DOI: 10.1002/ejoc.200700162

Triuracils – 1,3-Bis[ω-(*N*-methyluracil-1-yl)alkyl]thymines and Their 5,5′-Cyclic Counterparts

Vyacheslav E. Semenov,*[a] Leisan F. Galiullina,[a] Olga A. Lodochnikova,[a] Olga N. Kataeva,[a] Aidar T. Gubaidullin,[a] Alla V. Chernova,[a] Yurij Y. Efremov,[a] Shamil K. Latypov,[a] and Vladimir S. Reznik[a]

Keywords: Nucleobases / Macrocycles / Structure elucidation

A series of acyclic compounds with two 3,6-dimethyluracil or 3-methyluracil units attached to a a thymine or isocyanurate fragment by polymethylene or xylylene spacers are investigated. Ring-closure reactions with paraformaldehyde in aqueous HCl in the presence of copper(I) chloride afforded pyrimidinophanes which can be considered macrocyclic counterparts of the acyclic triuracils. By X-ray diffraction data the structures of the macrocycles in the solid state are characterised by a close arrangement of the uracil units, but there are no π-π contacts between them. On the contrary, significant hypochromism of the macrocyclic triuracils compared with their acyclic counterparts indicates stacking between the thymine and 3,6-dimethyluracil units in chloroform and H_2O solutions. The conformational behaviour of the acyclic and macrocyclic compounds in solution has been determined by NMR, UV and computational methods.

Introduction

Pyrimidinophanes are cyclophanes containing pyrimidine bases as the aromatic rings. Pyrimidinophanes are of interest in connection with their stacking structures in DNA, the formation of pyrimidine photodimers in DNA by ultraviolet light,[1] mechanistic studies on DNA photolyase,[2] and their complexation properties[3] and biological activity.[4] At the present time a variety of pyrimidinophanes are known and one can observe some features from the review of these compounds. Most of the pyrimidinophanes synthesised contain uracil or 5- or 6-substituted uracil units in which N_1 and N_3 are bridged by xylylene[3c,5] or polymethylene[6] spacers. The spacers can include one or more heteroatoms (O, N, S)[6b,7a–7d] and different functional groups, in particular OH or C=O.[4,7e,7f] A key step in the preparation of most of the (1,3)-pyrimidinophanes containing uracil units is the interaction of their disodium salt or *O*,*O*′-bis(trimethylsilyl)derivatives with a halogen-containing reagent. Pyrimidine rings can be bridged by their carbon atoms. For instance, [2.2](2,5)- and 2,11-dithia[3.3](2,5)-pyrimidinophanes[8a] have been synthesised starting from 2,5-dimethylpyrimidine, and the reaction of 1,3-bromophenyllithium with unsubstituted pyrimidine gave a series of (4,6)-phenylpyrimidinophanes.[8b,8c] Pyrimidinophanes with units bridged by nitrogen or sulfur in the substituents on the pyrimidine rings have also been reported.[9] The principal method of their preparation is the reaction of thio- or aminopyrimidine sodium salts with appropriate connecting agents. A series of macrocycles containing two 4-amino-2-mercapto-6-methylpyrimidines and one 6-methyluracil have been synthesised by the reaction of the disodium salts of *N*,*N*′-bis(2-mercapto-6-methylpyrimidine-4-yl)alkylenediamines with 1,3-bis(bromoalkyl)-6-methyluracils[9e] and these pyrimidinophanes were studied in detail by potentiometry, UV, ^{1}H NMR[10a,10b] and IR[10c,10d] spectroscopy. Pyrimidine rings have been involved in crown-ethers.[3a,3b,6b,11] Pyrimidino-crown ethers were prepared by treating the appropriate oligoethylene glycol with 2,4- or 4,6-substituted pyrimidine derivatives and tested for their complexation ability.

Although electrophilic substitution at C(5) position of the pyrimidine ring is much more favoured than such an attack at positions 2, 4 or 6, only a few examples of pyrimidinophanes with bridges at the carbon are known.[8a,12] The ability of uracil and its derivatives to give products with a C(5),C(5′) methylene bridge by reacting with paraformaldehyde in H_2O is well-known.[13] The first pyrimidinophane in which the uracil units are linked by a C(5),C(5′) methylene spacer has been synthesised using that reaction with paraformaldehyde to afford 5,5′-methylenebis[(2-hydroxyethyl)-3,6-dimethyluracil] starting from (2-hydroxyethyl)-3,6-dimethyluracil. Subsequently, the replacement of the hydroxyls with thiol groups and oxidation to disulfide bridges gave a macrocycle.[14] Recently we have reported a ring-closure reaction of acyclic bis(3,6-dimethyluracil-1-yl)-butane and 1,3-bis[4-(3,6-dimethyluracil-1-yl)butyl]thymine

[a] A.E. Arbuzov Institute of Organic and Physical Chemistry, Kazan, 420088, Arbuzov str. 8, Russian Federation
E-mail: sve@iopc.kcn.ru
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

with paraformaldehyde in H_2O in the presence of copper(I) chloride. Pyrimidinophanes containing four[15a] and three[15b] 3,6-dimethyluracil fragments, respectively, were obtained. Herein we present the synthesis of a series of acyclic 1,3-bis[ω-(3-methyl- or 3,6-dimethyluracil-1-yl)alkyl- or methylbenzene]thymines (**1**) as precursors for their C(5),C(5′) methylene counterparts (**2**) and the study of these triuracils in solution and as solids.

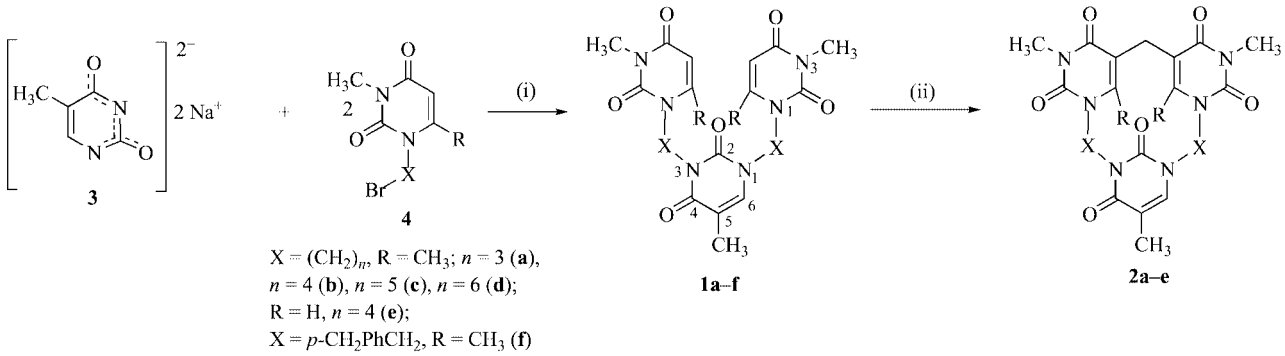
Acyclic compounds **1** consist of a thymine unit linked with two 3,6-dimethyluracil or 3-methyluracil fragments by hydrocarbon spacers and can be considered as simplified models of oligouridines, particularly triuracils. 3,6-Dimethyluracil, 3-methyluracil and thymine fragments are used as uracil units and hydrocarbon spacers are used as sugar phosphates. The rigidity of the spacers can be altered by varying the number of methylene groups in the alkyl chains or introducing a benzene ring. Such a system provides an opportunity to examine nucleotide-base interactions in the absence of the normal sugar phosphate structures that usually constrain them to Watson–Crick hydrogen-bonding interactions. Models of oligonucleotides consisting of two nucleotide bases (uracils or adenines or their combination) bridged by a polymethylene chain have been well-known for almost 40 years[16] and at present they are studied in particular by means of NMR spectroscopy.[17] Meanwhile there are very few examples of more complicated models especially with cleft-like topology which is represented by two nucleotide bases tethered to a rigid platform. Shall and Gokel prepared and carried out an NMR study of lariat ethers based upon 4,13-diaza-18-crown-6 having $–(CH_2)_3–$ sidearms terminated in adenine or thymine.[18] The data showed that these cleft-like ethers allow one to simulate intra- or intermolecular hydrogen-bond boxes between or among nucleotide bases which are additionally organised by π-stacking. In compounds **1** *N*-methyl-substituted uracil fragments terminate $–(CH_2)_n–$ or xylylene sidearms attached to a rigid pyrimidine ring. In this case the classical hydrogen bonding between the units is excluded due to the absence of imido groups and the observed effects are determined only by the π-π interactions of the uracil fragments. These acyclic compounds present the opportunity to determine the contribution of a "pure" stacking effect in the mutual arrangement of nucleotide bases in a three-dimensional structure since the contribution of hydrogen bonds is absent.

Pyrimidinophanes **2** can be considered macrocyclic counterparts of acyclic compounds **1**. *N*-(3)-Methyl uracil units in the macrocycles are bridged to form a 5,5′-(uracilyl)-methane moiety. How does the cyclisation influence conformational behaviour, the lability of the pyrimidinophanes, the mutual arrangement of uracil units with respect to acyclic counterparts? What interactions are responsible for conformational alterations due to ring closure especially in solution? The acyclic and macrocyclic triuracils **1** and **2** offer suitable models for NMR and UV methods in solution to observe conformational alterations which accompany variations in the rigidity of the compounds, to determine the driving forces of the mutual orientation of the uracil units. These structural data have a direct connection with the study of the behaviour of oligonucleotides in solutions, particularly those containing *N*-methyl uracils, which are minor components of nucleic acids.

Results and Discussion

Synthesis of Acyclic and Macrocyclic Triuracils

The synthesis of compounds **1** and **2** is represented in Scheme 1. Acyclic triuracils **1a**–**g** were prepared in moderate yields by the reaction of the disodium salt of thymine **3** with a two-fold excess of 1-(ω-bromoalkyl)uracil **4a**–**e** or 1-[4-(bromomethyl)phenylmethyl-1]-3,6-dimethyluracil **4f**. Yields with **4a**–**d** increase from 30% to 67% as the polymethylene-chain length increases with the exception of compound **1c** (30% yield). The subsequent ring-closing acid-catalysed reaction with paraformaldehyde in 0.5 M HCl in the presence of copper(I) chloride (**5**) afforded the macrocyclic triuracils **2a**–**e** in 3–30% yield. The other products of the reactions were not purified and it seemed they had a non-cyclised topology. Macrocyclisation into pyrimidinophanes **2a**–**e** was unambiguously confirmed by EIMS and NMR spectroscopic data. In the high-resolution mass spectra of the pyrimidinophanes the molecular ion peak is the



Scheme 1. Synthesis of the acyclic and macrocyclic triuracils. Reagents and conditions: (i) DMF, 60–70 °C; (ii) paraformaldehyde, Cu_2Cl_2, 0.5 M HCl, reflux.

most intense and its mass was in very good agreement with the calculated value. The only fragment in the region of heavy masses was $[M - CH_3]^+$.

Pyrimidinophane **2a** was obtained in low yield (3%); however when there are 4, 5 or 6 methylene groups in the spacers the yields dramatically increase to 28–30%. A small yield of **2a** can be explained by the arrangement of the 3,6-dimethyluracil units not being suitable for C(5)CH_2C(5′) bridge formation. Attempts to cyclise compound **1f** under the same conditions were unsuccessful due to concurrent reactions of formaldehyde with the benzene rings. In pyrimidinophane **2e** 3-methyluracil units were introduced, the reaction time was 70 h, and the yield was only 12% instead of 35 h and 28% for **2b**, which has the same number of the methylene groups in the spacers. It is obvious that the absence of an electron-releasing substituent at C(6) of the 3-methyluracil fragment causes a low yield under these conditions. The electrophilic attack at C(5) of the uracils by formaldehyde is more favoured when there is at least a methyl group at C(6). It is known that the presence of the strongly electron-releasing amino group at C(6) position allows the preparation of diverse 5,5′-bis(uracilyl)methanes even in neutral medium by the reaction with not only formaldehyde but also with other aldehydes.[13a]

At first we used salt **5** in the synthesis of pyrimidinophanes containing four 3,6-dimethyluracil units.[15a] Also the introduction of **5** into the reaction of acyclic compound **1a**–**e** with paraformaldehyde afforded the 5,5′-cyclic product. It was shown by EIMS of the reaction mixtures that in the absence of **5** only traces of the desired pyrimidinophanes were formed. Moreover using copper(II) salts instead of **5** did not promote the ring closure. The participation of monovalent copper ions in the reactions of the cyclisation is not clear. It can be proposed that copper(I) ions are able to coordinate the *N*-alkylated uracil facilitating the formation of the C(5)CH_2C(5′) spacer.

The complete structure elucidation of compounds **1** and **2** was carried out by a variety of correlation NMR methods

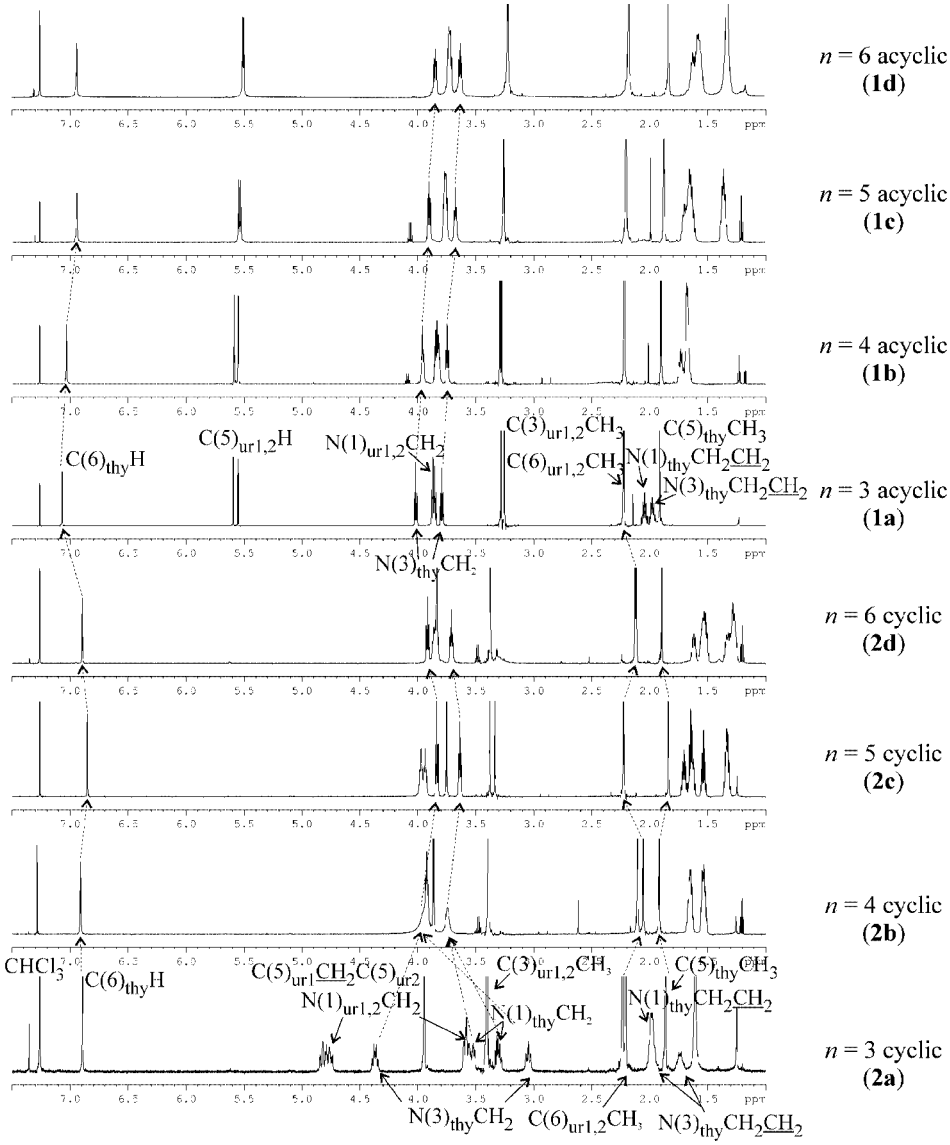


Figure 1. ^{1}H NMR spectra of compounds **1a**–**d** and **2a**–**d** in $CDCl_3$ (303 K).

(COSY, TOCSY, HSQC, HMBC, and NOESY).[19] The analysis will be considered in detail only for the pyrimidinophane **2a**. For the other macrocycles and acyclic counterparts an analogous approach was applied unless stated otherwise.

The ^{1}H NMR spectrum of **2a** is presented in Figure 1. Firstly, the two spin systems related to the aliphatic spacers were distinguished. The process started from the easily assigned $C(6)_{thy}H$ (δ_H = 6.91 ppm).[20] The observed NOE between $C(6)_{thy}H$ and the two terminal NCH_2 protons allowed us to assign unambiguously these resonances to the geminal $N(1)_{thy}CH_2$ protons. Then other proton resonances were identified by analysing the observed TOCSY correlations (Figure 2A). There were NOESY cross peaks between $N(1)_{ur1}CH_2$ and $C(6)_{ur1}CH_3$ and between $N(1)_{ur2}CH_2$ and $C(6)_{ur2}CH_3$. Therefore the signals of the $C(6)CH_3$ groups were also assigned. Based on HSQC experiment data the signals of the $C(5)_{thy}$, NCH_3 and $C(5)_{ur1}CH_2C(5)_{ur2}$ were identified, and based on HMBC correlations (Figure 2A) of C(2), C(4) and C(6) these signals of thymine and *N*-methyluracils were also identified. In addition cross peaks between $C(6)_{thy}H$ and $N(1)_{thy}CH_2$ confirmed the accuracy of aliphatic spacer assignment. There were cross peaks between $C(2)_{thy}$ and the $N(1)_{thy}CH_2$ and $N(3)_{thy}CH_2$ protons of the aliphatic chains in the 2D HMBC spectrum, which proved that the thymine unit and the three methylene spacers were coupled. Moreover cross peaks between $N(1)_{ur1}CH_2$ protons and $C(2)_{ur1}$ and $C(6)_{ur1}$ were observed. These similar cross peaks indicate the coupling of the second spacer with the second uracil moiety. There were also cross peaks in the 2D HMBC spectrum between $C(5)_{ur1}$, $C(5)_{ur2}$ and the $C(5)_{ur1}CH_2C(5)_{ur2}$ bridge protons.

The chemical structure of **1a** was determined analogously. In contrast to the ^{1}H NMR spectrum of pyrimidinophane **2a** in the ^{1}H NMR spectrum of its acyclic counterpart **1a** the geminal CH_2 protons of the middle carbon of the spacer were found to be equivalent (Figure 1). The key TOCSY and HMBC correlations for compound **1a** are summarised in Figure 2B. Similar NMR 2D experiments were performed for the macrocycles and their acyclic counterparts with longer spacers (n = 4–6). The observed homo- and heteronuclear correlations unambiguously confirmed the chemical structure of all the title compounds. The details can be found in the Supporting Information.

To elucidate the role of the thymine fragment in the structural features and conformational behaviour of the title triuracils it was proposed to replace the thymine unit with another *N*-heterocyclic moiety. Acyclic and macrocyclic compounds **6** and **7** based on methyl-substituted isocyanuric acid (Scheme 2) have been synthesised under the same conditions as were used for pyrimidinophanes **2a**–**e**

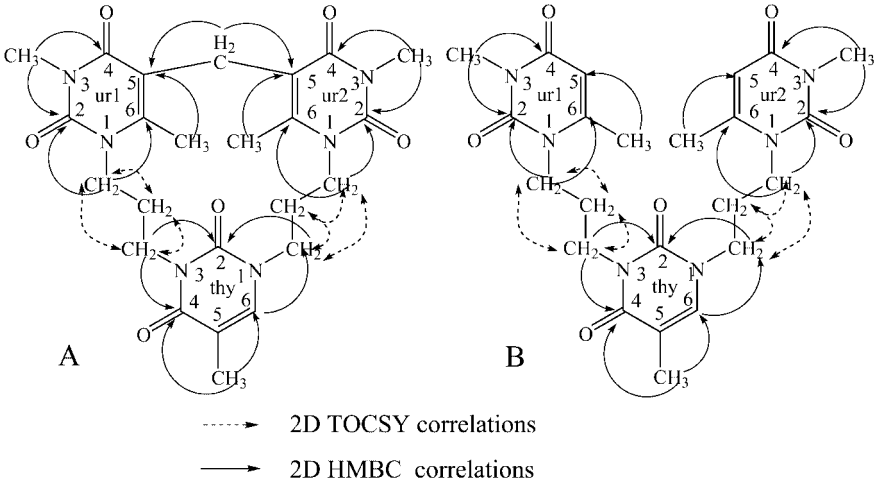
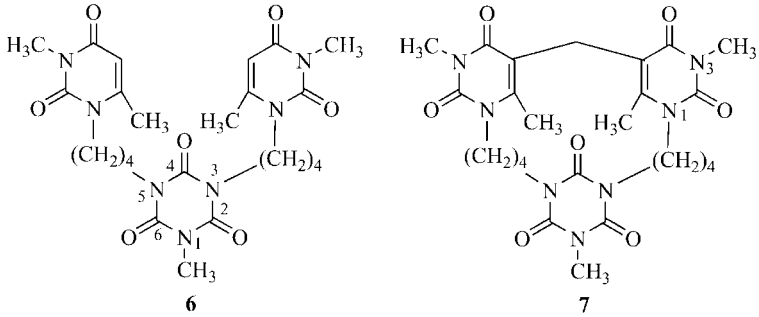


Figure 2. The TOCSY and HMBC key correlations for the compounds **2a** (A) and **1a** (B). In this figure the thymine unit is designated as thy and the 3,6-dimethyluracil or 3-methyluracil moieties attached to $N(3)_{thy}$ and $N(1)_{thy}$ are designated as ur1 and ur2, respectively.



Scheme 2. Acyclic and macrocyclic compounds with isocyanurate and 3,6-dimethyluracil units.

replacing **3** with the disodium salt of nonaromatic 1-methyl-1,3,5-triazin-2,4,6(1*H*,3*H*,5*H*)-trione. It is worth noting that macrocycle **7** was isolated in 46% yield, which significantly exceeds the yields of the thymine-based macrocycles.

Solid-State X-ray Studies

Pyrimidinophane **2b** crystallised from DMSO as a **2b**·DMSO·H_2O complex. It was found that one carbonyl group on the thymine unit was disordered and the oxygen of the group exhibits a 50% occupation at C(22) and C(24) (Figure 3, parts A and B). The structure in Figure 3 (A) would be absolutely identical with the structure shown in part B of the figure if the thymine unit was turned 180°. These structures can be considered as configurational isomers. It is evident that the molecules with different orientation of the thymine fragment were formed upon cyclisation, and they can be distinguishable only in crystal but not in solution.

Pyrimidinophane **2b** contains extended polymethylene chains with prevailing *trans* conformations, and as a result there are no short contacts between the thymine and either uracil. The distances between the centres of the thymine ring N(1)C(25)N(21)C(22)C(23)C(24) and 3,6-dimethyluracil rings N16C15N14C13C12C26 (ur1), N6C7N8C9C10C27 (ur2), are 6.05 Å and 6.34 Å, respectively. The dihedral angles are 48.48° and 31.57°, respectively. The dihedral angle between the planes of ur1 and ur2 is about 80° and the distance between their centres is 5.10 Å.

When polymethylene spacer length increases up to five methylene groups, the geometry of pyrimidinophane molecules in the crystal alters. This was demonstrated by the X-ray data for macrocycle **2c**, which was crystallise from

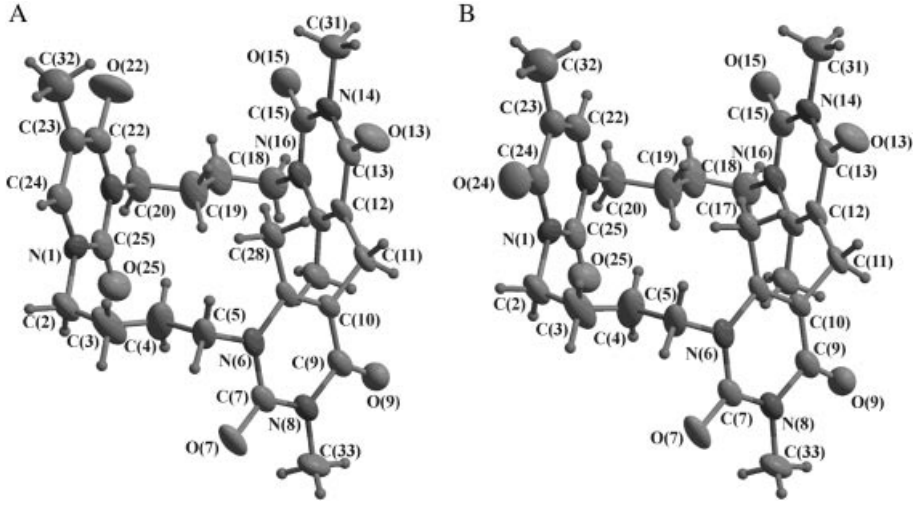


Figure 3. X-ray crystal structure of pyrimidinophane **2b** with carbonyl oxygen at (A) C(22) and (B) C(24) of the thymine unit.

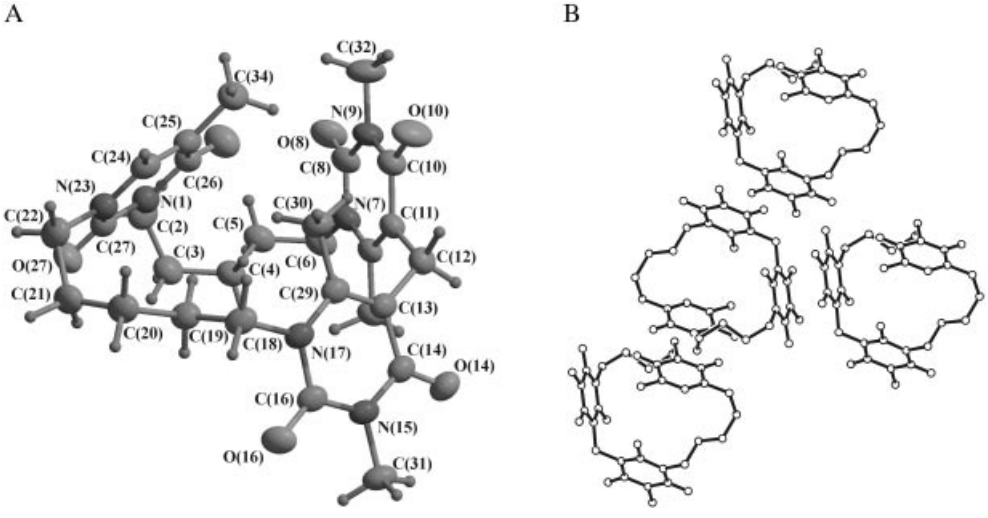


Figure 4. (A) X-ray crystal structure of pyrimidinophane **2c** crystallising from CH_3CN solution. The solvate CH_3CN molecules are not shown. (B) Diagram showing the π-π interactions of pyrimidinophane **2c** with three neighbouring molecules.

CH_3CN and DMSO solutions. In both cases the macrocycle crystallised with solvent molecules and have almost the same geometry. The X-ray crystal structure of the pyrimidinophane from DMSO showed the presence of two crystallographically independent molecules (A and B) in the unit cell, which had the same environment around themselves and therefore the same bonds and angles. The geometry of **2c** is depicted in Figure 4 (A). In contrast to **2b** gauche conformations in the polymethylene spacers prevail, and the C2–C6 chain is more bent. As a result the thymine unit is in proximity with the 3,6-dimethyluracil fragment defined as the N7C8N9C10C11C28 (ur1). In particular, the distance between C8 and O26 is 3.16 Å, indicating that these atoms are in van der Waals contact. The distance between the centres of the thymine and ur1 centroids is 5.42 Å, while that between the centres of the thymine ring and ur2 defined as C13C14N15C16N17C29 is 6.16 Å. The dihedral angle between the planes of ur1 and ur2 is 79.64°, which is almost the same as that for pyrimidinophane **2b**. However the dihedral angles between thymine and ur1 and thymine and ur2 are larger than those for **2b** (61.33° and 65.86°, respectively). Thus, in pyrimidinophane **2c** the uracil and thymine units are closer than they are in **2b** and in general the structure of **2c** can be considered folded. At the same time there is no evidence for intramolecular π-π interactions in **2b** as there is in **2c**, since the pyrimidine rings of the thymine and uracil moieties are not in parallel planes and the distance between their centres significantly exceeds 4 Å.

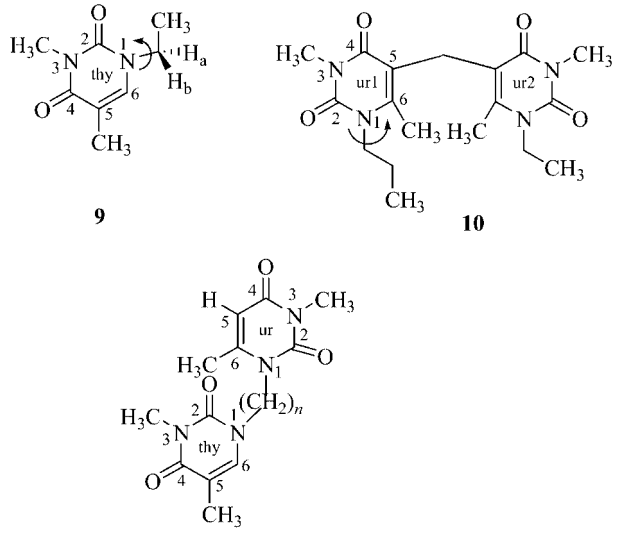
On the other hand the macrocycles **2b** and **2c** show the same crystal packing. Each pyrimidinophane molecule of is connected to three other symmetry-related molecules through intermolecular face-to-face π-π interactions of the uracil units, as is shown in part B of Figure 4. The distances between the rings are 3.3–4.3 Å, and these rings are practically in parallel planes.

Solution-State NMR and Computational Studies

A preliminary analysis of ^1H (Figure 1) and ^{13}C NMR spectra of pyrimidinophanes and their acyclic counterparts (see the Supporting Information for details) showed that the NMR spectra of the macrocycles are much different from that of their acyclic analogues. It was also observed that the NMR spectra of the macrocycles depended strongly on the length of the spacers. In the ^1H NMR spectrum of macrocycle **2a** (Figure 1) with three methylene groups in the spacers the geminal CH_2 protons are non-equivalent. This result corresponds to slow conformational exchange on the NMR time scale and means that the three-dimensional structure of this molecule is rigid. When the length of the spacers increase, the exchange rate rises. In the spectrum of pyrimidinophane **2b** with four methylene groups in the spacers each CH_2 group has only one signal, but the $N(1)_{thy}CH_2$ and $N(3)_{thy}CH_2$ signals are broadened. Thus, macrocycle **2b** takes part in some conformational exchange process with a medium exchange rate on the NMR time scale at 303 K. When the length of the spacers increase up to five or six methylene groups, the lines of the signals are narrowed, and the ^1H NMR spectra are observed under conditions of fast conformational exchange on the NMR time scale. The chemical shifts (δ) of $C(6)_{ur1,ur2}CH_3$, $C(6)_{thy}H$ and $N(1)_{thy}CH_2$ and $N(3)_{thy}CH_2$ of pyrimidinophanes change with the variation of spacer length. Moreover the δ of $C(6)_{ur1}$ and $C(6)_{ur2}$ of macrocycle **2a** are deshielded compared with the ones in macrocycles **2b** and **2c**. Some differences in the δ of the protons and carbons of the $C(5)_{ur1}CH_2C(5)_{ur2}$ bridge are also observed which could be related to the different mutual arrangement of the 3,6-dimethyluracil units.

In acyclic triuracils **1a**–**d** when the spacer length increases, the δ of the proton signals does not change except for $C(6)_{thy}H$. In all the spectra of the acyclic compounds the geminal protons of CH_2 groups of the aliphatic chains are found to be equivalent. Thus we can conclude that acyclic compounds are in fast conformational exchange on the NMR time scale and the rate of exchange does not depend on spacer length. The carbon δ of the acyclic triuracils with different numbers of methylene groups in the spacers are almost the same. The exceptions are the δ of $N(1)_{thy}CH_2$ and $N(3)_{thy}CH_2$ which are deshielded with the lengthening of the spacers.

To explain the observed effects the δ changes of the acyclic and macrocyclic compounds were analysed theoretically. Optimisation of the geometry was carried out at the RHF level using the 6-31G basis set. GIAO DFT calculations of δ values were performed at the RB3LYP/6-31G(d) theory level.[21] The δ values of models **9**, **10** and **11a**–**d** (Scheme 3) were calculated in order to see if the proton and carbon δ changes of the thymine unit and $N(1)_{thy}CH_2$ group of the spacers are caused by geometrical parameters and/or electron-density transfer through chemical bonds.



Scheme 3. Model compounds for the calculation of ^{13}C NMR δ of the thymine and uracil units, and $N(1)_{thy}CH_2$ group of the spacers.

Firstly, to evaluate the dependence of δ on the valence angles between the corresponding bonds ^1H and ^{13}C δ calculations of model **9** were carried out on the different orientations of the spacer around the $N(1)_{thy}$–CH_2 bond. The results are represented in Figure 5. As one can see the protons of the $N(1)CH_2$ group are the most sensitive to the spacer orientation. When the angle between the thymine plane and the aliphatic spacer {[O=C(2)–N(1)–CH_2]–CH_2} is about 90°, the difference between the δ of $N(1)CH_a$ and $N(1)CH_b$ is ca. 1.5 ppm. This is very close to the experimental value of the δ difference for these protons in pyrimidinophane **2a**, and it can be well explained by conformational features of this compound, in particular by the angles between the spacers and the thymine plane. In addition according to theory the δ of $C(6)_{thy}H$ should strongly depend on the angle between the spacer and the thymine plane. Therefore, taking into account that the experimental δ of $C(6)_{thy}H$ is almost the same for all compounds one can conclude that the angle between the spacers and the thymine plane remains approximately the same in all these structures.

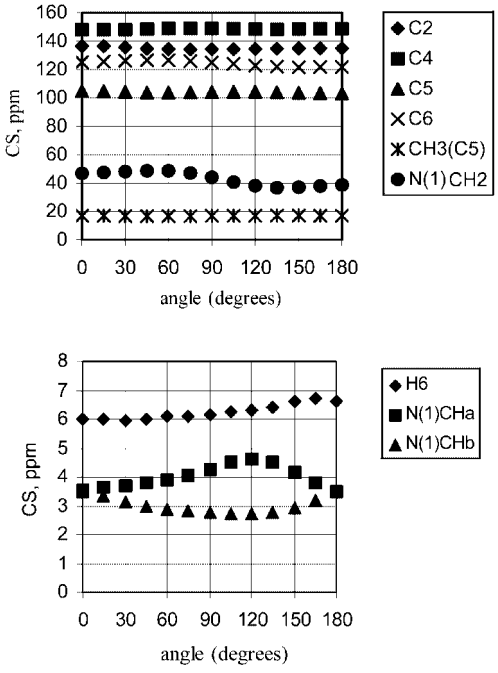


Figure 5. The dependence of ^1H and ^{13}C NMR δ of model **9** on the [O=C(2)–N(1)–CH_2]–CH_2 angle.

Model **10** is used to explain the change of δ of the $C(6)_{ur1}$ and $C(6)_{ur2}$ signals with the orientation of the spacers in compounds **2a**–**d**. As one can see the δ of these carbon atoms depend remarkably on the dihedral angle (Figure 6). At 0° the $C(6)_{ur1}$ signal is deshielded and it shifts upfield by about 2.5–3 ppm at –30° or 30°. Thus, taking into account that in macrocycle **2a** $C(6)_{ur}$ carbons resonate at lower fields [151.4(ur1) ppm and 151.2(ur2) ppm] than the same carbons in macrocycles **2b**, **2c**, and **2d** (148.9 ppm and 149.1 ppm, 149.0 ppm and 148.6 ppm and 149.2 ppm and 148.9 ppm, respectively) we can conclude that the angle between the spacers and the uracil plane in pyrimidinophane **2a** is close to 0°, while in pyrimidinophanes **2b**–**2d** it increases up to 20°.

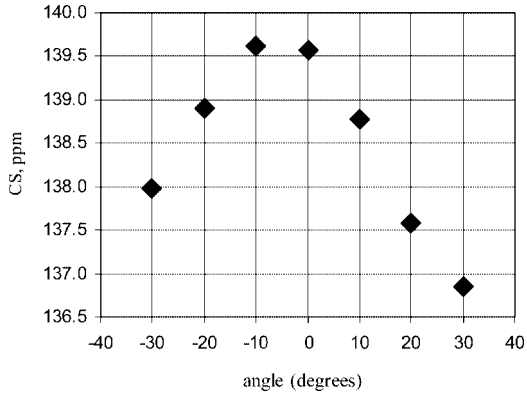


Figure 6. The dependence of the δ of $C(6)_{ur1}$ on the C–C bond angle in the $N(1)_{ur1}CH_2$–CH_2 fragment.

Finally, to explain the dependence of the δ of the $N(1)_{thy}CH_2$ and $N(1)_{ur}CH_2$ signals on spacer length in the spectra of acyclic triuracils **1a**–**d** non-empirical calculations of optimised geometry and δ values of model compounds **11a**–**d** with different spacer lengths were carried out. For all compounds **11a**–**d** there is good agreement between theoretically and experimentally obtained ^1H and ^{13}C δ values of the spacer signals. According to the calculations in compound **11b** the $N(1)_{thy}CH_2$ and $N(1)_{ur}CH_2$ signals are deshielded by 3.8 ppm and 2.4 ppm, respectively, in comparison with those for compound **11a**. With a further increase of the spacer length the deshielding decreases and in compound **11c** the same δ values are 1.4 ppm and 0.7 ppm, respectively. In compound **11d** the δ values of $N(1)_{thy}CH_2$ and $N(1)_{ur}CH_2$ remain almost the same. All these effects are in agreement with experimental δ values. Thus, experimentally observed differences in the δ of $N(1)_{thy}CH_2$ and $N(1)_{ur}CH_2$ evidently can be explained by the increasing distance between the thymine and uracil units alone. In the case of compound **11a** with $n = 3$ there is a γ-effect of uracil influence, but with **11b** ($n = 4$) the δ-effect takes place and so on for **11c**,**d**. The theoretically obtained spectra of **11a**–**d** are shown in Figure 7.

Thus, based on theoretical investigations we can propose some hypotheses about the conformations of the pyrimidinophanes in $CDCl_3$ solution. Namely, the angle between the spacer and the thymine plane is close to 90° and it leads to an overall folded conformation of the macrocycle. On the other hand alterations of the ^{13}C δ values of $N(1)_{thy}CH_2$ and $N(3)_{thy}CH_2$, and $N(1)_{ur1,2}CH_2$ are explained by the different influence of the uracil units on those methylene groups. The shifts in the δ of $C(6)_{ur1,ur2}$ are caused by the increasing angle between the CH bonds of the spacer and the uracil plane with increasing spacer length.

To determine the 3D structure of compounds **1** and **2** NOESY experiments in $CDCl_3$ were carried out. For acyclic triuracils **1a**–**e** there are no NOEs which can be evidence of an especially rigid conformation. At the same time

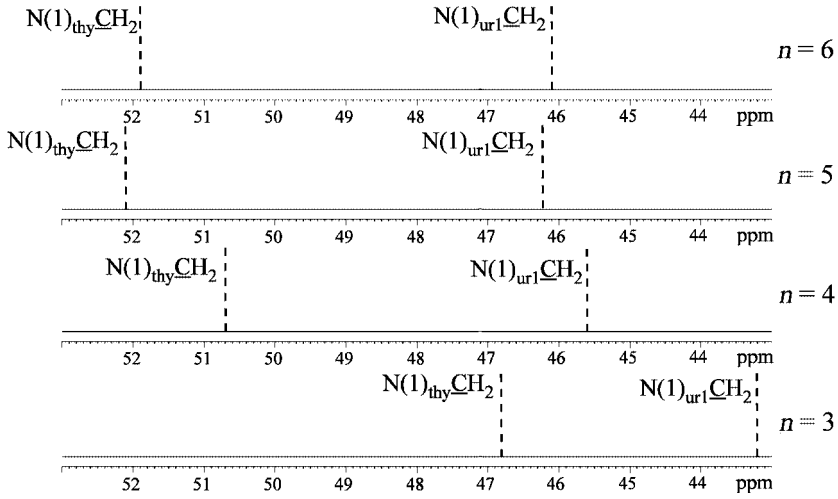


Figure 7. Schematic presentation of theoretically obtained partial ^{13}C NMR spectra for models **11a**–**d**.

for their macrocyclic counterparts there are a number of indicative NOEs. Especially for **2a** with three methylene groups in the spacers there are NOEs between $N(1)_{ur1}CH_2$, $N(1)_{ur2}CH_2$, $N(1)_{thy}CH_2CH_2$, and $N(3)_{thy}CH_2CH_2$ of the spacers and $C(6)_{thy}H$ (Figure 8, A). Thus we can conclude that the most stable conformation of this macrocycle in solution is folded. For the pyrimidinophane **2b** with four methylene groups in the spacers cross peaks in the NOESY spectrum between $C(6)_{ur1,ur2}CH_3$ and $N(3)_{thy}CH_2$ are also indicative of a folded conformation, which correlates with the structure of **2b** in the solid state and in particular with the 5.0–5.7 Å distance between those protons. Also in the spectrum of macrocycle **2c** (n = 5) NOEs between $C(5)_{thy}CH_3$ and $N_{ur1}CH_3$, $C(5)_{thy}CH_3$ and $N_{ur2}CH_3$, and $C(6)_{thy}H$ and $N_{ur1}CH_3$ are observed. Consequently in solution a folded conformation dominates for pyrimidinophane **2c**. Additionally in the solid state these distances are quite short (2.8–3.1 Å) and the uracil units are in proximity. Finally for the macrocycle **2d** with six methylene groups in the spacers there are no NOEs. This is probably due to the spacer length and to the fact that this molecule exists in solution in a fast exchange between several forms on the NMR time scale.

Further, the 3D structure of the macrocycle **2e** was investigated. There is a great difference between the δ values of the bridging $C(5)_{ur1}CH_2C(5)_{ur2}$ in pyrimidinophanes **2a**–**d** and **7** (3.75–3.96 ppm) which contain 3,6-dimethyluracil units and pyrimidinophane **2e** (δ = 3.39 ppm) which contains 3-methyluracil units. In Figure 9 the ^1H NMR spectrum of pyrimidinophane **2e** is compared with the spectrum of pyrimidinophane **2b**. The δ of $C(5)_{thy}CH_3$, $N(3)_{ur1,2}CH_3$ and $C(6)_{thy}H$ change very little. Some differences for the spacer signals are observed. The most significant changes are found for the protons of the $C(5)_{ur1}CH_2C(5)_{ur2}$ bridge.

Non-empirical calculations of the optimised geometries of macrocycles **2b** and **2e** and their δ values were carried out to explain the observed differences. The most stable conformation of both pyrimidinophanes is almost the same except for insignificant changes in the value of the angle between the two uracil unit planes in the 5,5′-(*N*-methyluracilyl)methane fragment. The results agree well with experi-

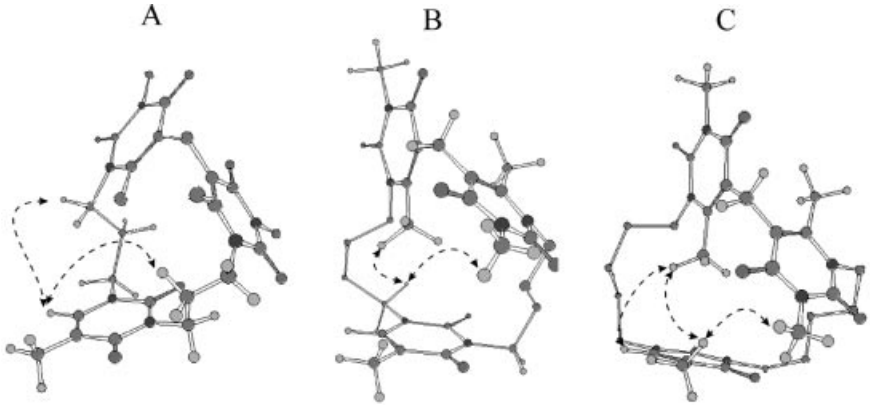


Figure 8. The observed NOEs (dashed lines) for the pyrimidinophanes **2a** (A), **2b** (B) and **2c** (C). Some protons of the spacers are omitted for clarity.

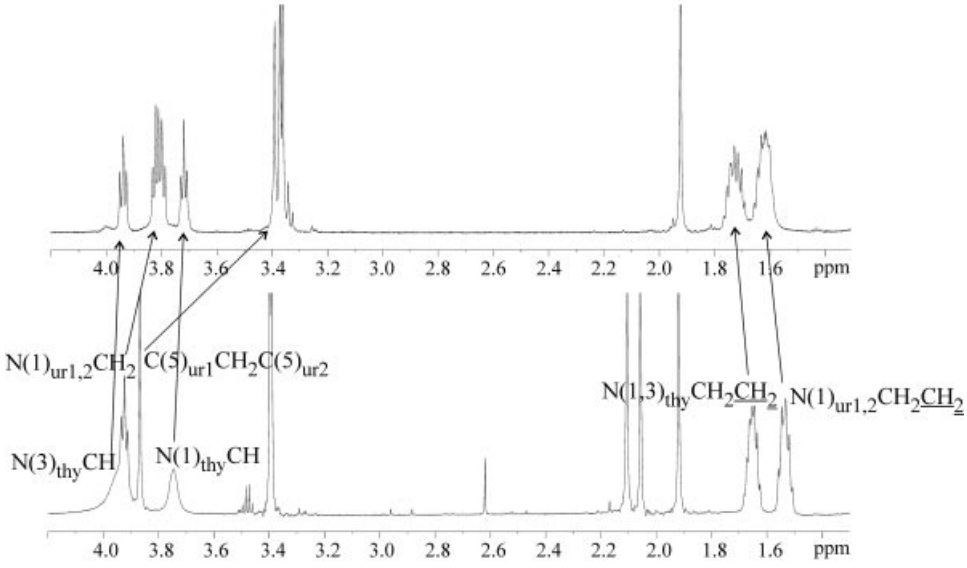


Figure 9. ^{1}H NMR spectra of pyrimidinophanes **2b** (bottom spectrum) and **2e** (upper spectrum) in $CDCl_3$ at 303 K.

mental data. Calculations show that the maximal difference is observed for the $C(5)_{ur1}CH_2C(5)_{ur2}$ bridge signals ($\Delta\delta$ = 0.3 ppm). This qualitatively agrees with experimental results ($\Delta\delta$ = 0.5 ppm). Thus, we can conclude that changing the substituent at $C(6)_{ur1,2}$ has little influence on the spatial structure of the macrocycle.

The absence of any significant shift of the indicative $C(6)_{thy}H$ proton signal in **2b** and **2e** additionally confirms that the conformational structure of the macrocycle does not change. In the NOESY spectrum of **2e** an NOE between $N(1)_{ur1,2}CH_2$ and $C(6)_{thy}H$ is observed. It proves that the most stable conformation of macrocycle **2e** in solution is also folded. It is interesting that unlike the spectrum of pyrimidinophane **2b** the ^{1}H NMR spectrum of pyrimidinophane **2e** shows the $N(1,3)_{thy}CH_2$ signals as resolved triplets (i.e. this spectrum corresponds to fast conformational exchange on the NMR time scale). Such changing of the macrocycle dynamics is not surprising. The introduction of a methyl group at $C(6)_{ur1,2}$ inevitably must lead to an increase of the rotational barrier around the $N(1)_{ur1,2}$–CH_2 bond for steric reasons. Thus, the replacement of the proton at $C(6)_{ur1,2}$ with a methyl substituent produces only a minor decrease of the energy barrier of interconversion and has little influence on the conformational structure of the most stable form.

As was mentioned above the ^{1}H NMR spectrum of pyrimidinophane **2b** with four methylene groups in the spacers corresponds to intermediate conformational exchange on

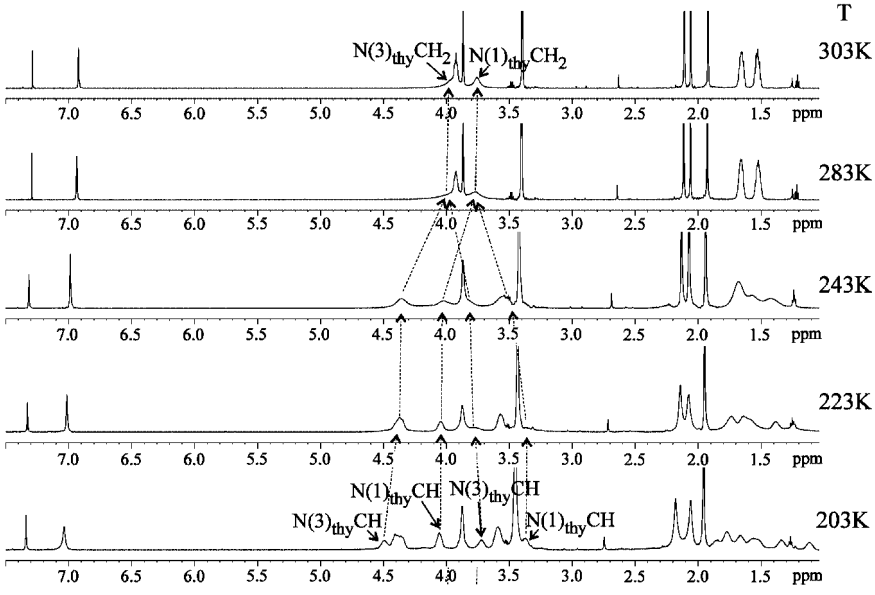


Figure 10. ^{1}H NMR spectra of pyrimidinophane **2b** in $CDCl_3$ at different temperatures.

the NMR time scale. To slow down this exchange process variable-temperature experiments have been performed (Figure 10). With temperature decreasing the lineshape in the ^{1}H NMR spectrum of the macrocycle dramatically changed. At the beginning the signals of the CH_2 groups of the aliphatic spacers are broad and the signals coalesce with decreasing temperature. Finally at 203 K the ^{1}H NMR spectrum of **2b** corresponds to slow conformational exchange on the NMR time scale. The geminal protons of the CH_2 groups of the aliphatic spacers become non-equivalent at low temperatures. Lineshape analysis at 208 K allowed us to determine the free activation energy (ΔG_0) at this temperature as 10.1 kcal/mol. This value agrees well with empirical data for analogous macrocycles.[22]

Thus, all the acyclic compounds are in fast conformational exchange between several forms on the NMR time scale. For the pyrimidinophanes the rate of exchange increases with spacer length. For macrocycle **2a** with three methylene groups in the spacers there is slow exchange on the NMR time scale. For macrocycles with four methylene groups in the spacers the rate constant corresponds to intermediate conformational exchange on the NMR time scale. For macrocycles with five and six methylene groups the exchange becomes fast on the NMR time scale. The most stable conformation for the macrocycles with n = 3–5 is folded.

Solution-State UV Studies

UV spectra of the compounds have been interpreted in terms of hyperchromic and hypochromic effects (increased or decreased light absorbance, respectively, compared with monomeric compounds). The latter phenomenon has been widely used as the evidence of stacked structures of various π-systems, including nucleic-acid bases in solution.[16] According to the theories of Tinoco[23a] and Rhodes,[23b] depending on the relative orientation of the transition moments, hypochromism (parallel stacking of the chromophores) or hyperchromism (linear array of the chromophores) is observed. Hypochromism [H (%)] values were calculated with Equation (1) which gives the oscillator strength, f, of the studied compounds and monomeric reference compounds, which simulate their building units.

$$f = 4.32 \times 10^{-9} \int [\varepsilon(\lambda) / \lambda^2] d\lambda \quad (1)$$

Acyclic triuracils **1a**–**d** and their macrocyclic counterparts **2a**–**d** consist of thymine and 3,6-dimethyluracil units which are simulated by the reference compounds 1,3-dibutylthymine (**8**) and **4b**, respectively. To simulate 3-methyluracil units in triuracils **1e** and **2e** the compound **4e** was used. The H values of compounds **1a**–**d** and **2a**–**d**, **1e** and **2e**, and **6** and **7** are described by Equations (2), (3) and (4), respectively. To calculate the H for acyclic triuracil **1f** reference compounds **8** and **4f** were used [Equation (5)].

$$\%H_{1a-d,2a-d} = \{1 - [f_{1a-d,2a-d} / (2f_{4b} + f_8)]\}100 \quad (2)$$

$$\%H_{1e,2e} = \{1 - [f_{1e,2e} / (2f_{4e} + f_8)]\}100 \quad (3)$$

$$\%H_{6,7} = \{1 - [f_{6,7} / 2f_{4b}]\}100 \quad (4)$$

$$\%H_{1f} = \{1 - [f_{1f} / (2f_{4f} + f_8)]\}100 \quad (5)$$

For example, in calculating the H of trimeric compound **1e** or **2e**, $f_{1e,2e}$ is the oscillator strength of **1e** or **2e**, and $2f_{4e} + f_8$ is the sum of the oscillator strengths of reference compounds **4e** and **8**. The light absorbance of compounds **6** and **7** in the UV region was determined by the 3,6-dimethyluracil units and only monomeric reference compound **4b** was used. Recently this approach has been applied to the first representatives of acyclic and macrocyclic triuracils **1b** and **2b**.[15b] Table 1 represents UV data, calculated oscillator strengths and H values of the studied compounds in different solvents. It should be noted that the concentrations used are low enough to preclude the formation of intermolecular aggregates so that the observed effects are determined only by intramolecular forces, in particular by π-π interactions of the uracil units. Moreover this was confirmed by the observation of a linear relationship between concentration and absorbance (the Beer–Lambert law) at 0.01–1 mM. Figure 11 shows comparative UV spectra of acyclic and macrocyclic counterparts **1b** and **2b** and monomeric reference compound **4b** at appropriate concentrations. The Figure demonstrates a dramatic decrease of light absorbance of macrocyclic triuracil compared with acyclic triuracil and model compound in chloroform and H_2O.

Table 1. UV absorption spectra and percentage hyper- or hypochromism of the acyclic and macrocyclic compounds and reference monomeric compounds in $CHCl_3$ and H_2O[a].

Entry		$CHCl_3$[b]				H_2O[b]			
		λ_{max}	$\varepsilon \times 10^{-3}$	f	H (%)	λ_{max}	$\varepsilon \times 10^{-3}$	f	H (%)
1	**1a**	267	31.8	0.658	–12.7	268	26.4	0.611	–0.5
2	**2a**	275	16.2	0.360	38.4	275	10.0	0.220	63.9
3	**1b**	267	28.7	0.615	–5.4	268	22.6	0.478	21.5
4	**2b**	273	19.6	0.438	25.1	274	16.3	0.354	41.9
5	**1c**	268	25.1	0.545	6.7	269	28.0	0.583	4.1
6	**2c**	274	23.6	0.508	12.9	275	21.8	0.469	22.9
7	**1d**	268	29.9	0.602	–3	268	31.1	0.621	–2.1
8	**2d**	274	20.6	0.442	24.3	275	19.4	0.425	30.0
9	**1e**	267	24.9	0.544	4.7	268	24.3	0.549	–7.8
10	**2e**	270	23.1	0.525	8.0	270	18.7	0.434	14.7
11	**1f**	266	28.1	0.596	13.4	–	–	–	–
12	**6**[c]	265	19.9	0.402	0.1	–	–	–	–
13	**7**[c]	277	17.2	0.408	–1.5	277	18.1	0.424	3.2
14	**4b**	266	9.0	0.201	–	267	11.1	0.219	–
15	**4e**	265	9.5	0.195	–	267	9.0	0.169	–
16	**4f**	262	13.0	0.253	–	–	–	–	–
17	**8**	272	8.5	0.182	–	273	8.4	0.171	–

[a] λ, wavelength in nm; ε, molar extinction coefficient in $M^{-1}cm^{-1}$; f, oscillator strength; H, hyper- or hypochromism value. [b] Concentration is 0.1–0.3 mM. [c] For compounds **6** and **7** measurements were carried out in the uracil absorption region.

The significant hypochromic effects and redshift of pyrimidinophanes **2a**–**d** indicate intramolecular π-π interactions between the thymine and 3,6-dimethyluracil units in $CHCl_3$ and H_2O solutions. In H_2O those effects are larger probably due to attractive interactions between the uracil units medi-

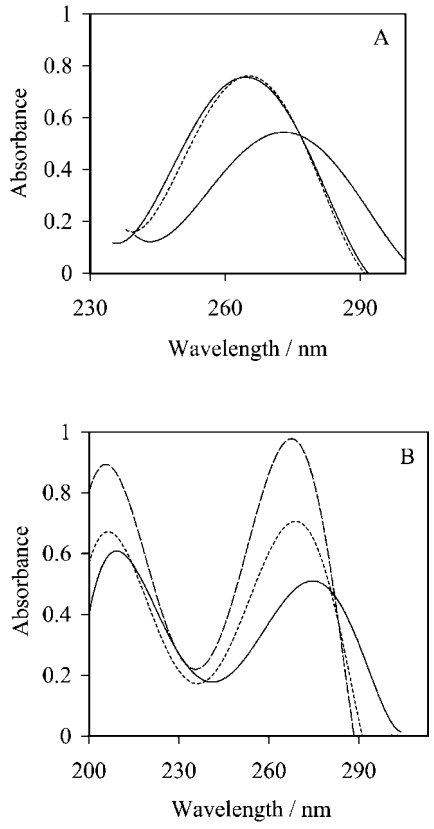


Figure 11. UV spectra of 0.2 mM chloroform (A) and H_2O (B) solutions of compounds **1b** (dotted line), **2b** (solid line) and a 0.9 mM solution of compound **4b** (dashed line).

ated by H_2O. The presence of π-π contacts implies on the one hand a small distance between the thymine and 3,6-dimethyluracil units and on the other hand a proper mutual arrangement of the 3,6-dimethyluracil units in the bis(3,6-dimethyluracil-5-yl)methane fragment to allow these contacts. It is interesting to note that when the H values of the macrocyclic uracils increase, the δ of the bridging C(5)-CH_2C(5′) protons shift downfield. In ^{1}H NMR spectrum of pyrimidinophane **2e** with 3-methyluracil units the signals of the protons are significantly shifted upfield (δ = 3.39 ppm) compared with those in the spectra of pyrimidinophane **2a**–**d** with 3,6-dimethyluracil units (3.96, 3.86, 3.75 and 3.84 ppm, respectively), and **2e** exhibits a much smaller hypochromic effect than **2a**–**d**.

Pyrimidinophane **2a** exhibits a dramatic decrease of light absorption with respect to its acyclic counterpart **1a**. The macrocycle **2a** shows the greatest H among the studied compounds both in $CHCl_3$ and H_2O probably due its having the shortest bridges, which provide the shortest distance between the 3,6-dimethyluracil and thymine units. To the best of our knowledge, these H values (38.4% in $CHCl_3$ and 63.9% in H_2O) even exceed the ones determined for macrocycles consisting of purines, which have a more expanded aromatic ring than pyrimidines.[24] However the H value of **2d** with 6 methylene groups in the $N(1)_{th}$–$N(1)_{ur}$ spacers increases again and is approximately equal to that of **2b** in $CHCl_3$. Moreover the ^{1}H NMR spectrum of **2d** in $CDCl_3$ is similar to the spectrum of **2b** due to downfield shift of the C(5)CH_2C(5′) protons and upfield shifts of the $C(6)_{ur1,2}CH_3$ protons in comparison with their δ values for **2c**.

Ultimately, the UV and ^{1}H NMR spectroscopic data do not allow us to determine the unambiguous conformations of macrocyclic triuracils **2a**–**2d** in solution but a trend is obvious; in chloroform and H_2O folded conformations take place in which one or both of the 3,6-dimethyluracil units stacks with the thymine unit and the interplanar distance between them is quite short. The presence of the thymine unit in the studied acyclic and macrocyclic triuracils is crucial, and it is confirmed by the UV spectra of isocyanurate-based compounds **6** and **7**. The UV absorbance of macrocycle **7** in different solvents is the sum of the absorbance of two 3,6-dimethyluracil units and H values are close to zero. In our opinion this proves that the hypochromic effect of macrocycles **2a**–**2d** is caused by the π-π interactions (stacking) between the thymine unit and the 3,6-dimethyluracil units. Moreover there is some dependence of H values of the pyrimidinophanes on the mutual orientation of the *N*-methyluracil units in the bis(*N*-methyluracilyl-5)methane fragment.

In general the acyclic triuracils **1a**–**e** do not have any steric restraints and exhibit a hyperchromic effect (negative values of H) or slight hypochromic effect. According to theory[23] negative values of H indicate a linear array of uracil units. The ^{1}H δ values of **1a**–**e** are close to those of the model compounds and in some cases are quite different from those of macrocyclic counterparts **2a**–**e** which corresponds with the linear array proposal for **1a**–**e**. Ring closure which is afforded by the introduction of the C(5)CH_2C(5′) spacer dramatically alters the conformation, and as a result alterations of the spectral features of the macrocycles occur. It is worth noting that the cyclisation implies that the mutual arrangement of the 3,6-dimethyluracil fragments in the acyclic triuracils is such that methylene bridge formation can proceed.

In some way the results of the UV study are in contradiction with the structures determined by X-ray diffraction. As was discussed above, in the crystals of the pyrimidinophanes, in particular **2b** and **2c** there is no evidence of intramolecular π-π interactions between the uracil units. However in solution the uracil units are situated closer to each other, and the UV data obviously indicate a possibility of intramolecular stacking between them. It can be supposed that in solution the mutual arrangement of the uracil moieties in these pyrimidinophanes is affected by attractive interactions between the units. These interactions are mediated by solvent ($CHCl_3$ or H_2O) and in aqueous solution significant H is explained by the mediation of many polar H_2O molecules in the attraction of pyrimidinophane fragments rather than by a hydrophobic effect.[25]

Conclusions

A series of acyclic triuracils – 1,3-bis[ω-(3-methyl- or 3,6-dimethyluracil-1-yl)alkyl]thymines with polymethylene or

xylylene spacers – has been prepared. Ring closure of the acyclic triuracils with paraformaldehyde in aqueous HCl in the presence of copper(I) chloride afforded pyrimidinophanes which can be considered macrocyclic counterparts of the acyclic triuracils. The thymine fragment in the acyclic and macrocyclic counterparts can be replaced by another heteroaromatic base, in particular by the isocyanuric acid derivative 1-methyl-1,3,5-triazin-2,4,6(1*H*,3*H*,5*H*)-trione. The introduction of a methylene bridge between the *N*-methyluracil units alters the conformational behaviour of the compounds. Both in the solid state and in chloroform and H_2O solutions the pyrimidinophanes exhibit a folded geometry with short distances between the thymine and *N*-methyluracil units. However in the solid state their mutual arrangement is not suitable for π-π contacts, while in solution the H values are indicative of their stacking. Larger H values indicate stronger π-π interactions between the thymine and 3,6-dimethyluracil units. H values for the pyrimidinophane with 3-methyluracil units is less than that for macrocycles with 3,6-dimethyluracil units. This is explained by the different mutual orientation of the uracil units in the bis(3,6-dimethyluracil-5-yl)methane fragment compared with that in the bis(3-methyluracil-5-yl)methane fragment. The acyclic triuracils do not have a folded structure and the uracil units in these compounds are probably arranged in a linear array. There is no evidence of any special rigid 3D structure of the acyclic triuracils. The dynamics of the macrocycles in solution depends on the length of the spacers. The pyrimidinophane with three methylene groups in the spacers has a rigid framework, but when the spacers lengthen the flexibility increases. The most stable conformation for the macrocycles with $n = 3–5$ is a folded one. However, based on NMR and UV data it is possible to determine a set of conformations of the acyclic and macrocyclic triuracils which prevail in solution.

Experimental Section

General: The mass spectra (EI) were obtained with a Finnigan MAT-212 mass spectrometer (resolution was 1000; data were processed using the MSS MASPEC II data system 32; direct inlet of the sample into the ion source, programming of the temperature from 20–300 °C, the energy of ionising electrons was 70 eV, the electron emission current was 1.0 mA). High resolution mass measurements were performed with the same instrument by a mass-matching procedure, and the reference substance was perfluorokerosene. UV spectra were measured with a Specord UV/Vis spectrophotometer, and the spectra of the acyclic and macrocyclic triuracils and the corresponding reference compounds were determined a minimum of three times provided that they were reproducible, and average parameters were reported. Oscillator strength was calculated from Equation (1) based on the integral intensity of the corresponding absorption band.

Intensity data measurements of macrocycle **2b** were carried out with an Enraf–Nonius four circle diffractometer using graphite-monochromated Cu-K_α (λ = 1.54178 Å) radiation. Macrocycle **2c** was studied with a Nonius Kappa CCD diffractometer using Mo-K_α (λ = 0.71073 Å) radiation. All structures were solved and refined using the SHELXTL[26] software package.

CCDC-603393, -603394, and -603395 contain the supplementary crystallographic data for this paper, specifically the X-ray structures of pyrimidinophanes **2b** and **2c** (from CH_3CN and DMSO). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

NMR experiments were carried out with a Bruker AVANCE-600 spectrometer (14.1 T) equipped with a pulsed-gradient unit capable of producing magnetic field pulse gradients in the *z* direction of 56 G cm^{-1}. All spectra were acquired in a 5 mm inverse probehead in 5 mm tubes. Chemical shifts (ppm) are internally referenced to the TMS signal (δ = 0 ppm) in all cases. In some cases the 1D DPFGNOE method in the rotating frame was used to measure NOEs.[27] Hermite shaped pulses were used for selective irradiation.

Line shape analysis of signals broadened by chemical exchange was carried out by the GNMR v.4.1 program.[28] Activation parameters were calculated by the Eyring equation.[29]

Full geometry optimisations were done at the ab initio RHF/6-31G level as implemented in GAUSSIAN 98[30] with an AuthenticAMD Athlon (Im) computer.

Elemental analyses was determined by the Analitical Laboratory at the A.E. Arbuzov Institute of Organic and Physical Chemistry of Kazan. Microanalyses of C, H, and N were performed with a CHN-3 analyser. Melting points were measured with a Boetius hot-stage apparatus. Thin layer chromatography was performed with Silufol-254 plates; visualisation was carried out with UV light. For column chromatography silica gel (60 mesh) from Fluka and neutral Al_2O_3 (activity II) were used.

All solvents were dried according to standard protocols. 1-(3-Bromoprop-1-yl)-3,6-dimethyluracil (**4a**) and 1-(4-bromobut-1-yl)-3,6-dimethyluracil (**4b**) have been prepared by the reaction of the sodium salt of 3,6-dimethyluracil with the appropriate α,ω-dibromoalkane according to a known protocol.[31] Compounds **4c**, **4d** and **4e** were obtained by the same procedure. 1,3-Dibutylthymine **8** was prepared by a published procedure.[15b]

1-(5-Bromopent-1-yl)-3,6-dimethyluracil (4c): Yield 67%; m.p. 71–72 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.54 (m, 2 H, $N_{ur}CH_2CH_2CH_2$), 1.67 (m, 2 H, $N_{ur}CH_2CH_2CH_2CH_2$), 1.92 (m, 2 H, $N_{ur}CH_2CH_2$), 2.27 [s, 3 H, $C(6)_{pyr}CH_3$], 3.32 (s, 3 H, $N_{ur}CH_3$), 3.43 (t, J = 6.4 Hz, 2 H, CH_2Br), 3.82 (t, J = 7.3 Hz, 2 H, $N_{pyr}CH_2$), 5.60 [s, 1 H, $C(5)_{pyr}H$] ppm. $C_{11}H_{17}BrN_2O_2$ (289.17): calcd. C 45.69, H 5.93, Br 27.63, N 9.69; found C 45.74, H 6.00, Br 27.54, N 9.66.

1-(6-Bromohex-1-yl)-3,6-dimethyluracil (4d): Yield 67%; m.p. 80–81 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.74 (m, 4 H, $N_{pyr}CH_2CH_2CH_2CH_2$), 1.66 (m, 2 H, $N_{ur}CH_2CH_2CH_2CH_2CH_2$), 1.92 (m, 2 H, $N_{ur}CH_2CH_2$), 2.24 [s, 3 H, $C(6)_{ur}CH_3$], 3.31 (s, 3 H, $N_{ur}CH_3$), 3.40 (t, J = 6.8 Hz, 2 H, CH_2Br), 3.80 (t, J = 7.7 Hz, 2 H, $N_{pyr}CH_2$), 5.59 [s, 1 H, $C(5)_{pyr}H$] ppm. $C_{12}H_{19}BrN_2O_2$ (303.20): calcd. C 47.54, H 6.32, Br 26.35, N 9.24; found C 47.77, H 6.21, Br 26.04, N 9.26.

1-(4-Bromobut-1-yl)-3-methyluracil (4e): Yield 75%; m.p. 34–35 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.90 (m, 4 H, $N_{ur}CH_2CH_2CH_2$), 3.33 (s, 3 H, $N_{ur}CH_3$), 3.46 (t, J = 5.4 Hz, 2 H, CH_2Br), 3.96 (t, J = 7.1 Hz, 2 H, $N_{ur}CH_2$), 5.60 [d, J = 7.6 Hz, 1 H, $C(5)_{ur}H$], 7.24 [d, J = 7.2 Hz, 1 H, $C(6)_{pyr}H$] ppm. $C_9H_{13}BrN_2O_2$ (261.12): calcd. C 41.40, H 5.02, Br 30.60, N 10.73; found C 41.47, H 5.11, Br 30.43, N 10.69.

1-[4-(Bromomethyl)phenylmethyl]-3,6-dimethyluracil (4f): *p*-Xylylene dibromide (40 g, 150 mmol) was added to a suspension of the sodium salt of 3,6-dimethyluracil (7 g, 43 mmol) in DMF (150 mL),

and the reaction mixture was stirred at room temperature for 4 h. The precipitate was filtered off, the filtrate was concentrated under vacuum to approximately ¼ the initial volume, and the solid formed was filtered off again. The filtrate was fully concentrated, treated with benzene and filtered. The resulted solution was concentrated to 10–15 mL and transferred to a column of Al_2O_3. The column was successively washed with petroleum ether and petroleum ether/EtOAc (3:1). From the fractions of petroleum ether/EtOAc compound **4f** was obtained. Yield 5.5 g (40%); m.p. 138–140 °C [hexane/EtOAc mixture (1.4:1)]. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.18 [s, 3 H, $C(6)_{ur}CH_3$], 3.37 (s, 3 H, $N_{ur}CH_3$), 4.47 (s, 2 H, CH_2Br), 5.11 (s, 2 H, $N_{ur}CH_2$), 5.65 [s, 1 H, $C(5)_{pyr}H$], 7.15 (d, J = 8.1 Hz, 2 H, Ar*H*), 7.37 (d, J = 8.1 Hz, 2 H, Ar*H*) ppm. $C_{14}H_{15}BrN_2O_2$ (323.19): calcd. C 52.03, H 4.68, Br 24.72, N 8.67; found C 51.81, H 4.79, Br 25.03, N 8.69.

Synthesis of Acyclic Compounds 1a–f and 6 (General Procedure): A two-fold excess of the appropriate compound **4** was added to a suspension of **3** or the disodium salt of 1-methyl-1,3,5-triazin-2,4,6(1*H*,3*H*,5*H*)-trione in DMF and the mixture was stirred at 60–70 °C. The reaction was complete if a pH test of the reaction mixture showed a neutral medium, which occurred usually after stirring for 6–8 h. The solvent was removed under vacuum, and the residue was dissolved in chloroform and filtered off. The crude product in chloroform was purified by either recrystallisation or column chromatography with SiO_2.

1,3-Bis[3-(3,6-dimethyluracil-1-yl)propyl]thymine (1a): Yield 30%; m.p. 166–167 °C (acetone). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.91 [s, 3 H, $C(5)_{thy}CH_3$], 1.97 [m, 2 H, $N(3)_{thy}CH_2CH_2$], 2.04 [m, 2 H, $N(1)_{thy}CH_2CH_2$], 2.22 [s, 3 H, $C(6)_{ur1}CH_3$], 2.23 [s, 3 H, $C(6)_{ur2}CH_3$], 3.25 (s, 3 H, $N_{ur1}CH_3$), 3.28 (s, 3 H, $N_{ur2}CH_3$), 3.79 [m, 2 H, $N(1)_{thy}CH_2$], 3.86 [m, 2 H, $N(1)_{ur1}CH_2$], 3.87 [m, 2 H, $N(1)_{ur2}CH_2$], 4.02 [m, 2 H, $N(3)_{thy}CH_2$], 5.55 [s, 1 H, $C(5)_{ur1}H$], 5.59 [s, 1 H, $C(5)_{ur2}H$], 7.07 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = th: 13.0 (CH_3), 110.3 [C(5)], 138.3 [C(6)], 151.3 [C(2)], 163.5 [C(4)]; ur1: 19.6 (CH_3), 27.8 (NCH_3), 101.6 [C(5)], 150.8 [C(6)], 152.1 [C(2)], 162.3 [C(4)]; ur2: 19.6 (CH_3), 27.8 (NCH_3), 102.0 [C(5)], 150.4 [C(6)], 152.4 [C(2)], 162.1 [C(4)]; spacers: 27.3 [$N(3)_{thy}CC$], 28.5 [$N(1)_{thy}CC$], 38.8 [$N(3)_{thy}C$], 42.3 [$N(1)_{ur2}C$], 43.0 [$N(1)_{ur1}C$], 47.1 [$N(1)_{thy}C$] ppm. $C_{23}H_{30}N_6O_6$ (486.52): calcd. C 56.78, H 6.22, N 17.27; found C 56.67, H 6.14, N 17.33.

1,3-Bis[4-(3,6-dimethyluracil-1-yl)butyl]thymine (1b): Compound **1b** was isolated by column chromatography with CH_2Cl_2/CH_3OH (40:1) as the eluent. Yield 43%; m.p. 175–176 °C [EtOAc/$CHCl_3$ (1.5:1)]. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.68 [m, 6 H, $N(1)_{ur2}CH_2CH_2$, $N(1)_{ur1}CH_2CH_2$, $N(3)_{thy}CH_2CH_2$], 1.73 [m, 2 H, $N(1)_{thy}CH_2CH_2$], 1.90 [s, 3 H, $C(5)_{thy}CH_3$], 2.21 [s, 3 H, $C(6)_{ur1}CH_3$], 2.22 [s, 3 H, $C(6)_{ur2}CH_3$], 3.28 (s, 3 H, $N_{ur1}CH_3$), 3.29 (s, 3 H, $N_{ur2}CH_3$), 3.75 [m, 2 H, $N(1)_{thy}CH_2$], 3.83 [m, 2 H, $N(1)_{ur1}CH_2$], 3.85 [m, 2 H, $N(1)_{ur2}CH_2$], 3.96 [m, 2 H, $N(3)_{thy}CH_2$], 5.55 [s, 1 H, $C(5)_{ur1}H$], 5.58 [s, 1 H, $C(5)_{ur2}H$], 7.03 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 110.0 [C(5)], 138.5 [C(6)], 151.4 [C(2)], 163.6 [C(4)]; ur1: 19.7 (CH_3), 27.8 (NCH_3), 101.5 [C(5)], 150.9 [C(6)], 152.2 [C(2)], 162.4 [C(4)]; ur2: 19.7 (CH_3), 27.8 (NCH_3), 101.8 [C(5)], 150.6 [C(6)], 152.4 [C(2)], 162.2 [C(4)]; spacers: 25.0 [$N(3)_{thy}CC$], 25.8 [$N(1)_{thy}CC$], 26.1 [$N(1)_{ur1}CC$], 26.3 [$N(1)_{ur2}CC$], 40.7 [$N(3)_{thy}C$], 44.3 [$N(1)_{ur2}C$], 44.9 [$N(1)_{ur1}C$], 48.7 [$N(1)_{thy}C$] ppm. $C_{25}H_{34}N_6O_6$ (514.57): calcd. C 58.35, H 6.66, N 16.33; found C 58.41, H 6.74, N 16.37.

1,3-Bis[5-(3,6-dimethyluracil-1-yl)pentyl]thymine (1c): Compound **1c** was isolated by column chromatography with CH_2Cl_2/CH_3OH (20:1) as the eluent. Yield 30%; m.p. 150–152 °C (EtOAc). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.36 [m, 4 H, $N(1)_{thy}CH_2CH_2CH_2$, $N(3)_{thy}CH_2CH_2CH_2$], 1.65 [m, 6 H, $N(1)_{ur1}CH_2CH_2$, $N(1)_{ur2}CH_2CH_2$, $N(3)_{thy}CH_2CH_2$], 1.70 [m, 2 H, $N(1)_{thy}CH_2CH_2$], 1.88 [s, 3 H, $C(5)_{th}CH_3$], 2.21 [s, 6 H, $C(6)_{ur1}CH_3$, $C(6)_{ur2}CH_3$], 3.25 (s, 3 H, $N_{ur1}CH_3$), 3.26 (s, 3 H, $N_{ur2}CH_3$), 3.68 [m, 2 H, $N(1)_{thy}CH_2$], 3.76 [m, 2 H, $N(1)_{ur1}CH_2$], 3.77 [m, 2 H, $N(1)_{ur2}CH_2$], 3.91 [m, 2 H, $N(3)_{thy}CH_2$], 5.53 [s, 1 H, $C(5)_{ur1}H$], 5.55 [s, 1 H, $C(5)_{ur2}H$], 6.94 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = th: 13.0 (CH_3), 110.0 [C(5)], 138.3 [C(6)], 151.4 [C(2)], 163.7 [C(4)]; ur1: 19.7 (CH_3), 29.8 (NCH_3), 101.5 [C(5)], 151.1 [C(6)], 152.3 [C(2)], 162.5 [C(4)]; ur2: 19.7 (CH_3), 27.8 (NCH_3), 101.7 [C(5)], 150.8 [C(6)], 152.2 [C(2)], 162.3 [C(4)]; spacers: 23.6 [$N(1)_{thy}CCC$], 24.1 [$N(3)_{thy}CCC$], 27.1 [$N(3)_{thy}CC$], 28.6 [$N(1)_{thy}CC$], 28.4 [$N(1)_{ur1}CC$], 28.4 [$N(1)_{ur2}CC$], 41.0 [$N(3)_{thy}C$], 44.8 [$N(1)_{ur2}C$], 45.1 [$N(1)_{ur2}C$], 49.0 [$N(1)_{thy}C$] ppm. $C_{27}H_{38}N_6O_6$ (542.63): calcd. C 59.76, H 7.06, N 15.49; found C 59.63, H 6.98, N 15.47.

1,3-Bis[6-(3,6-dimethyluracil-1-yl)hexyl]thymine (1d): Compound **1c** was isolated by column chromatography with EtOAc as the eluent. Yield 67%; m.p. 80–81 °C [benzene/petroleum ether (1:1) mixture]. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.33 [m, 8 H, $N(1)_{ur1}CH_2CH_2CH_2$, $N(1)_{ur2}CH_2CH_2CH_2$, $N(1)_{thy}CH_2CH_2CH_2$, $N(3)_{thy}CH_2CH_2CH_2$], 1.58–1.63 [m, 8 H, $N(1)_{ur1}CH_2CH_2$, $N(1)_{ur2}CH_2CH_2$, $N(1)_{thy}CH_2CH_2$, $N(3)_{thy}CH_2CH_2$], 1.84 [s, 3 H, $C(5)_{thy}CH_3$], 2.18 [s, 6 H, $C(6)_{ur1}CH_3$, $C(6)_{ur2}CH_3$], 3.22 (s, 6 H, $N_{ur1}CH_3$, $N_{ur2}CH_3$), 3.63 [m, 2 H, $N(1)_{thy}CH_2$], 3.72 (m, 4 H, $N_{ur1}CH_2$, $N_{ur2}CH_2$), 3.85 [m, 2 H, $N(3)_{thy}CH_2$], 5.50 [s, 1 H, $C(5)_{ur1}H$], 5.51 [s, 1 H, $C(5)_{ur2}H$], 6.94 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 110.0 [C(5)], 138.4 [C(6)], 151.3 [C(2)], 163.7 [C(4)]; ur1: 19.7 (CH_3), 27.7 (NCH_3), 101.3 [C(5)], 151.3 [C(6)], 152.7 [C(2)], 162.4 [C(4)]; ur1: 19.7 (CH_3), 27.7 (NCH_3), 101.3 [C(5)], 151.3 [C(6)], 152.7 [C(2)], 162.4 [C(4)]; ur2: 19.7 (CH_3), 27.8 (NCH_3), 101.4 [C(5)], 151.2 [C(6)], 152.2 [C(2)], 162.3 [C(4)]; spacers: 26.0 [$N(1)_{ur1}CCC$], 26.2 [$N(1)_{ur2}CCC$], 26.3 [$N(3)_{thy}CCC$], 26.5 [$N(1)_{thy}CCC$], 27.3 [$N(3)_{thy}CC$], 28.9 [$N(1)_{thy}CC$], 28.7 [$N(1)_{ur1}CC$], 28.7 [$N(1)_{ur2}CC$], 41.1 [$N(3)_{thy}C$], 45.0 [$N(1)_{ur2}C$], 45.2 [$N(1)_{ur21}C$], 49.2 [$N(1)_{thy}C$] ppm. $C_{29}H_{42}N_6O_6$ (570.68): calcd. C 61.03, H 7.42, N 14.73; found C 61.17, H 7.51, N 14.64.

1,3-Bis[4-(3-methyluracil-1-yl)butyl]thymine (1e): Yield 48%; m.p. 123–124 °C (EtOAc). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.68 [m, 2 H, $N(3)_{th}CH_2CH_2$], 1.73 [m, 6 H, $N(1)_{ur1}CH_2CH_2$, $N(1)_{ur2}CH_2CH_2$, $N(1)_{th}CH_2CH_2$], 1.93 [s, 3 H, $C(5)_{thy}CH_3$], 3.33 (s, 3 H, $N_{ur1}CH_3$), 3.34 (s, 3 H, $N_{ur2}CH_3$), 3.77 [m, 2 H, $N(1)_{thy}CH_2$], 3.81 (m, 4 H, $N_{ur1}CH_2$, $N_{ur2}CH_2$), 3.99 [m, 2 H, $N(3)_{thy}CH_2$], 5.72 [d, J = 7.8 Hz, 1 H, $C(5)_{ur1}H$], 5.76 [d, J = 7.8 Hz, 1 H, $C(5)_{ur2}H$], 7.01 [s, 1 H, $C(6)_{thy}H$], 7.16 [d, J = 7.8 Hz, 1 H, $C(6)_{ur2}H$], 7.22 [d, J = 7.8 Hz, 1 H, $C(6)_{ur1}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 110.2 [C(5)], 138.4 [C(6)], 151.5 [C(2)], 163.7 [C(4)]; ur1: 27.8 (NCH_3), 101.4 [C(5)], 142.4 [C(2)], 150.9 [C(6)], 163.3 [C(4)]; ur2: 27.8 (NCH_3), 101.8 [C(5)], 141.9 [C(6)], 151.8 [C(2)], 163.09 [C(4)]; spacers: 24.4 [$N(3)_{thy}CC$], 25.9 [$N(1)_{thy}CC$], 25.9 [$N(1)_{ur2}CC$], 26.1 [$N(1)_{ur1}CC$], 40.4 [$N(3)_{thy}C$], 48.6 [$N(1)_{thy}C$], 48.9 [$N(1)_{ur2}C$], 49.3 [$N(1)_{ur1}C$] ppm. $C_{23}H_{30}N_6O_6$ (486.52): calcd. C 56.78, H 6.22, N 17.27; found C 56.85, H 6.31, N 17.24.

1,3-Bis[4-(3,6-dimethyluracil-1-yl)methylphenylmethyl]thymine (1f): Compound **1f** was isolated by column chromatography with EtOAc as the eluent. Yield 22%; m.p. 109–111 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.89 [s, 3 H, $C(5)_{thy}CH_3$], 2.17 [s, 3 H, $C(6)_{ur1}CH_3$], 2.18 [s, 3 H, $C(6)_{ur1}CH_3$], 3.35 (s, 3 H, $N_{ur1}CH_3$), 3.36 (s, 3 H, $N_{ur2}CH_3$), 4.88 [m, 2 H, $N(1)_{thy}CH_2$], 5.13 [m, 6 H, $N(3)_{thy}CH_2$,

$N_{ur1}CH_2$, $N_{ur2}CH_2$], 5.63 [s, 1 H, $C(5)_{ur1}H$], 5.65 [s, 1 H, $C(5)_{ur2}H$], 6.97 [s, 1 H, $C(6)_{thy}H$], 7.18 (d, J = 8.1 Hz, 2 H, ArH), 7.26 (d, J = 8.1 Hz, 2 H, ArH), 7.46 (d, J = 8.1 Hz, 2 H, ArH), 7.46 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.1 (CH_3), 110.6 [C(5)], 137.9 [C(6)], 151.8 [C(2)], 163.5 [C(4)]; ur1 and ur2: 19.9 (CH_3), 28.1 (NCH_3), 101.9, 102.0 [C(5)], 151.2, 151.5 [C(6)], 152.8 [C(2)], 162.2, 162.3 [C(4)]; Ar: 126.3, 126.9, 128.6, 129.8, 135.4, 135.5, 136.5, 136.7; spacers: 44.3, 51.7 [$N(1)_{thy}C$, $N(3)_{thy}C$], 47.7, 47.8 ($N_{ur1}C$, $N_{ur2}C$) ppm. $C_{33}H_{34}N_6O_6$ (610.66): calcd. C 64.91, H 5.61, N 13.76; found C 65.05, H 5.57, N 13.84.

3,5-Bis[4-(3,6-dimethyluracil-1-yl)butyl]-1-methylisocyanurate (6): Yield 59%; m.p. 190 °C (EtOAc). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.70 [m, 8 H, $N(1)_{ur}CH_2CH_2$, NCH_2CH_2], 2.26 [s, 6 H, $C(6)_{ur}CH_3$], 3.31 (s, 6 H, $N_{ur}CH_3$), 3.34 (s, 3 H, NCH_3), 3.85 [t, J = 7.3 Hz, 4 H, $N(1)_{ur}CH_2$], 3.93 (t, J = 6.4 Hz, 4 H, NCH_2), 5.60 [s, 2 H, $C(5)_{ur}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = isocyanurate unit: 29.3 (NCH_3), 149.0 [C(2)], 149.1 [C(6) and C(4)]; ur: 19.6 (CH_3), 27.8 (NCH_3), 101.7 [C(5)], 150.7 [C(6)], 152.28 [C(2)], 162.3 [C(4)]; spacers: 25.1 (NC*C*), 26.1 ($N_{ur}CC$), 42.4 (NCH_2), 44.6 ($N_{ur}CH_2$) ppm. $C_{24}H_{33}N_7O_7$ (531.56): calcd. C 54.23, H 6.26, N 18.45; found C 54.35, H 6.37, N 18.41.

Synthesis of Pyrimidinophanes 2a–e and 7 (General Procedure): H_2O (600 mL) was added to acyclic triuracils **2a**–**e** or **6** (2 mmol), and the resulting mixture was heated with stirring for partial or full dissolving of the compound. Copper(I) chloride (0.2 g, 1 mmol) dissolved in concentrated HCl (20 mL) was added to the mixture, and at 94–97 °C a solution of paraformaldehyde (0.08 g, 2.7 mmol) in aqueous HCl (1.4 M, 170 mL) was added dropwise over 1 h. The mixture was refluxed with stirring for 35 h in the case of macrocycles **2a**–**d**, and **7** and 70 h in the case of pyrimidinophane **2e**. The mixture was concentrated to 100 mL, and the residue was extracted with $CHCl_3$ (4 × 100 mL). The organic layer was separated, dried ($MgSO_4$), concentrated to 10–15 mL and transferred to a column of SiO_2. The column was successively washed with a CH_2Cl_2/CH_3OH gradient starting from CH_2Cl_2/CH_3OH (100:1). The target macrocyclic compound obtained from the fractions of the eluent was washed with diethyl ether and dried under vacuum (1 Torr) at 80–100 °C.

7,13,21,24,25-Pentamethyl-1,5,7,13,15,19-hexaazatetracyclo-[17.3.1.1^{5,9}.1^{11,15}]pentacosa-9(24),11(25),21(22)-triene-6,8,12,14,20,23-hexaone (2a): Pyrimidinophane **2a** was isolated by column chromatography with CH_2Cl_2/CH_3OH (70:1) as the eluent. Yield 0.03 g (3%); m.p. 259–260 °C. HRMS (EI): calcd. for $C_{24}H_{30}N_6O_6$ 498.2227; found 498.2230. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.75 [m, 1 H, $N(3)_{thy}CH_2CH$], 1.88 [s, 3 H, $C(5)_{thy}CH_3$], 1.99 [m, 3 H, $N(3)_{thy}CH_2CH$, $N(1)_{thy}CH_2CH_2$], 2.23 [s, 3 H, $C(6)_{ur1}CH_3$], 2.25 [s, 3 H, $C(6)_{ur2}CH_3$], 3.07 [m, 1 H, $N(3)_{thy}CH$], 3.32 [m, 1 H, $N(1)_{thy}CH$], 3.40 (s, 3 H, $N_{ur1}CH_3$), 3.41 (s, 3 H, $N_{ur2}CH_3$), 3.54 [m, 1 H, $N(1)_{thy}CH$], 3.58 [m, 1 H, $N(1)_{ur2}CH$], 3.60 [m, 1 H, $N(1)_{ur1}CH$], 3.96 [s, 2 H, $C(5)_{ur1}CH_2C(5)_{ur2}$], 4.39 [m, 1 H, $N(3)_{thy}CH$], 4.78 [m, 1 H, $N(1)_{ur2}CH$], 4.83 [m, 1 H, $N(1)_{ur1}CH$], 6.91 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 109.6 [C(5)], 138.4 [C(6)], 150.7 [C(2)], 163.4 [C(4)]; ur1: 16.6 (CH_3), 28.9 (NCH_3), 110.9 [C(5)], 151.4 [C(6)], 152.9 [C(2)], 163.0 [C(4)]; ur2: 16.5 (CH_3), 28. 9 (NCH_3), 110.5 [C(5)], 151.2 [C(6)], 152.7 [C(2)], 162.9 [C(4)]; spacers: 20.5 [$C(5)_{ur1}CC(5)_{ur2}$], 26.8 [$N(3)_{thy}CC$], 27.5 [$N(1)_{thy}CC$], 36.6 [$N(3)_{thy}C$], 46.9 [$N(1)_{thy}C$], 41.1 [$N(1)_{ur2}C$], 41.5 [$N(1)_{ur1}C$] ppm. MS (EI): m/z (%) = 499 (11) [M + 1]$^+$, 498 (32) [M]$^+$, 483 (100) [M – 15]$^+$, 345 (13), 306 (10), 207 (34), 193 (31), 179 (32), 167 (45), 166 (42), 153 (19), 122 (17). $C_{24}H_{30}N_6O_6$ (498.53): calcd. C 57.82, H 6.07, N 16.86; found C 57.69, H 6.14, N 16.93.

8,14,23,26,27-Pentamethyl-1,6,8,14,16,21-hexaazatetracyclo-[19.3.1.1^{6,10}.1^{12,16}]heptacosa-10(26),12(27),23(24)-triene-7,9,13,15,22,25-hexaone (2b): Compound **2b** was isolated by column chromatography with CH_2Cl_2/CH_3OH (50:1) as the eluent. Yield 0.3 g (28%); m.p. 272–274 °C. HRMS (EI): calcd. for $C_{26}H_{34}N_6O_6$ 526.2540; found 526.2538. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.53–1.65 [m, 8 H, $N(1)_{ur1}CH_2CH_2$, $N(1)_{ur2}CH_2CH_2$, $N(1)_{thy}CH_2CH_2$, $N(3)_{thy}CH_2CH_2$], 1.92 [s, 3 H, $C(5)_{thy}CH_3$], 2.06 [s, 3 H, $C(6)_{ur1}CH_3$], 2.11 [s, 3 H, $C(6)_{ur2}CH_3$], 3.39 (s, 3 H, $N_{ur1}CH_3$), 3.40 (s, 3 H, $N_{ur2}CH_3$), 3.74 [m, 2 H, $N(1)_{thy}CH_2$], 3.86 [s, 2 H, $C(5)_{ur1}CH_2C(5)_{ur2}$], 3.92 [m, 2 H, $N(3)_{thy}CH_2$], 3.93 [m, 2 H, $N(1)_{ur1}CH_2$], 3.96 [m, 2 H, $N(1)_{ur2}CH_2$], 6.91 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 110.5 [C(5)], 138.0 [C(6)], 151.8 [C(2)], 163.3 [C(4)]; ur1: 16.6 (CH_3), 28.7 (NCH_3), 111.5 [C(5)], 148.9 [C(6)], 151.2 [C(2)], 162.9 [C(4)]; ur2: 16.9 (CH_3), 28.6 (NCH_3), 110.9 [C(5)], 149.1 [C(6)], 151.4 [C(2)], 163.1 [C(4)]; spacers: 20.6 [$C(5)_{ur1}CC(5)_{ur2}$], 24.6 [$N(1)_{thy}CC$], 25.9 [$N(3)_{thy}CC$], 25.2 [$N(1)_{ur2}CC$], 25.9 [$N(1)_{ur1}CC$], 40.9 [$N(3)_{thy}C$], 48.2 [$N(1)_{thy}C$], 43.9 [$N(1)_{ur1}C$], 44.6 [$N(1)_{ur2}C$] ppm. MS (EI): m/z (%) = 527 (23) [M + 1]$^+$, 526 (78) [M]$^+$, 511 (100) [M – 15]$^+$, 373 (38), 333 (18), 292 (37), 235 (17), 206 (31), 193 (48), 181 (63), 166 (46), 153 (52), 141 (21), 127 (22), 122 (19). $C_{26}H_{34}N_6O_6$ (526.59): calcd. C 59.30, H 6.51, N 15.96; found C 59.39, H 6.63, N 15.83.

9,15,25,28,29-Pentamethyl-1,7,9,15,17,23-hexaazatetracyclo-[21.3.1.1^{7,11}.1^{13,17}]nonacosa-11(28),13(29),25(26)-triene-8,10,14,16,24,27-hexaone (2c): Compound **2c** was isolated by column chromatography with CH_2Cl_2/CH_3OH (55:1) as the eluent. Yield 0.32 g (29%); m.p. 222–223 °C. HRMS (EI): calcd. for $C_{28}H_{38}N_6O_6$ 554.2853; found 554.2849. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.33 [m, 4 H, $N(1)_{thy}CH_2CH_2CH_2$, $N(3)_{thy}CH_2CH_2CH_2$], 1.54 [m, 2 H, $N(3)_{thy}CH_2CH_2$], 1.64–1.71 [m, 6 H, $N(1)_{ur1}CH_2CH_2$, $N(1)_{ur2}CH_2CH_2$, $N(1)_{thy}CH_2CH_2$], 1.84 [s, 3 H, $C(5)_{thy}CH_3$], 2.23 [s, 6 H, $C(6)_{ur1}CH_3$, $C(6)_{ur2}CH_3$], 3.34 (s, 3 H, $N_{ur1}CH_3$), 3.38 (s, 3 H, $N_{ur2}CH_3$), 3.64 [m, 2 H, $N(1)_{thy}CH_2$], 3.75 [s, 2 H, $C(5)_{ur1}CH_2C(5)_{ur2}$], 3.84 [m, 2 H, $N(3)_{thy}CH_2$], 3.94 [m, 2 H, $N(1)_{ur2}CH_2$], 3.97 [m, 2 H, $N(1)_{ur1}CH_2$], 6.85 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 109.6 [C(5)], 138.4 [C(6)], 151.3 [C(2)], 163.7 [C(4)]; ur1: 16.5 (CH_3), 28.5 (NCH_3), 110.5 [C(5)], 151.9 [C(2)], 149.0 [C(6)], 162.8 [C(4)]; ur2: 16.7 (CH_3), 28.5 (NCH_3), 111.0 [C(5)], 148.6 [C(6)], 151.9 [C(2)], 163.0 [C(4)]; spacers: 22.0 [$C(5)_{ur1}CC(5)_{ur2}$], 23.2 [$N(1)_{thy}CCC$], 23.7 [$N(3)_{thy}CCC$], 27.1 [$N(3)_{thy}CC$], 27.8 [$N(1)_{ur1}CC$], 27.9 [$N(1)_{ur2}CC$], 28.0 [$N(1)_{th}CC$], 40.7 [$N(3)_{th}C$], 44.6 [$N(1)_{ur1}C$], 44.9 [$N(1)_{ur2}C$], 48.9 [$N(1)_{th}C$] ppm. MS (EI): m/z (%) = 555 (33) [M + 1]$^+$, 554 (98) [M]$^+$, 539 (100) [M – 15]$^+$, 401 (31), 387 (17), 361 (12), 347 (14), 292 (30), 277 (22), 207 (22), 195 (24), 179 (20), 167 (22), 166 (32), 153 (29), 141 (15), 127 (17). $C_{28}H_{38}N_6O_6$ (554.64): calcd. C 60.63, H 6.91, N 15.15; found C 60.71, H 7.00, N 15.22.

10,16,27,30,31-Pentamethyl-1,8,10,16,18,25-hexaazatetracyclo-[23.3.1.1^{8,12}.1^{14,18}]hentriaconta-12(30),14(31),27(28)-triene-9,11,15,17,26,29-hexaone (2d): Compound **2d** was isolated by column chromatography with CH_2Cl_2/CH_3OH (65:1) as the eluent. Yield 0.35 g (30%); m.p. 115–116 °C. HRMS (EI): calcd. for $C_{30}H_{42}N_6O_6$ 582.3166; found 582.317. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.28 [m, 8 H, $N(1)_{ur1}CH_2CH_2CH_2$, $N(1)_{ur2}CH_2CH_2CH_2$, $N(1)_{th}CH_2CH_2CH_2$, $N(3)_{th}CH_2CH_2CH_2$], 1.33 [m, 2 H, $N(1)_{ur2}CH_2CH_2$], 1.51–1.55 [m, 4 H, $N(1)_{thy}CH_2CH_2$, $N(1)_{ur1}CH_2CH_2$], 1.62 [m, 2 H, $N(3)_{thy}CH_2CH_2$], 1.89 [s, 3 H, $C(5)_{thy}CH_3$], 2.12 [s, 3 H, $C(6)_{ur1}CH_3$], 2.13 [s, 3 H, $C(6)_{ur2}CH_3$], 3.38 (s, 6 H, $N_{ur1}CH_3$, $N_{ur2}CH_3$), 3.71 [m, 2 H, $N(1)_{thy}CH_2$], 3.84 [s, 2 H, $C(5)_{ur1}CH_2C(5)_{ur2}$], 3.86 (m, 4 H, $N_{ur1}CH_2$, $N_{ur2}CH_2$), 3.92 [m, 2 H, $N(3)_{thy}CH_2$], 6.90 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.0 (CH_3), 110.1 [C(5)], 138.1 [C(6)], 151.4 [C(2)],

163.6 [C(4)]; ur1: 16.5 (CH_3), 28.6 (NCH_3), 111.0 [C(5)], 149.2 [C(6)], 151.7 [C(2)], 163.1 [C(4)]; ur2: 16.7 (CH_3), 28.67 (NCH_3), 111.2 [C(5)], 148.9 [C(6)], 151.5 [C(2)], 163.2 [C(4)]; spacers: 20.8 [$C(5)_{ur1}CC(5)_{ur2}$], 25.9 [$N(1)_{ur1}CCC$], 26.0 [$N(1)_{ur2}CCC$], 26.3 [$N(3)_{thy}CCC$], 26.7 [$N(1)_{thy}CCC$], 27.4 [$N(3)_{thy}CC$], 28.8 [$N(1)_{thy}CC$], 28.9 [$N(1)_{ur2}CC$], 28.9 [$N(1)_{ur1}CC$], 41.3 [$N(3)_{thy}C$], 44.9 [$N(1)_{ur2}C$], 45.1 [$N(1)_{ur1}C$], 49.2 [$N(1)_{thy}C$] ppm. MS (EI): *m/z* (%) = 583 (34) $[M + 1]^+$, 582 (100) $[M]^+$, 567 (52) $[M - 15]^+$, 429 (14), 415 (11), 361 (10), 292 (17), 221 (11), 209 (16), 193 (11), 179 (20), 167 (14), 166 (22), 154 (14), 153 (19), 141 (15), 127 (20). $C_{30}H_{42}N_6O_6$ (582.69): calcd. C 61.84, H 7.27, N 14.42; found C 61.69, H 7.23, N 14.51.

8,14,23-Trimethyl-1,6,8,14,16,21-hexaazatetracyclo[19.3.1.1^{6,10}.1^{12,16}]heptacosa-10(26),12(27),23(24)-triene-7,9,13,15,22,25-hexaone (2e): Compound **2e** was isolated by column chromatography with CH_2Cl_2/CH_3OH (70:1) as the eluent. Yield 0.12 g (12%); m.p. 112–113 °C. HRMS (EI): calcd. for $C_{24}H_{30}N_6O_6$ 498.2227; found 498.223. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.62 [m, 2 H, $N(3)_{thy}CH_2CH_2$], 1.65 [m, 2 H, $N(1)_{ur12}CH_2CH_2$], 1.72 [m, 2 H, $N(1)_{thy}CH_2CH_2$], 1.65 [m, 2 H, $N(1)_{ur1}CH_2CH_2$], 1.92 [s, 3 H, $C(5)_{thy}CH_3$], 3.36 (s, 3 H, $N_{ur1}CH_3$), 3.37 (s, 3 H, $N_{ur2}CH_3$), 3.39 [s, 2 H, $C(5)_{ur1}CH_2C(5)_{ur2}$], 3.72 [m, 2 H, $N(1)_{thy}CH_2$], 3.80 [m, 2 H, $N(1)_{ur2}CH_2$], 3.92 (m, 2 H, $N_{ur1}CH_2$), 3.94 [m, 2 H, $N(3)_{thy}CH_2$], 6.75 [s, 1 H, $C(6)_{ur2}H$], 6.90 [s, 1 H, $C(6)_{ur1}H$], 6.91 [s, 1 H, $C(6)_{thy}H$] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = thy: 13.1 (CH_3), 110.59 [C(5)], 138.0 [C(6)], 151.8 [C(2)], 163.2 [C(4)]; ur1: 28.2 (NCH_3), 109.9 [C(5)], 140.0 [C(6)], 151.3 [C(2)], 163.1 [C(4)]; ur2: 28.2 (NCH_3), 111.3 [C(5)], 138.6 [C(6)], 151.3 [C(2)], 163.1 [C(4)]; spacers: 24.5 [$N(3)_{thy}CC$], 24.7 [$N(1)_{ur2}CC$], 25.1 [$C(5)_{ur1}CC(5)_{ur2}$], 25.7 [$N(1)_{ur1}CC$], 26.0 [$N(1)_{thy}CC$], 40.6 [$N(3)_{thy}C$], 48.3 [$N(1)_{thy}C$], 48.9 [$N(1)_{ur2}C$], 49.2 [$N(1)_{ur1}C$] ppm. MS (EI): *m/z* (%) = 499 (26) $[M + 1]^+$, 498 (100) $[M]^+$, 319 (14), 192 (11), 180 (12), 179 (12), 96 (17). $C_{24}H_{30}N_6O_6$ (498.53): calcd. C 57.82, H 6.07, N 16.86; found C 57.75, H 6.18, N 16.98.

8,14,23,26,27-Pentamethyl-1,6,8,14,16,21,23-heptaazatetracyclo-[21.1.1.1^{6,10}.1^{12,16}]heptacosa-10(27),12(26)-diene-7,9,13,15,22,24,25-heptaone (7): Compound **7** was isolated by column chromatography with CH_2Cl_2/CH_3OH (70:1) as the eluent. Yield 0.50 g (46%); m.p. 226 °C. HRMS (EI): calcd. for $C_{25}H_{33}N_7O_7$ 543.2441; found 543.244. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.62 [m, 8 H, NCH_2CH_2, $N(1)_{ur}CH_2CH_2$], 3.34 (s, 3 H, NCH_3), 3.40 (s, 6 H, $N_{ur}CH_3$), 3.88 [s, 2 H, $C(5)_{ur}CH_2C(5)_{ur}$], 3.90 [m, 8 H, $N(1)_{ur}CH_2$, NCH_2] ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = isocyanurate unit: 29.5 (NCH_3), 148.8 [C(2) and C(6)], 148.9 [C(4)]; ur: 16.8 (CH_3), 28.7 (NCH_3), 111.3 [C(5)], 151.4 [C(2)], 149.6 [C(6)], 163.0 [C(4)]; spacers: 20.6 [$C(5)_{ur}CC(5)_{ur}$], 24.7, 25.7 ($N_{ur}CC$, NCC), 42.4 (NCH_2), 44.2 [$N(1)_{ur}CH_2$] ppm. MS (EI): *m/z* (%) = 544 (38) $[M + 1]^+$, 543 (100) $[M]^+$, 528 (66), 512 (21), 404 (12), 391 (22), 390 (30), 376 (15), 292 (22), 261 (17), 206 (13), 193 (19), 192 (13), 191 (13), 181 (13), 179 (17), 167 (25), 166 (47), 154 (19), 153 (24), 144 (20), 140 (12), 122 (11), 109 (16). $C_{25}H_{33}N_7O_7$ (543.57): calcd. C 55.24, H 6.12, N 18.04; found C 55.38, H 6.15, N 18.11.

Supporting Information (see also the footnote on the first page of this article): 1D and 2D NMR spectra of the studied acyclic and macrocyclic compounds.

Acknowledgments

This work was partially supported by the Russian Foundation for Basic Research (05-03-33008, 05-03-32558-a and 07-03-00392-a). This investigation was carried out in the NMR department of the Federal Collective Spectral Analysis Center for Physical and Chemical Investigations of Structure, Properties and Composition of Matter and Materials (CKP SAC) and Federal CKP for Physical and Chemical Investigations of Matter and Materials (FCKP PCI) (state contracts of the Russian Federation Ministry of Education and Science, 02.451.11.7036 and 02.451.11.7019). The authors are grateful to Dr. S. G. Fattakhov for a sample of 1-methylisocyanuric acid. The authors are thankful to Dr. R. Fröhlich and Prof. G. Erker for providing for X-ray studies using the KappaCCD diffractometer at the University of Münster, Germany. One of us (Sh. L.) acknowledges the Russian Science Support Foundation for a doctoral research grant.

[1] a) N. J. Leonard, R. S. McCredie, M. W. Logue, R. L. Cundall, *J. Am. Chem. Soc.* **1973**, *95*, 2320–2324; b) H. Koroniak, K. Golankiewicz, *Pol. J. Chem.* **1978**, *52*, 567–570; c) J. L. Flippen, R. D. Gilard, I. L. Karle, *Acta Crystalogr. Sect. B* **1972**, 360–367.

[2] H. P. Diogo, A. R. Dias, A. Dhalla, M. E. Minas da Piedale, T. P. Begley, *J. Org. Chem.* **1991**, *56*, 7340–7345.

[3] a) J. T. Redd, J. S. Bradshaw, P. Huszthy, R. M. Izatt, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1997**, 301–308; b) J. T. Redd, J. S. Bradshaw, P. Huszthy, R. M. Izatt, D. N. Kent, *J. Heterocycl. Chem.* **1998**, *35*, 1–8; c) S. Kumar, D. Pall, H. Singh, *J. Inclusion Phenom. Macrocyclic Chem.* **2000**, 371–382.

[4] V. P. Krivonogov, G. A. Tolstikov, G. G. Kozlova, G. A. Sivkova, D. N. Lazareva, Yu. I. Murinov, F. S. Zarudii, V. A. Myshkin, A. F. Ismagilova, L. V. Spirikhin, I. B. Abdrakhmanov, in *Proceedings of the I International Conference on "The Chemistry and Biological Activity of Nitrogen-Containing Heterocycles and Alkaloids"* (Eds.: V. G. Kartsev, G. A. Tolstikov), Iridium-Press, Moscow, **2001**, vol. 1, p. 348–353.

[5] a) S. Kumar, D. Paul, H. Singh, *Tetrahedron Lett.* **1997**, *38*, 3607–3608; b) S. Kumar, G. Hundal, D. Paul, M. S. Hundal, H. Singh, *J. Org. Chem.* **1999**, *64*, 7717–7726.

[6] a) Y. S. Shvetsov, I. S. Salikhov, V. S. Reznik, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1976**, 1103–1106; b) M. M. Htay, O. Meth-Cohn, *Tetrahedron Lett.* **1976**, *17*, 79–82; c) Y. S. Shvetsov, I. S. Salikhov, V. S. Reznik, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1978**, 2079–2084; d) K. Golankiewicz, B. Skalski, *Pol. J. Chem.* **1978**, *52*, 1365–1373; e) T. Itahara, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 3239–3246; f) V. Caplar, L. Tumir, M. Zinic, *Croat. Chem. Acta* **1996**, *68*, 1617–1631.

[7] a) T. Kinoshita, S. Odawara, K. Fukumura, S. Furukawa, *J. Heterocycl. Chem.* **1985**, *22*, 1573–1576; b) A. F. Cichy, R. Saibaba, H. I. El Subbagh, R. P. Panzica, E. Abushanab, *J. Org. Chem.* **1991**, *56*, 4653–4658; c) S. G. Fattakhov, S. E. Solov'eva, Yu. Ya. Efremov, I. Kh. Rizvanov, V. S. V. S. Reznik, *Russ. J. Gen. Chem.* **2001**, *71*, 469–470; d) R. Kh. Giniyatullin, A. S. Mikhailov, V. E. Semenov, V. D. Akamsin, V. S. Reznik, A. V. Chernova, G. M. Doroshkina, A. A. Nafikova, S. K. Latypov, Y. Y. Efremov, D. R. Sharafutdinova, A. T. Gubaidullin, I. A. Litvinov, *Russ. Chem. Bull.* **2003**, *112*, 1595–1599; e) S. Kumar, D. Paul, S. Singh, *J. Chem. Soc. Perkin Trans. 1* **2000**, 1037–1043; f) S. Kumar, G. Hundal, D. Paul, M. S. Hundal, S. H. Singh, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2295–2301.

[8] a) U. Eiermann, C. Krieger, F. A. Neugebauer, *Chem. Ber.* **1990**, *123*, 1885–1889; b) T. Kauffmann, B. Muke, R. Otter, D. Tigler, *Angew. Chem.* **1975**, *87*, 746–747; c) B. Muke, T. Kauffmann, *Chem. Ber.* **1980**, *113*, 2739–2748.

[9] a) A. S. Mikhailov, N. G. Pashkurov, V. S. Reznik, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1982**, 930–932; b) V. M. Cherkasov, T. A. Dashevskaya, *Ukr. Khim. Zh.* **1983**, 1308–1310; c) A. S. Mikhailov, V. I. Skuzlova, N. G. Pashkurov, V. S. Reznik, *Zh. Obshch. Khim.* **1996**, *66*, 514–518; d) T. Itahara, *J. Heterocycl. Chem.* **1997**, *34*, 687–688; e) A. S. Mikhailov, R. Kh. Giniyatullin, V. E. Semenov, V. S. Reznik, A. A. Nafikova, S. K. Latypov, Y. Y. Efremov, D. R. Sharafutdinova, *Russ. Chem. Bull.* **2003**, *112*, 1399–1402.

[10] a) L. S. Kuznetsova, A. R. Mustafina, A. S. Mikhailov, V. E. Kataev, V. S. Reznik, *J. Solution Chem.* **2002**, *31*, 895–904; b) A. R. Mustafina, L. S. Kuznetsova, A. S. Mikhailov, V. E. Kataev, A. I. Konovalov, W. D. Habicher, *J. Solution Chem.* **2004**, *33*, 1257–1276; c) R. R. Shagidullin, A. V. Chernova, G. M. Doroshkina, V. E. Kataev, Z. G. Bazhanova, S. A. Katsyba, V. S. Reznik, A. S. Mikhailov, R. Kh. Giniyatullin, N. G. Pashkurov, Yu. Ya. Efremov, A. A. Nafikova, *Zh. Obshch. Khim.* **2002**, *72*, 1725–1732; d) R. R. Shagidullin, A. V. Chernova, Z. G. Bazhanova, L. Jenn-Huei, V. E. Kataev, S. A. Katsyuba, V. S. Reznik, *J. Mol. Struct.* **2004**, 1–9.

[11] a) G. R. Newkome, A. Nayak, J. Otemad, D. A. Van, W. H. Benton, *J. Org. Chem.* **1978**, *43*, 3362–3367; b) G. R. Newkome, A. M. Nayak, G. Sorci, W. H. Benton, *J. Org. Chem.* **1979**, *44*, 3812–3816.

[12] R. E. Cramer, V. Fermin, E. Kuwabara, R. Kirkup, M. Selman, *J. Am. Chem. Soc.* **1991**, *113*, 7033–7034.

[13] a) W. Pfleiderer, F. Sagi, L. Grozinger, *Chem. Ber.* **1966**, *99*, 3530–3538; b) M. Kondo, H. Tanaka, S. Furukawa, *Synthesis* **1986**, 857–859.

[14] T. Kinoshita, H. Tanaka, S. Furukawa, *Chem. Pharm. Bull.* **1986**, 1809–1813.

[15] a) V. E. Semenov, V. D. Akamsin, V. S. Reznik, Y. Y. Efremov, D. R. Sharafutdinova, A. A. Nafikova, N. M. Azancheev, *Mendeleev Commun.* **2001**, 97–98; b) V. E. Semenov, V. D. Akamsin, V. S. Reznik, A. V. Chernova, G. M. Dorozhkina, Y. Y. Efremov, A. A. Nafikova, *Tetrahedron Lett.* **2002**, *43*, 9683–9686.

[16] a) D. T. Browne, J. Eisinger, N. J. Leonard, *J. Am. Chem. Soc.* **1968**, *90*, 7302–7323; b) N. J. Leonard, *Acc. Chem. Res.* **1979**, *12*, 423–429.

[17] a) T. Itahara, *J. Chem. Soc., Perkin Trans. 1* **1996**, 2695–2700; b) T. Itahara, *Bull. Chem. Soc. Jpn.* **2002**, *75*, 285–290; c) Y. Kuroda, J. M. Lintuluoto, H. Ogoshi, *J. Chem. Soc., Perkin Trans. 2* **1996**, 333–339.

[18] a) O. F. Shall, G. W. Gokel, *J. Am. Chem. Soc.* **1994**, *116*, 6089–6100; b) O. F. Shall, G. W. Gokel, *J. Org. Chem.* **1996**, *61*, 1449–1458.

[19] a) A. E. Derome, *Modern NMR Techniques for Chemistry research*, Pergamon Press, **1988**; b) E. Breitmaier, W. Voelter, *Carbon-13 NMR Spectroscopy: High Resolution Methods and Applications in Organic Chemistry and Biochemistry*, VCH, Weinheim, **1987**; c) H. Günther, *NMR Spectroscopy: An Introduction*, John Wiley & Sons, New York, **1987**.

[20] L. Galiullina, A. Nikolaev, V. Semenov, V. Reznik, Sh. Latypov, *Tetrahedron* **2006**, *62*, 7021–7033.

[21] a) R. M. Gomila, D. Quinonero, C. Rotger, C. Garau, A. Frontera, P. Ballester, A. Costa, P. M. Deya, *Org. Lett.* **2002**, *4*, 399; b) E. Kolehmainen, J. Koivisto, V. Nikiforov, M. Perakyla, K. Tuppurainen, K. Laihia, R. Kauppinen, S. Miltsov, V. Karavan, *Magn. Reson. Chem.* **1999**, 743; c) P. Rossi, G. S. Harbison, *J. Magn. Reson.* **2001**, 1; d) I. Alkorta, J. Elguero, A. Fruchier, N. Jagerovic, G. P. A. Yap, *J. Mol. Struct.* **2004**, 251–254; e) I. Alkorta, J. Elguero, *New J. Chem.* **1998**, *22*, 381–385; f) I. Alkorta, J. Elguero, *J. Magn. Reson. Chem.* **2004**, 955–961; g) A. A. Balandina, A. A. Kalinin, V. A. Mamedov, B. Figadere, Sh. K. Latypov, *Magn. Reson. Chem.* **2005**, 816–828; h) A. Balandina, D. Saifina, V. Mamedov, Sh. Latypov, *J. Mol. Struct.* **2006**, 77–81; i) C. Bassarello, P. Cimino, L. Gomez-Paloma, R. Riccio, G. Bifulco, *Tetrahedron* **2003**, *59*, 9555; j) P. Cimino, L. Gomez-Paloma, D. Duca, R. Riccio, G. Bifulco, *Magn. Reson. Chem.* **2004**, S26; k) A. Balandina, V. Mamedov, X. Franck, B. Figadere, Sh. Latypov, *Tetrahedron Lett.* **2004**, 4003–4007.

[22] a) L. Ernst, *Progr. Nucl. Magn. Reson. Spectrosc.* **2000**, 47–190; b) M. Lin, K. F. Mok, Y.-H. Lai, *Tetrahedron. Lett.* **2003**, 3527–3530; c) D. N. Butler, M. D. Shang, M. Mann, R. Johnston, *ARKIVOC* **2001**, 23–34; d) L. Galiullina, M. Shulaeva, S. Fattahov, V. Reznik, Sh. Latypov, *J. Mol. Struct.* **2007**, 245–251.

[23] a) J. Tinoco Jr, *J. Am. Chem. Soc.* **1960**, *82*, 4785–4790; b) W. J. Rhodes, *J. Am. Chem. Soc.* **1961**, *83*, 3609–3617.

[24] F. Seyama, K. Akahori, Y. Sakata, S. Misumi, M. Aidd, C. Nagata, *J. Am. Chem. Soc.* **1988**, *110*, 2192.

[25] C. A. Hunter, *J. Am. Chem. Soc.* **1990**, *112*, 5525–5534.

[26] G. M. Sheldrick, *SHELXL97*, A computer program for crystal structure determination, University for Göttingen (Germany), **1997**.

[27] K. Stott, J. Stonehouse, J. Keeler, T. L. Hwang, A. J. Shaka, *J. Am. Chem. Soc.* **1995**, *117*, 4199.

[28] Cherwell Scientific, Oxford, UK.

[29] H. Friebolin, *Basic one and two-dimensional NMR spectroscopy*, VCH, Weincheim, **1991**.

[30] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery Jr, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, *GAUSSIAN 98, Revision A.6*, Gaussian, Pittsburgh, PA, **1998**.

[31] V. S. Reznik, Y. S. Shvetsov, I. S. Salikhov, B. E. Ivanov, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1977**, 880–882.

Received: February 21, 2007
Published Online: July 17, 2007

