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Synthesis and crystal structure of copper (II) uracil ternary polymeric complex with 1,10-phenanthroline along with the Hirshfeld surface analysis of the metal binding sites for the uracil ligand

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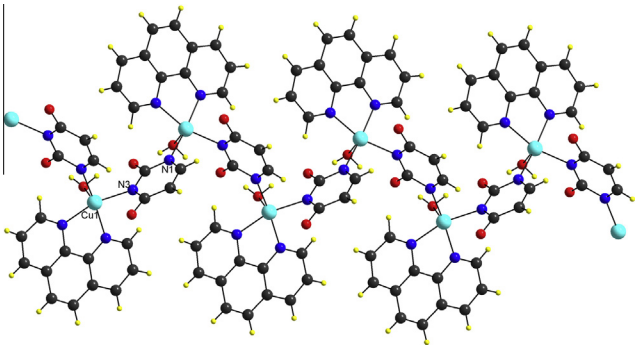
HIGHLIGHTS

- Ternary complex of copper-uracil-phenanthroline as a biomimic model.
- The complexes crystallized as *solvatomorphs*.
- Unique binding of uracil with N1 and N3 nitrogen atom of the six membered ring.
- First 1-D polymer with uracil as bridging ligand.
- Subtle differences of *solvatomorphs* quantified with Hirshfeld surface analysis.

GRAPHICAL ABSTRACT



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ABSTRACT

The study of models for "metal-enzyme-substrate" interaction has been a proactive area of research owing to its biological and pharmacological importance. In this regard the ternary copper uracil complex with 1,10-phenanthroline represents metal-enzyme-substrate system for DNA binding enzymes. The synthesis of the complex, followed by slow evaporation of the reaction mixture forms two concomitant *solvatomorph* crystals viz., {[Cu(phen)(μ-ura)(H_2O)]$_n$·H_2O **(1a)**} and {[Cu(phen)(μ-ura)(H_2O)]$_n$·CH_3OH **(1b)**}. Both complexes are structurally characterized, while elemental analysis, IR and EPR spectra were recorded for **1b** (major product). In both complexes, uracil coordinates uniquely via N1 and N3 nitrogen atom acting as a bidentate bridging ligand forming a 1-D polymer. The two *solvatomorphs* were quantitatively analyzed for the differences with the aid of Hirshfeld surface analysis.

Introduction

Metal–nucleic acid interaction is of vital importance in most of the biological processes. These processes are characterized by interaction between enzymes or proteins with DNA or RNA constituents mediated through a metal ion [1]. Thus elucidation of these interactions can be done by characterization of metal–amino acid–nucleobase ternary complexes acting as a biomimetic model [2,3].

Among the nucleobases, uracil present in RNA is a part of various enzymatic processes, wherein it is involved in site recognition through non covalent interactions in the presence of metal ions [4–7]. Uracil as a ligand has multiple coordination sites available and these binding sites vary with metal ions [8]. Thus documentation of these sites with different metal ions is of physiological

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importance. X-ray diffraction studies have provided unambiguous results for possible binding modes of uracil with transition metals like Zinc [7], Platinum [9,10] and Osmium [11]. In these complexes uracil acts as monodentate ligand [7] (coordinating via the nitrogen atom N1/N3), bidentate [11] (N1 and O1) or tridentate (N1, N3 and O4) and tetradentate (N1, O2, N3 and O4) bridging ligand for the cyclic tetramer Platinum complexes [9] (Fig. 1).

Copper, which is an important transition metal, forms the active site of many enzymes. The binding affinity of copper to DNA and nucleic acids is high as compared to other divalent metal ions [12]. Various copper uracil complexes have been characterized by Infrared spectra, elemental analysis [13,14] and theoretical studies in gas phase [12,15] but so far only two crystallographic reports are available for the direct copper uracil interaction. In both cases uracil acts as a monodentate ligand coordinating via nitrogen atom N1 [16,17].

In continuation of our ongoing work on nucleobases [18], herein we report the synthesis and crystallographic characterization of copper uracil ternary complex with 1,10-phenanthroline, as a coligand, wherein the two potential sites of the base [N1 and N3] are taking part simultaneously in coordination to two different metal centers. The subtle difference between the two *solvatomorphs* obtained was quantitatively analyzed with the Hirshfeld surface analysis.

Materials and methods

All the chemicals and reagents were obtained from commercial sources (S. D. Fine Chemicals, India; Sigma Aldrich, USA) and used without further purification. The elemental analyses were performed on Thermo Scientific Flash 2000 Organic Elemental Analyzer. The infrared spectra of the complexes and the ligands were recorded using Bruker Alpha FT-IR spectrometer. The EPR spectrum was recorded on the Bruker ER O41X Microwave bridge X band spectrometer.

*Synthesis of the Precursor complex **1***

The precursor was prepared according to reported procedure [19] with some modification. To the methanolic solution of copper chloride (500 mg, 2.932 mmol); 1,10-phenanthroline(581.3 mg, 2.932 mmol) in methanol (5 ml) was added and the reaction mixture was stirred for about 1 h. The green precipitate thus formed was filtered, washed with methanol and kept for vacuum drying over fused calcium chloride (yield 1.7129 g, 93.4% for **1**; Scheme 1).

*Synthesis of Cu(II) complexes[**1a**, **1b**]*

Complex $[Cu(phen)(\mu\text{-ura})(H_2O)]_n{\cdot}H_2O$ **(1a)** and $[Cu(phen)(\mu\text{-ura})(H_2O)]_n{\cdot}CH_3OH$ **(1b)** were prepared by mixing aqueous solution of $Cu_2(phen)_2(\mu\text{-}Cl)_2Cl_2$ [50 mg, 0.0798 mmol], to the methanolic solution of uracil [17.8 mg, 0.159 mmol]. The pH of reaction mixture was adjusted to 12 with dilute NaOH (1 M), the reaction mixture was then stirred for 17 h. The blue color solution obtained gave few diffraction quality crystals on slow evaporation of **1a** [green plate like] and **1b** [green needle shape] of which **1b** is the major product. The polymer obtained is insoluble in any common solvents [yield 49.7 mg, 76.8% for **1b**; Scheme 1] Anal. Calcd for **1b**: C, 50.56; H, 3.99; N, 13.87. Found: C, 50.49; H, 3.91; N, 13.85. Selected IR data (cm^{-1}): ν[OH] 3380br, 3216br; ν[C=O] and ν[C=C] 1644w, 1588vs (vs very strong; s, strong; m, medium; w, weak; br, broad).

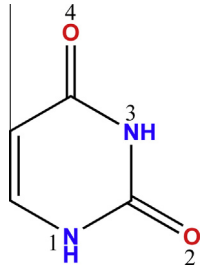
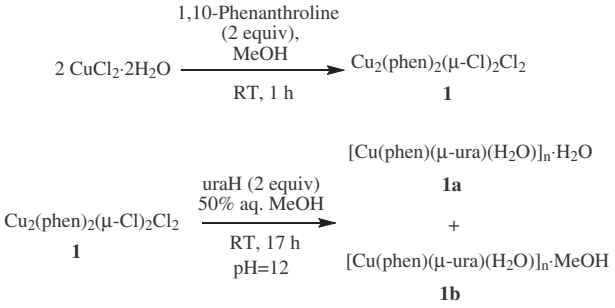


Fig. 1. Uracil with the numbering scheme.



Scheme 1.

X-ray crystallography

Single crystal X-ray diffraction studies were carried out for both complexes. Crystal data for **1a** was collected on BRUKER AXS SMART APEX CCD diffractometer whereas for **1b** the diffraction data was recorded on BRUKER KAPPA APEX-II CCD diffractometer. The crystal data were collected at 293 K with the operating voltage of 50 kV and 35 mA. The data for **1a** was collected with the combination of phi and omega scans with a scan width of 0.5° [sample to

Table 1
Selected crystallographic data for the structures **1a** and **1b.**

	$[Cu(phen)(\mu\text{-ura})(H_2O)]_n{\cdot}H_2O$ **1a**	$[Cu(phen)(\mu\text{-ura})(H_2O)]_n{\cdot}CH_3OH$ **1b**
Empirical formula	$C_{16}H_{14}CuN_4O_4$	$C_{17}H_{16}CuN_4O_4$
Formula weight	389.85	403.88
Crystal size (mm)	0.15 × 0.09 × 0.06	0.15 × 0.13 × 0.03
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
a (Å)	9.150(3)	9.272(1)
b (Å)	21.086(7)	21.357(2)
c (Å)	9.066(3)	8.980(1)
α (°)	90.0	90.0
β (°)	118.6(1)	115.5(1)
γ (°)	90.0	90.0
V (Å^3)	1535.7(8)	1605.0(3)
Z	4	4
ρ_c (g cm^{-3})	1.686	1.671
μ (mm^{-1})	1.454	1.394
$F(000)$	796	828
Reflections collected	15,542	16,938
Unique reflections	3031	3150
Observed reflections	2149	1752
L.S. parameters	261	238
R_{int}	0.1072	0.0961
$R_1[I > 2\sigma(I)]$	0.0666	0.0680
$wR_2[I > 2\sigma(I)]$	0.1217	0.1505
Goodness-of-fit on F^2	1.090	1.021
$\Delta\rho_{(max/min)}$ (eÅ^{-3})	0.506/−0.594	0.687/−0.751
CCDC deposition numbers	CCDC 951696	CCDC 951697