Carbohydrate Research, 143 (1985) 21–41
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

A ^{13}C-N.M.R. INVESTIGATION OF GLYCOSYL AZIDES AND OTHER AZIDO SUGARS: STEREOCHEMICAL INFLUENCES ON THE ONE-BOND ^{13}C–^{1}H COUPLING CONSTANTS

LÁSZLÓ SZILÁGYI* AND ZOLTÁN GYÖRGYDEÁK

Department of Organic Chemistry and Antibiotics Research Group of the Hungarian Academy of Sciences, Lajos Kossuth University, P.O.B. 20, H-4010 Debrecen (Hungary)

(Received January 17th, 1985; accepted for publication, April 26th, 1985)

ABSTRACT

Unambiguous ^{13}C assignments have been obtained, using 2D-n.m.r. techniques, for several glycosyl azides, 6-deoxyglycosyl azides, 2-acylamino-2-deoxyglycosyl azides, and some 2- and 3-azido monosaccharide derivatives. For *non-anomeric* C–H bonds the $^{1}J_{C,He}$ values are 4–9 Hz larger than the $^{1}J_{C,Ha}$ values. A substituent (hydroxyl, acetoxyl, alkoxyl, azido, *etc.*) in 1,3-diaxial relationship with H*a* significantly increases the value of $^{1}J_{C,Ha}$. Bond-angle distortions in the fused-ring bicyclic systems of some isopropylidene derivatives result in $^{1}J_{C,Ha}$ values being larger than $^{1}J_{C,He}$ values. Electronic and steric effects of substituents at non-anomeric carbons may alter the $^{1}J_{C,H}$ values for *anomeric* carbons to such an extent that they may no longer be useful for diagnosing anomeric configuration. Bond-angle deformations also influence the ^{13}C chemical shift differences in α- and β-anomers at C-5 and, to a lesser extent, at C-3.

INTRODUCTION

Glycosyl azides are useful synthesis intermediates[1] and are now readily available[2]. We recently described the syntheses of several 6-deoxyhexopyranosyl azides[3] and the use of ^{1}H-n.m.r. data for determining conformation and anomeric configuration. Although, for the majority of glycosyl azides, the ^{1}H-n.m.r. data allow the stereochemistry to be deduced, ambiguities may still arise as noted[3], for example, with 6-deoxy-L-talopyranosyl azides. Although ^{13}C chemical shifts and $^{1}J_{C,H}$ values are well-established n.m.r. parameters for determining anomeric configuration, relatively few such data have been published for azido sugars[1g,h] and we have therefore undertaken a systematic study. Whereas $J_{C\text{-}1,H\text{-}1}$ values are known for many carbohydrate derivatives[4] and have been used extensively for configurational determinations[5,6], this is not so for $^{1}J_{C,H}$ couplings associated with non-anomeric carbons. Assignment problems, overlap in the ^{1}H-coupled ^{13}C-n.m.r.

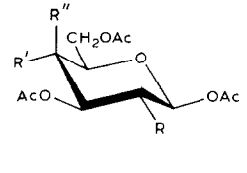
*To whom correspondence should be addressed.

0008-6215/85/$ 03.30

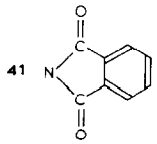
spectra, and, as a result, poor accuracy and reliability of these data are largely responsible. With the advent of modern, especially 2D-n.m.r., methodology, however, these problems can be overcome. The n.m.r. data to be discussed below were obtained mainly from spectra for which self-consistent, unambiguous assignments[7] were, in turn, obtained by the use of 2D-n.m.r. techniques.

RESULTS AND DISCUSSION

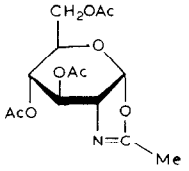
The derivatives **1–23, 25,** and **29** have been described[2c,d,3], and **36–38** have been prepared by published procedures[8,9]. The majority of the 2-acylamino-2-deoxyhexopyranosyl azides are available[2a] by the reaction of 3,4,6-tri-*O*-acetyl-2-acylamino-2-deoxyhexopyranosyl halides with NaN_3, LiN_3, or AgN_3. The halogenoses are usually obtained from acetylated 2-acylamino-2-deoxyglucopyranoses, but the preparation of pure anomers often involves[10] lengthy procedures. We have therefore applied our procedure[2c] for the preparation of **26, 33**, and **35**. The appropriate 1,2-*trans* isomers of acetylated 2-acylamino-2-deoxy-β-D-glycopyranoses **39–41** were treated with $Me_3SiN_3/SnCl_4$ in dichloromethane to give the glycosyl azides.



	R	R'	R''
39	NHAc	H	OAc
40	NHAc	OAc	H



41 OAc H



42

The *gluco*-azide **33** can also be obtained from the oxazoline **42**[11], whereas, under similar conditions, 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose was unreactive, probably due to steric hindrance of the formation of the oxocarbonium ion essential[2c] for reaction.

2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl azide (**24**) was prepared by using the procedure[2d] for the synthesis of 1,2-*cis*-azides. Treatment of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl chloride with NaN_3 in hexamethylphosphoric triamide gave **24** exclusively; the β-anomer **25** was not detected. Likewise, the azide **34** was obtained from 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide. The reaction of 1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranose[12] with Me_3SiN_3 in the presence of a Lewis acid gave 3,4,6-tri-*O*-acetyl-2-

azido-2-deoxy-α,β-D-galactopyranosyl azide (**27** and **28**). 1,2-*cis*-Azides preponderate[2g] in the displacement reactions with Me_3SiN_3 when the 1-*O*-acylpyranoses bear a non-participating group at position 2. However, in the above reaction, the stereoselectivity was low and the anomers were not separable by column chromatography.

^{13}C–^{1}H Coupling constants. — For a ^{1}H-n.m.r. spectrum with noncoincident signals, the 2D ^{13}C–^{1}H chemical shift correlation[13] is the method of choice for obtaining correct, non-heuristic ^{13}C assignments. Unless otherwise stated, the ^{13}C chemical shifts were obtained by using a version[14] of this method in which the proton–proton couplings were suppressed. In general, the ^{1}H chemical shifts were obtained by straightforward first-order analyses. For some compounds, recourse was made to the 2D proton–proton chemical-shift correlation technique in order to unravel more-complicated spectra. For example, Fig. 1 shows the COSY45[15] map of **27** and **28**; these derivatives were available only as an anomeric mixture. Based on the ^{1}H assignment shown, the ^{13}C spectrum could also be unambigously assigned with the aid of the 2D ^{13}C–^{1}H chemical-shift correlation map (Fig. 2). Obviously, this method is not useful when the ^{1}H spectrum is degenerate, and a non-empirical ^{13}C assignment can be achieved then by tracing the carbon–carbon connectivities through $^{1}J_{C,C}$ couplings with the aid of 1D[16] (or 2D[17]) double-quantum spectra (INADEQUATE). The ^{13}C assignment of **11** was accomplished by matching the $^{1}J_{C,C}$ couplings as revealed in a 1D INADEQUATE experiment. The $^{1}J_{C,H}$ couplings were determined from splittings in the ^{1}H-coupled ^{13}C spectra. Partial overlap and signal broadening due to incompletely resolved $^{2}J_{C,H}$ and $^{3}J_{C,H}$ couplings (even after heavy resolution enhancement had been employed) often make evaluations inaccurate or even unreliable. These difficulties could be overcome most conveniently by selectively exciting the individual multiplets using the DANTE[18] pulse sequence. In addition to the high digital resolution that is an advantage of this method and results in accurate coupling constant data, it is also preferred[19] to the use of 2D *J*-resolved spectra because of advantages in measurement time and disk storage space when the number of carbons is ≤10.

^{13}C Chemical shifts. — The chemical shift of the signal of an anomeric carbon bearing an equatorial substituent is at lower field (by ~5 p.p.m.) than that with an axial one[20]. However, there are many exceptions to this rule, or else, the difference is very small or insignificant, especially when the 2-substituent is axial or when the aglycon is chiral[21].

The δ (C-1) values of the hexopyranosyl azides studied here fall in the range 84.5–90.5 p.p.m. (Table I). However, inspection of the data shows that the Δδ (C-1) values for anomeric pairs (Table II) are not suitable for establishing the anomeric configurations in this series. Not only is this so for *manno, rhamno,* or *talo* derivatives, where the 2-substituent is axial, but also for the *galacto* (**24, 25, 27, 28**) and *gluco* (**33, 34**) pairs having an equatorial 2-substituent.

Also shown in Table II are the chemical shift differences for the signals of non-anomeric carbons of α,β-pairs. In accordance with earlier findings[20,22], a

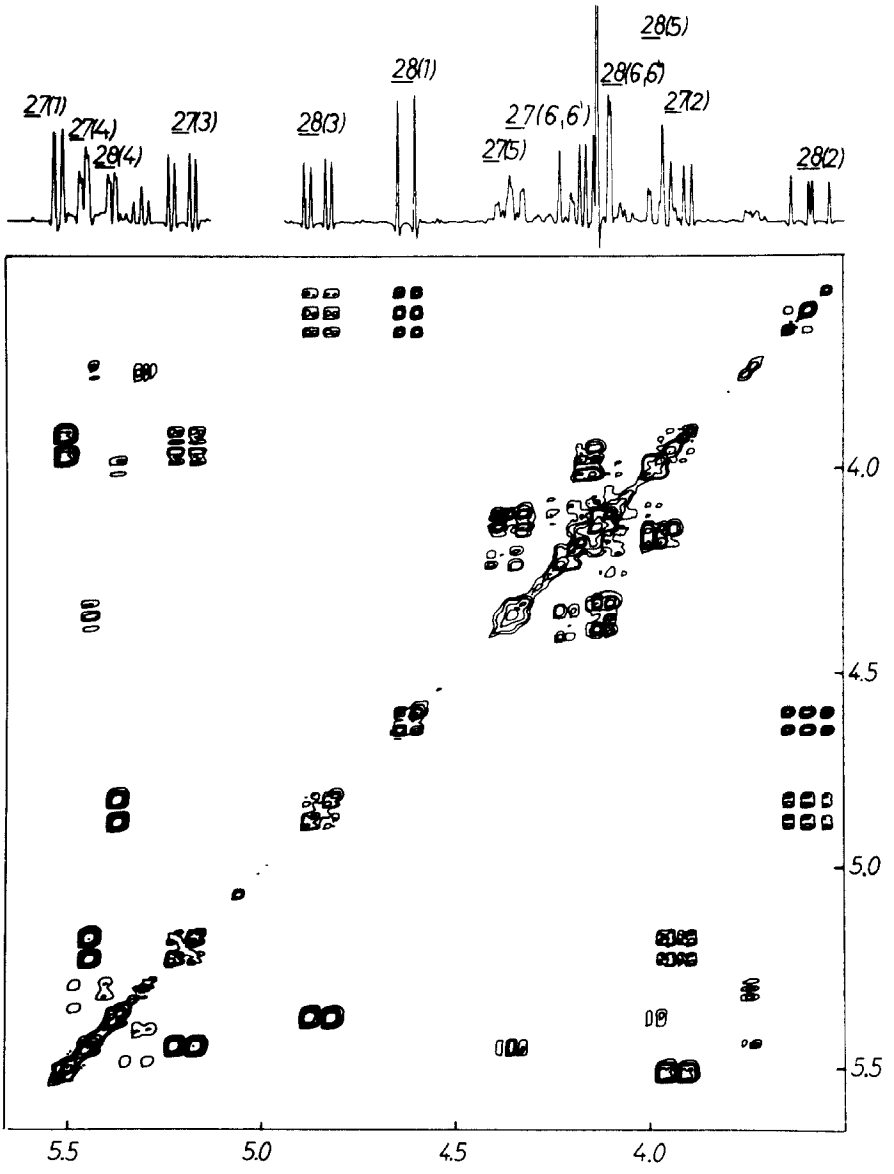


Fig. 1. ^1H–^1H Chemical-shift correlation map (COSY45) of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α,β-D-galactopyranosyl azides (**27** and **28**), together with the normal ^1H spectrum (above) showing the assignments. Time-domain data matrix: 1 K (t_2 direction) × 256 (t_1 direction) data points for a spectral width of 600 Hz. Before Fourier transformation, sinebell apodization was applied in both directions and the transformed data were "symmetrised" in order to eliminate artefacts.

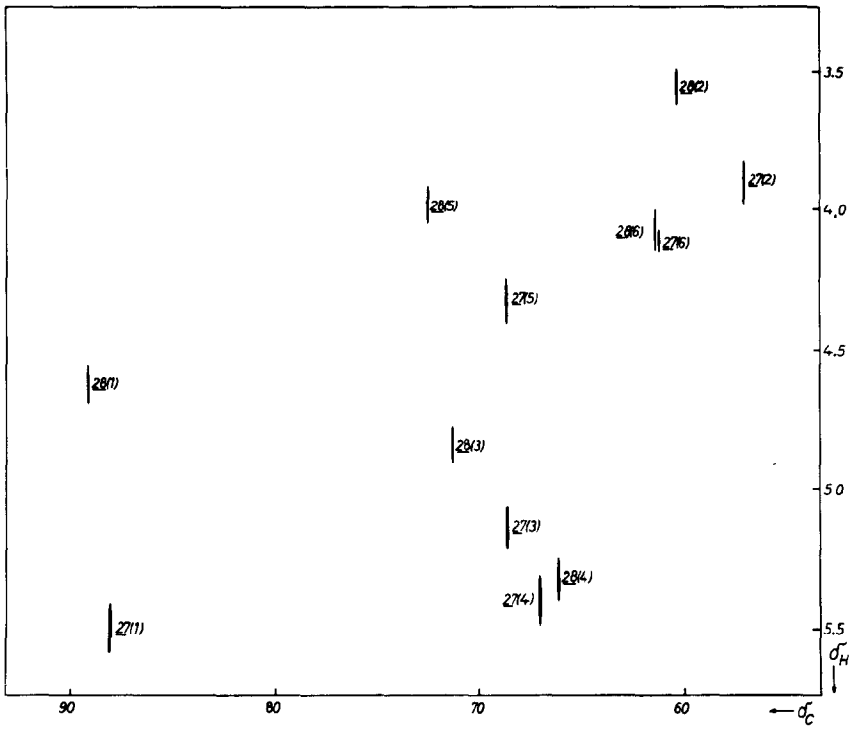


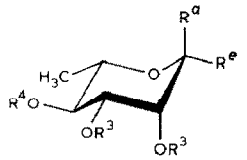
Fig. 2. ^{13}C–^{1}H Chemical-shift correlation map of **27** + **28** (see Fig. 1) produced with the aid of a pulse sequence[14] in order to eliminate ^{1}H–^{1}H couplings in the F_1 (^{1}H chemical shifts) direction. Time-domain data matrix: 2 K (^{13}C; spectral width, 100 p.p.m.) × 32 (^{1}H; spectral width, 2.5 p.p.m.) data points. These were subjected to Gaussian and squared sinebell apodizations in the t_2 and t_1 directions, respectively, and Fourier-transformed, after zero filling to 128 words in the t_1 direction.

significant upfield shift, attributable to the steric *γ-gauche* effects of the axial groups at C-1, is observed for the signals of C-3 and C-5 in the α-anomers compared to those of the β-isomers. Chemical shift differences at other carbons are small and irregular (the pair **27/28** is an exception). In all of the examples investigated here, the α/β chemical shift differences are consistently larger at C-5 than at C-3. It is also remarkable that this asymmetry of the $\Delta\delta$ values is increased significantly in the bicyclic isopropylidene derivatives **5/6, 7/8, 9/10, 15/16**, and **17/18** in comparison with the monocyclic compounds **1/2, 3/4, 11/12, 13/14, 24/25, 29/30**, and **34/35**.

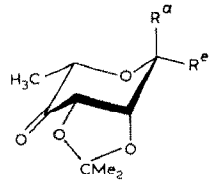
The hexopyranose ring in the bicyclic, fused-ring isopropylidene derivatives listed above exists[3] in a distorted chair form. Therefore, it is plausible to assume that the bond-angle changes associated with the deformation of the ring contribute to the observed decrease of $\Delta\delta$ (C-3) by a mechanism suggested[23] as a "generalised *γ-gauche* effect". Molecular models indicate[3] that it is C-3 which undergoes the largest displacement in space and, consequently, the largest bond-angle deformation, on fusion of the dioxolane and hexopyranose rings. This deformation is also reflected in the respective $^{1}J_{C,H}$ values discussed below.

TABLE I

^{13}C CHEMICAL SHIFTS [a] (50 MHz)

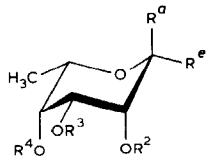


	R^a	R^e	R^3	R^4
1	N_3	H	H	H
2	H	N_3	H	H
3	N_3	H	Ac	Ac
4	H	N_3	Ac	Ac
5	N_3	H	CMe_2	H
6	H	N_3	CMe_2	H
7	N_3	H	CMe_2	Ac
8	H	N_3	CMe_2	Ac



	R^a	R^e
9	N_3	H
10	H	N_3

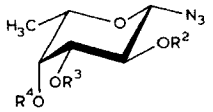
Compound *Solvent*	**1**[3] D_2O	**2**[3] D_2O	**3**[3] $CDCl_3$	**4**[3] $CDCl_3$	**5**[3] $CDCl_3$	**6**[3] $CDCl_3$	**7**[3] $CDCl_3$	**8**[3] $CDCl_3$	**9**[3] $CDCl_3$	**10**[3] $CDCl_3$
C-1	89.82	87.34	87.33	84.51	87.11	85.20	86.92	84.62	87.08	85.20
C-2	69.95	71.24	69.27	69.31	75.50	75.00	75.35	74.89	78.56	77.94
C-3	69 70	72.58	68.13	70.61	78.14	79.55	75.09	76.10	75.52	76.46
C-4	71 73	71.64	70.27	69.68	74.13	73.84	73.59	72.90[b]	202.89	203.37
C-5	70.73	74.46	68.45	72.44	68.14	73.31	66.58	72.79[b]	71.78	77.32
C-6	16.84	16.67	17.27	16 96	17.18	17 67	16.79	17.89	15.60	16.36



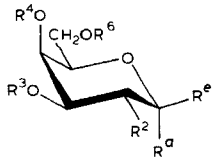
	R^a	R^e	R^2	R^3	R^4
11	N_3	H	H	H	H
12	H	N_3	H	H	H
13	N_3	H	Ac	Ac	Ac
14	H	N_3	Ac	Ac	Ac
15	N_3	H	CMe_2		H
16	H	N_3	CMe_2		H
17	N_3	H	CMe_2		Ac
18	H	N_3	CMe_2		Ac
19	H	N_3	H	CMe_2	

Compound *Solvent*	**11**[3] D_2O	**12**[3] D_2O	**13**[3] $CDCl_3$	**14**[3] $CDCl_3$	**15**[3] $CDCl_3$	**16**[3] $CDCl_3$	**17**[3] $CDCl_3$	**18**[3] $CDCl_3$	**19**[3] $CDCl_3$
C-1	90.53	87.75	88.19	85.62	87.16	85.49	87.34	85.27	86.48
C-2	69.47	70.82	66.52	66.89	73.10	72.45	72.74	72.48	67.09
C-3	65.02	68.15[c]	65.01[c]	68.06	72.78	74.43[c]	70.81	72.70	73.28
C-4	71.79	70.93	68.18	67.52	66.70	66.68	66.93	66.49	73.95
C-5	69.42	73.56[c]	66.92	72.10	67.57	72.45	66.15	71.23	70.29
C-6	15.80	15.40	15.88	15.93	16.73	16.59	16.53	16.48	16.38

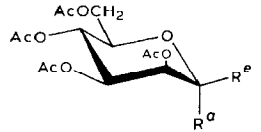
TABLE I (continued)



	R^2	R^3	R^4
20	H	H	H
21	Ac	Ac	Ac
22	H	CMe_2	
23	Ac	CMe_2	

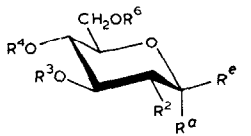


	R^e	R^a	R^2	R^3	R^4	R^6
24	H	N_3	OAc	Ac	Ac	Ac
25	N_3	H	OAc	Ac	Ac	Ac
26	N_3	H	NHAc	Ac	Ac	Ac
27	H	N_3	N_3	Ac	Ac	Ac
28	N_3	H	N_3	Ac	Ac	Ac



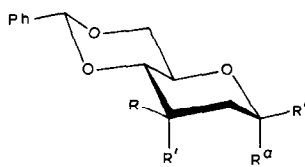
	R^e	R^a
29	H	N_3
30	N_3	H

Compound *Solvent*	**20**[3] D_2O	**21**[3] $CDCl_3$	**22**[3] $CDCl_3$	**23**[3] $CDCl_3$	**24** $CDCl_3$	**25**[2a] $CDCl_3$	**26** $CDCl_3$	**27** $CDCl_3$	**28** $CDCl_3$	**29**[2c] $CDCl_3$	**30**[2d] $CDCl_3$
C-1	90.51	87.90	89.68	87.14	86.56	87.94	88.54	87.91	88.95	87.26	84.84
C-2	70.10	68.07	73.08	71.71	67.17	67.87	50.36	56.95	60.24	68.97	69.09
C-3	72.85	70 92	78.67	76.03	67.01	70.45	69.79	68.49	71.21	68.09	70.72
C-4	71.17	69 78	76.07	75.70	67.45	66.70	66.59	68.89	66.01	65.47	65.24
C-5	73.14	71.27	71.13	70.68	68 39	72.58	76.62	68.49	72.43	70.46	74.30
C-6	15.39	15.69	16.40	16.07	61.27	61.01	61.46	61.01[b]	61.22[b]	61.97	62.07



	R^e	R^a	R^2	R^3	R^4	R^6
31	N_3	H	NHAc	H	H	H
32	N_3	H	NPhth	H	H	H
33	N_3	H	NHAc	Ac	Ac	Ac
34	H	N_3	NPhth	Ac	Ac	Ac
35	N_3	H	NPhth	Ac	Ac	Ac
36	H	AcO	N_3	Ac	Ac	Ac

Phth = phthaloyl



	R^e	R^a	R	R'
37	H	OMe	N_3	H
38	OMe	H	H	N_3

Compound *Solvent*	**31**[d] D_2O	**32** D_2O	**33** $CDCl_3$	**34** $CDCl_3$	**35** $CDCl_3$	**36** $CDCl_3$	**37**[8a] $CDCl_3$	**38**[8b] $CDCl_3$
C-1	88.65	86.06	88.10	87.33	85.50	89.82	98.00	99.20
C-2	55.09	56.32	53.75	53.00	54.02	60.23	35.37	35.89
C-3	73.71	70.78	72.01	66.73	70.42	70.62	56.26	57.56
C-4	69.59	70.32	68.30	69.53	68.50	67.93	82.00	79.45
C-5	77.95	78.31	73.57	69.75	74.00	69.64	63.03	64.07
C-6	60.65	60.79	61.86	61.51	61.71	61.35	68.92	69.15

[a] δ Scale, internal $CDCl_3$ (δ 77.00 for solutions in $CDCl_3$) or to external Me_4Si (for solutions in D_2O). [b] Assignments may be interchanged. [c] Assignments based on the $\Delta\delta$ values (Table II). [d] Assignments based on analogy with those for 2-acetamido-2-deoxy-β-D-glucopyranose[39].

TABLE II

^{13}C $\Delta\delta$ VALUES[a]

Atom	**1/2**	**3/4**	**5/6**	**7/8**	**9/10**	**11/12**	**13/14**	**15/16**	**17/18**
C-1	1.48	2.82	1.91	2.30	1 88	1 78	2.57	1.67	2.07
C-2	−1.29	−0.04	0.50	0.46	0.62	−1.35	−0 37	0.65	0.26
C-3	−2.88	−2.48	−1.41	−1.00	−0.94	−3.13	−3.05	−1 65	−1.89
C-4	0.09	0.59	0.29	0.69	—	0.86	0.66	0.02	0.44
C-5	−3.73	−3.99	−5.17	−6.21	−5.54	−4 14	−5 18	−4.88	−5.08
C-6	0.17	0.31	−0.50	−1.10	−0.76	0.40	−0.05	0.14	0.07

Atom	**24/25**	**27/28**	**29/30**	**34/35**
C-1	−1.38	−1.04	2.42	1.83
C-2	−0.70	−3 29	−0.12	−1 02
C-3	−3.44	−2.72	−2.63	−3.69
C-4	0.75	2.88	0.23	1.03
C-5	−4.19	−3.94	−3.84	−4.25
C-6	0.26	−0.21	−0.10	−0 20

[a]Defined as δ_C (α-anomer) − δ_C (β-anomer).

Evidence for the operation of the *γ-anti* effect[24] in carbohydrate derivatives is both scarce[25] and controversial[26]. Although nitrogen equatorially bonded to C-1 should cause upfield shifts[24] of the signals for C-3 and C-5, the present data provide no support for such a *γ-anti* effect of the azido group. On the contrary, the upfield shifts of the signals for C-3 and C-5 in the α-anomers having axial azido groups at C-1 clearly indicate the absence of any sizeable *γ-anti* upfield effect of the equatorial azido substituent.

$^1J_{C,H}$ *Values for anomeric carbons.* — The data in Table III show that the general rule, $J_{C\text{-}1,H\text{-}1e} \approx J_{C\text{-}1,H\text{-}1a} + 10$ Hz, established[4,6] for many carbohydrate derivatives, applies qualitatively to the glycosyl azides. However, the ΔJ ($J_{C\text{-}1,H\text{-}1\alpha} - J_{C\text{-}1,H\text{-}1\beta}$) values show a considerable scatter from 13.3 (**13** *vs.* **14**) down to 5.7 Hz (**34** *vs.* **35**). This is mainly due to the variation in $J_{C\text{-}1,H\text{-}1a}$ values (from 155.5 Hz in **18** to 164.8 Hz in **35**), the $J_{C\text{-}1,H\text{-}1e}$ values being fairly constant at 170 Hz. A small, but significant, decrease of the latter, accompanied by a similar decrease of $J_{C\text{-}1,H\text{-}1a}$ in the respective β-anomers, was observed for the isopropylidene derivatives. It seems probable that these changes, like those observed for other $J_{C,H}$ values (see

below), reflect the deformation of the hexopyranose ring in these fused-ring bicyclic systems. On the other hand, a significant *increase* of $J_{C\text{-}1,H\text{-}1a}$ was observed for the phthalimido derivatives **32** and **35**. Although, in principle, the increased value of $J_{C\text{-}1,H\text{-}1}$ in **32** might be attributed to a solvent effect in view of the known[27] trend that, in general, higher $^{1}J_{C,H}$ values are obtained for solutions in D_2O than in other solvents, this might not be so here since $J_{C\text{-}1,H\text{-}1}$ was only 0.7 Hz smaller for **35**, the acetylated counterpart of **32**, when measured for a solution in $CDCl_3$ (Table III). It is plausible to attribute this effect to the presence of the bulky phthalimido group at position 2 since $J_{C\text{-}1,H\text{-}1a}$ assumes "normal" values (~160 Hz) in the 2-acetamido derivatives **31** and **33**. Increase of the electronegativity of the 2-substituent in **35** as compared to **33**, C=O lone-pair interactions with H-1*a* (for which the probability in **35** is twice that in **33**), and bond-angle deformations due to the increase of steric crowding in **35** might be invoked also in explaining this effect. More experimental evidence is needed before an attempt is made to rationalise it in terms of any of the factors mentioned. It should be emphasised that the lowest value for $J_{C\text{-}1,H\text{-}1e}$ (167.5 Hz in **7**) in this series was only ~3 Hz larger than the highest value (164.8 Hz in **35**) for $J_{C\text{-}1,H\text{-}1a}$. Therefore, it might be misleading to deduce the anomeric configuration from $J_{C\text{-}1,H\text{-}1}$ values *alone* since the electronic and/or steric influences of substituents at non-anomeric carbons may alter them to such an extent that the difference between $J_{C\text{-}1,H\text{-}1e}$ and $J_{C\text{-}1,H\text{-}1a}$ may become negligible even when the ring heteroatom is oxygen and the aglycon (N_3 in this instance) is the same. Replacement of the ring oxygen by sulfur reduces[25] ΔJ to such a low value that it is no longer useful for determining the anomeric configuration. The phenomena just discussed are not limited to glycosyl azides and therefore due attention should be paid to the possible influence of substituents at non-anomeric carbons upon the value of $J_{C\text{-}1,H\text{-}1}$. Negligible or moderately small influences of 2-substituents on the value of $J_{C\text{-}1,H\text{-}1e}$ have been observed[5,27].

$^{1}J_{C,H}$ *Values of non-anomeric carbons.* — Differences between $^{1}J_{C,He}$ and $^{1}J_{C,Ha}$ values have been noted for some non-anomeric carbons *adjacent* to a ring oxygen in six-membered rings, *e.g.*, in pentopyranoses[6c] and 1,3-dioxanes[25]. The rule $^{1}J_{C,He} > {}^{1}J_{C,Ha}$ may be more general than implied previously. In particular, for hexopyranose rings in the unstrained chair conformation, $^{1}J_{C,He}$ values are significantly larger than $^{1}J_{C,Ha}$ values for *all* carbons. In fact, $J_{C\text{-}2,H\text{-}2e}$ *vs.* $J_{C\text{-}3,H\text{-}3a}$ (and $J_{C\text{-}5,H\text{-}5a}$) in **2, 4,** and **30** as well as $J_{C\text{-}4,H\text{-}4e}$ *vs.* $J_{C\text{-}3,H\text{-}3a}$ in **25, 26**, and **28** show up differences from 4.4 to 8.7 Hz in favour of $^{1}J_{C,He}$. Inspection of other data in Table III, however, also reveals serious departures from this picture, including examples where significant differences exist between $^{1}J_{C,Ha}$ values, *e.g.*, $J_{C\text{-}2,H\text{-}2}$ *vs.* $J_{C\text{-}3,H\text{-}3}$ in **21**. In some instances, $^{1}J_{C,Ha}$ even exceeds $^{1}J_{C,He}$, *e.g.*, $J_{C\text{-}3,H\text{-}3}$ vs. $J_{C\text{-}4,H\text{-}4}$ in **15**. Such phenomena may be rationalised in terms of steric effects leading to bond-angle distortions[23,28,29].

For the monocyclic derivatives, it was recognised that increased $^{1}J_{C,H}$ values are obtained for axial protons when in 1,3-diaxial relationship with an axial substituent. Thus, in **21**, the increase of $J_{C\text{-}2,H\text{-}2a}$ with respect to $J_{C\text{-}3,H\text{-}3a}$ can be

TABLE III

$^1J_{C,H}$ VALUES[a]

Compound	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
$J_{C\text{-}1,H\text{-}1}$	169.4	158.8	170.3	158.2	167.7	157.2	167.5	157.0	167.9	158.1	169.8
$J_{C\text{-}2\ H\text{-}2}$	149.5	148.5	156.6	155.0	152.1	150.6	152.6	152.0	155.2[b]	155.0	[c]
$J_{C\text{-}3,H\text{-}3}$	143.9	141.8	150.7	147.6	151.5	150.2	153.2	152.6	153.1[b]	152.2	142.0
$J_{C\text{-}4,H\text{-}4}$	143.3	146.8[b]	154.3	153.2[b]	146.6	146.6	152.0	[c]	—	—	147.2
$J_{C\text{-}5,H\text{-}5}$	142.6	143.1[b]	145.4	143 1[b]	145.3	141.0	143.4	[c]	144.4[b]	141.8	[c]
$J_{C\text{-}6,H\text{-}6}$	127.6	128.2	128.0	128.2	127.6	127.6	127 6	128.2	129.8	130.0	127.3
$J_{C\text{-}6,H\text{-}6'}$											

Compound	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**
$J_{C\text{-}1,H\text{-}1}$	158.4	170.2	156 9	168.9	157.1	167.9	155.5	157.7	159.9	158.3	156.4
$J_{C\text{-}2,H\text{-}2}$	[c]	156.4	154.2	152.5	149.8	151.4	150.4	148 5	147.7	154.6	147.5
$J_{C\text{-}3,H\text{-}3}$	140.9[b]	143.3[b]	141.6	150.0	147.9	148 9	149.7	149.0	142.7[b]	147 9	150.0
$J_{C\text{-}4,H\text{-}4}$	[c]	151.2[b]	151.1	148.0	147 4	150.2	147.8	147.1	146.0	152.3	146.5
$J_{C\text{-}5,H\text{-}5}$	141 6	142.7	140.1	141 3	142.4	142.2	139 4	140.0	142.2[b]	140 9	139.9
$J_{C\text{-}6,H\text{-}6}$	127.5	128.7	128.1	128.1	127.8	128.2	128.2	128.8	127.6	128.1	128.2
$J_{C\text{-}6,H\text{-}6'}$											

Compound	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**
$J_{C\text{-}1,H\text{-}1}$	157.5	171.0	159.1	160.4	170.4	160.0	170.9	158.4
$J_{C\text{-}2,H\text{-}2}$	152.4	150.0	154.8	144.4	147.0	147.3	156.2	155.4
$J_{C\text{-}3,H\text{-}3}$	151.7	150.0	149.1	146.7[b]	[c]	146.3	150.9	148.4
$J_{C\text{-}4,H\text{-}4}$	147.3	152.9	153.5	155.4	154.7	152.9	155.1	~154
$J_{C\text{-}5,H\text{-}5}$	139.9	146.5	143.7	144.0[b]	[c]	139.6	146.3	144.7
$J_{C\text{-}6,H\text{-}6}$	128.2	150.2	150.5	150.2	150.9[b]	150.4[d]	149.1	148.3
$J_{C\text{-}6,H\text{-}6'}$		150.2	150.5	150.2	150.9	150.4	149.1	148.3

Compound	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**
$J_{C\text{-}1,H\text{-}1}$	161.8	165.5	160.9	170.5	164.8	178.0	169.1	161.3
$J_{C\text{-}2,H\text{-}2}$	143.2	138.7	143.6	142.0	144.3[b]	144.9	129.6 133.3	129.0 132.5
$J_{C\text{-}3,H\text{-}3}$	~145	141.0	151.7	158.2	153.1[b]	148.9	145.0	148.4
$J_{C\text{-}4,H\text{-}4}$	~146	144.6	154.4	153.9	152.6[b]	148.3	145.0	143.9
$J_{C\text{-}5,H\text{-}5}$	~143	143.3	~144	146.6	145.0	147.2	149.2	149.3
$J_{C\text{-}6,H\text{-}6}$	144.4	143.3	~148	152.1	147.9	147.7	148.9	[c]
$J_{C\text{-}6,H\text{-}6}$	144.4	143.3	~148	152.1	147.9	150.6	150.1	[c]

[a]In Hz; accuracy ±0.2 Hz, and ±1 Hz for those marked ~. [b]Determined by the DANTE method. [c]Overlap of signals prevented measurement of the coupling constant with reasonable accuracy. [d]May be interchanged.

attributed to a 1,3-diaxial interaction of H-2 and AcO-4. This effect is of such magnitude ($\Delta J_{2,3}$ 6.7 Hz) that, in this instance, $J_{C\text{-}2,H\text{-}2a}$ becomes larger than $J_{C\text{-}4,H\text{-}4e}$. A similar relationship (although somewhat smaller in magnitude) in **20** holds for these coupling constants. In **25**, the interaction of AcO-4 with H-2*a* also accounts for the relative magnitudes of the coupling constants for H-2*a*, H-3*a*, and H-4*e*. Interaction of the axial azido group with H-5*a* may explain the difference (~3 Hz) between the $J_{C\text{-}5,H\text{-}5}$ values in the anomers **24** and **25**. The $J_{C\text{-}5,H\text{-}5a}$ values in the α-anomers generally exceed those in the respective β anomers (see Table III); $J_{C\text{-}3,H\text{-}3a}$ is equal to $J_{C\text{-}4,H\text{-}4a}$ in **35**, whereas in **34** it is larger by 4.8 Hz. This difference is of the right sign for a H-3*a* · · · N_3 diaxial interaction, but larger in magnitude than those found in other α-anomers. It is conceivable that bond-angle distortions at C-3 induced by steric crowding of N_3 with the bulky *N*-phthaloyl group in *cis*-position also contributes to the increase of $J_{C\text{-}3,H\text{-}3a}$.

Acetoxyl groups in 1,3-diaxial disposition to axial hydrogens seem to enhance the magnitude of $^1J_{C,Ha}$ to a greater extent than either azido and, possibly, hydroxyl or alkoxyl. Thus, the differences between the $J_{C\text{-}3,H\text{-}3}$ or $J_{C\text{-}5,H\text{-}5}$ values in the α- and β-anomers **29** and **30** (interaction with the axial azido group) are smaller (1.6–2.5 Hz) than that between $J_{C\text{-}3,H\text{-}3}$ and $J_{C\text{-}4,H\text{-}4}$ in the β-anomer **30** (interaction of H-4 with AcO-2).

The value of $J_{3,4}$ in **29** is smaller than that in **30** because of a 1,3-diaxial interaction of H-3 and the azido group in the former. Not surprisingly, the respective coupling constants in **3** and **4** display closely analogous behaviour. In **1**, $\Delta J_{3,4}$ is ~0, which indicates that axial azido and hydroxyl groups exert an effect of roughly equal magnitude upon $^1J_{C,H}$ of an axial hydrogen three bonds away. In the β-anomer **2**, $J_{C\text{-}3,H\text{-}3}$ becomes smaller, as expected (absence of a 1,3-diaxial interaction with N_3), but $J_{C\text{-}4,H\text{-}4}$ is increased by 3.5 Hz. This difference, which has no parallel in the acetylated compounds, may be due to a minor conformational change brought about by differences in the hydrogen-bonding networks of the two anomers **1** and **2** in aqueous solution. The present data are insufficient for the quantitative evaluation of the effect of the axial OH and OAlk groups. The required situation for evaluating the HO · · · H 1,3-diaxial effect on $^1J_{C,Ha}$ occurs in only two derivatives, namely, **2** and **20**. The former has been discussed above, whereas in **20**, $\Delta J_{2,3}$ is 5.0 Hz (presence and absence of 1,3-diaxial interaction with H-2 and H-3, respectively). The $J_{C\text{-}5,H\text{-}5}$ values in **37** and **38** are significantly larger than either $J_{C\text{-}4,H\text{-}4a}$ in these derivatives or $J_{C\text{-}5,H\text{-}5a}$ in comparable *gluco* derivatives (Table III), reflecting 1,3-diaxial interaction of H-5 with the methoxyl and azido groups in **37** and **38**, respectively. The similar $J_{C\text{-}5,H\text{-}5}$ values in these derivatives suggest that these groups make contributions of similar magnitude in enhancing $^1J_{C,Ha}$. By the same reasoning, the value of $J_{C\text{-}3,H\text{-}3a}$ in **37** is probably enhanced by MeO-1*a*. Electronegativity considerations are also in keeping with this assumption, *i.e.*, $J_{C\text{-}3,H\text{-}3a}$ would be expected to be smaller than $J_{C\text{-}4,H\text{-}4a}$ due to the lower electronegativity of N compared to O.

In the talopyranosyl azides **11** and **12**, overlap of resonances in the ^{1}H-

coupled spectra precluded the determination of all the coupling constants. Of those measured, $J_{C\text{-}3,H\text{-}3}$ and $J_{C\text{-}4,H\text{-}4}$ in **11** are of interest since, on the basis of their magnitudes (see above), they can be assigned to C-H*a* and C-H*e* bonds, respectively. This, taken together with the value of $J_{C\text{-}1,H\text{-}1'}$ unambiguously establishes the configuration (α) and conformation [$^1C_4$(L)] of **11**. This problem could not be solved by using ^{1}H-data alone[3]. In the acetylated 6-deoxytalopyranosides **13** and **14**, $J_{C\text{-}2,H\text{-}2}$ has the magnitude expected for a AcO–C-H*e* fragment (*cf.* the appropriate values in **3, 4, 29, 30**) in analogous structures. However, extremely low values are obtained for $J_{C\text{-}3,H\text{-}3}$ in both anomers (the corresponding coupling constants are 6–6.8 Hz larger in **3, 4, 29**, and **30**) and the $J_{C\text{-}4,H\text{-}4}$ values are also slightly decreased in comparison to "typical" $^1J_{C,He}$ values such as $J_{C\text{-}4,H\text{-}4}$ in **24–28** or **21** (differences of 1.8–4.7 Hz). The decrease in $J_{C\text{-}3,H\text{-}3}$ is of such magnitude that it completely counterbalances the opposite effect due to the increased electronegativity of OAc as compared to OH. The value of $J_{C\text{-}3,H\text{-}3}$ in the α-anomer **13** is larger by ~3 Hz than in the β anomer **14**, a feature which can be explained, as in the examples above (**3, 4, 29**, and **30** for instance), by a 1,3-diaxial interaction with N_3 in the α-anomer. The same applies to the difference (2.7 Hz) observed between the values of $J_{C\text{-}5,H\text{-}5}$ of the two anomers.

In searching for a rationale for the strikingly low $J_{C\text{-}3,H\text{-}3}$ values and the smaller but significant decrease of $J_{C\text{-}4,H\text{-}4}$ as compared to the "normal" value (154–156 Hz) for $^1J_{C,He}$, it should be noted that the values of $J_{C\text{-}2,H\text{-}2}$ clearly establish an equatorial H-2 for both anomers and, consequently, the preponderance of the $^1C_4$(L) conformation for both **13** and **14**. Since this conformation has been established for the rhamnose derivatives **1–4**, the data for taloses can be best evaluated with reference to those obtained for rhamnoses. Therefore, it is plausible to assume that the differences, noted above, between the respective coupling constants in rhamnose and talose derivatives reflect steric interactions of *cis*-substituents in the latter. In fact, all of the substituents in **14** (and all but one in **13**) lie on the same side of the hexopyranose ring. In **14**, there are four *gauche* interactions involving vicinal *cis*-groups, whereas there are only two in the corresponding rhamnose derivative **4**.

Linear correlations between the magnitude of $^1J_{C,H}$ couplings and the *s*-character of the C–H bond are well established[4]. Since bond angles are physically observable quantities for evaluating the *s*-character, variations in the magnitude of $^1J_{C,H}$ have been rationalised in terms of bond-angle effects[23,28,29]. In another approach, interaction of the C–H bond with the lone pairs on neighboring heteroatoms (O, N, S) have been invoked[30] to explain the observed trend, *e.g.*, $^1J_{C,He} > {}^1J_{C,Ha}$. Recently, a Karplus-type dependence of $^1J_{C,H}$ on the torsional angle between the C–H bond and a neighbouring *p*-orbital of nitrogen has been suggested[31]. Both explanations seem to be applicable here. Unfavorable 1,3-diaxial interactions of OAc groups in positions 2 and 4 in **13** and **14** and/or 1,2-*gauche* interactions of five (**14**, four in **13**) substituent groups may deform the ring such that the changes in bond angles in the region of the C-3–C-4 bond result in largely

(for $J_{C\text{-}3,H\text{-}3}$) or moderately (for $J_{C\text{-}4,H\text{-}4}$) diminished values of the respective coupling constants. Alternatively, it may be assumed that these interactions result in preferred conformations for the OAc groups in positions 2–4 that, on average, diminish the values of the coupling constants by interactions of the oxygen lone-pairs in the C=O groups with the respective C–H bonds. The steric interactions cited above are missing or largely diminished in **3** and **4**, chosen for reference.

In 2,3-*O*-isopropylidene derivatives, the value of $J_{C\text{-}3,H\text{-}3}$ is significantly increased (by 7–10 Hz) with respect to that in their monocyclic counterparts. The $J_{C\text{-}2,H\text{-}2}$ values are only moderately higher (by ~2–3 Hz) in the dioxolane derivatives, whereas the $^1J_{C,H}$ values of non-bridgehead carbons remain virtually unaffected by the formation of cyclic acetals. Thus, $J_{C\text{-}3,H\text{-}3}$ increases from 143.9 Hz in **1** to 151.4 Hz in **5** (ΔJ 7.5 Hz), whereas the respective differences are only 2.6 and 2.1 Hz for $J_{C\text{-}2,H\text{-}2}$ and 3.3 and −0.2 Hz for $J_{C\text{-}4,H\text{-}4}$. In the *talo* series, $J_{C\text{-}4,H\text{-}4}$ in **15** is only 0.8 Hz larger than in **11**. In the 3,4-*O*-isopropylidene derivatives **22** and **23**, the $J_{C\text{-}3,H\text{-}3}$ values are higher by 7.3 and 9.0 Hz, respectively, than in **20**, in contrast to the $J_{C\text{-}2,H\text{-}2}$ and $J_{C\text{-}4,H\text{-}4}$ values which show virtually no variation on going from **20** to **22** or **23**. The increased value of $J_{C\text{-}2,H\text{-}2}$ in **23** as compared to that in **20** is due to the increased electronegativity of AcO-2. Due to these effects, the differences between $^1J_{C,He}$ and $^1J_{C,Ha}$ vales in these fused-ring bicyclic dioxolane derivatives disappear for the bridgehead carbons or, in some instances, larger values are obtained for $^1J_{C,Ha}$ than for $^1J_{C,He}$ (*e.g.*, **22** and **23**, Table III). Clearly, the observed trends cannot be accounted for by invoking an increase in the electronegativity, associated with the formation of a cyclic acetal, of the substituents at bridgehead carbons. This should affect approximately equally the values of $^1J_{C,H}$ on both bridgehead carbons. In the bicyclic dioxolane derivatives discussed here, the hexopyranose ring is distorted[3] towards a flattened chair conformation in which C-3 is close to the quasi-plane involving C-1,2,4,5. A study of molecular models makes it clear that such a distortion affects the bond angles of C-3 to a much greater extent than those of the neighbouring carbons. Therefore, it is plausible to rationalise the increase of the $J_{C\text{-}3,H\text{-}3}$ values in **5–8**, **15–19**, and **23** on the formation of cyclic acetals in terms of the bond-angle distortion theory[24,28,29]. In fact, the C-3–H-3 bond occupies a position intermediate of axial and equatorial directions in these derivatives.

EXPERIMENTAL

Melting points were determined on a Boetius micro hot-stage. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. I.r. spectra were recorded for KBr pellets with a Perkin–Elmer Model 283 spectrophotometer. A VG Analytical 7035 instrument was used to obtain mass spectra. Dichloromethane was dried by distillation from P_4O_{10} and stored over molecular sieve 4Å, as was hexamethylphosphoric triamide. The cation-exchange resin used was Serdolit-Rot (Serva). Ether–light petroleum (b.p. 40–60°) (3:1) or toluene–ethanol

(3:1) was used for t.l.c. ^{1}H- (200 MHz) and ^{13}C-n.m.r. (50 MHz) spectra were recorded on a Bruker WP 200 SY instrument. For the measurement of $^{1}J_{C,H}$ values, ^{1}H-coupled ^{13}C spectra were acquired by the gated-decoupling technique, using the smallest possible spectral width (4–5 kHz). After Lorentzian to Gaussian transformation for resolution enhancement, the f.i.d.'s were Fourier-transformed with zero-filling to 32k words, resulting in a digital resolution of 0.15–0.25 Hz in the transformed spectra. The line spacings were extracted from the peak lists of interpolated frequency data provided by the peak-picking routine of the standard Bruker software (DISNMRP). The $^{1}J_{C,H}$ values obtained are believed to be accurate within ±0.2 Hz. ^{1}H-Coupled multiplets of individual carbons were obtained by using the DANTE[18] method for selective excitation under the following conditions: spectral width, 200–300 Hz; excitation selectivity, 10–20 Hz (corresponding to 100 or 50 ms, respectively, for the total length of the DANTE pulse train); time-domain data points, 0.5–1 K. Zero-filling to 4 K, after resolution enhancement, resulted in a digital resolution of 0.1 Hz in the transformed spectra. The COSY 45[15] variant of the homonuclear chemical-shift correlation experiment was employed for the ^{1}H–^{1}H correlation maps and the ^{1}H–^{13}C chemical-shift correlation maps were produced with the aid of a pulse sequence[14] devised for elimination of the ^{1}H–^{1}H couplings. Experimental details mentioned in the captions to Figs. 1 and 2 are representative values for all of the data reported here.

2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl azide (**24**). — 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl chloride[32] (2.2 g, 6 mmol) was added to a suspension of NaN_3 (1.125 g) in hexamethylphosphoric triamide (10.5 mL), and the mixture was vigorously stirred at room temperature for 16 h and then poured into ice–water (100 mL). The solid (2.23 g, 99%) was collected, washed with water, and dried. Recrystallisation from ether–light petroleum gave **24** as needles (1.62 g, 72.3%), m.p. 77–78°, $[\alpha]_D$ +199° (*c* 0.97, chloroform); ν_{max} 2117 (N_3), 1753 cm^{-1} (C=O). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.69 ($J_{1,2}$ 3.5 Hz, H-1), 5.20 ($J_{2,3}$ 10.5 Hz, H-2), 5.25 ($J_{3,4}$ 2.6 Hz, H-3), 5.46 ($J_{4,5}$ 1.2 Hz, H-4), 4.38 (H-5), 4.16 ($J_{5,6}$ 6.0 Hz, H-6), 3.95 ($J_{5,6'}$ 7.0 Hz, H-6').

Anal. Calc. for $C_{14}H_{19}N_3O_9$: C, 45.05; H, 5.13. Found: C, 45.42; H, 5.01.

2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl azide (**26**). — To a suspension of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-β-D-galactopyranose[33] (**39**; 1.17 g, 3 mmol) in dichloromethane (15 mL) were added trimethylsilyl azide (0.48 mL) and $SnCl_4$ (0.18 mL), and the mixture was stirred for 24 h; **39** dissolved within 15 min. The solution was then diluted with dichloromethane (20 mL), washed with aqueous $NaHCO_3$ and water, dried ($CaCl_2$), and concentrated to dryness. The product crystallised from ethanol–light petroleum to give **26** as prisms (0.82 g, 73.4%), m.p. 174–176°, $[\alpha]_D$ −36° (*c* 2.1, chloroform) {lit.[34] m.p. 164–166°, $[\alpha]_D$ −0.4° (*c* 0.95, chloroform)}; ν_{max} 3258 and 3087 (NH), 2107 (N_3), 1742 and 1731 (C=O), 1649 cm^{-1} (amide). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.81 ($J_{1,2}$ 9.4 Hz, H-1), 5.25 ($J_{2,3}$ 11.1, $J_{3,4}$ 3.4 Hz, H-3), 5.39 ($J_{4,5}$ 1.1 Hz, H-4), 6.04 ($J_{NH,2}$ 8.9 Hz, NH), 3.90–4.20 (H-2,5,6,6').

Anal. Calc. for $C_{14}H_{20}N_4O_8$: N, 15.05. Found: N, 14.59.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α,β-D-galactopyranosyl azides (**27** *and* **28**). — To a solution of 1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-α-D-galactopyranose[12] (1.11 g, 3 mmol) and trimethylsilyl azide (0.41 mL) in dichloromethane (6 mL) was added $SnCl_4$ (0.15 mL), and the mixture was kept at room temperature for 20 h and then worked-up as described for **26** to give a syrup (0.86 g, 80.4%) which spontaneously crystallised after storage for 2 months. ^{1}H-N.m.r. data ($CDCl_3$): **27**, δ 5.51 ($J_{1,2}$ 4.1 Hz, H-1), 3.93 ($J_{2,3}$ 10.1 Hz, H-2), 5.20 ($J_{3,4}$ 3.1 Hz, H-3), 5.45 ($J_{4,5}$ 1.5 Hz, H-4), 4.55 ($J_{5,6} \sim J_{5,6'} \sim$ 6.0 Hz, H-5), 4.2 (H-6,6′); **28**, δ 4.63 ($J_{1,2}$ 9.0 Hz, H-1), 3.59 ($J_{2,3}$ 10.7 Hz, H-2), 4.85 ($J_{3,4}$ 3.3 Hz, H-3), 5.37 ($J_{4,5}$ 1.3 Hz, H-4), 4.15 (H-6,6′).

Anal. Calc. for $C_{12}H_{16}N_6O_7$: C, 40.45; H, 4.52; N, 23.59. Found: C, 40.39; H, 4.51; N, 23.10.

2-Acetamido-2-deoxy-β-D-glucopyranosyl azide (**31**). — To a solution of 2-acetamido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl azide (**33**; 1.86 g, 5 mmol) in dry methanol (11 mL) was added methanolic M NaOMe (0.3 mL), and the solution was kept at room temperature for 30 min, then neutralised, and concentrated to dryness. The residue was recrystallised from ethanol–ethyl acetate to give **31** (1.04 g, 84.5%), m.p. 146–147°, $[\alpha]_D$ −45° (*c* 0.6, water); lit.[35] m.p. 142° (dec.), $[\alpha]_D$ −30° (*c* 1, water). ^{1}H-N.m.r. data (D_2O): δ 4.74 ($J_{1,2}$ 9.0 Hz, H-1), 3.66 ($J_{2,3}$ 9.0 Hz, H-2), 3.57 ($J_{3,4}$ 7.5 Hz, H-3), 3.46 ($J_{4,5}$ 9.5 Hz, H-4), 3.93 ($J_{5,6}$ 1.5 Hz, H-6), 3.75 ($J_{5,6'}$ 5 Hz, H-6′).

2-Deoxy-2-phthalimido-β-D-glucopyranosyl azide (**32**). — A solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide (**35**; 2.30 g, 5 mmol) in methanolic 0.1M NaOMe (10 mL) was stored for 15 min at room temperature, then neutralised with Serdolit-Rot (H^+) resin, and concentrated to dryness, and the residue was recrystallised from ethanol to yield **32** (1.35 g, 74.0%), m.p. 187–189° (dec.), $[\alpha]_D$ −24° (*c* 0.5, water). ^{1}H-N.m.r. data (D_2O): δ 5.61 ($J_{1,2}$ 9.5 Hz, H-1), 3.97 ($J_{2,3}$ 10.1 Hz, H-2), 4.35 ($J_{3,4}$ 8.5 Hz, H-3), 3.55 ($J_{4,5}$ 8.8 Hz, H-4), 3.5 (H-5), 3.85 (H-6), 3.8 (H-6′).

Anal. Calc. for $C_{14}H_{14}N_4O_6$: N, 16.76. Found: N, 16.82.

2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl azide (**33**). — (*a*) Prepared from 2-acetamido-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose[36] (**40**), as described for **26**, **33** (74%) had m.p. 167–168°, $[\alpha]_D$ −40° (*c* 1.3, chloroform); lit.[37] m.p. 166–168°, $[\alpha]_D$ −50° (chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.81 ($J_{1,2}$ 9.3 Hz, H-1), 3.93 ($J_{2,3}$ 10.1 Hz, H-2), 5.28 ($J_{3,4}$ 9.0 Hz, H-3), 5.11 ($J_{4,5}$ 9.0 Hz, H-4), 3.83 ($J_{5,6}$ 5.0 Hz, H-5), 4.28 (H-6), 4.17 ($J_{5,6'}$ 5.0 Hz, H-6′), 4.28 (H-6), 4.17 ($J_{5,6'}$ 2.6 Hz, H-6′), 6.23 ($J_{NH,2}$ 9.0 Hz, NH).

Anal. Calc. for $C_{14}H_{20}N_4O_8$: C, 45.16; H, 5.41; N, 15.04. Found: C, 45.13; H, 5.39; N, 14.92.

(*b*) To a solution of 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline[11] (**42**; 1.65 g, 5 mmol) and trimethylsilyl azide (0.68 mL) in dichloromethane (17 mL) was added $SnCl_4$ (0.68 mL), and the mixture was left at room temperature for 40 h. Work-up then gave a crude product (1.65 g)

which, on recrystallisation (ethyl acetate–light petroleum), afforded **33** (1.48 g, 79.5%), m.p. 165–166°, $[\alpha]_D$ −42° (*c* 1.2, chloroform).

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-α-D-glucopyranosyl azide (**34**). — Prepared from 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide[38], as described for **24**, crude **34** was recrystallised from ethyl acetate–light petroleum to yield material (73%) having m.p. 181–183°, $[\alpha]_D$ +204° (*c* 0.9, chloroform); ν_{max} 2112 (N_3), 1759 (C=O), and 1726 cm^{-1} (C=O). Mass spectrum: *m/z* 418 (6.7%) ($M^+ - N_3$). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.59 ($J_{1,2}$ 4.2 Hz, H-1), 4.60 ($J_{2,3}$ 10.2 Hz, H-2), 6.52 ($J_{3,4}$ 9.1 Hz, H-3), 5.08 ($J_{4,5}$ 10.0 Hz, H-4), 4.4 (H-5).

Anal. Calc. for $C_{20}H_{20}N_4O_9$: N, 12.17. Found: N, 12.14.

3,4,6-Tri-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide (**35**). — Prepared from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose[38] (**41**), as described for **26**, **35** (86.9%) had m.p. 142–143° (from ethanol–light petroleum), $[\alpha]_D$ +38° (*c* 1, chloroform); ν_{max} 2117 (N_3), 1784 (CO-N-CO), 1758 and 1720 cm^{-1} (C=O). Mass spectrum: *m/z* 418 (6.3%) ($M^+ - N_3$). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.66 ($J_{1,2}$ 9.4 Hz, H-1), 4.25 ($J_{2,3}$ 9.5 Hz, H-2), 5.82 ($J_{3,4}$ 9.0 Hz, H-3), 5.20 ($J_{4,5}$ 10.0 Hz, H-4), 3.97 (H-5), 4.36 ($J_{5,6}$ 4.5, H-6), 4.21 ($J_{5,6'}$ 2.5 Hz, H-6′).

Anal. Calc. for $C_{20}H_{20}N_4O_9$: C, 52.17; H, 4.38; N, 12.17. Found: C, 52.29; H, 4.33; N, 12.07.

ACKNOWLEDGMENTS

We thank the Hungarian Academy of Sciences for financial support, Professor R. Bognár for his interst, Dr. Gy. Batta for implementing the carbon–proton shift-correlation pulse sequence, Dr. R. E. Dávid and her staff for the microanalysis, and Dr. Z. Dinya and his staff for the i.r. and mass spectra. One of us (Z. Gy.) acknowledges the Alexander von Humboldt-Stiftung for a scholarship and thanks Professor H. Paulsen for advice.

REFERENCES

1 (*a*) B. Helferich and A. Mitrowsky, *Chem. Ber.*, 85 (1952) 1–8; (*b*) M. Tanaka and I. Yamashina, *Carbohydr. Res.*, 27 (1972) 175–183; (*c*) H. Paulsen, Z. Györgydeák, and M. Friedmann, *Chem. Ber.*, 107 (1974) 1590–1613; (*d*) A. Messmer, I. Pintér, and F. Szego, *Angew. Chem., Int. Ed. Engl.*, 3 (1964) 228–229; (*e*) W. A. Szarek, O. Achmatowicz, Jr., J. Plenkiewicz, and B. K. Radatus, *Tetrahedron*, 34 (1978) 1427–1433; (*f*) J. Kovács, I. Pintér, F. Szego, G. Tóth, and A. Messmer, *Acta Chim. Acad. Sci. Hung.*, 101 (1979) 7–16; (*g*) T. Takeda, Y. Sugiura, Y. Ogihara, and S. Shibata, *Can. J. Chem.*, 58 (1980) 2600–2603; (*h*) T. Takeda, Y. Sugiura, C. Hamada, R. Fujii, K. Suzuki, Y. Ogihara, and S. Shibata, *Chem. Pharm. Bull.*, 29 (1981) 3196–3201; (*i*) T. Ogawa, S. Nakabayashi, and S. Shibata, *Agric. Biol. Chem.*, 47 (1983) 281–285, 1213–1218, 1353–1356; (*j*) F. Chrétien and B. Gross, *Tetrahedron*, 38 (1982) 103–112; (*k*) R. E. Harmon, R. A. Earl, and S. K. Gupta, *J. Org. Chem.*, 36 (1971) 2553–2556; (*l*) R. A. Earl and L. B. Townsend, *Can. J. Chem.*, 58 (1980) 2550–2561; (*m*) R. Alonso, M. J. Camarasa, and F. G. de las Heras, *Eur. J. Med. Chem.*, 15 (1980) 105–109; (*n*) F. G. de las Heras, R. M. Sanches-Perez, and M. L. Aquado, *ibid.*, 16 (1981) 339–344; (*o*) W. Schörkhuber and E. Zbiral, *Justus Liebigs Ann. Chem.*, (1980) 1455–1469; (*p*) W. Schörkhuber and E.

ZBIRAL, *Chem. Ber*, 114 (1981) 3165–3169; (*r*) W. SCHORKHUBER AND E. ZBIRAL, *Justus Liebigs Ann. Chem.*, (1982) 1870–1880; (*s*) M. W. LOGUE AND B. H. HAN, *Carbohydr. Res.*, 121 (1983) 299–301.

2 (*a*) F. MICHEEL, *Adv. Carbohydr. Chem.*, 16 (1961) 85–103; (*b*) W. PFLEIDERER AND E. BUHLER, *Chem. Ber.*, 99 (1966) 3022–3039; (*c*) H. PAULSEN, Z. GYORGYDEÁK, AND M. FRIEDMANN, *ibid.*, 107 (1974) 1568–1578; (*d*) Z. GYORGYDEÁK AND H. PAULSEN, *Justus Liebigs Ann. Chem.*, (1977) 1987–1991; (*e*) R. J. M. NOLTE, J. A. J. VAN ZOMEREN, AND J. W. ZWIKKER, *J. Org. Chem.*, 43 (1978) 1972–1975; (*f*) F. CHRÉTIEN, B. CASTRO, AND B. GROSS, *Synthesis*, (1979) 937–939; (*g*) Z. GYORGYDEAK, I. LING, AND R. BOGNÁR, *Justus Liebigs Ann. Chem.*, (1983) 279–289; (*h*) M W. LOGUE AND B. H. HAN, *Carbohydr. Res.*, 121 (1983) 287–297.

3 Z. GYORGYDEÁK AND L. SZILÁGYI, *Justus Liebigs Ann. Chem.*, (1985) 103–112.

4 P E. HANSEN, *Progr Nucl Magn. Reson. Spectrosc.*, 14 (1980) 249–251.

5 K. BOCK AND C. PEDERSEN, *J. Chem. Soc., Perkin Trans. 2*, (1974) 293–297.

6 (*a*) A. S. PERLIN AND B. CASU, *Tetrahedron Lett.*, (1969) 2921–2924; (*b*) K. BOCK, I. LUNDT, AND C. PEDERSEN, *ibid.*, (1973) 1037–1040; (*c*) K. BOCK AND C. PEDERSEN, *Acta Chem. Scand., Ser. B*, 29 (1975) 258–264; (*d*) J. A. SCHWARCZ AND A. S. PERLIN, *Can. J. Chem.*, 50 (1972) 3667–3676.

7 L. SZILAGYI, *Carbohydr. Res*, 118 (1983) 269–275.

8 (*a*) A. C. RICHARDSON, *Carbohydr. Res.*, 4 (1967) 422–428; (*b*) I. PELYVAS, F. SZTARICSKAI, L. SZILÁGYI, R. BOGNAR, AND J. TAMÁS, *ibid.*, 68 (1979) 321–330.

9 H. PAULSEN AND W STENZEL, *Chem. Ber.*, 111 (1978) 2334–2347; N. V. BOVIN, S. E. ZURABYAN, AND A. Y KHORLIN, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1981) 1638–1641.

10 N. PRAVDIĆ, I. FRANJIĆ-MIHALIĆ, AND B. DANILOV, *Carbohydr. Res.*, 45 (1975) 302–306; M A. NASHED, C. W. SLIFE, M. KISO, AND L ANDERSON, *ibid.*, 82 (1980) 237–252.

11 K. L. MATTA AND O P. BAHL, *Carbohydr. Res.*, 21 (1972) 460–464; V K. SRIVASTAVA, *ibid.*, 103 (1982) 286–292.

12 H. PAULSEN, A RICHTER, V. SINNWELL, AND W. STENZEL, *Carbohydr. Res.*, 64 (1978) 339–362; R. U LEMIEUX AND R. M. RATCLIFFE, *Can. J. Chem.*, 57 (1979) 1244–1251; N. V. BOVIN, S. E. ZURABYAN, AND A. Y. KHORLIN, *Bioorg. Khim.*, 5 (1979) 1257–1258.

13 A A. MAUDSLEY, L. MULLER, AND R. R. ERNST, *J. Magn. Reson.*, 28 (1977) 463–469; R. FREEMAN AND G. A. MORRIS, *J. Chem. Soc., Chem. Commun.*, (1978) 684–686.

14 A. BAX, *J. Magn. Reson.*, 53 (1983) 517–520.

15 A. BAX AND R. FREEMAN, *J. Magn. Reson.*, 44 (1981) 542–561.

16 A. BAX, R. FREEMAN, AND S. P. KEMPSELL, *J. Am. Chem. Soc.*, 102 (1980) 4849–4851

17 A. BAX, R. FREEMAN, T. A. FRENKIEL, AND M. H. LEVITT, *J. Magn. Reson.*, 43 (1981) 478–483.

18 G. A. MORRIS AND R FREEMAN, *J. Magn. Reson.*, 29 (1978) 433–462.

19 L. D. HALL AND G. A. MORRIS, *Carbohydr Res.*, 82 (1980) 175–184.

20 A. S. PERLIN, *MTP Int. Rev. Sci., Org. Chem. Ser. 2*, (1976) 1–34.

21 S. SEO, Y. TOMITA, K. TORI, AND Y. YOSHIMURA, *J. Am. Chem. Soc.*, 100 (1978) 3329–3331; A. S. SHASHKOV, *Bioorg. Khim.*, 9 (1983) 246–253.

22 R. KASAI, M. OKIHARA, J. ASAKAWA, K. MIZUTANI, AND O. TANAKA, *Tetrahedron*, 35 (1979) 1427–1432.

23 D. G. GORENSTEIN, *J. Am. Chem. Soc.*, 99 (1977) 2254–2258.

24 E. L. ELIEL, W. F. BAILEY, L. D. KOPP, R. L. WILLER, D. M. GRANT, R. BERTRAND, K. A. CHRISTENSEN, D. K. DALLING, M. W DUCK, E. WENKERT, F. M. SHELL, AND D. W. COCHRAN, *J. Am. Chem. Soc.*, 97 (1975) 322–330.

25 K. BOCK AND L. WIEBE, *Acta Chem. Scand*, *Ser. A*, 27 (1973) 2676–2678; V. S. RAO AND A S. PERLIN, *Carbohydr. Res.*, 92 (1981) 141–148.

26 R. G. RITCHIE, N. CYR, AND A. S. PERLIN, *Can. J. Chem.*, 54 (1976) 2301–2309.

27 K. BOCK AND C PEDERSEN, *Carbohydr. Res.*, 71 (1979) 319–321.

28 G. SZALONTAI, *Tetrahedron*, 39 (1983) 1783–1788.

29 L. ÅKERSTROM AND R. ANDERSSON, *Chem. Scr.*, 23 (1984) 101–115.

30 Ref. 4, section 8.3.3.

31 D B. DAVIES, M. MACCROSS, AND S. D DANYLUK, *J. Chem. Soc., Chem. Commun.*, (1984) 536–538.

32 W. KORYTNYK AND J. A. MILLS, *J. Chem. Soc.*, (1959) 636–649.

33 B. WEISSMANN, *J. Org. Chem.*, 31 (1965) 2505–2509.

34 D DUNSTAN AND L. HOUGH, *Carbohydr. Res.*, 25 (1972) 246–248.

35 F. MICHEEL AND H. WULFF, *Chem. Ber.*, 89 (1956) 1521–1530.
36 O. WESTPHAL AND H. HOLTZMANN, *Ber.*, 75 (1942) 1274–1282; D. HORTON, *J. Org. Chem.*, 29 (1964) 1776–1782.
37 C. H. BOLTON AND R. W. JEANLOZ, *J. Org. Chem.*, 28 (1963) 3228–3230; A. YAMAMOTO, C. MIYASHITA, AND H. TSUKAMOTO, *Chem. Pharm. Bull.*, 13 (1965) 1036–1041; M. SPINOLA AND R. W. JEANLOZ, *J. Biol. Chem.*, 245 (1970) 4158–4162; D. E. COWLEY, L. HOUGH, AND C. M. PEACH, *Carbohydr. Res.*, 29 (1971) 231–241; B. PAUL AND W. KORYTNYK, *ibid.*, 67 (1978) 457–468.
38 G. BALUJA, B. H. CHASE, G. W. KENNER, AND A. TODD, *J. Chem. Soc.*, (1960) 4678–4681; R. U. LEMIEUX, S. Z. TAKEDA AND B. Y. CHUNG, *ACS Symp. Ser.*, 39 (1976) 99–115.
39 D. R. BUNDLE, H. J. JENNINGS, AND I. C. P. SMITH, *Can. J. Chem.*, 51 (1973) 3812–3819.