

# SYNTHESIS AND CHARACTERIZATION OF MIXED DITHIOCARBAMATE-CYCLOPENTADIENYL COMPLEXES CONTAINING Ti(IV)

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## ABSTRACT

Complexes of the type  $[\text{Cp}_2\text{Ti}(\text{pddtc})\text{Cl}]$ ,  $[\text{Cp}_4\text{Ti}_2\{\text{pz}(\text{dtc})_2\}\text{Cl}_2]$ , where  $[\text{pz}(\text{dtc})_2]$  = piperazine bisdithiocarbamate,  $[\text{pddtc}]$  = piperidinedithiocarbamate, Cp = cyclopentadienyl have been synthesized and characterized by elemental analyses, IR, electronic,  $^1\text{H}$ NMR spectral data and conductivity measurements. The spectroscopic evidence suggests that both the complexes have five coordinate geometry around the metal ion. The conductivity measurements data (1mmol solution) implies non-electrolytic behavior for both the complexes as evident by their low conductivity values obtained at room temperature. A symmetrical bidentate coordination has been observed for the dithiocarbamate moiety rendering the metal five coordinate.

## KEYWORDS

Titanocene dichloride, spectroscopic measurements, dithiocarbamate,

## INTRODUCTION

The chemistry of the metallocene dihalides ( $\text{Cp}_2\text{TiCl}_2$ ) has attracted significant interest since its antitumor activity was first reported by Kopf and Kopf-Maier.[1]  $\text{Cp}_2\text{TiCl}_2$  is the first non-platinum metal complex to enter clinical trials.[2-4] It has been confirmed that non-platinum complexes may offer significant benefits in chemotherapy.[5-6] DNA has been implicated as the principal cellular target of  $\text{Cp}_2\text{TiCl}_2$  in vivo, as the complex induces significant and pronounced inhibition of nucleic acid synthesis.[7] Titanium is found in the nucleic acid rich regions of solid Ehrlich Ascites tumor cells which have been treated with a complex containing titanium metal.[8] However, complete structural characterization of the mode of interaction of  $\text{Cp}_2\text{TiCl}_2$  with DNA has not been possible, mainly due to the hydrolytic instability of  $\text{Cp}_2\text{TiCl}_2$  at physiological pH.[9-10] Several efforts have been made to facilitate the synthesis of planar, chiral cyclopentadienyl metal complexes in terms of their potential as mediators or catalyst in asymmetric organic synthesis.[11] In fact, planar, chiral cyclopentadienyl group IV metal complexes were successfully used as catalysts in asymmetric organic synthesis and polymerization.[12]

Dithiocarbamates are known to inhibit the growth of bacteria and fungi.[13] Since the activity of the ligand is altered in the presence of metal ions it was thought worthwhile to study metal complexes of piperidine dithiocarbamate and piperazine bisdithiocarbamates that contain cyclopentadienyl group.

## Experimental

Titanocene (Merck), piperazine, piperidine,  $\text{CS}_2$  (Fluka) and THF (Merck), were used as received. Elemental analyses (C, H, N, S) were carried out with a 1106 Carlo Erba analyzer. The metals were determined by complexometric titration using EDTA and chlorine was determined gravimetrically. The IR spectra ( $4000\text{-}500\text{ cm}^{-1}$ ) were recorded on an Agilent technologies spectrometer using KBr discs. The conductivity measurements were carried out with a Systronics conductivity bridge in chloroform (Table I). The electronic spectra were recorded on a Cintra 5GBC spectrophotometer in  $\text{CHCl}_3$ .  $^1\text{H}$  NMR spectra were recorded on a Bruker ACF 300 spectrometer at 300.12 MHz, using TMS as a reference in  $\text{DMSO-d}_6$ .

### Synthesis of sodium salt of piperidine dithiocarbamate Na(pddtc) where pd = piperidine and dtc = dithiocarbamate

To a methanolic solution (50 ml) of piperidine (1.0 ml, 10 mmol) carbon disulfide (0.61 ml, 10 mmol) was added dropwise with continuous stirring in an ice bath followed by the addition of NaOH (0.4 g, 10 mmol) dissolved in minimum amount of aqueous methanol. The product obtained was filtered, washed with aqueous methanol and dried over phosphorous pentoxide in vacuo.

### Synthesis of sodium salt of piperazine bisdithiocarbamate Na[(pz)(dtc)<sub>2</sub>] where pz = piperazine and dtc = dithiocarbamate

To a methanolic solution (50 ml) of piperazine (0.861 g, 10 mmol) carbon disulfide (1.22 ml, 20 mmol) was added dropwise with continuous stirring in an ice bath followed by the addition of NaOH (0.8 g, 20 mmol) dissolved in minimum amount of aqueous methanol. The product obtained was filtered, washed with aqueous methanol and dried over phosphorous pentoxide in vacuo.

### Synthesis of [Ti(C<sub>5</sub>H<sub>5</sub>)<sub>2</sub>(pddtc)Cl] where pd = piperidine and dtc = dithiocarbamate

A solution of the sodium salt of piperidine dithiocarbamate (5 mmol) in THF (20 mL) was treated with 20 mL of a THF solution of (Cp)<sub>2</sub>TiCl<sub>2</sub> (5 mmol, 1.24 g) in a 100 ml round bottomed flask. The mixture was continuously stirred over a period of half an hour at room temperature. The precipitates thus obtained was filtered, washed with diethyl ether, recrystallized from CHCl<sub>3</sub> and dried in vacuo. Yield 51%

### Synthesis of [Ti<sub>2</sub>(C<sub>5</sub>H<sub>5</sub>)<sub>4</sub>{pz(dt<sub>2</sub>)Cl<sub>2</sub>] where pz = piperazine and dtc = dithiocarbamate

A solution of the sodium salt of piperazine bisdithiocarbamate (5 mmol) in THF (20 mL) was treated with 20 mL of a THF solution of (Cp)<sub>2</sub>TiCl<sub>2</sub> (5 mmol, 1.24 g) in a 100 ml round bottomed flask. The mixture was continuously stirred over a period of half an hour at room temperature. The precipitates thus obtained was filtered, washed with diethyl ether, recrystallized from CHCl<sub>3</sub> and dried in vacuo. Yield 47%

### RESULTS AND DISCUSSION

The reactions of the Cp<sub>2</sub>TiCl<sub>2</sub>, with the sodium salts of piperidine dithiocarbamate (pddtc) and piperazine bisdithiocarbamate {pz(dt<sub>2</sub>)} yield [Cp<sub>2</sub>Ti(pddtc)Cl] and [Cp<sub>4</sub>Ti<sub>2</sub>{pz(dt<sub>2</sub>)Cl<sub>2</sub>}] respectively. They are formed by the replacement of chloride ions by dithiocarbamates according to the schemes shown in Figures 1-2.

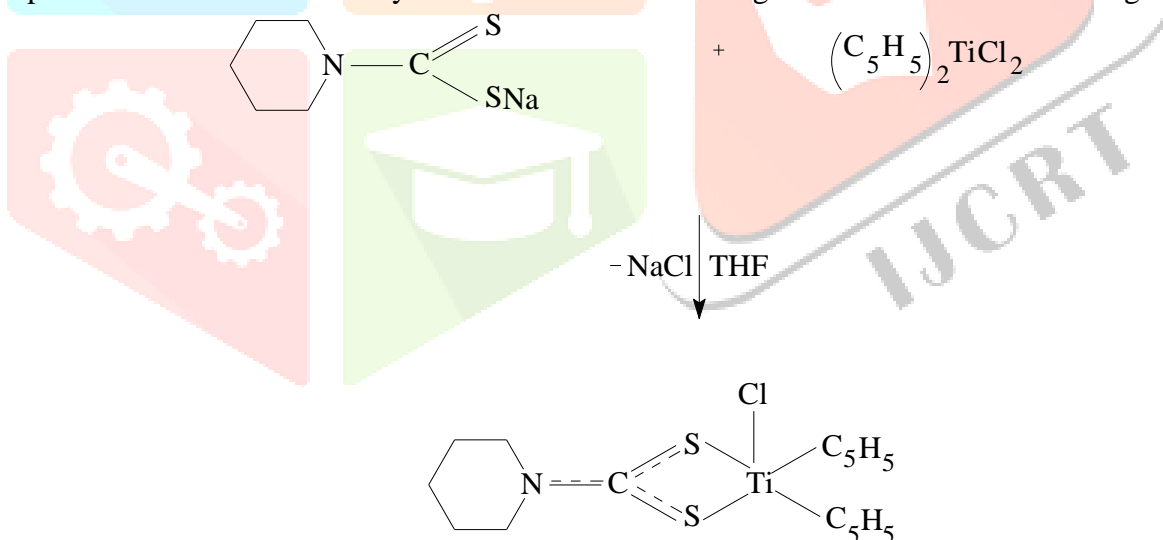


Fig.1. Synthesis of [Ti(C<sub>5</sub>H<sub>5</sub>)<sub>2</sub>(pddtc)Cl]

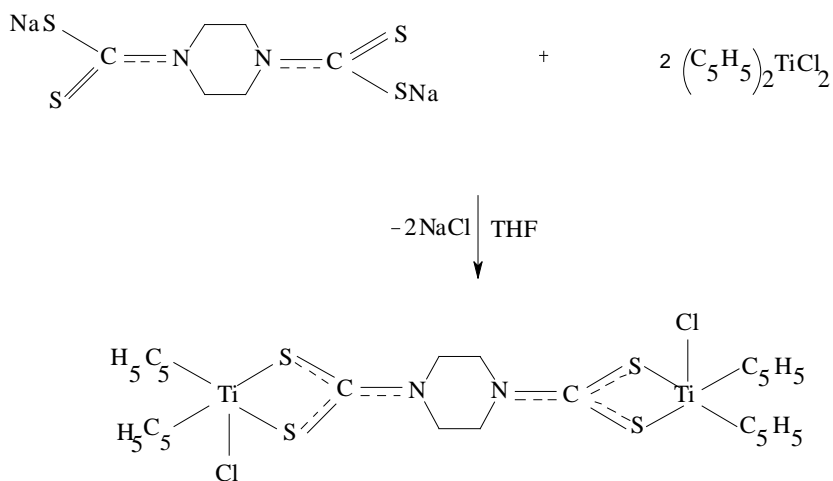


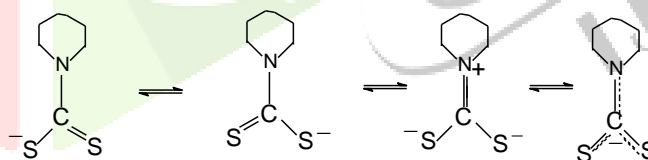
Fig.2. Synthesis of  $[\text{Ti}_2(\text{C}_5\text{H}_5)_4\{\text{pz}(\text{dtc})_2\}\text{Cl}_2]$

The molar conductance of the complexes measured in DMF ( $17\text{-}18 \text{ ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ ) indicate that they are non-electrolytes. [14]

### IR spectra

The IR spectral region  $3300\text{-}3500 \text{ cm}^{-1}$  of all the complexes, is devoid of any absorption indicating the absence of N–H groups.[15] Attempts have been made to deduce the denticity of piperazine bisdithiocarbamate and piperidine dithiocarbamate using  $\nu(\text{C}-\text{N})$  and  $\nu(\text{C}-\text{S})$ . The  $950\text{-}1050 \text{ cm}^{-1}$  region has been shown to be reliable for determining the mono or bidentate nature of the ligand. According to Brinkhoff and Grotenz,[16] the presence of only one strong C-S stretching vibration in the  $950\text{-}1050 \text{ cm}^{-1}$  region, is indicative of bidentate bonding of the dithiocarbamate ligand, while bonding is unidentate if this peak splits into two closely spaced bands. In the IR spectra of all the complexes, a strong absorption band is observed around  $1000 \text{ cm}^{-1}$  suggesting the bidentate nature of the piperidine and piperazine bisdithiocarbamate rendering the metal five coordinate. A similar five coordinate organozirconium dithiocarbamate has been reported.[16]

The thioureide bands appeared between  $1420$  and  $1490 \text{ cm}^{-1}$ , range which is intermediate between  $\nu(\text{C}=\text{N})$  and  $\nu(\text{C}-\text{N})$  indicating a partial double bond character between carbon and nitrogen. In all the complexes bands in the range of  $513\text{-}515 \text{ cm}^{-1}$  are observed which may be assigned to a coordinated chloro group.[17] New absorption bands were also observed in complexes in the region  $555\text{-}574 \text{ cm}^{-1}$  and are assigned to Ti-S stretching frequencies.[18]



### UV-Vis Spectra

The electronic spectra of all the complexes were recorded in  $\text{CHCl}_3$ . The UV spectra of dithiocarbamate exhibited two bands in the range of  $250$  to  $290 \text{ nm}$  due to the  $\pi - \pi^*$  transition of the N-C-S groups and a  $n - \pi^*$  transition involving the lone pairs of electrons located on the sulfur atoms. These bands are shifted to higher wavelength after complexation, showing the involvement of NCS<sub>2</sub> group in coordination.

### <sup>1</sup>H NMR Spectra

The <sup>1</sup>H NMR spectra of  $[\text{pz}(\text{dtc})_2]$ ,  $[\text{pddtc}]$ ,  $[\text{Ti}(\text{C}_5\text{H}_5)_2(\text{pddtc})\text{Cl}]$  and  $[\text{Ti}_2(\text{C}_5\text{H}_5)_4\{\text{pz}(\text{dtc})_2\}\text{Cl}_2]$  were recorded in DMSO-*d*<sub>6</sub>. In the free  $[\text{pz}(\text{dtc})_2]$ , a single proton signal at  $\delta 3.2$  corresponding to the piperazine moiety (8H, s) was observed. On complexation with  $[\text{Ti}(\text{Cp})_2\text{Cl}_2]$ , the singlet slightly shifts to  $\delta 3.7$  indicating the formation of the complex. The resonances due to the cyclopentadienyl protons were found as a multiplet between  $\delta 7.3$  and  $7.7$ .

Depending on the chemical environment of the protons in  $[\text{pddtc}]$  three signals were envisaged. They were found at C<sub>1</sub> (4H, br) at  $\delta 2.73$ , C<sub>2</sub> (4H, q) at  $\delta 1.54$  and C<sub>3</sub> (2H, q) at  $\delta 1.47$ . On complexation with  $[\text{Cp}_2\text{TiCl}_2]$ , all these three peaks slightly shift to  $\delta 3.27$  (4H, br, C<sub>1</sub> and C<sub>1'</sub> protons),  $\delta 1.79$  (4H, q, C<sub>2</sub> and C<sub>2'</sub> protons) and  $\delta 1.57$  (2H, q, C<sub>3</sub> protons) in  $[\text{Ti}(\text{C}_5\text{H}_5)_2(\text{pddtc})\text{Cl}]$  indicating the formation of complex. The resonances due to the cyclopentadienyl protons were found as a multiplet between  $\delta 7.1$  to  $7.7$ .

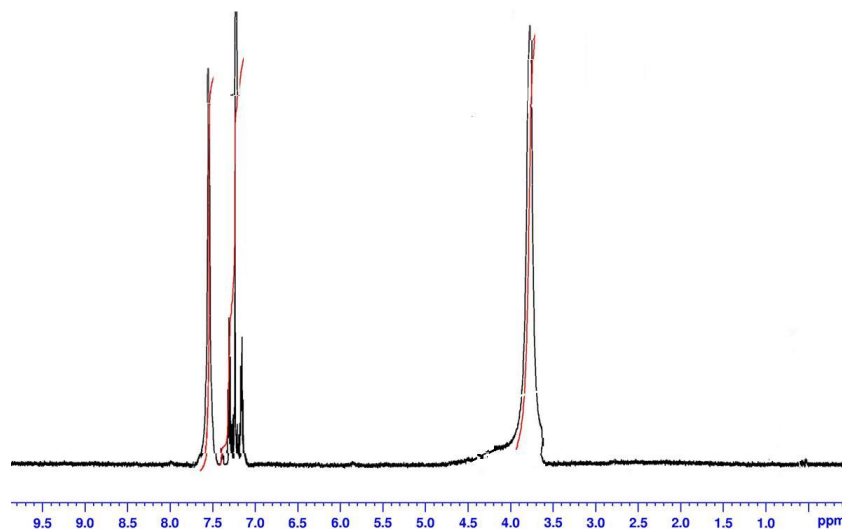


Fig.3.  $^1\text{H}$  NMR spectrum of  $[\text{Cp}_4\text{Ti}_2\{\text{pz}(\text{dte})_2\}\text{Cl}_2]$

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Table I. Physical Properties and Analytical Data for Metal Chelates

	Compounds (Formula weight)	Yield (%)	Colour	M.p. (°C)	Molar conductance (ohm <sup>-1</sup> cm <sup>2</sup> mol <sup>-1</sup> )	% Analysis Found (Calcd).				
						C	H	N	S	Ti
(1)	[Ti(C <sub>5</sub> H <sub>5</sub> ) <sub>2</sub> (pddtc)Cl] (373.38)	51	Pale yellow	260 d	18	47.03 (47.32)	5.31 (5.56)	10.89 (11.04)	24.92 (25.27)	12.31 (12.82)
(2)	[Ti <sub>2</sub> (C <sub>5</sub> H <sub>5</sub> ) <sub>4</sub> {pz(dtc) <sub>2</sub> }Cl <sub>2</sub> ] (662.63)	47	Pale yellow	275 d	17	47.19 (46.97)	5.51 (5.52)	11.04 (10.95)	24.76 (25.05)	13.98 (14.44)

Table II. Important IR Bands (cm<sup>-1</sup>) of Ligands and their Metal Chelates

	Compounds	v(C-N)	v(C=S)	v(M-Cl)	v(M-S)
(1)	[Ti(C <sub>5</sub> H <sub>5</sub> ) <sub>2</sub> (pddtc)Cl]	1415(s)	991(s)	515	555
(2)	[Ti <sub>2</sub> (C <sub>5</sub> H <sub>5</sub> ) <sub>4</sub> {pz(dtc) <sub>2</sub> }Cl <sub>2</sub> ]	1432(s)	996(s)	513	574