*Journal of Sulfur Chemistry*
Vol. 31, No. 6, December 2010, 515–524

Taylor & Francis
Taylor & Francis Group

# Studies on chromium(III) complexes with active nitrogen, oxygen and sulfur donor ketimines synthesized under microwave conditions

Sumit Shrivastava, Nighat Fahmi and R.V. Singh*

*Department of Chemistry, University of Rajasthan, Jaipur-302004, India*

(*Received 14 July 2009; final version received 31 July 2010*)

Heterocyclic ketimines, 1-(2-furanyl)ethanonehydrazincarbothioamide ($L^1H$), 1-(2-furanyl)ethanonehydrazincarboxamide ($L^2H$), 1-(2-thienyl)ethanone hydrazincarbothioamide ($L^3H$) and 1-(2-thienyl) ethanonehydrazincarboxamide ($L^4H$), were prepared by the condensation of thiosemicarbazide and semicarbazide hydrochloride (in the presence of sodium acetate) in ethanol with the respective ketones by using microwave as well as conventional methods. Chromium(III) complexes have been prepared by mixing $CrCl_3 \cdot 6H_2O$ in 1:1 and 1:2 molar ratios with monobasic bidentate ketimines. The authenticity of the ligands and their complexes has been established by elemental analyses, melting point determinations, molecular weight determinations, EPR, infrared and UV spectral and X-ray powder diffraction studies. These studies showed that the ligands coordinated to the metal atom in a monobasic bidentate mode, coordinating through the nitrogen and sulfur/oxygen donor system. Thus, an octahedral environment around the metal atoms has been proposed. The growth-inhibiting potential of the ligands and complexes has been assessed against a variety of fungal and bacterial strains.

**Keywords:** chromium(III) complexes; heterocyclic ketimines; spectral studies; antimicrobial activity

## 1. Introduction

Increasing attention for environmental protection during the last decades has led both modern academic and industrial groups to develop chemical processes with the maximum yield and minimum cost while using non-toxic reagents, solvents and catalysts (*1*). Microwave (MW) synthesis represents one of the important dimensions of modern chemistry attracting a considerable amount of attention (*2*). Metal complexes, in particular of transition metal ions, are important in many areas of science, including catalysis, medicine (diagnosis and therapy), design of high value materials, analytical chemistry and as model compounds with the structure and function of metalloproteins (*3, 4*). The metal oxidation state, the type and number of donor atoms, as well as their relative disposition within the ligand, are major factors determining the structure–activity relationship of the metal complexes (*5*). Chromium(III) is a unique transition metal, which has been established

*Corresponding author. Email: rvsjpr@hotmail.com

ISSN 1741-5993 print/ISSN 1741-6000 online

DOI: 10.1080/17415993.2010.513438
http://www.informaworld.com

to be biologically significant at all the levels of living organisms (*6*). Out of the two stable oxidation states of chromium, chromium(III) has been shown to play a positive role in controlling carbohydrate and lipid metabolism (*7*). For instance, even at the prokaryotic level, chromic chloride has been shown to maintain the glucose levels in the yeast, *Saccharomyces cerevisiae* (*8*). Ketimine complexes of chromium(III) are efficient inhibitors for the pathogenic microorganism and have invasive potential of *Shigella dysenteriae* (*9*). Thiosemicarbazones usually act as chelating ligands with the transition metal ion, bonding through the sulfur and azomethine nitrogen atoms. The chemistry of thiosemicarbazones has received considerable attention in view of their variable bonding modes, promising biological implications, structural diversity and ion-sensing ability (*10*). Semicarbazones and thiosemicarbazones have been used as drugs and are reported to possess a wide variety of biological activities against bacteria, fungi and certain types of tumors, and they are also a useful model for bioinorganic processes (*11*).

Because of the wide range of medicinal applications of semicarbazones and thiosemicarbazones and their abilities to coordinate with the transition metal ions, it is highly desirable to synthesize and characterize the transition metal complexes with such ketimines. Keeping all these facts under consideration during the present investigations, we have synthesized, characterized and screened the biologically potent ligands and their chromium(III) complexes against a variety of pathogenic fungal and bacterial strains.

## 2. Results and discussion

The resulting chromium(III) complexes are green solids, soluble in MeOH, DMF and DMSO and sparingly soluble in $H_2O$. Molecular weight determinations indicate their monomeric nature. The reactions of $CrCl_3 \cdot 6H_2O$ with the ligands were carried out in unimolar and bimolar ratios in methanol. The successive replacement of chloride resulted in the formation of products $[CrCl_2(L)(H_2O)_2]$ and $[(CrCl(L)_2(H_2O)]$ as shown in Equations (1) and (2).

$$CrCl_3 \cdot 6H_2O + LH + NaOH \xrightarrow[MeOH]{1:1} [CrCl_2(L)(H_2O)_2] + NaCl + 5H_2O \quad (1)$$

$$CrCl_3 \cdot 6H_2O + 2LH + 2NaOH \xrightarrow[MeOH]{1:2} [(CrCl(L)_2(H_2O)] + 2NaCl + 7H_2O. \quad (2)$$

The physical properties and analytical data of the ligands and their metal complexes, synthesized by green chemical approach as well as conventional method, are enlisted in Tables 1 and 2.

### 2.1. *Electronic spectra*

The electronic spectra of the complexes were recorded in DMSO. In the electronic spectra of chromium(III) complexes, three transitions are expected and are also observed experimentally. A consistent treatment for the bands is to assign the band near 15,550–17,900 $cm^{-1}$ as the $^4A_2g \rightarrow {}^4T_2g$ ($\nu_1$) transition; the band at 22,850–24,040 $cm^{-1}$ as the $^4A_2g \rightarrow {}^4T_1g$ ($\nu_2$) transition and that at 32,700–30,080 $cm^{-1}$ as the $^4A_2g \rightarrow {}^4T_1g$ (P) ($\nu_3$) transition. These three transitions suggest an octahedral geometry around the $Cr^{+3}$ ion (*12, 13*). Various ligand field parameters such as Dq, $B$, and $\beta$ have been calculated and given in Table 3. The energy of the first spin-allowed transition [$^4A_2g(F) \rightarrow {}^4T_2g$ (F)] directly gives the value of 10Dq. The ligand field spectral parameters for chromium(III) complexes are found to be Dq = 1790–1680 $cm^{-1}$, $B$ = 471–882 $cm^{-1}$ and $\beta$ = 0.51–0.96. The reduction in the Racah parameter ($B$) from the free-ion value of 918–654 $cm^{-1}$ and the value of $\beta$ indicate the covalent nature of the chromium(III) complexes.

Table 1. Analytical data and physical properties of the ligands and their complexes synthesized by conventional heating.

| Compounds | Color | Melting point (°C) | Found (calculated) (%) | | | | | Molecular weight found (calculated) |
|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | S | M | |
| $L^1H$ | Brown | 108–110 | 45.01 (45.88) | 4.87 (4.91) | 22.09 (22.93) | 16.99 (17.50) | – | 186.30 (183.23) |
| $L^2H$ | White | 160–162 | 49.95 (50.29) | 4.96 (5.42) | 25.71 (25.14) | – | – | 169.75 (167.09) |
| $L^3H$ | Yellow | 130–132 | 41.85 (42.18) | 4.21 (4.55) | 20.90 (21.08) | 32.96 (32.17) | – | 205.37 (199.30) |
| $L^4H$ | White | 187–190 | 45.01 (45.88) | 4.42 (4.95) | 22.15 (22.93) | 17.18 (17.50) | – | 185.32 (183.23) |
| $[CrCl_2(L^1)(H_2O)_2]$ | Green | 140–143 | 24.14 (24.62) | 3.67 (3.54) | 11.84 (12.03) | 10.97 (9.39) | 15.44 (15.29) | 343.32 (341.14) |
| $[CrCl(L^1)_2(H_2O)]$ | Green | 160–164 | 34.77 (35.78) | 3.92 (3.86) | 17.98 (17.03) | 13.06 (13.64) | 10.91 (11.07) | 471.31 (469.89) |
| $[CrCl_2(L^2)(H_2O)_2]$ | Green | 262–265 (d) | 25.96 (25.84) | 3.51 (3.72) | 10.80 (11.08) | – | 16.10 (16.18) | 329.25 (325.07) |
| $[CrCl(L^2)_2(H_2O)$ | Green | 223–225 (d) | 38.78 (38.11) | 3.75 (4.14) | 15.78 (15.30) | – | 10.13 (10.97) | 496.36 (491.26) |
| $[CrCl_2(L^3)(H_2O)_2]$ | Green | 180–200 (d) | 22.66 (23.52) | 2.84 (3.38) | 12.03 (12.11) | 17.52 (17.97) | 14.86 (14.56) | 360.46 (357.01) |
| $[CrCl(L^3)_2(H_2O)]$ | Green | 215–225 (d) | 32.45 (33.49) | 3.10 (3.61) | 16.07 (16.74) | 25.17 (25.54) | 10.72 (10.37) | 505.34 (501.03) |
| $[CrCl_2(L^4)(H_2O)_2]$ | Green | 190–200 (d) | 23.43 (24.64) | 3.88 (3.52) | 12.25 (12.69) | 9.86 (9.39) | 15.00 (15.29) | 346.34 (341.14) |
| $[CrCl(L^4)_2(H_2O)]$ | Green | 150–160 (d) | 36.21 (35.84) | 3.13 (3.86) | 18.09 (17.88) | 13.11 (13.65) | 11.79 (11.07) | 471.19 (469.90) |

Note: d, decomposition.

Table 2. Analytical data and physical properties of the ligands and their complexes synthesized by MW method.

| Compounds | Color | Melting point (°C) | Found (calculated) (%) | | | | | Molecular weight found (calculated) |
|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | S | M | |
| $L^1H$ | Brown | 108–110 | 45.12 (45.88) | 4.97 (4.91) | 22.87 (22.93) | 17.46 (17.50) | – | 184.51 (183.23) |
| $L^2H$ | White | 160–162 | 50.15 (50.29) | 5.89 (5.42) | 25.10 (25.14) | – | – | 168.99 (167.05) |
| $L^3H$ | Yellow | 130–132 | 41.83 (42.18) | 4.52 (4.55) | 21.45 (21.08) | 32.12 (32.17) | – | 200.55 (199.30) |
| $L^4H$ | White | 187–190 | 46.01 (45.88) | 4.88 (4.95) | 22.91 (22.93) | 17.38 (17.50) | – | 185.90 (183.23) |
| $[CrCl_2(L^1)(H_2O)_2]$ | Green | 140–143 | 24.54 (24.62) | 3.60 (3.54) | 12.56 (12.03) | 9.31 (9.39) | 15.78 (15.29) | 342.22 (341.14) |
| $[CrCl(L^1)_2(H_2O)]$ | Green | 160–164 | 34.77 (35.78) | 3.05 (3.86) | 17.00 (17.03) | 13.46 (13.64) | 11.15 (11.07) | 470.76 (469.89) |
| $[CrCl_2(L^2)(H_2O)_2]$ | Green | 262–265 (d) | 25.92 (25.84) | 3.01 (3.72) | 11.24 (11.08) | – | 16.09 (16.18) | 327.42 (325.07) |
| $[CrCl(L^2)_2(H_2O)$ | Green | 223–225 (d) | 37.74 (38.11) | 3.97 (4.14) | 15.16 (15.30) | – | 10.81 (10.97) | 492.25 (491.26) |
| $[CrCl_2(L^3)(H_2O)_2]$ | Green | 180–200 (d) | 23.66 (23.52) | 3.05 (3.38) | 12.19 (12.11) | 17.83 (17.97) | 14.72 (14.56) | 359.92 (357.01) |
| $[CrCl(L^3)_2(H_2O)]$ | Green | 215–225 (d) | 32.99 (33.49) | 3.58 (3.61) | 16.57 (16.74) | 25.68 (25.54) | 10.21 (10.37) | 503.64 (501.03) |
| $[CrCl_2(L^4)(H_2O)_2]$ | Green | 190–200 (d) | 24.43 (24.64) | 3.49 (3.52) | 12.69 (12.69) | 9.46 (9.39) | 15.33 (15.29) | 343.83 (341.14) |
| $[CrCl(L^4)_2(H_2O)]$ | Green | 150–160 (d) | 35.11 (35.84) | 3.37 (3.86) | 17.29 (17.88) | 13.69 (13.65) | 10.95 (11.07) | 470.88 (469.90) |

Note: d, decomposition.

Table 3. Electronic spectral data ($cm^{-1}$) of the chromium(III) complexes.

| Compounds | Transitions | Spectral bands $cm^{-1}$ (nm) | Dq | $B^\circ$ | $\beta = B/B^\circ$ | $\nu_2/\nu_1$ |
|---|---|---|---|---|---|---|
| $[CrCl_2(L^1)(H_2O)_2]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 16,800 (595) | 1680 | 617 | 0.67 | 1.37 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 23,100 (432) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 30,080 (332) | | | | |
| $[CrCl(L^1)_2(H_2O)]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 17,340 (576) | 1734 | 651 | 0.70 | 1.38 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 23,950 (417) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 32,050 (312) | | | | |
| $[CrCl_2(L^2)(H_2O)_2]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 15,550 (643) | 1555 | 882 | 0.96 | 1.47 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 22,995 (434) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 30,314 (329) | | | | |
| $[CrCl(L^2)_2(H_2O)]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 17,540 (570) | 1754 | 635 | 0.69 | 1.37 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 24,040 (415) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 32,356 (309) | | | | |
| $[CrCl_2(L^3)(H_2O)_2]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 17,900 (553) | 1790 | 471 | 0.51 | 1.28 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 23,050 (433) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 31,500 (317) | | | | |
| $[CrCl(L^3)_2(H_2O)]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 17,210 (581) | 1721 | 552 | 0.60 | 1.33 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 23,000 (434) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 30,300 (330) | | | | |
| $[CrCl_2(L^4)(H_2O)_2]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 17,380 (575) | 1739 | 563 | 0.61 | 1.34 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 23,290 (429) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 32,700 (306) | | | | |
| $[CrCl(L^4)_2(H_2O)]$ | $^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ | 17,035 (586) | 1704 | 563 | 0.61 | 1.34 |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ | 22,850 (436) | | | | |
| | $^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ | 31,780 (315) | | | | |

Note: B, Complex; Bo, free ion.

### 2.2. *ESR spectra and magnetic moment*

The electron spin resonance spectra of 1:1 and 1:2 chromium(III) complexes were recorded at room temperature. These consist of a single broad peak in each case and from which the Lande splitting factor ("*g*" values) has been calculated which lie in the range 1.9289–1.9431, with $g_{iso}$ (2.04) which are characteristic of an octahedral geometry (*14*). The room temperature magnetic moment for the chromium(III) chelates is slightly less than the required environment. The observed magnetic moment value of 3.92–4.20 BM and the electronic spectra of the complexes support the octahedral structure of the complexes (*15*).

### 2.3. *Infrared spectra*

The infrared (IR) spectra of the thiosemicarbazones ($L^1H$ and $L^3H$) and semicarbazones ($L^2H$ and $L^4H$) display a sharp band at 1610–1600 $cm^{-1}$, which is shifted to a lower frequency, in the spectra of the corresponding metal complexes, probably due to the coordination of the azomethine nitrogen to the metal atom. In the spectra of the free ligands, bands appearing due to $\nu$(NH) vibrations in the regions 3240–3230 $cm^{-1}$disappear in the spectra of the complexes, indicating deprotonation of the functional groups on complexation. Medium-intensity bands due to $\nu$(C=S)/$\nu$(C=O) vibrations appear in the regions 1050–1040/1690–1680 $cm^{-1}$ in the spectra of ligands and shifted to the lower frequency in the spectra of the complexes. This fact is further corroborated by the observation of the new bands due to $\nu$(C–O) and $\nu$(C–S) modes at lower frequency in the spectra of chromium(III)

complexes. In the spectra of chromium(III) complexes, a band is observed in the range 870–860 $cm^{-1}$, which may be attributed to the coordinated water molecule. Further, a broad band around 3480–3400 $cm^{-1}$ may be due to $\nu$(O–H) of water molecule. The far IR spectra of these metal complexes exhibited new bands, which are not present in the spectra of the ligands. The single band observed at ca. 320–315 $cm^{-1}$ is due to $\nu$(Cr–Cl), suggesting thereby that the complexes have a *trans* structure (*16*) and the presence of $\nu$(Cr–N), $\nu$(Cr–S) (*17*) and $\nu$(Cr–O) vibrations around $535 \pm 10$, 360–335 and $610 \pm 10$ $cm^{-1}$ indicate that complexation takes place through the nitrogen and sulfur/oxygen atoms.

## 2.4. *NMR spectra ($^1$H and $^{13}$C)*

The proposed structures of the ligands get further support by the $^1$H NMR and $^{13}$C spectra of the ligands. The significant $^1$H NMR and $^{13}$C NMR spectral data of the ligands, ($L^1$H, $L^2$H, $L^3$H) and ($L^4$H) along with their tentative assignments are reported in Table 4.

On the basis of above studies, octahedral environment around the metal atoms has been proposed, and the expected structures are as shown in Figures 1 and 2.

Table 4. $^1$H NMR and $^{13}$C NMR spectral data ($\delta$, ppm) of the ligands.

| | $^1$H NMR spectra ($\delta$, ppm) | | | | $^{13}$C NMR spectra ($\delta$, ppm) | | | |
|---|---|---|---|---|---|---|---|---|
| Ligands | $-C(CH_3)=N-$ proton | NH proton | $NH_2$ proton | Aromatic protons | Azomethine carbon | Amido/thiolo carbon | Methyl carbon | Aromatic carbon |
| $L^1$H | 1.8 | 9.9 | 2.83 | 7.80–6.60 | 178.51 | 198.71 | 12.3 | 150.81, 134.75, 114.74, 146.14 |
| $L^2$H | 1.78 | 10.68 | 2.55 | 7.89–6.32 | 160.07 | 177.35 | 12.33 | 153.02, 144.19, 139.80, 112.17 |
| $L^3$H | 1.68 | 10.68 | 2.81 | 8.68–7.16 | 146.2 | 179.78 | 13.74 | 143.40, 128.54, 128.05, 128.91 |
| $L^4$H | 2.3 | 10.68 | 2.84 | 7.84–7.20 | 152.76 | 178.62 | 13.17 | 140.31, 126.45, 126.70, 125.37 |

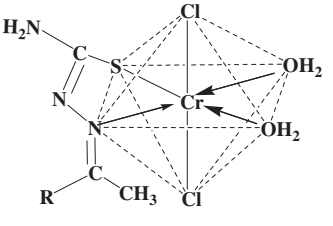


Figure 1. Suggested structures for chromium(III) complexes. 1:1 complex.

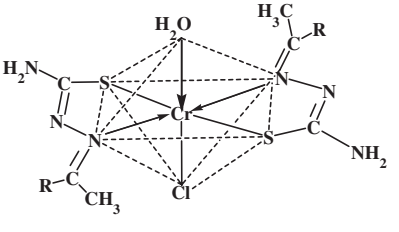


Figure 2. Suggested structures for chromium(III) complexes. 1:2 complex.

### 2.5. *X-ray powder diffraction study*

The possible lattice dynamics of the finely powdered product, $[CrCl_2(L^1)(H_2O)_2]$, has been deduced on the basis of X-ray powder diffraction studies. The observed interplanar spacing values ("*d*" in Å) have been measured from the diffractogram of the compound (Figure 3); the Miller indices *h*, *k* and *l* have been assigned to each *d* value and $2\theta$ angles are reported in Table 5. The results show that the compound belongs to "orthorhombic" crystal system having unit cell parameters as $a = 9.63$, $b = 17.37$ $c = 21.15$, maximum deviation of $2\theta = 0.045°$ and $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$.

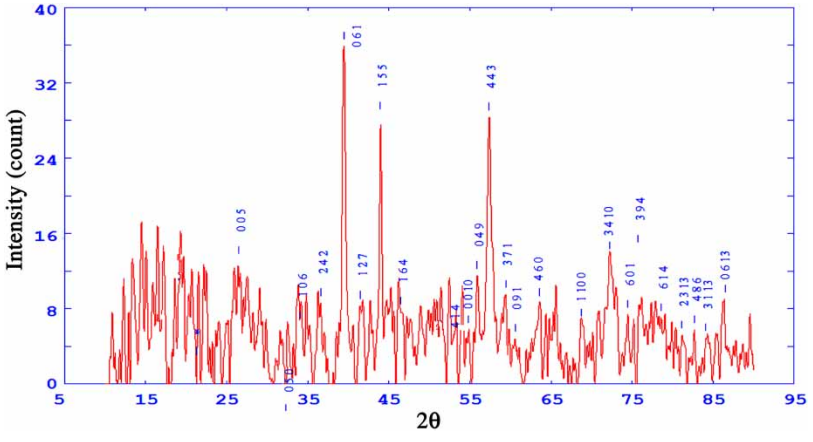


Figure 3. X-ray powder diffraction spectra of $[CrCl_2(L^1)(H_2O)_2]$.

Table 5. X-ray diffraction data of $[CrCl_2(L^1)(H_2O)_2]$.

| *h* | *k* | *l* | $2\theta$ (°) (Exp.) | $2\theta$ (°) (Calc.) | $2\theta$ (°) (Diff.) | *d* (Å) (Exp.) | *d* (Å) (Calc.) | Intensity (Exp.) |
|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 5 | 26.451 | 26.476 | −0.025 | 4.23388 | 4.23000 | 13.07 |
| 0 | 5 | 0 | 32.335 | 32.380 | −0.045 | 3.47874 | 3.47400 | −3.94 |
| 1 | 0 | 6 | 34.071 | 34.030 | 0.041 | 3.30634 | 3.31020 | 6.16 |
| 2 | 4 | 2 | 36.597 | 36.650 | −0.008 | 3.08518 | 3.08453 | 8.59 |
| 0 | 6 | 1 | 39.450 | 39.475 | −0.025 | 2.86999 | 2.86825 | 35.84 |
| 1 | 2 | 7 | 41.464 | 41.468 | −0.004 | 2.73629 | 2.73607 | 8.29 |
| 1 | 5 | 5 | 43.953 | 43.995 | −0.042 | 2.58840 | 2.58604 | 28.41 |
| 1 | 6 | 4 | 46.456 | 46.469 | −0.013 | 2.45603 | 2.45537 | 7.68 |
| 4 | 1 | 4 | 52.903 | 52.922 | −0.019 | 2.17456 | 2.17384 | 2.91 |
| 0 | 0 | 10 | 54.543 | 54.514 | 0.028 | 2.11358 | 2.11500 | 4.88 |
| 0 | 4 | 9 | 55.907 | 55.896 | 0.011 | 2.06641 | 2.06677 | 11.49 |
| 4 | 4 | 3 | 57.379 | 57.386 | −0.007 | 2.01772 | 2.01750 | 28.30 |
| 3 | 7 | 1 | 59.402 | 59.407 | −0.005 | 1.95499 | 1.95482 | 9.48 |
| 0 | 9 | 1 | 60.571 | 60.526 | 0.045 | 1.92072 | 1.92201 | 4.79 |
| 4 | 6 | 0 | 63.135 | 63.106 | 0.028 | 1.85032 | 1.85106 | 5.82 |
| 1 | 10 | 0 | 69.016 | 69.034 | −0.018 | 1.70980 | 1.70941 | 6.13 |
| 3 | 4 | 10 | 72.604 | 72.610 | −0.006 | 1.63610 | 1.63598 | 11.05 |
| 6 | 0 | 1 | 74.475 | 74.494 | −0.019 | 1.60074 | 1.60040 | 7.37 |
| 3 | 9 | 4 | 75.695 | 75.701 | −0.006 | 1.57861 | 1.57861 | 14.29 |
| 6 | 1 | 4 | 78.595 | 78.568 | 0.027 | 1.52984 | 1.52984 | 7.01 |
| 2 | 3 | 13 | 81.164 | 81.134 | 0.030 | 1.48945 | 1.48945 | 5.17 |
| 4 | 8 | 6 | 82.679 | 82.694 | −0.014 | 1.46627 | 1.46627 | 5.74 |
| 3 | 1 | 13 | 84.116 | 84.105 | 0.011 | 1.44614 | 1.44614 | 4.87 |
| 0 | 6 | 13 | 86.162 | 86.150 | 0.012 | 1.41830 | 1.41830 | 7.99 |

### 2.6. *Antimicrobial assay*

The heterocyclic ketimines and their chromium(III) complexes were evaluated for their antimicrobial activity against two bacteria *Bacillus subtilis* (Gram-positive) and *Escherichia coli* (Gram-negative) and two fungi *Candida albicans* and *Aspergillus niger* and the results are summarized in Table 6. The ligands were found to be biologically active and the chromium complexes are more active than their respective ligands. This indicated that the complexation to metal enhances the activity of the ligand. This may be explained by Tweedy's chelation theory (*18*), according to which chelation reduces the polarity of the central metal atom because of partial sharing of its positive charge with the ligand, due to which the lipophilic character of the metal chelate increases and favors its permeation through the lipid layer of cell membrane. It has also been proposed that the ultimate action of the compounds is the denaturation of one or more proteins of the cell as a result of which normal cellular processes are impaired (*19*).

## 3. Conclusions

MW irradiation is an efficient and environmentally benign method to accomplish various inorganic syntheses to afford purer products in higher yields in shorter reaction periods. All the ligands behave as a monofunctional bidentate with metal ion in different reaction conditions. Based on the analytical and spectral data, a hexacoordinated environment around the metal ion has been proposed. The antimicrobial activity of the complexes and the ligands showed that the complexes are more active than the parent ligands.

## 4. Experimental

The $CrCl_3 \cdot 6H_2O$ was purchased from Alfa aesar. All the reagents were dried and distilled before use. 2-Acetylfuran and 2-acetylthiophene were purchased and used as received. All preparations were done under anhydrous conditions.

Table 6. Antifungal and antibacterial screening data for the ligands and their complexes.

| | (Antifungal activity) (%) Inhibition after 96 h (concentration in ppm) | | | | | | (Antibacterial activity) Diameter (mm) of inhibition zone after 24 h (concentration in ppm) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *C. albicans* | | | *A. niger* | | | *B. subtilis* | | *E. coli* | |
| Compounds | 50 | 100 | 200 | 50 | 100 | 200 | 500 | 1000 | 500 | 1000 |
| $L^1H$ | 28 | 47 | 50 | 25 | 32 | 52 | 11 | 13 | 10 | 11 |
| $L^2H$ | 27 | 44 | 52 | 24 | 30 | 53 | 10 | 11 | 8 | 9 |
| $L^3H$ | 28 | 46 | 53 | 26 | 33 | 53 | 11 | 14 | 10 | 13 |
| $L^4H$ | 25 | 42 | 51 | 23 | 30 | 50 | 11 | 12 | 9 | 11 |
| $[CrCl_2(L^1)(H_2O)_2]$ | 30 | 49 | 55 | 28 | 35 | 56 | 13 | 14 | 11 | 14 |
| $[CrCl(L^1)_2(H_2O)]$ | 32 | 50 | 59 | 29 | 38 | 59 | 14 | 15 | 12 | 15 |
| $CrCl_2(L^2)(H_2O)_2]$ | 29 | 49 | 54 | 28 | 36 | 56 | 12 | 13 | 11 | 13 |
| $[CrCl(L^2)_2(H_2O)]$ | 32 | 52 | 60 | 30 | 42 | 65 | 14 | 13 | 12 | 14 |
| $[CrCl_2(L^3)(H_2O)_2]$ | 30 | 51 | 59 | 31 | 37 | 58 | 12 | 15 | 12 | 16 |
| $[CrCl(L^3)_2(H_2O)]$ | 33 | 53 | 62 | 32 | 44 | 66 | 15 | 16 | 13 | 16 |
| $CrCl_2(L^4)(H_2O)_2]$ | 29 | 48 | 57 | 27 | 35 | 57 | 13 | 15 | 11 | 13 |
| $[CrCl(L^4)_2(H_2O)]$ | 31 | 51 | 59 | 30 | 40 | 60 | 14 | 16 | 12 | 15 |
| Nystatin (standard fungicide) | 50 | 85 | 100 | 52 | 89 | 99 | – | – | – | – |
| Streptomycin (standard bactericide) | – | – | – | – | – | – | 16 | 18 | 15 | 18 |

### 4.1. *Preparation of the ligands*

Two different routes were employed for the synthesis of the ligands.

(1) In MW-assisted synthesis, the ligands, thiosemicarbazones ($L^1H$, $L^3H$) and semicarbazones ($L^2H$, $L^4H$), were prepared by the condensation of 2-acetylfuran and 2-acetylthiophene with thiosemicarbazide and semicarbazide hydrochloride (in the presence of sodium acetate), respectively, in 1:1 molar ratio through a conventional MW oven by taking 2–4 ml of ethanol as a solvent. The reactions were completed in a short period of 4–7 min.
(2) For comparison purpose, the above ligands were also synthesized by a thermal method as described previously (*20*). The parent ligands exist in the tautomeric forms depicted in Figure 4. A comparison between thermal method and MW method is given in Table 7.


### 4.2. *Preparation of the complexes*

The complexes were also prepared by two different routes.

(1) In MW-assisted synthesis, the complexes were prepared by irradiating the reaction mixture of chromium trichloride and the respective ligand in appropriate stoichiometric proportions using NaOH in dry methanol. The products were recovered from the MW oven and dissolved in a 2–5 ml of dry methanol, where the precipitate of sodium chloride formed during the course of the reaction was removed by filtration and the filtrate was then concentrated under

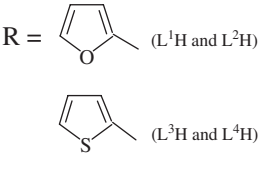


Figure 4. Structure of the ligands.

Table 7. Comparison between MW and thermal method.

| | Yield (%) | | Solvent (ml) | | Time | |
|---|---|---|---|---|---|---|
| Compounds | Thermal | MW | Thermal | MW | Thermal (h) | MW (m) |
| $L^1H$ | 80 | 87 | 100 | 4 | 4 | 5 |
| $L^2H$ | 79 | 89 | 100 | 3 | 4 | 4 |
| $L^3H$ | 80 | 86 | 100 | 3 | 4.5 | 7 |
| $L^4H$ | 80 | 88 | 100 | 2 | 3.5 | 5 |
| $[CrCl_2(L^1)(H_2O)_2]$ | 76 | 83 | 50 | 5 | 15 | 4 |
| $[CrCl(L^1)_2(H_2O)]$ | 73 | 87 | 35 | 2 | 15 | 7 |
| $[CrCl_2(L^2)(H_2O)_2]$ | 70 | 89 | 30 | 3 | 14 | 5 |
| $[CrCl(L^2)_2(H_2O)]$ | 72 | 86 | 40 | 2 | 13 | 5 |
| $[CrCl_2(L^3)(H_2O)_2]$ | 69 | 87 | 55 | 2 | 12 | 4 |
| $[CrCl(L^3)_2(H_2O)]$ | 75 | 81 | 30 | 5 | 15 | 7 |
| $[CrCl_2(L^4)(H_2O)_2]$ | 70 | 84 | 30 | 2 | 14 | 7 |
| $[CrCl(L^4)_2(H_2O)]$ | 74 | 80 | 40 | 3 | 15 | 4 |

reduced pressure. The resulting compounds were washed with cyclohexane and recrystallized with methanol.

(2) These complexes were also synthesized by the thermal method where instead of 4–7 min, reactions were completed in 12–15 h and the yield of the products was also less than that obtained by the MW-assisted synthesis. In this method, the methanolic solution of $CrCl_3 \cdot 6H_2O$ was added to the methanolic solution of ligands in 1:1 and 1:2 molar ratios using NaOH in appropriate stoichiometric proportions. The resulting mixture was heated under reflux for 12–15 h, filtered to remove NaCl and the solvent was concentrated under reduced pressure. The product was dried in *vacuum*. The resulting compounds were washed with cyclohexane and recrystallized with methanol.

### 4.3. *Physical measurements and analytical methods*

The molecular weights were determined by the Rast Camphor method (*21*). The metal contents were analyzed gravimetrically. Sulfur and nitrogen were determined by Messenger's (*22*) and Kjeldahl's methods (*23*), respectively. Carbon and hydrogen analyses were performed at the CDRI, Lucknow. IR spectra were recorded on a Nicolet Megna FTIR-550 spectrophotometer using KBr pellets. The electronic spectra were recorded on a Varian–Cary/5E spectrophotometer at SAIF, IIT Madras, Chennai. EPR spectra of the complexes were monitored on Varian E-4X band spectrometer at SAIF, IIT Madras, Chennai.

### 4.4. *Antifungal screening*

The antifungal activity of the ligands and their chromium complexes was tested by agar plate technique (*24*) against the two pathogenic fungi *C. albicans* and *A. niger* using the potato dextrose agar medium having the composition: glucose 20 g, starch 20 g, agar–agar 20 g and distilled water 1000 ml. Solutions of the test compounds in methanol at 50, 100 and 200 ppm concentrations were prepared and then were mixed with the medium. The medium then was poured into Petri plates and the spores of fungi were placed on the medium with the help of inoculum's needle. These Petri plates were wrapped in the polythene bags containing a few drops of alcohol and were placed in an incubator at $25 \pm 2\,^{\circ}C$. The activity was determined after 96 h of incubation at room temperature ($25\,^{\circ}C$). The controls were also run and three replicates were used in each case. The linear growth of the fungus was obtained by measuring the fungal colony diameter in Petri plates after 4 days. The percentage inhibition was calculated as

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

where $C$ and $T$ are the diameters of the fungus colony in the control and test plates, respectively.

### 4.5. *Antibacterial screening*

*In vitro* antibacterial screening is generally performed by disc diffusion method (*25*) for the primary selection of the compounds as therapeutic agents. The method is essentially a qualitative or a semi-quantitative test indicating the sensitivity or resistance of microorganisms to the test materials as well as the bacteriostatic or bactericidal activity of a compound. The antibacterial activity of the ligands and their chromium complexes was evaluated against Gram-positive (*B. subtilis*) and Gram-negative (*E. coli*) bacteria. The nutrient agar medium having the composition: peptone 5 g, beef extract 5 g, NaCl 5 g, agar–agar 20 g and distilled water 1000 ml was pipetted into the Petri plates. When it solidified, 5 ml of warm seeded agar was applied. The seeded agar

was prepared by cooling the molten agar to 40 °C and then 10 ml of bacterial suspension was added. The compounds were dissolved in methanol in 500 and 1000 ppm concentrations. Paper discs of Whatman No. 1 filter paper 5 mm in diameter were soaked in these solutions of varied concentrations. The discs were dried and placed on the medium previously seeded with organisms in Petri plates at a suitable distance. The Petri plates were stored in an incubator at $28 \pm 2$ °C for 24 h. The diameters of the zone of inhibition produced by the compounds were compared with the standard antibiotic (Streptomycin). The zone of inhibition thus formed around each disc containing the test compounds was measured accurately in millimetres.

## Acknowledgements

The authors are thankful to CSIR, New Delhi, and UGC, New Delhi, for financial assistance through grant no. 01(2307)/09/EMR-II and 36-1/2008(RAJ)(SR), respectively.

## References

(1) Kidwai, M.; Thakur, R.; Mohan, R. *Acta Chim. Slov*. **2005,** *52*, 88–92.
(2) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002,** *35*, 209–217.
(3) Yoshikawa, Y.; Ueda, E.; Kawabe, K.; Miyabe, K.; Takino, T.; Sakurai, H;. Kojima, Y. *J. Biol. Inorg. Chem*. **2002,** *7*, 68–73.
(4) Glusker, J.P.; Katz, A.K.; Bock, C.W. *Rigaku J*. **1999,** *16*, 8–16.
(5) Amado, A.M.; Ribeiro-Claro, P.J.A. *J. Inorg. Biochem*. **2004,** *98*, 561–568.
(6) Juturu, V.; Komorowski, J.R. *Am. J. Clin. Nutr*. **2003,** *78*, 192–193.
(7) Ryan, G.J.; Wanko, N.S.; Redman, A.R.; Cook, C.B. *Ann. Pharmacother*. **2003,** *37*, 876–885.
(8) Zetic, V.G.; Stehlik-Tomas, V.; Grba, S.; Lutilsky, L;. Kozlek, D. *J. Biosci*. **2001,** *26*, 217–223.
(9) Yamini Shrivastava, H.; Niranjali Devaraj, S.; Unni Nair, B. *J. Inorg. Biochem.* **2004,** *98*, 387–392.
(10) Mishra, D.; Naskar, S.; Drew, M.G.B.; Chattopadhyay, S.K. *Inorg. Chim. Acta* **2006,** *359*, 585–592.
(11) Kizilcikli, I.; Ulkuseven, B.; Daşdemir, Y.; Akkurt. B. *Synth. React. Inorg. Met-Org. Chem.* **2004,** *34*, 653–665.
(12) Aranha, P.E.; dos Santos, M.P.; Romera, S.; Dockal, E.R. *Polyhedron* **2007,** *26*, 1373–1383.
(13) Dubey, R.K.; Dubey, U.K.; Mishra, C.M. *Indian. J. Chem.* **2008,** *47A*, 1208–1212.
(14) El-ajaily, M.M.; Maihub, A.A.; Hudere S.S.; Bensaber, S.M. *Asian J. Chem*. **2006,** *18*, 2427–2430.
(15) Saydam, S.; Yilmaz, E. *Spectrochim. Acta A* **2006,** *63*, 506–510.
(16) Byun, J.C.; Han Bull, C.H. *J. Korean Chem. Soc.* **2005,** *26*, 1395–1402.
(17) Shukla, D.; Gupta, L.K.; Chandra, S. *Spectrochim. Acta A* **2008,** *71*, 746–750.
(18) Tweedy, B.G. *Phytopathology* **1964,** *55*, 910–914.
(19) Lehninger, A.L. *Biochemistry*, 2nd ed.; Worth Publishers: New York, 1975; pp 519–520.
(20) Saxena, C.; Singh, R.V. *Synth. React. Inorg. Met.-Org. Chem.* **1992,** *2*, 1061–1072.
(21) Vogel, A.I. *A Textbook of Organic Quantitative Analysis*, 5th ed.; Pearson Education Ltd.: Thames Polytechnique, London, 2004; p 243.
(22) Vogel, A.I. *A Textbook of Quantitative Chemical Analysis*, 6th ed.; Pearson Education Ltd.: Thames Polytechnique, London, 2006; pp 498–499.
(23) Vogel, A.I. *A Textbook of Quantitative Chemical Analysis*, 6th ed.; Pearson Education Ltd.: Thames Polytechnique, London, 2006; p 387.
(24) Fahmi, N.; Saxena, C.; Singh, R.V. *Bull. Chem. Soc. Jpn.* **1996,** *69*, 963–969.
(25) Jain, M.; Kumar, D.; Singh, R.V. *Main Group Met. Chem.* **2003,** *26*, 99–109.