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SYNTHESIS OF COMPLEXES OF URIC ACID WITH GROUP I AND II B METALS

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ABSTRACT. Complexes of uric acid (UA) with Zn^{2+}, Cd^{2+}, Hg^{2+}, Cu^{2+}, and Ag^{+} were obtained from aqueous solution between pH 7.0 and 9.0. Elemental analyses are consistent with the formula $M(UA)_2.nH_2O$ (M = Zn, Cd , Cu, and n = 2 and M = Hg, n = 6) and $Na[Ag(UA)_2].2H_2O$. The IR spectra of the four complexes with M = Zn, Hg, Cu and Ag indicate that the metal is coordinated to nitrogen of the imidazole ring and the carbonyl of the pyrimidine ring in UA, while the Cd in $Cd(UA)_2.2H_2O$ is coordinated to the nitrogen and the carbonyl of the imidazole ring. Except for Cd^{2+} all the metal ions form five membered ring complexes with uric acid. The calculated integral absorbance shows all the complexes contain triketo-form of uric acid. The stability constants and metal : UA ratio were also measured at two different pH (7.4 and 10) values.

INTRODUCTION

Uric acid (UA, **1**) complexes of some 3d [1], 5d [2] metal salts, lanthanides [3], and of groups I [4], II [5,6], IV A [7] metals have been reported. All class B metals (e.g. Co, Ni, Cd, Hg, and Zn) easily coordinate to nitrogen and form stable amide complexes while heterocyclic amides such as uric acid readily coordinate transition metals. Metals like Na, K and Mg that seldom coordinate nitrogen form salts with uric acid [7].

Complexes and salts of UA are of interest because of their stereochemistry, their analytical application and in understanding of their role in physiological systems [8-10]. We therefore have synthesized and characterized uric acid complexes of group I and IIB metals for the first time.

EXPERIMENTAL

The complexes were prepared in aqueous medium between pH 7.0-9.0 and handled in air. Since UA is slightly soluble in water, its monosodium salt was prepared by dissolving UA, 0.84 g. (0.005 mole) in 0.1 NaOH to give 5 mg/mL solution. The excess NaOH was neutralized with 0.01 N HCl to the desired pH before use. The monosodium salt was used in all the preparations.

Reagents and equipment. All reagents were prepared in double distilled water. UA, $Cd(NO_3)_2.4H_2O$, $ZnSO_4.7H_2O$, $HgCl_2$, $CuCl_2$ and $AgNO_3$ were all of reagent grade. The IR

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spectra were recorded over the range 4000 cm^{-1} to 600 cm^{-1} with a Perkin Elmer, 1600 series FTIR Model in KBr disks. UV spectra were recorded on a Beckman DU-65 spectrophotometer. The pH of solutions were measured with a Beckman Chem-Mate pH meter and melting points were determined with a Kofler Block melting point apparatus.

Elemental analysis. Nitrogen of uric acid was determined by the Kjeldahl method [11] using a catalyst containing 0.2 g $CuSO_4$ and 5 g of K_2SO_4. Zinc and Hg were determined by complexometric titration with EDTA, Cu by a back titration method of EDTA. Ag and Ni were determined by indirect complexometric titration with EDTA. Sodium was determined with a flame photometer, water of crystallization was estimated by weight loss at 150°C, chloride was determined with $AgNO_3$ and sulphate as barium sulphate [12]. The average of triplicate analyses are given for all the elements measured.

Synthesis of complexes

Preparation of $Zn(UA)_2.2H_2O$. $ZnSO_4.7H_2O$ (1.435 g, 0.005 mole) was dissolved in 50 mL water and 50 mL of a solution of UA (5 mg/mL) was added at room temperature and then heated to 60°C while stirring. The precipitate was filtered off, washed with cold water and left in a desiccator to dry for three days to give light brown crystals. Yield: 0.92 g (59.3%); m.p.: change color to light green at 320°C; melts at 345°C. Elemental analysis, found (calcd.)%: Zn, 15.35 (15.03); UA, 76.74 (76.69); H_2O, 7.83 (8.27); UV λ_{max} nm: 250, 270 and 305; IR $\nu_{C=O}$ cm^{-1}: 1701, 1616, 1655; $\nu_{O\text{-}H}$ cm^{-1}: 3420.

Preparation of $Cd(UA)_2.6H_2O$. $Cd(NO_3)_2.4H_2O$ (1.54 g, 0.005 mole) was dissolved in 50 mL water and mixed with a 50 mL solution of UA (5 mg/mL). The temperature of the mixture was raised to 40°C and the mixture was concentrated to two thirds of its volume by evaporation to give light green fine needles. The crystals were filtered, washed with cold water and dried in a desiccator for four days. Yield: 0.67 g (41.5%), m.p.: >360°C. Elemental analysis, found (calcd.)%: Cd, 24.80 (24.24); UA, 70.70 (69.22); H_2O, 8.22 (7.46). UV λ_{max} nm: 259, 270, 312; IR $\nu_{C=O}$ cm^{-1}: 1733, 1673, 1609; $\nu_{O\text{-}H}$ cm^{-1}: 3750.

Preparation of $Hg(UA)_2.6H_2O$. $HgCl_2$ (1.36 g, 0.005 mole) was dissolved in 50 mL water and mixed with a 50 mL solution of UA (5 mg/mL). The mixture was heated to 50°C. The precipitate was filtered off, washed with cold water and dried in a desiccator for three days to give grey crystals. Yield: 0.91 g (60%), m.p.: color changes to reddish brown at 260°C and melts at 331 - 335°C. Elemental analysis, found (calcd.)%: Hg 31.14 (31.20); UA, 51.90 (52.47); H_2O, 15.82 (16.80). UV λ_{max} nm: 248, 266, 318; IR $\nu_{C=O}$ cm^{-1}: 1701, 1616, 1655; $\nu_{O\text{-}H}$ cm^{-1}: 3538.

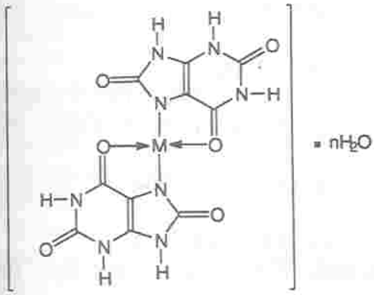
Preparation of $Cu(UA)_2.2H_2O$. $CuCl_2$ (0.68 g, 0.005 moles) in 50 mL water was mixed with a 50 mL solution of UA (5 mg/mL) and the pH of the mixture was adjusted to 7.5. The mixture was concentrated to two thirds of its volume and then cooled to give brown-black crystals which were filtered and washed with a small amount of water. The crystals were dried in a desiccator. Yield: 0.71 g (47%); m.p.: decomposes at 240°C. Elemental analysis: found (calcd.)%: Cu, 14.56 (14.65); UA, 77.16 (77.07); H_2O, 9.61 (8.80). UV λ_{max} nm: 236, 282, 304; IR $\nu_{C=O}$ cm^{-1}: 1694, 1646; $\nu_{O\text{-}H}$ cm^{-1}: 3650.

Preparation of $Na[Ag(UA)_2].2H_2O$. $AgNO_3$ (0.83 g, 0.005 moles) was dissolved in 50 mL water and a 50 mL solution of UA (5 mg/mL) was added. The mixture was allowed to react in the dark, and the precipitate was filtered off, washed with cold water and left in a desiccator for three days to give reddish brown crystals. Yield: 0.74 g (59.10%), m.p.: >360°C. Elemental analysis, found (calcd.)%: Ag, 21.40 (21.36); Na, 4.40 (4.60); UA, 67.35 (66.81); H_2O, 6.14 (7.23). UV λ_{max} nm: 271, 295; IR $\nu_{C=O}$ cm^{-1}: 1710, 1658, 1609 cm^{-1}; ν_{O-H} cm^{-1}: 3745; ν_{N-H} cm^{-1}: 3358, 3295.

RESULTS AND DISCUSSION

The chemical and physical data are consistent with the proposed chemical formulas of the respective compounds. All the compounds are colored crystalline materials with m.p. greater than 330°C. Qualitative analysis showed that inorganic anions (chloride, nitrate, sulphate) are not involved in complex formation and that coordinated UA is present in the monoanionic form. The low temperature of dehydration of the complexes and IR data indicate that all the water molecules present are in the outer sphere. The UV spectrum of uric acid has a maximum at 292 nm [13] that can be described as a $n-\pi^*$ transition involving C=O groups. If ionization is accompanied by tautomeric transformation (Figure 1), a shift to a longer wavelength of this band in alkaline solution must take place [13,14]. This was not observed, indicating that the triketo form is the most stable.

Figure 1. Keto-enol tautomerism of uric acid.



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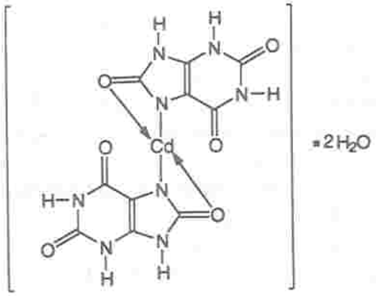
M = Zn, Cd, Cu and n = 2, and M= Hg, n= 6



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The integral absorption of $\nu_{C=O}$ was calculated to examine whether or not the keto-enol tautomeric transformation takes place during complex formation. The calculated values (9.0 - 11.6 x 10^{-4} kg $mol^{-1}cm^2$) for all the complexes, uric acid (4.44 x 10^{-4} kg $mol^{-1}cm^2$) and the theoretical values for alloxan (10.1x10^{-4} kg $mol^{-1}cm^2$) [15] containing three keto-groups are in agreement, confirming that uric acid exists in the triketo form in the synthesized complexes.

The IR spectrum of uric acid exhibits three different C=O absorption bands. The 1701 and 1671 cm^{-1} bands are due to the carbonyl of the pyrimidine ring, (NH-CO-NH and NH-CO-OH, respectively) and the third at 1655 cm^{-1} corresponds to the carbonyl of the imidazole ring [15]. The IR spectra of all the complexes except for Cd^{2+} exhibit a shift from 1671 to 1609 cm^{-1}

of the carbonyl of the pyrimidine ring nearer to the imidazole fragment indicating its involvement in bond formation together with the deprotonated NH group of the imidazole ring (**2**). In the cadmium complex the band at 1655 cm^{-1} (the imidazole carbonyl) shifts to lower frequency (1609 cm^{-1}), which probably shows that the Cd^{2+} and carbonyl of the imidazole ring interact together with the deprotonated NH group of the imidazole ring (**3**).

The absorbances of the reaction mixtures for the determination of stability constants [16] (calculated by mole ratio method) and metal: UA ratio [17] (1:2 for M = Zn, Hg, Cu and Ag) were recorded at 250 nm (pH 7.4) and 310 nm (pH 10) . The results of the two measurements are close to each other. From the data it can be inferred that Ag ($\log \beta_2 = 11.2$) and Hg ($\log \beta_2 = 10.9$) complexes are more stable than the rest ($\log \beta_2 = 9.3$ for Cu, and 9.2 for Zn). The previously reported stability constants for Ag and Hg complexes ($\log \beta_2 =$ 8-14) [18,19] are in agreement with our finding.

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