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Certain new dicyclopentadienyl titanium complexes derived from sterically impeded heterocyclic beta-diketones and beta-diketones: Generation, spectroscopic characterization and structure- antimicrobial activity relationship

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Abstract

A set of new dicyclopentadienyl titanium complexes was generated by the reactions of titanocene dichloride with sterically impeded heterocyclic beta-diketones ($L_{(1)}H$=4-acetyl-2,4 dihydro-5-methyl-2-phenyl-3H-pyrazol-3-one, $L_{(2)}H$=4-propanoyl-2,4 dihydro-5-methyl-2-phenyl 3H-pyrazol-3-one and $L_{(3)}H$=4-(4-chloro)benzoyl-2,4 dihydro-5-methyl-2-phenyl 3H-pyrazol-3-one), beta-diketones ($L'_{(1)}H$=pentane-2,4-dione, $L'_{(2)}H$=1-phenylbutane-1,3-dione and $L'_{(3)}H$=1,3-diphenylpropane-1,3-dione) and triethylamine in 1:1:1:2 molar ratio in refluxing dry THF. Plausible structures of these newly generated complexes were suggested based on spectroscopic and mass studies. Some representative complexes were also screened for their antimicrobial activity.

Keywords: Titanocene complexes, Heterocyclic beta-diketones, Antimicrobial activity.

Introduction

The superior properties, technological applications[1,2] and biological relevance[3-5] of organic-inorganic hybrid materials have made new strides and important advances in the field of material chemistry. Organic-inorganic hybrid complexes of titanocene dichloride[6-7] constitute an important facet of the material chemistry[8] and these complexes were structurally characterized with the aid of spectroscopic studies[6,9,10], DFT[11-13]and single-crystal X-ray analysis[14-16]. A number of titanocene complexes are receiving attention due to their interesting structural chemistry[9] and wide range of applications in organic synthesis[7], olefin polymerization[17,18], catalysis[19,20], nanotechnology[21,22] and in the manufacture of new materials. Some titanocene complexes are associated with significant biological activities such as antitumor[3,4], antiviral[3], insecticidal[3] and antiinflammatory[3], etc. Heterocyclic β-diketones and β-diketones are excellent organic ligands owing to their coordination ability, interesting bonding modes and potential biological applications of their metal complexes[6,23-25].

β-Diketones demonstrate various pharmacological activities and also antioxidant potential. The structure-activity relationship[26] of titanocene complexes is an important concept which is used to correlate certain structural features of titanocene complexes with their biological activities. To study the antimicrobial activity, some titanocene complexes were generated by the reactions of titanocene dichloride with sterically impeded heterocyclic β-diketones and β-diketones in the presence of triethylamine.

Materials and methods

The sterically impeded heterocyclic β-diketones were generated by the reported method[27]. Titanocene dichloride and β-diketones were commercially available. Standard methods were used to dry the solvents. All the chemical reactions were carried out under strictly anhydrous conditions. Infrared spectra (4000-400 cm^{-1}) of the samples were recorded on SHIMADZU, FTIR 8400 spectrophotometer, and samples were prepared as KBr pellets. ^1H and ^{13}C Nuclear Magnetic Resonance spectra of titanocene complexes were obtained in $CDCl_3$ on a JEOL-ECS 400 DELTA 2-NMR spectrometer. Mass spectrum of titanocene complex was recorded on WATERS-G2S-QTOF-YDA 200 mass spectrometer.

The titanocene complexes were generated using a similar method. The synthesis of one representative complex is described in detail and analytical data of other complexes are given in Table-1.

Synthesis of [$TiCp_2$ (p-ClC_6H_4CO $\overline{C:C(O)N(C_6H_5)N:C}CH_3$) ($CH_3COCHCOCH_3$)]: A THF solution of the two organic ligands, sterically impeded heterocyclic beta-diketone,*4-(4-chloro)benzoyl-2,4dihydro-5-methyl-2-phenyl 3H-pyrazol-3-one* L_3H (1.33gm, 4.25mmol) and β-diketone, *pentane-2,4-dione* $L_1'H$ (0.42gm, 4.25mmol) was mixed with a THF solution of $(C_5H_5)_2TiCl_2$ (1.05gm,4.25mmol) followed by drop wise addition of triethylamine (0.86gm, 8.50mmol). The yellow colour of the solution changed to reddish-brown.

The reaction contents were refluxed for 7-8 hours. Triethylamine hydrochloride, so formed, was filtered out. The excess solvent was removed under reduced pressure. Consequently a coloured solid product was obtained which was recrystallized from benzene n-hexane mixture.

Antimicrobial Activity: The antimicrobial activity of some titanocene complexes of sterically impeded heterocyclic β-diketones and β-diketones have been investigated against *S. aureus, E.coli* and *P. aeruginosa*. These complexes were also screened for their antifungal activity against *A.niger* and *C. albicans*. Antibacterial activity and antifungal activity testing were done by Kirby-Bauer Well Diffusion method. Itraconazole was used as positive control and DMSO as negative control for antifungal activity. Positive control for antibacterial activity is streptomycin where as clotrimazole is for antifungal activity.

Micro-organisms used: The clinical laboratory bacterial isolates of *S. aureus, P. aeruginosa, E. coli* and fungal isolates such as *A. niger and C. albicans* were collected from the stock cultures of Microbiology Laboratory, SMS Medical College, Jaipur, India.

Determination of Antibacterial Assay: In vitro antibacterial activity of the complex 3, $(C_5H_5)_2TiL_{(2)}L'_{(1)}$, was investigated against positive and negative bacterial strains by the agar well diffusion method[29].

Determination of antifungal assay: Antifungal activity of the complex 3, $(C_5H_5)_2TiL_{(2)}L'_{(1)}$, was studied by agar well diffusion method[29].

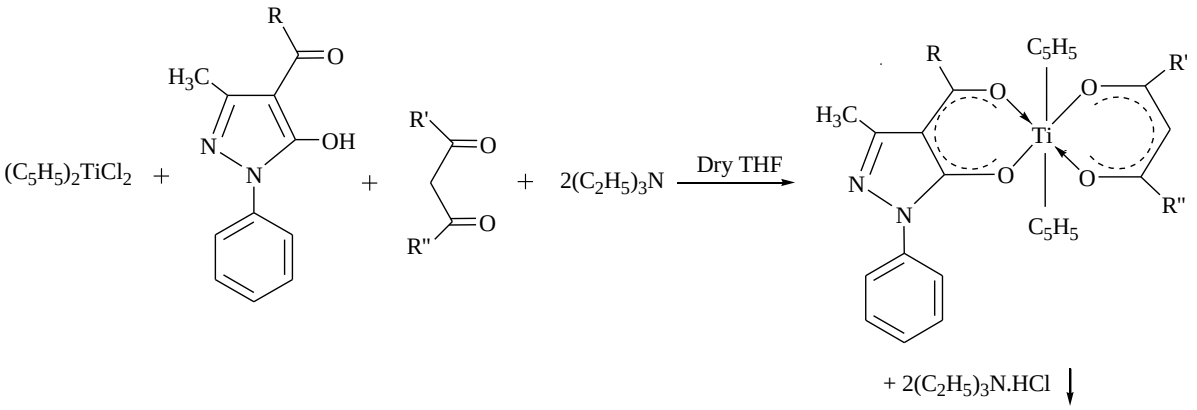
Evaluation of antibacterial activity of titanocene complexes against *S.aureus* and *P.aeruginosa:* Study protocols: For the processing of samples (complex 7 and complex 8), two concentrations (1X and 0.5X. where 1X=5mg/ml and 0.5X=2.5 mg/ml) of the test complexes of the stock solution were prepared and 100µL was used in each well. Streptomycin was used as positive control and DMSO was employed as a negative control for antibacterial activity. Kirby-Bauer well diffusion method was used for testing of antibacterial activity. Muller Hinton agar medium is used for antibacterial activity by disk/ well diffusion susceptibility testing. *S.aureus* and *P.aeruginosa* were cultured on blood plate agar and kept for 24 hours at 37°C. The bacterial suspension was prepared in pentane water compared to 0.5 McFarland Turbidity standards. Cultures were swabbed on Mueller Hinton agar surface 100µl were loaded on respective well. A disk of streptomycin was used as positive control and DMSO was used as a negative control. The plates were kept for incubation at 37°C for 24 hrs.

Results and Discussion

Titanocene complexes having the general formula $[Cp_2TiLL']$ [where LH=$RCOC{:}C(OH)\,N\,(C_6H_5)N{:}CCH_3$ and L'H= $R'COCH_2COR''$ where R=-CH_3($L_{(1)}H$), R=-CH_2CH_3 ($L_{(2)}H$), R=p-ClC_6H_4 ($L_{(3)}H$) and R'=R"=-CH_3, ($L'_{(1)}H$), R'=-CH_3, R"=-C_6H_5($L'_{(2)}H$), R'=R" =-C_6H_5 ($L'_{(3)}H$)] were generated by the reactions of $(C_5H_5)_2TiCl_2$ with sterically impeded heterocyclic beta-diketones, beta-diketones and triethylamine in a 1:1:1:2 molar ratio in refluxing dry THF (Scheme 1).

Table-1: Analytical data of titanocene (IV) complexes.

Complex No.	Complexes/ Empirical formula	Reagents in gm (mmol)					% yield
		Et_3N	LH	L'H	Cp_2TiCl_2	Et_3N.HCl (calculated)	
1.	$Cp_2TiL_{(1)}L'_{(2)}$ $C_{32}H_{30}N_2O_4Ti$	0.75gm (7.46mmol)	0.80 gm (3.73 mmol)	0.60 gm (3.73mmol)	0.92 gm (3.73mmol)	1.00gm (1.02gm)	49
2.	$Cp_2TiL_{(1)}L'_{(3)}$ $C_{37}H_{32}N_2O_4Ti$	0.82gm (8.10mmol)	0.87gm (4.05mmol)	0.90gm (4.05mmol)	1.00gm (4.05mmol)	1.09gm (1.11gm)	51
3.	$Cp_2TiL_{(2)}L'_{(1)}$ $C_{28}H_{30}N_2O_4Ti$	0.84gm (8.34mmol)	0.96gm (4.17mmol)	0.41gm (4.17mmol)	1.04gm (4.17mmol)	1.13gm (1.15gm)	54
4.	$Cp_2TiL_{(2)}L'_{(2)}$ $C_{33}H_{32}N_2O_4Ti$	0.74gm (7.32mmol)	0.84gm (3.66mmol)	0.58gm (3.66mmol)	0.91gm (3.66mmol)	0.99gm (1.00gm)	49
5.	$Cp_2TiL_{(2)}L'_{(3)}$ $C_{38}H_{34}N_2O_4Ti$	0.79gm (7.84mmol)	0.90gm (3.92mmol)	0.87gm (3.92mmol)	0.97gm (3.92mmol)	1.08gm (1.10gm)	48
6.	$Cp_2TiL_{(3)}L'_{(1)}$ $C_{32}H_{29}ClN_2O_4Ti$	0.86gm (8.50mmol)	1.33gm (4.25mmol)	0.42gm (4.25mmol)	1.05gm (4.25mmol)	1.15gm (1.17gm)	56
7.	$Cp_2TiL_{(3)}L'_{(2)}$ $C_{37}H_{31}ClN_2O_4Ti$	0.87gm (8.66mmol)	1.35gm (4.33mmol)	0.70gm (4.33mmol)	1.07gm (4.33mmol)	1.18gm (1.19gm)	52
8.	$Cp_2TiL_{(3)}L'_{(3)}$ $C_{42}H_{33}ClN_2O_4Ti$	0.96gm (9.50mmol)	1.48gm (4.75mmol)	1.06gm (4.75mmol)	1.18gm (4.75mmol)	1.29gm (1.30gm)	57



Scheme-1: Synthesis of Complexes (1-8).

Where
R=-CH_3, R'=-CH_3, R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(1)}L'_{(2)}$ Complex 1,
R=-CH_3, R'=R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(1)}L'_{(3)}$ Complex 2,
R=-CH_2CH_3, R'= R"=-CH_3, $(C_5H_5)_2Ti\ L_{(2)}L'_{(1)}$Complex 3,
R=-CH_2CH_3, R'=-CH_3, R" =-C_6H_5 $(C_5H_5)_2Ti\ L_{(2)}L'_{(2)}$ Complex 4,
R= -CH_2CH_3, R'= R"=-$C_6H_5(C_5H_5)_2Ti\ L_{(2)}L'_{(3)}$ Complex 5,
R= p-ClC_6H_4, R'=R"=-CH_3, $(C_5H_5)_2Ti\ L_{(3)}L'_{(1)}$ Complex 6,
R= p-Cl C_6H_4, R'=-CH_3, R"=-$C_6H_5(C_5H_5)_2Ti\ L_{(3)}L'_{(2)}$ Complex 7,
R= p-Cl C_6H_4, R'= R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(3)}L'_{(3)}$ Complex 8.

$(C_2H_5)_3N.HCl$ formed during the course of these reactions, was filtered out. The excess solvent was removed under reduced pressure. The reddish-yellow solid products, so obtained, were recrystallised from the chloroform-hexane mixture in 48-57% yield. The melting points of these solid products were found in the range 150-200°C. Plausible structures of these monomeric coloured solid products were suggested on the basis of mass study and spectroscopic evidences.

Spectroscopic studies: IR spectra: The IR spectra of these titanocene complexes of sterically impeded heterocyclic beta-diketones and beta-diketones were recorded as KBr pellets in the region 4000-400cm^{-1}. In the IR spectra of titanocene complexes, two new medium intensity bands were observed in the regions 610±10cm^{-1} and 520±10cm^{-1} which may be attributed to Ti-O bonds[6]. In the IR spectra of sterically impeded heterocyclic beta-diketones, $\nu_{(>C=O)}$ stretching vibration[25] appeared at 1545cm^{-1}. This carbonyl frequency shifts to lower wave number (1525±5cm^{-1}) in the IR spectra of titanocene complexes. This indicates that coordination is taking place through carbonyl oxygen and also suggests the bidentate nature of this ligand. The bands present at 1590cm^{-1} and at 1570cm^{-1} may be assigned to phenyl and $\nu_{(>C=C/>C=N-)}$ stretchings, respectively.

The IR spectra of beta-diketones demonstrate a strong band[6] in the region 1620-1650cm^{-1} which may be assigned to $\nu_{(>C=O)}$ stretching vibrations. This band shifts to a lower wave number in the IR spectra of the complexes which indicates the bidentate nature of these ligands in the complexes. A medium intensity band appearing in the region 460-445cm^{-1} may be due to $\nu_{(Ti\text{-}ring)}$ vibrations[6]. The medium intensity bands present in the regions 1030-1000cm^{-1} and 850-820cm^{-1} may be assigned to $\nu_{(C\text{-}H)}$ in plane and $\nu_{(C\text{-}H)}$ out of plane vibrations[6], respectively.

^{1}H NMR spectra: The ^{1}H NMR spectra of some representative titanocene complexes were recorded in $CDCl_3$ solution and TMS was used as an internal standard. The ^{1}H NMR data are summarized in Table-2. In the ^{1}H NMR spectra of sterically impeded heterocyclic beta- diketones and beta- diketones, the broad signals of enolic –OH are observed in the regions δ 10.20 – 12.18 and δ 15.46–16.95, respectively. These broad signals were found to be absent in the ^{1}H NMR spectra of titanocene complexes.

This clearly indicates the deprotonation of these two ligands and also supports the formation of Ti-O bond. The methylene protons of β-diketones ($L'_{(1)}H$ and $L'_{(2)}H$) were observed as a singlet in the region[24] δ3.61-4.10. This singlet disappeared in the spectra of titanocene complexes. The methine (=CH-) proton appeared in the region δ4.51-6.49 in the spectra of the complexes. In the spectra of titanocene complexes, aromatic protons were observed as a complex pattern in the region δ7.10-8.25. In this region, aromatic protons of sterically impeded heterocyclic β-diketones are overlapping with the aromatic protons of β-diketones. The signals for cyclopentadienyl ring protons appeared in the region δ6.26-6.69.

^{13}C NMR Spectra: The ^{13}C NMR spectrum of one representative titanocene complex was recorded in $CDCl_3$ and is summarized in Table-3. In the ^{13}C NMR spectrum of complex 3, the C_3, C_4 and C_6 carbon signals experience some shift in their positions as compared to their positions in the parent ligands. This indicates delocalization of electrons in quasi-aromatic ring and also the bidentate nature of sterically impeded heterocyclic beta-diketones. In the ^{13}C NMR spectrum of beta-diketone $L_1'H$, the carbon signal of >C=O was observed at δ 202.28 and δ191.32[24].
In the ^{13}C NMR spectrum of titanocene complex 3, there is some shift in the position of this carbonyl carbon signal. This observation supports the bidentate nature of L'_1H (acetylacetone).

The cyclopentadienyl ring carbon signal was observed at δ119.67 in the ^{13}CNMR spectrum of complex 3. The aromatic carbon signal appeared in the region δ148.57-120.61.

Table-2: ^{1}H NMR data of ligands and titanocene (IV) complexes in (δ)ppm.

Ligand/ Complex	RCOC:C(OH) N(C_6H_5)N:CCH_3 (LH)						R'COCH_2COR"(L'H)					
Complex no.	OH	Ring CH_3	Ring C_6H_5	p-ClC_6H_4	CH_2	CH_3	OH	CH	CH_2	CH_3	C_6H_5	C_5H_5
L_1H	11.30 (bs)	2.41 (s)	7.24-7.81(m)			2.43(s)						
L_2H	12.18 (bs)	2.42 (s)	7.22-7.81(m)		2.71,2.72, 2.74,2.76(q)	1.19,1.21, 1.23(t)						
L_3H	10.20 (bs)	2.10 (s)	7.24-7.85(m)	*								
L'_1H**							15.46 (bs)	5.52 (s)	3.61 (s)	2.00(s) 2.21(s)		
L'_2 H**							16.16 (bs)	6.18 (s)	4.10 (s)	2.22(s)	7.25-7.95(m)	
$L_3'H$							16.95 (bs)	4.62 (s)			7.46-8.00(m)	
$Cp_2TiL_1L_2'$ (1)	-	2.21 (s)	7.24-7.54(m)			2.60 (s)	-	6.13 (b)	-	1.90(s) 2.21(s)	*	6.34(b)
$Cp_2TiL_2L_1'$ (3)	-	2.21 (s)	7.35-8.25(m)		2.44,2.36, 2.26,2.24(q)	1.01,0.993, 0.795(t)	-	6.49 (bs)	-	2.23(s) 2.14(s)	*	6.57(b) 6.69(b)
$Cp_2TiL_2L_2'$ (4)	-	2.55 (bs)	7.10-7.69(m)		3.12(q) unresolved	1.43,1.41, 1.39(t)	-	6.46 (s)	-	***	*	6.51(s)
$Cp_2TiL_3L_1'$ (6)	-	2.66 (s)	7.24-7.86(m)	*			-	4.51 (s)	-	1.15(s) 1.18(s)	*	6.47(s) 6.26(s)

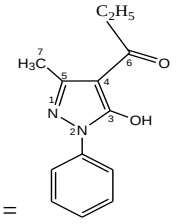
* merge with phenyl region, (b)= broad signal, ** reference 24, (bs)= broad singlet,*** merge with ring CH_3, s= singlet, t=triplet, q=quartet, m=multiplet.

LH=RCOC:C(OH) N(C_6H_5)N:CCH_3 [Where: R=-CH_3(L_1H), R=-CH_2CH_3(L_2H), R=p-ClC_6H_4(L_3H)] L'H=R'COCH_2COR" [where R'=R"=-CH_3($L_1'H$), R'=-CH_3, R"=-C_6H_5 ($L_2'H$), R'=R"=-C_6H_5($L_3'H$)]

Table-3 ^{13}C NMR data of ligand and titanocene (IV) complex in (δ) ppm.

Ligand/ Complex (Complex no.)	RCOC:C(OH) N(C_6H_5)N:CCH_3 (LH)								R'COCH_2COR" (L'H)				
	C_3	C_4	C_5	C_6	C_7	N-⟨⟩	CH_2	CH_3	-CO	-CH-	CH_3	CH_2	C_5H_5
L_2 H*	160.4	103.4	137.0	198.0	15.9	147.0,129.0, 126.4,120.8	32.6	8.4					
L'_1H**									191.32 202.28	100.50	24.81 30.85	58.49	
$Cp_2TiL_2L_1'$(3)	161.53	109.22	138.22	197.91	15.69	148.57,126.71, 120.61,129.73	31.14	8.98	191.73 197.9	N.O.	24.34 ***	-	119.67

*Reference 28, **Reference 24, *** merge with CH_2 , N.O.= not observed.



L_2H =

$L_1'H = CH_3COCH_2COCH_3$

Mass spectrum: The mass spectrum of one newly generated representative complex was recorded. Mass spectrum of titanocene complex showed a number of peaks which indicated the formation of various fragments due to loss of side-chain and ligand.

Structure: With the help of mass study and spectroscopic evidences, the following tentative structure (Figure-1) having a distorted trans octahedral geometry may be proposed for these titanocene complexes-

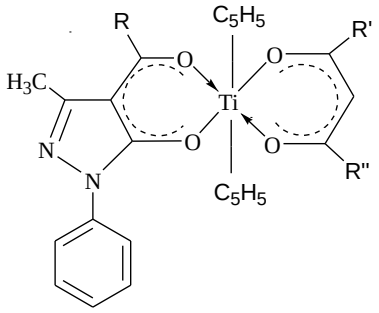


Figure-1: Structure of Complex

$(C_5H_5)_2Ti(RCOC{:}C(O)\ N\ (C_6H_5)N{:}CCH_3)(R'COCHCOR")$.

Where

R=-CH_3, R'=-CH_3, R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(1)}L'_{(2)}$ Complex 1.
R=-CH_3, R'=R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(1)}L'_{(3)}$ Complex 2.
R=-CH_2CH_3, R'=R"=-CH_3, $(C_5H_5)_2Ti\ L_{(2)}L'_{(1)}$ Complex 3.
R=-CH_2CH_3, R'=-CH_3, R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(2)}L'_{(2)}$ Complex 4.
R=-CH_2CH_3, R'=R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(2)}L'_{(3)}$ Complex 5.
R=p-Cl C_6H_4, R'=R"=-CH_3, $(C_5H_5)_2Ti\ L_{(3)}L'_{(1)}$ Complex 6.
R=p-Cl C_6H_4, R'=-CH_3, R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(3)}L'_{(2)}$ Complex 7.
R=p-Cl C_6H_4, R'=R"=-C_6H_5 $(C_5H_5)_2Ti\ L_{(3)}L'_{(3)}$ Complex 8.

In these complexes, the central titanium is surrounded by two six-membered rings and two C_5H_5 rings present trans to each other.

Antimicrobial Activity: Various factors such as the nature of the metal atom, geometry as well as coordination number of the complexes were used to discuss the antibacterial activity of these dicyclopentadienyl titanium (IV) complexes. The presence of dicyclopentadienyl titanium (IV) moiety in the complexes appears to be an important factor for imparting activity to these complexes. The structure-antibacterial activity relationship of these newly generated titanocene complexes was investigated against various bacteria.

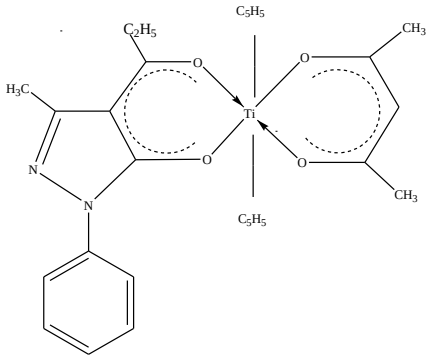


Figure-2: Structure of Complex 3

$(C_5H_5)_2Ti(C_2H_5CO\ C{:}C(O)N(C_6H_5)N{:}CCH_3)(CH_3COCHCOCH_3)$.

In the case of *S. aureus* (Table-4), at 30µl concentration, the antibacterial activity of complex 3, $(C_5H_5)_2TiL_{(2)}L'_{(1)}$, (Figure-2) is nil.

The antibacterial activity increases with the increase of concentration. This complex demonstrates highest activity at 120µl concentration. The presence of two cyclopentadienyl rings directly appended to titanium appears to be an important contributor for imparting antibacterial activity to this complex.

In the case of *E.coli* (Table-4), at 30µl concentration, complex 3, $(C_5H_5)_2TiL_{(2)}L'_{(1)}$ (Figure-2) did not show antibacterial activity. The activity increases with the increase of concentration and this complex exhibits maximum activity at 120µl concentration. The presence of $(C_5H_5)_2Ti$ moiety in this complex may be an important factor for the antibacterial activity of this complex.

Table-4: Antibacterial activity of complex 3 against *S.aureus* and *E. Coli.*

Organism	S	30µl	60µl	90µl	120µl
S.aureus	30mm	nil	13mm	14mm	19mm
E.coli	30mm	nil	14mm	16mm	18mm

The antibacterial activity of complex 7 and complex 8 was also investigated against *S. aureus*.

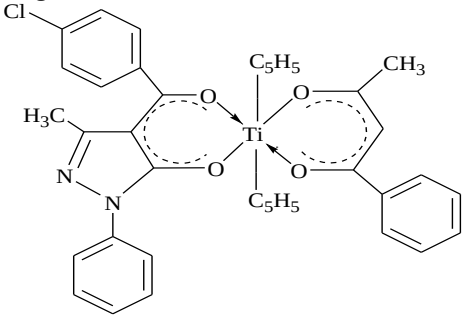


Figure-3: Structure of Complex 7.

$(C_5H_5)_2Ti(p\text{-}ClC_6H_4CO\ C{:}C(O)N(C_6H_5)N{:}CCH_3)(CH_3COCHCOC_6H_5)$.

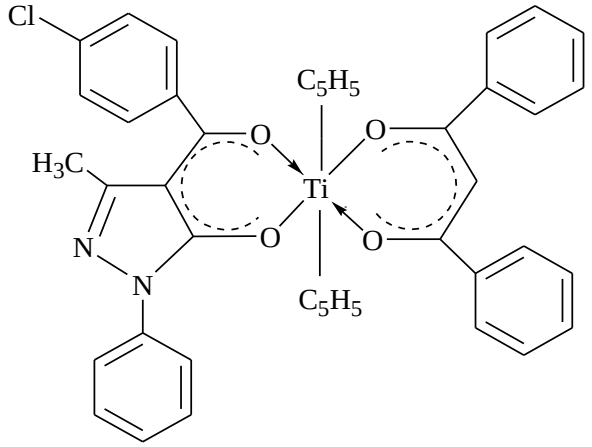


Figure-4: Structure of Complex 8,
$(C_5H_5)_2Ti(p\text{-}ClC_6H_4CO\ C{:}C(O)N(C_6H_5)N{:}CCH_3)(C_6H_5COCHCOC_6H_5)$.

The positive control of the two complexes is the same, at 1X (where 1X= 5mg/ml) concentration. Complex 8 is slightly more active than complex 7. However, at 0.5X (where 0.5X=2.5 mg/ml) concentration, the antibacterial activity of the two complexes remains the same.

Table-5: Antibacterial activity of complex 7 and complex 8 against *S. aureus* and *P. aeruginosa.*

ORGANISM	Complex	P C	NC	1X	0.5X
S.aureus	Complex7	24mm	NZ	14mm	12mm
	Complex 8	24mm	NZ	15mm	12mm
P.aeruginosa	Complex 7	25mm	NZ	NZ	NZ
	Complex 8	20mm	NZ	NZ	NZ

NZ: No zone of inhibition, PC: Positive control, NC: Negative control, X= concentration of the complex.

The antibacterial activity of complex 7 and complex 8 was also studied against *P. aeruginosa*. Positive controls of complex 7 and complex 8 were found to be 25mm and 20mm, respectively. The complexes exhibit no activity at 1X (where 1X= 5mg/ml) and 0.5X (where 0.5X=2.5mg/ml) concentrations.

The structure-antifungal activity relationship of complex 3, $(C_5H_5)_2\ TiL_{(2)}\ L'_{(1)}$,was also studied against various fungi. In the case of *A.niger* (Table-6), complex 3, $(C_5H_5)_2TiL_{(2)}L'_{(1)}$ (Figure-2) shows no antifungal activity at 30µL concentration. The antifungal activity increases with the increase of concentration and attains the highest activity at 120µl concentration. The presence of two cyclopentadienyl rings in the complex may be an important factor for this activity.

Table-6: Antifungal activity of complex 3 against *A.niger* and *C. albicans.*

Organism	S	30µl	60µl	90µl	120µl
A.niger	28mm	nil	11mm	16mm	23mm
C.albicans	27mm	nil	15mm	18mm	23mm

In the case of *C. albicans* (Table-6), at 30µL concentration, complex 3, $(C_5H_5)_2TiL_{(2)}L'_{(1)}$, demonstrates no activity. The antifungal activity increases with the increase of concentration of titanocene complex. This complex exhibits the highest activity at 120µL concentration. The most plausible explanation for this antifungal activity may be the presence of two cyclopentadienyl rings directly attached to the central titanium atom along with two six-membered rings in this complex.

Conclusion

Some new titanocene complexes were prepared by the reactions of titanocene dichloride with sterically impeded heterocyclic β-diketones and β-diketones. Plausible structures of these complexes were suggested based on mass study and spectroscopic evidences. Some representative titanocene complexes were also screened for their antimicrobial activity. The structure-antimicrobial activity relationship has been studied.

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