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NMR Studies on Uranyl(VI) Complexes with L-Histidine, Imidazole and Derivatives

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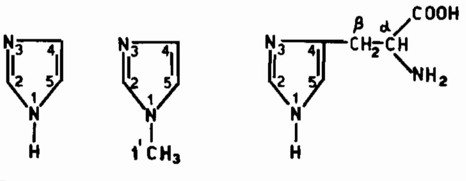
The interaction of L-histidine, imidazole and N-methylimidazole with uranyl nitrate and acetate has been investigated both in D_2O *and* CD_3OD *by* ^1H *and* ^{13}C *NMR measurements.*

The results suggest the formation of complexes of uranyl(VI) ion with imidazole and methylimidazole through a nitrogen atom only in CD_3OD *solutions. No direct involvement of the ring nitrogen donors in uranyl ion binding seems to occur in aqueous solutions at pH 3.3 or 4.0, either for imidazole or the imidazole side-chain of L-histidine molecule. The major coordination site of the latter ligand is the carboxylate group.*

Introduction

Imidazole, a side-chain donor system of L-histidine seems to play an important role in metal ion binding in many bioinorganic systems (see *e.g.* [1]). Uranyl(VI) ion as a cation seems to prefer oxygen donor set and, at least in its complexes with amino-acids in suitable pH regions, it interacts mostly with carboxyl groups [2–7]. Our previous physico-chemical measurements on 1:2 and 1:1 solid dioxo-uranium(VI) complexes of imidazole suggested a coordination at the pyridine nitrogen (N-3) when the imidazole ring was reacted with uranyl nitrate in ethyl acetate and at both N-1 and N-3 atoms when the same imidazole solution was reacted with uranyl acetate [8]. In the latter coordination a polymeric structure is probably the result as found for imidazole complexes of Co(II) and Zn(II) [9].

Recent X-ray work of Perry *et al.* [10] has shown that, under the conditions used in aqueous solution, the formed complex contains imidazole molecule but no direct binding to uranyl ion was found. One of the reasons of the lack of direct binding between uranyl ion and imidazole molecule could be the high pK_{imid} value (~6.0). To increase the possibility of UO_2^{2+} binding to imidazole we have carried out experiments in aqueous and methanol solutions by ^1H and ^{13}C NMR measurements.



Imidazole N-Methylimidazole L-Histidine

Experimental

Materials

Imidazole(Imid), N-methylimidazole(N-M-Imid) and L-histidine (His) were purchased from Fluka A.G. $UO_2(NO_3)_2 6H_2O$ and $UO_2(CH_3COO)_2 2H_2O$ were obtained from Carlo Erba. Tetradeuteromethanol (99.5%) and deuterium oxide (99.8%) were Ega-Chemie products.

Methods

^1H and ^{13}C NMR spectra of 0.2 *M* and 0.1 *M* ligands in CD_3OD or ^2H_2O were recorded at 28 °C at varying dioxouranium(VI)/ligand molar ratios by using T-60 and FT-80 Varian spectrometers. The spectra in ^2H_2O of imidazole or L-histidine upon UO_2^{2+} addition were measured at pH 3.3 or pH ~ 4.0 respectively, since precipitation occurred at higher pH. The pH values adjusted with NaOH, HNO_3 or CH_3COOH were measured with a Radiometer TTT2 pH meter. No correction for the D_2O solvent was applied. Chemical shifts expressed in δ/ppm were related to TMS as internal standard for CD_3OD solutions and to dioxane converted to TMS scale for D_2O solutions.

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TABLE I. $^{1}H^{a}$ and $^{13}C^{b}$ NMR Chemical Shifts of Free L-Histidine and UO_2 Nitrate Containing Solutions in D_2O at pH = 3.95 in ppm (δ).

Compound	C-2-H	C-5-H	α-CH	β-CH_2	COO^-	C-2	C-4	C-5	α-CH	β-CH_2
Histidine	8.85, 1H	7.57, 1H	4.19, 1H	3.47, 2H	105.93	67.46	60.79	51.21	−12.93	−40.77
Histidine + UO_2 nitrate 1:0.25	8.81, 1H	7.55, 1H	4.24, 1H	3.49, 2H						
Histidine + UO_2 nitrate 1:0.5	8.80, 1H	7.54, 1H	4.28. 1H	3.52, 2H						
Histidine + UO_2 nitrate 1:1	8.82, 1H	7.58, 1H	4.38, 1H	3.60, 2H	107.75	67.46	60.79	51.21	−12.34	−40.65
Histidine + UO_2 nitrate 1:2	8.80, 1H	7.59 1H	4.41, 1H	3.67, 2H	107.26	67.46	60.91	51.21	−12.38	−40 65
Δ ppm =	−0.05	+0.02	+0.22	+0.20	+1.33	0.00	+0.12	0.00	+0.55	+0.12

[a] ^{1}H nmr chemical shifts are measured downfield from TMS, using dioxane as an internal standard. [b] ^{13}C nmr chemical shifts are measured downfield from dioxane used as an internal standard.

TABLE II. ^{1}H and $^{13}C^{a}$ NMR Chemical Shifts of Free Imidazole and UO_2 Nitrate Containing Solutions in CD_3OD in ppm (δ).

Compound	C-2-H	C-4-H C-5-H	C-2	C-4 C-5
Imidazole	7.77, 1H	7.15, 2H	136.48	122.74
Imidazole + UO_2 nitrate 1:0.2	8 20, 1H	7.35, 2H	136.20	121.94
Imidazole + UO_2 nitrate 1·0.5	8.75, 1H	7.60, 2H	135.81	120.92
			Δ ppm = −0.67	−1.82
Imidazole + UO_2 nitrate 1:1	8.87, 1H	7.61, 2H		
Imidazole + UO_2 nitrate 1:2	8.88, 1H	7.60, 2H		
Δ ppm =	+1 11	+0.45		

[a] ^{1}H and ^{13}C nmr chemical shifts are measured downfield from TMS used as an internal standard.

Results and Discussion

UO_2^{2+} Interaction with L-Histidine and Imidazole in Aqueous Solutions

The changes of ^{1}H and ^{13}C chemical shifts upon UO_2^{2+} addition in the solutions containing imidazole up to pH ~ 3.3 are very small and do not suggest any direct involvement of the ligand nitrogens in uranyl ion binding. This result is in agreement with the recent X-ray work mentioned above [10]. Also the NMR results obtained for the UO_2^{2+}–His solutions do not indicate any imidazole involvement in metal ion binding as reported in Table I. The major changes in the chemical shifts of α-CH and β-CH_2 protons as well as carbon chemical shifts of COO^- and α-CH suggest however that histidine may coordinate to dioxouranium(VI) ion via the carboxyl donor. These changes are similar to those found in the other aminoacid systems [2–7] in which carboxyl coordination was proposed. The involvement of the uranyl ion in the binding of L-histidine may also be suggested from IR spectrum of D_2O solutions. The asymmetric stretching band of O–U–O group, ν_3, observed at 952 cm^{-1} in the free ligand solutions occurs at lower frequencies, *i.e.* to ~910 cm^{-1}, when histidine is added.

The profiles obtained by plotting the chemical shifts of α-CH and β-CH_2 protons as a function of the UO_2^{2+}:Histidine molar ratio, in D_2O at pH 4, show a break at 1:1 molar ratio. This suggests the

TABLE III. ^{1}H and ^{13}C[a] NMR Chemical Shifts of Free Imidazole and UO$_2$ Acetate Containing Solutions in CD$_3$OD in ppm (δ).

Compound	C-2-H	C-4-H C-5-H	CH$_3$ acet.	C-2	C-4 C-5	CH$_3$ acet.
Imidazole	7.77, 1H	7.15, 2H		136.48	122.75	
Imidazole + UO$_2$ acetate 1:0.2	7.95, 1H	7.27, 2H	2.47	136.85	122.78	25.72
Imidazole + UO$_2$ acetate 1:0.5	8.12, 1H	7.34, 2H	2.53	137.42	122.88	26.40
				Δ ppm = +0.94	+0.13	
Imidazole + UO$_2$ acetate 1:1	8.40, 1H	7.41, 2H	2.54			
Imidazole + UO$_2$ acetate 1:2	8.52, 1H	7.44, 2H	2.58			
Δ ppm =	+0.75	+0.29				

[a] Chemical shifts are measured downfield from TMS used as an internal standard.

TABLE IV. ^{1}H and ^{13}C NMR Chemical Shifts* of Free N-Methylimidazole and UO$_2$ Nitrate Containing Solutions in CD$_3$OD in ppm (δ).

Compound	C-2-H	C-5-H	C-4-H	1'-CH$_3$	C-2	C-5	C-4	C-1'
N-M-Imid	7.67, 1H	7.15, 1H	7.05, 1H	3.78, 3H	139.20	129.18	121.84	33.55
N-M-Imid + UO$_2$ nitrate 1:0.25	8.24, 1H	7.37, 2H		3.89, 3H	139.10	126.68	122.97	34.68
N-M-Imid + UO$_2$ nitrate 1:0.5	8.68, 1H	7.53, 2H		3.95, 3H	139.00	125.85	123.20	34.93
					Δ ppm = −0.20	−3.33	+1.36	+1.38
N-M-Imid + UO$_2$ nitrate 1:1	8.88, 1H	7.62, 2H		4.00, 3H				
N-M-Imid + UO$_2$ nitrate 1:2	8.92, 1H	7.64, 2H		4.02, 3H				
Δ ppm =	+1.25	+0.54		+0.24				

*Chemical shifts are taken downfield from TMS used as an internal standard. Abbreviation: N-M-Imid = N-Methylimidazole.

formation of 1:1 complexes, with both uranyl nitrate and uranyl acetate as major species in solution.

UO$_2^{2+}$ Interaction with Imidazole and Its Derivative in CD$_3$OD

The UO$_2^{2+}$ interaction with imidazole in methanol solution is much more evident than that found for the aqueous solutions, as shown in Tables II and III. The downfield shift of C$_2$H and C$_4$H, C$_5$H protons in the presence of uranyl ion depends on UO$_2^{2+}$: imidazole molar ratio and the obtained plot may indicate that the major species in the UO$_2^{2+}$ nitrate containing solution is the 1:2 UO$_2^{2+}$: imid complex. A similar though less univocal dependence may suggest that UO$_2^{2+}$ acetate binds only one molecule of imidazole in the dominant complex species.

The ^{13}C NMR results support the involvement of imidazole nitrogen in uranyl ion binding (Tables II, III). The interesting feature of carbon spectra is the chemical shift variation upon coordination of uranyl nitrate and acetate. Each of the latter salts displaces the resonance signal in different directions *i.e.* downfield (acetate) or upfield (nitrate). This strongly suggests a direct influence of the anion (NO$_3^-$ and CH$_3$COO$^-$) on the coordination mode of the imidazole molecule. Such an influence can occur when one (acetate) or both

TABLE V. ^{1}H and ^{13}C NMR Chemical Shifts* of Free N-methylimidazole and UO$_2$ Acetate Containing Solutions in CD$_3$OD in ppm (δ).

Compound	C-2-H	C-5-H	C-4-H	1'-CH$_3$	CH$_3$ $_{\text{acet.}}$	C-2	C-5	C-4	C-1'	CH$_3$ $_{\text{acet.}}$
N-M-Imid	7.67, 1H	7.15, 1H	7.05, 1H	3.78, 3H		139.20	129.18	121.84	33.55	
N-M-Imid + UO$_2$ acetate 1:0.25	7.91, 1H	7.23, 1H	7.20, 1H	3.82, 3H	2.48	139.45	128.85	122.12	33.66	26.03
N-M-Imid + UO$_2$ acetate 1:0.5	8.10, 1H	7.32, 1H	7.30, 1H	3.82, 3H	2.52	139.47	128.42	122.27	34.11	25.73
						Δ ppm = +0.27	−0.76	+0.43	+0.56	
N-M-Imid + UO$_2$ acetate 1:1	8.32, 1H	7.39, 2H		3.82, 3H	2.55					
N-M-Imid + UO$_2$ acetate 1:2	8.50, 1H	7.42, 2H		3.80, 3H	2.58					
	Δ ppm = +0.83	+0.32		+0.02						

*Chemical shifts are measured downfield from TMS used as an internal standard. Abbreviation: N-M-Imid = N-Methylimidazole.

the anions are also directly involved in metal ion coordination in the studied solutions.

The different behaviour of uranyl acetate and nitrate is also observed in their coordination to the N-methyl derivative of imidazole. The involvement of N3 donor in uranyl ion binding could be suggested by the considerable changes of proton and carbon chemical shifts upon UO$_2^{2+}$ coordination as shown in Tables IV and V. The features observed for the chemical shifts dependence on UO$_2^{2+}$:ligand molar ratio are very close to those found for imidazole containing solutions. Thus, the plots suggest that N-methylimidazole forms as a major species a 1:1 complex with UO$_2^{2+}$ acetate and a 2:1 complex with UO$_2^{2+}$ nitrate as found above for imidazole.

The present results suggest that the imidazole donors are involved in the binding of uranyl ion, and are in good agreement with the results obtained with the solid complexes [8]. The results obtained in aqueous solution are negative because the pH range available for the measurements is too acidic to allow such coordination to occur. It seems clear, however, that imidazole may be involved in UO$_2^{2+}$ binding as histidine side-chain in proteins where the pH problem met in this study does not exist.

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