

Synthesis and fungicidal activity of the complexes of *N*-alkylphenothiazines with titanium(IV) and zirconium(IV)

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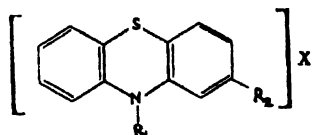
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Complexes of the type $[\text{Ti}(\text{C}_2\text{O}_4)_2\text{L}]\cdot 2\text{H}_2\text{O}$ and $[\text{Zr}(\text{NO}_3)_4\text{L}]$, where L = *N*-alkylphenothiazines, have been synthesized. The coordination behavior of the ligands has been determined. The fungicidal activity of the complexes has been evaluated.

In continuation of our work¹, we now report the synthesis, characterization and fungicidal activity on the complexes of titanium(IV) and zirconium(IV) with methoxypromazine (MP), prochlorperazine (PCP) and trifluoperazine (TFP).



	R ₁	R ₂	X
Methoxypromazine maleate (MPM)			
10-[3-(Dimethylamino)propyl]-2-methoxyphenothiazine maleate	(CH ₂) ₃ N(CH ₃) ₂	OCH ₃	C ₄ H ₄ O ₄
Prochlorperazine dimaleate (PCPD)			
10-[3-(4-Methyl-1-piperazinyl)propyl]-2-chlorophenothiazine dimaleate	(CH ₂) ₃ C ₄ H ₈ N-CH ₃	Cl	2C ₄ H ₄ O ₄
Trifluoperazine hydrochloride (TFPH)			
10-[3-(4-Methyl-1-piperazinyl)propyl]-2-trifluoromethylphenothiazine hydrochloride	(CH ₂) ₃ NC ₄ H ₈ N-CH ₃	CF ₃	HCl

Results and Discussion

The interaction of potassium titanyl oxalate dihydrate or zirconium nitrate with *N*-alkylphenothiazines in the form of maleate or hydrochloride in aqueous medium yields titanium(IV) or zirconium(IV) complexes. The maleate and chloride ions of the ligand go into solution during the reaction and do not participate in coordination with metal ions.

The analytical data of the complexes suggest a general formula $[\text{M}(\text{C}_2\text{O}_4)_2\text{L}]\cdot 2\text{H}_2\text{O}$ for titanium(IV) and $[\text{M}(\text{NO}_3)_4\text{L}]$ for zirconium(IV) complexes (where, L = methoxypromazine, prochlorperazine or trifluoperazine). The complexes are coloured, non-hygroscopic and stable at room temperature. They are soluble in DMF and DMSO and insoluble in water and common organic solvents. They

do not possess sharp melting points. The molar conductances are 10.2–12.4 and 26.5–38.9 $\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ for Ti-NAP and Zr-NAP complexes, respectively, indicating their non-electrolytic nature. The magnetic susceptibility values indicate that the complexes are diamagnetic. These results are consistent with the stoichiometry proposed for the complexes on the basis of analytical data.

Electronic spectra : The electronic spectra of the complexes show bands at the 404–414 nm for Ti^{IV} and 425–440 nm for Zr^{IV} complexes which may be assigned to charge transfer transition². The band at 250–265 nm found in the NAP and the corresponding titanium complexes may be attributed to $\pi \rightarrow \pi^*$ transition. However, this band is not observed in the spectra of the Zr complexes. The band at 300–320 nm in the free ligands may be assigned to the $n \rightarrow \pi^*$ transition. This band is found slightly shifted towards higher energy region in the spectra of the corresponding complexes evidently due to coordination.

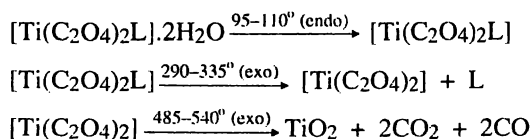
Infrared spectra : It was reported³ that the ions R₃N⁺H combine with Cl⁻ ion present in *N*-alkylphenothiazines giving rise to a broad band at 2500–2300 cm⁻¹. A broad band observed at 2600–2350 cm⁻¹ in the free ligands corresponds to the $-(\text{CH}_2)_2\text{N}^+\text{H}(\text{CH}_3)$ in MPM, $-(\text{CH}_2)_3\text{HN}^+-\text{C}_4\text{H}_8\text{N}-\text{CH}_3$ in PCPD and TEPH combined with X⁻ anion (X⁻ = maleate or chloride). This band is absent in the spectra of the corresponding Ti^{IV} and Zr^{IV} complexes, showing that the tertiary nitrogen atom of the side-chain is a site of coordination. In far-IR region, the complexes exhibit new bands at 540–525 (Ti-N)⁴ and 545–530 cm⁻¹ (Zr-N)⁵.

In aromatic derivatives ν_{CSC} generally appears as a weak or moderate intensity band in 705–670 cm⁻¹ region⁶. However, some difficulty is experienced in recognising the

ν_{CSC} mode in *N*-alkylphenothiazines due to the presence of the intense CH out-of-plane deformation band in this region⁷. In all the complexes studied, ν_{CSC} suffers a significant positive shift by 10–30 cm^{-1} . This is attributed to coordination from sulfur atom. This is supported by the band at 335–325 (Ti-S)⁴ for Ti^{IV} and 340–330 cm^{-1} (Zr-S)⁵ for Zr^{IV} complexes. This supports the fact that sulfur atom present in the NAP ring is the second site of coordination. The coordination of the bidentate oxalate is confirmed by the bands at 1700–1680 (asymmetric COO) and 1400–1380 cm^{-1} (symmetric COO)⁸ for the Ti^{IV} complexes. The absence of bands at 1360 and 830 cm^{-1} for the Zr^{IV} complexes indicates the absence of ionic nitrate. The small separation (20–30 cm^{-1}) of the coordination bands ($\nu_1 + \nu_4$) at 1800–1700 cm^{-1} and the bands at 1480–1450, 1260–1230 and 760–740 cm^{-1} confirm the monodentate nature of nitrate groups².

¹H NMR spectra : ¹H NMR spectra of titanium and zirconium complexes recorded in CDCl_3 and $\text{DMSO-}d_6$, respectively, exhibit chemical shifts at lower fields for N-CH_3 protons which appears at δ 2.75–2.95 for the Ti and 2.75–2.85 for the Zr complexes compared with the free ligands (δ 2.55–2.70), probably due to the coordinating effect of tertiary nitrogen atom which results in the deshielding of the protons attached to it. These studies confirm the participation of the tertiary nitrogen atom of the alkyl side-chain of NAP in coordination. The integrated proton ratios correspond to the proposed formula.

Thermogravimetric studies : The studies of the titanium complexes indicate the decomposition in three steps, i.e. the loss of water molecules, decomposition of organic moiety and the loss of oxalate followed by the formation of TiO_2 in the temperature ranges 85–155°, 180–380° and 400–545°, respectively. The intermediates were identified by mass-loss. The differences between found and calculated mass-losses lie in the range 0.2–0.9%. The decomposition scheme of $[\text{Ti}(\text{C}_2\text{O}_4)_2\text{L}]\cdot 2\text{H}_2\text{O}$ in air and DTA peak temperatures for each step are as follows :



In case of the zirconium complexes, the decomposition starts at 185–225°, slow in the beginning but rapid afterwards. As the decomposition was complete in one step without involving distinct stages, intermediates were not isolated. All the complexes attained constant weight in the temperature range 485–600°. The weight-loss observed in each case was in good agreement with that calculated on the

basis of the stoichiometry assumed for the complexes. The thermal data, thus give further support to the formula assumed for the complexes.

Antifungal activity : Antifungal activity was tested against *Aspergillus flavus* and *Alternaria tenuis* at 0.01 and 0.25% concentrations by the poisoned food technique⁹. The results reveal that the titanium complexes exhibit 5 and 4 times greater fungitoxicity with respect to *A. flavus* and *A. tenuis* than potassium titanyl oxalate and the free ligands and the zirconium complexes exhibit 4 and 3 times greater toxicity than zirconium nitrate and the free ligands, respectively. Further, the studies indicate that the fungitoxicity of the complexes increases with increase in concentration of the fungi.

Experimental

Potassium titanyl oxalate dihydrate, zirconium nitrate, methoxypropazine maleate, prochlorperazine dimaleate (Rhone poulenc) and trifluoperazine hydrochloride (Bayers A.G. Lever-kusen) were used. The purity of the NAP ligands was checked by volumetric estimation using ceric sulfate⁹. Ether, DMF and DMSO were of AnalaR grade.

Preparation of the complexes : Aqueous solutions (60 ml) of *N*-alkylphenothiazines (1 mmol) were added separately to aqueous solution (50 ml) of potassium titanyl oxalate dihydrate (1 mmol) with stirring. The complexes formed were set aside for 1 h, then filtered, washed with water and ether and dried under reduced pressure over fused CaCl_2 . The complexes of zirconium were prepared in a similar manner by adding aqueous solutions (150 ml) of *N*-alkylphenothiazines (1 mmol) to aqueous solution (120 ml) of zirconium nitrate (1 mmol) containing 1 *M* sulfuric acid (5–10 ml).

C, H and N were determined with a Carlo-Erba 1106 analyzer. Molar conductance was measured in 10^{-3} DMF solutions using an Elico CM-82T conductivity bridge. IR spectra (KBr) were recorded on a Shimadzu FTIR 470 spectrophotometer, ¹H NMR spectra on a Hitachi R-600 spectrometer and electronic spectra (DMF) on a Jasco-UVIDEC-610 spectrophotometer. Magnetic susceptibility was determined by Gouy method at room temperature using $\text{Hg}[\text{Co}(\text{SCN})_4]$ as calibrant. Thermal analysis was carried out on a Rigaku-TAS-100 instrument with a linear heating rate of 10° min^{-1} in static air.

Acknowledgement

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