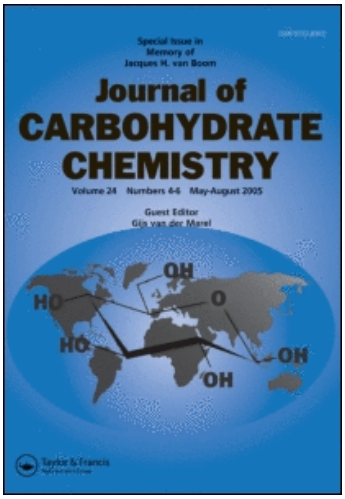


Journal of Carbohydrate Chemistry

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

THE STRUCTURE AND CONFORMATIONS OF METHYL 3,4,6-TRI- *O*-ACETYL-2-DEOXY-2-(3',3'-DICYCLOHEXYLUREIDO)-β- d-GLUCOPYRANOSIDE

Iwona Wawer[a]; Andrzej Temeriusz[b]; Romana Anulewicz-Ostrowska[b]; Dieter Ströhl[c]
[a] Department of Physical Chemistry, Medical Academy, Warsaw, Poland [b] Department of Chemistry, Warsaw University, Warszawa, Poland [c] Institute of Organic Chemistry, Martin-Luther-University, Halle (Saale), Germany

Online publication date: 06 April 2002

To cite this Article Wawer, Iwona , Temeriusz, Andrzej , Anulewicz-Ostrowska, Romana and Ströhl, Dieter(2002) 'THE STRUCTURE AND CONFORMATIONS OF METHYL 3,4,6-TRI- *O*-ACETYL-2-DEOXY-2-(3',3'-DICYCLOHEXYLUREIDO)-β- d-GLUCOPYRANOSIDE', Journal of Carbohydrate Chemistry, 21: 3, 235 — 246
To link to this Article: DOI: 10.1081/CAR-120004335
URL: http://dx.doi.org/10.1081/CAR-120004335

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

J. CARBOHYDRATE CHEMISTRY, 21(3), 235–246 (2002)

THE STRUCTURE AND CONFORMATIONS OF METHYL 3,4,6-TRI-*O*-ACETYL-2-DEOXY-2-(3′,3′-DICYCLOHEXYLUREIDO)-β-D-GLUCOPYRANOSIDE

Iwona Wawer,[1] Andrzej Temeriusz,[2,*] Romana Anulewicz-Ostrowska,[2] and Dieter Ströhl[3]

[1]Department of Physical Chemistry, Medical Academy, Banacha 1, 02097 Warsaw, Poland
[2]Department of Chemistry, Warsaw University, Pasteura 1, 02093 Warszawa, Poland
[3]Institute of Organic Chemistry Martin-Luther-University, Kurt-Mothes Str.2, 06120 Halle (Saale), Germany

ABSTRACT

The title compound was studied by ^{1}H and ^{13}C NMR in CD_2Cl_2 solution and by ^{13}C CPMAS NMR and X-ray diffraction in the solid phase. Low-temperature NMR spectra showed separate signals for the two cyclohexyl rings, located *E* and *Z* with respect to C2′═O. Distinct resonances of cyclohexyl carbons are also present in the solid state ^{13}C NMR spectrum. The barrier to rotation around C-2′–N-3′ bond is 41.5 kJ/mol. Separate signals for H-1, H-2 and H-3 of the sugar unit indicate also that rotation around C-2′–N-1′ is hindered; the barrier height is 39.5 kJ/mol. The *Z* conformation is preferred (4:1) over *E* at 193 K. In the crystals the glucopyranose ring is located *Z* with respect to C2′═O, and the molecules are linked by the N1′H···O═C (acetyl group at C-6) hydrogen bond.

Key Words: Ureido sugars; ^{13}C CP MAS solid-state analysis; ^{1}H-NMR; ^{13}C-NMR; X-ray diffraction analysis

* Corresponding author. Fax: 48(22)8225996; E-mail: atemer@chem.uw.edu.pl

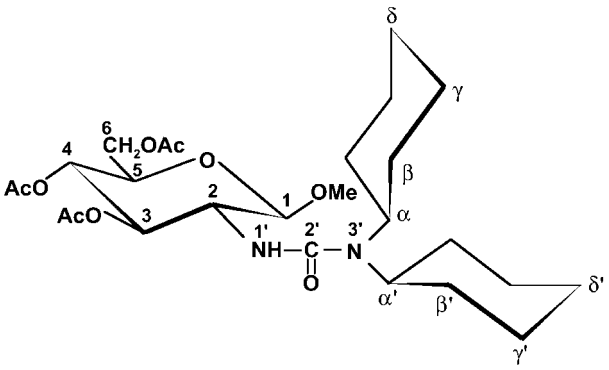
INTRODUCTION

Several series of ureido sugars have been obtained as starting materials in the synthesis of new nitrosoureido sugars, some of which are active as antitumor agents (e.g. streptozotocin, chlorozotocin).[1] Ureido sugars with amine and amino acid ester residues have been studied by means of NMR spectroscopy in solution and in the solid state.[2] Derivatives of methyl 2-deoxy-β-D-glucopyranoside and secondary amines are sterically crowded; separate signals of the two alkyl groups were observed in low-temperature NMR spectra studied, and the barrier to rotation of the N-3′–R_2 fragment was 40.4 kJ/mol for diethyl and 39.2 kJ/mol for di-*n*-hexyl substituents.[3] The molecular structure and conformations of the ureido glucopyranoside with two cyclohexyl substituents are presented here.

RESULTS AND DISCUSSION

The structure and conformational dynamics of the ureido sugar methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**) are interesting because, as confirmed by molecular modeling, it is a compound with large crowding at N-3′. There is neither enough space for rotation around the C-2′–N-3′ bond, nor for simultaneous rotation of the two saturated rings (Scheme 1).

Steric hindrance results in correlated rotation and/or an increase of the respective barriers. The cyclohexyl rings are rigid, i.e., there is no interchange of chair↔boat↔twisted boat (chair) conformations (or it is slow, on an NMR time-scale). Similarly as seen in the ^{1}H spectrum of dicyclohexylamine ($CDCl_3$), 500 MHz, separate groups of multiplets for equatorial and axial protons are observed. The signals from equatorial protons of the cyclohexyl groups appear between 1.60 and 1.86 ppm and those from axial protons between 1.00 and 1.24 ppm; chemical shifts decrease in the order: H-$\alpha_a \gg$ H-$\beta_e >$ H-$\gamma_e >$ H-$\delta_e \gg$ H-$\gamma_a >$ H-$\delta_a >$ H-β_a. The involvement of a dicyclohexylamine residue in a



1

Scheme 1. Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**).

ureido sugar results in a deshielding of H-α (of 0.75 ppm) and H-β (H-β_a of 0.60 and H-β_e of 0.19 ppm). The room temperature ^{1}H NMR spectrum of the cyclohexyl fragments of **1** shows a triplet of triplets for H-α (2 H), and vicinal coupling of H-α to axial H-β (11.8 Hz) and to equatorial H-β (3.7 Hz) indicating that H-α is axial. The signal from axial H-δ (4 H) appears as a quartet of triplets ($^2J = 14.5$, $^3J = 13$ and 3.5 Hz). The H-γ_e and H-γ_a form multiplets (4 H) separated by ca. 0.5 ppm; the H-δ_e, H-β_e and H-β_a contribute to a complex multiplet between 1.5 and 1.8 ppm. The 2D g-HSQC, COSY and ROESY spectra enabled the assignment of carbons and protons from the cyclohexyl rings, and the established order of chemical shifts is: H-$\alpha_a \gg$ H-$\gamma_e >$ H-$\beta_e >$ H-$\delta_e \approx$ H-$\beta_a >$ H-$\gamma_a >$ H-δ_a. The difference in shielding between equatorial and axial protons in the cyclohexyl ring amounts typically to ca. 0.5 ppm, reaching 0.86 ppm for H-β protons in the free amine; however in the cyclohexyl rings of **1** this difference is reduced to 0.06 ppm. In the ^{13}C spectrum of **1** the signals from the C-β and C-γ methylene carbons of the two rings appeared as doublets separated by 0.33 ppm (C-β, C-β′) and 0.03 ppm (C-γ, C-γ′), while the resonance of more distant carbons C-δ appeared as a singlet.

The 2D ROESY spectrum (Figure 1) allowed us to draw some conclusions as to the solution conformation of **1**. The cross-peaks between H-1, H-3 and H-5, which are axial and on the same side of the β-D-glucopyranose ring, as well as the cross-peak between H-4 and H-2 (on another side) confirm a $^4C_1$ conformation. Other ROESY cross-peaks appear for H-α_a and H-γ_a, thus indicating that both are axial neighbours in the cyclohexane ring to H-β_e.

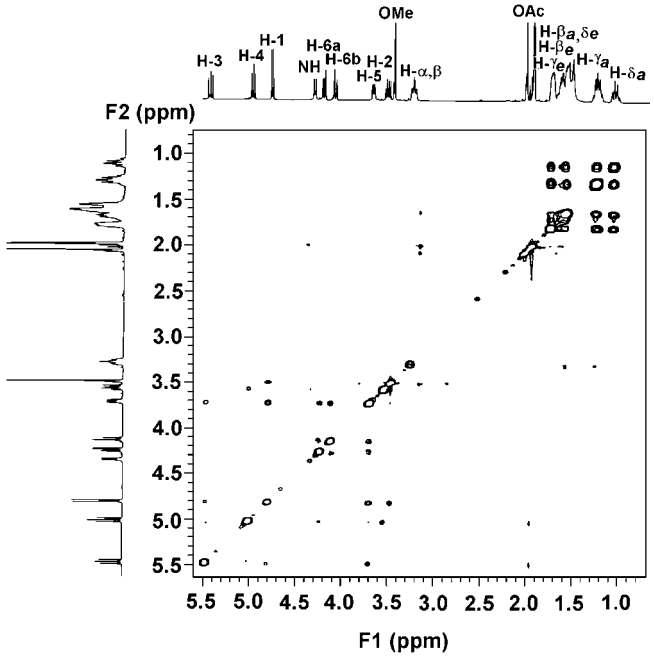


Figure 1. 2D ROESY spectrum of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**).

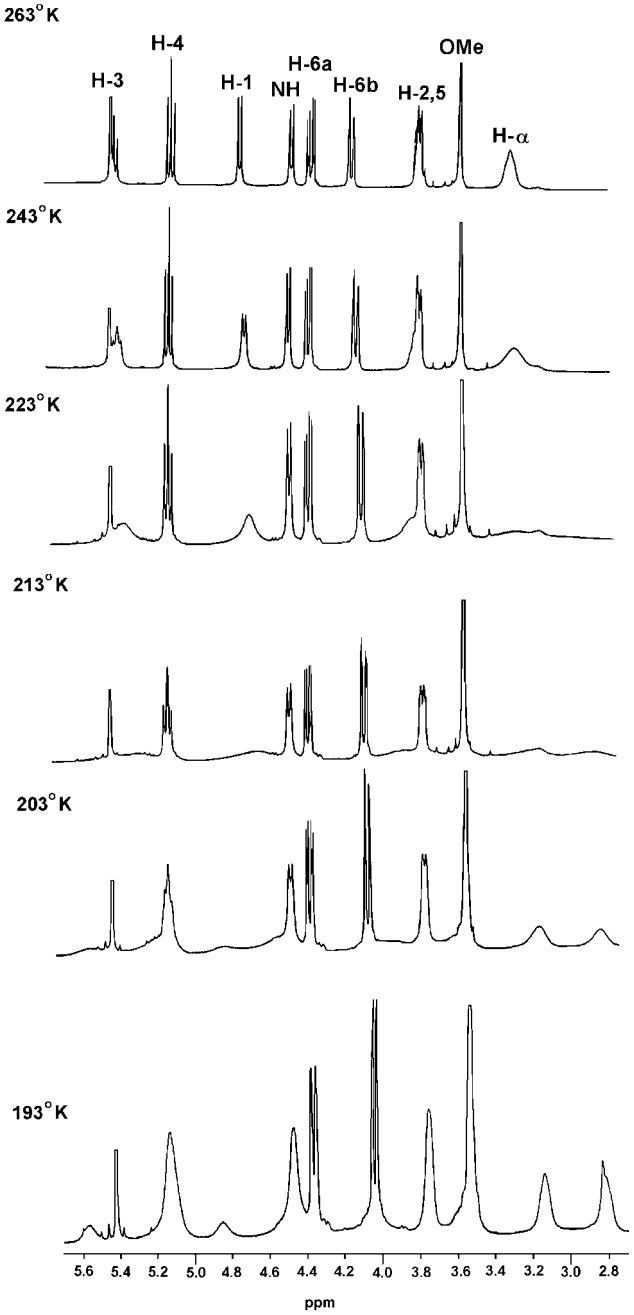


Figure 2. Portion of the ^{1}H NMR spectrum of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**) at various temperatures.

There are several possible dynamic processes averaging the chemical shifts of protons and carbons: 1) hindered rotation around the C-2′–N-3′ and C-2′–N-1′ bonds in the ureido skeleton; 2) rotation of cyclohexyl rings (around N-3′–C-α); and 3) the nitrogen inversion. As mentioned, the ^{1}H spectra indicated that the inversion of cyclohexyl rings, i.e., the interchange of chair↔boat↔twisted boat (chair)↔chair conformation is slow on the NMR time scale. The inversion of a nitrogen free electron pair is usually fast (with the exception of small cyclic amines).[4] In order to attribute the changes in the spectra to any of the dynamic phenomena a series of ^{1}H and ^{13}C spectra at various temperatures were recorded.

In the ^{1}H spectrum recorded at 223 K the signal of H-α protons decoalesces, and below 213 K two separate signals from cyclohexyl rings *E* and *Z* to C2′═O can be observed. Portions of ^{1}H spectra recorded at low temperatures are illustrated in Figure 2. It is evident that H-α protons from the *E* and *Z* rings are anisochronous, and the reason for this is extreme steric crowding. Even when the rotation around the C-2′–N-3′ bond is frozen the ring rotation around the N-3′–C-α bonds could be fast. This process is probably hindered by the neighbouring OCH_3 group, which is close to *E*-cyclohexyl, and the acetyl group at C-3, which is close to the *Z*-cyclohexyl ring.

An attempt was made to calculate the rate constants for hindered rotation by line shape analysis of the ^{1}H spectra using a computer program for two-site exchange.[5] At low temperature the *J*-splitting pattern remains unresolved. The signal due to H-α at 263 K can be treated as a broad singlet, which decoalesces into two broad resonances (at 193 K, without exchange broadening, the width at half height is ca. 30 Hz, which is accounted for in T_2* values) of 1:1 intensity.

The signals of sugar hydrogens H-1, H-2 and H-3 become broader with decreasing temperature (Figure 2) and at 203 K they almost disappear indicating that the coalescence temperature has been reached. At 193 K separate resonances from the two environments can be observed, unfortunately partially overlapped with other signals. The calculated signal intensities indicate that the population of the two conformations is 20%:80%. The high frequency component of the H-1, H-2 and H-3 signals is smaller, and can be assigned to the less populated conformer with the sugar unit located *Z* with respect to the imido C═O. In the low temperature ^{13}C spectra, the signals of sugar carbons C-2, C-3 and C-4 are broader, and at 193 K appear as unequal doublets (ca. 1:4). The separation of C-3 is 1.9 ppm, of C-4 0.73 ppm (the signal of C-2 is overlapped with solvent), and the resonance of ureido C2′═O exhibits two unequal components ($\approx$1:4) separated by 0.74 ppm.

Below 213 K the signals of methylene carbons C-β and C-γ begin to split further. The high frequency component of the C-β doublet is broad, and at 203 K it separates into two lines (ca. 1:1). At 193 K four C-β resonances can be distinguished. One broad signal is observed for C-γ at 213 K, two resonances C-γ and C-γ′ at 203 K (ca. 2:2), however the low frequency component is broader. In the spectrum recorded at 193 K it is split into two lines (1:1); therefore the C-γ signal intensities are 2:1:1. Cooling the sample to 193 K was sufficient to obtain separate ^{13}C signals of particular carbons from the *E* and *Z* cyclohexyl rings. The chemical shifts are included in Table 1.

The kinetic data can be obtained much more easily from the analysis of the ^{13}C NMR spectra. Therefore, line shape analysis of carbon signals was carried out to obtain life-times using a computer program.[5] Convergent solutions were found on iteration with populations, life-times τ and transverse relaxation times T_2. The initial values of T_2

Table 1. ^{1}H and ^{13}C Chemical Shifts (δ, ppm) for CD_2Cl_2 Solution and Solid State for Methyl 3,4,6-Tri-*O*-Acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**)

	^{1}H NMR			^{13}C NMR	
Carbon or Hydrogen	263 K, CD_2Cl_2	193 K, CD_2Cl_2	263 K, CD_2Cl_2	193 K, CD_2Cl_2	Solid State
1	4.66	4.84; 4.48	102.48	101.70	103.56
2	3.72	4.03; 3.55	55.48	55.90;*	56.32
3	5.35	5.56; 5.12	72.82	72.80; 70.92	75.72
4	5.03	5.10	68.67	67.65; 66.92	69.62
5	3.70	3.72	71.63	70.65	71.71
6	4.29; 4.07	4.36; 4.03	62.19	61.27	63.85
OMe	3.51	3.53	57.14	56.97	57.18
N-1′–H	4.39	4.45	–	–	–
C═O	–	–	156.19	155.8;155.1	156.5
α	3.22_a	3.16; 2.84	55.26	*	55.16; 54.18
β	1.71; 1.62	2.30; 1.25	31.73; 31.28	30.89; 30.45 30.13; 30.00	32.78; 30.14; 30.04
γ	1.76_e; 1.30_a	1.78; 1.33	26.50; 26.44	26.15; 25.43; 25.24	26.88; 26.50
δ	1.60; 1.10	1.61; 1.10	25.57	24.92	25.76
AcCO	–	–	170.8 (×2); 169.7	170.8 (×2); 169.5	171.7; 169.7; 168.9
$AcCH_3$	2.08; 2.00; 1.98	2.13; 2.05; 2.01	20.84 (×2); 20.80	20.67 (×3)	20.60; 20.13 (×2)

*Overlapped with solvent.

for iteration were obtained from the observed line width of the C-6 carbon signal of glucose. Several estimations of the rate constant could be obtained from one ^{13}C spectrum. The rate constants ($k = 1/\tau$) and kinetic parameters for C-N rotation are collected in Table 2.

The rate constants obtained for the temperatures close to coalescence of the respective doublets were used to determine the free energy of activation; these values of $G^{\neq}$ have been taken as a measure of rotational barrier. The barrier to rotation of the *N*-3′–cyclohexyl fragment ($G^{\neq}$) obtained by analysis of cyclohexyl ^{1}H and ^{13}C resonances (intensity 1:1) is 41.5 kJ/mol, for the *N*-dicyclohexyl substituent. The rotation of one of the cyclohexyl rings (probably *Z* with respect to C2′═O) is faster than the rotation of the whole dicyclohexyl fragment. The coalescence of the two components of C-γ′ at 199 K enabled the rough estimation of the barrier for rotation around the N-3′–C-α′ bond as 40.3 kJ/mol.

The barrier for rotation around the N-1′–C-2′O bond, calculated from the kinetic parameters for sugar and C2′═O carbons is slightly smaller (39.4 kJ/mol), however it could not be determined precisely. Since the equilibrium constant depends on temperature, the calculations of the rate constant assuming 1:4 populations of conformers are correct only at 193 K. At higher temperatures broad ^{1}H resonances hinder the determination of integrals (the populations were obtained by iteration procedure).

Table 2. Kinetic Parameters for Methyl 3,4,6-Tri-*O*-Acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**)

Temperature °(K)	τ (s)	k (s^{-1})	Signal (Population)	$\Delta G^{\#}$ (kJ/mol)
193	0.015	66.7	C═O (≈1:4)	
	0.015	66.7	C-3 (≈1:4)	
	0.015	66.7	H-1 (1:4)	
	0.015	66.7	H-3 (1:4)	
203	0.004*	250	C═O	39.7
	0.003	333	C-3	39.3
	0.003	333	H-3	39.3
207	0.002	500	C-3	39.4
213	0.001	1000	C═O	39.3
	0.001	1000	C-3	
193	0.008	125	H-α (1:1)	
	0.009	111	C-β (1:1)	
	0.006	166	C-γ (1:1)	
199	0.0196*	94	C-γ (≈1:1)	40.3
203	0.0045	222	H-α (1:1)	
	0.0065	154	C-β (≈1:1)	
	0.004	250	C-β (≈2:2)	
213	0.003	333	H-α	
	0.0042*	238	C-β	41.8
	0.0035	285	C-γ	41.5
221	0.00152*	658	H-α	41.6
223	0.0013	769	H-α	41.7
	0.00135	740	C-β	41.8
	0.0008	1250	C-γ	
243	0.0003	3333	H-α	

*τ_c life-time of coalescence.

In order to compare the low-temperature conformation of **1** with the crystal structure the ^{13}C CP MAS spectrum of solid ureido sugar was recorded. The resonances can be assigned by comparison with solution data, and the chemical shifts are collected in Table 1. The most interesting feature is the appearance of separate C-α, C-β and C-γ signals of the *E* and *Z* cyclohexyl rings, whereas one set of sugar carbons can be seen (Figure 3). As confirmed by the X-ray diffraction study (see further) only one conformation is present in the solid phase, with the glucopyranose ring located *Z* to C═O.

X-ray Diffraction

The view of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**) is presented in Figure 4 and the crystal packing pattern in Figure 5. The crystal data and structure refinement parameters are included in Table 3; selected bond lengths and angles are given in Table 4. Thermal ellipsoids, drawn at 50% probability are large for C═O atoms of the acetyl group at C-3. The β-D-glucopyranose

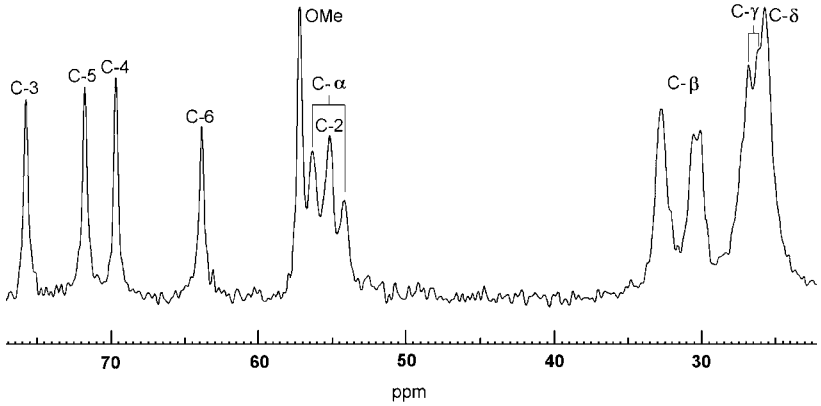


Figure 3. ^{13}C CP MAS spectrum of methyl 3,4,6-tri-O-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**) in the region of sugar carbons.

ring exists in a $^4C_1$ conformation; all acetyl groups are almost planar. The fragment C2N1′C═O adopts a *Z* conformation and is planar, like the urea moiety (the C-2 atom is only 1° out of the plane C-2–N-1′–C-β–N-3′). The C-α and C-α′ atoms are 8.9° and 15.1° below or above the plane of the ureido moiety. In the crystals of ureido sugars studied previously[6] the molecules were associated by intermolecular hydrogen bonds

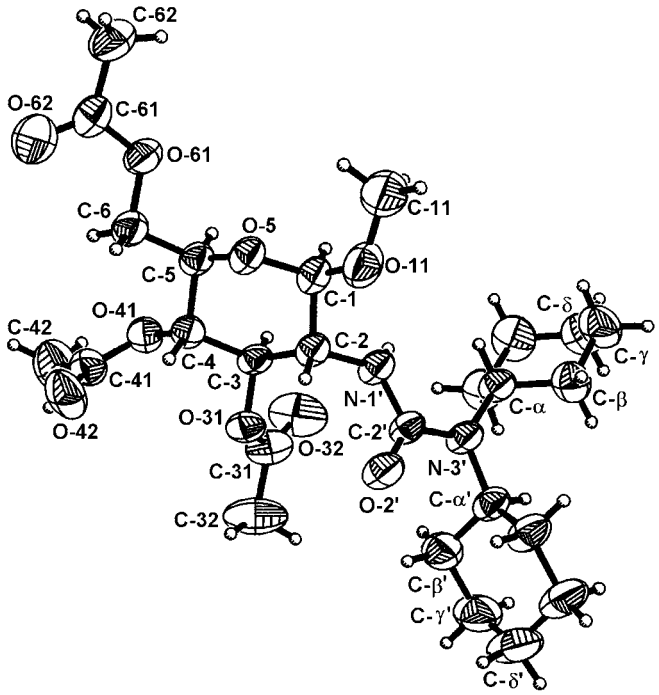


Figure 4. Molecular structure and atom numbering of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**).

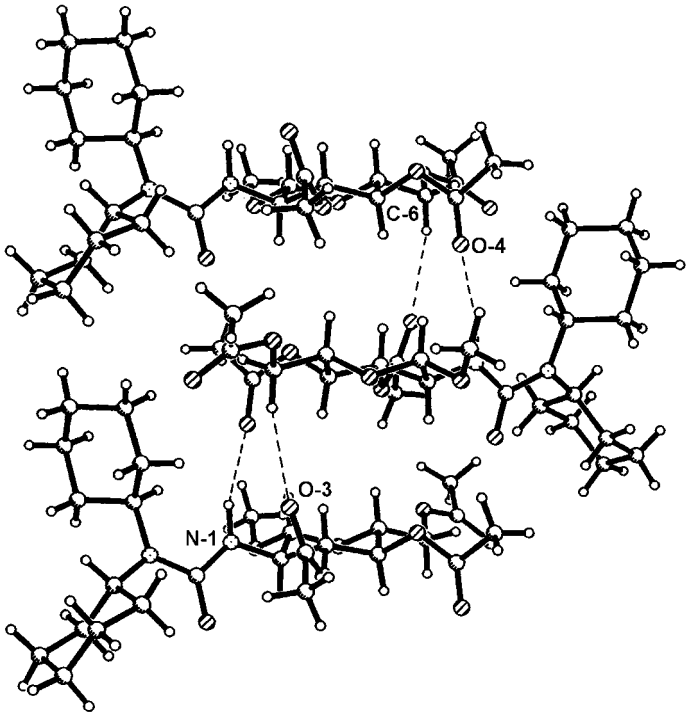


Figure 5. The crystal structure of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**). The intermolecular hydrogen bonds and short contacts are indicated by broken lines.

NH···O═C, formed by the ureido carbonyl group. The *Z* orientation of the sugar substituent enables such hydrogen bonding also in this case.

In the crystal lattice of the β-D-glucopyranose rings are stacked in a column (Figure 5); however, because of voluminous cyclohexyl rings the proton donor, N-1′–H, is close to C═O of the acetyl group at C-6. The N-1′···O distance is 3.160 Å (the length of hydrogen bond is 2.449 Å). The structure is stabilised by the C6H···O═C interaction involving the carbonyl oxygen of the acetyl group at C-3 of the parent molecule. The intermolecular C-6. . .O distance is 2.532 Å.

EXPERIMENTAL

The methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**) was synthesized from methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(4-nitrophenoxycarbonylamino)-β-D-glucopyranoside and dicyclohexyl amine according to the published procedure.[7] The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Plus-500 MHz spectrometer equipped with a variable temperature probe (the precision of the temperature measurements was ±1 deg) and with an inverse detection 5 mm probe. The spectra were collected for $CDCl_3$ and CD_2Cl_2 solutions. The 2D experiments were run

Table 3. Crystal Data and Structure Refinement for Methyl 3,4,6-Tri-*O*-Acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**)

Empirical formula	$C_{26}H_{42}N_2O_9$
Formula weight	526.62
Melting point (°, K)	429–430
$[\alpha]_D^{20}$(°, *c* 1, chloroform)	+12.8
Temperature (°, K)	293(2)
Wavelength (Å)	1.54178
Crystal system	orthorombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions (Å)	a = 9.408(2) α = 90°
	b = 17.548(3) β = 90°
	c = 18.190(4) γ = 90°
Volume (Å^3)	3003.0(11)
Z (molecules/cell)	4
Density (calculated, Mg cm^{-1})	1.165
Absorption coefficient (mm^{-1})	0.726
F(000)	1136
Crystal size (mm)	0.5 × 0.3 × 0.3
θ range for data collection (°)	3.50 to 79.41
Index ranges data for collection (°)	$1 \le h \le 10, -1 \le k \le 19, -1 \le l \le 20$
Reflections collected	4035
Independent reflections	3854 [*R*(int) = 0.0429
Refinement method	Full-matrix least-squares on F^2
Data (restraints) parameters	3851/0/380
Goodness-of-fit on F^2	1.056
Final *R* indices [$I > 2(I)$]	$R_1 = 0.0585$, $wR_2 = 0.1526$
Extinction coefficient	0.0051(6)
Absolute structure parameter	0.1(3)
R indices (all data)	$R_1 = 0.0717$, $wR_2 = 0.1734$
Largest diff. peak and hole (e Å^{-3})	0.377 and −0.270

using standard Varian software. The COSY spectrum was acquired in absolute value mode with 2810 Hz spectral windows along both axes, 1024 data points and time increments (zero filled to 2048), and 8 transients per increment. The ROESY spectrum was measured in the phase sensitive mode, using the same spectral windows and data points as for COSY, 16 transient per increment, 256 increments and delays of 2.3 s. The gradient-HSQC spectrum was recorded with an ^{1}H spectral window of 2810 Hz and data points as above, a ^{13}C spectral window of 17,000 Hz, 256 increments and relaxation delay of 2 s.

The CP MAS solid state ^{13}C NMR spectrum was recorded on a Bruker MSL-300 instrument at 75.5 MHz. Powder sample was spun at 4 kHz and a contact time of 5 ms; a repetition time of 6 s and a spectral width of 20 kHz were used for accumulation of 800 scans. Chemical shifts were calibrated indirectly through the glycine CO signal recorded at 176.0 ppm relative to TMS. X-ray measurements of the crystal were performed on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated MoKα radiation. The crystal was positioned at 65 mm from the KM4CCD camera; 512 frames were measured at 1.0° intervals with a counting time of 10 sec. The data were corrected for

Table 4. Selected Bond Lengths and Angles for Crystalline Methyl 3,4,6-Tri-*O*-Acetyl-2-deoxy-2-(3′,3′-dicyclohexylureido)-β-D-glucopyranoside (**1**)

Atoms	Bond Length (Å)	Atoms	Angles (°)
N-1′–C-2′	1.377(4)	N-1′–C-2′–N-3′	116.5
N-3′–C-2′	1.364(4)	C-2–N-1′–C-2′	122.0
C-2′–O-2′	1.232(4)	C-α–N-3′–C-2′	120.0
N-3′–C-α	1.467(4)	C-2–N-1′–C-2′–O-2′	− 2.0(5)
N-3′–C-α′	1.477(4)	C-2–N-1′–C-2′–N-3′	179.0(3)
N-1′–C-2	1.447(4)	N-1′–C-2′–N-3′–C-α	− 164.9
		N-1′–C-2′–N-3′–C-α′	8.9

Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Kuma Diffraction (Wroclaw) programs.

The structure was solved by direct methods[8] and refined using SHELXL.[9] The refinement was based on F^2 for all reflections except those with very negative F^2. The weighted R factors wR and all goodness-of-fit S values are based on F^2. Conventional R factors are based on F with F set to zero for negative F^2. The $F_o^2 > 2s(F_o^2)$ criterion was used only for calculating R factors and is not relevant to the choice of reflections for the refinement. The R factors based on F^2 are about twice as large as those based on F. All hydrogen atoms were located from a differential map and refined isotropically. Scattering factors were taken from International Tables for X-ray Crystallography.[10]

Full crystallographic details, excluding structure features, have been deposited with the Cambridge Crystallographic Data Centre. (CCDC Identification Number 159583) These data may be obtained, on request, from The Directory, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www:http://www.csdc.cam.ac.uk).

ACKNOWLEDGMENTS

Financial support from the Warsaw University (BST-663/14/2000) is gratefully acknowledged. The X-ray measurements were undertaken in the Crystallographic Unit of the Physical Chemistry Laboratory at the Chemistry Department of the Warsaw University.

REFERENCES

1. Gnewuch, C.T.; Sosnowsky, G.A. Critical appraisal of the evolution of *N*-nitrosourea as anticancer drugs. Chem. Rev. **1997**, *97*, 829–1013.
2. Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A. ^{13}C CP MAS and high-resolution ^{1}H, ^{15}N NMR study of ureido sugars. Carbohydr. Res. **1995**, *267*, 167–176; Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A. ^{13}C CP MAS and high-Resolution ^{1}H, ^{13}C, ^{15}N NMR study of new ureido sugars, derivatives of 2-amino-2-deoxy-β-D-glucopyranose and L-amino acid. Carbohydr. Res. **1995**, *279*, 83–91; Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A. ^{13}C, ^{15}N CP MAS and high-

resolution multinuclear NMR study of methyl 3,4,6-tri-*O*-acetyl-2-(3′arylureido)-2-deoxy-β-D-glucopyranosides. Carbohydr. Res. **1996**, *290*, 137–146; Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A.; Potrzebowski, M.; Ciesielski, W. ^{13}C CP MAS NMR study of ureido sugars, derivatives of 2-amino-2-deoxy-β-D-glucopyranose and dipepdites. Solid State Nucl. Magn. **1998**, *12*, 45–50.

3. Wawer, I.; Weychert, M.; Klimkiewicz, J.; Piekarska-Bartoszewicz, B.; Temeriusz, A. NMR study of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(alkylureido)-β-D-glucopyranosides. Magn. Reson. Chem. **1999**, *37*, 189–194.
4. Witanowski, M.; Stefaniak, L.; Webb, G.A., Eds.; Annual Reports on NMR Spectroscopy, Academic Press, 1986; Vol. 18, Ch. VII.
5. Wawer, I. ^{1}H and ^{13}C NMR study of hindered rotation in N1, N1,-dimethyl-N2-substituted phenylacetamidines. Magn. Reson. Chem. **1988**, *26*, 601–607.
6. Anulewicz, R.; Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A. Crystal structure and solid-state NMR analysis of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-[3-(2-phenyl)-ureido]-β-D-glucopyranoside. Carbohydr. Res. **1996**, *281*, 1–10; Anulewicz, R.; Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A. Crystal structure and solid state NMR analysis of *N*-(methyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside)-*N*′-carbamoyl-D-valine ethyl ester. J. Carbohydr. Chem. **1997**, *16*, 739–749; Anulewicz, R.; Wawer, I.; Piekarska-Bartoszewicz, B.; Temeriusz, A. Crystal structure and solid state ^{13}C NMR analysis of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(3-phenylureido)-β-D-glucopyranoside. J. Carbohydr. Chem. **1999**, *18*, 617–628.
7. Piekarska-Bartoszewicz, B.; Temeriusz, A. A new method for synthesis of ureido sugars. Carbohydr. Res. **1990**, *203*, 302–307.
8. Sheldrick, G.M. Phase annealing in SHELX-90: direct methods for larger structures. Acta Crystallogr., Sect. A **1990**, *46*, 467–473.
9. Sheldrick, G.M. SHELXL93. Program for the Refinement of Crystal Structures; University of Göttingen, Germany, 1993.
10. *International Tables for Crystallography*; Wilson, A.J.C., Ed.; Kluwer: Dordrecht, 1992; Vol. C.

Received March 19, 2001
Accepted January 25, 2002