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On the memory of professor Giorgio Anderegg (Laboratory for Inorganic Chemistry, ETH Zürich)

Giorgio Anderegg was born 15-th August 1926 in Turin (Italy). He studied at the University of Turin, where he received the doctor's degree in 1951, and then he held a research fellowship at Chemical Institute of the University of Zurich. In 1956 he moved to the ETH-Zurich, where he remained until his retirement in 1993. From 1967, he was Associate Professor of inorganic chemistry. He received the Werner Award of the Swiss Chemical Society in 1964. He was active member of the IUPAC Commission on Equilibrium Data (1970-1993). G. Anderegg wrote more than 150 scientific papers and collaborated in the publications of different '*IUPAC Tabulations and Critical Surveys on Stability Constants*'. In recent time, he was involved in TDB project in which two books '*Chemical Thermodynamics of Technetium*' and '*Chemical Thermodynamics of Compounds and Complexes of U, Np, Pu, Am, Tc, Se, Ni, and Zr with Selected Organic Ligands*' were published. In the following list, some of the relevant publications are presented for the illustration of broad region in scientific research.

G. Anderegg's research interests were concerned with the investigations of equilibria, mostly in aqueous solutions, between metal ions and complexing agents (e.g. chelators), and in the determination of the corresponding equilibrium constants, as well as the thermodynamic functions of such processes. They allow description of the equilibria in terms of speciation and have extensive practical applications in connections with the regulation of the metal-ion concentration, particularly in relation with environmental, agricultural, industrial, and health aspects. He was also engaged, for more ten years, with the investigation of the chemistry of radioactive artificial technetium.

Giorgio Anderegg died 31-th August 2006 in Olomouc. He was open-minded gentleman and his laboratory was opened for people coming from the countries around the whole world. The scientific world lost in his person one of the well-known respected experts in the field of solution equilibria.

List of representative scientific contributions

Books

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THE PROTECTIVE EFFECT AGAINST REACTIVE OXYGEN SPECIES

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Abstract

The photodynamic effect produces the reactive oxygen species (ROS) by electron transfer (Type I, superoxide) or by energy transfer (Type II, singlet oxygen). We can determine the level of destruction by lifetime of *Paramecium caudatum*. Also the protective effect of antioxidant against ROS can be determined by changes of lifetime of *Paramecium caudatum*. Other method to determine the protective ability of the antioxidant is chemiluminescent determination of the TEAC (Trolox Equivalent Antioxidant Capacity). As a source of antioxidants we have chosen the black and green tea. We have compared them with ascorbic acid and trolox.

Key Words: *photodynamic effect, reactive oxygen species (ROS), black and green tea*

Introduction

The photodynamic effect involves the combination of light, photosensitizer and molecular oxygen. Upon irradiation by laser, the photosensitizer is excited to the first

excited singlet state, which can react in two ways. A *Type I* mechanism involves hydrogen-atom abstraction or electron-transfer reactions to yield free radicals and radical ions. A *Type II* results from an energy transfer and generates singlet oxygen. The photodynamic generation of reactive oxygen species is the base of the cancer treatment known as photodynamic therapy (PDT).

All aerobic organisms have developed more or less complex systems to neutralize the reactive oxygen species (ROS) before their potentially harmful effect is activated. But nutritional elements are also extremely important. Foods that have potential or definite antioxidant capacities are mainly vegetables and fruits, as well as beverages like red wine, tea and beer.

The lifetime of reactive oxygen species is extremely short, and if a physiological acceptor does not immediately neutralize them, ROS can damage biological systems. Tea is a source of epigallocatechin gallate in green tea, and theaflavin and the associated thearubigins, in black tea. For example, cancer in the colon, breast, prostate and pancreas may be caused by a new class of carcinogens - the heterocyclic amines, formed during the broiling or frying of creatinine-containing foods, including fish and meats. Their formation and action can be inhibited by antioxidants such as those in soy and tea. Black tea is a powerful chemopreventor of reactive oxygen species and seems to be more efficient than green tea.

A sensitive and simple chemiluminescent (CL) method for measuring antioxidant activity was developed. The determination of TEAC (Trolox Equivalent Antioxidant Capacity) is based on the inhibition of CL intensity of luminol by an antioxidant.

Materials and methods

Reagents: methylene blue, eosin B, fluorescein, copper(II) phthalocyanine-tetrasulfonic acid tetrasodium salt (CuPcS₄), luminol (5-amino-2,3-dihydro-1,4-phthalazinedione), horseradish peroxidase (HRP), E.C. 1.11.1.7., Grade II, hydrogen peroxide, trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid 98% pure, water soluble vitamin

E analogue used as reference antioxidant to determine antioxidant capacity) were Sigma-Aldrich (Germany) compounds.

The photodynamic effect. The experiments were done in Petri dishes with *Paramecium caudatum* solution (density about 25 individuals in 1 ml, total volume 10 ml). The lifetime means the time when all P.c. were dead (motionless). The stock solution of tea was prepared from 2 g of dry leaves (Ceylon and Gunpowder) and 100 ml boiling water. 1 ml of this solution was used. Final concentration of ascorbic acid was 0,57 μ M and of trolox was 50 μ M (the concentrations of ascorbic and trolox were tested for 24 hours without killing effect).

Chemiluminescent mixture: 100 μ L of the 10 mM hydrogen peroxide solution was added to 200 μ L of the luminol solution (2.0 mM). This mixture (10 mL) was protected against the light with aluminum foil. *Calibration curve:* from the stock solution 1 mM Trolox in 0.1 M phosphate buffer, pH 7.6, stored in a freezer until use, several working solutions were prepared in the range 0.1-1 mM.

Chemiluminescent assay: 20 μ L of the peroxidase solution was added to 180 μ L of the chemiluminescent mixture to trigger the luminol oxidation reaction. This mixture was the reference system representing 100% light emission in the absence of inhibition by the sample or standard antioxidant solutions. To determine the total antioxidant capacity of the samples, 20 μ L of the sample or standard solutions were injected into the microplate. The light signal was immediately inhibited, reaching values close to zero, which were maintained for a certain time then gradually increased to return to values close to those observed prior to sample injection. The time between sample injection and the return to maximal emission was measured. The value obtained (in seconds) was a function of the antioxidant capacity of the sample examined. This antioxidant capacity was expressed, fitting the times obtained on the relative calibration curve, in concentration of trolox (mM).

Preparation of tea solution: leaves were dissolved in hot water (under 100°C) for 3 min (2g/100mL). The extracted solutions were filtered and allowed to cool at room temperature. The tea solutions were neither made fresh or frozen.

Results and discussion

The aim of this work was to compare the killing effect of the photosensitizer (methylene blue, fluorescein, eosin B, phthalocyanine) on *Paramecium caudatum* and the protective effect of the antioxidant (black and green tea, ascorbic acid and trolox – water-soluble analog of vitamin E). The table 1 shows the lifetime dependence on presence of the photosensitizer and on the presence of the photosensitizer and antioxidant together. All antioxidants have protected *Paramecium caudatum* against ROS; the highest protection was determined in case of black tea.

Table 1: The lifetime (sec) of *Paramecium caudatum* in the solution of the photosensitizer only and in the solution of the photosensitizer and antioxidant (black and green tea, ascorbic acid, trolox)

Photosensitizer (mM)	Lifetime (sec)				
	Methylene Blue	Black tea	Green tea	Ascorbic Acid	Trolox
0,025	413	7633	4672	2142	850
0,050	281	4361	4224	1034	565
0,100	210	3393	3395	519	437
0,200	135	2956	2942	441	309
Photosensitizer (mM)	Lifetime (sec)				
	Eosin B	Black tea	Green tea	Ascorbic Acid	Trolox
0,25	1481	2643	1438	1875	4994
0,50	895	1926	1094	1764	3528
1,00	402	681	843	1477	1674
2,00	207	563	752	1262	1037

Photosensitizer (mM)	Lifetime (sec)				
	CuPcS ₄	Black tea	Green tea	Ascorbic Acid	Trolox
0,25	4620	8507	6825	10824	14323
0,50	2688	7093	6257	4581	10812
1,00	1669	5261	5294	2926	3927
2,00	1128	2281	1585	2648	2638
Photosensitizer (mM)	Lifetime (sec)				
	Fluorescein	Black tea	Green tea	Ascorbic Acid	Trolox
2,50	2094	7302	5489	7094	3286
5,00	1266	6065	2387	5085	2708
7,50	803	4176	1330	2456	2284
10,00	643	2361	914	1756	608

The graph shows the dependence of TEAC (Trolox Equivalent Antioxidant Capacity) on the different types of tea. The tea solutions were neither made fresh - the white column - nor frozen for one year - the grey column. Major part of tea samples have manifested again at least minimal TEAC.

Sample: 1. SHOU MEE, **2.** PU – ERH, **3.** CHE XANH, **4.** SHUI HSIEN, **5.** CEYLON BOP HIGH FOREST, **6.** ZHU HA, **7.** UVA, **8.** SENCHA KJOTO, **9.** TZA´ - O- LONG, **10.** DARJEELING, **11.** GUN POWDER, **12.** CHINA OP YUNNAN, **13.** ROOIBOS SUPERIOR, **14.** MATE RANHCHO, **15.** NEPAL 1 FIKKAL ILLAM, **16.** TURKEY BOP, **17.** VIETNAM, **18.** JAPAN HOJICHA, **19.** JAVA OP , **20.** NILGIRI- SOUTH

INDIA FOP, **21.** FORMOSA FINE OOLONG, **22.** GRUSIA OP, **23.** EARL GREY, **24.** ASSAM OP KHONGEA, **25.** ASSAM TG FOP-1CL, **26.** LAPACHO, **27.** LUNG CHING, **28.** KOKEICHA, **29.** JAVA OP TALOON, **30.** BANCHA, **31.** GOLDEN TIPPY, **32.** LAPSANG SOUCHONG, **33.** PAHARGOOMIAH, **34.** GOLDEN MARINYM

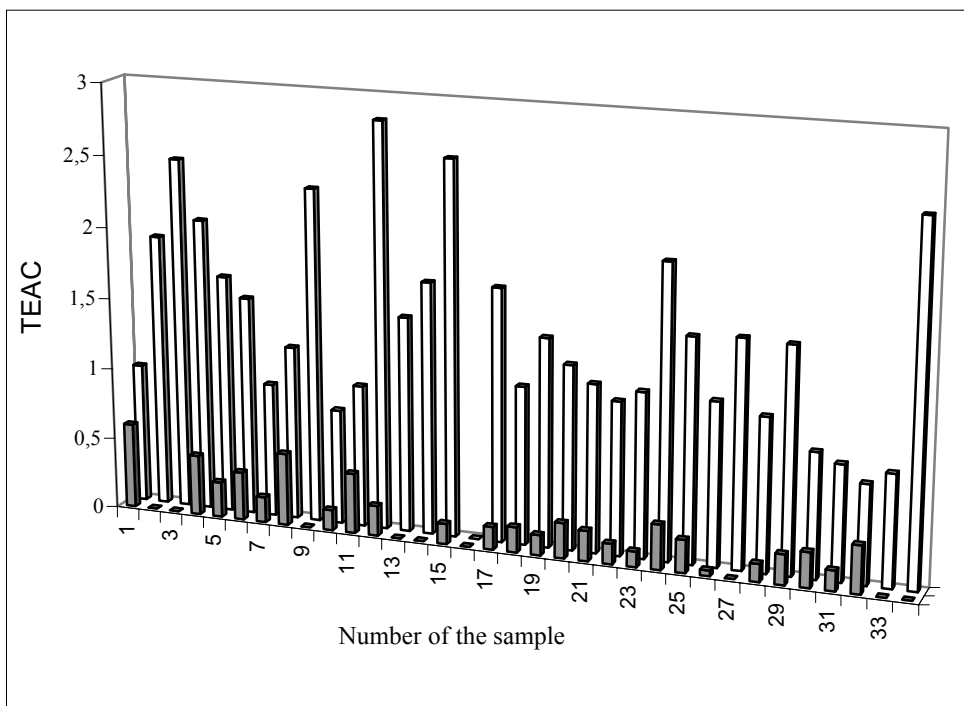


Figure 1. The dependence of TEAC on the type of tea (the number of sample). The white columns are the fresh tea solutions; the grey columns are the frozen tea solution (for one year)

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SYNTHESIS OF N-[[4-[2-(DIMETHYLAMINO)ETHOXY]PHENYL]METHYL]-3,4-DIMETHOXYBENZAMID MONOHYDROCHLORIDE

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Abstract

Technological details about preparation of *N*-[[4-[2-(dimethylamino)ethoxy]phenyl]-methyl]-3,4-dimethoxybenzamid monohydrochloride (**4**) are described.

Key words: *synthesis, amide, technology*

Introduction

N-[[4-[2-(dimethylamino)ethoxy]phenyl]methyl]-3,4-dimethoxybenzamid monohydrochloride (**4**) is a compound with biological effects on the gastrointestinal tract, it is a peristaltic stimulant and dopamine D2 antagonist with gastroprokinetic and antiemetic characteristics¹. For the time being, the substance is patent-protected and the

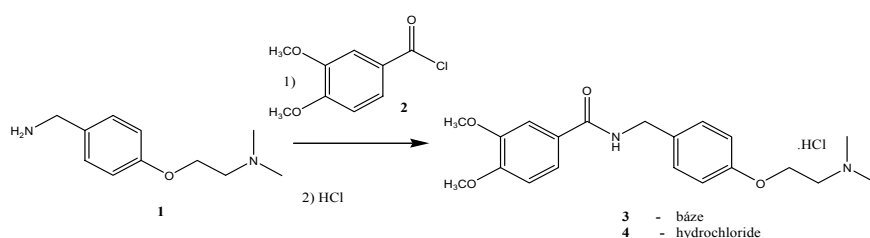
entry into market is expected in 2008. At present, the substance is called itoprid and is sold under the commercial name Itax or Ganaton.

Results and discussion

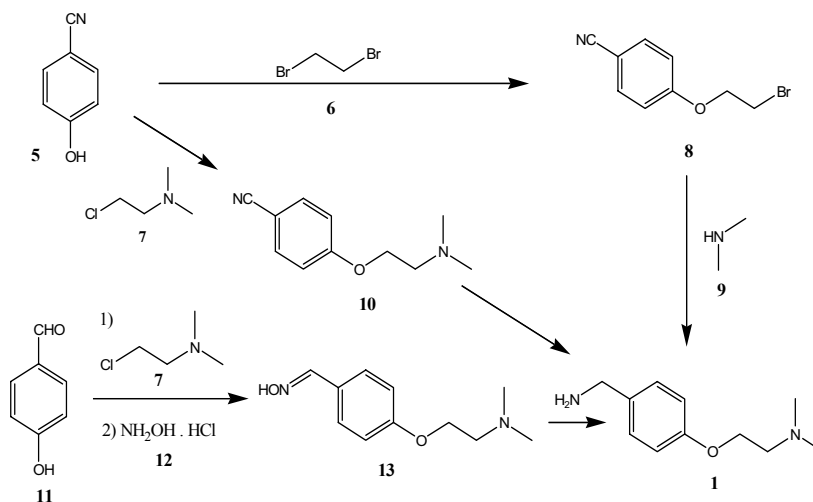
The only known synthesis (Scheme 1) is based on 3,4-dimethoxy benzoic acid from which its chloride **2** will be prepared by means of thionylchloride that will undergo condensation with the substituted benzylamine **1**. The prepared base **3** is transferred to hydrochloride **4** that is the effective substance itself.

The other described procedures differ only in the used conditions. Several synthetic methods are known for the synthesis of the key intermediate - benzylamine **1** (Scheme 2).

Scheme 1:



Scheme 2:



The procedure we used is very similar to the procedures described in the literature.^{2,3} However compared to them, different technological conditions were used. Especially safer and cheaper solvents were used. The main change is the replacement of diisopropyl ether used in the literature. This compound forms peroxides easily which is not much suitable for the industrial use. Its replacement with one solvent common for the whole synthesis failed, but each synthetic step was solved individually. Toluene that is cheaper and safer was used for the acylation and preparation of the raw base **3** and its crystallisation. Also in the case of the final hydrochloride **4**, its precipitation from the alcoholic solution with diisopropylether was replaced with the crystallisation from acetone. Under these conditions, high yields of sufficiently clean substance were obtained, while solvents can be easily recovered.

The synthetic ways leading to the starting benzylamine **1** are described in the works^{2,3,4}. In principle, the procedures are described based on 4-hydroxybenzotrile (**5**), where after the alkylation of the hydroxyl group the nitrile group is reduced, or on 4-hydroxybenzaldehyde (**11**). In this case, the first step is the formation of ether and after that the creation of oxime **13** and its reduction to the amino group. The outline of methods is illustrated in the scheme 2. However, we have not dealt with this part of synthesis with respect to the price of benzylamine **1**. This intermediate is commonly purchased from Asia.

Experimental part

During synthetic works, the analytic service was ensured with continuous control of purity by HPLC instrumentation Agilent 1100 with UV detection and the structure of clean samples was verified with the MS spectral analysis on the direct probe of DEP instrumentation GCMS Polaris Q – Thermo Finnigan.

Chloride of 3,4-dimethoxy benzoic acid (2)

Thionylchloride (5.25 ml, 70.7 mmol) was added dropwise to the suspension of 3,4-dimethoxy benzoic acid (5.0 g, 27.4 mmol) in toluene (55.0 ml). The reaction mixture was stirred and heated under the reflux with anhydrous calcium chloride closure for 4 hours. Then the excess of thionylchloride was distilled off together with toluene in vacuum. The residual solid was dissolved in toluene (20 ml) and it was evaporated in vacuum to dryness. This operation was repeated twice. After that the residual solid was dissolved in toluene (50 ml), filtered with charcoal and then it was directly used for another reaction.

***N*-[[4-[2-(dimethylamino)ethoxy]phenyl]methyl]-3,4-dimethoxybenzamid (3)**

Benzylamine **1** (4.57 g, 24 mmol) was dissolved in toluene (100.0 ml) and the toluene solution of substance **2** was added to solution of **1** at the laboratory temperature. The white precipitate was formed immediately, the reaction mixture will get thicken and was spontaneously heated up to 46°C. Then the reaction mixture was stirred at the laboratory temperature for another 2.5 hours. Then water was added (100.0 ml) and the formed emulsion was acidified with the concentrated hydrochloric acid (1.0 ml). The layers were separated, the water layer was extracted with toluene (50.0 ml) and then water layer was alkalified with the water solution of ammonia to pH 11. The formed suspension was stirred for 30 minutes while being cooled down to the temperature of 0°C and the formed product was filtered off, washed with water and dried in the vacuum at the temperature of 70°C. The yield of substance **3** was 7.74 g, i.e. 92% theory with purity above 99.0 % HPLC. This crude substance **3** (7.74 g, 21.5 mmol) was re-crystallised from hot toluene (100.0 ml). After the filtration with charcoal and after cooling down, the substance **3** was filtered off and washed with cooled toluene. The obtained crystalline substance was dried in the vacuum at the temperature of 70°C to constant weight. By the crystallisation, 6.76 g, i.e. 87.3 % of the substance **3** of purity 99.27 % HPLC and the melting point 109 – 110.5°C was obtained.

***N*-[[4-[2-(dimethylamino)ethoxy]phenyl]methyl]-3,4-dimethoxybenzamid hydrochloride (4)**

The recrystallised base **3** (6.0g, 16.7 mmol) was dissolved in hot methanol. The solution was acidified with 20 % isopropanolic solution of hydrochloric acid (6.0 ml). After 5 minutes of stirring, one third of solvent was evaporated off. The residual oil was diluted with acetone (60.0 ml). The formed suspension was cooled down in ice bath and after 1 hour of stirring the solid portion was filtered off and washed with acetone (20.0 ml). The crystalline product was dried in vacuum at the temperature of 70°C. The yield of substance **4** was 6.4 g, i.e. 96.4 % theory, and of purity 99.52 % HPLC. This crude product was dissolved in methanol (50.0 ml). After the filtration with charcoal the solution was concentrated in the vacuum, acetone (80.0 ml) was added to evaporation residue, the precipitated product **4** was cooled down, stirred 1 hour and filtered off. After washing with acetone (20.0 ml) it was dried in vacuum at the temperature of 70°C. The yield of hydrochloride **4** was 5.24 g, i.e. 82.3 % theory, and purity 99.88 % by HPLC. Melting point was 192 – 196 °C.

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ON THALLIUM(III) COMPLEXES WITH TRIS(2-AMINOETHYLAMINE) (*tren*)

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Abstract

The coordination compound $[\text{Tl}(\textit{tren})_2](\text{NO}_3)_3 \cdot \text{H}_2\text{O}$ was prepared and characterized by elemental analysis and IR spectroscopy. The compound is well soluble in water and its aqueous solution is stable for several weeks. The protonation constants of complex were determined by acidimetric titration of the aqueous solution of complex at ionic strength $I = 1.00 \text{ M}$ (NaNO_3) and temperature $(25.0 \pm 0.1) \text{ }^\circ\text{C}$. On the base of experimental facts, the possible structural formula of prepared compound has been proposed.

* deceased 31.8.2006

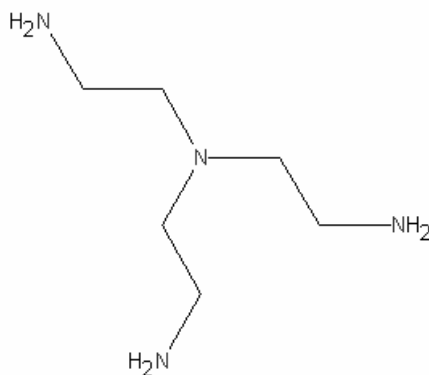
Key Words: *Thallium(III), polyamine complexes, equilibrium constants, 2,2',2''-triaminotriethylamine.*

Introduction

The study of amine chelates with a variety of metal ions has been very intensive^{1,2}, mostly with ethylenediamine (*en*) which is considered as “God’s gift to the coordination chemists”^{1,2}. Thallium(III) ion belongs to the group of soft metal ions and it shows the strong affinity to ligands having nitrogen donor atoms^{1,3,4}. The thallium(III) solution chemistry is rather complicated because of its strong oxidizing ability against several organic or inorganic ligands and extensive metal ion hydrolysis even in acidic solutions, when the hydroxo species $[\text{Tl}(\text{OH})_n]^{3-n}$ ($n = 1-3$) or the solid brown Tl_2O_3 can start to be formed at $-\log [\text{H}^+] \approx 1$ especially in presence of bases^{1,5,6,7}. The solution equilibria study of thallium(III) complex species with polyamines^{5,6} (pyridine, ammonia, ethylenediamine, 2,2'-bipyridyl, 1,10-phenantroline) shows that the stability of thallium(III) complexes is increasing in the order, however the formation of ternary mixed thallium(III)-hydroxo-amine species was observed for simple amines⁵ (pyridine, ammonia, ethylenediamine) due to formation of more stable hydroxo complex $[\text{Tl}(\text{OH})]^{2+}$ ($\log K_1 \approx 13.4$) than ammonia complex $[\text{Tl}(\text{NH}_3)]^{3+}$ ($\log K_1 \approx 9.1$)⁴. This fact was confirmed by Musso⁷ who observed the fast hydrolysis of freshly prepared thallium(III) ammonia and ethylenediamine salts in aqueous solution. The physico-chemical and structural properties of binary and ternary thallium(III) complexes with ethylenediamine^{1,7,9}, diethylenetriamine^{7,8}, triethylenetetraamine^{7,9} and auxiliary ligands bromide⁷ and cyanide⁹ were investigated and the stepwise stability constants were determined in pyridine solvent in case of ethylenediamine ligand¹. Increasing the coordination number of thallium(III) ion in compounds with N,N,N',N'-tetrakis(2-aminoethyl)ethane-1,2-diamine (*penten*)¹⁰ and N,N,N',N'-tetrakis(2-pyridylmethyl)ethane-1,2-diamine (*tpen*)¹¹, the complexes become inert in aqueous solution and they are capable of formation of ternary species with halogenides and

pseudohalogenides having the total thallium(III) coordination number seven and eight^{10,11}.

In this work, the complex $[\text{Tl}(\text{tren})_2](\text{NO}_3)_3$ was prepared for the first time and its structure was proposed on the base of experimental facts. In addition, the attempt for estimation of stability constant of $[\text{Tl}(\text{tren})]^{3+}$ complex species was done using LFER approach.



Scheme 1. Formula of the ligand 2,2',2''-triaminotriethylamine (*tren*).

Materials and methods

Synthesis of complex

The coordination compound was prepared as follows. The liquid *tren* amine (see **Scheme 1**, Fluka, the highest available purity) dissolved in dry methanol was added slowly dropping to methanolic solution of $\text{Tl}(\text{NO}_3)_3$ (Fluka, $\text{Tl}(\text{NO}_3)_3 \cdot 3\text{H}_2\text{O}$). Yellowish precipitate of coordination compound is formed after mixing reagent species in respective molar ratio. The mixture was stirred 30 minutes after end of the mixing up. The synthesis was done in argon atmosphere to protect formation of mixed carbonate-species. The precipitate has been filtered off and washed by dry methanol. The

substances were dried in vacuum desiccator. The chemical substances were characterized by elemental analysis, $[\text{Tl}(\text{tren})_2](\text{NO}_3)_3 \cdot \text{H}_2\text{O}$ (Calc. for C 20.56%, H 5.46%, N 21.98%; found: C 20.75%, H 5.35%, N 21.71%). The elemental analysis (C, H, N) was done in Microlab for Analytical Chemistry ETH Zürich.

IR spectroscopy

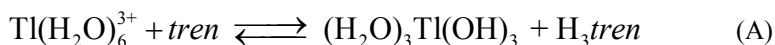
Infrared (IR) spectra were measured on PERKIN-ELMER 883 equipment as KBr pastils. The prepared compound $[\text{Tl}(\text{tren})_2](\text{NO}_3)_3 \cdot \text{H}_2\text{O}$ (s) shows absorption peaks in cm^{-1} : 3427 (s,br), 3186 (vs), 3100 (s), 2954 (vs), 2916 (vs), 2875 (vs), 2394(m), 1760 (m), 1577 (m), 1382 (m), 1066 (m), 1010 (s), 992 (m), 891 (m), 745 (m), 633 (m), 571 (m), 531 (m), 413 (m). The characteristic absorption bands for thallium(III)-amine compounds are about those frequencies 1760, 1580, 1380, 1010 and 820 cm^{-1} ref. 7. Frequency 820 and 1380 cm^{-1} are respected to free uncoordinated nitrate, whereas 1010 cm^{-1} frequency is monodentately coordinated nitrate. The band about 1580 cm^{-1} is assigned to antisymmetric NH_2 deformation vibration and the 1760 cm^{-1} band can be assigned for some C-N valence vibration. This band position appears only for thallium(III)-amine complexes (spectrum of pure amine does not concern any peaks of this band). This vibration is excited probably by formation of strong thallium(III)-nitrogen bonding.

Potentiometric titrations

Prepared substance was dissolved in water and titrated by 0.1 M HNO_3 solution at temperature $(25.0 \pm 0.1) \text{ }^\circ\text{C}$. Ionic strength was adjusted by sodium nitrate to be equal one. Titration instrumentation was the same as described elsewhere¹¹. The calculations were done by means of SUPERQUAD program¹².

Results and discussion

The synthesis of coordination compound $[\text{Tl}(\text{tren})_2](\text{NO}_3)_3$ was not carried out in aqueous solution due to possible reaction



as the consequence of strong affinity of basic *tren* ligand to protons. The methanol was used the solvent in which the synthesis of complex is more straight-forward and the undesired chemical reactions are excluded.

The thallium(III) coordination compound $[\text{Tl}(\text{tren})_2](\text{NO}_3)_3 \cdot \text{H}_2\text{O}$ is very good soluble in water (several grams of compound in 1 ml water). The aqueous solution of above discussed compound is stabile several weeks and it does not show any start of thallium(III) ion hydrolysis in compound while this phenomena is observed in acidic medium ($-\log [\text{H}^+] < 3$).

The aqueous solutions of freshly prepared compound were titrated adding the nitric acid solution. The titrations were carried out for different concentrations of complex in region 1-5 mM. The titration curves are shown in Fig. 1. The degree of protonation of coordination compounds was calculated as

$$Z = \frac{c_{\text{H}^+} - [\text{H}^+] + [\text{OH}^-]}{c_{\text{species}}} \quad (1)$$

As it can be seen on Fig. 1, the discussed compound consumed two protons and this protonation process is not dependent on complex concentration. On the contrary, the addition of the third proton leads systematically to $-\log [\text{H}^+]$ decrease with the increased complex concentration which can be explained by the hydrolytic reaction with simultaneous formation of polymeric species analogously to metal ion hydrolysis^{13,14}. Only three protonation constants can be estimated and the calculated overall and stepwise protonation constants of thallium(III) complex are collected in Table 1. The protonation constants of *tren* ligand under the same experimental conditions are given also for comparison there¹⁵.

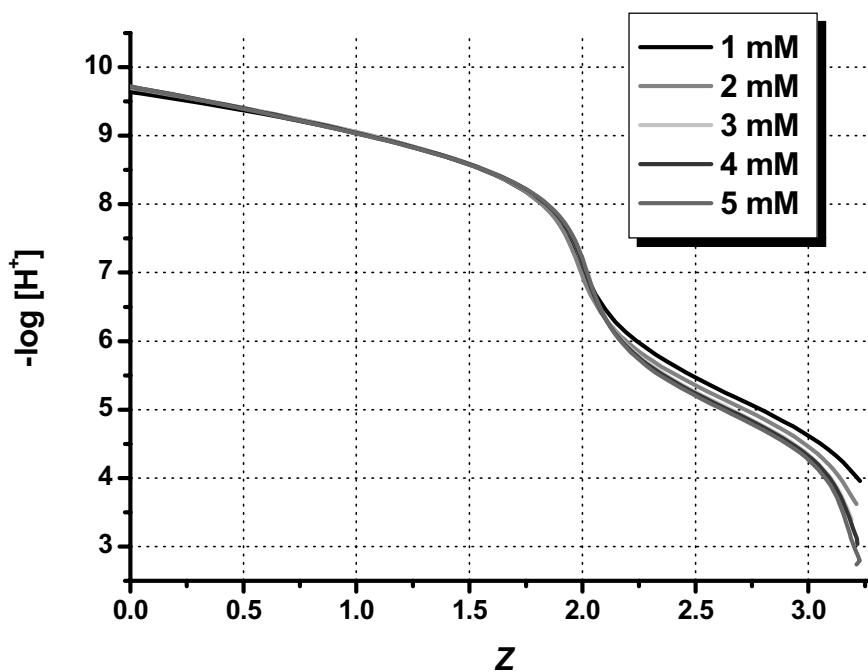


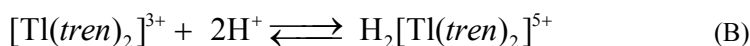
Fig. 1: The normalized titration curves of aqueous solutions of $[\text{Tl}(\text{tren})_2](\text{NO}_3)_3 \cdot \text{H}_2\text{O}$ compound in concentration levels 1 - 5 mM. The other experimental details are given in text.

Table 1 The logarithmic values of overall and stepwise protonation constants for thallium(III) chelate of *tren* polyamine

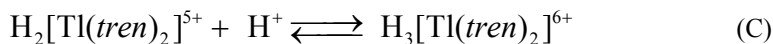
i	$\text{H}_i\text{tren}^{\text{a}}$		$\text{H}_i[\text{Tl}(\text{tren})_2]$	
	$\log \beta_{p,i}$	$\log K_{p,i}$	$\log \beta_{p,i}$	$\log K_{p,i}$
1	10.39	10.39	8.89 ± 0.03	8.89
2	20.20	9.81	17.73 ± 0.03	8.84
3	29.09	8.89	22.40 ± 0.04	4.67

a) Ref. 15

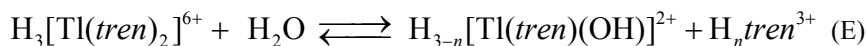
The first two protonation constants of $[\text{Tl}(\text{tren})_2]^{3+}$ complex species are almost the same (8.89 and 8.84) which means that two protons can attack either the most basic coordinated or uncoordinated nitrogen atoms in each *tren* molecule. Those nitrogen atoms are each other sufficiently separated from steric point of view and there is no electrostatic repulsion between functional groups which behave independently. This phenomenon was observed also in case of some macrocyclic ligands¹⁶. The estimated last protonation constant is much lower in comparison with two other protonation constants. In addition, the first two protonation constants of the thallium(III) complex and ligand are not so different as the last constant. Therefore the double protonation of complex species in solution can be described as



while the consumption of the third proton

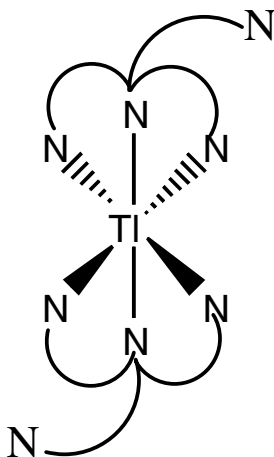


can be explained by several reactions where the hydrolytic decomposition of protonated complexes with simultaneous formation of brown solid thallium(III) hydroxide or formation of polymeric species (*e.g.* in the system Tl^{3+} -*trien*⁷) can take place:



The theoretical coordination number of thallium(III) ion in this compound can achieve eight due to the nitrogen donor atoms of two ligand molecules but the real coordination number in studied compound will be six. If all nitrogen donor atoms are bound by thallium(III) ion (*e.g.* Tl^{3+} -*penten* system¹¹), the protonation constants of nitrogen atoms in complex dropped several order of magnitude in comparison to free ligand. This is not fulfilled in our case therefore it can be suggested that the two nitrogen atoms are not bound to thallium(III) ion. In addition, it is difficult to decide which kind of nitrogen atom of *tren* ligand (tertiary or primary nitrogen atom) is free and it will be protonated in the first step because both do have almost the same protonation ability¹⁷.

There are several possible structural formulas but taking into account the above mentioned facts and the structures of $[\text{Tl}(\text{en})_3]^{3+}$ ref. 1, $[\text{Tl}(\text{dien})_2]^{3+}$ ref. 8, $[\text{Tl}(\text{trien})(\text{CN})]^{2+}$ ref. 9, $[\text{Tl}_2(\text{trien})_3]^{6+}$ ref. 7 and $[\text{Tl}(\text{penten})]^{3+}$ ref. 10 complexes obtained by means of X-ray diffraction analysis, the most probable looks this one given in **Scheme 2**.



Scheme 2. The possible structural formula of $[\text{Tl}(\text{tren})_2]^{3+}$ complex in aqueous solution.

In order to estimate the stability of $[\text{Tl}(\text{tren})]^{3+}$ complex species, the Linear Free Energy Relationship (LFER) approach was applied^{3,4}. The protonation and stability constants for metal complexes with hexadentate *penten* ligand¹⁰ and our studied tetradentate *tren* ligand taken from NIST database¹⁸ shows straight correlation (see Fig. 2) which is independent on ionic strength employed in the determination of equilibrium constants (0.1 M vs. 1.0 M) as can be seen on the obtained LFER parameters: $\log \beta(\text{M}(\text{penten}), I = 1.0 \text{ M}) = (1.27 \pm 0.04) \times \log \beta(\text{M}(\text{tren}), I = 0.1 \text{ M})$ and $\log \beta(\text{M}(\text{penten}), I = 1.0 \text{ M}) = (1.22 \pm 0.04) \times \log \beta(\text{M}(\text{tren}), I = 1.0 \text{ M})$. Generally the stability constants for metal complexes with *penten* are about 25-30 % higher than with *tren* due to higher ligand denticity. Using the LFER parameters, one obtains the estimates of stability constants for $[\text{Tl}(\text{tren})]^{3+}$ species: $\log \beta(I = 0.1 \text{ M}) \approx 29.3$ and $\log \beta(I = 1.0 \text{ M}) \approx 30.3$ which reflects the high affinity of thallium(III) ion to form stable complexes with polyamine ligands predicted theoretically^{3,4}.

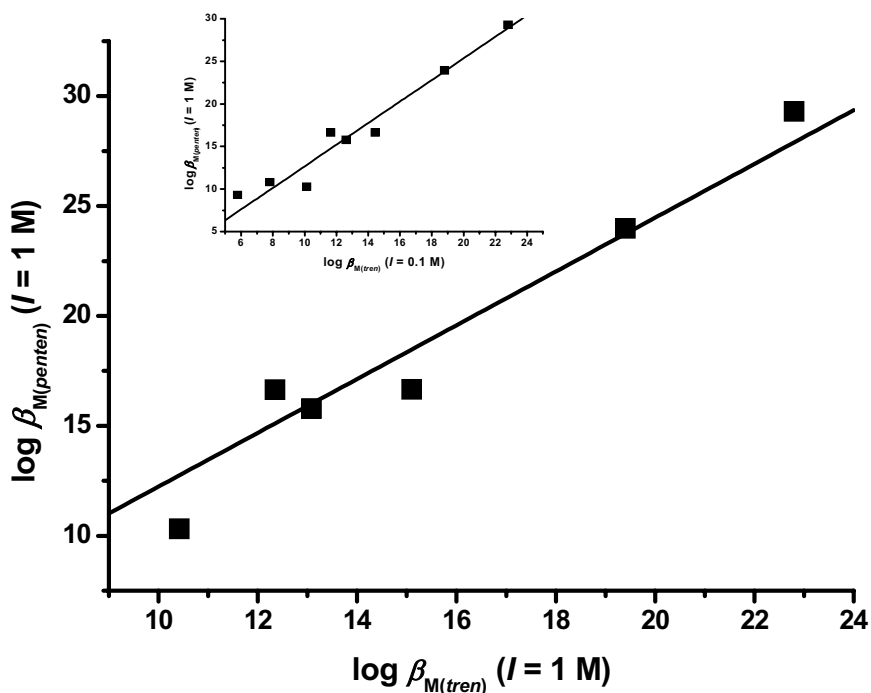


Fig. 2: The LFER of complexes of **penten** and **tren** polyamine ligands with proton and transition metal ions (Co^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+}) for ionic strength $I = 1 \text{ M}$. In offset, LFER for ionic strength $I = 0.1 \text{ M}$ is extended for Ag^+ and Mn^{2+} metal ions.

Acknowledgment

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INFLUENCE OF HALIDE ANION ON PREPARATION OF SILVER COLLOID PARTICLES

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Abstract

Within the presented paper there has been studied the influence of bromide and iodide ions on the preparation of silver colloid particles. The preparation was based on the reduction of silver salt by glucose in the presence of ammonia. The obtained results have shown that the silver particles originate in direct reduction of the appropriate silver halide precipitate, the prepared silver particles were of approx. 100 nm in size. A significant influence of the ammonia presence was observed only in the system containing bromide ions. Still in many cases they have proved a tendency to agglomeration.

Key Words: *Colloid silver, nanoparticles, bromide, iodide, reduction, glucose.*

Introduction

Metal colloid particles or more precisely metal nanoparticles represent one of the building stones in today's dynamic nanotechnology development. The transfer from a metal macro phase into metal particles of definite sizes in range from nanometres to tens of nanometres causes fundamental changes in behaviour. The key changes can be observed both in chemical and physical properties. Chemical changes are reflected especially in their high catalytic activity.^{1,2} Characteristic physical properties of the metal nanoparticles are mainly connected with the existence of the surface plasmon.³ Besides gold, silver has become one of the first metal with practical usage because of its unique properties. It has been used already since the beginning of the 1980s especially in the field of the surface enhanced Raman Spectroscopy (SERS).^{4,5} Silver nanoparticles have shown also other properties that can be used in practice – the most recently studied property is its high antibacterial activity which can be used e.g. for textile fabric modification.⁶⁻⁹

A fundamental problem is found in the preparation of monodisperse systems of metal nanoparticles with defined sizes.¹⁰ This problem is then encountered especially in the case of silver nanoparticles that are most frequently prepared via chemical reduction of soluble silver salt.¹¹ Unfortunately these methods do not still offer the desired variability in nanoparticle sizes with sustaining highly monodisperse system at the same time.^{12,13} Therefore there have been searched other possibilities enabling to control the sizes and polydispersity of the prepared nanoparticles using different types of additives as e.g. surface active substances (surfactants) and polymer substances side by side with inorganic substances.^{14,15} Methods that do not reduce directly the soluble silver salt but its insoluble compound present in the system in the form of colloid particles (e.g. the most frequently used hydrated silver oxide) provide us with another possibility of the influence on the prepared colloid system.¹⁶ Also only slightly soluble silver halides, mainly bromides and iodides, can fulfil comparable role.¹⁷ The preparation of silver nanoparticles, considering the dependency of the sizes of the formed silver colloid

particles on the sizes of the primarily formed silver halide, via reduction of their halides has not been devoted such attention it would deserve.

Experimental Part

Silver nitrite, ammonia (25% w/w aqueous solution), sodium hydroxide, sodium bromide, and sodium iodide p.a. purity (Lachema) were used without any additional purification. Reducing sugar – glucose p.a. (Penta) was also used without any further purification. All the prepared solutions were purified prior their use from solid particles by filtration through 0.2 μm filter (Sigma).

Silver colloid particles were prepared via the reduction of silver halide precipitate by glucose in the presence of ammonia. In the system the value of pH was maintained at 11.5 by means of appropriate addition of certain amount of sodium hydroxide solution. Starting concentrations in reaction mixture were for ammonia 0.01 $\text{mol}\cdot\text{dm}^{-3}$, for AgNO_3 10^{-3} $\text{mol}\cdot\text{dm}^{-3}$ and for glucose 10^{-2} $\text{mol}\cdot\text{dm}^{-3}$. Concentration of sodium bromide or sodium iodide was adjusted in the range from $5\cdot 10^{-5}$ to $5\cdot 10^{-3}$ $\text{mol}\cdot\text{dm}^{-3}$. The halide was added to the system together with the solution of the reducing sugar. The course of the reduction was continuously monitored by measurements of turbidity of evolving dispersion. The simple photometry equipment prepared from titration accessory for spectrophotometer Specol (30 ml cuvette) was used. A high luminance LED ($\lambda = 660$ nm, luminance 1500 mcd) was used as the light source. All measurements were performed at laboratory temperature (approx. 20 °C) and the temperature in cuvette during reduction was not controlled.

Particle size distribution of the prepared hydrosols was measured by means of ZetaPlus (Brookhaven, USA), using a dynamic light scattering (DLS) method. True particle size distribution was modelled by unimodal lognormal distribution by the Brookhaven original software package.

Results and discussion

Regarding the difference in behaviour of the system influenced by addition of bromide and iodide ions the results in these two systems will be primarily discussed separately.

A) Influence of bromide ions

Bromide ions create together with silver ions a precipitate. Its solubility product (pK_s) is equal to 12,31 and conveys the concentration of silver ions in pure aqueous solution of approx. 10^{-6} mol/l. Considering the constant (pK_2') of stability of the $[Ag(NH_3)_2]^+$ complex cation equal to 7,03 it is also possible to estimate the concentration of free silver ions in aqueous solution of this complex cation to approximately 10^{-6} mol/l (regarding the concentration rates corresponding to the experimental adjustment). Therefore the silver bromide can dissolve in the presence of ammonia although much worse than chloride. Thanks to this worsened solubility the silver bromide precipitate is derived in this reaction system as it can be proved by the measurements of the particle sizes for the case that the reducing substance was not added to the reaction system (see table 1). The sizes of these silver bromide particles were ranged from 100 to 150 nm. Relatively narrow range of particle sizes in the silver bromide precipitate points out at the significant influence of the ammonia, present in the system, on the development of these particles. In the systems without ammonia with equimolar rates of silver and halide ions there have been gained particles with sizes from micrometers up to tens of micrometers.

The reduction of silver ions by glucose in the presence of bromide ions, the reaction takes place on the surface of the already existing silver bromide particles. These particles play the role of not only source of silver ions but also of a catalyst. This statement can be supported by the obtained dependencies of the sizes of the particles on the bromide ions concentration, which is valid not only for silver bromide but also for the final silver colloid particles. Both dependencies have proved similar tendencies and the sizes of the prepared silver colloid particles copied the sizes of the silver bromide

(see figure 1). In the course of the reduction the primarily generated particles were slightly enlarged which could have been caused by their deformation. They were deformed during the process of the reduced silver atoms storage on the silver bromide surface of the already existing particles in the reaction centres. The final silver particles were then of irregular shapes as it can be observed from the TEM images (see figure 3a).

Table 1: Basic characteristics of silver colloid particles prepared via reduction of $[\text{Ag}(\text{NH}_3)_2]^+$ complex cation by the solution of glucose in the presence of KBr based on the dependency of its presence in the system (d – size of the particles, h.w. –half-width of the distribution curve). At the same time there are presented also sizes of primarily formed AgBr particles.

c_{KBr} , mol/l	AgBr particles d [nm]	Ag particles		
		d [nm]	h.w. [nm]	polydispersity
0.00005	97	133	73	0.31
0.0001	97	112	59	0.26
0.0002	103	98	53	0.33
0.0005	126	171	76	0.21
0.001	152	189	71	0.15
0.002	118	134	54	0.18
0.005	103	103	37	0.13

B) Influence of iodide ions

In the case of addition of iodide ions into the reaction system the situation is diametrically different to the case in the system influenced by addition of bromide ions. Solubility product constant of silver iodide is of such a low value ($pK_s=16,08$) that

solubility of this compound ($c_{\text{Ag}^+} \approx 10^{-8}$ mol/l) does not allow the complex cation $[\text{Ag}(\text{NH}_3)_2]^+$ to exist, and even more exactly, does not allow the silver iodide to dissolve in ammonia. Also in the case when the precipitate is performed in the presence of ammonia the formed silver iodide particles are influenced especially when there are more silver ions present in the system in comparison to the iodide.

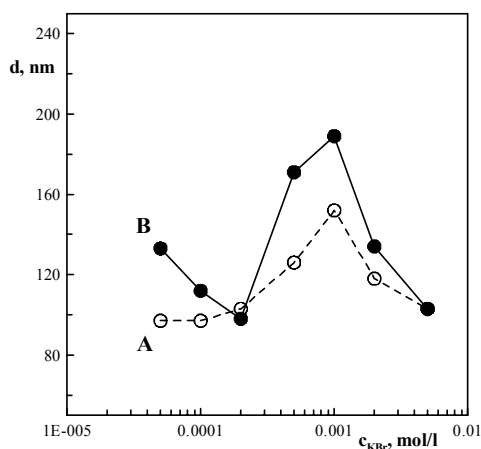


Figure 1: Comparison of the size dependency of the particles of AgBr coagulation (A) and subsequently reduced silver colloid particles (B) on the concentration of silver bromide in the reaction system with ammonia concentration equal to 0.01 mol/l.

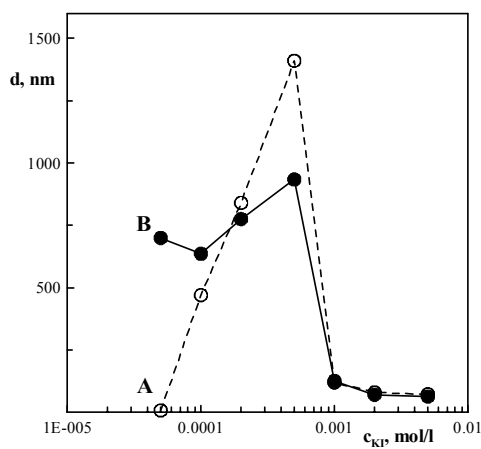


Figure 2: Comparison of the size dependency of the particles of AgI coagulation (A) and subsequently reduced silver colloid particles (B) on the concentration of silver iodide in the reaction system with ammonia concentration equal to 0.01 mol/l.

Surplus of the silver ions remains bounded into the complex cation, which is adsorbed on the surface of the AgI particle less likely than Ag^+ itself. This effect causes decrease in agglomeration stability. The maximum of the particle sizes is then reached earlier than in the equimolar amount of Ag^+ and I^- ions. Thus the agglomerations gain the sizes over $1\ \mu\text{m}$ comparable to the case with the system with ammonia (see Table 2). The prepared AgI agglomerations are not entirely compact because smaller silver particles occur in the course of the following reduction although in agglomeration form again, which can be observed from the TEM images (see figure 3b). The agglomeration is stopped not until the higher KI concentrations, in comparison to the equimolar adjustment, occur in the system. The individual particles are smaller in size - under hundred of nanometres. Simultaneously the sizes of the original silver iodide particles remain the same although their polydispersity becomes relatively high (see figure 3c).

C) Differences in the behaviour of bromide and iodide ions in the system

The gained results of the preparation of the silver nanoparticles, prepared in the reduction process in the presence of bromide and iodide, have undoubtedly proved the influence of the silver halide on the resulting sizes of the reduced silver nanoparticles. The resulting sizes of the silver nanoparticles copy the tendency in sizes of the primarily formed particles of the silver halide precipitate. These particles have proved to play the key role in the whole process of silver nanoparticle preparation, which is reflected in their resulting sizes. Silver iodide, which is insoluble in ammonia, is not actually influenced by the presence of ammonia and therefore the size of the primarily formed particles of silver iodide, leading to negative influence on stabilization, approaches the size of micrometers (μm). Meanwhile in the case of silver bromide the presence of ammonia leads to stabilization of the particles sizes in the range of nanometres (nm).

Table 2: Basic characteristics of silver colloid particles prepared via reduction of $[\text{Ag}(\text{NH}_3)_2]^+$ complex cation by the solution of glucose in the presence of KI based on the dependency of its presence in the system (d – size of the particles, h.w. –half-width of the distribution curve). At the same time there are presented also sizes of primarily formed AgI particles.

c_{KI} , mol/l	AgI particles d [nm]	Ag particles		
		d [nm]	h.w. [nm]	polydispersity
0.00005	7	699	158	0.068
0.0001	470	635	239	0.181
0.0002	840	775	196	0.188
0.0005	1410	933	342	0.173
0.001	119	125	53	0.179
0.002	79	70	29	0.167
0.005	72	63	28	0.199

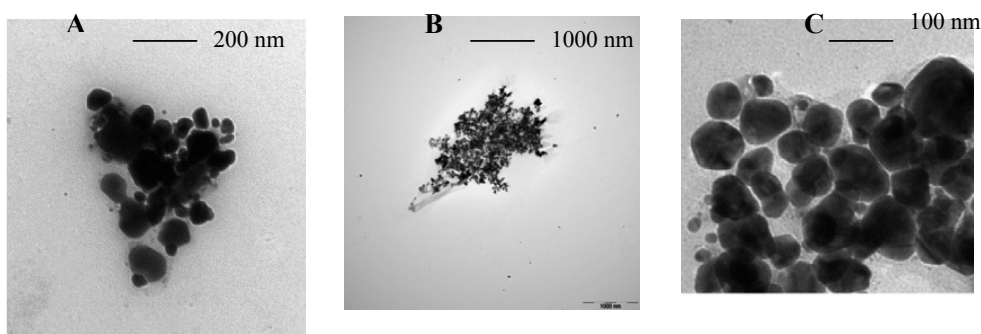


Fig. 3: TEM microphotographs of the prepared silver colloid particles in the presence of the bromide (A) and iodide (B, C) ions.

Conclusion

The performed experiments have studied mainly the influence of halide ions on the preparation of the silver nanoparticles obtained in the reduction process of the $[\text{Ag}(\text{NH}_3)_2]^+$ complex cation by glucose. This study has proved especially the principle influence on the size of the prepared silver nanoparticles. The size of the primarily formed silver halide is crucial in this process and therefore the tailored preparation of the silver nanoparticles could be hence performed through the tailored preparation of the silver halide. Unfortunately the experimental adjustment does not allow to prepare silver nanoparticles smaller than the particles obtained in the original process (approx. from 50 to 60 nm).¹³ Therefore this kind of improvement, in the field of particle size modification, could be possible via different methods that would also influence sizes of the primarily formed silver halide particles.

Acknowledgments

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TETRACYANOPALLADNATES(II) AND TETRACYANOPLATINATES(II) OF COPPER(II) WITH TRIAMINES OR TETRAMINES AS CHELATING LIGANDS

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Abstract

Eight new complexes of composition $[\text{Cu}(\text{L})\text{Pd}(\text{CN})_4] \cdot x\text{H}_2\text{O}$ (L = bappz (1,4-bis(3-aminopropyl)piperazine), $x = 0$ (**1**); L = bapen (*N,N'*-bis(3-aminopropyl)-1,2-diaminoethane, $x = 1$ (**2**); L = dpt (dipropylenetriamine), $x = 0$ (**3**); L = ept (*N*-(2-aminoethyl)-1,3-diaminopropane), $x = 2$ (**4**)) and $[\text{Cu}(\text{L})\text{Pt}(\text{CN})_4]$ (L = bappz (**5**), bapen (**6**), dpt (**7**) or ept (**8**)) have been prepared by the reactions of $\text{K}_2[\text{M}(\text{CN})_4] \cdot 3\text{H}_2\text{O}$ (M = Pd, Pt) with complex $[\text{Cu}(\text{L})](\text{ClO}_4)_2$ (L = bappz or bapen) or $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ and appropriate triamine (dpt or ept) in water and have been characterized by IR spectroscopy and magnetic measurements. The temperature dependence of magnetic susceptibility (85 – 295 K) was measured for compound **2**, but exchange interaction between copper(II) atoms was not found.

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Keywords: *Tetracyanopalladate(II); tetracyanoplatinate(II); copper(II); magnetic properties; cyano-bridged complexes.*

Introduction

Consistently with the diversity of crystal structures and interesting properties, especially in the context of their magnetic behavior, cyano-bridged complexes unceasingly keep attracting much attention in coordination chemistry¹⁻⁵.

Cyano-bridged tetracyanometallates²⁻ (a tetracyanometallate anion is centered by a divalent d⁸ transition metal: Ni, Pd or Pt) are suitable model compounds for magnetic studies at low temperatures as the tetracyanometallate anion may bridges paramagnetic ions partially coordinated with amine ligands and thus to form molecular, 1D, 2D and 3D structures. Since copper(II) ion is normally four-, five- or six-coordinated, it was anticipated that the coupling of a copper(II) to the [M(CN)₄]²⁻ (M = Ni, Pd or Pt) ion might lead to the formation of a novel family of magnetic compounds. Recently, molecular⁵⁻¹², 1D^{4,12-18}, 2D¹⁹⁻²¹ and 3D²¹ structures of copper(II) tetracyanometallates (the central atom is Ni(II), Pd(II) or Pt(II)) have been described. The number of structural studies on tetracyanopalladates(II) or tetracyanoplatinates(II) of copper(II) is surprisingly low. Only four structural examples of these compounds have been reported: binuclear complex [Cu(NH₃)₄Pt(CN)₄]⁵, tetranuclear complex [{Cu(bpy)(H₂O)Pt(CN)₄}₂].2H₂O (bpy = 2,2'-bipyridine)¹⁰, one-dimensional complex [Cu(en)₂Pd(CN)₄] (en = ethylenediamine)⁴ and two-dimensional complex [Cu(bpy)Pt(CN)₄]²¹.

A variety of multidimensional structures have been obtained in which [M(CN)₄]²⁻ (M = Ni(II), Pd(II) or Pt(II)) forms a tetra-monodentate cross joint, by using all the N atoms^{12,18,19}, or a di-monodentate bridge, by using the N atoms of *trans*-^{4,11,15-17} or *cis*-^{7-10,16,21} CN groups, bounded to the copper(II) centers. Recently, some examples of T-type three-bonded coordination²⁰ and monodentate ligation⁵⁻⁷ of [M(CN)₄]²⁻ to the copper(II) atom have been reported.

Magnetochemical study showed the presence of a very weak antiferromagnetic interaction between the copper(II) atoms through diamagnetic $[M(CN)_4]^{2-}$ ion (super-exchange interaction parameter J is in the range from -0.08 cm^{-1} to -1.96 cm^{-1})^{4,11,12,16,22}.

The μ -cyano tetracyanopalladates(II) or tetracyanoplatinates(II) of copper(II) with monodentate and bidentate *N*-ligands were studied but no triamine or tetraamine ligand was used as a blocking ligand in these compounds. Therefore, we carried out the reaction of $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ and triamine ligand (dipropylenetriamine (dpt) or *N*-(2-aminoethyl)-1,3-diaminopropane (ept)) or $[\text{Cu}(\text{L})](\text{ClO}_4)_2$ (L = tetraamine ligand 1,4-bis(3-aminopropyl)piperazine (bappz) or *N,N'*-bis(3-aminopropyl)ethylenediamine (bapen)) and $\text{K}_2[\text{M}(\text{CN})_4] \cdot 3\text{H}_2\text{O}$ (M = Pd or Pt) in water. Eight new complexes of composition $[\text{Cu}(\text{L})\text{Pd}(\text{CN})_4] \cdot x\text{H}_2\text{O}$ (L = bappz, $x = 0$ (**1**); L = bapen, $x = 1$ (**2**); L = dpt, $x = 0$ (**3**); L = ept, $x = 2$ (**4**)) and $[\text{Cu}(\text{L})\text{Pt}(\text{CN})_4]$ {L = bappz (**5**), bapen (**6**), dpt (**7**) or ept (**8**)} were obtained.

Materials and methods

All chemicals (commercial products of reagent grade) were used without further purification. Starting materials $[\text{Cu}(\text{bappz})](\text{ClO}_4)_2$ and $[\text{Cu}(\text{bapen})](\text{ClO}_4)_2$ were prepared by reaction $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ with bappz or bapen in 1:1 molar ratio in the aqueous solution. Elemental analyses for carbon, hydrogen and nitrogen were carried out with an EA 1108 CHN analyser (Fisons Instruments). IR spectra ($4000 - 400 \text{ cm}^{-1}$) were recorded on a Specord M 80 instrument (Carl Zeiss, Jena) (complexes **1** and **5**) or on a FT-IR Spectrum One instrument (Perkin Elmer) (complexes **2-4** and **6-8**) using the nujol technique. The magnetic susceptibilities were measured at the room temperature (complexes **1**, **3-8**) and in the liquid nitrogen temperature range and room temperature (complex **2**) by Faraday method using device constructed in Palacký University with $\text{Co}[\text{Hg}(\text{NCS})_4]$ as a calibrant²⁴. The molar susceptibilities of all complexes were corrected for diamagnetism using Pascal's constants²⁵.

Syntheses of the complexes

[Cu(bappz)Pd(CN)₄] (1)

A solution of 0.27 g (0.58 mmol) of [Cu(bappz)]ClO₄)₂ in water (30 cm³) was added to a solution of 0.20 g (0.58 mmol) of K₂[Pd(CN)₄]·3H₂O in water (25 cm³). The blue solid appeared was filtered off, washed with water and dried on air. Yield: 0.16 g (58%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2124(s), 2132(sh), 2156(s) cm⁻¹; $\mu_{\text{eff}} = 1.86 \text{ BM} / 294 \text{ K}$. Anal. calcd. for C₁₄H₂₄CuN₈Pd: C 35.45, H 5.10, N 23.62; found: C 35.13, H 4.24, N 23.06 (%).

[Cu(bapen)Pd(CN)₄]·H₂O (2)

The compound was prepared analogously as **1** from 0.25 g (0.57 mmol) of [Cu(bapen)](ClO₄)₂ and 0.20 g (0.58 mmol) of K₂[Pd(CN)₄]·3H₂O as blue solid. Yield: 0.08 g (31%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2100(sh), 2126(s) cm⁻¹; $\mu_{\text{eff}} = 1.86 \text{ BM} / 295 \text{ K} - 1.82 \text{ BM} / 85 \text{ K}$. Anal. calcd. for C₁₂H₂₂CuN₈Pd·H₂O: C 30.90, H 5.19, N 24.03; found: C 31.27, H 5.62, N 24.26 (%).

[Cu(dpt)Pd(CN)₄] (3)

A solution of 0.22 g (0.59 mmol) of Cu(ClO₄)₂·6H₂O and 0.08 cm³ (0.57 mmol) of dipropylenetriamine in water (30 cm³) was added to a solution of 0.20 g (0.58 mmol) of K₂[Pd(CN)₄]·3H₂O in water (30 cm³). The blue precipitate was filtered off, washed with water and dried on air. Yield: 0.12 g (52%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2142(s), 2160(sh), 2184(s) cm⁻¹; $\mu_{\text{eff}} = 1.87 \text{ BM} / 297 \text{ K}$. Anal. calcd. for C₁₀H₁₇CuN₇Pd: C 29.64, H 4.23, N 24.19; found: C 29.93, H 4.90, N 24.17 (%).

[Cu(ept)Pd(CN)₄]·2H₂O (4)

This compound was obtained similarly as **3** from 0.22 g (0.59 mmol) of Cu(ClO₄)₂·6H₂O, 0.07 ml (0.56 mmol) of ept and 0.20 g (0.58 mmol) of K₂[Pd(CN)₄]·3H₂O as blue solid. Yield: 0.14 g (58%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2127(sh),

2141(s), 2182(s) cm^{-1} ; $\mu_{\text{eff}} = 1.86 \text{ BM} / 295 \text{ K}$. Anal. calcd. for $\text{C}_9\text{H}_{15}\text{CuN}_7\text{Pd}\cdot 2\text{H}_2\text{O}$: C 25.30, H 4.48, N 22.95; found: C 25.84, H 4.57, N 23.32 (%).

[Cu(bappz)Pt(CN)₄] (5)

This compound was synthesized analogously as **1** from 0.26 g (0.60 mmol) of [Cu(bappz)](ClO₄)₂ and 0.24 g (0.56 mmol) of K₂[Pt(CN)₄] \cdot 3H₂O as blue solid. Yield: 0.14 g (44%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2120(s), 2128(sh), 2152(s) cm^{-1} ; $\mu_{\text{eff}} = 1.88 \text{ BM} / 294 \text{ K}$. Anal. calcd. for $\text{C}_{14}\text{H}_{24}\text{CuN}_8\text{Pt}$: C 29.87, H 4.30, N 19.90; found: C 29.48, H 3.52, N 19.46 (%).

[Cu(bapen)Pt(CN)₄] (6)

This compound was prepared analogously as **1** from 0.26 g (0.59 mmol) of [Cu(bapen)](ClO₄)₂ and 0.26 g (0.60 mmol) of K₂[Pt(CN)₄] \cdot 3H₂O as blue solid. Yield: 0.18 g (31%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2128(s), 2166(sh) cm^{-1} ; $\mu_{\text{eff}} = 1.83 \text{ BM} / 294 \text{ K}$. Anal. calcd. for $\text{C}_{12}\text{H}_{22}\text{CuN}_8\text{Pt}$: C 26.84, H 4.13, N 20.87; found: C 26.76, H 4.62, N 20.93 (%).

[Cu(dpt)Pt(CN)₄] (7)

This compound was prepared as blue precipitate analogously as **3** from 0.19 g (0.51 mmol) of Cu(ClO₄)₂ \cdot 6H₂O, 0.07 ml (0.50 mmol) of dpt and 0.22 g (0.51 mmol) of K₂[Pt(CN)₄] \cdot 3H₂O. Yield: 0.20 g (81%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2139(s), 2162(sh), 2187(sh) cm^{-1} ; $\mu_{\text{eff}} = 1.86 \text{ BM} / 295 \text{ K}$. Anal. calcd. for $\text{C}_{10}\text{H}_{17}\text{CuN}_7\text{Pt}$: C 24.32, H 3.47, N 19.85; found: C 24.49, H 3.39, N 19.75 (%).

[Cu(ept)Pt(CN)₄] (8)

This compound was obtained as blue solid similarly as **3** from 0.22 g (0.59 mmol) of Cu(ClO₄)₂ \cdot 6H₂O, 0.08 ml (0.63 mmol) of ept and 0.26 g (0.60 mmol) of

$\text{K}_2[\text{Pt}(\text{CN})_4]\cdot 3\text{H}_2\text{O}$. Yield: 0.26 g (92%). IR (nujol): $\nu(\text{C}\equiv\text{N})$ 2127(s), 2138(s), 2179(s) cm^{-1} ; $\mu_{\text{eff}} = 1.82 \text{ BM} / 294 \text{ K}$. Anal. calcd. for $\text{C}_9\text{H}_{15}\text{CuN}_7\text{Pt}$: C 22.53, H 3.15, N 20.43; found: C 22.35, H 3.61, N 20.28 (%).

Results and discussion

The new coordination compounds have been prepared by precipitation $[\text{CuL}]^{2+}$ (L = bappz, bapen, dpt or ept) and $[\text{Pd}(\text{CN})_4]^{2-}$ or $[\text{Pt}(\text{CN})_4]^{2-}$ in water and characterized by elemental analysis, IR spectroscopy and magnetic susceptibility measurements.

In the infrared spectra, for $\nu(\text{C}\equiv\text{N})$ characteristic vibrations were assigned. The presence of cyano-bridge is shown by the splitting of the $\nu(\text{CN})$ stretching band which appears at about 2000 - 2200 cm^{-1} for cyano-complexes²⁶. According to the literature data, the formation of the cyano-bridge shifts $\nu(\text{CN})$ towards higher frequencies²⁷ { $\nu(\text{CN})$ is at 2122 cm^{-1} for free $[\text{Pt}(\text{CN})_4]^{2-}$ }¹⁰. In the present complexes the strong bands in 2152 - 2184 cm^{-1} range may be probably attributed to the $\nu(\text{CN})$ of the bridging cyanides and the remaining ones (2100 - 2141 cm^{-1}) are probably caused by the terminal cyanides.

Due to the diamagnetism of $[\text{Pd}(\text{CN})_4]^{2-}$ and $[\text{Pt}(\text{CN})_4]^{2-}$ anions, the paramagnetism of the prepared complexes is caused by the copper(II) ($S = 1/2$). The observed values of magnetic moments at room temperature (1.82 – 1.88 BM) are in accordance with the literature data for magnetically diluted compounds of Cu(II) (1.9 - 2.2 BM)²⁸. The temperature dependence of the magnetic susceptibility of complex $[\text{Cu}(\text{bapen})\text{Pd}(\text{CN})_4]\cdot\text{H}_2\text{O}$ (**2**) was measured in the temperature range 85 – 295 K, but no exchange interaction was found (see Figure 1). The temperature dependence of the magnetic susceptibility of this complex obeys the Curie-Weiss law, according to which the calculated values of the Weiss and Curie constants were not significant [$C = 0.38 \text{ cm}^3 \text{ K mol}^{-1}$, $\theta = 5.2 \text{ K}$ and $N\alpha = 1.4 \times 10^{-4} \text{ cm}^3 \text{ mol}^{-1}$]. Some interactions between

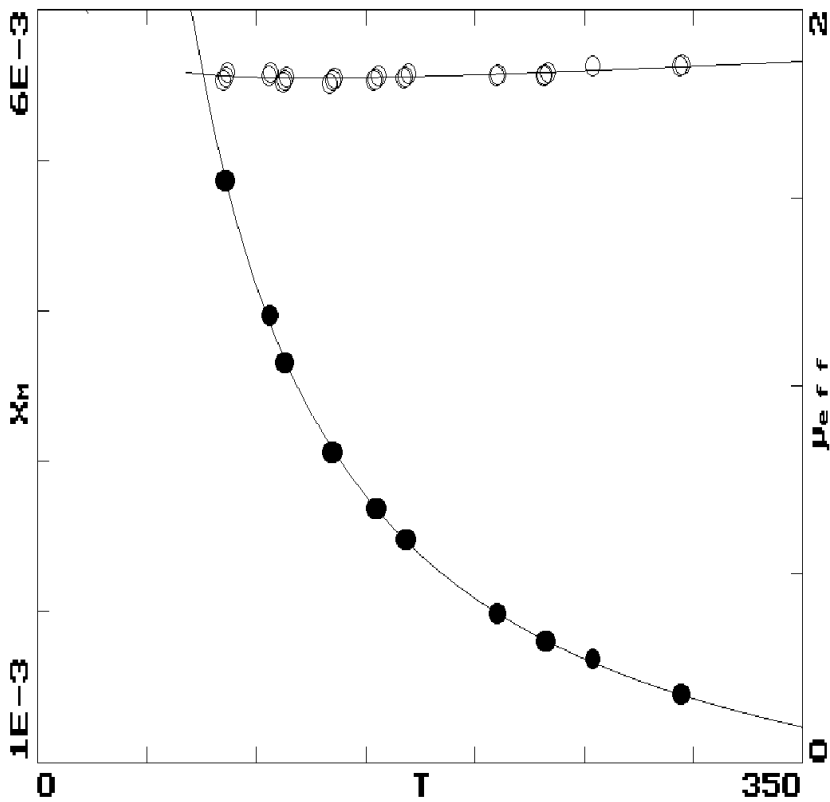


Fig. 1. Experimental magnetic data of $[\text{Cu}(\text{bapen})\text{Pd}(\text{CN})_4]\cdot\text{H}_2\text{O}$ (**2**) plotted as a molar magnetic susceptibility ($\text{cm}^3 \text{mol}^{-1}$) (\bullet) and μ_{eff} (BM) (\circ) vs. temperature (K). Solid lines represent the best least – squares fit of the experimental data to the Curie-Weiss law.

copper(II) atoms (even if, very weak) are possible, but the measurement at the liquid helium temperature would be necessary to prove this possible interaction.

Our attempts to prepare single-crystals for X-ray analysis unfortunately failed. The new compounds of the $[\text{Cu}(\text{tetramine})\text{M}(\text{CN})_4]$ type (**1**, **2**, **5** and **6**; M = Pd or Pt) exhibit probably a structure with tetra-coordinated M(II) in the square-planar arrangement (chromophore MN_4) and five- or six-coordinated Cu(II) with chromophores CuN_5 or CuN_6 . All newly prepared complexes of the $[\text{Cu}(\text{triamine})\text{M}(\text{CN})_4]$ type (**3**, **4**, **7** and **8**; M = Pd or Pt) exhibit probably structure that consists of alternating $\{\text{Cu}(\text{triamine})\}^{2+}$ and $[\text{M}(\text{CN})_4]^{2-}$ moieties linked by two cyanide ligands of the $[\text{Ni}(\text{CN})_4]^{2-}$ di-anion, giving rise to an one-dimensional chain structure $[\mu\text{-(NC)-M}(\text{CN})_2\text{-}\mu\text{-(CN)-Cu}(\text{triamine})]_n$, as was found for the similar $[\text{Cu}(\text{dpt})\text{Ni}(\text{CN})_4]$ complex¹⁶.

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**PYRIMIDINE-BASED 13- AND 14-MEMBERED
PENTAAZA MACROCYCLIC LIGANDS AND THEIR
FIRST ROW TRANSITION METAL COMPLEXES:
SYNTHESIS, CHARACTERIZATION AND
ANTIMICROBIAL STUDIES**

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Abstract

Two 13- and 14-membered pentaazamacrocycles, namely, 1,4,7,9,12-pentaaza-10,11-dioxo-8,9,12,13-bis-(1',3'-dioxo-2'-hydropyrimidine)-trideca-7,13-diene, (L^1) and 1,4,7,9,12-pentaaza-10,12-dioxo-8,9,13,14-bis-(1',3'-dioxo-2'-hydropyrimidine)tetradeca-7,14-diene, (L^2) have been synthesized. Their complexes with Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) have also been prepared. *Author for correspondence.

The macrocyclic ligands and their complexes have been characterized by elemental analysis, IR, UV-visible spectroscopy, magnetic moment, ¹H NMR, EPR, and molar conductance measurements. On the basis of electronic spectra and magnetic moment measurements, the Cr(III) and Fe(III) complexes are octahedral, while the divalent metal complexes are tetrahedral except Ni(II) and Cu(II) complexes which have square planar geometry. All of the metal complexes are paramagnetic except for Ni(II) and Zn(II) complexes that show diamagnetic behavior. All the ligands and their complexes have been screened against gram (+) bacteria, *Staphylococcus aureus* and gram (-) *Escherichia coli* and they inhibit bacteria growth.

Keywords: *Pentaazamacrocycles, bivalent and trivalent metal complexes, magnetic properties, antibacterial studies*

Introduction

The design of new macrocyclic ligands has driven much attention and interest¹. The macrocyclic ligands exhibit interesting coordination properties and often remarkable metal ion binding stabilities. If large cavity size macrocycle is formed, containing nitrogen, oxygen and sulfur donor atoms, it can encapsulate two or more metal ions selectively². A variety of macrocyclic ligands have been prepared and evaluated as suitable chelates to bind specific radionuclides^{3,4}. The use of the macrocyclic complexes in chemotherapy has grown impressively in recent years⁵⁻⁷, as the result of an advanced understanding of biological structure and function⁸. The chemistry of macrocyclic ligands is rich and they have proved to be excellent compounds due to their technological applications as a catalyst⁹, as building blocks for assembling supramolecular architectures¹⁰, as immunosuppressive drugs and anti-inflammatory drugs¹¹. The gadolinium(III) complexes of macrocyclic ligand have been used as magnetic resonance imaging (MRI) contrast agents¹². The macrocyclic complexes are also significant due to their use as models in naturally occurring system, as well as they have more biological importance¹³. The presence of pyrimidine group in the macrocyclic

framework offers the opportunity to obtain highly stable metal complexes. Due to the diverse applications of the pyrimidine derivatives and macrocycles in biological system, we have synthesized two new pyrimidine-based macrocycles 1,4,7,9,12-pentaaza-10,11-dioxo-8,9,12,13-bis-(1',3'-dioxo-2'-hydro-pyrimidine)-trideca-7,13-diene, (L^1) from barbituric acid, diethylenetriamine, diethyl oxalate and 1,4,7,9,12-pentaaza-10,12-dioxo-8,9,13,14-bis-(1',3'-dioxo-2'-hydro-pyrimidine)-tetradeca-7,14-diene, (L^2) from barbituric acid, diethylenetriamine, diethyl malonate. Their complexes with Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) ions have also been synthesized and characterized. The antibacterial activities of the ligands and their complexes have also been tested.

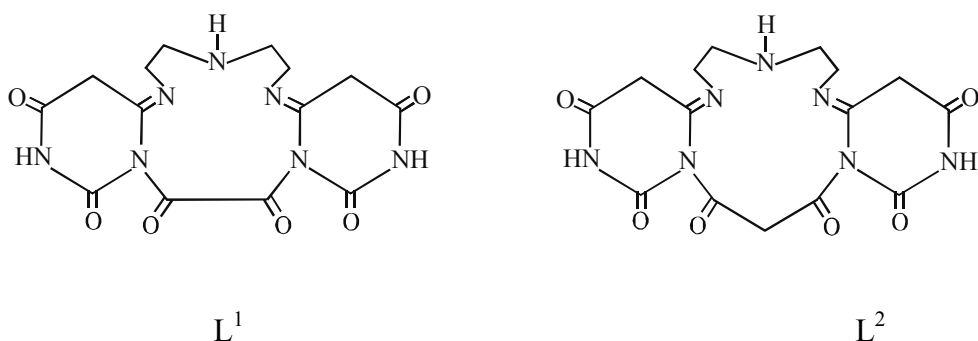


Figure1. Suggested structures of the ligands (L^1 and L^2)

Materials and methods

Materials

Barbituric acid (E. Merck), diethylenetriamine, diethyl oxalate, diethyl malonate (BDH), transition metal(II) and metal(III) chloride (s.d. fine chem. Ltd.) were used as received.

Preparation of Ligands (L^1 and L^2)

1,4,7,9,12-pentaaza-10,11-dioxo-8,9,12,13-bis-(1',3'-dioxo-2'-hydropyrimidine)-trideca-7,13-diene, (L^1)

The barbituric acid (40 mmol, 5.12 g) in 150 cm³ ethanol is taken in three necked round bottom flask and in this refluxed and stirred solution 20 mmol of diethyl oxalate (2.76 cm³) and 20 mmol of diethylenetriamine (2.16 cm³) are added very slowly for 1 h. The resulting mixture was refluxed for 4-5 h and then cooled to room temperature and kept in refrigerator for two days. A light orange precipitate formed was collected by filtration, washed with hexane and dry diethyl ether and dried in vacuum desiccator. Yield: 63%.

1,4,7,9,12-pentaaza-10,12-dioxo-8,9,13,14-bis-(1',3'-dioxo-2'-hydropyrimidine)-tetradeca-7,14-diene, (L^2)

To a refluxed and stirred solution 40 mmol of barbituric acid (5.12 g) in 150 cm³ of ethanol were added 20 mmol of diethyl malonate (3.05 cm³) and 20 mmol of diethylenetriamine (2.16 cm³) drop-wise for 1 h. The resulting mixture was refluxed with stirring for 5 h and cooled to room temperature. It was kept in refrigerator for two days. An off white product formed was collected by filtration, washed with hexane and dry ethanol and dried in vacuum desiccator. Yield: 55%.

Synthesis of complexes with ligand (L^1)

To a stirred solution 10 mmol of L^1 (3.8 g) in ethanol (50 cm³) and conc. HCl (2 cm³) was added slowly a solution 10 mmol of chromium(III) chloride (1.6 g). The resulting mixture was refluxed with constant stirring for 3 h and then stirred for 6 h at room temperature; the light green precipitate was collected by filtration, washed with acetone, hexane and dry diethyl ether and dried in vacuum desiccator. Yield: 55%.

Iron(III) complex was prepared by a similar procedure. The light brown compound was collected by filtration, washed with acetone, hexane and dry diethyl ether and dried in vacuum desiccator. Yield: 60%.

The refluxed and well stirred solution 10 mmol of L^1 (3.8 g) in ethanol(50 cm³) and conc. HCl (2 cm³) and solution 10 mmol of nickel(II) chloride (2.4 g) in 25 cm³

ethanol was added very slowly for 1 h. The reaction mixture was refluxed for 5 h. After being stirred for 7 h at room temperature the bluish green precipitate that formed, was filtered, washed with acetone, hexane and dry diethyl ether and dried in vacuum desiccator. Yield: 48%.

A similar procedure was employed for the synthesis of Mn(II), Co(II), Cu(II), Zn(II) complexes. The precipitates were filtered, washed with hexane and dry diethylether and dried in vacuum desiccator. Yields: 46-56%.

Synthesis of the complexes with ligand (L²)

A stirred solution 10 mmol of Cr(III) chloride (1.6 g) was added slowly in the refluxed and stirred solution 10 mmol of the ligand L² (3.9 g) in ethanol (40 cm³) and conc. HCl (2 cm³) for 2 h. The resulting solution was refluxed with constant stirring for 5-6 h. The light green product was filtered, washed with hexane and dry diethyl ether and dried in vacuum desiccator. Yield: 50%.

For the preparation of Mn(II), Co(II), Ni(II) and Zn(II) complexes with ligand L² similar above procedure was carried out. The precipitates were filtered, washed with acetone, hexane and dry diethyl ether and dried in vacuum desiccator. Yields: 48-60%.

Fe(III) complex was prepared by the same method. The light brown product was obtained by filtration, washed with hexane and dry Et₂O and dried in vacuum desiccator. Yield: 63%.

The copper(II) complex with ligand L² was synthesized by using a stirred solution 10 mmol of Cu(II) chloride (1.7 g) in ethanol (25 cm³) was added drop-wise to the refluxed solution 10 mmol of L² (3.9 g) in ethanol (50 cm³) and conc. HCl (2 cm³). The resulting solution was refluxed with constant stirring 7-8 h. The sky blue product thus obtained was filtered, washed with acetone, hexane and dry diethyl ether and dried in vacuum desiccator. Yield: 57%.

Inhibitory activity of microorganism

Antibacterial screening of the ligands and their complexes in dimethyl sulfoxide (DMSO) was evaluated *in vitro* by the agar diffusion method¹⁴. The sample solution of ligands and their metal complexes and were prepared by dissolving 50 µg and 100 µg of each compound in 1 cm³ of DMSO. Filter paper (Whatman No. 4) discs (6 mm diameter) were dipped in the solution of test compound of 50-100 µg/cm³ concentration in DMSO and placed over seeded plates after drying to remove the solvent and incubated at 37 °C for 24 h. The bacteria were grown in nutrient broth at 37 °C for 24 h. The compounds diffuse on nutrient agar plates and inhibit the growth of bacteria in the zone around the disc. At the end of the incubation period the inhibitory zones around the wells were measured in mm. DMSO was used as a control. Gentamicin was also screened under similar condition for comparison as a reference standard. So the results indicate that the compounds inhibit the growth of bacteria to a greater extent as concentration of the compounds is increased.

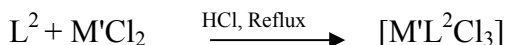
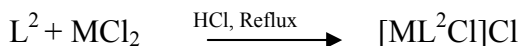
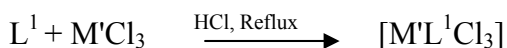
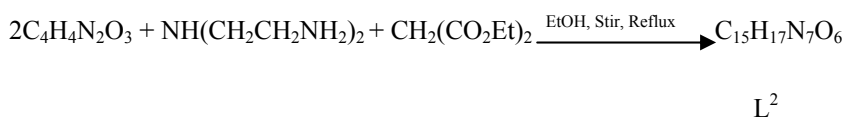
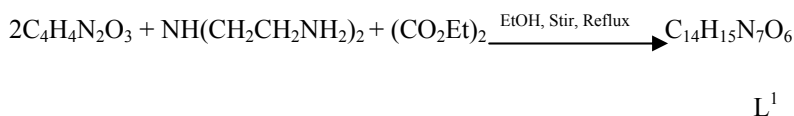
Physical measurements

Elemental analyses (C,H,N) were performed with a Carlo Erba 1106 Thomas and Coleman analyzer. The metals were determined by complexometric titration¹⁵ and chlorine was determined gravimetrically¹⁶. IR spectra (4000-200 cm⁻¹) for KBr disks pellets were recorded on a model 621 Perkin-Elmer spectrometer. The molar conductivity measurements were carried out on a CM-82T Elico conductivity bridge in DMSO. The UV-visible spectra were recorded in DMSO on a Perkin Elmer Lambda EZ201 spectrometer with quartz cuvettes and magnetic susceptibility measurement was done with an Allied Research model 155 vibration sample magnetometer at room temperature. The ¹H NMR spectrum of diamagnetic complexes was run in DMSO-d₆ on a JOEL-FX-100 spectrometer. The EPR spectra of the Cu(II) complexes of the ligands (L¹ and L²) were recorded on a Bruker Scientific X-band ESP-300 spectrometer.

Results and discussion

The new macrocycles L^1 and L^2 were synthesized by condensation reaction of barbituric acid, diethylenetriamine, diethyl oxalate (2:1:1) and barbituric acid, diethylenetriamine, diethyl malonate (2:1:1), respectively in ethanol.

The reactions are represented as



where $M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II)$, $M' = Cr(III), Fe(III)$

The colour, melting point, yield percentage, molar conductance and analytical data of the ligands and their complexes are given in Table 1. Elemental analysis correspond to the composition $[ML^1Cl]Cl$, $[ML^2Cl]Cl$, where $M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II)$, and $[M'L^1Cl_3]$, $[M'L^2Cl_3]$, where $M' = Cr(III), Fe(III)$. The complexes were found to be air stable and soluble in DMSO and CH_3CN . The molar conductance of 10^{-3} M solution of the complexes in DMSO ($52-72 \text{ S cm}^2 \text{ mole}^{-1}$) reveal the 1:1 electrolytic behavior of divalent metal complexes, while for trivalent metal complexes

the values fall in range (15-31 S cm² mole⁻¹) suggesting the non-electrolytic behavior of these complexes¹⁷.

IR spectra

The relevant infrared spectral bands and their assignments are given in Table 2. As a consequence of the reaction of barbituric acid, diethylenetriamine and diethyl oxalate, barbituric acid, diethylenetriamine and diethyl malonate, there is the formation of ligands L¹ and L². In the macrocyclic ligands (L¹ and L²), out of two N-H bands of barbituric acid, one weak N-H band disappears while the other band appears at 3230 cm⁻¹. The free ligands (L¹ and L²) exhibit $\nu(\text{C}=\text{O})$ of barbituric acid (1625 cm⁻¹)¹⁸, $\nu\text{C}=\text{O}$ (oxalate group) at 1618 cm⁻¹ and $\nu\text{C}=\text{O}$ (malonate group) at 1622 cm⁻¹. The strong band at 1665 cm⁻¹ is assigned to $\nu(\text{C}=\text{N})$ vibration¹⁹. The IR spectrum shows a band at 3275 cm⁻¹ associated with the $\nu(\text{N-H})$ vibration of secondary amine. The absorption bands occurring at 1435 cm⁻¹ indicate the coupling band of $\nu(\text{C-N})$ and $\delta(\text{N-H})$ vibration. The ring stretching vibration persists at same wave number region (1318 m, 1400 m, 1455 m). In the transition metal complexes of ligands $\nu(\text{C}=\text{N})$ and $\nu(\text{N-H})$ secondary amine) are found to be shifted to lower frequency (25-55 cm⁻¹) while the other bands persist at the same wave number region suggesting the coordination of metal ion via nitrogen atom. In the complexes some new bands also appear at the lower frequency region. All the metal ions exhibit strong intensity M-N bands in 275-410 cm⁻¹ range, while the bands at 255-320 cm⁻¹ are assigned as $\nu(\text{M-Cl})$ stretches.

Electronic spectra and magnetic moment

The observed electronic spectral bands of macrocyclic complexes have been recorded in DMSO and the magnetic moment values are given in Table 3.

The Cr(III) complexes of ligands L¹ and L² show three bands at 31,250 cm⁻¹, 25,320 cm⁻¹, 18,870 cm⁻¹, and 31,680 cm⁻¹, 25,890 cm⁻¹, 19,115 cm⁻¹, respectively, which are assigned to ${}^4\text{T}_{1\text{g}}(\text{P}) \leftarrow {}^4\text{A}_{2\text{g}}(\text{F})$, ${}^4\text{T}_{1\text{g}}(\text{F}) \leftarrow {}^4\text{A}_{2\text{g}}(\text{F})$ and ${}^4\text{T}_{2\text{g}}(\text{P}) \leftarrow {}^4\text{A}_{2\text{g}}(\text{F})$ transitions, respectively. The magnetic moment values (3.52 B.M. and 3.22 B.M.) are

well within the range for three unpaired electrons. The electronic spectral bands and magnetic moment studies suggest an octahedral geometry around the chromium(III) ion.

The majority of Mn(II) complexes are high-spin and high-spin d^5 configuration gives an essentially spin only magnetic moment of 5.8 B.M., which is slightly lower than that of calculated for five unpaired electrons. In the manganese(II) complexes of ligands (L^1 and L^2), two bands have been observed at 22,730 cm^{-1} , 19,800 cm^{-1} and 23,100 cm^{-1} , 19,605 cm^{-1} , respectively, assigned to ${}^4A_1(G) \leftarrow {}^6A_1$ and ${}^4A_1(G) \leftarrow {}^6A_1$ transitions, which are characteristic of tetrahedral geometry around Mn(II) ion²⁰.

$[\text{FeL}^1\text{Cl}_3]$ and $[\text{FeL}^2\text{Cl}_3]$ complexes show three bands at 27,770 cm^{-1} , 26,315 cm^{-1} , 17,850 cm^{-1} and 28,570 cm^{-1} , 26,455 cm^{-1} , 18,180 cm^{-1} respectively, which are assigned to ${}^4E_g(D) \leftarrow {}^6A_1$, ${}^4T_{2g}(D) \leftarrow {}^6A_{1g}$ and ${}^4T_{1g}(G) \leftarrow {}^6A_{1g}$ transitions, respectively. The μ_{eff} value is slightly different from those calculated due to coupling interaction. The observed magnetic moment values (5.72 B.M. for L^1 and 5.65 B.M. for L^2) and the spectral assignment suggest an octahedral arrangement of ligand around iron(III) ion²¹.

For cobalt(II) complexes of L^1 and L^2 the μ_{eff} value we have observed 3.42 B.M. and 3.50 B.M. respectively, which indicates the tetrahedral geometry around cobalt(II) ion. The $[\text{CoL}^1\text{Cl}]\text{Cl}$ and $[\text{CoL}^2\text{Cl}]\text{Cl}$ complexes exhibit two bands at 23,800 cm^{-1} , 11,760 cm^{-1} and 24,100 cm^{-1} , 11,900 cm^{-1} . The first band is due to the charge transfer while the other is assigned to ${}^4T_1(F) \leftarrow {}^4A_2(F)$ transition, in a tetrahedral structure for the complexes²².

The magnetic moment of Cu(II) complexes of ligands (1.65 B.M. for L^1 and 1.80 B.M. for L^2) falls in the normal range for a copper(II) species with $s = \frac{1}{2}$. The nickel(II) complexes and copper(II) complexes in square planar field have two spin-allowed bands (Table 3), assigned to ${}^1B_{1g} \leftarrow {}^1A_{1g}$, ${}^1A_{2g} \leftarrow {}^1A_{1g}$ and ${}^2A_{1g} \leftarrow {}^2B_{1g}$, ${}^2E_g \leftarrow {}^2B_{1g}$, transitions, respectively²².

¹HNMR spectra

The ¹HNMR spectra of ligands L¹ and L² in DMSO-d₆ exhibit two triplets at δ(2.32-2.82 ppm) and δ(2.90-3.55 ppm) of two types of -CH₂- protons of secondary amine²³ and one singlet of pyrimidine group at δ(3.4-3.6 ppm). The broad band of N-H proton appears at δ(7.5-9.2 ppm) of pyrimidine and secondary amine at δ(4.55-4.66 ppm). However, in the ligand L² an additional singlet of CH₂ at δ(3.6 ppm). The above values broadly confirmed the structure of ligands L¹ and L². The other characteristic peaks are represented in Table 4.

The characteristic peaks for Ni(II) complexes of ligands (L¹ and L²) for the -CH₂- protons during complex formation shifted towards low field that is high δ value confirming the coordination with these groups. This is attributed due to the decrease in electron density after complex formation.

EPR spectra

The EPR spectra of the copper(II) complexes of macrocycles L¹ and L² have been recorded at room temperature and they show single broad signals. The g_{||} and g_⊥ have been observed in the 2.22-2.37 and 2.048-2.086 regions respectively. This is therefore, for a Cu(II) center with an unpaired electron in the d_{x²-y²} orbital without super hyperfine structure. In the copper(II) complexes the higher values of g_{||} than g_⊥ show a square planar geometry around Cu(II) ion.

Bacterial screening

Results of antibacterial screening are shown in Table 5, a comparative study of the ligands and their complexes indicate that the metal complexes exhibit higher antibacterial activity than that of the free ligands and the control. These synthesized macrocyclic metal complexes inhibit the growth of bacteria to a greater extent and

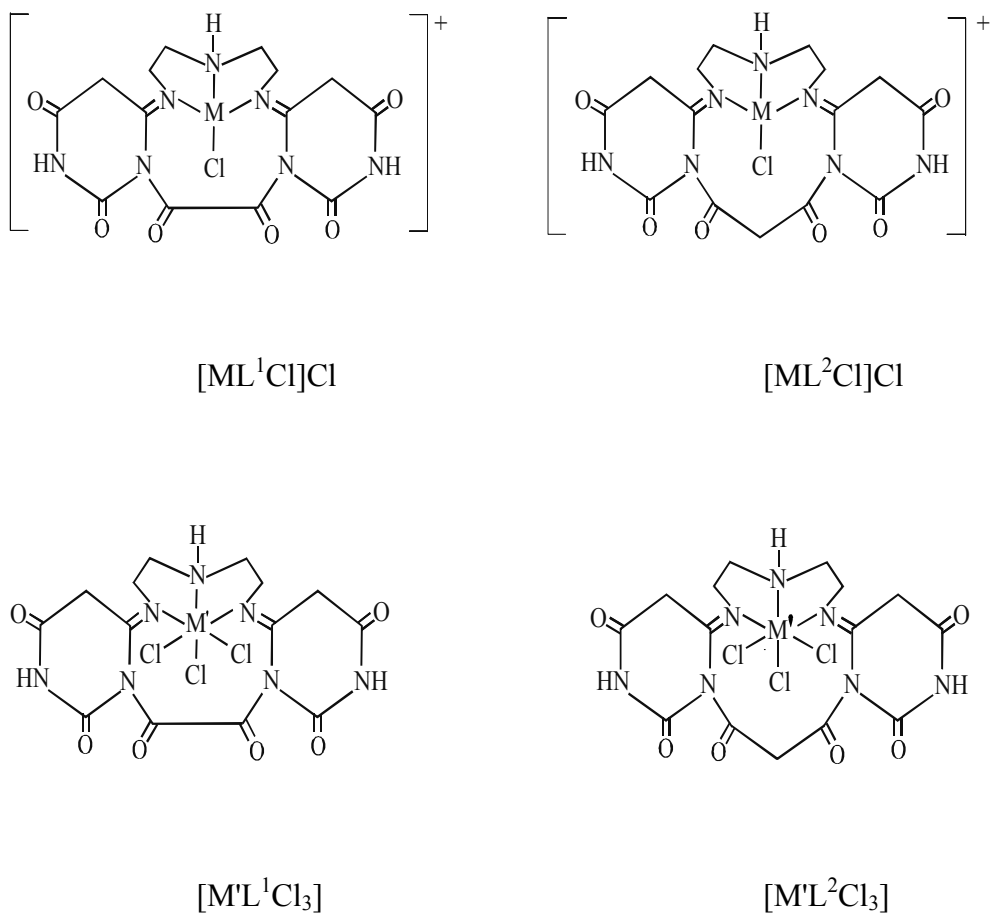


Figure 2. Suggested structures of the metal complexes of ligands L^1 and L^2 .

Key: $M = Mn(II), Co(II), Ni(II), Cu(II), Zn(II)$ and $M' = Cr(III), Fe(III)$

enhance their biological activity as antimicrobial agents. The rate of antibacterial activities of the ligands and their metal complexes on microorganisms depends on the concentration of the compounds used. The increase in the antibacterial activity of the

Table 1. Analytical data, melting points, colours, percent yield and molar conductance of the ligands (L¹, L²) and complexes

Compound (Formula weight)	Colour	M.p. (°C)	Yield (%)	Λ_M (S cm ² mole ⁻¹)	Analysis, Found (Calcd.) %				
					C	H	N	Cl	M
C ₁₄ H ₁₅ N ₇ O ₆ , (L ¹) (377.14)	Light orange	170	63	-	44.62 (44.58)	3.95 (4.00)	25.90 (25.98)	-	-
[CrL ¹ Cl ₃] [C ₁₄ H ₁₅ N ₇ O ₆ CrCl ₃] (535.5)	Light green	>300 d	55	31	31.30 (31.37)	2.80 (2.82)	18.26 (18.3)	19.82 (19.86)	9.68 (9.70)
[MnL ¹ Cl]Cl [C ₁₄ H ₁₅ N ₇ O ₆ MnCl]Cl (503.0)	Grey	>300 d	52	60	33.4 (33.4)	2.96 (3.0)	19.42 (19.48)	14.02 (14.09)	10.90 (10.92)
[FeL ¹ Cl ₃] [C ₁₄ H ₁₅ N ₇ O ₆ FeCl ₃] (539.35)	Light brown	285 d	60	15	31.09 (31.15)	2.75 (2.80)	18.15 (18.16)	19.75 (19.71)	10.30 (10.35)
[CoL ¹ Cl]Cl [C ₁₄ H ₁₅ N ₇ O ₆ CoCl]Cl (506.93)	Blue	288 d	56	72	33.10 (33.14)	3.04 (3.0)	19.30 (19.33)	13.98 (13.98)	11.60 (11.62)
[NiL ¹ Cl]Cl [C ₁₄ H ₁₅ N ₇ O ₆ NiCl]Cl (506.47)	Bluish green	>300 d	48	52	33.07 (33.15)	2.92 (2.98)	19.32 (19.33)	13.95 (14.0)	11.60 (11.58)
[CuL ¹ Cl]Cl [C ₁₄ H ₁₅ N ₇ O ₆ CuCl]Cl (511.93)	Sky blue	260 d	54	67	32.75 (32.81)	2.98 (2.95)	19.18 (19.14)	13.80 (13.85)	12.40 (12.41)
[ZnL ¹ Cl]Cl [C ₁₄ H ₁₅ N ₇ O ₆ ZnCl]Cl (513.39)	Color less	292 d	46	70	32.74 (32.72)	2.90 (2.94)	18.96 (19.0)	13.75 (13.81)	12.70 (12.73)

Table 1. Contd.....

$C_{15}H_{17}N_7O_6$, (L ²) (391.15)	Off white	148	55	-	46.10 (46.02)	4.22 (4.38)	25.10 (25.05)	-	-
[CrL ² Cl ₃] [C ₁₅ H ₁₇ N ₇ O ₆ CrCl ₃] (549.65)	Light green	275 d	50	25	32.70 (32.75)	3.04 (3.11)	17.85 (17.82)	19.30 (19.35)	9.38 (9.45)
[MnL ² Cl]Cl [C ₁₅ H ₁₇ N ₇ O ₆ MnCl]Cl (517.0)	Light Pink	300 d	48	55	34.90 (34.81)	3.25 (3.31)	18.88 (18.95)	12.85 (12.9)	10.60 (10.62)
[FeL ² Cl ₃] [C ₁₅ H ₁₇ N ₇ O ₆ FeCl ₃] (553.36)	Light brown	>300 d	63	19	32.50 (32.53)	3.00 (3.09)	17.65 (17.70)	19.18 (19.22)	10.00 (10.09)
[CoL ² Cl]Cl [C ₁₅ H ₁₇ N ₇ O ₆ CoCl]Cl (521.0)	Dark blue	278 d	60	64	34.48 (34.55)	3.35 (3.28)	18.9 (18.8)	13.54 (13.60)	11.36 (11.31)
[NiL ² Cl]Cl [C ₁₅ H ₁₇ N ₇ O ₆ NiCl]Cl (520.7)	Bluish green	>300 d	55	58	34.50 (34.56)	3.22 (3.28)	18.76 (18.82)	13.55 (13.61)	11.35 (11.27)
[CuL ² Cl]Cl [C ₁₅ H ₁₇ N ₇ O ₆ CuCl]Cl (535.94)	Sky blue	252 d	57	60	33.47 (33.58)	3.14 (3.20)	18.20 (18.28)	13.20 (13.22)	11.92 (11.85)
[ZnL ² Cl]Cl [C ₁₅ H ₁₇ N ₇ O ₆ ZnCl]Cl (527.40)	Color less	268 d	52	63	34.10 (34.13)	3.19 (3.24)	18.60 (18.58)	13.50 (13.44)	12.34 (12.40)

Table 2. IR spectra of the ligands (L¹, L²) and complexes (cm⁻¹)

Compound	$\nu(\text{N-H})$ Pyrimidine	$\nu(\text{N-H})$ (secondary amine)	$\nu(\text{C=O})$	$\nu(\text{C=O})$ (oxalate group)	$\nu(\text{C=N})$	$\delta(\text{N-H})$	Ring stretching Mode	$\nu(\text{M-N})$	$\nu(\text{M-Cl})$
Ligand _s (L1)	3230 m	3275 m	1625 m	1618 m	1665 m	1435	1318, 1400, 1455	-	-
[CrL1Cl3]	3228 m	3250 m	1625 m	1620 m	1610 m	1440	1322, 1405, 1452, 1450, 1545	385 s	248 m
[MnL1Cl]Cl	3225 m	3238 m	1632 m	1625 m	1620 m	1438	1320, 1412, 1458, 1565, 1542	275 s	292 m
[FeL1Cl]3	3234 m	3247 m	1634 m	1620 m	1635 m	1436	1325, 1410, 1455, 1562, 1545	410 s	255 m
[CoL1Cl]Cl	3236 m	3240 m	1635 m	1622 m	1615 m	1442	1322, 1415, 1456, 1565, 1540	380 s	320 m
[NiL1Cl]Cl	3230 m	3235 m	1630 m	1618 m	1620 m	1445	1325, 1408, 1458, 1560, 1545	375 s	288 m
[CuL1Cl]Cl	3228 m	3245 m	1626 m	1620 m	1630 m	1434	1320, 1410, 1452, 1558, 1545	392 s	310 m

S=strong, m=medium

Table 3. Electronic Spectral Bands, Magnetic Moment Values and Ligand Field Parameters of the Macrocyclic Complexes

Compound	Magnetic moment (B.M.)	Electronic bands (cm ⁻¹)	Possible Assignment	10 Dq (cm ⁻¹)	B (cm ⁻¹)	β
[CrL ¹ Cl ₃]	3.52	31,250 25,320 18,870	⁴ T _{1g} (P) ← ⁴ A _{2g} (F) ⁴ T _{1g} (F) ← ⁴ A _{2g} (F) ⁴ T _{2g} (P) ← ⁴ A _{2g} (F)	12,810	866	0.89
[MnL ¹ Cl]Cl	5.50	22,730 19,800	⁴ A ₁ (G) ← ⁶ A ₁ ⁴ A ₁ (G) ← ⁶ A ₁	-	-	-
[FeL ¹ Cl ₃]	5.72	27,770 26,315 17,850	⁴ E _g (D) ← ⁶ A _{1g} ⁴ T _{2g} (D) ← ⁶ A _{1g} ⁴ T _{1g} (G) ← ⁶ A _{1g}	9,413	568	0.58
[CoL ¹ Cl]Cl	3.42	23,800 11,760	Charge Transfer ⁴ T ₁ (F) ← ⁴ A ₂ (F)	-	-	-
[NiL ¹ Cl]Cl	Diamagnetic	22,120 18,790	¹ B _{1g} ← ¹ A _{1g} ¹ A _{2g} ← ¹ A _{1g}	-	-	-
[CuL ¹ Cl]Cl	1.65	15,620 13,890	² A _{1g} ← ² B _{1g} ² E _g ← ² B _{1g}	-	-	-
[ZnL ¹ Cl]Cl	Diamagnetic	-	-	-	-	-

Table 3. Contd....

Compound	Magnetic moment (B.M.)	Electronic bands (cm ⁻¹)	Possible assignment	10 Dq (cm ⁻¹)	(B) (cm ⁻¹)	β
[CrL ² Cl ₃]	3.22	31,680 25,890 19,115	⁴ T _{1g} (P) ← ⁴ A _{2g} (F) ⁴ T _{1g} (F) ← ⁴ A _{2g} (F) ⁴ T _{2g} (P) ← ⁴ A _{2g} (F)	12,610	890	0.85
[MnL ² Cl]Cl	5.35	23,100 19,605	⁴ A ₁ (G) ← ⁶ A ₁ ⁴ A ₁ (G) ← ⁶ A ₁	-	-	-
[FeL ² Cl ₃]	5.65	28,570 26,455 18,180	⁴ E _g (D) ← ⁶ A _{1g} ⁴ T _{2g} (D) ← ⁶ A _{1g} ⁴ T _{1g} (G) ← ⁶ A _{1g}	8,780	567	0.55
[CoL ² Cl]Cl	3.50	24,100 11,900	Charge Transfer ⁴ T ₁ (F) ← ⁴ A ₂ (F)	-	-	-
[NiL ² Cl]Cl	Diamagnetic	21,740 19,230	¹ B _{1g} ← ¹ A _{1g} ¹ A _{2g} ← ¹ A _{1g}	-	-	-
[CuL ² Cl]Cl	1.80	15,380 13,700	² A _{1g} ← ² B _{1g} ² E _g ← ² B _{1g}	-	-	-
[ZnL ² Cl]Cl	Diamagnetic	-	-	-	-	-

Table 4. ^1H NMR spectra of the ligands and their complexes δ (ppm)

Compound	N-H Pyrimidine, (1H)	N-H (2 ^o amine), (1H)	-CH ₂ - (4H)	-CH ₂ - (4H), (4H)	-CH ₂ - (malonate group), (2H)
(L ¹)	7.5-9.2 b	4.55 b	3.6 s	(2.32-2.80) t, (2.90-3.50) t	-
(L ²)	7.8-9.5 b	4.66 b	3.4 s	(2.30-2.82) t, (2.85-3.55) t	3.6 s
[NiL ¹ Cl]Cl	7.3-8.8 b	4.88 b	3.0 s	(2.40-3.00) t, (3.15-3.68) t	-
[NiL ² Cl]Cl	6.9-9.2 b	4.68 b	2.9 s	(2.45-2.85) t, (3.00-3.65) t	3.8 s

Table 5. Antibacterial activity of the ligands and their complexes

Compound	<i>S. aureus</i>		<i>E. coli</i>	
	50 µg/cm ³	100 µg/cm ³	50 µg/cm ³	100 µg/cm ³
*Gentamycin	7	10	7	9
*Control	10	15	11	17
(L ¹)	13	17	15	18
(L ²)	11	14	13	15
[CrL ¹ Cl ₃]	22	27	20	25
MnL ¹ Cl]Cl	25	33	23	32
[FeL ¹ Cl ₃]	27	35	26	36
[CoL ¹ Cl]Cl	25	34	27	32
[NiL ¹ Cl]Cl	21	29	23	30
[CuL ¹ Cl]Cl	22	27	20	35
[ZnL ¹ Cl]Cl	29	36	27	31
[CrL ² Cl ₃]	23	29	21	27
[MnL ² Cl]Cl	26	32	24	34
[FeL ² Cl ₃]	22	31	21	33
[CoL ² Cl]Cl	27	35	29	37
[NiL ² Cl]Cl	24	33	25	32
[CuL ² Cl]Cl	31	37	28	35
[ZnL ² Cl]Cl	29	36	30	38

*Bactericides

metal complexes with increase in concentration is due to the effect of metal ion on the normal cell process.

The 10 Dq value also depends upon the ring size. M-N distance and the chelate effect are responsible for the variation of the void. On the basis of above studies the structures in Figure 2 have been proposed for the divalent and trivalent metal complexes. Unfortunately, our attempts to prepare crystals for X-ray analysis were unsuccessful.

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