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The X-ray crystal structure of *N*-(1-hexadecyl)-D-gluconamide and powder diffraction studies on its lower and higher homologues ($n = 9 - 18$) ☆

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Abstract

The crystal structure of *N*-(1-hexadecyl)-D-gluconamide [$a = 4.8072(6)$ Å, $b = 46.771(5)$ Å, $c = 5.2885(7)$ Å, $\beta = 94.37(1)°$; monoclinic $P2_1$, $Z = 2$] displays the same molecular conformation and the same monolayer packing-arrangement as its lower homologues described previously. This is at seeming variance with most recent CPMAS ^{13}C NMR solid-state investigations describing a bilayer packing. It can be shown that the bilayer arrangement is the result of a kinetically driven crystallisation process, whereas the monolayer packing is the thermodynamically stable polymorph of the title compound. Powder spectra of dried self-assembled layers of *N*-(1-alkyl)-D-gluconamides showed only one-dimensional order and exhibited at most two periodicities. These could be assigned to a mono- and bilayer arrangement, respectively. Derivatives with long alkyl chains proved to have a smaller tendency towards monolayer assembling than homologues with a short tail.

Keywords: *N*-(1-Hexadecyl)-D-gluconamide; Diffraction studies

☆ Dedicated to Professor Dr Hans Bradaczek, Freie Universität Berlin, on the occasion of his 65th birthday.

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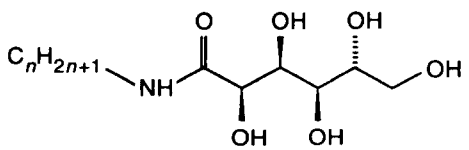
1. Introduction

Amphiphilic *N*-(1-alkyl)-D-gluconamides [1–3] (n_{alkyl} = 7–12) display a head-to-tail arrangement in the crystalline state. This packing, which is also found for *N*-(1-alkadiyne) derivatives [4,5], is usually not observed with amphiphilic compounds which tend to display tail-to-tail packing [6]. Increasing the chain length of the alkyl tail of *N*-alkyl gluconamides should increase its influence on the crystallisation process. Therefore it may be expected that certain chain lengths might trigger a reversal from the monolayer to a bilayer packing.

Just recently, this expectation was confirmed experimentally: CPMAS ^{13}C NMR of powder samples of *N*-(1-alkyl)gluconamides demonstrated that the derivatives having chain lengths beyond C15 display a bilayer arrangement [7,8]. These findings were supported by DSC-thermograms which showed that longer alkyl chains caused crystal-to-crystal transitions accompanied by low endothermic enthalpy changes. In contrast, the derivatives with shorter alkyl tails displayed high enthalpy values during their crystal-to-crystal transitions upon heating. The high enthalpy values were interpreted as accompanying a monolayer-to-bilayer rearrangement. It was concluded from the low enthalpy values that the longer alkyl derivatives did not rearrange, since they already occurred in a bilayer structure at room temperature [8].

This work is part of our studies on the crystalline behaviour of acylic-sugar lipid derivatives which include so far *N*-(1-octyl)-D-gulonamide [9], *N*-(1-octyl)-D-talonamide [10], *N*-(1-dodecyl)-D-ribonamide [11], *N*-(1-octyl)-D-arabinonamide [11], *N*-trideca-5,7-diyne-D-gluconamide [5] and the tetradeca-6,8-diyne derivative [4] of it and the double-headed (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane [12].

The CPMAS observations prompted us to determine the crystal structure of the gluconamide derivative with the shortest alkyl chain at which the bilayer packing still should be observable, namely *N*-(1-hexadecyl)-D-gluconamide (**1**). Furthermore, X-ray powder diffraction spectra of self-assembled layers of dried *N*-alkyl-D-gluconomide solutions (n = 9–18) were taken which might provide further insight into the solid-state behaviour of these compounds.



1 : n = 16
N-(1-alykl)-D-gluconamides : n = 9–18

2. Experimental

Single crystal X-ray analysis.—Colourless single crystals of **1** of sufficient size for X-ray work were obtained at 4°C in a closed vial (1 week) from 70:29:1 $CHCl_3$–C_2H_5OH–H_2O. Precise lattice constants were calculated by a least-squares fitting to the

accurately determined positions of 45 setting reflections ($70° \leq 2\Theta \leq 80°$) on a Stoe four-circle diffractometer. The data collection was performed at room temperature in the $\omega - 2\Theta$-scan mode using Ni-filtered CuK α-radiation.

The structure was solved with direct methods using [13] SHELXS86 and was refined with [14] XTAL2.2. All hydrogen atoms were located in difference Fourier maps. Non-hydrogen atoms were refined with anisotropic, and all hydrogen atoms with isotropic, temperature parameters with no restraints applied. The final refinement cycle resulted in an unweighted R-value of 0.031 (weighted R-value 0.032). Therefore, this is an exceptional case where high quality data could be obtained for an amphiphile with a rather long tail, namely a hexadecanoyl moiety.

Powder diffraction.—Samples of *N*-(1-alkyl)-D-gluconamide ($n = 9$–18) were kindly provided by B. Kling and Dr S. Svenson, Freie Universität Berlin. Dried self-assembled layers of all gluconamides were prepared from solutions in 70:29:1 $CHCl_3$–C_2H_5OH–H_2O which were dropped onto glass supports. The solvent was allowed to evaporate at room temperature; this took < 15 min.

Table 1
Experimental and crystal data for **1**

Molecular formula	$C_{22}H_{45}NO_6$
Molecular weight (g mol^{-1})	419.6
Crystal size (mm^3)	0.72 × 0.18 × 0.08
Colour	colourless, clear
Space group	monoclinic $P2_1$
Lattice constants (Å,°)	
a	4.8072(6)
b	46.771(5)
c	5.2885(7)
β	94.37(1)°
Cell volume (Å^3)	1185.60
Z	2
Calculated density D_x (g cm^{-3})	1.175
Wavelength of used radiation (CuK α) (Å)	1.5418
Absorption coefficient μ (cm^{-1})	6.84
$T_{measurement}$ (K)	295
Measured reflections	2232 ($6 \leq 2\Theta_{max} \leq 128°$ for h:0 → 5, k:0 → 54, l:−6 → 5)
Independent reflections	1992
R_{int} (480 repl. measurements)	0.013
Observed ($I > 2\sigma(I)$)	1667
Structure refinement based on	$w(\|F_0\| - \|F_R\|)^2$ ($w = 1/\sigma^2$, σ from counting statistics)
R	0.031
R_w	0.032
GOF	3.2
Final residual of electron density (e Å^{-3})	0.168

The information obtained from the spectra of the forgoing samples may be biased by preferential orientation of the molecules into lamellar layers parallel to the glass support. Therefore, self-assembled layers of $n = 10$ and $n = 18$ prepared as compound just described were scratched from their glass supports and cautiously powdered. These samples, which were regarded as exhibiting no further preorientation on the glass support, were also subjected to powder diffraction.

All powder spectra were taken on a Philips PW 1050 powder diffractometer using Ni-filtered and graphite-monochromated CuKα radiation. The spectra were measured between 1 and 30° in 2Θ in the $\omega - 2\Theta$-scan mode with steps of 0.02° in 2Θ and 5 s measurement time per step.

Table 2
Atomic parameters and U_{eq}- and U-values for **1** (U_{eq} and U in Å$\times 10^2$) [a]

Atom	x	y	z	U_{eq}
C-1	0.2430(6)	0.59320(-)	0.3551(6)	3.5(1)
O-1	0.3062(6)	0.60034(9)	0.1449(5)	6.2(1)
C-2	0.0547(6)	0.56736(9)	0.3753(6)	3.18(9)
H-2	−0.102(6)	0.5699(7)	0.251(5)	3.1(8)
O-2	−0.0309(5)	0.56436(8)	0.6275(5)	4.25(8)
H-O2	−0.169(9)	0.561(1)	0.599(8)	6(1)
C-3	0.2174(6)	0.54108(9)	0.2987(6)	2.88(9)
H-3	0.312(5)	0.5472(6)	0.145(5)	2.0(7)
O-3	0.4258(4)	0.53431(8)	0.4991(5)	3.32(7)
H-O3	0.365(7)	0.5277(8)	0.611(7)	4(1)
C-4	0.0413(6)	0.51497(9)	0.2193(5)	2.88(9)
H-4	−0.089(6)	0.5213(7)	0.082(6)	2.8(8)
O-4	−0.1049(5)	0.50377(9)	0.4214(4)	3.55(7)
H-O4	−0.212(8)	0.5137(9)	0.428(7)	5(1)
C-5	0.2156(6)	0.4903(1)	0.1289(6)	3.10(9)
H-5	0.361(6)	0.4837(7)	0.263(6)	3.0(8)
O-5	0.3646(5)	0.50094(9)	−0.0748(4)	3.76(7)
H-O5	0.486(7)	0.4917(7)	−0.097(6)	1.9(9)
C-6	0.0452(7)	0.4645(1)	0.0434(7)	3.8(1)
H-61	−0.051(7)	0.4565(7)	0.186(6)	3.8(9)
H-62	0.160(6)	0.4491(7)	−0.010(6)	3.3(8)
O-6	−0.1633(5)	0.47080(9)	−0.1558(5)	3.64(8)
H-O6	−0.097(7)	0.4793(8)	−0.268(7)	4(1)
N	0.3399(6)	0.60623(9)	0.5671(5)	3.76(9)
H-N	0.277(6)	0.6000(7)	0.732(6)	2.5(7)
C-7	0.5301(8)	0.6305(1)	0.5516(7)	4.0(1)
H-71	0.429(7)	0.6457(8)	0.475(7)	5(1)
H-72	0.681(8)	0.6245(7)	0.459(7)	4(1)
C-8	0.6485(8)	0.6404(1)	0.8102(7)	4.0(1)
H-81	0.767(8)	0.6244(8)	0.869(7)	5(1)
H-82	0.504(8)	0.6426(8)	0.928(7)	5(1)
C-9	0.8294(8)	0.6668(1)	0.7927(7)	4.0(1)
H-91	0.717(7)	0.6822(8)	0.700(7)	4.4(9)
H-92	0.974(7)	0.6626(7)	0.688(7)	4(1)
C-10	0.9383(8)	0.6783(1)	1.0509(7)	4.1(1)
H-101	1.054(9)	0.6641(9)	1.147(8)	7(1)

Table 2 (continued)

Atom	x	y	z	U_{eq}
H-102	0.789(7)	0.6801(8)	1.174(7)	4(1)
C-11	1.1156(9)	0.7052(1)	1.0366(7)	4.3(1)
H-111	1.268(7)	0.7003(7)	0.936(6)	3.3(9)
H-112	1.001(8)	0.7200(8)	0.947(7)	4(1)
C-12	1.2166(9)	0.7171(1)	1.2940(7)	4.4(1)
H-121	1.330(8)	0.7017(9)	1.393(8)	6(1)
H-122	1.057(7)	0.7201(7)	1.405(7)	4.0(9)
C-13	1.3929(9)	0.7443(1)	1.2806(7)	4.4(1)
H-131	1.279(8)	0.7589(9)	1.187(7)	5(1)
H-132	1.541(8)	0.7399(8)	1.183(7)	5(1)
C-14	1.4937(9)	0.7561(1)	1.5381(7)	4.4(1)
H-141	1.595(9)	0.741(1)	1.648(8)	7(1)
H-142	1.336(8)	0.7589(9)	1.650(7)	6(1)
C-15	1.6680(9)	0.7830(1)	1.5242(7)	4.6(1)
H-151	1.554(8)	0.7977(9)	1.430(7)	6(1)
H-152	1.814(8)	0.7786(8)	1.419(7)	4(1)
C-16	1.7694(9)	0.7952(1)	1.7813(7)	4.6(1)
H-161	1.605(7)	0.7966(7)	1.898(7)	4.3(9)
H-162	1.872(8)	0.782(1)	1.884(8)	6(1)
C-17	1.9427(9)	0.8222(1)	1.7679(7)	4.7(1)
H-171	2.101(8)	0.8180(9)	1.675(7)	6(1)
H-172	1.828(8)	0.8378(9)	1.678(8)	6(1)
C-18	2.0454(9)	0.8344(1)	2.0236(7)	4.8(1)
H-181	1.896(9)	0.8368(9)	2.126(8)	6(1)
H-182	2.159(8)	0.8188(9)	2.121(8)	7(1)
C-19	2.2157(9)	0.8614(1)	2.0067(7)	4.9(1)
H-191	2.089(9)	0.876(1)	1.910(8)	7(1)
H-192	2.363(8)	0.8573(8)	1.905(7)	5(1)
C-20	2.3165(9)	0.8744(1)	2.2604(7)	4.9(1)
H-201	2.415(8)	0.8606(9)	2.381(8)	7(1)
H-202	2.18(1)	0.877(1)	2.370(9)	8(1)
C-21	2.485(1)	0.9015(1)	2.2402(8)	6.3(2)
H-211	2.38(1)	0.917(1)	2.13(1)	12(2)
H-212	2.62(1)	0.896(1)	2.12(1)	13(2)
C-22	2.578(1)	0.9149(1)	2.492(1)	7.9(2)
H-221	2.42(1)	0.919(1)	2.61(1)	10(2)
H-222	2.65(1)	0.902(1)	2.63(1)	12(2)
H-223	2.68(1)	0.932(1)	2.47(1)	10(2)

[a] ESD values in parentheses.

3. Results and discussion

The crystal data and experimental details are given in Table 1. Table 2 gives the co-ordinates of **1**. Bond lengths and angles are displayed in Tables 3 and 4, respectively. Torsion angles are given in Table 5; the hydrogen bonding geometry — with O–H and N–H distances normalized to 0.97 and 1.0 Å, respectively — is displayed in Table 6. Table 7 shows the lamellar spacings for powder spectra of the dried self-assembled layers of DGLUn the $n_{alkyl} = 9 - 18$ compound. Figure 1 displays the molecular

Table 3
Bond lengths (Å) of **1**

C-1–O-1	1.221(4)	C-1–C-2	1.519(4)
C-1–N	1.329(4)	C-2–O-2	1.432(4)
C-2–C-3	1.528(6)	C-3–O-3	1.437(4)
C-3–C-4	1.526(5)	C-4–O-4	1.423(4)
C-4–C-5	1.525(6)	C-5–O-5	1.428(4)
C-5–C-6	1.507(6)	C-6–O-6	1.428(4)
N–C-7	1.464(6)	C-7–C-8	1.513(5)
C-8–C-9	1.519(7)	C-9–C-10	1.522(5)
C-10–C-11	1.525(7)	C-11–C-12	1.517(6)
C-12–C-13	1.530(7)	C-13–C-14	1.516(5)
C-14–C-15	1.516(7)	C-15–C-16	1.519(6)
C-16–C-17	1.518(7)	C-17–C-18	1.515(6)
C-18–C-19	1.512(7)	C-19–C-20	1.519(6)
C-20–C-21	1.513(7)	C-21–C-22	1.510(7)

[a] ESD values in parentheses.

conformation of **1** and the numbering scheme used. Figure 2 shows a SCHAKAL [15]-stereo plot of the crystal packing and the hydrogen-bonding pattern.

Powder diffraction.—The assignment of packing arrangements from powder diffraction spectra is to a certain extent ambiguous, especially when different space groups come into play. Since, however, the spectra of the powdered samples gave — aside the lamellar reflections — no evidence which would have could indicated that the occurring state of order was higher than one-dimensional, extinction rules for certain space groups obviously were not applicable.

The powder diffraction pattern of the dried, self-assembled layer samples exhibiting between six and ten orders showed at most two periodicities which could be assigned to

Table 4
Bond angles (°) of **1** [a]

O-1–C-1–C-2	118.2(3)	O-1–C-1–N	123.2(3)
C-2–C-1–N	118.6(3)	C-1–C-2–O-2	111.0(3)
C-1–C-2–C-3	107.5(2)	O-2–C-2–C-3	110.9(3)
C-2–C-3–O-3	108.9(3)	C-2–C-3–C-4	115.6(3)
O-3–C-3–C-4	111.5(3)	C-3–C-4–O-4	112.5(3)
C-3–C-4–C-5	112.7(3)	O-4–C-4–C-5	105.8(3)
C-4–C-5–O-5	107.0(3)	C-4–C-5–C-6	113.6(3)
O-5–C-5–C-6	110.2(3)	C-5–C-6–O-6	113.1(4)
C-1–N–C-7	119.2(3)	N–C-7–C-8	112.4(3)
C-7–C-8–C-9	111.8(3)	C-8–C-9–C-10	113.0(3)
C-9–C-10–C-11	113.6(3)	C-10–C-11–C-12	113.6(3)
C-11–C-12–C-13	113.8(3)	C-12–C-13–C-14	113.7(4)
C-13–C-14–C-15	113.6(3)	C-14–C-15–C-16	114.0(3)
C-15–C-16–C-17	114.1(3)	C-16–C-17–C-18	114.4(4)
C-17–C-18–C-19	113.7(4)	C-18–C-19–C-20	114.8(4)
C-19–C-20–C-21	114.2(4)	C-20–C-21–C-22	114.1(4)

[a] ESD values in parentheses.

Table 5
Torsion angles (°) of **1** [a]

Sequence	
O-1–C-1–C-2–O-2	−171.8(3)
O-1–C-1–C-2–C-3	66.7(3)
N–C-1–C-2–O-2	10.9(4)
N–C-1–C-2–C-3	−110.6(3)
O-1–C-1–N–C-7	0.5(6)
C-2–C-1–N–C-7	177.7(3)
C-1–C-2–C-3–O-3	73.5(3)
C-1–C-2–C-3–C-4	−160.0(2)
O-2–C-2–C-3–O-3	−48.1(3)
O-2–C-2–C-3–C-4	78.4(3)
C-2–C-3–C-4–O-4	−64.3(4)
C-2–C-3–C-4–C-5	176.2(3)
O-3–C-3–C-4–O-4	60.8(4)
O-3–C-3–C-4–C-5	−58.7(3)
C-3–C-4–C-5–O-5	−56.8(3)
C-3–C-4–C-5–C-6	−178.5(3)
O-4–C-4–C-5–O-5	180(1)
O-4–C-4–C-5–C-6	58.1(3)
C-4–C-5–C-6–O-6	57.5(4)
O-5–C-5–C-6–O-6	−62.4(4)
C-1–N–C-7–C-8	−172.8(3)
N–C-7–C-8–C-9	−176.0(3)
C-7–C-8–C-9–C-10	176.8(3)
C-8–C-9–C-10–C-11	−178.8(4)
C-9–C-10–C-11–C-12	178.2(4)
C-10–C-11–C-12–C-13	−179.6(4)
C-11–C-12–C-13–C-14	−180(2)
C-12–C-13–C-14–C-15	−180(1)
C-13–C-14–C-15–C-16	179.8(6)
C-14–C-15–C-16–C-17	−179.7(4)
C-15–C-16–C-17–C-18	−179.8(7)
C-16–C-17–C-18–C-19	−179.6(4)
C-17–C-18–C-19–C-20	178.8(4)
C-18–C-19–C-20–C-21	−179.5(4)
C-19–C-20–C-21–C-22	178.4(5)

[a] ESD values in parentheses.

a monolayer and a bilayer arrangement, respectively. The percentage of the mono- and bi-layer arrangement within the corresponding sample was roughly estimated by the relative intensities of the mono- and bi-layer peaks.

The monolayer spacing of $n = 11$ gluconamide of 19.6 Å matches the d-value of the 010 reflection ($d = 19.5$ Å) as calculated for the powder diffraction spectrum from its known crystal structure [16]. On the other hand, the corresponding bilayer value of 39.7 Å is compatible with the value of 39.4 Å given for the bilayered crystal phase of *N*-undecyl-D-gluconamide obtained both upon heating to 90°C and after cooling down to room temperature [16]. The same holds for the monolayer spacings of $n = 10$ (d =

Table 6
Hydrogen bond geometry [a,b] of **1** in Å and degrees

D	A	H···A	D···A	D-H···A	Symop. for A		A···H···H [c]
N	O-1	2.17(3)	3.085(4)	152(2)	*x,y,*	1+*z*	
N	O-2	2.27(3)	2.683(5)	104(2)	*x,y,*	*z*	104(1)[360(3)]
O-2	O-3	2.07(4)	2.998(4)	158(4)	−1+*x,y,*	*z*	
O-3	O-5	1.88(4)	2.775(4)	152(3)	*x,y,*	1+*z*	
O-4	O-3	1.79(4)	2.728(4)	162(4)	−1+*x,y,*	*z*	
O-5	O-6	1.77(3)	2.733(4)	173(3)	1+*x,y,*	*z*	
O-6	O-4	1.85(4)	2.748(4)	153(3)	*x,y,*	−1+*z*	
O-6	O-5	2.54(4)	2.906(4)	103(2)	*x,y,*	*z*	99(2)[355(4)]

[a] ESD values in parentheses. [b] O-H and N-H bond lengths normalized to 0.97 and 1.0 Å, respectively. ESD values for D-H ≤ 0.04 Å. [c] Sum of angles in square brackets.

Table 7
Lamellar spacings [a] of *N*-(1-alkyl)-D-gluconamides (n = 9–18) in Å

n	Bilayer	Monolayer	Percentage [b] of bilayer	Monolayer
9	-	17.7	0	100
10	39.6	17.9	13	87
11	39.7	19.6	1	99
12	44.1	19.7	97	3
13	43.6	21.3	1	99
14	48.2	21.4	99	1
15	49.3	22.9	97	3
16	52.2	23.2	64	36
	51.9 [c]	-	100 [c]	-
17	51.8	-	100	0
18	56.5	25.1	90	10

[a] No other periodicities were visible in the powder diffraction patterns indicating one-dimensional order. [b] The error of the percentages is assumed to be ±5%. [c] This spacing is found in the raw material as obtained from synthesis.

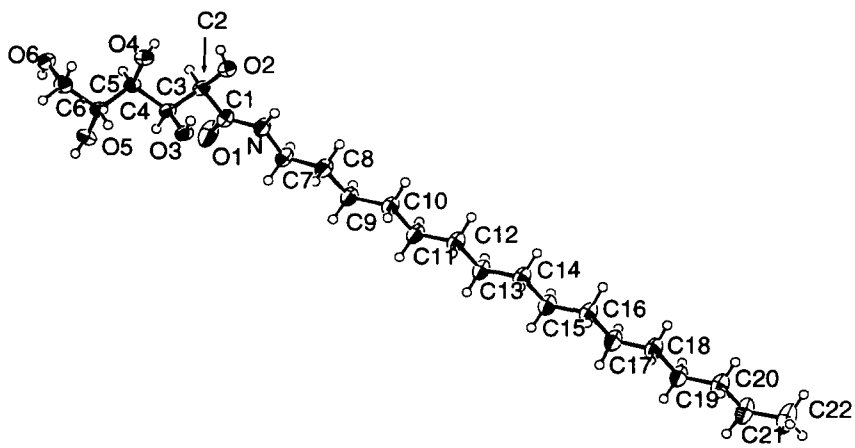


Fig. 1. Molecular conformation and atomic numbering scheme of **1** (ellipsoids represent 50% probability).

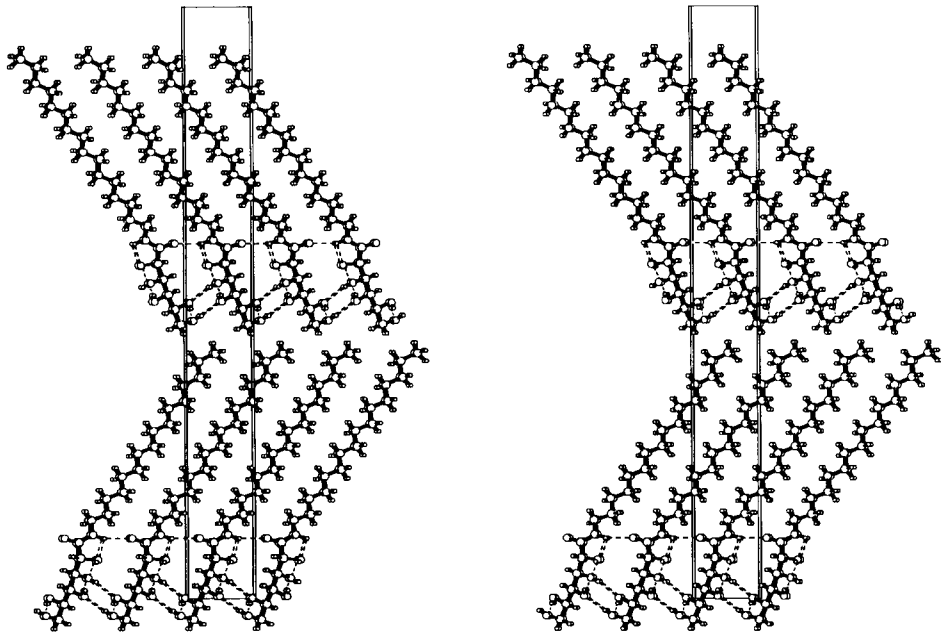


Fig. 2. Stereo plot of the crystal packing and the hydrogen bonding scheme of **1**. The viewing direction is [−1 0 0].

17.9 Å), $n = 12$ ($d = 19.7$ Å) and $n = 16$ gluconamide ($d = 23.2$ Å) agreeing with half the *b*-axis of decyl (ref. [2]), docecyl-D-gluconamide (ref. [1]), and **1**, respectively.

For the odd-numbered gluconamides, the percentage of the tail-to-tail oriented bilayer increases continuously from C-9 to C-17. The bilayer arrangement preponderates within the even-numbered series, beginning with $n = 12$. Therefore, the influence of the alkyl tail's length on the rearrangement from bilayer to monolayer packing is observable in both series. Notably, the powder patterns indicate that the molecules in self-assembled layers of the $n = 9$, 10 and 11 gluconamides occur almost completely in a monolayered arrangement. It is remarkable that the bilayer spacings do not become larger on a regular compound-by-compound basis, but rather on a stepwise odd-to-even basis: the bilayer spacings of an even- and its next-higher odd-numbered homologue are merely identical, whereas the lamellar spacing increases by ~4 Å going to the next even-numbered derivative. The inverse holds for the monolayer spacings. Here the spacing increases by ~2 Å on going from an even-to its next-higher odd-numbered homologue.

Single crystal X-ray analysis.—The bond lengths and angles are in the range usually found in alditols [17] and deserve no further discussion. The alkyl tail is extended and ordered-as found in all *N*-(1-alkyl)-aldonamides studied so far [1–5,10,11,16,18] the only exception being *N*-(1-octyl)-D-gulonamide [9] where the alkyl chain is quasi-fluid. The head group conformation of 1 is identical to those of other gluconamides, that is it is extended by tolerating a 1,3-syndiaxial interaction [19] between O-2 and O-4. Notably, all O_{OH}–C–C–O_{OH} torsion angles — except O-5–C-5–C-4–O-4 which is trans — are in the ±gauche range. Therefore, gauche effects [20] contribute to the

stabilization of the molecule. There exists, however, a destabilization due to the O-2–O-4 interaction the magnitude of which is a matter of heavy debate. In fact, recently published statistical data support the view that 1,3-syndiaxial effects have been over-emphasized in the past [21]. The discussion concerning these interactions is, however not yet finished. Therefore, the relative importance of the gauche effect and 1,3-syndiaxial interactions for the conformational behaviour of **1** cannot be estimated reasonably. *N*-alkyl/alkadiyne-gluconamides display an odd-even effect by crystallising in different space groups and differing conformationally within the 'hinge' region [2] (C-1–*N*–C-7–C-8 and *N*–C-7–C-8–C-9). The corresponding torsion angles of **1** amounting to −172.8(3) and −176.0(3), respectively, are both in the *ap* range; thus **1** has the same overall conformation as its even-numbered homologous compounds (see Table 4 in ref. [12] for a list of torsion angles of gluconamide head groups). Some aspects of the odd-even-effect of amphiphilic gluconamides were discussed in ref. [5] where a complete list of the hinge region's torsion angles for *N*-alkyl-and *N*-alkadiyne-gluconamides was also given (ref. [5], Table 4).

The hydrogen-bonding scheme consists of a homodromic, quadrilateral cycle formed by $O\text{-}3_{x,y,z} \rightarrow O\text{-}5_{x,y,-1+z} \rightarrow O\text{-}6_{-1+x,y,-1+z} \rightarrow O\text{-}4_{-1+x,y,z} \rightarrow O\text{-}3_{x,y,z}$ and endless chains of the kind *N*–H · · · O = C–*N*–H · · · O = C etc. with an intramolecular branch from *N*–H to O-2. Both the cycles as well as the amide bond chains — including the intramolecular branch — are also found in all other *N*-(1-alkyl)- [22] and *N*-(1-alkadiyne) derivatives. These hydrogen patterns also occur in (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane, which contains two gluconamide moieties in its structure [12]. In this structure the homodromic cycle is formed by only two molecules instead of four, but nevertheless the cycle of the latter compound and **1** are completely identical. As discussed recently [12], differences amongst the *N*-alkyl/alkadiynyl-gluconamide homologues solely emerge from O-2. In **1**, it is involved in an intermolecular hydrogen bond with O-3; thus O-2 behaves identically in **1** and *N*-(1-trideca-5,7-diyne)-D-gluconamide [5]. Notably, this hydrogen bond has also been found in the neutron crystal structure of *N*-(2-chloroethyl)-D-gluconamide [23].

The most interesting question of this structure analysis is the packing arrangement of the molecules in the crystal. As already suggested by the similarity of the hydrogen bonding of 1 with that of other gluconamides, the crystal packing of **1** (Fig. 2) reveals the same monolayer arrangement as found for the shorter alkyl chain homologues [22]. This seems to be at variance with the findings of the earlier cited solid-state NMR investigation [8]. Moreover, the lamellar spacing of 51.9 Å (Table 7), found in the powder diffraction experiment for the untreated material of **1** as obtained from synthesis likewise shows unambiguously the existence of a bilayer.

If the crystallization process were driven only by the thermodynamical gradient, then the resulting crystal structure would represent the thermodynamically most stable form of the compound under investigation. The existence of polymorphism, that is the occurrence of more than one crystal structure for a given compound, shows that crystallization can also be driven kinetically.

It is quite obvious that the solid-state NMR investigation and the powder diffraction of the non-recrystallised sample on the one hand and the crystal structure depicted for **1** on the other side describe different solid-state forms of **1**.

Polymorphism has been reported for *N*-(1-undecyl)-D-gluconamide. It has been reported that the molecules rearrange from a mono- into a bi-layer packing upon heating crystals to 90°C and that this bilayer is kept after slow cooling down to room temperature [16]. However, no crystal structure is available for the bilayer packing. The existence of two different crystal forms of the related compound *N*-dodecanoyl-*N*-methylglucamine has also been reported recently [24], but again no detailed data are available.

Which form of **1** is now the thermodynamically most stable one? The monolayer crystal-packing of **1** presented here was found in a crystal obtained by a slow crystallisation process (~ 1 week) and at 4°C, that is below room temperature. In contrast to this, the sample used for the solid-state NMR-study was obtained by cooling from a hot methanol solution of **1** [25]. After ~ 2 h the solution had reached room temperature [25].

Similar conditions [7] occurred during the synthesis of **1** explaining why identical forms of **1** were found in the CPMAS study and the powder diffraction experiment for the untreated sample of **1**.

Therefore, thermodynamic crystallisation conditions are found in the former case, whereas the crystallisation is kinetically driven in the latter. Thus, a bilayer arrangement is a metastable solid-state form of *N*-(1-alkyl)gluconamides, whereas the crystalline monolayer packing stabilised by a quadrilateral hydrogen-bond cycle constitutes the thermodynamically more stable form of these compounds.

It has been reported recently, that the homodromic hydrogen-bond cycle, now found in **1**, actually occurs in the crystal structures of many other — and not only amphiphilic [22]! — open-chain carbohydrate derivatives in a completely identical form [26]. One may wonder if the crystal structures exhibiting this special hydrogen-bond cycle also represent the thermodynamically most stable forms of each corresponding compound. Lattice-energy calculations on hypothetical and real crystal structures would be necessary for answering this question on a quantitative basis. However, chemical intuition suggests that this need not necessarily be so; there is no indication that kinetically and thermodynamically driven crystallisation processes of non-identical compounds should not result in similar or identical packing arrangements.

It should be mentioned that there exists another example — namely aliphatic *p*-alkanamidobenzoic acids [27] — where powder diffraction and single crystal X-ray structure analysis also give opposite packing arrangements, thereby likewise indicating polymorphism. Powder spectra indicate that the pentane derivative displays the same bilayer arrangement found in the crystal structures of its butane and nonane homologues, respectively. In contrast to that, the former compounds display in the crystalline state a packing arrangement in which the molecules are oriented anti parallel. It is noteworthy that both the bilayer and the anti parallel arrangement involve the same hydrogen-bonding schemes, namely carboxylic acid dimers and endless chains of the kind N–H $\cdots$ O = C–N–H $\cdots$ O = C, and so on. It is important to stress that the different packing patterns definitively can not be traced back to an odd-even-effect, since the bilayer arrangement is found with derivatives with both an odd- and an even-numbered alkyl tail. Taking into account the powder patterns, which indicate that the bilayer arrangement can be adopted by all amidobenzoic acid derivatives, it becomes obvious that this

series of homologues represent a mixture of stable and metastable crystal structures. In this case, however, there are no data providing evidence that the structure under consideration represents a stable or a metastable form.

Acknowledgments

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