ISSN No:-2456-2165

Synthesis of Two Cadmium Complexes of 6-Thioguanosine by Different Ways

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Abstract:-In this paper, two complexes of6-ThioGuowithcadmium ions weresynthesised. The binding ratio of 6-ThioGuo ligand withCd^{+2} in the complex,1was revealed to be two ligands to one $Cd^{+2}$where one of the ligands is deprotonated. On the other hand, in the situation of complex,2the binding ratio of 6-ThioGuo ligand withCd^{+2} was shown to be two deprotonated ligands to one cadmium (II) ion. These complexes were characterised by ES-MS, IR, ^{1}H-NMR and elemental analysis.

Keywords:*-6-thioguanosine" cadmium ion" complexes.*

I. INTRODUCTION

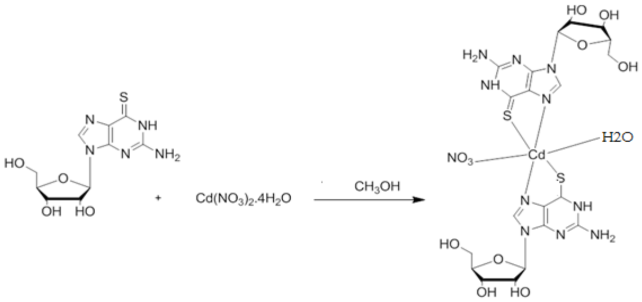
Recently, thiopurines have attractive attentions for many researches,as they have several applications. For example, 6-mercaptopurine (**6-MP**) and 6-thioguanine(**6-TG**)have immune- suppressive and anticancer activities.[1-3] In addition,6-MP has a clinical treatment for lymphoblast leukemia[4]and **6-TG** is used in the myelocyticleukaemia treatment.[5,6]

Moreover, the interactions of thiopurines with metal ions have attracted considerable initial investigation mostly focussed on understanding the essential aspects of the coordination chemistry.[7]for instant, it has been found that some complexes of thiopurines with metals such as **6-MP**, inparticlar those of platinum and palladium , show activity toward antitumor which in some satuations is enhanced with respect to the free ligand activity.[8,9]

Lately, intrest in possible applications of systems containing nucleobases and metal ions in the framework of nanotechnology based on DNA and associated systems [10-12]propelled researchers to consider these complexes as promising applicants in the field of molecular materials. Especially, the systems of the **6-MP** have the ability for metal ions assembly, either as metal complexes high nuclearity or as(1D) one dimension coordination polymer such as $[M(6\text{-}MP)_2]$ that bear similarity to the suggested structure for M-DNA.[13]Filex and his group was able to form 1D-coordination polymer $[Cd(6\text{-}MP)_2]_n$ of **6-MP** and Cd(II).[14] In addition, they demonstrated the isolation of single molecular chain of this polymer on a surface.However, it was found that these systems insulating.[15] Moreover, they found that**6-MP** and**6-TG** form 1D-coordination polymers with Ni(II) ions that revealsemiconducting behaviour.[10] In the recent, the complexes of 6-thioguanosine (**6-ThioGuo**) and 2'-deoxy-6-thioguanosine (**2'-d-6-ThioGuo**) with cobalt and nickel ions were reported.[16]It was found that, their binding ratio was three ligands coordinating to one metal ion. In this study, we report the synthesis and characterisation of two new complexes of **6-ThioGuo** with cadmium (II) ions (Cd^{2+}) by different methods.

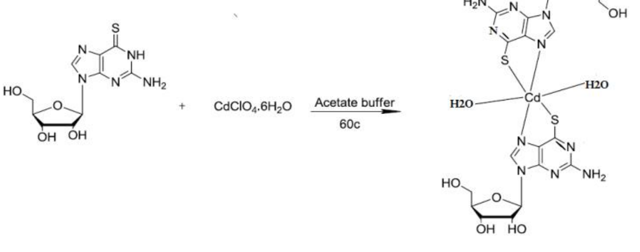
II. SYNTHESIS OF CADMIUM COMPLEXES

The cadmium complex,**1**was prepared by the direct reaction of two equivalents of **6-ThioGuo**with one equivalent of cadmium nitrate in methanol as seen in **scheme 1**according to procedure described by Zamora,*el al*.[17]The yellow powder was obtained after one day.



Scheme 1. Synthesis of cadmium(II) complex,**1**

While, the complex,**2** was prepared according to general procedure of Gosh and Chatterjee[18]and more details of synthesis have been previously reported by Dubler and Gry[19]. 6-**ThioGuo**was dissolved in the hot buffer solution of acetic acid/sodium acetate, and then the same buffer solution of cadmium perchlorate was added as seen in **scheme 2**. After two days yellowish white powderof complex,**2** was obtained.



Scheme 2. Synthesis of cadmium (II) complex, **2**

Spectroscopic characterization was used to determine the chemical structure of these complexes.In complex,**1** the ES-MS indicatedtheforming of a complexhaving two ligands of **6-ThioGuo**coordinating to one $Cd^{2+}C_{20}H_{25}O_8N_{10}S_2Cd$ (M+H) (m/z found 711.0049). Similarly in the case of thecomplex, **2**ES-MS showedthe complex comprises oftwo deprotonated**6-ThioGuo**ligands coordinating to one $Cd^{2+}C_{20}H_{24}O_8N_{10}S_2Cd$ (M+Na) is (733.0159).

The IR spectra ofcomplexes of Cd (II) were studied to suggest the bestpossible structures of complexes,(**1**and**2**). The IRspectra of complex,**1**andcomplex,**2**were comparedwith the respective free ligand **6-ThioGuo.**In the free**6-ThioGuo,**the C=S stretching frequency absorbs at 1207 cm^{-1}while this band in the complex,**1** is moved to 1194 cm^{-1}see **Figure 1.**

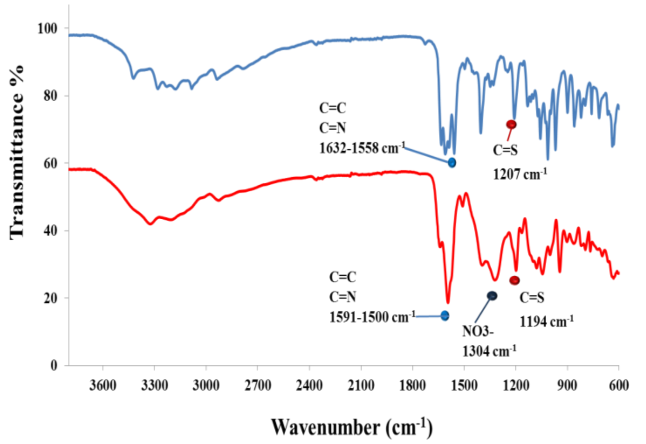


Figure 1 . The comparison of IR spectra between**6-ThioGuo** (blue line) and Cd (II) complex, **1** (red line)

However,the C=S stretching of the complex,**2** is moved to 1199 cm^{-1}compared with free ligand **6-ThioGuo**as seen in**Figure 2**. These results are evidences for the involvement of the thione group in the complexation.

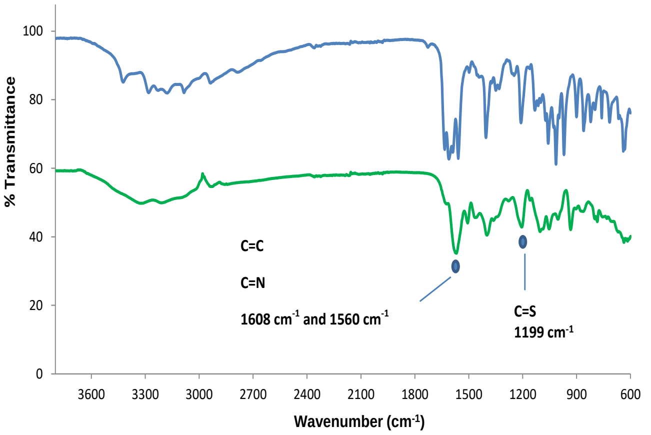


Figure 2 . The comparison of IR spectrabetween**6-ThioGuo** (blue line) and Cd(II)complex, **2**(green line).

Inthe**6-ThioGuo**,the stretching band of (C=C) is 1632 cm^{-1} whereas the (C=N) stretching bandis 1558 cm^{-1}. Subsequently, in the complex formation these bands in the complex, **1**shifted to about 1591 cm^{-1} and 1500 cm^{-1}Although**,**in the complex,**2** these bands moved to about1608 cm^{-1} and 1560cm^{-1}respectively.These results are indicative of N-7 and C6 of free ligands are involved in the complexes of cadmium (II).The obtained data were compared with the results of Sodhis' on the forming of a 6-thioguanine complex with mercury metal.[20]In addition,in the complex**, 1**there is a new broad band at about 1304 cm^{-1} pointed to nitrate group NO_3^-. This result, suggests the involvement of the NO_3^- in the complex as shown in **Figure 1**. The finding data are parallel to Zamora results for the formation of cobalt(II) complexes.[16]

^{1}H-NMR of Cadmium (II) complexes

The spectrum of ^{1}H-NMR of cadmium (II) complex,**1**appearsoverall downfield shift and broadening for the protons compared to the free ligand**6-ThioGuo**. In particular, the N(1) proton, H(8)and NH_2 peaks as seen in **Figure 3**. In the free ligand **6-ThioGuo,**the signal at δ 11.9 in the ^{1}H-NMRspectrum is related to N (1) proton. After, the complex, **1**was formed, this peak shifted to δ 12.7 ppm. Moreover, theprotons ofH(8) and NH_2in the complex,**1**are shifted to 8.1 and 6.7 ppm respectively compared to when in the free ligand, 8.4 & 7.1 ppm. The obtained finding agree with the previous research for the complexformation ofmercaptopurine with cadmium.[17]Furthermore, the peaks ofN(1) proton, H(8) and NH_2 integrated as 1:1:2 respectively in the**6-ThioGuo** ligand. In the complex,**1** these peaks were integrated as 1:2:4 respectively as shown in**Figure 3**.These resultsshowforming complex contains two ligands coordinate to one Cd^{2+} where one of the ligands is deprotonated and involves the highlighted structure given alongside thespectrum of NMR below. This complex in other words has a deprotonated ligand (anionic thiol ligand) and a neutral ligand (thione ligand).

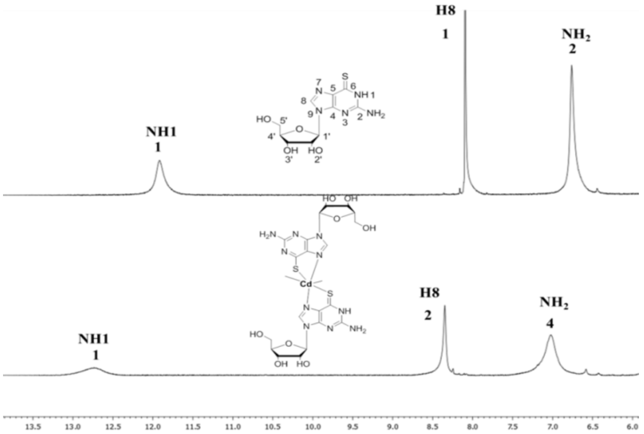


Figure 3. Thecomparison of^{1}H-NMR between **6-ThioGuo (top)**and Cd (II) complex **1 (below)** in d^6-DMSO.

Thedata of^{1}H-NM of the complex,**2**were shown sharp peaks, see **Figure 4.** This is possibly because the Cd^{2+} in hexa-coordinated complexnow reveals diamagnetic properties.[21]This is because of its low spinpaired electron configuration.[6]TheH(8) and NH_2 protons of the complex ,**2** shifts as well, however, the NH_2shifts were toward up fieldcompared with the outcome resultsof the NH_2 of complex,**1**that shifted towards downfield.In addition, the N(1) proton is about 11.9 ppm in the freeligand **6-ThioGuo**, where this proton disappeared in the spectrum of the complex,**2** as shown in the **Figure 4**. These findings are agreed with previously report for the complex of **6-ThioGuo** with Co (III) ion.[16]These findings suggesting the deprotonation of**6-ThioGuo**ligands during complex formation.Furthermore, the integration ofN(1) proton, H(8) and NH_2 peaks were as 0:2:4 respectively. This indicates the creation of complex containing two deprotonated **6-ThioGuo** ligands bound to one cadmium (II) ion.

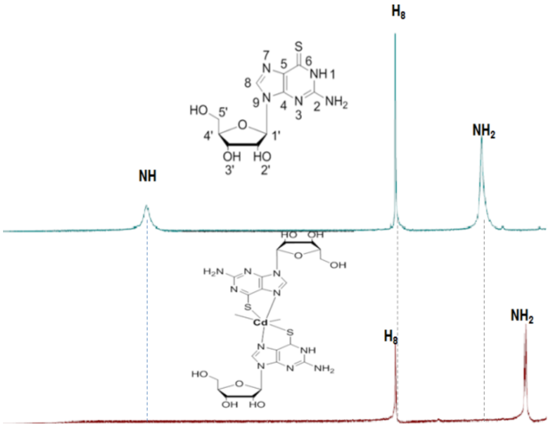


Figure 4.^{1}H-NMR comparison between **6-ThioGuo**and cadmium complex **2** in d^6-DMSO.

Because of the lack of a crystal structure of the Cd (II) complexes with **6-ThioGuo**, the molecular formula and structure of the complexes were measured byES-MS, IR, ^{1}H NMR and elemental analysis.These resultsproposes that the complex,**1**consist of two ligands (neutral and anionic ligands) bound to one Cd (II) ion via N7 and C6. Additionally, the inner sphere of cadmium (II) complex is anionic as one of the two ligands is deprotonated (thiol form). As a result, the one nitrate group neutralize the complex. As previous report the geometry for cadmium complex of meracuptopurine is octahedral arrangement.[17] Therefore it was expected for this complex to have the octahedral geometry as seen in **Figure 5**. Moreover, elemental analysis of complex, **1** is consistent with this suggested structure. The C, H, N analysis of the complex,**1**indicated the formula of the complex was $C_{20}H_{27}N_{11}O_{12}S_2Cd.2H_2O$, Calcd (found): C, 29.08 (29.05); H, 3.78 (3.09); N, 18.65 (17.12).

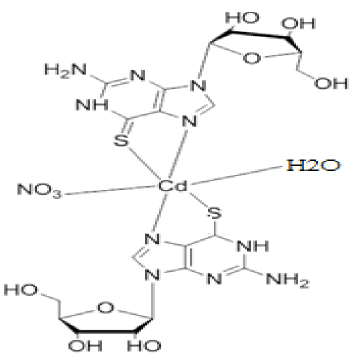


Figure 5.Proposedchemical structure of cadmium complex, **1**

Whereas the results of ES-MS, IR, ^{1}H-NMR and elemental analysis of complex,**2**proposed the complex formed of two deprotonated ligands(anionic ligands-thiol form)bound to one $Cd^{2+}$by N7 and C6. Therefore the inner sphere of the cadmium (II) complex,**2** is anionic. In addition, there are two H_2O molecules coordinate to the cadmium ion to obtain the octahedral geometry as shown in **Figure 6**.Additionally,The C, H, N analysis of the complex,**2**showed the formula of the complex was $C_{20}H_{28}N_{10}O_{10}S_2Cd$. CH_3COONa. $4H_2O$, Calcd (found): C, 29.70 (29.66); H, 3.80 (4.38); N, 14.98 (15.73).

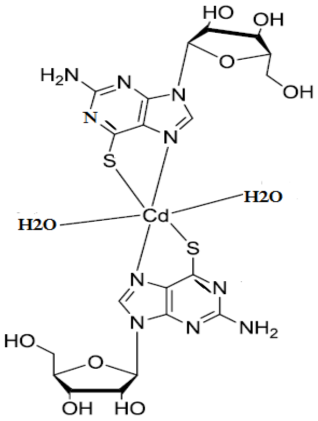


Figure 6.Proposed chemical structure of cadmium complex, **2.**

III. SUMMARY

Overall, two complexes of**6-ThioGuo**withcadmium ions wereperformed. The formation of complexes was characterizedbyES-MS, IR, ^{1}HNMR and elemental analysis. The results revealed, the binding ratio of **6-ThioGuo** ligand withCd^{+2}in complex, **1**was shown to be two ligands to one $Cd^{+2}$where one of the ligands is deprotonated.However, in the case of complex, **2**the binding ratio of **6-ThioGuo** ligand withCd^{+2} was revealed to be two deprotonated ligands to one cadmium (II) ion.

Experiment

NMR spectrum was measured on a 400 MHz Delta Jeol. IR analysis was performed on a Varian 800 FT-IR and ESI-MS was performed on a Waters- LCT-Premier mass spectrometer. A Carlo-Erba CE1108, configured for % CHN was used. All chemicals were purchased from Sigma-Aldrich.

Synthesis of complex, 1[Cd(6-ThioGuoH)(6-ThioGuo)NO_3H_2O]

6-ThioGuo (56 mg, 0.2 mmole**)**was dissolved in 10 ml methanol, and a solution of cadmium nitrate $Cd(NO_3)_2.4H_2O$(30 mg, 0.1 mmole) was added in the same solvent .The mixture was stirred at 80°Cfor overnight. After 24 h, a yellow powder was obtained and filtered and was dried at room temperature (33 mg, 59 %). Anal.Calcd (found) for $C_{20}H_{27}N_{11}O_{12}S_2Cd.2H_2O$, Calcd (found): C, 29.08 (29.05); H, 3.78 (3.09); N, 18.65 (17.12).IR selected data: 3294 (s), 3181 (w), 3115 (s), 2966 (m), 2876 (s), 1591(s), 1500 (s), 1371 (s), 1304 (s), 1194 (s), 1038 (w), 941 (s), 854 (m), 630 (m). ^{1}H-NMR (399.78 MHz, DMSO-*d*6):δ 12.74 (br, 1H, NH), 8.40 (s, 1H, H_8), 7.11 (br, 2H, NH_2), 5.69 (d,1H, J= 5.01 Hz,$H_{1'}$), 5.47 (br, 1H, 2'-OH), 5.18 (br, 1H, 3'-OH), 5.06 (br, 1H, 5'-OH), 4.41 (br, 1H, $H_{3'}$), 4.07 (br, 1H, $H_{4'}$), 3.87 (m, 2H, $H_{5',5''}$), 3.52 (m, 1H, $H_{2'}$). ES-MS: m/z (positivemode)$C_{20}H_{25}O_8N_{10}S_2Cd$ (M+H) (m/z found 711.0049 (calcd for $C_{20}H_{25}O_8N_{10}S_2Cd$ (M+H) 711.0334.

Synthesis of complex, 2 [Cd(6-ThioGuo)$_2$(H_2O)]

A(31.13 mg 0.1 mmol)of $CdC1O_4.6H_2O$ was dissolved in the 100 ml of 0.1 M acetic acid/sodium acetate buffer (pH 4.6) then was added to the solution of (52.4 mg,0.175 mmol) of **6-ThioGuo** in 400 ml of 0.1 M acetic acid/sodium acetate buffer (pH 4.6) at 95 ^{O}C and it was stirred for3mins after that kept at 60 ^{O}C. The yellowish white powder was filtered after two days and the percentage of the yield was (40 mg, 76.33%).Anal.Calcd (found) for $C_{20}H_{28}N_{10}O_{10}S_2Cd$. CH_3COONa. $4H_2O$, Calcd (found): C, 29.70 (29.66); H, 3.80 (4.38); N, 14.98 (15.73).IR selected data: 3296 (w), 3192 (w), 2947 (m), 2876 (s), 1608 (m), 1560 (s), 1509 (m), 1396 (s), 1198 (s), 1085 (w), 931 (s), 804 (w), 636 (m). ^{1}H-NMR (399.78 MHz, DMSO-*d*6): δ 8.00 (s, 1H, H_8), 6.11 (s, 2H, NH_2), 5.7 (d, 1H, J= 5.01 Hz, $H_{1'}$), 5.3 (br, 1H, 2'-OH), 5.1 (br, 1H, 3'-OH), 4.4 (br, 1H, 5'-OH), 4.00 (br, 1H, $H_{3'}$), 3.9 (br, 1H, $H_{4'}$), 3.5(m, 2H, $H_{5',5''}$), 3.4 (m, 1H, $H_{2'}$). ES-MS: m/z (positivemode)for$C_{20}H_{24}O_8N_{10}S_2Cd$ (M+Na)m/z found is (733.0159).(calcd for $C_{20}H_{24}O_8N_{10}S_2Cd$ (M+Na)733.0153.

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