Russian Journal of General Chemistry, Vol. 73, No. 8, 2003, pp. 1208–1212. Translated from Zhurnal Obshchei Khimii, Vol. 73, No. 8, 2003, pp. 1279–1283.
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Macrocyclic Systems on the Basis of Phosphorus Acids and 2,7-Dihydroxynaphthalene

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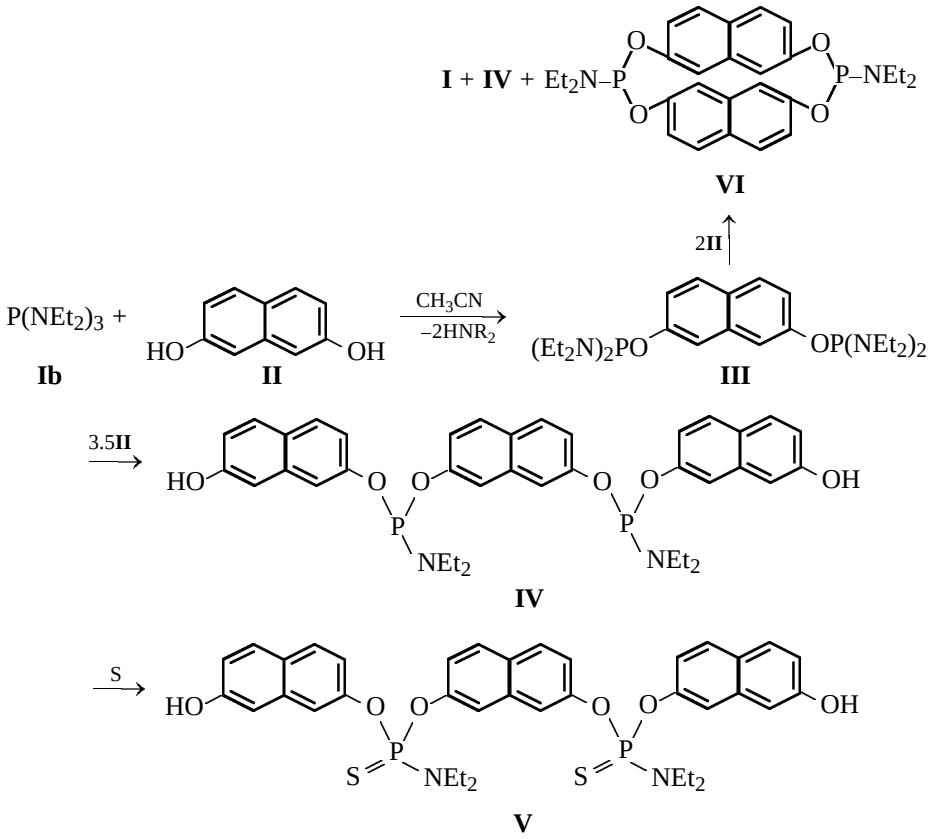
Received October 9, 2001

Abstract — Syntheses of macrocyclic systems containing three 2,7-dihydroxynaphthalene residues and three residues of thiophosphoric and phosphorous amides in various ratios are developed. Chemical properties of the obtained compounds are studied.

We earlier prepared [1] on the basis of dihydroxynaphthalenes first representatives of biscyclophosphoramidites whose molecules contain regular combinations of two aromatic fragments and two phosphorous amide **I** residues. In the present work we set our selves the task to prepare analogous macrocyclic compounds with a larger molecular cavity. Systems whose molecules contain three 2,7-dihydroxynaph thalene (**II**) and phosphorus acid residues were chosen as target compounds. During these investigations we made use of our experience in designing analogous but simpler macrorings on the basis of resorcinol and hexaalkylphosphorous triamides [2]. First we intended to prepare the target macrorings by the molecular assembly method that consists in consecutive binding naphthyl and phosphorous amide fragments. However, one this way we faced difficulties associated with the tendency of the intermediate linear oligonaphthylene phosphoroamidites for disproportionation leading to formation of biscyclophosphoramidites. Therefore, we



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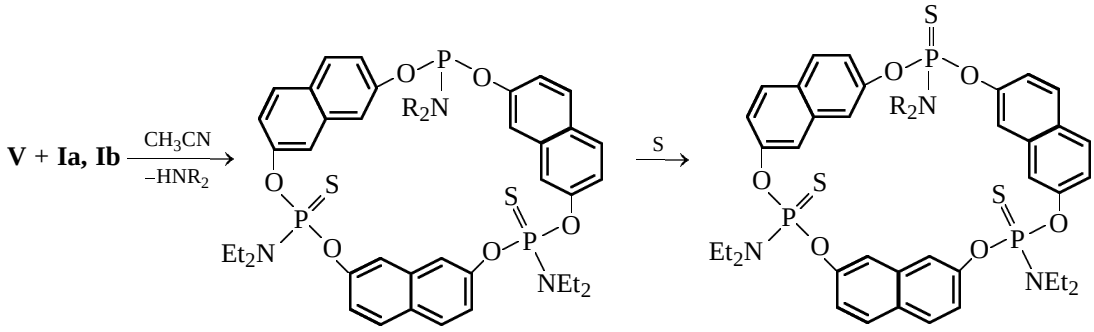
have modified this scheme and, to enhance stability of linear intermediates, introduced the stage of their conversion into thiophosphates.

With this additional stage, we have accomplished two variants of assembly of the target systems.

The first variant involved using tetraethylphosphorodiamidite **III** derived from 2,7-dihydroxynaphthalene [1]. This compound was reacted with 2,7-dihydroxynaphthalene to obtain diol **IV** which was immediately stabilized as disulfate **V**. Note that the target product **IV** was almost quantitatively formed only with excess diol **II**. With equimolar reagent amounts, the major product was biscyclophosphoroamidite **VI**. Note that a linear oligomer containing three aromatic fragments **IV** could only be prepared with hexaethylphosphorous triamide (**Ib**). With hexamethylphosphorous triamide (**Ia**), an extremely fast disproportionation of linear triphosphite was observed, which prevented its preparative conversion to thiophosphate **V**.

Thiophosphate **V** was isolated by column chromatography as an oil. Its ^{31}P NMR spectrum contained a singlet at δ_P 67.30 ppm, characteristic of monoamidothiophosphates. In the ^{1}H NMR spectrum, signals of all proton groups were observed, including that of two hydroxy groups with an expected integral intensity ratio.

Further on phosphocyclization of compound **V** with with 1 mol of hexaalkylphosphorous triamide **Ia** or **Ib** was performed.

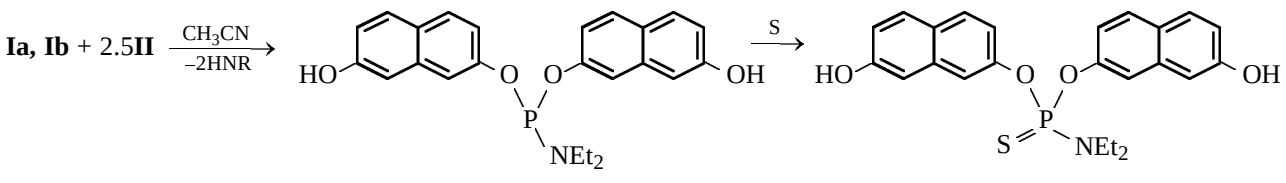


VIIa, VIIb **VIIIa, VIIIb**

R = Me (**VIIa, VIIIa**), Et (**VIIb, VIIIb**).

Products **VIIa, VIIb** were viscous oils. Their ^{31}P NMR spectra contained two singlets at Δ_P 139.70 and 66.67 (**VIIa**) and 140.70 and 66.67 ppm (**VIIb**) with an integral intensity ratio of 1:2. These compounds readily disproportionated on handling, and, therefore, they were stabilized by sulfurization. After purification by column chromatography, thiophosphates **VIIIa, VIIIb** were obtained as low-melting powders. The ^{31}P NMR spectrum of compound **VIIIa** contained two signals at δ_P 68.13 and 66.67 ppm (1:2), whereas the spectrum of ethyl derivative **VIIIb**, one singlet at δ_P 66.67 ppm; these signals all are characterisic of amidothiophosphates. Note an interesting feature of the ^{1}H NMR spectra: When the system contained different alkyl substituents on nitrogen, nonequivalence of all proton groups was observed, whereas in the case of the same substituents on nitrogen, such a nonequivalence was lacking.

The second variant involved synthesis of dinaphthyl phosphoramidites **IXa, IXb** and their subsequent phosphocyclization with phosphorylated diols **IIIa, IIIb**.

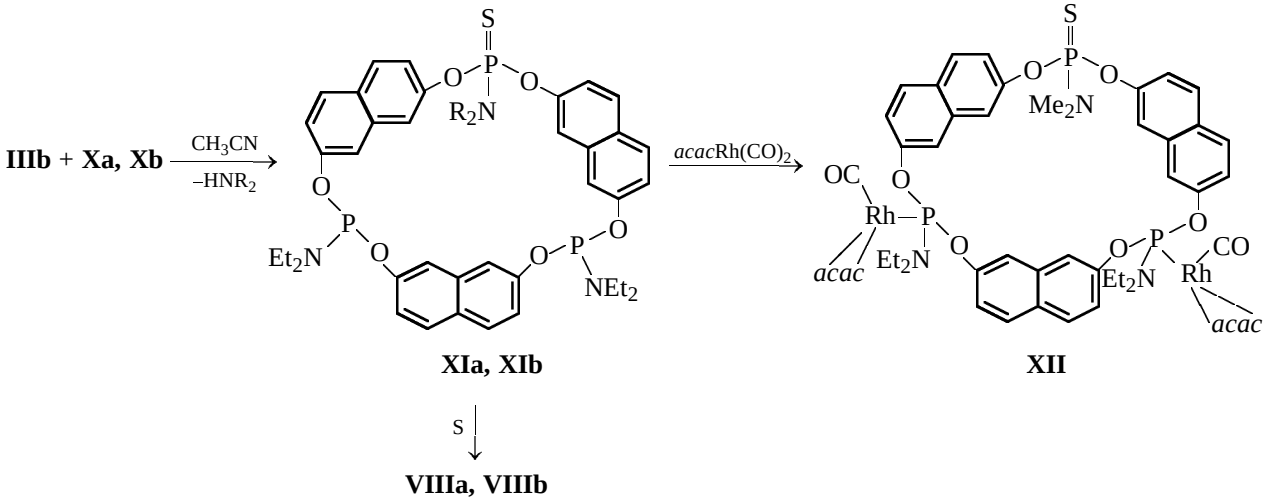


IXa, IXb **Xa, Xb**

R = Me (**IXa, Xa**), Et (**IXb, Xb**).

It was shown that using excess diol **II** in the synthesis of compounds **IXa, IXb** completely excludes formation of cyclic products. However, in this case, chromatographic isolation of **IXa, IXb** is required, which sharply decreases their yield. For this reason, we converted crude phosphoramidites **IXa, IXb** into thiophosphates **Xa, Xb**. These latter were isolated pure in high yields and completely characterized. Their ^{31}P NMR spectra contained signals characteristic of amidothiophosphates: δ_P 68.47 (**Xa**) and 66.88 ppm (**Xb**). The ^{1}H NMR spectra of **Xa, Xb** were identical to those of **IXa, IXb**.

For the subsequent cyclization, thiophosphates **Xa, Xb** were added to phosphorylated diol **IIIb**, more specifically, to a mixture of amide **Ib** and diol **II** ten minutes after phosphorylation had began (using a freshly prepared compound **IIIb** is very important, since it tends to disproportionate on handling to give a mixture of products).



As a result, an oily substance readily soluble in methylene chloride and dioxane separated from the solution. The ^{31}P NMR spectra of compounds **XIa, XIb** contained signals of two types of phosphorus centers at δ_P 68.18 and 140.85 (**XIa**) and 66.88 and 140.87 ppm (**XIb**). The integral intensity ratios were 1:2. The products obtained after sulfurization and isolated by column chromatography were fully identical to compounds **VIIIa, VIIIb**.

To provide further evidence for the formation of compounds **XIa, XIb**, we brought the latter compound into complex fomation with AcacRh(CO)$_2$. Complex **XII** was isolated by reprecipitation and looked as a dark brown powder after drying. Its ^{31}P NMR spectrum contained a doublet at δ_P 134.07 ppm, characteristic of phosphamides coordinated with Rh, and a singlet at δ_P 68.63 ppm, characteristic of thiophosphate phosphorus. The integral intensity ratio of these two signals was 2:1.

Compounds **VIIIa, VIIIb**, having molecular cavities, tend to form inclusion compounds. This is proved by the fact that the ^{1}H NMR spectra of **VIIIa, VIIIb** subjected to prolonged vacuum drying (50°C, 1 mm) contained signals of amines liberated during their synthesis and also of solvents, including methylene chloride.

Hence, we established that 2,7-dihydroxynaphthalene behaves quite differently from resorcinol in the synthesis of arylene amidophosphacyclanes. Stable tris(arylene phosphacyclanes) can be prepared either with mixed phosphorus or with $(R_2N)P{=}S$ functions.

EXPERIMENTAL

The IR spectra were measured on a Specord IR-75 instrument in NaCl cells in methylene chloride. The ^{1}H NMR spectra were measured in $CDCl_3$ on a Bruker H-250 (250 MHz) spectrometer against TMS. The ^{31}P NMR spectra were obtained on a Bruker WP-80SY spectrometer (32.4 MHz) against 85% phosphoric acid.

Column chromatography was performed on Silica gel L 100/250. Thin-layer chromatography was performed on Silufol plates, elution with benzene–dioxane, 3:1 (A), benzene–dioxane, 5:1 (B), chloroform–ethanol, 3:1 (C), and chloroform–ethanol, 5:1

(D), development in iodine vapor. All operations were carried out in dry solvents under argon.

2,7-Bis[(7-hydroxy-2-naphthyl)(diethylamino)-thiophosphoryloxy]naphthalene (V). A mixture of 0.8 g of amide **Ib** and 0.26 g of diol **II** in 5 ml of dry acetonitrile was stirred for 10 min at room temperature and then an additional diol **II** (1.3 g in 7 ml of dry acetonitrile) was added. After 4-h stirring, 0.1 g of sulfur was added, and the resulting mixture was left to stand for 1 day, after which it was filtered, the solvent was removed in a vacuum, and the residue was chromatographed (eluent benzene–dioxane, 7 : 1). Compound **V** was isolated and dried in a vacuum for 2 h (60°C, 1 mm). Yield 0.39 g (32%), oil. R_f 0.60 (A), 0.51 (B). ^{1}H NMR spectrum, δ, ppm: 1.19 t (12H, CH_3), 3.52 m (8H, CH_2), 6.92 br.s (2H, OH), 7.22 d, 7.34 d, 7.52 s, 7.56 s, 7.78 d, 7.81 d (18H, CH). ^{31}P NMR spectrum, δ_P, ppm: 67.3 s (CH_3CN). Found, %: C 61.00; H 5.36; N 3.72; P 8.23. $C_{38}H_{40}N_2O_6P_2S_2$. Calculated, %: C 61.11; H 5.40; N 3.75; P 8.29.

Cyclic thiophosphates VIIIa, VIIIb. *a*. To a solution of 2 mmol of amide **Ia, Ib** in 7 ml of acetonitrile, 2 mmol of compound **V** was added with stirring at room temperature. The resulting mixture left to stand for a day. An oily precipitate formed and was washed with acetonitrile, dissolved in 5 ml of methylene chloride, and treated with 2 mmol of sulfur. After a day, the reaction mixture was filtered, and the solvent was removed in a vacuum. The residue was chromatographed on a column of silica gel, eluent benzene–dioxane, 9 : 1. The eluent was evaporated at reduced pressure and the residue was dried in a vacuum (1 mm) for 2 h at 50°C.

b. A solution of 1 mmol of diol **II** in 6 ml of acetonitrile was added with stirring at room temperature to 2 mmol of amide **Ib**. After 10-min stirring, 1 mmol of thiophosphate **Xa, Xb** was added. The reaction mixture was left to stand for a day. A precipitate formed and was washed with acetonitrile, dissolved in 5 ml of methylene chloride, and 2 mmol of sulfur was added. After 10 h, the mixture was filtered, the solvent was removed in a vacuum, and the residue was purified as described above.

Compound VIIIa. Yield 0.53 g (50%), mp 108–109°C, R_f 0.56 (A), 0.41 (B). ^{1}H NMR spectrum, δ, ppm: 3.02 d (6H, CH_3, $^3J_{PH}$ 12.1 Hz), 6.00 br.s (2H, OH), 7.00 d, 7.03 s, 7.63 d (6H, CH), 7.22 d, 7.48 s, 7.70 d (6H, CH). ^{31}P NMR spectrum (CH_2Cl_2), δ_P, ppm: 68.47 s. Found : *M* 818 (cryoscopy). Calculated: *M* 852.

Compound VIIIb. Yield 78%, mp 93–94°C, R_f 0.79 (B). ^{1}H NMR spectrum, δ, ppm: 1.17 t (18H, CH_3), 3.5 m (12H, CH_2), 7.35 d, 7.63, 7.79 d (18H, CH, $^3J_{PH}$ 13.75 Hz). ^{31}P NMR spectrum (CH_2Cl_2), δ_P, ppm: 67.15 s. Found, %: C 57.32; H 5.49; N 4.78; P 10.56. $C_{42}H_{48}N_3O_6P_3S_3$. Calculated, %: C 57.34; H 5.5; N 4.76; P 10.52.

Bis(7-hydroxy-2-naphthyl) diethylphosphoramidite (IXb). To a solution of 0.31 g of compound **Ib** in acetonitrile, 0.5 g of diol **II** was added with stirring at room temperature. After 4 h, the solvent was removed in a vacuum, and the residue was chromatographed on a column of silica gel, eluent benzene–dioxane, 7 : 1. The product was dried for 2 h in a vacuum (1 mm) for 50°C. Yield 0.07 g (12%), oil, R_f 0.62 (D). ^{1}H NMR spectrum, δ, ppm: 1.19 t (6H, CH_3), 3.51 m (4H, CH_2, $^3J_{PH}$ 14.3 Hz), 4.80 br.s (2H, OH), 7.02 d, 7.07 s, 7.69 d (6H, CH), 7.22 d, 7.51 s, 7.78 d (6H, CH). ^{31}P NMR spectrum (CH_3CN), δ_P, ppm: 140.81 s.

***O,O*-Bis(7-hydroxy-2-naphthyl) (dialkylamido)-thiophosphates Xa, Xb.** Diol **II**, 7.5 mmol, was added at room temperature to 2.5 mmol of hexaalkylphosphorous triamide **Ia, Ib**. The resulting mixture was stirred for 3 h, after which 2.5 mmol of sulfur was added, and stirring was continued for an additional 3 h. The mixture was then filtered, the solvent was removed in a vacuum, and the residue was chromatographed on a column of a silica gel. Compound **Xa** was eluted with benzene–dioxane, 7 : 1, and compound **Xb**, with benzene–dioxane, 9 : 1. The products were dried in a vacuum (1 mm) for 2 h at 60°C.

***O,O*-Bis(7-hydroxy-2-naphthyl) (dimethylamido)thiophosphates (Xa)**. Yield 50%, mp 108–109°C, R_f 0.56 (A), 0.41 (B). ^{1}H NMR spectrum, δ, ppm: 3.02 d (6H, CH_3), 6.00 br.s (2H, OH), 7.00 d, 7.63 s (6H, CH_3, $^3J_{PH}$ 12.1 Hz). ^{31}P NMR spectrum (CH_3CN), δ_P, ppm: 68.47 s.

***O,O*-Bis(7-hydroxy-2-naphthyl) (diethylamido)thiophosphates (Xa).** Yield 62%, mp 112–113°C, R_f 0.48 (B), 0.81 (C). ^{1}H NMR spectrum, δ, ppm: 1.19 t (6H, CH_3), 3.53 m (4H, CH_2), 7.00 d, 7.05 s, 7.66 d (6H, CH), 7.24 d, 7.51 s, 7.72 d (6H, CH), 7.4 br.s (2H, OH). ^{31}P NMR spectrum (CH_3CN), δ_P, ppm: 66.88 s. Found, %: C 63.56; H 5.33; N 3.08; P 6.84. $C_{24}H_{24}NO_4PS$. Calculated, %: C 63.58; H 5.31; N 3.04; P 6.85.

Complex XII. To a solution of 0.5 g of compound **XIa** in 5 ml of methylene chloride, a solution of 0.15 g of dicarbonylrhodium(I) acetylacetonate in 7 ml of methylene chloride was added with stirring at room temperature. The reaction mixture was left to

stand for a day, and the resulting complex was precipitated with hexane and dried in a vacuum (1 mm) for 2 h at 60°C. Yield 0.39 g (49%), mp 51–52°C. IR spectrum, ν, cm^{-1}: 1990 (Rh–CO), 1510, 1570 (acac CO). ^1H NMR spectrum, δ, ppm: 1.13 t (12H, CH_3), 1.45 s, 1.96 s (12H, acac CH_3), 3.00 d (6H, CH_3), 3.63 m (8H, CH_2), 5.31 s (2H, acac CH), 7.35 d, 7.44 s, 7.74 d (12H, CH), 7.31 d, 7.57 s, 7.70 d (6H, CH, $^3J_{PH}$ 11.55 Hz). ^{31}P NMR spectrum (CH_2Cl_2), δ_P, ppm: 134.08 d ($^1J_{PRh}$ 265 Hz), 68.63 s.

ACKNOWLEDGMENTS

The work was financially supported by the *Fundamental'nye issledovaniya vysshei shkoly v oblasti estestvennykh i gumanitarnykh nauk. Universitety Rossii* Program (grant no. 990 986).

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