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New *P,N*–Containing Cyclophanes with Exocyclic Pyridyl–Containing Substituents on Phosphorus Atoms

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The synthesis of 28- and 36-membered P,N-containing cyclophanes with two 1,5-diaza-3,7-diphosphacyclooctane rings in the macrocyclic frameworks and exocyclic pyridine-2-yl or 2-(pyridine-2-yl)ethyl substituents on all phosphorus atoms is described. These cyclophanes have been obtained by Mannich-like condensations in three components systems: pyridyl-containing primary phosphines–formaldehyde–primary diamines with spatially divided amine groups (bis(4-aminophenyl)methane, bis(4-aminophenyl)sulfide or 1,3-bis(4'-aminophenoxy)benzene), and the selectivity of the macrocyclization depends on the lengths the diamine spacers unlike previously described analogous condensations with the participation of arylphosphines. The condensations of pyridyl-containing phosphines with formaldehyde and diamines containing relatively short spacers formed by two phenylene groups bonded with one-atom bridges proceed as covalent self-assembly and lead to the predominant formation of 28-membered cyclophanes which have been isolated in moderate yields (17–21 %) whereas the condensations with the participation of 1,3-bis(4'-aminophenoxy) benzene containing three phenylene groups in the spacer are much less selective, and 36-membered cyclophanes have been obtained in low yields (7–9 %). It shows the strong influence of the starting phosphine nature on the selectivity of the Mannich-like condensation reactions. The treatment of 28-membered P-pyridylethyl substituted cyclophanes with hydrochloric acid in chloroform leads to the corresponding monohydrochlorides as a result of the protonation of pyridyl nitrogen atom, and in the solutions the fast migration of the proton between all pyridyl nitrogen centers is observed.

Keywords: Macrocycle, cyclophane, pyridyl-containing phosphine, diamine, condensation, covalent self-assembly.

Новые *P,N*–содержащие циклофаны с экзоциклическими пиридилсодержащими заместителями при атомах фосфора

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Описан синтез 28- и 36-членных P,N-содержащих циклофанов с двумя 1,5-диаза-3,7-дифосфациклооктановыми фрагментами в скелете макроциклов и экзоциклическими пиридин-2-ильными и 2-(пиридин-2-ил)этильными заместителями при всех атомах фосфора. Данные циклофаны были получены конденсацией типа Манниха в трехкомпонентных системах: пиридилсодержащие первичные фосфины – формальдегид – первичные диамины с пространственно разделенными аминогруппами (бис(4-аминофенил)метан, бис(4-аминофенил)сульфид или 1,3-бис(4'-аминофенокси)бензол). Показано, что селективность макроциклизации зависит от длины спейсеров диаминов в отличие от ранее описанных аналогичных конденсаций с участием арилфосфинов. Конденсации пиридилсодержащих фосфинов с формальдегидом и диаминами, содержащими относительно короткие спейсеры, образованные двумя фениленовыми фрагментами, связанными одноатомными мостиками, протекают как ковалентная самосборка и приводят к преимущественному образованию 28-членных циклофанов, выделенных с умеренным выходом (17–21 %), тогда как конденсации с участием 1,3-бис(4'-аминофенокси)бензола, содержащего три фениленовые группы в спейсере, значительно менее селективны, и 36-членные цикло-

фаны были получены с низким выходом (7–9 %); это показывает сильное влияние природы исходного фосфина на селективность конденсаций типа Манниха. Обработка 28-членных P-пиридилэтилзамещенных циклофанов соляной кислотой в хлороформе приводит к соответствующим моногидрохлоридам в результате протонирования атома азота пиридильной группы, причем в растворах наблюдается быстрая миграция протона по всем пиридильным азотным центрам.

Ключевые слова: Макроцикл, циклофан, пиридилсодержащий фосфин, диамин, конденсация, ковалентная самосборка.

Introduction

Pyridylphosphines are multifunctional ligands which have the ability to act as hybrid *P,N*-ligands,[1-9] so pyridyl-containing phosphines on the cyclic aminomethylphosphine platform should combine the properties of two systems – pyridylphosphine and aminomethylphosphine.[10] The introduction of *o*-pyridyl fragments bound with phosphorus atoms both directly and through the spacer should expand the coordination modes of these ligands. On the other hand, the presence of photoactive pyridyl radicals should result in the increase of metal complexes luminescence.[3-9] Indeed polynuclear gold(I) complexes of recently described *P*-pyridyl substituted 1,5-diaza-3,7-diphosphacyclooctanes[10] and *P,N*-chelate copper(I) complexes of their *P*-pyridylethyl substituted analogues[11] have represented unusual photoluminescence and were medium luminophors with quantum yields up to 40 %.[11]

A very important source of a fast growing interest to the chemistry of cyclic *P,P*-chelating aminomethylphosphines is the remarkable catalytic activity of their complexes with abundant inexpensive metals (mainly nickel and cobalt) at electrochemical processes in particular the hydrogen production and hydrogen oxidation.[12-15] One of the main reasons of this activity is the presence of the amine bases incorporated in *P,N*-containing rings, which function as proton relays,[12-14] so the introduction of additional nitrogen basic centers into the ligands periphery is able to increase the catalytic activity of their complexes. 1,5-Diaza-3,7-diphosphacyclooctanes with nitrogen-containing heterocyclic fragments (including pyridyl rings) on intracyclic nitrogen atoms have appeared to be very promising ligands for the creation of electrocatalytic systems.[15,16] Recently Ni^{II} complexes of several representatives of 1,5-diaza-3,7-diphosphacyclooctanes with pyridine-2-yl substituents on phosphorus atoms have demonstrated a unique effectiveness in hydrogen evolution and fuel cell tests probably due to the presence of additional pendant bases situated in close proximity to the coordination sphere of the transition metal.[10,17]

The promising results achieved in the chemistry of aminomethylphoshines with pyridyl-containing substituents on phosphorus atoms make expedient the next step of its development namely the synthesis of *P,N*-containing cyclophanes with 1,5-diaza-3,7-diphosphacyclooctane fragments in the macrocyclic framework and peripheral pyridyl-containing fragments. The inclusion of two *P*-pyridyl substituted diazadiphosphacyclooctane rings into the macrocycle could definite their spatial positions, change their conformational and coordination behavior. In addition the cyclophanes should have internal molecular cavities which are capable to bind various organic substrates,[18-20] and this phenomenon could influence on the catalytic and luminescent properties of the metal complexes of the proposed ligands. The approach to the synthesis of this type of cyclophanes has been previously developed for *P*-aryl, benzyl- and alkyl-substituted compounds and is based on the covalent self-assembly by Mannich-like condensations between primary phosphines, formaldehyde and primary aromatic diamines with spatially divided amine groups. The successful use of this strategy has resulted in the synthesis of a series of 28–38-membered cage macrocyclic tetraphoshines with two diazadiphosphacyclooctane rings and various phane fragments depending on the nature of starting diamines.[18,21,22] The use of available pyridyl-containing primary phosphines, namely (pyridine-2-yl)phosphine[10,23] and [2-(pyridine-2-yl)ethylphosphine[24] in analogous condensations could become a route to the synthesis of functionalized *P,N*-containing cyclophanes with pyridyl-containing groups on the periphery.

In the present paper we describe the synthesis of the first representatives of 28- and 36-membered cage *P,N*-containing macrocycles with pyridyl- and pyridylethyl substituents on phosphorus atoms on the basis of the covalent self-assembly approach.

Experimental

General

^{1}H and ^{31}P NMR spectra were recorded on a spectrometer BrukerAvance-DRX 400, operating at 400 and 162 MHz respectively; chemical shifts (δ, ppm) were referenced to TMS (^{1}H) or to external 85 % H_3PO_4 (^{31}P). Spin-spin coupling constants (*J*) are given in Hz. MALDI mass-spectra were obtained on a Bruker ULTRALEX III mass-spectrometer (laser Nd: YAG, l = 335 nm, matrix: *p*-nitroaniline). The melting points were determined on a Boetius apparatus and are uncorrected.

(Pyridine-2-yl)phosphine[10,23] and [2-(pyridine-2-yl)ethylphosphine[24] were obtained according to the described methods. All manipulations with the primary phosphines and solutions of macrocycles were carried out by standard high-vacuum and dry-nitrogen techniques in dry degassed solvents which were purified by standard methods.

Preparations

*$1^{3},1^{7},5^{3},5^{7}$-Tetra[2-(pyridine-2-yl)ethyl]-1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphane (**1**).* A mixture of 2-[(pyridine-2-yl)ethyl]phosphine (0.891 g, 6.41 mmol) and paraformaldehyde (0.385 g, 12.83 mmol) was stirred at 90 °C until the homogenization. *Bis*(hydroxymethyl)[2-(pyridine-2-yl)ethyl]phosphine obtained was dissolved in DMF

(5 ml) and a solution of *bis*(4-aminophenyl)methane (0.635 g, 3.21 mmol) in DMF (12 ml) was added. The reaction mixture was stirred at 100–110 °C for 14 h and cooled. The precipitate formed was filtered off, washed with DMF, was washed twice carefully with acetonitrile and dried at 0.05 torr for 4 h. Yield: 0.285 g (17 %). M.p.: 210–212 °C. Found, %: C, 70.63; H, 6.74; N, 10.81; P, 11.69. $C_{62}H_{68}N_8P_4$. Calculated, %: C, 70.98; H, 6.53; N, 10.68; P, 11.81. ^{1}H NMR (400 MHz, $CDCl_3$, 303 K) δ_H ppm: 8.57 (4H, br. s, C^{3}H), 7.67 (4H, dd, $^3J_{HH}\approx{}^3J_{HH}\approx$7.3, C^{5}H), 7.29 (4H, br.d, $^3J_{HH}\approx$7.3, C^{6}H), 7.16 (4H, m, C^{4}H), 7.01 (8H, d, $^3J_{HH}$=7.6, C^{9}H), 6.39 (8H, d, $^3J_{HH}$=7.6, C^{8}H), 4.11 (8H, dd, $^2J_{HH}$=14.2, $^2J_{PH}$=15.1, C^{1}H$_{eq}$), 3.56 (4H, s, C^{11}H), 3.37 (8H, br.d, $^2J_{HH}$=14.2, C^{1}H$_{ax}$), 3.07–3.18 (8H, m, C^{12}H), 1.73–1.82 (8H, m, C^{13}H). ^{31}P NMR (162 MHz, $CDCl_3$, 303 K) δ_P ppm: -55.92 (s). Mass spectrum (MALDI-TOF) *m/z* (%): 1047 (100.0) $[M-H]^+$, 1048 (80.0) $[M]^+$, 1049 (84.0) $[M+H]^+$, 1064 (61.0) $[M+O]^+$, 1079 (38.0) $[M+2O-H]^+$.

*1^3,1^7,5^3,5^7-Tetra[2-(pyridine-2-yl)ethyl]-3,7-dithia-1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphane (**2**)*. **2** was obtained like **1** from 2-[(pyridine-2-yl) ethyl]phosphine (1.033 g, 7.43 mmol), paraformaldehyde (0.440 g, 14.67 mmol) and *bis*(4-aminophenyl)sulfide (0.804 g, 3.72 mmol). The reaction time was 2.5 days at 100–110 °C. Yield: 0.42 g (21 %). M.p. 222–224 °C. Found, %: C, 66.08; H, 6.07; N, 10.45; P 11.09; S, 5.76. $C_{60}H_{64}N_8P_4S_2$. Calculated, %: C, 66.40; H, 5.94; N, 10.33; P, 11.42; S, 5.91. ^{1}H NMR (400 MHz, DMSO-d_6, 303 K) δ_H ppm: 8.53 (4H, br. d, $^3J_{HH}$=4.9, C^{3}H), 7.76 (4H, ddd, $^3J_{HH}$=7.8, $^3J_{HH}$=7.5, $^4J_{HH}$=1.8, C^{5}H), 7.40 (4H, d, $^3J_{HH}$=7.8, C^{6}H), 7.31 (8H, d, $^3J_{HH}$=8.8, C^{9}H), 7.24 (4H, dd, $^3J_{HH}$=7.5, $^3J_{HH}$=4.9, C^{4}H), 6.40 (8H, d, $^3J_{HH}$=8.8, C^{8}H), 3.94 (8H, dd, $^2J_{HH}$=15.6, $^2J_{PH}$=13.3, C^{1}H$_{eq}$), 3.80 (8H, dd, $^2J_{HH}$=15.6, $^2J_{PH}$=5.1, C^{1}H$_{ax}$), 3.00–3.09 (8H, m, C^{12}H), 1.76–1.84 (8H, m, C^{13}H). ^{31}P NMR (162 MHz, DMSO-d_6, 303 K) δ_P ppm: -52.82 (s). Mass spectrum (MALDI-TOF) *m/z* (%): 1083 (100.0) $[M-H]^+$, 1084 (71.0) $[M]^+$, 1085 (56.0) $[M+H]^+$, 1100 (38.0) $[M+O]^+$, 1116 (19.0) $[M+2O]^+$.

*{1^3,1^7,5^3,5^7-Tetra[2-(pyridine-2-yl)ethyl]-1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphane}hydrochloride (**3**)*. A solution of 37 % aqueos hydrochloric acid (0.011 g, 0.114 mmol) in chloroform (0.5 ml) was added to a solution of **1** (0.020 g, 0.019 mmol) in chloroform (3 ml) and stirred for 10 min. A precipitate formed was filtered off, washed with chloroform and dried at 0.05 torr for 1 h. Yield: 0.017 g (82 %). M.p.: 168–180 °C (dec.). Found, %: C, 68.36; H, 6.58; N, 10.48; P, 11.30; Cl, 3.14. $C_{62}H_{69}ClN_8P_4$. Calculated, %: C, 68.59; H, 6.41; N, 10.68; P, 11.41; Cl, 3.27. ^{1}H NMR (400 MHz, DMSO-d_6, 303 K) δ_H ppm: 8.75 (4H, br. s, C^{3}H), 8.34 (4H, m, C^{5}H), 7.91 (4H, m, C^{6}H), 7.76 (4H, br.s, C^{4}H), 7.01 (8H, d, $^3J_{HH}$=7.9, C^{9}H), 6.41 (8H, d, $^3J_{HH}$=7.9, C^{8}H), 4.10 (8H, dd, $^2J_{HH}$=14.9, $^2J_{PH}$=10.4, C^{1}H$_{eq}$), 3.90 (8H, br.d, $^2J_{HH}$=14.9, C^{1}H$_{ax}$), 3.16–3.24 (8H, m, C^{12}H), 1.79–1.87 (8H, m, C^{13}H) (the signal of C^{11}H is masked by the signal of H_2O in DMSO-d_6). ^{31}P NMR (162 MHz, DMSO-d_6, 303 K) δ_P ppm: -53.21 (s).

*{1^3,1^7,5^3,5^7-Tetra[2-(pyridine-2-yl)ethyl]-3,7-dithia-1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphane} hydrochloride (**4**)*. **4** was obtained like **3** from **2** (0.020 g, 0.018 mmol) and 37 % aqueos hydrochloric acid (0.011 g, 0.114 mmol). Yield: 0.018 g (85 %). M.p.: 170–176 °C (dec.) Found, %: C, 64.08; H, 5.97; N, 9.87; P, 10.86; S, 5.63; Cl, 3.07. $C_{60}H_{65}ClN_8P_4S_2$. Calculated, %: C, 64.25; H, 5.84; N, 9.99; P, 11.05; S, 5.72; Cl, 3.27. ^{1}H NMR (400 MHz, DMSO-d_6, 303 K) δ_H ppm: 8.63 (4H, br. d, $^3J_{HH}\approx$ 4.0, C^{3}H), 7.99 (4H, m, C^{5}H), 7.59 (4H, br.d, $^3J_{HH}\approx$7.5, C^{6}H), 7.45 (4H, m, C^{4}H), 7.32 (8H, d, $^3J_{HH}$=8.8 Hz, C^{9}H), 6.42 (8H, d, $^3J_{HH}$=8.8 Hz, C^{8}H), 4.01 (8H, dd, $^2J_{HH}$=14.8 Hz, $^2J_{PH}$=13.1, C^{1}H$_{eq}$), 3.86 (8H, dd, $^2J_{HH}$=14.8, $^2J_{PH}$=4.5, C^{1}H$_{ax}$), 3.08–3.19 (8H, m, C^{12}H), 1.80–1.89 (8H, m, C^{13}H). ^{1}H NMR (400 MHz, DMSO-d_6+ D_2O 1:1, 303 K) δ_H ppm: 8.61 (4H, d, $^3J_{HH}$=5.3, C^{3}H), 8.40 (4H, dd, $^3J_{HH}$=8.3, $^3J_{HH}$=7.5, C^{5}H), 7.93 (4H, br.d, $^3J_{HH}$=7.5, C^{6}H), 7.81 (4H, dd, $^3J_{HH}$=8.3, $^3J_{HH}$=5.3, C^{4}H), 7.36 (8H, d, $^3J_{HH}$=8.7, C^{9}H), 6.43 (8H, d, $^3J_{HH}$=8.7, C^{8}H), 4.07 (8H, dd, $^2J_{HH}$=15.6, $^2J_{PH}$=11.7, C^{1}H$_{eq}$), 3.83 (8H, dd, $^2J_{HH}$=15.6, $^2J_{PH}$=4.8, C^{1}H$_{ax}$), 3.20–3.29 (8H, m, C^{12}H), 1.83–1.92 (8H, m, C^{13}H). ^{31}P NMR (DMSO-d_6, 303 K) δ_P ppm: -52.24 (s); (162 MHz, DMSO-d_6+D_2O 1:1, 303 K) δ_P ppm: -53.13 (s).

*1^3,1^7,7^3,7^7-Tetra(pyridine-2-yl)-3,5,9,11-tetraoxa-1,7(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,6,8,12(1,4),4,10(1,3)-hexabenzenacyclododecaphane (**5**)*. A mixture of (pyridine-2-yl) phosphine (0.43 g, 3.87 mmol) and paraformaldehyde (0.23 g, 7.75 mmol) was stirred at 110 °C until the homogenization. *Bis*(hydroxymethyl)(pyridine-2-yl)phosphine obtained was dissolved in DMF (6 ml) and was added to a solution of 1,3-*bis*(4-aminophenoxy)benzene (0.57 g, 1.95 mmol) in DMF (10 ml) under stirring at 50–60 °C. The reaction mixture was stirred at 100 °C for 24 h and the gradient formation of a white precipitate was observed. After the cooling of the reaction mixture up to the ambient temperature the precipitate formed was filtered off, washed carefully with DMF and twice with acetonitrile and dried at 0.05 torr for 4 h. Yield: 0.10 g (9 %). M.p.: 208–210 °C. Found, %: C, 68.06; H, 5.29; N, 10.21; P, 10.97. $C_{64}H_{56}N_8O_4P_4$. Calculated, %: C, 68.32; H, 5.02; N, 9.96; P, 11.01. ^{1}H NMR (400 MHz, DMSO-d_6, 303 K) δ_H ppm: 8.75 (4H, ddd, $^3J_{HH}$=4.9, $^4J_{HH}$=1.7, $^4J_{HH}$=1.0, C^{3}H), 7.82 (4H, ddd, $^3J_{HH}$=7.8 Hz, $^3J_{HH}$=7.3, $^4J_{HH}$=1.7, C^{5}H), 7.77 (4H, br.d, $^3J_{HH}$=7.8, C^{6}H), 7.34 (4H, ddd, $^3J_{HH}$=7.3, $^3J_{HH}$=4.9, $^4J_{HH}$=1.3, C^{4}H), 7.13 (2H, t, $^3J_{HH}$=8.3, C^{13}H), 6.98 (8H, d, $^3J_{HH}$=9.0, C^{9}H), 6.89 (8H, d, $^3J_{HH}$=9.0, C^{8}H), 6.37 (4H, dd, $^3J_{HH}$= 8.3, $^4J_{HH}$=2.4, C^{12}H), 5.98 (2H, t, $^4J_{HH}$=2.4, C^{14}H), 4.66 (8H, dd, $^2J_{HH}$=14.3, $^2J_{PH}$=10.0, C^{1}H$_{eq}$), 4.48 (8H, dd, $^2J_{HH}$=14.3, $^2J_{PH}$=5.9, C^{1}H$_{ax}$). ^{31}P NMR (162 MHz, DMSO-d_6, 303 K) δ_P ppm: -45.59 (s). Mass spectrum (MALDI-TOF) *m/z* (%): 1140 (78.0) $[M+O]^+$, 1157 (100.0) $[M+2O+H]^+$, 1172 (81.0) $[M+3O]^+$.

*1^3,1^7,7^3,7^7-Tetra[2-(pyridine-2-yl)ethyl]-3,5,9,11-tetraoxa-1,7(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,6,8,12(1,4),4,10(1,3)-hexabenzenacyclododecaphane (**6**)*. A mixture of 2-[(pyridine-2-yl)ethyl]phosphine (0.553 g, 3.98 mmol) and paraformaldehyde (0.239 g, 7.97 mmol) was stirred at 90 °C until the homogenization. *Bis*(hydroxymethyl)[2-(pyridine-2-yl)ethyl]phosphine obtained was dissolved in DMF (5 ml) and was added to a solution of 1,3-*bis*(4-aminophenoxy)benzene (0.581 g, 1.98 mmol) in DMF (10 ml) under stirring at 50–60 °C. The reaction mixture was stirred at 100–110 °C for 7 days and cooled. The reaction mixture was filtered off a small amount of a dark solid, the filtrate was concentrated *in vacuo* up to ¼ of the initial volume and allowed to stand at -15 °C for 4 days. The precipitate formed was filtered off at -10 – -20 °C, washed with cold DMF and twice with acetonitrile and dried at 0.05 torr for 4 h. Yield: 0.090 g (7 %). M.p.: 180–182 °C. Found, %: C, 69.66; H, 5.97; N, 9.32; P, 9.88. $C_{72}H_{72}N_8O_4P_4$. Calculated, %: C, 69.89; H, 5.87; N, 9.06; P, 10.01. ^{1}H NMR (400 MHz, DMSO-d_6, 303 K) δ_H ppm: 8.48 (4H, br.d, $^3J_{HH}$=4.9, C^{3}H), 7.73 (4H, ddd, $^3J_{HH}$ =$^3J_{HH}$= 7.3, $^4J_{HH}$=1.7, C^{5}H), 7.39 (4H, d, $^3J_{HH}$=7.3, C^{6}H), 7.21 (4H, dd, $^3J_{HH}$=7.3, $^3J_{HH}$=4.9, C^{4}H), 7.10 (2H, t, $^3J_{HH}$=8.3, C^{13}H), 6.81 (8H, d, $^3J_{HH}$=8.8, C^{9}H), 6.48 (8H, d, $^3J_{HH}$=8.8, C^{8}H), 6.31 (4H, dd, $^3J_{HH}$=8.3, $^4J_{HH}$=2.4, C^{12}H), 5.84 (2H, t, $^4J_{HH}$=2.4, C^{14}H), 3.98 (8H, dd, $^2J_{HH}\approx{}^2J_{PH}\approx$13.7, C^{1}H$_{eq}$), 2.99–3.06 (8H, m, C^{15}H), 1.81 (8H, m, C^{16}H) (the signal of C^{1}H$_{ax}$ is masked by the signal of H_2O in DMSO-d_6). ^{31}P NMR (162 MHz, DMSO-d_6, 303 K) δ_P ppm: -56.35 (s). Mass spectrum (MALDI-TOF) *m/z* (%): 1023 (100.0) [M-2(C_7H_8N)-H]+, 1130 (11.0) $[M-C_7H_8N]^+$, 1253 (8.0) $[M+O+H]^+$.

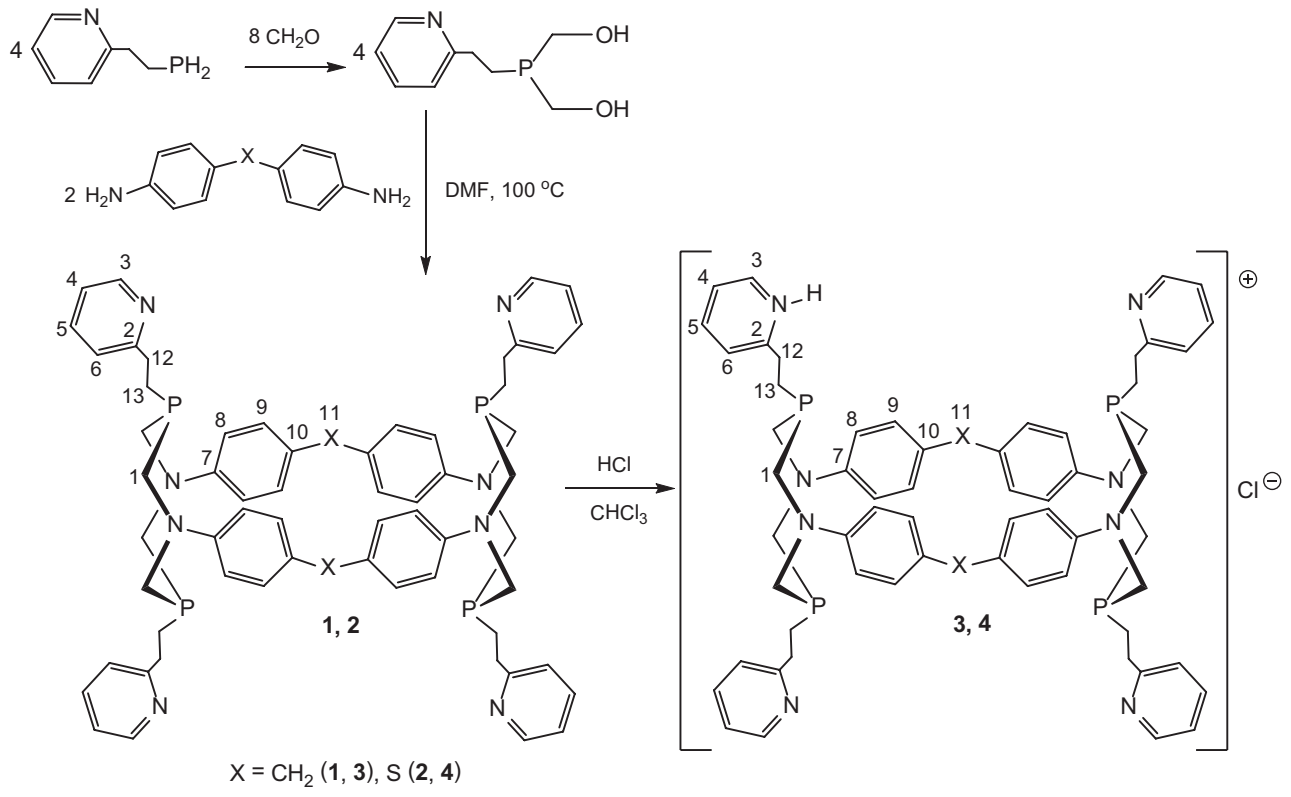
Results and Discussion

The studies of the condensation reactions in the systems: pyridyl-containing primary phosphine – formaldehyde – primary diamine with spatially divided amine groups and various lengths and the flexibilities of the spacers – were performed in order to synthesized cage *P,N*-containing cyclophanes with pyridyl-containing substituents on phosphorus atoms. The condensations were performed in two

steps like previously described analogous macrocyclizations on the basis of primary aryl- and benzylphosphines.[18,24,25] At the first step (pyridine-2-yl)- or [2-(pyridine-2-yl) ethyl]phosphine have reacted with solid paraformaldehyde at elevated temperature (90–110 °C) to give corresponding *bis*(hydroxymethyl)organylphoshine.[10] On the second step the obtained diol has interacted with primary aromatic diamine in DMF at 100–110 °C. The reaction times depended strongly on the nature of primary diamines and phosphines.

The condensation of *bis*(hydroxymethyl)(pyridine-2-yl)phoshine with *bis*(4-aminophenyl)methane was unsuccessful because of premature precipitation of practically insoluble oligomeric aminomethylphosphines which prevented from the further self-assembly of the desired macrocycle. However the condensations of *bis*(hydroxymethyl) [2-(pyridine-2-yl)ethyl]phosphine with *bis*(4-aminophenyl) methane or *bis*(4-aminophenyl)sulfide at the concentration range 0.3–0.4 M smoothly led to the formation of desired 28-membered *P,N*-containing macrocycles **1** and **2** (Scheme 1) with two 1,5-diaza-3,7-diphosphacyclooctane fragments in the macrocyclic frameworks. The formation of **1** and **2** has proceeded for 14 h and 2.5 days, respectively. The signals of **1** and **2** at δ_p -55.3 and -52.6 ppm prevailed in the spectra of the corresponding final reaction mixtures to indicate the phenomenon of the covalent self-assembly. Individual cyclophanes **1** and **2** were isolated by the spontaneous crystallization from the cooled reaction mixtures in moderate yields (17 and 21 %, respectively).

Compounds **1** and **2** are microcrystalline white solids, and in the solid state they are stable to the oxidation. Macrocycle **1** is satisfactorily soluble in chloroform and methylene chloride whereas **2** is soluble in DMSO and chloroform but it is very sensitive to acidic impurities in the latter solvent to give a precipitate that is probably the corresponding hydrochloride. The structure elucidation of these compounds was based on ^{31}P and ^{1}H NMR spectroscopy, mass-spectrometry and elemental analysis. MALDI mass-spectra of **1** and **2** show the peaks of the mass-ions of the corresponding [2+2]-condensation products with *m/z* = 1048 and 1084, respectively, and the peaks of corresponding mono- and dioxides. It should be mentioned that the oxidation of analogous *P*-aryl and *P*-benzyl substituted 28-membered macrocyclic tetraphosphines was often observed earlier under the conditions of the registration of MALDI mass-spectra.[25] Indeed ^{31}P NMR spectra of **1** and **2** show only one narrow signal of each macrocyclic phosphine at δ_p -55.3 ppm (**1**, $CDCl_3$) and -52.82 ppm (**2**, DMSO-d_6) that gives the evidence of the symmetrical structure of the macrocycles. The values of the chemical shifts indicate that the cyclophanes contain 1,5-diaza-3,7-diphosphacyclooctane fragments.[25-27] ^{1}H NMR spectra also confirm the structures of 1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphanes **1** and **2**. The signals of the methylene protons of diazadiphosphacyclooctane fragments at C^1 form typical $(AB)_2X$ systems for the chair-chair conformation of the heterocyclic fragments with equatorial positions of the substituents on phosphorus atoms and axial positions of their lone electron pairs, namely two doublets of doublets with coupling constants $^{2}J_{HH}$ values of 14.2–15.6 Hz and $^{2}J_{PH}$ values of 13.3–15.1 Hz for equatorial protons and 0–5.1 Hz for axial protons.[24-26] Both phane fragments are equivalent and the signals of their protons are typical *p*-phenylene AB systems (for **1** also a singlet of central methylene protons at C^{11} is observed); all 2-(pyridine-2-yl)ethyl substituents



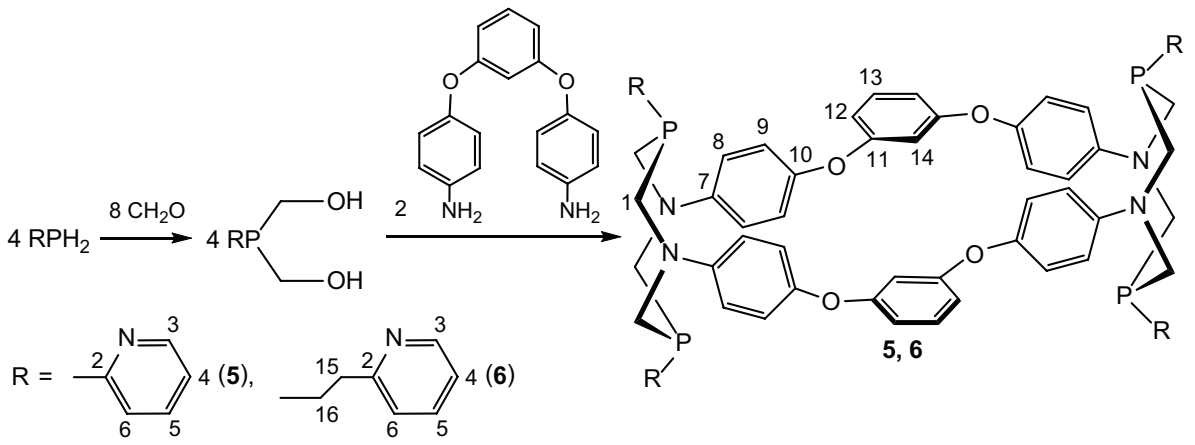
Scheme 1.

on phosphorus atoms are also equivalent and the patterns of their protons signals are very similar for the macrocycles **1** and **2** and include the most low-field broad singlet or doublet of the proton at C^3 at δ_H 8.53–8.57 ppm, a doublet of doublets of the proton at C^5 at δ_H 7.67–7.77 ppm, a doublet of the proton at C^6 at δ_H 7.29–7.59 ppm, a broadened multiplet or a doublet of doublets of the proton at C^4 at δ_H 7.16–7.24 ppm and two multiplets of the methylene groups bound with pyridyl ring and with phosphorus atom at δ_H 3.00–3.18 and 1.73–1.84 ppm. The signals in ^{1}H NMR spectra of **1** and **2** corresponding to their framework parts are similar to the analogous signals of previously described 28-membered *P,N*-containing 1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphanes; it should be mentioned that their structures have been confirmed by the X-ray analysis.[25] The data obtained indicate that the structures of cyclophanes **1** and **2** are similar to that of previously described 28-membered cage *P,N*-containing macrocycles with two diazadiphosphacyclooctane fragments in chair-chair conformations with axial lone electron pairs of phosphorus atoms directed inward the macrocyclic cavity.[18,21,25]

The treatment of **1** and **2** with the excess of aqueous hydrochloric acid in chloroform leads to the formation of the microcrystalline precipitates of their monohydrochlorides **3** and **4** (Scheme 1) according to the elemental analysis data. **3** and **4** are soluble in DMSO. Their signals in ^{31}P NMR spectra are not essentially shifted in comparison with the signals of **1** and **2**. The ^{1}H NMR spectra of **3** and **4** are also similar to ones of the initial cyclophanes **1** and **2**. Only the signals of the protons of the pyridyl fragments are broadened and show low-field shifts. For **4** these shifts are equal *ca.* 0.10–0.23 ppm. In the case of **3** the low-field shifts are 0.18–0.7 ppm but the comparison is not completely correct because different solvents have been used ($CDCl_3$ for **1** and DMSO-d_6 for **3**). It should be mentioned that the positions and the character of other signals have not been essentially changed and the signals of the heterocyclic fragments are registered as $(AB)_2X$ systems which are typical for their chair-chair conformations like those of the initial compounds **1** and **2**, so the total macrocyclic frameworks retain unchanged and only exocyclic pyridyl groups participate in protonation. The equivalence of all pyridylethyl fragments indicates the migration of the proton between all pyridyl nitrogen centers which is fast or intermediate in the NMR time scale. Salts **3** and **4** are not soluble in neat water, but **4** is not precipitated by D_2O from its solution in DMSO-d_6. The ^{1}H and ^{31}P NMR spectra of **4** in DMSO-d_6:D_2O mixture (1:1) are similar to the spectra in DMSO-d_6 giving the evidence of its stability in this medium which may be favorable for the use of this ligand as a potential basis of electrocatalysts acting in water-organic media.[15]

The condensation of *bis*(hydroxymethyl)(pyridine-2-yl)phoshine with 1,3-*bis*(4'-aminophenoxy)benzene was also performed in DMF at 100–110 °C for 24 h. The graduate formation of a white microcrystalline precipitate was observed during the reaction. This precipitate appeared to be the desired 36-membered 3,5,9,11-tetraoxa-1,7(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,6,8,12(1,4),4,10(1,3)-hexabenzenacyclododecaphane **5** (Scheme 2) which was isolated in an yield of 9 %. It should be mentioned that the signal of **5** at δ_P -43.97 ppm was the most intensive one in the ^{31}P NMR spectrum of the final reaction mixture, but its content was only 48 % of all phosphorus-containing products, so the selectivity of the covalent self-assembly of the macrocycle has decreased in comparison with analogous condensations of primary arylphosphines where the macrocycle contents were 70–80 %.[18,26] The interaction of this diamine with *bis*(hydroxymethyl)[2-(pyridine-2-yl)ethyl]phosphine under analogous conditions was very slow and less selective. ^{31}P NMR monitoring of the reaction has shown that at the initial steps of the reaction the main products were probably oligomeric aminomethylphosphines which provided a wide intensive signal at δ_P -54.9 ppm. A narrow signal of the macrocycle at δ_P -57.27 ppm was minor one and after 1 day of the heating the ratio of the intensities of these signals was 5.2:1. In the course of the prolonged heating the reaction mixture was slowly enriched by the macrocycle and after 7 days this ratio became equal ca 3:1, but it did not change further. As a result the 36-membered macrocycle **6** (Scheme 2) was isolated in the yield of only 7 % by the fractional crystallization of the concentrated reaction mixture at -15 °C.

Macrocycles **5** and **6** are also microcrystalline white solids which are air-stable in the solid state. Both compounds are restrictedly soluble in hot DMF and DMSO. Their structures were elucidated on the basis of ^{31}P and ^{1}H NMR spectroscopy, mass-spectrometry and elemental analysis.



Scheme 2.

MALDI mass-spectrum of **5** shows the peaks of the monoxide of the corresponding 3,5,9,11-tetraoxa-1,7(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,6,8,12(1,4),4,10(1,3)-hexabenzenacyclododecaphane with *m/z* = 1140, of its protonated dioxide with *m/z* = 1157 and trioxide with *m/z* = 1172. The MALDI mass-spectrum of **6** shows a low-intensive peak of the corresponding protonated monoxide of 36-membered macrocyclic tetraphosphine with *m/z* = 1253, whereas the most intensive peaks are ones which correspond to the loss of two (*m/z* = 1023) and one pyridylethyl fragment (*m/z* = 1130) by the mass-ion. The analogous oxidation of *P,N*-containing cyclophanes during the registration of MALDI mass-spectra was earlier observed for the macrocycles of various sizes.[19,25] NMR-spectra of both macrocycles **5** and **6** give the evidence of their symmetrical structures. Their signals in ^{31}P NMR spectra in DMSO-d_6 are narrow singlets at δ_P -45.59 ppm (**5**) and -56.35 (**6**). These values of the chemical shifts are typical for the corresponding 1,5-diaza-3,7-diphosphacyclooctanes.[10,11] All pyridyl or pyridylethyl fragments and both phane fragments are mutually equivalent. The patterns of pyridyl protons signals are similar to ones observed for macrocycles **1** and **2**. ^{1}H NMR spectrum confirms that phane fragments are formed by two terminal *p*-phenylene and one central *m*-phenylene rings. The $(AB)_2X$ spin system of heterocyclic methylene protons of macrocycle **5** with the coupling constants values $^2J_{HH}$ of 14.3 Hz and $^2J_{PH}$ of 10.0 Hz for equatorial protons and 5.9 Hz for axial protons undoubtedly indicates the chair-chair conformations of 1,5-diaza-3,7-diphosphacyclooctane fragments of the cyclophane with equatorial pyridyl substituents and axial lone electron pairs of the phosphorus atoms. At the ^{1}H NMR spectrum of the macrocycle **6** the signal of the axial protons of eight-membered fragments is masked by the wide signal of water in the solvent at 3.3 ppm, but the signal of the corresponding equatorial protons is a doublet of doublets at δ_H = 3.98 ppm with close coupling constants $^2J_{HH}$ and $^2J_{PH}$ of *ca*. 13.7 Hz. This type of the signal is usual for the diazadiphosphacyclooctane fragments in their the most typical chair-chair conformations with equatorial substituents on phosphorus atoms,[27] so the analogous conformation is the most probable for the heterocyclic fragments of the cyclophane **6** like previously described 36-membered *P,N*-containing cyclophanes of the structures confirmed by X-ray analysis.[18,26]

36-Membered cyclophanes **5** and **6** also contain exocyclic basic nitrogen centers, but their low solubility did not allow to obtain their individual protonated derivatives.

The attempts to synthesized 38-membered cage *P,N*-containing cyclophanes with pyridyl containing substituents were unsuccessful. The use of diamines with longer spacers (1,4-*bis*[α-(4'-aminophenyl)isopropyl]benzene and 1,4-*bis*(4'-aminophenoxy)benzene) has additionally decreased the selectivity of their condensation with pyridyl-containing *bis*(hydroxymethyl)organylphosphines and the macrocycles appeared to be minor products. The replacement of DMF as a reaction medium by toluene was also ineffective due to premature precipitation of acyclic and oligomeric intermediates. So the synthetic approach based on the covalent self-assembly has essential restrictions in the preparation of the cage *P,N*-containing cyclophanes with pyridyl-containing exocyclic substituents. However it is effective enough for the synthesis of pyridyl-functionalized 28-membered *P,N*-containing cyclophanes and allows to obtain pyridyl-containing representatives of 36-membered *P,N*-containing cyclophanes with diazadiphosphacyclooctane fragments in the macrocyclic framework. These macrocycles with additional peripheral basic and donor centers have the enriched coordination abilities and may be considered as a potential ligand basis of electrocatalytical and luminescent systems.

Conclusions

The Mannich-like condensations in three component systems: primary [2-(pyridine-2-yl)ethyl]phosphine – formaldehyde – primary diamine with the spacer formed by two *p*-phenylene fragments linked by the one-atom bridge – proceeded as covalent self-assembly and led to the selective formation of 28-membered cage *P,N*-containing cyclophanes – 1,5(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,4,6,8(1,4)-tetrabenzenacyclooctaphanes with pyridylethyl substituents on phosphorus atoms. The condensations between pyridyl-containing primary phosphine, formaldehyde and diamines with longer spacers formed by three phenylene fragments were essentially less selective unlike the analogous reactions with the participation of arylphosphines and allowed to obtain only 36-membered *P,N*-containing cyclophanes – 3,5,9,11-tetraoxa-1,7(1,5)-di(1,5-diaza-3,7-diphosphacyclooctana)-2,6,8,12(1,4),4,10(1,3)-hexabenzenacyclododecaphanes with pyridyl- and pyridylethyl substituents on phosphorus atoms which were isolated in low yields. It shows the strong influence of the starting phosphine nature on the selectivity of the Mannich-like condensation reactions.

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