Binuclear and polynuclear transition metal complexes with macrocyclic ligands

3.* New polydentate macrocyclic ligands in reactions of 4-alkyl-2,6-diformylphenols with 1,2-diaminobenzenes

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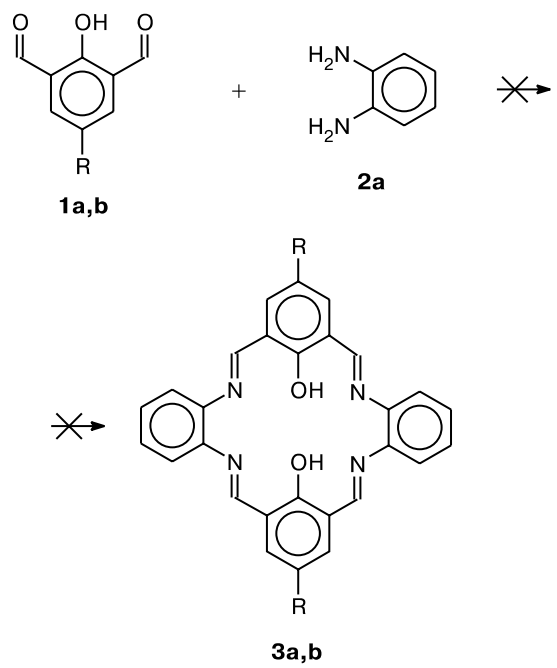
The mechanism of abnormal condensation of 2,6-diformyl-4-R-phenols with 1,2-diaminobenzenes accompanied by the reduction of two of four double C=N bonds in macrocyclic Schiff´s bases formed was studied by DFT (gradient-corrected PBE functional, TZ2p basis set). In the first step, [1+1] Schiff´s base is formed and disproportionates further to afford amine and benzoimidazolylphenols. Two new macrocyclic polydentate ligands containing two CH_2—NH moieties in the rings were synthesized. The reduction of one of these ligands with sodium borohydride gave the new macrocyclic ligand, whose structure and conformations were studied by the DFT method.

Key words: polydentate ligands, Schiff´s bases, 2,6-diformylphenols, DFT method.

Condensations of 2,6-diformyl-4-R-phenols **1** with 1,2-diaminobenzenes **2** occur abnormally. The reactions of 2,6-diformyl-4-methylphenol (**1a**) and 4-chloro-2,6-diformylphenol (**1b**) with 1,2-diaminobenzene (**2a**) in boiling MeOH unexpectedly afford partially hydrogenated macrocycles **4a,b** in which two of four C=N azomethine bonds are reduced to the CH_2NH moieties instead of the expected products of [2+2] condensation: macrocyclic Schiff´s bases **3a,b** (Scheme 1).[2] The reaction of 4-*tert*-butyl-2,6-diformylphenol (**1c**) with 1,2-diamino-3,4,5,6-tetrafluorobenzene (**2b**) in the presence of Co^{II} and Mn^{II} perchlorates gives free partially hydrogenated macrocyclic Schiff´s base **4c** in 40% yield instead of the expected binuclear complexes of [2+2]-macrocyclic Schiff´s base.[3] Although none of these works indicates which of the agents acts as a reducing agent in these condensations, it is convincingly demonstrated[2] that the reduction occurs at the step of synthesis rather than during the isolation and further purification of the reaction products.

Scheme 1



1, 3: R = Me (**a**), Cl (**b**)

Results and Discussion

We showed in the previous work[1] that the reaction of phenol **1c** with diamine **2a** in boiling EtOH affords, in fact, two products in a molar ratio of 1 : 1, *viz.*, partially hydrogenated Schiff´s base (**4d**) and 2,6-bis(benzoimidazol-2-yl)-4-*tert*-butylphenol (**5a**) (Scheme 2). Continuing these studies, in this work we found that phenols **1a,c** react with 1,2-diamino-4,5-dimethylbenzene (**2c**) to form mixtures of products with the similar structure: **4e** and **5b**, **4f** and **5c**, respectively. In addition, phenol **5d**

* For Part 2, see Ref. 1.

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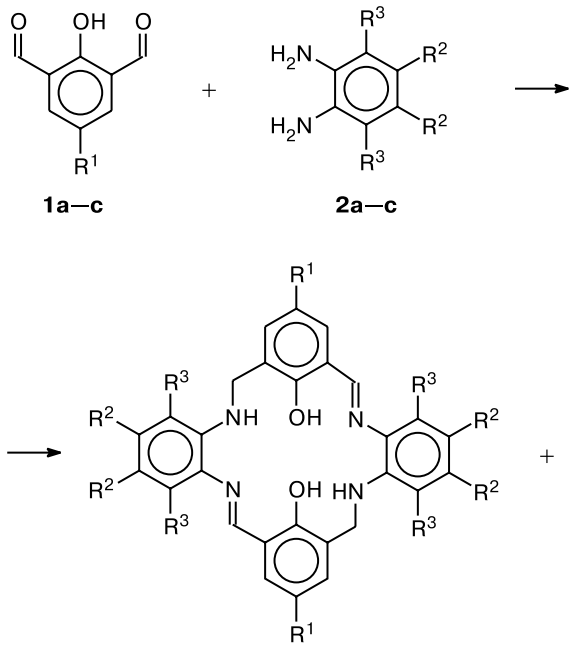
along with the known azomethine **4a** was isolated from the reaction of **1a** with **2a** (*cf.* Ref. 2).

Scheme 2



1a + **2a** —*i*→ **4a**
1b + **2a** —*i*→ **4b**
1c + **2b** —*iii*→ **4c**
1c + **2a** —*ii*→ **4d** + **5a**
1a + **2c** → **4e** + **5b**
1c + **2c** → **4f** + **5c**
1a + **2a** → **4a** + **5d**

Note. *i*. See Refs. 2, 3. *ii*. See Ref. 1. *iii*. See Ref. 3.

1: R^1 = Me (**a**), Cl (**b**), Bu^t (**c**);
2: $R^2 = R^3$ = H (**a**); $R^2 = R^3$ = F (**b**); R^2 = Me, R^3 = H (**c**)

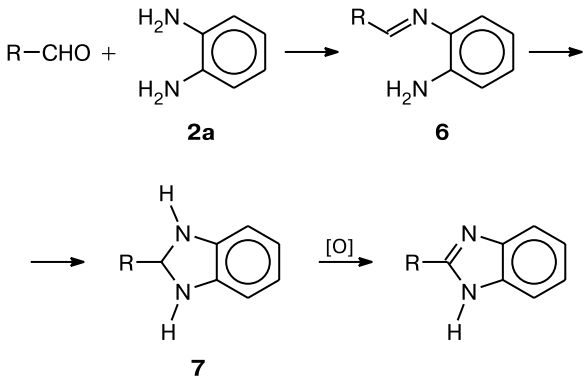
4	**a**	**b**	**c**	**d**	**e**	**f**
R^1	Me	Cl	Bu^t	Bu^t	Me	Bu^t
R^2	H	H	F	H	Me	Me
R^3	H	H	F	H	H	H

5	**a**	**b**	**c**	**d**
R^1	Bu^t	Me	Bu^t	Me
R^2	H	Me	Me	H

The variation of ratios of the reactants and solvent (going from anhydrous EtOH to 1,2-dimethoxyethane and their mixtures with water) and additives of such reducing agents as hydroquinone and ascorbic acid to the reaction mixture do not substantially change the ratio of formed products **4** and **5**. The presence of reducing agents and an excess of compound **2a** only decrease the yields of the latter, clearly indicating that 1,2-diaminobenzene itself is not the reducing agent in this reaction.

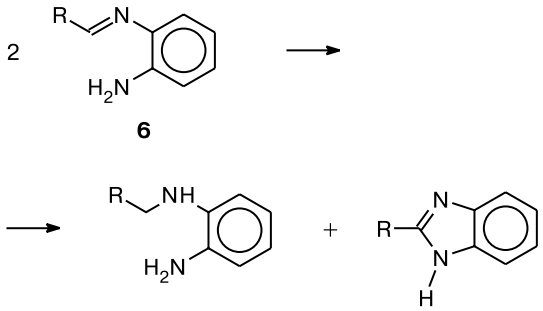
The formation of benzoimidazoles in the reaction of aldehydes with diaminobenzene **2a** and its derivatives has been described more than a century ago,[4] and this reaction is sufficiently well studied.[4—7] Schiff´s base[4] **6** appeared in the first step undergoes intramolecular ring closure to form imidazoline **7**, which is further dehydrogenated by air oxygen[4,5] or oxidants specially added to the reaction mixture (mercury oxide,[5,6] copper acetate,[5,7] or nitrobenzene[5]) (Scheme 3).

Scheme 3



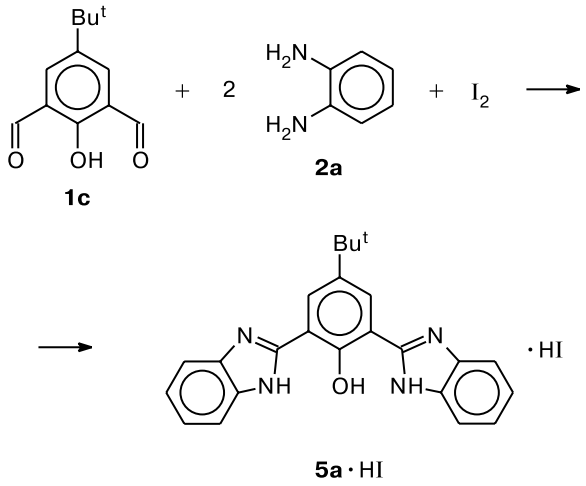
It has been proposed comparatively long ago[4] that Schiff´s base **6** itself can act as an oxidant toward imidazoline **7**. In this case, the base disproportionates (Scheme 4).

Scheme 4



We carried out the reaction of compounds **1c** and **2a** at ~20 °C in the presence of iodine as a weak oxidant to obtain salt **5a** · HI in ~100% yield (Scheme 5).

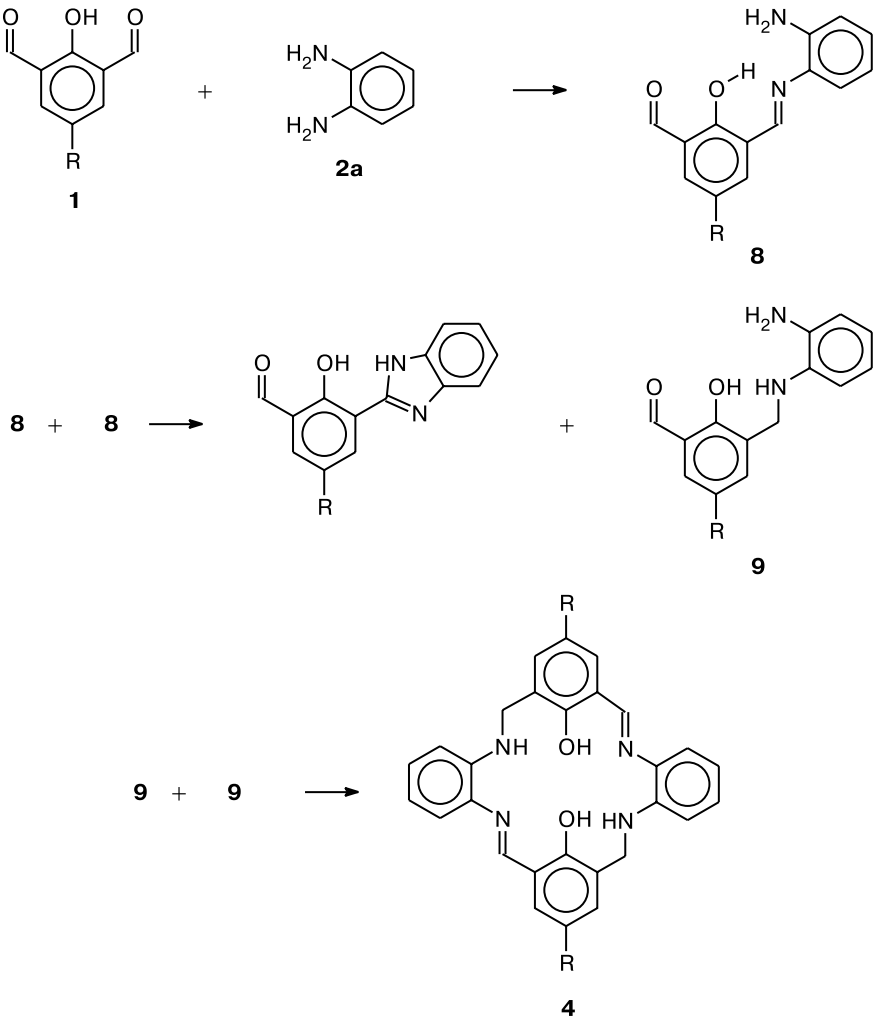
Scheme 5



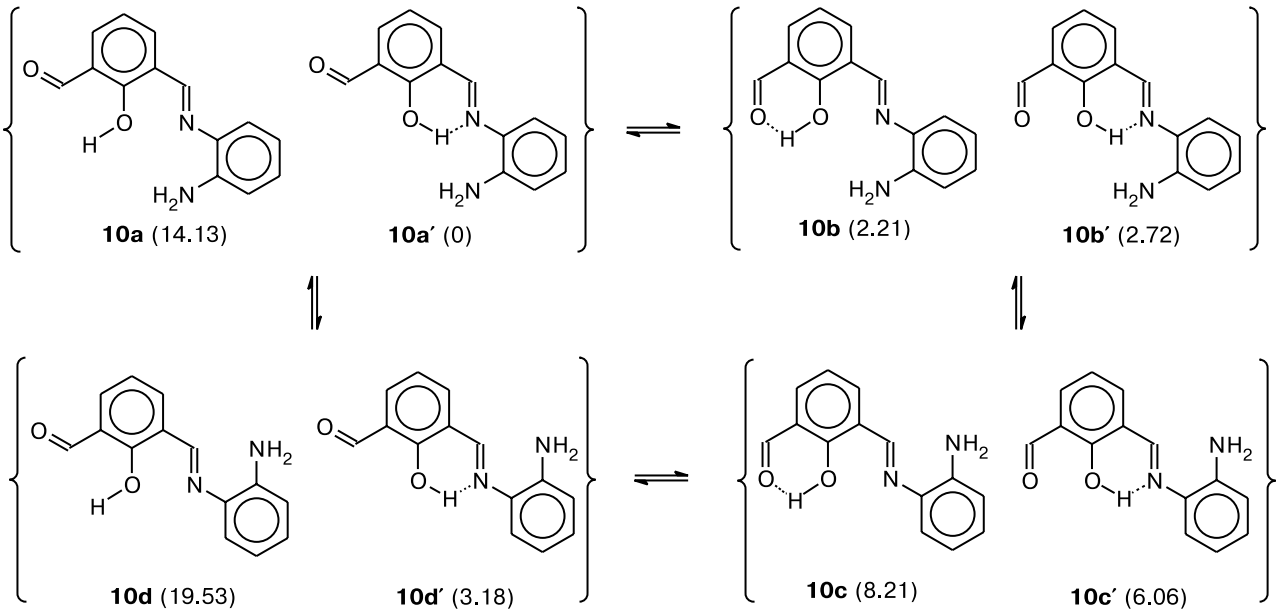
These experimental results and published data make it possible to propose a sufficiently reliable general scheme of formation of products **4** and **5** in reactions of compounds **1** and **2**, including several steps (Scheme 6). Undoubtedly, [1+1]-Schiff's base **8** is formed in the first step and undergoes further disproportionation. Two molecules of *N*-(3-formylbenzyl-2-hydroxy)-1,2-diaminobenzene (**9**) that formed are condensed to form macrocycle **4**.

To obtain more detailed data on the thermodynamics of the processes under study, we theoretically simulated the main steps of the sequence of reactions proposed for diformylphenol **1d** (R = H) with diaminobenzene **2a** by the DFT method using the gradient-corrected PBE functional and extended split TZ2p basis sets.[8] Schiff's base **10** formed in the first step can exist as four conformers. Conformation **10a**′ corresponds to the total energy minimum (Scheme 7).

Scheme 6



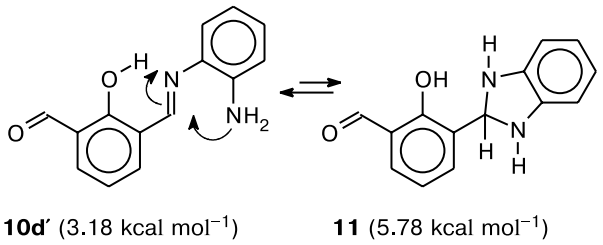
Scheme 7



Note. Relative energies of conformers are presented in parentheses (in kcal mol^{-1}).

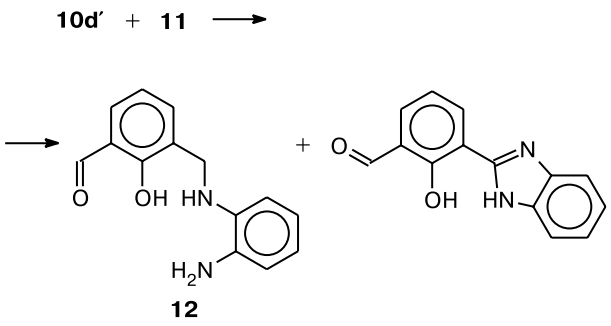
In conformer **10d**′, whose energy is higher by 3.18 kcal mol^{-1}, the distance between the N atom of the amino group and C atom of the imino group is ~3.5 Å, which favors intramolecular ring closure (Scheme 8). The process is characterized by the early transition state and a sufficiently high activation barrier (21.9 kcal mol^{-1}). However, as it is shown by the preliminary study, in the case of involvement of one or two solvent molecules in the transition state, the activation barrier can be decreased. More detailed data on this problem will be published elsewhere. Since the **10d**′ → **11** process is endothermic, the equilibrium concentration of imidazoline **11** should be very low. However, the equilibrium shift to the right occurs easily at a relatively low activation barrier, if **11** is rapidly leaves the reaction sphere due to oxidation, which occurs, in fact, for the reaction of **1c** with **2a** and iodine (see Scheme 5).

Scheme 8



Indeed, benzoimidazoline **11** is a strong reducing agent. Its interaction with Schiff′s base **10d**′ results in the reduction of the latter to diamine **12** and is accompanied, according to the calculation, by the energy gain equal to 27.3 kcal mol^{-1} (Scheme 9).

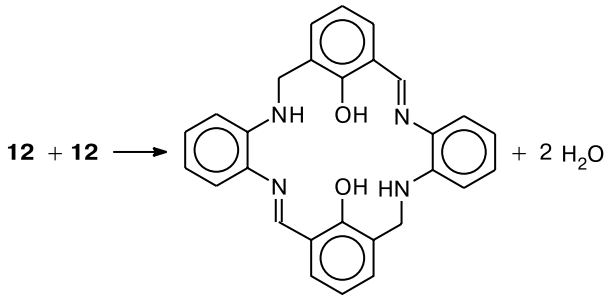
Scheme 9



The final step of condensation of two molecules of compound **12** gives a weak enthalpy gain (−0.12 kcal mol^{-1}) but it is favorable in entropy. Therefore, ΔG° of this reaction is −9.15 kcal mol^{-1} (Scheme 10).

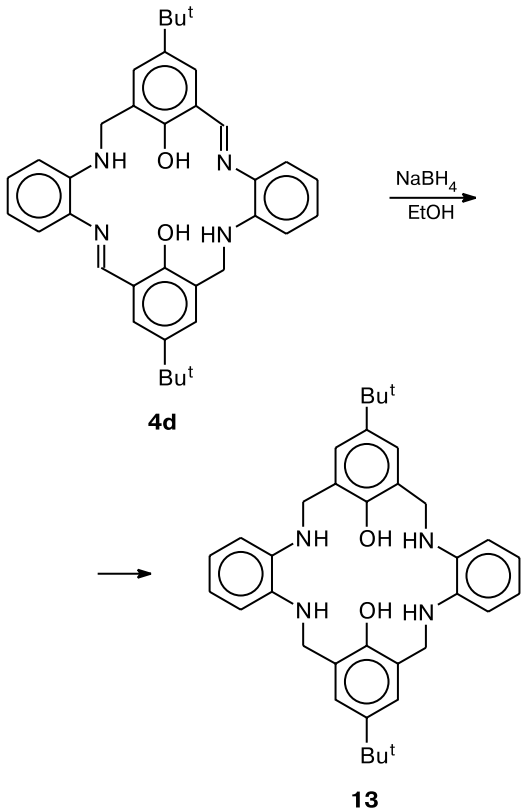
Macrocyclic Schiff′s bases **4** are readily reduced by $NaBH_4$ in EtOH to macrocyclic tetramines, which are very promising as ligands due to their high hydrolytic stability and favorably differ, in this respect, from the starting bases. The reduction of compound **4d** affords macrocycle **13** in high yield (Scheme 11). This yellow substance is soluble in organic solvents and water-insoluble. It forms binuclear complexes with copper(II), cobalt(II), nickel(II), and palladium(II) salts, which will

Scheme 10



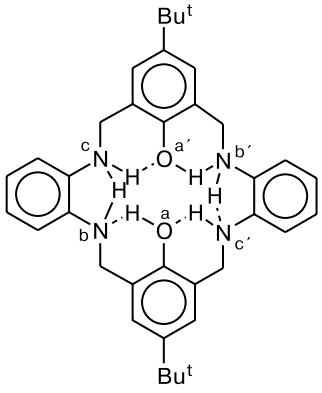
be described elsewhere. The structure of macrocycle **13** was established from the data of NMR spectroscopy, IR spectroscopy, and mass spectrometry and confirmed by elemental analysis. In the ^{1}H NMR spectra of macrocycle **13**, the signals of the NH and OH groups are considerably broadened, indicating hydrogen exchange.

Scheme 11



The macrocycles with close structures have been obtained previously[9] by the reduction of the respective macrocyclic Schiff´s bases based on diformylpyridine and phthalaldehydes. The DFT study of the structure of macrocycle **13** showed that the potential energy surface of this compound contains several local minima corresponding to different molecular conformers, which insignificantly differ from each other in energy and separated low barriers. The "saddle" conformation (**13´**) shown in three projections in Fig. 1 is the most thermodynamically stable.

Table 1. Lengths (*d*) of intracyclic hydrogen bonds D—H...A in conformer **13´**



13´

D—H	*d*/Å	H...A	*d*/Å
O_a—H_a	1.0040	H...N_b	1.8063
N_b—H_b	1.0256	H...N_c	2.3696
N_c—H_c	1.0227	H...$O_{a'}$	2.1463
$O_{a'}$—$H_{a'}$	1.0041	H...$N_{b'}$	1.8056
$N_{b'}$—$H_{b'}$	1.0246	H...$N_{c'}$	2.3706
$N_{c'}$—$H_{c'}$	1.0227	H...O_a	2.1466

Note. D is donor, and A is acceptor.

All intracyclic protons and O and N atoms in **13´** are included into a system of strong hydrogen bonds with short interatomic distances between protons and donor atoms (Table 1).

The second stable conformer, *viz.*, "boat" **13´´** (Fig. 2), lies by 3.94 kcal mol^{-1} higher in energy than **13´**. In this conformer, only two pairs of the O and N atoms are linked with each other by two hydrogen bonds each. The NH...O distances are 2.794 Å, and the OH...N distances are 2.654 Å.

The diameter of the internal cavity of macrocycle **13** in different conformers can vary from 3.5 to 4 Å. Therefore, in addition to the formation of complexes with one or two metal cations, compound **13** can likely bind various anions and donor molecules, such as ammonia, amines, water, and alcohols, due to the formation of hydrogen bonds with OH and NH groups. Compound **13** and similar macrocycles formed by the reduction of the CH=N bonds of macrocyclic Schiff´s bases represent a new type of polydentate ligands relative to nitrogen-containing crown ethers, calixarenes, and calixpyrroles by coordination ability. Their coordination properties are presently under study.

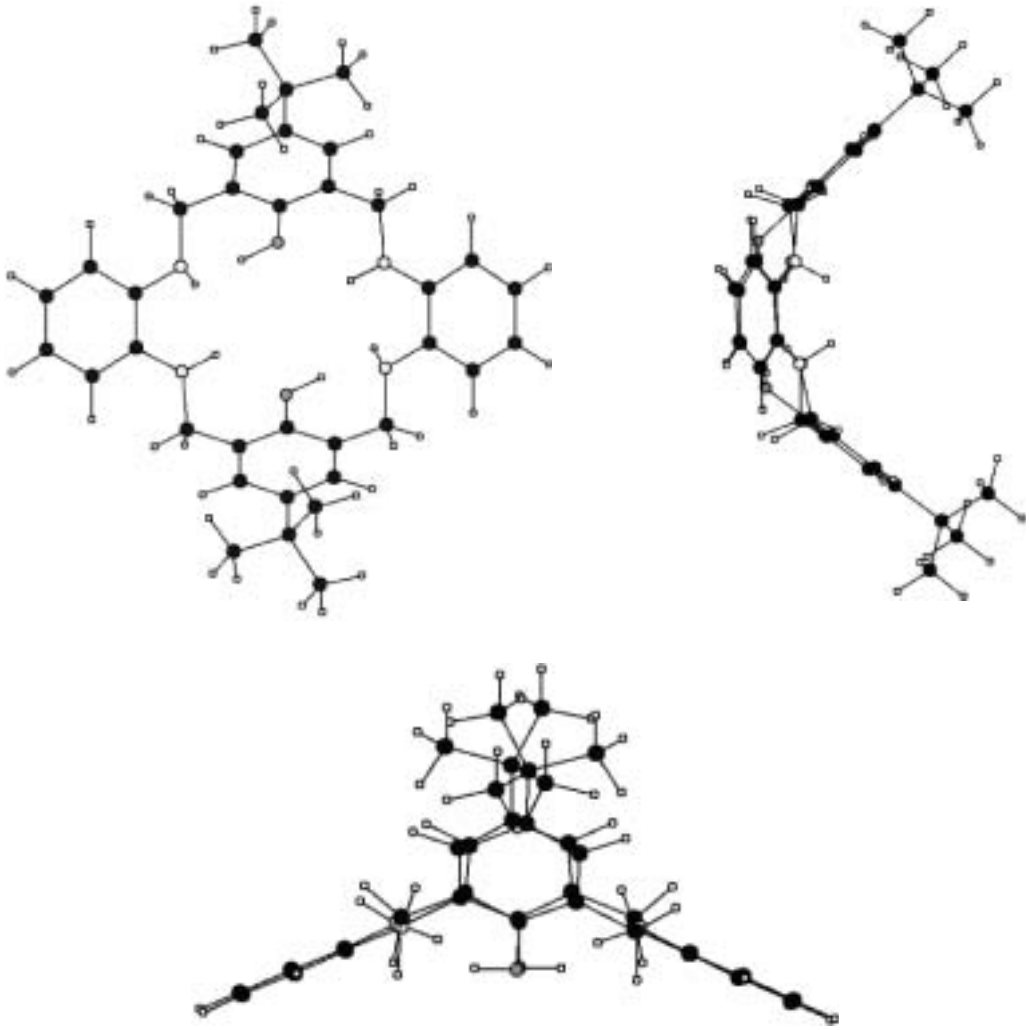


Fig. 1. Structure of the "saddle" conformer (**13´**) of macrocycle **13** according to the calculation data.

Experimental

NMR spectra were recorded on a Bruker DPX-300 instrument at 24 °C. IR spectra were recorded on Specord M-80 (in KBr pellets) and UR-2 (in Nujol) spectrometers. Mass spectra were obtained on a Finigan MAT 212 instrument (EI, 70 eV).

Condensation of compounds 1 and 2 (general procedure). Diformylphenol **1** (0.84 mmol) and diaminobenzene **2** (1.68 mmol) were dissolved in boiling anhydrous EtOH (25 mL), and the mixture was refluxed for 3 h. The precipitate of macrocycle **4** was filtered off. The filtrate was concentrated, and the residue was dissolved in $CHCl_3$ (1 mL). The insoluble derivative of benzoimidazole **5** was filtered off, and an additional amount of **4** was isolated from filtrate by chromatography on silica gel using AcOEt as the eluent. The constants of earlier characterized compounds **4a**,[2] **4d**,[1] and **5a** [1] coincide with the published values.

6,13,14,21,28,29-Hexamethyl-2,10,17,25-tetraazapentacyclo[24.4.1^{4,8}.1^{19,23}.0^{11,16}]dotriaconta-4,6,8(31),9,11,13,15,19,21,23(32),24,26,28,30-tetradecaene-31,32-diol (4e). M.p. 299—300 °C. ^{1}H NMR ($CDCl_3$), δ: 2.24 (s, 6 H, 2 Me); 2.31 (s, 12 H, 4 Me); 4.39 (s, 4 H, 2 CH_2); 6.79 (s, 2 H, 2 CH); 6.84 (s, 2 H, 2 CH); 7.14 (s, 2 H, 2 CH); 7.19 (s, 2 H, 2 CH); 8.55 (s, 2 H, 2 CH=N); 13.61 (s, 2 H, 2 OH). MS, m/z (I_{rel} (%)): 532 $[M]^+$ (5), 266 $[0.5\ M]^+$ (100).

6,21-Di(*tert*-butyl)-13,14,28,29-tetramethyl-2,10,17,25-tetraazapentacyclo[24.4.1^{4,8}.1^{19,23}.0^{11,16}]dotriaconta-4,6,8(31),9,11,13,15,19,21,23(32),24,26,28,30-tetradecaene-31,32-diol (4f). M.p. 306—307 °C. ^{1}H NMR ($CDCl_3$), δ: 1.30 (s, 18 H, 2 Bu^t); 2.20 (s, 6 H, 2 Me); 2.33 (s, 6 H, 2 Me); 4.43 (s, 4 H, 2 CH_2); 6.20 (br.s, 2 H, 2 NH); 6.78, 6.85, 7.30, 7.39 (all s, 2 H each, 8 CH); 8.58 (s, 2 H, 2 CH=N); 13.54 (s, 2 H, 2 OH). MS, m/z (I_{rel} (%)): 616 $[M]^+$ (6), 308 $[0.5\ M]^+$ (75), 293 $[0.5\ M - Me]^+$ (100). IR (Nujol), ν/cm^{-1}: 3420 (N—H), 1610 (C=N).

2,6-Bis(5,6-dimethylbenzoimidazol-2-yl)-4-methylphenol (5b). M.p. 228—230 °C. ^{1}H NMR (DMSO-d_6), δ: 2.34 (s, 12 H, 4 Me); 2.41 (s, 3 H, Me); 7.43 (s, 4 H, 4 CH): 8.08 (s, 2 H, 2 CH). ^{13}C NMR (DMSO-d_6), δ: 20.5, 20.7, 116.0, 128.3, 129.6, 131.5, 149.8, 154.1. MS, m/z (I_{rel} (%)): 396 $[M]^+$ (100). IR (Nujol), ν/cm^{-1}: 3620 (O—H), 3410 (N—H).

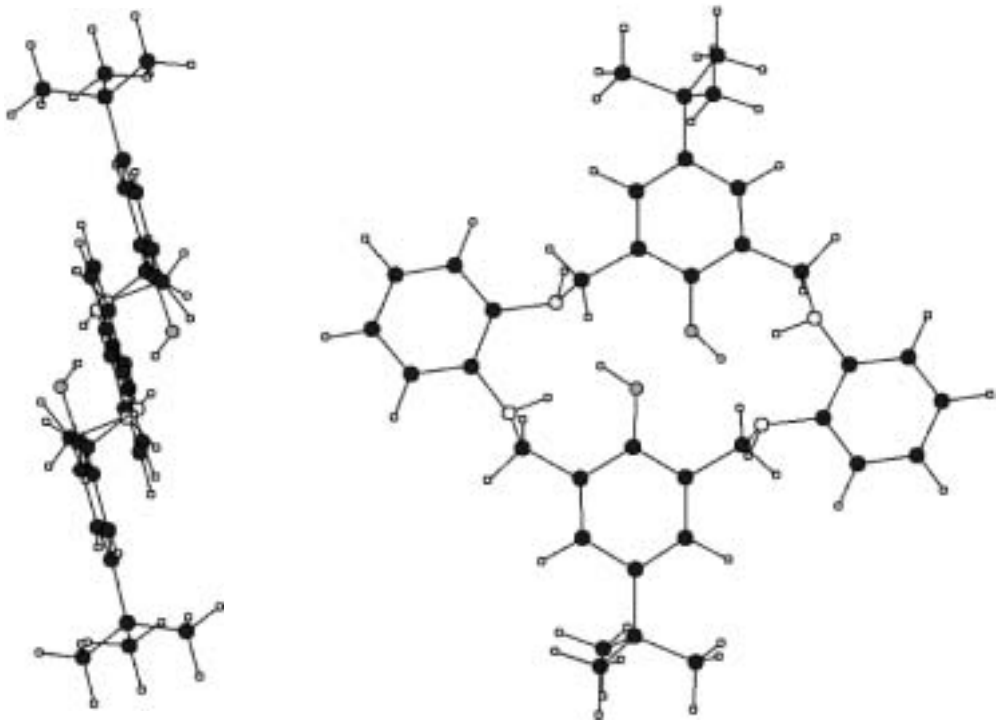


Fig. 2. Structure of the "boat" conformer (**13´´**) of macrocycle **13** according to the calculation data.

2,6-Bis(5,6-dimethylbenzoimidazol-2-yl)-4-*tert*-butylphenol (5c). M.p. 300—303 °C. MS, m/z (I_{rel} (%)): 438 $[M]^+$ (100), 423 $[M - CH_3]^+$ (75). IR (Nujol), ν/cm^{-1}: ~3400 (N—H, O—H).

2,6-Bis(benzoimidazol-2-yl)-4-methylphenol (5d). M.p. 270—272 °C. ^{1}H NMR (DMSO-d_6), δ: 2.44 (s, 3 H, Me); 7.27, 7.68 (both m, 8 H each, 16 CH); 8.17 (s, 2 H, 2 CH); 13.50 (br.s, 3 H, OH, 2 NH). ^{13}C NMR (DMSO-d_6), δ: 20.3, 111.8, 115.4, 124.1, 128.1, 130.9, 135.4, 150.2, 154.1. MS, m/z (I_{rel} (%)): 340 $[M]^+$ (100). IR (Nujol), ν/cm^{-1}: ~3400 (N—H, O—H).

Salt 5a·HI. Crystalline iodine (426 mg, 1.68 mmol) was added to a hot solution of diformylphenol **1c** (173 mg, 0.84 mmol) in anhydrous EtOH (20 mL). The resulting mixture was introduced into a hot solution of diaminobenzene **2a** (182 mg, 1.68 mmol) in anhydrous EtOH (5 mL), and the mixture was refluxed for 30 min. After cooling, large black crystals of **5a**·HI salt were filtered off. The filtrate was evaporated, and an additional amount of **5a**·HI salt was isolated from the residue after recrystallization from $CHCl_3$. After drying in air, **5a**·HI salt was obtained in 76% yield (360 mg). Found (%): C, 50.83; H, 5.14. $C_{24}H_{23}N_4O \cdot HI \cdot 3H_2O$. Calculated (%): C, 51.07; H, 5.18.

6,21-Di(*tert*-butyl)-2,10,17,25-tetraazapentacyclo[24.4.1^{4,8}.1^{19,23}.0^{11,16}]dotriaconta-4,6,8(31),11,13,15,19,21,23(32),24,26,28,30-dodecaene-31,32-diol (13). Small portions of $NaBH_4$ (311 mg, 8.2 mmol) were added for 1.5 h to a warm suspension of macrocycle **4d** (459 mg, 0.82 mmol) in anhydrous EtOH (80 mL). The reaction mixture was boiled for 15 min, cooled, and acidified with AcOH until gas release stopped. The precipitate was filtered off, dried, and washed with $CHCl_3$. The solvent was evaporated, and compound **13** was isolated by recrystallization from the dry residue in 93% yield (430 mg), m.p. 195—198 °C. Found (%): C, 64.69; H, 6.74; N, 8,07. $C_{36}H_{44}N_4O_2 \cdot CHCl_3$. Calculated (%): C, 64.96; H, 6.63; N, 8.19. ^{1}H NMR ($CDCl_3$), δ: 1.31 (s, 18 H, 2 Bu^t); 4.23 (br.s, 4 H, 4 NH); 4.33 (br.s, 8 H, 4 CH_2); 6.91, 6.99 (both m, 4 H each, 8 CH); 7.22 (s, 4 H, 4 CH); 8.92 (s, 2 H, 2 OH). ^{13}C NMR ($CDCl_3$), δ: 31.5, 34.1, 47.3, 112.0, 120.3, 123.5, 126.6, 128.3, 137.2, 142.9, 153.2. MS, m/z (I_{rel} (%)): 280 $[0.5\ M - 2\ H]^+$ (100). IR (KBr), ν/cm^{-1}: 2864, 2960 (CH), 3048 (OH), 3352 (NH).

Procedure of theoretical study. Potential energy surfaces for molecule **9** were studied by the DFT method using the PRIRODA program[8] and the PBE functional that includes the electron density gradient.[10]

The TZ2p-atomic basis sets of grouped Gaussian functions were used to solve the Kohn—Sham equations. The orbital basis sets included the contracted sets (5s1p)/[3s1p] for H and (11s6p2d)/[6s3p2d] for C, N, and O atoms. The electron density expansion in the auxiliary basis set of the atom-centered nongrouped Guassian functions (4s1p) for H and (3s2d1f) for C, N, and O atoms were used for the calculation of the matrix elements of the Coulomb and exchange-correlation potential.[8] The geometry optimization was performed without restrictions imposed on the molecular symmetry. The character of the stationary points was determined by the analytical calculation of the second derivatives of the energy.

The same method and program have previously been successfully used in studies of the structures and reactivity of silicon-containing organophosphorus betaines and the mechanism of alkane activation by the cationic titanium and zirconium complexes.[11]

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