ISSN 1070-3632, Russian Journal of General Chemistry, 2013, Vol. 83, No. 12, pp. 2453–2459. © Pleiades Publishing, Ltd., 2013.

Synthesis, Characterization, and Antimicrobial Activity of Heterobimetallic Complexes of Sn(IV) and Zn(II) with 4-Aminophenylacetic Acid[1]

S. Iram[a], S. Ali[b], S. Shahzadi[a], and M. Shahid[c]

[a] *Department of Chemistry, GC University, Faisalabad, Pakistan*
e-mail: sairashahzadi@hotmail.com

[b] *Department of Chemistry, Quaid-i-Azam University, Islamabad-45320, Pakistan*
e-mail: drsa54@yahoo.com

[c] *Department of Chemistry and Biochemistry, University of Agriculture, Faisalabad, Pakistan*

Received November 8, 2013

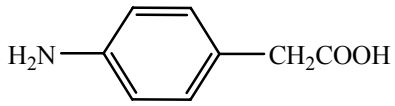
Abstract—A series of new heterobimetallic complexes of zinc and tin with 4-aminophenylacetic acid has been prepared. Their composition and structure in solid state and in solution have been elucidated by elemental analysis, IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. IR spectroscopy results have confirmed the bidentate nature of the ligand, its molecules being arranged in planar square [Zn(II)] and trigonal bipyramid [Sn(IV)] around the metal ions. NMR studies have revealed four-coordinated geometry in the solution. The complexes containing both Sn(IV) and Zn(II) are better antimicrobial agents as compared to the Zn-only analog.

DOI: 10.1134/S1070363213120426

Complexes of organic compounds of tin(IV) and zinc(II) have been intensively studied in view of their potential biological activity, reactivity, and industrial applications [1]. In particular, such complexes may act as antiviral and antineoplastic agents, bactericides, fungicides, marine antifouling paints, surface disinfectants, wood preservatives; they are used in organic synthesis and fingerprint detection as well [2].

High coordination numbers of metal ions can be achieved in complexes including tin and zinc bonds with electronegative atoms, such as oxygen, nitrogen, and sulfur [3, 4]. Such compounds are important in the development of coordination chemistry fields related to catalysis, enzymatic reactions, magnetism, and molecular architectures [4]. The well known structural diversity of organotin compounds is attributed to ambi-dentate character of the carboxylate ligands [5]. Steric and electronic properties of organic part of the ligand influence greatly the structure of tin carboxylates. For instance, dithiocarbamate ligand strongly bonds to metal ions and can stabilize metal complexes with high oxidation number [6]. Organotin(IV) dithiocarbamate complexes have been widely studied due to special features of Sn–S bond affecting the complex biological properties [7, 8].

Extending the above-mentioned studies, this work aimed to probe the biological properties of the novel heterobimetallic complexes of Sn(IV) and Zn(II) with 4-aminophenylacetic acid (HL), and to elucidate the complexes structure.



4-Aminophenylacetic acid (HL).

The structures of complexes **I–VI** are given in the Experimental section. All the prepared complexes were solid substances with distinct melting points, soluble in common organic solvents. The elemental analysis data coincided with the proposed formula of the complexes. The physical properties are reported in Table 1.

Infrared spectroscopy. The major IR bands of the ligand and the metal complexes are listed in Table 2. The characteristic ν(NH) and ν(NH_2) bands were observed at 3235 and 3350 cm^{-1}, respectively, in the ligand spectrum, they were not shifted significantly

[1] The text was submitted by the authors in English.

Table 1. Physical properties of Zn(II) and Sn(IV) complexes with 4-aminophenylacetic acid

Comp. no.	Formula	FW, g/mol	Yield, %	mp, °C	Elemental analysis			
					C, wt % calculated (found)	H, wt % calculated (found)	N, wt % calculated (found)	S, wt % calculated (found)
HL	$C_8H_9O_2N$	151.16	–	208–209	63.50 (63.54)	5.95 (5.93)	9.26 (9.30)	–
Zn product	$C_{16}H_{20}O_6N_2Zn$	401.75	75	280–283	47.83 (47.80)	5.02 (5.05)	6.97 (6.94)	–
I	$C_{19}H_{25}O_6N_2S_2ClZnSn$	661.11	62	255–257	34.52 (34.49)	3.81 (3.84)	4.24 (4.29)	9.70 (9.74)
II	$C_{25}H_{37}O_6N_2S_2ClZnSn$	745.27	59	229–231	40.29 (40.25)	5.00 (5.04)	3.76 (3.71)	8.60 (8.65)
II	$C_{29}H_{29}O_6N_2S_2ClZnSn$	785.25	70	129–131	44.36 (44.31)	3.72 (3.76)	3.57 (3.62)	8.17 (8.11)
IV	$C_{20}H_{28}O_6N_2S_2ZnSn$	640.39	75	218–219	37.47 (37.52)	4.37 (4.32)	4.37 (4.41)	9.99 (9.95)
V	$C_{29}H_{46}O_6N_2S_2ZnSn$	766.94	55	158–159	45.42 (45.47)	6.05 (6.09)	3.65 (3.71)	8.36 (8.41)
VI	$C_{35}H_{34}O_6N_2S_2ZnSn$	826.9	60	192–194	50.84 (50.80)	4.14 (4.11)	3.39 (3.44)	7.76 (7.71)

Table 2. Infrared absorption bands (ν, cm^{-1}) of Zn(II) and Sn(IV) complexes with 4-aminophenylacetic acid

Comp. no.	ν(H_2O)	ν(NH_2)	ν(COO)		Δν	ν(C=S)	ν(C–S)	ν(NH)	ν(Zn–O)	ν(Sn–C)	ν(Sn–S)	ν(Sn–Cl)
			ν(COO_{asym})	ν(COO_{sym})								
HL	3460	3350	1597	1382	215	–	–	3235	–	–	–	–
Zn product	3430	3349	1590	1429	161	–	–	3230	315	–	–	–
I	3441	3337	1593	1428	165	1073	950	3221	331	544	472	239
II	3436	3341	1580	1440	140	1088	937	3228	327	566	471	230
II	3435	3345	1581	1408	173	1094	920	3230	319	239	476	234
IV	3410	3350	1580	1392	188	1095	919	3230	321	535	479	–
V	3440	3344	1580	1389	191	1092	925	3232	336	530	468	–
VI	3449	3339	1590	1427	163	1079	932	3231	317	254	462	–

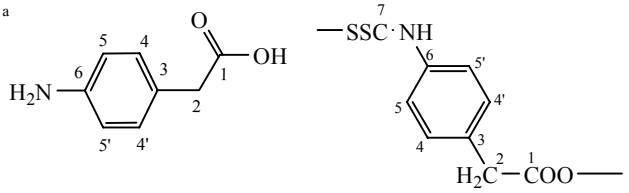
upon formation of complexes **I–VI**. The carboxyl group stretching frequencies ν(COO_{asym}) and ν(COO_{sym}) are indicative of the structure and bonding of the ligand in the complexes [9]. Upon complexation, the asymmetric stretching band was shifted to higher frequency as compared to HL spectrum, whereas the symmetric stretching band was shifted to lower frequency, thus revealing the bonding between the metal ion and carboxylate oxygen atom. The difference between ν(COO_{asym}) and ν(COO_{sym}) in the complexes, Δν, was below 200 cm^{-1}, indicating the bidentate nature of carboxylate group [10].

The presence of ν(Zn–O) bands in the range of 315–336 cm^{-1} in all the complexes confirmed the interaction between zinc and carboxylate. As was reported in [11], a single ν(C=S) band around 1000 cm^{-1} was indicative of dithiocarbamate groups, bonded symmetrically or bidentate. In the spectra of **I–VI**, strong absorption bands of ν(C=S) were found at

Table 3. The ^{1}H NMR spectral data[a–c] of Zn(II) and Sn(IV) complexes with 4-aminophenylacetic acid

Proton	δ, ppm							
	HL	Zn product	**I**	**II**	**III**	**IV**	**V**	**VI**
2	3.32 s	3.32 s	3.32 s	3.32 s	3.32 s	3.32 s	3.32 s	3.32 s
4,4'	6.47–6.51 m	6.45–6.48 m	7.03–7.05 m	7.04–7.11 m	7.05–7.12 m	7.03–7.12 m	7.07–7.12 m	7.03–7.11 m
5,5'	6.81–6.90 m	6.87–6.90 m	7.14–7.17 m	7.14–7.19 m	7.17–7.22 m	7.14–7.21 m	7.17–7.24 m	7.14–7.21 m
$-NH_2$	4.82 s	4.83 s	4.82 s	4.82 s	4.82 s	4.82 s	4.82 s	4.82 s
–NH	3.86 s	3.86 s	3.86 s	3.86 s	3.86 s	3.86 s	3.86 s	3.86 s
–OH	11.53 s	–	–	–	–	–	–	–
R	–	–	1.10s [96]	0.85 t (7.2) 1.26–1.37 m 1.63–1.87 m	6.42–6.85 m 6.11–6.52 m	0.37 s [97]	0.89 t (7.2) 1.61–1.69 m 1.73–1.79 m	6.68–6.91 m 6.61–6.32 m

[a]



[b] $^nJ[^{119}Sn–^1H]$ in Hz.
[c] $^3J(^1H, ^1H)$ in Hz.

1073–1094 cm^{-1}, and ν(C–S) bands appeared at lower frequency, 919–950 cm^{-1} [12]. The Sn–S bond formation in **I**–**VI** was confirmed by appearance of ν(Sn–S) band in the range of 462–479 cm^{-1} [13]. The strong band in the region of 230–239 cm^{-1} was assigned to ν(Sn–Cl).

The ν(Sn–C) band was observed at 530–547 cm^{-1} in the cases of **I** and **II**–**V**. However, the same bands were found at 239 cm^{-1} (**III**) and at 254 cm^{-1} (**VI**) in the spectra of di- and triphenyltin derivatives. The absence of any band in the range of 420–440 cm^{-1}, commonly assigned to ν(Sn–N) mode in similar compounds [14, 15] contradicted possible amino group coordination to tin, thus supporting the coordination via carboxylate oxygen [16] and dithioate sulfur in all the prepared complexes.

^{1}H NMR Spectroscopy. The characteristic signals in ^{1}H NMR spectra of the ligand and the complexes are collected in Table 3. Characteristics of all the proton signals (location and intensity) coincided with the respective values calculated by incremental method [17]. In the ^{1}H NMR spectrum of the ligand, singlets at 4.82 and 3.86 ppm were assigned to $-NH_2$ and –NH protons, respectively [18], whereas aromatic protons were observed at 6.47–6.90 ppm as multiplet. The singlet at 11.53 ppm was assigned to –OH group, its disappearance in the complexes spectra confirmed the carboxylic group coordination with Zn [19].

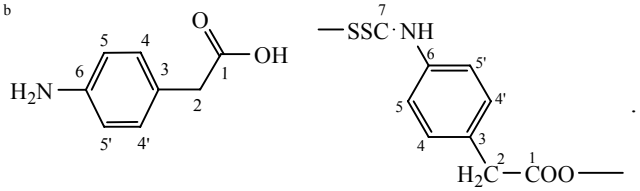
The signals of CH_3 protons of **I** and **IV** appeared as singlets at 1.10 and 0.37 ppm with $^2J[^{119}Sn–^1H]$ of 96 and 97 Hz, respectively, thus supporting the five-coordinated tin atom presence in the solution [20]. In the spectra of **II** and **V**, butyl group protons appeared as multiplets in the region of 1.26–1.87 and 1.61–1.79 ppm, respectively. The terminal CH_3 group of butyl gave triplets at 0.85 and 0.89 ppm with $^3J[^1H–^1H]$ value of 7.2 Hz in the cases of **II** and **V**, respectively. In triphenyltin(IV) derivatives spectra, phenyl protons signals formed two groups. The *ortho* protons were observed at 6.42–6.85 and 6.68–6.91 ppm, whereas the *meta* and *para* protons resonated at 6.11–6.52 and 6.61–6.32 ppm, respectively, in the cases of **III** and **VI**.

^{13}C NMR Spectroscopy. The characteristic signals of ^{13}C NMR spectra of the ligand and the complexes are given in Table 4. The aromatic carbons were

Table 4. ^{13}C NMR spectral data of Zn(II) and Sn(IV) complexes with 4-aminophenylacetic acid[a,b]

Carbon	δ, ppm							
	HL	Zn product	**I**	**II**	**III**	**IV**	**V**	**VI**
1	173.8	178.1	175.2	175.1	175.2	175.3	175.1	175.2
2	40.8	40.7	40.8	40.8	40.7	40.8	40.7	40.8
3	122.2	124.9	122.3	122.4	122.3	122.1	122.2	122.3
4,4'	130.1	130.0	130.1	130.1	130.2	130.1	130.2	130.1
5,5'	114.2	114.1	114.5	114.6	114.5	114.5	114.5	114.5
6	147.6	146.9	140.3	140.2	140.2	140.4	140.2	140.3
7	–	–	204.2	204.1	204.2	204.3	204.1	204.2

[a] **I**: Sn–CH_3Cl, (C^{α}) 28.3; **II**: Sn–C_4H_9Cl, (C^{α}) 28.3, (C^{β}) 27.6, (C^{γ}) 26.3, (C^{δ}) 14.3; **III**: Sn–C_6H_5Cl, (C^{α}) 147.4, (C^{β}) 137.6, (C^{γ}) 135.4, (C^{δ}) 129.3; **IV**: Sn–CH_3, (C^{α}) –2.1 ^{1}J[395.6]; **V** Sn–C_4H_9; (C^{α}) 28.6, (C^{β}) 26.8, (C^{γ}) 25.6, (C^{δ}) 14.6; **VI**: Sn–C_6H_5, (C^{α}) 142.2 ^{1}J[638.1], (C^{β}) 136.3 ^{2}J[47.8], (C^{γ}) 135.7, (C^{δ}) 129.7. $^{n}J[^{119}Sn,^{13}C]$ in Hz are listed in square brackets.

[b] 

assigned to 114.2–130.1 ppm signals in the ligand spectra, those signals did not change significantly upon complexation. The carboxylic carbon (COO) signal observed at 173.8 ppm in the ligand spectrum [19, 20] was shifted downfield to 175.3–175.7 ppm (**I**–**VI**) and 178.1 ppm (Zn product) upon complexation, thus indicating the participation of carboxylate anions in coordination with Sn(IV) and Zn(II). The chemical shift of carbon bonded to sulfur (CS_2) was observed at 204.1–204.3 ppm in the spectra of **I**–**VI**. The $^{1}J(^{119}Sn–^{13}C)$ coupling constants of 395.6 and 638.1 Hz in the cases of **IV** and **VI**, respectively, were indicative of the four-coordinated geometry [21] in solution.

Antibacterial activity. Antibacterial activity of the ligand, the complexes, and the reference drug was tested against Gram-positive and Gram-negative bacterial strains: *Escherichia coli, Bacillus subtilis, Pasturella multocida*, and *Stephlococcus aureus*. The measured growth inhibition zones are listed in Table 5. The complexes exhibited significantly higher antibacterial activity as compared to the free ligand. The ligand and Zn product showed no or little activity against the tested bacterial strains. Complex **VI** revealed the highest activity against all the strains, only slightly lower than that of the reference drug. Thus, the complex with Zn only was not efficient as antibacterial drug, but its coordination with Sn(IV) enhanced the antibacterial activity significantly. In line with [22], the complexes containing methyl and phenyl groups showed highest inhibitory effect on bacteria growth. Therefore, the tested bimetallic complexes can be potentially used as bactericides.

Antifungal activity. The antifungal activity of the ligand, the complexes, and the reference drug was tested against selected fungal strains: *Alternaria alternata, Ganoderma lucidium, Aspergilus flavus and Aspergilus niger*. The measured growth inhibition zones are listed in Table 6. In general, all the tested compounds revealed lower antifungal activity against *Aspergilus flavus and Aspergilus niger* as compared to that against *Alternaria alternate* and *Ganoderma lucidium*. The observed growth inhibition by complexes **I**, **IV**–**VI**, and by the free ligand was roughly similar, however somewhat weaker than that in the case of reference drug. Therefore, all the tested complexes can be potentially used as fungicides.

EXPERIMENTAL

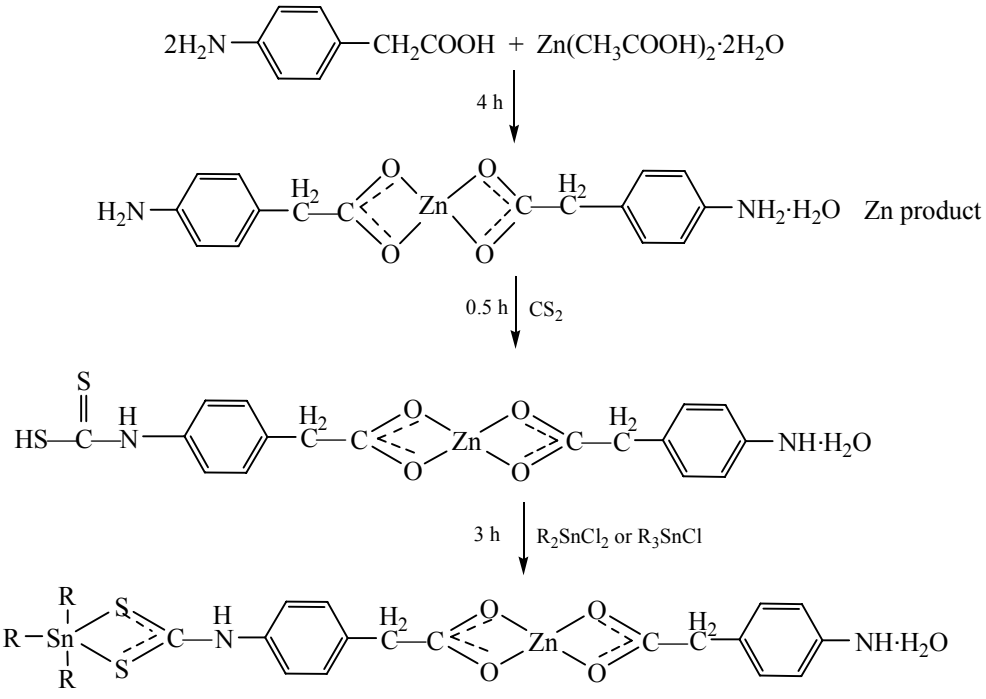
All glassware was used after cleaning and drying at 120°C. Trimethyltin chloride, tributyltin chloride, triphenyltin chloride, dimethyltin dichloride, dibutyltin dichloride, and diphenyltin dichloride (all – Aldrich);

4-aminophenylacetic acid, zinc acetate dehydrate, and chloroform (all – Merck); ethanol and DMSO (both – Lab-scan); acetone, methanol, and CS_2 (all – Riedel-de-Haen); nutrient agar and potato dextrose (both – Oxoid) were used as received. The melting points were determined with Stuart SMP3 electrothermal melting point apparatus in capillary tubes, and were not corrected. Elemental analysis was performed with CHNS-932 Leco analyzer. IR spectra of KBr/CsBr pellets were recorded with Perkin Elmer FT-IR-1000 spectrophotometer at 4000–250 cm^{-1}. ^1H and ^{13}C NMR spectra were recorded with Bruker AM-250 FT-NMR 300 MHZ spectrometer in $CDCl_3$ using the solvent signals as internal standard.

Complexes preparation *(general procedure). a. (Zn product).* 2 mmol of 4-aminophenylacetic acid was dissolved in 30 mL of acetone under constant stirring during 0.5 h. Then, solution of 1 mmol of zinc acetate dihydrate in 10 mL of distilled water was added dropwise, and the mixture was refluxed during 4 h. The formed precipitate was filtered off and dried in air.

b. (Zn-Sn product). The Zn product obtained at *a* (1 mmol) was dissolved in 50 mL of methanol in a round bottom flask under constant stirring during 0.5 h. Then, 1 mmol of CS_2 was added dropwise at 0°C to a stirred mixture. After 0.5 h, solid R_2SnCl_2 or R_3SnCl (1 mmol) was added in several portions. The mixture was refluxed during 3 h. The solid product obtained after slow evaporation of the solvent was recrystallized from chloroform–*n*-hexane (1 : 1).

The schemes of the occurring processes are shown below.



X = Cl (**I–III**), X = R (**IV–VI**), R = Me (**I, IV**), R = *n*-Bu (**II, V**), R = Ph (**III, VI**).

Antibacterial activity by disc diffusion method. The complexes antibacterial activity was determined by disc diffusion method [9]. Nutrient agar was dissolved in distilled water and autoclaved at 121°C. After cooling the molten agar to about 40°C, bacterial inoculum (100 μL/100 mL) was added. The media was spread onto the sterile Petri dishes, and even coverage was ensured before agar solidification. Sterile discs containing 100 μL of the tested sample (Wicks paper, 6 mm in diameter) were put flat onto the growth medium. Ampicillin was used as reference drug. The Petri dishes with bacterial strains were incubated at 37°C overnight. The activity was determined by measuring the diameter of the inhibition zone (mm) using zone reader [10].

Antifungal activity by disc diffusion method. The complexes antifungal activity was determined by disc

Table 5. The antibacterial activity data of Zn(II) and Sn(IV) complexes with 4-aminophenylacetic acid[a]

Compound no.	Inhibition zone, mm			
	B. subtilis	*P. multocida*	*S. aureus*	*E. coli*
HL	No activity	No activity	No activity	1419±11
Zn Product	No activity	No activity	No activity	2019±11
I	2519±12	2119±12	1819±11	19±1
II	1819±11	2419±12	2419±12	No activity
III	21± 2	2319±12	2819±12	2319±12
IV	2719±12	2319±12	1919±11	2019±11
V	1919±11	2519±12	2019±11	2819±12
VI	2819±12	2719±12	2919±12	3119±12
Ampicillin (reference)	3319±12	2919±12	3919±12	4019±12

[a] Results are reported as mean19±1S.D. of three samples analyzed individually in triplicate.

Table 6. The antifungal activity data of Zn(II) and Sn(IV) complexes with 4-aminophenylacetic acid[a]

Compound no.	Inhibition zone, mm			
	G. lucidium	*A. alternata*	*A. flavus*	*A. niger*
HL	2619±12	2619±12	2419±12	2819±12
Zn Product	1919±11	2219±11	No activity	No activity
I	1919±11	1419±11	2719±12	2519±12
II	1919±11	2119±12	No activity	No activity
III	2019±11	1719±12	2819±12	No activity
IV	2119±11	1719±11	2819±12	2719±12
V	2619±12	2219±12	2819±12	2819±12
VI	2419±11	2419±11	2919±12	2919±11
Flucanazol (reference)	3019±11	2919±12	4019±11	3919±12

[a] Results are reported as mean19±1S.D. of three samples analyzed individually in triplicate.

diffusion method [9]. Potato dextrose agar was dissolved in distilled water and autoclaved at 121°C. After cooling the molten agar to about 40°C, fungal inoculum (100 μL/100 mL) was added. The culture (60 mL) was spread onto the sterile Petri dishes, and even coverage was ensured before agar solidification. Sterile discs containing 100 μL of the tested sample (Wicks paper, 6 mm in diameter) were put flat onto the growth medium. Flucanazole was used as reference drug. The Petri dishes were incubated at 25°C during 48 h. The activity was determined by measuring the diameter of the inhibition zone (mm) using zone reader [10].

ACKNOWLEDGMENTS

HEC (project no. 20-1623/R&D/10/4402) is acknowledged for financial support.

REFERENCES

1. Ji-Chun, C., Yan-Lng, Q., Long-Hua, D., and Han-Dong, Y., *Chin. J. Stru. Chem.*, 2010, vol. 29, no. 12, p. 1784.
2. Jamil, K., Wajid, R., Bakhtiar, M., and Danish, M., *J. Iran. Chem. Soc.,* 2010, vol. 7, no. 2, p. 495.
3. Ali, S., Shahzadi, S., Shahid, K., Yousaf, M., Sharma, S.K., and Qanungo., K., *J. Chin. Chem. Soc.*, 2010, vol. 57, p. 659.
4. You, Z., Liub, W., and Zhua, H., *Inorg. Allgem. Chem.,* 2004, vol. 630, p. 1617.
5. Sadiq-ur-Rehman, K., Shahid, S., Ali, M.H., Bhatti, and M., Parvez, *J. Organomet. Chem.*, 2005, vol. 690, p. 1396.
6. Heard, P.J., *Progress in Inorganic Chemistry*, Karlin, D., Ed., vol. 53, New York: John Wiley & Sons, 2005.
7. Thoonen, S., Deelman, B., and Koten, G., *J. Organomet. Chem*., 2004, vol. 689, p. 2145.
8. Hussain, H., Ahmad, V.U., Green, I.R., Krohn, K., Hussain, J., and Badshah, A., *Arkivoc,* 2007, vol. 89, p. 299.
9. Awang, N., Yamin, B.M., Othman, M., and Baba, I., *Ameri. J. Appl. Sci.*, 2011, vol. 8(4), p. 310.
10. Shah, F.A., Shahzadi, S., and Ali, S., *J. Iran. Chem. Soc.*, 2010, vol. 7, no. 1, p. 59.
11. Kumar, A. and Garg, *Inorg. Chim. Acta*, W., 2006, vol. 346, p. 227.
12. Amin, M.M., Ali, S., Shahzadi, S., Sharma, S.K., and Qanungo, K., *J. Coord. Chem.*, 2011, vol. 64, no. 2, p. 337.
13. Singh, R. and Kaushik, N.K., *Spectrochim. Acta Part A*, 2008, vol. 71, p. 669.
14. Singh, H.L. and Singh, J.B., *Inter. J. Inorg. Chem.*, 2006, vol. 2012, p. 1.
15. Sexana, A.K., Tandon, J.P., Molloy, K.C., and Zukermann, J.J., *Inorg. Chim. Acta*, 1982, vol. 63, p. 71.
16. Saxena, A.K., Singh, H.B., and Tandon, J.P., *Synth. React. Inorg. Met.-Org. Chem.*, 1980, vol. 10, p. 117.
17. Kalinowski, H.O., Berger, S., and Brown, S., *^{13}C NMR Spectroscopy*, Stuttgart: Thieme Verlag, 1984.
18. Singh, K. and Puri, P., *Turk. J. Chem.*, 2010, vol. 34, p. 499.
19. Kumar, D. and Garg, B., *Spectrochim. Acta, Part A*, 2006, vol. 64, p. 141.
20. Shahid, K., Ali, S., Bhatti, M.H., Mazhar, M., Mahmood, S., and Rehman, S., *Turk. J. Chem.*, 2002, vol. 26, p. 589.
21. Affan, M.A., Foo, I.P., Fasihuddin, B.A., and Hapipah, M.A., *The Malay. J. Anal. Sci.*, 2009, vol. 13, no. 1, p. 73.
22. Joseyphus, R. and Nair, M., *Mycobiol.*, 2008, vol. 36, no. 2, p. 93.
23. CLSI (The Clinical Laboratory Standards Institute), Agar Dilution and Disc Diffusion Susceptibility Testing of Campylobacter spp, *Clinical Microbiol.*, 2007, vol. 45, p. 2758.
24. Huang, G., Moore, S., Jiaxin, J., and Dehui, D., *J. Food Sci. Technol.,* 2001, vol. 11, no. 1, p. 25.