J. Indian Chem. Soc.,
Vol. 92, November 2015, pp. 1669-1681

Mono- and disubstituted aryldithiocarbonates of titanium(IV) and zirconium(IV)

Savit Andotra, Nidhi Kalgotra, Bhawana Gupta and Sushil K. Pandey*

Department of Chemistry, University of Jammu, Baba Sahib Ambedkar Road, Jammu-180 006, Jammu & Kashmir, India

E-mail : kpsushil@rediffmail.com

Manuscript received online 11 February 2015, revised 09 April 2015, accepted 06 May 2015

Abstract : New dithiocarbonates of titanium(IV) and zirconium(IV) corresponding to $[(ROCS_2)_nM(C_5H_5)_2Cl_{2-n}]$ (R = *o*-, *m*- or *p*-$CH_3C_6H_4$, and 4-Cl-3-$CH_3C_6H_3$; n = 1 or 2; M = Ti or Zr) have been isolated by the reaction of sodium salt of dithiocarbonates with titanocene or zirconocene dichloride in 1 : 1 and 1 : 2 molar ratio in $CHCl_3$. These have been characterized by elemental analyses, mass, IR and heteronuclear NMR (^1H and ^{13}C) spectroscopic analyses. Thermal and redox properties of complexes were studied by thermogravimetric analysis and cyclic voltammetry. Based on analytical results, penta- and hexa-coordinate geometries are concluded around the Ti or Zr atom. The antimicrobial test of these complexes has been conducted against the bacteria *Klebsiella pneumonia* and *Enterococcus faciolus* and fungus *Rhizopus nigricans*. The cytotoxic properties of the few ligands and complexes were also measured *in vitro* using the cultivated human cell lines.

Keywords : Xanthate, dithiocarbonate, metallocene, cyclic voltammetry, antimicrobial, anticancer.

Introduction

Metallocene complexes of Group IV metals have attracted increasing attention owing to their versatile applications like asymmetric catalyses, stoichiometric reactions and isotactic polymerization of propylene[1]. Interestingly, modifications to the classical ligands is very effective way of varying the physical and chemical properties of the parent metallocenes over a very wide range in order to incorporate novel reactivity and optimize existing properties[2]. Transition metal dithiolate complexes exhibited a rich and interesting chemistry that has been studied extensively[3]. The synthetic and structural chemistry of xanthates witnessed increased attention through the pioneering work of Winter *et al.*[4,5] and Hoskins *et al.*[6,7]. Subsequently, extensive structural analyses were performed by Haiduc and Tiekink[8], which showed monodentate, isobidentate or anisobidentate chelation of ligands to the metals. Applications of xanthates as vulcanizers[9], fungicides[10] and flotation agents[11,12] in metallurgy have been described in literature. More recent applications of xanthates and other thio-compounds are in the production of nano-particles of metal sulfides[13,14] and NLO properties[15,16]. Metal xanthates are extensively used as pesticides[17], corrosion inhibitors[18], agricultural reagents[19], and quite recently in therapy for HIV infections[20]. Moreover, xanthates are also known to show antitumor properties[21,22] and their antioxidant properties could be of importance for treating Alzheimer's disease[23]. Continuing our studies on tolyl dithiocarbonates[9,16,24–26] it was thought worthy to synthesize and characterize new metallocene complexes of titanium and zirconium and also to find out biological features of these metallocene complexes and the ligands as well. This paper also reports the comparative study of cytotoxicity of dithiocarbonate ligand and its complexes.

Experimental

Materials and methods :

Chloroform (Thomas Baker, b.p. 61 °C) was dried and distilled before use. Moisture was carefully excluded throughout the experimental manipulations by using standard Schlenk's technique. Titanocene dichloride (Cp_2TiCl_2) and zirconocene dichloride (Cp_2ZrCl_2) were procured from Sigma Aldrich and these were used as received. The ligands were synthesized according to a literature procedure[9]. Titanium and zirconium were estimated gravimetrically as TiO_2 and ZrO_2[27]. Chlorine was estimated volumetrically by Volhard's method[27]. Elemen-

tal analyses (C, H, N, S) were conducted using the Elemental Analyser Vario EL-III. Infrared spectra were recorded in the range of 4000–200 cm^{-1} on Perkin-Elmer FTIR spectrometer. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Brucker Avance III 400 MHz using TMS as internal reference. The ESI mass spectra were recorded on ESI-esquires 3000 Bruker Daltonics spectrophotometer. The thermogram (up to 1000 °C) was analyzed by using Perkin-Elmer, Diamond TG/DTA instrument using recrystallized alumina sample holder and the heating rate of 20 °C per minute. The experiment was carried out under a flow rate of 50 ml per minute of nitrogen atmosphere. The cyclic voltammograms were recorded on Metrohm Autolabs. The potential is applied between the reference electrode (Ag/AgCl) and the working electrode (gold electrode) and the current is measured between the working electrode and the counter electrode (platinum wire). For all the measurements, 0.1 *M* phosphate buffer solution (pH 7) was used. Also the antifungal and antibacterial activity were tested under laboratory condition in the Bioassay Lab, Department of Chemistry, University of Jammu, Jammu, using classical poison food technique and agar well diffusion method.

Synthesis of [(o-$CH_3C_6H_4OCS_2$)Ti(C_5H_5)$_2$Cl] (**1**) :

Complex **1** was prepared by dropwise addition of chloroform solution of 1.20 g (4.82 mmol) titanocene dichloride, $(C_5H_5)_2TiCl_2$, to a chloroform suspension of 1.00 g (4.84 mmol) sodium *o*-tolydithiocarbonate, *o*-$CH_3C_6H_4OCS_2Na$, with constant stirring at room temperature. The contents were further stirred for 6 h followed by refluxing for 3 h. The color of the contents was changed to intense red from red. The precipitated sodium chloride was removed by filtration using funnel fitted with G-4 disc. The removal of volatiles from the filtrate *in vacuo* yielded the complex **1** as dark red solid. Yield : 1.73 g (91%); m.p. 180–184 °C (dec.); Anal. Calcd. for $C_{18}H_{17}OCS_2ClTi$: Calcd. (%) : C, 54.49; H, 4.32; S, 16.16; Cl, 8.94; Ti, 12.06, Found (%) : C, 54.45; H, 4.30; S, 16.14; Cl, 8.91; Ti, 12.04; FTIR (cm^{-1}) : 3334b [ν(C–H)], 1618s [ν(C–C)], 1236s [ν(C–O–C)], 1015b [ν(S–C–S)], 444w [νTi–S], 363w [νTi–Cl]; ^1H NMR ($CDCl_3$) : 2.21 (3H, s, CH_3), 6.28 (1H, d, *ortho*), 6.91–7.32 (2H, m, *meta*), 7.23 (1H, t, *para*), 5.35 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 20.81 (CH_3), 121.90 (C-*ortho*), 124.60 (C–CH_3), 129.52 (C-*para*), 130.14–138.30 (C-*meta*), 147.71 (C–O), 121.32 (C_5H_5), 168.90 (OCS_2) ppm; ESI-MS : *m/z* (%) = $[M^+]$** 396.7(15) 398.7(10) 340.7(3) [(*o*-$CH_3C_6H_4OCS_2$)Ti(C_5H_5)$_2$Cl]; $[M^+]$ 361.3(8) [(*o*-$CH_3C_6H_4OCS_2$)Ti(C_5H_5)$_2$]; $[M^+]$ 231.1(9) [(*o*-$CH_3C_6H_4OCS_2$)Ti]; $[M^+]$ 183.0(5) [*o*-$CH_3C_6H_4OCS_2$]; $[M^+]$ 107.0(18) [*o*-$CH_3C_6H_4O$].

Synthesis of [(m-$CH_3C_6H_4OCS_2$)Ti(C_5H_5)$_2$Cl] (**2**) :

Complex **2** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.84, mmol) of sodium *m*-tolydithiocarbonate, *m*-$CH_3C_6H_4OCS_2Na$, and 1.20 g (4.82 mmol) of titanocene dichloride, $(C_5H_5)_2TiCl_2$, was used to yield complex **2** as dark red solid. Yield : 1.69 g (89%); m.p. 175–177 °C (dec.); Anal. Calcd. for $C_{18}H_{17}OCS_2ClTi$: Calcd. (%) : C, 54.49; H, 4.32; S, 16.16; Cl, 8.94; Ti, 12.06, Found (%) : C, 54.48; H, 4.30; S, 16.13; Cl, 8.90; Ti, 12.01; FTIR (cm^{-1}) : 3367b [ν(C–H)], 1571s [ν(C–C)], 1230s [ν(C–O–C)], 1029b [ν(S–C–S)], 448w [νTi–S], 375w [νTi–Cl]; ^1H NMR ($CDCl_3$) : 2.33 (3H, s, CH_3), 6.52–6.73 (2H, m, *ortho*), 6.82 (1H, d, *para*), 7.00 (1H, t, *meta*), 5.50 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 19.99 (CH_3), 113.40–132.51 (C-*ortho*), 120.52 (C-*para*), 127.24 (C-*meta*), 128.95 (C–CH_3), 152.50 (C–O), 117.42 (C_5H_5), 169.50 (OCS_2) ppm.

Synthesis of [(p-$CH_3C_6H_4OCS_2$)Ti(C_5H_5)$_2$Cl] (**3**) :

Complex **3** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.84 mmol) of sodium *p*-tolydithiocarbonate, *p*-$CH_3C_6H_4OCS_2Na$, and 1.20 g (4.82 mmol) of titanocene dichloride, $(C_5H_5)_2TiCl_2$, was used to yield complex **3** as dark red solid. Yield : 1.71 g (90%); m.p. 188–189 °C (dec.); Anal. Calcd. for $C_{18}H_{17}OCS_2ClTi$: Calcd. (%) : C, 54.49; H, 4.32; S, 16.16; Cl, 8.94; Ti, 12.06, Found (%) : C, 54.47; H, 4.29; S, 16.12; Cl, 8.90; Ti, 12.03; FTIR (cm^{-1}) : 3356b [ν(C–H)], 1572s [ν(C–C)], 1230s [ν(C–O–C)], 1038b [ν(S–C–S)], 434w [νTi–S], 372w [νTi–Cl]; ^1H NMR ($CDCl_3$) : 2.25 (3H, s, CH_3), 6.68 (2H, d, *ortho*), 6.94 (2H, d, *meta*), 5.32 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 20.25 (CH_3), 127.20 (C-*ortho*), 129.71 (C–CH_3), 131.38 (C-*meta*), 149.25 (C–O), 119.36 (C_5H_5), 166.63 (OCS_2) ppm.

Synthesis of [(4-Cl-3-$CH_3C_6H_3OCS_2$)Ti(C_5H_5)$_2$Cl] (**4**) :

Complex **4** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.15 mmol) of sodium 4-chloro-3-methylphenyldithiocarbonate, 4-Cl-3-$CH_3C_6H_4OCS_2Na$, and 1.03 g (4.13 mmol) of titanocene dichloride, $(C_5H_5)_2TiCl_2$, was used to yield complex **4** as dark red solid. Yield : 1.16 g (92%); m.p. 187–188 °C (dec.); Anal. Calcd. for $C_{18}H_{16}OCS_2Cl_2Ti$: Calcd. (%) : C, 50.90; H, 3.61; S, 20.91; Cl, 11.56; Ti, 7.80, Found (%) : C, 50.88; H, 3.60; S, 20.89; Cl, 11.54; Ti, 7.78; FTIR (cm^{-1}) : 3353b [ν(C–H)], 1576s [ν(C–C)], 1233s [ν(C–O–C)], 1029b [ν(S–C–S)], 434w [νTi–S], 367w [νTi–Cl]; ^1H NMR ($CDCl_3$) : 2.22 (3H, s, CH_3), 6.23–6.51 (2H, m, *ortho*), 7.10 (1H, d, *meta*), 5.44 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 19.10 (CH_3), 114.03–116.13 (C-*ortho*), 128.02 (C–CH_3), 118.17 (C-*meta*), 116.41 (C-*para*), 152.27 (C–O), 117.20 (C_5H_5), 162.12 (OCS_2) ppm; ESI-MS : *m/z* (%) = [M^+]** 431.2(20) 433.2(16) 435.2(10) [(4-Cl-3-$CH_3C_6H_3OCS_2$)Ti(C_5H_5)$_2$Cl]; [M^+]** 395.7(10) 397.7(8) 399.7(4) [(4-Cl-3-$CH_3C_6H_3OCS_2$)Ti(C_5H_5)]; [M^+]** 265.5(8) 267.5(6) 269.5(1) [(4-Cl-3-$CH_3C_6H_3OCS_2$)Ti]; [M^+]** 217.7(15) 219.7(10) 221.7(5) [(4-Cl-3-$CH_3C_6H_3OCS_2$)]; [M^+] 182.2(15) [$CH_3C_6H_3OCS_2$]; [M^+] 106.1(16) [($CH_3C_6H_3O$)].

Synthesis of [(o-$CH_3C_6H_4OCS_2$)$_2$Ti(C_5H_5)$_2$] (**5**) :

Complex **5** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.84 mmol) of sodium *o*-tolyldithiocarbonate, *o*-$CH_3C_6H_4OCS_2Na$, and 0.60 g (2.41 mmol) of titanocene dichloride, $(C_5H_5)_2Cl_2$, was used to yield complex **5** as dark red solid. Yield : 1.17 g (90%); m.p. 198–199 °C (dec.); Anal. Calcd. for $C_{26}H_{24}O_2S_4Ti$: Calcd. (%) : C, 57.34; H, 4.44; S, 22.55; Ti, 8.79, Found (%) : C, 57.33; H, 4.40; S, 22.53; Ti, 8.77; FTIR (cm^{-1}) : 3350b [ν(C–H)], 1572s [ν(C–C)], 1230s [ν(C–O–C)], 1038b [ν(S–C–S)], 449w [νTi–S]; ^1H NMR ($CDCl_3$) : 2.23 (6H, s, CH_3), 6.17 (2H, d, *ortho*), 6.90–7.01 (4H, m, *meta*), 7.32 (2H, t, *para*), 5.15 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 19.81 (CH_3), 117.62 (C-*ortho*), 128.88 (C–CH_3), 135.48 (C-*para*), 133.31–136.32 (C-*meta*), 149.27 (C–O), 120.19 (C_5H_5), 167.57 (OCS_2) ppm.

Synthesis of [(m-$CH_3C_6H_4OCS_2$)$_2$Ti(C_5H_5)$_2$] (**6**) :

Complex **6** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.84 mmol) of sodium *m*-tolyldithiocarbonate, *m*-$CH_3C_6H_4OCS_2Na$, and 0.60 g (2.41 mmol) of titanocene dichloride, $(C_5H_5)_2TiCl_2$, was used to yield complex **6** as dark red solid. Yield : 1.15 g (88%); m.p. 194–193 °C (dec.); Anal. Calcd. for $C_{26}H_{24}O_2S_4Ti$: Calcd. (%) : C, 57.34; H, 4.44; S, 22.55; Ti, 8.79, Found (%) : C, 57.32; H, 4.41; S, 22.53; Ti, 8.76; FTIR (cm^{-1}) : 3027b [ν(C–H)], 1591s [ν(C–C)], 1232s [ν(C–O–C)], 1021b [ν(S–C–S)], 447w [νTi–S]; ^1H NMR ($CDCl_3$) : 2.32 (6H, s, CH_3), 6.62–6.82 (4H, m, *ortho*), 6.19 (2H, d, *para*), 7.11 (2H, t, *meta*), 5.05 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 19.74 (CH_3), 114.05–128.45 (C-*ortho*), 117.21 (C-*para*), 117.51 (C-*meta*), 128.70 (C–CH_3), 152.27 (C–O), 116.51 (C_5H_5), 164.00 (OCS_2) ppm.

Synthesis of [(p-$CH_3C_6H_4OCS_2$)$_2$Ti(C_5H_5)$_2$] (**7**) :

Complex **7** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.84 mmol) of sodium *p*-tolyldithiocarbonate, *p*-$CH_3C_6H_4OCS_2Na$, and 0.60 g (2.41 mmol) of titanocene dichloride, $(C_5H_5)_2TiCl_2$, was used to yield complex **7** as dark red solid. Yield : 1.17 g (90%); m.p. 199–200 °C (dec.); Anal. Calcd. for $C_{26}H_{24}O_2S_4Ti$: Calcd. (%) : C, 57.34; H, 4.44; S, 22.55; Ti, 8.79; FTIR (cm^{-1}) : 3357b [ν(C–H)], 1587s [ν(C–C)], 1239s [ν(C–O–C)], 1028b [ν(S–C–S)], 441w [νTi–S]; ^1H NMR ($CDCl_3$) : 2.13 (6H, s, CH_3), 6.90 (4H, d, *ortho*), 7.12 (4H, d, *meta*), 5.54 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 20.42 (CH_3), 113.01 (C-*ortho*), 139.43 (C–CH_3), 127.52 (C-*meta*), 150.67 (C–O), 119.05 (C_5H_5), 162.55 (OCS_2) ppm; ESI-MS : *m/z* (%) = [M^+] 544.5(6) [(*p*-$CH_3C_6H_4OCS_2$)$_2$Ti(C_5H_5)$_2$]; [M^+] 414.4(8) [(*p*-$CH_3C_6H_4OCS_2$)$_2$Ti]; [M^+] 231.1(9) [(*p*-$CH_3C_6H_4OCS_2$)Ti]; [M^+] 183.0(5) [*p*-$CH_3C_6H_4OCS_2$]; [M^+] 107.0(18) [*p*-$CH_3C_6H_4O$].

Synthesis of [(4-Cl-3-$CH_3C_6H_3OCS_2$)$_2$Ti(C_5H_5)$_2$] (**8**) :

Complex **8** was synthesized according to the protocol as described for complex **1**; 1.00 g (4.15 mmol) of sodium 4-chloro-3-methylphenyldithiocarbonate, 4-Cl-3-$CH_3C_6H_4OCS_2Na$, and 0.51 g (2.40 mmol) of titanocene dichloride, $(C_5H_5)_2TiCl_2$, was used to yield complex **8** as dark red solid. Yield : 1.16 g (93%); m.p. 197–198 °C (dec.); Anal. Calcd. for $C_{26}H_{22}O_2S_4Cl_2Ti$: Calcd. (%) : C, 50.90; H, 3.61; S, 20.90; Cl, 11.56; Ti, 7.80, Found (%) : C, 50.87; H, 3.59; S, 20.87; Cl, 11.53; Ti, 7.77; FTIR (cm^{-1}) : 3354b [ν(C–H)], 1574s [ν(C–C)], 1234s

[ν(C–O–C)], 1040b [ν(S–C–S)], 449w [νTi–S]; ^{1}H NMR ($CDCl_3$) : 2.32 (6H, s, CH_3), 6.61–6.29 (4H, m, *ortho*), 7.21 (2H, d, *meta*), 5.50 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 17.51 (CH_3), 118.13–121.80 (C-*ortho*), 125.88 (C–CH_3), 129.00 (C-*meta*), 131.06 (C-*para*), 150.05 (C–O), 117.05 (C_5H_5), 168.55 (OCS_2) ppm.

Synthesis of [(o-$CH_3C_6H_4OCS_2$)Zr(C_5H_5)$_2$Cl] (**9**) :

Complex **9** was prepared by dropwise addition of chloroform solution of 1.41 g (4.79 mmol) zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, to chloroforrm suspension of 1.00 g (4.84 mmol) sodium *o*-tolyldithiocarbonate, *o*-$CH_3C_6H_4OCS_2Na$, with constant stirring. The contents were further stirred for 6 h followed by refluxing for 3 h. The turbidity due to formation of sodium chloride was removed by filtration using alkoxy funnel fitted with G-4 disc. The removal of volatiles from the filtrate *in vacuo* yielded the complex **9** as yellow solid. Yield : 1.19 g (90%); m.p. 209–210 °C (dec.); Anal. Calcd. for $C_{18}H_{17}OS_2ClZr$: Calcd. (%) : C, 49.12; H, 3.89; S, 14.57; Cl, 8.06; Zr, 20.73, Found (%) : C, 49.10; H, 3.86; S, 14.54; Cl, 8.04; Zr, 20.70; FTIR (cm^{-1}) : 3351b [ν(C–H)], 1586s [ν(C–C)], 1239s [ν(C–O–C)], 1036b [ν(S–C–S)], 409w [νZr–S], 330w [νZr–Cl]; ^{1}H NMR ($CDCl_3$) : 2.32 (3H, s, CH_3), 6.09 (1H, d, *ortho*), 6.90–17.27 (2H, m, *meta*), 7.30 (1H, t, *para*), 5.58 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 20.18 (CH_3), 121.9 (C-*ortho*), 124.06 (C–CH_3), 128.99 (C-*para*), 131.99–138.22 (C-*meta*), 147.47 (C–O), 121.36 (C_5H_5), 169.59 (OCS_2) ppm.

Synthesis of [(m-$CH_3C_6H_4OCS_2$)Zr(C_5H_5)$_2$Cl] (**10**) :

Complex **10** was synthesized according to the protocol as described for complex **9**; 1.00 g (4.84 mmol) of sodium *m*-tolyldithiocarbonate, *m*-$CH_3C_6H_4OCS_2Na$, and 1.41 g (4.79 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **10** as yellow solid. Yield : 1.86 g (88%); m.p. 212–213 °C (dec.); Anal. Calcd. for $C_{18}H_{17}OS_2ClZr$: Calcd. (%) : C, 49.12; H, 3.89; S, 14.57; Cl, 8.06; Zr, 20.73, Found (%) : C, 49.09; H, 3.87; S, 14.55; Cl, 8.03; Zr, 20.71; FTIR (cm^{-1}) : 3368b [ν(C–H)], 1574s [ν(C–C)], 1229s [ν(C–O–C)], 1025b [ν(S–C–S)], 412w [νZr–S], 367w [νZr–Cl]; ^{1}H NMR ($CDCl_3$) : 2.30 (3H, s, CH_3), 6.52–6.70 (2H, m, *ortho*), 6.81 (1H, d, *para*), 7.01 (1H, t, *meta*), 5.32 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 19.09 (CH_3), 113.44–132.25 (C-*ortho*), 121.05 (C-*para*), 127.02 (C-*meta*), 129.88 (C–CH_3), 152.51 (C–O), 116.94 (C_5H_5), 169.99 (OCS_2) ppm; ESI-MS : *m/z* (%) = [M$^+$]** 440.1(16) 442.1(15) 444.1(9) [(*m*-$CH_3C_6H_4OCS_2$)Zr(C_5H_5)$_2$Cl]; [M$^+$] 404.6(12) [(*m*-$CH_3C_6H_4OCS_2$)Zr(C_5H_5)$_2$]; [M$^+$] 274.4(6) [*m*-$CH_3C_6H_4OCS_2$)Zr]; [M$^+$] 183.0(15) [*m*-$CH_3C_6H_4OCS_2$]; [M$^+$] 107.0(18) [*m*-$CH_3C_6H_4O$].

Synthesis of [(p-$CH_3C_6H_4OCS_2$)Zr(C_5H_5)$_2$Cl] (**11**) :

Complex **11** was synthesized according to the protocol as described for complex **9**; 1.00 g (4.84 mmol) of sodium *p*-tolyldithiocarbonate, *m*-$CH_3C_6H_4OCS_2Na$, and 1.41 g (4.79 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **11** as yellow solid. Yield : 2.01 g (95%); m.p. 216–217 °C (dec.); Anal. Calcd. for $C_{18}H_{17}OS_2ClZr$: Calcd. (%) : C, 49.12; H, 3.89; S, 14.57; Cl, 8.06; Zr, 20.73; Found (%) : C, 49.10; H, 3.84; S, 14.53; Cl, 8.03; Zr, 20.69; FTIR (cm^{-1}) : 3436b [ν(C–H)], 1558s [ν(C–C)], 1239s [ν(C–O–C)], 1022b [ν(S–C–S)], 410w [νZr–S], 335w [νZr–Cl]; ^{1}H NMR ($CDCl_3$) : 2.41 (3H, s, CH_3), 6.38 (2H, d, *ortho*), 7.70 (2H, d, *meta*), 5.45 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 21.04 (CH_3), 124.30 (C-*ortho*), 138.04 (C–CH_3), 128.92 (C-*meta*), 150.02 (C–O), 120.15 (C_5H_5), 168.99 (OCS_2) ppm.

Synthesis of [(4-Cl-3-$CH_3C_6H_3OCS_2$)Zr(C_5H_5)$_2$Cl] (**12**) :

Complex **12** was synthesized according to the protocol as described for complex **9**; 1.00 g (4.15 mmol) and of sodium 4-chloro-3-methylphenyldithiocarbonate, 4-Cl-3-$CH_3C_6H_4OCS_2Na$, 1.21 g (4.14 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **12** as yellow solid. Yield : 1.76 g (90%); m.p. 210–212 °C (dec.); Anal. Calcd. for $C_{18}H_{16}OS_2Cl_2Zr$: Calcd. (%) : C, 45.55; H, 3.40; S, 13.51; Cl, 14.94; Zr, 19.22, Found (%) : C, 45.52; H, 3.37; S, 13.48; Cl, 14.91; Zr, 19.20; FTIR (cm^{-1}) : 3040b [ν(C–H)], 1597s [ν(C–C)], 1233s [ν(C–O–C)], 1035b [ν(S–C–S)], 415w [νZr–S], 373w [νZr–Cl]; ^{1}H NMR ($CDCl_3$) : 2.32 (3H, s, CH_3), 6.30–6.67 (2H, m, *ortho*), 7.04 (1H, d, *meta*), 5.78 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 18.99 (CH_3), 119.40–121.79 (C-*ortho*), 129.76 (C–CH_3), 129.82 (C-*meta*), 132.83 (C-*para*), 151.49 (C–O), 117.11 (C_5H_5), 168.66, (OCS_2) ppm.

Synthesis of [(o-$CH_3C_6H_4OCS_2$)$_2$Zr(C_5H_5)$_2$] (**13**) :

Complex **13** was synthesized according to the proto-

col as described for complex **9**; 1.00 g (4.84 mmol) of sodium *o*-tolyldithiocarbonate, *o*-$CH_3C_6H_4OCS_2Na$, and 0.70 g (2.39 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **13** as yellow solid. Yield : 1.26 g (90%); m.p. 221–223 °C (dec.); Anal. Calcd. for $C_{26}H_{24}O_2S_4Zr$: Calcd. (%) : C, 53.11; H, 4.11; S, 21.81; Zr, 15.52, Found (%) : C, 53.09; H, 4.07; S, 21.80; Zr, 15.50; FTIR (cm^{-1}) : 3359b [ν(C–H)], 1581s [ν(C–C)], 1238s [ν(C–O–C)], 1032b [ν(S–C–S)], 423w [νZr–S]; ^1H NMR ($CDCl_3$) : 2.43 (6H, s, CH_3), 6.65 (2H, d, *ortho*), 6.89–7.52 (4H, m, *meta*), 7.24 (2H, t, *para*), 5.72 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 21.29 (CH_3), 126.88 (C-*ortho*), 149.59 (C–CH_3), 124.37 (C-*para*), 137.51–139.07 (C-*meta*), 151.80 (C–O), 119.43 (C_5H_5), 165.71 (OCS_2) ppm; ESI-MS : *m/z* (%) = $[M^+]$ 587.9(7) [(*m*-$CH_3C_6H_4OCS_2)_2Zr(C_5H_5)_2$]; $[M^+]$ 457.7(12) [(*m*-$CH_3C_6H_4OCS_2)_2Zr$]; $[M^+]$ 274.4(9) [*m*-$CH_3C_6H_4OCS_2)Zr$]; $[M^+]$ 183.0(10) [*m*-$CH_3C_6H_4OCS_2$]; $[M^+]$ 107.0(20) [*m*-$CH_3C_6H_4O$].

Synthesis of [(m-$CH_3C_6H_4OCS_2)_2Zr(C_5H_5)_2$] (**14**) :

Complex **14** was synthesized according to the protocol as described for complex **9**; 1.00 g (4.84 mmol) of sodium *m*-tolyldithiocarbonate, *m*-$CH_3C_6H_4OCS_2Na$, and 0.70 g (2.39 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **14** as yellow solid. Yield : 1.27 g (91%); m.p. 219–220 °C (dec.); Anal. Calcd. for $C_{26}H_{24}O_2S_4Zr$: Calcd. (%) : C, 53.11; H, 4.11; S, 21.81; Zr, 15.52, Found (%) : C, 53.07; H, 4.10; S, 21.79; Zr, 15.49; FTIR (cm^{-1}) : 3340b [ν(C–H)], 1591s [ν(C–C)], 1232s [ν(C–O–C)], 1036b [ν(S–C–S)], 420w [νZr–S]; ^1H NMR ($CDCl_3$) : 2.32 (6H, s, CH_3), 6.76–6.98 (4H, m, *ortho*), 6.90 (2H, d, *para*), 7.12 (2H, t, *meta*), 5.75 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 20.24 (CH_3), 117.64–129.55 (C-*ortho*), 120.91 (C-*para*), 121.80 (C-*meta*), 136.58 (C–CH_3), 150.90 (C–O), 114.20 (C_5H_5), 166.72 (OCS_2) ppm.

Synthesis of [(p-$CH_3C_6H_4OCS_2)_2Zr(C_5H_5)_2$] (**15**) :

Complex **15** was synthesized according to the protocol as described for complex **9**; 1.00 g (4.84 mmol) of sodium *p*-tolyldithiocarbonate, *p*-$CH_3C_6H_4OCS_2Na$, and 0.70 g (2.39 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **15** as yellow solid. Yield : 1.28 g (92%); m.p. 220–221 °C (dec.); Anal. Calcd. for $C_{26}H_{24}O_2S_4Zr$: Calcd. (%) : C, 53.11; H, 4.11; S, 21.81; Zr, 15.52, Found (%) : C, 53.07; H, 4.08; S, 21.79; Zr, 15.48; FTIR (cm^{-1}) : 3362b [ν(C–H)], 1585s [ν(C–C)], 1233s [ν(C–O–C)], 1039b [ν(S–C–S)], 402w [νZr–S]; ^1H NMR ($CDCl_3$) : 2.21 (6H, s, CH_3), 6.90 (4H, d, *ortho*), 7.31 (4H, d, *meta*), 5.85 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 20.14 (CH_3), 127.02 (C-*ortho*), 129.47 (C–CH_3), 132.36 (C-*meta*), 154.03 (C–O), 117.14 (C_5H_5), 165.98 (OCS_2) ppm.

Synthesis of [(4-Cl-3-$CH_3C_6H_3OCS_2)_2Zr(C_5H_5)_2$] (**16**) :

Complex **16** was synthesized according to the protocol as described for complex **9**; 1.00 g (4.15 mmol) of sodium 4-chloro-3-methylphenyldithiocarbonate, 4-Cl-3-$CH_3C_6H_4OCS_2Na$, and 0.60 g (2.05 mmol) of zirconocene dichloride, $(C_5H_5)_2ZrCl_2$, was used to yield complex **16** as yellow solid. Yield : 1.21 g (91%); m.p. 223–224 °C (dec.); Anal. Calcd. for $C_{26}H_{22}O_2S_4Cl_2Zr$: Calcd. (%) : C, 47.54; H, 3.38; S, 19.53; Cl, 10.79; Zr, 13.38, Found (%) : C, 47.51; H, 3.36; S, 19.50; Cl, 10.77; Zr, 13.36; FTIR (cm^{-1}) : 3365b [ν(C–H)], 1574s [ν(C–C)], 1232s [ν(C–O–C)], 1040b [ν(S–C–S)], 416w [νZr–S]; ^1H NMR ($CDCl_3$) : 2.43 (6H, s, CH_3), 6.76–6.98 (4H, m, *ortho*), 7.11 (2H, d, *meta*), 5.45 (10H, s, C_5H_5) ppm; ^{13}C NMR ($CDCl_3$) : 17.05 (CH_3), 119.30–121.99 (C-*ortho*), 124.65 (C–CH_3), 129.07 (C-*meta*), 130.16 (C-*para*), 151.35 (C–O), 117.85 (C_5H_5), 168.05 (OCS_2) ppm; ESI-MS : *m/z* (%) = $[M^+]$** 656.8 (18) 658.8(13) 660.8(6) [(4-Cl-3-$CH_3C_6H_3OCS_2)_2Zr(C_5H_5)_2$]; $[M^+]$** 526.6(12) 528.6(8) 530.8(3) [(4-Cl-3-$CH_3C_6H_3OCS_2)_2Zr$]; $[M^+]$** 308.9(8) 310.8(4) 312.8(3) [(4-Cl-3-$CH_3C_6H_3OCS_2)Zr$]; $[M^+]$** 217.7(17) 219.7(12) 221.7(7) [(4-Cl-3-$CH_3C_6H_3OCS_2$)]; $[M^+]$ 182.2(18) [$CH_3C_6H_3OCS_2$]; $[M^+]$ 106.1(13) [($CH_3C_6H_3O$)].

Antifungal activity :

The antifungal activities of the complexes were evaluated by the poisoned food technique against pathogenic strain of fungus *Rhizopus nigricans*[28]. Potato dextrose medium (PDA) was prepared in a flask and sterilized; 100 mm^3 of each sample was added to the PDA medium and poured into each sterilized Petri plate. Mycelial discs taken from the standard culture of fungi were grown on PDA medium for 7 days. These cultures were used for aseptic inoculation in the sterilized Petri dish. Standard cultures, inoculated at 28 ± 1 °C, were used as the con-

** Isotopic peaks of chlorine complexes.

trol. The efficiency of each sample was determined by measuring the radial fungal growth. The radial growth of the colony was measured in two directions at right angles to each other, and the average of two replicates was recorded in each case. Data were expressed as percent inhibition over the control from the size of the colonies. The percent inhibition was calculated using the formula

$$\% \text{ Inhibition} = ((C - T)/C) \times 100,$$

where C is the diameter of the fungus colony in the control plate after 96 h incubation and T is the diameter of the fungus colony in the tested plate after the same incubation period.

Antibacterial activity :

The antibacterial activity was tested using agar well diffusion method[29]. Test samples were prepared in different concentrations (250, 500, 1000 ppm) in DMSO. Agar medium (20 mL) was poured into each Petri plate. The plates were swabbed with broth cultures of the respective microorganisms (*Klebsiella pneumonia* and *Enterococcus faciolus*) and kept for 15 min for adsorption to take place. Using a punch, ≈6-mm diameter wells were bored in the seeded agar plates, and 100 mm^3 of the DMSO solution of each test compound was added into the wells. DMSO was used as the control for all the test compounds. After holding the plates at room temperature for 2 h to allow diffusion of the compounds into the agar, the plates were incubated at 37 °C for 24 h. The antibacterial activity was determined by measuring the diameter of the inhibition zone. The entire tests were made in triplicates, and the mean of the diameter of inhibition was calculated.

Cytotoxic activity :

The cytotoxicity was measured *in vitro* using the cultivated human cell lines involving lung adeno carcinoma cell line A-549, leukemia cell line THP-1, lung cervical node cell line NCI-H322 and colorectal cancer cell line HCT-116. The inhibition capacity was assessed using the sulforhodamine B (SRB) protein staining assay by 96-well technique described previously by Skehan *et al.*[30]. The seeded 96-well plates are incubated for 48 h after addition of test samples. Then the cells were fixed in 30% trichloroacetic acid (TCA) and placed for 1 h at 4 °C followed by washing with distilled water. After air-drying, the fixed cells were stained with 0.4% SRB (prepared in 1% acetic acid), left at room temperature for 30 min washed with 1% acetic acid and dried. Solubilization is carried out with 10 mM tris buffer followed by recording the optical density (OD) with ELISA reader at 540 nm wavelength.

Results and discussion

Reactions of bis(cyclopentadienyl)titanium(IV) or zirconium(IV) dichloride, Cp_2MCl_2 (M = Ti or Zr), with sodium salt of dithiocarbonates in 1 : 1 and 1 : 2 stoichiometric ratio in chloroform yielded titanocene or zirconocene dithiocarbonates corresponding to $[(ROCS_2)_nM(C_5H_5)_2Cl_{2-n}]$ [R = *o*-$CH_3C_6H_4$, *m*-$CH_3C_6H_4$ or *p*-$CH_3C_6H_4$ and 4-Cl-3-$CH_3C_6H_3$; n = 1 or 2; M = Ti or Zr] as dark red and yellow solid. The reaction appears to be sluggish since ~3 h of refluxing was required (Scheme 1).

$$nROCS_2Na + (C_5H_5)_2MCl_2 \xrightarrow[\text{Reflux } \sim 3 \text{ h}]{CHCl_3} \underset{\text{-NaCl}}{} [(ROCS_2)_nM(C_5H_5)_2Cl_{2-n}]$$

(1-16)

[R = *o*-$CH_3C_6H_4$ (**1**,**5**,**9**,**13**), *m*-$CH_3C_6H_4$ (**2**,**6**,**10**,**14**), *p*-$CH_3C_6H_4$ (**3**,**7**,**11**,**15**) and 4-Cl-3-$CH_3C_6H_3$ (**4**,**8**,**12**,**16**), n = 1 or 2; M = Ti or Zr]

Scheme 1. Reactions of $ROCS_2Na$ with $(C_5H_5)_2MCl_2$.

These compounds are soluble in chloroform, dichloromethane, ethanol and acetone. These compounds appear to be bit moisture sensitive; however, these can be kept unchanged under anhydrous atmosphere. These compounds are non-volatile even under the reduced pressure and tend to decompose on heating as dark brown mass which could not be identified.

IR :

Comparison of IR spectra of these complexes with literature reports[9,16,31–33] and starting materials has given seminal information. Three main regions are of interest in dithiocarbonate compounds i.e. 1250–1200 cm^{-1} region primarily associated with the stretching of the C–O–C of $ROCS_2$, 1050–950 cm^{-1} region associated with $\nu(CS_2)$ and 420–250 cm^{-1} region which is associated with ν(M–S). The 1050–950 cm^{-1} region has been shown to be reliable for determining whether the ligand is bidentate or unidentate. According to Bonati and Ugo[33], presence of only one strong bond in the 1040–1005 cm^{-1} region is

associated with ν(C⎓S) stretching vibrations, which indicates complete symmetric bidentate bonding by dithiocarbonate ligand. Thus in complexes (**1**-**16**), the sharp bands were observed in the range 1040–1015 cm^{-1} owing to the bidentate mode of bonding by the dithiocarbonate ligand to the respective metal centre. The characteristic sharp band for ν(C–O–C) and broad band for ν(C=C) (tolyl ring stretching) were appeared in the region 1239–1229 and 1558–1618 cm^{-1}, respectively. The presence of new bands ascribed to ν(Ti–S) and ν(Zr–S) in the region 449–434 and 420–402 cm^{-1} also authenticate the chelation of dithio ligand with metal[27]. The weak band in the region 375–361 and 373–330 cm^{-1} may be attributed to [νTi–Cl] and [νZr–Cl], respectively[29].

^1H NMR :

The ^1H NMR spectra did not show any appreciable difference compared to the parent moieties. The protons of the cyclopentadienyl moiety were resonated as singlet in the region 5.05–5.85 ppm. The signal for the $-CH_3$ protons (tolyl ring) were observed as singlet at 2.13–2.43. The protons of the C_6H_4 (tolyl ring) in the complexes gave chemical shift in the range 6.17–7.70 with their usual splitting pattern. There were two resonances for the ring protons of *para* complexes (**3**, **7**, **11**, **15**) whereas four resonances were observed for *ortho* (**1**, **5**, **9**, **13**) and *meta* (**2**, **6**, **10**, **14**) derivatives. The splitting pattern and intensities of peaks in the spectra of all these complexes are found to be consistent with their structures.

^{13}C NMR :

The ^{13}C NMR spectra of all complexes show resonances for the carbon nuclei of the cyclopentadienyl ring in the region 114.20–121.36 ppm. The signals for methyl ($-CH_3$) carbon occurred in the range 17.05–21.04 ppm, respectively. The carbon nuclei of phenyl groups ($-C_6H_4$) displayed their resonance in the region 113.01–139.43 ppm. The signal in the region 147.71–154.03 ppm was due to the carbon attached to the oxygen in the tolyl derivatives. The chemical shift for the dithiocarbonate carbon ($-OCS_2$) was appeared at 162.12–169.94 ppm with an upfield shift (30–36 ppm) compared to the parent ligands. Presumably, this reflects the fact that environment around the CS_2 carbon is the one most affected by the formation of the Ti–S and Zr–S bond.

Mass :

The mass spectra of few representative complexes (**1**, **4**, **7**, **10**, **13** and **16**) depicted molecular ion peaks [M^+] at m/z = 396.7 (**1**), 431.2 (**4**), 544.5 (**7**), 440.1 (**10**), 587.9 (**13**) and 656.8 (**16**). In addition to the molecular ion peak, several other peaks of different fragments were also observed, which were formed after consecutive dismissal of different groups. The occurrence of molecular ion peak in the complexes is supporting the monomeric nature of the complexes. Furthermore, the presence of chlorine atoms in these complexes (**1**, **4**, **10** and **16**) resulted in the appearance of isotopic peaks at intervals of M, M+2 and M+4 in the mass spectra. The masses of the fragmented ions are calculated using one chlorine atom mass equal to 35 amu as it is the most abundant isotope of chlorine atom.

Thermogravimetric analysis :

The results are in good agreement with the composition of the complexes as calculated mass change agrees with experimental values. The thermogram from thermal studies performed on the complex [(*p*-$CH_3C_6H_4OCS_2$)$Ti(C_5H_5)_2Cl$] (**3**) is shown in Fig. 1(a). The results show a loss of weight 8.1% (obsd.) [8.9% (calcd.)] due to the removal of chloride group at approximately at 161.8 °C. Further heating up to 266.8 °C shows a gradual weight loss of 41.7% (theoretical weight loss 41.3%) attributable to the formation of [(*p*-$CH_3C_6H_4OCS_2$)Ti]. The weight loss (obsd. 44.1%, calcd. 45.1%) continues beyond this temperature and leads to formation of [$(C_6H_4OCS_2)$Ti] at 271.8 °C and finally attains a constant mass corresponding to TiS_2 (obsd. 68.1%, calcd. 68.7%) at 431.8 °C.

Similarly, the complex, [(*o*-$CH_3C_6H_4OCS_2)_2$Zr-$(C_5H_5)_2$] (**13**) displayed a thermolysis step that covers a temperature range from 150 to 900 °C. The thermogram exhibited the decline curve characteristic for dithiocarbonate complexes (Fig. 1(b)). The diagnostic weight loss of initial weight occurs in the steeply descending segment of the TGA curve. The weight loss i.e. 5.1% (obsd.) at 118.4 °C is due to the formation of the dithiocarbonate corresponding to [$(C_6H_5OCS_2)_2Zr(C_5H_5)_2$], weight loss 5.0% (calcd.) as an intermediate product, which agrees with thermogravimetric data for dithiocarbonates. Another important weight loss 27.2% (obsd.) occur at 253.4 °C temperature corresponding to the formation of

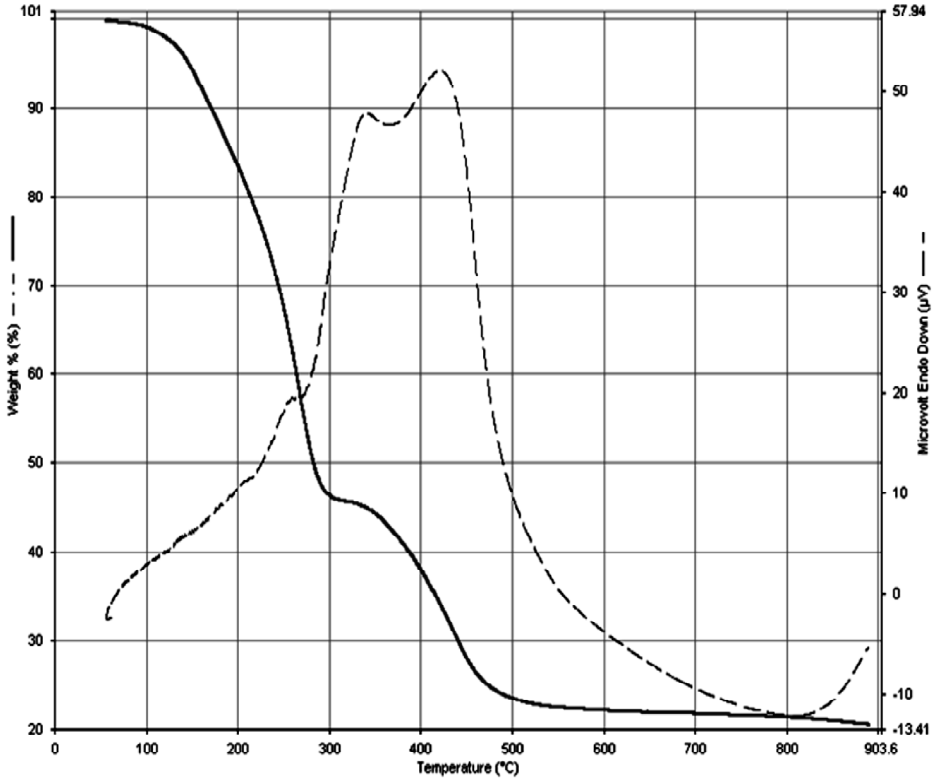

Fig. 1(a). TGA curve of [(*p*-$CH_3C_6H_4OCS_2$)Ti(C_5H_5)$_2$Cl] (**3**).

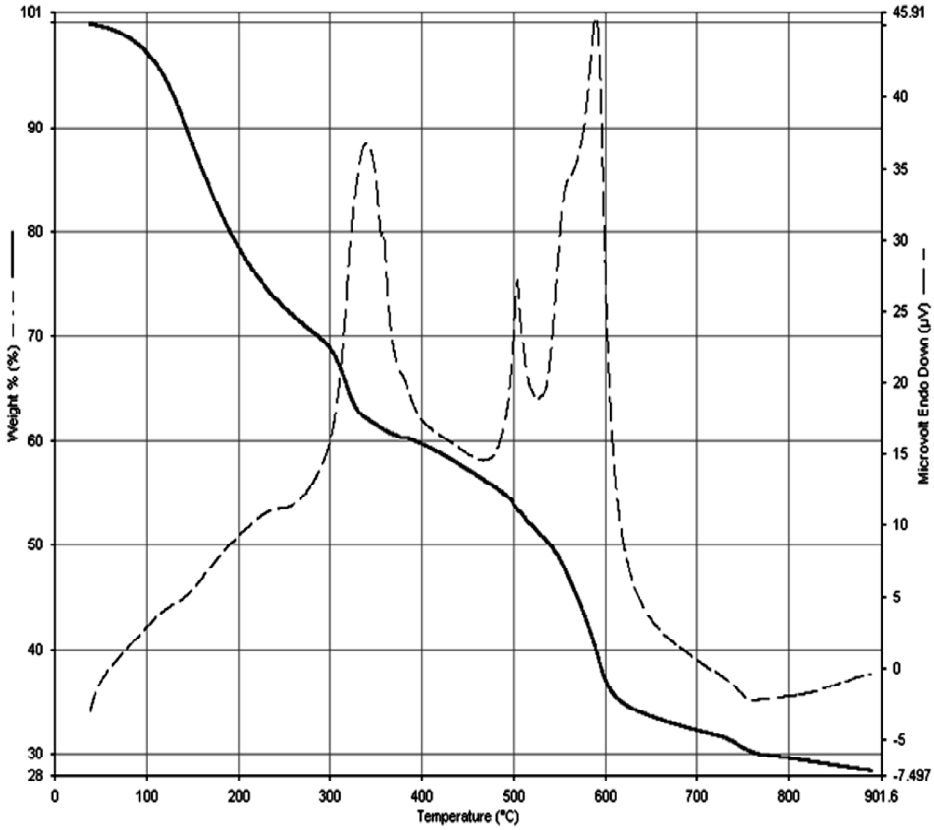

Fig. 1(b). TGA curve of [(*o*-$CH_3C_6H_4OCS_2$)$_2$Zr(C_5H_5)$_2$] (**13**).

$[(C_6H_5OCS_2)_2Zr]$ 27.5% (calcd.). The decomposition continues to about 878.4 °C at which most of the organic part of the compound has been lost. This sharp decomposition period brings about 71.4% (obsd.), 71.4% (calcd.), weight loss in the zirconium complex and led to the complete formation of ZrS_2.

Redox behaviour :

The redox behaviour of $[(m\text{-}CH_3C_6H_4OCS_2)Ti(C_5H_5)_2Cl]$ (**2**) in methanol at scan rate 100 V s^{-1} was recorded (Fig. 2a). The cyclic voltagramm depicts a cathodic peak (E_{pc}) at 0.88 V and the anodic peak (E_{pa}) at 1.14 V. The cathodic peak current (i_c) and the anodic peak current (i_a) were found to be -2.9×10^{-5} A and 5.4×10^{-5} A, respectively.

For the complex, $[(p\text{-}CH_3C_6H_4OCS_2)_2Zr(C_5H_5)_2]$ (**15**), the anodic peak (E_{pc}) and cathodic peak (E_{pa}) were found at –0.26 V and 0.62 V, respectively (Fig. 2b). The corresponding anodic current (i_a) was found -1.4×10^{-5} A while and cathodic currents (i_c) 1.6×10^{-5} A. The ratio to anodic and cathodic current (i_c/i_a) was found to be 1.14, which is close to unity corresponding to simple one-electron process.

The presence of new bands in the IR ascribed to ν(Ti–S) and ν(Zr–S) authenticate the chelation of dithio ligand

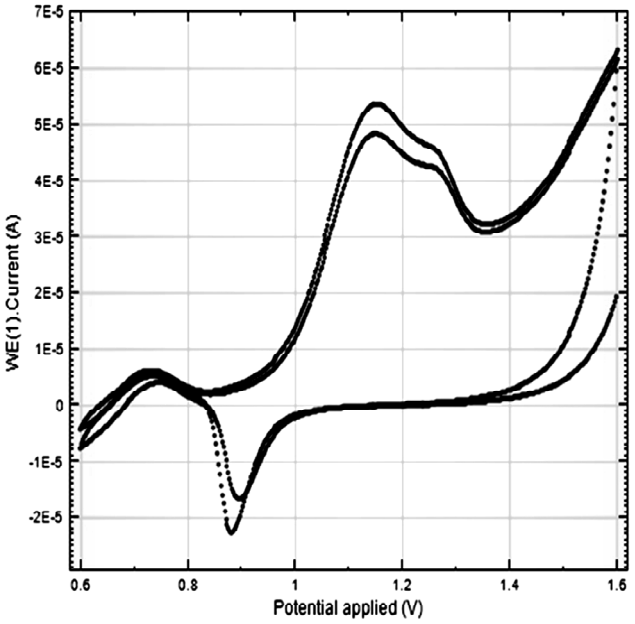

Fig. 2(a). Cyclic voltammetric curve of $[(m\text{-}CH_3C_6H_4OCS_2)Ti(C_5H_5)_2Cl]$ (**2**).

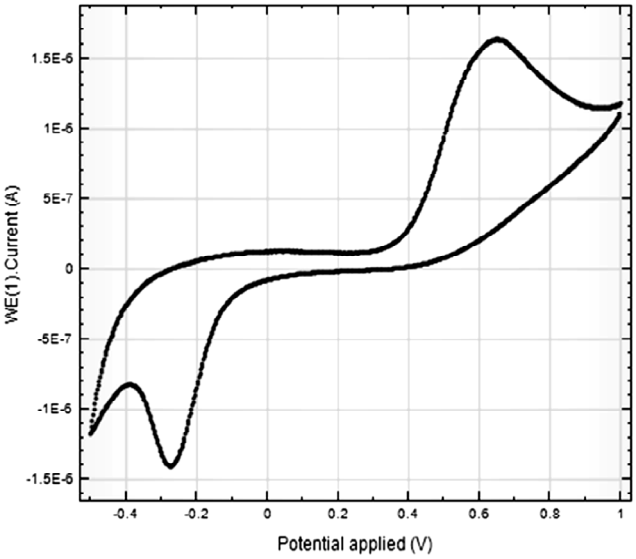

Fig. 2(b). Cyclic voltammetric curve of $[(p\text{-}CH_3C_6H_4OCS_2)_2Zr(C_5H_5)_2]$ (**15**).

with the titanium and zirconium. The mass spectra show the molecular ion peak (*m/z*). ^1H and ^{13}C NMR spectra also support the formation of these complexes as these have depicted the chemical shift for each proton and carbon nuclei. In conjunction with the literature reports[9,16,27,31–33], trigonal bipyramidal (t_{bp}) (pentacoordinate) and octahedral (O_h) (hexacoordinate) geometries may tentatively be proposed around the titanium(IV) or zirconium(IV) atom as consequence of bidentate mode of bonding in the complexes corresponding to $[(ROCS_2)M(C_5H_5)_2Cl]$ (**1-4**, **9-12**) and $[(ROCS_2)_2M(C_5H_5)_2]$ **(5-8**, **13-16),** respectively (Figs. 3 and 4).

Antifungal activity :

The antifungal activity of the complexes against *Rhizo-*

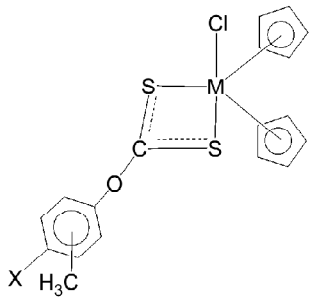

Fig. 3. Proposed pentacoordinate geometry for the complexes $[(ROCS_2)M(C_5H_5)_2Cl]$(**1-4**, **9-12**) (R = *o*-, *m*-, *p*-$CH_3C_6H_4$ and 4-Cl-3-$CH_3C_6H_3$, M = Ti or Zr).

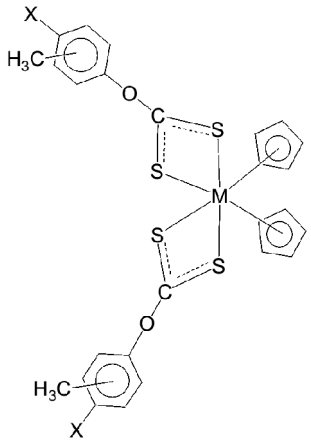

Fig. 4. Proposed hexacoordinate geometry for the complexes $[(ROCS_2)_2M(C_5H_5)_2]$ (**5**-**8**, **13**-**16**) (R = *o*-, *m*-, *p*-$CH_3C_6H_4$ and 4-Cl-3-$CH_3C_6H_3$, M = Ti or Zr).

pus nigricans establishes a linear relationship between concentration and percent inhibition. All the complexes inhibited the growth of fungus significantly on enhancing the concentration of the complex. The increase of inhibition might be due to faster diffusion of the complexes whole through the cell membrane or due to combined activity effect of the metal and ligand[34]. Moreover, the complexes may also indulge in the formation of bridge between the coordinated chloride anion with the active centre of cell constituents. The factors capable of increasing lipophilicity are expected to enhance the antimicrobial activity. Among all, the complex $[(4\text{-Cl-3-}CH_3C_6H_3OCS_2)_2Ti(C_5H_5)_2]$ (**8**) showed remarkable antifungal activity (Table 1). Antifungal data shows that titanium complexes are more potential compared to zirconium complexes. The results of fungitoxicity analysis have been illustrated as a bar graph in Fig. 5.

Antibacterial activity :

Antibacterial *in vitro* studies against Gram-negative *Klebsiella pneumonia* and Gram-positive *Bacillus cereus* using penicillin as standard antibacterial drug are summarized in Table 2. The ligands did not exhibit appreciable inhibition in comparison to the complexes. The slight modification of the ligand's ability to inhibit bacteria is attributed to the general principle based on chelation[34]. It has also been observed that concentration plays a vital role in increasing the degree of inhibition as it increases with higher concentration. The complex [(4-Cl-

Table 1. *In vitro* evaluation of complexes against the fungus *Rhizopus nigricans*

Sl. no.	Conc. (ppm)	Colony diameter (mm)	%Inhibition $I = [(C - T)/C] \times 100$
o-$CH_3C_6H_3OCS_2Na$	50	4.7	0
	100	4.3	9
	150	4.1	13
	200	3.9	17
	250	3.8	19
4-Cl-3-$CH_3C_6H_3OCS_2Na$	50	3.5	25
	100	3.0	36
	150	2.0	57
	200	1	79
	250	0.5	89
2	50	4.1	15
	100	3.0	32
	150	2.2	51
	200	2.0	60
	250	1.5	70
7	50	4.2	13
	100	4.0	36
	150	3.0	53
	200	2.8	57
	250	2.0	68
8	50	2.0	57
	100	1.5	68
	150	1.0	79
	200	0.2	96
	250	0	100
9	50	4.0	11
	100	3.2	15
	150	2.3	36
	200	1.9	40
	250	1.4	57
15	50	4.1	13
	100	3.5	25
	150	3.1	34
	200	2.5	47
	250	2.1	55
16	50	2.5	47
	100	2.0	57
	150	1.6	66
	200	0.3	94
	250	0	100

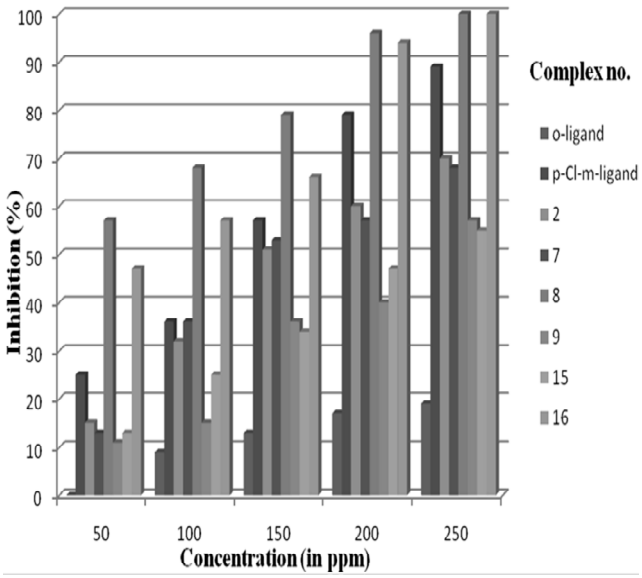

Fig. 5. Graph showing comparative result of antifungal activity.

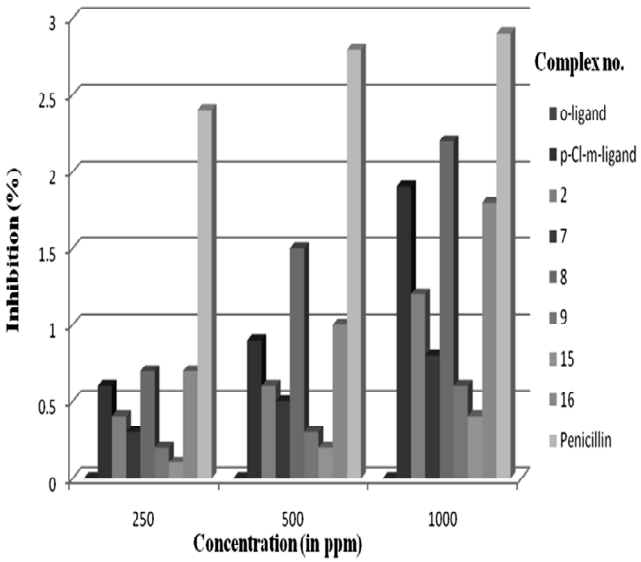

Fig. 6(b). Graph showing comparative result of antibacterial activity for bacteria *Bacillus cereus* (+).

3-$CH_3C_6H_3OCS_2)_2Ti(C_5H_5)_2$] **(8)** shows pronounced activity against *Klebsiella pneumonia* and *Bacillus cereus* amongst all. Antibacterial data also reveals that titanium complexes are more active than zirconium complexes. The comparison of antibacterial activity of ligands and some of the complexes is described diagrammatically in Fig. 6(a-b).

Cytotoxic analysis :

In the present study, the comparative evaluation of cytotoxicity of the ligands, *o*-$CH_3C_6H_4OCS_2Na$, 4-Cl-3-$CH_3C_6H_3OCS_2Na$ and representative complexes, [(*m*-$CH_3C_6H_4OCS_2)Ti(C_5H_5)_2Cl$] **(2)**, [(4-Cl-3-$CH_3C_6H_3OCS_2)$-$Ti(C_5H_5)_2Cl$] **(4)**, [(*o*-$CH_3C_6H_4OCS_2)_2Ti(C_5H_5)_2$] **(5)** and [(4-Cl-3-$CH_3C_6H_3OCS_2)_2Ti(C_5H_5)_2$] **(8)** has been done. Titanocene dichloride has been recognized as active anticancer drug against breast and gastrointestinal carcinomas. The active species of titanocene dichloride responsible for antitumor activity *in vivo* and the mechanism of action have been discussed in literature reports[35–37]. DNA was supposed to be its target in a manner similar to cisplatin due to the similarity in Cl-Cl distances. But the aqueous chemistry of titanocene dichloride displaced the anticancer activity because of inhibition of collagenase type IV activity, which is involved in regulation of cellular proliferation, protein kinase C and DNA topoisomerase II activities. The titanocene dichloride is believed to be accumulated via the transferrin-dependent pathways. The cytotoxic properties of the complex [(4-Cl-3-$CH_3C_6H_3OCS_2)Ti(C_5H_5)_2Cl$] (**4**) exhibited maximum antitumor potency as compared to the ligands (Table 3). The metal complex is rather more effective than the pure ligand, and it is likely that the metal serves as a protective carrier for the ligand, ensuring to intact at the active site. The maximum cytotoxic activity was observed against

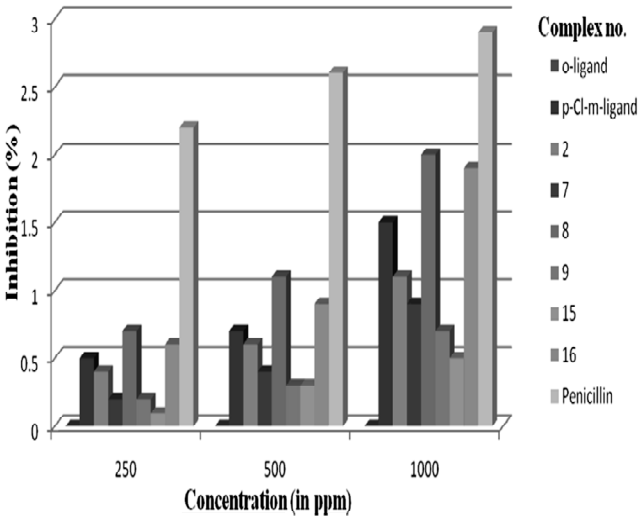

Fig. 6(a). Graph showing comparative result of antibacterial activity for bacteria *Klebsiella pneumonia* (–).

Table 2. *In vitro* evaluation of complexes for antibacterial activity

Sl. no.	Diameter of inhibition zone (cm) (conc. in ppm)					
	Klebsiella pneumonia (–)			*Bacillus cereus* (+)		
	250 ppm	500 ppm	1000 ppm	250 ppm	500 ppm	1000 ppm
o-$CH_3C_6H_3OCS_2Na$	0	0	0	0	0	0
4-Cl-3-$CH_3C_6H_3OCS_2Na$	0.5	0.7	1.5	0.6	0.9	1.9
2	0.4	0.6	1.1	0.4	0.6	1.2
7	0.3	0.4	0.9	0.3	0.5	0.8
8	0.7	1.1	2.0	0.7	1.5	2.2
9	0.2	0.3	0.7	0.2	0.3	0.6
15	0.1	0.3	0.5	0.1	0.2	0.4
16	0.6	0.9	1.9	0.7	1.0	1.8
Penicillin	2.2	2.6	2.9	2.4	2.8	2.9

Table 3. *In vitro* evaluation cytotoxicity activity of dithiocarbonate ligands and its titanium(IV) complexes

Cell line type		THP-1	HCT-116	NCI-H322	A549
Sl. no.	Conc. (μM)	% Growth inhibition			
o-$CH_3C_6H_3OCS_2Na$	100	0	65	24	34
4-Cl-3-$CH_3C_6H_3OCS_2Na$	100	11	86	29	69
2	100	0	82	29	63
4	100	96	96	70	94
5	100	0	75	22	53
8	100	52	37	4	30

the leukemia cell line THP-1 and colorectal cancer cell line HCT-116. The comparative cytotoxicity data is well illustrated in the form of bar graphs in Fig. 7.

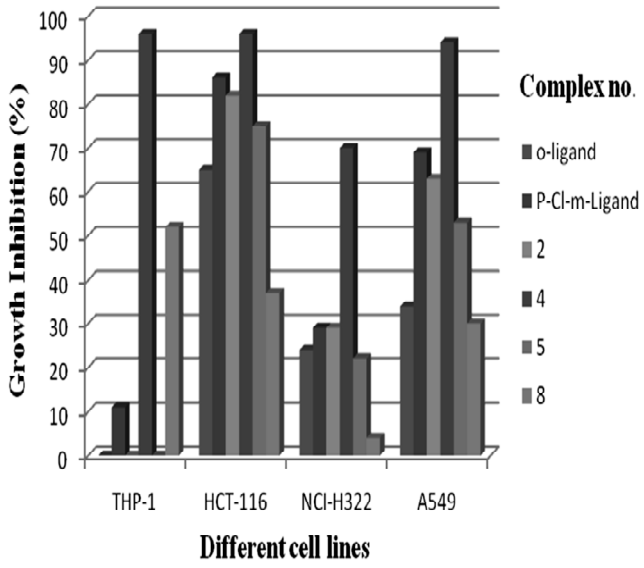

Fig. 7. Comparative cytotoxic activity of dithiocarbonate ligands and its titanium(IV) complexes.

Conclusions

We have reported synthesis and characterization of some new metallocene complexes of titanium and zirconium with mono- and di-substituted phenyldithiocarbonates, having methyl and chlorine substituents, corresponding to $[(ROCS_2)_nM(C_5H_5)_2Cl_{2-n}]$ (R = *o*-, *m*- or *p*-$CH_3C_6H_4$, $C_6H_5CH_2$ and 4-Cl-3-$CH_3C_6H_3$; n = 1 or 2; M = Ti or Zr). Further, electrochemical study depicted one electron redox process of the metal. Antimicrobial screening data show that titanium complexes are more potential compared to zirconium complexes. The cytotoxic properties of the complex [(4-Cl-3-$CH_3C_6H_3OCS_2$)-$Ti(C_5H_5)_2Cl$] (**4**) exhibited maximum antitumor potency compared to other complexes and free ligands.

Acknowledgement

We are grateful to the Sophisticated Analytical Instrumentation Facility, Panjab University, Chandigarh and NMR Lab (PURSE Programme), Department of Chemistry, University of Jammu, Jammu, for providing spectral facilities. We are also thankful to the Division of Pharmacology, IIIM, Jammu, for providing cytotoxicity analysis.

References

1. O. P. Pandey, S. P. Sengupta and C. M. Tripathi, *Molecules*, 2005, **10**, 653.
2. Y. Quin, J. Huang, M. D. Bala, B. Lian and H. Zhang, *Chem. Rev.*, 2003, **103**, 2633.
3. A. O. Gorgulu, H. Celikkanb and M. Arslan, *Acta Chim. Slov.*, 2009, **56**, 334.
4. G. Winter, *Rev. Inorg. Chem.*, 1980, **2**, 253.
5. E. R. T. Tiekink and G. Winter, *Rev. Inorg. Chem.*, 1992, **12**, 183.
6. B. F. Hoskins and C. D. Pannan, *J. Chem. Soc. Chem.*, 1975, 408.
7. D. Dakternieks, R. Di. Giacomo, R. W. Gable and B. F. Hoskins, *J. Am. Chem. Soc.*, 1988, **110**, 6762.
8. E. R. T. Tiekink and I. Haiduc, *Progress Inorg. Chem.*, 2005, **54**, 127.
9. B. Gupta, N. Kalgotra, S. Andotra and S. K. Pandey, *Monatsh Chem.*, 2012, **143**, 1087.
10. O. V. Bakbardina, I. J. Pukhnyarskaya, M. A. Gazalieva, S. D. Fazylov and E. M. Makarov, *Rus. J. App. Chem.*, 2006, **79**, 1726.
11. A. A. Abramov and K. S. E. Forssberg, *Miner. Process Extr. Metall. Rev.*, 2005, **26**, 77.
12. S. Chaudari and V. Tare, *J. Appl. Polym. Sci.*, 1999, **71**, 1325.
13. K. Xu and W. Ding, *Mater. Lett.*, 2008, **62**, 4437.
14. Q. Han, J. Chen, X. Yang, L. Lu and X. Wang, *J. Phys. Chem. (C)*, 2007, **111**, 14072.
15. D. E. Zelmon, Z. Gebeyehu, D. Tomlin and Th. M. Copper, *Mater. Res. Soc. Symp. Proc.*, 1998, **519**, 395.
16. N. Kalgotra, B. Gupta, K. Kumar and S. K. Pandey, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2012, **187**, 364.
17. W. M. Doane, B. S. Shasha and C. R. Russel, *Controlled Release Pesticides*, 1977, **53**, 74.
18. M. Scendo, *Corrosion Science*, 2005, **47**, 1738.
19. W. J. Orts, R. E. Sojka and G. M. Glenn, *Agro. Food Industry*, 2002, **37**, 1078.
20. O. A. Gorgulu, M. Arslan and E. Cil, *J. Coord. Chem.*, 2006, **59**, 637.
21. A. C. Larsson and S. Oberg, *J. Phys. Chem. (A)*, 2011, **115**, 1396.
22. E. Amtmann, *Drugs Exp. Clin. Res.*, 1996, **22**, 287.
23. M. Perluigi, G. Joshi, R. Sultana, V. Calabrese, C. DeMarco, R. Coccia and D. A. Butterfirld, *Neuroscience*, 2006, **138**, 1161.
24. N. Kalgotra, B. Gupta, S. Andotra, S. Kumar and S. K. Pandey, *Int. J. Inorg Chem.*, 2013, **2013**, 1.
25. S. Andotra, N. Kalgotra and S. K. Pandey, *Bioinorg. Chem. Appl.*, 2014, **2014**, 1.
26. B. Gupta, D. Kumar, N. Kalgotra, S. Andotra, G. Kour, V. K. Gupta, R. Kant and S. K. Pandey, *Acta Chim. Slov.*, In press.
27. A. I. Vogel, "Quantitative Inorganic Analysis", 3rd ed., Longmans, London, 1961.
28. D. P. Singh, V. Malik, R. Kumar and K. Kumar, *J. Serb. Chem. Soc.*, 2010, **75**, 763.
29. M. Kamboj, D. P. Singh and K. Jain, *Int. J. Chem. Res.*, 2012, **3**, 21.
30. P. Skehan, R. Storeng, D. Scudiero, A. Monks, J. McMahon, D. Vistica, J. T. Warren, H. Bokesch, S. Kenney and M. R. Boyd, *J. Natl. Cancer Inst.*, 1990, **82**, 1107.
31. A. A. S. El-Khaldy, A. R. Hussien, A. M. Abu Shanab and M. A. Wassef, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2011, **186**, 589.
32. K. Nakamoto, "Infrared and Raman Spectra of Inorganic and Coordination Compounds", 4th ed., Wiley-Interscience, New York, 1986.
33. F. Bonati and R. Ugo, *J. Organomet. Chem.*, 1967, **10**, 257.
34. B. G. Tweedy and C. Loeppky, *Phytopathology*, 1968, **58**, 1522.
35. J. R. Boyles, M. C. Baird, B. G. Campling and N. Jain, *J. Inorg. Biochem.*, 2001, **84**, 159.
36. A. M. Pizarro, A. Habtemariam and P. J. Sadler, *Top. Organomet. Chem.*, 2010, **32**, 21.
37. X. Stachtea, N. Karamanos and N. Klouras, *Anticancer Res.*, 2009, **29**, 3227.