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Synthesis of novel N,O-macrocyclic ligands, functionalized by phosphine oxide groups

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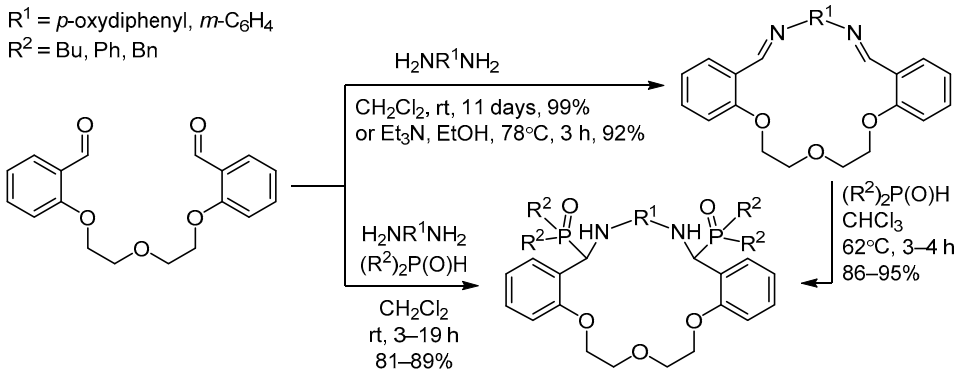


As a result of the implementation of two approaches, the Pudovik reaction (the reaction of macrocyclic azomethines with secondary phosphine oxides) and the Kabachnik–Fields reaction (three-component one-pot process involving dialdehydes, diamines, and secondary phosphine oxides), novel N,O-containing macrocyclic ligands with phosphine oxide groups were first obtained. The synthesized macrocycles are a kind of α-aminophosphoryl compounds that can be used in the synthesis of supramolecular systems.

Keywords: α-aminophosphoryl compounds, N,O-macrocyclic ligands, Kabachnik–Fields reaction, Pudovik reaction.

The synthesis of compounds with high affinity for various targets and high selectivity for binding to them is one of the most important tasks of supramolecular chemistry.[1] Such compounds include heteroatomic macrocycles, which, due to their special chemical and physicochemical properties, have found wide application in the creation of host–guest supramolecular systems.[2–5] One of the main features of these compounds is the unusual stability of macrocyclic complexes, known as the macrocyclic effect.[6]

An important place among macrocyclic heteroatomic ligands is occupied by compounds containing both nitrogen and oxygen atoms in the cycle, which differ in both electron-donating properties and ability to have different spatial arrangement (exo- or endodentate) within the macrocyclic structure.[6] N,O-containing macrocyclic ligands are even more unique in having the so-called pendant-arms, that is, various functional groups associated with ring atoms, for example, amine[7] or phosphoryl.[8–12]

Two phosphorus-containing groups were introduced into macrocycles in a number of studies[8–12] *via* the Pudovik reaction, the addition of hydrophosphoryl compounds to two intracyclic C=N bonds. Recently, we presented an example of the phosphorylation of macrocyclic azomethine containing four C=N bonds with diphenyl phosphine oxide, resulting in a ligand with four groups bonded to carbon atoms of the macrocycle.[13] These compounds are referred to as α-aminophosphoryl compounds due to the presence of the P(O)CNH group and are known for unique biologically active properties and complex-forming ability.[14] For example, trivial acyclic α-aminophosphoryl compounds containing only one P(O)CNH group exhibit high

efficiency and selectivity in the processes of liquid extraction of metal ions and mineral acids, as well as in the membrane transport of organic and mineral acid substrates.[14] These properties are largely because of the ability of the aminophosphoryl group to form a five-membered chelate structure due to the interaction P=O···H–N. In macrocyclic aminophosphoryl compounds, these properties can be significantly enhanced due to a combination of chelate and macrocyclic effects, which are known to significantly increase the thermodynamic stability of the host–guest complex.[15]

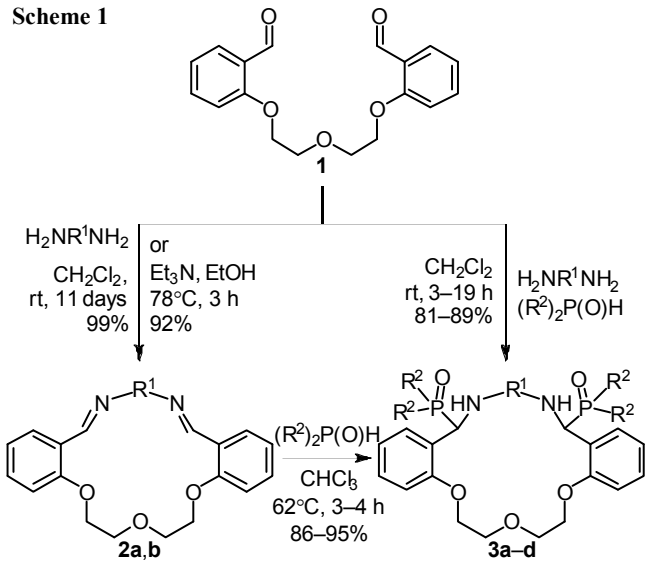
In this work, we synthesized novel N,O-macrocyclic ligands **3a**–**d** containing phosphine oxide fragments using two classical methods for the synthesis of α-aminophosphoryl compounds, the Pudovik and Kabachnik–Fields reactions.

The N,O-containing macrocyclic compounds **2a**,**b**, which have a C=N bond in their composition, necessary for the Pudovik reaction to take place, were obtained by condensation of dialdehyde **1** with 4,4'-diaminodiphenyl ether and *m*-phenylenediamine, respectively (Scheme 1). The synthesis of macrocyclic azomethine **2a** was previously described and involved the reaction of dialdehyde **1** with 4,4'-diaminodiphenyl ether upon heating in MeOH.[16] However, under the indicated conditions, the resulting reaction product contains a significant amount of impurities, and therefore we carried out the reaction in CH_2Cl_2 at 20°C for 10–12 days (control by ^{1}H NMR spectroscopy monitoring the change in intensity of the signals of aldehyde proton and protons of the amino group). The reaction product was obtained with a yield of 99% (calculated for compound **2a**) under the conditions employed by us, however, the content of the product itself was about 93%, since the ^{1}H NMR spectrum contains aldehyde proton signals (~5% of the starting material) and protons of the NH_2 group (~7% of the starting material). An attempt to isolate compound **2a** in a purer form by recrystallization or using column chromatography did not lead to success. Therefore, compound **2a** was used without further purification for subsequent phosphorylation. Its spectral characteristics (IR, ^{1}H and ^{13}C NMR spectra) match literature data,[16] while the macrocyclic structure of the adduct is confirmed by mass spectrometry.

The synthesis of macrocyclic bisazomethine **2b**, which was not previously described in the literature, was carried out under conditions similar to the preparation of structurally similar macrocyclic compounds, *via* the reaction of dialdehyde **1** with *m*-phenylenediamine in the presence of Et_3N using absolute EtOH as the solvent.[6] Composition and structure of compound **2b** was confirmed by elemental analysis, mass spectrometry, IR spectroscopy, ^{1}H, ^{13}C NMR, and correlation NMR spectroscopy data. Thus, in the IR spectrum of compound **2b**, there is an absorption band characteristic of the C=N bond at 1687 cm^{-1}, and the ^{13}C NMR spectrum contains a signal of the carbon atom of this group at 158.7 ppm.

The molecular structure of bisazomethine **2b** was determined by X-ray structural analysis (Fig. 1). The achiral compound **2b**, which has close to Cs symmetry,

Scheme 1



2a, **3a–c** R^1 = oxybis(4,1-phenylene), **2**, **3 d** R^1 = *m*-C_6H_4
3 a,**d** R^2 = Ph, **b** R^2 = Bn, **c** R^2 = Bu

crystallizes in the chiral space group $P2_12_12_1$ with one independent molecule in the unit cell. Its main geometric parameters are close to those of macrocyclic Schiff base **4** (Fig. 2), in which the oxygen bridge connecting the benzene rings contains a carbon atom instead of the central oxygen atom.[6] In compound **2b**, a conformation is realized in which oxygen atoms have an endodentate arrangement, and nitrogen atoms, on the contrary, are exodentate. The geometry of the central macrocyclic fragment in the molecule **2b** is such that all heteroatoms are located in the same plane with a standard deviation of 0.015 Å. The distances from oxygen atoms to the geometric center of the 18-membered ring in compound **2b** are from 2.74 Å (O(2) atom) to 2.83 Å (O(1) and O(3) atoms). To compare the conformations of molecules **2b** and **4**, it is convenient to use dihedral angles between the planes of the aromatic fragments. So, if the values of the angles between rings A and B, as well as A and C differ slightly, then the difference in the values of the angles between rings B and C reaches 20° (Table 1). It should be noted that the observed changes are most likely not due to the presence of an additional oxygen atom, but are probably a consequence of the flexibility of this macrocyclic system and the effect of crystal packing. Indeed, the calculation of the geometry of compound **2b** in the B3LYP/def-2-TZVP approximation showed that optimization of the molecule leads to some flattening of it, in which the value of the dihedral angle between rings B and C in an isolated molecule is much closer to the those in compound **4**, and the angles between rings A and B and A and C, on the contrary, are smaller than in compound **4** and in the crystal of compound **2b**. Since this compound is of interest as a potential ligand, in addition to analyzing the shape of the molecule, we also calculated the charges obtained by integrating atomic pools within the framework of the quantum theory "Atoms in Molecules".[17] The charges of oxygen atoms vary in a narrow range –1.09 ÷ –1.04 e, and the charges of nitrogen atoms are –1.16 e. An

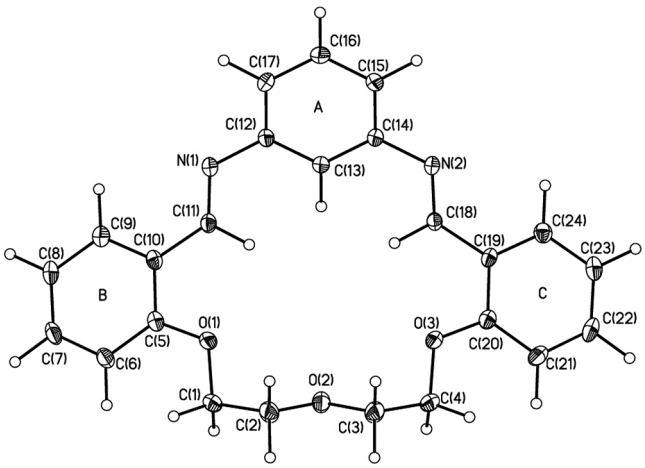


Figure 1. Molecular structure of compound **2b** with atoms represented as thermal vibration ellipsoids of 50% probability.

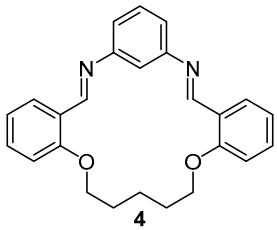


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Figure 2. The structural formula of macrocyclic Schiff base **4**.

Table 1. Dihedral angles between aromatic fragments in compounds **2b** and **4**

Compound	Fragment		
	A–B	A–C	B–C
2b (DFT)	39.0	39.0	50.8
2b (solid state)	46.5	46.5	36.3
4	53.1	59.4	56.1

analysis of the crystalline packing showed that, unlike compound **4**, no stacking interactions are observed in bisazomethine **2b**, and all contacts correspond to weak van der Waals interactions, such as C–H···O, C–H···N, and C–H···π. The greatest number of H···H and C–H···O interactions is observed between the atoms of the "internal cavity" of the macrocycle and the hydrogen atoms of the aromatic ring A.

The Pudovik reaction, which involves the addition of hydrophosphoryl compounds to the C=N bond of azomethines, was carried out by the interaction of macrocyclic azomethines **2a**,**b** with secondary phosphine oxides (diphenyl, dibenzyl, and dibutyl phosphine oxides) at a molar ratio of 1:2 by heating in $CHCl_3$ under reflux (Scheme 1). The phosphine oxides used were selected as the most active among hydrophosphoryl compounds.[14] The reaction progress was monitored by the change in the intensity of phosphorus atom signals in the ^{31}P NMR spectra, namely, by a decrease in the integral intensity of doublets of hydrophosphoryl compounds at 21.5 ppm, J_{PH} = 479.0 Hz (for diphenylphosphine oxide), 36.2 ppm, J_{PH} = 469.0 Hz (for dibenzylphosphine oxide), and 35.5 ppm, J_{PH} = 449.0 Hz (for dibutylphosphine oxide), as well as by the increase in the integral intensity of singlets in the spectra of the formed phosphorylated macrocyclic compounds **3a**–**d**.

Compounds **3a**–**d**, obtained in 86–95% yields, are white or slightly colored powders, highly soluble in $CHCl_3$, CH_2Cl_2, poorly soluble in EtOH, PhH, EtOAc, insoluble in Et_2O, hexane. The structure of macrocyclic α-aminophosphoryl compounds was established using IR, ^1H, ^{13}C, ^{31}P NMR spectroscopy and correlation spectroscopy. The composition was confirmed by elemental analysis and mass spectrometry (electrospray ionization). The IR spectra contain absorption bands of the P=O groups (1144–1169 cm^{-1}) and NH groups (3384–3393 cm^{-1}). In the ^{31}P NMR spectra, the signals at 33.2 ppm (compound **3a**), 33.3 ppm (compound **3d**), 45.5 ppm (compound **3b**), and 50.8 ppm (compound **3c**) have values characteristic of respectively tertiary diphenyl-, dibenzyl-, and dibutylalkylphosphine oxides. The ^1H NMR spectra contain broadened signals of protons of the P(O)CH groups (5.06–6.14 ppm) and NH groups (4.96–5.20 ppm), while in the ^{13}C NMR spectra the signals of the carbon atom of the P(O)CH groups are present (doublets at 47.4–49.4 ppm, J_{PC} = 63.3–74.8 Hz), which indicates the addition of secondary phosphine oxides to the C=N bond. This is also confirmed by the absence of signals of the carbon atom of the imino group.

We obtained phosphorylated N,O-containing macrocyclic ligands **3a**–**d** also by the Kabachnik–Fields reaction, which is a three-component reaction of dialdehyde **1**, the corresponding diamine (4,4'-diaminodiphenyl ether and *m*-phenylenediamine), and secondary phosphine oxide (diphenyl-, dibenzyl-, and dibutylphosphine oxide) carried out as a one-pot process. The reaction was carried out in CH_2Cl_2 at 20°C with the dialdehyde–diamine–phosphine oxide molar ratio of 1:1:2.1 to almost complete conversion (control by ^1H and ^{31}P NMR spectroscopy). The yields of final products **3a**–**d** are 81–89%, which practically coincides with the yields of the same compounds obtained by the Pudovik reaction. All spectral data of compounds **3a**–**d** synthesized by both the Pudovik reaction and the Kabachnik–Fields reaction are identical.

To conclude, novel N,O-containing macrocyclic compounds with phosphine oxide groups were obtained as a result of the implementation of two approaches, the Pudovik and Kabachnik–Fields reactions. Such ligands can be used to create supramolecular systems.

Experimental

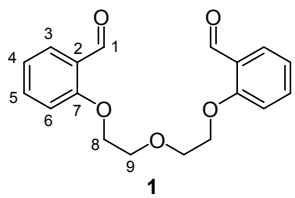
IR spectra were registered on a Shimadzu FTIR-8400S spectrophotometer (in $CHCl_3$ solution). ^1H, ^{13}C, and ^{31}P NMR spectra were acquired on a Bruker Avance 400 spectrometer (400, 100, and 162 MHz, respectively) in $CDCl_3$, with residual solvent signals (7.26 ppm for ^1H nuclei, 77.0 ppm for ^{13}C nuclei) as the internal reference.

The assignment of signals in ^{13}C NMR spectra was verified using spectra recorded in the DEPT mode, as well as from two-dimensional experiments: ^1H–^{13}C HMQC, ^1H–^{13}C HMBC, and homocorrelation ^1H–^1H COSY. For

clarity of the assignment of signals of hydrogen and carbon atoms, after the description of the spectral data of each compound, the structural formula with the numbering of carbon atoms is given in the same way as in published works.[3,18] High-resolution mass spectra were recorded on a Bruker micrOTOF 10223 mass spectrometer (electrospray ionization), eluent MeOH or MeOH–CH_2Cl_2. Elemental analysis was performed on a Carlo Erba 1106 Elemental analyzer, while the content of phosphorus was determined spectrophotometrically on a Cary-100 apparatus.[19] Melting points were determined on a PTP(M) apparatus.

2,2'-Dichlorodiethyl ether ("Glavkhimreaktiv") was purified by distillation. The starting dibenzyl- and dibutylphosphine oxides were obtained by a published procedure: the reaction of diethylphosphite with the corresponding Grignard reagent under an argon atmosphere.[20] Diphenylphosphine oxide was synthesized by hydrolysis of chlorodiphenylphosphine with 1 N HCl under an argon atmosphere.[21]

1,7-Bis(2-formylphenyl)-1,4,7-trioxaheptane (1) was obtained following a modified literature method.[16] K_2CO_3 (27.64 g, 0.20 mol) was added to a solution of salicylic aldehyde (24.42 g, 0.20 mol) in DMF (400 ml), and the reaction mixture was stirred at 20°C for 30 min. Then a solution of 2,2'-dichlorodiethyl ether (15.00 g, 0.10 mol) in DMF (40 ml) was added dropwise. The resulting mixture was stirred at 150–155°C for 10 h under an argon atmosphere, then at 20°C for 4 h. As the reaction progressed, the color of the solution changed from light-yellow to brown. The dialdehyde was precipitated by addition of H_2O until the color of the solution changed from dark-brown to light-yellow. The formed mixture was kept at 0–4°C for 48 h. The formed light-yellow precipitate was filtered off, washed with H_2O, recrystallized from EtOH, and dried under reduced pressure. Yield 21.7 g (69%), beige needles, mp 72–73°C (EtOH) (mp 75–76°C (EtOH),[16] mp 59–61°C (Me_2CO),[18] mp 73°C ($CHCl_3$),[22] mp 73.5°C (MeOH)[23]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.99–4.02 (4H, m, 9-CH_2); 4.27–4.30 (4H, m, 8-CH_2); 7.00 (2H, d, *J* = 8.3, H-6); 7.04 (2H, t, *J* = 7.5, H-5); 7.54 (2H, td, *J* = 7.8, *J* = 1.8, H-4); 7.83 (2H, dd, *J* = 7.7, *J* = 1.6, H-3); 10.51 (2H, s, 1-CH).



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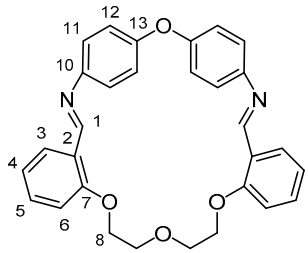
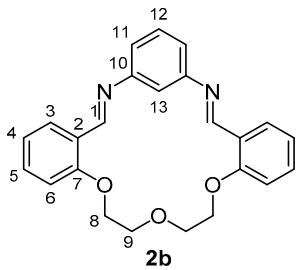
2,7,10,13-Tetraoxa-4,16-diaza-1,3(1,4),6,14(1,2)-tetrabenzenacyclohexadecaphane-4,15-diene (2a). A solution of dialdehyde **1** (0.16 g, 0.50 mmol) in CH_2Cl_2 (10 ml) was added dropwise with stirring to a solution of 4,4'-diaminodiphenyl ether (0.10 g, 0.50 mmol) in CH_2Cl_2 (40 ml). The reaction mixture was stirred at 20°C for 11 days. The solvent was evaporated under reduced pressure. Yield 0.24 g (99%), yellow glass, mp 104–108°C (mp 95°C (PhMe)[16]). IR spectrum, ν, cm^{-1}: 1162 (C–O Alk), 1243 (C–O Ar), 1452, 1496, 1601 (C–C Ar), 1688 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.94–4.00 (4H, m, 9-CH_2); 4.21–4.28 (4H, m, 8-CH_2); 6.92–7.01 (6H, m, H-6,12); 7.04–7.05 (2H, m, H-5); 7.17–7.20 (4H, m, H-11); 7.38–7.42 (2H, m, H-4); 8.13–8.16 (2H, m, H-3); 8.94 and 8.96 (2H, both s, 1-CH). ^{13}C NMR spectrum, δ, ppm: 68.3 (C-8); 69.8 (C-9); 112.7 (C-6); 119.3 (C-12); 121.5 (C-5); 122.5 (C-11); 125.2 (C-2); 127.6 (C-3); 132.7 (C-4); 147.9 (C-10); 155.5 (C-1); 158.6 (C-7,13). Found, *m*/*z*: 479.1981 [M+H]$^+$. $C_{30}H_{27}N_2O_4$. Calculated, *m*/*z*: 479.1965.



2a

(2*E*,5*E*)-8,11,14-Trioxa-3,5-diaza-1,7(1,2),4(1,3)-tribenzenacyclotetradecaphane-2,5-diene (2b). A mixture of dialdehyde **1** (0.48 g, 1.50 mmol), anhydrous EtOH (40 ml), and Et_3N (0.15 g, 1.50 mmol) was heated to boiling, and a solution of *m*-phenylenediamine (0.21 g, 2.00 mmol) in anhydrous EtOH (20 ml) was added dropwise. The reaction mixture was heated under reflux for 3 h, then kept at 0–4°C for 48 h. The formed precipitate was filtered off, dried under reduced pressure, and recrystallized from CH_2Cl_2. Yield 0.53 g (92%), brown needles, mp >240°C. IR spectrum, ν, cm^{-1}: 1247 (C–O Ar), 1452, 1487, 1601 (C–C Ar), 1687 (C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.90–3.92 (4H, m, 9-CH_2); 4.25–4.27 (4H, m, 8-CH_2); 6.90 (2H, d, *J* = 8.2, H-6); 7.00 (1H, s, H-13); 7.04 (2H, t, *J* = 7.5, H-5); 7.27 (2H, dd, *J* = 7.8, *J* = 1.7, H-11); 7.39–7.44 (3H, m, H-4,12); 8.20 (2H, dd, *J* = 7.8, *J* = 1.4, H-3); 9.22 (2H, s, 1-CH).^{13}C NMR spectrum, δ, ppm: 67.2 (C-8); 70.8 (C-9); 109.6 (C-13); 111.2 (C-6); 121.2 (C-11); 121.4 (C-5); 124.2 (C-2); 127.2 (C-3); 129.2 (C-12); 133.1 (C-4); 154.7 (C-10); 158.7 (C-1); 159.0 (C-7). Found, *m*/*z*: 387.1717 [M+H]$^+$. $C_{24}H_{23}N_2O_3$. Calculated, *m*/*z*: 387.1703. Found, %: C 74.44; H 5.56; N 7.28. $C_{24}H_{22}N_2O_3$. Calculated, %: C 74.59; H 5.74; N 7.25.

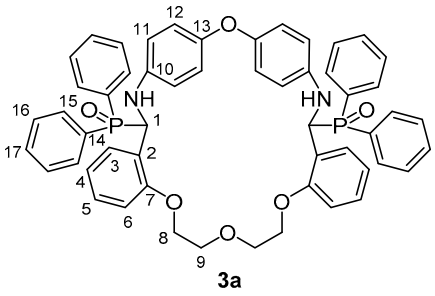


2b

Synthesis of compounds 3a–d by the Pudovik reaction (General method). The corresponding phosphine oxide

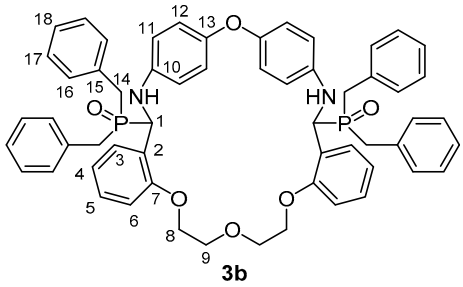
(0.50 mmol) in $CHCl_3$ (5 ml) was added to compound **2a** or **2b** (0.25 mmol) under an argon atmosphere. The reaction mixture was heated under reflux for 3–4 h. The solvent was evaporated under reduced pressure. For compounds **3a**,**b**,**d**, the residue was recrystallized, while for compound **3c**, it was washed with hot Et_2O.

2,7,10,13-Tetraoxa-4,16-diaza-1,3(1,4),6,14(1,2)-tetrabenzenacyclohexadecaphane-5,5-diylbis(diphenylphosphine oxide) (3a). Yield 147 mg (86%), white powder, mp 166–170°C (PhH). IR spectrum, ν, cm^{-1}: 1120 (C–O Alk), 1169 (P=O), 1242 (C–O Ar), 1452, 1500, 1600 (C–C Ar), 3393 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.42–3.44 (2H, m, 8-CH_2); 3.74–3.75 (4H, m, 9-CH_2); 3.86–3.87 (2H, m, H-8'); 5.20 (2H, br. s, NH); 5.79 (2H, d, *J* = 10.1, 1-CH); 6.35 (2H, t, *J* = 9.0, H-6); 6.46–6.54 (8H, m, H-11,12); 679–6.84 (2H, m, H-5); 6.95–6.96 (2H, m, H-4); 7.05–7.31 (16H, m, H-15,16); 7.50–7.54 (2H, m, H-3); 7.85–7.86 (4H, m, H-17). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 49.4 (d, *J* = 67.1, C-1); 66.7 (C-8); 70.0 (C-9); 110.4 (C-6); 114.5 (C-12); 119.5 (C-11); 121.5 (C-5); 124.2 (C-2); 127.5; 128.8; 131.5; 131.6; 131.7; 132.2 (C-3,4,15–17); 132.7 (C-14); 142.0 (C-10); 150.1 (C-13); 155.5 (C-7). ^{31}P NMR spectrum, δ, ppm: 33.2. Found, *m*/*z*: 905.2908 $[M+Na]^+$. $C_{54}H_{48}N_2NaO_6P_2$. Calculated, *m*/*z*: 905.2880. Found, %: C 73.32; H 5.32; N 3.30; P 7.32. $C_{54}H_{48}N_2O_6P_2$. Calculated, %: C 73.46; H 5.48; N 3.17; P 7.02.



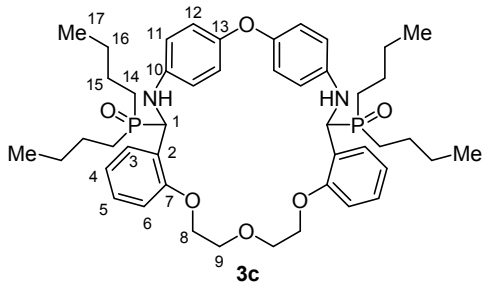
3a

4,16-Diaza-1,3(1,4),6,14(1,2)-tetrabenzena-2,7,10,13-tetraoxacyclohexadecaphane-5,15-diylbis(dibenzylphosphine oxide) (3b). Yield 205 mg (87%), beige powder, mp 154–161°C (EtOH). IR spectrum, ν, cm^{-1}: 1130 (C–O Alk), 1165 (P=O), 1240 (C–O Ar), 1454, 1498, 1601 (C–C Ar), 3384 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.69–2.83 (4H, m, H-14); 3.16 (2H, t, *J* = 14.0, H-14'); 3.34 (2H, t, *J* = 13.7, H-14"); 3.62–3.66 (4H, m, 9-CH_2); 4.02–4.03 (4H, m, 8-CH_2); 5.15–5.16 (4H, m, NH, 1-CH); 6.41–6.43 (4H, m, H-12); 6.58–6.60 (4H, m, H-11); 6.69–6.71 (2H, m, H-6); 6.89–6.93 (2H, m, H-5); 7.06–7.20 (22H, m, H-4,16–18); 7.46–7.47 (2H, m, H-3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 32.0 (d, *J* = 61.4, C-14); 34.7 (d, *J* = 61.4, C-14'); 47.4 (d, *J* = 63.3, C-1); 67.2 (C-8); 69.8 (C-9); 110.9 (C-6); 114.5 (C-12); 119.4 (C-11); 122.1 (C-5); 124.2 (C-2); 127.0; 128.6; 128.7; 129.2; 130.0; 130.1 (C-3,4,16–18); 131.4; 132.4 (C-15,15'); 141.9 (C-10); 150.3 (C-13); 155.7 (C-7). ^{31}P NMR spectrum, δ, ppm: 45.5. Found, *m*/*z*: 961.3526 $[M+Na]^+$. $C_{58}H_{56}N_2NaO_6P_2$. Calculated, *m*/*z*: 961.3506. Found, %: C 73.96; H 6.06; N 2.99; P 6.94. $C_{58}H_{56}N_2O_6P_2$. Calculated, %: C 74.19; H 6.01; N 2.98; P 6.60.



3b

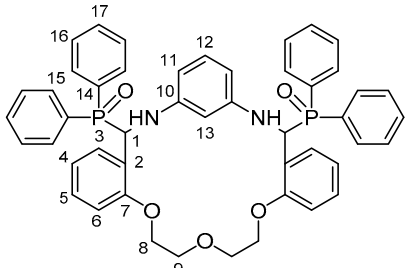
2,7,10,13-Tetraoxa-4,16-diaza-1,3(1,4),6,14(1,2)-tetrabenzenacyclohexadecaphane-5,15-diylbis(dibutylphosphine oxide) (3c). Yield 283 mg (95%), beige powder, mp 130–145°C. IR spectrum, ν, cm^{-1}: 1144 (P=O), 1238 (C–O Ar), 1452, 1499, 1600 (C–C Ar), 3385 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.70–0.75 (6H, m, 17-CH_3); 0.87–0.91 (6H, m, 17'-CH_3); 1.13–1.45 (16H, m, 15,16-CH_2); 1.55–1.58 (4H, m, 14-CH_2); 1.87–1.89 (4H, m, 14'-CH_2); 3.92–3.94 (4H, m, 9-CH_2); 4.14–4.17 (4H, m, 8-CH_2); 5.06–5.07 (4H, m, NH, 1-CH); 6.49–6.51 (4H, m, H-12); 6.53–6.54 (4H, m, H-11); 6.75–6.77 (2H, m, H-6); 6.87–6.90 (2H, m, H-5); 7.10–7.14 (2H, m, H-4); 7.43–7.44 (2H, m, H-3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 13.6; 13.8 (C-17); 23.1; 24.3; 24.4 (C-15,16); 25.3 (d, *J* = 65.2, C-14); 27.4 (d, *J* = 65.2, C-14'); 48.5 (d, *J* = 63.3, C-1); 67.4 (C-8); 70.0 (C-9); 110.8 (C-6); 114.5 (C-12); 119.4 (C-11); 122.0 (C-5); 125.0 (C-2); 128.8 (C-3); 129.0 (C-4); 142.0 (C-10); 150.1 (C-13); 155.6 (C-7). ^{31}P NMR spectrum, δ, ppm: 50.8. Found, *m*/*z*: 825.4132 $[M+Na]^+$. $C_{46}H_{64}N_2NaO_6P_2$. Calculated, *m*/*z*: 825.4132. Found, %: C 68.60; H 8.05; N 3.32; P 7.59. $C_{46}H_{64}N_2O_6P_2$. Calculated, %: C 68.81; H 8.03; N 3.49; P 7.71.



3c

8,11,14-Trioxa-3,5-diaza-1,7(1,2),4(1,3)-tribenzenacyclotetradecaphane-2,6-diylbis(diphenylphosphine oxide) (3d). Yield 174 mg (88%), light-brown powder, mp 176–186°C (PhH). IR spectrum, ν, cm^{-1}: 1121 (C–O Alk), 1169 (P=O), 1247 (C–O Ar), 1452, 1490, 1604 (C–C Ar), 3388 (NH). 1H NMR spectrum, δ, ppm (*J*, Hz): 3.37–3.40 (2H, m, 8-CH_2); 3.47–3.52 (2H, m, 9-CH_2); 3.82–3.87 (2H, m, 8'-CH_2); 3.90–3.94 (2H, m, 9'-CH_2); 4.96–5.00 (2H, m, NH); 6.03 (2H, dd, *J* = 7.8, *J* = 2.0, H-11); 6.08–6.14 (1H, m, 1-CH); 6.29 (1H, s, H-13); 6.52 (2H, d, *J* = 8.2, H-6); 6.75 (1H, t, *J* = 7.9, H-12); 6.97 (2H, t, *J* = 7.5, H-5); 7.15–7.19 (6H, m, H-15); 7.29–7.39 (10H, m, H-15',16); 7.46 (2H, t, *J* = 7.5, H-4); 7.54 (2H, d, *J* = 7.6, H-3); 7.74 (2H,

d, *J* = 7.6, H-17); 7.76 (2H, d, *J* = 7.6, H-17'). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 47.8 (d, *J* = 74.8, C-1); 67.7 (C-8); 69.7 (C-9); 96.0 (C-13); 107.1 (C-11); 110.3 (C-6); 121.6 (C-5); 124.5 (C-2); 127.6; 127.7 (C-15); 128.7; 128.8; 128.9 (C-16); 129.0 (C-12); 129.6 (C-3); 130.7 (C-14); 131.6; 132.0 (C-4,17); 147.4 (C-10); 156.0 (C-7). ^{31}P NMR spectrum, δ, ppm: 33.3. Found, *m*/*z*: 791.2791 $[M+H]^+$. $C_{48}H_{45}N_2O_5P_2$. Calculated, *m*/*z*: 791.2798. Found, %: C 72.66; H 5.60; N 3.34; P 7.74. $C_{48}H_{44}P_2N_2O_5$. Calculated, %: C 72.90; H 5.61; N 3.54; P 7.83.



3d

Synthesis of compounds 3a–d by the Kabachnik–Fields reaction (General method). A solution of compound **1** (0.31 g, 1.0 mmol) in CH_2Cl_2 (5 ml) was added dropwise with stirring under argon atmosphere to a solution of 4,4'-diaminodiphenyl ether or *m*-phenylenediamine (1.0 mmol) in CH_2Cl_2 (30 ml). Then a solution of phosphine oxide (2.1 mmol) in CH_2Cl_2 (7 ml) was added dropwise; the reaction mixture became bright-yellow. The reaction mixture was stirred at 20°C for 3–19 h. The solvent was evaporated under reduced pressure. Purification of the obtained compounds was carried out in the same way as in their synthesis by the Pudovik reaction. Yields of compounds: **3a** – 756 mg (86%), **3b** – 811 mg (86%), **3c** – 718 mg (89%), **3d** – 643 mg (81%).

X-ray structural analysis of single crystals of compound 2b was performed on a Bruker APEX II CCD diffractometer (λ(MoKa) 0.71072 Å, ω-scanning, 2Θ < 58°). Single crystals of compound **2b** were obtained from $CHCl_3$ solution ($C_{24}H_{22}N_2O_3$, *M* 386.43, μ 0.87 cm^{-1}, d_{calc} 1.303 $g \cdot cm^{-3}$); they are rhombic (at 120 K), space symmetry group $P2_12_12_1$; *a* 8.3883(4), *b* 10.6916(5), *c* 21.9716(10) Å; *V* 1970.5(16) Å^3. A total of 23556 reflections were collected; 5248 independent reflections (R_{int} 0.02920) were used in further refinement. The structure was solved with the direct method and refined against F_{hkl}^2 by the least-squares technique in the full-matrix anisotropic approximation. Hydrogen atom positions were calculated geometrically and were refined according to the "rider" model in isotropic approximation. The final probability factor values: wR_2 0.1041 and *GOF* 1.009 for all independent reflections (R_1 0.0385 were calculated against *F* for 4957 reflections with $I > 2\sigma(I)$). All calculations were performed using the SHELXTL software package.[24] The full set of X-ray structural data and atomic coordinates were deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1907415).

Optimization of an isolated molecule 2b carried out by the density functional method (B3LYP/def-2-TZVP) in Gaussian 09[25] program using empirical dispersion correction of total energy[26] and Becke–Jonson damping (DFT-D3)[27]. Topological analysis of theoretically calculated function ρ(*r*) was done by AIMAll programm.[28]

References

1. Park, H. S.; Lin, Q.; Hamilton, A. D. *J. Am. Chem. Soc.* **1999**, *121*, 8.
2. Tabushi, I.; Yamamura, K. *Top. Curr. Chem.* **1983**, *113*, 146.
3. Reyes-Marquez, V.; Tiburcio, J.; Hopfl, H.; Sanchez-Vazquez, M.; Hernandez-Ahuactzi, I. F.; Moreno-Corral, R.; Lara, K. O. *J. Phys. Org. Chem*. **2012**, *25*, 1042.
4. Erkin, A. V.; Gurzhiy, V. V.; Krutikov,V. I. *Chem. Heterocycl. Compd.* **2018**, *54*, 1168. [*Khim. Geterotsikl. Soedin.* **2018**, *54*, 1168.]
5. Ostrovskii, V. A.; Mazur, M. S.; Mikhailenko, V. V.; Aksenov, N. A.; Aksenov, A. V. *Chem. Heterocycl. Compd.* **2016**, *52*, 849. [*Khim. Geterotsikl. Soedin.* **2016**, *52*, 849.]
6. Balic, T.; Markovic, B.; Jazwinski, J.; Matkovic-Calogovic, D. *Inorg. Chim. Acta* **2015**, *435*, 283.
7. Vicente, M.; Bastida, R.; Lodeiro, C.; Macias, A.; Parola, A. J.; Valencia, L.; Spey, S. E. *Inorg. Chem.* **2003**, *42*, 6768.
8. Rohovec, J.; Vojtisek, P.; Lukes, I. *Phosphorus*, *Sulfur Silicon Relat. Elem.* **1999**, *148*, 79.
9. Bilge, S.; Nadzagdorj, A.; Akduran, N.; Hokelek, T.; Kilic, Z. *J. Mol. Struct.* **2002**, *611*, 169.
10. Ilter, E. E.; Kilic, Z. *Spectrochim. Acta*, *Part A* **2008**, *70*, 542.
11. Bilge, S.; Kilic, Z.; Davies, D. B. *Spectrochim. Acta*, *Part A* **2011**, *81*, 441.
12. Kocak, S. B.; Uckardes¸ H. *Heteroat. Chem.* **2012,** *23*, 583.
13. Trishin, Yu. G.; Kudryavtseva, A. I.; Shafeeva, M. V.; Avdeeva, E. A.; Karpova, E. A. *Russ. J. Gen. Chem.* **2013**, 83, 2345. [*Zh. Obshch. Khim.* **2013**, *83*, 2062.]
14. Cherkasov, R. A.; Galkin, V. I. *Russ. Chem. Rev.* **1998**, 67, 857. [*Usp. Khim.* **1998**, *67*, 940.]
15. Stid, Dzh. V.; Etvud, Dzh. L. *Supramolecular Chemistry* [Russian translation]; IKTs "Akademkniga": Moscow, 2007, Vol. 1, p. 159.
16. Kedy, S.; Almhna, N.; Kandil, F. *Jordan J. Chem.* **2012**, *7*, 73.
17. Beider, R. *Atoms in Molecules. A Quantum Theory* [Russian translation]; Mir: Moscow, 2000.
18. Moreno-Corral, R.; Hopfl, H.; Machi-Lara, L.; Lara, K. O. *Eur. J. Org. Chem.* **2011**, 2148.
19. Gel'man, N. E.; Terent'eva, E. A; Shanina, T. M.; Kiparenko, L. M.; Rezl, V. *Methods of Quantitative Organic Elemental Microanalysis* [in Russian]; Gel'man, N. E., Ed.; Khimiya: Moscow, 1987.
20. Keglevich, G.; Jablonkai, E.; Balazs, L. B. *RSC Adv.* **2014**, *4*, 22808.
21. Kabat, M. M.; Garofalo, L. M.; Daniewski, A. R.; Hutchings, S. D; Liu, W.; Okabe, M.; Radinov, R.; Zhou, Y. *J. Org. Chem.* **2001**, *66*, 6141.
22. Yapar, G.; Erk, C. *J. Inclusion Phenom. Macrocyclic Chem.* **2002**, *43*, 299.
23. Adam, K. R.; Leong, A. J.; Lindoy, L. F.; Lip, H. C.; Skelton, B. W.; White, A. H. *J. Am. Chem. Soc.* **1983**, *105*, 4645.
24. Sheldrick, G. M. *SHELXTL v.6.14. Structure Determination Software Suite*; Bruker AXS: Madison, 2000.
25. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.;

Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, *Revision D.01*; Gaussian, Inc.: Wallingford, 2016.

26. Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. *J. Chem. Phys.* **2010**, *132*, 154104.
27. Grimme, S.; Ehrlich, S.; Goerigk, L. *J. Comput. Chem.* **2011**, *32*, 1456.
28. Keith, T. *AIMAll (Version 16.08.17)*; TK Gristmill Software: Overland Park, 2016.