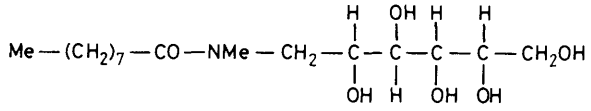
Molecular and Crystal Structure of a Nonionic Detergent: Nonanoyl-*N*-methylglucamide

Anke Müller-Fahrnow, Volker Zabel, Manfred Steifa, and Rolf Hilgenfeld*†

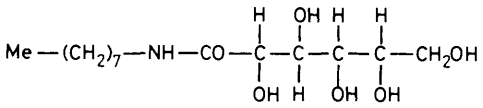
Abteilung Saenger, Institut für Kristallographie, Freie Universität Berlin, Takustr. 6, D-1000 Berlin 33, F.R.G.

In crystals of the nonionic detergent nonanoyl-*N*-methylglucamide, molecules are packed parallel in sheets with adjacent sheets being arranged in a head-to-tail fashion; an unusual conformation of the polar head moiety explains why this compound forms micelles whereas the related alkylglyconamides do not.

Crystallization of membrane proteins depends critically on the detergent used. Small nonionic detergents have been found useful for growing three-dimensional crystals of such proteins.[1,2] In our attempts to improve the size and diffraction of crystals[3] of the mitochondrial pore-protein from *Neurospora crassa*,[4] we use, among others, nonanoyl-*N*-methylglucamide (**1**) (MEGA-9)[5] as detergent. At concentrations above the critical micelle concentration (c.m.c.), this amphiphile readily forms micelles at room temperature whereas the related compound n-octyl-D-gluconamide (**2**) does so only when heated to 90 °C.[6] The crystal structure analysis of the latter molecule, which differs from MEGA-9 mainly by a reversed amide group and by lacking the *N*-methyl group, revealed an all-*trans* conformation of both the alkyl chain and the glucose moiety.[7] In order to shed light on the structural foundations of the different properties of MEGA-9, we have now determined its molecular and crystal structure by *X*-ray



(**1**)



(**2**)

† *Present address:* Angewandte Physik, Hoechst Aktiengesellschaft, D-6230 Frankfurt 80, FRG.

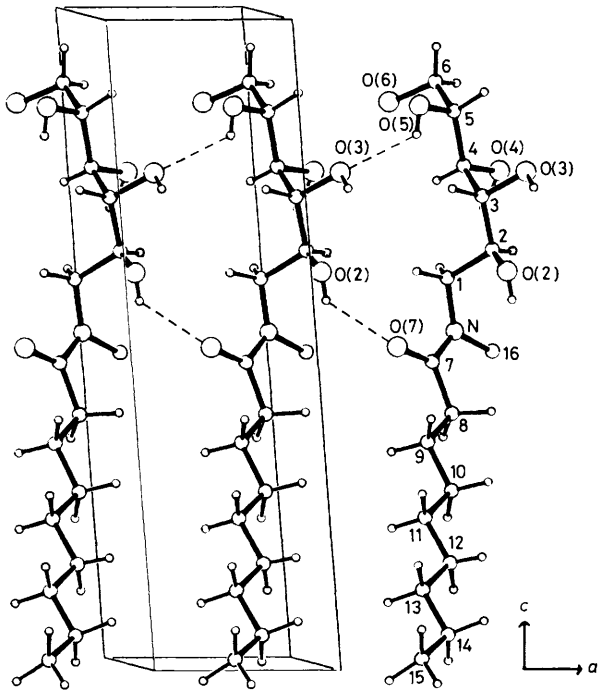


Figure 1. The crystal structure of MEGA-9 (**1**) with the atom numbering scheme, showing the parallel packing of molecules.

Table 1. Hydrogen bond geometry in crystals of nonanoyl-*N*-methylglucamide (MEGA-9). Distances in Å, angles in °; standard deviations in parentheses; D, donor atom; A, acceptor atom.

D–H···A	Translation	D···A distance	H···A distance	D–H–A angle
O(2)–H(O2)···O(7)	$1+x,y,z$	2.85(1)	2.25(2)	132.2(8)
O(3)–H(O3)···O(4)	$x,1+y,z$	2.75(2)	1.74(3)	154.4(9)
O(4)–H(O4)···O(2)	$x,1-y,z$	3.38(2)	2.40(3)	148.6(9)
O(5)–H(O5)···O(3)	$1-x,y,z$	2.76(2)	2.44(3)	122.5(9)
O(6)–H(O6)···O(5)	$x,1-y,z$	2.76(1)	1.81(2)	166.4(8)

diffraction.‡ Owing to inherent difficulties in obtaining single crystals of nonionic detergents, the only other *X*-ray structure reported of such a compound is, to the best of our knowledge, that of 1-decyl-α-D-glucopyranoside.[8]

The molecular structure of MEGA-9 is shown in Figure 1 together with the atom numbering scheme. As in n-octyl-D-gluconamide (**2**),[7] the alkyl chain is in an all-*trans* conformation which includes the amide bond. However, there is an important difference in the polar head moiety, where a kink is introduced in MEGA-9 by the synclinal torsion angle C(1)–C(2)–C(3)–C(4) [−57(1)°].

The molecules of MEGA-9 are packed parallel in sheets in the *ac*-plane, resulting in a head-to-tail packing of molecules (along *c* axis) in adjacent sheets. The same unusual feature has been observed with octyl-D-gluconamide (**2**).[7] However, the hydrogen bonding is quite different in the two structures owing to the methylation of the amide group and the different conformation of the polar head moiety in MEGA-9. The latter is involved in five intermolecular hydrogen bonds three of which are rather weak (Table 1). In contrast, hydrogen bonding between the polar head groups in adjacent octyl-D-gluconamide molecules (**2**) is much stronger[7] favouring the aggregation to aqueous gels observed with this compound.[6]

From this observation it appears that not too strong hydrogen bonding of the polar head moieties is a pre-requisite for micelle formation.

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‡ *Crystal data:* crystals of MEGA-9 (Oxyl, Bobingen, FRG) grown from acetone–methanol (1:1), $C_{16}H_{33}NO_6$, M = 335, triclinic, space group $P\bar{1}$, a = 4.985(2), b = 5.603(2), c = 17.449(7) Å, α = 85.4(3), β = 86.0(3), γ = 76.2(3)°, U = 468.5 Å^3, Z = 1, D_c = 1.19 g cm^{-1}, μ(Cu-K_α) = 0.67 cm^{-1}.

1445 unique intensity data ($2\theta_{max}$ = 120°) were recorded on a redesigned[9] Stoe four-circle diffractometer using Ni-filtered Cu-K_α-radiation and a $2\theta/\omega$ scan technique. The structure was solved by a combination of direct methods and difference Fourier techniques, and refined by full-matrix least-squares (all non-hydrogen atoms were anisotropic). All hydrogen atoms could be located from difference syntheses and isotropically refined. The final conventional *R*-factor was 0.055.

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1, 1986.

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