NMR Studies of Sugar Amides and Thioamides

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Configurational and conformational NMR analyses of amido and thioamido groups in pyranoid sugar derivatives are described. *Z*, *E* isomers about the N–CX bond were unequivocally identified. Also, the disposition of this functional group with respect to the sugar ring has been determined on the basis of some NMR parameters. A relevant parameter was the chemical shift of the α-sugar proton to the amide or thioamide group. The scope and limitations of other ^1H and ^{13}C NMR data have been studied.

Chemical and biological properties of organic compounds depend on their structure and conformation, and therefore their correct determination is not a trivial question. Many natural products and their derivatives have a *N*-acyl group joined to a sugar moiety. NMR data of some *N*-alkyl-*N*-glycosyl fatty acid amides,[1] that enhance the production of antibodies against various antigens, indicate the presence of two conformational isomers in solution due to the hindered rotation about the amide C–N bond. This structural feature appears in antibiotics such as *N*-acetylcalicheamicins,[2] istamycins,[3] glycocinnamoylspermidines,[4] and streptomycins.[5] In these cases, signals for individual conformers were not identified and nor was a preferred conformation in solution established. Although the amide *Z*/*E* isomerism has been extensively studied,[6,7] works dealing with the configuration and conformation of amido- and thioamido sugar fragments are scarce and, in our opinion, some useful data for the assignment of both isomers in this type of molecule should be reported. For this reason, we have studied some simple *N*-acyl or *N*-thioacyl aminosugars which have been gathered into three series (**I–III**):

Su-NH-CXH	Su-NR^1-CXR	Su-NH-CXR
I	**II**	**III**

Su = *O*-acylated pyranoid sugar; X = O, S; R = Me, Ph; R^1 = alkyl group

In all cases, the conformational rigidity of the sugar ring simplifies the structural study of these molecules.

Results and Discussion

Series **I**.—*N*-Formylaminopyranoses have been previously studied[8–14] by NMR spectroscopy. In some of these compounds, both rotamers could be identified and a preference for the *Z* isomer was always observed.[9–15] However, *N*-thioformyl aminosugars have recently been synthesised[14] and for that, the study of **1–5** will now be considered (see Fig. 1).

When NMR spectra of some thioformamides were recorded occasionally, a variation of the isomeric ratio was observed. For instance, when **3** was dissolved in $CDCl_3$, the solution contained initially only the *Z*-isomer. Later however, the *E*-isomer would appear. Compound **5** displayed an opposite behaviour, in this case the *E*-isomer was detected first (Table 1). For **1**, both isomers were initially observed with the *Z*-isomer slowly increasing. These changes were also observed by specific rotation measurement. The variation of isomeric ratio can be explained if only one isomer crystallises. When amorphous solids are isolated the isomeric ratio does not change. At the equilibrium, the *Z*-isomer of **1–3** and **6** was predominant whereas for **4** and **5**, *Z* and *E* configurations showed similar abundance.

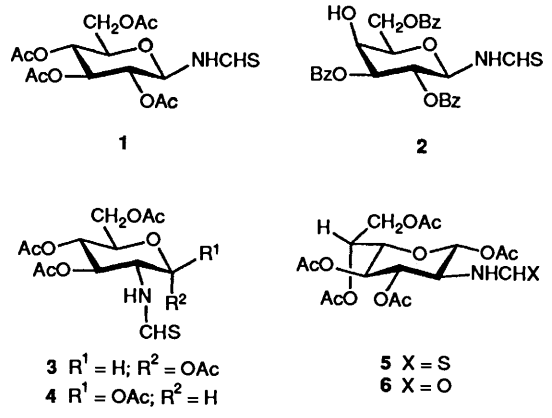


Fig. 1 Compounds of series **I**

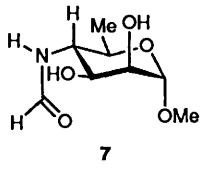


Fig. 2 W Arrangement between 4-H and H-CO in the *syn*-periplanar conformation for *Z* isomer of compound **7**

Z/*E* configurations of **1–6** could be assigned by $J_{NH,CHX}$ measurements. For **1–5**, thioformyl proton signals appear as doublets with larger coupling constants for *E*($J_{NH,CHS}$ 9.5–14.1 Hz) than for *Z* ($J_{NH,CHS}$ 5.0–6.1 Hz) isomers (Table 2). In the *N*-formyl series, $J_{NH,CHO}$ 9.2-11.3 Hz for *E* and < 1.0 Hz for *Z* were measured.[13]

Anti- and/or syn-periplanar conformations about the sugar–NHCXR bond have been found.[11,13,17–22] Although the Karplus equation[23] is not able to discriminate between the *syn*- and *anti*-conformations, the observed values for $J_{NH,CH}$ (8.0–10.9 Hz) are generally considered consistent with a preferred antiperiplanar disposition[13,17–22] for all compounds of series **I** (and **III**, see later). However, Kenne *et al.*[11] have found a long-range coupling constant (W arrangement) that suggests also the existence of a synperiplanar conformation for the *Z*-isomer of **7** (see Fig. 2).

In this series, the $J_{NH,C(1\text{ or }2)H}$ coupling constant and the chemical shift of the sugar proton geminal to the amide group enable a correct assignment of the preferred conformation. For **1–5**, this proton resonated at lower field for *Z* than for *E* isomers

Table 1 Series I; ^{1}H NMR chemical shifts

	1-H	2-H	3-H	4-H	5-H	6-H	6′-H
1*Z*	5.96 t	5.23–4.95 m	5.40 t	5.23–4.95 m	3.92 ddd	4.33 dd	4.10 dd
1*E*	4.86 t	5.23–4.95 m	5.30 t	5.23–4.95 m	3.85 ddd	4.27 dd	4.13 dd
2*Z*	6.34 t	6.06 t	5.63 dd	4.52 ~d	4.80–4.40 m	4.60 dd	4.36 dd
2*E*	5.14 t	6.08 t	5.54 dd	4.80–4.40 m	4.80–4.40 m	4.80–4.40 m	4.40–4.00 m
3*Z*	6.37 d	5.45–5.20 m	5.44 t	5.27 t	4.17–4.00 m	4.29 dd	4.17–4.00 m
3*E*	6.28 d	4.19–3.96 m	5.39 t	5.15 t	4.19–3.96 m	4.29 dd	4.19–3.96 dd
4*Z*	5.92 d	5.54–5.32 m	5.54–5.32 m	5.20 t[a]	4.00–3.90 m	4.33 dd[a]	4.17 dd[a]
4*E*	5.85 d	3.79 ddd-q	5.54–5.32 m	5.10 t[a]	4.00–3.90 m	4.31 dd[a]	4.13 dd[a]
5*Z*	5.82 d	5.38 q	5.36–5.24 m	5.25 t	3.97 dd	5.36–5.24 m	—
5*E*	5.73 d	3.78 ddd-q	5.36–5.24 m	5.10 t	3.97 dd	5.36–5.24 m	—
5*Z*[b]	5.85 d	5.06 q	5.33 t	4.91 t	4.26 dd	5.22–5.11 m	—
5*E*[b]	5.74 d	4.24–4.00 m	5.25 t	4.86 t	4.24–4.00 m	5.22–5.11 m	—
6*Z*	5.74 dd	4.34 ddd	5.36–5.16 m	5.16 t	3.94 dd	5.36–5.16 m	—
6*E*	5.65 d	3.57 ddd	5.36–5.16 m	5.11 t	3.95 dd	5.36–5.16 m	—
6*Z*[b]	5.74 d	4.01 q	5.23 t	4.85 t	4.24–3.93 m	4.24–3.93 m	—
6*E*[b]	5.61 d	3.72 q	5.13 t	4.85 t	4.24–3.93 m	4.24–3.93 m	—

	7-H	7′-H	NH	CHX	OAc	OH	OBz
1*Z*	—	—	8.60–8.40 m	9.52 d	2.10–2.04 m	—	—
1*E*	—	—	8.60–8.40 m	9.40 d	2.10–2.04 m	—	—
2*Z*	—	—	9.17 dd	9.58 d	—	4.80–4.40 m	8.20–7.12 m
2*E*	—	—	9.17 dd	9.51 d	—	4.80–4.40 m	8.20–7.12 m
3*Z*	—	—	8.08 dd	9.40 d	2.19, 2.11, 2.07	—	—
3*E*	—	—	8.22–8.00 m	9.22 d	2.25, 2.18, 2.09, 2.06	—	—
4*Z*	—	—	8.32 dd	9.49 d	2.17, 2.15, 2.09, 2.06	—	—
4*E*	—	—	8.51 dd	9.19 d	2.10, 2.08, 2.06, 2.04	—	—
5*Z*	4.34 dd	4.16 dd	7.95 dd	9.49 d	2.17, 2.14, 2.13, 2.11	—	—
5*E*	4.32 dd	4.15 dd	8.21 dd	9.17 d	2.09, 2.05, 2.03	—	—
5*Z*[b]	4.24–4.00 m	4.24–4.00 m	10.26 dd	9.39 d	2.11–1.88	—	—
5*E*[b]	4.24–4.00 m	4.24–4.00 m	10.17 dd	9.21 d	2.11–1.88	—	—
6*Z*	4.33 dd	4.14 dd	6.45 d	8.17 s	2.12, 2.11, 2.05, 2.05, 2.02	—	—
6*E*	4.33 dd	4.14 dd	6.65 t	7.98 d	2.16, 2.10, 2.07, 2.03	—	—
6*Z*[b]	4.24–3.93 m	4.24–3.93 m	8.17 d	8.04 s	2.17–1.85	—	—
6*E*[b]	4.24–3.93 m	4.24–3.93 m	7.82 t	7.95 d	2.17–1.85	—	—

[a] Assignments may be interchanged between *Z* and *E* isomers. [b] In [$^2H_6$]DMSO.

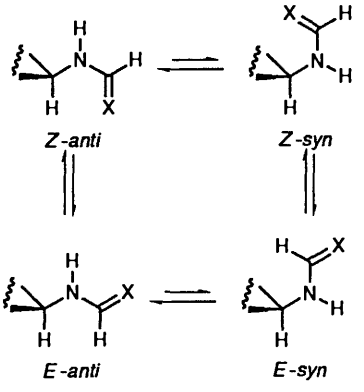


Fig. 3 Syn- and anti-periplanar conformations for *Z* and *E* isomers

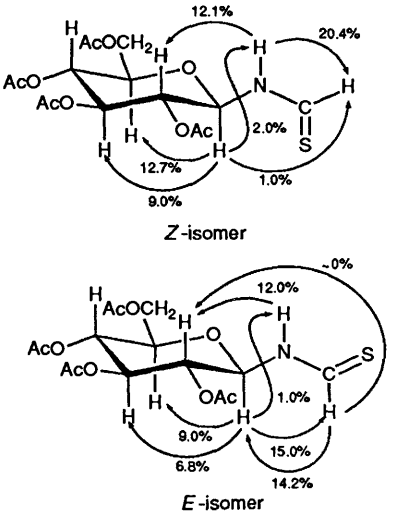


Fig. 4 NOE data for *Z* and *E* isomers of 1

(Δδ 0.8–1.6 ppm). In the case of formamides,[13] this difference is smaller (for instance, 0.3 and 0.8 ppm in DMSO and $CDCl_3$, respectively, for **6**). This deshielding of the *Z*-isomer would justify the assignment of an *anti*-conformation.[7] Although this proton always lies in the plane of the amido group in accordance with the high value of $J_{NH,C(1\text{ or }2)H}$, in a *Z-anti* disposition this proton is nearer to the C=X group than in other arrangements (Fig. 3). The similar value of $J_{NH,C(1\text{ or }2)H}$ for the *E*-isomer, allows us also to propose an antiperiplanar conformation. Furthermore, in the *syn*-conformation the *N*-acyl group causes 1,3-diaxial interactions and would induce remarkable variations in the chemical shifts of the β-sugar protons. The antiperiplanar conformation was also supported by the NOE data shown in Fig. 4.

On the other hand, the CHX proton always resonated at slightly higher field for *E* than for *Z* rotamers.

In the ^{13}C NMR spectra of this series, two salient features must be emphasised: (*a*) the sugar carbon joined to the functional group resonates at higher field for *Z* than for *E* isomers (Δδ = 7.6–8.9 ppm for **1**–**5** and 4.7 ppm for **6**), as previously described,[13,24,25] and (*b*) the signal of C=X is more deshielded for *E* than for *Z* isomers (Δδ = 1.4–1.9 ppm for **1**–**5** and 3.1 for **6**) (Table 3).

Series **II**.—Although many compounds related to this series

Table 2 Series I; ^{1}H NMR coupling constants

	CHX,NH	NH,1	NH,2	1,2	2,3	3,4	4,5	5,6	5,6′	6,6′	6,7	6,7′	7,7′
1*Z*	5.3	9.1	—	9.1	9.4	9.4	10.0	5.0	1.9	12.5	—	—	—
1*E*	13.8	9.0	—	8.9	9.4	9.4	10.0	4.8	2.0	12.2	—	—	—
2*Z*	5.8	9.0	—	9.0	9.9	2.8	~0	5.6	6.1	11.6	—	—	—
2*E*	12.1	~8	—	~8	10.4	2.8					—	—	—
3*Z*	5.9	—	8.0	3.2	9.7	9.7	9.7	3.4		12.3	—	—	—
3*E*	13.9	—		3.6	10.5	10.2	10.2	3.4		12.3	—	—	—
4*Z*	6.0	—	9.0	8.4		9.7	9.7	4.0	2.1	12.5	—	—	—
4*E*	14.1	—	9.9	8.6	9.7	9.7	9.7	4.0	2.1	12.5	—	—	—
5*Z*	6.0	—	8.4	8.3	8.4	8.8	8.8	2.1	—	—	4.8	7.6	11.7
5*E*	13.7	—	10.0	8.7	8.0	9.7	9.7	2.1	—	—	4.9	7.6	11.7
5*Z*[a]	6.1	—	~9	8.7	9.9	9.9	9.8	1.8	—	—			
5*E*[a]	13.7	—	9.5	8.7	9.8	9.8	9.6		—	—			
6*Z*	~0	—	9.7	8.9	~9.5	9.7	9.8	2.2	—	—	4.8	5.7	9.6
6*E*	11.3	—	10.9	8.6	~9.0	9.7	9.8	2.2	—	—	4.8	5.7	9.6
6*Z*[a]	~0	—	9.3	8.8	9.8	9.7	9.7		—	—			
6*E*[a]	11.1	—	9.8	8.7	9.8	9.7	9.7		—	—			

[a] In DMSO.

Table 3 Series I; ^{13}C NMR chemical shifts

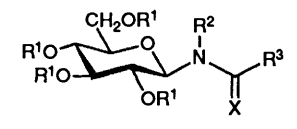
	C=X	C-1	C-2	C-3	C-4	C-5	C-6	C-7	O-*C*(O)-CH$_3$	O-*C*(O)-Ph	O-*C*(O)-Ph	Ph
1*Z*	192.48	78.49	70.50[a]	72.40[a]	68.04[a]	73.79[a]	61.51	—	170.99, 170.57, 169.82, 169.51	20.41	—	—
1*E*	193.84	86.43	70.17[a]	72.22[a]	67.73[a]	73.79[a]	61.51	—	170.50, 169.90, 168.74, 169.30	20.41	—	—
2*Z*	192.56	78.90	69.37	73.97[a]	67.42	74.49[a]	62.90	—	—	—	166.92, 166.62, 165.67	133.74–128.10
2*E*	194.06	87.22	68.98	73.89[a]	67.15	74.32[a]	63.04	—	—	—		
3*Z*	190.77	~88.2	53.07	70.03[a]	67.05[a]	69.45[a]	61.20	—	171.35, 170.56, 168.91, 169.30	20.75–20.30	166.57, 166.14, 165.76	133.74–128.10
3*E*	192.71	89.72	60.67	69.63[a]	65.52[a]	69.45[a]	61.06	—	170.38, 169.97, 169.13, 168.44	20.75–20.30	—	—
4*Z*	191.26	91.84	54.19	72.23	67.68	72.56	61.51	—	171.40–168.77	20.79–20.40	—	—
4*E*	192.98	90.90	63.09	71.29	67.55	72.44	61.30	—	171.40–168.77	20.79–20.40	—	—
5*Z*	191.37	92.38	54.34	72.41[a]	66.61[a]	73.08[a]	66.34[a]	62.34	171.42, 170.72, 170.32, 169.65, 169.22	20.74–20.47	—	—
5*E*	193.02	91.45	63.06	71.51[a]	66.61[a]	72.96[a]	66.34[a]	62.12	170.64, 170.57, 170.10, 169.50, 168.71	20.74–20.47	—	—
6*Z*	161.35	92.39	56.01	72.25[a]	66.97	72.87[a]	66.45[a]	62.26	171.00, 170.60, 170.44, 169.36, 169.29	20.71, 20.56, 20.39	—	—
6*E*	164.42	92.18	51.35	71.95[a]	66.87	72.87[a]	66.45[a]	62.13	170.54, 170.27, 170.11, 169.51, 168.74	20.71, 20.56, 20.39	—	—

[a] Assignments may be interchanged in each isomer.

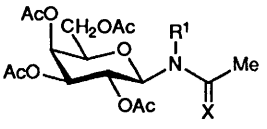
have been structurally studied,[1–3,5,26] no reports about the assignation of *Z*/*E* isomers could be found. Some interest has been paid to sugar derivatives, whose endocyclic oxygen was replaced by a *N*-acyl group[7,27,28] (see Fig. 5).

At room temperature, NMR spectra of *N*-acetylglycosylamines **8**,[29] **11**, **14**,[30] **16**[31] and **17**,[32] *N*-thioacetylglycosylamines **9**, **12** and **15**, and *N*-(ethylacetamido)heptopyranose **20** showed two signal sets and the *Z*/*E* isomeric ratio (60–82% of *Z* in $CDCl_3$) did not change over time. Isomeric ratios for **8** and **9** showed a strong dependence on the solvent (25% of *Z* in DMSO). These signals coalesced when the temperature increased. NMR spectra of the perbenzoylglycosylamines **10** and **13**, and perbenzoyl-2-aminosugars[31,33,34] **18**, **19** and **21**–**23**, showed, at room temperature, broad signals that made their interpretation difficult. Nevertheless, single sets of signals for each isomer could be obtained when spectra were recorded at low temperature (see Tables 4–6 and 10). The long-range coupling observed for the *Z* isomer of **21**, $J_{3,5}$ 1.3, also supports the D-glycero-D-*ido* configuration in the $^0S_2$ conformation[35] previously described.[34] However, the $J_{1,2}$ values (~1.7 and 2.8 Hz for *Z* and *E* isomers, respectively) are not indicative of the anomeric configuration.[35,36]

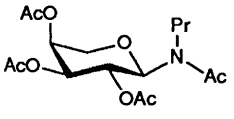
In this series, the sugar proton geminal to the amide group showed chemical shifts related to those described in Series I. For the *N*-acylglycosylamines **8**, **10**, **11**, **13**, **14**, **16** and **17**, 1-H protons resonated in two unoverlapping spectral regions (6.69–5.79 and 5.53–4.93 ppm). For the *N*-thioacetylglycosylamines **9**, **12** and **15**, the thiocarbonyl group anisotropy also causes large differences in the chemical shift of these protons. In the *N*-acyl-2-aminosugars 2-H showed a similar behaviour. These results are in accordance with the *Z*-configuration for the isomer whose proton (geminal to the amide group) resonates at lower field, and the *E* configuration for the other one. Both isomers show the same antiperiplanar conformation between the aforementioned proton and the *N*-alkyl substituent. This conclusion is in agreement with the NOE data shown in Fig. 6.



8 R^1 = Ac; R^2 = Pr; R^3 = Me; X = O
9 R^1 = Ac; R^2 = Pr; R^3 = Me; X = S
10 R^1 = Bz; R^2 = Pr; R^3 = Ph; X = O
11 R^1 = Ac; R^2 = Bn; R^3 = Me; X = O
12 R^1 = Ac; R^2 = Bn; R^3 = Me; X = S
13 R^1 = Bz; R^2 = Bn; R^3 = Ph; X = O



14 R^1 = Et; X = O
15 R^1 = Et; X = S



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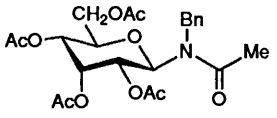

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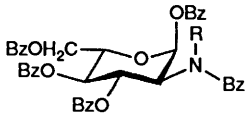
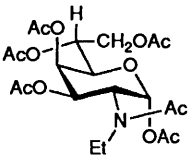


18 R = Et
19 R = Pr



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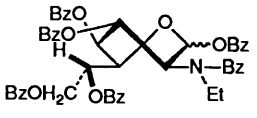

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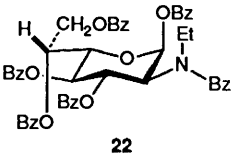

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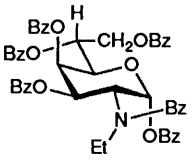

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Fig. 5 Compounds of series II

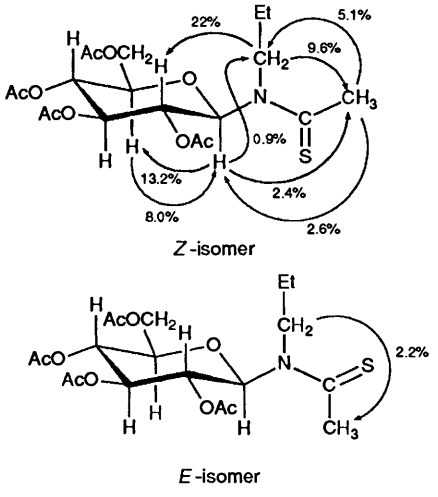
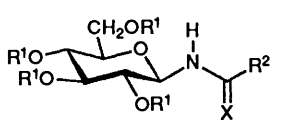


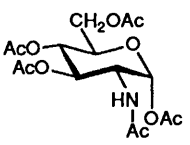
Fig. 6 NOE data for *Z* and *E* isomers of **9**

NMR data of *N*-alkyl groups rarely have diagnostic value.[37] Sometimes, geminal protons, N-CH_2-R, appear together in different regions for each isomer; however, this behaviour is not general and spectra are often very complex (Table 4).

In the case of thioacetamides **9**, **12** and **15**, *N*-CS-CH_3 protons were more deshielded for *E* than for *Z* isomers. However, this



24 R^1 = Ac; R^2 = Me; X = O
25 R^1 = Ac; R^2 = Me; X = S
26 R^1 = Bz; R^2 = Ph; X = O
27 R^1 = Bz; R^2 = Ph; X = S



28

Fig. 7 Compounds of series III

methyl group could not be promptly identified in acetamides because it appears along with ester protons.

Some ^{13}C NMR signals can also have diagnostic value. Thus, sugar carbon atoms joined to the amide group were more shielded for *Z* than for *E* isomers. This is in accordance[24,25] with the relative disposition of this carbon with respect to the C=X in each isomer. Unlike series **I**, $\Delta\delta$ for C-1 atoms of **9**, **12** and **15** are smaller than for the corresponding oxoanalogues **8**, **11** and **14**.

For the *E* isomer, the *N*-alkyl group adopts a *syn* disposition with respect to the C=X double bond. For this reason, the carbon atom joined to nitrogen is more shielded than for the *Z* isomer.[24,25] However, thioacetamides show exceptions to this behaviour. Thus, the sequence of both isomers changed in **15** and, in the case of **9** and **12**, the carbons mentioned had an identical chemical shift.

On the other hand, unlike Series **I**, the N–CHX carbon resonated further downfield for *Z* than for *E* isomers. In the case of the *E* isomer of acetamides, assignment of this signal can sometimes be difficult because it appears along with those of carbonyl groups.

For *N*-alkylaminosugar derivatives, the methyl carbon of the NC(X)Me group resonated at higher field for *Z* than for *E* isomers as in **8**, **9**, **14**–**16** and **20**. This sequence changed for **11**, **12** and **17** wherein a *N*-Bn instead of an *N*-alkyl group is present.

These compounds also allow us to observe the effect of the inversion of one chiral carbon (**11** and **17**), O/S exchange (**8**, **11** and **14** with respect to **9**, **12** and **15**), and *N*-alkyl substitution (**8** and **9** with respect to **11** and **12**) on the *Z*/*E* isomeric ratio observed.

Series **III**.—Many natural products can be classified in this series (see Fig. 7). Only one signal set has been found for these compounds,[7,19,28,38] and the antiperiplanar conformation of the *Z* configuration has been proposed, based on the $J_{NH,CH}$ coupling constant.[17,18] This assignment, which is in accordance with X-ray crystallography data, has been fully accepted.[15,21,39,40] However, Thornton[9,41] has found a *syn* conformation, stabilised by hydrogen bonding, in some derivatives of *N*-acylneuraminic acid. On the other hand, a dynamic equilibrium between *syn* and *anti* conformations has been proposed[42] for some 2-acetamido-2-deoxy sugars, and recently, contribution of three conformers has been assumed[43] for *N*-acyl-D-ribofuranosylamines. Also, configurational and conformational information about the sugar fragment has been collected by NMR studies of diacylamino derivatives.[7,28]

Accordingly, NMR spectra of **24**,[44] **25**–**27** and **28**[45] showed only one signal set even at 200 K in [$^2H_6$]acetone (Tables 7–9).

Again, the resonance of the sugar proton geminal to the amide group may provide valuable information about the structure of this type of compound. We have observed a great similarity between the chemical shift of this proton in the *Z* isomer of **1**, **6** and other related compounds,[11,13] with that of the same proton of **24**,[44] **25**, **28**[45] and others.[11,13,46] These similar chemical shifts are indicative of identical geometries,

Table 4 Series II; ^{1}H NMR chemical shifts

	1-H	2-H	3-H	4-H	5-H	5′-H	6-H	6′-H	7-H	7′-H	Ph	α-CH_2	β-CH_2	X-CH_3	NAc, OAc	C(S)-CH_3
8*Z*	5.94 d	5.10 t	5.34 t	5.08 t	3.89–3.79 m	—	4.23–4.13 m	4.23–4.13 m	—	—	—	3.17 t	1.76–1.42 m	0.91 t	2.11, 2.07, 2.05, 2.01, 1.98	—
8*E*	5.26–5.04 m	5.26–5.04 m	5.32 t	5.26–5.04 m	3.89–3.79 m	—	4.23–4.13 m	4.23–4.13 m				3.5–3.3 m 3.0–2.8 m	1.76–1.42 m	0.86 t	2.16, 2.07, 2.05, 2.01, 1.98	—
8*Z*[a]	5.90 d	5.12 t	5.38 t	5.05 t	4.21–3.98 m	—	4.21–3.98 m	4.21–3.98 m	—	—	—	3.34–3.05 m	1.62–1.28 m	0.84 t	2.10–1.88	—
8*E*[a]	5.49 d	5.12 t	5.44 t	5.05 t	4.21–3.98 m	—	4.21–3.98 m	4.21–3.98 m	—	—	—	3.05–2.80 m	1.62–1.28 m	0.77 t	2.10–1.88	—
8[b]	5.55 b s	5.12 t	5.38 t	5.02 t	4.18–4.05 m	—	4.18–4.05 m	4.18–4.05 m	—	—	—	3.30–2.90 m	1.60–1.17 m	0.81 t	2.07, 2.00, 1.94	—
9*Z*	7.12 d	5.11 t	5.44 t	5.11 t	3.88 m	—	4.23–4.08 m	4.23–4.08 m	—	—	—	3.51–3.33 m	1.85–1.58 m	0.93 t	2.09, 2.06, 2.02, 1.99	2.65 s
9*E*	5.31 d	5.29 t	5.39 t	5.16 t	3.88 m	—	4.21 dd	4.10 dd				3.51–3.33 m	1.85–1.58 m	0.88 t	2.10, 2.06, 2.03, 2.01	2.74 s
9*Z*[a]	7.02 d	5.18 t	5.41 t	5.23–4.90 m	4.30–3.95 m	—	4.30–3.95 m	4.30–3.95 m			—	3.95–3.72 m 3.63–3.24 m	1.76–1.26 m	0.85 t	2.08–1.87	2.56 s
9*E*[a]	5.87 d	5.23 t	5.48 t	5.08 t	4.30–3.95 m	—	4.30–3.95 m	4.30–3.95 m	—	—	—	3.95–3.72 m 3.63–3.24 m	1.76–1.26 m	0.78 t	2.08–1.87	2.64 s
10*Z*[c]	6.54 d	5.90–5.62 m	6.21 t	5.90–5.62 m	4.48–4.28 m	—	4.86 d	4.48–4.28 m	—	—	8.22–7.15 m	3.40–3.20 m	1.30–1.20 m 1.60–1.50 m	0.50 t	—	—
10*E*[c]	5.36 d	5.87 t	5.90–5.62 m	5.90–5.62 m	4.10–3.90 m	—	4.81 d	4.41 dd	—	—	8.22–7.15 m	3.95–3.77 m 3.40–3.20 m	1.86–1.60 m	0.94 t	—	—
10[b]	5.81 d	5.90 t	6.04 t	5.77 t	4.50–4.40 m	—	4.68 dd	4.53 dd	—	—	8.10–7.33 m	3.63 ddd 3.39 ddd	1.85–1.42 m	0.79 t	—	—
11*Z*	6.09 d	5.09 d	5.41 t	5.04 t	4.00–3.80 m	—	4.24–4.06 m	4.24–4.06 m	—	—	7.38–7.15 m	4.65 d 4.37 d	—	—	2.26–1.88	—
11*E*	5.31–4.99 m	5.31–4.99 m	5.31 t	5.31–4.99 m	4.00–3.80 m	—	4.24–4.06 m	4.25–4.06 m		—	7.38–7.15 m	4.52 s	—	—	2.26–1.88	—
12*Z*	7.34–7.20 m	5.14 t	5.51 t	5.07 t	4.13–3.98 m	—	4.13–3.98 m	4.13–3.98 m	—	—	7.34–7.20 m	4.82 d 4.64 d	—	—	2.07–1.95	2.42 s
12*E*	5.56–5.02 m	5.56 t	5.56–5.02 m	5.56–5.02 m	4.13–3.98 m	—	4.13–3.98 m	4.13–3.98 m	—	—	7.34–7.20 m	4.95–4.29 m	—	—	2.07–1.95	2.83 s
13*Z*[c]	6.69 d	5.94–5.64 m	6.35 t	5.94–5.64 m	5.00–4.00 m	—	5.00–4.00 m	5.00–4.00 m	—	—	8.30–6.75 m	5.00–4.00 m	—	—	—	—
13*E*[c]	5.53 d	5.94–5.64 m	5.94–5.64 m	5.94–5.64 m	5.00–4.00 m	—	5.00–4.00 m	5.00–4.00 m			8.30–6.75 m	5.00–4.00 m	—	—	—	—
14*Z*	5.91 d	5.24 t	5.24–5.09 m	5.45 d	4.20–4.05 m	—	4.20–4.05 m	4.20–4.05 m	—	—	—	3.33 q	—	1.24 t	2.19–1.99	—
14*E*	5.03 d	5.39 t	5.24–5.09 m	5.45 d	4.20–4.05 m	—	4.20–4.05 m	4.20–4.05 m	—	—	—	3.70–3.45 m 3.30–3.05 m	—	1.14 t	2.19–1.99	—
15*Z*	7.11 d	5.60–5.16 m	5.60–5.16 m	5.60–5.16 m	4.40–4.00 m	—	4.40–4.00 m	4.40–4.00 m	—	—	—	3.67 q	—	1.30 t	2.19, 2.06, 2.00	2.67 s
15*E*	5.60–5.16 m	5.60–5.16 m	5.60–5.16 m	5.60–5.16 m	4.40–4.00 m	—	4.40–4.00 m	4.40–4.00 m	—	—	—	3.67 q	—	1.26 t	2.21, 2.04, 2.03, 2.00	2.74 s
16*Z*	5.79 d	5.37–5.22 m	5.14 dd	5.37–5.22 m	4.01 dd	3.76 dd	—	—	—	—	—	3.20 t	1.80–1.46 m	0.93 t	2.18–2.00	—
16*E*	4.93 d	5.42 t	5.14 dd	5.37–5.22 m	4.07 dd	3.76 dd	—	—	—	—	—	3.56–3.36 m 3.17–2.92 m	1.80–1.46 m	0.88 t	2.18–2.00	—
17*Z*	6.38 d	5.02–4.80 m	5.69 t	5.02–4.80 m	4.32–3.97 m	—	4.32–3.97 m	4.32–3.97 m	—	—	7.36–7.12 m	4.63 d 4.42 d	—	—	2.20, 2.01, 1.93	—
17*E*	5.42 d	5.02–4.80 m	5.69 t	5.02–4.80 m	4.32–3.97 m	—	4.32–3.97 m	4.32–3.97 m		—	7.36–7.12 m	4.78 d 4.33 d	—	—	2.31, 2.17, 2.09, 2.01, 1.73	—
18*Z*[d]	6.78 d	5.81 ddd	6.37 t	5.99 t	4.70–4.27 m	—	4.70–4.27 m	4.70–4.27 m	—	—	8.32–7.00 m	3.60–3.40 m	—	0.63 t	—	—
18*E*[d]	6.66 d	4.70–4.27 m	6.32 t	5.49 t	4.70–4.27 m	—	4.70–4.27 m	4.70–4.27 m	—	—	8.32–7.00 m	3.90–3.72 m 3.60–3.40 m	—	1.08 t	—	—
19*Z*[d]	6.79 d	5.80 ddd	6.42 t	6.03 t	4.74–4.26 m	—	4.74–4.26 m	4.74–4.26 m	—	—	8.30–6.90 m	3.38 m	1.78 m	0.18 t	—	—
19*E*[d]	6.71 d	4.74–4.26 m	6.35 t	5.52 t	4.74–4.26 m	—	4.74–4.26 m	4.74–4.26 m	—	—	8.30–6.90 m	3.69 t 3.38 t	1.78 m 1.36–0.87 m	0.63 t	—	—
19[b]	6.66 d	4.84 m	6.41 dd	5.52 t	4.73 dt	—	4.44 d	4.44 d	—	—	8.28–7.19 m	3.39–3.25 m	1.38–1.12 m	0.43 t	—	—
20*Z*	6.16 d	5.23 dd	5.50 dd	5.53 ~s	4.25 d	—	5.08 ddd	—	4.40 dd	4.07 dd	—	3.53–3.10 m	—	1.11 t	2.15, 2.13, 2.11, 1.99	—
20*E*	6.20 d	4.47–4.33 m	5.57–5.40 m	5.57–5.40 m	4.25 d	—	5.08 ddd	—	4.40 dd	4.07 dd	—	3.53–3.10 m	—	1.00 t	2.19, 2.18, 2.00, 1.99	—
20*Z*[a]	5.94 d	5.03 dd	5.50 dd	5.41 ~d	4.32–4.20 m	—	5.06–5.00 m	—	4.45 d	4.07 dd	—	3.50–3.14 m	—	1.05 t	2.19, 2.13, 2.10, 2.04, 1.99, 1.97	—
20*E*[a]	6.29 d	4.33 dd	5.48 dd	5.50–5.40 m	4.32–4.20 m	—	5.06–5.00 m	—	4.49 d	4.07 dd	—	3.50–3.14 m	—	0.92 t	2.23, 2.15, 1.95	—
20[b]	6.11 b s	5.15–4.85 m	5.56 dd	5.51 dd	4.43 dd	—	5.04 ddd	—	4.34 dd	4.09 dd	—	3.37 dq 3.30 dq	—	1.07 t	2.21, 2.14, 2.12, 2.04, 2.00, 1.98	—
21*Z*[c]	6.82 d	6.04–5.85 m	6.21 ddd	5.75 t	5.13 dd	—	6.04–5.85 m	—	4.92 dd	4.84–4.53 m	8.21–6.98 m	3.60–3.30 m	—	0.63 t[a]	—	—
21*E*[c]	6.74 d	4.84–4.53 m	6.35 dd	5.42 t	4.84–4.53 m	—	6.11 ddd	—	4.84–4.53 m	4.45 dd	8.21–6.98 m	3.92–3.72 m 3.70–3.53 m	—	1.04 t[a]	—	—
22*Z*[c]	6.87 d	5.95 dd	6.38 t	5.61 t	4.88–4.40 m	—	5.74 dd	—	4.88–4.40 m	4.88–4.40 m	8.67–7.00 m	3.79 m	—	0.59 t	—	—
22*E*[c]	6.75 d	4.88–4.40 m	6.34 t	5.55 t	4.88–4.40 m	—	5.99 dd	—	4.88–4.40 m	4.88–4.40 m	8.67–7.00 m	3.57 m	—	1.06 t	—	—
22[b]	6.81 d	4.97 dd	6.52 dd	5.56 t	4.99 dd	—	5.71 dt	—	4.61 d	4.61 d	8.38–7.01 m	3.53 q	—	0.87 t	—	—
23*Z*[c]	6.94[e]	6.47[e]	6.42 dd	6.08 s	5.77 d[e]	—	5.23–4.48 m	—	5.23–4.48 m	5.23–4.48 m	8.35–6.98 m	3.54–3.30 m	—	0.64 t	—	—
23*E*[c]	6.71 d	5.10 dd	6.22 dd	6.08 d	5.47 d	—	4.83 d	—	4.72 d	4.60 d	8.35–6.98 m	3.77 dq 3.56 dq	—	1.07 t	—	—
23[b]	6.82 d	5.13 dd	6.47 dd	6.13 d	5.17 d	—	5.46 ddd	—	4.77 dd	4.53 dd	8.30–7.23 m	3.77–3.43 m	—	0.93 t	—	—

[a] In DMSO. [b] At coalescence in DMSO. [c] At 248 K in $CDCl_3$. [d] At 273 K in $CDCl_3$. [e] Tentative assignment.

Table 5 Series II; ^{1}H NMR coupling constants

	1,2	2,3	3,4	4,5	4,5′	5,5′	5,6	5,6′	6,6′	6,7	6,7′	7,7′	α-CH_2 gem	α-CH_2, β-CH_2	β-CH_2, CH_3
8*Z*	9.4	9.1	9.4	9.7	—	—	2.7	2.7		—	—	—	~0.0	8.2	7.4
8*E*		9.4	9.4		—	—				—	—	—	14.5	7.6	7.4
8*Z*[a]	8.2	9.2	8.8	9.3	—	—				—	—	—			6.8
8*E*[a]	8.8				—	—				—	—	—			7.2
8[b]	9.2	9.5	9.4	9.4	—	—				—	—	—			7.3
9*Z*	9.1	9.4	9.5	9.5	—	—				—	—	—			7.4
9*E*	9.1	9.1	9.2	9.2	—	—	4.0	2.4		—	—	—			7.4
9*Z*[a]	8.9	9.6	9.6		—	—				—	—	—			7.0
9*E*[a]	8.7	9.3	9.4	9.5	—	—				—	—	—			7.2
10*Z*[c]	9.3	9.6	9.6		—	—				—	—	—			6.5
10*E*[c]	8.5	9.0			—	—	~0	6.2	12.4	—	—	—	12.3	7.0	7.0
10[b]	8.8	8.7	9.0	9.4	—	—	2.2	4.7	11.2	—	—	—	14.3	8.8 5.6	7.3
11*Z*	9.2	9.6	9.3	9.9	—	—				—	—	—	17.4	—	—
11*E*		9.3	9.3		—	—				—	—	—	~0.0	—	—
12*Z*	9.6	9.6	9.6	9.7	—	—				—	—	—	16.8	—	—
12*E*					—	—				—	—	—		—	—
13*Z*[c]	9.4	9.3	9.3												
13*E*[c]	8.0														
14*Z*	8.0	9.0	2.4	~0	—	—				—	—	—	~0	—	7.2
14*E*	8.7	9.0	2.4	~0	—	—				—	—	—	13.8	—	6.9
15*Z*	8.0				—	—				—	—	—		—	7.0
15*E*					—	—				—	—	—		—	7.6
16*Z*	9.0	10.0	3.2	1.7	1.0	13.3	—	—	—	—	—	—	~0	8.2	7.5
16*E*	9.0	9.6	3.2	1.7	1.0	13.3	—	—	—	—	—	—	15	~9	7.5
17*Z*	9.8	~3.7	~3.7	9.5									~15	—	—
17*E*	9.5	~3.7	~3.7										~16	—	—
18*Z*[d]	~3	9.1	9.1	9.0	—	—				—	—	—	~14	—	~7
18*E*[d]	~3	9.1	9.1	8.9	—	—				—	—	—	~14	—	~7
19*Z*[d]	2.7	10.5	9.8	9.5	—	—				—	—	—			6.2
19*E*[d]	2.9	10.0	9.6	9.6	—	—				—	—	—	~13	~6.6	6.9
19[b]	2.7	11.0	9.5	10.2	—	—	3.9	3.9	~0	—	—	—		4.4	7.3
20*Z*	3.2	10.5	2.8	~0	—	—	9.8	—	—	2.2	3.7	12.2		—	7.0
20*E*	3.2			~0	—	—	9.8	—	—	2.2	3.7	12.2		—	6.8
20*Z*[a]	3.4	~11	~3		—	—		—	—	~0	4.8	12.2		—	6.8
20*E*[a]	3.1	11.1	~3		—	—		—	—	~0	4.8	12.2		—	6.6
20[b]	~3	11.7	3.4	2.6	—	—	9.2	—	—	~2	5.2	12.2		—	6.8
21*Z*[c]	1.7	10.2	2.6	2.9	—	—	9.7	—	—	~1				—	6.9
21*E*[c]	2.8	9.2	5.4	4.8	—	—		—	—		5.1	12.4	14.9	—	6.9
22*Z*[c]	~3.3	8.8	8.8	9.5	—	—	7.2	—	—	~9	~0			—	~7
22*E*[c]	~3.3	8.8	8.8	9.5	—	—	~7	—	—	~9	~0			—	~7
22[b]	3.6	11.1	9.5	10.0	—	—	1.9	—	—	6.3	6.4	~0		—	6.8
23*Z*[c]					—	—	10	—	—					—	
23*E*[c]	2.7	11	~2.5	~0	—	—	9.8	—	—	~0	~0	11.8	~12.6	—	5.8
23[b]	2.5	11.5	3.2	0	—	—	9.2	—	—	2.5	4.2	12.3	~13	—	6.9

[a] In DMSO. [b] At coalescence in DMSO. [c] At 248 K in $CDCl_3$. [d] At 273 K in $CDCl_3$.

and are in accordance with a *Z* configuration in an antiperiplanar disposition. The NOE data on **25** confirm this assumption (Fig. 8).

Conclusions

Compounds of series **III** only appear as one stereoisomer of *Z* configuration about the amide or thioamide C–N bond. However, for compounds of series **I** and **II** mixtures of *Z* and *E* rotamers can be observed when equilibrium is reached (Table 10). A very useful parameter for the identification of these rotamers is the chemical shift of the sugar proton directly joined to the carbon that supports the substituent. Furthermore, the ^{1}H NMR signal of this proton and its coupling constant with the NH proton allow us to determine the preferential conformation for these compounds in which C-H sugar and NH or NR groups adopt an *anti* disposition. Several useful rules for configurational assignment in compounds of series **I** and **II** are given in Table 11.

There are many references about the presence of rotamers unassigned in acylaminosugar frameworks. For instance, *N*-alkyl-*N*-glycosyl fatty acid amides as glycolipid analogues have recently been studied.[1] Both the ^{1}H and ^{13}C NMR spectra show the duplicity of some signals which indicates the presence of two conformational isomers in solution although they are not identified by the authors. From the spectroscopic data reported[1] for these glycosylamides (compounds of series **II**), *Z* and *E* isomers can be identified and their predominant conformations in solution established as shown for **29** in Fig. 9.

N-Acetylcalicheamicins[2] and some of their degradation products contain an *N*-acetyl-*N*-alkylamino group joined to a sugar fragment which can show *Z*, *E* isomerism. Thus, some of the ^{13}C NMR signals of the simplified model **30** appear to be duplicated.[2] Assignment of *Z* and *E* rotamers has been made in Fig. 10.

N-(Benzyloxycarbonyl) derivatives of 3″-epidihydrostreptomycin gave, at room temperature, a mixture of rotamers.[5] The same behaviour is shown by **31** which has a double set of signals in its ^{1}H NMR spectrum. The identification of these isomers appears in Fig. 11.

Other compounds wherein the thioformylic or formylic protons of series **I** are replaced by different frameworks, as in acylated thioureylenedisaccharides,[22,47] sugar thioureas,[48]

Table 6 Series II; ^{13}C NMR chemical shifts

	C·1	C·2	C·3	C·4	C·5	C·6	C·7	C = X	N·CX·CH_3	α·CH_2	β·CH_2	CH_2·CH_3	O·CO·CH_3	O·CO·CH_3	O·CO·Ph	Ph
8*Z*	79.98	68.34[a]	72.92	67.88[a]	73.54	61.46	—	171.39	21.36	45.60	23.76	11.06	170.03, 169.40, 169.16	20.24–20.08	—	—
8*E*	85.28	68.57[a]	73.04	67.59[a]	73.54	61.46	—	170.03[b]	21.77	~43.2	~23.8	11.06	169.69, 169.40, 168.94, 168.63	20.24–20.08	—	—
9*Z*	84.99	69.54[a]	72.53[a]	68.06[a]	74.00[a]	61.55	—	204.73	32.87	49.42	23.37	11.27	170.39, 170.16, 169.66, 169.53	20.54–20.10	—	—
9*E*	86.23	68.77[a]	72.75[a]	67.68[a]	74.31[a]	61.55	—	201.76	33.21	49.42	20.22	11.18	170.39, 169.99, 169.22, 168.75	20.54–20.10	—	—
10*Z*[c]	~81.0	~68.2[a]	72.56	68.93[a]	73.93	~61.5	—	172.95	—	~46.7	~24.0	11.10	—	—	165.76, 165.60, 165.25	135.01–125.77
10*E*[c]	86.33	68.14	72.93	68.24	73.62	62.25	—	172.10	—	43.63	21.85	11.46	—	—	165.76, 165.35, 164.88, 164.43	135.01–125.77
11*Z*	79.71	68.89[a]	72.70	68.13[a]	73.53	61.75	—	172.29	22.19	47.14	—	—	169.98, 169.52, 169.43, 169.18	20.17	—	137.55–126.38
11*E*	85.27	68.89[a]	73.05	67.56[a]	73.60	61.62	—	170.44[b]	21.80	~45.0	—	—	169.98, 169.76, 168.94, 168.32	20.17	—	137.55–126.38
12*Z*	84.40	69.80[a]	72.20	68.12[a]	73.63	61.67	—	206.39	33.84	50.65	—	—	170.34–168.44	20.50–20.02	—	136.27–126.22
12*E*	86.01	68.92[a]	72.64	67.58[a]	73.98	~62.5	—	~203	32.97	50.65	—	—	170.34–168.44	20.50–20.02	—	136.27–126.22
13*Z*[c]	80.06	68.80[a]	72.10[a]	69.68[a]	73.90[a]	62.95[a]	—	173.31	—	48.20	—	—	—	—	165.72, 165.34, 164.87, 163.80	138.22–125.35
13*E*[c]	86.11	68.45[a]	72.90[a]	68.60[a]	73.71[a]	62.59	—	172.08	—	45.56	—	—	—	—	165.72, 165.21, 164.50, 163.60	138.22–125.35
14*Z*	80.56	67.02[a]	70.99[a]	66.24[a]	72.30	61.06	—	171.27	21.31	38.52	—	15.92	—	20.26–20.15	—	—
14*E*	85.89	67.02[a]	71.21[a]	66.37[a]	72.41	61.06	—	169.92[b]	21.80	~36.5	—	14.01	169.92–168.72	20.26–20.15	—	—
15*Z*	85.19	66.90	70.17	66.71	72.48	60.82	—	203.87	32.35	42.20	—	15.10	169.93–168.42	20.13–19.91	—	—
15*E*	86.42	66.65	70.43	66.09	72.59	60.82	—	200.82	32.85	42.49	—	12.16	169.93–168.42	20.13–19.91	—	—
16*Z*	81.12	71.13[a]	68.16[a]	66.66[a]	66.07	—	—	171.53	21.53	46.02	23.97	11.33	169.88–168.87	20.69, 20.37	—	—
16*E*	86.54	71.22[a]	68.16[a]	66.84[a]	66.07	—	—	170.24[b]	21.91	43.66	21.91	11.33	169.88–168.87	20.69, 20.37	—	—
17*Z*	77.40	66.48[a]	68.22	66.13[a]	71.47	62.25	—	172.93	22.56	46.89	—	—	170.51, 170.00, 169.14	20.75–20.05	—	137.29–126.25
17*E*	82.77	66.94[a]	68.04	65.74[a]	71.84	62.25	—	171.40	21.98	~44.5	—	—	169.43, 169.09, 168.95, 168.17	20.75–20.05	—	137.81–126.25
18*Z*[d]	91.85	54.44	69.92[a]	68.68	69.71[a]	62.22	—	173.57	—	40.32	—	15.65	—	—	165.90, 165.60, 164.95, 164.23	135.83–125.84
18*E*[d]	92.11	59.97	69.71	68.04	69.71	62.38	—	172.96	—	38.61	—	13.68	—	—	165.72, 165.18, 164.95, 164.23	135.83–125.84
19*Z*[d]	91.76	54.28	69.68	68.71	69.68	62.34	—	174.22	—	47.40	23.68	10.99	—	—	165.81, 165.09, 164.09	135.56–125.76
19*E*[d]	91.91	59.94	69.68	68.02	69.68	62.34	—	173.52	—	45.32	21.41	10.58	—	—	165.64, 164.88, 164.09	135.56–125.76
20*Z*	91.15	49.96	67.43[a]	65.43[a]	66.82[a]	65.38[a]	61.55	171.98	21.42	38.83	—	15.01	170.11, 169.88, 169.78, 169.07, 167.99	20.57–20.17	—	—
20*E*	91.56	54.13	67.32[a]	65.65[a]	67.02[a]	65.20[a]	61.44	170.86[b]	21.96	37.10	—	13.37	169.78, 169.66, 169.40, 169.07, 167.78	20.57–20.17	—	—
21*Z*[c]	91.56[e]	52.09	71.16	68.68	69.82	68.09	63.16	174.32	—	40.15	—	15.53	—	—	165.94–164.44	135.58–125.64
21*E*[c]	91.80[e]	58.75	70.52	~68.4	69.82	66.55	~63.0	173.60	—	38.73	—	13.62	—	—	165.94–164.44	135.58–125.64
22*Z*[c]	91.48	53.95	69.54[a]	67.94[a]	68.61[a]	66.48[a]	60.98	173.59	—	~40.1	—	15.59	—	—	165.75–163.95	135.39–125.64
22*E*[c]	91.76	59.82	69.23[a]	67.94[a]	68.04[a]	66.48[a]	60.57	172.94	—	38.69	—	13.61	—	—	165.75–163.95	135.39–125.64
23*Z*[c]	92.13	*f*	*f*	*f*	*f*	*f*	~62.5	*f*	—	*f*	—	~15.5	—	—	*f*	135.45–125.84
23*E*[c]	92.62	55.66	67.51	65.57	67.31[a]	66.00[a]	61.47	173.06	—	37.85	—	13.52	—	—	165.29, 164.99, 164.56, 163.82	135.45–125.84

[a] Assignments may be interchanged in each isomer. [b] These assignments may be interchanged with the corresponding carbonyl groups. [c] At 248 K in $CDCl_3$. [d] At 273 K in $CDCl_3$. [e] Assignments may be interchanged between *Z* and *E* isomers. [f] Signal unidentified.

Table 7 Series III; ^{1}H NMR chemical shifts

	1-H	2-H	3-H	4-H	5-H	6-H	6′-H	NH	Ac	Ph	CS-CH_3
25	5.90 t	5.07 t	5.42 t	5.09 t	3.93 ddd	4.33 dd	4.12 dd	8.42 d	2.08, 2.07, 2.06, 2.04	—	2.52 s
26	6.01 t	5.75 t	6.26 t	5.90 t	4.57–4.37 m	4.70 dd	4.55 dd	7.48–7.08 m	—	8.14–7.09 m	—
27	6.26 dd	5.66 t	6.20 t	5.79 t	4.39 ddd	4.66 dd	4.48 dd	8.70 d	—	8.08–7.24 m	—

Table 8 Series III; ^{1}H NMR coupling constants

	NH,1	1,2	2,3	3,4	4,5	5,6	5,6′	6,6′
25	8.6	9.0	9.5	9.4	9.9	4.9	1.7	12.5
26	9.1	9.4	9.5	9.6	9.8	2.5	4.1	11.2
27	8.0	9.2	9.4	9.6	9.6	2.4	5.4	11.8

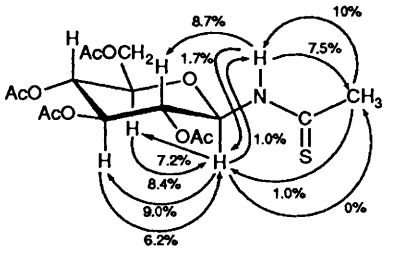


Fig. 8 NOE data on **25**

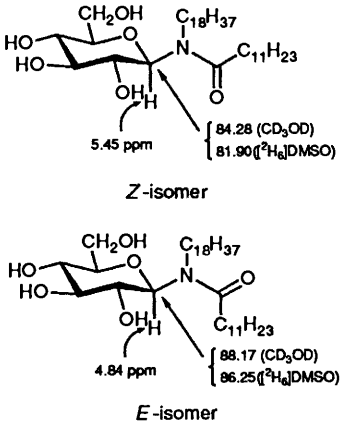
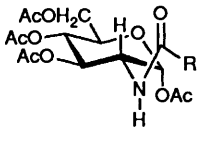
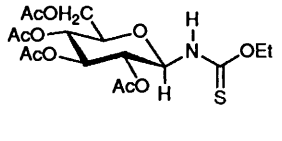


Fig. 9 Spectroscopic data and conformation of *Z* and *E* isomers of **29**

ureas,[49] thiocarbamates,[49] *etc.* can also be compared with the respective members of series **I** and **III**. Thus, chemical shifts of sugar α-protons to the substituent are similar to those found for *Z*-thioformamides or formamides. Thus, the 2-H chemical shifts for **31** and **32** are respectively 4.43 and 4.40 ppm (δ 4.56 and 3.80 ppm for *Z*-**33** and *E*-**33**, respectively,[13] and 1-H in the thiocarbamate **34** appears at 5.56 ppm (see $\delta_{H\text{-}1}$ for *Z*-**1** in Table 1). Ureido bridges are present in glycocinnamoylspermidine antibiotics.[4]



31 R = PhNH
32 R = 4-ClC$_6$H$_4$NH
33 R = H



34

Thus, the structural analysis that we report, can be applied to the study of biological molecules related to compounds of series **I**–**III** (glycoproteins, polysaccharides, glycolipids, antibiotics, *etc.*), and can probably help with the interpretation of molecular recognition processes.

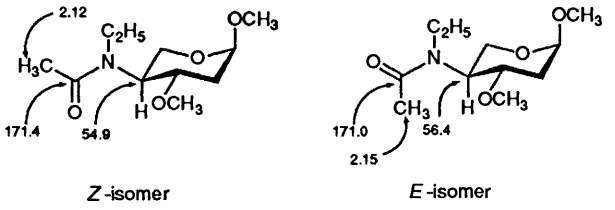


Fig. 10 Spectroscopic data and conformation of *Z* and *E* isomers of **30**

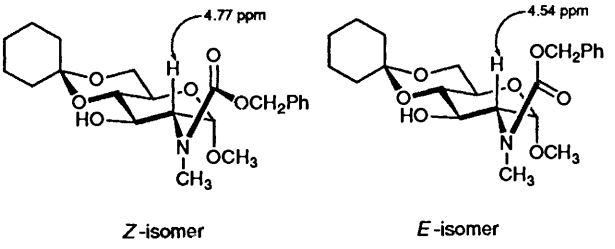


Fig. 11 Spectroscopic data and conformation of *Z* and *E* isomers of **31**

Experimental

General Methods.—M.p.s were determined on a Gallenkamp apparatus and are uncorrected. Optical rotations were measured at 20 ± 5°C on a Perkin-Elmer 141 polarimeter. IR spectra (KBr discs) were recorded on a Perkin-Elmer 399 spectrophotometer and UV spectra on a Pye-Unicam SP8-250 instrument. The ^{1}H (200 MHz) and ^{13}C NMR (50.3 MHz) spectra were recorded on a Bruker AC 200-E spectrometer. Unless otherwise indicated, spectral data refers to samples at equilibrium at 295 K using $CDCl_3$ as solvent. Assignments were confirmed by homo- and hetero-nuclear double-resonance experiments, and DEPT. TMS was used as the internal standard and all *J* values are given in Hz. EI mass spectra (35 and 70 eV) were measured on a Kratos MS-80RFA spectrometer. Analytical TLC was performed with silicagel 60 GF_{254} (Merck) and flash column chromatography with silica gel 60, 230–400 mesh, (Merck) using the following eluents: (a) benzene: diethyl ether (3:1); (b) diethyl ether:light petroleum (b.p. 40–60 °C) (2:1); (c) diethyl ether:light petroleum (3:1); (d) diethyl ether:toluene (3:1).

Materials.—Synthesis of some per-*O*-acylated amidosugars used in this study (**8**,[29] **14**,[30] **16**,[31] **17**,[32] **18**,[31] **19**,[30] **21**,[34] **22**,[34] **23**,[33] **24**[50] and **28**,[13]), has been described elsewhere. Compounds **10**, **11**, **13**, **20** and **26** were prepared by conventional acylation from unprotected aminosugars. On the other hand, the syntheses of thioformamides **1**–**5** have recently been reported[16] in a preliminary communication. Thioamides **9**, **12**, **15**, **25** and **27** were obtained by thiation of the corresponding amides. Use of P_4S_{10} for this conversion in carbohydrate substrates is known,[51] although it has been accelerated using ultrasonic irradiation.[52]

1,3,4,6,7-*Penta*-O-*acetyl*-2-*deoxy*-2-*formamido*-α-D-*glycero*-L-gluco-*heptopyranose* **6**. To a suspension of 1,3,4,6,7-penta-*O*-acetyl-2-amino-2-deoxy-α-D-glycero-L-glucoheptopyranose hydrochloride[22] (0.025 g, 0.55 mmol) in diethyl ether (3 cm^3) at 0°, acetic–formic anhydride (0.1 cm^3) was added. After 3 h, the solvent was evaporated to give a syrup that crystallised from ethanol (0.021 g, 79%), m.p. 160–161 °C; $[\alpha]_D$ +18° (*c* 0.5 in $CHCl_3$); ν_{max}/cm^{-1} 3400m, 1765s, 1695s and 1535m (Found: C,

Table 9 Series III; ^{13}C NMR chemical shifts

	C-1	C-2	C-3	C-4	C-5	C-6	N-*C*X-R	N-C(X)-*C*H$_3$	O-*C*O-R	O-CO-*C*H$_3$	Ph
24	78.04	70.59[a]	72.90[a]	68.16[a]	73.48[a]	61.77	170.75[b]	23.26	170.67, 170.65, 169.89, 169.62	20.72, 20.65, 20.57	—
25	81.45	70.54[a]	72.22	67.90[a]	73.37	61.41	204.76	33.94	170.54, 170.32, 169.46, 169.32	20.31, 20.22 20.18, 20.15	—
26	79.33	71.86	73.22	69.59	73.89	63.09	167.59[b]	—	166.91, 166.12, 165.70, 165.23	—	133.72–127.28
27	82.86	71.99	72.81	69.29	74.24	62.87	202.18	—	167.53, 166.12, 165.63, 165.15	—	140.33–126.91
28	90.70	51.03	70.66[a]	67.53[a]	69.73	61.56	166.72	23.04	171.69, 170.74, 170.07, 169.15	20.96, 20.73, 20.60	—

[a] Assignments may be interchanged. [b] These assignments may be interchanged with the corresponding carbonyl signals.

Table 10 *Z*/*E* Isomer ratios and coalescence temperatures for compounds of the series **I, II, III**

	Z/*E* Ratios							
No.	Equilibrium	*t*/h	Off equilibrium	*t*/min	Other[a]	Conc./mol dm^{-3}	*T*/K	Coalescence *T*/K
1	71/29	2 h	60/40	3 m		0.35	295	
2	67/33					0.55	295	
3	79/21	24 h	99/1	3 m		0.55	295	
4	52/48					0.85	295	
5	49/51	24 h	0/100	3 m		0.11	295	
5[b]	44/56	24 h	0/100	3 m		0.11	295	>365
6	68/32					0.10	295	
6[b]	70/30					0.10	295	>365
8	58/42					0.93	295	
8[b]	25/75					0.47	335	~335
9	68/32					0.31	295	
9[b]	25/75					0.90	295	>365
10					16/84	0.43	248	~345
11	70/30					0.84	295	
12	83/17					0.81	295	
13					25/75	0.51	248	
14	60/40					1.20	295	
15	63/37					0.93	295	
16	60/40					0.81	295	
17	65/35					0.13	295	
18					40/60	0.28	273	
19					38/62	0.43	273	~345
20	64/36					0.65	295	
20[b]	70/30					0.65	295	>360
21					50/50	0.16	248	
22					58/42	0.23	248	~355
23					13/87	0.28	248	~355
24	100/0					1.03	295	
25	100/0					0.99	295	
26	100/0					0.88	295	
27	100/0					0.29	295	
28	100/0					1.03	295	

[a] Spectra were recorded just after the temperature diminished. [b] In [$^2H_6$]DMSO.

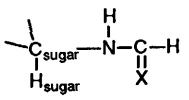
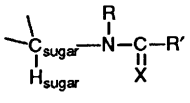
47.95; H, 5.65; N, 3.0. Calc. for $C_{18}H_{25}NO_{12}$: C, 48.3; H, 5.6; N, 3.1%).

2,3,4,6-*Tetra*-O-*acetyl*-N-*propyl*-N-*thioacetamido*-β-D-*glucopyranosylamine* **9**. To a solution of **8** (5.4 g, 12.5 mmol) in anhydrous THF (40 cm^3), P_4S_{10} (3.37 g, 7.59 mmol) was added and the reaction mixture was irradiated with an ultrasonic laboratory cleaner until disappearance of starting amide (4 h, solvent d). The solvent was evaporated and the residue was extracted with dichloromethane (2 × 25 cm^3). The extracts were combined and evaporated to give **9** as a syrup that crystallised from ethanol (3.8 g, 68%), m.p. 112–113 °C; $[\alpha]_D$ + 19° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 274 (ε/dm^3 mol^{-1} cm^{-1} 19 600); ν_{max}/cm^{-1} 1740s and 1475m (Found: C, 50.75; H, 6.8; N, 3.2. Calc. for $C_{19}H_{29}NO_9S$: C, 51.0; H, 6.5; N, 3.1%).

N-*Benzoyl*-2,3,4,6-*tetra*-O-*benzoyl*-N-*propyl*-β-D-*glucopyranosylamine* **10**. To a solution of *N*-propyl-D-glucopyranosylamine[29] (10.0 g, 48 mmol) in pyridine (200 cm^3) at 0 °C, benzoyl chloride was gradually added (60 cm^3, 518 mmol). After cooling at 4 °C for 24 h, the reaction mixture was poured into ice–water (750 cm^3) and extracted with dichloromethane (3 × 100 cm^3). The combined extracts were washed with 3 mol dm^{-3} hydrochloric acid, saturated aqueous sodium hydrogencarbonate, and water, dried with anhydrous sodium sulfate and concentrated to give **10** as a syrup that crystallised from ethanol (30.0 g, 85%), m.p. 190–192 °C; $[\alpha]_D$ +28° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 281, 273 and 230 (ε/dm^3 mol^{-1} cm^{-1} 52 300, 4500 and 3500); ν_{max}/cm^{-1} 1743s, 1663s and 1615m, 1598w and 1505w (Found: C, 71.2; H, 5.5; N, 2.05. Calc. for $C_{44}H_{39}NO_{10}$: C, 71.2; H, 5.3; N, 1.9%).

N-*Acetyl*-2,3,4,6-*tetra*-O-*acetyl*-N-*benzyl*-β-D-*glucopyrano-*

Table 11 Rules for configurational assignment in compounds of series I and II

Series I	Series II
	
(1) $\delta_{H_{sugar}}(Z) > \delta_{H_{sugar}}(E)$	(1) $\delta_{H_{sugar}}(Z) > \delta_{H_{sugar}}(E)$
(2) $\delta_{C_{sugar}}(Z) < \delta_{C_{sugar}}(E)$	(2) $\delta_{C_{sugar}}(Z) < \delta_{C_{sugar}}(E)$
(3) $\delta_{CX}(Z) < \delta_{CX}(E)$	(3) $\delta_{CX}(Z) > \delta_{CX}(E)$
(4) $\delta_{CHX}(Z) > \delta_{CHX}(E)$	(4) When R = sat. alkyl group: $\delta_{CXCH_3}(Z) < \delta_{CXCH_3}(E)$
(5) $J_{NH,CHO} \sim 0$ (Z) $J_{NH,CHO}$ 9.2–11.3 (E) $J_{NH,CHS}$ 5.0–6.1 (Z) $J_{NH,CHS}$ 9.5–14.1 (E)	When R = benzyl group: $\delta_{CXCH_3}(Z) > \delta_{CXCH_3}(E)$

sylamine **11**. To a solution of *N*-benzyl-D-glucopyranosylamine[56] (10.0 g, 37.4 mmol) in pyridine (100 cm^3) at 0 °C, acetic anhydride was gradually added (50 cm^3, 530 mmol). The reaction mixture was processed as described for **10** to give **11** (11.0 g, 61%), m.p. 120–122 °C; $[\alpha]_D$ −20° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 206 (ε/dm^3 mol^{-1} cm^{-1} 9900); ν_{max}/cm^{-1} 1765s, 1748s, 1683s, 1618w, 1598w and 1508w (Found: C, 57.8; H, 5.6; N, 2.9. Calc. for $C_{44}H_{39}NO_{10}$: C, 58.0; H, 5.5; N, 2.9%).

2,3,4,6-*Tetra*-O-*acetyl*-N-*benzyl*-N-*thioacetyl*-β-D-*glucopyranosylamine* **12**. Thiation of **11** (0.95 g, 2.0 mmol) with P_4S_{10} (0.44 g, 1.0 mmol) as described for **9** (8 h) gave **12** (0.70 g, 71%), m.p. 93–94 °C; $[\alpha]_D$ −68° (*c* 0.12 in $CHCl_3$); λ_{max}(EtOH)/nm 276 (ε/dm^3 mol^{-1} cm^{-1} 7000); ν_{max}/cm^{-1} 1742s, 1659m and 1477s (Found: C, 55.9; H, 5.9; N, 2.7. Calc. for $C_{23}H_{29}NO_9S$: C, 55.75; H, 5.9; N, 2.8%).

N-*Benzoyl*-2,3,4,6-*tetra*-O-*benzoyl*-N-*benzyl*-β-D-*glucopyranosylamine* **13**. *N*-Benzyl-D-glucopyranosylamine[56] (10.0 g, 37.4 mmol) was processed as described for the preparation of **10** to give **13** (14.0 g, 48%), m.p. 186–187 °C; $[\alpha]_D$ +48° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 229, 273 and 281 (ε/dm^3 mol^{-1} cm^{-1} 62 100, 5200 and 3900); ν_{max}/cm^{-1} 1737s, 1660m, 1612m, 1595w and 1502w (Found: C, 73.2; H, 5.0; N, 1.7. Calc. for $C_{48}H_{39}NO_{10}$: C, 73.0; H, 5.0; N, 1.8%).

2,3,4,6-*Tetra*-O-*acetyl*-N-*ethyl*-N-*thioacetamido*-β-D-*galactopyranosylamine* **15**. Thiation of **14** (0.83 g, 2.0 mmol) with P_4S_{10} (0.44 g, 1.0 mmol) as described for **9** (7 h) gave **15** (0.65 g, 76%), m.p. 157–158 °C; $[\alpha]_D$ +23° (*c* 0.5 in $CHCl_3$); λ_{max} (EtOH)/nm 274 (ε/dm^3 mol^{-1} cm^{-1} 16 900); ν_{max}/cm^{-1} 1742s, 1659m and 1477s (Found: C, 49.8; H, 6.2; N, 3.2. Calc. for $C_{18}H_{26}NO_9S$: C, 50.0; H, 6.1; N, 3.2%).

1,3,4,6,7-*Penta*-O-*acetyl*-2-*deoxy*-2-(N-*ethylacetamido*)-α-D-glycero-D-galacto-*heptopyranose* **20**. 2-Deoxy-2-(*N*-ethylamino)-α-D-*glycero*-D-*galacto*-heptopyranose hydrochloride[33] (1.0 g, 3.7 mmol) was processed as described for the preparation of **11** to give **20** (0.5 g, 25%), m.p. 138–140 °C; $[\alpha]_D$ +121° (*c* 0.5 in $CHCl_3$); ν_{max}/cm^{-1} 1750s, 1730s and 1640m (Found: C, 51.2; H, 6.5; N, 2.9. Calc. for $C_{21}H_{31}NO_{12}$: C, 51.5; H, 6.4; N, 2.9%).

2,3,4,6-*Tetra*-O-*acetyl*-N-*thioacetyl*-β-D-*glucopyranosylamine* **25**. Thiation of **24** (30.0 g, 63.6 mmol) with P_4S_{10} (20.0 g, 45.0 mmol) as described for **9** (7 h) gave **25** (22.3 g, 87%), m.p. 114–115 °C; $[\alpha]_D$ +67° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 267 (ε/dm^3 mol^{-1} cm^{-1} 15 000); ν_{max}/cm^{-1} 3280m, 1785s and 1538m (Found: C, 47.5; H, 5.6; N, 3.4. Calc. for $C_{16}H_{23}NO_9S$: C, 47.4; H, 5.7; N, 3.5%).

N-*Benzoyl*-2,3,4,6-*tetra*-O-*benzoyl*-β-D-*glucopyranosylamine* **26**. To a solution of D-glucopyranosylamine[50] (10.0 g, 56 mmol) in pyridine (80 cm^3) at 0 °C benzoyl chloride was gradually added (45.2 cm^3, 391 mmol). After 24 h at 4 °C, the mixture was poured into a cold saturated solution of sodium hydrogen carbonate to give a crude product that was recrystallised from ethanol (36.7 g, 96%), m.p. 106–108 °C; $[\alpha]_D$ +13° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 229, 272 and 280 (ε/dm^3 mol^{-1} cm^{-1} 51 400, 54 00 and 4400); ν_{max}/cm^{-1} 3370m, 1735s, 1690m, 1670m, 1612m, 1595w and 1535m (Found: C, 72.1; H, 4.7; N, 2.2. Calc. for $C_{41}H_{33}NO_9$: C, 72.0; H, 4.9; N, 2.05%).

2,3,4,6-*Tetra*-O-*benzoyl*-N-*thiobenzoyl*-β-D-*glucopyranosylamine* **27**. Thiation of **26** (10.3 g, 15.0 mmol) with P_4S_{10} (4.44 g, 10.0 mmol) as described for **9** (60 h) gave **27** (10.5 g, 70%), m.p. 191–192 °C; $[\alpha]_D$ −111° (*c* 0.5 in $CHCl_3$); λ_{max}(EtOH)/nm 232 and 283 (ε/dm^3 mol^{-1} cm^{-1} 43 000 and 7000); ν_{max}/cm^{-1} 3325m, 1730s, 1605m, 1590w and 1530m (Found: C, 68.7; H, 4.75; N, 1.8. Calc. for $C_{41}H_{33}NO_9S$: C, 68.8; H, 4.65; N, 1.95%).

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