promoted by Lewis acids. Besides the expected β-D-glycosides, cyclisation and rearrangement side-products were often encountered in such glycosylations.

INTRODUCTION

The high reactivity of 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose **1** as donor in glycosylation reactions has been demonstrated using various alcohols.[1-4] In order to extend the field of application of the method to donors disubstituted on nitrogen, we prepared *N*-acyl-*N*-alkoxycarbonyl and *N*,*N*-dialkoxycarbonyl analogues of compound **1**.

To our knowledge, other than the well-known phthalimido derivatives,[5] only a few examples of *N,N*-diacyl derivatives of D-glucosamine have been reported in the literature. These compounds have been previously prepared by *N*-acetylation or *N*-benzoylation of 2-acetamido and 2-benzamido-D-glucose derivatives.[6-8]

RESULTS AND DISCUSSION

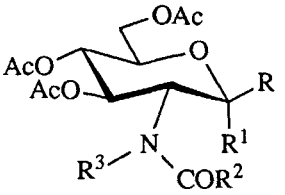
U. Ragnarsson and co-workers have recently described a general method for exhaustive *tert*-butoxycarbonylation of amides[9] and carbamates[10] under very mild conditions, by treatment with di-*tert*-butyl pyrocarbonate and a catalytic amount of 4-dimethylaminopyridine in dry acetonitrile. Similar protection of the amine function (*N,N*-dialkoxycarbonyl derivative) was reported earlier by F. M. F. Chen and N. L. Benoiton[11] in the field of aminoacids.

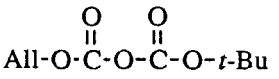
Application of the *N-tert*-butoxycarbonylation method to 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose **1** and to 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose **2** afforded compounds **3** and **4** in high yields (87 % and 85 %, respectively).

However, as we reported earlier,[12] the *N-tert*-butoxycarbonyl group was not stable enough to be used as a protecting group in glycosylation reactions catalyzed by Lewis acids. Therefore, we tried to prepare *N,N*-diallyloxycarbonyl derivatives of D-glucosamine. Attempts to use the commercially available diallyl pyrocarbonate[13] as acylating agent for compound **1** under Ragnarsson's conditions gave rather discouraging results. The lower reactivity of the latter reagent, compared with the di-*tert*-butyl pyrocarbonate and its limited stability in the presence of 4-dimethylaminopyridine, could explain this observation already reported with dimethyl pyrocarbonate.[9]

Nevertheless the reaction of compound **1** with the mixed allyl *tert*-butyl pyrocarbonate **5**, prepared by condensation of allyl chloroformate with sodium *tert*-butyl carbonate, allowed the synthesis of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-diallyloxycarbonylamino-β-D-glucopyranose **6** in good yield (81 %). As expected, the attack on the other carbonyl function of compound **5** was disfavored for steric reasons; the compound **3** was nevertheless formed as a by-product (13 % yield).

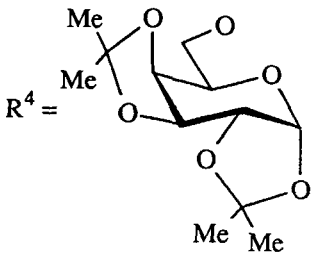
The syntheses of other *N,N*-diacyl derivatives of D-glucosamine were also attempted in the aim of obtaining new glycosyl donors. The *N*-allyloxycarbonyl derivative **1** could not be benzoylated contrariwise to the analogous 2-acetamido compound **2** which could be transformed into the 2-acetamido-1,3,4,6-tetra-*O*-acetyl-*N*-benzoyl-2-deoxy-β-D-glucopyranose **7**[6] in 65 % yield by direct benzoylation with benzoyl chloride in pyridine.

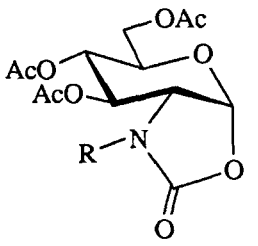




5

1 R = OAc, $R^1 = R^3 = H$, R^2 = OAll
2 R = OAc, $R^1 = R^3 = H$, R^2 = Me
3 R = OAc, R^1 = H, R^2 = OAll, R^3 = COO*t*-Bu
4 R = OAc, R^1 = H, R^2 = Me, R^3 = COO*t*-Bu
6 R = OAc, R^1 = H, R^2 = OAll, R^3 = COOAll
7 R = OAc, R^1 = H, R^2 = Ph, R^3 = COMe
8 R = OAc, R^1 =H, R^2 = Me, R^3 = COOAll
9 R = OAc, R^1 = H, R^2 = Ph, R^3 = COOAll
10 R = OEt, R^1=H, R^2 = OAll, R^3 = COOAll
11 R = O*i*-Pr, R^1 = H, R^2 = OAll, R^3 = COOAll
12 R = R^4, R^1 = H, R^2 = OAll, R^3 = COOAll
15 R = OEt, R^1 = H, R^2 = Me, R^3 = COOAll
16 R = O*i*-Pr, R^1 = H, R^2 = Me, R^3 = COOAll
17 R = R^4, R^1 = H, R^2 = Me, R^3 = COOAll
18 R = H, R^1 = OAc, R^2 = OAll, R^3 = H
20 R = H, R^1 = OBz, R^2 = OAll, R^3 = H





13 R = COOAll
14 R = H
19 R = COPh

Nevertheless, the preparation of a *N*-acetyl-*N*-allyloxycarbonyl compound **8** was realized by *N*-acetylation of the compound **1**, using an *in situ* formed mixed anhydride. The first attempt at acetylation of compound **1** using a mixed anhydride prepared from acetic acid, isobutyl chloroformate and tributylamine[14] was negative and did not afford the expected compound **8**. Another mode of preparation of mixed anhydrides was then considered. As already described by Pozdnev,[15] dialkyl pyrocarbonates could be used for the

TABLE I. ^{1}H NMR chemical shifts of *N*-acylated and *N*-alkoxylated derivatives of D-glucosamine [a]

	Solvent	T(°C)	H-1	H-2	H-3	H-4	H-5	H6a	H6b	NAc	% rotamer
1	CD_3COCD_3	25	5.86	3.85	5.33	5.04	3.94	4.27	4.08		
3	CD_3COCD_3	25	6.36	4.37	5.77	5.07	3.99	4.29	4.17		
4[b]	CD_3SOCD_3	25	6.38	4.31	5.71	4.95	3.99	4.20	4.02	2.18	0.40
			6.23	4.83	5.60	4.95	3.99	4.20	4.02	2.39	0.60
4	CD_3SOCD_3	90	6.30	4.62	5.69	4.95	3.95	4.20	4.08	2.30	
6	CD_3COCD_3	25	6.37	4.45	5.78	5.09	3.99	4.30	4.08		
7	CD_3SOCD_3	90	6.40	4.34	5.78	4.94	4.02	4.20	4.06		
8[b]	CD_3SOCD_3	25	6.38	4.30	5.71	4.97	4.02	4.21	4.01	2.25	0.45
			6.23	4.83	5.60	4.97	4.02	4.21	4.01	2.37	0.55
	CD_3SOCD_3	90	6.29	4.60	5.68	4.97	3.99	4.2	4.07	2.30	
9	CD_3COCD_3	25	6.48	4.58	5.87	5.16	4.07	4.34	4.12		
10	CD_3COCD_3	25	5.24	4.27	5.68	5.02	3.85	4.28	4.10		
11	CD_3COCD_3	25	5.30	4.23	5.69	5.00	3.85	4.28	4.08		

TABLE I (continued).

	Solvent	T(°C)	H-1	H-2	H-3	H-4	H-5	H6a	H6b	NAc	% rotamer
12	CD_3COCD_3	25	5.36	4.30	5.70	5.03	3.93-3.83	4.28	4.11		
			5.44[c]	4.32[c]	4.59[c]	4.21[c]	3.93-3.83[c]	3.93-3.83[c]	3.66[c]		
15[b]	CD_3SOCD_3	25	5.29	4.09	5.61	4.87	3.86	4.19	4.07	2.28	0.43
			5.07	4.62	5.50	4.90	3.86	4.19	4.07	2.36	0.57
	CD_3SOCD_3	90	5.18	4.42	5.57	4.88	3.83	4.19	4.07	2.33	
16[b]	CD_3SOCD_3	25	5.28	4.08	5.63	4.86	3.85	4.21	4.00	2.27	0.47
			5.13	4.59	5.52	4.89	3.85	4.21	4.00	2.35	0.53
	CD_3SOCD_3	90	5.20	4.40	5.58	4.86	3.82	4.19	4.04	2.31	
17	CD_3SOCD_3	90	5.21	4.52	5.59	4.89	3.80	4.19	4.07	2.35	
			5.40[c]	4.29[c]	4.55[c]	4.15[c]	3.80[c]	3.85[c]	3.52[c]		
18	CD_3COCD_3	25	6.18	4.15	5.30	5.13	4.17	4.24	4.05		
20	CD_3COCD_3	25	6.50	4.31	5.52	5.12	4.08	4.31	4.29		

a. Chemical shifts in ppm from internal TMS
b. Two rotamers were observed
c. Galactopyranose moiety

TABLE II. ^{1}H NMR coupling constants of *N*-acylated and *N*-alkoxylated derivatives of D-glucosamine, in deuteroacetone.

Product	Solvent	T(°C)	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	J_{5a6a}	$J_{6a,6b}$
1	CD_3COCD_3	25	8.8	10.5	9.4	10	4.8	2.4	12.5
3	CD_3COCD_3	25	8.6	10.6	9.2	10.2	4.6	2.1	12.4
4[b]	CD_3SOCD_3	25	7.9	9.7	8.6	10.2	4.5	2.1	12.6
			8.5	10.8	9.3	10.0	4.5	2.1	12.6
4	CD_3SOCD_3	90	8.5	10.6	8.9	10.1	4.7	2.5	12.5
6	CD_3COCD_3	25	8.5	10.7	9.1	10.1	4.5	2.1	12.5
7	CD_3SOCD_3	90	8.5	10.5	9.0	10.1	5.0	2.5	12.5
8[b]	CD_3SOCD_3	25	7.9	9.8	8.5	10.2	4.3	2.1	12.6
			8.5	10.7	9.4	10.0	4.3	2.1	12.6
8	CD_3SOCD_3	90	8.3	10.5	9.0	10.1	4.7	2.5	12.4
9	$CDCl_3$	25	8.7	10.6	9.2	9.7	4.4	2.1	12.3
10	CD_3COCD_3	25	8.1	10.8	9.1	10.1	4.6	2.4	12.2
11	CD_3COCD_3	25	8.1	10.8	9.0	10.2	5.0	2.4	12.2
12	CD_3COCD_3	25	8.1	10.7	9.0	10.1	4.0	2.2	12.2
			4.9[c]	2.2[c]	7.9[c]	1.3[c]	-	8.5[c]	12.5[c]

TABLE II (continued).

Product	Solvent	T(°C)	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	J_{5a6a}	$J_{6a,6b}$
15[b]	CD_3SOCD_3	25	8.0	11.0	8.9	10.0	4.2	2.0	12.4
			7.9	11.0	8.9	10.0	4.2	2.0	12.4
15	CD_3SOCD_3	90	8.5	11.0	9.0	10.1	5.0	2.7	12.2
16[b]	CD_3SOCD_3	25	8.4	11.2	8.8	10.0	-	-	-
			8.0	11.0	8.9	10.0	-	-	-
16	CD_3SOCD_3	90	8.0	11.1	9.0	10.0	5.1	2.5	12.2
17	CD_3SOCD_3	90	8.0	11.3	8.9	10.0	4.7	2.6	12.2
			4.9[c]	2.4[c]	7.9[c]	1.8[c]	4.4[c]	6.9[c]	10.7[c]
18	CD_3COCD_3	25	3.4	9.8	9.5	10	4.2	1.8	12.1
20	CD_3COCD_3	25	3.6	10.9	9.5	10.1	4.1	-	12.3

a. Coupling constants in Herz.
b. Two rotamers were observed.
c. Galactopyranose moiety.

TABLE III. ^{13}C NMR Chemical shifts of *N*-acylated and *N*-alkoxylated derivatives of D-glucosamine, in deuteroacetone at room temperature

	C-1	C-2	C-3	C-4	C-5	C-6	NCOOR	NCOR	$NCOCH_3$
1	93.19	55.80	73.27	69.36	73.39	62.58	156.61		
3	91.83	60.39	70.98	69.72	73.26	62.39	ind.		
4[b]	91.54	61.10	70.77	69.55	73.12	62.39	154.14	174.18	27.25
	92.13	56.11	71.67	69.55	73.34	62.39	152.37	173.40	26.40
6	91.72	60.78	70.88	69.52	73.22	62.34	154.27;154.27		
7	91.72	61.84	70.76	69.85	73.26	62.39	ind.	174.96	27.07
8[b]	91.37	61.06	70.78	69.18	73.16	62.06	155.02	174.02	27.22
	92.08	56.40	71.43	69.18	73.16	62.36	153.78	173.21	26.41
9	91.78	59.62	70.71	69.76	73.33	62.36	ind.	172.79	
10	100.12	61.85	71.20	70.30	72.34	62.73	154.43, 153.72		
11	99.10	62.03	71.19	70.36	72.28	62.85	154.45, 153.70		

TABLE III (continued).

	C-1	C-2	C-3	C-4	C-5	C-6	NCOOR	NCOR	$NCOCH_3$
12	101.00	61.96	71.27	70.25	72.34	62.77	154.30, 153.65		
	97.00[c]	71.46[c]	71.14[c]	67.65[c]	71.63[c]	69.14[c]			
15[b]	99.79	62.28	71.13	70.40	72.42	62.85	155.37	174.15	27.27
	100.52	57.66	71.83	70.40	72.42	62.85	154.17	173.19	26.46
16[b]	98.70	62.40	71.10	70.40	72.25	62.89	155.41	174.18	27.24
	99.50	57.80	71.79	70.40	72.25	62.89	154.21	173.11	26.46
17[b]	100.86	62.21	71.19	70.30	72.30	62.80	155.02	174.10	27.48
	102.06	57.18	71.87	70.30	72.30	62.80	153.94	173.41	26.81
	97.34[c]	71.67[c]	71.19[c]	67.87[c]	71.59[c]	69.87[c]			
18	91.20	53.76	70.50	69.16	71.56	62.44	156.73		
20	92.11	54.00	70.87	69.41	71.53	62.46	156.85		

a. Chemical shifts in ppm from internal TMS.
b. Two rotamers were observed.
c. Galatopyranose moiety.

activation of carboxylic acids in the presence of a base. In particular, di-*tert*-butyl pyrocarbonate reacted with carboxylic acids in the presence of pyridine to afford a mixed anhydride of carboxylic and *tert*-butylcarbonic acids. Thus, treatment of a solution of compound **1**, with acetic acid (2.5 equiv), di-*tert*-butyl pyrocarbonate (5 eq) and a catalytic amount of 4-dimethylaminopyridine in acetonitrile afforded 2-acetamido-1,3,4,6-tetra-*O*-acetyl-*N*-allyloxycarbonyl-2-deoxy-β-D-glucopyranose **8** in high yield (90 %). The use of a twofold excess of di-*tert*-butyl pyrocarbonate *versus* acetic acid was necessary to avoid the formation of acetic anhydride by reaction of acetic acid with the mixed anhydride formed in the reaction mixture.[15]

The similar reaction of the mixed anhydride of benzoic and *tert*-butylcarbonic acids (formed *in situ* by reaction of di-*tert*-butyl pyrocarbonate and benzoic acid) with compound **1** did not show any regioselectivity. A mixture of the *N*-allyloxycarbonyl-*N*-*tert*-butoxycarbonyl derivative **3** and the expected *N*-allyloxycarbonyl-*N*-benzoyl compound **9** was thus obtained in respective yields of 46% and 45% due to the reaction of the *N*-allyloxycarbonylamino function on both carbonyl groups of the mixed anhydride.

The structures of compounds **3, 4, 6-9** were established on the basis of ^{1}H and ^{13}C NMR data (Tables I, II and III). *N*-Acetylation or *N*-alkoxycarbonylation of **1** resulted in a substantial deshielding of H-1, H-2 and H-3 (0.4 - 0.7 ppm, Table I). ^{1}H NMR spectra of **4, 7** and **8** revealed the presence of two conformers, the proportions of which were dependent on their structures (**4** : 40/60; **7** : 75/25; **8** : 45/55). This observation could be due to restricted rotations around the amide bond. On increasing the temperature, a coalescence of signals appeared at 60 °C for H-1 and H-3 and at 90 °C for H-2 (FIG. 1). ^{13}C NMR spectra of compounds **4** and **8**, also confirmed the presence of two rotamers at room temperature (chemical shift differences in the range 0.7-0.9 ppm for C-1 and C-3 and 4.6-5.0 ppm for C-2 between both conformations). In the case of the acetamido-*N*-benzoyl compound **7**, the ^{13}C NMR spectrum presented broadened singlets for C-1, C-2 and C-3. Surprisingly the ^{1}H and ^{13}C NMR spectra of the *N*-benzoyl carbamate **9** displayed one form only at room temperature, which could either indicate free rotation around the amide bond or the predominance (>95:5) of one conformer.

Afterwards, compounds **6** and **8** were used as donors in 1,2-*trans* glycosylation reactions, under the conditions reported earlier with the donor **1**.[1-4, 12] The reactions were conducted with a slight excess of alcohol (1.1 equiv.) and one equivalent of trimethylsilyl trifluoromethanesulfonate, with respect to the β-acetate **6** or **8**, at -30 °C, in dichloromethane.

Glycosylation of **6** with ethanol, 2-propanol and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose afforded the expected β-glycosides **10**(81 %), **11**(59 %) and **12**(75 %) together with the *N*-allyloxycarbonyl oxazolidinone by-product **13** (16 %, 36 % and 22 %

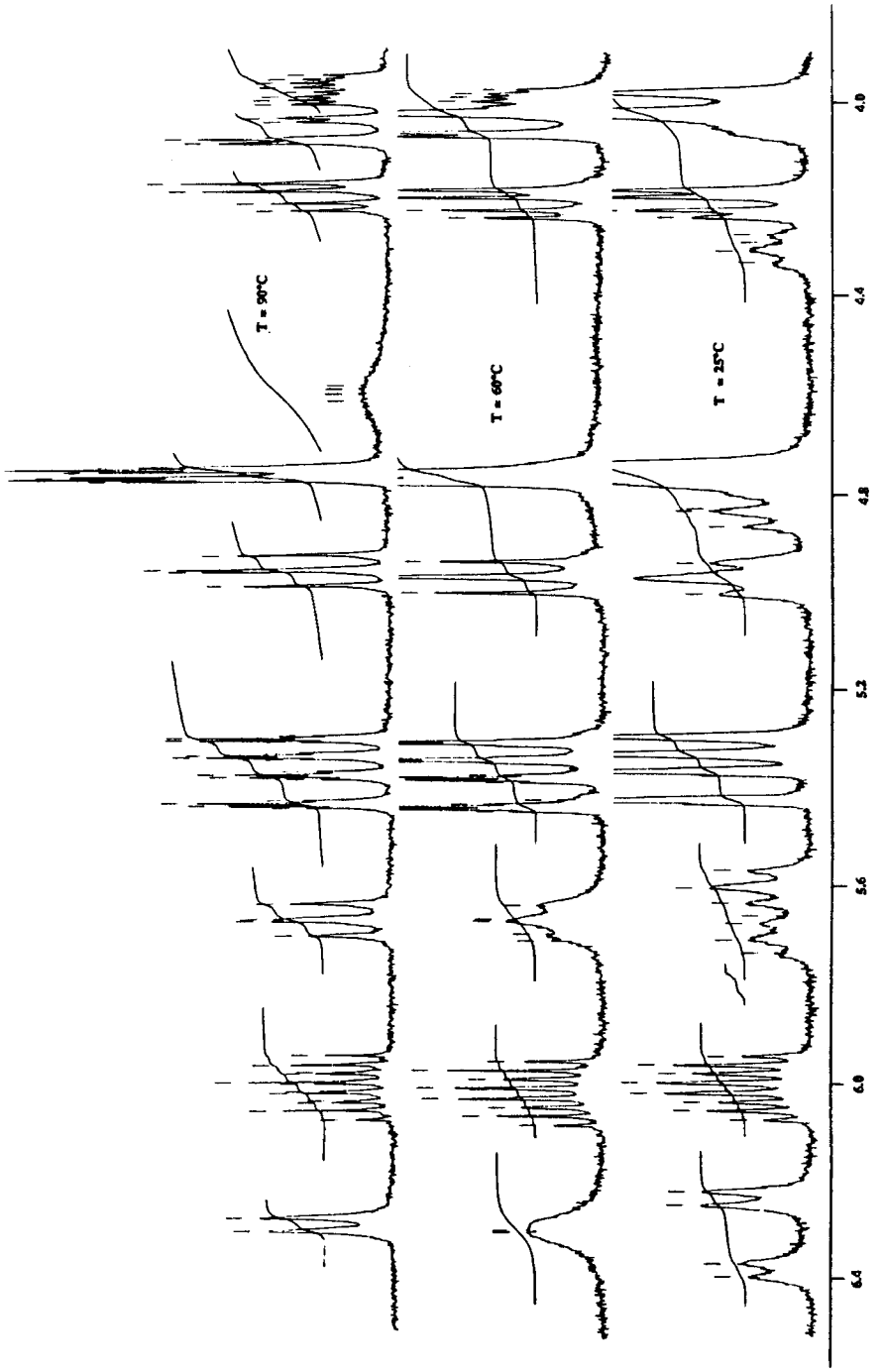


FIG. 1. ^{1}H NMR spectra of compound **8** at different temperatures.

yields, respectively). As we reported earlier,[12] the amount of the cyclization compound **13** increased with the decreasing reactivity of the alcohol. When *tert*-butyl alcohol was used as the acceptor, the latter derivative was obtained as the main product.

In the absence of alcohol, the reaction of **6** with trimethylsilyl trifluoromethanesulfonate afforded the oxazolidinone **13** in 89 % yield. Compound **13** could also be prepared by direct allyloxycarbonylation of the oxazolidinone **14**[16] with allyl chloroformate and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) in dichloromethane.

Under the same conditions, glycosylation of **8** with the same acceptors (ethanol, 2-propanol and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose) afforded the expected β-glycosides **15**(68 %), **16**(56 %) or **17**(60 %), together with 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-α-D-glucopyranose **18**[1] (respective yields: 27 %, 30 % and 28 %). The formation of the α-acetate **18** was probably due to an intramolecular rearrangement, with *N* ->*O* acetyl migration as already observed by Inch *et al.* with the 2-acetamido-*N*-benzoyl-2-deoxy-D-glucopyranose.[6,7]

In order to confirm the latter assessment, compound **8** was treated with trimethylsilyl trifluoromethanesulfonate in the absence of alcohol, under the same conditions. A mixture of two compounds was thus recovered, the ^{1}H NMR spectrum of which exhibited the presence of an anomeric α-acetate for the first one (δ H-1 6.18 ppm, $J_{1,2}$ = 3.4 Hz) and of a *N*-acetylallyloxycarbonylamino function for the second one (δ CH_3 = 2.40 ppm) in the ratio 3:2. Attempts to separate these two compounds were unsuccessful since the slower moving product rearranged to the faster one during column chromatography. We suggest that the slower moving product (tentatively assigned as 2-acetamido-3,4,6-tri-*O*-acetyl-*N*-allyloxycarbonyl-2-deoxy-D-glucopyranose) could have been formed with the allyloxycarbonylamino function acting as the participating group. The faster moving derivative (identical with compound **18**) could have been formed, contrariwise, *via* a *N* ->*O* acetyl migration, with the acetamido function acting as the participating group.

The structure of the glycosides **10** - **12** and **15** - **17** were ascertained by ^{1}H and ^{13}C NMR . The β-configurations were characterized by the values of $J_{1,2}$ and δ C-1 in ^{1}H and ^{13}C NMR spectra respectively (Tables II and III). As reported for compounds **4**, **7** and **8**, the NMR spectra of compounds **15**-**17** also showed mixtures of conformers, at room temperature, in ratios depending on the solvent. When the temperature was raised to 90 °C, rotation around the amide bond became too fast for a spectroscopic differentiation of the rotamers (Tables I, II and III).

The β-acetate **9** was also tested as glycosyl donor under the same conditions. However, glycosylation with 2-propanol gave a complex mixture of compounds which was not analyzed. Furthermore, when the reaction was realized in the absence of alcohol, two major products were obtained in the mixture. Attempts to separate them were un-

successful, but ^{1}H and ^{13}C NMR spectra allowed assignment of the structure **19** to the minor one (17 % yield) and **20** to the major one (68 % yield). The formation of the latter could have resulted from a benzoyl migration from the nitrogen atom to the anomeric oxygen, as already observed starting from **8**.

The structures of compounds **19** and **20** were confirmed by chemical proofs. Thus, the benzoylation of the oxazolidinone **14** in pyridine afforded the *N*-benzoyl oxazolidinone **19** in 92 % yield, and the cleavage of the anomeric acetate of **1** with hydrazine acetate in dimethylformamide,[17] followed by benzoylation of the free anomeric hydroxyl group gave a 6/1 α/β anomeric mixture of **20** (yield 77 %) from which the α-anomer could be isolated in a pure form.

In conclusion, use of the mixed anhydrides or mixed pyrocarbonates allowed us to synthesize *N*-acyl-*N*-alkoxycarbonyl and *N*,*N*-dialkoxycarbonyl derivatives of D-glucosamine in high yields. These products could be used as donors in 1,2-*trans*-glycosylations, but cyclizations and rearrangements in the glycosylation conditions, gave by-products, limiting their interest as donors.

EXPERIMENTAL

General Procedures. Acetonitrile and dichloromethane were dried by refluxing respectively with calcium hydride and phosphorus pentoxide for six hours, then distilled and stored over 4 Å molecular sieves. Tetrahydrofuran was refluxed with sodium-benzophenone mixture under a nitrogen atmosphere until a blue color was obtained, then distilled and stirred over 4 Å molecular sieves. Melting points were determined on an Electrothermal 9100 apparatus and were uncorrected. TLC analyses were performed on aluminium sheets coated with silica gel 60 F 254 Merck. Compounds were visualized by UV light or by spraying the TLC plates with dilute 15 % aqueous sulfuric acid, followed by charring at 150 °C for a few minutes. Column chromatography was performed on Merck-Kieselgel (230-400 mesh ASTM). Optical rotations were measured on a Perkin Elmer 241 polarimeter in a 1 dm cell. ^{1}H and ^{13}C NMR spectra were recorded with a Brucker AM-300 spectrometer at 300 or 75.5 MHz respectively with tetramethylsilane as internal standard. Elemental analyses were realized by the "Laboratoire Central d'Analyses du CNRS" (Solaize, France).

Compounds **1** and **2** were prepared by published methods.[1,18]

1,3,4,6-Tetra-*O*-acetyl-2-allyloxycarbonylamino-*N*-*tert*-butoxycarbonyl-2-deoxy-β-D-glucopyranose (3). A solution of 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose (**1**) (0.432 g, 1 mmol) in dry acetonitrile

(5 mL) was treated with 4-dimethylaminopyridine (0.012 g, 0.1 mmol) and di-*tert*-butyl pyrocarbonate (0.262 g, 1.2 mmol) at room temperature overnight. The solution was then concentrated *in vacuo* and the residue was applied to the top of a silica gel column and then eluted with ethyl acetate/hexane (1:1, v/v) to give the pure compound **3** (0.463 g, 87 %) as a colorless oil: R_f 0.63 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ +24.6 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{23}H_{33}NO_{13}$ (531.50): C, 51.97; H, 6.26; N, 2.64. Found: C, 51.89; H, 6.27; N, 2.68.

2-Acetamido-1,3,4,6-tetra-*O*-acetyl-*N*-*tert*-butoxycarbonyl-2-deoxy-β-D-glucopyranose (4). Compound **4** was obtained from 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose (**2**) as described for the preparation of **3** from **1**. The crude product was purified by column chromatography (ethyl acetate/hexane 2:1, v/v) to give **4** as a colorless oil (0.420 g, 85 %): R_f 0.68 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ +14.8 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{21}H_{31}NO_{12}$ (489.46): C, 51.53; H, 6.38; N, 2.86. Found: C, 51.39; H, 6.41; N, 2.86.

Allyl *tert*-Butyl Pyrocarbonate (5). To a 100 mL, three-necked flask, fitted with a mechanical stirrer, a 50 mL pressure equalizing dropping funnel and a gas-inlet tube (6 mm internal diameter) extending nearly to the bottom of the flask, was poured a solution of sodium *tert*-butoxide (3.8 g, 39.6 mmol) in dry tetrahydrofuran (40 mL), under nitrogen. The reaction flask was immersed in an ice-salt bath maintained at -15 °C, and a stream of anhydrous carbon dioxide was passed through the cold solution for 0.5 h, with stirring. The formation of a thick slurry in the reaction flask was thus observed. Allyl chloroformate (4.6 mL, 43.3 mmol) was then added dropwise followed by tetrahydrofuran (15 mL). When the addition was complete, the solution was allowed to reach room temperature and stirring was maintained for 3 h. The solution was concentrated *in vacuo*, the residue was dissolved in dichloromethane (100 mL) and the organic phase washed twice with water, dried and concentrated to dryness. Finally, the obtained residue was centrifugated to afford a crude colorless syrup **5** which was directly used for the further step (4.8 g, 60 % yield). ^1H NMR ($CDCl_3$) δ 5.95 (m, 1H, C*H*=), 5.47-5.30 (m, 2H, CH_2=), 4.78-4.70 (m, 2H, allyl -CH_2), 1.57 (s, 9H, 3CH_3); ^{13}C NMR ($CDCl_3$) δ 148.92, 148.29 (2 *C*=O), 130.43 (=*C*H-), 120.00 (*C*H_2=), 85.94 (*C*(CH_3)$_3$), 69.73 (allyl *C*H_2-), 27.39 (C(*C*H_3)$_3$).

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-diallyloxycarbonylamino-β-D-glucopyranose (6). Compound **6** was obtained from **1** (1.078 g, 2.5 mmol) and **5** (0.758 g, 3.75 mmol) as already described for the preparation of **3** from **1**. The crude product was purified by column chromatography (ethyl acetate/hexane 1:1 v/v) to afford success-

ively the by-product **3** (0.173 g, 13 % yield) and the expected product **6** as a colorless oil (1.044 g, 81 % yield): R_f 0.58 (ethyl acetate/hexane 1:1 v/v); $[\alpha]_D$ +16.2 (*c* 1.8, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{22}H_{29}NO_{13}$ (515.46): C, 51.26; H, 5.67; N, 2.72. Found: C, 51.04; H, 5.83; N, 2.74.

2-Acetamido-1,3,4,6-tetra-*O*-acetyl-*N*-benzoyl-2-deoxy-β-D-glucopyranose (7). A solution of **2** (1g, 2.57 mmol) and benzoyl chloride (0.3 mL, 0.363 g, 2.56 mmol) in pyridine (10 mL) was stirred overnight at room temperature. After concentration *in vacuo*, the crude residue was directly applied to a silica gel column (ethyl acetate/hexane 3: 2, v/v) to afford the chromatographically pure product **7** as an amorphous solid (0.799 g, 63 %): R_f 0.40 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -22.0 (*c* 1.0, chloroform) (lit.[6] $[\alpha]_D$ - 22; *c* 0.85, chloroform); ^1H and ^{13}C NMR Tables I, II and III.

2-Acetamido-1,3,4,6-tetra-*O*-acetyl-*N*-allyloxycarbonyl-2-deoxy-β-D-glucopyranose (8). Acetic acid (0.297 mL, 5.2 mmol) was added dropwise to a cold (-10 °C) solution of di-*tert*-butyl pyrocarbonate (2.27 g, 10.4 mmol) in dry acetonitrile (10 mL), followed by a catalytic amount of 4-dimethylaminopyridine (0.020 g, 0.16 mmol). The mixture was stirred for 0.5 h at -10 °C and a solution of **1** (0.897 g, 2.08 mmol) in acetonitrile (5 mL) was added in once. The reaction mixture was allowed to reach room temperature and stirring was continued overnight. After concentration *in vacuo*, the brown residue was directly applied to a column of silica gel (ethyl acetate/hexane 1 :1 v/v) to give the pure compound **8** (0.886 g, 90 % yield) as a colorless oil which crystallized from ethanol and hexane: mp 99 °C; R_f 0.55 (ethyl acetate/hexane 1:1 v/v); $[\alpha]_D$ +9.4 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{20}H_{27}NO_{12}$ (473.42): C, 50.74; H, 5.75; N, 2.96. Found: C, 50.53; H, 5.66; N, 3.08.

1,3,4,6-Tetra-*O*-acetyl-2-allyloxycarbonylamino-*N*-benzoyl-2-deoxy-β-D-glucopyranose (9). Benzoic acid (0.767 g, 6.28 mmol) was added to a cold (-10 °C) solution of di-*tert*-butyl pyrocarbonate (1.83 g, 8.38 mmol) in dry acetonitrile (10 mL) followed by a catalytic amount of 4-dimethylaminopyridine. The mixture was stirred for 0.5 h at -10 °C and a solution of **1** (1.083 g, 2.51 mmol) in acetonitrile was added in once. After the same work-up procedure as precedingly, the crude product was purified by column chromatography (ethyl acetate/hexane 2:3 v/v) to afford the pure compounds **3** (0.613 g, 46 %) and **9** (0.605 g, 45 %). Compound **9** was recrystallized from ethanol: mp 130 °C; R_f 0.65 (ethyl acetate/hexane 1:2, v/v); $[\alpha]_D$ +22.3 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{25}H_{29}NO_{12}$ (535.49): C, 56.07; H, 5.46; N, 2.62. Found: C, 56.22; H, 5.36; N, 2.68.

General procedure for glycosylation reactions. The β-acetate **6** or **8** (0.5 mmol) and the acceptor alcohol (0.55 mmol) were added to dry alcohol-free dichloromethane (25 mL). The reaction mixture was flushed with nitrogen while cooling to -30 °C. Trimethylsilyl trifluoromethanesulfonate (FLUKA) (95.2 μL, 0.525 mmol) was then introduced through a syringe and the nitrogen flush maintained for 0.5 h. The mixture was stirred for 16 h at - 30 °C and the reaction was quenched by addition of triethylamine (0.148 mL, 1.05 mmol). The mixture was then poured into a saturated aqueous solution of sodium hydrogencarbonate and the products were extracted with dichloromethane. After drying and concentration *in vacuo*, the organic phase led to a mixture which was purified by column chromatography.

Ethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-diallyloxycarbonylamino-β-D-glucopyranoside (10). Prepared following the general glycosylation procedure (**6** as donor, ethanol as acceptor alcohol). Purification of the residue on a silica gel column (ethyl acetate/hexane 1:1, v/v) afforded compound **10** (0.203 g, 81 %) as a colorless oil: R_f 0.68 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -9.5 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{22}H_{31}NO_{12}$ (501.47): C, 52.69; H, 6.23; N, 2.79. Found: C, 52.74; H, 6.25; N, 2.87.

Further elution afforded compound **13** (0.037 g, 16 %), R_f 0.38.

Isopropyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-diallyloxycarbonylamino-β-D-glucopyranoside (11). Prepared following the general glycosylation procedure (**6** as donor, 2-propanol as acceptor alcohol). Purification of the residue on a silica gel column afforded compound **11** (0.152 g, 59 %) as a colorless oil: R_f 0.63 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -18.8 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{23}H_{33}NO_{12}$ (515.50): C, 53.58; H, 6.45; N, 2.72. Found: C, 53.38; H, 6.50; N, 2.68.

Further elution afforded compound **13** (0.075 g; 36 %).

6-*O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-diallyloxycarbonylamino-β-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (12). Prepared following the general glycosylation procedure (**6** as donor, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose as acceptor alcohol). Purification on a column of silica gel afforded compound **12** (0.270 g, 75 %) as a colorless oil: R_f 0.59 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -44.5 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{32}H_{45}NO_{17}$ (715.69): C, 53.70; H, 6.34; N, 1.96. Found: C, 53.98; H, 6.39; N, 2.02.

Further elution afforded a mixture of compound **13** (0.031 g; 15 %) and unreacted acceptor alcohol (0.033 g, 22 %).

3-Allyloxycarbonyl-[3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano]-*[2,1-d]*-2-oxazolidinone (13). Method A : Compound **13** could be prepared from **6** as previously described for glycosylation reactions but in absence of alcohol, with a 89 % yield after column chromatography (ethyl acetate/hexane 1:1 v/v). The product **13** crystallized from dichloromethane-hexane and was recrystallized from ethanol: mp 106 °C (ethanol); R_f 0.38 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -25.7 (*c* 1.0, chloroform); ^1H NMR (CD_3COCD_3) δ 6.13 (d, 1H, $J_{1,2}$ = 7.1 Hz, H-1), 5.99 (m, 1H, -C*H*=), 5.55 (dd, 1H, $J_{2,3}$ = 4.0 Hz, $J_{3,4}$ = 4.2 Hz, H-3), 5.44 and 5.25 (m, 2H, CH_2=), 5.02 (ddd, 1H, $J_{2,4}$ = 0.6Hz, $J_{4,5}$ = 7.4 Hz, H-4), 4.79 - 4.68 (m, 2H, allyl -CH_2-), 4.67 (ddd, 1H, H-2), 4.27 (dd 1H, $J_{5,6a}$ = 5.5 Hz, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.22 (dd, 1H, $J_{5,6b}$ = 3.6 Hz, H-6b), 4.08 (ddd, 1H, H-5), 2.06, 2.01, 1.99 (3s, 9H, 3CH_3CO). ^{13}C NMR (CD_3COCD_3) δ 170.64, 169.74, 169.63 (3C, *C*=O acetates), 150.97, 150.18 (2C, N-*C*=O), 132.47 (*C*H=), 118.82 (*C*H_2=), 94.85 (C-1), 70.14 , 68.50, 67.15 (C-3,4,5), 68.07 (*C*H_2-allyl), 63.79 (C-6), 55.14 (C-2), 20.76, 20.60, 20.58 (3C, *C*H_3 acetates).

Anal. Calcd for $C_{17}H_{21}NO_{11}$ (415.345): C, 49.16; H, 5.10; N, 3.37. Found: C, 48.98; H, 5.10; N, 3.50.

- Method B : A solution of the oxazolidinone **14**[12] (0.780 g, 2.3 mmol) in dry dichloromethane was stirred for 2 h with 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) (1.7 mL, 11.5 mmol, 5 eq) and allyl chloroformate (0.6 mL, 5.6 mmol). After concentration *in vacuo*, the crude residue was purified by column chromatography to give the pure product **13** (0.760 g) in 85 % yield.

Ethyl 2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-allyloxycarbonyl-2-deoxy-β-D-glucopyranoside (15). Prepared following the general glycosylation procedure (**8** as donor, ethanol as acceptor alcohol). Purification of the residue on a column of silica gel (ethyl acetate/hexane 1:1, v/v) afforded compound **15** as a colorless oil (0.156 g, 68 %): R_f 0.58 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -17.0 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{20}H_{29}NO_{11}$ (459.44): C, 52.28; H, 6.36; N, 3.05. Found: C, 52.31; H, 6.43; N, 3.10.

Further elution afforded compound **18** (0.058 g, 27 %).

Isopropyl 2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-allyloxycarbonyl-2-deoxy-β-D-glucopyranoside (16). Obtained, following the general glycosylation procedure (**8** as donor, 2-propanol as acceptor alcohol), in 56 % yield after chromatographic purification; **16** was a colorless oil: R_f 0.73 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -23.8 (*c* 1.0, chloroform); ^1H and ^{13}C NMR Tables I, II and III.

Anal. Calcd for $C_{21}H_{31}NO_{11}$ (473.46): C, 53.27; H, 6.60; N, 2.96. Found: C, 53.13; H, 6.55; N, 3.20.

Further elution afforded the compound **18** (0.065g, 30 %).

6-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-allyloxycarbonyl-2-deoxy-β-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (17). Prepared as described above from **8** (0.50 mmol) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.55 mmol). Purification of the residue on a column of silica gel (ethyl acetate/hexane 1:2, v/v) afforded successively the disaccharide **17** (0.202 g, 60 %) and the α-acetate **18** (0.058 g, 27 %) followed by the unreacted alcohol (0.041 g, 28 %). Compound **17** was a colorless oil: R_f 0.58 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -43.7 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $C_{30}H_{43}NO_{14}$ (672.65): C, 53.48; H, 6.43; N, 2.08. Found: C, 53.22; H, 6.45; N, 2.05.

1,3,4,6-Tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-α-D-glucopyranose (18). Compound **8** (0.50 mmol) was treated overnight with trimethylsilyl trifluoromethanesulfonate (0.50 mmol) at -30 °C in dichloromethane (25 mL). After usual work-up, TLC of the crude product showed the presence of two compounds (R_f 0.70 and R_f 0.52 in dichloromethane/acetone 6:1, v/v) and ^1H NMR exhibited an anomeric acetate (δ H-1 6.18 ppm) and a *N*-acetyl group (δ CH_3 ~ 2.40 ppm) in the ratio 3:2. Attempts to separate the two compounds on a column of silica gel with the same eluent afforded only the first product (R_f = 0.70) in 82 % yield, which crystallized from ether. Compound **18** had mp 120 °C (lit.[1] mp 119-121 °C); R_f 0.51 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ +91.7 (*c* 1.0, chloroform); ^1H and ^{13}C NMR, Tables I, II and III.

3-Benzoyl-[3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano]-*[2,1-d]*-2-oxazolidinone (19). To a cold (0 °C) solution of oxazolidinone **14**[12] (0.200 g, 0.60 mmol) in dry pyridine was added benzoyl chloride (0.14 mL, 2 eq) and 4-dimethylaminopyridine (0.005 g). The solution was allowed to reach room temperature and stirring was maintained overnight. After concentration of the solution, the residue was applied to the top of a silica gel column (ethyl acetate/hexane 1:1, v/v) to give product **20** which crystallized from ethanol (0.240 g, 92 % yield): mp 162 °C; R_f 0.63 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ -69.3 (*c* 1.0, chloroform); ^1H NMR (CD_3COCD_3) δ 7.77-7.44 (m, 5H, H aromat.), 6.21 (d, 1H, $J_{1,2}$ = 7.1 Hz, H-1), 5.55 (dd, 1H, $J_{3,2}$ = 3.5 Hz, $J_{3,4}$ = 2.6 Hz, H-3), 5.11 (m, 1H, $J_{4,5}$ = 6.1 Hz, H-4), 4.98 (ddd, 1H,$J_{2,4}$ = 1.2 Hz, H-2), 4.35-4.25 (m, 3H, H-5,6a,6b), 2.10, 2.04, 1.87 (3S,.9 H, 3C*H*$_3$CO). ^{13}C NMR (CD_3COCD_3) δ 170.69, 169.70, 169.68, 169.50 (4 *C*=O), 152.66 (N-*C*=O), 134.27 - 128.60 (C aromat.), 94.87 (C-1), 69.73, 67.54, 67.27 (3C, C-3,4,5), 64.18 (C-6), 53.85 (C-2), 20.73, 20.60, 20.60 (3C, *C*H_3 acetates).

Anal. Calcd for $C_{20}H_{21}NO_{10}$ (435.37): C, 55.17; H, 4.86; N, 3.22. Found: C, 55.04; H, 4.98; N, 3.14.

3,4,6-Tri-*O*-acetyl-2-allyloxycarbonylamino-1-*O*-benzoyl-2-deoxy-α-D-glucopyranose (20). The β-acetate **1** (1g, 2.32 mmmol) was treated for 5 min at 50 °C with hydrazine acetate (0.195 g, 2.78 mmol) in dry dimethylformamide. After addition of ethyl acetate, the mixture was washed with brine (2 x 5 mL), and the organic phase dried and concentrated *in vacuo*. The residue was quickly purified by column chromatography to afford the α,β-hemiacetal (0.768 g, 85 %) which was dissolved in pyridine (5 mL) and treated overnight with benzoyl chloride (0.46 mL, 2 eq). After concentration, the crude residue was purified by column chromatography (ethyl acetate/hexane 1:1, v/v) to afford successively the pure α-anomer **20** (0.390 g, 40 %) and an α,β-mixture (0.360 g, 37 %, α:β=7:3). Compound **20α** was an amorphous solid, R_f 0.60 (ethyl acetate/hexane 1:1, v/v); $[\alpha]_D$ +115.7 (*c* 1.0, chloroform); ^1H NMR and ^{13}C NMR, Tables I, II and III.

Anal. Calcd for $_{23}H_{27}NO_{11}$ (493.45): C, 55.98; H, 5.52; N, 2.84. Found: C, 55.63; H, 5.66; N, 2.77.

Compound **20β** had R_f 0.58 (ethyl acetate/hexane 1:1, v/v); ^1H NMR ($CDCl_3$) δ 6.00 (1H, H-1, $J_{1,2}$ = 6.8 Hz).

REFERENCES

1. P. Boullanger, J. Banoub and G. Descotes, *Can. J. Chem.*, **65**, 1343 (1987).
2. P. Boullanger, D. Lafont, J. Banoub and G. Descotes, *J. Carbohydr. Chem.*, **8**, 343 (1989).
3. D. Lafont, P. Boullanger, J. Banoub and G. Descotes, *Can. J. Chem.*, **68**, 828 (1990).
4. D. Lafont, S. Manaudier, P. Boullanger and G. Descotes, *Bull. Chim. Soc. Fr.*, **127**, 576 (1990).
5. B. R. Baker, J. P. Joseph, R. E. Schaub and J. H. Williams, *J. Org. Chem.*, **19**, 1786 (1954).
6. T. D. Inch and H. G. Fletcher Jr., *J. Org. Chem.*, **31**, 1815 (1966).
7. T. D. Inch and H. G. Fletcher Jr., *J. Org. Chem.*, **31**, 1821 (1966).
8. R. U. Lemieux and M.H. Burzynska, *Can. J. Chem.*, **60**, 76 (1982).
9. L. Grahn, K. Gunnarsson and U. Ragnarsson, *Acta. Chem. Scand., Ser. B*, **40**, 745 (1986).
10. K. Gunnarsson and U. Ragnarsson, *Acta. Chem. Scand., Ser. B*, **44**, 944 (1990).
11. F. M. F. Chen and N.L. Benoiton, *Can. J. Chem.*, **65**, 1228 (1987).

12. P. Boullanger, M. Jouineau, B. Bouammali, D. Lafont and G. Descotes, *Carbohydr. Res.*, **202**, 151 (1990).

13. G. Sennyey, G. Barcelo and J. P. Senet, *Tetrahedron Lett.*, **28**, 5809 (1987).

14. R. A. Boissonnas, *Helv. Chim. Acta.*, **34**, 874 (1951).

15. V. F. Pozdnev, *Zh. Org. Khim.*, **19**, 882 (1983).

16. T. Suami, S. Ogawa and S. Umezawa, *Bull. Chem. Soc. Jpn.*, **36**, 459 (1963).

17. G. Excoffier, D. Gagnaire and J. P. Utille, *Carbohydr. Res.*, **39**, 368 (1975).

18. M. Bergmann and L. Zervas, *Chem. Ber.*, **64**, 975 (1931).