

Dioxobridged complexes of molybdenum (IV) and tungsten (IV) with N-alkylphenothiazines and their interactions with L-cysteine and L-histidine

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Abstract. Six new dioxobridged complexes of molybdenum (IV) and tungsten (IV) with N-alkylphenothiazines having the general formula $M_2O_4(L)_2(H_2O)_2$ [where M = molybdenum or tungsten and L = N-alkylphenothiazines] have been synthesised. The complexes have been characterised on the basis of analytical, molar conductance, magnetic susceptibility, spectral data, TGA and DTA. The low magnetic moments for the complexes are due to spin–spin interaction or metal–metal bonding. The interactions of these complexes with some biologically important amino acids have been studied.

Keywords. Dioxobridged complexes of Mo(IV) & W(IV); N-alkylphenothiazines; complexes of amino acids.

1. Introduction

Molybdenum as a trace element plays an important role in metabolic processes¹. Complexes of molybdenum (V) and molybdenum (VI) with cysteine², histidine³ and organic sulphur compounds⁴ are of interest as models for molybdenum-containing enzymes. These enzymes are known to catalyse a number of important biological oxo-transfer reactions where the valence of molybdenum alternates between molybdenum (VI) and molybdenum (IV) states in reactions with substrates and subsequent reactivation⁵. N-alkylphenothiazines (NAP) are versatile anticholinergic, antihistamine and antiemetic compounds⁶. The study of metal–phenothiazine complexes has gained much importance in recent years due to their potential pharmacological activities⁷. The possible use of metal–phenothiazine complexes as fungicides and considerable increase in their fungicidal activity by complexation of phenothiazines with copper (II)⁸, dioxo-uranium (VI)⁹, yttrium (III)¹⁰ and lanthanides (III)¹¹ have been reported.

In the present paper, we report the isolation and structural investigation of dioxobridged molybdenum (IV) and tungsten (IV) complexes with methoxypropazine (MP), prochlorperazine (PCP) and trifluoperazine (TFP) and their interactions with biologically important compounds such as L-cysteine and L-histidine.

*For correspondence

2. Experimental

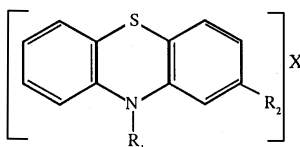
2.1. Materials

Ammonium molybdate tetrahydrate, $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$, sodium tungstate dihydrate, $\text{Na}_2\text{WO}_4\cdot 2\text{H}_2\text{O}$, L-cysteine and L-histidine hydrochloride monohydrate were of analytical grade. Methoxypromazine maleate (Rhone Poulenc, France), prochlorperazine dimaleate and trifluoperazine hydrochloride (M/s Bayer A G, Leverkusen, Germany) were used as received. Ethanol, ether, DMF and DMSO used were of analytical grade. Trivial and systematic names of the above N-alkylphenothiazines are given in table 1.

2.2. Preparation of the complexes

An ethanolic solution (50 cm^3) of methoxypromazine maleate (2.9 g, 6.74 mmol) was added to ammonium molybdate tetrahydrate. (2.0 g, 1.62 mmol) dissolved in 2 M hydrochloric acid (30 cm^3) with constant stirring at room temperature. The complex separated was set aside for 2 h, filtered, washed several times with water and then with ethanol and dried *in vacuo* over fused CaCl_2 . The same procedure was repeated for the preparation of other molybdenum (IV)–NAP complexes. The yield varied from 65–72%. The tungsten (IV)–NAP complexes were prepared by adding ethanolic solutions (50 cm^3) of NAP (2.7 g, 4.46–6.27 mmol) to an aqueous solution (40 cm^3) of sodium tungstate dihydrate (1.6 g, 4.85 mmol), containing a few drops of 2 M hydrochloric acid, with vigorous stirring at room temperature. The complexes were separated and washed as mentioned above. The yield varied from 60–64%.

Table 1. N-alkylphenothiazines.



Trivial and systematic names of ligand	R ₁	R ₂	X
<i>Methoxypromazine maleate (MPM)</i>			
10-[3-(Dimethylamino)propyl] 2-methoxy phenothiazine maleate	$-(\text{CH}_2)_3\text{N}(\text{CH}_3)_2$	$-\text{OCH}_3$	$\text{C}_4\text{H}_4\text{O}_4$
<i>Prochlorperazine dimaleate (PCPD)</i>			
10-[3-(4-Methyl-1-piperazinyl)propyl] 2-chloro phenothiazine dimaleate	$-(\text{CH}_2)_3\text{N} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{N}-\text{CH}_3$	$-\text{Cl}$	$2\text{C}_4\text{H}_4\text{O}_4$
<i>Trifluoperazine hydrochloride (TFPH)</i>			
10-[3-(4-Methyl-1-piperazinyl)propyl] 2-trifluoromethyl phenothiazine hydrochloride	$-(\text{CH}_2)_3\text{N} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{N}-\text{CH}_3$	$-\text{CF}_3$	HCl

2.3 Interactions of M(IV)–NAP complexes with L-cysteine and L-histidine

The M(IV)–NAP complex [where M = molybdenum or tungsten] (1.4 or 1.3 g) in DMF (50 or 40 cm³) was treated with L-cysteine (2.6 or 1.5 g) in 2 M hydrochloric acid (80 or 60 cm³) or with an aqueous solution of L-histidine (2.75 or 1.8 g). The solid complexes that separated immediately were filtered, washed several times with ethanol and dried *in vacuo* over fused CaCl₂.

2.4 Measurements

C, H and N contents were determined with a Carlo–Erba 1106 elemental analyser. The metal content of the complexes was determined by the atomic absorption method (AA/AE spectrophotometer, model 751) after decomposing the complexes with 1:1 mixture of concentrated sulphuric and nitric acids. Molar conductance of the complexes were measured in 10⁻³ M DMF solutions using ELICO-model CM-82T conductivity bridge. The magnetic susceptibility were determined by the Gouy method at room temperature using Hg[Co(SCN)₄] as calibrant ($c_g = 16.4$ c.g.s.u.). Molar susceptibilities were corrected for the diamagnetism for the constituent molecules and magnetic moments calculated according to the formula $m = 2.84 (c_M^1)^{1/2} \text{BM}$ where c_M^1 is the corrected molar susceptibility¹². The infrared spectra of the ligands and the complexes were recorded on a Shimadzu FT–IR model 470 spectrophotometer using KBr disc technique. Electronic spectra in DMF were measured on a Jasco-Uvidec-610 double beam spectrophotometer. Thermal analysis was carried out on a Stanton Redcraft TG 750/770 electrobalance with a linear heating rate of 6°C min⁻¹ in static air.

3. Results and discussion

The interaction of ammonium molybdate tetrahydrate or sodium tungstate dihydrate with N-alkylphenothiazines results in the formation of M(IV)–NAP complexes. The reduction of M(VI) to M(IV) may be attributed to the behaviour of N-alkylphenothiazines which are excellent electron donors¹³. The maleate or chloride ions of the ligand go into solution during the reaction and do not participate in the coordination with metal ions. The analytical data (table 2) correspond with the formula [M₂O₄(L)₂(H₂O)₂] (where M = molybdenum or tungsten and L = methoxypromazine, prochlorperazine or trifluoperazine).

The complexes are coloured, non-hygroscopic and stable at room temperature for long periods. They do not possess sharp melting points. The complexes are insoluble in water and common organic solvents but soluble in DMF and DMSO. The molar conductance values measured in DMF indicate the non-electrolytic nature of the complexes (table 2). Ion-exchange studies show that the complexes are neutral. These results are consistent with the stoichiometry assumed for the complexes on the basis of analytical data.

3.1 Magnetic properties

The low values of magnetic moments of the complexes (table 2) are concordant with the dinuclear formulation of the M(IV) complexes in which there are metal–metal interactions or spin–spin interactions between two metal atoms through the oxygen-bridging atoms. Formation of a metal–metal bond is more favourable for dioxobridged

Table 2. Characterisation data of M(IV)–NAP complexes [M = Mo(IV) or W(IV)].

Complex	Colour	Found (Calcd.), %				Λ_M^a	m_{ff} (BM)
		C	H	N	Mo/W		
Mo ₂ O ₄ (MP) ₂ (H ₂ O) ₂	Pale yellow	47.08 (47.48)	4.81 (4.83)	6.08 (6.15)	21.0 (21.1)	19.55	0.18
Mo ₂ O ₄ (PCP) ₂ (H ₂ O) ₂	Pale blue	45.45 (46.21)	4.60 (4.62)	8.06 (8.09)	18.38 (18.47)	20.42	0.16
Mo ₂ O ₄ (TFP) ₂ (H ₂ O) ₂	Pale yellow	45.20 (45.57)	4.33 (4.34)	7.52 (7.59)	17.30 (17.35)	18.63	0.17
W ₂ O ₄ (MP) ₂ (H ₂ O) ₂	Pale yellow	39.35 (39.79)	4.02 (4.05)	5.13 (5.16)	33.77 (33.87)	15.65	0.19
W ₂ O ₄ (PCP) ₂ (H ₂ O) ₂	Violet	39.21 (39.52)	3.90 (3.95)	6.86 (6.91)	30.02 (30.27)	17.42	0.22
W ₂ O ₄ (TFP) ₂ (H ₂ O) ₂	Pale yellow	39.08 (39.32)	3.72 (3.74)	6.52 (6.55)	28.55 (28.69)	16.06	0.20

^a(Ohm⁻¹ cm² mol⁻¹) in DMF as solvent

complexes than for monooxobridged complexes due to the shorter bond lengths between the metal atoms^{14,15}.

3.2 Electronic spectra

The electronic spectra of the dinuclear M(IV) complexes (table 3) with dioxobridges exhibit two bands at 650–740 nm and 528–598 nm for Mo–NAP complexes and at 643–715 nm and 550–594 nm for W–NAP complexes which are assigned to ²B₂ → ²E(I) and ²B₂ → ²B₁ ligand field transitions respectively^{16,17}. In the ultraviolet region, the three bands observed at 304–318, 270–298 and 248–268 nm for molybdenum complexes and 308–344, 274–296 and 246–260 nm for tungsten complexes are attributed to intraligand transitions. The electronic spectra of N-alkylphenothiazines exhibit three bands at similar wavelengths and the differences are not significant.

3.3 Infrared spectra

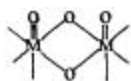
The selected infrared frequencies of the dioxobridged M(IV)–NAP complexes are given in table 4. The infrared spectra of the ligands observed at 2860–2825 cm⁻¹ region may be assigned to the heterocyclic nitrogen atom attached to an alkyl group¹⁸. In the infrared spectra of the corresponding complexes, this band either disappears or is shifted to higher frequencies ($\Delta\nu = 30\text{--}40\text{ cm}^{-1}$) suggesting the coordination of the heterocyclic nitrogen atom. It was reported that the ions R₃N⁺H combine with Cl⁻ ion present in the molecules of N-alkylphenothiazines giving a broad band in the 2500–2300 cm⁻¹ region⁶. A broad band observed at 2600–2350 cm⁻¹ region in the infrared spectra of the free ligands corresponds to the $\text{--}(\text{CH}_2)_2\text{N}^+\text{H}(\text{CH}_3)_2$ in MPM and $\text{--}(\text{CH}_2)_3\text{HN}^+\text{N-CH}_3$

Table 3. Electronic spectra of M(IV)–NAP complexes.

Complex	λ (nm)	$\bar{\nu}$ (cm ⁻¹)	ϵ	Transition
Mo ₂ O ₄ (MP) ₂ (H ₂ O) ₂	690	15.8	286	² B ₂ → ² E(I)
	594	16.7	325	² B ₂ → ² B ₁
	312	32.2	25258	Intraligand
	278	32.9	17354	Intraligand
	255	38.8	60765	Intraligand
Mo ₂ O ₄ (PCP) ₂ (H ₂ O) ₂	730	14.2	65	² B ₂ → ² E(I)
	546	18.3	728	² B ₂ → ² B ₁
	308	32.8	15780	Intraligand
	288	34.9	27695	Intraligand
	255	38.8	36585	Intraligand
Mo ₂ O ₄ (TFP) ₂ (H ₂ O) ₂	702	14.4	270	² B ₂ → ² E(I)
	598	16.6	425	² B ₂ → ² B ₁
	306	32.6	16356	Intraligand
	272	35.5	29654	Intraligand
	250	39.7	36547	Intraligand
W ₂ O ₄ (MP) ₂ (H ₂ O) ₂	655	15.4	25	² B ₂ → ² E(I)
	554	18.1	34	² B ₂ → ² B ₁
	316	28.3	9145	Intraligand
	288	35.4	16152	Intraligand
	250	39.3	23156	Intraligand
W ₂ O ₄ (PCP) ₂ (H ₂ O) ₂	656	15.3	24	² B ₂ → ² E(I)
	562	17.8	65	² B ₂ → ² B ₁
	320	27.4	8640	Intraligand
	292	34.1	15940	Intraligand
	254	39.4	23094	Intraligand
W ₂ O ₄ (TFP) ₂ (H ₂ O) ₂	715	13.9	12	² B ₂ → ² E(I)
	595	17.0	23	² B ₂ → ² B ₁
	342	29.1	12980	Intraligand
	296	33.7	16212	Intraligand
	258	38.4	21318	Intraligand

in PCPD and TFPH combined with the X⁻ anion (X⁻ = maleate or chloride). In the infrared spectra of the corresponding molybdenum and tungsten complexes, this band totally disappears indicating that the tertiary nitrogen atom of the side chain is another site of coordination. This shows that the N-alkylphenothiazines act as bidentate ligands with the heterocyclic nitrogen atom and the tertiary nitrogen atom as the two coordination sites. The sharp band observed at 750 cm⁻¹ in the spectra of the N-alkylphenothiazines assignable to $\nu(\text{CSC})$ stretching frequency¹⁹ remains unaffected in the spectra of the corresponding complexes suggesting the non-participation of the sulphur atom in coordination.

The infrared spectra of M₂O₄(L)₂(H₂O)₂ complexes contain five bands assignable to the



moiety. The strong bands observed at 960–942 cm⁻¹ for molybdenum

Table 4. Infrared spectral data (cm^{-1}) of M(IV)–NAP complexes.

Complex	$n_s\text{M}=\text{O}$	$n_a\text{M}=\text{O}_b$	$n_s\text{M}=\text{O}_b$	$n\text{M}=\text{N}$	$n\text{H}_2\text{O}$
$\text{Mo}_2\text{O}_4(\text{MP})_2(\text{H}_2\text{O})_2$	950	668	445	342	3120 3490
$\text{Mo}_2\text{O}_4(\text{PCP})_2(\text{H}_2\text{O})_2$	954	670	446	355	3110 3445
$\text{Mo}_2\text{O}_4(\text{TFP})_2(\text{H}_2\text{O})_2$	948	656	450	346	3110 3450
$\text{W}_2\text{O}_4(\text{MP})_2(\text{H}_2\text{O})_2$	978	818	436	340	3190 3480
$\text{W}_2\text{O}_4(\text{PCP})_2(\text{H}_2\text{O})_2$	980	822	452	345	3196 3492
$\text{W}_2\text{O}_4(\text{TFP})_2(\text{H}_2\text{O})_2$	976	824	446	340	3215 3500

complexes and at $982\text{--}970\text{ cm}^{-1}$ for tungsten complexes are due to the symmetric stretching modes of terminal $\text{M}=\text{O}$ bond. But the antisymmetric stretching mode is not observed. However the presence of the symmetric stretching mode is quite sufficient to designate a *cis* disposition for the two terminal $\text{M}=\text{O}$ in the dimeric complexes¹⁵. Antisymmetric and symmetric vibrations due to the $\text{M}=\text{O}$ bridge are found at $680\text{--}658\text{ cm}^{-1}$ and $452\text{--}425\text{ cm}^{-1}$ respectively for molybdenum complexes and at $825\text{--}808\text{ cm}^{-1}$ and $454\text{--}432\text{ cm}^{-1}$ respectively for tungsten complexes. These values are in good agreement with those found in complexes suggested to have an MO_2M bridge^{16,20}. The medium intense bands observed at $354\text{--}334\text{ cm}^{-1}$ for molybdenum complexes and at $354\text{--}332\text{ cm}^{-1}$ for tungsten complexes are assigned to the $\text{M}=\text{N}$ bond²¹. All the complexes exhibit strong and broad bands at $3500\text{--}3180\text{ cm}^{-1}$ which may be attributed to coordinated water molecules.

3.4 Thermogravimetric studies

Thermogravimetric studies indicate the coordination of water molecules in the complexes and also that the decomposition occurs in two steps. The first step involves the loss of the coordinated water molecules in the temperature range $118\text{--}184^\circ\text{C}$ and $110\text{--}220^\circ\text{C}$ for molybdenum and tungsten complexes respectively. The second step consists of the decomposition of the organic moiety and the formation of MO_3 . The weight loss becomes constant at $\approx 690^\circ\text{C}$ and this agrees with that calculated on the basis of the stoichiometry proposed for the complexes. In both the cases, the intermediate product MO_4L_2 was identified by elemental analysis and the infrared spectra. DTA studies show that the loss of water molecules is accompanied by an endothermic process at $\approx 140^\circ\text{C}$ and the formation of MO_3 at $\approx 690^\circ\text{C}$ by an exothermic process.

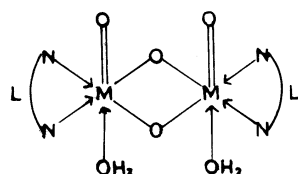
3.5 Interactions of M(IV)–NAP complexes with L-cysteine and L-histidine

The interactions of M(IV)–NAP complexes with biologically important compounds such as L-cysteine and L-histidine were carried out to determine the ease of substitution of the coordinated ligands. These interactions result in the immediate formation of solid complexes by displacement of the NAP ligands. The complexes thus obtained are

Table 5. Characterization data of M(IV)-substituted complexes.

Complex	% Carbon ^a	% Hydrogen	% Nitrogen	% Metal	m_{eff} in BM
$[\text{Mo}_2\text{O}_4(\text{Cyst})_2(\text{H}_2\text{O})_2]^{2-}$	13.38 (13.49)	2.61 (2.62)	5.22 (5.24)	35.88 (35.94)	0.22
$[\text{Mo}_2\text{O}_4(\text{Hist})_2(\text{H}_2\text{O})_2]^{2-}$	23.85 (23.92)	2.97 (2.99)	13.95 (13.96)	31.44 (31.88)	0.32
$[\text{W}_2\text{O}_4(\text{Cyst})_2(\text{H}_2\text{O})_2]^{2-}$	10.10 (10.14)	1.96 (1.97)	3.92 (3.94)	51.76 (51.81)	0.24
$[\text{W}_2\text{O}_4(\text{Hist})_2(\text{H}_2\text{O})_2]^{2-}$	18.46 (18.52)	2.30 (2.31)	10.78 (10.80)	47.10 (47.28)	0.28

^aCalculated values in parentheses



[M = Mo(IV) or W(IV) and L = N-alkylphenothiazine]

Figure 1. Structure of M(IV)-NAP complexes.

quite stable for long periods. They exhibit low magnetic moments in accordance with dimeric M(IV)-NAP complexes due either to spin-spin interaction or to direct metal-metal bond. The analytical and magnetic data of the complexes given in table 5 show that there is no significant change in the composition or structure of the substituted products. The infrared spectra of these molybdenum complexes contain strong bands at 972–932 cm^{-1} and those of the tungsten complexes at 974–952 cm^{-1} , which are assigned to the stretching vibration of the M=O bond. The bridged vibrations of the MO_2M group occur at 750–742 cm^{-1} and 460–432 cm^{-1} for molybdenum complexes and at 810–794 cm^{-1} and 436–422 cm^{-1} for tungsten complexes. The presence of the coordinated water molecules is confirmed by the broad bands in the 3460–3320 cm^{-1} region. All these Mo(IV) complexes exhibit medium intense bands at 3240–3218 cm^{-1} and at 1654–1588 cm^{-1} due to NH_2 and COO stretching modes respectively. Similarly, for W(IV) complexes, these modes were observed at 3280–3218 cm^{-1} and at 1645–1580 cm^{-1} respectively. The above assignments are in good agreement with those of some metal-amino acid complexes^{2,3,21,22}.

4. Conclusion

Based on the above discussions, we propose the structure shown in figure 1 for the M(IV)-NAP complexes.

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