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MOLECULAR AND CRYSTAL STRUCTURES OF *N*-(*n*-HEPTYL)- AND *N*-(*n*-DECYL)-D-GLUCONAMIDE*

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ABSTRACT

The crystal structures are described of *N*-(*n*-heptyl)-D-gluconamide (**1**) [space group $P1$, $a = 5.183(7)$, $b = 16.18(1)$, $c = 4.803(5)$ Å, $\alpha = 94.2(1)°$, $\beta = 96.1(1)°$, $\gamma = 99.0(1)°$] and of *N*-(*n*-decyl)-D-gluconamide (**2**) [space group $P2_1$, $a = 5.255(2)$, $b = 35.97(1)$, $c = 4.807(2)$ Å, $\beta = 94.81(3)°$], and compared with that of *N*-(*n*-octyl)-D-gluconamide (**3**). In contrast to other amphiphilic molecules which form bilayers and crystallise in the tail-to-tail mode, the *N*-(*n*-alkyl)-D-gluconamides form monolayers and crystallise in sheet-like head-to-tail arrangements stabilised by intra- and inter-molecular N–H · · · O and O–H · · · O hydrogen bonds. Compounds (**2** and **3**) with an even number of alkyl carbon atoms crystallise in space group $P2_1$ and those (**1**) with odd numbers in $P1$. This situation is correlated with a change in torsion angles around the first C–C bond in the alkyl chain and the packing is such that the head CH_2OH group interacts virtually identically with the tail group CH_2CH_3 in each crystal structure. This specific interaction might explain why these molecules form gels in aqueous solution.

INTRODUCTION

Naturally occurring membranes consist of a variety of different lipid molecules and have been studied extensively. It has proved valuable to investigate model membranes composed of only one type of molecule, *e.g.*, lipids isolated from natural membranes or synthetic amphiphilic substances. Among the latter, the alkylgluconamides are of particular interest because those with alkyl chains $>C_8$ form stable monolayers when dissolved in water, whereas those with alkyl

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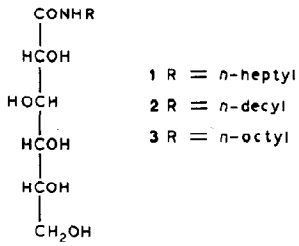
chains $<C_7$ tend to form micelles[1]. For the closely related "alkanoyl-*N*-methylglucamides", micelles are observed also for the higher homologues.

Recently, representatives of each structural family, *N*-(*n*-octyl)-D-gluconamide[2] and "nonanoyl-*N*-methylglucamide[3]", have been crystallised and the structures elucidated. Surprisingly, these studies established that the molecules are arranged in a head-to-tail packing mode and not in the tail-to-tail configuration usually observed for amphiphilic, membrane-forming molecules[4]. We now report the crystal structures of two further analogues of the gluconamide series, namely, *N*-(*n*-heptyl)- (**1**) and *N*-(*n*-decyl)-D-gluconamide (**2**), and compare them with the crystal structure of *N*-(*n*-octyl)-D-gluconamide (**3**).



EXPERIMENTAL

Crystals of **1** and of **2** were grown from methanolic solutions. Identical crystals were obtained from aqueous solutions or gels, as verified by X-ray powder diffraction, but they are too small for single crystal analysis. The crystals were mounted on glass fibers. Weissenberg and precession photographs served to derive space groups and initial unit-cell constants, which were later refined by least-squares methods with the angular positions of 16 (**1**) and 23 (**2**) reflections accurately determined with a STOE four-circle diffractometer. The crystallographic data are given in Table I.

The X-ray intensity data were collected up to $2\theta = 120°$, using Ni-filtered CuK_α radiation from a fine focus sealed tube, and corrected for Lorentz and polarisation effects. The structures were solved by direct methods[5] which provided the co-ordinates of most of the non-hydrogen atoms. The remaining atoms were located from difference Fourier maps. Full matrix least-squares refinement with anisotropic temperature factors[6] converged smoothly for **2**; for **1**, C-12 and C-13 had to be held fixed in the final cycles because of excessive co-ordinate shifts. Most, but not all, of the O–H and the N–H hydrogen atoms were located from difference Fourier maps, and the positions of the C–H hydrogen atoms were calculated. The final *R*-factors, given in Table I, are relatively high because the crystals were not of good quality and the reflection profiles were broad.

TABLE I

CRYSTALLOGRAPHIC DATA FOR *N*-(*n*-HEPTYL)-D-GLUCONAMIDE (**1**) AND *N*-(*n*-DECYL)-D-GLUCONAMIDE (**2**)

	1	**2**
Formula	$C_{13}H_{27}NO_6$	$C_{16}H_{33}NO_6$
Mol. wt.	293	335
Space group	triclinic *P*1	monoclinic $P2_1$
Cell constants *a*	5.183(7)	5.255(2)
b	16.18(1)	35.97(1)
c	4.803(5)	4.807(2)
α	94.2(1)	90.0
β	96.1(1)	94.81(3)
γ	99.0(1)	90.0
Cell volume (Å^3)	394	905
Z	1	2
D_c (g/cm^3; calc.)	1.24	1.23
Number of X-ray data	1,339	1,598
Unobserved data $<2\sigma(F)$		
Final *R*-factor	0.117	0.096
R_w	0.092	0.053

RESULTS AND DISCUSSION

The atomic parameters for **1** and **2** are listed in Table II and the relevant torsion angles are given in Table III. Bond angles and distances in **1** and **2** are comparable to those calculated for *N*-(*n*-octyl)-D-gluconamide[2]. The hydrogen-bonding distances given in Table IV should be regarded with some reservation because the location of the H atoms from X-ray difference Fourier maps can be ambiguous if the data are of modest quality, as in the present study.

A comparison of torsion angles (Table III) and the illustrations in Fig. 1 indicate that the carbon skeletons of the D-glucose moieties in **1–3** display the same all-*trans* conformation that is generally preferred. Only the torsion angle C-3–C-2–C-1–N-1 deviates and is in the (−)anticlinal (−ac) range (−114° in **1** and **2**, and −111.7° in **3**), probably because then the C-2–O-2 and C-1–O-1 dipoles are in favorable antiparallel orientation and the intramolecular N-1–H · · · O-2 hydrogen bond can form, which appears to be a characteristic feature of this class of molecules. The conformation of the alkyl chain is also all-*trans* in **2** and **3** but, as the torsion angles in Table III indicate, the conformation around C-7 is different in **1**. It appears that this methylene group is the least sterically hindered because it is adjacent to the relatively small N–H group and thus may serve as a hinge when the D-gluconamide and alkyl chains have to rotate relative to each other.

Comparison of the packing diagrams in Fig. 2 shows that all three molecules are not arranged in the tail-to-tail mode as usually observed for amphiphilic substances[4,7,8], but are head-to-tail, consistent with the observation that these molecules form monolayers but no bilayers[1]. Although the packing patterns change

TABLE II

FINAL ATOMIC PARAMETERS[a]

N-(n-*Heptyl*)-D-*gluconamide*

Atom	x	y	z	U11	U22	U33	U12	U13	U23
O-1	0.409(3)	0.453(1)	0.806(3)	0.053(5)	0.129(8)	0.106(7)	0.029(5)	0.036(5)	0.047(6)
O-2	0.903(3)	0.563(1)	0.446(3)	0.050(5)	0.095(6)	0.060(5)	0.015(4)	0.032(4)	0.010(4)
O-3	0.824(3)	0.647(1)	0.943(3)	0.035(4)	0.111(6)	0.036(4)	0.016(4)	0.010(3)	0.015(4)
O-4	0.777(3)	0.736(1)	0.430(3)	0.047(4)	0.085(6)	0.049(5)	0.003(4)	0.017(4)	0.011(4)
O-5	0.290(3)	0.747(1)	0.912(3)	0.046(4)	0.106(7)	0.049(5)	0.013(4)	0.027(4)	0.008(5)
O-6	0.247(3)	0.836(1)	0.407(3)	0.060(5)	0.077(5)	0.043(5)	0.017(4)	0.010(4)	0.010(4)
N-1	0.830(3)	0.441(1)	0.779(4)	0.069(7)	0.089(7)	0.061(6)	0.035(6)	0.021(5)	0.024(5)
C-1	0.621(3)	0.476(1)	0.719(4)	0.041(7)	0.086(9)	0.067(8)	0.018(6)	0.011(6)	0.017(7)
C-2	0.640(4)	0.550(1)	0.539(4)	0.040(6)	0.106(9)	0.060(7)	0.020(6)	0.012(5)	0.022(7)
C-3	0.605(3)	0.626(1)	0.725(3)	0.035(6)	0.098(9)	0.043(7)	0.013(6)	0.011(5)	0.010(6)
C-4	0.556(3)	0.701(1)	0.570(3)	0.037(6)	0.089(8)	0.046(6)	0.015(5)	0.014(5)	0.005(6)
C-5	0.515(3)	0.779(1)	0.772(4)	0.037(6)	0.081(8)	0.064(8)	0.004(5)	0.021(6)	0.001(7)
C-6	0.464(3)	0.855(1)	0.628(4)	0.054(7)	0.058(7)	0.062(8)	0.008(5)	0.026(6)	0.009(6)
C-7	0.851(3)	0.375(1)	0.957(4)	0.066(8)	0.093(9)	0.077(9)	0.030(8)	0.024(7)	0.032(8)
C-8	0.831(3)	0.292(1)	0.807(4)	0.059(8)	0.11(1)	0.10(1)	0.023(8)	0.029(8)	0.049(9)
C-9	0.564(–)	0.258(–)	0.633(–)	0.062(9)	0.13(1)	0.10(1)	0.025(9)	0.037(8)	0.03(1)
C-10	0.557(4)	0.168(1)	0.484(4)	0.07(1)	0.11(1)	0.11(1)	0.020(8)	0.033(9)	0.04(1)
C-11	0.291(4)	0.128(1)	0.331(4)	0.08(1)	0.12(1)	0.08(1)	0.024(9)	0.028(9)	0.04(1)
C-12	0.279(4)	0.041(1)	0.192(4)	0.10(1)	0.11(1)	0.13(2)	0.001(9)	0.03(1)	0.03(1)
C-13	0.007(5)	0.001(2)	0.065(6)	0.09(1)	0.17(2)	0.17(2)	0.01(1)	−0.01(1)	0.01(2)

N-(n-*Decyl*)-D-*gluconamide*

Atom	x	y	z	U11	U22	U33	U23	U13	U12
O-1	0.4995(9)	−0.3129(3)	0.276(1)	0.039(1)	0.091(1)	0.076(1)	−0.029(1)	−0.01(1)	0.004(1)
O-2	0.0065(8)	−0.2663(3)	0.624(1)	0.039(1)	0.062(1)	0.054(1)	−0.004(1)	0.008(1)	−0.017(1)
O-3	0.1374(9)	−0.2273(3)	0.1584(9)	0.037(1)	0.054(1)	0.026(1)	−0.008(1)	−0.005(1)	0.004(1)
O-4	0.2201(8)	−0.1876(3)	0.6885(9)	0.033(1)	0.065(1)	0.019(1)	−0.009(1)	−0.007(1)	0.006(1)
O-5	0.7123(9)	−0.1839(3)	0.2121(9)	0.046(1)	0.073(1)	0.026(1)	−0.008(1)	−0.014(1)	0.016(1)
O-6	0.7946(8)	−0.1444(3)	0.7463(9)	0.039(1)	0.055(1)	0.025(1)	0.009(1)	−0.012(1)	−0.015(1)
N-1	0.0688(9)	−0.3205(3)	0.245(1)	0.022(1)	0.051(1)	0.028(1)	−0.019(1)	−0.006(1)	0.003(1)
C-1	0.288(1)	−0.3036(3)	0.345(1)	0.078(1)	0.032(1)	0.033(1)	0.001(1)	−0.004(1)	0.002(1)
C-2	0.253(1)	−0.2704(4)	0.524(1)	0.085(1)	0.039(1)	0.039(1)	−0.002(1)	−0.024(1)	−0.006(1)
C-3	0.345(1)	−0.2358(4)	0.367(1)	0.032(1)	0.061(1)	0.034(1)	0.007(1)	−0.014(1)	0.012(1)
C-4	0.414(1)	−0.2023(3)	0.543(1)	0.027(1)	0.034(1)	0.035(1)	−0.002(1)	−0.007(1)	−0.004(1)
C-5	0.499(1)	−0.1708(3)	0.373(1)	0.044(1)	0.029(1)	0.028(1)	−0.005(1)	−0.017(1)	0.008(1)
C-6	0.581(1)	−0.1356(4)	0.539(1)	0.059(1)	0.058(1)	0.051(1)	0.011(1)	−0.004(1)	0.008(1)
C-7	0.091(1)	−0.3531(4)	0.055(1)	0.011(1)	0.066(1)	0.073(1)	0.002(1)	−0.014(1)	0.001(1)
C-8	−0.175(1)	−0.3665(4)	−0.060(1)	0.054(1)	0.055(1)	0.042(1)	−0.014(1)	−0.013(1)	−0.006(1)
C-9	−0.155(1)	−0.4005(3)	−0.237(1)	0.039(1)	0.047(1)	0.047(1)	−0.001(1)	−0.002(1)	0.002(1)
C-10	−0.414(1)	−0.4155(4)	−0.355(1)	0.017(1)	0.077(1)	0.067(1)	0.005(1)	−0.016(1)	−0.005(1)
C-11	−0.388(1)	−0.4516(4)	−0.525(1)	0.029(1)	0.054(1)	0.077(1)	−0.018(1)	−0.025(1)	−0.008(1)
C-12	−0.658(1)	−0.4663(4)	−0.626(1)	0.035(1)	0.055(1)	0.082(1)	−0.002(1)	−0.015(1)	0.001(1)
C-13	−0.635(1)	−0.5023(4)	−0.803(1)	0.045(1)	0.061(1)	0.064(1)	−0.006(1)	−0.032(1)	0.001(1)
C-14	−0.896(1)	−0.5190(4)	−0.903(1)	0.035(1)	0.073(1)	0.041(1)	0.002(1)	−0.002(1)	−0.014(1)
C-15	−0.860(1)	−0.5539(4)	−1.074(1)	0.105(1)	0.041(1)	0.053(1)	−0.009(1)	−0.032(1)	−0.006(1)
C-16	−1.130(1)	−0.5723(4)	−1.149(1)	0.099(1)	0.111(1)	0.108(1)	−0.001(1)	−0.048(1)	−0.029(1)

[a]Atomic co-ordinates are fractional. Standard deviations obtained from least-squares correlation matrix are given in parentheses.

TABLE III

COMPARISON OF TORSION ANGLES IN *N*-(*n*-HEPTYL)-, *N*-(*n*-OCTYL)-, AND *N*-(*n*-DECYL)-D-GLUCONAMIDES[a]

Torsion angles (degrees)	D-*Gluconamide*		
	N-(n-*heptyl)*	N-*(*n-*decyl)*	N-(n-*octyl)*
O-6–C-6–C-5–C-4	55(2)	59	57.8(4)
C-6–C-5–C-4–C-3	180(2)	−178	−179.1(3)
C-5–C-4–C-3–C-2	178(1)	180	177.4(3)
C-4–C-3–C-2–C-1	−167(1)	−159	−166.1(3)
C-3–C-2–C-1–N-1	−114(2)	−114	−111.7(4)
C-2–C-1–N-1–C-7	176(1)	178	177.9(3)
*C-1–N-1–C-7–C-8	101(2)	−175	−172.8(4)
*N-1–C-7–C-8–C-9	−64(2)	−177	−175.6(4)
C-7–C-8–C-9–C-10	−179(1)	179	176.8(4)
C-8–C-9–C-10–C-11	174(1)	−177	−178.0(4)
C-9–C-10–C-11–C-12	−180(1)	177	177.5(4)
C-10–C-11–C-12–C-13	173(1)	179	−179.9(4)
C-11–C-12–C-13–C-14		178	178.3(4)
C-12–C-13–C-14–C-15		180	
C-13–C-14–C-15–C-16		176	

[a]The torsion angles which differ and represent a molecular hinge are marked*.

TABLE IV

HYDROGEN-BOND GEOMETRY[a] IN **1–3**

	A H B	*A–H*	*H–B*	*A–B*	*A–H–B*	*Sym. op.*
***1**	N-1–H · · · O-1	1.24	1.97	2.959	133.3	$x+1, y, z$
***2**		1.04	2.07	3.016	142.3	$x+1, y, z$
***3**		0.82(5)	2.32(5)	3.052(5)	150(4)	$x+1, y, z$
***1**	N-1–H · · · O-2	1.24	2.18	2.647	97.5	x, y, z
***2**		1.04	2.18	2.712	106.3	x, y, z
***3**		0.82(5)	2.28(5)	2.693(4)	112(4)	x, y, z
1	O-3–H · · · O-5	1.06	1.82	2.710	138.4	$x+1, y, z$
2		1.08	1.85	2.759	138.9	$x+1, y, z$
3		0.95(5)	1.99(5)	2.771(4)	144(5)	$x+1, y, z$
1	O-6–H · · · O-4	1.00	1.94	2.73	133.6	$x-1, y, z$
2		1.05	1.88	2.755	141	$x-1, y, z$
3		0.91(6)	1.93(6)	2.748(4)	148(5)	$x-1, y, z$
1	O-4 · · · O-3			2.71		$x, y, z-1$
2	O-4–H · · · O-3	0.86	1.89	2.735	175.5	$x, y, z-1$
3	O-4–H · · · O-3	0.84(5)	1.89(5)	2.725(4)	171(5)	$x, y, z-1$
1	O-5 · · · O-6			2.74		$x, y, z+1$
2	O-5 · · · O-6			2.72		$x, y, z+1$
3	O-5–H · · · O-6	0.82(6)	1.93(6)	2.727(4)	163(6)	$x, y, z+1$

[a]Distances in Å, angles in degrees, with standard deviations in parentheses. Hydrogen bonds marked * are of the three-centre (bifurcated) type.

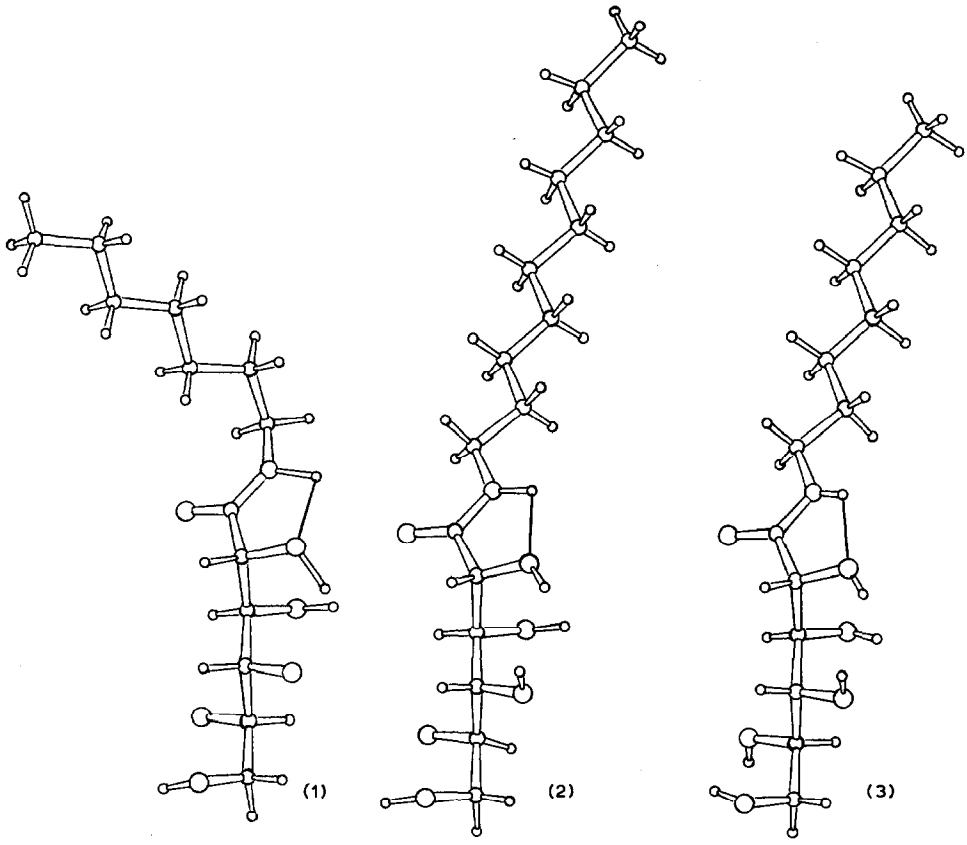


Fig. 1. Comparison of molecular structures of **1–3** projected on a plane through C-5, C-6, and O-5.

from pure translation in **1** (space group $P1$) to a fishbone-type arrangement in **2** and **3** (space group $P2_1$), the D-gluconamide moieties are in nearly the same orientation and environment. The hydrogen-bonding schemes are similar, as shown in Table IV. The N-1–H · · · O-1 interaction of the peptide groups represents one leg of a three-centre (bifurcated) hydrogen bond, the other leg being the intramolecular N-1–H · · · O-2 bond.

The intricate inter-glucose hydrogen bonding, apparently, is the underlying basis for the observed crystal packing, probably because the favoured all-*trans* form of the D-gluconamide moiety positions the O–H and amide groups in well-defined orientations. This arrangement determines the formation of molecular hydrogen bonds between O–H and amide groups, which is stronger than the van der Waals interactions of the alkyl chains and therefore dominates.

The molecules **2** and **3** with an even number of alkyl carbon atoms pack almost identically and in the same space group $P2_1$, as illustrated in Figs. 1 and 2. This packing can be predicted for all such molecules, because then the relative

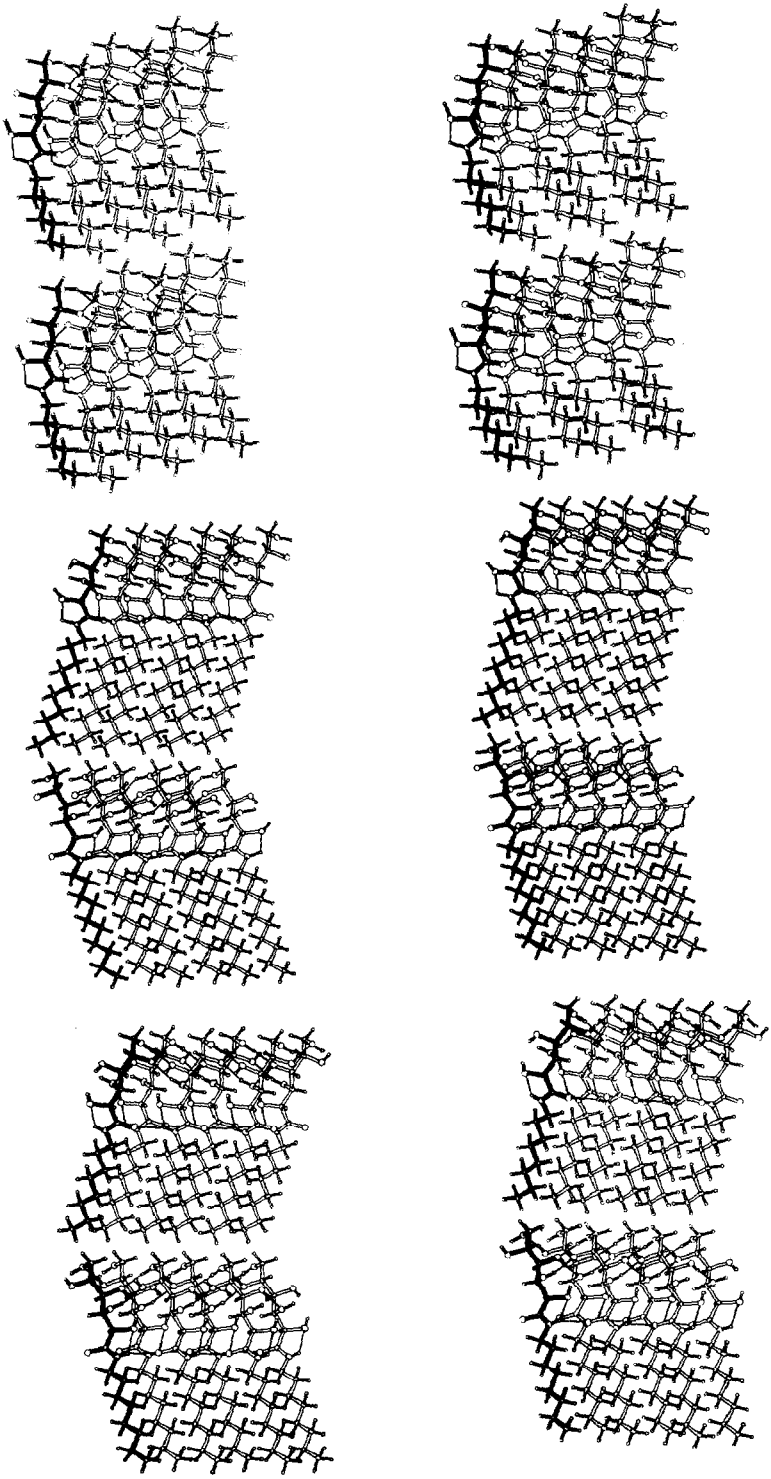


Fig. 2. Packing diagrams of **1–3**.

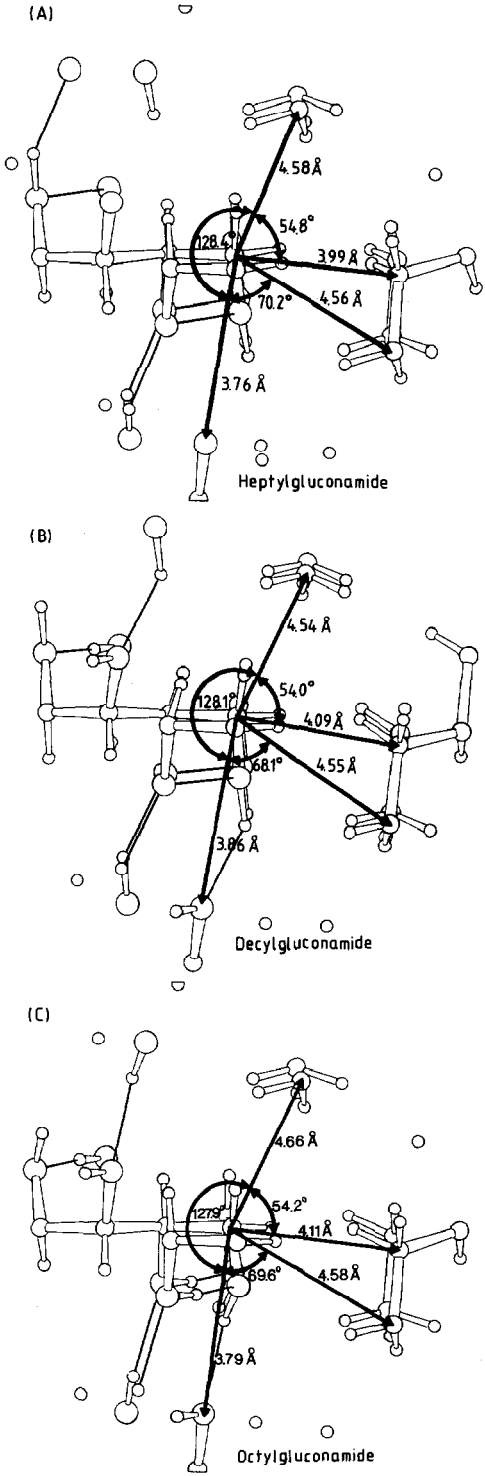


Fig. 3. Comparison of structural details in a sphere of 5-Å radius drawn around C-6 as centre, for *N*-(*n*-heptyl)-, *N*-(*n*-decyl)- and *N*-(*n*-octyl)-D-gluconamide.

orientation of the end groups (alkyl CH_2CH_3 and D-gluconamide $CHOHCH_2OH$) is maintained (Fig. 3). When the alkyl chain has an odd number of carbon atoms, as in **1**, the contacts between the end groups were different if molecular conformation and space group were the same as in **2** and **3**. This appears to be unfavourable and therefore both conformation *and* space group are changed in **1** so as to enable an identical interaction of the end groups as observed in **2** and **3**.

Thus, it is concluded that, in some respects, this well-defined, practically identical head-to-tail association in the *N*-(*n*-alkyl)-D-gluconamides is specific. It is made possible by two structural changes which are correlated and occur on different levels, namely (*a*) in *molecular packing* which changes from the simple *c*-translation in space group *P*1 (**1**) to the fishbone-type arrangement in space groups $P2_1$ (**2** and **3**), and (*b*) in *molecular conformation* where the alkyl chain which is all-*trans* in **2** and in **3** adopts a kink in **1** at the least sterically hindered CH_2 group, which is next to the amide N–H.

Work is in progress concerning the reasons for the aggregation of the alkyl-gluconamides in gels and the fine structure in ropes.

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