Макрогетероциклы
http://macroheterocycles.isuct.ru

DOI: 10.6060/mhc2011.4.08

Novel P,N−Containing Cyclophane with a Chiral Hydrophobic Cavity

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The effective self-assembly process between phenylphosphine, formaldehyde and racemic N-alkyl-2,6-diamino-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximides results in the formation of novel heterocyclophanes with chiral intramolecular cavity. Compounds of this type can be regarded as potential precursors for a new kind of enantioselective molecular reactors.

Keywords: Chiral cyclophanes, phosphines, 2,6-diaminoanthracene, covalent self-assembly.

Introduction

Macrocycles containing aromatic or heterocyclic units within the macrocyclic core draw an increasing attention for the last few decades.[1] The aromatic units, being rigid building blocks, allow the design and synthesis of molecular cavities with defined spatial characteristics, and also serve as binding sites for hosts capable of interacting with their π-electron systems.[1b-d] On the other side heterocyclic rings are also of special interest for the construction of cyclophane-type molecules[2] because the presence of donor heteroatoms provides means for the incorporation of a binding site for transition metals within the macrocyclic structure. Macrocycles formed both by the aromatic and the heterocyclic units with three-coordinated phosphorus atoms as donors[3] are able to provide a variety of the donor-acceptor and the non-valent interactions so they are of interest both for supramolecular chemistry (in particular as selective sensors[4]) and as unusual ligands for transition metal catalyzed reactions in organic synthesis,[5] as the geometry and well-defined position of the complexing donor centers could lead to specific catalytically active complexes.[6] However, the chemistry of cyclophane ligands containing phosphine groups as donor centers within the macrocyclic skeleton is less developed than that of their oxygen or nitrogen analogues.[3] This fact has been mainly attributed to the air sensitivity of these compounds and the poor yields obtained in their preparations by high-dilution[3,7] or template methods,[3] although the high-yield synthesis of a few types of phosphamacrocycles has been reported.[3,8] To the best of our knowledge there are no examples of *P*-containg cyclophanes with chiral intramolecular cavity. But we are sure that if *P*-containing cyclophanes, especially chiral, with a unique shape, distinct architecture, and set of functional groups become easily available from natural or synthetic sources, they would start to inspire the imagination of supramolecular chemists to devise and synthesize novel sophisticated receptors, machines, and devices,[1-3,6,8] as well as new types of molecular reactors.[9]

Recently, a highly effective self-assembly process giving macrocyclic tetraphosphines with a relatively large hydrophobic prismatic or helical twisted cavities by condensation of the three-component system diamine/formaldehyde/phosphine was discovered.[10] In the present work diamines possessing inherent chirality, namely *N*-alkyl-2,6-diamino-9,10-dihydro-9,10-ethanoanthracene-*cis*-11,12-dicarboximide **2-4**,[11] were used as spatially divided diamine component of the self-assembling system to prepare a novel type of *P*,*N*-containing cyclophanes with chiral intramolecular cavity.

Experimental

General

^{1}H NMR spectra (Bruker Avance-600, 30ºC, 600.00 MHz; BrukerAvance-DRX 400, 162 MHz; standard): Me_4Si. ^{31}P NMR spectra (Bruker Avance-600, 242.937 MHz; BrukerAvance-DRX 400, 162 MHz; CXP-100, 36.47 MHz; standard): external 85% H_3PO_4. IR-spectra were obtained on Vector-22 (Bruker) in the range 400-4000 cm^{-1} in nujol mulls. ESI_{pos} mass-spectra were obtained on Esquire3000 plus mass-spectrometer. The melting points were determined on a Boetius apparatus and are uncorrected.

Phenylphosphine,[12] 2,6-diaminoanthracene (**1**)[11] and *N*-methyl-2,6-diamino-9,10-dihydro-9,10-ethanoanthracene-*cis*-11,12-dicarboximide (**2**)[11] were obtained according to the described methods. All manipulations were carried out by standard high-vacuum and dry-nitrogen techniques in dry degassed solvents which were purified by standard methods.

Preparations

*N-Ethyl-2,6-diamino-9,10-dihydro-9,10-ethanoanthracene-cis-11,12-dicarboximide (**3**).* The mixture of **1** (0.8 g, 3.85 mmol) and *N*-ethylmaleimide (0.58 g, 4.64 mmol) in chlorobenzene (75 ml) was stirred under reflux for 3 days and cooled. The resulting white crystals were collected by filtration, washed with chlorobenzene and then with hexane. The solvent of the filtrate was removed in vacuo, the residue was dissolved in chloroform (4 ml) and was precipitated with hexane (20 ml). The resulting precipitate was washed with hexane, combined with the first portion and dried at 0.1 torr for 4 h. Yield 0.75 g (58 %); m.p. 228°C. Found: C 72.07, H 5.71, N 12.61 %. $C_{20}H_{19}N_3O_2$ [333] requires C 71.78, H 5.69, N 12.79 %. ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.00 (d, 2H, $^3J_{HH}$ = 7.8 Hz, C^{8}H or C^{4}H), 6.78 (d, 1H, $^3J_{HH}$ = 7.7 Hz, C^{4}H or C^{8}H), 6.61 (d, 1H, $^4J_{HH}$ = 1.8 Hz, C^{5}H or C^{1}H), 6.41 (d, 1H, $^4J_{HH}$ = 1.8 Hz, C^{1}H or C^{5}H), 6.27 (dd, 1H, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.8 Hz, C^{7}H or C^{3}H), 6.22 (dd, 1H, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.8 Hz, C^{3}H or C^{7}H), 4.88 (br.s., 4H, NH_2), 4.29 (br.d, 2H, $^3J_{HH}$ = 6.6 Hz, C^{11}H + C^{12}H), 3.06 (br.s., 2H, C^{9}H + C^{10} H), 3.01 (q, 2H, $^3J_{HH}$= 7.0 Hz, CH_2), 0.42 (t, 3H, $^3J_{HH}$= 7.0 Hz, CH_3).

*N-Propyl-2,6-diamino-9,10-dihydro-9,10-ethanoanthracene-cis-11,12-dicarboximide (**4**).* **4** was prepared like **3** from **1** (1.05 g, 5.05 mmol) and *N*-propylmaleimide (0.83 g, 6.06 mmol). Yield 1.1 g (63 %); m.p. 196°C. Found: C 72.23, H 6.37, N 12.43 %. $C_{21}H_{21}N_3O_2$ [347] requires C 72.62, H 6.05, N 12.10 %. ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.00 (2H, d, $^3J_{HH}$ = 7.7 Hz, C^{8}H or C^{4}H), 6.80 (1H, d, $^3J_{HH}$ = 7.7 Hz, C^{4}H or C^{8}H), 6.62 (1H, d, $^4J_{HH}$ = 1.8 Hz, C^{5}H or C^{1}H), 6.42 (1H, d, $^4J_{HH}$ = 1.8 Hz, C^{1}H or C^{5}H), 6.28 (1H, dd, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.8 Hz, C^{7}H or C^{3}H), 6.23 (1H, dd, $^3J_{HH}$ = 7.7 Hz, $^4J_{HH}$ = 1.8 Hz, C^{3}H or C^{7}H), 4.92 (4H, br.s, NH_2), 4.30 (2H, br.d, $^3J_{HH}$ = 5.1 Hz, C^{11}H + C^{12} H), 3.07 (2H, br.s, C^{9}H + C^{10} H), 2.95 (2H, t, $^3J_{HH}$ = 7.3 Hz, N-CH_2), 0.79-0.93 (2H, m, CH_2), 0.47 (3H, t, $^3J_{HH}$= 7.3 Hz, CH_3).

*1^3,1^7,7^3,7^7-Tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphospha-cyclooctana)-2,4-di[11,12-(cis-N-methyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena]cyclotetraphane (**5**).* A mixture of phenylphosphine[12] (0.97 g, 8.81 mmol) and paraformaldehyde (0.53 g, 17.66 mmol) was heated to 110°C up to the homogenization, then the reaction mixture was dissolved in DMF (5 ml) and a solution of **2** (1.43 g, 4.4 mmol) in DMF (17 ml) was added under stirring. The reaction mixture was stirred at 110 ^{0}C for 3 days and cooled. The resulting white crystals were collected by filtration, washed with DMF and acetonitrile and dried in vacuo. According to the data of ^{1}H, ^{31}P NMR and mass-spectra the crystalline product was an 1:1 mixture of *1^3,1^7,7^3,7^7-tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4(2,6)-di-(R,R/S,S)-[11,12-(cis-N-methyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena] cyclotetraphane* (**5a**) and *1^3,1^7,7^3,7^7-tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4-di-[11,12-(cis-N-methyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena] cyclotetraphane* (**5b**). Yield 1.21 g; m.p. > 270°C. *m/z* (ESI_{pos}) (%): 1175 (100) $[M+H]^+$. IR (KBr, nujol) ν_{max} cm^{-1}: 1696 s, 1774 m (C=O). Found: C 71.08, H 5.69, N 6.88; P 10.23 %. $C_{70}H_{62}N_6O_4P_4$ [1174] requires C 71.55, H 5.28, N 7.16, P 10.56 %. δ_P ([D_6]DMSO, 303 K) -55.89 (d, J_{PP} = 6.7 Hz) (**5a**), -55.96 (s) (**5b**), -56.24 (s) (**5b**), -56.31 (d, J_{PP} = 6.7 Hz) (**5a**).

The obtained equimolar mixture of **5a** and **5b** (0.1 g) was recrystallized from DMF (6 ml). The resulting crystals of **5a** of 90 % purity were collected by filtration, washed with DMF and acetonitrile and dried in vacuo. Yield 0.03 g, m.p. > 270°C.

Spectral data for **5a**: ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.72-7.79 (8H, m, *m*-C_6H_5), 7.46-7.55 (12H, m, *o,p*-C_6H_5),7.15 (2H, d, $^3J_{HH}$ = 8.3 Hz, C^{8}H or C^{4}H), 6.93 (2H, d, $^3J_{HH}$ = 8.3 Hz, C^{4}H or C^{8}H), 6.64 (2H, s, C^{5}H or C^{1}H), 6.37 (2H, s, C^{1}H or C^{5}H), 6.20 (4H, br.d, $^3J_{HH}$ = 7.3 Hz, C^{3}H + C^{7}H), 4.59-4.64 (4H, m, P-C^{15}H$_a$-N + P-C^{16}H$_a$-N), 4.42 (2H, dd, $^2J_{HH}$ = 14.2 Hz, $^2J_{PH}$ = 5.4 Hz, P-C^{13}H$_a$-N), 4.36 (2H, dd, $^2J_{HH}$ ≈ 14.7 Hz, $^2J_{PH}$ = 5.4 Hz, P-C^{14}H$_a$-N), 4.34 (4H, br.s, C^{11}H + C^{12} H), 4.14 (2H, dd, $^2J_{HH}$ ≈ $^2J_{PH}$ ≈ 13.2 Hz, P-C^{16}H$_e$-N), 4.05 (2H, dd, $^2J_{HH}$ ≈ $^2J_{PH}$ ≈ 13.7 Hz, P-C^{15}H$_e$-N), 3.98 (2H, dd, $^2J_{HH}$ ≈ $^2J_{PH}$ ≈14.7 Hz, P-C^{14}H$_e$-N), 3.89 (2H, dd, $^2J_{HH}$ ≈ $^2J_{PH}$ ≈ 14.2 Hz, P-C^{13}H$_e$-N), 3.08 (2H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 2.9 Hz, C^{9}H or C^{10} H), 2.97 (2H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 2.4 Hz, C^{9}H or C^{10} H), 2.32 (6H, s, CH_3). ^{31}P NMR ([D_6]DMSO, 303 K) δ_P ppm: -55.89 (d, J_{PP} = 6.7 Hz), -56.31 (d, J_{PP} = 6.7 Hz).

The filtrate of the reaction mixture was concentrated in vacuo up to ½ of the initial volume and allowed to stand at -10 ^{0}C. The resulting powder was collected by filtration, washed with DMF and acetonitrile and dried in vacuo. According to ^{1}H and ^{31}P spectra these mictocrystals were the 1:2 mixture of **5a** and **5b.** Yield 0.10 g. Combined yield of **5a** and **5b** was 1.31 g, 51 %.

Spectral data for **5b:** ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.70-7.79 (8H, m, *m*-C_6H_5), 7.46-7.57 (12H, m, *o,p*-C_6H_5), 7.13 (2H, d, $^3J_{HH}$ = 8.8 Hz, C^{8}H or C^{4}H), 6.95 (2H, d, $^3J_{HH}$ = 8.1 Hz, C^{4}H or C^{8}H), 6.67 (2H, s, C^{5}H or C^{1}H), 6.34 (2H, s, C^{1}H or C^{5}H), 6.21 (d, $^3J_{HH}$ = 8.8 Hz, C^{7}H or C^{3}H), 6.19 (d, $^3J_{HH}$ = 8.1 Hz, C^{3}H or C^{7}H) (total intensity 4H), 4.65 (2H, dd, $^2J_{HH}$ = 16.1 Hz, $^2J_{PH}$ = 5.4 Hz, P-C^{16}H$_a$-N), 4.58 (2H, dd, $^2J_{HH}$ = 16.0 Hz, $^2J_{PH}$ = 4.9 Hz, P-C^{15}H$_a$-N), 4.39 (4H, dd, $^2J_{HH}$ ≈ 14.2 Hz, $^2J_{PH}$ = 3.5 Hz, P-C^{13,14}H$_a$-N), 4.35 (4H, br.s, C^{11}H + C^{12} H), 3.95-4.13 (6H, m, P-C^{14,15,16}H$_e$-N), 3.86 (2H, dd, $^2J_{HH}$ ≈ $^2J_{PH}$ ≈ 14.2 Hz, P-C^{13}H$_e$-N), 3.08 (2H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 2.4 Hz, C^{9}H or C^{10} H), 2.97 (2H, dd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 2.4 Hz, C^{10}H or C^{9}H), 2.32 (6H, s, CH_3). ^{31}P NMR ([D_6]DMSO, 303 K) δ_P ppm: -55.96 (s), -56.24 (s).

*1^3,1^7,7^3,7^7-Tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4(2,6)-di-(R,R/S,S)-[11,12-(cis-N-ethyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena] cyclotetraphane (**6a**).* **6a** was prepared like **5a** from phenylphosphine (0.48 g, 4.36 mmol), paraformaldehyde (0.26 g, 8.67 mmol) and **3** (0.72 g, 2.16 mmol). The crude reaction product was practically individual **6a**, which was recrystallized from DMSO, washed with acetonitrile and dried in vacuo. Yield 0.09 g, 6.8 %; m.p. 246°C. Found: C 71.34, H 5.80, N 6.54, P 10.07 %. $C_{72}H_{66}N_6O_4P_4$ [1202] requires C 71.88, H 5.49, N 6.98, P 10.31 %. IR (KBr, nujol) ν_{max} cm^{-1}: 1695 s, 1774 m (C=O). ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.72-7.79 (8H, m, *m*-C_6H_5), 7.45-7.58 (12H, m, *o,p*-C_6H_5), 7.16 (2H, d, $^3J_{HH}$ = 8.4 Hz, C^{4}H or C^{8}H), 6.92 (2H, d, $^3J_{HH}$ = 8.1 Hz, C^{8}H or C^{4}H), 6.64 (2H, br.s, C^{1}H or C^{5}H), 6.37 (2H, br.s, C^{5}H or C^{1}H), 6.21 (2H, br.d, $^3J_{HH}$ = 8.4 Hz, C^{3}H or C^{7}H), 6.18 (2H, br.d, $^3J_{HH}$ = 8.1 Hz, C^{7}H or C^{3}H),4.59-4.63 (4H, m, P-C^{15,16}H$_a$-N), 4.34 (br.d, J_{HH}= 3.3 Hz, C^{11}H + C^{12}H), 4.31-4.47 (m, P-C^{13,14}H$_a$-N) (total intensity 8H), 3.94-4.16 (6H, m, P-C^{14,15,16}H$_e$-N), 3.87 (2H, dd, $^2J_{HH}$ ≈ $^2J_{PH}$ ≈ 14.1 Hz, P-C^{13}H$_e$-N), 3.06 (2H, dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 3.5 Hz, C^{9}H or C^{10} H), 2.96 (2H, dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 3.2 Hz, C^{10}H or C^{9}H), 2.87-2.93 (4H, m, CH_2), 0.29 (6H, t, $^3J_{HH}$ = 7.3 Hz, CH_3). ^{31}P NMR ([D_6]DMSO, 303 K) δ_P ppm: -55.95 (d, J_{PP} = 6.7 Hz), -56.62 (d, J_{PP} = 6.7 Hz).

*1^3,1^7,7^3,7^7-Tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4(2,6)-di[11,12-(cis-N-propyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena] cyclotetraphane (**7**).* The reaction of phenylphosphine (0.67 g, 6.09 mmol), paraformaldehyde (0.36 g, 12.18 mmol) and **4** (1.05 g, 3.02 mmol) was performed like the analogous reaction with **2**. The hot reaction mixture was filtered off the unidentified dark residue, cooled and concentrated in vacuo up to 1/3 of the inintial volume. After the standing at -15^{0}C overnight the crystalline precipitate was formed, which was collected by filtration, washed with cold DMF and acetonitrile and dried in vacuo. According to ^{1}H and ^{31}P spectra the crude product (0.21 g) was practically individual *1^3,1^7,7^3,7^7-tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4(2,6)-di-(R,R/S,S)-[11,12-(cis-N-propyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena]cyclotetraphane* (**7a**)**,** which was recrystallized from DMSO, washed with acetonitrile and dried. Yield of **7a** 0.11 g, 6.3%; m.p. 252°C. Found: C 71.87, H 5.93, N

6.62, P 9.87 %. $C_{74}H_{70}N_6O_4P_4$ [1230] requires C 72.19, H 5.69, N 6.82, P 10.08 %. IR (KBr, nujol) ν_{max} cm^{-1}: 1696 s, 1774 m (C=O). ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.73-7.80 (8H, m, *m*-C_6H_5). 7.45-7.61 (12H, m, *o,p*-C_6H_5), 7.15 (2H, d, $^3J_{HH}$ = 8.1 Hz, C^4H or C^8H), 6.92 (2H, d, $^3J_{HH}$ = 8.1 Hz, C^8H or C^4H), 6.64 (2H, br.s, C^1H or C^5H), 6.38 (2H, br.s, C^5H or C^1H), 6.21 (2H, br.d, $^3J_{HH}$ = 8.1 Hz, C^3H or C^7H), 6.18 (2H, br.d, $^3J_{HH}$ = 8.1 Hz, C^7H or C^3H), 4.62 (4H, dd, $^2J_{HH}$ = 15.0 Hz, $^2J_{PH}$ = 5.9 Hz, P-$C^{15,16}H_a$-N), 4.34-4.45 (m, P-$C^{13,14}H_a$-N), 4.34 (br.d, J_{HH} = 2.9 Hz, $C^{11}H + C^{12}H$) (total intensity 8H), 3.93-4.15 (6H, m, P-$C^{14,15,16}H_e$-N), 3.86 (2H, dd, $^2J_{HH} \approx {}^2J_{PH} \approx$ 14.1 Hz, P-$C^{13}H_e$-N), 3.06 (2H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 3.7 Hz, C^9H or C^{10} H), 2.96 (2H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 3.1 Hz, $C^{10}H$ or C^9H), 2.80-2.88 (4H, m, N-CH_2), 0.66-0.88 (4H, m, CH_2), 0.30 (6H, t, $^3J_{HH}$ = 7.3 Hz, CH_3). ^{31}P NMR ([D_6]DMSO, 303 K) δ_p ppm: -55.60 (d, J_{PP} = 6.6 Hz), -55.94 (d, J_{PP} = 6.6 Hz).

The filtrate of the reaction mixture was repeatedly concentrated in vacuo up to ~ 1/2 of the initial volume and allowed to stand at -15 ^{0}C for 1 day. The resulting precipitate (0.05 g) was collected by filtration, washed with cold DMF and acetonitrile and dried in vacuo. This precipitate was a mixture of **7a** and *1^3,1^7,7^3,7^7-tetraphenyl-1,3(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4-di-[11,12-(cis-N-propyldicarboximido)-9,10-dihydro-9,10-ethanoanthracena]cyclotetraphane* (**7b**) in the ratio 2:5. The combined yield of **7a** and **7b** was 0.26 g , 14 %.

Spectral data for **7b:** ^{1}H NMR ([D_6]DMSO, 303 K) δ_H ppm: 7.70-7.82 (8H, m, *m*-C_6H_5), 7.45-7.61 (12H, m, *o,p*-C_6H_5), 7.14 (2H, d, $^3J_{HH}$ = 8.1 Hz, C^4H or C^8H), 6.95 (2H, d, $^3J_{HH}$ = 8.1 Hz, C^8H or C^4H), 6.66 (2H, br.s, C^1H or C^5H),6.36 (2H, br.s, C^5H or C^1H),6.21 (2H, br.d, $^3J_{HH}$ = 8.1 Hz, C^3H or C^7H), 6.18 (2H, br.d, $^3J_{HH}$ = 8.1 Hz, C^7H or C^3H), 4.65 (2H, dd, $^2J_{HH}$ = 15.0 Hz, $^2J_{PH}$ = 4.8 Hz, P-$C^{15}H_a$-N), 4.59 (2H, dd, $^2J_{HH}$ = 12.0 Hz, $^2J_{PH}$ = 5.1 Hz, P-$C^{16}H_a$-N), 4.40 (dd, $^2J_{HH}$ = 14.7 Hz, $^2J_{PH}$ = 4.8 Hz, P-$C^{13,14}H_a$-N), 4.35 (br.d, J_{HH} = 3.3 Hz, $C^{11}H + C^{12}H$) (total intensity 8H), 3.93-4.16 (6H, m, P-$C^{14,15,16}H_e$-N), 3.84 (2H, dd, $^2J_{HH} \approx {}^2J_{PH} \approx$ 15.0 Hz, P-$C^{13}H_e$-N), 3.06 (2H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 3.7 Hz, C^9H or C^{10} H), 2.96 (2H, dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 3.1 Hz, $C^{10}H$ or C^9H), 2.80-2.88 (4H, m, N-CH_2), 0.66-0.89 (4H, m, CH_2), 0.29 (6H, t, $^3J_{HH}$ = 7.3 Hz, CH_3). ^{31}P NMR ([D_6]DMSO, 303 K) δ_p ppm: -55.77 (s), -55.83 (s).

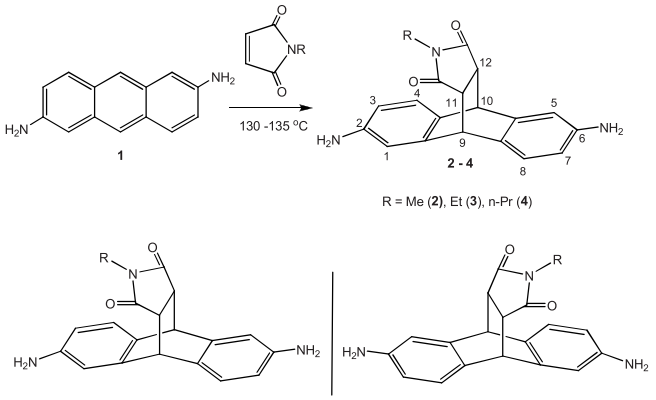
X-Ray Crystallography

Single crystals of **5a** were grown from DMSO, and measured on a Nonius KappaCCD sealed tube diffractometer with graphite-monochromated Mo K_α radiation. Programs used: data collection COLLECT,[13] cell refinement with Dirax/lsq,[14] data reduction with EvalCCD.[15] Multi-scan empirical absorption corrections using SADABS,[16] structure solution with <SIR2004>,[17] structure refinement against F^2 using SHELXL-97.[18] Crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as a supplementary publication no. CCDC 853218. Copy of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223/336-033).

Crystal Data: $C_{70}H_{62}N_6O_4P_4 \cdot 7\ C_2H_6OS + H_2O$ (**5a**), M = 1738.03, colorless crystal 0.19 x 0.18 x 0.17 mm, a = 14.836(3), b = 15.408(3), c = 18.992(4) Å, α = 91.27(3), β = 91.40(3), γ = 90.05(3)º, V = 4339.1(15) Å^3, ρ_{calc} = 1.330 g cm^{-3}, μ= 0.318 mm^{-1}, semiempirical absorption correction from equivalents (94.20≤ T ≤ 94.79), Z = 2, triclinic, space group *P-1*, λ= 0.71073 Å, T = 198(2) K, ω and φ scans (2.14 ≤θ≤25.10º), 18300 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 Å^{-1}, 12553 independent (R_{int} = 0.1006) and 5198 observed reflections [$I \geq 2\ \sigma(I)$], 1061 refined parameters, $R(I \geq 2\sigma(I))$ = 0.1085, wR^2 = 0.2649, max. residual electron density 1.01 (-0.68) e Å^{-3}. The completeness of the data set is 0.81 due to crystal deterioration.

Results and Discussion

Starting diamine **1** was obtained via reduction of corresponding commercially available 2,6-diaminoanthraquinone by zinc powder.[11] Further Diels-Alder reaction of **1** with *N*-alkylmaleimides led to the racemic mixtures of the corresponding diamines **2-4**[11] (Scheme 1).

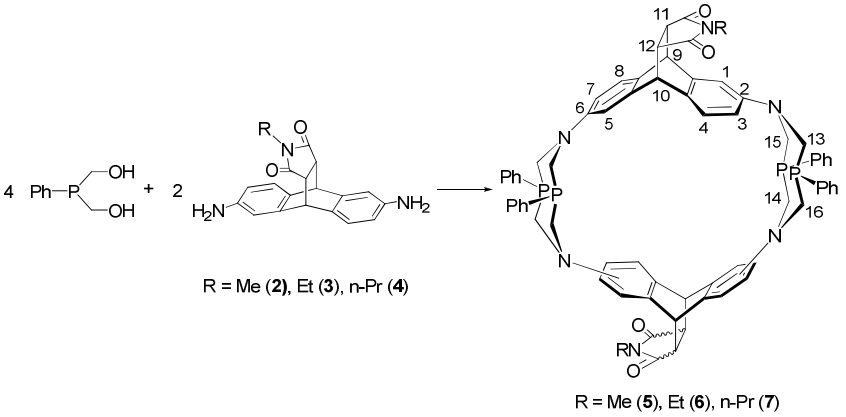


Scheme 1.

To the best of our knowledge *N*-alkyl-2,6-diamino-9,10-dihydro-9,10-ethanoantracene-*cis*-11,12-dicarboximides **3-4** are new organic compounds and diamines of that type have never been used for cyclophane design before, though 11,12-disubstituted 2,6-dioxy-9,10-dihydro-9,10-ethenoanthracenes were key starting reagents for the synthesis of chiral cyclophanes which showed the strong binding properties toward organic ammonium salts.[19]

Diamines **2-4** possess inherent chirality due to the asymmetric disposition of amino groups relative to bicyclic framework and had been obtained as racemic mixtures of enantiomers. The attempts to separate pure enathiomers via diastereomeric salt formation with *D*-tartaric or (1*S*)-(+)-10-camphorsulfonic acid have been unsuccessful yet. Spatial arrangement of amino groups resembles that of diamines (4,4'-diaminodiphenylmethane, 4,4'-thiodianiline and bis(4-aminophenyl)sulfone) previously exploited for the efficient self-assembly of *P,N*-containing cyclophanes.[10a]

Macrocyclization was performed according recently developed procedure of covalent self-assembly in the course of Mannich-type condensation.[10] Two equivalents of formaldehyde were heated with one equivalent of phenylphosphine, and the resulting transparent mixture was dissolved in DMF. Then one equivalent of *N*-alkyl-2,6-diamino-9,10-dihydro-9,10-ethanoanthracene-*cis*-11,12-dicarboximides **2-4** was added and the reaction mixtures were stirred at 80 - 110 °C for 3 days (Scheme 2), the starting phosphine concentrations being 0.2-0.4 M. According to the NMR monitoring data of the reaction mixtures the products with 1,5-diaza-3,7-diphosphacyclooctane fragments incorporated into the macrocyclic frameworks were predominant after 3 days of reactions. The appearance of a number of signals with chemical shifts in the narrow region -55 ÷ -57 ppm in ^{31}P NMR spectra was explained by the formation of the products of homo- and heterochiral [2+2] macrocyclization (corresponding *rac*- and *meso*-isomers) with head-to-tail and probably head-to-head orientations



Scheme 2.

of bicyclic fragments and the inequivalence of phosphorus atoms forming chiral intramolecular cavity (Figure 1). The white crystals of cyclophanes **5-7** were isolated in moderate yields (51 %, 7 % and 14 %, respectively) (Scheme 2) as the adducts with few DMF molecules according to ^{1}H NMR spectra. The solvent was removed by washing of the crude crystalline products with acetonitrile.

Cyclophane **5** was obtained as a mixture of two isomers according to NMR data. The crude crystalline product was recristallized from DMF to give one isomer **5a** of 90 % purity in moderate yield (17 %). Two other macrocycles **6a** and **7a** were crystallized from the reaction mixtures as practically individual stereoisomers though in the case of the macrocycle **7** the reaction mixture's filtrate was enriched by the second isomer **7b**.

Macrocycles are restrictedly soluble in DMF and DMSO like 1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphanes described earlier.[10a]

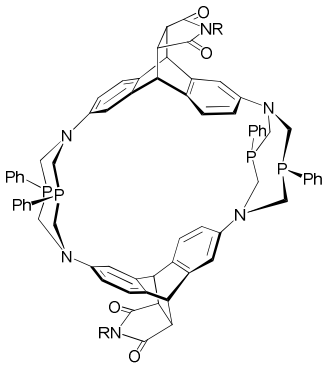
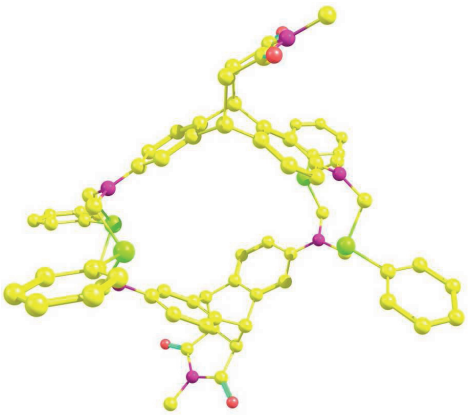
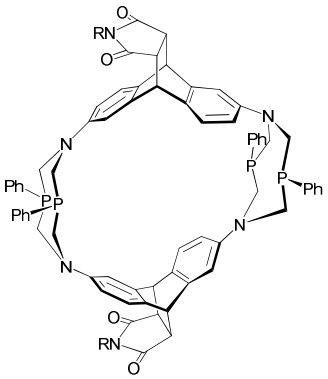
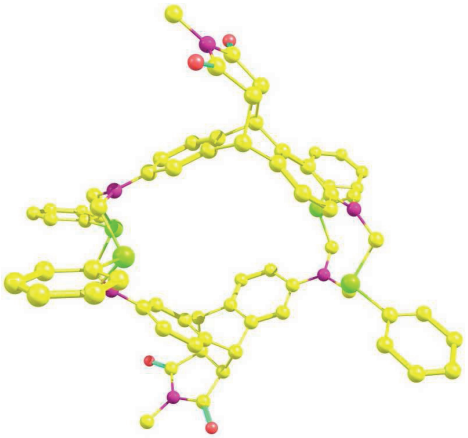
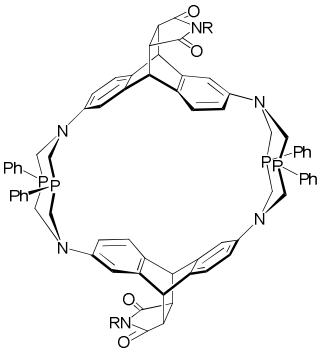
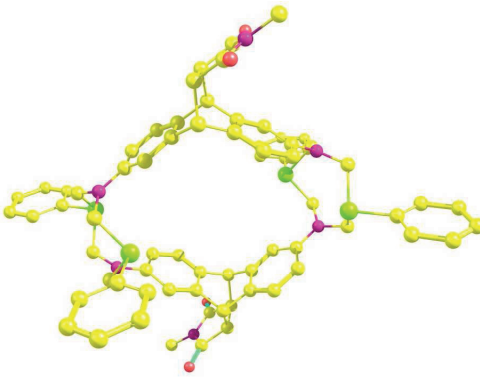
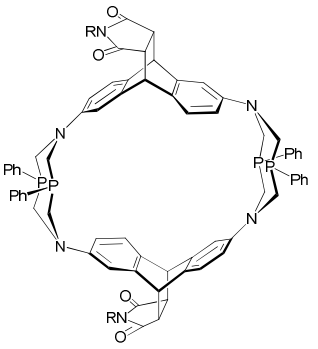
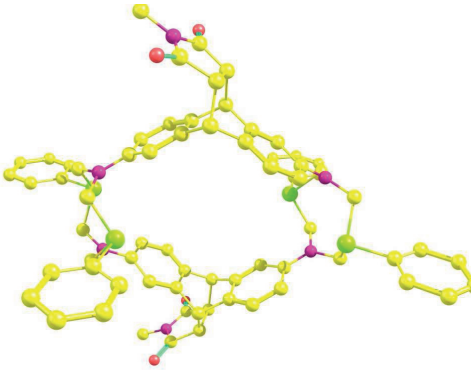
Taking into account two possible ways of mutual coupling of diamine fragments into the [2+2]-macrocycles two principial types of cyclophanes could be formed (Table 1). The first type with slightly twisted cyclophane framework is possible for homochiral *rac*-isomers with head-to-tail and head-to-head orientations of phane fragments. According to quantum-chemical calculations for cyclophane **5** by "Priroda" method[20] their optimized structures (Table 1, entries 1 and 2) differ only by the directions of exocyclic imido groups and show the dihedral angles of about 30.7-30.8° between PP-axes of two eight-membered fragments. The second type with untwisted framework and near rhombohedral cavities is possible for both heterochiral *meso*-isomers with head-to-tail and head-to-head orientation of the phane fragments (Table 1, entries 3 and 4). In these cases the PP-axes of the heterocyclic fragments of the optimized calculated structures are parallel and the only difference between these *meso*-isomers would be also the directions of imido groups. According to quantum-chemical calculations of the full energies E_0 the *rac*-head-to-head isomer is the most stable one, but ΔE_0 for the *rac*-head-to-tail isomer is only 0.1364 kJ·mol^{-1} (0.0326 kkal·mol^{-1}), whereas for *meso*-head-to-tail and *meso*-head-to-head isomers ΔE_0 are 15.3145 kJ·mol^{-1} (3.660 kkal·mol^{-1}) and 16.1074 kJ·mol^{-1} (3.849 kkal·mol^{-1}). So there are no noticeable energy gaps between all four possible isomers of the cyclophane **5**.

In contrast to the previously described ^{31}P NMR spectra of *P*,*N*-containing cyclophanes[10] the signals of the less soluble isomers **5a-7a** represent two doublets due to the inequivalence of two pairs of phosphorus atoms incorporated into the chiral macrocyclic framework. The ^{31}P NMR chemical shifts of **5a-7a** (δ_P -55.60 and -56.31 ppm (J_{PP} = 6.6 Hz) (**5a**); -55.95 and -56.62 ppm (J_{PP} = 6.7 Hz) (**6a**); -55.60 and -55.94 ppm (J_{PP} = 6.6 Hz) (**7a**)) are similar to those of previously described 3,7-diphenyl-l,5-diaza-3,7-diphosphacyclooctanes[21] and macrocycles with analogous heterocyclic fragments.[10a,b] Inequivalence of P-atoms has been described recently for *P*,*N*-corands containing exocyclic chiral sustuents on nitrogens,[22] however coupling constant J_{PP} in the cyclic -PCH_2NCH_2P- fragments to the best of our knowledge is observed for the first time.

The ^{1}H NMR spectra of **5a-7a** show the inequivalence of all methylene groups of the diazadiphosphacyclooctane fragments. The one set of signals for two equivalent phane fragments confirms that **5a-7a** are single isomers; six aromatic protons of these fragments are mutually inequivalent like the corresponding protons of starting chiral diamines **2-4**. The observed spectral picture can be explained by the total asymmetry of macrocyclic molecules. The X-ray study of the single crystal of **5a** (see below) showed that it was *rac*-head-to-tail isomer. **6a** and **7a** were also analogous *rac*-head-to-tail isomers according to the similarity of their NMR spectra with the spectra of **5a**.

The concentration of the filtrates of the corresponding reaction mixtures gave the fractions enriched by more soluble isomers **5b** and **7b** (in the case of the macrocycle **6** this attempt was unsuccessful). In both cases their ^{31}P NMR spectra showed two singlets at δ_P -55.96, -56.24 ppm (**5b**) and at δ_P -55.77, -55.83 ppm (**7b**). The ^{1}H NMR spectra of **5b** and **7b** were also similar and showed the presence of four inequivalent methylene groups of the diazadiphosphacyclooctane fragments and one set of the signals for two chiral phane fragments which confirmed that both signals in ^{31}P NMR spectra correspond to the single isomer. However the spectral data do not allow to make a choice between three possible structures with asymmetrical heterocyclic fragments and close energies (Table 1). It should be mentioned, that the spectra of the reaction mixtures did not show the signals of the diazadiphosphacyclooctane-containing products (in the range -50 ÷ -60 ppm) other than isolated isomers **a** (*rac*-head-to-tail) and these more soluble

Table 1. Structures and relative full energies ΔE_0 of possible isomers of cyclophane **5**.

	Isomer	Chemical structure	Optimized calculated structure	ΔE_0, kJ·mol^{-1}
1	*rac*-head-to-tail			0.1364
2	*rac*-head-to-head			0.00
3	*meso*-head-to-tail			15.3145
4	*meso*-head-to-head			16.1074

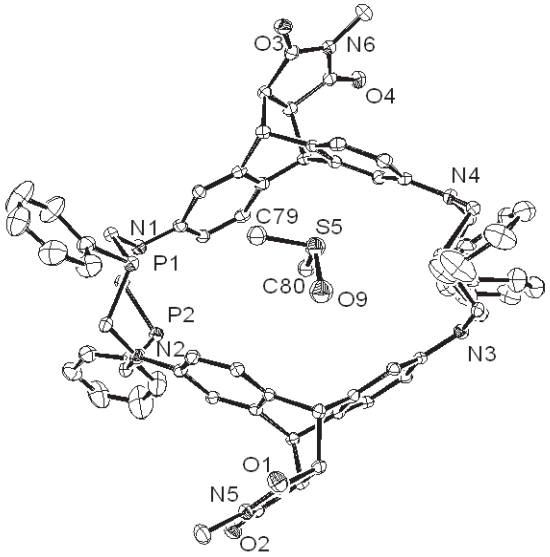


Figure 1a. The molecular structure of the cyclophane **5a** with one DMSO molecule penetrating the cavity (hydrogen atoms and other DMSO molecules are omitted for clarity).

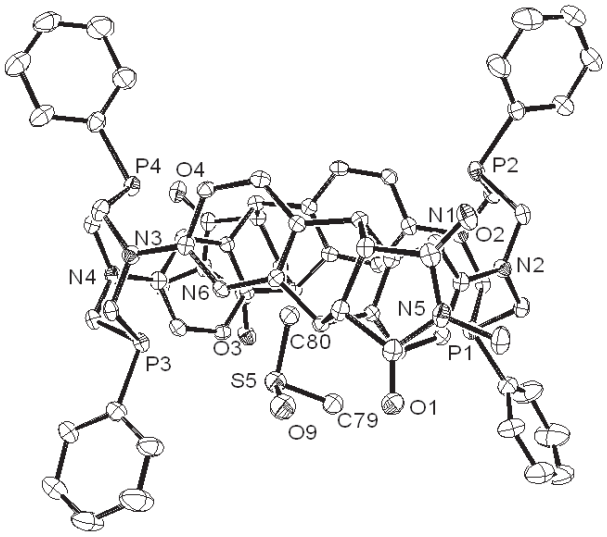


Figure 1b. The molecular structure of the cyclophane **5a** with one DMSO molecule penetrating the cavity (side view, hydrogen atoms and other DMSO molecules are omitted for clarity).

isomers **b**, so only two isomers from four possible ones are formed as a result of the macrocyclization. It demonstrates the stereoselectivity of the covalent self-assembly processes.

Crystals of **5a** suitable for X-ray analysis were obtained by slow recrystallization from DMSO. The unit cell contains the macrocycle **1** (Figure 1), seven disordered DMSO molecules and one water molecule. The X-ray analysis data showed that **5a** was a racemate of homochiral macrocycle with phane fragments linked in "head-to-tail" mode with the opposite mutual direction of the exocyclic dicarboximide groups. The molecule of **5a** is asymmetric and slightly twisted. Unlike the previously described 1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphanes[10a] nitrogen atoms are not located in the same plane and the dihedral angle N1N2N3N4 is 27.49º, whereas the angle between phosphorus-phosphorus axes of two heterocyclic fragments is 28.16º. The aromatic rings which form the cavity walls are practically orthogonal to the calculated medium plane of four nitrogen atoms (the dihedral angles are 79.84 - 83.01º) so the cavity is relatively deep. Nitrogen atoms are coordinated in near trigonal-planar fashion (the sums of their bond angles are 357.2 - 360º) due to the conjugation of their electron lone pairs with the π-systems of the aromatic rings. Both eight-membered fragments adopt chair-chair conformations. The slightly different positions of their exocyclic phenyl substituents are probably determined by the solvate DMSO molecules. The diagonal P1-P4 and P2-P3 distances are 9.72 и 9.64 Å respectively and are close to the corresponding distances of 1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6, 8(1,4)-tetrabenzenacyclooctaphanes (about 9.4 Å[10a]), but the distances between opposite phenylene rings are less (7.25 - 7.45 Å *vs*. 8.8 Å[10a]). The free volume of the cavity is about 80 Å^3. The single crystal of **5a** is a true racemic mixture of both enantiomers.

The methyl group of one DMSO molecule penetrates the macrocyclic cavity like the previously described DMF solvates of *P,N*-containing cyclophanes.[10a,b] The solvate complex with DMSO is not very stable and prolonged washing with acetonitrile gives solvent-free microcrystalline cyclophane **5a**.

In summary, a novel type of heterocyclophanes with chiral intramolecular cavities which are also potential bis-chelating ligands for transition metals has been obtained.

Conclusions

The condensations of bis(hydroxymethyl)phenylphosphine with racemic diamines containing chiral *N*-alkyl-*cis*-11,12-dicarboximido-9,10-dihydro-9,10-ethanoanthracene-2,6-diyl spacers proceed as the covalent self-assembly to give two isomers of corresponding [2+2]-macrocycles as the main products. The products of homochiral condensation, namely racemic head-to-tail isomers of these cyclophanes, have been isolated and the structure of their *N*-methyl substituted representative has been studied by the X-ray analysis which has showed the slightly twisted structure of the cyclophane molecule with chiral hydrophobic cavity. These results indicate that the use of enantiopure diamines with similar 9,10-dihydro-9,10-ethanoanthracene-2,6-diyl spacers in analogous condensations may be considered as a perspective approach to the synthesis of optically active *P,N*-containing cyclophanes, which are of interest for the design of stereoselective catalysts, molecular recognition systems and molecular reactors.

Acknowledgements. This work was supported by the Russian Foundation for Basic Research (grant 10-03-00380_a), a President of Russia grant for the support of leading scientific schools (grant NSh-3831.2010.3), Ministry of Education and Science of Russian Federation (state contract 02.740.11.0633).

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Received 05.06.2011
Accepted 01.08.2011