J Incl Phenom Macrocycl Chem (2008) 61:367–375
DOI 10.1007/s10847-008-9431-7

ORIGINAL ARTICLE

Structure of benzo- and dibenzocrown ethers and their H-bonded adducts. 4. Structural motifs in the 2,4-dithiouracil complexes with 4-bromo- and 4-nitrobenzo-18-crown-6, [2.4]dibenzo- and thia[1.5]dibenzo-18-crown-6

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Received: 9 October 2007 / Accepted: 26 February 2008 / Published online: 1 April 2008

Abstract Four novel complexes of 2,4-dithiouracil (pyrimidine-2,4(1*H*,3*H*)-dithione, DTU) with 18-membered benzo- and dibenzo-crown ethers were synthesized in approximately the same conditions and studied by single crystal diffraction. Hydrogen bonding was observed to be the most important for the complexation in the solid state but π–π interactions also contribute to it. The crystalline monohydrates of the 1:1:1 stoichiometry are recorded for 4-bromo- and 4-nitrobenzo-18-crown-6 (complexes **1** and **2**), while complexes with [2.4]dibenzo- and thia[1.5]dibenzo-18-crown-6 (complexes **3** and **4**) represent anhydrous adducts of the 2:2 ratio. The crystal structures reveal three supramolecular structural motifs: the alternative chain for the ternary complex **1** and two types of capsules for complexes **2**–**4** where the DTU dimers are encapsulated inside the space restricted by two crown molecules.

Keywords Benzo- and dibenzocrown ethers · Complexes · 2,4-Dithiouracil · Hydrogen bonding · Synthesis · Crystal structure

Introduction

In 2007 the chemical scientific community marked the fortieth anniversary of the publication in the Journal of the American Chemical Society of the synthesis and cation binding properties of crown ethers by Charles J. Pedersen [1, 2]. The fields of anionic synthetic reagents, phase-transfer catalysis, biological ion transport, enzyme mimics, molecular devices and machines and other emerging disciplines benefited profoundly from the discovery of crown ethers. Enormous excellent reviews describe thousands of crown structures and crown applications in chemistry [3]. The deep analysis of the hydrogen bond formation and understanding of factors controlling the formation of complexes are still required.

For the last two decades along with the others we were involved in the host–guest chemistry of the crown ethers with an accent on their interaction with biologically important molecules (drugs, heterocyclic bases etc.). These studies have been developed in two directions: construction of extended supramolecular networks sustained by conventional hydrogen bonds using the unique property of classic crown ethers to serve as the double-face spacers for the organic molecules with the variety of H-donor groups (NH_2, $C(=S)NH_2$, $C(=O)NH_2$ etc.) that serve as the linkers [4], and the structural study of the host–guest complexes on the base of the novel crown ethers [5].

For part 3 see *JIPh*., **56**, 345 (2006).

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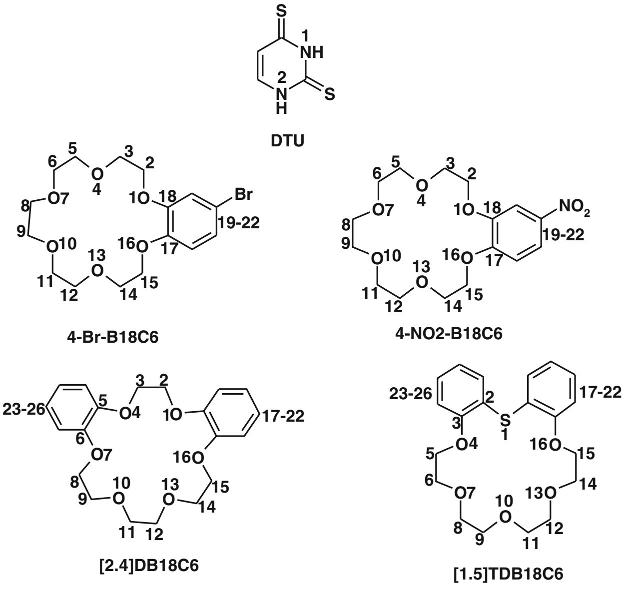
Heterocyclic bases such as pyrimidine, imidazole and purine and their derivatives are of great importance in biological systems due to their proton acceptor and hydrogen bonding abilities. Pursiainen et al. [6] thoroughly studied the complexation of tropylium, pyridinium derivatives and five-membered N-heteroatomic cations with crown ethers. In our turn we have demonstrated the formation of ionic complexes between pyrimidine derivatives and aza-crown ethers with the proton transfer from the pyrimidine molecule to the macrocyclic nitrogen atom [7]. Alongside with uracil, its sulfur substituted analogues 2-thiouracil, 2,4-dithiouracil (DTU) are intensively studying both by the computational [8] and crystallographic methods [9] with an emphasis on the preferable forms of the DTU existence in the solid and gas phases, the estimation of the comparative affinity of the DTU binding sites for the protonation and participation in the metal complexation and hydrogen bonding. Our investigations [5a, 10] appeared to be the pioneering ones in the preparation and X-ray study of the genuine molecular complexes of the DTU with classic crown ethers (18C6, *cis*-isomers of dicyclohexano-18C6, benzo-18C6 and [1.5]dibenzo-18C6). By that study we showed that of six possible isomers namely dithione isomer actually forms the crystalline complexes, and the CE···DTU interactions occur via one NH···O hydrogen bond through the nitrogen atom being in the position “2” of the DTU ring (see Scheme 1 for the numbering in the DTU molecule) and the subsidiary CH···O interaction through one additional carbon atom of the DTU ring. The coupling of two DTU molecules via $R_2^2(8)$ homosynthon [11] built on two NH···S hydrogen bonds has been registered in the complexes with dicyclohexyl-18C6 and [1.5]dibenzo-18C6, while the incorporation of water molecule that blocks the nitrogen atom in the position “1” of the DTU ring and completely destroys the hydrogen bonding network typical for the pure DTU [9a] results in the reproducible 1D supramolecular motif for 18C6, B18C6 or *cis-syn-cis*-DCH18C6 with the alternation of the CE, DTU and water molecules in the chain. These three earlier reported supramolecular motifs are reproduced in Fig. 1.

In continuation of this research we report here the synthesis and crystal structures of four complexes of DTU with benzo-crown ethers. Four monomers used in this study are shown in Scheme 1. They are two mono- and two dibenzo-derivatives of 18C6, namely 4-bromo-, 4-nitrobenzo-18C6, [2.4]dibenzo- and thia[1.5]dibenzo-18C6. Four novel complexes were characterised by elemental analysis, ^{1}H NMR and X-ray investigation.

It is known [3b] that an attachment of the benzene ring to the crown ether framework influences the flexibility of the oxyethylene chain and decreases the accessibility of the oxygen atoms relative to it for the hydrogen bonding



Scheme 1 Structural formulas and crystallographic numbering for studied compounds

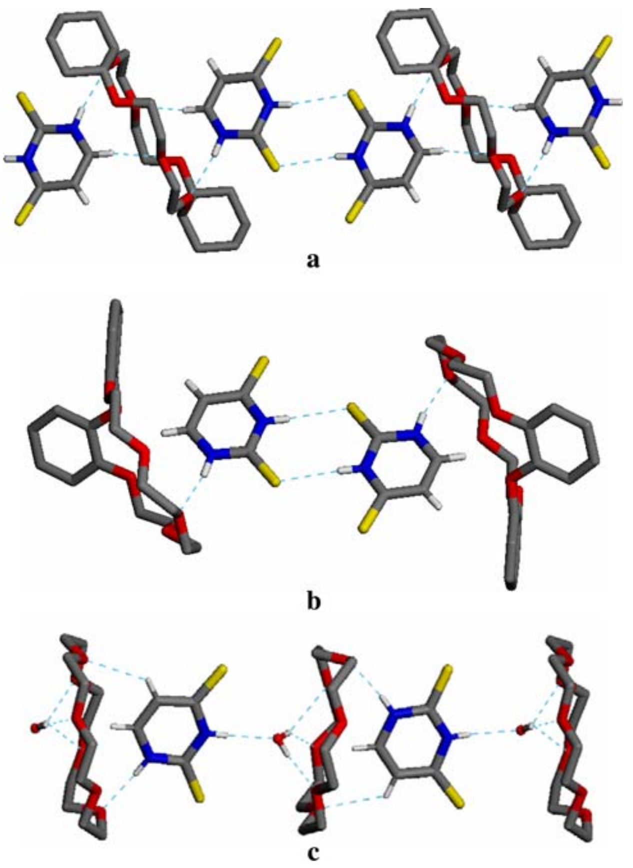


Fig. 1 Structural motifs in the DTU complexes with crown ethers: (**a**) fragment of the chain in the complex *cis-anti-cis*-DCH18C6·2DTU [10], refcode CATCIK in CSD [12]); (**b**) molecular capsule in the complex [1.5]DB18C6·DTU [5a], refcode YAXNAN in CSD; (**c**) fragment of the chain in the complex 18C6·DTU·H_2O [12], refcode CATCEG in CSD

interaction, the second aromatic ring arranged in a close proximity to the first one in the macrocyclic molecule is expected to make additional impediments for the macrocyclic oxygens for intermolecular interactions. On the other hand, the availability of the aromatic units in the macrocyclic molecule enhances the contribution of the π–π interactions in the overall system of the crown ether–DTU interactions. This study aims to register the preferable modes of DTU interactions with benzo-crown ethers with the estimation of the contribution of π–π component in an overall system of interactions. The divalent sulfur atoms are significantly larger than oxygen. Being incorporated in the macrocyclic framework, the sulfurs prefer an exocyclic conformation [13]. It seems to be interesting to compare the structural peculiarities of the previously reported DTU—[1.5]dibenzo-18C6 complex [5a] with its thia-analogue, thia[1.5]dibenzo-18C6.

Experimental

Synthesis

4-Bromo-B18C6 and 4-nitro-B18C6 were obtained as described in [14] and [15] respectively, and [2.4]DB18C6 as reported in [16]. Thia[1.5]DB18C6 was synthesized by us according to the originally developed procedure. Commercially available DTU (Aldrich Chemical Co) was used in its initial state. The thin layer chromatographic control of the substances purity was performed on Silufol UV-254 plates. Complexes **1–4** were obtained in a similar way by mixing of the methanol solutions of DTU and the corresponding crown ether. The ratio of the components varied from 1:1 till 1:3 (excess of the crown ether). Only four complexes described in this article were obtained. Complexes were analyzed for C, H, Br, N and S in a Perkin Elmer 240C instrument. Crystals suitable for the X-ray diffraction experiments were isolated from the mass of the crystals obtained. Suitable microanalyses were obtained for all compounds. ^{1}H NMR spectra were recorded in DMSO$_{d6}$ (99.9%) and $CDCl_3$ (99.8%) on the 299.95 MHz Varian WXP-300 instrument using TMS as internal standard. ^{1}H NMR spectra recorded only the peaks typical for the separate components (crown ether and DTU), no solution studies were fulfilled. Mass spectrum was obtained with a MX-1321 spectrometer equipped with a direct inlet; ionization voltage 70 eV, ionization chamber temperature 200 °C.

Synthesis of thia[1.5]DB18C6

Sodium hydroxide (4.0 g, 100 mmol) was added with an effective stirring to the solution of 2,2^{I}-dihydroxydiphenyl sulfide (10.91 g, 50 mmol) and tetraethyleneglycol ditosylate (19.10 g, 51 mmol) in dry 1,4-dioxane (150 ml). The resulting mixture was stirred during 20 h at 100 °C, then cooled and acidified by concentrated hydrochloric acid to pH 3−4. The residue was filtered, washed by cool 1,4-dioxane (2 × 10 ml) and filtrate was treated by activated charcoal. The solvent was evaporated at reduced pressure. The residue was extracted by boiling *n*-heptane (4 × 150 ml) and combined extracts were cooled to 5–10 °C and filtered off. The residue was washed by boiling *n*-heptane (2 × 30 ml) and crystallized from *iso*-propanol. White crystals M.P. 107–108 °C were obtained with the yield 3.76 g (20%). Found, C, 63.72; H, 6.50; S, 8.46 for $C_{20}H_{24}O_5S$. Calculated, %: C, 63.81; H, 6.43; S; 8.52. ^{1}H NMR ($CDCl_3$, 299.95 MHz): 3.57, m; 3.67, m; 4.08, m (16H, CH_2); 6.72, t; 6.78–6.99, m; 7.09 t (8H, CH_{Ar}). Mass spectra, *m/z* (I%): 377 (20.8), 376 (100.0), 218 (34.2), 200 (10.7), 171 (10.6), 151 (47.6), 137 (81.8), 120 (14.6), 96 (13.6), 94 (25.1), 91 (20.1), 45 (73.8), 43 (38.7).

Synthesis of 4-bromo-B18C6 · DTU · H_2O (1)

DTU (36 mg, 0.25 mmol) and 4-bromo-B18C6 (98 mg, 0.25 mmol) were dissolved in methanol (20 ml) at 64 °C. Ethyl acetate (30 ml) was added, and the mixture was remained to crystallize at room temperature and spontaneous evaporation of solvents. Yellow transparent crystals M.P. 260–262 °C (with decomposition) suitable for X-ray analysis were obtained with the yield 117 mg (85%). Found, C, 43.44; H, 5.25; Br, 14.49; N, 5.13; S, 11.64 for $C_{20}H_{29}BrN_2O_7S_2$. Calculated, %: C, 43.40; H, 5.28; Br, 14.44; N, 5.06, S; 11.59. ^{1}H NMR (DMSO$_{d6}$, 299.95 MHz): 3.55 m, 3.59 m, 3.73 m, 4.07 m (20H, CH_2) and 7.05 d, 7.10 s (3H, CH_{Ar})—crown ether; 6.50 d, 7.25 d (2H, CH)—pyrimidine-2,4(1*H*,3*H*)-dithione.

Synthesis of 4-nitro-B18C6 · DTU · H_2O (2)

DTU (36 mg, 0.25 mmol) and 4-nitro-B18C6 (89 mg, 0.25 mmol) were dissolved in methanol (3 ml) at 64 °C. Ethyl acetate (6 ml) was added, and the mixture was remained to crystallize at room temperature and spontaneous evaporation of solvents. Yellow transparent crystals, M.P. 253–254 °C (with decomposition) suitable for X-ray analysis were obtained with the yield 118 mg (91%). Found, C, 46.18; H, 5.67; N, 8.13; S, 12.39 for $C_{20}H_{29}N_3O_9S_2$. Calculated, %: C, 46.23; H, 5.63; N, 8.09; S, 12.34. ^{1}H NMR (DMSO$_{d6}$, 299.95 MHz): 3.57 m, 3.62 m, 3.76 m, 4.23 m (20H, CH_2) and 7.25 d, 7.73 s (3H, CH_{Ar})—crown ether; 6.50 d, 7.25 d (2H, CH)—pyrimidine-2,4(1*H*,3*H*)-dithione.

Synthesis of [2.4]DB18C6 · DTU (3)

A solution of [2.4]DB18C6 (360 mg, 1 mmol) and DTU (144 mg, 1 mmol) in the methanol:ethyl acetate mixture (20 ml:40 ml) was stored during 3–4 days at 20–25 °C in an open flask. The resulting transparent yellow crystals, suitable for X-ray analysis, M.P. 236–238 °C (with decomposition) were separated with the yield of 80% (400 mg). Found, C, 57.08; H, 5.63; N, 5.58; S, 12.75 for $C_{24}H_{28}N_2O_6S_2$. Calculated, %: C, 57.12; H, 5.59; N, 5.55; S, 12.71. ^{1}H NMR ($DMSO_{d6}$, 300 MHz): 3.59 m, 3.72 m, 4.07 m, 4.28 m (16H, CH_2) and 6.96 m (8H, CH_{Ar})—crown ether; 6.49 d, 7.25 d (2H, CH)—pyrimidine-2,4(1*H*,3*H*)-dithione.

Synthesis of thia[1.5]DB18C6 · DTU (4)

DTU (36 mg, 0.25 mmol) and thia[1.5]DB18C6 (94 mg, 0.25 mmol) were dissolved in methanol (2 ml) at 64 °C. Ethyl acetate (2 ml) and *n*-butanol (1 ml) were added, and the mixture was remained to crystallize at room temperature and spontaneous evaporation of solvents. Yellow transparent crystals M.P. 250–252 °C (with decomposition) suitable for X-ray analysis were obtained with the yield 114 mg (88%). Found, C, 55.53; H, 5.38; N, 5.43; S, 18.52 for $C_{24}H_{28}N_2O_5S_3$. Calculated, %: C, 55.36; H, 5.42; N, 5.38; S, 18.48. ^{1}H NMR ($DMSO_{d6}$, 299.95 MHz): 3.59 m, 3.66 m, 4.12 m (16H, CH_2) and 6.99 m, 7.25 m (8H, CH_{Ar})—crown ether; 6.50 d, 7.25 d (2H, CH)—pyrimidine-2,4(1*H*,3*H*)-dithione.

Data collection and structure refinement

Unit cell dimensions and intensity data collection were performed at a room temperature on a Philips PW1100 diffractometer equipped with graphite monochromated MoKα radiation for **1**, **2**, **4** and CuKα radiation for **3**. All the data sets were collected by ω-2θ scan mode. There was no significant intensity decay. Structure solutions were performed by direct methods (SHELXS-97) and refined by full-matrix least-squares methods on F^2 (SHELXL-97) [17]. All non-disordered non-hydrogen atoms were refined anisotropically. In all structures H atoms attached to carbons were included in idealized positions in a riding model with isotropic temperature factors (1.2 times the carbon temperature factor), whereas those on N and O (water) atoms were found from difference Fourier maps at an intermediate stage of the refinement and refined with isotropic temperature factors (1.5 times the parent N(O) temperature factor) subjected to the geometrical restraints for the distance (N–H and O–H = 0.86 Å). In complex **2** the 4-Br-1,2-phenylene moiety is disordered over two positions with the occupancies equal to 0.811(3) and 0.189(3), correspondingly, the minor component being refined in an approximation of the rigid group with all but Br atom being isotropic. In complex **4** two atoms of the oxyethylene chain, O10 and C9 were found to be disordered over two positions with the occupancies equal to 0.723(1) and 0.277(1), correspondingly, the minor component being refined in an isotropic approximation.

The X-ray data and details of the refinement for **1–4** are summarized in Table 1, hydrogen bonding geometry—in Table 2, torsion angles—in Table 3.

Results and discussion

DTU–CE complex organisation

The retrieval of CSD (CSD version 5.28, November 2006, three updates 2007) [12] reveals only very few examples of the crystalline complexes of the CEs shown in Scheme 1 [18]. Moreover, among them only 1:1 adduct of thia[1.5]DB18C6 with antimony trifluoride represents a genuine host–guest complex where the components are held together through electronic interactions [18f]. We present here the single crystal structures for the molecular complexes **1–4**. All compounds crystallize in the centric space groups, triclinic *P*−1 for complexes **1** and **2** and monoclinic $P2_1/n$ and $P2_1/c$ for complexes **3** and **4,** correspondingly. Complexes **1** and **2** represent the monohydrates of the 1:1:1 ratio, while complexes **3** and **4** represent the binary adducts of the 2:2 ratio. The formula units for **1–4** are shown in Fig. 2. The asymmetric unit contains one ternary complex for **1** (Fig. 2a) and **2** (Fig. 2b), one binary complex for **3** (Fig. 2c) and one half of the binary complex for **4** (Fig. 2d). Below we summarize the differences in the complex organisation dictated by the structure of the corresponding CE.

The common feature for **1–4** is a weakness of intermolecular hydrogen bonding. Similar to the earlier discussed DTU complexes [5a, 10] in the complexes **1–4** the DTU-CE units are held together via an NH···O hydrogen bond with the sterically non-hindered N2 nitrogen atom of the DTU ring and by the subsidiary weak CH···O interaction with the neighboring CH-group (Table 2). The π–π stacking interactions between the pyrimidine ring of DTU molecule and the aromatic moieties in the macrocyclic molecules (varying number of phenylene rings) and the nature of the substituents (Br, NO_2) influence the mutual arrangement of the components in the complexes **1–4**. The mutual arrangement of the DTU and CE molecules is completely described by two dihedral angles, the first one (angle 1) is between the planes through the heterocyclic pyrimidine ring in the DTU molecule and the plane through six oxygen atoms in the macrocyclic

Table 1 Crystallographic data for complexes **1**–**4**

Complex	**1**	**2**	**3**	**4**
Composition	$C_{20}H_{29}BrN_2O_7S_2$	$C_{20}H_{29}N_3O_9S_2$	$C_{24}H_{28}N_2O_6S_2$	$C_{24}H_{28}N_2O_5S_3$
CCDC numbers	663173	663172	663170	663171
Formula weight	553.48	519.58	504.60	520.66
Wavelength (Å)	0.71073	0.71073	1.54180	0.71073
Space group	*P*-1	*P*-1	$P2_1/n$	$P2_1/c$
a (Å)	8.8461(18)	7.2210(14)	21.739(4)	9.0864(18)
b (Å)	9.4941(19)	11.535(2)	9.1700(18)	17.611(4)
c (Å)	15.663(3)	15.025(3)	25.360(5)	16.400(4)
α (°)	104.21(3)	91.14(3)	90.0	90.0
β° (°)	90.10(3)	95.94(3)	90.11(3)	99.04(3)
γ (°)	101.47(3)	92.81(3)	90.0	90.0
V (Å^3)	1248.0(4)	1242.9(4)	5055.4(17)	2591.7(9)
Z	2	2	8	4
*D*calc (g cm^{-3})	1.473	1.388	1.326	1.334
μ (mm^{-1})	1.856	0.268	2.261	0.323
F(000)	572	548	2128	1096
Reflections collected/unique	11272/4852	4877/4877	9815/9602	22203/5049
Reflections with $I > 2\sigma(I)$	2307	2602	6047	5049
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	4852/6/323	4877/2/315	9602/4/630	5049/2/323
Goodness-of-fit on F^2	1.021	1.009	0.998	1.016
R_1, wR_2 [$I > 2\sigma(I)$]	0.0647, 0.1913	0.0662, 0.1608	0.0429, 0.1029	0.0541, 0.1227
R_1, wR_2 (all data)	0.1396, 0.2092	0.1291, 0.1786	0.0746, 0.1146	0.0707, 0.1297
Largest diff. peak and hole e˙ Å^{-3}	0.302/−0.426	0.450/−0.457	0.499/−0.451	0.281/−0.364

molecule in complexes **1**–**3** and S_1O_5 set in complex **4**; and the second angle (angle 2) is between the same plane of the DTU molecule and the plane through the 1,2-phenylene ring in the CE molecule (it is one such angle for complexes **1** and **2** and two angles for complexes **3** and **4,** further they will be designated as angles 2/3, correspondingly). The angle 1 is equal to 50.7(2)° in **1**, 57.0(1)° in **2**, 77.3(1)/74.1(1)° for units A and B in complex **3** and 83.4(2)° in complex **4**, respectively. The gradual increase of this torsion angle with the approaching to the practically perpendicular arrangement of the DTU molecule towards the least-square plane of S_1O_5 atom set in the complex **4** is observed. The dihedral angle 2 has the values of 50.8(3)° and 9.8(1)° in complexes **1** and **2**, respectively. The dihedral angles 2/3 in complexes **3** and **4** adopt the values 44.8(1)/80.5(1)° and 45.4(1)/70.1(1)° for units A and B in **3**, and 57.2(3)/75.6(3)° in **4**. The inspection of these values evidently reveals the most pronounced contribution of stacking component in complex **2**, where the planar moieties of the DTU and CE molecules are displayed in practically parallel planes with the distance between the centroids of the DTU and benzene rings equal 3.811 Å. It is concerted with the typical π–π interactions and demonstrates the function of the electron-seeking nitro-group in the phenylene ring of CE that increases the planar π-electronic system and the π–π component of the intermolecular interaction. Contrary, the electron-withdrawing Br substituent in the 4-Br-B18C6 molecule in complex **1** impoverishes the π-electronic system of the crown that results in the lack of π–π stacking and instead demonstrates the close to the T-shape mode arrangement of the phenyl and DTU rings in the complex. In both complexes **1** and **2** the DTU arrangement occurs on the concave side of the macrocycle with the water molecule displayed on its convex side. The 4-Br-B18C6 and 4-NO_2-B18C6 molecules provide both sides of the molecule for the hydrogen bonding interactions. In contrary, arranged in a close proximity phenylene rings in the dibenzocrown ethers in complexes **3** and **4** preclude any interaction on one side of the macrocycle.

In the 4-Br-B18C6 and 4-NO_2-B18C6 molecules the oxygen atoms of the macrocyclic ring adopt a half-boat shape with five oxygen atoms that define its bottom being coplanar within ±0.12 and ±0.16 Å, correspondingly and the O7 atom deviating from this plane at 0.97 and 0.70 Å, correspondingly. The macrocyclic conformation is

Table 2 Hydrogen bonds for complexes **1**–**4** [Å and °]

D–H···A	d(D–H), Å	d(H···A), Å	d(D···A), Å	∠(DHA), [°]	Symmetry transformation for acceptor
1					
N(1)–H(1N1)···O(1W)	0.90(2)	1.97(3)	2.814(6)	156(6)	*x* + 1, *y*, *z*
N(2)–H(1N2)···O(10)	0.91(2)	2.02(4)	2.835(6)	148(6)	−*x* + 1, −*y* + 1, −*z* + 1
C(25)–H(25)···O(13)	0.93	2.58	3.458(8)	157	*x*, *y*, *z*
O(1W)–H(1W)···O(7)	0.85(2)	2.41(8)	2.971(6)	124(7)	−*x* + 1, −*y* + 1, −*z* + 1
O(1W)–H(2W)···O(1)	0.86(2)	2.51(2)	3.283(6)	151(4)	−*x* + 1, −*y* + 1, −*z* + 1
2					
N(1)–H(1N)···S(1)	0.86(2)	2.49(2)	3.340(3)	170(3)	−*x*, −*y* + 2, −*z* + 1
N(2)–H(2N)···O(13)	0.86(2)	2.20(3)	2.953(4)	144(4)	*x*−1, *y*, *z*
N(2)–H(2N)···O(10)	0.86(2)	2.53(3)	3.137(4)	127(3)	*x*−1, *y*, *z*
O(1W)–H(1W)···O(7)	0.84	2.26	2.937(5)	137	*x*, *y*, *z*
O(1W)–H(2W)···O(13)	0.92	2.52	3.425(5)	168	*x*, *y*, *z*
C(25)–H(25)···O(7)	0.93	2.45	3.369(4)	168	*x*−1, *y*, *z*
3					
N(2A)–H(2NA)···O(16A)	0.82(2)	2.49(2)	3.074(3)	129(2)	*x*, *y*, *z*
N(2A)–H(2NA)···O(1A)	0.82(2)	2.18(2)	2.946(2)	156(2)	*x*, *y*, *z*
C(28A)–H(28A)···O(10A)	0.93	2.44	3.133(3)	131	*x*, *y*, *z*
N(1A)–H(1NA)···S(1B)	0.83(2)	2.49(2)	3.305(2)	172(2)	*x* + 1/2, −*y* + 3/2, *z* + 1/2
N(1B)–H(1NB)···S(1A)	0.81(1)	2.62(1)	3.425(2)	174(2)	*x*−1/2, −*y* + 3/2, *z*−1/2
N(2B)–H(2NB)···O(7B)	0.82(2)	2.57(2)	3.181(2)	132(2)	*x*, *y*, *z*
N(2B)–H(2NB)···O(4B)	0.82(2)	2.22(2)	2.984(2)	155(2)	*x*, *y*, *z*
C(28B)–H(28B)···O(13B)	0.93	2.29	3.052(3)	139	*x*, *y*, *z*
4					
N(1)–H(1)···S(2)	0.86(2)	2.47(2)	3.297(2)	161(3)	−*x* + 1, −*y* + 1, −*z*
N(2)–H(2)···O(10)	0.86(2)	1.93(3)	2.789(3)	172(3)	*x*, *y*, *z*

Table 3 Torsion angles along the macrocyclic framework in crown molecules in complexes **1**–**4**

Complex	**1**	**2**	**3** (A)	**3** (B)	**4**
C(18)–O(S)(1)–C(2)–C(3)	−177.3(5)	−171.7(4)	−179.6(2)	−162.8(2)	−166.1(2)
O(1)–C(2)–C(3)–O(4)	−71.0(7)	73.9(5)	67.5(3)	−64.9(2)	−0.1(3)
C(2)–C(3)–O(4)–C(5)	−176.5(5)	−179.0(4)	167.1(2)	178.0(2)	160.1(2)
C(3)–O(4)–C(5)–C(6)	−172.2(6)	165.7(4)	179.7(2)	−170.2(2)	−167.9(2)
O(4)–C(5)–C(6)–O(7)	68.8(7)	−68.9(4)	−3.0(3)	−0.1(3)	66.6(3)
C(5)–C(6)–O(7)–C(8)	178.6(6)	−175.2(3)	−172.8(2)	176.1(2)	−168.7(3)
C(6)–O(7)–C(8)–C(9)	169.9(5)	173.6(3)	170.8(2)	−162.7(2)	160.1(4)
O(7)–C(8)–C(9)–O(10)	−75.0(6)	77.1(5)	−63.3(2)	68.4(2)	55.2(7)
C(8)–C(9)–O(10)–C(11)	176.5(5)	−177.0(3)	−174.2(2)	173.5(2)	175.4(4)
C(9)–O(10)–C(11)–C(12)	−82.0(6)	89.7(4)	−172.2(2)	172.9(2)	73.7(6)
O(10)–C(11)–C(12)–O(13)	−77.6(6)	65.7(4)	74.9(2)	−72.4(2)	49.0(5)
C(11)–C(12)–O(13)–C(14)	−179.1(5)	179.7(3)	−171.8(2)	168.3(2)	166.6(3)
C(12)–O(13)–C(14)–C(15)	−178.1(5)	−179.1(3)	−166.5(2)	166.3(2)	175.8(3)
O(13)–C(14)–C(15)–O(16)	72.5(6)	−75.5(4)	−67.8(2)	63.2(3)	−70.3(3)
C(14)–C(15)–O(16)–C(17)	−179.8(5)	167.3(3)	153.7(2)	−171.6(2)	−86.2(3)
C(15)–O(16)–C(17)–C(18)	−179.6(5)	−178.5(3)	−166.0(2)	169.2(2)	163.2(2)
O(16)–C(17)–C(18)–O(1)	1.5(8)	−2.1(5)	−2.5(3)	6.4(3)	−9.4(3)
C(17)–C(18)–O(S)(1)–C(2)	−169.6(6)	179.9(4)	174.9(2)	176.9(2)	85.1(2)

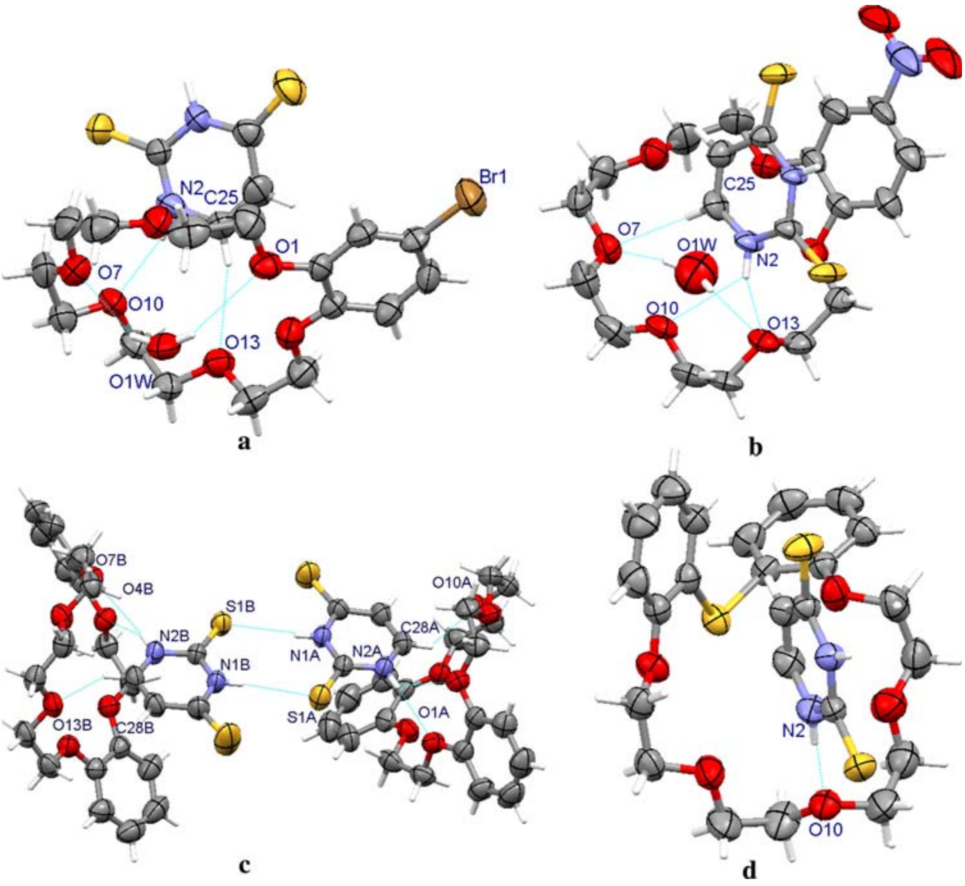


Fig. 2 ORTEP view for complexes **1**–**4**: (**a**) complex **1**; (**b**) complex **2**; (**c**) complex **3**; (**d**) complex **4**. Ellipsoids for non-hydrogen atoms are drawn at the 50% probability level. Only atoms involved in hydrogen bonding (and Br1 in complex **1**) are labeled

described by five *gauche*- and one *cis*- C–C torsion angles and 11 *anti*- and one *gauche*- C–O torsion angles (Table 3). Two DB18C6 macrocycles in complex˙**3** (A and B) adopt very close conformations with six oxygen atoms being coplanar within ±0.16 Å, all C–O bonds being in *anti*-conformation, two C–C bonds that belong to the 1,2-phenylene rings being in *cis*-conformation, four other C–C bonds being *gauche*. The dihedral angle between two phenylene rings in the molecule A is equal to 57.1(1)°, in the molecule B—60.2(1)°. In the thia[1.5]DB18C6 molecule in complex **4** five oxygen atoms are coplanar within ±0.05 Å, and sulfur atom deviates from this plane at 1.52 Å. In the macrocyclic framework one C–S bond is in *anti*-, and one—in *gauche*-conformation, of ten C–O bonds 8 being in *anti*- and 2—in *gauche*-conformation, of 6 C–C bonds two that belong to the phenylene rings are *cis*- and four others—are *gauche* (Table 3). The dihedral angle between the phenylene rings in the molecule adopts the value 88.1(3)°.

Supramolecular organisation

As we noted in Introduction, three different modes of supramolecular organisation of the DTU–CE units have been found so far (Fig. 1): for the ternary complexes which incorporate water molecules it is a chain organisation with the alternation of the components; for the binary complexes it is a chain organization again with the alternation of the CE molecules and the dimers of the inversion-related DTU molecules and the capsule organisation with the incorporation of the DTU dimer inside two CE molecules. Complex **1** reveals the first type of supramolecular organization, whilst complexes 2–**4** reveal the different modes of capsules (Figs. 2c, 3).

In the complex **1** the O(1W) water molecule is situated on the convex face of the crown ether with the O(1W)···O(crown) distances being in the range 2.971(6) (till O7)–3.905(7) Å (till O10) (Table 2) and at the distance of 1.815(6) Å from the least-square plane of six oxygen atoms. It is weakly bound with the macrocycle. The water molecule blocks the second amino group of the DTU ring, thus precluding the typical nucleic bases pairing [9, 19] via $R_2^2(8)$ NH···S synthon [11]. The strong intermolecular H-bonding, N(1)–H(1)···O(1W) is described by the N(1)···O(1W) separation of 2.819(7) Å and N(1)–H(1)···O(1w) angle of 157(4)°. The components are organized in the chain running along *c* axis in the crystal (Fig. 3a).

In the ternary complex **2**, similar to **1**, water molecule is displayed on the convex face of the macrocyclic cavity at the distances 2.937(5)–3.864(5) Å from the crown oxygen atoms being weakly bounded with the macrocycle via only

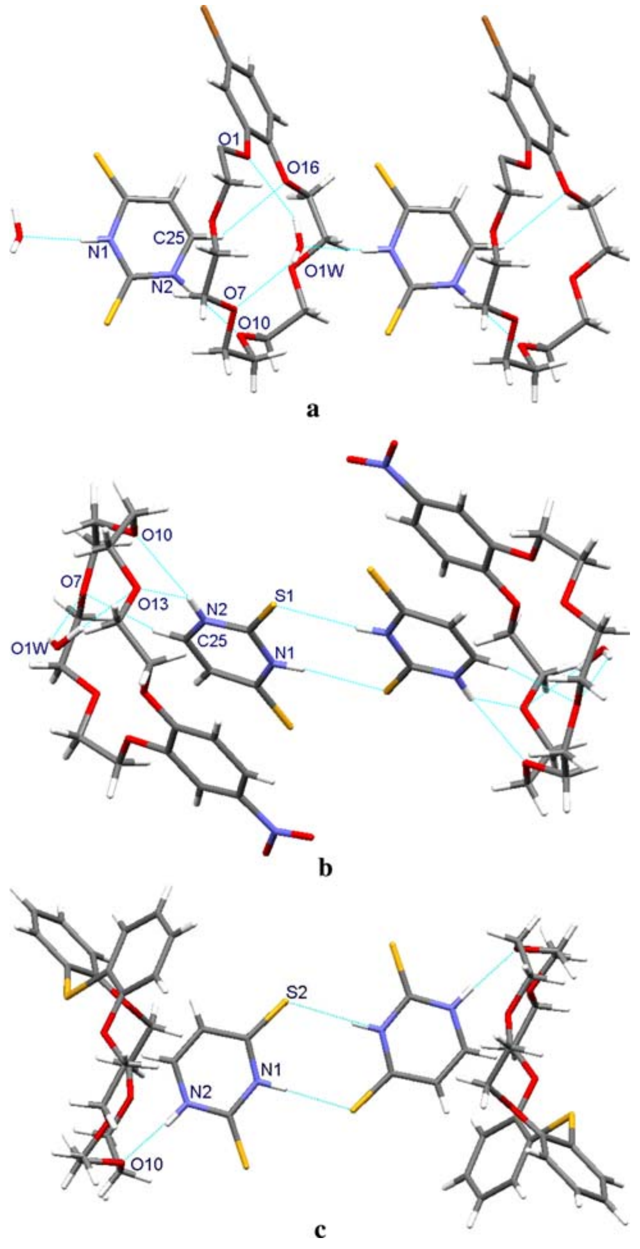


Fig. 3 Supramolecular organisation for **1**, **2**, **4**: (**a**) the chain fragment for **1**; (**b**) supramolecular capsule for **2**; (**c**) supramolecular capsule for **4**

one OH···O hydrogen bond (Table 2). The water molecule deviates at 1.802(4) Å from the least-square plane of six oxygen atoms of the CE, which are coplanar within ±0.262 Å. In this complex the water molecule does not exhibit its typical bridging function, and does not have any direct contacts with the DTU molecule. We observe here the novel six-membered type of the capsule (Fig. 3b).

The binary complexes **3** and **4** represent the fine examples of the four-membered capsules relative to that one previously reported for the [1.5]DB18C6 [5a]. The unusual feature of **3** is a lack of the inversion center within the capsule. The N···S distances are slightly different, the dihedral angle between two planar S1/C27/N2/H2N moieties in the eight-membered H-bonded ring is equal to 9.9(3)°, and this deviation from the planarity confirms the P1 capsule symmetry (Fig. 2c).

Conclusion

Four novel complexes of 2,4-dithiouracil (DTU) with 18-membered benzo- and dibenzo-crown ethers (CE) were synthesized in approximately the same conditions and characterized by X-ray diffraction analysis. From six possible tautomeric forms of DTU, only 2,4-dithione form was registered in all crystalline products. The crystal structures revealed the three structural motifs: 1D chain ···***CE***···***water***···***DTU***···***CE***···, and two types of capsules $\boldsymbol{CE\cdots(DTU)_2\cdots CE}$ and $\boldsymbol{water\cdots CE\cdots (DTU)_2\cdots CE\cdots water}$. These supramolecular motifs are sustained by the diverse hydrogen bonding. In the first motif *all* hydrogen bonding interactions typical for the pure DTU were substituted by the interactions with the oxygen atoms of the water and crown ether molecules as the stronger hydrogen acceptors. In the two types of capsules the only $R_2^2(8)$ NH···S base-pairing supramolecular synthon responsible for the coupling of the DTU molecules remains as a part of the DTU self-assembling in the pure form.

Supplementary material

Crystallographic data (excluding structure factors) for the structures in this article have been deposited with the Cambridge Crystallographic Data Center, deposition numbers CCDC 663173 (**1**), CCDC 663172 (**2**), CCDC 663170 (**3**), CCDC 663171 (**4**). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1233-336-033; E-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

References

1. Pedersen, C.J.: Cyclic polyethers and their complexes with metal salts. J. Am. Chem. Soc. **89**, 7017–7036 (1967)
2. Pedersen, C.J.: The discovery of crown ethers (noble lecture). Angew. Chem. Int. Ed. Engl. **27**, 1021–1027 (1988)
3. (a) Bradshaw, J.S., Krakowiak, K.E., Izatt, R.M.: Aza-Crown Compounds, vol. 51, 885 pp. Wiley, New York (1993); (b) Gokel, G.W., Leevy, W.M., Weber, M.E.: Crown ethers: sensors for ions and molecular scaffolds for materials and biological models. Chem. Rev. **104,** 2723–2750 (2004); (c) Gokel, G.W., Carasel, I.A.: Biologically active, synthetic ion transporters. Chem. Soc. Rev. **36**, 378–389 (2007); (d) Steed, J.W.: First- and second-sphere coordination chemistry of alkali metal crown ether complexes. Coord. Chem. Rev. **215**, 171–221 (2001); (e) Bond, A.H.,

Dietz, M.L., Chiarizia, R.: Incorporating size selectivity into synergistic solvent extraction: a review of crown ether-containing systems. Ind. Eng. Chem. Res. **39**(10), 3442–3464 (2000); (f) Cusack, P.A., Smith, P.J.: Crown ethers in tin chemistry. Appl. Organometal. Chem. **4**, 311–317 (1990)

4. (a) Simonov, Yu.A., Fonari, M.S., Zaworotko, M.J., Abourahma, H., Lipkowski, J., Ganin, E.V., Yavolovskii, A.A.: From 1D strands to extended supramolecular assemblies in the binary compounds of dithiooxamide and dithiobiurea with crown ethers. Org. Biomol. Chem. **1**, 2922–2929 (2003); (b) Fonari, M.S., Simonov, Yu.A., Kravtsov, V.Ch., Lipkowski, J., Ganin, E.V., Yavolovskii, A.A.: Hydrogen bonding assemblies in the host-guest complexes with 18-crown-6. J. Mol. Struct. **647**(1–3), 129–140 (2003)
5. (a) Ganin, E.V., Fonari, M.S., Simonov, Yu.A., Bocelli, G., Basok, S.S., Tkachuk, V.V., Kotlyar, S.A., Kamalov, G.L.: Structure of dibenzocrown ethers and their H-bonded adducts. 2. [1.5]Dibenzo-18-crown-6, a suitable building block to modulate the supramolecular assemblages sustained by conventional and weak hydrogen bonds. J. Incl. Phenom. **52**, 63–74 (2005); (b) Kotlyar, S.A., Fonari, M.S., Simonov, Yu.A., Bocelli, G., Shishkin, O.V., Shishkina, S.V., Tkachuk, V.V., Grigorash, R.Ya., Kamalov, G.L.: Structure of dibenzocrownethers and their H-bonded adducts. 1. [1.5]Dibenzo-18-crown-6 and biphenyl-20-crown-6: complexes with amidosulfuric acid. J. Incl. Phenom. **52,** 75–84 (2005)
6. Kiviniemi, S., Nissinen, M., Kolli, T., Jalonen, J., Rissanen, K., Pursiainen, J.: Crown ether complexes of six-membered N-heteroaromatic cations. J. Incl. Phenom. **40**, 153–159 (2001)
7. (a) Simonov, Yu.A., Fonari, M.S., Lipkowski, J., Yavolovskii, A.A., Ganin, E.V.: Preparation and X-ray study of inclusion complexes of (4*Z*,5*E*)-pyrimidine-2,4,5,6(1*H*, 3*H*)-tetraone 4,5-dioxime and the product of its cyclization, (1,2,5)-oxadiazolo(3,4-*d*)-pyrimidine-5,7(4*H*,6*H*)-dione with two 18-membered macrocycles. J. Incl. Phenom. **46**(1–2), 27–36 (2003); (b) Fonari, M.S., Simonov, Yu.A., Chumakov, Yu.M., Bocelli, G., Ganin, Ed.V., Yavolovskii, A.A.: The dihydropyrimidine-2,4-(1H,3H)-dione functionality: a suitable module for novel crown-containing hydrogen-bonded supramolecular assemblies. Supramol. Chem. **16**(1), 23–30 (2004)
8. (a) Rostkowska, H., Szczepaniak, K., Nowak, M.J., Leszczynski, J., KuBulat, K., Person, W.B.: Thiouracils. 2. Tautomerism and infrared spectra of thiouracils. Matrix-isolation and ab initio studies. J. Am. Chem. Soc. **112**, 2147–2160 (1990); (b) Leszczynski, J., Lammertsma, K.: 2,4-Dithiouracil tautomers: structures and energies. J. Phys. Chem. **95**, 3128–3132 (1991); (c) Leš, A., Adamowicz, L.: Tautomerism of 2- and 4-thiouracil. Ab initio theoretical study. J. Am. Chem. Soc. **112**, 1504–1509 (1990); (d) Lapinski, L., Rostkowska, H., Nowak, M., Kwiatkowski, J., Leszczynski, J.: Infrared spectra of thiouracils: experimental matrix isolation and ab initio Hartree-Fock, post-Hartree-Fock and density functional theory studies. Vib. Spectrosc. **13**, 23–40 (1996); (e) Yekeler, H.: Ab initio study on tautomerism of 2-thiouracil in the gas phase and in solution. J. Comput. Aided Mol. Des. **14**, 243–250 (2000); (f) Wang, H., Meng, F., Xu, W., Liu, C.: The effects of incorporating 2,4-dithiouracil into uracil tetrad: a theoretical study. J. Mol. Struct. THEOCHEM **716**, 137–141 (2005); (g) Gomzi, V., Herak, J.N.: Ionization potentials of nucleobase analogs using partial third-order electron propagator method. J. Mol. Struct. THEOCHEM **683**, 155–157 (2004); (h) Yang, Z., Rodgers, M.T.: Influence of thioketo substitution on the properties of uracil and its noncovalent interactions with alkali metal ions: threshold collision-induced dissociation and theoretical studies. J. Phys. Chem. A **110**(4), 1455–1468 (2006)
9. (a) Shefter, E. Mautner, H.G.: The crystal and molecular structure of 2,4-dithiouracil. J. Am. Chem. Soc. **89**, 1249–1253 (1967); (b) Tiekink, E.R.T.: Crystal structure of 2-thiouracil. Z. Kristallogr. **187**, 79–84 (1989); (c) Fonari, M.S., Simonov, Yu.A., Ganin, E.V., Yavolowski, A.A., Luboradzki, R.: Crystal and molecular structures of the 1:2 “host-guest” complex between *cis-anti-cis* isomer of dicyclohexano-18-crown-6 and 2-thiouracil. Crystallogr. Rep. **44**, 1006–1009 (1999)
10. Wang, W.-J., Ganin, E.V., Fonari, M.S., Simonov, Yu.A., Bocelli, G.: 2,4-Dithiouracil: the reproducible H-bonded structural motifs in the complexes with 18-membered crown ethers. Org. Biomol. Chem. **3**, 3054–3058 (2005)
11. Etter, M.C., Frankenbach, G.A.: Hydrogen-bond directed cocrystallization as a tool for designing acentric organic solids. Chem. Mater. **1**, 10–12 (1989)
12. Allen, F.N.: The Cambridge Structural Database: a quarter of a million crystal structures and rising. Acta Crystallogr. **B58**, 380–388 (2002)
13. (a) Goldberg, I.: Geometry of the ether, sulphide and hydroxyl Groups and structural chemistry of macrocyclic and non-cyclic polyether compounds. In: Patai, S., Rappaport, Z. (eds.) Crown Ethers and Analogs, pp. 359–476. Wiley (1989); (b) Abramson, S., Berkovich-Berger, D., Dagan, S., Goldberg, I., Golender, L., Grabarnik, M., Lemcoff, N.G., Weinman, S., Fuchs, B.: Polythiacrown macro- and gigantocycles with chiral diacetal cores. Eur. J. Org. Chem. 1957–1975 (2007)
14. Kotlyar, S.A., Pluzhnik-Gladyr, S.M.: The development of convenient synthesis methods of halogenosubstituted benzo- and dibenzocrown ethers. In: Monomers for Thermotolerant Polymers (Russ.). Moscow. NIITECHIM, 74–80 (1990)
15. Ivanov, O.V., Markovich, I.S., Blokhina, L.I., Nikolaenko, S.P., Filatova, M.P.: The method of nitration of benzocrown ethers. Patent USSR, № 1544754 (1990). Bull. 1990, №7
16. Gorodnuyk, V.P., Ivanov, O.V., Kotlyar, S.A.: Simple synthesis of unsymmetrical dibenzocrown ethers. Chem. Heterocycl. Comp. (Russ.). **26**, 1414–1415 (1990) (translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1697–1698, 1990)
17. Sheldrick, G.M.: SHELXS97 and SHELXL97. Programs for Crystal Structure Solution and Refinement. University of Göttingen, Germany (1997)
18. (a) Kotlyar, S.A., Shishkina, S.V., Shishkin, O.V., Pluzhnik-Gladyr, S.M., Kiriyak, A.V., Chuprin, G.N., Kamalov, G.L.: (4-Bromobenzo-18-crown-6)potassium chlorochromate. Acta Crystallogr. **E62**, m120–m122 (2006); (b) Hlavata, D., Hasek, J., Huml, K.: The crystal and molecular structure of 4-nitrobenzo-1,4,7,10,13,16-hexaoxacyclooctadecane. RbSCN, $C_{17}H_{23}O_8N_2SRb$. Acta Crystallogr. **B34**, 416–420 (1978); (c) Hasek, J., Hlavata, D., Huml, K.: Crystal and molecular structure of a complex formed by caesium thiocyanate and 4-nitrobenzo-1,4,7,10,13,16-hexaoxacyclooctadecane (4-nitrobenzo-18-crown-6). Acta Crystallogr. **B33**, 3372–3376 (1977); (d) Calleja, M., Johnson, K., Belcher, W.J., Steed, J.W.: Oxonium ions from aqua regia: isolation by hydrogen bonding to crown ethers. Inorg. Chem. **40**, 4978–4985, (2001); (e) Talanova, G.G., Elkarim, N.S.A., Talanov, V.S., Hanes Junior, R.E., Hwang, H.-S., Bartsch, R.A., Rogers, R.D.: The “picrate effect” on extraction selectivities of aromatic group-containing crown ethers for alkali metal cations. J. Am. Chem. Soc. **121**, 11281–11290 (1999); (f) Fonari, M.S., Ganin, E.V., Gelmboldt, V.O., Lipkowski, J., Kotlyar, S.A., Kamalov, G.L.: The 1:1 adduct of antimony trifluoride with [1.5]dibenzothia-18-crown-6. Acta Crystallogr. **E62**, m1021–m1023 (2006)
19. (a) Brewer, A.D., Ferguson, G., Parvez, M.: Triethylammonium salt of 1,2,3,4-tetrahydro-6-hydroxy-4-oxo-N-phenyl-2-thio-5-pyrimidinecarboxamide, ethanol solvate. Acta Crystallogr. **C43**, 144–147 (1987); (b) Tiekink, E.R.T.: Crystal and molecular structure of 5-carboxy-2-thiouracil monohydrate. Z. Kristallogr. **216**, 122–125 (2001)