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N-(3-Hydroxymethyl-5-nitrophenyl)-acetamide dimethyl sulfoxide solvate

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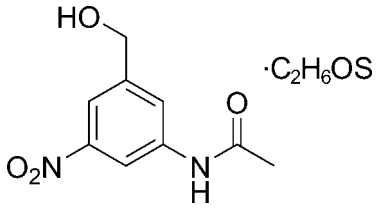
Key indicators: single-crystal X-ray study; T = 89 K; mean σ(C–C) = 0.003 Å; R factor = 0.038; wR factor = 0.103; data-to-parameter ratio = 14.0.

The title compound, $C_9H_{10}N_2O_4\cdot C_2H_6OS$, was prepared by the selective hydrolysis of 3-acetamido-5-nitrobenzyl acetate with sodium hydroxide in ethanol. The crystal structure contains a dimethyl sulfoxide solvent molecule. The title compound is an intermediate in the synthesis of DNA minor-groove-binding polybenzamide agents. N—H···O and O—H···O hydrogen bonds are present in the crystal structure.

Related literature

For related literature on the biological activity of polybenzamide DNA binding agents, see: Lelkes & Pollard (1987); Lown *et al.*(1986); Petering *et al.* (2000); Storl *et al.* (1993). For related literature on natural and synthetic minor-groove-binding agents, see: Arcamone *et al.* (1964); Atwell *et al.* (1995); Baraldi *et al.* (1999, 2004, 2007); Turner & Denny (2000); Turner *et al.* (1999); Wemmer (2000); Xie *et al.* (1996); Yan *et al.* (1997).



Experimental

Crystal data

$C_9H_{10}N_2O_4\cdot C_2H_6OS$
M_r = 288.32
Triclinic, $P\overline{1}$
a = 7.2124 (4) Å
b = 10.1722 (6) Å
c = 10.4117 (6) Å
α = 65.904 (1)°
β = 76.889 (1)°
γ = 74.014 (1)°
V = 664.62 (7) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.26 mm^{-1}
T = 89 (2) K
0.32 × 0.20 × 0.10 mm

Data collection

Siemens SMART CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1997)
T_{min} = 0.672, T_{max} = 0.981
6112 measured reflections
2506 independent reflections
2078 reflections with $I > 2\sigma(I)$
R_{int} = 0.026

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.103
S = 1.02
2506 reflections
179 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.50 e Å^{-3}
$\Delta\rho_{min}$ = −0.38 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O5^{i}	0.86	1.98	2.835 (2)	171
O4—HO4···O1^{ii}	0.83 (3)	1.86 (3)	2.6941 (19)	177 (3)

Symmetry codes: (i) $x, y, z-1$; (ii) $x, y-1, z$.

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPIII* (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXTL* (Siemens, 1995).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: PK2041).

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supplementary materials

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N-(3-Hydroxymethyl-5-nitrophenyl)acetamide dimethyl sulfoxide solvate

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Comment

Oligopeptides are a growing area of interest due to their strong biological activities (Lown *et al.*, 1986, Lelkes & Pollard, 1987, Xie *et al.*, 1996, Turner & Denny, 2000, Petering *et al.*, 2000). Some natural oligopeptides are powerful DNA minor groove-binding agents but their cytotoxity precludes their use as medicines (Arcamone *et al.*, 1964, Baraldi *et al.*, 2004, Wemmer, 2000, Storl *et al.*, 1993). To increase the DNA binding affinity and sequence specificity and to minimize the undesired physiological activities, many synthetic analogues have been prepared (Baraldi *et al.*, 2007). The title compound is a key intermediate required in the synthesis of a novel polybenzamide DNA minor groove-binding agent. For background information on polybenzamide DNA binding agents see (Atwell *et al.*, 1995, Turner *et al.*, 1999, Yan *et al.*, 1997)

Experimental

To a solution of 3-acetamido-5-nitrobenzyl acetate (990 mg, 3.93 mmol) in ethanol (20 ml), was added a solution of sodium hydroxide (315 mg, 7.85 mmol) in water (5 ml). The resulting solution was stirred at room temperature for 3 h before water (15 ml) was added to quench the reaction. The ethanol was removed *in vacuo*, and the resulting aqueous solution extracted with ethyl acetate (3 *x* 20 ml). The organic extracts were combined, dried (Na_2SO_4), and the solvent removed *in vacuo*, to give the crude product, which was purified by flash chromatography (9:1 dichloromethane-methanol), to afford the title compound (810 mg, 98%) as white solid which was recrystallized from DMSO for single-crystal analysis. Mp 450–451 K. ν_{max} (NaCl)/cm^{-1} 3298, 1681, 1529, 1348. δ_H (400 MHz, $(CD_3)_2SO$) 2.09 (3*H*, s, NHCOC*H*$_3$), 4.58 (2*H*, s, C*H*$_2$OH), 5.55 (OH), 7.83 (1*H*, s, Ar—H), 7.85 (1*H*, s, Ar—H), 8.49 (1*H*, br s, Ar—H) and 10.43 (NH). δ_C (100 MHz, $(CD_3)_2SO$) 24.1 (CH_3, NHCO*C*H$_3$), 61.9 (CH_2, *C*H$_2$OH), 111.4 (CH, Ar—C), 115.0 (CH, Ar—C), 122.3 (CH, Ar—C), 140.3 (quat. Ar—C), 145.5 (quat. Ar—C), 147.9 (quat. Ar—C) and 169.1 (C=O). m/*z* (EI$^+$) 210 (M^+, 27%), 168 (M^+—C_2H_2O, 100), 43 ($COCH_3$, 93). Found M^+ 210.06318, $C_9H_{10}N_2O_4$ requires 210.06406.

Refinement

Hydrogen atoms were placed in calculated positions and refined using the riding model [C—H 0.93–0.97, N—H 0.86 Å), with U_{iso}(H) = 1.2 or 1.5 times U_{eq}(C). Atom HO4 was located from a difference map, and refined individually with an isotropic temperature factor.

Figures

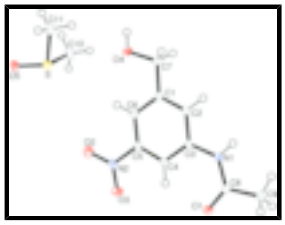

Fig. 1. The molecular structure showing 50% probability displacement ellipsoids for non-hydrogen atoms and hydrogen atoms as arbitary spheres (Burnett & Johnson, 1996).

N-(3-Hydroxymethyl-5-nitrophenyl)acetamide dimethyl sulfoxide solvate

Crystal data

$C_9H_{10}N_2O_4 \cdot C_2H_6OS$	$Z = 2$
$M_r = 288.32$	$F_{000} = 304$
Triclinic, $P\overline{1}$	$D_x = 1.441$ Mg m^{-3}
Hall symbol: -P 1	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
$a = 7.2124$ (4) Å	Cell parameters from 3933 reflections
$b = 10.1722$ (6) Å	$\theta = 2.2$–$25.7°$
$c = 10.4117$ (6) Å	$\mu = 0.26$ mm^{-1}
$\alpha = 65.904$ (1)°	$T = 89$ (2) K
$\beta = 76.889$ (1)°	Needle, colourless
$\gamma = 74.014$ (1)°	0.32 × 0.20 × 0.10 mm
$V = 664.62$ (7) Å^3	

Data collection

Siemens SMART CCD diffractometer	2506 independent reflections
Radiation source: fine-focus sealed tube	2078 reflections with $I > 2\sigma(I)$
Monochromator: graphite	$R_{int} = 0.026$
$T = 89(2)$ K	$\theta_{max} = 25.7°$
Area detector ω scans	$\theta_{min} = 2.2°$
Absorption correction: multi-scan (SADABS; Sheldrick, 1997)	$h = -8 \rightarrow 8$
$T_{min} = 0.672$, $T_{max} = 0.981$	$k = -12 \rightarrow 12$
6112 measured reflections	$l = -12 \rightarrow 12$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.038$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.103$	$w = 1/[\sigma^2(F_o^2) + (0.0528P)^2 + 0.4021P]$

	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.02$	$(\Delta/\sigma)_{max} < 0.001$
2506 reflections	$\Delta\rho_{max} = 0.50$ e Å^{-3}
179 parameters	$\Delta\rho_{min} = -0.38$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

Experimental. After primary data collection, a portion of the first block of data was re-measured to check for crystal decay. No decay was detected.

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.7428 (2)	0.74152 (14)	0.49286 (14)	0.0194 (3)
O2	0.7892 (2)	0.12848 (16)	0.93095 (15)	0.0275 (4)
O3	0.8474 (2)	0.34423 (16)	0.87491 (15)	0.0240 (3)
O4	0.7515 (2)	−0.04223 (15)	0.57626 (15)	0.0223 (3)
HO4	0.751 (4)	−0.107 (3)	0.547 (3)	0.033 (7)*
N1	0.7253 (2)	0.61369 (17)	0.36153 (16)	0.0143 (3)
H1	0.7122	0.6232	0.2779	0.017*
N2	0.8098 (2)	0.25090 (18)	0.84407 (17)	0.0176 (4)
C1	0.7568 (3)	0.2115 (2)	0.5149 (2)	0.0144 (4)
C2	0.7386 (3)	0.3575 (2)	0.4214 (2)	0.0139 (4)
H2	0.7207	0.3813	0.3282	0.017*
C3	0.7466 (2)	0.4693 (2)	0.4645 (2)	0.0130 (4)
C4	0.7726 (3)	0.4339 (2)	0.6049 (2)	0.0144 (4)
H4	0.7801	0.5056	0.6362	0.017*
C5	0.7867 (3)	0.2879 (2)	0.6955 (2)	0.0148 (4)
C6	0.7804 (3)	0.1751 (2)	0.6555 (2)	0.0152 (4)
H6	0.7915	0.0785	0.7201	0.018*
C7	0.7482 (3)	0.0950 (2)	0.4630 (2)	0.0174 (4)
H7A	0.6301	0.1233	0.4201	0.021*
H7B	0.8583	0.0868	0.3913	0.021*
C8	0.7231 (3)	0.7392 (2)	0.3791 (2)	0.0150 (4)
C9	0.6964 (3)	0.8784 (2)	0.2486 (2)	0.0200 (4)
H9A	0.5845	0.9475	0.2689	0.030*
H9B	0.6779	0.8556	0.1721	0.030*

H9C	0.8098	0.9204	0.2219	0.030*
S	0.67034 (7)	0.73548 (5)	0.95105 (5)	0.02010 (16)
O5	0.6536 (2)	0.62318 (16)	1.10091 (14)	0.0233 (3)
C10	0.9074 (3)	0.6815 (2)	0.8663 (2)	0.0250 (5)
H10A	1.0039	0.6890	0.9118	0.038*
H10B	0.9197	0.7450	0.7681	0.038*
H10C	0.9260	0.5817	0.8735	0.038*
C11	0.5368 (3)	0.6896 (2)	0.8558 (2)	0.0239 (5)
H11A	0.5771	0.5865	0.8722	0.036*
H11B	0.5612	0.7457	0.7562	0.036*
H11C	0.4003	0.7118	0.8879	0.036*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0281 (8)	0.0156 (7)	0.0178 (7)	−0.0067 (6)	−0.0044 (6)	−0.0074 (6)
O2	0.0426 (9)	0.0201 (8)	0.0169 (8)	−0.0079 (7)	−0.0058 (7)	−0.0019 (6)
O3	0.0330 (8)	0.0257 (8)	0.0206 (8)	−0.0106 (6)	−0.0079 (6)	−0.0107 (6)
O4	0.0395 (9)	0.0121 (7)	0.0175 (8)	−0.0085 (6)	−0.0073 (6)	−0.0038 (6)
N1	0.0188 (8)	0.0137 (8)	0.0115 (8)	−0.0041 (6)	−0.0035 (6)	−0.0044 (7)
N2	0.0187 (8)	0.0191 (9)	0.0141 (9)	−0.0033 (7)	−0.0019 (6)	−0.0059 (7)
C1	0.0116 (9)	0.0157 (10)	0.0175 (10)	−0.0024 (7)	−0.0012 (7)	−0.0082 (8)
C2	0.0140 (9)	0.0158 (9)	0.0118 (9)	−0.0031 (7)	−0.0032 (7)	−0.0043 (8)
C3	0.0109 (9)	0.0140 (9)	0.0141 (9)	−0.0029 (7)	−0.0018 (7)	−0.0049 (8)
C4	0.0151 (9)	0.0144 (9)	0.0153 (10)	−0.0034 (7)	−0.0020 (7)	−0.0069 (8)
C5	0.0132 (9)	0.0186 (10)	0.0127 (9)	−0.0034 (7)	−0.0021 (7)	−0.0056 (8)
C6	0.0141 (9)	0.0133 (9)	0.0168 (10)	−0.0026 (7)	−0.0025 (7)	−0.0038 (8)
C7	0.0205 (10)	0.0142 (9)	0.0177 (10)	−0.0043 (7)	−0.0034 (8)	−0.0052 (8)
C8	0.0116 (9)	0.0142 (9)	0.0193 (10)	−0.0034 (7)	−0.0008 (7)	−0.0063 (8)
C9	0.0242 (10)	0.0144 (10)	0.0209 (11)	−0.0046 (8)	−0.0038 (8)	−0.0054 (8)
S	0.0245 (3)	0.0192 (3)	0.0170 (3)	−0.0062 (2)	−0.00436 (19)	−0.0052 (2)
O5	0.0322 (8)	0.0263 (8)	0.0121 (7)	−0.0112 (6)	−0.0045 (6)	−0.0035 (6)
C10	0.0227 (11)	0.0296 (12)	0.0182 (11)	−0.0070 (9)	−0.0048 (8)	−0.0021 (9)
C11	0.0223 (10)	0.0329 (12)	0.0165 (11)	−0.0096 (9)	−0.0052 (8)	−0.0052 (9)

Geometric parameters (Å, °)

O1—C8	1.235 (2)	C5—C6	1.386 (3)
O2—N2	1.230 (2)	C6—H6	0.9300
O3—N2	1.228 (2)	C7—H7A	0.9700
O4—C7	1.410 (2)	C7—H7B	0.9700
O4—HO4	0.83 (3)	C8—C9	1.512 (3)
N1—C8	1.357 (2)	C9—H9A	0.9600
N1—C3	1.413 (2)	C9—H9B	0.9600
N1—H1	0.8600	C9—H9C	0.9600
N2—C5	1.473 (2)	S—O5	1.5130 (14)
C1—C2	1.393 (3)	S—C11	1.785 (2)
C1—C6	1.394 (3)	S—C10	1.788 (2)
C1—C7	1.510 (3)	C10—H10A	0.9600

C2—C3	1.401 (3)	C10—H10B	0.9600
C2—H2	0.9300	C10—H10C	0.9600
C3—C4	1.399 (3)	C11—H11A	0.9600
C4—C5	1.387 (3)	C11—H11B	0.9600
C4—H4	0.9300	C11—H11C	0.9600
C7—O4—HO4	110.7 (18)	O4—C7—H7B	109.5
C8—N1—C3	127.59 (16)	C1—C7—H7B	109.5
C8—N1—H1	116.2	H7A—C7—H7B	108.1
C3—N1—H1	116.2	O1—C8—N1	123.12 (18)
O3—N2—O2	123.43 (17)	O1—C8—C9	121.40 (17)
O3—N2—C5	118.31 (16)	N1—C8—C9	115.48 (17)
O2—N2—C5	118.26 (16)	C8—C9—H9A	109.5
C2—C1—C6	119.66 (17)	C8—C9—H9B	109.5
C2—C1—C7	119.49 (17)	H9A—C9—H9B	109.5
C6—C1—C7	120.85 (17)	C8—C9—H9C	109.5
C1—C2—C3	121.52 (18)	H9A—C9—H9C	109.5
C1—C2—H2	119.2	H9B—C9—H9C	109.5
C3—C2—H2	119.2	O5—S—C11	105.62 (9)
C4—C3—C2	119.39 (17)	O5—S—C10	106.87 (9)
C4—C3—N1	123.66 (16)	C11—S—C10	97.05 (10)
C2—C3—N1	116.94 (16)	S—C10—H10A	109.5
C5—C4—C3	117.43 (17)	S—C10—H10B	109.5
C5—C4—H4	121.3	H10A—C10—H10B	109.5
C3—C4—H4	121.3	S—C10—H10C	109.5
C6—C5—C4	124.38 (18)	H10A—C10—H10C	109.5
C6—C5—N2	118.08 (17)	H10B—C10—H10C	109.5
C4—C5—N2	117.54 (16)	S—C11—H11A	109.5
C5—C6—C1	117.60 (17)	S—C11—H11B	109.5
C5—C6—H6	121.2	H11A—C11—H11B	109.5
C1—C6—H6	121.2	S—C11—H11C	109.5
O4—C7—C1	110.61 (16)	H11A—C11—H11C	109.5
O4—C7—H7A	109.5	H11B—C11—H11C	109.5
C1—C7—H7A	109.5		

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O5^{i}	0.86	1.98	2.835 (2)	171
O4—HO4···O1^{ii}	0.83 (3)	1.86 (3)	2.6941 (19)	177 (3)

Symmetry codes: (i) *x*, *y*, *z*−1; (ii) *x*, *y*−1, *z*.

Fig. 1