## ACS NEW ORLEANS 2008

### CHED 1263 - Thiosemicarbazone and diimine complexes of transition metals: Synthesis and reactivity toward DNA

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The thiosemicarbazone of 9-anthraldehyde, (9-ATSC) and its group 12 metal complexes have been synthesized. The compounds have been characterized by IR, electronic and NMR spectrometries, molar conductivity, melting points and elemental analysis. In all the complexes, the 9-ATSC coordinates through the sulfur and the azomethinic nitrogen. The zinc (II) complex shows a 1:2 metal to ligand stoichiometry while the mercury(II) complex exhibit 1:1 metal-ligand composition. In addition, organometallic ruthenium type [($\eta^6$-*p*-cymene)RuCl(XY)] (XY = dipyrido[3,2,-d:2′,3′-f]quinoxaline (dpq), dipyrido[3,2,-a:2′,3′-c]phenazine-11-carboxylic acid (dppz-$CO_2H$) and 9-ATSC) were also synthesized.We will present the preliminary results of the biochemical reactivity (absorption and melting titrations) of most of these compounds with DNA. The results indicate that all of the complexes interact with DNA to some degree. It was expected that the complexes would bind DNA via intercalation but it was observed that none of the complexes exhibited strong evidence for this type of mechanism.

## ACS SALT LAKE CITY 2009

### CHED 585 - Mixed ligand diimine-thiosemicarbazone complexes of ruthenium(II): Synthesis, biophysical reactivity and cytotoxicity

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A series of novel mixed ligand ruthenium(II) containing diimines and thiosemicarbazones have been synthesized using microwave energy. The compounds have the general formula [Ru(N-N)$_2$(N-S)]($PF_6$)$_2$ where N-N = bipyridine or 1,10-phenanthroline and N-S = 9-anthraldehyde thiosemicarbazone and the 4-alkyl substituted (R = methyl, ethyl and phenyl) analogs. The compounds have been characterized spectroscopically (NMR, IR, UV-Vis and fluorescence) as well as by elemental analysis, magnetic susceptibility and cyclic voltammetry. The compounds quench the fluorescence of the complex between ethidium bromide and calf-thymus DNA with the Stern-Volmer quenching constants in the range 1.18 – 2.71 x $10^4$ $M^{-1}$. Results from viscometric experiments suggest that the interaction with calf thymus DNA is a possible combination of partial intercalation and groove binding. Thermal denaturation studies supported the proposal that the complexes interact with DNA in a mostly non-intercalative manner. Results from the cytotoxicity studies with various human cancer cell lines will be presented.

**CHED 633 - Synthesis, characterization and cytotoxicity of copper and ruthenium complexes of a series of thiosemicarbazones derived from piperonal.**

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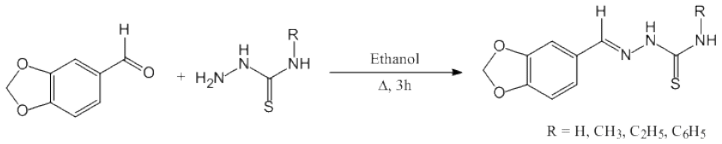
Novel piperonal thiosemicarbazones have been synthesized by the acid-catalyzed condensation of piperonal with thiosemicarbazide and the appropriate 4-alkyl substituted thiosemicarbazides in ethanol. The copper complexes of general formula $Cu(N\text{-}S)_2Cl_2$ (N-S = thiosemicarbazone) have been synthesized from the reaction with copper(II) chloride and have been characterized spectroscopically as well as by elemental analyses, conductivity measurements and cyclic voltammetry. Elemental analysis suggests that the piperonal 4-methyl-3-thiosemicarbazone complex is dimeric and is best formulated as $[Cu(N\text{-}S)Cl]_2$. Conductivity measurements show that the compounds are non-electrolytes in dimethyl sulfoxide solutions. The microwave synthesis of the ruthenium complexes $[Ru(phen)_2(N\text{-}S)](PF_6)_2$ (phen = 1,10-phenanthroline) and their characterization is also being reported. Results from the cytotoxicity studies with various human cancer cell lines will be presented.




**INOR 587 - The bioorganometallic chemistry of thiosemicarbazones.**

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Reaction of the dimers $[(\eta^6\text{-p-cymene})RuCl_2]_2$ and $[(\eta^6\text{-benzene})RuCl_2]_2$ with a series of thiosemicarbazones from 9-anthraldehyde and piperonal causes the cleavage of the chloride bridges to form complexes of the type $[(\eta^6\text{-arene})RuCl(N\text{-}S)]^+$ (N-S = thiosemicarbazone and the 4-alkyl substituted (alkyl = methyl, ethyl and phenyl) analogs). The compounds have been characterized by NMR, IR, UV-Vis and fluorescence spectroscopies as well as elemental analyses and cyclic voltammetry. The compounds utilizing 9-anthraldehyde 4-methyl-3-thiosemicarbazone and piperonal 4-phenyl-3-thiosemicarbazone have also been characterized by single crystal X-ray crystallography. Preliminary results from biophysical experiments suggest that compounds interact weakly with ds DNA. Antimicrobial susceptibility studies as executed by the disk diffusion method showed that the complexes have no appreciable antibacterial activity against common bacteria. Results from the cytotoxicity studies against various human tumor cell lines will also be presented.

## ACS SAN FRANCISCO 2010

### 225 - Microwave synthesis of mixed ligand diimine-thiosemicarbazone complexes of ruthenium(II): Reactivity with DNA and human serum albumin

***Floyd Beckford, Dr., Michael Shaloski, Jeffrey Thessing, Charles Morgan, . Department of Chemistry, Lyon College, Batesville, AR, United States***

A novel microwave-assisted synthetic method has been used to synthesize a series of mixed ligand ruthenium(II) compounds containing diimine as well as bidentate thiosemicarbazone ligands. The compounds contain the diimine 1,10-phenanthroline (phen) or 2,2-bipyridine (bpy) and the thiosemicarbazone is derived from piperonal. Based on elemental analyses and spectroscopic data, the compounds are best formulated as $[(phen)_2Ru(thiosemicarbazone)](PF_6)_2$ and $[(phen)_2Ru(thiosemicarbazone)](PF_6)_2$ where thiosemicarbazone = piperonal thiosemicarbazone, piperonal-N(4)-methylthiosemicarbazone, and piperonal-N(4)-ethylthiosemicarbazone. The complexes were partially characterized by elemental analysis, UV-vis and infra-red spectrometries and cyclic voltammetry. The interaction of the complexes with DNA and human serum albumin (HSA) was studied by UV-vis, infrared and fluorescence spectrometries. The complexes can cleave pBR322 plasmid DNA in the presence of long wavelength UV light.

### 768 - Synthesis and reactivity of ruthenium(II) compounds containing piperonal thiosemicarbazones

***Diedra Dourth, Floyd Beckford, Dr., PhD . Department of Chemistry Lyon College Batesville AR United States***

A series of ruthenium(II)-dmso complexes containing piperonal thiosemicarbazones have been synthesized. The complexes are best formulated as $Ru(dmso)_2(Cl)_2(RpTSC)$ where RpTSC = alkyl-substituted piperonal thiosemicarbazones and R = H, $CH_3$, $C_2H_5$, and $C_6H_5$. The complexes have been characterized by elemental analyses, infrared and UV-Vis spectrometry and cyclic voltammetry. The binding of the complexes with DNA was studied via UV-Vis absorption, titrations and viscometry. The results suggest that the interaction between the complexes and DNA occurred by a non-intercalative mechanism. Fluorescence competition experiments were done to further establish the mode of the binding as well as the extent of binding. A Stern-Volmer analysis of the data from the ethidium bromide and Hoechst 33258 competition studies supports the idea of a non-intercalative mode of binding and suggest binding in the grooves.

### 769 - DNA interaction studies of binuclear ruthenium-iron thiosemicarbazone complexes

***Vernon Crowell, Floyd Beckford, Dr. Department of Chemistry Lyon College Batesville AR United States***

As part of a continuing project to metal-centered pharmaceuticals we have prepared a number of binuclear mixed-metal compounds by combining two organometallic pharmacophores - namely the (*p*-cymene)Ru and ferrocenyl fragments. The complexes are best formulated as [(*p*-cymene)Ru(Cl)(AcFe-R-TSC)]X and [(*p*-cymene)Ru(Cl)(HFe-R-TSC)]X where AcFe-R-TSC and HFe-R-TSC are thiosemicarbazones derived from acetylferrocene and ferrocene carbaldehyde

respectively; R = H, $CH_3$, $C_2H_5$ and $C_6H_5$; and X = $Cl^-$ or $PF_6^-$. The compounds were partially characterized by elemental analyses, UV-Vis and infrared spectrometry and cyclic voltammetry. The binding of the complexes with DNA was studied via UV-vis absorption titrations and viscometry as well as fluorescence competition experiments with ethidium bromide (EB) and Hoechst 33258. A Stern-Volmer analysis of the data provided an apparent binding constant of 4.07 x $10^4$ $M^{-1}$ and 1.94 x $10^4$ $M^{-1}$ for the EB and Hoechst 33258 respectively at 20 Â°C. We infer from the results that the complexes bind to DNA by groove binding and to a lesser extent, intercalation.

**771 - Synthesis and reactivity of ruthenium (II)-dimethyl sulfoxide complexes containing ferrocenyl thiosemicarbazones**

***Jason Woods, Floyd Beckford, Dr. . Department of Chemistry Lyon College Batesville AR United States***

Ruthenium(III)-dmso complexes containing imidazole or indazole ligands are known to be potent anti-tumor complexes. Thiosemicarbazones are also known to have very good biological activity. In this study we have prepared a series of ruthenium(II)-dmso complexes that contain an organometallic thiosemicarbazone. The complexes were synthesized by reacting the ferrocenyl thiosemicarbazones (from acetylferrocene or ferrocene carbaldehyde) with cis-$RuCl_2(dmso)_4$ either thermally or with microwave energy. The compounds were partially characterized by elemental analyses, UV-Vis and infrared spectrometry and cyclic voltammetry. The binding of the complexes with DNA was studied via UV-vis absorption titrations and viscometry as well as fluorescence competition experiments with ethidium bromide (EB) and Hoechst 33258. Based on the results we cannot conclusively say what is the preferred mode of DNA binding - intercalative or groove binding.

**866 - Interaction of anticancer copper complexes with DNA and human serum albumin**

***Jeffrey Thessing, Charles Morgan, Floyd Beckford, Dr. . Department of Chemistry Lyon College Batesville AR United States***

A number of copper compounds containing piperonal thiosemicarbazones or 9-anthraldehyde thiosemicarbazones have been synthesized. The complexes show varied and novel structural motifs with the parent thiosemicarbazone (piperonal or 9-anthraldehyde) forming a bimetallic compound and the phenyl substituted analog forming a mixed tautomer complex -one thiosemicarbazone ligand is neutral and the other is anionic. The compounds are biologically active showing promising anticancer activity against breast cancer cell lines (MCF-7 and MDA-MB-231) as well as colon cancer cell lines (HCT116 and HT29), with $IC_{50}$ values ranging from 1.4 to 28 mM. Initial results suggest that the compounds do not cleave pBR322 DNA. Further investigations of the compounds with DNA and human serum albumin using various spectroscopic techniques will be reported.

## ACS BOSTON 2010

**INOR 27 - Investigations of transition metal-thiosemicarbazone complexes as medicinal agents**

***Dr. Floyd Beckford. Department of Chemistry, Lyon College, Batesville, AR, United States***

We have investigated the development and use of organometallic and inorganic ruthenium and

copper complexes bearing thiosemicarbazone ligands as anti-tumor agents. These compounds have been found to be cytotoxic to breast cancer (MCF-7 and MDA-MB-231) and colon cancer (HT29 and HCT116) cell lines with $IC_{50}$ values ranging from 2.7 to 40 mM. We have also examined their biophysical reactivity with DNA and human serum albumin (HSA). These compounds interact with DNA *in vitro* which might imply it is a target for their biological activity. The binding constants for the organometallic complexes with DNA are on the order of $10^3$ $M^{-1}$ but the inorganic ruthenium and copper compounds have binding constants that are an order of magnitude higher. The complexes bind strongly to HSA. For instance, $[Ru(bpy)_2(EtpTSC)](PF_6)_2$ binds with K = 1.20 x $10^5$ $M^{-1}$, $[(\eta^6\text{-cymene})Ru(EtATSC)Cl]Cl$ with K = 1.37 x $10^5$ $M^{-1}$, and $[Cu(\mu\text{-}Cl)_2(HpTSC)_2]$ with K = 8.21 x $10^4$ $M^{-1}$.

## ACS ANAHEIM 2011

### INOR 129 - Investigations of ruthenium, gallium and copper complexes that contain thiosemicarbazone ligands as medicinal agents

***Dr Floyd A Beckford PhD*, *Alyssa Brock, Vernon Crowell, Jacob Didion, Diedra Dourth, Gabriel Leblanc, Michael Shaloski, Jeffrey Thessing, Liya Li PhD, Antonio Gonzalez-Sarrias PhD, Navindra P Seeram PhD. Science Division, Lyon College, Batesville, AR, United States; University of Rhode Island, Kingston, RI, United States***

We have investigated the development and use of organometallic and inorganic ruthenium as well as gallium and copper complexes bearing thiosemicarbazone ligands as anti-tumor agents and antibacterial agents. These compounds have been found to be cytotoxic to breast and colon cancer cell lines with $IC_{50}$ values ranging from 1.0 - 200 mM. The compounds exhibited less cytotoxicity against the non-tumorigenic cell line (CCD-18Co). We have also examined their biophysical reactivity with DNA and human serum albumin (HSA). These compounds interact with DNA which might imply that it is a target for their biological activity. The binding constants for the organometallic complexes with DNA are on the order of $10^3$ $M^{-1}$ but the inorganic compounds have binding constants that are an order of magnitude higher. We have discovered that the organometallic ruthenium complexes have strong potential as inhibitors of human topoisomerase II. The complexes also bind strongly to human serum albumin.

### INOR 207 - Novel chemotherapeutic agents of vanadium(IV) with thiosemithiocarbazones and Schiff bases as ligands: Structural and *in vitro* studies

***Ms. Nerissa A. Lewis*, *Ms. Fang Liu, Mr. Tony Magnusen, Mr. Travis Erves, Ms. Jessa Faye Arca, Dr. Floyd A. Beckford Ph.D., Dr. Ramaiyer Venkatraman Ph.D., Dr. Antonio Gonzalez Sarrias Ph.D., Dr. Liya Li Ph.D., Mr. Suman Parajuli, Dr. Navindra Seeram Ph.D., Dr. Aimin Liu Ph.D., Dr. William Jarrett Ph.D., Dr. Wujian Miao Ph.D., Dr. Alvin A. Holder Ph.D.. Department of Chemistry and Biochemistry, The University of Southern Mississippi, Hattiesburg, Mississippi, United States; Department of Chemistry, Georgia State University, Atlanta, Georgia, United States; Science Division, Lyon College, Batesville, Arkansas, United States; Department of Chemistry and Biochemistry, Jackson State University, Jackson, Mississippi, United States; Department of Biomedical and Pharmaceutical Sciences, University of Rhode Island, Kingston, Rhode Island, United States***

A series of novel mixed-ligand vanadium (IV) complexes containing thiosemicarbazones and Schiff

bases as ligands were synthesized and characterized. The novel complexes were characterized by elemental analysis, ESI MS, IR, UV-visible, EPR, and $^{1}H$ and $^{13}C$ NMR spectroscopy, and electrochemistry. $^{51}V$ NMR spectroscopy was used to identify the oxidized species in DMSO solutions on standing at room temperature. *In vitro* studies were carried on three colon cancer cell lines, viz., HTC-116, Caco-2, and HT-29, with a comparative anti-proliferative activity on non-cancerous colonic myofibroblasts, CCD18-Co. All three compounds exhibited less inhibitory effects in human normal CCD-18Co cells, indicating a possible cytotoxic selectivity towards colon cancer cells. In general, those compounds which exhibited anti-proliferative activity on cancer cells but did not affect normal cells may have a potential in chemoprevention.

**663 - Synthesis, characterization, and biological evaluation of semicarbazone and thiosemicarbazone complexes of gallium**

***Ms Alyssa Brock, Professor Floyd A Beckford PhD, Dr. Antonio Gonzalez-Sarrias PhD, Professor Navindra P Seeram PhD. Science Division, Lyon College, Batesville, AR, United States; Department of Biomedical and Pharmaceutical Sciences, University of Rhode Island, Kingston, RI, United States***

We have synthesized a series of gallium(III) complexes containing a semicarbazone (ASC) or thiosemicarbazone (ATSC, EtATSC, and PhATSC) based on 9-anthraldehyde. The compounds are best formulated as $Ga(L)_3$ where L is the tautomer of the semicarbazone or thiosemicarbazone. The interaction of the complexes with calf-thymus DNA and human serum albumin (HSA) have been investigated and the initial results clearly suggest quite strong binding to both biomolecules. The compound $Ga(ATSC)_3$ interacts with HSA with a binding constant of $3.30 \times 10^5$ $M^{-1}$ at 298 K and binds DNA with a binding constant of $2.65 \times 10^5$ $M^{-1}$. We are also reporting the nuclease activity of the complexes against ct-DNA and the antioxidant activity of $Ga(ATSC)_3$ as determined by the 2,2-diphenyl-1-picrylhydrazyl (dpph) radical assay. The compounds that were evaluated were shown to be more active *in vitro* against two human colon cancer cell lines (HCT-116 and Caco-2) than against a non-tumorigenic line (CCD-18Co) with $IC_{50}$ values in the micromolar range.

**659 - Synthesis, characterization, and biological evaluation of ruthenium and gallium complexes containing thiosemicarbazone ligands**

***Mr Canisius Mbarushimana, Professor Floyd A Beckford PhD. Science Division, Lyon College, Batesville, AR, United States***

A series of thiosemicarbazones derived from *o*-vanillin (**vTSC**) and 3-formylchromone (**fcTSC**) have been synthesized. The compounds were characterized by elemental analysis, nuclear magnetic resonance (NMR) and infrared spectrometries. The thiosemicarbazones exist as the thione tautomer in both the solid and liquid state. We have also synthesized organometallic ruthenium complexes containing **vTSC**. The complexes are formulated as [(*p*-cymene)Ru(**vTSC**)Cl]Cl primarily from elemental analysis results. The complexes have been characterized by NMR and infrared spectrometries. We report on the preliminary results of the interaction of the complexes with DNA from ethidium bromide competition experiments and viscosity studies. The binding with DNA is moderate as reflected by the binding constants that are on the order of $10^3$ $M^{-1}$. We have also synthesized and characterize gallium complexes of **Et-fcTSC** and **Ph-fcTSC**. These complexes contain the thiosemicarbazone coordinated as the anion of the thiol tautomer. We report on the preliminary results of the biological evaluation of the ruthenium complexes as antibacterial agents.

**660 - First-row transition metal complexes of thiosemicarbazones containing extended aromatic rings**

***Mr Marc-Andre Leblanc, Professor Floyd A Beckford PhD, Mr Gabriel Leblanc, Mr Canisius Mbarushimana. Science Division, Lyon College, Batesville, AR, United States***

We have synthesized a series of thiosemicarbazones from anthracene-9-carboxaldehyde, phenanthrene-9-carboxaldehyde and 2-acetonaphthone by reaction with thiosemicarbazide. The ligands have been characterized by elemental analysis and spectroscopic methods. We have synthesized Cu(II), Co(II) and Zn(II) complexes utilizing these ligands. These complexes have also been characterized by elemental analysis and spectroscopic methods. We will report on the preliminary results from biophysical experiments involving the interaction of the complexes with DNA and human serum albumin. Results from the initial evaluation of the anticancer properties of the complexes will also be presented.

**747 - Biological evaluation of ferrocenyl-ruthenium complexes and their evaluation as potential human topoisomerase II inhibitors**

***Mr Jacob Didion, Professor Floyd A Beckford PhD, Mr Vernon Crowell. Science Division, Lyon College, Batesville, AR, United States***

We report on the synthesis of organometallic ruthenium complexes of the type [(*p*-cymene)Ru(R-Fe-R'TSC)Cl]X (where R-Fe-R'TSC = a ferrocenyl thiosemicarbazone - R = H or $CH_3$, R' = H, $CH_3$ or $C_6H_5$; X = $Cl^-$ or $PF_6^-$), their biological evaluation as anticancer and antibacterial agents and their potential as anti-topoisomerase II (topo II) agents. The compounds binds moderately to DNA and human serum albumin. The active compounds behave as enzyme inhibitors rather than poisons with varying degrees of activity amongst them. The compound type [(*p*-cymene)Ru(Me-Fe-PhTSC)Cl]$PF_6$ can inhibit topo II activity at 25 mM but [(*p*-cymene)Ru(H-Fe-PhTSC)Cl]$PF_6$ do not show activity at this concentration. On the other hand [(*p*-cymene)Ru(Me-Fe-PhTSC)Cl]Cl also has activity at 25 mM. So it may be suggested that a phenyl group on the thiosemicarbazone enhances enzyme inhibitory activity but the complex counter anion does not. It general it was seen that all of the complexes studied can inhibit the enzyme at concentrations ≥50 mM.

## ANNUAL BIOMEDICAL RESEARCH CONFERENCE FOR MINORITY STUDENTS - NOVEMBER 9 - 12, 2011

**A Novel Chemotherapeutic Agent of Copper(II) With a Thiosemicarbazone as Ligand: Structural and *in vitro* Studies**

**Justin R. Moreira,** Alvin A. Holder, Rosella M. Taylor, Rodney Ballard, Antonio Gonzalez-Sarrias, Tiffany B. Edwards, Navindra Seeram and Floyd A. Beckford.

The American Cancer Society estimates that in 2011 about 141,210 people will be diagnosed with colorectal cancer; and that about 49,380 people will die of colorectal cancer in the U.S.A. In both men and women, colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death. The limited efficacy of current treatments for advanced colon cancer

serves an impetus for a concerted effort to identify chemo-preventive agents for treatment. This process has always involved metal complexes. Cisplatin is widely used for the treatment of many cancers despite its undesirable side effects, due to high toxicity, and problems with drug resistance in primary and metastatic cancers. These limitations have spurred a growing interest in novel non-platinum metal complexes that can show anti-cancer properties. For example, copper(II) complexes have been reported to possess several favorable properties suited to rational anti-cancer drug design. Recently, copper(II) thiosemicarbazone complexes have been the focus of investigation as metallodrugs through various medical applications. These applications include their use as anti-cancer agents. In this study, the main hypothesis is as follows: ***a copper(II) complex with thiosemicarbazone as a ligand, which is derived from 2-acetylthiazole and 4-ethyl-3-thiocarbazide, can inhibit colorectal cancer growth***. For this study, a novel copper(II) complex containing a thiosemicarbazone (which was derived from 2-acetylthiazole and ethyl-3-thiocarbazide), was synthesized and characterized. The novel complex was characterized by elemental analysis, TGA, FT IR, UV-visible, EPR spectroscopy, ESI MS, and electrochemistry. *In vitro* studies were carried on three colon cancer cell lines, viz., HTC-116, Caco-2, and HT-29, with a comparative anti-proliferative activity on non-cancerous colonic myofibroblasts, CCD18-Co. The novel complex was found to have better efficacy against the cancer cell lines when compared with etoposide, which was used as a control. These results may suggest that this complex can affect only the colorectal oncogenes that can cause cancer cell proliferation. In conclusion, this complex may have potential in ameliorating or inhibiting colorectal cancer growth.

## ACS SAN DIEGO 2012

### INOR 13 - Synthesis, biophysical reactivity and medicinal evaluation of a series of half-sandwich ruthenium complexes with a 1,4,7-trithiacyclononane face-cap

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Four complexes of the type [9]ane$S_3$Ru(ATSC)Cl]Cl where ATSC = 9-anthraldehyde thiosemicarbazones with a N3-alkyl (H, $CH_3$, $C_2H_5$ or $C_6H_5$) substituent were synthesized. The complexes bind to DNA moderately with binding constants ranging from 3.21 x $10^4$ - 1.27 x $10^5$ $M^{-1}$. Electronic absorption spectral analysis of the reaction of the complexes with model proteins did suggest that they can bind to the proteins. In addition, the complexes bind to human serum albumin with the binding constants on the order of $10^4$ $M^{-1}$. We have investigated the cytotoxicity of the complexes against 22Rv1 (human prostate) cells, HCT-116 (human colorectal) and MCF-7 (human breast) cancer cell lines along with a non-tumorigenic CCD-18Co (human colon fibroblasts) cell line. Against the 22Rv1 cell line the complex bearing a phenyl group on N3 was the most active. They show good antibacterial profiles against gram-positive bacterial strains but showed no activity against the gram-negative strains we studied.[p]

### INOR 14 - Half-sandwich ruthenium complexes with thiosemicarbazones ancillary ligands

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Half-sandwich ruthenium complexes particularly those containing an organometallic face-capping group have recently been shown to be good structural motifs for investigating the development of metallodrugs. In our lab we have synthesized a series of complexes of the type [(face-cap)Ru(dmabTSC)Cl]X, where face-cap = benzene, *p*-cymene or [9]aneS$_3$, dmabTSC = dimethylaminobenzaldehyde thiosemicarbazone and X = $Cl^-$ or $PF_6^-$. We have investigated the biochemical and biophysical reactivity of the complexes by examining their interactions with calf-thymus DNA, human serum albumin and other model proteins. The compounds have been tested for anticancer activity against 22Rv1 (human prostate carcinoma), HCT-116 (human colorectal carcinoma), Caco-2 (human colorectal adenocarcinoma) or MCF-7 (human breast adenocarcinoma) along with a non-tumorigenic CCD-18Co (human colon fibroblasts). Against the 22Rv1 cell line the *p*-cymene complex is the most active followed by the [9]aneS$_3$ complex and then the benzene complex. The activity versus HCT-116 and Caco-2 was minimal with $IC_{50}$ values above 350 μM.[p]

**INOR 456 - Comparison of half-sandwich ruthenium-thiosemicarbazone complexes with [9]aneS$_3$ or *p*-cymene face-caps**

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We have synthesized two series of half-sandwich ruthenium complexes containing vanillin thiosemicarbazones (vTSCs); the complexes have the general formula [([9]aneS$_3$)Ru(vTSC)Cl]Cl and [(*p*-cymene)Ru(vTSC)Cl]$^+$. We have compared the cytotoxicity profiles (of the two sets) against two human colon cancer cell lines, HCT-116 and Caco-2. The $IC_{50}$ values for the *p*-cymene series range from 2.7 μM to 59.7 μM against HCT-116 and 3.7 μM to 60.3 μM for Caco-2. There is only slight cytotoxic selectivity for the cancer cell lines versus the non-tumorigenic CCD-18Co cells. The [([9]aneS$_3$)Ru(vTSC)Cl]Cl complexes were also tested against MCF-7 (human breast cancer) cells. The members of both series of complexes can bind to DNA. For instance, from electronic absorption titrations the [(*p*-cymene)Ru(vTSC)Cl]$^+$series bind to calf-thymus DNA with binding constants that range from1.71 - 7.08 x $10^4$ $M^{-1}$. The complexes also interact with human serum albumin and we have also investigated their reactions with ubiquitin, hen egg white lysozyme and horse cytochrome c.

**INOR 457 - Benzene-ruthenium organometallic complexes: Synthesis, characterization, and biophysical reactivity**

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We have synthesized two half-sandwich ruthenium complexes of the type [($C_6H_6$)Ru(ATSC)Cl]$PF_6$, where ATSC = 9-anthraldehyde thiosemicarbazone (**1** ) or 9-anthraldehyde ethylthiosemicarbazone (**2** ). The complexes were characterized by elemental analysis and various spectroscopic techniques. The complexes displays variegate cytotoxic profiles against HCT-116 and Caco-2 (human colon cancer cells. The $IC_{50}$ values for **1** were 104 μM and 59.8 μM respectively and **2** had $IC_{50}$ values of 23.3 μM and 29.7 μM for HCT-116 and Caco-2 respectively. In addition, we noted that

the complexes displayed some cytotoxic selectivity being half as cytotoxic to non-tumorigenic CCD-18Co cells. We have studied the reactions of the complexes with model proteins and have detected, by mass spectrometry, two ruthenated-ubiquitin species. The complexes bind to DNA with binding constants on the order of $10^4$ $M^{-1}$. The complexes bind strongly to human serum albumin; competition experiments with flufenamic acid and phenylbutazone did not prove conclusively which binding site on the protein is targeted.

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**INORG 21 - Curcuminoids as ligands in half-sandwich organometallic ruthenium piano-stool complexes: Synthesis and biophysical reactivity**

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A set of structurally diverse [(aryl)hepta-1,6-diene-3,5-dione]s (curcuminoids) were synthesized by the reaction of 2,5-pentanedione with the appropriate aldehyde in the presence of tributylborate and n-butylamine as catalyst. These curcuminoids were used as mono-anionic bidentate ligands in the synthesis of half-sandwich organometallic ruthenium complexes of the type [($\eta^6$-arene)Ru(curcuminoid)Cl] where arene = benzene or *p*-cymene. The complexes have been characterized and initial investigations of reactions with DNA as well as some model proteins have been carried out. A number of the complexes show a weak ability to uncoil pBR322 plasmid DNA but this ability disappears under irradiation with 365 nm UV light. Spectroscopic and viscometric experiments suggest that the complexes interact with DNA via weak intercalation. On the other hand the interaction, as measured by the binding constant, with human serum albumin is strong.

**CHED 700 - Synthesis, characterization, and initial biophysical reactivity of [$\eta^6$-($C_6H_6$)Ru(curcuminoid)Cl] complexes**

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We have synthesized a series of organometallic ruthenium piano-stool complexes with curcuminoids as co-ligands from the reaction of $[(C_6H_6)RuCl_2]_2$ with the curcuminoid in a methanolic solution containing potassium hydroxide. The complexes have been characterized by elemental analysis and various spectroscopic methods. The hydrolysis (defined as the replacement of the chloride ligand by a water molecule) of the complexes shows a complicated behavior with rates constants ranging from $1.1 \times 10^{-5}$ $s^{-1}$ to $1.2 \times 10^{-4}$ $s^{-1}$. We have also investigated the interaction of the complexes with calf-thymus DNA using absorption and fluorescence spectroscopies as well as viscometric methods. From UV-Vis absorption spectrophotometry the binding constant with calf-thymus DNA is $10^3$ - $10^4$ $M^{-1}$.