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Synthesis and Extraction Properties of First Representatives of 2-(Phosphorylamido)-Substituted 1,8-Naphthyridines

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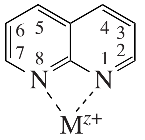
Liquid radioactive waste, which is formed in large amounts in the process of spent fuel treatment, is a serious environmental hazard since it contains considerable amounts of long-lived radionuclides, mainly radioactive isotopes of *f* elements, actinides and lanthanides [1]. One of the most promising methods of liquid waste treatment is extraction with the use of different types of organic and organoelement compounds as extractants. Organoelement extractants of greatest interest are neutral organophosphorus ligands, first of all, bidentate ones, capable of efficiently extracting tetra- and hexavalent actinides from acid media. Unfortunately, these ligands are, as a rule, considerably less efficient in extraction of trivalent actinides and lanthanides [2]. At the same time, it was shown that trivalent actinides (for example, americium and curium) can be efficiently extracted from acid media by means of various polydentate nitrogen-containing heterocycles, such as tripyridyltriazines, terpyridines, bis(benzimidazolyl)pyridines, bis(benzothiazolyl)pyridines, and especially polyalkyl-substituted 2,6-bis(1,2,4-triazin-3-yl)pyridines [3–5].

It might be expected that design of neutral organophosphorus extractants with molecules containing polynitrogen heterocyclic moieties would make it possible to extend the field of application of the resulting hybrid structures and to find compounds with a unique combination of useful properties.

As such a heterocyclic moiety, 1,8-naphthyridine deserves special attention. In its molecule, the arrangement of the nitrogen atoms is optimal for chelation of various metal cations, including lanthanide ions [6, 7].



In this case, the potentially best conditions for complex formation can be achieved when a phosphoryl-containing substituent is introduced into the 2-position of the naphthyridine ring and especially when an imide bridge is used as the linker between the ligating fragments (the heterocycle and the phosphoryl group). The presence of this bridge not only optimizes the distance between the endocyclic nitrogen atoms and the phosphorus atom but also ensures delocalization of the electron system of the chelating center.

In this work, we synthesized for the first time a series of various 2-(phosphorylamido)-substituted 1,8-naphthyridines and demonstrated that compounds of this type can selectively extract lanthanides from carbonate media.

These compounds were obtained by direct phosphorylation of 2-amino-1,8-naphthyridines with phosphoryl chlorides (Scheme 1).

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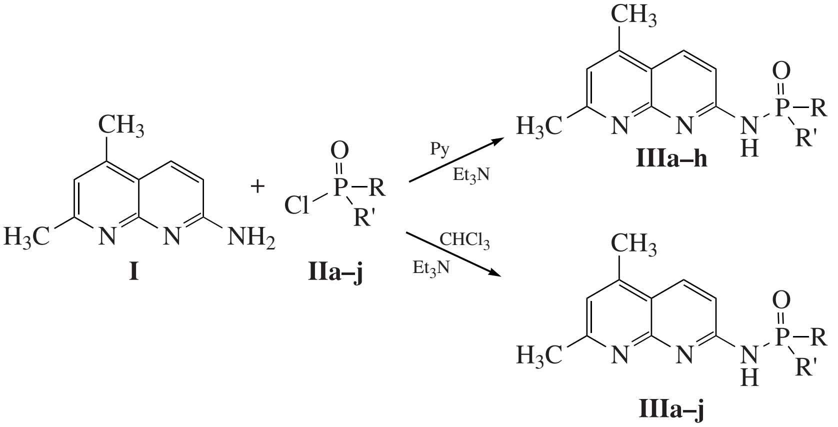

II, **III**: **a** R = R' = Ph; **b** R = R' = PhO; **c** R = R' = *o*-MeC_6H_4O; **d** R = R' = *m*-MeC_6H_4O; **e** R = R' = *p*-MeC_6H_4O; **f** R = Ph, R' = Me; **g** R = Me, R' = PhO; **h** R = Ph, R' = EtO; **i** R = Me, R' = EtO; **j** R = R' = EtO.

Scheme 1.

2-Amino-5,7-dimethyl-1,8-naphthyridine (**I**), which is readily synthesized from inexpensive commercially available reagents, was used as the initial amino-substituted naphthyridine. Various phosphoric, phosphonic, and phosphinic monochlorides **IIa**–**IIj** were used as phosphorylating agents, so that the nature of the substituents at the ligating phosphoryl group varies in a wide range.

Taking into account the fact that initial heterocyclic amine **I** is poorly soluble in most organic solvents, 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines **III** were first synthesized by refluxing a pyridine solution of amine **I** with a phosphorylating agent in the presence of triethylamine as the hydrogen chloride acceptor, which is considerably more basic than pyridine (method A). However, it turned out that, while phosphorylamides **IIIa**–**IIIg** are obtained in rather high yields (71–83%) by this method (Table 1), the yield of **IIIh** sharply decreases (to 45%), and phosphoramides **IIIi** and **IIIj** are not synthesized at all because of the destruction of the corresponding initial acid chlorides **II** under the conditions used.

Therefore, we developed an alternative variant of synthesis of 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines under much milder conditions. The method consists in the reaction of chlorides **IIa**–**IIj** under heating with a suspension of aminonaphthyridine **I** in chloroform in the presence of triethylamine (method B). Under these conditions, we succeeded in synthesizing phosphoramides **IIIi** and **IIIj**, and the yields of compounds **IIIa**–**IIIh** were higher (in the case of **IIIh**, considerably higher) than those afforded by method A (Table 1).

All synthesized 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines **IIIa**–**IIIj** are white or light yellow air-stable solids readily soluble in dimethylformamide, dimethyl sulfoxide, pyridine, benzene, and chloroform, poorly soluble in hexane and ether, and insoluble in water. The structure of the compounds was confirmed by elemental analysis data and $^{31}P\{^1H\}$ NMR (Table 1). In all cases, the $^{31}P\{^1H\}$ NMR spectra show a singlet in the region typical of the corresponding environment of the phosphorus atom.

The next step of the work was to study the possibilities of using the synthesized 2-(phosphorylamido)-subsituted 1,8-naphthyridines for extraction of 4*f* and 5*f* elements from nitric acid and carbonate media. The study was performed for 5,7-dimethyl-2-(diphenylphosphinamido)-1,8-naphthyridine **IIIa** and La(III), Nd(III), Th(IV), and U(VI) as an example. We found that this phosphorus–nitrogen ligand taken in concentration of 0.01 mol/L in chloroform selectively extracts lanthanides(III) from carbonate media, whereas the distribution ratios in nitric acid media are low for the metals tested (Table 2).

Taking into account that carbonate solutions are not typical media for the extraction of *f* elements by neutral organophosphorus compounds (both mono- and polydentate), our findings concerning the extraction with 2-(phosphorylamido)-substituted 1,8-naphthyridines allow us to draw the conclusion that these hybrid extractants have unique properties.

It is worth noting that, according to preliminary data, phosphoryl-containing 1,8-naphthyridines **III** do act as tridentate ligands in complexation of lanthanide cations. Both nitrogen atoms of the heterocycle and the phosphoryl oxygen atom are involved in the coordination of the metal [8].

EXPERIMENTAL

The $^{31}P\{^1H\}$ NMR spectra of solutions in $CDCl_3$ were recorded at 298 K on a Bruker Avance-400 spectrometer operating at 161.98 MHz with 85% H_3PO_4 as the external reference. Standard tubes 5 mm in diameter were used. The concentration of solutions was 0.02 mol/L. Elemental analysis was carried out in the

Table 1. Yields and properties of 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines **IIIa–IIIj**

Compound	Yield*, %	T_m, °C	Found/calculated, %				Empirical formula	$^{31}P\{^1H\}$ NMR, δ, ppm, s
			C	H	N	P		
IIIa	86 (78)	191–193	$\frac{70.85}{70.77}$	$\frac{5.29}{5.40}$	$\frac{11.30}{11.25}$	$\frac{8.45}{8.30}$	$C_{22}H_{20}N_3OP$	16.8
IIIb	80 (71)	67–69	$\frac{65.18}{65.18}$	$\frac{5.03}{4.97}$	$\frac{10.21}{10.37}$	$\frac{7.46}{7.64}$	$C_{22}H_{20}N_3O_3P$	–3.0
IIIc	82 (80)	138–140	$\frac{66.37}{66.50}$	$\frac{5.49}{5.58}$	$\frac{9.70}{9.69}$	$\frac{7.10}{7.15}$	$C_{24}H_{24}N_3O_3P$	–2.7
IIId	80 (74)	97–99	$\frac{66.61}{66.50}$	$\frac{5.52}{5.58}$	$\frac{9.74}{9.69}$	$\frac{7.23}{7.15}$	$C_{24}H_{24}N_3O_3P$	–3.5
IIIe	84 (83)	127–129	$\frac{66.42}{66.50}$	$\frac{5.60}{5.58}$	$\frac{9.78}{9.69}$	$\frac{7.07}{7.15}$	$C_{24}H_{24}N_3O_3P$	–3.2
IIIf	83 (72)	229–231	$\frac{65.74}{65.59}$	$\frac{5.80}{5.83}$	$\frac{13.50}{13.50}$	$\frac{9.67}{9.95}$	$C_{17}H_{18}N_3OP$	30.1
IIIg	79 (74)	186–187	$\frac{62.14}{62.38}$	$\frac{5.49}{5.54}$	$\frac{12.75}{12.84}$	$\frac{9.43}{9.46}$	$C_{17}H_{18}N_3O_2P$	29.4
IIIh	78 (45)	98–100	$\frac{63.40}{63.34}$	$\frac{5.94}{5.91}$	$\frac{12.35}{12.31}$	$\frac{9.01}{9.07}$	$C_{18}H_{20}N_3O_2P$	18.4
IIIi	82 (0)	203–205	$\frac{55.83}{55.91}$	$\frac{6.44}{6.50}$	$\frac{15.11}{15.05}$	$\frac{10.97}{11.09}$	$C_{13}H_{18}N_3O_2P$	29.5
IIIj	71 (0)	117–119	$\frac{54.55}{54.36}$	$\frac{6.41}{6.52}$	$\frac{13.66}{13.59}$	$\frac{10.10}{10.01}$	$C_{14}H_{20}N_3O_3P$	1.8

* The yields of 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines by method A are parenthesized.

laboratory for microanalysis at the Institute of Organoelement Compounds, RAS.

All operations were carried out in an argon atmosphere. Solvents purified and dried by known procedures [9] and saturated with argon were used. Diphenylphosphinic chloride **IIa**, diphenyl chlorophosphate **IIb**, methylphenylphosphinic chloride **IIf**, and diethyl chlorophosphate **IIj** (Aldrich) were purified by vacuum distillation. 2-Amino-5,7-dimethyl-1,8-naphthyridine **I** [10], bis(*o*-tolyl) chlorophosphate **IIc** [11], bis(*m*-tolyl) chlorophosphate **IId** [12], bis(*p*-tolyl) chlorophosphate **IIe** [11], *O*-phenyl chloromethylphosphonate **IIg** [13], *O*-ethyl chlorophenylphosphonate **IIh** [14], and *O*-ethyl chloromethylphosphonate **IIi** [15] were synthesized by known procedures.

Table 2. Distribution ratios

Concentration, mol/L	U(VI)	Th(IV)	La(III)	Nd(III)
HNO_3 0.77	0.10	–	0.05	0.15
HNO_3 2.81	0.17	0.05	0.1	0.27
HNO_3 5.40	0.36	–	0.23	0.32
Na_2CO_3 0.47	0.02	0.2	1.43	2.00

Synthesis of 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines IIIa–IIIg (method A). To a suspension of 867 mg (5 mmol) of aminonaphthyridine **I** and 606 mg (6 mmol) of abs. triethylamine in 10 mL of abs. pyridine, 5 mmol of corresponding chloride **II** was added dropwise at room temperature. The reaction mixture was heated under reflux for 5 h, pyridine was removed in the vacuum of a water-jet pump, and the residue was dissolved in 20 mL of $CHCl_3$, washed with water (2 × 15 mL), dried over $MgSO_4$, and chromatographed on 8 g of Al_2O_3 (elution with $CHCl_3$). The solvent was removed from the eluate, and the residue was recrystallized from *tert*-butyl methyl ether.

Synthesis of 5,7-dimethyl-2-(phosphorylamido)-1,8-naphthyridines IIIa–IIIj (method B). To a suspension of 867 mg (5 mmol) of aminonaphthyridine **I** in 20 mL of abs. $CHCl_3$, 5 mmol of corresponding chloride **II** was added dropwise. The mixture was stirred for 5 min at room temperature, and 606 mg (6 mmol) of abs. triethylamine was added dropwise. The reaction mixture was refluxed until complete dissolution of the initial aminonaphthyridine, cooled, washed with water

(2 × 20 mL), dried over $MgSO_4$, and treated further as in method A.

Extraction of U(VI), Th(IV), La(III), and Nd(III). In test tubes with ground-glass stoppers, the following components were placed: 1.5 mL of a solution of HNO_3 of different concentrations or Na_2CO_3, 0.5 mL of a metal solution in 0.01 M HNO_3, and 2 mL of a 0.01 M solution of 5,7-dimethyl-2-(diphenylphosphinamido)-1,8-naphthyridine **IIIa** in chloroform (the ligand solution was prepared by dissolving a weighed sample). The phases were allowed to contact for 15 min. Phase separation was performed by centrifuging. The phases were isolated, and an aliquot of the aqueous phase was sampled for spectrophotometric analysis for U(VI), Th(IV), La(III), and Nd(III) with Arsenazo III followed by calculation of metal distribution ratios. The distribution ratios were determined as the ratio of the metal content in the organic phase to its content in the aqueous phase. Extraction was studied under static conditions at 20 ± 1°C.

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