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The X-ray crystal structure of the double-headed amphiphile (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane

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Abstract

If a mixture of diastereomeric and enantiomeric 1,2-diaminocyclohexanes is amidated with D-glucono-1,5-lactone, only one of the four diasteroeomeric amides, namely the title compound, crystallizes from the mixture. The same amide was also synthesized and crystallized from enantiomerically pure *S*,*S*-diamino-cyclohexane. The 1*R*,2*R*-diamide was also synthesized, but could not be crystallized. (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane, $C_{18}H_{34}N_2O_{12}$, $M_r = 470.47$, orthorhombic $P2_12_12_1$, $a = 4.877$ (1), $b = 18.962$ (5), $c = 23.432$ (9) Å, $V = 2166.9$ Å^3, $Z = 4$, $D_x = 1.422$ g cm^{-3}, λ (Cu$K\alpha$) = 1.5418 Å, $\mu = 10.49$ cm^{-1}, $F(000) = 1008.0$, $T = 295$K, final $R = 0.057$ and $R_w = 0.054$ for 1808 reflections with $F > 2\sigma(F)$. When compared to crystal structures of other gluconamides, the title compound exhibits regular differences in its gluconamide moieties. These differences are explained by an equilibrium between the tendency to form an extended hydrogen bonding net, the tendency of gluconamide chains to adopt an all-*trans* conformation and the restrictions imposed on the sugar chains by the topology. The hydrophobic parts of the molecule form parallel 'oil-tubes' in the crystal rather than hydrophobic sheets, a pattern never observed before.

1. Introduction

In our studies on the conformational and packing behaviour of acyclic sugar derivatives [1–4] we describe here the crystal structure of (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane (**1**), an amphiphilic molecule bearing two hydrophilic residues. The compound was synthesized in order to test its aptitude as a mediator for incorporation of hydrophobic substances into chiral superstructures formed by *N*-(1-alkyl)aldonamides [5–8].

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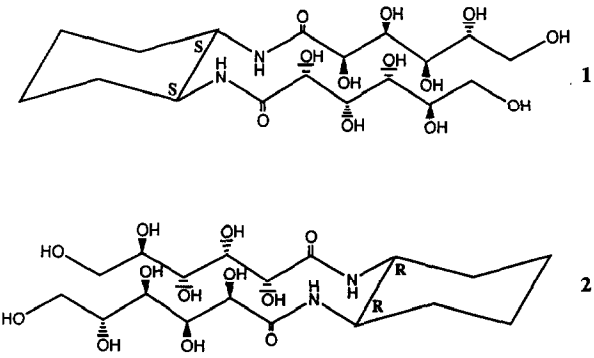
2. Experimental

Preparation.—D-Gluconic acid-1,5-lactone (10 g, 56.13 nmol) was refluxed under Ar for 5 h in 200 mL of dry MeOH until the lactone was completely dissolved. Thereafter 3.44 mL (28.07 nmol) of freshly distilled 1,2-diaminocyclohexane (*cis/trans* mixture) were added dropwise to the refluxing solution with stirring. After 1 h, a white product precipitated and 200 mL of dry MeOH was added to obtain a stirrable mixture. After another 6 h of refluxing, the white precipitate was filtered off, washed with MeOH and finally crystallized from MeOH–water; yield: 4 g (30%) of white crystals; mp 222°C.

As the yield of a sharply melting product was relatively small, it was supposed that only one stereoisomer had been formed; a study of the corresponding literature showed that the pure enantiomer (+)-(1*S*,2*S*)-1,2-diaminocyclohexane, for example, can be obtained by fractional crystallization of the D-tartaric acid salt [9]. The fact that, in our case, also a resolution of the racemate can be effected under the influence of the D-gluconic acid-1,5-lactone, was confirmed by the analysis of the crystal structure of the substance obtained, as well as by the synthesis of the same compound with the pure enantiomer (1*S*,2*S*)-(+)-(1,2)-diamino-cyclohexane.

The second synthesis of **1** was performed as just described, the only difference being that now 5 g (28.06 nmol) D-gluconic acid-1,5-lactone and 1.60 g (14.03 nmol) of (+)-(1*S*,2*S*)-1,2-diaminocyclohexane were used; yield: 4.2 g (64%); mp 222°C; $[\alpha]_D^{25}$ +56.5°. ^{1}H NMR (Me_2SO-d_6, 250 MHz): δ (ppm) 1.24 (m, 4 H, $-CH_2-$), 1.66 (m, 2 H, $-CH_2-$), 1.90 (m, 2 H, $-CH_2-$), 3.38 (m, 2 H, 6′-H), 3.48 (m, 4 H, 4-H and 5-H), 3.55 (m, 2 H, –CH–NH–), 3.57 (m, 2 H, 6-H), 3.90 (m, 2 H, 3-H), 3.97 (t, 2 H, 2-H), 4.31 (t, 2 H, OH-6), 4.38 (d, 2 H, OH-3), 4.43 (d, 2 H, OH-4), 4.53 (d, 2 H, OH-5), 5.28 (d, 2 H, OH-2), 7.42 (d, 2 H, –NH–); ^{13}C NMR (Me_2SO-d_6, 250 MHz): δ (ppm) 24.30 ($-CH_2-\underline{C}H_2-CH_2-$), 31.52 ($-CH_2-\underline{C}H_2-$CH–NH–), 51.90 ($CH_2-\underline{C}H-NH-$), 63.41 (C-6), 70.37 (C-3), 71.55 (C-5), 72.37 (C-4), 73.49 (C-2), and 171.73 (C=O).



Scheme 1. Structural formula of (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane (1) and its corresponding 1*R*,2*R* diastereomer **2**.

X-ray crystal structure.—A colorless, needle-shaped single crystal (0.15 × 0.07 × 1.45 mm) was used for the data collection on a Stoe four-circle diffractometer controlled by a DEC Mikro PDP-11 computer. Lattice parameters were obtained from least-squares refinement of 52 reflections with $30 < 2\theta < 60°$. At room temperature one octant of independent reflections was measured in the ω-2θ scan mode up to $(\sin\theta/\lambda)_{max} = 0.528$ Å^{-1} with Ni-filtered Cu$K\alpha$ radiation. The number of independent reflections was 1913, of which 107 were regarded as unobserved [$F < 2\sigma(F)$]. A Lorentz polarisation, but no absorption correction, was applied.

The structure solution with SHELXS-86 [10] revealed all non-H atoms. A conventional full-matrix least-squares refinement of atomic positional and thermal parameters, scale factor, and an isotropic extinction parameter was performed with the XTAL system [11]. The quantity minimized was $\Sigma w(|F_0| - |F_c|)^2$ with $w = 1/\sigma^2(F_0)$ ($\sigma^2(F_0)$ values from counting statistics).

All non-H-atoms were refined with anisotropic thermal parameters and all H-atoms were located in difference Fourier maps and refined with isotropic thermal parameters. The positions of H(05A) and H(05B) are debatable due to the large C–O–H bonding angles of 143 (9) and 133 (6)°.

The final R value was 0.057 and $R_w = 0.054$, based on 1808 reflections and 425 variables, (goodness of fit, $S = 5.389$).

3. Discussion

Final atomic coordinates and equivalent isotropic temperature factors are given in Table 1 *. Fig. 1 shows on ORTEP-plot [12] of the crystal conformation and the numbering scheme of the title compound. Tables 2, 3, and 4 record bond lengths, angles, and selected torsion angles, respectively. The geometrical data of the hydrogen bonds are given in Table 5. The C–C and C–OH bond lengths in the sugar moieties lie in the range usually found in alditols [13]. The N–C-1 and N–C-1A bond lengths lie between a C–N double (1.29 Å) and a C–N single bond (1.49 Å) indicating the partial double bond character of the amide bond. The C–C–C bond angles of the sugar moieties are on average larger than those of the cyclohexane ring: 113.0 (1.6)° and 111.6 (1.3)°, supposedly due to the sterical influence of the OH groups. The C–C bonds in the ring lie between 1.48 and 1.52 Å with an average value of 1.51(1) Å; the C–C bonds in which the substituted carbon atoms C-7 and C-8 are involved are generally longer than the other C–C bonds of the cyclohexane ring. This phenomenon has also been observed in other 1,2-disubstituted cyclohexane derivatives [14–17]. The substituents obviously pull apart the ring atoms to whom they are bonded.

* A complete atom list, including the hydrogen atom and displacement parameters, together with the list of observed and calculated structure-factors for 1 can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2, 1EZ, UK.

Table 1
Atomic parameters and U_{eq} and U-values for 1 [a]

Atom	x	y	z	U_{eq} / U
N-A	0.031(1)	0.5307(3)	0.0926(2)	5.3(2)
C-1	−0.169(1)	0.5703(3)	0.1146(2)	5.0(2)
O-1	−0.3966(9)	0.5457(2)	0.1250(2)	6.6(2)
C-2	−0.094(1)	0.6453(3)	0.1285(3)	5.4(2)
O-2	0.078(1)	0.6709(2)	0.0843(2)	6.3(2)
C-3	0.047(1)	0.6525(3)	0.1866(3)	5.3(2)
O-3	0.172(1)	0.7199(2)	0.1884(2)	6.1(1)
C-4	−0.148(1)	0.6452(3)	0.2371(2)	5.0(2)
O-4	−0.3366(9)	0.7023(2)	0.2383(2)	5.7(1)
C-5	0.009(1)	0.6418(3)	0.2937(3)	5.7(2)
O-5	0.169(1)	0.5800(3)	0.2932(2)	7.1(2)
C-6	−0.172(2)	0.6440(4)	0.3460(3)	6.5(2)
O-6	−0.356(1)	0.5864(3)	0.3496(2)	7.1(2)
N-B	−0.053(1)	0.4098(3)	0.1645(2)	5.4(2)
C-1B	0.003(1)	0.3729(3)	0.2105(3)	5.1(2)
O-1B	0.189(1)	0.3275(2)	0.2117(2)	6.5(2)
C-2B	−0.177(1)	0.3862(3)	0.2620(2)	5.1(2)
O-2B	−0.312(1)	0.4506(3)	0.2542(2)	6.1(2)
C-3B	−0.006(1)	0.3850(3)	0.3165(3)	5.2(2)
O-3B	0.1858(9)	0.4415(2)	0.3160(2)	5.6(1)
C-4B	−0.167(1)	0.3829(3)	0.3717(3)	5.2(2)
O-4B	−0.323(1)	0.4450(3)	0.3815(2)	6.1(2)
C-5B	0.015(1)	0.3725(3)	0.4238(2)	5.3(2)
O-5B	0.179(1)	0.3127(3)	0.4137(2)	6.2(2)
C-6B	−0.141(2)	0.3663(4)	0.4786(3)	6.5(3)
O-6B	−0.328(1)	0.3094(3)	0.4753(2)	8.0(2)
C-7	−0.004(1)	0.4606(4)	0.0697(3)	5.3(2)
C-8	0.088(1)	0.4027(4)	0.1102(3)	5.5(2)
C-9	0.048(2)	0.3308(4)	0.0832(3)	6.9(3)
C-10	0.191(2)	0.3240(5)	0.0262(4)	7.7(3)
C-11	0.097(2)	0.3825(5)	−0.0131(3)	8.0(3)
C-12	0.133(2)	0.4540(4)	0.0115(3)	6.9(3)
H-NA	0.17(2)	0.557(3)	0.084(3)	7(2)
H-O2	0.10(2)	0.720(3)	0.100(3)	8(2)
H-O3	0.30(4)	0.730(7)	0.193(6)	26(7)
H-O4	−0.27(2)	0.748(3)	0.254(3)	9(2)
H-O5	0.28(2)	0.564(6)	0.309(4)	15(5)
H-O6	−0.30(2)	0.532(5)	0.358(3)	14(3)
H-NB	−0.18(1)	0.449(2)	0.166(2)	3(1)
H-O2B	−0.42(2)	0.464(6)	0.269(4)	15(5)
H-O3B	0.09(2)	0.488(4)	0.306(3)	10(3)
H-O4B	−0.42(2)	0.450(4)	0.357(3)	10(3)
H-O5B	0.26(2)	0.287(4)	0.434(3)	11(4)
H-O6B	−0.37(2)	0.307(4)	0.510(3)	9(3)

[a] Numbers in parentheses are esd values.

The C–N–C angle is 125.1(6)° and 124.6(5)° in the A- and B-chain, respectively, differing significantly from the almost ideal value of 120.8(5)° in *N*-cyclohexyl-D-gluconamide [18]. Thus it seems that the widening of the angle is necessary to

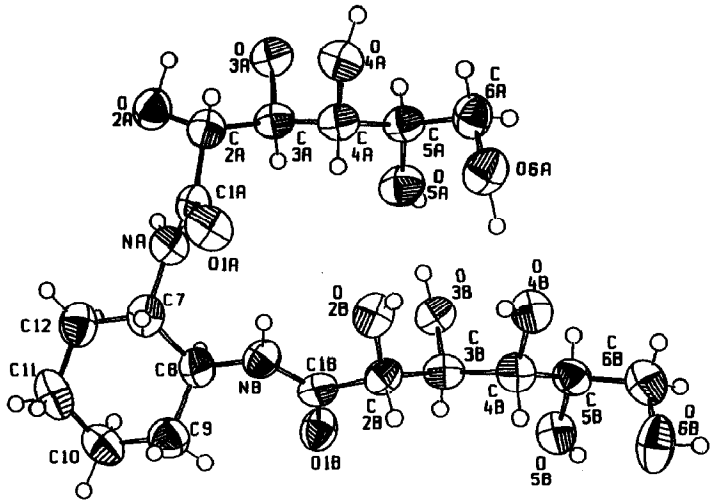


Fig. 1. ORTEP-plot showing the conformation and the numbering scheme of **1**.

separate the large, diequatorial substituents from each other rather than from the ring.

The two gluconamide moieties of **1** are in parallel alignment. The B-chain displays an all-*trans* conformation whereas the A-chain exhibits two gauche interactions along C-1–C-2 and C-2–C-3. A comparison with the crystal structure of other gluconamides (Table 4) shows that all other derivatives except the *N*,*N*-diethyl compound, also prefer for the sugar chain an all-*trans* conformation, thereby tolerating the 1,3-syndiaxial interaction between O-2 and O-4.

Table 2
Bond lengths (Å) in **1** [a]

N-1–C-1A	1.335(8)	N-B–C-1B	1.313(7)
N-A–C-7	1.443(9)	N-B–C-8	1.456(8)
C-1A–C-2A	1.506(9)	C-1B–C-2B	1.514(9)
C-2A–C-3A	1.532(9)	C-2B–C-3B	1.524(9)
C-3A–C-4A	1.525(9)	C-3B–C-4B	1.515(9)
C-4A–C-5A	1.531(9)	C-4B–C-5B	1.521(9)
C-5A–C-6A	1.51(1)	C-5B–C-6B	1.500(9)
C-1A–O-1A	1.228(7)	C-1B–O-1B	1.250(8)
C-2A–O-2A	1.419(8)	C-2B–O-2B	1.398(8)
C-3A–O-3A	1.416(7)	C-3B–O-3B	1.421(7)
C-4A–O-4A	1.422(7)	C-4B–O-4B	1.420(8)
C-5A–O-5A	1.407(8)	C-5B–O-5B	1.406(8)
C-6A–O-6A	1.415(9)	C-6B–O-6B	1.42(1)
C-7–C-8	1.52(1)	C-7–C-12	1.52(1)
C-8–C-9	1.52(1)	C-9–C-10	1.51(1)
C-10–C-11	1.51(1)	C-11–C-12	1.48(1)

[a] The esd's are in parentheses.

Table 3
Valence angles (°) in 1 [a]

C-1A–N-A–C-7	125.1(6)	C-1B–C-2B–C-3B	110.4(5)
N-A–C-1A–O-1A	121.5(6)	O-2B–C-2B–C-3B	112.3(5)
N-A–C-1A–C-2A	115.9(5)	C-2B–C-3B–O-3B	110.0(5)
O-1A–C-1A–C-2A	122.5(6)	C-2B–C-3B–C-4B	115.7(5)
C-1A–C-2A–O-2A	108.0(5)	O-3B–C-3B–C-4B	111.5(5)
C-1A–C-2A–C-3A	112.7(5)	C-3B–C-4B–C-5B	112.7(5)
O-2A–C-2A–C-3A	110.7(5)	C-3B–C-4B–O-4B	113.2(5)
C-2A–C-3A–O-3A	107.5(5)	C-5B–C-4B–O-4B	107.0(5)
C-2A–C-3A–C-4A	113.7(5)	C-4B–C-5B–O-5B	107.6(5)
O-3A–C-3A–C-4A	109.1(5)	C-4B–C-5B–C-6B	113.5(6)
C-3A–C-4A–O-4A	110.5(5)	O-5B–C-5B–C-6B	111.7(5)
C-3A–C-4A–C-5A	111.3(5)	C-5B–C-6B–O-6B	109.9(6)
O-4A–C-4A–C-5A	109.8(5)	N-A–C-7–C-8	113.4(5)
C-4A–C-5A–O-5A	107.8(5)	N-A–C-7–C-12	111.0(6)
C-4A–C-5A–C-6A	114.2(6)	C-8–C-7–C-12	111.7(6)
O-5A–C-5A–C-6A	110.6(5)	N-B–C-8–C-7	109.8(6)
C-5A–C-6A–O-6A	113.4(6)	N-B–C-8–C-9	112.7(6)
C-1B–N-B–C-8	124.6(5)	C-7–C-8–C-9	110.5(6)
N-B–C-1B–O-1B	122.6(6)	C-8–C-9–C-10	112.6(7)
N-B–C-1B–C-2B	116.3(5)	C-9–C-10–C-11	109.6(7)
O-1B–C-1B–C-2B	121.1(5)	C-10–C-11–C-12	113.5(7)
C-1B–C-2B–O-2B	108.3(5)	C-7–C-12–C-11	111.9(7)

[a] The esd's are in parentheses.

The angles between two least-squares planes through C–N–C-1–C-2–O-1 and C-2–C-3–C-4–C-5–C-6 are 108.0(2)° and 43.2(5)° in the A- and B-chain, respectively. These values both differ significantly from the corresponding angle in the crystal structure of *N*-(2-chloroethyl)- (69.8°, ref 19), *N*-isopropyl- (62.7°, ref 20), *N*,*N*-diethyl- (76.3°, ref 20), *N*-benzyl (69.5°, ref 21), and *N*-cyclohexyl-D-gluconamide (61.7°), where the interplane angles all lie within a comparable range.

The cyclohexane ring is in an almost undistorted chair conformation as indicated by the ring puckering parameters according to Cremer and Pople [22]: $Q = 0.548(9)$, $\theta = 1.5(9)°$, and $\Phi = 123(25)°$ (standard deviation in parentheses according to Norrestam [23]). Reference atom 1 is C-7 and the direction in the ring used for the calculation of the parameters is given by C-8 being atom 2. The torsion angle in the ring along C-7–C-8 is −53.2(8)° and is therefore closer to the ideal chair geometry (60°) than the torsion angles in (±)-*trans*-1,2-cyclohexanedicarboxylic acid [16] and (+)-*trans*-1,2-cyclohexanedicarboxylic acid [14] being 47.0(3)° and −50.0(5)°, respectively. The authors discuss the sterical influence of the carboxylic groups that should be separated as far as possible. However, the sugar chains must not be seperated too far, because this would restrict the chances for an extended H-bonding network.

All hydroxyl protons of the title compound are involved in an extended hydrogen-bonding network that spans the crystal (Table 5) with a high percentage of bifurcated H-bonds. The atoms of both amide bonds take part in endless chains

Table 4
Comparison of selected torsion angles (°) of different gluconamides

Sequence	A	B	C	D	E	F [a]	G [b]	H [b]
C–N-C-1–C-2	177.9	−176.6	−179.6 [c]	174.7	179.3	174.0	−171.8(6)	−177.6(6)
N–C-1–C-2–O-2	10.7	−3.4	102.5	5.3	0.6	9.2	39.7(7)	−17.8(7)
N–C-1–C-2–C-3	−111.7	−126.6	−135.9	−114.2	−123.0	−112.2	−82.8(7)	−141.2(5)
C-1–C-2–C-3–C-4	−160.1	−172.5	57.9	−161.4	−170.3	165.2	74.5(6)	−168.1(5)
C-2–C-3–C-4–C-5	177.4	−177.5	−178.7	178.4	180.0	177.8	171.6(5)	172.7(5)
C-3–C-4–C-5–C-6	−179.1	−173.3	172.5	174.8	−175.8	179.9	172.5(5)	−176.9(5)
O-1–C-1–C-2–O-2	−171.7	−177.8	−79.9	−176.3	179.5	−175.5	−143.2(6)	164.3(5)
O-2–C-2–C-3–O-3	−47.7	−57.0	−61.0	−53.6	−56.4	−52.5	43.6(6)	−56.6(7)
O-3–C-3–C-4–O-4	60.9	61.5	−65.2	63.3	60.5	63.2	53.7(6)	61.0(7)
O-4–C-4–C-5–O-5	180.0	−176.3	171.2	−178.6	−175.7	179.8	173.2(5)	−177.5(5)
O-5–C-5–C-6–O-6	−62.7	−66.4	57.2	−67.1	−65.2	−63.9	−59.9(8)	−63.9(7)

A, *N*-(1-octyl)-D-gluconamide (FAKFUS) [d]
B, *N*-isopropyl-D-gluconamide (DAYVUU) [d]
C, *N,N*-diethyl-D-gluconamide (DAYWAB) [d]
D, *N*-benzyl-D-gluconamide (FATXUT) [d]
E, *N*-cyclohexyl-D-gluconamide (CIBWIT) [d]
F, *N*-(2-chloroethyl-D-gluconamide (CEGLCA, CEGLCA01) [d]
G, title compound (A-chain)
H, title compound (B-chain)

[a] The signs of all torsion angles had to be reversed, since the atomic coordinates describe the L enantiomer.
[b] The esd's are in parentheses.
[c] The second C–N–C-1–C-2 angle is −24.8°.
[d] Reference code taken from the Cambridge Structural Database (ref 28).

of the kind –H···O=C–N–H···O=C– with intramolecular side-branches from the amide hydrogen atom to O-2. A homodromic, quadrilateral hydrogen bonding pattern of the kind $O\text{-}3B_{x,y,z} \rightarrow O\text{-}5A_{x,y,z} \rightarrow O\text{-}6A_{1+x,y,z} \rightarrow O\text{-}4B_{1+x,y,z} \rightarrow O\text{-}3B_{x,y,z}$ is formed between any molecule and its counterpart in the next cell in the *x*-direction (Fig. 2). Since O-2B donates an intramolecular hydrogen bond to O-4B, which is involved in the homodromic cycle, the hydrogen-bond network N-B–H-NB → O-2B → $O\text{-}4_{\text{homodromic cycle}}$ emerges. It must be noted that this network has also been observed with exactly the same connectivity in *N*-(1-alkyl)-D-gluconamides [24,25] as discussed by Jeffrey [26]. The cycle and the amide bond hydrogen chains, not however the O-2–O-4 hydrogen bond, are also found in the crystal structures of the corresponding *N*-alkadiyne derivatives [4,27]. O-2 donates an intermolecular hydrogen bond to O-3 in the trideca-5,7-diyne-amphiphile [4]; this hydrogen bond is also observed in the neutron crystal structure of *N*-(2-chloroethyl)-D-gluconamide [29]. In contrast, the tetradeca-6,8-diyne-derivative displays [27] an intermolecular hydrogen bond between O-2 and O-1. Thus, the latter compound is the only gluconamide where the hydrogen bonds formed by the atoms of the amide bond are not in cooperativity with the homodromic cycle, since the trideca-5,7-diyne and the *N*-(2-chloroethyl) derivative have the network N–H-N → O-2 → $O\text{-}3_{\text{homodromic cycle}}$.

Table 5
Geometry of the hydrogen bonds in **1** [a]

D–H···A [b]	D···A	D–H	H···A	D–H···A	O···H···O [c]
N-A–H-NA···O-2A^{I}	2.676(5)	0.87(7)	2.22(7)	112(6)	
N-A–H-NA···O-1A^{II}	2.906(7)	0.88(7)	2.31(8)	125(5)	106(3) [344(8)]
O-2A–H-O2A···O-3A^{I}	2.651(6)	1.01(6)	2.10(6)	112(5)	
O-2A–H-O2A···O-5B^{IV}	2.968(7)	1.01(6)	2.24(7)	128(6)	105(3) [345(8)]
O-3A–H-O3A···O-4A^{II}	2.687(7)	0.7(2)	2.1(2)	142(15)	
O-4A–H-O4A···O-1B^{IV}	2.744(6)	0.99(7)	1.76(7)	172(7)	
O-5A–H-O5A···O-6A^{II}	2.671(8)	0.7(1)	2.1(1)	143(11)	
O-5A–H-O5A···O-3B^{I}	2.682(7)	0.7(1)	2.4(1)	108(10)	109(5) [360(10)]
O-6A–H-O6A···O-4B^{I}	2.788(7)	1.10(9)	1.74(9)	159(9)	
N-B–H-NB···O-2B^{I}	2.569(7)	0.96(5)	2.16(4)	104(3)	
N-B–H-NB···O-1A^{I}	3.209(7)	0.96(5)	2.33(5)	151(4)	105(2) [360(5)]
O-2B–H-O2B···O-3B^{III}	2.852(7)	0.7(1)	2.3(1)	147(12)	
O-2B–H-O2B···O-4B^{I}	2.985(7)	0.7(1)	2.7(1)	108(10)	69(3) [324(9)]
O-3B–H-O3B···O-5A^{I}	2.682(7)	1.02(8)	1.82(7)	140(7)	
O-3B–H-O3B···O-2B^{I}	2.831(7)	1.02(8)	2.40(8)	104(5)	112(4) [357(10)]
O-4B–H-O4B···O-3B^{III}	2.846(7)	0.76(8)	2.14(9)	155(8)	
O-4B–H-O4B···O-2B^{I}	2.985(7)	0.76(8)	2.48(8)	126(8)	76(2) [357(10)]
O-5B–H-O5B···O-6B^{II}	2.804(7)	0.77(8)	2.3(1)	125(8)	
O-6B–H-O6B···O-2A^{V}	2.855(7)	0.83(7)	2.08(7)	157(8)	

[a] In Å and degree; the esd's are in parentheses.
[b] Codes for the symmetry operations of A: I: x, y, z; II: $1+x, y, z$; III: $-1+x, y, z$; IV: $-x, 1/2+y, 1/2-z$; V: $-1/2-x, 1-y, 1/2+z$.
[c] Sum of angles in square brackets.

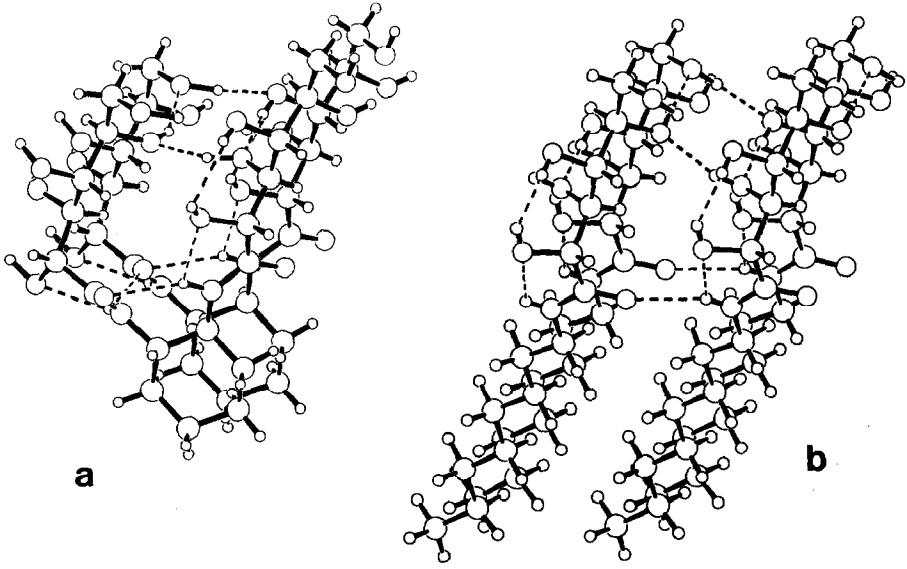


Fig. 2. Identical packing of the gluconamide moieties and identical hydrogen-bond networks in the crystal structures of **1** (a) and *N*-(1-octyl)-D-gluconamide (b).

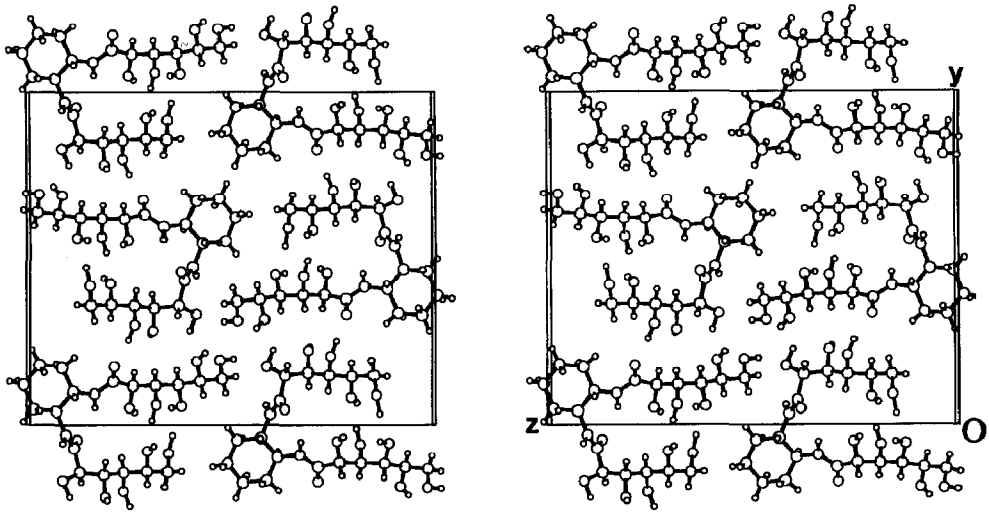


Fig. 3. Crystal packing of **1**, projected along the $-x$ direction.

However, it is common to all crystal structures of *N*-alkyl- and *N*-alkadiyne-gluconamides that there are four separate molecules involved in the cycle, since these compounds only have one gluconamide moiety in their molecular structure. The gluconamides moieties of two molecules of **1**, therefore, mimic the packing arrangement of four separate long-chain gluconamide molecules. The general importance of such a homodromic cycle for other open-chain carbohydrate derivatives has been discussed recently [3].

Naturally occurring membrane lipids [30] display two (or in their lysoform: one) hydrophobic alkane chain(s) attached to the hydrophilic head group; one alkane tail and one head group are found in amphiphilic aldonamides, which have been studied intensively [1,2,4,24–27,31,32]. In contrast, the title compound exhibits one peculiarity in its molecular structure: it has two hydrophilic sugar chains attached to neighboring atoms of one bis-chiral, comparatively small, hydrophobic cyclohexane ring. The aliphatic ring, therefore, does not serve as a hydrophobic spacer as in bola-amphiphiles [33] and the molecule keeps its anisotropical hydrophilicity.

Fig. 3 depicts the packing of the molecules of **1**. The gluconamide moieties are approximately parallel to the *c*-axis and their lipophilic methylene groups point towards the cyclohexane ring of a neighbor molecule. It has already been noted that the gluconamide moieties of two molecules of **1** show the same packing arrangement of four separate long-chain gluconamide molecules. This is correct as far as it concerns the formation of the homodromic hydrogen-bond cycle. It does not, however, hold for the whole crystal, since the crystal packing of **1** differs from the ones of the amphiphilic gluconamides.

The distribution of hydrophobic and hydrophilic ranges within the crystal structure of **1** is exceptional: the hydrophobic ranges form parallel 'tubes' in the crystal structure of the title compound running along the *c*-axis. These tubes are

formed mainly by the cyclohexane rings and are totally surrounded by the lipophobic sugar chains, which point with their lipophilic CH_2-groups towards them. Thus these 'oily tubes' are completely separated from each other. To the best of our knowledge, such 'oily tubes' have never been observed before. The hydrophobic and hydrophilic ranges usually are distributed in alternating parallel layers through the crystal in all crystal structures of glycolipids published so far. The occurrence of these alternating layers is independent of the orientation of the amphiphiles within the crystal. They are found in the crystal structures of long-chain ribon [31,32] and glucon-amides [4,24,25,27], which crystallize in the unusual head-to-tail arrangement and they occur in the crystals of membrane lipids [30] and other aldonamides [1,2] which exist in the tail-to-tail (bilayer) orientation.

All particularities of the title compound may be explained by an interplay of three effects: (*1*) the tendency of gluconamide chains to adopt a linear, all-*trans* conformation in spite of the resulting O//O interaction; (*2*) the restraints imposed by the topology that prevent the A-chain from adopting the fully extended conformation; because (*3*) a parallel alignment of the sugar moieties results in a close packing with an energetically favorable quadrilateral homodromic hydrogen-bond cycle. Such a pattern is accomplished best when the hydrophobic parts of the molecule are separated from the hydrophilic parts; because there are two hydrophilic moieties in the molecule, this separation causes the unusual 'oily-tubes' in the crystal.

As indicated in the Experimental, the title compound crystallizes from a mixture of the four diasteromeric cyclohexane-1,2-digluconamides. It is readily understood that the *cis*-configured diastereomers having one gluconamide group in axial and the other in equatorial disposition are much more water-soluble and do not crystallize well, because no intramolecular ordering of the gluconamide groups is possible. Less obvious is the easy separation of the diamide formed from D-gluconic acid and 1*S*,2*S*-cyclohexylamine, which crystallizes readily even from mixtures of four diastereomers, and the corresponding 1*R*,2*R*-diamine, where even the pure compound could not be crystallized. A possible explanation is given by the stereochemical structures shown in Scheme 1. There is a strong 1,3-hydrogen bond between the NH- and the carbonyl group in the crystallizing 1*S*,2*S*-diastereomer **1** (Fig. 2a). Under the conditions that the homodromic cycle is kept, that the gluconamide side-chains are kept linear, no such stabilizing hydrogen bond is possible. It is very probable, that both gluconamide chains become bent in diastereomer **2**, thus impeding its crystallization.

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References

[1] Ch. André, P. Luger, S. Svenson, and J.-H. Fuhrhop, *Carbohydr. Res.*, 230 (1992) 31–40.
[2] Ch. André, P. Luger, S. Svenson, and J.-H. Fuhrhop, *Carbohydr. Res.*, 240 (1993) 47–56.
[3] Ch. André, P. Luger, J.-H. Fuhrhop, and B. Rosengarten, *Acta Crystallogr., Sect. B*, 49 (1993) 375–382.
[4] J.-H. Fuhrhop, P. Blumtritt, C. Lehmann, and P. Luger, *J. Am. Chem. Soc.*, 113 (1991) 7437–7439.
[5] J.-H. Fuhrhop and C. Boettcher, *J. Am. Chem. Soc.*, 112 (1990) 1768–1776.
[6] J.-H. Fuhrhop, P. Schnieder, E. Boekema, and W. Helfrich, *J. Am. Chem. Soc.*, 110 (1988) 2861–2867.
[7] J.-H. Fuhrhop, P. Schnieder, J. Rosenberg, and E. Boekema, *J. Am. Chem. Soc.*, 109 (1987) 3387–3390.
[8] J.-H. Fuhrhop, S. Svenson, C. Boettcher, E. Rössler, and H.-M. Vieth, *J. Am. Chem. Soc.*, 112 (1990) 4307–4312.
[9] F.M. Jaeger and L. Bijikerk, *Z. Anorg. Chem.*, 233 (1937) 97–139.
[10] G.M. Sheldrick, in G.M. Sheldrick, C. Krüger, and R. Goddard (Eds.), *Crystallographic Computing 3*, Oxford University Press, Oxford, 1985, pp 175–189.
[11] S.R. Hall and J.M. Stewart (Eds.), XTAL 2.2. User Manual, University of Western Australia, Australia and Maryland, 1987, USA.
[12] C.K. Johnson, ORTEP, Report ORNL-3794, Oak Ridge Nat. Laboratory, Tennessee, 1965.
[13] G.A. Jeffrey and H.S. Kim, *Carbohydr. Res.*, 14 (1970) 207–216.
[14] E. Benedetti, P. Corradini, and C. Pedone, *J. Am. Chem. Soc.*, 91 (1969) 4075–4077.
[15] E. Benedetti, C. Pedone, and G. Allegra, *J. Phys. Chem., 74* (1970) 512–516.
[16] E. Benedetti, P. Corradini, C. Pedone, and B. Post, *J. Am. Chem. Soc.*, 91 (1969) 4072–4074.
[17] A. Pawel, K.-H. Woller, M. Strümpel, and P. Luger, *Cryst. Struct. Commun.*, 11 (1982) 647–652.
[18] N. Darbon, Y. Oddon, J.M. Lacombe, E. Decoster, A.A. Pavia, and J.P. Reboul, *Acta Crystallogr., Sect. C*, 40 (1984) 1105–1107.
[19] L.O.G. Satzke and M.F. Mackay, *Acta Crystallogr., Sect. B*, 31 (1975) 1128–1132.
[20] N. Darbon-Meyssonnier, Y. Oddon, E. Decoster, A.A. Pavia, G. Pepe, and J.P. Reboul, *Acta Crystallogr., Sect. C*, 41 (1985) 1324–1327.
[21] Y. Oddon, N. Darbon-Meyssonnier, J.P. Reboul, G. Pepe, E. Decoster, and A.A. Pavia, *Acta. Crystallogr., Sect. C*, 42 (1986) 1764–1766.
[22] D. Cremer and J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.
[23] R. Norrestam, *Acta Crystallogr., Sect. A*, 37 (1981) 764–765.
[24] A. Müller-Fahrnow, R. Hilgenfeld, H. Hesse, W. Saenger, and B. Pfannemüller, *Carbohydr. Res.*, 176 (1988) 165–174.
[25] V. Zabel, A. Müller-Fahrnow, R. Hilgenfeld, W. Saenger, B. Pfannemüller, V. Enkelmann, and W. Welte, *Chem. Phys. Lipids*, 39 (1986) 313–327.
[26] G.A. Jeffrey, *Molec. Cryst. Liq. Cryst.*, 185 (1990) 209–213.
[27] Ch. André, P. Luger, and J.-H. Fuhrhop, *Chem. Phys. Lipids*, (1994) accepted.
[28] F.H. Allen, S. Bellard, M.D. Brice, B.A. Cartwright, A. Doubleday, H. Higgs, T. Hummelink, B.G. Hummelink-Peters, O. Kennard, W.D. Motherwell, J.R. Rodgers, and D.G. Watson, *Acta Crystallogr., Sect. B*, 35 (1979) 2331–2339.
[29] A. Sindt, and M.F. Mackay, *Acta Crystallogr., Sect. B*, 33 (1977), 2659–2662.
[30] I. Pascher, M. Lundmark, P.-G. Nyholm, and S. Sundell, *Biochim. Biophys. Acta*, 1113 (1992) 339–373.
[31] C. André, P. Luger, R. Bach, and J.-H. Fuhrhop, *Carbohydr. Res.*, (1994) submitted.
[32] B. Tinant, J.P. Declercq, and M. Van Meersche, *Acta Crystallogr. Sect. C*, 42 (1986) 579–581.
[33] A. Müller-Fahrnow, W. Saenger, D. Fritsch, P. Schnieder, and J.-H. Fuhrhop, *Carbohydr. Res.*, 242 (1993) 11–20.