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cis-anti-cis-Dicyclohexyl-18-crown-6–thiacetazone–methanol (1/2/2)

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Key indicators

Single-crystal X-ray study
T = 153 K
Mean σ(C–C) = 0.003 Å
R factor = 0.043
wR factor = 0.123
Data-to-parameter ratio = 14.5

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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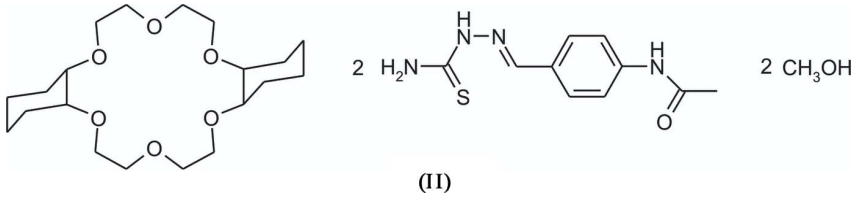
In the title compound [systematic name: 2,5,8,15,18,21-tricyclo[20.4.0.0^{9,14}]hexacosane–4-acetylaminobenzaldehyde thiosemicarbazone–methanol (1/2/2)], $C_{20}H_{36}O_6\cdot 2C_{10}H_{12}N_4OS\cdot 2CH_3OH$, the *cis-anti-cis*-dicyclohexyl-18-crown-6 molecule resides on an inversion center, and two thiacetazone molecules are linked to the macrocycle *via* N—H···O hydrogen bonds of the terminal amino group [N···O = 3.017 (2) and 3.092 (2) Å]. These units are further associated into chains *via* bridging methanol molecules acting both as an H-atom donor [*via* an O—H···S contact, with O···S = 3.182 (3) Å] and as an H-atom acceptor [*via* an N—H···O contact, with N···O = 2.848 (3) Å].

Comment

In continuation of our earlier research devoted to the interaction of macrocyclic ligands with drug molecules, we studied the system that includes the 18-membered classic crown ether, *cis-anti-cis*-dicyclohexyl-18-crown-6 (DCH6B) and the antimicrobial drug thiacetazone, (I). The aim of our study was to elucidate the mode of interaction of the drug molecule with the macrocycle and to compare the crystal packing of the complex with the crystal packing of the pure drug form. Previously we have shown that the primary amino group of streptocide (Dvorkin *et al.*, 1989), diacarb (Fonari *et al.*, 1989), hypothiazide (Dvorkin *et al.*, 1990) and 4-aminobenzoic acid (Fonari *et al.*, 1994) always interacts with the classic 18-membered crown ethers *via* a pair of N—H···O hydrogen bonds. The mode of mutual interaction is more predictable in the case of DCH6B, as its geometry is predisposed to the generation of an inversion center within the molecule and an equal-face coordination. This is not always the case for 18-crown-6, which, for example, in the complex with hypothiazide (Dvorkin *et al.*, 1990) reveals C_1 symmetry and different-face coordination of the drug molecule.



(II)

The structure of thiacetazone, (I), itself has been reported previously [Karlsen *et al.*, 1988; refcode GANGEH in the Cambridge Structural Database (Version 5.26, plus three 2005 updates; Allen, 2002)]. In (I), the self-assembly of the molecules occurs *via* a diverse system of hydrogen bonding; the

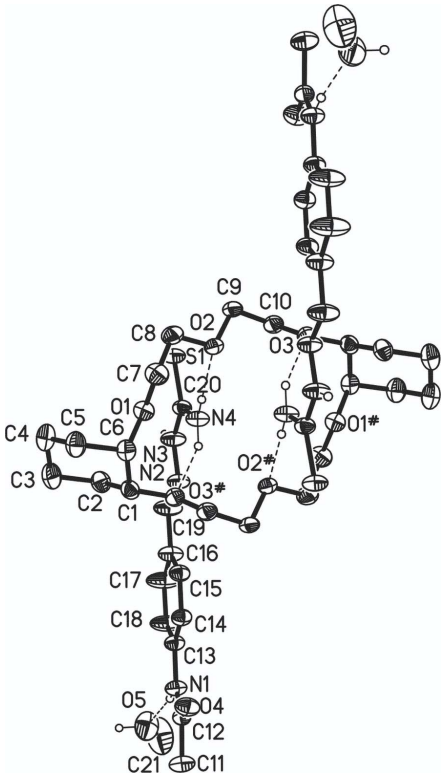


Figure 1
A view of the molecular structure of (II), showing the atomic labeling scheme and displacement ellipsoids drawn at the 30% probability level. Hydrogen bonds are shown as dashed lines. Atoms marked with a hash (#) are in the symmetry position $(2 - x, 2 - y, 1 - z)$ [C-bound H atoms have been omitted for clarity].

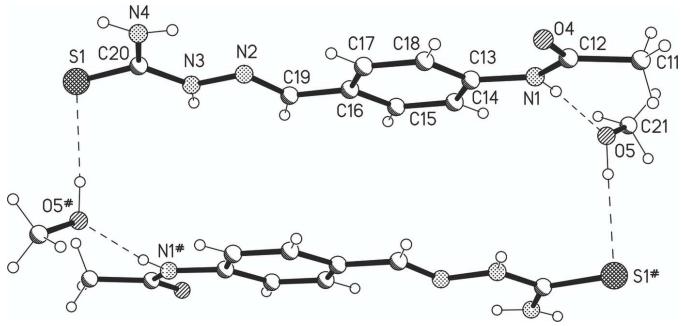


Figure 2
The centrosymmetric heterotetramer in the structure of compound (II), sustained by N—H···O and O—H···S hydrogen bonds (dashed lines). Atoms marked with a hash (#) are in the symmetry position $(2 - x, 2 - y, 1 - z)$.

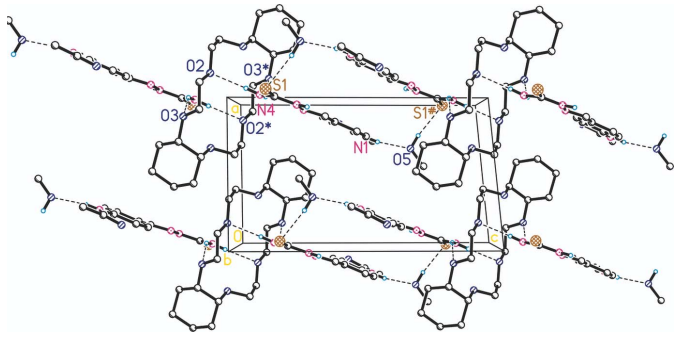


Figure 3
The crystal packing of the chains in compound (II) viewed along the *b* axis. Atoms marked with an asterisk (*) and a hash (#) are at the symmetry positions $(2 - x, 2 - y, -z)$ and $(2 - x, 2 - y, 1 - z)$, respectively [C-bound H atoms have been omitted for clarity].

molecules form the centrosymmetric dimer *via* a pair of N—H···O hydrogen bonds with the participation of the NH group of the thiourea fragment and an $R_2^2(22)$ ring is generated. These dimers are further associated into chains, again *via* N—H···O hydrogen bonds, with the participation of the terminal amino groups; $R_2^2(26)$ rings are generated. These chains are combined into layers *via* typical thiosemicarbazone centrosymmetric planar $R_2^2(8)$ synthons, based on two N—H···S hydrogen bonds. In the title compound, (II), a complete rearrangement of the hydrogen bonds occurs.

The structure of (II) is shown in Fig. 1, and selected geometric parameters are given in Table 1. The crown ether lies on an inversion center. The geometry of all the molecules forming the complex is in reasonable agreement with the precise data obtained for crown ethers and for (I) (Karlsen *et al.*, 1988). The thiacetazone molecule adopts an almost planar conformation, all the non-H atoms being coplanar within ±0.079 Å. The macrocycle in (II) adopts a C_i symmetric conformation with the O atoms coplanar within ±0.15 Å. The torsion angles of the DCH6B ring are given in Table 1. The dihedral angle between the least-squares planes through all the crown O atoms and the thiacetazone molecular skeleton is 89.70 (4)°. In the 1:2 centrosymmetric unit DCH6B–thiacetazone, the components are held together *via* two pairs of N—H···O hydrogen bonds involving the primary amino group, with atom N4 displaced by 2.057 (2) Å from the least-squares plane of the DCH6B O atoms. The NH H atom of the thiourea group is blocked by the methanol molecule *via* a N—H···O hydrogen bond.

Two symmetry-related thiacetazone and methanol molecules form a centrosymmetric tetramer *via* a pair of N—H···O and a pair of O—H···S hydrogen bonds (Fig. 2). Thus, the methanol molecule acts as a single donor and a single acceptor, and an approximate regular rectangle is formed with the short axis between the planar fragments equal to 3.53 Å, and a long axis of *ca* 12.1 Å. The alternation of these tetramers and macrocyclic molecules forms corrugated chains packing along [100] in the unit cell (Fig. 3).

In conclusion, we underline again the complete rearrangement of the hydrogen bonding in complex (II) compared with that in the crystal structure of the pure drug, compound (I); neither of the supramolecular synthons remains in the ternary complex, (II), discussed above.

Experimental

A solution of DCH6B (0.372 g, 1 mmol) and thiacetazone (0.236 g, 1 mmol) in methanol (25 ml), and ethyl acetate (25 ml), was stored for 3–4 d at 293–298 K in an open flask. Colorless transparent crystals of (II) separated out in a yield of 81% (0.370 g). Compound (II) is soluble in methanol, ethanol and acetone [m.p. > 513 K (decom-

position)]. ^{1}NMR (DMSO-d6, 300 MHz): 2.04 (*s*, 6H, CH_3-thiacetazone), 1.22–1.71 (*m*) and 3.55 (*m*, 36H, B-isomer DCH-6), 7.58 (*d*) and 7.69 (*d*, 8H, CH-thiacetazone), 7.97, 10.05 and 11.31 (*s*, 8H, HN). Analysis calculated for $C_{42}H_{68}N_8O_{10}S_2$: C 55.48, H 7.54, N 12.33, S 7.05%; found: C 55.53, H 7.51, N 12.37, S 7.09%.

Crystal data

$C_{20}H_{36}O_6{\cdot}2C_{10}H_{12}N_4OS{\cdot}2CH_4O$
M_r = 909.16
Triclinic, $P\overline{1}$
a = 9.6712 (18) Å
b = 9.9236 (18) Å
c = 14.849 (4) Å
α = 93.17 (3)°
β = 91.38 (2)°
γ = 118.649 (7)°
V = 1246.7 (5) Å^3
Z = 1
D_x = 1.211 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 4.4–12.5°
μ = 0.17 mm^{-1}
T = 153 (2) K
Prism, colorless
0.42 × 0.26 × 0.20 mm

Data collection

Siemens *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: ψ scan (*XSCANS*; Siemens, 1996)
T_{min} = 0.928, T_{max} = 0.967
4658 measured reflections
4371 independent reflections
3488 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 25.0°
$h = -1 \rightarrow 11$
$k = -11 \rightarrow 10$
$l = -17 \rightarrow 17$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.123
S = 1.03
4371 reflections
302 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.058P)^2 + 0.2974P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—C20	1.7034 (18)	C11—C12	1.509 (3)
O4—C12	1.214 (2)	C13—C18	1.384 (3)
O5—C21	1.310 (4)	C13—C14	1.386 (3)
N1—C12	1.358 (2)	C14—C15	1.380 (3)
N1—C13	1.409 (2)	C15—C16	1.387 (3)
N2—C19	1.262 (3)	C16—C17	1.388 (3)
N2—N3	1.384 (2)	C16—C19	1.464 (3)
N3—C20	1.339 (2)	C17—C18	1.376 (3)
N4—C20	1.313 (3)		
C12—N1—C13	128.89 (17)	C14—C13—N1	115.93 (17)
C19—N2—N3	115.99 (17)	C15—C14—C13	120.16 (19)
C20—N3—N2	119.86 (17)	C14—C15—C16	121.4 (2)
O4—C12—N1	123.72 (18)	C15—C16—C17	117.58 (18)
O4—C12—C11	122.43 (18)	C18—C17—C16	121.50 (17)
N1—C12—C11	113.83 (19)	C17—C18—C13	120.34 (16)
C18—C13—C14	118.96 (17)	N2—C19—C16	122.59 (19)
C18—C13—N1	125.11 (17)	N4—C20—N3	117.77 (17)
C1—C6—O1—C7	−160.6 (2)	O2—C9—C10—O3	−65.4 (2)
C6—O1—C7—C8	−177.5 (2)	C9—C10—O3—C1^i	112.0 (2)
O1—C7—C8—O2	−70.1 (2)	C10—O3—C1^i—C6^i	140.9 (2)
C7—C8—O2—C9	−171.5 (2)	O3—C1^i—C6^i—O1^i	96.9 (2)
C8—O2—C9—C10	−177.8 (2)		

Symmetry code: (i) $-x+2, -y+2, -z+1$.

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

D—H···A	D—H	H···A	D···A	D—H···A
O5—H1O···S1^i	0.89 (2)	2.30 (2)	3.182 (3)	174 (4)
N1—H1A···O5	0.85 (2)	2.01 (2)	2.848 (3)	169 (2)
N3—H3A···O4^{ii}	0.84 (2)	2.15 (2)	2.980 (2)	167 (2)
N4—H4A···O3^{iii}	0.86 (3)	2.38 (2)	3.092 (2)	140 (2)
N4—H4B···O2	0.86 (2)	2.16 (2)	3.017 (2)	175 (2)

Symmetry codes: (i) $-x+2, -y+2, -z+1$; (ii) $x, y+1, z$; (iii) $-x+2, -y+2, -z$.

C-bound H atoms were placed in calculated positions, with C—H distances of 0.95-1.00 Å, and were treated using a riding-model approximation, with U_{iso}(H) = 1.2U_{eq}(C) for all H atoms except methyl H atoms, for which U_{iso}(H) = 1.5U_{eq}(C). NH and OH H atoms were located in difference Fourier maps and allowed to refine isotropically, with the O—H distance restrained to 0.86 (3) Å.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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