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3-(1-Pyridinio)propanesulfonate and 3-(benzyldimethylammonio)propanesulfonate monohydrate

Katarzyna D. Koclega,[a,b] Maksymilian Chruszcz,[a] Anna Gawlicka-Chruszcz,[c] Marcin Cymborowski[a] and Wladek Minor[a]*

[a]University of Virginia, Department of Molecular Physiology and Biological Physics, 1340 Jefferson Park Avenue, Charlottesville, VA 22908, USA, [b]Technical University of Lodz, Faculty of Biotechnology and Food Sciences, Institute of Technical Biochemistry, Stefanowskiego 4/10, 93-923 Lodz, Poland, and [c]HKL Research Inc., 310 Old Ivy Way, Charlottesville, VA 22903, USA
Correspondence e-mail: wladek@iwonka.med.virginia.edu

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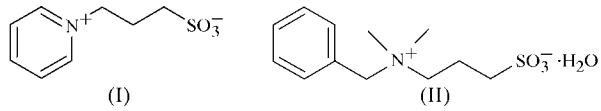
3-(1-Pyridinio)propanesulfonate, $C_8H_{11}NO_3S$, and 3-(benzyldimethylammonio)propanesulfonate monohydrate, $C_{12}H_{19}NO_3S\cdot H_2O$, used as additives during protein refolding and crystallization, both crystallize in the monoclinic system in the $P2_1/c$ space group, with one molecule (or one set of molecules) per asymmetric unit. The solvent water molecule present in the second crystal structure results in the formation of a dimer through hydrogen bonds. The conformation of the propanesulfonate moiety is similar in both structures.

Comment

Non-detergent sulfobetaines (NDSBs), to which the title compounds belong, are zwitterionic molecules. NDSB-201 or 3-(1-pyridinio)propanesulfonate, (I), and NDSB-256 or 3-(benzyldimethylammonio)propanesulfonate, of which the monohydrate structure, (II), is reported here, are members of a larger family of compounds that was mainly developed to facilitate protein solubilization, as well as for improvement of protein stability (Vuillard *et al.*, 1995). It was discovered that compounds from this group are very useful during protein refolding (Goldberg *et al.* 1995; Vuillard *et al.*, 1998; Expert-Bezançon *et al.* 2003; Swope Willis *et al.*, 2006) and purification (Vuillard *et al.*, 1995). NDSBs prevent protein aggregation and are used as additives to protein solutions in isoelectric focusing. Recently, Collins *et al.* (2006) demonstrated the usefulness of NDSB-201 in differential scanning calorimetry. The properties of NDSBs with respect to protein solutions have also been noticed by protein crystallographers (Vuillard *et al.*, 1994, 1996). During crystallization, a protein has to be stable in highly concentrated solution for a prolonged period of time, and the presence of chemicals preventing the formation of an amorphous precipitate could be crucial for the success of a crystallization experiment.



NDSB-201 and NDSB-256 crystallize in the $P2_1/c$ space group, with one molecule or one set of molecules per asymmetric unit (Figs. 1 and 2). Both compounds have aromatic rings that influence packing in the crystal structures. Weak interactions also play an important role in crystal packing, especially in the case of the structure of (I); the contacts between H and O atoms that are at least 0.3 Å shorter than the sum of the van der Waals radii are listed in Table 1. In the case of (II), hydrogen bonds mediated by water molecules are important for the packing (Table 2). The NDSB-256 molecules in the structure of (II) form dimers through hydrogen bonds involving water molecules (Fig. 3). The hydrogen-bonding pattern corresponds to an $R_4^4(12)$ motif, as described by Bernstein *et al.* (1995). Atom O1, which does not form hydogen bonds with water molecules, is involved in short contacts with benzyl atom H6*B* and atom H9 from the aromatic ring. The distances H6*B*$\cdots$O1($-x, \frac{1}{2}+y, \frac{1}{2}-z$) and H9$\cdots$O1($1+x, y, z$) are 2.35 and 2.48 Å, respectively, while the distances C6$\cdots$O1($-x, \frac{1}{2}+y, \frac{1}{2}-z$) and C9$\cdots$O1($1+x, y, z$) are 3.262 (2) and 3.167 (2) Å, respectively. The angles C6—H6*B*$\cdots$O1($-x, \frac{1}{2}+y, \frac{1}{2}-z$) and C9—H9$\cdots$O1($1+x, y, z$) are 156 and 131°, respectively.

NDSBs with a three-carbon bridge between the S and N atoms (sulfopropyl non-detergent betaines) have been found to be superior for work with proteins (Vuillard *et al.*, 1995). It was proposed that a sulfopropyl NDSB may adopt a cyclic conformation, with a six-atom ring and an ionic link between N^+ and SO_3^- in solution. The resulting hydrocarbon cluster might take part in hydrophobic protein–protein interactions. Our results show that for NDSB-201 and NDSB-256, such a conformation of the sulfopropyl moiety is not observed in the crystal structures, but of course it cannot be concluded that at least some of the molecules do not adopt the cyclic conformation in solution. In the crystal structures reported by us, the torsion angles S1—C1—C2—C3 and C1—C2—C3—N1 are −178.3 (1) and 171.3 (1)°, respectively, for NDSB-201, while for NDSB-256 they are 178.8 (1) and 169.2 (1)°.

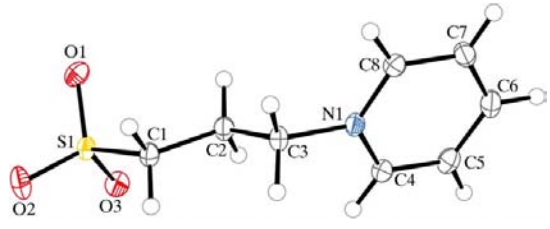


Figure 1
The molecular structure of compound (I). Displacement ellipsoids are drawn at the 50% probability level.

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In the Cambridge Structural Database (CSD, Version 5.27, update of January 2006; Allen, 2002), there are 12 structures with the sulfopropyl moiety attached to an N atom, forming ternary or quaternary amines. In the structures reported in the CSD, there is also no example in which the cyclic conformation of the $^{+}N-CH_2-CH_2-CH_2-SO_3^{-}$ fragment is observed. It is also quite surprising that, although NDSB molecules are quite often used during protein refolding, there are only a few structures in the Protein Data Bank (PDB; Berman *et al.*, 2000) for which the use of non-detergent sulfobetaines is reported in REMARK 280 (REMARK 280 contains information about crystals, solvent content and crystallization conditions). A search of the PDB in September 2006 revealed that for only six structures were NDSBs used for crystallization. NDSB-195 was used in two cases (PDB codes 2AUW and 2G4B), NDSB-201 was used in three cases (PDB codes 1NAX, 1UA2 and 2FGC), and the usage of NDSB-256 was reported in only one case (PDB code 2F96). It was noted that the application of NDSB-201 (Lolli *et al.*, 2004) helped to prevent excessive nucleation and promoted crystal growth. Most probably the influence of compounds from the NDSB family in protein solution is similar to that observed in the case of arginine (Baynes & Trout, 2004) and NDSBs may be treated as 'neutral crowder' additives (Baynes & Trout, 2004).

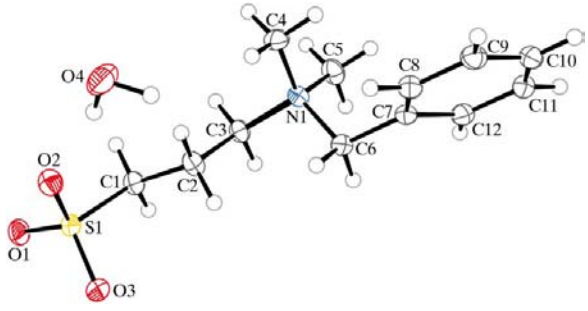

Figure 2
The molecular structure of compound (II). Displacement ellipsoids are drawn at the 50% probability level.

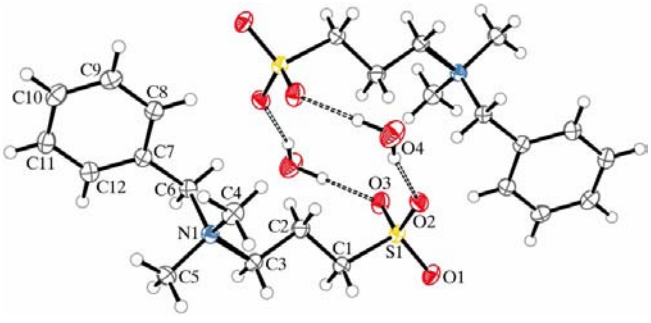

Figure 3
Hydrogen bonds (dashed lines) in the crystal structure of (II). Labelled and unlabelled molecules are related by the symmetry code ($-x$, $1-y$, $-z$).

Experimental

Both NDSB-201 and NDSB-256 were purchased from Anatrace. Crystallization was performed at room temperature and the crystals used for X-ray diffraction experiments were obtained by slow evaporation; NDSB-201 was crystallized from a 1:1 mixture of methanol and 70% ethanol, while NDSB-256 was crystallized from 10% propionic acid.

Compound (I)

Crystal data

$C_8H_{11}NO_3S$
M_r = 201.24
Monoclinic, $P2_1/c$
a = 5.699 (1) Å
b = 7.428 (1) Å
c = 20.053 (2) Å
β = 93.384 (7)°
V = 847.4 (2) Å^3
Z = 4
D_x = 1.577 Mg m^{-3}
Cu $K\alpha$ radiation
μ = 3.20 mm^{-1}
T = 103 (2) K
Prism, colourless
0.5 × 0.4 × 0.3 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans with χ offset
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.27, T_{max} = 0.38
78761 measured reflections
1641 independent reflections
1636 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 72.2°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.082
S = 1.05
1641 reflections
163 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0455P)^2 + 0.5835P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.45 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0253 (12)

Table 1
Hydrogen-bond geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
C4—H4···O1^{i}	0.94 (2)	2.26 (2)	3.175 (2)	165.6 (16)
C3—H3A···O3^{i}	0.996 (19)	2.397 (19)	3.347 (2)	159.2 (14)
C7—H7···O2^{ii}	0.93 (2)	2.41 (2)	3.155 (2)	136.5 (16)
C5—H5···O1^{iii}	0.96 (2)	2.41 (2)	3.206 (2)	139.8 (16)

Symmetry codes: (i) $-x, y+\frac{1}{2}, -z+\frac{1}{2}$; (ii) $x+1, -y+\frac{3}{2}, z+\frac{1}{2}$; (iii) $x, -y+\frac{3}{2}, z+\frac{1}{2}$.

Compound (II)

Crystal data

$C_{12}H_{19}NO_3S\cdot H_2O$
M_r = 275.37
Monoclinic, $P2_1/c$
a = 12.628 (1) Å
b = 11.209 (1) Å
c = 9.982 (1) Å
β = 107.260 (4)°
V = 1349.3 (2) Å^3
Z = 4
D_x = 1.356 Mg m^{-3}
Cu $K\alpha$ radiation
μ = 2.21 mm^{-1}
T = 103 (2) K
Block, colourless
0.45 × 0.15 × 0.11 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans with χ offset
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.710, T_{max} = 0.780
36458 measured reflections
2600 independent reflections
2449 reflections with $I > 2\sigma(I)$
R_{int} = 0.057
θ_{max} = 72.1°

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0464P)^2 + 0.8011P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.039$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.102$	$\Delta\rho_{max} = 0.36$ e Å^{-3}
$S = 1.08$	$\Delta\rho_{min} = -0.47$ e Å^{-3}
2600 reflections	Extinction correction: *SHELXL97* (Sheldrick, 1997)
172 parameters	Extinction coefficient: 0.0169 (8)
H atoms treated by a mixture of independent and constrained refinement	

Table 2
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
O4—H1···O3^{i}	0.83 (3)	2.00 (3)	2.812 (2)	167 (3)
O4—H2···O2	0.87 (3)	2.05 (3)	2.921 (2)	178 (3)

Symmetry code: (i) $-x, -y+1, -z$.

All H atoms in NDSB-201, (I), were located in a difference map and their positional and isotropic displacement parameters were refined. In the case of NDSB-256 monohydrate, (II), water H atoms were located in a difference map and their positional and isotropic displacement parameters were refined. All other H atoms were included in the refinement in calculated positions and refined using a riding-model approximation, with C—H = 0.93 (aromatic), 0.96 (CH_3) or 0.97 Å (CH_2), and with U_{iso}(H) = 1.2U_{eq}(C) for aromatic CH and CH_2, or 1.5U_{eq}(C) for CH_3 hydrogens.

For both compounds, data collection: *HKL-2000* (Otwinowski & Minor, 1997); cell refinement: *HKL-2000*; data reduction: *HKL-2000*; program(s) used to solve structure: *HKL-3000SM* (Minor *et al.*, 2006) and *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *HKL-3000SM* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *HKL-3000SM*, *ORTEPIII* (Burnett & Johnson, 1996) and *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *HKL-3000SM*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3054). Services for accessing these data are described at the back of the journal.

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