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Synthesis, Characterization and Biological Studies of Selenium Dithiocarbamates and their Ni^{+2} and Cu^{+2} Complexes

Nabeel H. Buttrus
Department of Chemistry
College of Science
Mosul University

Wadala N. AL-Ani
Department of Dental basic Science
College of Dentistry
Mosul University

Amena F. AL-Omari
Department of Chemistry
College of Science
Mosul University

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ABSTRACT

Selenium metal react with $(RNHC(S)S)_2$ where R= (Ph or *o*-tolyl) in refluxing toluene to give the compounds $Se\{RNHC(S)S\}_4$. New complexes of the type $[M_2Se\{RNHC(S)S\}_4Cl_4]$, where M=$Ni^{+2}$ or Cu^{+2}, were prepared by reaction of $Se\{RNHC(S)S\}_4$ with the metal chloride salts in 1:2 molar ratio.The compounds and complexes were characterized by atomic absorption, Infrared, U.V-Visible spectra, conductivity and magnetic measurements.Biological activity studies of the compounds and complexes as antimicrobial agents and the comparison of their activities with well known antibiotic (Ampicillinc, Gentamycine and Nystatine) using different straine of bacteria gram (+ve) and gram (-ve) in addition to fungi strain candida albicans.

The results indicated that complexes of the type $[M_2Se\{S_2CNHPh\}_4Cl_4]$ are more active than $[M_2Se\{S_2CNHPhCH_3\text{-}o\}_4Cl_4]$ while the selenium compounds $Se(S_2CNHPh)_4$ and $Se(S_2CNHPhC_2H_5)_4$ have moderate antimicrobial activity.

تحضير وتشخيص و الدراسات البايولوجية لمركبات دايثايوكاريميت السيلينيوم ومعقداته مع الـNi^{+2} وCu^{+2}

الملخص

يتفاعل فلز السلينيوم مع $(RNHC(S)S)_2$ عندما R= Ph او *o*-Tolyl في التولوين المغلي ليعطي المركب $Se\{RNHC(S)S\}_4$. تم تحضير المعقدات ثلاثية النوى الجديدة ذوات الصيغة $[M_2Se\{RNHC(S)S\}_4Cl_4]$ عندما M= Ni^{+2} او Cu^{+2} من تفاعل أملاح الفلزات والمركب $Se\{RNHC(S)S\}_4$ وبنسبة مولية 1:2.تم تشخيص المركبات والمعقدات المحضرة بواسطة الامتصاص الذري، اطياف الأشعة تحت الحمراء وفوق البنفسجية والتوصيلية والقياسات المغناطيسية .تمت دراسة

الفعالية البايولوجية للمركبات والمعقدات كعوامل مضادة للبكتريا ومقارنتها مع المضادات القياسية (Ampicillinc, Gentamycine and Nystatine) وذلك باستخدام أنواع من البكتريا غرام موجب وغرام سالب بالإضافة للفطريات ومنها(candida albicans).

بينت النتائج بان المعقدات ذوات الصيغ $[M_2Se\{S_2CNHPh\}_4Cl_4]$ هي أكثر فعالية من $[M_2Se\{S_2CNHPhCH_3\text{-}o\}_4Cl_4]$ بينما اظهرت مركبات السلينيوم ذوات الصيغ $Se(S_2CNHPh)_4$ و $Se(S_2CNHPhC_2H_5)_4$ فعالية متوسطة ضد المايكروبات.

INTRODUCTION

Metal complexes play an important role in plant and animal life due to their physico-chemical properties. Organosulphur compounds, in the form of their metal complexes, exhibit awide range of biological properties. The complication has a profound effect on the uptake of micronutrient metal ions. Among sulphur containing compounds, dithiocarbametes constitute a chemically as well as biologically important class. Metal dithiocarbametes have been reported to show fungicidal (Darian et al.,1999), insecticidal (Patel et al., 1999) and herbicidal (Daris, 1997) properties. They have been act as anticancer agents(Caruso et al., 2004).

Sharma et al. (2003) have been studied the isolation, sterochemical analysis and anti fungal activity of metal complexes of trantomerised o-tolylammonium dithiocarbamate with As(III),Sb(III) and Bi(III) metal ions Arora and Arora (2003) studied the synthesis and explore their plant growth regulators and shoot weight and chlorophyll content of leaves in the leguminous corp.

The preparation and characterization of triorganophosphine gold (1) complexes containing anion derived from thiobenzoic acid are described and their cytotoxity has been investigated by Vicenti et al.,(2001). The complexes showed moderate to high cytoxity 1D50 (250-2500ng/ml).

Our interest in metal complexes with antimicrobial activity propted us to synthesis these type of compounds and complexes because it is closely related to active tetrahedral and trigonal Se(IV) and Bi(III) compounds $Se(Spy)_4$ and $Bi(Spy)_3$ (Buttrus et al., 2005) we describe in this work the antibacterial activity of selenium compound and their complexes with Ni^{+2} and Cu^{+2} ions against different strains of bacteria and fungi strain candida albicans.

Experimental:

Selenium ,toluene, aniline and substituted aniline were used as supplied.The disulfide was synthesized by standard method (Kumar et al., 1988) metal content were determined spectrophotometry using Shimadzo AA670. In frared spectra were recorded on a Perkin Elmer 580B IR spectrophotometer in the 4000-200 cm^{-1} range using CsI pellets. U.V/Vis spectra were recorded an a Shimadzu UV-Vis. Recording Spectro-photometer UV/160 .Conductivity measurements were carried out at room temperature in DMSO solution 10^{-3}M using a Jenway 4070. conductivity meter .magnetic measurements.

Synthesis:

[Se(RNHC(S)S)$_4$], (R=Ph or *o*-Tolyl)

A mixture of selenium metal (0.79 g,1 mmol) and thiuram disulfide (RNHC(S)S)$_2$ (2.0 mmol) in toluene or tetarhydrofuran (40 cm^3) was refluxed for 10 h. The reaction mixture was filtered through celite to remove the unreacted selenium metal (0.01 g) and the resulted solution was reduced to Ca 1/4 of its volume by evaporation under reduced pressure. The solid thus obtained, after cooling, solid was collected by filtration and washed by diethylether and dried in vacuum.

[M$_2$Se{RNHC(S)S}$_4$Cl$_4$], (M=Ni(II),Cu(II))

The compound [Se(RNHC(S)S)$_4$], (0.75 g,1.0mmol) in (10 cm^3) ethanol was added to alcoholic solution of metal (II) chloride (2mmol) in (10 cm^3) ethanol .The reaction mixture was stirred under reflux for 2h. during which time a precipitate was formed. It was collected by filtrations, washed with dietheylether and dried in vacuum.

Biological activity:

The antibacterial activity of selenium compounds and their complexes were selected for screening by disc diffusion technique (Bauer et al., 1966). The test disc were containing 100 microgram per disc of the compounds .

The activity was shown against Gram (+ve) bacteria (Staphylococcus and Streptococcus), and Gram (-ve) bacteria (Psendomonas and Protens) in addition to fungus strain candida alblicans. Ampicillin, Gentamycine and Nystatin were used as standard drug.The inhibition zone (mm) for the selenium compound and complexes are listed in Table 3.

Results and discussion:

The compounds of the type [Se(RNHC(S)S)$_4$] were prepared by direct oxidative addition reaction of thiuramdisulfide with selenium metal. The reaction was occured in two steps, the reduction of thiuram disulfide through the scission of the S – S bond results in the incorporation of dithiocarbamate fragments into the selenium coordination sphere . The oxidation insertion process is clearly analogous to known reactions involving the conversions of $In^o \longrightarrow In^{+3}$ or $Sn \longrightarrow Sn^{+4}$ (Buttrus,1998).

The complexes of the type [M$_2$Se{RNHC(S)S}$_4$Cl$_4$] were prepared by adding an alcoholic solution of metal (II) chloride to the alcoholic solution of the selenium compounds .The electron pair on the sulfur atoms in selenium compounds are responsible for the complexes formation.

The physical properties of the complexes are tabulated in Table 1. The complexes are stable to heat and they are soluble in dimethyl- sulfoxide (DMSO).

The most important assignment of the selenium compounds are listed in Table (2). The IR bands of the free disulfide exhibit three bands due to the υ(C – S), υ(C = S) and υ(C – N) at (995,1050 and 1460 cm^{-1}). In the selenium compounds the υ(C – N) band observed at higher frequency due to increase of bond order, the υ(C = S) band appear at the same postion, while the υ(C – S) band observed at lower frequency ahich indicate it was shared in corrdination with selenium. Further support for this coordination is provided by the appearance of new bands at (370-375cm^{-1}) ranges which tentatively attributed to υ(Se – S). The complexes display bands characteristic of coordinated dithiocarbamate ligands strong absorption in the 1460-1550 and 990-1050 cm^{-1} region due to υ(C – N), υ(C – S) and υ(C = S) modes, indicate bidentate bridging nature of dithiocarbamate (Singh and Prassed (1998)) , A shift to higher frequency in the υ(C – N) band of the complexes comparable to the dithiocarbamate ligands, indicate an increase in the double bond character of the υ(C–N) bond (Nakamoto, 1986). The shift to lower frequency in the υ(C=S) band indicating the involvement of sulphur atom of the ligand in the coordination with Ni(II) or Cu(II) metal ions, the bands occurring near 385-392 cm^{-1} and 240-315 cm^{-1} have been assigned to the υ(M - S) and υ(M - Cl) modes (Singh and Prassed, 1998).

The electronic spectra of selenium compounds and their complexes were recorded as 10^{-3} M solutions in DMSO and the results presented in Table (2). The bands observed in range 32150-40100 cm^{-1} are due to π – π* or n – π* with the dithiocarbamate group, as well as new band was observed in the range 21142-22350 cm^{-1}. This can be attributed to the charge transfer from filled ligand orbitals to the vacant selenium orbitals.

The electronic spectra of Ni(II) complexes show a band in the visible region at 11001-13450 cm^{-1} due to a transition from F state $^3T_1(F) \longrightarrow {}^3T_1(p)$ state , which is consistent with tetrahedral geometry. In the Cu(II) complexes the observed band at 14000-14600 cm^{-1} which correspond to the transition $^2T_2 \longrightarrow {}^2E$ and others at 30900 cm^{-1} which correspond to charge transfer which is consistent with tetrahedral geometry (Buttrus et al., 2006).

The results of the magnetic moment measurements are presented in Table (1) throw light on the stereochemistry of these complexes. The magnetic value of Ni(II) complexes are 3.89 and 3.83 B.M suggested a tetrahedral geometry of the complexes (Buttrus et al., 2006).The magnetic moment of Cu(II) complexes has been found 1.63 and 1.98 B.M. This corresponds to the presence of one unpaired electron in the complexes. These values with the electronic spectra indicate the complexes have tetrahedral geometry .On the basis of spectral and magnetic values, structures could be assigned to the metal complexes as shown in Fig 1.

The biological studies revealed that both compounds and complexes are effective against different microorganisms. The biological study proved that the complexes No.(3,4) with R group (phenyl) were markedly the most effective toward all microorganisms (Nawas et al., 1994) (Table 3) ,that is may be due to the effect of the subsistent as electron releasing toward the metal ions. It is also obvious that the compounds and complexes are more effective toward (*staphylococus & candida* albicans) as shown in (Table 3),in addition they showed to have better activity than the standard refrences (Ampicillinc , Gentamycine and Nystatine) and as shown in Fig 2.

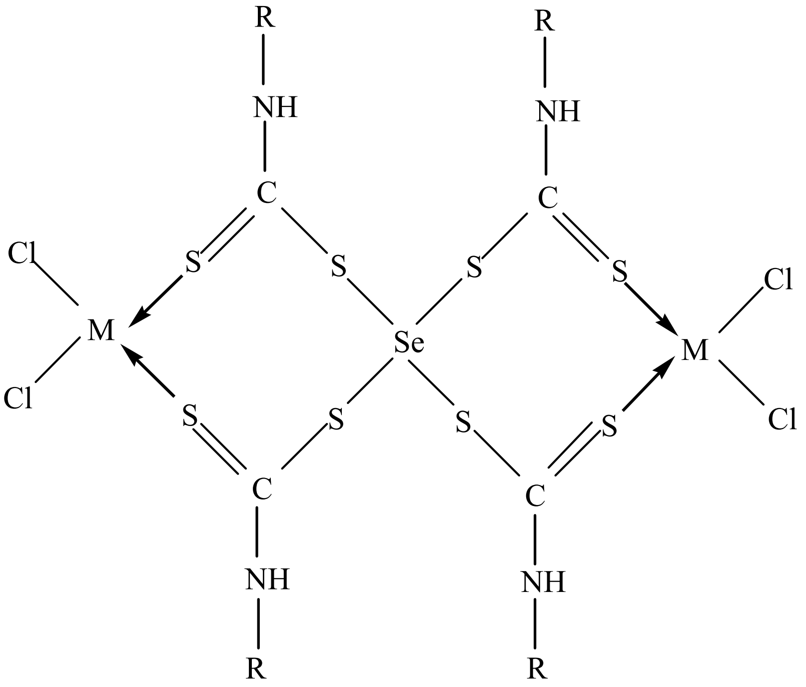


Fig 1: Suggested structure for the complexes $[M_2Se\{RNHC(S)S\}_4Cl_4]$
M= Cu(II),Ni(II)
R=Ph or *o*-tolyl

Table 1: Physical properties of compounds and complexes

No.	compound	colour	M.p (°C)	Analysis % Found(calc.)		μ_{eff}	Ω $ohm^{1}.cm^{2}.mol^{-1}$
				Se	M		
1	$[Se(S_2CNHC_6H_5)_4]$	Pale yellow	119*	10.48 (10.51)	---	---	12
2	$[Se(S_2CNHC_7H_8)_4]$	Dark gray	115	9.69 (9.74)	---	---	14
3	$[Ni_2Se(S_2CNHC_6H_5)_4Cl_4]$	Green	147	7.76 (7.81)	11.59 (11.62)	3.89*	10
4	$[Cu_2Se(S_2CNHC_6H_5)_4Cl_4]$	Pale green	132	7.18 (7.74)	12.42 (12.46)	1.63*	14
5	$[Ni_2Se(S_2CNHC_7H_8)_4Cl_4]$	Dark green	240	7.31 (7.38)	10.89 (10.93)	3.83*	20
6	$[Cu_2Se(S_2CNHC_7H_8)_4Cl_4]$	Dark red	233	7.80 (7.81)	11.72 (11.76)	1.80*	16

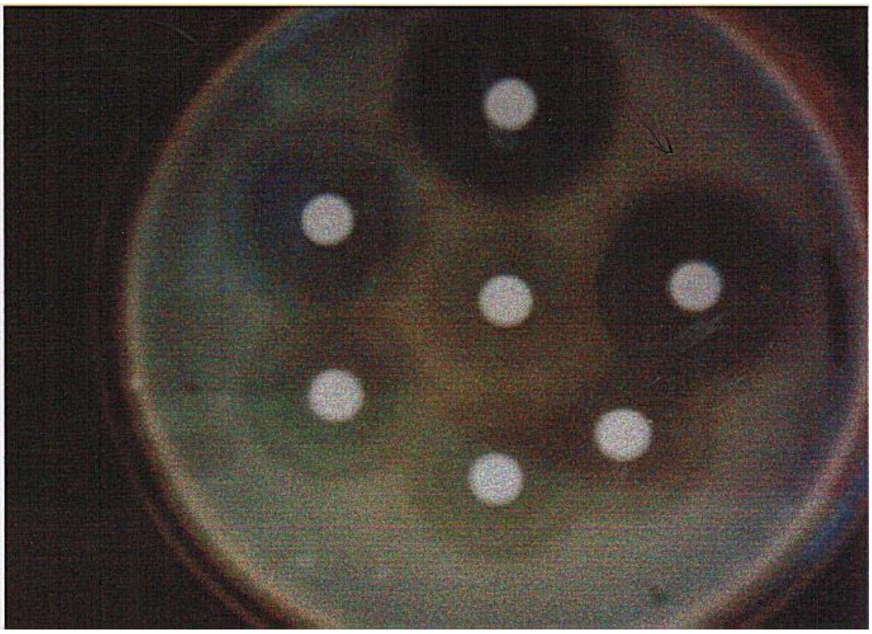
* values per metal ion

Table 2: Electronic and IR spectral data of compounds and complexes

Comp. No.	U.V-Vis bands cm^{-1}		C.T	Selected IR bands (cm^{-1})				
	$^3T_1(F)\longrightarrow{}^3T_1(p)$	$^2T_2\longrightarrow{}^2E$		υ(C-S)	υ(C = S)	υ(C=N)	υ(M-S)	υ(M-Cl)
$(S(S)CNHR)_2$			33000	995	1050	1460	---	----
1	----	----	32150, 36500	990	1050	1490	375	----
2	----	----	33450, 401000	965	1050	1550	370	300
3	11001,12900	----	22350	960	1020	1500	385	290
4	----	14000	21142	970	1015	1540	392	240
5	13450,11600	----	29000	975	1025	1550	390	290
6	----	14600	30900	980	1010	1530	385	315

Table 3: The antibacterial activities of the compounds and complexes against different

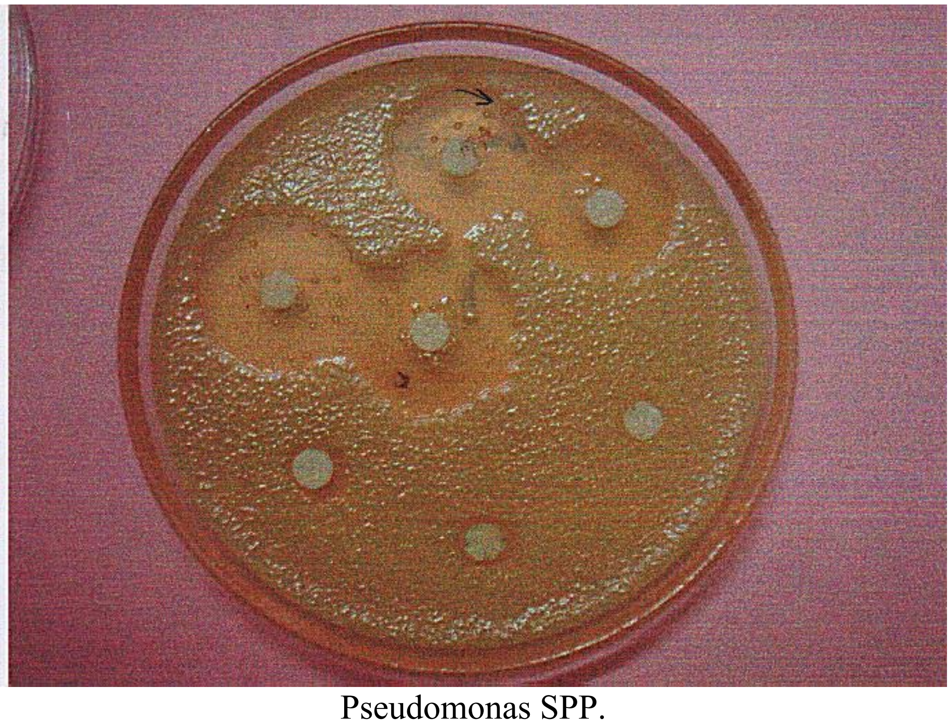
Micro-organism tested	**Compound**		**Complexes**				**Antibiotics**	
	1	**2**	**3**	**4**	**5**	**6**		
Staphylococcus	18	18	20	18	13	14	13	Ampcilline
Streptococcus	10	14	8	14	---	---	12	Ampcilline
Pseudomonas	10	---	10	22	18	20	18	Gentamycine
Proteus	---	8	22	20	---	25	14	Gentamycine
Candida albicans	20	24	18	16	22	14	15	Nystatine



Staphylococcus SPP.

(a)

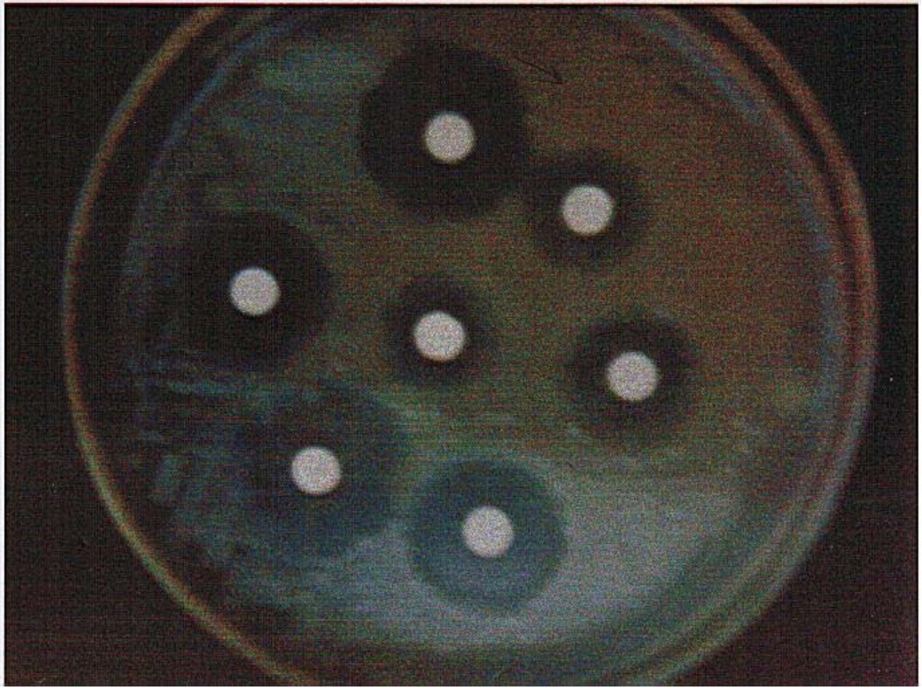
Staphylococcus SPP. on Neutrent Agar
(b)



Pseudomonas SPP.
(c)

Proteus SPP.

(d)



Candida SPP.

(e)

Fig 2: Antibacterial activities of the complexes and compounds a,b,c,d,e

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