



Bis (Cyclopentadienyl) titanium (IV) derivatives with isatin-2,3-Bis-Thiosemicarbazones

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ABSTRACT

A series of bis (cyclopentadienyl) titanium(IV) derivatives with isatin-2,3-bis-thiosemicarbazones have been synthesized. The complexes were characterized by analysis, electrical conductance, magnetic moment and spectral (UV-Vis, IR and ¹H NMR) data, The antibacterial activity of the ligands and complexes were evaluated against Gram-positive Bacillus subtilis and Gram-negative Escherichia coli.

Keywords : Titanium, UV-Vis, IR, Antibacterial activity

Introduction

The potential antitumor, antibacterial, antiviral, fungicidal, antimalarial and anticancer activities of thiosemicarbazones and their metal complexes have encouraged the study of the coordination chemistry of these ligands.¹⁻⁸ A number of papers have appeared on coordination behavior of isatin-3 and isatin-2 thiosemicarbazones. Their coordination behavior depends upon the pH of the medium, the nature of the substituents and the metal ion. However very few reports are available on coordination behavior of isatin-2,3-Bis thiosemicarbazones.

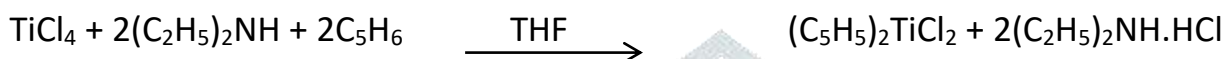
The present paper describes the synthesis and characterization of Bis (cyclopentadienyl) titanium (IV) derivatives with isatin-2,3, Bis-thiosemicarbazones.

Materials and methods

All the organic solvents used were of “Analytical Reagent” grade.

Preparation of bis(cyclopentadienyl) titanium (IV) chloride

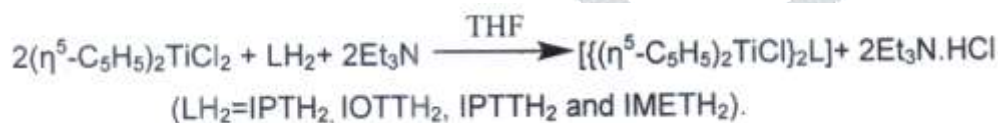
Bis(cyclopentadienyl) titanium (IV) chloride was prepared by the reaction of titanium tetrachloride with cyclopentadiene in the presence of diethylamine and tetrahydrofuran.



Titanium tetrachloride (60.0g) was added to tetrahydrofuran (300 cm³) and cyclopentadiene (120 cm³) was added. The reaction mixture was refluxed at (60-65 °C) for 8 h, cooled and filtered. The precipitate, which was mixture of bis(cyclopentadienyl) titanium(IV) dichloride and diethylaminehydrochloride was washed with tetrahydrofuran followed by petroleum ether at (40-60 °C). The precipitate so obtained, was added to 4N HCl (200 cm³) and the resulting slurry was stirred for ten minutes and filtered. The bis(cyclopentadienyl)titanium(IV) dichloride was washed with ice water and dried. The crude product was crystallized from chloroform. Yield : 82 %.

Results and Discussion

A systematic study of the reaction of bis(cyclopentadienyl)titanium(IV) dichloride with isatin-2,3-bis(thiosemicarbazone) in anhydrous tetrahydrofuran in the presence of Et₃ may be represented by the following reaction:



R	Abbreviation
C ₆ H ₅	IPTH ₂
(2-Me)C ₆ H ₄	IOTTH ₂
(4-Me)C ₆ H ₄	IPTTH ₂
(OMe)C ₆ H ₄	IMETH ₂

The above reaction is quite facile and the resulting complexes have been isolated in almost quantitative yields. The methods used for the preparation and isolation of these compounds give materials of good purity, as supported by their analysis and TLC. All these compounds are colored solid, soluble in tetrahydrofuran, dimethylformamide and dimethylsulphoxide. The electrical conductance measurements show that the complexes are non-electrolytes. Magnetic susceptibility measurements show that they are diamagnetic.

Electronic Spectra

The electronic spectra of the complexes show a single band in the region 465-438 nm, which can be assigned to the charge transfer band and is in accordance with an $(n-1)d^0ns^0$ electronic configuration. One more band is observed at ca. 286-312 nm, which is due to intra-ligand transition.

Infrared Spectra

The infrared spectral bands of ligands and titanium(IV) complexes are listed in Table 1. Isatin-2,3-bis(thiosemicarbazones) can exist either as thione or thiol tautomeric forms or as an equilibrium mixture of both forms, since they have a thioamide, $-NH-C(=S)$ function. The infrared spectra of thiosemicarbazones in the solid state do not show any $\nu(S-H)$ band but exhibit a medium $\nu(N-H)$ [at (2) or (2')] band at ca. 3200 cm^{-1} , indicating that, in the solid state, they remain mainly in the thione form. However, in solution (basic medium) they readily convert to the thiol tautomeric form with concomitant formation of the titanium(IV) complexes of the protonated mercapto form of the ligands. This is indicated by the absence of $-NH$ band in the complexes. The IR spectra of the complexes also show a new band at ca. 620 cm^{-1} , owing to the conversion of $C=S$ to $C-S$. The band in the complexes at ca. $375-385\text{ cm}^{-1}$ assigned to $\nu(Ti-S)$ shows that sulphur is bonded to the metal atom. The $\nu(C=N)$ shift to the thiosemicarbazone ligands from $1585-1600\text{ cm}^{-1}$ to lower energy in the spectra of the complexes indicates¹¹ the coordination of two imine nitrogens (3 and 3'). However, the $N^{(2,2')}=C(S)$, indicated by the appearance of a weak band at ca. 1615 cm^{-1} in the spectra of the complexes. Bands in the $450-465\text{ cm}^{-1}$ region are assigned to $\nu(Ti-N)$ and support coordination of both the imine nitrogens¹². In addition, the spectra of thiosemicarbazones show two bands at ca. 3180 cm^{-1} and 3150 cm^{-1} , assignable to $\nu(N-H)$ (at 1 or 1') and $\nu(N-H)$ of isatin moiety respectively. These bands remain almost at the same position in the spectra of the complexes, suggesting non-coordination of these two (N-H) groups to metal ion.

Absorption bands occurring at ca. 3000 cm^{-1} for $\nu(\text{C-H})$, CA. 1420 cm^{-1} for $\nu(\text{C-C})$ and ca. 1010 and 810 cm^{-1} for $\nu(\text{C-H out of plane deformation})$ in the complexes are due to the cyclopentadienyl ring. These bands are similar to those reported for bis(cyclopentadienyl)titanium(IV) dichloride and their appearance indicates that the ($\eta^5\text{-C}_6\text{H}_5$) group persist in the complexes.

Proton Magnetic Resonance Spectra

The Proton Magnetic Resonance Spectra of the complexes (Table. 2) have been recorded in deuterated dimethylsulphoxide. Coupling between various groups complicates the spectra, but a comparison of the spectra of the ligands with those of the complexes can lead to the following conclusions :

1. The 6.65-6.80 signals may be assigned to the cyclopentadienyl ring protons and indicate the rapid rotation of the ring about the metal ring axis.
2. The signal of $\text{N}^{(2)}\text{H}$ is seen at ca. 7.0, in isatin-2,3-bis(thiosemicarbazones), which disappears in their corresponding complexes.
3. The signal due to $-\text{NH}$ proton of isatin ring appears at ca. 4.45 in the ligands, which also persists in the complexes.
4. The chemical shift due to the aromatic ring appears at ca. 7.60-8.50ppm, which slightly shifts downfield in the complexes. This may be due to the decrease in electron density after forming the complex.

^{13}C NMR Spectra

^{13}C NMR spectra of the complexes were recorded in DMSO and described in Table 3. The following are the salient features :

1. The peak due to cyclopentadienyl groups appears at ca. 116 (relative to TMS).
2. The ligands show thioamide-C signal at ca. 180. In the complexes, this signal is at significantly at higher field which is due to enolization of thione group and formation of new azomethine linkage.
3. The ligands show signals at ca. 150 and 145 due to two azomethine-Cs(C-2 and C-3) in the ligands. These signals undergo downfield shift, indicating coordination of both the azomethine nitrogens to metal.
4. For aromatic ring, a number of signals appear.

Thus, the above studies suggest that two thiol sulphur atoms and two azomethine nitrogen atoms of the ligands are involved in the chelation. Casas et al¹³ studied the reactions of SnMe_2O with identical isatin-2,3-bis(thiosemicarbazone) ligands are reported spectral

Table 1: Infrared spectral bands of isatin-2, 3-bis(thiosemicarbazones) and their bis(cyclopentadienyl)titanium(IV) derivatives

Ligand/ complex	Data cm ⁻¹
IPTH ₂	3200m, 3180m, 3150s, 2980w, 2850w, 1585m, 1460w, 1360m, 1160s, 980w, 840w, 720m, 640w
IOTTH ₂	3210m, 3175m, 3145s, 2985w, 2860w, 1600m, 1520w, 1450w, 1360m, 1320w, 1150s, 940w, 820w, 740w, 650w .
IPTTTH ₂	3200m, 3170m, 3140s, 2980w, 2840w, 1595m, 1510w, 1460w, 1350m, 1310w, 1165s, 960w, 850w, 720m, 640w, 520w
IMETH ₂	3205m, 3180m, 3150s, 2950w, 2820w, 1600m, 1450w, 1350s, 1240w, 1160s, 950w, 860w, 710m, 650w
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IPT)]	3185m, 3150s, 3000m, 2980w, 2850w, 1615w, 1565m, 1460w, 1420m, 1360m, 1010m, 955w, 840w, 810m, 710m, 640w, 620m, 450m, 375m
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IOTT)]	3175m, 3145s, 3010m, 2985w, 2860w, 1620w, 1575m, 1520w, 1455w, 1410m, 1365m, 1320w, 1000m, 945w, 820w, 800m, 750w, 610m, 460m, 380m
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IPTT)]	3170m, 3140s, 3005m, 2980w, 2840w, 1618w, 1570m, 1510w, 1460w, 1415m, 1360m, 1310w, 1015m, 950w, 850w, 810m, 720m, 640w, 625m, 520w, 455m, 385m
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IMET)]	3180m, 3150s, 3000m, 2950w, 2820w, 1615w, 1580m, 1450w, 1420m, 1355s, 1240w, 1010m, 950w, 860m, 805m, 710m, 650m, 615m, 465m, 380m



Where,

IPTH₂ = (2Z)-2, 2'-(indoline-2, 3-diylidene)-bis (N-phenyl hydrazine carbothioamide)

IOTTH₂ = (2Z)-2, 2'-(indoline-2, 3-diylidene)-bis (N-*o*-tolyl hydrazine carbothioamide)

IPTTTH₂ = (2Z)-2, 2'-(indoline-2, 3-diylidene)-bis (N-*p*-tolyl hydrazine carbothioamide)

IMETH₂ = (2Z)-2, 2'-(indoline-2, 3-diylidene)-bis [N-(2-methoxyphenyl) hydrazine carbothioamide]

Table 2: ¹H-NMR spectral bands (δ, ppm) of bis(cyclopentadienyl)titanium(IV) derivatives with isatin-2, 3-bis(thiosemicarbazone)

Complexes	N ^{1H} -H	η ⁵ -C ₅ H ₅	N-H isatin	Aromatic ring
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IPT)]	10.70 s	6.85 s	4.42 s	7.75-8.05 m
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IOTT)]	10.65 s	6.80 s	4.50 s	7.65-7.95 m
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IPTT)]	10.60 s	6.82 s	4.45 s	7.60-8.50 m
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IMET)]	10.62 s	6.70 s	4.40 s	7.70-8.25 m

Where,

IPTH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis (N-phenyl hydrazine carbothioamide)

IOTT₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis (N-o-tolyl hydrazine carbothioamide)

IPTT₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis (N-p-tolyl hydrazine carbothioamide)

IMETH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis [N-(2-methoxyphenyl) hydrazine carbothioamide]

Applications

**Table 3.** ¹³C-NMR spectral bands (δ, ppm) of bis(cyclopentadienyl)titanium(IV) derivatives with isatin-2, 3-bis(thiosemicarbazone)

Complexes	η ⁵ -C ₅ H ₅	(C-10)	(C-2, C-3)	Aromatic ring
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IPT)]	116.2	165	150.1, 152.8	146.8, 139.2, 134.5, 131.5, 129.8, 128.7, 125.3, 123.2, 120.5, 118.8, 117.5, 115.0
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IOTT)]	116.2	160	154, 152	148.2, 140.5, 135.6, 130.8, 130.2, 129.8, 125.2, 124.8, 120.4, 117.5, 115.6
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IPTT)]	115.5	162	156, 154	147.8, 136.2, 133.8, 131.5, 129.8, 129.5, 125.2, 124.2, 120.6, 118.6, 117.8, 115.2
[[[(η ⁵ -C ₅ H ₅) ₂ TiCl] ₂ (IMET)]	116.2	164.8	151.6, 153.4	158.8, 148.2, 135.2, 131.6, 129.8, 126.3, 125.8, 123.2, 121.0, 118.5, 117.8, 115.2

Where,

IPTH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis(N-phenyl hydrazine carbothioamide)

IOTT₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis(N-o-tolyl hydrazine carbothioamide)

IPTT₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis(N-p-tolyl hydrazine carbothioamide)

IMETH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis[N-(2-methoxyphenyl) hydrazine carbothioamide]

antibacterial activity was evaluated by the paper-disc plate method. The antibacterial activity was focused against two bacteria, viz, Gram-positive *Bacillus subtilis* and Gram-negative *Escherichia coli*. The results (Table.4) show that activity increases on chelation. The activity of the ligands is affected by the nature of substituent¹⁴⁻¹⁵. This in relation to the lipophilicity of the ligands and their membrane permeability, a key factor in determining their entry inside the cell. The results lead to following conclusions :

1. The complexes are slightly more toxic than the parent ligands.
2. The presence of chloro / methoxy group at the phenyl ring of the ligands increases the antibacterial activity of the derivatives.
3. The compounds exhibit a better effect on the Gram-negative form.

Table 4: Antibacterial activity of isatin-2, 3-bis (thiosemicarbazones) and their bis(cyclopentadienyl)titanium(IV) derivatives

Ligand / compound	Diameter of inhibition zone (mm)	
	<i>B. subtilis</i> (Gram +ve)	<i>E. coli</i> (Gram -ve)
IPTH ₂	5	7
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IPT)]	9	12
IOTTH ₂	3	5
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IOTT)]	6	10
IPTHH ₂	4	6
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IPTT)]	8	11
IMETH ₂	7	10
[[$(\eta^5\text{-C}_5\text{H}_5)_2\text{TiCl}$] ₂ (IMET)]	12	19
Streptomycin (standard)	20	32

Where,

IPTH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis (N-phenyl hydrazine carbothioamide)

IOTTH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis (N-o-tolyl hydrazine carbothioamide)

IPTHH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis (N-p-tolyl hydrazine carbothioamide)

IMETH₂ = (2Z)-2, 2'-(indoline-2, 3-diyldiene)-bis [N-(2-methoxyphenyl) hydrazine carbothioamide]

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