



Synthesis and chemical characterization of some transition metal complexes with a 6-acetyl-1,3,7-trimethylumazine ligand

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Abstract

In order to continue our studies in coordination chemistry with pteridine derivatives, ligand pyridinylhdrazone of 6-acetyl-1,3,7-trimethylumazine (PZLMH) and its mononuclear Cu(II), Ag(I), Cd(II), Hg(II) and Gd(III) complexes have been synthesized. Ligand and metal complexes were characterized by elemental analyses, ¹H- and ¹³C-NMR and IR studies. The result suggest that the mononuclear complexes have a metal to ligand mole ratio of 1:1 and the metal ions are coordinated with the phenolic oxygen and imine nitrogen atoms.

1. Introduction

It is well known that the heterocyclic hydrazones have a great biological relevance, as these compounds constitute an important class of biologically active molecules which have attracted attention of medicinal chemists due to their wide ranging pharmacological properties and their potential application as antitumor, antineoplastic, antiviral and antiinflammatory agents [1-6].

Specifically on the antitumor activity of aroylhydrazones, it has been shown to possess significant inhibiting effect on DNA synthesis and cell growth in a number of human and rodent cell lines [7]. It has been postulated that inhibition is due to their ability to penetrate cell membranes and disrupt the intracellular metabolism of essential metal ions [8-9]. The exact nature of such disruptions and the extent to which they may be exploited for therapeutic purposes require deeper studies because biological activities of many of these organic compounds are increased when they are administered as metal complexes [10], so several metal chelates have been used as antitumour agents [11-12].

A literature survey indicated that the scientists are mostly impressed by biochemical qualities of pteridines, and their derivatives which have attracted the attention from several points of view, since they are capable of simulating the reactivity of metal sites in several enzymes [13-16].

On the other hand, the pyridine ring itself is a part of many natural and synthetically prepared pharmaceuticals. In addition, the pyridine moiety plays a significant role in many biological processes like nicotinamide adenine dinucleotide phosphate NADP or vitamin B6 [17-18]. Nowadays, the metal complexes of these heterocycles have recently been studied as models to mimic the reactivity of the metal site of some metalloenzymes and they carry out diverse biological functions, being present in a number of biological systems involving several biochemist reactions of physiological relevance [19-24].

Furthermore, the functionalized 6-acetyl-1,3,7-trimethylumazine pro-ligand (lumazine:pteridine-2,4(1H,3H)-dione) has been already used as a precursor compound to build some thiosemicarbazone and hydrazone hybrid coordinative systems [25-26]. Thus, this work is aimed to describe the synthesis and chemical characterization of a new pteridine derivative, the pyridinehydrazone of 6-acetyl-1,3,7-trimethylumazine (PZLMH) (Figure.1) and a number of new metal complexes, with Cu(II), Cd(II), Hg(II), Ag(I) and Gd(III) metals, providing a detailed spectroscopic (IR, ¹H and ¹³C-NMR).

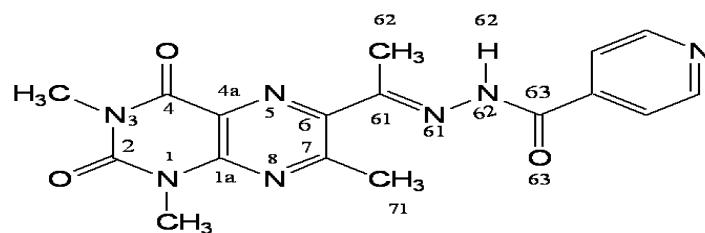


Figure 1: Numbering scheme for chemical structure of pyridinylhydrazone of 6-acetyl-1,3,7-trimethyllumazine (PZLMH) (1).

2. Experimental details

2.1. Measurements

Elemental analyses were carried out with Thermo Finnigan Flash EA 1112. The IR spectra were performed between 4000 and 400 cm^{-1} using KBr pellets on a Bruker TGA-IR Tensor 27; the intensity of reported IR signals is defined as s = strong, m = medium, w = weak. ^1H and ^{13}C -NMR spectra (DMSO- d_6) were recorded on a Bruker Avance 400; the chemical shifts were referenced to residual solvent resonance external TMS (tetramethylsilane) in the ^1H and ^{13}C spectra; the splitting of proton resonances in the reported ^1H NMR spectra is defined as s = singlet, d = doublet, and m = multiplet

2.2 Materials

Metallic nitrates and perchlorates were purchased from standard commercial sources. Reagent-grade solvents were used without further purification.

2.3 Synthesis of compounds

2.3.1 Synthesis of pyridinylhydrazone of 6-acetyl-1,3,7-trimethyllumazine (PZLMH)(1)

The pro-ligand 6-acetyl-1,3,7-trimethyllumazine (DLMACEM) was prepared by standard Timmis reaction between 6-amino-5-nitrosopyrimidines and 1,3-dicarbonylic derivatives by the method described by Kim et al [27]. The pyridinylhydrazone ligand (PZLMH) (1) was prepared by condensation of equimolar amounts of lumazine derivative (DLMACEM) (2.5 g, 10 mmol) and pyridinylhydrazone (1.4g, 10mmol) in ethanol (30 mL) with 0.5 mL of acetic acid used as catalyst (Figure.2).

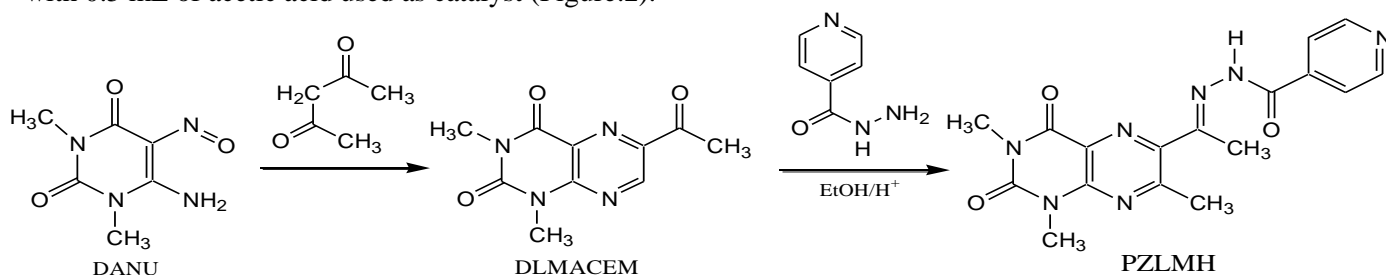


Figure 2: Synthesis of PZLMH ligand.

The mixture was refluxed for 3 h at 80 °C and then was left to stand to room temperature. The beige solid formed (3.02 g) in high yield (82%) was filtered and washed with ethanol and diethyl ether. Elemental analysis found (%), C, 55.48; H, 4.70; N, 26.62. Calc. For $\text{C}_{17}\text{H}_{17}\text{N}_7\text{O}_3$ (367.47): C, 55.58; H, 4.66; N, 26.69. IR (KBr, cm^{-1}): 3455, 3331 (m, $\nu(\text{N-H})$); 1711, 1679, 1656 (vs, $\nu(\text{C=O})$); 1587 (w, $\nu(\text{N=C-CH}_3)$); 1549 (m, $\nu(\text{C=N})$); 1432, 1288 (m, $\nu(\text{C=C}) + \nu(\text{C-N})$); 1024 (w, $\nu(\text{N-N})$). ^1H NMR ((CD_3) $_2\text{SO}$, d, ppm): 2.47 (s, C62-H); 2.93 (s, C71-H); 3.31 (s, N3-Me); 3.55 (s, N1-Me); 7.55, 8.44 (meta, Ph); 8.75, 9.05 (ortho, Ph); 11.0 (s, N62-H). ^{13}C NMR ((CD_3) $_2\text{SO}$, d, ppm): 14.9 (C62); 25.63 (C71); 28.36 (C3); 28.87 (C1); 123.81 (C4A); 141.82 (C6); 123.40, 135.92 (C_{arom}); 144.55 (C61); 145.79 (C1A); 148.49 (C2); 150.49 (C7); 159.33 (C4).

2.3.2 Synthesis of the complexes

All complexes were prepared using the same method. They were obtained by reacting a suspension of ligand PZLMH (1/4 mmol) with a solution of metallic salt (1/4 mmol) in the ethanol. The reaction mixture was heated and stirred to about 60° for several hours. The resulting solids obtained were filtered and washed with ethanol and diethyl ether.

- 2.3.2.1. *Compound Ag(NO₃)(PZLMH).(2).* (0.12 g) Yield, ca. 92 %.Elemental analysis found, C, 37.48 ; H, 3.28 ; N, 20.66 ; Calc. for AgC₁₇H₁₇N₈O₆(537.34) C, 37.99 ; H, 3.19 ; N, 20.85. IR (KBr, cm⁻¹): 3516, 3332 (m, ν(N-H)); 1712, 1659 (s, ν(C=O)); 1589 (w, ν(C=N)_{azom}); 1549 (m, ν(C=N)); 1473,1290 (m, ν(C=C) + ν(C-N)); 1025 (w, ν(N-N)); 1384 (m, ν(N-O)_{nitrate}).
- 2.3.2.2. *Compound Cd(NO₃)₂(PZLMH).(3).* (0.14 g)Yield, ca. 92%.Elemental analysis found, C, 37.75 ; H, 3.75 ; N, 19.24 ; Calc. for CdC₁₇H₁₇N₉O₉(603.88) C, 33.82 ; H, 2.84 ; N, 20.24. IR (KBr, cm⁻¹): 3474 (m, ν(N-H)); 1720, 1665 (s, ν(C=O)); 1599 (w, ν(C=N)_{azom}); 1556 (m, ν(C=N)); 1500, 1298 (m, ν(C=C) + m(C-N)); 1056 (w, ν(N-N)); 1384 (m, ν(N-O)_{nitrate}).
- 2.3.2.3. *2.3.2.3. Compound Hg(ClO₄)₂(PZLMH).(4).* (0.10 g)Yield, ca. 52%.Elemental analysis found, C, 26.96 ; H, 2.45 ; N, 12.71 ; Calc. for HgC₁₇H₁₇N₇O₁₁Cl₂(766.96) C, 26.62 ; H, 2.23 ; N, 12.78. IR (KBr, cm⁻¹): 3453 (m, ν(N-H)); 1718, 1663 (s, ν(C=O)); 1580 (w, ν(C=N)_{azom}); 1554 (m, ν(C=N)); 1504, 1292 (m, ν(C=C) + m(C-N)); 1121, 1107, 1088, 627(m, ν(Cl-O)_{perchlorate}).
- 2.3.2.4. *Compound Cu(ClO₄)₂(PZLMH).(5).* (0.082 g) Yield, ca. 52%.Elemental analysis found, C, 32.54 ; H, 2.68 ; N, 15.74 ; Calc. for CuC₁₇H₁₇N₇O₁₁Cl₂(629.91) C, 32.41 ; H, 2.72 ; N, 15.56. IR (KBr, cm⁻¹): 3509 (m, ν(N-H)); 1720, 1672 (s, ν(C=O)); 1574 (w, ν(C=N)_{azom}); 1546 (m, ν(C=N)); 1519, 1289 (m, ν(C=C) + m(C-N)); 1034 (w, ν(N-N)); 1120, 1108, 1094, 625 (m, ν(Cl-O)_{perchlorate}).
- 2.3.2.5. *2.3.2.5. Compound Gd(NO₃)₃(PZLMH).(6).* (0.1 g) Yield, ca. 58%.Elemental analysis found, C, 27.50 ; H, 2.43 ; N, 19.16 ; Calc. for GdC₁₇H₁₇N₁₀O₁₂ (710.65) C, 28.70 ; H, 2.39 ; N, 19.70. IR (KBr, cm⁻¹): 3385 (m, ν(N-H)); 1718, 1650 (s, ν(C=O)); 1580 (w, ν(C=N)_{azom}); 1541 (m, ν(C=N)); 1474, 1294 (m, ν(C=C) + m(C-N)); 1091 (w, ν(N-N)); 1384 (m, ν(N-O)_{nitrate}).

3. Results and discussion

3.1. Infrared Spectra

IR data of the ligand and its complexes are given in table 1 and IR spectrum of ligand PZLMH it's represented in Figure 3. In the infrared spectrum of compounds, the bands about 3450 and 3330 cm⁻¹ can be assigned to the vibration ν(N-H) of N62 hydrazonic [28,29]. Two sharp and intense bands must be assigned to the combination of the stretching vibrations of both exocyclic carbonyl groups, the first one assignable to the vibration ν(C2=O), while the second corresponds to the ν(C4=O) [28,29]. In general, the ν(C63=O) mode can not be observed in the spectra of the complexes, because of the involvement in the coordination enlarges the bond shifting, consequently, the band to a lower wave-number region in which may be hidden by other lumazine vibrations; however the compounds Cd(NO₃)₂(PZLMH) and Gd(NO₃)₂(PZLMH) show a latter vibration (ν(C63=O)) displaced to 1644 and 1650 cm⁻¹, respectively, which appearing as become a shoulder in the ν(C4=O) bands [30,31].

Table 1.-Significant bands in the IR spectra of the ligand PZLMH and its metal complexes (cm⁻¹).

Complexes	ν(N-H)	ν(C=O)	ν(C=N) _{azom}	ν(C=N)	ν(C=C) + ν(C-N)	ν (N-N)	ν (M-X)
PZLMH	3455 3331	1711 1656	1587	1549	1432 1288	1024	-
Ag(NO ₃)(PZLMH)	3516 3332	1712 1659	1589	1549	1473 1290	1025	1384
Cd(NO ₃) ₂ (PZLMH)	3474 ^a	1720 1665	1599	1556	1500 1298	1056	1384
Hg(ClO ₄) ₂ (PZLMH)	3453	1718 1663	1580	1554	1504 1292	-	1121, 1107 1088, 627
Cu(ClO ₄) ₂ (PZLMH)	3509	1720 1672	1574	1546	1519 1289	1034	1120, 1108 1094, 625
Gd(NO ₃) ₃ (PZLMH)	3385	1718 1650	1580	1541	1474 1294	1091	1384

The azomethine mode tension ν(C=N) appears between 1570 and 1620 cm⁻¹, as found in literature [32, 33]. This band is weak or medium intensity infrared. Although often suffer displacement in both (10-30 cm⁻¹) as a result of the N5 and N61 coordination of the metal ion in some compounds remains virtually unchanged.

Below they can also be found other modes of vibration including atoms which may potentially act as donors, such as ν(C=C), strongly coupled with ν(C-N). This coupling results in two bands that are around 1450 and 1290 cm⁻¹, approximately, and corresponds to vibrations ring lumazine that involving primarily to nitrogen atoms N5 and N8 as well as carbon atoms C6 and C7. In general, a displacement is observed at higher wave

number of these bands respect to its position in the spectrum of the free ligand, possibly due to coordination of N5. The vibration tension N-N of the hydrazone appears as a much weaker band.

The vibrations $\nu(\text{N-O})$ own of nitrate groups are appearing located about 1384 cm^{-1} and corresponds, in all cases, with a very sharp band in the spectrum, suggest the presence of ionic nitrate in the complexes [34]. The vibration mode of the perchlorate ion, $\nu(\text{Cl-O})$, it appears split into two or three bands between 1080 and 1120 cm^{-1} , splitting that is produced as a result of loss of T_d geometry presenting the free perchlorate ions; moreover, the appearance in all cases of another band around $625\text{--}627\text{ cm}^{-1}$ assignable to the deformation $\delta(\text{O-Cl-O})$, is indicative of the presence of uncoordinated perchlorate ions [29, 35].

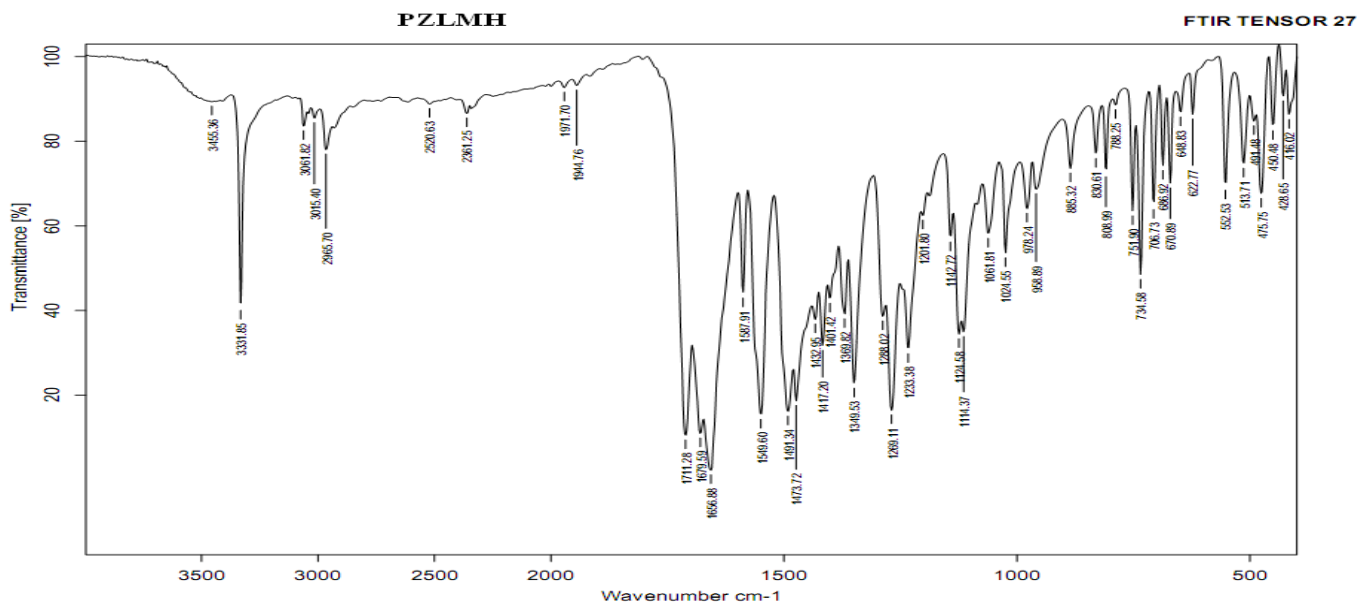


Figure 3: Infrared spectrum of ligand PZLMH.

2.2. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ Spectra

The $^1\text{H-NMR}$ spectra of the ligand was recorded in dimethylsulfoxide (DMSO- d_6) solution using tetramethylsilane (TMS) as internal standard. The $^1\text{H-NMR}$ spectrum of (**1**) shows a singlet at 2.47 and 2.93 ppm that may be assigned respectively to the protons of C62-H and C71-H. Aromatic singlets at 3.31 and 3.55 ppm that may be assigned to the proton of N3-Me and N1-Me, a signals between 7.55 and 9.05 ppm may be assigned to the aromatic protons (Figure 4).

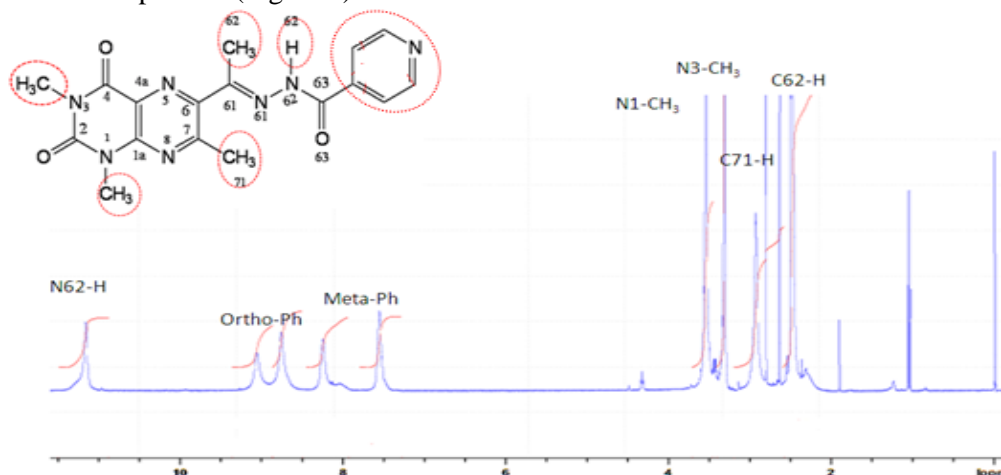


Figure 4: $^1\text{H-NMR}$ spectrum of ligand PZLMH

The $^{13}\text{C-NMR}$ of the ligand (**1**) shows peaks at range $123.40\text{--}159.33\text{ ppm}$, which are assignable to the carbons of the aromatic rings. The chemical shift for C3 and C1 was found at 28.36 and 28.87 respectively. The carbon atom of the methyl group was observed for C62 and C71 at 14.9 and 25.63 respectively. $^1\text{H-}$ and $^{13}\text{C-NMR}$ spectra data of the ligand in DMSO- d_6 confirm the proposed structure of the ligand (**1**) (Figure 5).

Single crystals of the complexes could not be isolated from any solutions, thus no definite structure could be described. However, according to literature [25-26, 29], these results and discussed through different techniques suggest below the proposed possible coordination for bidentate, tridentate and tetradentate ligand, shown in scheme 1-3.

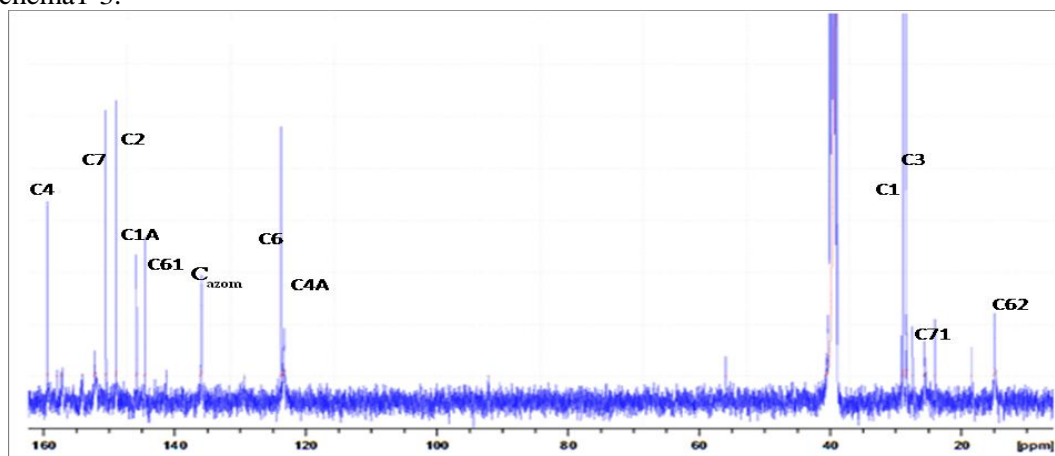
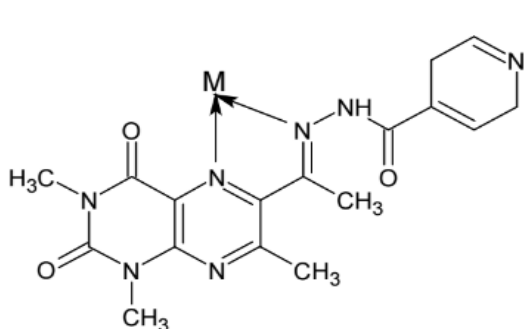
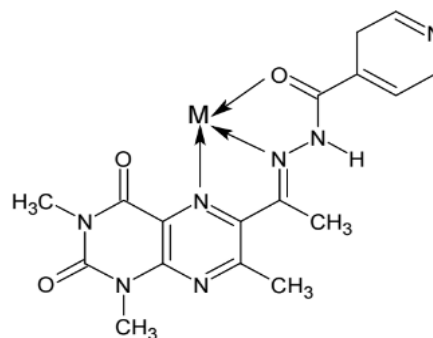


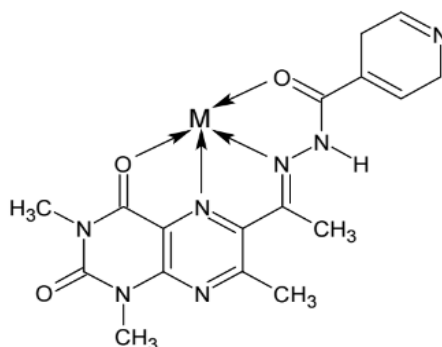
Figure 5: ^{13}C -NMR spectrum of ligand PZLMH



Scheme 1: Possible scheme of coordination for bidentate ligand PZLMH behavior.



Scheme 2: Possible scheme of coordination for tridentate ligand PZLMH behavior.



Scheme 3: Possible scheme of coordination for the complexes with a ligand bound to the metal tetradentate manner

Conclusions

In this paper, we reported the preparation, spectral identification, analytical data and coordination chemistry of pyridinylhydrazone of 6-acetyl-1,3,7-trimethylumazine (PZLMH) derived from the pro-ligand 6-acetyl-1,3,7-trimethylumazine (DLMACEM) by condensation and its metal complexes with Cu(II), Cd(II), Hg(II), Ag(I) and Gd(III) metals ions.

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