26. A ^{1}H-NMR Spectroscopic Investigation of the Conformation of the Acetamido Group in Some Derivatives of *N*-Acetyl-D-allosamine and -D-glucosamine

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The population of the conformations obtained by rotation around the C(2)–N and the N–C(O) bonds of AllNAc, GlcNAc, and GlcNMeAc derivatives was investigated by ^{1}H-NMR spectroscopy. The AllNAc-derived α-D- and β-D-pyranosides **4**–**7**, the AllNAc diazirine **16**, and the GlcNAc-derived axial anomers α-D-**8**–**10** prefer the (*Z*)-*anti*-conformation. A significant population of the (*Z*)-*syn*-conformer in the (*Z*)-*syn*/(*Z*)-*anti*-equilibrium for the equatorial anomers β-D-**8**–**10** and the GlcNAc diazirine **17** was evidenced by an upfield shift of H–C(2), downfield shifts of H–C(1) and H–C(3), and by NOE measurements. The population of the (*Z*)-*syn*-conformation depends on the substituent at C(1) and is highest for the hexafluoroisopropyl glycoside. The population of the (*Z*)-*syn*-conformation of β-D-**14** decreases with increasing polarity of the solvent, but a substantial population is still observed for solutions in D_2O. Whereas the α-D-anomers of the hemiacetal **22** and the methyl glycoside **21** prefer the (*Z*)-*anti*-conformation in D_2O solution, the corresponding β-D-anomers are mixtures of the (*Z*)-*anti*- and (*Z*)-*syn*-conformers. The diazirine **17** self-associates in CD_2Cl_2 solution at concentrations above 0.005M at low temperatures. The axial anomers of the GlcNMeAc derivatives α-D-**26**–**28** are 2:1 to 3:1 mixtures of (*Z*)-*anti*- and (*E*)-*anti*-conformers, whereas the corresponding β-D-glycosides are *ca.* 1:3:6 mixtures of (*Z*)-*syn*-, (*Z*)-*anti*-, and (*E*)-*anti*-conformers.

Introduction. – We have described an unprecedented neighboring-group participation of the acetamido group in the glycosidation of alcohols by the diazirines **16** and **17** derived from 2-acetamido-2-deoxyhexoses, leading preferentially to α-D-glycosides [1]. We rationalized this selectivity on the basis of a *bona fide* H-bond from the appropriately oriented acetamido group of the reactive intermediates to the glycosyl acceptor. This raises the question about the conformation of the NHAc–C(2) group, which is of evident importance considering the prominent biological role of *N*-acetylglucosamine and its glycosides. There is evidence that the conformational behavior of the NHAc–C(2) group depends upon the constitution and configuration of the saccharide. The extent of the dependence of the chemical shift of the H–N group on the temperature is a criterium for inter- *vs.* intramolecular H-bonds. It is linear and in agreement with an intramolecular H-bond for solutions in CD_2Cl_2 of the *N*-acetylallosamine-derived diazirine **16**, but nonlinear for the *N*-acetylglucosamine analogue **17** [1]; it is also linear and in agreement with an intramolecular H-bond for the hexafluoroisopropyl *N*-acetyl-allosamine α-D-**6** and for the hexafluoroisopropyl *N*-acetylglucosamine α-D-**9**, but again curved for the anomer β-D-**9**.

As a rule, the NMR spectra of secondary acetamides (RR′CH–NHAc) show the presence of a single conformer. The rather large vicinal J(C–*H*,N–*H*) value [2] is compatible with either the antiperiplanar or the synperiplanar arrangement of the C–H

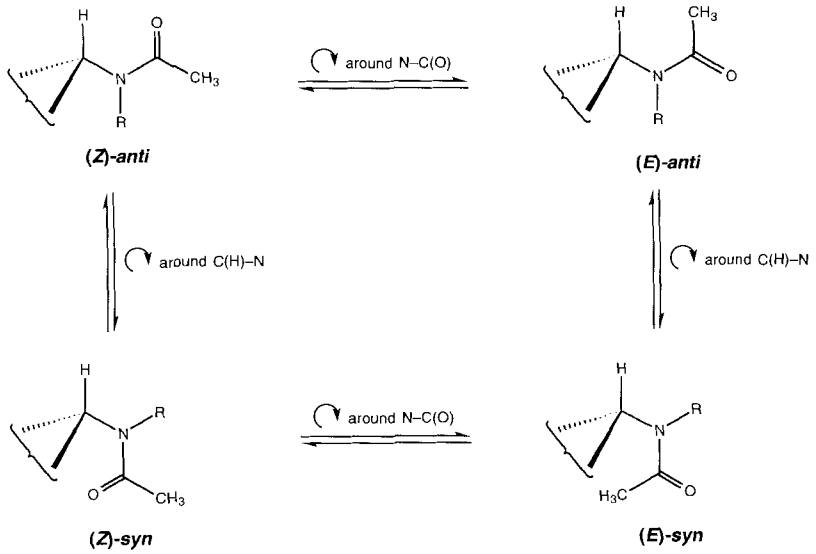
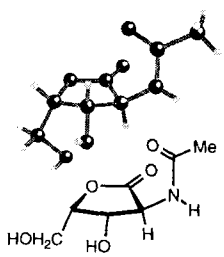


Fig. 1. *The equilibria obtained by rotation around C(H)–N and N–C(O) bonds of acetamides* (R = H or Me)

and the N–H bond[1]). The four conformers depicted in *Fig. 1* and the equilibria between them have to be evaluated. The (*E*)-conformers are less stable than the (*Z*)-conformers due to the unfavorable *cis*-interaction of the CH_3 and the RR'CH groups. Indeed, there are no examples for (*E*)-configurated acetamides in the *Cambridge Data Base*. The dominant part of the entries (*ca.* 250) show the (*Z*)-*anti*-conformation. Both the (*Z*)-*anti*- and (*Z*)-*syn*-conformers are present in a clathrate of *N*-acetylmethionine ethyl ester [14]. The L-arabinonolactone **1** is the only acetamide which crystallizes exclusively as the (*Z*)-*syn*-conformer [15].

The configuration and conformation of sugar amides and thioamides in solution has recently been reviewed [16]. Whereas formamides and *N*,*N*-disubstituted acetamides are



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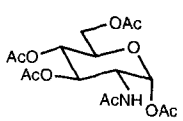

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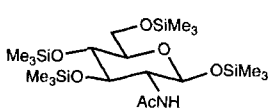

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[1]) According to the *Karplus* equation of *Bystrov* [3], $J(H–C,N–H)$ is 10.9 Hz for the antiperiplanar (*anti*; $\phi = 180°$) and 8.7 Hz for the synperiplanar (*syn*; $\phi = 0°$) arrangement of H–C and H–N. *Hirano* [4] favored the antiperiplanar conformation due to weaker steric interactions. In the following, the antiperiplanar arrangement is assigned on the basis of 'large' $J(C–H,N–H)$ values [5–13]. The assignment of the (*Z*)-*anti*-conformation (*cf. Fig. 1*) for protected β-D-GlcNAc derivatives [7] [12] [13] may be wrong.

mixtures of (*Z*)-*anti*- and (*E*)-*anti*-conformers, **2** and the few examples of β-D-glucopyranosylacetamides mentioned in [16] occur only as (*Z*)-*anti*-conformers above 200 K, as deduced from the similarity of their ^{1}H-NMR spectra with those of (*Z*)-*anti*-formamides [16]. However, *Vliegenthart* and coworkers [17] claimed to have detected the (*Z*)-*syn*-conformers of the β-D-GlcNAc derivative **3** and of its β-D-GalNAc analogue in acetone solution at $T < 235$ K. Also, a weak long-range coupling between the formyl H and H–C(4) of a 4-deoxy-4-formamido-mannopyranoside (W-arrangement) has been explained by the population of the (*Z*)-*syn*-conformation [18]. Recently, however, it has been shown that such long-range couplings occur both in (*Z*)-*anti*- and (*E*)-*anti*-formamides, and probably have to be interpreted as pseudoallylic couplings, considering the partial double-bond character of the N–C(O) bond [19].

The rotamer equilibria related to the C(H)–N bond of acetamides may be influenced by the substituents at neighboring C-atoms. Therefore, we investigated the conformation of NHAc–C(2) in α-D- and β-D-GlcNAc and α-D- and β-D-AllNAc derivatives, embodying the four fundamental types of diastereoisomers possessing an equatorial NHAc group.

Results and Discussion. – 1. *Molecular-Mechanics Calculations.* Methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-methyl-α/β-D-allopyranosides and -α/β-D-glucopyranosides (α/β-D-**14**) were used for molecular-mechanics calculations (Macromodel V. 4.5 [20], MM3* force field, gas phase). The energy of the conformers obtained by stepwise (20°) rotation around the C(2)–N bond was calculated. Maxima occur when the C=O group has close contact to a MeO group. The destabilization is due to unfavorable steric and dipole-dipole interactions that are stronger for equatorial than for axial MeO groups[2]). The conformers exhibiting the largest distances between the C=O and both MeO groups are global minima. The (*Z*)-*anti*-conformers of the *O*-methylated α-D-allo-, β-D-allo-, and α-D-glucopyranosides (dihedral angle H–C(2)–N–H of ±150, −135, and +135°, resp.) are 8.0, 2.7, and 2.8 kcal/mol more stable than the corresponding (*Z*)-*syn*-conformers (dihedral angle H–C(2)–N–H of *ca.* ±10°). The (*Z*)-*anti*-conformer of the *O*-methylated β-D-glucopyranoside, however, is destabilized by two equatorial MeO groups, and the (*Z*)-*syn*-conformer is 4.0 kcal/mol more stable[3]). Calculation shows also that the (*E*)-*anti*-conformers may be neglected in the rotamer equilibrium, being always *ca.* 4 kcal/mol higher in energy than the (*Z*)-*anti*-conformers.

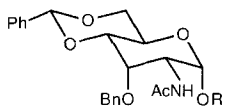
2. *Analysis of the ^{1}H-NMR Spectra of Protected 2-Acetamido-2-deoxy-*D*-allo- and -*D*-glucopyranosides.* The chemical-shift difference for the signals of H–C geminal to the *N*-substituent is characteristic for the conformations of sugar thioformamides and formamides [16]. H–C of the (*Z*)-*anti*-conformer (1,5-interaction of H–C and X=C = 1,3-diaxial-type interaction) is deshielded by *ca.* 0.8–1.6 ppm relative to H–C of the (*E*)-*anti*-conformer (1,5-interaction of H–C and H–C(X)), *i.e.* this deshielding is due to the proximity of the X=C group (*cf.* [21]). A similar chemical-shift difference is expected for the corresponding H–C signal of the (*Z*)-*anti*- and the (*Z*)-*syn*-conformers (synperipla-

[2]) Compare with similar barriers in *N*-phthaloylallosamine derivatives [21].

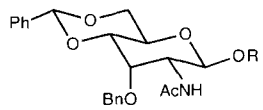
[3]) The (*Z*)-*syn*-conformer of β-D-GlcNAc derivatives is the most stable conformer according to empirical energy [22] and PCILO semi-empirical quantum chemical calculations [23]. Other semi-empirical quantum calculations, however, favor the (*Z*)-*anti*-conformer (MNDO: H–N antiperiplanar to H–C(2); CNDO, INDO, and PCILO: H–N synperiplanar to C(1)–C(2) [24]).

nar arrangement of H–C and H–N)[4]). The chemical shift of the H–C vicinal to the *N*-substituent (corresponding to H–C(1) and H–C(3) of 2-(acylamino)-2-deoxyhexoses) is not influenced by the (*E*)/(*Z*)-equilibrium (*cf.* [16]). The *anti*/*syn*-equilibrium, however, should affect the chemical shifts of the vicinal H–C, and one expects that a (*Z*)-*anti*/(*Z*)-*syn*-equilibrium of AllNAc and GlcNAc derivatives is reflected by the chemical-shift values of H–C(2), H–C(1), and H–C(3).

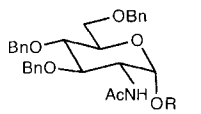
H–C(2) of the β-D-anomer of the alkyl 2-acetamido-2-deoxy-allopyranosides **4–6** [1] [29] resonates by *ca.* 0.1 ppm at higher field than H–C(2) of the corresponding α-D-anomer (solutions in $CDCl_3$; *Table 1*). H–C(2) of both anomers of the aryl 2-acetamido-2-deoxy-allopyranoside **7** [1] appears at the same position. Similar $\Delta\delta$ values[5]) as for



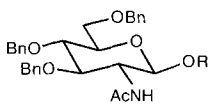
α-D-**4** R = Me
α-D-**5** R = Me_2CH
α-D-**6** R = $(F_3C)_2CH$
α-D-**7** R = $O_2NC_6H_4$



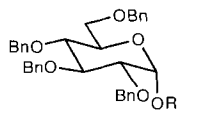
β-D-**4** R = Me
β-D-**5** R = Me_2CH
β-D-**6** R = $(F_3C)_2CH$
β-D-**7** R = $O_2NC_6H_4$



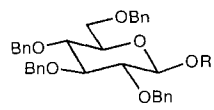
α-D-**8** R = Me
α-D-**9** R = $(F_3C)_2CH$
α-D-**10** R = $O_2NC_6H_4$



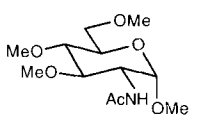
β-D-**8** R = Me
β-D-**9** R = $(F_3C)_2CH$
β-D-**10** R = $O_2NC_6H_4$



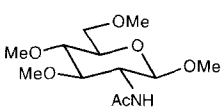
α-D-**11** R = Me
α-D-**12** R = $(F_3C)_2CH$
α-D-**13** R = $O_2NC_6H_4$



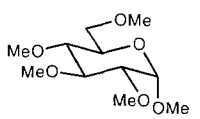
β-D-**11** R = Me
β-D-**12** R = $(F_3C)_2CH$
β-D-**13** R = $O_2NC_6H_4$



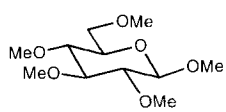
α-D-**14**



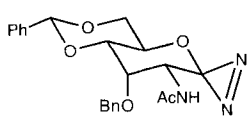
β-D-**14**



α-D-**15**



β-D-**15**



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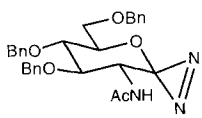

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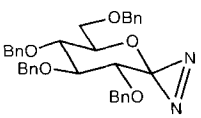

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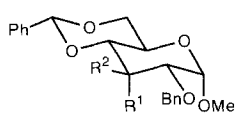

19 R^1 = OBn, R^2 = H
20 R^1 = H, R^2 = OBn

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[4]) The chemical-shift values for H–C of a pure (*Z*)-*syn*-acetamide is not known. H–C(1) of 2-azabicyclo-[2.2.2]octan-3-one resonates at 3.65 ppm [25] and is synperiplanar to H–N (dihedral angle H–C(1)–N–H of 0°), but some deshielding may be due to its bridgehead position. The axial H–C(2) of pyranosides derived from 2-amino-2-deoxyallose [26] and -glucose [27] [28] resonates at 2.7–3 ppm.

[5]) $\Delta\delta$ values are taken as the difference of the chemical-shift values δ(β-D-anomer) – δ(α-D-anomer) (*Chapt. 2* and *4*, *Tables 1–3* and *5*) or δ(diazirine) – δ(corresponding methyl α-D-pyranoside) (*Chapt. 3*, *Table 4*).

Table 1. *Selected Chemical-Shift Values* [ppm] *and Coupling Constants* [Hz] *of the AllNAc Glycosides* **4**–**7**, *the Alloside* **19**, *the GlcNAc Glycosides* **8**–**10**, *and the Glucosides* **11**–**13** *and* **20** *in* $CDCl_3$ *Solution*. In parentheses $\Delta\delta$ values[5]).

	H–C(1)	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H–N	J(2,NH)
α-D-**4** [1]	4.61	4.27	4.05	3.72	4.39–4.28	5.99	9.3
α-D-**5** [2]	4.83	4.26	4.05	3.72	4.43	6.02	9.3
α-D-**6** [1]	5.03	4.42–4.35	4.06	3.78	4.48	6.03	9.3
α-D-**7** [1]	5.59	4.50	4.16	3.83	4.39	6.07	9.3
β-D-**4** [29]	4.55 (−0.06)	4.18–4.09 (*ca.* −0.13)	4.18–4.09 (*ca.* +0.09)	3.74 (+0.02)	4.10 (*ca.* −0.24)	5.70	8.8
β-D-**5** [1]	4.64 (−0.19)	4.14–4.04 (*ca.* −0.17)	4.14–4.04 (*ca.* +0.04)	3.75 (+0.03)	4.14–4.04 (*ca.* −0.34)	5.62	9.2
β-D-**6** [1]	4.80 (−0.23)	4.27 (*ca.* −0.11)	4.11 (+0.05)	3.79 (+0.01)	4.48–4-37 (*ca.* −0.05)	5.63	9.7
β-D-**7** [1]	5.29 (−0.30)	4.49 (−0.01)	4.18 (+0.02)	3.86 (+0.03)	4.30 (−0.09)	5.75	9.6
α-D-**8** [29]	4.68	4.26	3.79–3.59	3.79–3.59	3.79–3.59	5.29	9.3
α-D-**9** [1]	5.14	4.28	3.69	3.88–3.79	3.88–3.79	5.06	8.7
α-D-**10** [1]	5.70	4.37	3.91–3.87	3.91–3.87	3.75	5.15	8.3
β-D-**8** [29]	4.71 (+0.03)	3.45 (−0.81)	4.06 (*ca.* +0.37)	3.79–3.59	3.79–3.59	5.51	8.1
β-D-**9** [1]	5.21 (+0.07)	3.26 (−1.02)	4.33 (+0.64)	3.76–3.59	3.76–3.59	5.60	7.3
β-D-**10** [1]	5.58 (−0.12)	3.91–3.85 (*ca.* −0.49)	4.13 (*ca.* +0.24)	3.75 (*ca.* −0.14)	3.91–3.85 (*ca.* +0.13)	5.84	7.9
α-D-**11** [30]	4.63	3.56	3.98	3.66–3.61	3.74	–	–
α-D-**12** [30]	5.15	3.65	3.97	3.71	3.88	–	–
α-D-**13** [4]	5.45	3.75	4.18	3.80	3.80–3.65	–	–
β-D-**11** [30]	4.32 (−0.31)	3.44 (−0.12)	3.65 (−0.33)	3.60 (*ca.* −0.03)	3.47 (−0.27)	–	–
β-D-**12** [30]	4.67 (−0.48)	3.54 (−0.11)	3.68–3.58 (*ca.* −0.34)	3.68–3.58 (*ca.* −0.08)	3.49 (−0.39)	–	–
β-D-**13** [31]	5.09 (−0.36)	3.82–3.73 (*ca.* +0.03)	3.82–3.73 (*ca.* −0.40)	3.71–3.62 (*ca.* −0.13)	3.82–3.73	–	–
19	4.72	3.45	4.20	3.50	3.70–3.62	–	–
20	4.61	3.57	4.06	3.61	3.84	–	–

Table 2. *Selected Chemical-Shift Values* [ppm] *and Coupling Constants* [Hz] *of the GlcNAc Glycosides* **8**–**14** *and the Glucosides* **11** *and* **15** *in* CD_2Cl_2 *Solution*. In parentheses $\Delta\delta$ values[5]).

	H–C(1)	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H–N	J(2,NH)
α-D-**8**	4.62	4.17	3.69	3.65	3.72	5.44	9.5
α-D-**9** [1]	5.12	4.24	3.70	3.80	3.86	5.22	8.8
α-D-**14**	4.56	4.05	3.29	3.18	*ca.* 3.56	5.64	8.9
β-D-**8**	4.49 (−0.13)	3.59 (−0.58)	3.81 (+0.12)	3.64 (−0.01)	3.52 (−0.20)	5.47	8.6
β-D-**9** [1]	5.09 (−0.03)	3.40 (−0.84)	4.14 (+0.44)	3.66 (−0.14)	3.57 (−0.29)	5.60	7.9
β-D-**14**	4.45 (−0.11)	3.43 (−0.62)	3.47 (+0.18)	3.16 (−0.02)	3.35 (*ca.* −0.21)	5.63	6.7
α-D-**11**	4.72	3.54	3.90	3.60	*ca.* 3.70	–	–
α-D-**15**	4.75	3.13	3.38	3.07	*ca.* 3.52	–	–
β-D-**11**	4.32 (−0.40)	3.37 (−0.17)	*ca.* 3.60 (*ca.* −0.30)	*ca.* 3.60 (*ca.* 0)	3.45 (*ca.* −0.25)	–	–
β-D-**15**	4.10 (−0.65)	2.89 (−0.24)	3.12 (−0.26)	3.07 (0)	3.23 (*ca.* −0.29)	–	–

H–C(2) of **4**, **5**, and **7** are observed for H–C(2) of the corresponding glucopyranosides **11**, **12**, and **13** [30] [31], respectively. The chemical-shift values for H–C(2) of **4**–**7** are similar to those of a (*Z*)-*anti*-formamide (4.34 ppm [16]). Thus, both anomers of these AllNAc glycosides prefer the (*Z*)-*anti*-conformation. The chemical shift for H–C(3) and H–C(4) of **4**–**7** depends only weakly on the anomeric configuration.

H–C(2) of the α-D-anomers of the GlcNAc derivatives **8**–**10** [1] [29] resonates in the narrow range of 4.26–4.37 ppm, indicating again the predominance of the (*Z*)-*anti*-conformation. H–C(2) of the β-D-anomers of **8**–**10**, however, resonates significantly at higher field ($\Delta\delta$ values of 0.81, 1.02, and *ca.* 0.5 ppm, resp.). H–C(1) of the α- and β-D-anomers of **8**–**10** resonates at the same position ($|\Delta\delta| \leq 0.12$ ppm). The H–C(3) signals of the β-D-anomers of **8**–**10** are shifted *downfield* by 0.24–0.64 ppm relative to those of the α-D-anomers. These $\Delta\delta$ values are significant, as evidenced by a comparison with the $\Delta\delta$ values for H–C(1) and H–C(3) of the anomers of the corresponding 2-*O*-benzyl-glucopyranosides **11**–**13**; here, the H–C(1) and H–C(3) signals of the β-D-anomers are shifted *upfield* by 0.3–0.5 ppm.

The $\Delta\Delta\delta$ values for H–C(1), H–C(2), and H–C(3) ($\Delta\delta$ values[5]) of the GlcNAc-glycosides – $\Delta\delta$ values of the glucosides) indicate a deviation of the experimental values from those expected for the (*Z*)-*anti*-conformers of the β-D-configurated 2-acetamido-2-deoxy-glucopyranosides. The $\Delta\Delta\delta$ values ($CDCl_3$ solution) express a *downfield* shift for H–C(1) (α/β-D-**8** *vs.* α/β-D-**11**: +0.34; α/β-D-**9** *vs.* α/β-D-**12**: +0.55; α/β-D-**10** *vs.* α/β-D-**13**: +0.22 ppm) and H–C(3) (α/β-D-**8** *vs.* α/β-D-**11**: *ca.* +0.70; α/β-D-**9** *vs.* α/β-D-**12**: *ca.* +0.98; α/β-D-**10** *vs.* α/β-D-**13**: *ca.* +0.64 ppm) and an *upfield* shift for H–C(2) (α/β-D-**8** *vs.* α/β-D-**11**: −0.69; α/β-D-**9** *vs.* α/β-D-**12**: −0.91; α/β-D-**10** *vs.* α/β-D-**13**: *ca.* −0.52 ppm) and reveal an equilibrium between the (*Z*)-*syn*- and (*Z*)-*anti*-conformers for 2-acetamido-2-deoxy-β-D-glucopyranosides. The preference for the (*Z*)-*syn*-conformers decreases from the hexafluoroisopropyl glycoside β-D-**9** to the methyl glycoside β-D-**8** and the 4-nitrophenyl glycoside β-D-**10**. This equilibrium is also evident from the smaller J(2, NH) values for the β-D-conformers of the GlcNAc derivatives (*Table 1*) in agreement with the *Karplus* equation of *Bystrov* [3].

Also for solutions in CD_2Cl_2, the chemical-shift values of β-D-**8** and β-D-**9** indicate the equilibrium between the (Z)-*syn*- and (*Z*)-*anti*-conformers (*Table 2*). The smaller $\Delta\Delta\delta$ values for H–C(1) (α/β-D-**8** *vs.* α/β-D-**11**: +0.27; α/β-D-**9** *vs.* α/β-D-**11**: +0.37 ppm), H–C(3) (α/β-D-**8** *vs.* α/β-D-**11**: *ca.* +0.42; α/β-D-**9** *vs.* α/β-D-**11**: *ca.* +0.74 ppm), and H–C(2) (α/β-D-**8** *vs.* α/β-D-**11**: −0.41; α/β-D-**9** *vs.* α/β-D-**11**: −0.67 ppm) indicate the same relative, but weaker preference for the (*Z*)-*syn*-conformers as it was observed for the solutions in $CDCl_3$. The $\Delta\delta$ values for the anomeric methylated methyl glycosides **14** [32] [33] and **15** [34] [35] are very similar to those for the corresponding benzylated methyl glycosides **8** and **11** (except for H–C(1) of the fucosides), respectively. This evidences that the Ph groups have no influence upon the position of the equilibrium of conformers relative to the C(2)–N bond of benzylated GlcNAc derivatives.

The conformer equilibria of the GlcNAc glycosides α-D-**8**, β-D-**8**, α-D-**14**, β-D-**14**, and β-D-**9** were further evidenced by NOE experiments. Irradiation of H–N of α-D-**8** in CD_2Cl_2 led to NOE's for H–C(1) and H–C(3) in agreement with the *anti*-conformation (*Fig. 2, a*). The enhancement at H–C(2) (2%) may indicate a weak population of the *syn*-conformer or a through-bond coupling. Irradiation of H–N of β-D-**8** gave NOE's for H–C(2) (7%) indicating a *syn*-conformation. Weaker NOE's for H–C(3) (5%) and

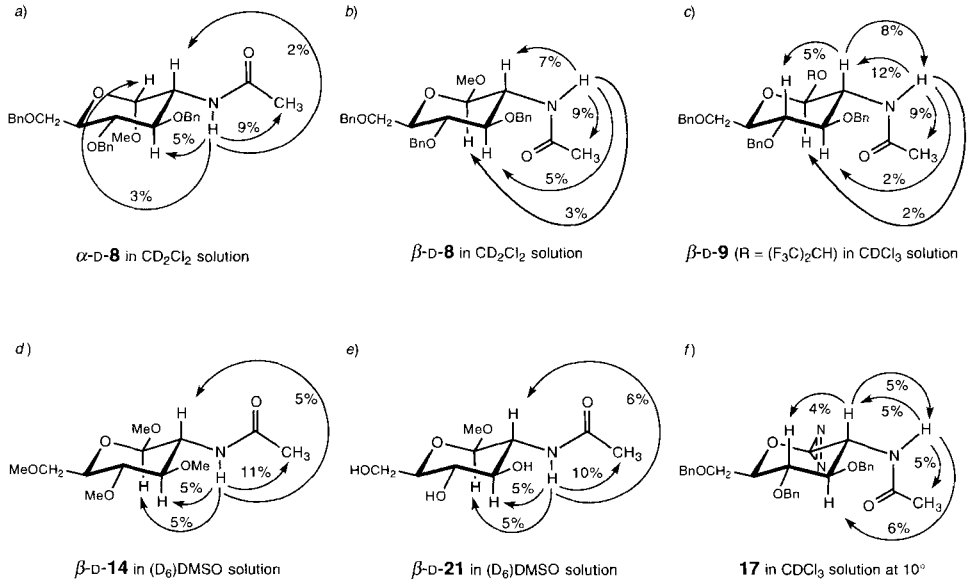


Fig. 2. *NOE data.* *a*) Irradiation at H–N of α-D-**8**; *b*) irradiation at H–N of β-D-**8**; *c*) irradiation at H–N and H–C(2) of β-D-**9**; *d*) irradiation at H–N of β-D-**14**; *e*) irradiation at H–N of β-D-**21**; *f*) irradiation at H–N and at H–C(2) of **17**.

H–C(1) (3%) indicate a lower population of the *anti*-conformation (*Fig. 2, b*). Similar NOE's as for α-D-**8** and β-D-**8** were observed upon irradiation of H–N of α-D-**14** and β-D-**14** (CD_2Cl_2; not shown in *Fig. 2*). They reveal the same rotamer equilibria in CD_2Cl_2 solutions for the benzylated and the methylated glycosides. Irradiation of H–N of β-D-**9** ($CDCl_3$) gave an even stronger NOE for H–C(2) (12%) and weaker NOE's for H–C(3) and H–C(1) (2% each), further evidencing the higher population of the *syn*-conformer of the hexafluoroisopropyl glycoside (*Fig. 2, c*). In addition, strong NOE's between N–H and the Me group of α-D-**8**, β-D-**8**, α-D-**14**, β-D-**14**, and β-D-**9** confirm the population of the (*Z*)-conformers of the α-D- and β-D-anomers which has been so far only assumed on the basis of the calculations. Low-temperature experiments for β-D-**8** in CD_2Cl_2 show some line broadening at 200–183 K that is presumably not only due to the increased viscosity, but also to a beginning coalescence, as the spectrum of **17** shows much less line broadening under analogous conditions. Unfortunately, the higher viscosity of a 1:1 mixture $CD_2Cl_2/CFCl_3$ did not allow to record well resolved spectra at temperatures below 200 K.

The solvent dependence of the rotamer *syn*/*anti*-equilibrium of the permethylated acetamides α-D- and β-D-**14** was then investigated. These glycosides are soluble in a wide range of solvents including H_2O. The population of the (*Z*)-*syn*-conformer decreases with increasing polarity of the solvent [36], as shown by the difference of the chemical-shift values ($\Delta\delta$) for H–C(1), H–C(2), and H–C(3) of the corresponding pairs of anomers (*Table 3*); it is highest in C_6D_6 ($\Delta\delta$ −1.23 for H–C(2), +0.18 for H–C(1), and +0.42 ppm for H–C(3)). The effect of solvent polarity soon levels off and the $\Delta\delta$ values for the spectra

Table 3. *Solvent Dependence of the Chemical-Shift Values* [ppm] *for H–C(1), H–C(2), H–C(3), and H–N and the Coupling Constant J(2,NH)* [Hz] *of* α-D-**14** *and* β-D-**14**. In parentheses $\Delta\delta$ values[5]).

Solvent		H–C(1)	H–C(2)	H–C(3)	H–N	*J*(2,NH)
C_6D_6	α-D-**14**	4.58	4.53	3.45	5.19	8.3
	β-D-**14**	4.76 (+0.18)	3.30 (−1.23)	3.87 (+0.42)	4.81	6.9
$CDCl_3$	α-D-**14**	4.66	4.19	3.31	5.59	8.9
	β-D-**14**	4.75 (+0.09)	3.24 (−0.95)	3.80 (+0.49)	5.75	7.7
CD_2Cl_2	α-D-**14**	4.56	4.05	3.29	5.64	8.9
	β-D-**14**	4.45 (−0.11)	3.43 (−0.62)	3.47 (+0.18)	5.63	6.7
(D_6)acetone	α-D-**14**	4.52	3.98	3.33	7.03	9.2
	β-D-**14**	4.39 (−0.13)	3.63–3.51 (*ca.* −0.41)	3.43 (+0.10)	7.14	7.3
CD_3CN	α-D-**14**	4.51	3.88	3.26	6.44	9.4
	β-D-**14**	4.22 (−0.29)	3.61–3.50 (*ca.* −0.33)	3.21 (−0.05)	6.39	8.7
(D_6)DMSO	α-D-**14**	4.47	3.77	3.32	8.00	8.8
	β-D-**14**	4.21 (−0.26)	3.55–3.44 (*ca.* −0.28)	3.25 (−0.07)	7.87	9.0
CD_3OD	α-D-**14**	4.55	3.95	3.41	–	–
	β-D-**14**	4.27 (−0.28)	3.67–3.60 (*ca.* −0.32)	3.28 (−0.13)	–	–
D_2O	α-D-**14**	4.68	3.96	3.55	–	–
	β-D-**14**	4.41 (−0.27)	3.73 (−0.23)	3.41 (−0.14)	–	–

in CD_3CN, (D_6)DMSO, CD_3OD, and D_2O differ only slightly from each other, revealing a similar population of the conformers. The $\Delta\delta$ values for H–C(2) of **14** in polar solvents are still *ca.* −0.30 ppm. The $\Delta\delta$ values for H–C(1) (*ca.* −0.28 ppm) and H–C(3) (*ca.* −0.1 ppm) are distinctly smaller than expected. The experimental $\Delta\delta$ values for pairs of anomeric glucosides, *ca.* −0.6 ppm for H–C(1), *ca.* −0.1 ppm for H–C(2), and *ca.* −0.3 ppm for H–C(3) are well known [37] and illustrated by **11**–**13**. Thus, H–C(1) and H–C(3) of β-D-**14** are relatively deshielded, and H–C(2) is relatively shielded. The influence of the AcNH group can only be rationalized by assuming a substantial population of the (*Z*)-*syn*-conformer also in polar solvents. In keeping with this, irradiation of H–N of β-D-**14** in (D_6)DMSO solution led to NOE's of the same intensity (5%) for H–C(1), H–C(2), and H–C(3) (*Fig. 2, d*).

3. *Analysis of the* ^{1}*H-NMR Spectra of the 2-(Acetamido)-2-deoxy-*D-*allosylidene- and* -D-*glucosylidene-Derived Diazirines* **16** *and* **17**. Glycosylidene-derived diazirines possess a pseudoaxial and a pseudoequatorial N-substituent at C(1), so that the population of the conformers relative to the C(2)–N bond of **16** and **17** is mainly influenced by the orientation of RO–C(3). The diazirine **16** crystallizes as the (*Z*)-*anti*-conformer. In the solid state, it possesses a dihedral angle H–C(2)–N–H of 158.6° and an intermolecular H-bond between the H–N and the O=C group [38]. The chemical shift of H–C(2) and perhaps H–C(3) of **16** [39] and **17** [29] should allow to deduce the preferred conformation of the AcNH–C(2) group in solution (*Table 4*). For this, one has to distinguish between the influence of the azi and of the acetamido groups in the *syn*/*anti*-conformers. This can be done by comparing the chemical-shift values of H–C(2) and H–C(3) of the diazirine **18** [40] and the diazirines **16** and **17**, on the one hand, and those of the diazirines and the corresponding methyl glycosides **4**, **8**, and **11**, on the other hand.

It is sufficient to compared the δ values for H–C(2) of the *gluco*-configurated diazirines with those of the corresponding methyl α-D-pyranosides since the $\Delta\delta$ values[5]) of the alkyl glucosides **11** and **12** are constant and small (*ca.* −0.1 ppm; *Table 1*). The $\Delta\delta$

Table 4. *Selected Chemical-Shift Values* [ppm] *and Coupling Constants* [Hz] *of the AllNAc and the GlcNAc Diazirines* **16**–**18** *in* $CDCl_3$ *Solution.* In parentheses $\Delta\delta$ values[5]).

	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H–N	*J*(2,NH)
16 [39]	4.85 (+0.58)	4.16 (+0.11)	3.92 (+0.20)	4.46 (+0.13)	5.21	9.2
17 [29]	4.35 (+0.09)	3.77 (*ca.* +0.08)	3.94	3.86	4.88	8.1
18 [40]	4.12 (+0.56)	3.99 (+0.11)	3.89 (*ca.* +0.25)	3.75 (+0.01)	–	–

values (value for the diazirine – value for the corresponding methyl α-D-pyranoside) for H–C(2) of the glucose diazirine **18** and the GlcNAc diazirine **17** are 0.56 and 0.09 ppm, respectively (*Table 4*). The former $\Delta\delta$ value reflects the combined influence of the azi group and the axial MeO group, and the latter $\Delta\delta$ value reflects the same combined influence and additionally the influence of NHAc in its accessible conformations. The assumption that the influence on the chemical shift of H–C(2) of the azi and of the MeO groups is the same for the corresponding pairs of compounds leads to a shielding of 0.47 ppm for H–C(2) of **17** by the influence of the NHAc group. Hence, a substantial population of the (*Z*)-*syn*-conformation of **17** is present in $CDCl_3$ solution.

The analysis of the AllNAc diazirine **16** is hampered, as the corresponding allose diazirine (AcNH replaced by BnO) is not known. However, one can correlate the chemical-shift value for H–C(2) of **16** with that for H–C(2) of **18**. The comparison of the δ values for H–C(2) of **19** [41], **20** [42], and α-D-**11** (3.45, 3.57, and 3.56 ppm; *Table 1*) shows that H–C(2) of the glucosides is deshielded by *ca.* 0.1 ppm relative to H–C(2) of the alloside and that the protecting groups of HO–C(4) and HO–C(6) have no influence upon the δ value of H–C(2) of the glucosides. Therefore, the $\Delta\delta$ values for H–C(2) (value for the diazirine – value for the corresponding methyl α-D-pyranoside) should be the same for **18** and the unknown allose diazirine analogue of **16** (0.56 ppm). The corresponding $\Delta\delta$ value for **16** is 0.58 ppm. Thus, one has to conclude that the NHAc group of the AllNAc diazirine **16** and of the corresponding glycoside α-D-**4** have a strong and similar preference for the (*Z*)-*anti*-conformation.

Is the population of the (*Z*)-*syn*-conformer higher in **17** or in the corresponding β-D-**8**? To answer this question, we compared the δ values for H–C(2) of α-D-**8** and the diazirine **17**, on the one hand, and of the anomeric glycosides **8**, on the other hand. The chemical-shift values for H–C(2) of α-D-**8** and of the AllNAc analogue α-D-**4** are very similar to each other, and the NHAc group of both glycosides adopts almost exclusively the (*Z*)-*anti*-conformation (see above). The expected δ value for H–C(2) of **17** in the (*Z*)-*anti*-conformation is given by δ(H–C(2)) for α-D-**8** and the contribution of the azi and the axial MeO groups (4.26 + 0.56 = 4.82 ppm). The expected δ value for H–C(2) of β-D-**8** in the (*Z*)-*anti*-conformation is given by δ(H–C(2)) for α-D-**8**, taking into account $\Delta\delta$(H–C(2)) for the formal anomerization, as derived from the chemical-shift values for the anomers of **11** (4.26 – 0.1 = 4.16 ppm). The difference between the expected and the observed values is 0.47 ppm for **17** and 0.71 ppm for β-D-**8**; hence, the population of the (*Z*)-*syn*-conformer is higher in β-D-**8** than in the diazirine **17**. The signals of H–C(3) were not taken into account for this conformational analysis, as the δ values responded only weakly to structural changes.

The (*Z*)-*syn*/(*Z*)-*anti*-equilibrium of **17** was corroborated by NOE measurements at 10° in $CDCl_3$ solution (*Fig. 2,f*). Upon irradiation of H–N, enhancements of similar

intensities were observed for the signals of H–C(2), H–C(3), and the Me group, evidencing the larger contribution of the (*Z*)-*anti*-conformer in **17** than in β-D-**8**. No trace of coalescence could be observed for **17** in CD_2Cl_2 solution in the temperature range from 283 to 183 K.

Is the temperature dependence of the (*Z*)-*syn*/(*Z*)-*anti*-equilibrium responsible for the nonlinear temperature dependence of the δ values for H–N of **17**? To answer this question, we measured ^{1}H-NMR spectra of **17** in CD_2Cl_2 at different concentrations and temperatures between 193 and 293 K. On the one hand, the temperature dependence of the (*Z*)-*syn*/(*Z*)-*anti*-equilibrium should lead to opposite chemical-shift changes for H–C(2) and H–C(3). On the other hand, the concentration dependence of H–N should reveal di- or oligomerization of **17** at low temperature. Indeed, the δ value for H–N of a 0.005M solution of **17** in CD_2Cl_2 solution shows a strong, linear dependence upon the

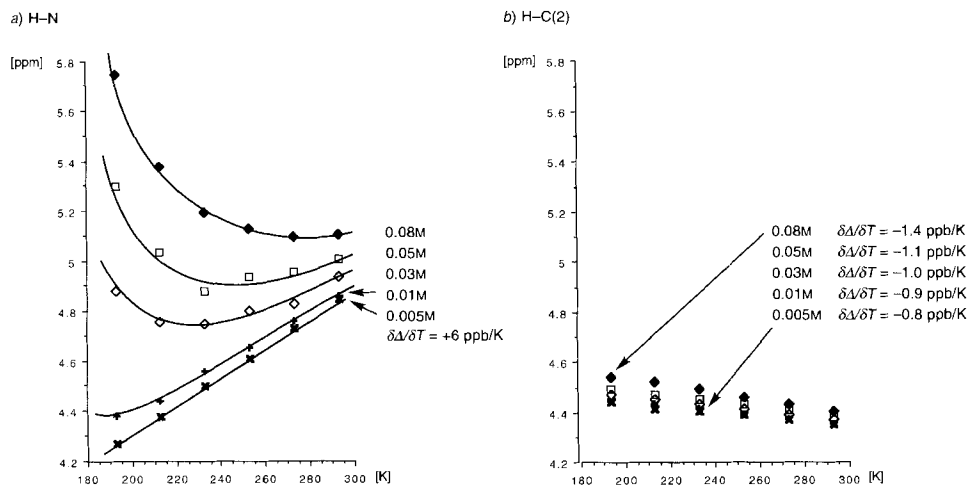


Fig. 3. *Temperature and concentration dependence of the chemical shift of* a) *H–N and* b) *H–C(2) of* **17** *in* CD_2Cl_2 *solution*

temperature (*Fig. 3, a*). The $\delta\Delta/\delta T$ value of +6 pp b/K evidences that H–N is not involved in an intramolecular H-bond[6]). With increasing concentration, the temperature dependence deviates more strongly from linearity. This is strong evidence for self-association of **17** at lower temperatures and at higher concentrations. The observed deshielding of H–N with increasing concentration is in agreement with H–N acting as a donor in a N–H···O=C H-bond. H–C(2) of **17** shows only a weak, linear dependence upon the temperature (*Fig. 3b*). The $|\delta\Delta/\delta T|$ value increases slightly from a 0.005M to a 0.08M solution (from −0.8 to −1.4 ppb/K, *Fig. 3, b*). The determination of the temperature dependence of H–C(3) is impeded by overlapping signal. Nevertheless, an increased

[6]) Positive $\delta\Delta/\delta T$ values for H–N of peptides in poorly H-bonding (chlorinated) solvents indicate, as a rule, completely buried H–N groups that are not involved in H-bondings [43]; small negative $\delta\Delta/\delta T$ values indicate intramolecularly H-bonded H–N groups [43–45].

shielding was observed upon lowering the temperature ($\delta\Delta/\delta T \approx +1$ ppb for 0.005–0.08M solutions). As expected, H–C(4) resonates at the same position for this temperature and concentration range ($\delta\Delta/\delta T = 0$ ppb). The $\Delta\delta$ values for H–C(2) and H–C(3) show opposite signs, but the absolute value are so small that the shift differences may be due to the self-association of **17** (both H–C(2) and H–C(3) are in the neighborhood of the AcNH group). Thus, the position of the (*Z*)-*syn*/(*Z*)-*anti*-equilibrium of **17** is (nearly) constant in the temperature range from 190 to 300 K.

The rationalization according to which the intermolecular H-bond N(Ac)–H···O(H)–R is responsible for the preferred α-D-selectivity in the glycosidation of the GlcNAc diazirine **17** [1] is compatible with the (*Z*)-*syn*/(*Z*)-*anti*-equilibrium. Such an H-bond of the (*Z*)-*syn*-conformer of **17** locates the ROH group far away from C(1). As a consequence, neither the α-D- nor the β-D-glycosides can be formed directly from this complex. In the (*Z*)-*anti*-conformer of **17**, however, such an H-bond locates the ROH group below the pyranose ring in a position that is favorable for the formation of the α-D-glycoside.

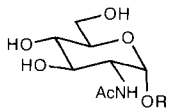
4. *Analysis of the ^{1}H-NMR Spectra of Unprotected 2-Acetamido-2-deoxy-*D*-glucopyranose, Its Methyl Glycosides, and Related Pseudosaccharides in D_2O Solution.* High-resolution ^{1}H-NMR spectra of GlcNAc (**22**), glucose (**24**), and their methyl pyranosides **21** and **23** in D_2O solution were measured by *Perkins et al.* [46] (*Table 5*). Similar $\Delta\delta$ values[5]) were

Table 5. *Selected Chemical-Shift Values* [ppm] *of the GlcNAc Derivatives* **21** *and* **22**, *the Pseudoglucose* **25**, *and the Glucose Derivatives* **23** *and* **24** *in D_2O Solution and of* **21** *in (D_6)DMSO Solution.* In parentheses $\Delta\delta$ values[5]).

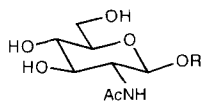
	H–C(1)	H–C(2)	H–C(3)	H–C(4)
α-D-**21** [46]	4.75	3.90	3.70	3.47
α-D-**22** [46]	5.19	3.86	3.75	3.48
α-D-**25** [47]	4.08	3.70	3.63	3.37
β-D-**21** [46]	4.44 (−0.31)	3.68 (−0.22)	3.52 (−0.18)	3.43 (−0.04)
β-D-**22** [46]	4.70 (−0.49)	3.66 (−0.20)	3.52 (−0.23)	3.44 (−0.04)
β-D-**25** [47]	3.60 (−0.48)	3.63 (−0.07)	3.31 (−0.32)	3.38 (+0.01)
α-D-**21**[a])	4.52	3.69–3.61	3.50–3.42	3.11
β-D-**21**[a])	4.17 (−0.35)	3.45–3.35 (*ca.* −0.25)	3.30–3.20 (*ca.* −0.21)	3.11–3.03 (*ca.* −0.04)
α-D-**23** [46]	4.80	3.55	3.66	3.39
α-D-**24** [46]	5.22	3.52	3.70	3.40
β-D-**23** [46]	4.37 (−0.43)	3.25 (−0.30)	3.48 (−0.18)	3.37 (−0.02)
β-D-**24** [46]	4.63 (−0.59)	3.23 (−0.29)	3.47 (−0.23)	3.39 (−0.01)

[a]) In (D_6)DMSO. Data for H–N: α-D-**21**: 7.74 (J = 8.1); β-D-**21**: 7.67 (J = 9.3).

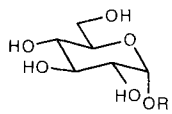
observed for H–C(1), H–C(2), and H–C(3) of **21**–**24**. This suggests a similar and presumably dominant population of the (*Z*)-*anti*-conformation of both anomers of **21** and **22** in water. The $\Delta\delta$ values for H–C(1), H–C(2), and H–C(3) of **21** for D_2O or (D_6)DMSO solutions (*Table 5*) differ only slightly from those of the permethylated analogue **14** in the same solvents (*Table 3*). A significant contribution of the (*Z*)-*syn*-conformer of β-D-**14** was deduced in *Chapt. 2*. This indicates a similar contribution of the (*Z*)-*syn*-conformer of β-D-**21** in D_2O or (D_6)DMSO solutions. In keeping with this, irradiation of H–N of β-D-**21** in (D_6)DMSO solution led to similar NOE's as observed



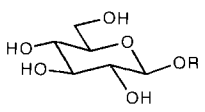
α-D-**21** R = Me
α-D-**22** R = H



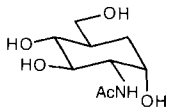
β-D-**21** R = Me
β-D-**22** R = H



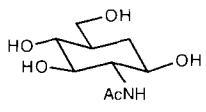
α-D-**23** R = Me
α-D-**24** R = H



β-D-**23** R = Me
β-D-**24** R = H



α-D-**25**

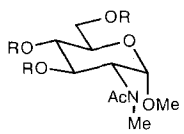


β-D-**25**

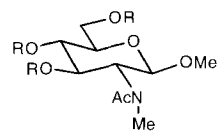
for β-D-**14** (*Fig. 2, e* and *d*). Hence, a significant population of the (*Z*)-*syn*-conformer of β-D-**21** is probable. The similarity of the $\Delta\delta$ values of **22** and the pseudosaccharides **25** [47] shows that the ring O-atom has no influence upon the position of the equilibirum of these conformers.

5. *Analysis of the NMR Spectra of 2-[Acetyl(methyl)amino]-2-deoxy-*D*-glucopyranosides.* The conformational equilibrium of NAlkylAc and NAlkylBz derivatives of glycopyranosyl-acetamides and 2-amino-2-deoxy-hexopyranoses has been investigated by *Avalos et al.* [16]. These authors observed equilibria between the (*Z*)-*anti*- and the (*E*)-*anti*-conformers (ratios of 3:2 to 4:1). As expected, the H geminal to the N-substituent of the (*Z*)-*anti*-conformers resonates at lower field than the one of the (*E*)-*anti*-conformers ($\Delta\delta$ > 0.8 ppm). β-D-Glycosides derived from GlcNRAc have not been included in *Avalos'* investigation; these glycosides are, however, of interest in the context of our studies.

Calculations of the energy of the conformers obtained by stepwise (20°) rotation around C(2)–N of (*E*)- and (*Z*)-α-D-**27** predict that the (Z)-*anti*- and the (*E*)-*anti*-con-



α-D-**26** R = Bn
α-D-**27** R = Me
α-D-**28** R = H



β-D-**26** R = Bn
β-D-**27** R = Me
β-D-**28** R = H

formers are most stable and possess the same energy. The (*Z*)-*syn*- and the (*E*)-*syn*-conformers are destabilized by 2.5 and 7.2 kcal/mol, respectively. For β-D-**27**, the (*Z*)-*syn*-conformer represents the global minimum; the (*E*)-*anti*-, the (*Z*)-*anti*-, and the (*E*)-*syn*-conformers are destabilized by 1.1, 2.5, and 5.7 kcal/mol, respectively. The rotational barriers for the NMeAc derivatives are higher than those for the NHAc derivatives. A comparison of the calculated and the spectroscopic data of the corresponding acetamides

(see above) shows that the calculation overestimates the destabilization of the (*Z*)-*anti*-conformer (due to O,O-interaction of O=C and the neighboring alkoxy group) of the β-D-glucopyranosides[7]).

On the basis of these considerations, one expects an equilibrium between the (*Z*)-*anti*- and the (*E*)-*anti*-conformers for the α-D-pyranosides of GlcNMeAc and an equilibrium between the (*Z*)-*syn*-, (*Z*)-*anti*-, and (*E*)-*anti*-conformers for the corresponding β-D-pyranosides. The chemical-shift values of H–C(1), H–C(2), and H–C(3) should allow the characterization of the conformers.

N-Methylation of α-D-**8**, β-D-**8**, α-D-**14**, and β-D-**14** with MeI in DMSO under basic conditions [50] gave the *N*-methylacetamides α-D-**26**, β-D-**26**, α-D-**27** [51], and β-D-**27** [51–53], respectively. Catalytic transfer hydrogenation [54] of α-D-**26** and β-D-**26** led to the triols α-D-**28** and β-D-**28**[8]), respectively.

The ^{1}H-NMR spectra of α-D-**26** and α-D-**27** in CD_2Cl_2 solution and of α-D-**28** in D_2O solution show the signals of two conformers each in the ratio of 67:33, 70:30, and 75:25, respectively. H–C(2) of the major isomer resonates at low field (> 4.3 ppm; *Table 6*) as expected for (*Z*)-*anti*-conformers. H–C(2) of the minor isomers resonates by 0.57–0.96 ppm at higher field. The (*E*)-*anti*-conformation was assigned to the minor conformer, as the chemical-shift values of H–C(1) and H–C(3) of both conformers are very similar to each other ($\Delta\delta$ < 0.15 ppm).

Table 6. *Selected Chemical-Shift Values* [ppm] *of the GlcNMeAc Glycosides* **26**–**28**. The spectra of the α-D-anomers were recorded at room temperature, those of the β-D-anomers at −50°.

		Ratio	Solvent	H–C(1)	H–C(2)	H–C(3)	H–C(4)	MeN	AcN
α-D-**26**	(*Z*)-*anti*	67	CD_2Cl_2	4.64	4.79	4.03	3.80–3.69	2.85	2.02
	(*E*)-*anti*	33		4.73	3.83	4.05	3.80–3.69	2.89	2.12
α-D-**27**[a])	(*Z*)-*anti*	70	CD_2Cl_2	4.56	4.54	3.68	3.28	2.97	2.08
	(*E*)-*anti*	30		4.64	3.61	3.67	3.26	2.90	2.07
α-D-**28**	(*Z*)-*anti*	75	D_2O	4.74	4.39	4.08	3.50	3.08	2.16
	(*E*)-*anti*	25		4.89	3.82	4.02	3.52	2.94	2.17
β-D-**26**	(*Z*)-*anti*	30	CD_2Cl_2	4.21	4.62–4.48	3.80–3.66	3.61–3.42	2.29	1.92
	(*E*)-*anti*	60		4.35	3.61–3.42	3.80–3.66	3.61–3.42	2.62	2.08
	(*Z*)-*syn*	10		5.15	3.61–3.42	3.80–3.66	3.61–3.42	2.99	1.89
β-D-**27**	(*Z*)-*anti*	30	CD_2Cl_2	4.21	4.44	3.50–3.46	3.36–3.23	2.84	2.03
	(*E*)-*anti*	60		4.29	3.36–3.23	3.50–3.46	3.36–3.23	2.76	2.03
	(*Z*)-*syn*	10		5.06	3.36–3.23	4.14	3.36–3.23	3.02	2.06
β-D-**28**	(*Z*)-*anti*	30	D_2O	4.52	4.41	3.75–3.65	3.48–3.31	2.98	2.13
	(*E*)-*anti*	60		4.59	3.48–3.31	3.75–3.65	3.48–3.31	2.86	2.12
	(*Z*)-*syn*	10		5.17	3.48–3.31	3.75–3.65	3.48–3.31	3.10	2.10

[a]) The spectrum in $CDCl_3$ solution ((*Z*)-*anti*/(*E*)-*anti* 58:42) is similar to the published one [51], except that H–C(2) of the (*E*)-*anti*-conformer resonates at high field between 3.68 and 3.38 ppm.

[7]) For this reason, the calculated (*Z*)-*anti*-rotamers of the β-D-allopyranoside and the α-D-glucopyranoside possess no intramolecular H-bonds between H–N and the neighboring axial OR group. A weak temperature dependence of H–N in the *allo*- and *gluco*-acetamides and CD measurements of glucosides [1] [48] [49] suggest such H-bonds.

[8]) Both anomers have been prepared by selective acetylation and methylation of GlcNMe [55].

At room temperature, the ^{1}H-NMR spectra of β-D-**26** and β-D-**27** in CD_2Cl_2 solution and the one of β-D-**28** in D_2O solution show signals of two conformers in ratios of 60:40, 65:35, and 55:45, respectively. Whereas the signals of the major conformer are sharp, the signals of the minor conformers are broad. This phenomenon has already been observed in the ^{1}H-NMR spectrum of β-D-**27** in $CDCl_3$ solution [51] [52]. Some ^{1}H- and ^{13}C-NMR signals of the minor isomers are not visible. This suggests two equilibria of three conformers with one coalescence temperature above and the other close to room temperature. If one excludes the unfavorable (*E*)-*syn*-conformer and considers that coalescence due to (*E*)/(*Z*)-isomerization of amides occurs at temperatures of 50–70° [56], one has to conclude that the broad signals are due to the equilibrating (*Z*)-*anti*- and (*Z*)-*syn*-conformers, and the sharp signals to the (*E*)-*anti*-conformer. Indeed, sharper ^{1}H-NMR signals are recorded for the minor conformers of β-D-**26** and β-D-**27** at 50° in $CDCl_3$ solution. The ^{1}H-NMR spectrum of β-D-**28** at 85° in D_2O shows only sharp signal of two conformers. The position of the equilibria at 50 and 85°, respectively (β-D-**26**: 60:40; β-D-**27**: 70:30; β-D-**28**: 50:50), differ only slightly from those at room temperature. At −50°, mixtures of the (*E*)-*anti*-, the (*Z*)-*anti*-, and the (*Z*)-*syn*-conformers were observed for solutions in CD_2Cl_2 of β-D-**26** and β-D-**27** and for β-D-**28** (CD_3OD) in the same ratio 60:30:10.

The assignment of the conformers is based on the characteristic chemical-shift values, with H–C(2) of the (*E*)-*anti*- and the (*Z*)-*syn*-conformers resonating at high field, and H–C(2) of the (*Z*)-*anti*- and H–C(1) of the (*Z*)-*syn*-conformers resonating at low field (*Table 6*). The same relative chemical-shift values are observed for H–C(1) of the (*Z*)-*anti*- *vs.* the (*E*)-*anti*-conformers (deshielding by 0.07–0.15 ppm) in **26**–**28**. Simi-

Table 7. *Selected ^{13}C-NMR Chemical-Shift Values* [ppm] *of* **8** *and the GlcNMeAc Glycosides* **26**–**28** *at Room Temperature*

		Solvent	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	MeN	AcN
α-D-**8**		$CDCl_3$	98.73	52.55	80.37	78.49	70.85	68.63	–	169.77, 23.48
α-D-**26**	(*Z*)-*anti*	$CDCl_3$	99.76	54.92	79.19	77.28	70.66	68.70	32.44	172.25, 23.39
	(*E*)-*anti*		100.40	61.28	79.47	77.55	70.25	68.33	30.11	172.05, 22.24
α-D-**27**	(*Z*)-*anti*	$CDCl_3$	99.56	54.45	80.09	77.55	70.40	71.09	32.40	171.96, 23.35
	(*E*)-*anti*		100.36	60.88	81.00	78.85	70.03	70.70	29.74	171.88, 22.00
α-D-**28**	(*Z*)-*anti*	D_2O	102.18	59.90	74.96	71.53	74.20	63.82	35.31	179.29, 24.65
	(*E*)-*anti*		102.77	64.46	74.96	71.80	74.00	63.82	32.45	178.74, 24.05
β-D-**8** [57]		$CDCl_3$	101.3	55.6	81.5	78.3	74.4	68.8	–	170.5, 23.4
β-D-**26**	(*E*)-*anti*	$CDCl_3$	100.63	63.43	79.32	78.96	74.86	68.50	27.76	172.48, 22.09
	(*Z*)-*syn*/(*Z*)-*anti*		100.23	[a])	[b])	[b])	74.75	68.86	[a])	171.36, [a])
β-D-**27**	(*E*)-*anti*	$CDCl_3$	100.50	63.12	81.61	80.28	74.61	70.89	27.83	172.69, 21.94
	(*Z*)-*syn*/(*Z*)-*anti*		100.15	59.32	81.00	[a])	[a])	71.26	[a])	171.35, 23.39
β-D-**27**[c])	(*E*)-*anti*	CD_2Cl_2	100.46	63.06	81.25	80.02	74.21	70.65	28.53	172.77, 23.03
	(*Z*)-*anti*		100.46	61.64	80.44	79.77	74.47	71.10	31.53	172.43, 23.43
	(*Z*)-*syn*		100.20	[a])	81.09	80.84	74.08	69.49	42.60	171.83, 23.29
β-D-**28**	(*E*)-*anti*	D_2O	102.60	66.53	73.35	73.22	78.52	63.44	30.43	178.49, 23.74
	(*Z*)-*syn*/(*Z*)-*anti*		102.51	[a])	72.92	72.92	[a])	63.39	33.21[d])	[a]), [a])

[a]) Hidden by other signals or not visible.
[b]) Broad signal at 79.84–79.47 ppm.
[c]) At −80°.
[d]) Broad signal.

larly, MeN of the (*E*)-*anti*-conformers of **27** and **28** is sightly shielded relative to the (*Z*)-*anti*-isomers. MeN for the (*Z*)-*anti*-conformers of α-D-**26** (0.04 ppm, 25°) and β-D-**26** (0.33 ppm, −50°), however, is shielded relative to the (*E*)-*anti*-conformer, presumably due to the anisotropy effect of the neighboring Ph group.

The ^{13}C-NMR spectra of the GlcNMeAc α-D-glycosides show a characteristic downfield shift of 4.6–6.4 ppm (*cf.* [16]) for C(2) of the (*E*)-*anti*-conformers as related to the corresponding (*Z*)-*anti*-conformers (*Table 7*). Upfield shifts were observed for MeN (2.3–2.9 ppm) and for *Me*CO (1.1–1.6 ppm) of the (*E*)-*anti*-conformers, whereas the chemical-shift values of the other C-atoms are hardly affected by the conformation ($|\Delta\delta| < 1$ ppm). At room temperature, the ^{13}C-NMR spectra ($CDCl_3$) of the GlcNMeAc β-D-glycosides are characterized by sharp signals for the (*E*)-*anti*-conformers (major isomers) and by broadened signals for equilibrating (*Z*)-*anti*/(*Z*)-*syn*-conformers (minor isomers). Some signals are invisible due to coalescence. Unfortunately, the low-temperature ^{13}C-NMR spectra (−80°) of β-D-**26** (CD_2Cl_2) and β-D-**28** (CD_3OD) are poorly resolved. The ^{13}C-NMR spectrum of β-D-**27** in CD_2Cl_2 solution at −80°, however, shows the presence of three conformers in the ratio of *ca.* 66:27:7 (deduced from the intensity of the strong C=O signals). The chemical-shift values of the dominant conformer agree well with those of the (*E*)-*anti*-conformer at room temperature in $CDCl_3$ solution and the shift values of the two minor isomers with those of the averaged (*Z*)-*anti*- and (*Z*)-*syn*-conformers at room temperature. The largest chemical-shift differences are observed for H–C(2) and MeN of the conformers of β-D-**27**.

6. *Conclusion.* Polar diequatorial substituents at the neighboring C-atoms of *N*-acetyl-hexosamines possessing an equatorial NHAc group favor a shift of the position of the equilibrium of the (*Z*)-*anti*- and (*Z*)-*syn*-conformers, so that substantial amounts of the latter conformer can be detected. Thus, β-D-GlcNAc derivatives occur as mixtures of the (*Z*)-*anti*- and (*Z*)-*syn*-conformers, evidenced by the observation that H–C(2) of β-D-GlcNAc and its unprotected glycosides resonate in D_2O solution *ca.* 0.2–0.3 ppm at higher field than H–C(2) of the corresponding α-D-GlcNAc derivatives [46] [47] (see also *e.g.*, [58] [59]). As a consequence, one or the other conformer may be preferred in oligo- or polymers containing β-D-GlcNAc residues or in complexes of β-D-GlcNAc derivatives with a given enzyme. To the best of our knowledge, this aspect has not been explicitly investigated[9]). The solid-state structures of β-D-GlcNAc derivatives found in the protein database (hyaluronic acid [60], keratan sulfate [61], and substrate-enzyme complexes of β-D-GlcNAc derivatives with lysozyme [62–66], wheat germ agglutinin [67] [68], and CD59 [69]), however, prefer exclusively the (*Z*)-*anti*-conformation. NOE Measurements of glycopeptides containing β-D-GlcNAc residues indicate a low population of the (*Z*)-*syn*-conformation in H_2O in one case [70] and a substantial population of the (*Z*)-*syn*-conformation of another glycopeptide in (D_6)DMSO [71].

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[9]) One may speculate that N-deacylases of GlcNAc-derived β-D-glycosides will attack the (*E*)- or (*Z*)-*syn*-conformer.

Experimental Part

General. See [39]. The following compounds were prepared according to literature procedures: α-D- and β-D-**9** by thermolysis of **17** in the presence of MeOH [1], α-D-**14** [32], β-D-**14** [33], and α-D- and β-D-**15** [34] [35] by methylation of α-D-**21** [72] [73], β-D-**21** [72] [74], and α-D- and β-D-**23**, resp., with Me_2SO_4/NaOH in CCl_4/H_2O [75], α-D- and β-D-**11** [30] [76] [77] by benzylation of α-D- and β-D-**23** with KOH and benzyl chloride (BnCl) in dioxane [78]. Anal. HPLC: *Merck-LiChrosorb-Si60* 250 × 4.6 mm cartridge; prep. HPLC: *Zorbax-Sil* 250 × 20 mm column. ^{1}H-NMR Spectra: chemical shifts in ppm rel. to $SiMe_4$ measured from residual $CHCl_3$ (δ 7.27 ppm) or $CDHCl_2$ (δ 5.32 ppm), or from sodium 3-(trimethylsilyl)propane-1-sulfonate (DSS; δ 0.00) as internal standard; in ambiguous cases, assignments based on selective homonuclear decoupling experiments or on ^{1}H,^{1}H-COSY and ^{1}H,^{13}C-HSQC spectra (α-D-**8**, β-D-**14**, and α-D-**27**).

*Methyl 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (α-D-**8**; for an anomeric mixture of **8**, see [29]). A soln. of α-D-**21** (0.25 g, 1.06 mmol) in DMF (7.5 ml) was treated with NaH (78 mg, 3.25 mmol), stirred at 25° for 10 min, treated with BnBr (40 µl, 3.37 mmol), stirred for further 30 min, and poured into H_2O (20 ml). The resulting precipitate was washed with H_2O (20 ml), dried, and recrystallized (AcOEt/hexane): anomerically pure α-D-**8** (0.43 g, 80%). R_f (AcOEt) 0.38. M.p. 157–160°. ^{1}H-NMR ($CDCl_3$): see [29] and *Table 1*. ^{13}C-NMR (75 MHz, $CDCl_3$): see *Table 7*; additionally, 138.50 (*s*); 138.10 (2*s*); 128.51–127.51 (several *d*); 75.01 (*t*), 74.82 (*t*), 73.49 (*t*, 3 PhCH_2); 54.99 (*q*, MeO).

*Methyl 2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (β-D-**8**) [52] [57]. As described for α-D-**8**, benzylation of β-D-**21** [72] [74] (0.65 g, 2.76 mmol) gave β-D-**8** (0.84 g, 60%). R_f (AcOEt) 0.38. M.p. 164–167° ([52]: 158–159°). ^{1}H-NMR ($CDCl_3$): see [29] [57] and *Table 1*. ^{13}C-NMR ($CDCl_3$): see *Table 7*.

*Methyl 2-[Acetyl(methyl)amino]-3,4,6-tri-*O*-benzyl-2-deoxy-α-*D*-glucopyranoside* (α-D-**26**). A stirred soln. of α-D-**8** (1.00 g, 1.98 mmol) in DMSO (5 ml) was treated with a soln. of dimethylsulfinyl carbanion [79] (5 ml), stirred for 3 h, treated dropwise with MeI (250 µl, 4.01 mmol), and stirred for further 48 h [50]. The soln. was treated with H_2O (25 ml) and extracted with $CHCl_3$ (3 × 25 ml). The org. layers were washed with H_2O (25 ml) and brine (25 ml), combined, dried (Na_2SO_4), and evaporated. FC (AcOEt/hexane 7:3) gave α-D-**26** (0.47 g, 46%). Oil. R_f (AcOEt) 0.55. $[\alpha]_D^{25} = +70.7$ ($c = 4.4$, $CHCl_3$). IR (0.03M, CH_2Cl_2): 3066*w*, 3033*w*, 2915*m*, 1644*s*, 1496*w*, 1453*m*, 1405*m*, 1365*m*, 1318*w*, 1280*w*, 1247*w*, 1211*w*, 1192*w*, 1128*s*, 1045*s*, 1028*s*, 914*w*, 603*w*. ^{1}H-NMR (500 MHz, CD_2Cl_2; (*Z*)-*anti*/(*E*)-*anti* 2:1): 7.38–7.21 (*m*, 15 arom. H); 4.86 (*d*, $J = 11.9$, 0.67 H, PhC*H*); 4.82 (*d*, $J = 11.1$, 0.33 H, PhC*H*); 4.795 (*d*, $J = 11.3$, 0.67 H, PhC*H*); 4.790 (*dd*, $J = 3.5$, 11.4, 0.67 H, H–C(2)); 4.73 (*d*, $J = 3.5$, 0.33 H), 4.64 (*d*, $J = 3.5$, 0.67 H, H–C(1)); 4.622 (*d*, $J = 11.2$, PhC*H*); 4.616 (*d*, $J = 11.3$, PhC*H*); 4.59 (*d*, $J = 11.1$, 0.33 H, PhC*H*); 4.58 (*d*, $J = 11.9$, 0.67 H, PhC*H*); 4.54 (*d*, $J = 11.2$, PhC*H*); 4.52 (*d*, $J = 12.1$, 0.33 H, PhC*H*); 4.05 (*dd*, $J = 8.3$, 10.5, 0.33 H), 4.03 (*dd*, $J = 8.0$, 11.4, 0.67 H, H–C(3)); 3.83 (*dd*, $J = 3.6$, 10.4, 0.33 H, H–C(2)); 3.80–3.69 (*m*, H–C(4), H–C(5), 2 H–C(6)); 3.37 (*s*, 1 H); 3.32 (*s*, 2 H, MeO); 2.89 (*s*, 1 H), 2.85 (*s*, 2 H, MeN); 2.12 (*s*, 1 H), 2.02 (*s*, 2 H, Ac). ^{13}C-NMR (75 MHz, $CDCl_3$; (*Z*)-*anti*/(*E*)-*anti* 2:1): see *Table 7*; additionally for the (*Z*)-*anti*-conformer, 138.89 (*s*); 138.08 (2*s*); 128.45–126.83 (several *d*); 74.71 (*t*), 73.56 (*t*), 72.56 (*t*, 3 PhCH_2); 54.79 (*q*, MeO); additionally for the (*E*)-*anti*-conformer, 138.01 (*s*); 137.98 (*s*); 137.22 (*s*); 74.94 (*t*), 74.72 (*t*), 73.70 (*t*, 3 PhCH_2); 54.93 (*q*, MeO). FAB-MS: 520.3 (100, $[M + 1]^+$), 488.2 (22, $[M - OMe]^+$), 412.2 (47, $[M - OBn]^+$), 380.2 (65), 91.0 (35, $C_7H_7^+$).

*Methyl 2-[Acetyl(methyl)amino]-3,4,6-tri-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (β-D-**26**). β-D-**8** (0.40 g, 0.79 mmol) was methylated as described for α-D-**26**. FC (AcOEt/hexane 7:3) gave β-D-**26** (0.24 g, 47%). Oil. R_f (AcOEt/hexane 7:3) 0.30. $[\alpha]_D^{25} = +9.9$ ($c = 3.5$, $CHCl_3$). IR (0.03M, CH_2Cl_2): 3060*w*, 3051*m*, 3034*m*, 2936*m*, 2870*m*, 1646*s*, 1496*m*, 1454*m*, 1408*m*, 1383*m*, 1359*m*, 1312*w*, 1279*w*, 1245*w*, 1216*m*, 1190*w*, 1113*s*, 1055*s*, 1028*s*, 914*w*, 814*w*, 651*w*, 601*w*. ^{1}H-NMR (50°, 300 MHz, $CDCl_3$; (*E*)-*anti*/((*Z*)-*anti* and (*Z*)-*syn*) 3:2): 7.33–7.18 (*m*, 15 arom. H); 4.86–4.73 (*m*, 2 PhC*H*); 4.67–4.54 (*m*, 0.4 H–C(1), 4 PhC*H*); 4.37 (*d*, $J = 7.3$, 0.6 H, H–C(1)); 3.79–3.67 (*m*, 0.4 H–C(2), H–C(3), H–C(5), 2 H–C(6)); 3.67–3.51 (*m*, 0.6 H, H–C(2)); 3.49 (*s*, 1.8 H), 3.47 (*s*, 1.2 H, MeO); 3.48–3.42 (*m*, H–C(4)); 3.04–2.84 (br. *s*, 1.2 H), 2.75 (*s*, 1.8 H, MeN); 2.16 (*s*, 1.8 H), 1.96 (*s*, 1.2 H, Ac). ^{1}H-NMR (−50°, 300 MHz, CD_2Cl_2; (*E*)-*anti*/(*Z*)-*anti*/(*Z*)-*syn* 6:3:1): 7.37–7.20 (*m*, 15 arom. H); 5.15 (*d*, $J = 8.0$, 0.1 H, H–C(1)); 4.84–4.72 (*m*, 2 PhC*H*), 4.62–4.48 (*m*, 0.3 H–C(2), 4 PhC*H*); 4.35 (*d*, $J = 7.8$, 0.6 H), 4.21 (*d*, $J = 8.9$, 0.3 H, H–C(1)); 3.80–3.66 (*m*, H–C(3), H–C(5), 2 H–C(6)); 3.61–3.42 (*m*, 0.7 H–C(2), H–C(4)); 3.45 (*s*, 1.8 H), 3.40 (*s*, 1.2 H, MeO); 2.99 (*s*, 0.3 H), 2.62 (*s*, 1.8 H), 2.29 (*s*, 0.9 H, MeN); 2.08 (*s*, 1.8 H), 1.92 (*s*, 0.9 H), 1.89 (*s*, 0.3 H, Ac). ^{13}C-NMR (75 MHz, $CDCl_3$; (*E*)-*anti*/((*Z*)-*anti* and (*Z*)-*syn*) 2:1): see *Table 7*; additionally for the (*E*)-*anti*-conformer, 137.93 (*s*); 137.87 (*s*); 137.57 (*s*); 128.54–127.61 (several *d*); 75.16 (*t*, PhCH_2); 75.05 (*t*, PhCH_2); 73.64 (*t*, PhCH_2); 57.11 (*q*, MeO); additionally for the (*Z*)-*anti*- and (*Z*)-*syn*-conformers, 138.67 (*s*); 138.24 (*s*); 74.75 (*t*, PhCH_2); 73.48 (*t*, PhCH_2). FAB-MS: 520.3 (34, $[M + 1]^+$), 488.2 (100, $[M - OMe]^+$), 412.2 (35, $[M - OBn]^+$), 91.0 (56, $C_7H_7^+$).

*Methyl 2-[Acetyl(methyl)amino]-2-deoxy-3,4,6-tri-*O*-methyl-α-*D*-glucopyranoside* (α-D-**27**) [51]. α-D-**14** (0.20 g, 0.72 mmol) was methylated as described for α-D-**26**. FC (AcOEt/MeOH 19:1) and HPLC (AcOEt/MeOH/hexane 19:1:24.4) gave α-D-**27** (0.13 g, 60%). Oil. Anal. HPLC (hexane/AcOEt/MeOH 20:19:1, 2 ml/min): t_R 5.9 min. R_f (AcOEt/MeOH 19:1) 0.37. ^{1}H-NMR (500 MHz, CD_2Cl_2; (*Z*)-*anti*/(*E*)-*anti* 7:3): 4.64 (*d*, *J* = 3.2, 0.3 H), 4.56 (*d*, *J* = 3.5, 0.7 H, H–C(1)); 4.54 (*dd*, *J* = 3.5, 11.2, 0.7 H, H–C(2)); 3.68 (*dd*, *J* = 8.5, 11.2, 0.7 H), 3.67 (br. *t*, *J* ≈ 9.0, 0.3 H, H–C(3)); 3.61 (*dd*, *J* = 2.9, 11.3, 0.3 H, H–C(2)); 3.60–3.52 (*m*, H–C(5), 2 H–C(6)); 3.52 (*s*, 0.9 H), 3.51 (*s*, 3 H), 3.49 (*s*, 2.1 H), 3.38 (*s*, 2.1 H), 3.37 (*s*, 0.9 H), 3.33 (*s*, 0.9 H), 3.29 (*s*, 2.1 H, 4 MeO); 3.28 (*dd*, *J* = 8.1, 10.6, 0.7 H), 3.26 (*dd*, *J* = 8.1, 10.6, 0.3 H, H–C(4)); 2.97 (*s*, 2.1 H), 2.90 (*s*, 0.9 H, MeN); 2.08 (*s*, 2.1 H); 2.07 (*s*, 0.9 H, Ac). ^{1}H-NMR (300 MHz, $CDCl_3$; (*Z*)-*anti*/(*E*)-*anti* 58:42): similar to [51], except H–C(2) of the (*E*)-*anti*-conformer at 3.68–3.38 ppm. ^{13}C-NMR (75 MHz, $CDCl_3$; (*Z*)-*anti*/(*E*)-*anti* 7:3): see *Table 7*; additionally for the (*Z*)-*anti*-conformer, 60.10, 59.13, 57.51, 54.78 (4*q*, 4 MeO); additionally for the (*E*)-*anti*-conformer, 60.33, 60.10, 59.13, 54.97 (4*q*, 4 MeO).

*Methyl 2-[Acetyl(methyl)amino]-2-deoxy-3,4,6-tri-*O*-methyl-β-*D*-glucopyranoside* (β-D-**27**) [51–53]. β-D-**14** (0.20 g, 0.72 mmol) was methylated as described for α-D-**26**. FC (AcOEt/MeOH 19:1) and HPLC (hexane/AcOEt/MeOH 20:19:1) gave β-D-**27** (70 mg, 33%). Oil. Anal. HPLC (hexane/AcOEt/MeOH 20:19:1, 2 ml/min): t_R 8.3 min. R_f (AcOEt) 0.25. ^{1}H-NMR (50°, 300 MHz, $CDCl_3$; (*E*)-*anti*/((*Z*)-*anti* and (*Z*)-*syn*) 7:3): 5.11–4.87 (br. *s*, 0.3 H), 4.32 (*d*, *J* = 8.1, 0.7 H, H–C(1)); 4.25–3.98 (br. *s*, 0.3 H, H–C(2)); 3.68–3.58 (*m*, 0.3 H–C(3), 2 H–C(6)); 3.55–3.50 (*m*, 0.7 H, H–C(3)); 3.55 (*s*, 2.1 H), 3.52 (*s*, 0.9 H), 3.50 (*s*, 3 H), 3.47 (*s*, 2.1 H), 3.45 (*s*, 0.9 H), 3.43 (*s*, 2.1 H), 3.41 (*s*, 0.9 H, 4 MeO); 3.40–3.27 (*m*, 0.7 H–C(2), 0.7 H–C(4), H–C(5)); 3.16 (br. *t*, *J* = 9.3, 0.3 H, H–C(4)); 3.05 (*s*, 0.9 H), 2.86 (*s*, 2.1 H, MeN); 2.13 (*s*, 2.1 H), 2.09 (*s*, 0.9 H, Ac). ^{1}H-NMR (−50°, 300 MHz, CD_2Cl_2; (*E*)-*anti*/(*Z*)-*anti*/(*Z*)-*syn* 6:3:1): 5.06 (*d*, *J* = 8.4, 0.1 H, H–C(1)); 4.44 (*d*, *J* = 8.5, 10.3, 0.3 H, H–C(2)); 4.29 (*d*, *J* = 7.9, 0.6 H), 4.21 (*d*, *J* = 8.7, 0.3 H, H–C(1)); 4.14 (*dd*, *J* = 9.0, 10.4, 0.1 H, H–C(3)); 3.59–3.51 (*m*, 2 H–C(6)); 3.50–3.46 (*m*, 0.9 H, H–C(3)); 3.47 (*s*, 1.8 H), 3.46 (*s*, 0.9 H), 3.44 (*s*, 1.8 H), 3.43 (*s*, 0.9 H), 3.42 (*s*, 1.2 H), 3.41 (*s*, 1.8 H), 3.39 (*s*, 0.9 H), 3.36 (*s*, 0.3 H), 3.34 (*s*, 2.1 H), 3.32 (*s*, 0.3 H, 4 MeO); 3.36–3.23 (*m*, 0.7 H–C(2), H–C(4), H–C(5)); 3.02 (*s*, 0.3 H), 2.84 (*s*, 0.9 H), 2.76 (*s*, 1.8 H, MeN); 2.06 (*s*, 0.3 H), 2.03 (*s*, 2.7 H, Ac). ^{13}C-NMR (75 MHz, $CDCl_3$; (*E*)-*anti*/((*Z*)-*anti* and (*Z*)-*syn*) 7:3): see *Table 7*; additionally for the (*E*)-*anti*-conformer, 60.64, 60.46, 59.32, 57.09 (4*q*, 4 MeO); additionally for the (*Z*)-*anti*- and the (*Z*)-*syn*-conformers, 60.20 (*q*), 56.80 (br. *q*, 2 MeO). ^{13}C-NMR (−80°, 75 MHz, CD_2Cl_2; (*E*)-*anti*/(*Z*)-*anti*/(*Z*)-*syn* 6:3:1): see *Table 7*; additionally for the (*E*)-*anti*-conformer, 61.56, 61.14, 59.57, 57.71 (4*q*, 4 MeO); additionally for the (*Z*)-*anti*-conformer, 61.21, 59.52, 57.71, 56.10 (4*q*, 4 MeO); additionally for the (*Z*)-*syn*-conformer, 60.36, 60.30, 57.66, 57.60 (4*q*, 4 MeO).

*Methyl 2-[Acetyl(methyl)amino]-2-deoxy-α-*D*-glucopyranoside* (α-D-**28**) [55]. A stirred soln. of α-D-**26** (225 mg, 0.43 mmol) in EtOH (3.75 ml) and cyclohexene (1.90 ml) was treated with 20% $Pd(OH)_2$/C (60 mg) and kept under reflux and N_2 for 6 h [54]. Filtration through *Celite* and evaporation fo the filtrate gave α-D-**28** (87 mg, 91%). Oil. R_f (AcOEt/MeOH 4:1) 0.30. ^{1}H-NMR (D_2O, 500 MHz; (*Z*)-*anti*/(*E*)-*anti* 3:1): 4.89 (*d*, *J* = 3.4, 0.25 H), 4.74 (*d*, *J* = 3.5, 0.75 H, H–C(1)); 4.39 (*dd*, *J* = 3.5, 11.3, 0.75 H, H–C(2)); 4.08 (*dd*, *J* = 8.6, 10.7, 0.25 H), 4.02 (*dd*, *J* = 8.6, 11.3, 0.75 H, H–C(3)); 3.89 (*dd*, *J* = 2.3, 12.2, 0.25 H), 3.88 (*dd*, *J* = 2.3, 12.3, 0.75 H, H–C(6)); 3.82 (*dd*, *J* = 3.4, 10.7, 0.25 H, H–C(2)); 3.78 (*dd*, *J* = 5.4, 12.3, H′–C(6)); 3.71 (*ddd*, *J* = 2.3, 5.5, 10.1, 0.25 H), 3.69 (*ddd*, *J* = 2.3, 5.4, 10.0, 0.75 H, H–C(5)); 3.52 (*dd*, *J* = 8.6, 10.0, 0.25 H), 3.50 (*dd*, *J* = 8.6, 10.0, 0.75 H, H–C(4)); 3.39 (*s*, 0.75 H), 3.36 (*s*, 2.25 H, MeO); 3.08 (*s*, 2.25 H), 2.94 (*s*, 0.75 H, MeN); 2.17 (*s*, 0.75 H), 2.16 (*s*, 2.25 H, Ac). ^{13}C-NMR (50 MHz, D_2O; (*Z*)-*anti*/(*E*)-*anti* 3:1): see *Table 7*; additionally, 58.22 (*q*, MeO).

*Methyl 2-[Acetyl(methyl)amino]-2-deoxy-β-*D*-glucopyranoside* (β-D-**28**) [55]. β-D-**26** (82 mg, 0.16 mmol) was debenzylated as described for α-D-**26** to afford β-D-**28** (33 mg, 83%). Oil. R_f (AcOEt/MeOH 4:1) 0.25. ^{1}H-NMR (85°, 200 MHz, D_2O; (*E*)-*anti*/((*Z*)-*anti* and (*Z*)-*syn*) 1:1): 4.75 (*d*, *J* = 8.8, 0.5 H), 4.69 (*d*, *J* = 8.2, 0.5 H, H–C(1)); 4.12–4.02 (br. *s*, 0.5 H, H–C(2)); 3.96–3.71 (*m*, H–C(3), H–C(4), H–C(5), 2 H–C(6)); 3.63–3.51 (*m*, 0.5 H, H–C(2)); 3.53 (*s*, 1.5 H), 3.50 (*s*, 1.5 H, MeO); 3.03 (*s*, 1.5 H), 2.87 (*s*, 1.5 H, MeN); 2.15 (*s*, Ac). ^{1}H-NMR (−50°, 300 MHz, CD_3OD; (*E*)-*anti*/(*Z*)-*anti*/(*Z*)-*syn* 6:3:1): 5.17 (*d*, *J* = 8.7, 0.1 H), 4.59 (*d*, *J* = 8.2, 0.6 H), 4.52 (*d*, *J* = 8.1, 0.3 H, H–C(1)); 4.41 (br. *t*, *J* = 9.1, 0.3 H, H–C(2)); 3.88 (br. *d*, *J* = 11.8, H–C(6)); 3.75–3.65 (*m*, H–C(3), H′–C(6)); 3.50 (*s*, 1.8 H, MeO); 3.48–3.31 (*m*, 0.7 H–C(2), H–C(4), H–C(5)); 3.46 (*s*, 0.9 H), 3.45 (*s*, 0.3 H, MeO); 3.10 (*s*, 0.3 H), 2.98 (*s*, 0.9 H), 2.86 (*s*, 1.8 H, MeN); 2.13 (*s*, 0.9 H), 2.12 (*s*, 1.8 H), 2.10 (*s*, 0.3 H, Ac). ^{13}C-NMR (75 MHz, D_2O; (*E*)-*anti*/((*Z*)-*anti* and (*Z*)-*syn*) 3:1): see *Table 7*; additionally for the (*E*)-*anti*-conformer, 59.93 (*q*, MeO); additionally for the (*Z*)-*anti*- and (*Z*)-*syn*-conformers, 59.47 (*q*, MeO).

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