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Synthesis of 3-(2-Hydroxyphenyl)-5-(2-Pyridinyl)-1,2,4-triazoles as a potential chelate ligand for Uranyl ion

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Two new uranyl complexes with the molecular formula **$[(UO_2)(H_2L^1)](CH_3OH)$** and **$[(UO_2)(H_3L^2)](CH_3OH)$** {**H_4L^1** = 2-[5-[[5-[[5-(2-pyridyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]phenol and **H_5L^2** = 2-[5-[[5-[[5-[[5-(2-pyridyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]phenol)} have been synthesized. All compounds have been characterized by NMR and IR spectroscopy. With **H_4L^1** and **H_5L^2** uranyl ion forms mononuclear complexes. In **$[(UO_2)(H_3L^2)](CH_3OH)$** pyridyl nitrogen was uncoordinated and bonding of **H_5L^2** was realized only through phenol oxygen and N^4-nitrogens of triazole cycles.

Introduction

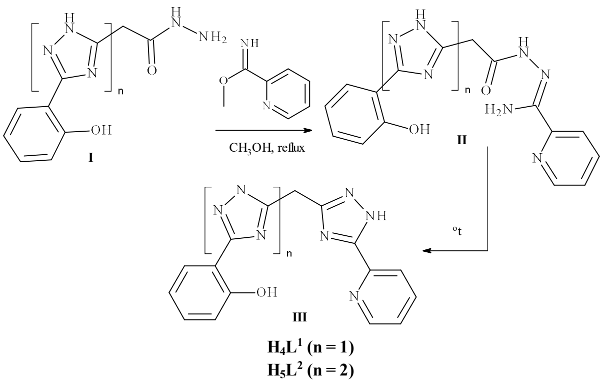
The enduring interest in the chemistry of actinides is associated not only with the use in nuclear energy, but also with the potential use in medicine and catalysis[1–4]. An example of the use of actinides in catalysis is hydrogenation of alkenes, hydroamination of terminal alkynes, hydrosilylation of aldehydes. Thus, there are a number of articles devoted the use actinides for targeted alpha therapy.

One of the most abundant and extensively studied metals in the actinide series are Uranium and uranyl ion based compounds as the most stable derivatives. The coordination compounds of uranyl and the uranyl-organic frameworks have found many applications that range from photoluminescence to photochemical reactions and photocatalysis [5–8]. As a consequence, the synthesis of new actinide compounds with improved properties is one of the rapidly developing areas of inorganic chemistry. Despite the considerable amount of available data on the physicochemical characteristics of uranium compounds, different classes of uranyl complexes have been studied very unevenly. Thus, coordination compounds of uranyl with ligands bearing the 1,2,4-triazolate moiety are poorly studied today. Previously we reported three coordination compounds of uranyl ion with 3-(2-hydroxyphenyl)-5-(2-pyridyl)-1,2,4-triazole and 2-[5-(2-pyridin-2-yl-4H-[1,2,4]triazol-3-ylmethyl)-4H-[1,2,4]triazol-3-yl]phenol [9,10]. In this work, two new 3-(2-hydroxyphenyl)-5-(2-pyridinyl)-1,2,4-triazole ligands containing three and four triazole cycles linked by a methylene group were synthesized and their interaction with uranyl ion was investigated.

Results and discussion

Compounds **H_4L^1** and **H_5L^2** were obtained by acylation of triazolylcarboxylic acid hydrazides by picolinic acid iminoester, with subsequent cyclization providing title compounds (**Scheme 1**), which is a common method for the preparation of 1,2,4-triazoles [11,12]. The first step of the reaction proceeds slowly over 2-3 days due to the low solubility of the starting hydrazides and leads to the formation of the intermediate amidrazone **II**. Further heating of the reaction mixture during 2 days leads to the intramolecular cyclization of amidrazone **II** into 1,2,4-triazole, only in trace amounts. Therefore, it was isolated and cyclized by heating to a melting point, since the process of intramolecular cyclization goes well at high temperatures.

Interaction of uranyl acetate with **H_4L^1** and **H_5L^2** leads to the formation of complexes with the following compositions: **$[(UO_2)(H_2L^1)](CH_3OH)$** and **$[(UO_2)(H_3L^2)](CH_3OH)$**. Signals of acetate ions are absent in the NMR and IR spectra of the complexes. This fact suggests that the complexes have a molecular structure and, probably, deprotonation of one of the triazole heterocycles takes place. This is supported by a strong low-field shift of the α-pyridine proton signal (Δδ = -1.79 ppm) in the spectrum of **$[(UO_2)(H_2L^1)](CH_3OH)$** complex, which is significantly greater than the shift of the α-pyridine proton signal (Δδ = -1.24 ppm).) for mono- and ditriazole complexes [10]. Such strong proton signal shifts are also characteristic of palladium and iridium complexes with 3-(2-pyridyl)-1,2,4-triazoles, where the triazole cycle is coordinated in the anionic form [13,14].



Scheme 1. Synthesis of H_4L^1 and H_5L^2

A negative charge at one of the triazole heterocycles accelerates the exchange of protons of non-deprotonated triazoles with water molecules present in DMSO and deprotonated triazole. This is evidenced by the absence of their signals in the usual region of 13-15 ppm and a slightly extended water proton signal at 3.34 ppm (**Figure 1**).

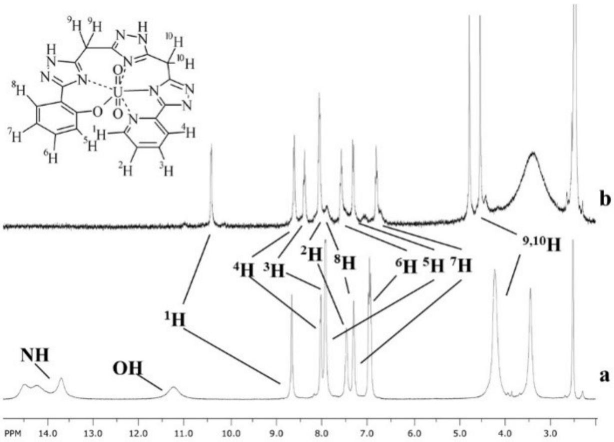


Figure 1. Fragments of ^{1}H NMR spectra of H_4L^1 (a) and $[(UO_2)(H_2L^1)](CH_3OH)$ (b).

In the ^{1}H NMR spectrum of the complex **$[(UO_2)(H_3L^2)](CH_3OH)$** the downfield shift of the pyridyl proton signals is not observed which is characteristic of pyridyl-triazole complexes (**Figure 2**). At the same time the specific signal shifts of the protons are belonging to the oxyphenyl moiety confirm the formation of a corresponding coordination bond.

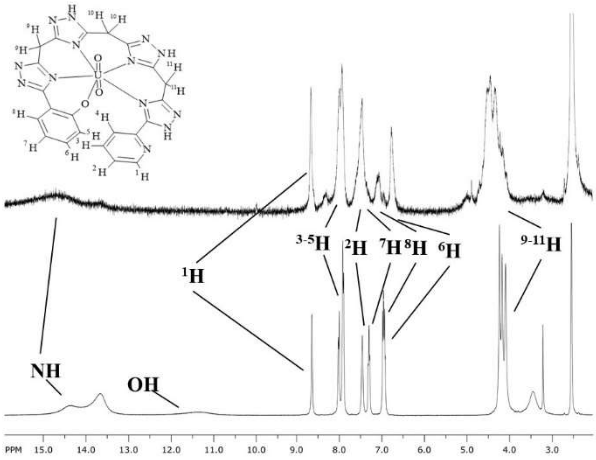


Figure 2. Fragments of ^{1}H NMR spectra of H_5L^2 (a) and $[(UO_2)(H_3L^2)](CH_3OH)$ (b).

The obtained complexes, especially **$[(UO_2)(H_3L^2)](CH_3OH)$,** so are poorly soluble in DMSO or other solvents, and therefore we were unable to obtain a suitable for analysis ^{13}C NMR spectrum for **$[(UO_2)(H_2L^1)](CH_3OH)$** or **$[(UO_2)(H_3L^2)](CH_3OH)$**. The LC/MS spectra of the obtained complexes were also uninformative. Uranyl complexes are labile and therefore easily decompose during ionization, so only the molecular peak of the ligand was observed in the spectrum. The destruction of the complex in the process of ionization can be confirmed by different release times of the ligand and the complex in the spectrum as shown in the example of **H_4L^1** and **$[(UO_2)(H_2L^1)](CH_3OH)$** (**Figure 3**). Because the mass spectra were not informative, we did not perform further studies of complex compounds by mass spectrometry.

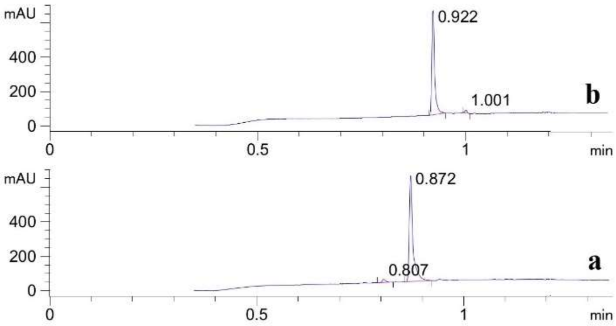
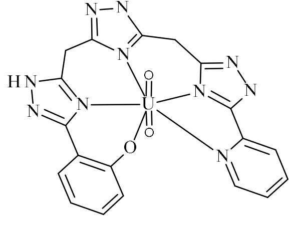
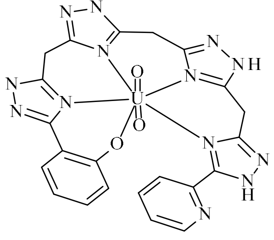


Figure 3. Retention time for H_4L^1 (a) and $[(UO_2)(H_2L^1)](CH_3OH)$ (b) in LC/MS spectrum.

Considering that the equatorial plane of the uranyl complexes usually contains from 4 to 6 donor atoms[15,16] the following structures of the complexes were proposed:



$[(UO_2)(H_2L^1)](CH_3OH)$



$[(UO_2)(H_3L^2)](CH_3OH)$

This structure of the compounds is confirmed by the results of elemental analysis, IR and NMR spectroscopy. In the case of **$[(UO_2)(H_3L^2)](CH_3OH)$**, coordination of oxyphenyl group is preferable compared to pyridine, which is due to the high affinity of uranium to oxygen donors compared to nitrogen. In this complex the pyridine nitrogen does not participate in coordination due to steric hindrances and due to saturated coordination polyhedron of uranium.

Experimental part

All used solvents and reagents are commercially available and were used without prior purification. Hydrazides 3-(2-hydroxyphenyl)-triazolyl acetic acids and methyl picolimidate were obtained by the previously described methods [17,18]. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 170 Avance 500 spectrometer (at 500 MHz for ^{1}H NMR and 126 MHz for ^{13}C NMR). IR spectra were recorded on a Spektrum BX Perkin Elmer. Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (CI)).

General procedure for the preparation of H_4L^1 and H_5L^2. **I** (9.72mmol) was added to the solution of methyl picolimidate (10.2 mmol) in methanol (50 ml) and resulting mixture was refluxed for 72 hours. White precipitate of amidrazone **II** was filtered off and melted without additional purification to give triazole **III**.

2-[5-[[5-[[5-(2-pyridyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]phenol (**H_4L^1**). Yield:57%. ^{1}H NMR (400MHz, DMSO-d$_6$) δ4.21 (s, 6H), 6.94 (d, 1H), 6.96 (t, 1H), 7.31 (t, 1H), 7.47 (t, 1H), 7.92 (t, 1H), 7.93 (t, 1H), 8.02 (d, 1H),8.67 (d, 1H), 11.15 (brs, 1H), 13.62 (brs, 1H), 14.44 (brs, 2H). ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 25.8, 111.8, 116.8, 119.4, 121.3, 124.9, 126.5, 137.7, 146.3, 149.5, 153.7, 156.0, 159.4. IR(KBr, cm^{-1}): 3059, 1551, 1493, 1413, 1267, 1136, 743. LC/MS (CI): m/z = 401 $[M+H]^+$.Anal. Calc. for $C_{19}H_{16}N_{10}O$ (%): C 57.00; H 4.03; N 34.98. Found: C 57.09; H 4.07; N 34.96.

2-[5-[[5-[[5-[[5-(2-pyridyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]phenol (**H_5L^2**). Yield: 66 %. ^{1}H NMR (400MHz, DMSO-d$_6$) δ4.05 (s, 2H), 4.13 (s, 2H), 4.19 (s, 2H), 6.93 (d, 1H), 6.97 (t, 1H), 7.31 (t, 1H), 7.48 (t, 1H), 7.92 (t, 1H), 7.93 (t, 1H), 8.03 (d, 1H); 8.67 (d, 1H), 11.25 (brs, 1H), 13.64 (brs, 2H), 14.46 (brs, 2H). ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 125.9, 113.1, 116.8, 119.4, 121.3, 124.7, 126.5, 131.2, 137.6, 146.6, 149.5, 153.8, 156.0, 158.9. IR(KBr, cm^{-1}): 3051, 1566, 1500, 1384, 1252, 1063, 722.LC/MS (CI): m/z = 482 $[M+H]^+$.Anal. Calc. for $C_{22}H_{19}N_{13}O$ (%): C 54.88; H 3.98; N 37.82. Found: C 54.91; H 3.95; N 37.81.

General procedure for the preparation of $[(UO_2)(H_2L^1)](CH_3OH)$ and $[(UO_2)(H_3L^2)](CH_3OH)$. The mixture of triazole **III** and $(UO_2)(CH_3COO)_2(H_2O)_2$ in methanol (25 ml) was refluxed for 1 hour. The red precipitate of uranyl complex was filtered off and dried in air to constant weight to give title compound.

$[(UO_2)(H_2L^1)](CH_3OH)$. Yield: 54%. ^{1}H NMR (400MHz, DMSO-d_6) δ4.58 (s, 2H), 4.81 (s, 2H), 6.85 (t, 1H), 7.36 (d, 1H), 7.26 (t, 1H), 8.10 (m, 2H), 8.42 (t, 1H), 8.64 (d, 1H), 10.46 (d, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 26.3, 29.5, 115.2, 119.0, 1220.8, 121.6, 124.8, 127.0, 151.4, 152.4, 156.4, 156.8, 158.1, 156.6, 159.0, 161.9, 166.6. IR(KBr, cm^{-1}): 3409, 2927, 1602, 1471, 1297, 1151, 904. Anal. Calc. for $C_{19}H_{15}N_9O_3U$, %: C 34.82; H 2.31; N 19.23. Found: C 34.82; H 2.33; N 19.22.

$[(UO_2)(H_3L^2)](CH_3OH)$. Yield: 47%. ^{1}H NMR (400MHz, DMSO-d_6) δ4.41 (m, 6H), 6.77 (s, 1H), 7.07 (s, 1H), 7.46 (s, 2H), 7.95 (s, 1H), 8.02 (m, 2H), 8.68 (s, 1H), 14.84 (brs, 3H). IR(KBr, cm^{-1}): 3370,2768, 1464, 1340, 1049, 904. Anal. Calc. for $C_{22}H_{17}N_{13}O_3U$ (%): C 35.26; H 2.29; N 24.30. Found: C 35.28; H 2.39; N 24.37.

Conclusions

Two new uranyl complexes with the molecular formula **$[(UO_2)(H_2L^1)](CH_3OH)$** and **$[(UO_2)(H_3L^2)](CH_3OH)$** {**H_4L^1** = 2-[5-[[5-[[5-(2-pyridyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]phenol and **H_5L^2** = 2-[5-[[5-[[5-[[5-(2-pyridyl)-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]methyl]-1H-1,2,4-triazol-3-yl]phenol)} have been synthesized. Compounds have been characterized by NMR, IR spectroscopy. Uranyl ion with **H_4L^1** and **H_5L^2** forms mononuclear complexes.

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