13th INTERNATIONAL VANADIUM SYMPOSIUM

22nd – 24th NOVEMBER 2023

BOOK OF ABSTRACTS

CALOUSTE GULBENKIAN FOUNDATION
LISBON, PORTUGAL

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WELCOME

Dear Colleagues,

It is with great pleasure that we welcome you to the **13th International Vanadium Symposium**, **V13**, at the Calouste Gulbenkian Foundation, Lisbon, Portugal.

It is the second time in 15 years that this key conference on Vanadium Chemistry is held in Lisbon after the 6th edition, V6, chaired by Professor João Costa Pessoa.

The outstanding quality of the presenter's research will surely serve as an innovative benchmark for the following decades, allowing a wider application of vanadium in a variety of fields and impacting the life quality of future generations. On top of the scientific program, V13 will offer opportunities for exploring historical sites and landscapes of unique natural beauty in and around Lisbon, as well as cultural events and delicious Portuguese cuisine and wines.

We sincerely hope that you enjoy a pleasant time from both the scientific and social points of view.

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The Organizing Committee is very grateful to the following companies and institutions for their kind sponsorship and support of V13.

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Vanitec is the global not-for-profit organization whose objective is to promote and defend the use of vanadium bearing materials around the world. Members include all of the world's major vanadium producers, vanadium users, and those involved in energy storage with the Vanadium Flow Battery. Vanitec supports technical investigations, market development and promotion, and health & safety research and advocacy.

PAST EVENTS

The meeting named "Chemistry, Biochemistry, and Therapeutic Applications of Vanadium Compounds" held within the 5th North American Chemical Congress (in Cancun, Mexico, 1997) was considered the 1st international meeting of the vanadium community, although the interest in vanadium centred meetings can be traced back to 1986, with the meeting entitled "Role of Vanadium in Biology", held within the Federation of American Societies for Experimental Biology Meeting.

The full list of past vanadium symposia is listed below.

	Year	City, Country	Chair(s)
V1	1997	Cancun, Mexico	Alan Tracey and Debbie C. Crans
V2	1999	Berlin, Germany	Dieter Rehder and Valeria Conte
V3	2001	Osaka, Japan	Toshikazu Hirao
V4	2004	Szeged, Hungary	Tamás Kiss
V5	2006	San Francisco, USA	Debbie C. Crans; co-chairs: João Costa Pessoa and Kenneth Kustin
V6	2008	Lisbon, Portugal	João Costa Pessoa
V7	2010	Toyama, Japan	Hitoshi Michibata, Kan Kanamori; co-chair: Toshikazu Hirao
V8	2012	Arlington, USA	Mitchell Cohen, Andrew Ghio and Craig C. McLauchlan
V9	2014	Padua, Italy	Giulia Licini and Valeria Conte
V10	2016	Taipei, Taiwan	Biing-Jiun Uang
V11	2018	Montevideo, Uruguay	Dinorah Gambino
V12	2021	Virtual Edition	Anastasios D. Keramidas

GENERAL INFORMATION

The 13th International Vanadium Symposium is held at the **Calouste Gulbenkian Foundation**. Main entrance – Berna Avenue (red arrow).

1 - Olissippo Hotel (4 *)
2 - Hotel Princípe Ávila (4 *)
3 - Hotel Princípe (3 *)
4 - Corinthia Hotel (5 *)

All lectures will take place in the main building – **Auditorium 3**, located below the main floor. Poster session will be held in **Sala 1**.

Internet networks: FCG Eventos or FCG Eventos 5 Ghz.

Password: #GULBENKIAN#

GENERAL INFORMATION

WELCOME COCKTAIL (Tuesday, 21st at 5 pm)

The cocktail reception will be held at *Instituto Superior Técnico*, University of Lisbon (Rovisco Pais 1 Avenue) in the Interdisciplinary Complex building (Map – blue square). This will be an excellent opportunity to meet friends and taste Portuguese pastries, savories and wine. Participants registration will start on this day.

LUNCHES

Lunches on Wednesday (22nd), Thursday (23rd) and Friday (24th) will be served at the Gulbenkian Foundation's canteen, and are included in the registration fee. We kindly ask all participants to present their lunch tickets to the staff.

CONFERENCE DINNER (Friday, 24th at 8 pm)

The conference dinner will be offered to all participants and will be served at **Gula's for Kitchen Lovers** (R. Dona Filipa de Vilhena 18A). Map – red square.

SOCIAL PROGRAM (Thursday, 23rd Nov after 4 pm)

After the poster session, guided tours to the Calouste Gulbenkian Museum collection will be offered. Full details will be given during the conference.

SCIENTIFIC INFORMATION

ORAL COMMUNICATIONS

Presentations should be prepared in PowerPoint with resolution 1920x1080 and format 16:9. Speakers of the **morning sessions** are kindly asked to give their ppt presentation **in advance**. The **afternoon session** speakers can give their presentation during lunch break.

Please take into account the maximum duration of your lecture (which must include a few minutes for Q&A):

Plenary Lectures: 35 min

Invited Lectures: 25 min

Oral Lectures: 20 min

Award lectures: 40 min

POSTER COMMUNICATIONS

The **poster session** will be held on the 23rd (Thursday) in the afternoon. Authors are requested to set up their posters for display on the morning, during coffee break, and remove them at the end of the poster session.

Authors should stay near their posters so they will be available to answer any questions from the participants and the evaluation panel, who will select the posters for the Poster Prize awards. **Posters should be prepared in portrait format and fit on A0 panels.**

Poster prizes are sponsored from the New Journal of Chemistry and Springer:

1st award: 250€ + 150€ ebook voucher

2nd award: 200€ + 150€ ebook voucher

3rd award: 150€

SCIENTIFIC INFORMATION

SPECIAL ISSUES

There will be Special Topics and Web Collections dedicated to the Vanadium Conference, in Frontiers in Chemical Biology and New Journal of Chemistry.

Please consider publishing your work in one of them.

Frontiers in Chemical Biology

Research topic: ***Vanadium Biochemistry – Highlights from the 13th International Vanadium Symposium***

Guest Editors: Debbie C. Crans and Isabel Correia

Site: https://www.frontiersin.org/research-topics/59347/vanadium-biochemistry---highlights-from-the-13th-international-vanadium-symposium

New Journal of Chemistry

Web collection: ***Vanadium Chemistry in the 21st Century***

Guest Editors: Armando Pombeiro, Isabel Correia and Manas Sutradhar

PROGRAMME

The conference programme can also be accessed via the Eventee app (Android and iOS) or by scanning the following QR code:

SCHEDULE

TUESDAY, 21ST NOVEMBER

5:00 **WELCOME RECEPTION** at Instituto Superior Técnico

WEDNESDAY, 22ND NOVEMBER

9:00	**OPENING SESSION (Rogério Colaço; President of IST)**
9:20	**PL1** - Debbie C. Crans
9:55	**OL1** - Rianne M. Lord
10:15	**OL2** - Mauro Carraro
10:35	**COFFEE BREAK**
11:05	**IL1** - Peter Lay
11:30	**IL2** - Thanos Salifoglou
11:55	**OL3** - Nádia Ribeiro
12:15	**OL4** - Gonzalo Scalese
12:35	**LUNCH BREAK**
13:55	**IL3** - Manuel Aureliano
14:20	**IL4** - Enrique González-Vergara
14:45	**OL5** - Juliana Missina
15:05	**OL6** - Fernando Avecilla
15:25	**OL7** - Matteo Marafante
15:45	**COFFEE BREAK**
16:15	**IL5** - Alexandra R. Fernandes
16:40	**OL8** - Skyler Markham
17:00	**VANADIS AWARD V9**
18:00	

SCHEDULE

THURSDAY, 23RD NOVEMBER

9:00	**PL2** - Kotohiro Nomura
9:35	**IL6** - Elisabete C.B.A. Alegria
10:00	**OL9** - Jana Pisk
10:20	**OL10** - Laura Orian
10:40	**COFFEE BREAK**
11:10	**IL7** - Toshiyuki Moriuchi
11:35	**OL11** - Marta Pawlak
11:55	**OL12** - Fátima Sanz
12:15	**OL13** - Venkata Narayana Kalevaru
12:35	**LUNCH BREAK**
13:55	**IL8** - Ronald Wever
14:20	
14:45	**POSTER SESSION**
16:00	
16:00	
16:50	**SOCIAL PROGRAM**
18:00	

SCHEDULE

FRIDAY, 24TH NOVEMBER

9:00	**PL3** - Eugenio Garribba
9:35	**IL9** - Anastasios D. Keramidas
10:00	**OL14** - Antonello Merlino
10:20	**OL15** - José Ferraz-Caetano
10:40	**COFFEE BREAK**
11:10	**IL10** - Manas Sutradhar
11:35	**OL16** - Andrew Bates
11:55	**OL17** - Leonor Côrte-Real
12:15	**OL18** - Rorie Gilligan
12:35	**LUNCH BREAK**
13:55	**IL11** - Craig C. McLauchlan
14:20	**OL19** - Diego Venegas-Yazigi
14:40	**OL20** - Kanticha Jaiyen
15:00	**OL21** - Yoshihito Hayashi
15:20	**COFFEE BREAK**
15:50	**IL12** - Annette Rompel
16:15	**IL13** - David White
16:40	**VANADIS AWARD V10**
17:40	**CLOSING SESSION**
18:00	
20:00	**CONFERENCE DINNER**

WEDNESDAY, 22ND NOVEMBER

Chair: João Costa Pessoa

PL1 - Vanadium combinatorial therapy prevents loss of pancreatic β cell mass and function while ameliorating insulin resistance in type 2 diabetes – **Debbie C. Crans**

OL1 - Vanadium Acetylacetonate Complexes in the Treatment of Cancer – **Rianne M. Lord**

OL2 - Lindqvist polyoxovanadate-peptides conjugates for cancer cell targeting – **Mauro Carraro**

Chair: Marvin Makinen

IL1 - Substitution Kinetics, Albumin and Transferrin Affinities, and Hypoxia all Affect Biological Activities of Anticancer Vanadium(V) Complexes – **Peter Lay**

IL2 - Ligand-specific structural features guide vanadium-dependent cell differentiation in adipogenesis – **Thanos Salifoglou**

OL3 - Hydrazide-hydrazone: a linkage feature with a preponderant role in coordination chemistry and biological activity – **Nádia Ribeiro**

OL4 - Comparing the effects on Trypanosoma cruzi of heteroleptic oxidovanadium (V) complexes with 8-hydroxyquinoline derivatives – **Gonzalo Scalese**

Chair: Dinorah Gambino

IL3 - Vanadium Effects on Lipid Peroxidation and Diseases – **Manuel Aureliano**

IL4 - Playing with Decavanadates and Tetravanadates: A Story Full of Surprises – **Enrique González-Vergara**

OL5 - Exploring decavanadate salts with cationic dyes: tackling multidrug resistance and colorant adsorption – **Juliana Missina**

OL6 - Vanadium complexes with hydrazone ligands and study of their biological interactions – **Fernando Avecilla**

OL7 - Multi-technique characterization and speciation of oxovanadium(IV) aqueous systems: interaction with 8-hydroxyquinoline-2-carboxylic acid and 6,7-dihydroxycoumarin – **Matteo Marafante**

Chair: Ron Wever

IL5 - In vitro and in vivo biological activity of dipicolinate oxovanadium(IV) complexes – **Alexandra R. Fernandes**

OL8 - Development of two vanadium(V) Schiff-Base catecholate complexes: Relating stability and biological activity to structural modifications – **Skyler Markham**

THURSDAY, 23RD NOVEMBER

Chair: Armando Pombeiro

PL2 - Vanadium(V)-Alkylidenes as Olefin Metathesis Catalysts – **Kotohiro Nomura**

IL6 - Selective oxidation of volatile organic compounds in liquid phase over homogeneous and supported vanadium catalysts – **Elisabete Alegria**

OL9 - Vanadium coordination compounds derived from simple acetic acid hydrazide as non-conventional semiconductors – **Jana Pisk**

OL10 - C-C oxidative bond cleavage in diols promoted by vanadium catalysts: insight from relativistic DFT calculations – **Laura Orian**

Chair: Valeria Conte

IL7 - Oxovanadium(V)-Catalyzed Synthesis of Ureas Using Carbon Dioxide – **Toshiyuki Moriuchi**

OL11 - Comparison of the catalytic activity of oxovanadium(IV) and cobalt(II) complex compounds in the oligomerization of ethylene – **Marta Pawlak**

OL12 - Photocatalytic oxidation of Lignin models using V^{v}-aminotriphenolate complexes – **Fátima Sanz**

OL13 - Green synthesis of 2-cyanopyrazine by gas phase ammoxidation using vanadium-containing catalysts – **Venkata Narayana Kalevaru**

Chair: Alison Butler

IL8 - Catalytic activity of vanadium chloroperoxidases and its applications – **Ronald Wever**

FRIDAY, 24TH NOVEMBER

Chair: Debbie C. Crans

PL3 - Vanadium-proteins. Structure, binding, characterization and biological implications – **Eugenio Garribba**

IL9 - Mechanism of the Reductive Activation of O_2 to O_2^{2-} from a Vanadium(IV) Species and Its Potential Use in Fuel Cells – **Anastasios Keramidas**

OL14 - Protein metalation by vanadium compounds: structural studies – **Antonello Merlino**

OL15 - Vanadium-based catalyst design guidelines using an explainable Machine Learning model for predicting epoxidation yields – **José Ferraz-Caetano**

Chair: Giulia Licini

IL10 - Oxidovanadium(V) complexes as reusable catalysts – **Manas Sutradhar**

OL16 - Increasing Temperature Sensitivity for ^{51}V NMR Thermometers through Ligand-to-Metal Charge Transfer – **Andrew Bates**

OL17 - Oxidovanadium(IV) complexes containing 8-hydroxyquinoline Schiff bases – synthesis, characterization and biological screening – **Leonor Côrte-Real**

OL18 - A comparative study of vanadium extraction from different concentrates by the salt roast-water leach process – **Rorie Gilligan**

Chair: Toshiyuki Moriuchi

IL11 - Adventures in vanadium coordination chemistry with the Kläui ligand – **Craig C. McLauchlan**

OL19 - Electronic properties of polyoxovanadoborates and alkoxylated polyoxovanadates – **Diego Venegas-Yazigi**

OL20 - Synthesis of Functionalized Bottlebrush Polymers by Cis-specific Metathesis Polymerization by Vanadium-Alkylidene Catalysts – **Kanticha Jaiyen**

OL21 - Alkali and alkaline-earth metal polyoxovanadates – **Yoshihito Hayashi**

Chair: Craig McLauchlan

OL21 - Alkali and alkaline-earth metal polyoxovanadates – **Yoshihito Hayashi**

IL12 - Understanding Polyoxometalate Speciation in Buffered Solutions: A Focus on Decavanadate – **Annette Rompel**

IL13 - Technical Challenges for USEPA's Assessment of Vanadium and Its Compounds – **David White**

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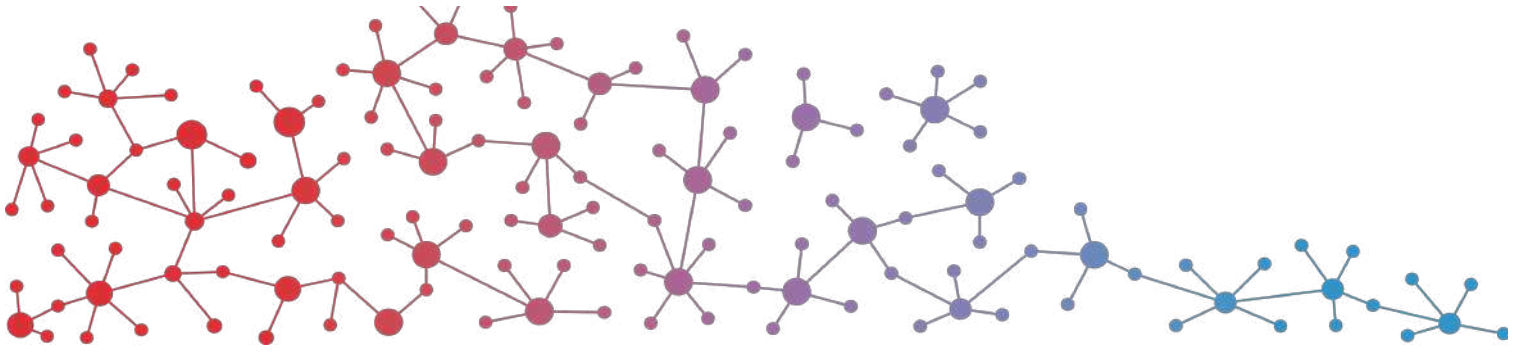
PLENARY LECTURES



PLENARY SPEAKERS

DEBBIE CRANS, *Colorado State University, USA*

Professor D. Crans's is a Professor of Organic, Inorganic and Biological Chemistry and of Cell and Molecular Biology at Colorado State University, where she also is a Professor Laureate of the College of Natural Sciences. Her main interest is in the fundamental chemistry and biochemistry of drugs with particular interest in vanadium and other transition metal ions as metals in medicine and their mechanisms of toxicity.

EUGENIO GARRIBBA, *Università degli Studi di Sassari, Italy*

Professor E. Garribba is a full professor in the Department of Medicine, Surgery and Pharmacy of the Università degli Studi di Sassari, in Italy. He graduated in Chemistry in 1995 and obtained his PhD from the Università degli Studi di Sassari, in Italy in 2001. His interests are the understanding of the role of vanadium enzymes and of vanadium compounds in biology, as well as the design of new vanadium-based species for catalysis, materials science and medicinal chemistry.

KOTOHIRO NOMURA, *Tokyo Metropolitan University, Japan*

Professor K. Nomura is a full professor in the Department of Chemistry, Tokyo Metropolitan University. He finished his undergraduate and master studies in Saitama University in 1986 and University of Tokyo in 1988, and joined Sumitomo Chemical Co., Ltd. He received his Ph.D. degree in 1993 from Osaka University and joined a group of Prof. R. R. Schrock (MIT, USA) as a postdoctoral fellow for 2 years. His main interests are vanadium complex catalysts for olefin metathesis, olefin polymerization and dimerization.

Vanadium combinatorial therapy prevents loss of pancreatic β cell mass and function while ameliorating insulin resistance in type 2 diabetes

B. Shang[a], Y. Dong[b], B. Feng[a], Z. Wang[a], D.C. Crans[d], X. Yang[a,c]

[a] State Key laboratories of Natural and mimetic drugs and Department of Chemical Biology, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing 100191, China.

[b] Institute of Translational Medicine, The Affiliated Hospital of Qingdao University, College of Medicine, Qingdao University, Qingdao 266021, China.

[c] SATCM Key Laboratory of Compound Drug Detoxification, Peking University Health Science Center, Beijing 100191, China.

[d] Department of Chemistry and Cell and Molecular Biology Program, College of Natural Science, Colorado State University, Fort Collins, CO 80523-1872, USA.

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To enhance insulin sensitivity meanwhile rescue the loss of insulin-secreting β cells in type 2 diabetes mellitus (T2DM), a novel vanadium-oestrogen combinatorial therapy was developed using the membrane permeable graphene quantum dots (GQDs) as delivery platform. Vanadyl acetylacetonate (VAC) and estradiol (E2) are integrated stably on the surface of GQDs (ϕ ~2.5nm) in desired amounts to form GQD-E2-VAC complexes. On *db*/*db* transgenetic type 2 dabetic mice, GQD-E2-VAC complexes (10 μmol/kg/day for vanadium; 250 nmol/kg/day for E2) exhibited a comprehensive anti-diabetic effects including fully control of hyperglycemia (normalizing fasting blood glucose, feed blood glucose, and urine glucose) and dyslipidemia, improvement of insulin sensitivity, correction of hyperinsulinemia, and restore of β-cell mass. Further analysis on tissue samples using a NIT-1 pancreatic cell model revealed that co-regulation of TXNIP activation by vanadium and oestrogen would contribute to the enhanced anti-diabetic effects of the combinational therapy. Moreover, dietary supplement of a potent mitochondrial protective antioxidant, coniferaldehyde (0.2 mmol/kg/day), can significantly potentiate the protective effects of GQD-E2-VAC complexes, supporting the

significance of correction of redox state in diabetes. Collectively, the present work provided a vanadium-oestrogen combinatorial approach that achieved simultaneously protection of β-cells and insulin enhancement using very low dose of vanadium close to the upper safety limit of daily intake of vanadium as an essential element. Our work may encourage further new multi-modal therapies towards the cure of type 2 diabetes.

Vanadium-proteins. Structure, binding, characterization and biological implications

E. Garribba,[a] F. Pisanu,[a] G. Sciortino,[b] D. Sanna,[c] V. Ugone,[c] A. Merlino,[d] G. Ferraro,[d] M. Paolillo,[d]

[a]*Department of Medicine, Surgery and Pharmacy, University of Sassari, I-07100, Sassari, Italy.*
[b]*Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology, 43007 Tarragona, Spain.*
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A growing interest for vanadium complexes (VCs) concerns their possible use in medicine.[1] In biological fluids VCs with pharmacological action may give several transformation processes, among which the formation of species with the bioligands of organism. In this context, the binding of VCs to proteins plays a crucial role in the processes of transport in organism and action mode,[2] even if for years little progress has been made in this area due to the complexity of studying these systems with usual techniques. The interaction depends on several factors: the structure of VC in aqueous solution, the number of available sites in the metal fragment, its thermodynamic stability, the presence of accessible residues on the protein structure, the stabilization of the adduct by secondary interactions, such as hydrogen bonds or van der Waals contacts,[3] making the description of these systems a demanding and stimulating challenge for the inorganic, bioinorganic and medicinal chemists. Both covalent and non-covalent interactions are possible, with Asp, Asn, Glu, Gln, His, Ser residues being involved in the first one and Asp, Asn, Glu, Gln, Arg, Cys and Lys in the second one, and with the binding of one or more metal moieties. In this communication, the binding of VCs with small proteins such as hen egg white lysozyme,[4,5] myoglobin,[6] ubiquitin,[7] cytochrome *c*,[8] ribonuclease A,[9] or larger proteins like G-actin,[10] human serum transferrin in the apo or holo form,[11] human serum albumin,[12] hemoglobin,[11] and immunoglobulin G[11] will be presented. It will be shown that a complete characterization is possible through a multi-technique approach based on spectrometry (MS), spectroscopy (EPR), computation (docking, DFT and molecular dynamics methods) and X-ray crystallography. The biological implications of VC–protein binding will also be discussed.

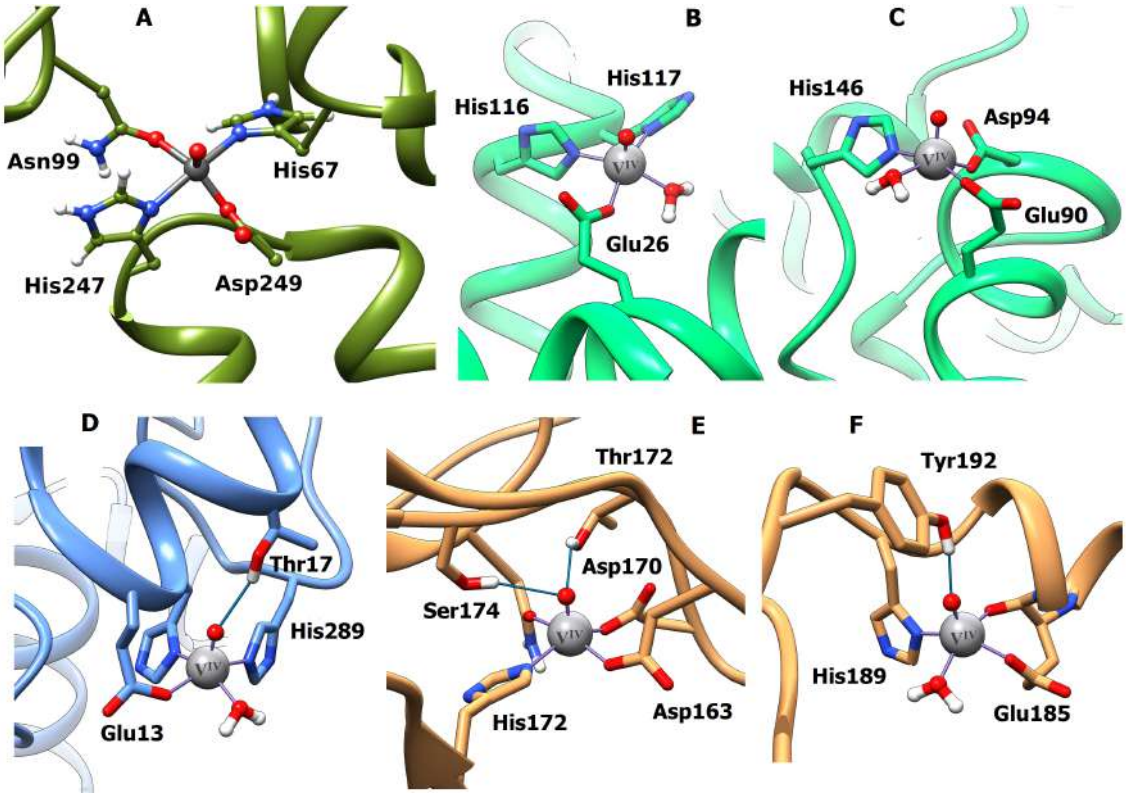

Figure 1 – Binding sites of $V^{IV}O^{2+}$ ion to: A) multi-metal site (MBS) of human serum albumin; B-C) γ and β of hemoglobin; D) C of transferrin and E-F) sites 3 and 2 of immunoglobulin G.

References

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Vanadium(V)-Alkylidenes as Olefin Metathesis Catalysts

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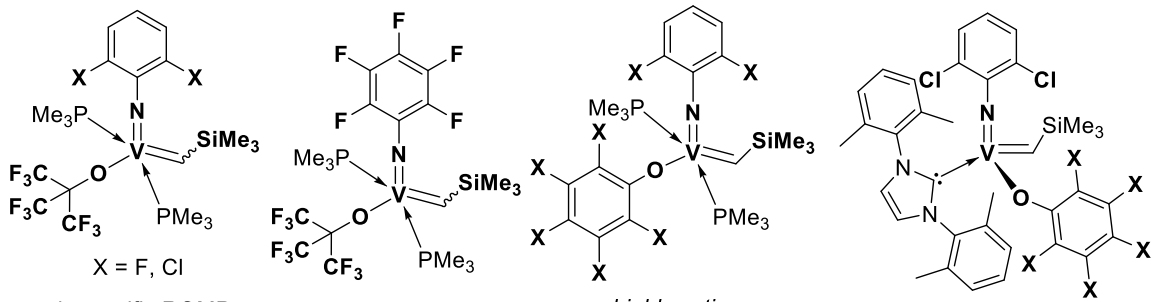
Certain high oxidation state early transition metal–alkylidene (carbene) species play an essential role in olefin metathesis.[1] In particular, the (arylimido)vanadium(V) complexes (Scheme 1) display promising capabilities especially for ring opening metathesis polymerization (ROMP) of cyclic olefins.[1,2] The perfluorinated alkoxides, $V(CHSiMe_3)(NAr)[OC(CF_3)_3](PMe_3)_2$, enabled to proceed *cis*-specific ROMP of norbornene even at 80 ºC,[2a,b] whereas c*is-syndiospecific* ROMP could be achieved by the NHC alkylidenes.[2e] The perchlorinated phenoxide, $V(CHSiMe_3)(N\text{-}2,6\text{-}Cl_2C_6H_3)(OC_6Cl_5)(PMe_3)_2$, enabled to proceed ROMP of low strained cyclic olefins.[2c]

In this lecture, the basic concept for the catalyst design and the application as olefin metathesis catalysts as well as ethylene polymerization/dimerization catalysts,[3] and more recent results in the *cis*/*trans* specific synthesis of bottlebrush ROMP polymers will be introduced.[4a] Moreover, the NHC supported catalysts enable to proceed exclusive ring-closing metathesis reactions in an efficient manner.[4b] Details including the overview will be thus introduced in the symposium.



Scheme 1

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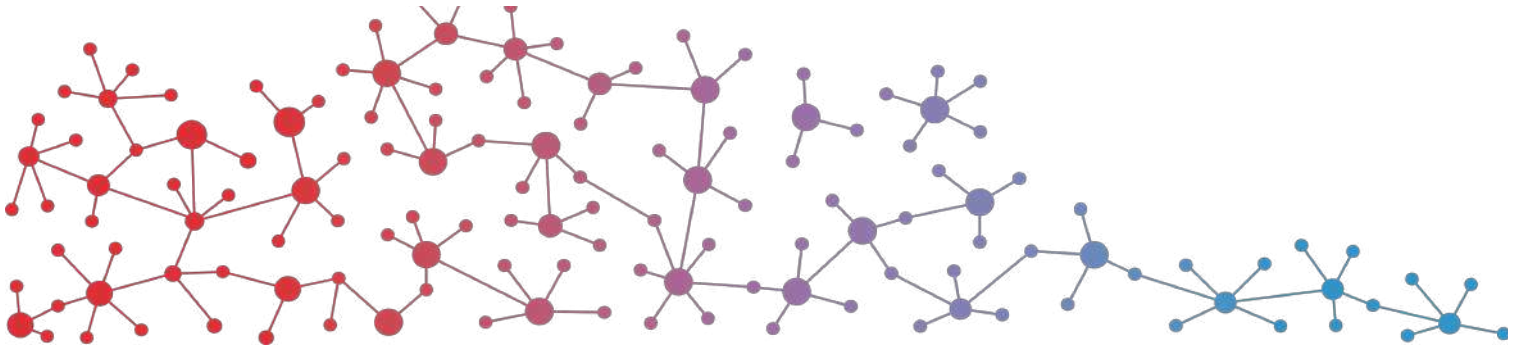
13th INTERNATIONAL VANADIUM SYMPOSIUM

22nd – 24th NOVEMBER 2023

INVITED LECTURES



INVITED SPEAKERS

Peter A. Lay, University of Sydney Australia

Thanos Salifoglou, Aristotle University of Thessaloniki, Greece

Manuel Aureliano, University of Algarve, Portugal

Enrique Gonzáles-Vergara, Benemérita Universidad Autónoma de Puebla, Mexico

Alexandra R. Fernandes, Universidade Nova de Lisboa Portugal

Elisabete Alegria, Instituto Superior de Engenharia de Lisboa, Portugal

Toshiyuki Moriuchi, Osaka Metropolitan University, Japan

Ron Wever, University of Amsterdam, The Netherlands

Anastasios D. Keramidas, University of Cyprus, Cyprus

Manas Sutradhar, Universidade Lusófona, Lisbon, Portugal

Crais C. McLauchlan, Illinois State University in Normal, IL, USA

Annette Rompel, University of Vienna, Austria

David White, Vanitec USA

Substitution Kinetics, Albumin and Transferrin Affinities, and Hypoxia all Affect Biological Activities of Anticancer Vanadium(V) Complexes

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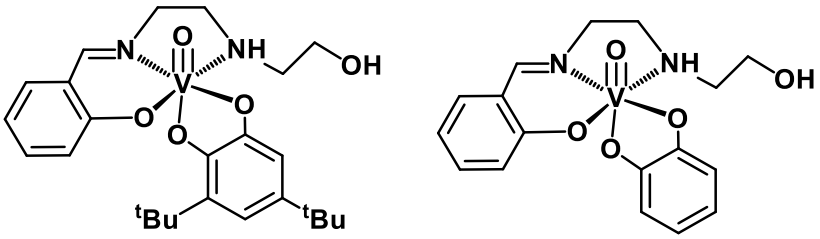
Limited stability of typical metal complexes in biological media has hampered their medicinal applications, but also created a potential for novel cancer treatments, such as intratumoral injections of cytotoxic but short-lived anticancer drugs.[1] Two related V(V) complexes, [VO(Hshed)(dtb)] (**1**) and [VO(Hshed)(cat)] (**2**), (H_2shed = *N*-(salicylideneaminato)-*N*′-(2-hydroxyethyl)-1,2-ethanediamine, H_2dtb = 3,5-di-*tert*-butyl)catechol and H_2cat = 1,2-catechol, decomposed within minutes in cell culture medium at 310 K ($t_{1/2}$ = 43 s and 9 s for **1** and **2**, respectively).[1-4] Despite this, both complexes showed high anti-proliferative activities in triple-negative human breast cancer (MDA-MB-231) cells, but the mechanisms of their activities were radically different. Complex **1** formed noncovalent adducts with human serum albumin, rapidly entered cells via passive diffusion, and was nearly as active in a short-term treatment (IC_{50} = 1.9 ± 0.2 □M at 30 min) compared with a long-term treatment (IC_{50} = 1.3 ± 0.2 □M at 72 h). The activity of **1** decreased about twenty-fold after its decomposition in cell culture medium for 30 min at 310 K. Complex **2** showed similar activities (IC_{50} ~12 □M at 72 h) in both fresh and decomposed solutions and was inactive in a short-term treatment. The activity of **2** was mainly due to the reactions between V(V) decomposition products, free catechol and O_2 in cell culture medium. As a result, the activity of **1** was less sensitive than that of **2** to hypoxic conditions that are characteristic of solid tumors and to the presence of apo-transferrin that acts as a scavenger of V(V/IV) decomposition products in blood serum.[5] These results demonstrate the importance of fine-tuning the ligand properties for optimization of biological activities of metal complexes.



[VO(Hshed)(dtb)] **1**

[VO(Hshed)(cat)] **2**

Scheme 1 – Structures of V(V) Schiff base -catecholato complexes, [VO(Hshed)(dtb)] (**1**) and [VO(Hshed)(cat)] (**2**).

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Ligand-specific structural features guide vanadium-dependent cell differentiation in adipogenesis

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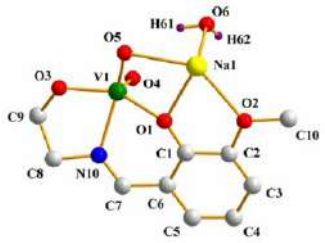
Metabolic syndromes have been plaguing the global community for decades on end, with incessant efforts on behalf of the scientific community to unravel cause and effect relationships at the molecular level, thereby bypassing painful drug administration to patients. Insulin emerges unequivocally at the center of the attention in Diabetes mellitus I and II, with repercussions due to insufficiently secreted quantities or absence hereof guiding pharmaceutical development and administration. Over the years, the side effects of known administered drugs have come to point out the need for alternative substances capable of alleviating symptoms of the disease, with potential candidates located in suitably formulated transition metal ions in the Periodic Table. Vanadium has been at the forefront of such research efforts with a certain number of molecular formulations synthesized and characterized physicochemically and biologically. Our approach has so far been based on the premise that atoxic forms of vanadium(IV,V) species could be produced through interactions of physiologically relevant substrates-binders, further bestowed with solubility and bioavailability, sufficient to warrant induction of early events in stem cell physiology that through adipogenesis could lead to mature adipocytes capable of taking up glucose and catabolizing it, thus contributing to the reduction of hyperglycemia.[1]

The approach was based on the synthesis of well formulated ligands, the structure of which emerged through modification of naturally occurring vanillin (and derivatives thereof), with binary partners a) exhibiting variable number of alcoholic moieties, capable increasing hydrophilicity while concurrently involved in hydrogen bond formation, and b) amply and efficiently pursuing Schiff base condensation to afford hybrid molecules, further seeking vanadium binding. The choice of vanadium oxidation state was made on the basis of the existing biologically relevant oxidation states of V(IV) and V(V), with the latter ion chosen for a start. The so interacting and arisen species were isolated in crystalline forms and characterized physicochemically

through an arsenal of techniques (e.g. FT-IR, NMR, CV, TGA, and finally X-ray crystallography) (**Scheme 1**). The characterized species were subsequently introduced in in vitro biological studies involving a) toxicity profile generation (viability, migration, proliferation, morphology), and b) cell differentiation studies involving known biomarkers linked to the processes of differentiation and subsequently maturation. The conducted work included cell lines akin to the pathology of the disease investigated, thereby providing insight into the potency of the employed binary V(V)-ligand species to induce adipocyte differentiation and maturation.

The results obtained suggest that a) the structure of the ligands binding V(V) plays an important role in tis chemistry and biological behavior, with the alcoholic moieties attached to that the ligand occupying metal ion binding sites, while concurrently participating in hydrogen bond formation, b) the adipogenic potential of the vanadium complex species relies on the nature of the ligand used and the number of alcoholic moieties differentiating the phenotypic behavior of vanadium inducing adipocyte differentiation. The collective physicochemical and biological results converge into formulated well-defined species of vanadium(V),[2] participating atoxically (in a concentration dependent fashion) to the adipocyte differentiation and maturation, thus setting the molecular basis of designing and synthesizing new hybrid molecular species[3] as potential candidates in assisting insulin or mimicking insulin to confront hyperglycemia in Diabetes mellitus II.



Scheme 1 – Structure of a representative V(V)-organic substrate species.

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Vanadium Effects on Lipid Peroxidation and Diseases

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Oxidation of lipids (i.e., LPO), is a process occurring in cells and tissues. LPO, a process that affects human health, can be induced by exposure to vanadium salts and compounds. LPO also relates to aspects of oxidative stress in disease. The primary biomarkers for LPO fall into several categories: ROS/RNS, LPO products, antioxidants and enzymes. Vanadium compounds interfere with these biomarkers. The extent of oxidative stress observed depends on the ratio of compounds with oxidative damage potential relative to the defense capacity of available antioxidants (Fig. 1). The variation in vanadium effects on cells, tissues or organisms results from vanadium's complex chemistry.

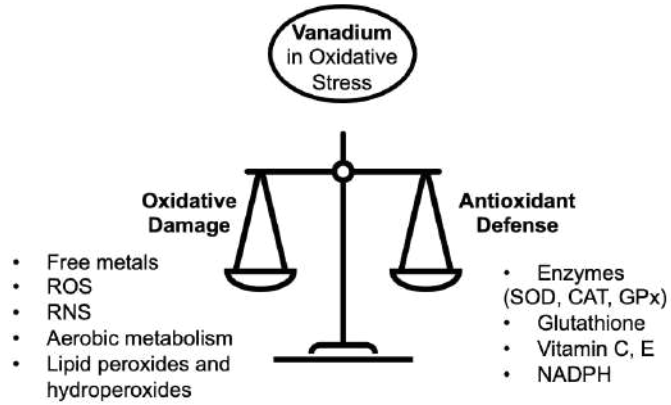

Figure 1. Molecules involved in oxidative stress with either unfavorable oxidative damage potential or the ability to provide antioxidant defense that is protective. Abbreviations: RNS, reactive nitrogen species; SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase[1].

Most published work studying LPO effects in biological systems has been carried out using vanadium salts. However, comparisons between the effects of monomeric vanadate (V_1) and decameric vanadate (decavanadate, V_{10}) highlight the marked differences in responses seen in studies using other vanadium compounds. This

communication will highlight the direct and/or indirect effects of LPO induced by V_{10}. V_{10} has been shown to have anticancer, antiviral and antibacterial activities, among others and, as a result, is perhaps the best-studied polyoxometalate (POM) in biology, affecting multiple biochemical and cellular processes[2,3].

In fact, the consequences of reactions of reactive oxygen species (ROS) and reactive nitrogen species (RNS) with major biomolecules such as proteins, lipids and nucleic acids, induces global structural modifications leading to denaturation and/or inactivation of proteins, lipid peroxidation, mitochondrial dysfunction, DNA damage and mutagenesis, among others (Fig. 2). Finally, the role of vanadium in lipid peroxidation and oxidative stress related on diseases processes, namely cancer, diabetes and neurological diseases such as Alzheimer and Parkinson will be analyzed.

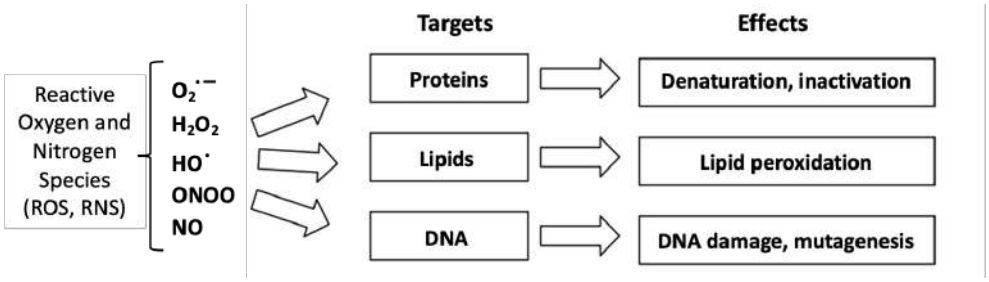

Figure 2. Vanadium induces changes in oxidative stress, leading to denaturation and/or inactivation of proteins, lipid peroxidation, DNA damage and mutagenesis[1].

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Playing with Decavanadates and Tetravanadates: A Story Full of Surprises

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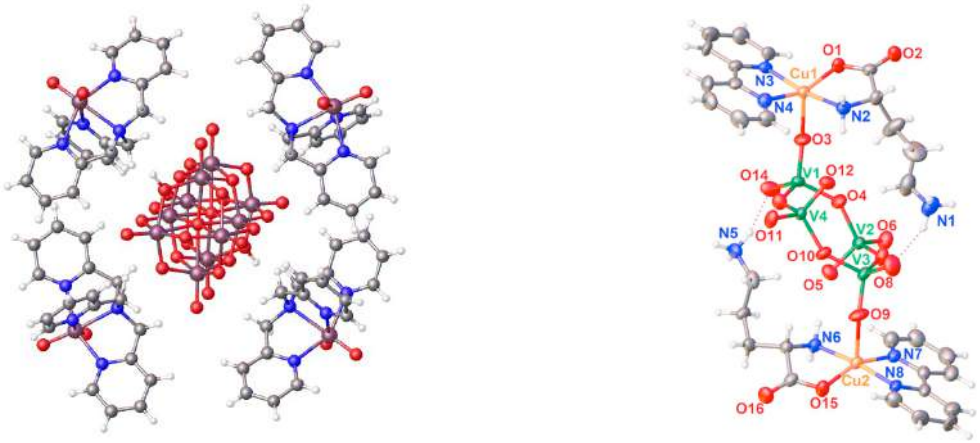
As often happens in science, serendipity appears unexpectedly. The unsuccessful synthesis of a bidentate ligand containing histamine for biomimetic purposes for heme-peroxidase model compounds ended with crystalline histaminium oxalate. By introducing a copper ion in between, the copper histamine oxalate complex was successfully prepared. A young student appeared in the lab, asking for a bachelor's thesis project. I thought inserting vanadyl ions in place of copper would be a good idea. Although we started with vanadyl sulfate, the vanadium was oxidized to vanadium (V), and beautiful yellow-orange crystals were obtained. Even though the refinement was difficult with histamine, we successfully crystallized the dimethylamino pyridinium decavanadate. Not only was it interesting from a structural point of view, but it also opened our biological studies on obesity, metabolic syndrome, and diabetes with encouraging results. To this, a series of Metforminium decavanadates followed by Cytosinium[1], 2-Aminopyrimidinium[2], and Tris (2-Pyridylmethylamine)$V(O)_2$ complexes as counter ions of Diprotonated Decavanadate[3], which are not only interesting structurally but with potential biomedical applications for diabetes and cancer. Knowing that decavanadate at physiological pH tends to form cyclotetravanadate ions, we have explored the possibility of copper-vanadium heterobimetallic compounds. We successfully synthesized casiopeina analogs containing lysine, ornithine, and glutamine coordinated with tetravanadate as possible double bullets for cancer therapy[4]. Thus, we are expecting more surprises in the future.



Scheme 1. Examples of Decavanadate and Tetravanadate compounds.

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In vitro and *in vivo* biological activity of dipicolinate oxovanadium(IV) complexes

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Vanadium compounds have been widely investigated due to a broad application in catalysis and a wide range of pharmacological properties. In the area of medicinal applications, the exploration of vanadium-based compounds has been focused on their insulin-mimetic properties, anticancer activities, antibacterial action, and effects on enzymes. Among oxidovanadium(IV) derivatives, a special attention has been devoted to bis(4,7-dimethyl-1,10-phenanthroline)-sulfatooxydovanadium(IV) (Metvan), which was found to induce apoptosis in leukemia, multiple myeloma, solid tumors such as breast, prostate, testis, and glioblastoma.
Most remarkably, Metvan is known to show high activity against cisplatin-resistant ovarian and testis tumor cell lines. The anticancer activity of vanadium coordination compounds can be assigned to different mechanisms, including DNA-binding, generating reactive oxygen species leading to oxidative stress, cell cycle arrest and programmed cell death, and it is widely modulated by ligand nature and geometry of the complex. Considering these data we have analysed the anticancer properties of dipicolinate (dipic) based vanadium(IV) complexes [VO(dipic)(N∩N)] bearing different diimines (2-(1*H*-imidazol-2-yl)pyridine, 2-(2-pyridyl)benzimidazole, 1,10-phenanthroline-5,6-dione, 1,10-phenanthroline and 2,2′-bipyridine), as well as differently 4,7-subsitiuted 1,10-phenanthrolines in different tumors (A2780, HCT116 and HCT116-DoxR) and normal (primary human dermal fibroblasts) cell lines. Our data reveals a high cytotoxic effect of [VO(dipic)(N∩N)] with 4,7-dimetoxy-phen (**5**), 4,7-diphenyl-phen (**6**) and 1,10-phenanthroline (**8**) against the HCT116-DoxR cells. The cytotoxicity differences between these complexes can be correlated with their different internalization by HCT116-DoxR

cells. Worthy of note, these three complexes were found to i) induce cell death through apoptosis and autophagy pathways, namely through ROS production; ii) not to be cytostatic; iii) interact with BSA protein; iv) do not promote tumor cell migration or a pro-angiogenic capability; v) show a slight *in vivo* anti-angiogenic capability, and vi) do not show *in vivo* toxicity in a chicken embryo.

Selective oxidation of volatile organic compounds in liquid phase over homogeneous and supported vanadium catalysts

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Volatile Organic Compounds (VOCs) emissions are a growing environmental concern, and catalytic oxidation is a promising approach due to its efficiency and cost-effectiveness, as well as the selective functionalization of aromatic hydrocarbons. However, the challenges associated with C-H bond breaking in industrial processes have driven the need for more efficient catalysts[1,2].

Vanadium complexes, specifically homogeneous and supported catalysts based on these complexes, were explored for the selective conversion of model substrates, toluene and xylenes[3-5]. The study explores various reaction parameters such as reaction time, temperature, type and amount of oxidant, and catalyst stability. The resulting catalytic systems yield oxygenated products such as benzyl alcohol, benzaldehyde, tolualdehyde, toluic acid, terephthalic acid, and benzoic acid, which have relevance in diverse industries including chemicals, agrochemicals, fragrances, pharmaceuticals, and polymers.

In summary, a comprehensive exploration of vanadium complexes as catalysts for the conversion of VOCs is presented, shedding light on their catalytic performance and potential applications in various industries.

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Oxovanadium(V)-Catalyzed Synthesis of Ureas Using Carbon Dioxide

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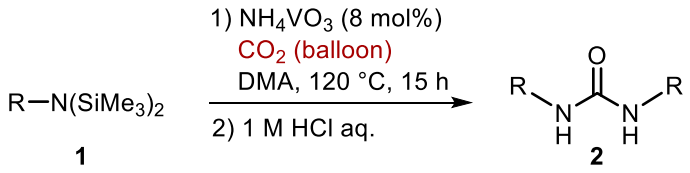
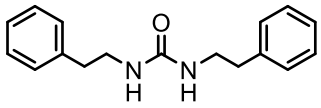
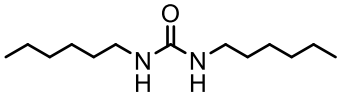
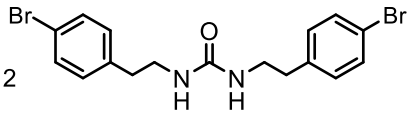
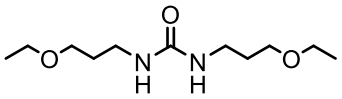
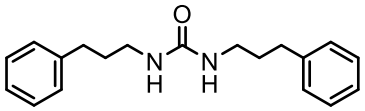
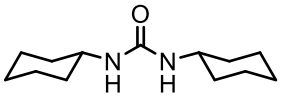
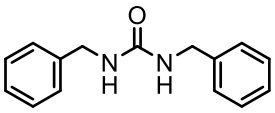
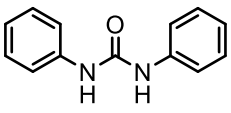
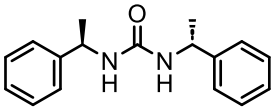
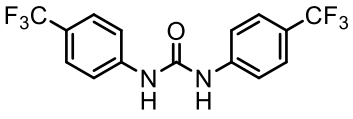
Ureas are important carbonyl compounds that widely used in pharmaceuticals, agricultural pesticides, and raw materials for resins. Conventionally, ureas are synthesized by using toxic or expensive reagent. Recently, the use of carbon dioxide as a carbon source for urea synthesis has attracted much attention. Some catalytic systems for urea synthesis using carbon dioxide have been reported, but generally require high carbon dioxide pressure. We have recently performed the oxovanadium(V)-catalyzed synthesis of ureas using carbon dioxide under ambient pressure.[1] In this catalytic system, the use of an air-sensitive oxovanadium(V) catalyst, MS3A as a dehydrating reagent, and *N*,*N*-diisopropylethylamine as a base were required. We herein report a practical catalytic system for urea synthesis from disilylamines and carbon dioxide under ambient pressure by using a commercially available easy-to-handle oxovanadium(V) compound.[2]

The reaction of 2-phenylethyl-*N*,*N*-bis(trimethylsilyl)amine (**1a**) with carbon dioxide (balloon) in the presence of catalytic amount of NH_4VO_3 was found to afford the corresponding urea **2a** in 95% yield (Table1, Entry 1). The catalytic reaction of alkyl-substituted disilylamines took place well to give the corresponding ureas in good yields (Entries 2-5). For example, 2-(4-bromophenyl)ethyl-*N*,*N*-bis(trimethylsilyl)amine (**1b**) was successfully converted into the corresponding urea **2b** in 76% isolated yield, in which the obtained urea can be utilized for further transformation using Br group (Entry 2). This catalytic system could be applied to the synthesis of the chiral urea **2e** (***R*,*R***) without loss of chirality (Entry 5). When disilylamines consisting of linear or cyclic alkyl groups were used, the catalytic

reaction proceeded smoothly to provide the corresponding ureas in good yields (Entries 6-8). In the case of phenyldisilylamines (Entries 9-10), the yields slightly decreased campared with those of alkyl-substituted disilylamines (Entries 1-8).

Table 1. $VO(O^iPr)_3$-catalyzed urea formation from **1** and carbon dioxide.[a]



Entry	Isolated yield [b]	Entry	Isolated yield [b]
1	 **2a**, 94%	6	 **2f**, 70%
2	 **2b**, 76%	7	 **2g**, 68%
3	 **2c**, 85%	8	 **2h**, 72%
4	 **2d**, 89%	9	 **2i**, 58%
5	 **2e (*R,R*)**, 77%	10	 **2j,** 54%

[a] Reaction conditions: **1** (0.60 mmol), NH_4VO_3 (8 mol%) in DMA (1.0 mL) under carbon dioxide (balloon) at 120 °C for 15 h. [b] Isolated yield (%) = [**2** (mmol) x 2 / **1** (mmol)] x 100.

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Catalytic activity of vanadium chloroperoxidase and its applications

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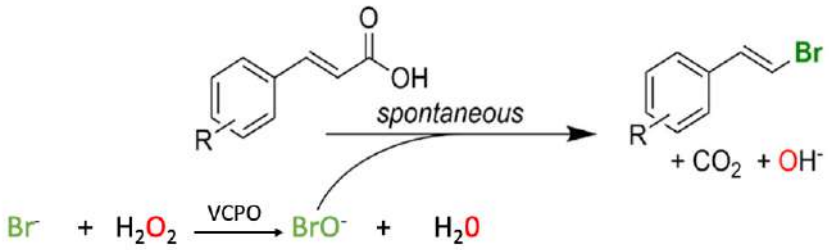
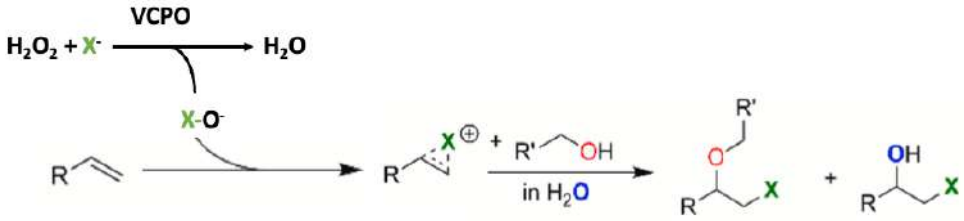
Activated electrophilic halogens are frequently used as common oxidants in organic synthesis and as halogenating agents. These highly reactive compounds yield in general undesired side products. In addition, these activated compounds are not stable and handling these compounds is a safety issue. Furthermore, considerable amounts of salt are generated. An alternative is to generate hypohalites form hydrogen peroxide and a halide using haloperoxidases. In the past the heme- containing chloroperoxidase from the fungus *Caldariomyces fumago* was used with limited success.[1] This was mainly due to the vulnerability of the enzyme to high concentration of hydrogen peroxide and its limited temperature stability. The vanadium chloroperoxidase (VCPO) from the fungus *Curvularia inaequalis* represent an alternative solution. This enzyme has a very high thermostability due to the compact packing of four alpha helices in its structure which exhibit a strong stabilizing effect. The enzyme also withstands very high concentrations of hydrogen peroxide of up to 0.5 M and furthermore most organic solvents do not influences the robustness of the enzyme.[2,3] Ethyl acetate in particular is a useful cosolvent since most substrates and products show good solubility and in addition it is easily removed by distillation.[3] A particular advance of the enzymatic catalytic system is that HOCl and HOBr are formed at a controlled rate and at a molecular level this results in the halogenation or modification of the most susceptible site of a molecule. In short, the VCPO has been successfully applied in the bromination of phenolics, formation of halohydrines and epoxides, halolactonisation of unsaturated carboxylic acids and alcohols, and the preparation of lactones at preparative scale. In general, the catalytic performance of VCPO with Br- as a substrate is superb,[4,5] the turnover frequencies are in the range of 15-70 sec^{-1} and the total turnover numbers (moles of product per mole of enzyme) are around 1 x 10^6. More recently the enzymatic bromo-decarboxylation of α,ß-unsaturated carboxylic acids was investigated.[6] I will discuss the previous conversions as well the more recent ones. Scheme 1 shows an example of decarboxylation catalyzed by VCPO. HOBr formed from Br^- and H_2O_2 reacts non-enzymatically with

the unsaturated carboxylic acid resulting in decarboxylation and the formation of vinyl bromide. Vinyl bromides are versatile intermediates in organic chemistry.



A problem in this reaction is that water interferes with this reaction by nucleophilic attack on the intermediate bromonium ion. As will be discussed this can be solved by medium engineering. The VCPO has also been used in intermolecular halo-ether synthesis (Scheme 2). In this case HOBr reacts with alkenes to form a bromonium intermediate which may react with water or an alcohol group as nucleophiles and both a halo-ether is formed as well as the unwanted halohydrin. The problems associated with this will be discussed.



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Mechanism of the Reductive Activation of O_2 to O_2^{2-} from a Vanadium(IV) Species and Its Potential Use in Fuel Cells

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The two electron reductive activation of O_2 to O_2^{2-} is of particular interest to scientific community mainly due to the use of peroxides as green oxidants and in powerful fuel-cells. Among the metal-ions which activate O_2, vanadium is of particular interest because of its numerous oxidative catalytic properties. Reaction of either $V^{IV}OSO_4{\cdot}3.5H_2O$ or $V^{IV}OCl_2$ with *N*-(8-quinolyl)pyridine-2-carboxamide (Hpbq) in CH_3OH solution under atmospheric O_2, at room temperature, resulted in the quick formation of $[V^{V}O(k^2\text{-}O_2)(pbq)(H_2O)]$(1). Compound 1 constitutes a rare example of formation of a (peroxo)oxidovanadium(V) complex from molecular O_2 and an oxidovanadium(IV) complex. The reaction of formation of compound 1*vs.* time was monitored by ^{51}V and ^{1}H NMR, UV-vis, cw-X-EPR, Resonance Raman spectroscopiesand cyclic voltammetry revealing the formation of a stable radical intermediate $[V^{V}O(k^2\text{-}O_2)(pbq)(H_2O)]^{+}$. Dynamic experiments in combination with computational calculations were used to elucidate the mechanism of the reaction. The galvanic cell $\{Zn|V^{III},V^{II}||$*cis*-$[V^{V}O_2(bpq)]$, $[V^{V}O(O_2)(bpq)(H_2O)]$,$[V^{IV}O(bpq)(H_2O)_2]^{+}|O_2|C(s)\}$ was manufactured, demonstrating that this technology can be used in $Zn|H_2O_2$ fuel cells generating H_2O_2 *in situ* from atmospheric O_2.

Acknowledgements: This work was co-funded by the European Regional Development Fund and the Republic of Cyprus through the Research and Innovation Foundation (Project: EXCELLENCE/1216/0515).

Oxidovanadium(V) complexes as reusable catalysts

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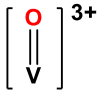
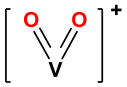
Vanadium complexes are well known as homogeneous catalysts and can exhibit interesting properties, such as high activity, enantioselectivity, and well-characterized structures.[1] However, their separation from the reaction products, recycling, and potential application to continuous-flow processes are difficult, which are easily achievable by heterogeneous catalysts. The possibility to combine the useful properties of homogeneous catalysts with the advantages of heterogeneous systems by anchoring them onto solid supports can overcome such limitations.[1,2]

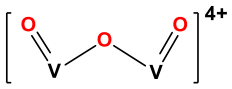
This presentation aims to explore the catalytic activity of various supported oxidovanadium(V) complexes towards different oxidation reactions (cyclohexane, 1-Phenylethanol and toluene oxidation) and compare their performances with homogeneous conditions.



Monooxidovanadium(V)



dioxidovanadium(V)



μ-oxido briged vanadium(V)

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Adventures in vanadium coordination chemistry with the Kläui ligand

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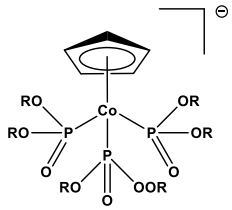
η^5-Cyclopentadienyltris-(dialkylphosphito-κ^1P) cobaltate(III), $(CpP^RCo)^-$ was first synthesized by Kläui, and it is often called the Kläui ligand (1), shown in Scheme 1. It has been recognized as a tridentate oxygen analogue of the well-used Tp (Trispyrazolylborate) ligand. Owing to the ligand's high stability, π-donation capability, and weak ligand field strength, organometallic complexes of $(CpP^RCo)^-$ were found to be quite different from the conventional Tp-based analogs. We have been using $(CpP^RCo)^-$ as a ligand to model the catalytic activity of industrially-used vanadium phosphate oxidation catalysts. Several vanadium precursors containing Kläui ligand have been synthesized and characterized. Also, the dinuclear organophoshorus-bridged vanadyl complexes with Kläui Ligand have been characterized as containing a VO_6 octahedral environment for the vanadium center. To explore the application of these vanadium-Kläui ligand complexes, the catalytic abilities were investigated employing 3,5-di-*tert*-butylcatechol to the corresponding quinone as a model reaction. We will present our latest work here, focusing on the coordination chemistry of the vanadium center.



R=Me, Et, Bu, ^{i}Pr

Scheme 1 – Structure of Kläui ligand, $(CpP^RCo)^-$.

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Understanding Polyoxometalate Speciation in Buffered Solutions: A Focus on Decavanadate

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Polyoxometalates (POMs), typically studied in their solid state, provide a structural foundation upon which solution chemistry is developed. Upon dissolution in aqueous environments, POM anions, like many compounds, can undergo protonation, hydrolysis, and even redox reactions, all of which influence the presence of active species[1]. As the utilization of POMs in aqueous solutions continues to expand, comprehending their speciation within various pH, temperature, incubation time, buffer type, presence of reducing or chelating agents, and ionic strength conditions becomes paramount. This knowledge is essential for attributing activity to the specific POM species present in solution.

In this contribution, we delve into the speciation profiles of commonly employed POMs with applications in catalysis and biology within aqueous solutions. For this study, we selected seven phosphorus-containing polyoxotungstates (POTs) of Keggin-, Wells-Dawson- and Preyssler-type, two polyoxomolybdates (POMos) of Keggin- and Wells-Dawson-type, two polyoxotungstates of Anderson-type and silicotungstic acid, as well as the prominent polyoxovanadate (POV) representative, decavanadate, $[V_{10}O_{28}]^{6-}$ (**V_{10}**, **Figure 1**). These selections were based on their widespread use in catalysis and biology and the presence of active NMR nuclei within the POM anions. Each of these ten POMs is meticulously characterized under 54 distinct conditions using a quantitative NMR spectroscopy-based approach, which is the most accessible method for elucidating processes within solutions. Our study focuses on the pH range from 3 to 9, which is often addressed using anionic buffers like acetic acid-sodium acetate, citric acid-sodium citrate, sodium phosphate (including phosphate saline buffer, PBS), and TRIS-HCl. Additionally, organic Good's buffers such as HEPES, MES, and glycine-NaOH cover this pH range. Biological investigations frequently require complex media to support the growth and well-being of the organisms being studied. Thus, we examined two media: Mueller-Hinton broth (MHB), which is a liquid medium for antibiotic susceptibility studies, and nutrient mixture F-12 Ham (Ham's), a serum-free medium for mammalian cell growth. The

speciation data were collected at pH values overlapping across different types of buffers. This approach allows us to not only assess the impact of solution pH but also consider the influence of buffer and media components. These components, typically perceived as relatively benign, can nonetheless play a crucial role in the stability, speciation, and effectiveness of POM applications.

This comprehensive speciation atlas of polyoxometalates not only advances our understanding but also establishes a new standard in the study of metal oxides in solution[2].

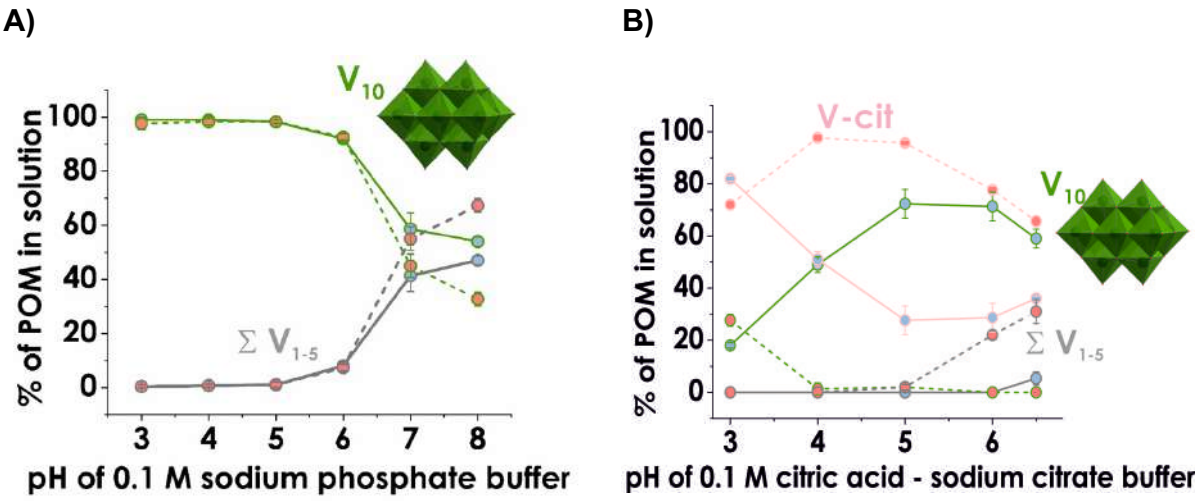

Figure 1 – POM concentration curves in $Na_2K_4[V^V_{10}O_{28}]$ (10 mM) in A) 0.1 M sodium phosphate buffer solutions and B) 0.1M citric acid – sodium citrate buffer solutions before before (solid line, blue dot in the middle) and after incubation (dash line, red dot in the middle) for 24 h at 37 °C.

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Technical Challenges for USEPA's Assessment of Vanadium and Its Compounds

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The US Environmental Protection Agency (USEPA) conducts health assessments of industrial compounds under a program known as the Integrated Risk Information System (IRIS).[1] IRIS assessments are widely recognized internationally. Previously, in 2011, an assessment of vanadium pentoxide was initiated but never completed, and it was deferred to a new assessment of vanadium compounds which was started in 2020. USEPA's assessment seeks to determine safe levels of vanadium substances in water and air, which are used by state and regional regulatory bodies to set discharge limits and evaluate permits. In addition, the assessments classify cancer risks, and a cancer risk assessment is conducted if it is determined to be needed. For the assessments of vanadium compounds USEPA decided to split the assessment into two parts, one for oral exposure[2] and one for inhalation[3]. The current IRIS process will be reviewed. USEPA's extensive documents from the first two steps in the IRIS process have been released from 2020-2023. The authors have raised a number of concerns about the reports issued so far and have pointed out flaws in separate submissions to the agency. Collectively, they have raised concerns for the accuracy and outcome of the assessments which are important since the outcome is likely affect the use allowable uses of vanadium in numerous jurisdictions internationally.

Chemistry errors in each of the documents are numerous and have obscured the clarity and identity of the compounds referred to in the assessment and these will be described from the released documents. In addition, references have been incorrectly cited for critical information. An important deficiency is that the form of vanadium that the public is exposed to is not known and opportunities exist for research in this important area.

Regarding the health information in the released documents key references have been omitted or incorrectly categorized as supplemental which raises concerns for the validity of the final assessment. Science questions have been formulated for

both the oral and inhalation assessments and these need to be revised to frame and provide direction for the development of science- based values. Data gaps in our knowledge will be discussed that need to be filled in to permit the assessment. The need for research will be described emphasizing important opportunities for future work. Finally, given the importance of vanadium as an official Critical Mineral in both the USA and EU, a case will be made for USEPA to host workshops to facilitate international expert vanadium scientists' discussions on environmental chemistry, identification of data gaps in our knowledge that will need to be filled in for the completion of the IRIS process.

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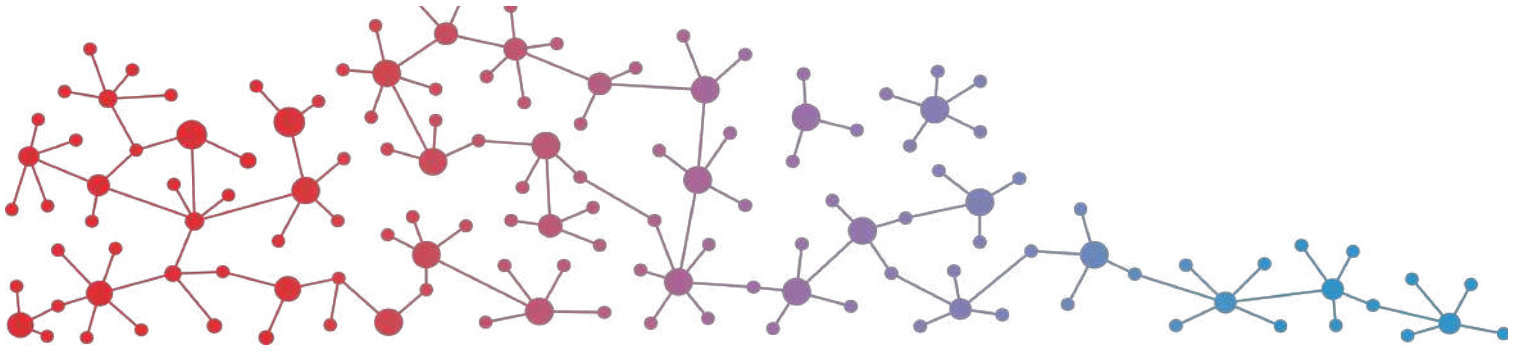
Acknowledgements: This work was funded by Vanitec.

13th INTERNATIONAL VANADIUM SYMPOSIUM

22nd – 24th NOVEMBER 2023

ORAL LECTURES



Vanadium Benzoylacetonate Complexes in the Treatment of Cancer

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[b]*Koç University, Sariyer, Istanbul, 34450, Turkey.*
[c] *TUBITAK, Kocaeli, 41470, Turkey.*
e-mail: r.ord@uea.ac.uk

The use of early metals as chemotherapeutics is very attractive, as they are cheap, readily available, and often better tolerated in the body than late/precious transition metals.[1] Over the past 5 years, there has been some progress in the use of vanadium for cancer therapy, emphasizing vanadium(V) compounds which interact with DNA,[2] and vanadium(IV) complexes which cause cell cycle arrest.[3] We developed a straightforward, fast (<5 mins), high yielding and environmentally friendly method for the synthesis of vanadium(IV) complexes.[4] The antiproliferative activity against a range of cancerous and normal cell lines was determined, highlighting particularly sensitive against lung carcinoma (A549). The compounds also interact with various DNA forms and show increased production of reactive oxygen species, whilst causing elevated levels of apoptosis and caspase-3/7.[4]

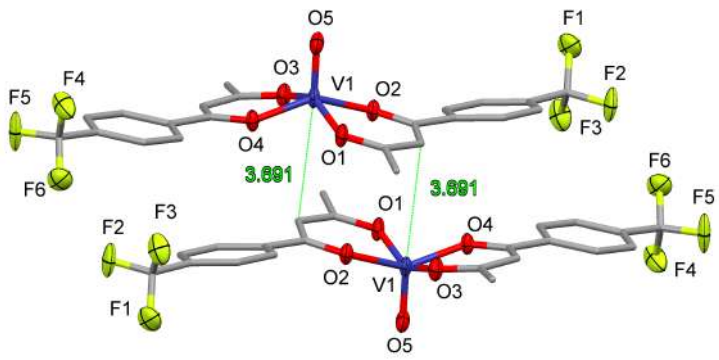

Figure 1 – An example of a vanadium(IV) benzoylacetonate complex.[4]

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Lindqvist polyoxovanadate-peptides conjugates for cancer cell targeting

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As reported in the literature, some polyoxometalates (POMs) exhibit anticancer activity: they are able to interfere with cellular redox processes, compete with ATP synthesis and inhibit different enzymes.[1] However, despite their interest, mostly related to the low cost of the drug candidates, POMs show low selectivity for cancer cells and turn to be too toxic.

In this communication, the antitumor activity and the selectivity of hybrid derivatives of the Lindqvist hexavanadate will be discussed.

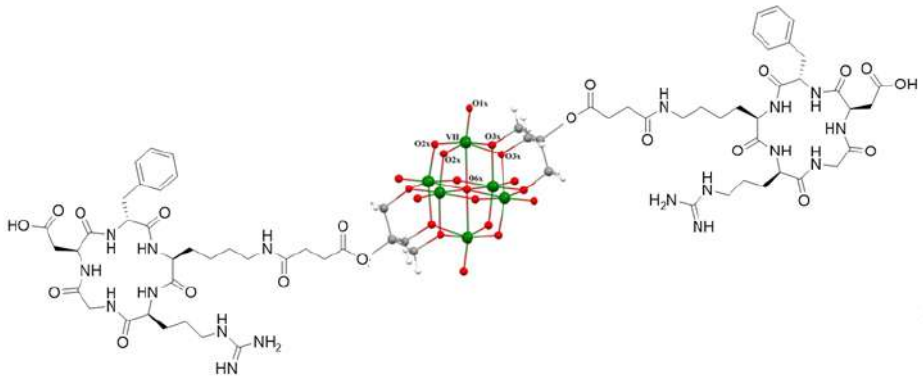

Figure 1: The hybrid organic-inorganic Lindqvist Hexavanadate $\{V_6O_{13}[(OCH_2)_3CCH_2OR]_2\}^{2-}$ used for peptide grafting (R=spacer + cyclopeptide).

The aim of the work is to explore the POMs' cytotoxicity when combined with suitable peptides (bombesin or RGD derivatives, Fig. 1), covalently attached to the POM. Spacers were also introduced to inhibit the interactions between the peptide and the POM, and avoid POM-induced undesired folding of the native peptide.[2] The synthesis and a combined 2D NMR, Circular Dichroism (CD) and Transmission Electron Microscopy (TEM) investigation will be presented to highlight the interplay between the two domains and the structural features of the most promising drug candidates, for which an increased biological activity, with respect to peptide-free POM, was finally assessed.

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Hydrazide-hydrazone: a linkage feature with a preponderant role in coordination chemistry and biological activity

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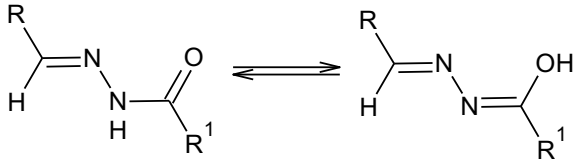
The high incidence of cancerous diseases, as well as other conditions, has led to the pursuit for new and improved chemotherapeutic drugs. In this respect, researchers sometimes use the combination of several bioactive molecules, and some linkage features seem to be advantageous. The hydrazide-hydrazone motif arises from the condensation of an aldehyde or ketone with a hydrazide, bearing the H_2N–NH–C(=O)– group, forming an imine-containing molecule. When starting materials are aromatic compounds, usually a final solid product is obtained that may be isolated with high purity. The presence of heteroatoms may provide this structure with coordination ability towards metal ions, especially when other donor atoms exist in the molecule. Such complexes exhibit several biological activities, namely as anticancer, antibacterial and antifungal.[1] However, a keto-iminol tautomeric equilibrium contributes to diversity in the coordination to the metal centers.



Scheme 1 – Keto-iminol tautomeric equilibrium of hydrazide-hydrazones.

Moreover, different species coexist, which will affect the results of *in vitro* and *in vivo* bioassays, as recently observed in our work with $V^{IV}O$-complexes.[2] Different examples of hydrazide-hydrazone containing complexes will be discussed, with a focus on their coordination modes and anticancer properties. Furthermore, the importance of speciation studies for the evaluation of the biological activity will be addressed. A quick survey over the literature reveals that often the antiproliferative ability is enhanced in the complex when compared to the ligand, an observation that will also be discussed, as well as a comparison of oxidovanadium(IV) systems with other metal complexes, namely Cu(II) and Zn(II).

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Comparing the effects on *Trypanosoma cruzi* of heteroleptic oxidovanadium (V) complexes with 8-hydroxyquinoline derivatives

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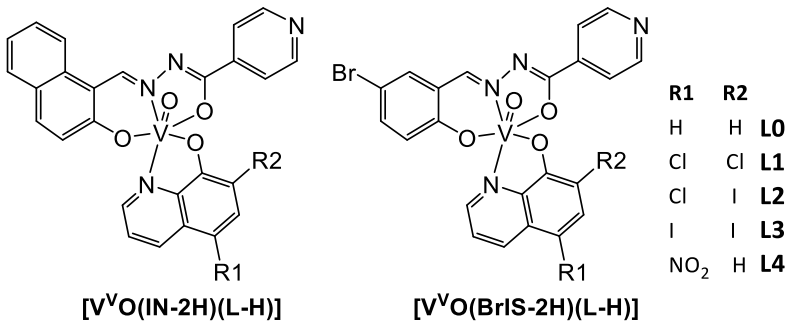
Chagas' disease is a neglected tropical disease (NTD-WHO) caused by the trypanosomatid parasite *Trypanosoma cruzi (T. cruzi)*. Searching for prospective vanadium-based drugs, we have previously developed complexes including 8-hydroxyquinoline derivatives as bioactive ligands (L) and a Schiff base tridentate ligand (IN), [V^{V}O(IN-2H)(L-H)][1]. In this work, we are extending the series incorporating a tridentate bromo-substituted Schiff base ligand (BrIS). Five new complexes, [V^{V}O(BrIS-2H)(L-H)], where synthesized and fully characterized. The complexes showed improved activity against the infective form of *T. cruzi* when compared with the previous series. Vanadium uptaken by the parasites was higher than the amount found for [V^{V}O(IN-2H)(L-H)] analogues and the accumulation in the insoluble proteins fraction increased. A trypanocide effect was observed when incubating with high doses of both series and the generation of ROS was suggested. Cell death mechanisms were analyzed, finding a higher apoptosis percentage for [V^{V}O(BrIS-2H)(L-H)] incubations. For [V^{V}O(IN-2H)(L-H)] series, the activation of autophagy as cell death mechanism was also suggested. This series could be considered prospective anti-*T. cruzi* agents that deserve further research.



[V^{V}O(IN-2H)(L-H)] **[V^{V}O(BrIS-2H)(L-H)]**

Scheme 1 – Previous series, [V^{V}O(IN-2H)(L-H)], and new series, [V^{V}O(BrIS-2H)(L-H)].

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Exploring decavanadate salts with cationic dyes: tackling multidrug resistance and colorant adsorption

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Polyoxovanadates (POVs), a subclass of polyoxometalates, includes decavanadate, $[V_{10}O_{28}]^{6-}$ or V_{10}, which deserves special attention due to its anticancer activities. Decavanadate is well known for interacting with phosphate-dependent proteins, such as ion pumps, ATPases and actin.[1] In spite of the numerous studies on the interaction of V_{10} and other higher-nuclearity POVs with a variety of biological targets and as anticancer drugs, no previous study has been carried out targeting ABC transporters associated with multidrug resistance. We investigated the use of POVs to inhibit the activity of ABC transporters by flow cytometry, using the fluorescent dye rhodamine 123 as a model substrate.[2] The POVs $[V_{10}O_{28}]^{6-}$ (**V_{10}**), $[H_6V_{14}O_{38}(PO_4)]^{5-}$ (**V_{14}**), $[V_{15}O_{36}Cl]^{6-}$ (**V_{15}**), and $[V_{18}O_{42}I]^{7-}$ (**V_{18}**) were evaluated in NIH3T3 fibroblasts overexpressing P-gp, ABCG2 and MRP1. All four POVs selectively inhibited P-gp, presenting IC_{50} values of: **V_{18}** (22.7 μmol L^{-1}) > **V_{10}** (25.4 μmol L^{-1}) > **V_{14}** (35.6 μmol L^{-1}) > **V_{15}** (58.8 μmol L^{-1}). Orthovanadate (**V_1**), a classic protein inhibitor, was 4 times less potent than **V_{10}**. No clear correlation was observed between the number of vanadium atoms and the potency of P-gp inhibition, since **V_{10}** and **V_{18}** were the two best inhibitors. To bring some light onto the inhibition mechanisms, two hybrid compounds containing V_{10} and fluorescent dyes that were not transported by P-gp, rhodamine B (RB) and methylene blue (MB), were synthesized. The novel $(RB)_4[H_2V_{10}O_{28}]\cdot 2RB\cdot 14H_2O$ (**RBV_{10}**) and $(MB)_4[H_2V_{10}O_{28}]\cdot 16H_2O$ (**MBV_{10}**) complexes were characterized by single-crystal and powder X-ray diffraction, spectroscopic techniques and thermogravimetric analysis. The inhibitory activity of **RBV_{10}** was similar to that determined for **V_{10}**, and confocal microscopy images suggested that the compound accumulates in the fibroblasts. **RBV_{10}** also inhibited P-gp-mediated efflux of two different well-known substrates, rhodamine 123 (Rho123) and the drug mitoxantrone. Moreover, a binding assay, using an antibody that recognizes conformational changes, suggested that V_{10} and V_{18} bind at different sites. **MBV_{10}**, in turn, was insoluble in water, preventing inhibitory studies with P-gp.

Still, this was the first time that single-crystal X-ray structures of a polyoxovanadate have been reported with these dyes. Noteworthy, the crystal packing of both V_{10} salts showed marked differences: in **MBV$_{10}$** alternating cations form a 1D chain defined by π-π interactions, while the V_{10} anion is fully embedded among de organic parts in **RBV$_{10}$** (Figure 1). Comparing the structures of the dyes with the packings observed in the salts was useful to explain our recent results involving the selective adsorption of MB over RB in heterogeneous aqueous media containing V_{10}.[3] Not only do these findings aid to overcome one of the major problems in oncology, but they might also contribute to improve the interaction models of cationic dyes when in the presence of large polyoxoanions.

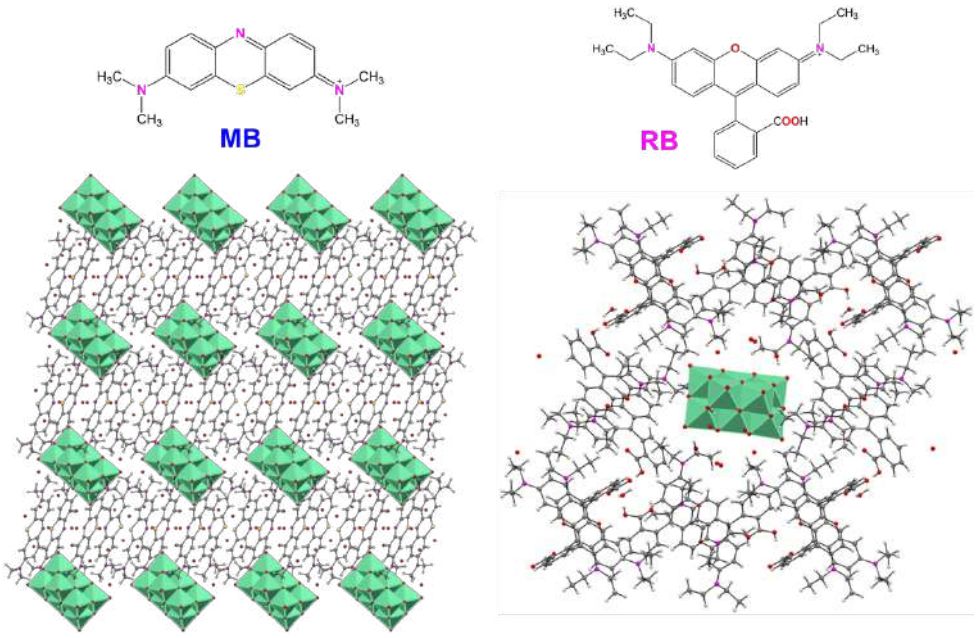

Figure 1 – Crystal packing of the salts $(MB)_4[H_2V_{10}O_{28}]\cdot 16H_2O$ (**MBV$_{10}$**, left) and $(RB)_4[H_2V_{10}O_{28}]\cdot 2RB\cdot 14H_2O$ (**RBV$_{10}$**, right).

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Vanadium complexes with hydrazone ligands and study of their biological interactions

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The interactions of the two series of hydrazone vanadium complexes with DNA by UV-vis spectroscopy and with BSA by UV-vis, fluorescence and circular dichroism spectroscopy were studied. The hydrazone ligands used were derived from pyridoxal monoaldehyde[1] and 2,6-diformyl-4-methylphenol, which condensed with different hydrazides. These compounds were characterized by elemental analyzed, IR, MS, ^{1}H NMR and X-ray diffraction of monocrystal (see two examples in **Figure 1**).

The DNA binding constants were calculated by the Benesi-Hildebrand equation[2]. The interaction constants, K_b, obtained are of the order of 10^3 and 10^4 M^{-1} (see an example in **Figure 2**).

BSA shows a strong fluorescence emission band at 340 nm when it is excited at 295 nm. The addition of increasing amounts of the compounds results in a gradual decrease of the emission band. Fluorescence quenching was used to quantify the binding interaction between the BSA and each compound by using the Stern-Volmer analysis[3]. The K_{SV} values obtained are of the order of 10^4-10^6 M^{-1} (see **Figure 3**). To study in which area of the BSA the compounds interact, the Stern-Volmer constant were calculated also in presence of site I and II markers (phenylbutazone and ibuprofen respectively).

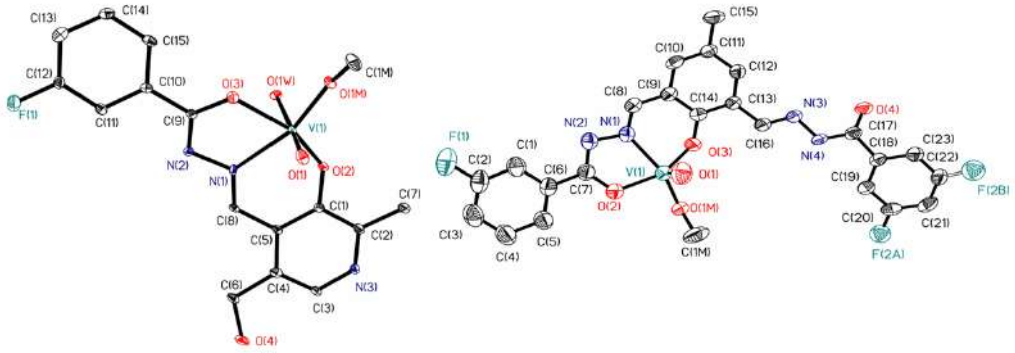

Figure 1 – X-ray crystal structures of vanadium complexes, **1** and **2**, respectively, with the ligands resulting in condensation of pyridoxal monoaldehyde (left) and 2,6-diformyl-4-mtehylphenol (right) with 3-fluorobenzoic hydrazide.

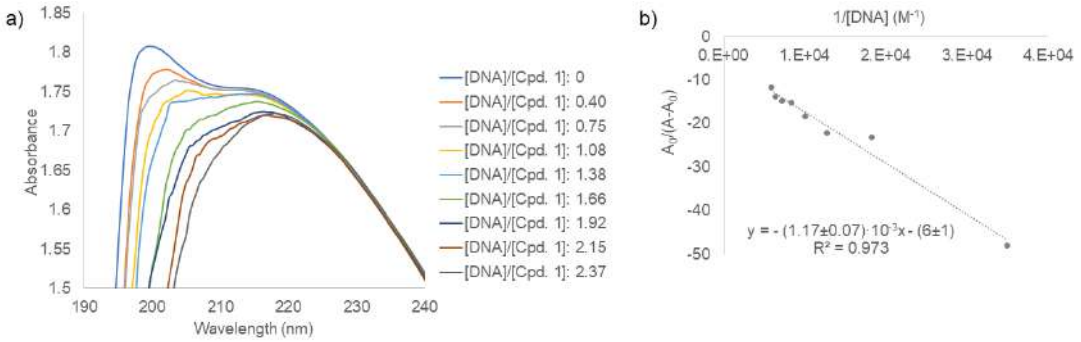

Figure 2 – Spectra of the vanadium complex **1**, with different concentrations of ct-DNA in PB solutions (pH = 7.2) with 10% of ethanol.

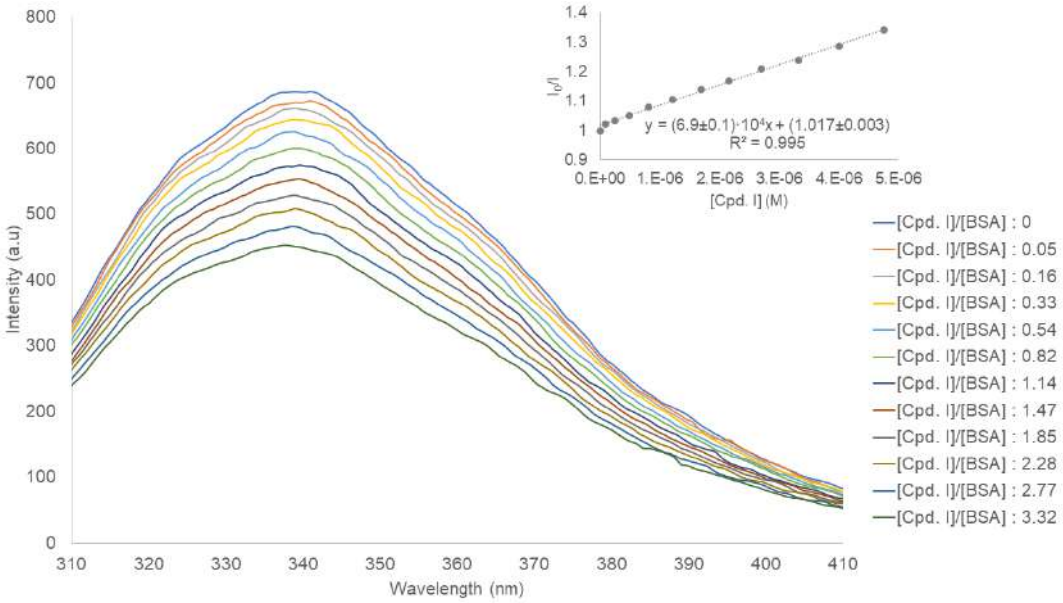

Figure 3 – Spectra of the vanadium complex **1**, with different concentrations of BSA in PBS solutions (pH = 7.2) with 5% of DMSO.

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Multi-technique characterization and speciation of oxovanadium(IV) aqueous systems: interaction with 8-hydroxyquinoline-2-carboxylic acid and 6,7-dihydroxycoumarin

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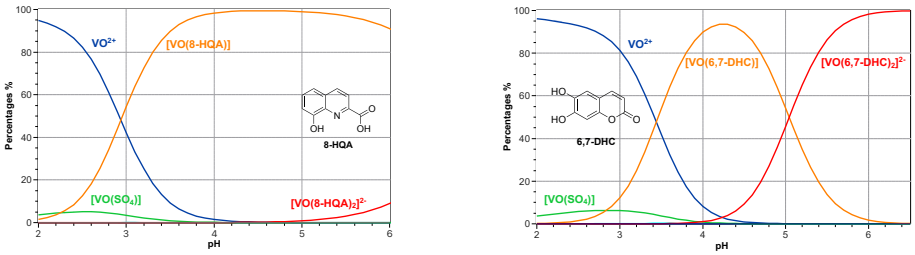
Vanadium ions possess interesting chemical and biological properties. Through all the oxidation states in which this metal could show off, the VO^{2+} ion represents one of the most relevant, having the ability to form coordination compounds with ligands such as metabolites, amino acid, and biomolecules.[1] Since the interaction of a certain ligand and a metal ion could enhance the biological activity of both components, several VO^{2+} coordination compounds showing different biological activities have been studied in the last decades.[2] Anyway, the aspects governing the stability of VO^{2+} coordination complexes, their biological activity and bioavailability are not yet fully understood . Therefore, the study of new coordination complexes of VO^{2+} and their speciation in aqueous solution and biological fluids remains an effective way to develop new biologically active compounds.

The interaction of VO^{2+} with quinolines and coumarins derivatives has been investigated in aqueous solution. 8-Hydroxyquinolines and hydroxycoumarins represent two families of naturally occurring compounds showing interesting biological properties and coordination abilities.[3,4] These two classes of compounds hold medicinal properties such as anti-inflammatory, antioxidant, antiallergic, hepatoprotective, antithrombotic, antiviral, antimicrobial, antineurodegenerative, anticancer, and antidiabetic activities. Specifically, the interaction of VO^{2+} with 8-hydroxyquinoline-2-carboxylic acid (8-HQA) and 6,7-dihydroxycoumarin (6,7-DHC) were considered. A multi-technique approach was adopted to describe the speciation of the VO^{2+}/8-HQA and VO^{2+}/6,7-DHC system in aqueous solution. Potentiometric and UV/Vis spectrophotometric titrations were performed, in $KCl_{(aq)}$ 0.2 $mol \cdot L^{-1}$ and T = 298.15 K. Voltammetric experiments as well as EPR and mass spectroscopy were

exploited to expand the characterization of the system. The binary systems were studied in solutions with a ratio of metal to ligand ranging (M:L) from 1:1 to 1:5, with a maximum concentration of the ligand of $1 \cdot 10^{-2}$ mol·L^{-1}. Since both systems showed instability due to the oxidation of the VO^{2+} ion at alkaline pH, experiments under oxygen exclusion were conducted to explore the system in the oxidation sensitive region. Combining the information obtained from all the different techniques, it was possible to achieve a good grade of knowledge about the chemistry of the two systems. The main species formed in the solutions at various pH values were identified. Hypotheses for stoichiometries and coordination modes were developed. Finally, the stability constants of the complexes were estimated and the speciation diagrams were obtained.



Scheme 1 – Speciation diagrams of (left) VO^{2+}/8-HQA (0.3/0.9 mmol·L^{-1}) and (right) VO^{2+}/8-HQA (0.3/0.9 mmol·L^{-1}) aqueous solutions.

The interaction between VO^{2+} and 8-HQA leads to the formation of two metal complexes, namely [VO(8-HQA)] and $[VO(8\text{-HQA})_2]^{2-}$, in the pH range considered (2-7). Similarly, in the VO^{2+}/6,7-DHC system two main complexes are observable (pH range 2-7): [VO(6,7-DHC)] and $[VO(6,7\text{-DHC})_2]^{2-}$. In both cases, the complexes are stable under aerobic conditions only up to pH 7. As previously mentioned, O_2 must be excluded to extend the stability range of the system.

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Development of two vanadium (V) Schiff-Base catecholate complexes: Relating stability and biological activity to structural modifications

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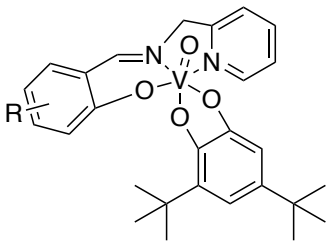
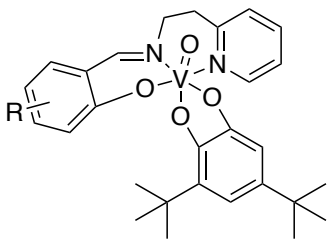
Development of therapeutics for difficult to treat or aggressive cancers, such as brain or pancreatic cancers, are needed.[1] The use of highly cytotoxic, short-lived metal-based complexes are advantageous to use for intratumoral injections to kill the cells and then rapidly decompose into less toxic components.[2] Recent publications from the Crans group have shown the development of several hydrophobic vanadium Schiff-base catecholate complexes with anticancer activity.[2,3] These complexes have been shown to be highly active, with the lead compound notable being twelve times more active than cis-platin, a commonly used anticancer therapeutic. Current design modifications have led to the use of pyridines as part of the Schiff-base scaffold, and with that two series of complexes have been designed and shown in Scheme 1: the [VO(SALIEP)(X)] series, and the [VOSALIMP)(X)] series, where X is a catecholate ligand (SALIEP = N-(salicylideneaminato)-N'-(ethylpyridine) and SALIMP = N-(salicylideneaminato)-N'-(methylpyridine)).[4,5] While these complexes are structurally very similar, their stability and biological activities are distinct and give further insight into the development of future complexes.



[VO(SALIMP)(dtb)]



[VO(SALIEP)(dtb)]

Scheme 1 – Structural comparison of [VO(SALIMP)(dtb)] and [VO(SALIEP)(dtb)].

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Vanadium coordination compounds derived from simple acetic acid hydrazide as non-conventional semiconductors

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Despite the extensive knowledge of various vanadium coordination complexes and their applications,[1,2] the investigation of their electrical/dielectric properties is still an unexplored, mystified area.[3,4] The literature abounds with vanadium compounds prepared by reactions of vanadium with different hydrazone ligands, most often aroyl-hydrazones. However, there is a scarcity of coordination complexes prepared from simple hydrazones, specifically acyl-hydrazones. Therefore, the synthetic aspect of this research was focused on the preparation of V complexes through reactions with hydrazones, derivatives of acetic acid hydrazide. For the hydrazone preparation 2-hydroxybenzaldehyde, 2-hydroxy-3-methoxybenzaldehyde, and 2-hydroxy-5-nitrobenzaldehyde were used. The aim was to investigate the influence of the substituents on the benzene ring of the ligand on the nature of the vanadium complex.

Further, the electrical characterization of the prepared vanadium complexes aimed to explore their (di)electric properties using the *in situ* method of Solid-State Impedance Spectroscopy (SS-IS) in a wide frequency and temperature range and to study how potential structural changes, induced by temperature, affect the electrical conductivity. The SS-IS method is sensitive enough to monitor structural changes and transformations that occur, and the obtained results are correlated with thermal and structural features. Obtained knowledge will contribute to the advancement and understanding of this group of materials.

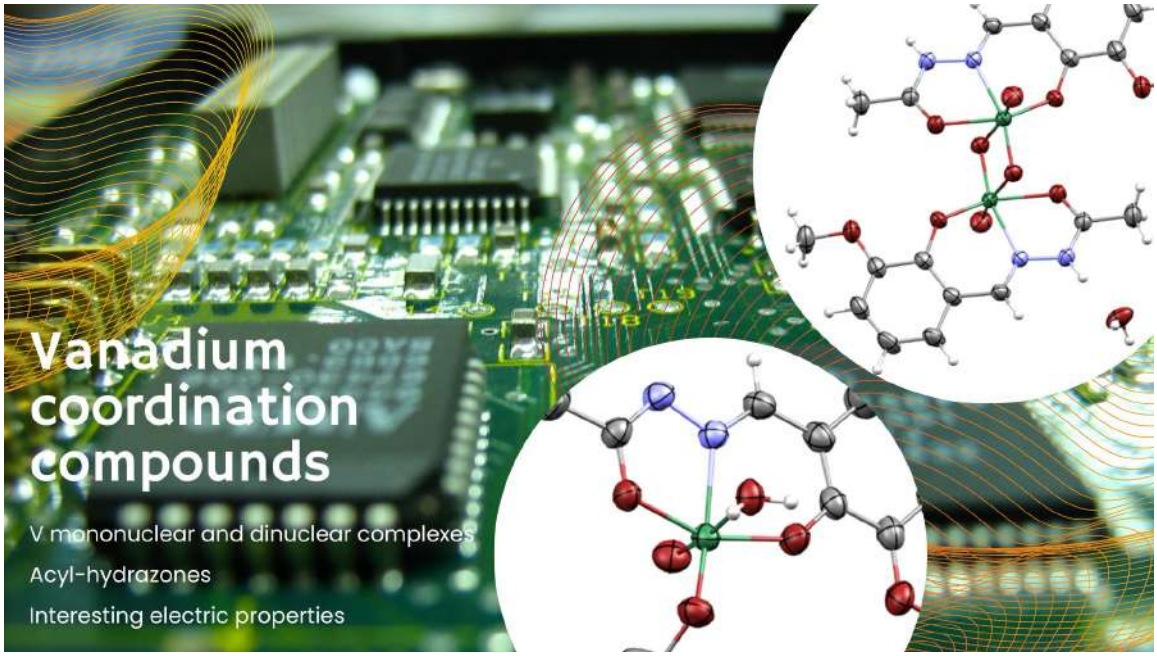

Figure 1 – Vanadium coordination compounds.

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C-C oxidative bond cleavage in diols promoted by vanadium catalysts: insight from relativistic DFT calculations

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An accurate computational analysis focused on C-C oxidative bond cleavage in diols in presence of the V^V-aminotriphenolate complex VO-TPA(Cl,Cl) is presented.[1] In particular, we investigate the role of the substituents on substrates of general formula $R_1R_2C(OH)C(OH)R_3R_4$ (R_i=H, CH_3, Ph) in the key-step of conversion of the alkoxide to the V-product (**Figure 1**).

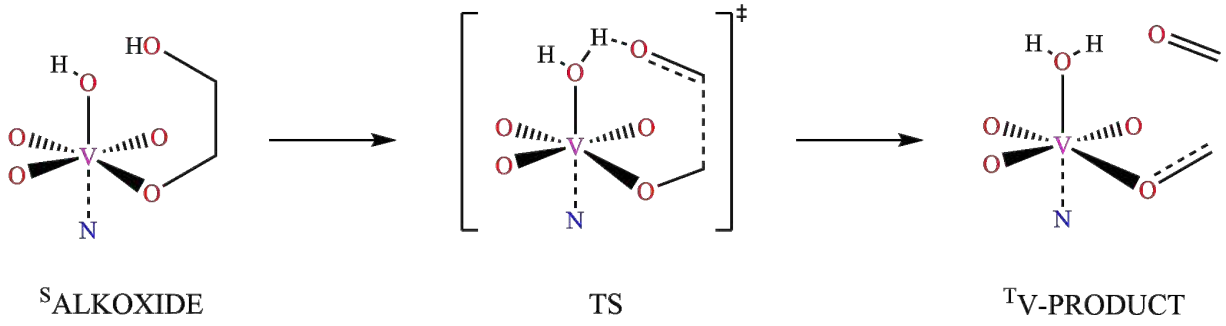

Figure 1 - C-C cleavage: schematic structural representation of alkoxide, transition state and V-product.

Since reactants and products lie on different electronic potential energy surfaces, the thermal mechanism on the singlet as well as triplet state is explored. The diradical nature of the transition state is analysed using the broken-symmetry formalism. Finally, spin orbit relativistic calculations are performed. By comparing the energetics and the separation between the electronic states of the different systems, we find nice agreement with the experimental evidence that, in vicinal diols, the presence of substituents leads to an easier C-C bond cleavage. The trends of the activation energies are rationalized in the frame of the activation strain model.[2]

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Comparison of the catalytic activity of oxovanadium(IV) and cobalt(II) complex compounds in the oligomerization of ethylene

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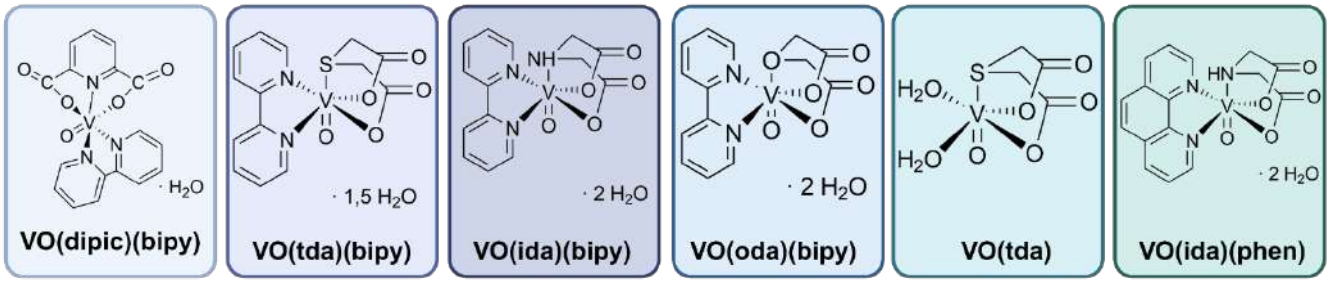
The process of oligomerization and polymerization of olefins, especially ethylene, is an ever-growing field in the world of polymer chemistry. Currently, research is largely focused on the search for new catalysts for the polymerization and oligomerization of this compound[1]. The most versatile and widespread polymeric material in the world is polyethylene, and the production of polymers and ethylene oligomers is of great importance especially in industry. Thanks to its versatility, it can be used, for example, in the production of packaging, films, tubes or bottle caps[2,3].

The discovery of complex catalysts by Brookhart's group in the 1960s ushered in a new generation of catalytic materials to produce polyethylene. With this finding, research on olefin polymerization catalysts increased in intensity and popularity. Since then, a multitude of complex compounds have been presented in the literature that can proudly act as active catalysts for the polymerization and oligomerization of ethylene. The catalysts presented so far are mainly based on copper(II), chromium(III) and nickel(II) ions. Processes using the presented catalysts have many disadvantages, such as the need for high pressure or instability at high temperatures and the use of environmentally hostile metal salts. Reviewing the literature, we will not find many publications concerning highly active catalysts for ethylene oligomerization; the articles appearing mainly concern the use of materials based on chromium(III) and nickel(II) ions. It is therefore of paramount importance to search for new catalytic materials that overcome the drawbacks of the currently used catalysts, consist of new safer metal ions, and revolutionize the world of ethylene polymerization[3,4].

We have conducted studies to assess the catalytic activity, in the ethylene oligomerization, of a series of 9 complex compounds containing oxovanadium(IV) and cobalt(II) ions, along with organic ligands in their structure.

The roles of the ligands were played by anions of organic compounds such as dipicolinate anion (dipic), 2,2'-bipyridyl (bipy), thiodiacetate anion (tda), oxydiacetate anion (oda), iminodiacetate anion (ida), 1,10-phenanthroline (phen) (**Scheme**).



Scheme - Vanadium(IV) complexes used as catalysts in the research.

Each compound was used as a precatalyst for the ethylene oligomerization reaction, after prior activation with modified methylaluminoxane (MAO-12). The process was carried out at relatively low temperatures of 80 °C, under a constant ethylene pressure of 0.5 bar and in a nitrogen atmosphere. The resulting oligomerization products were then analyzed by MALDI-TOF-MS, TG, DSC techniques and examined by SEM to determine the physicochemical parameters of the resulting oligomers. In a final step, the catalytic activity values of each of the tested compounds were determined and compared to determine the most active catalyst in ethylene oligomerization and to compare the influence of the structure of the complex compounds on the catalytic activity. All catalysts used in ethylene oligomerization showed activity in the range of 600-1700 g · $mmol^{-1}$· h^{-1}·bar^{-1}.

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Photocatalytic oxidation of Lignin models using V^v-aminotriphenolate complexes

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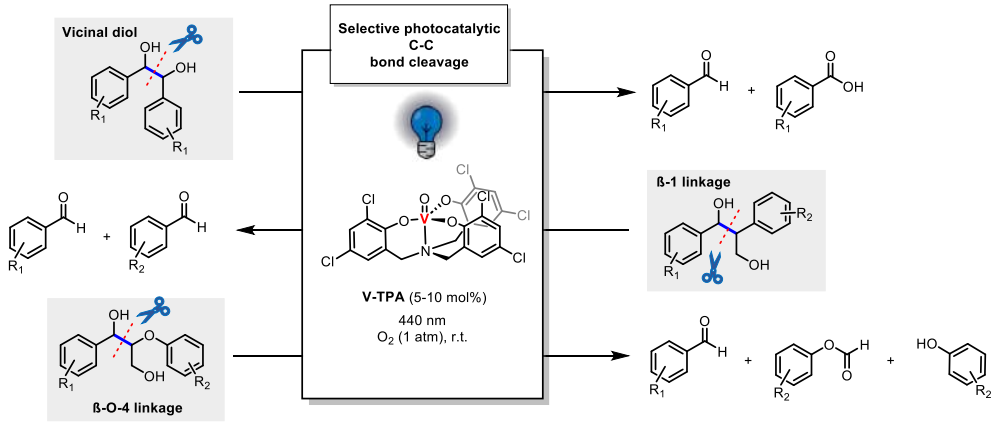
The exploitation of biomass waste materials, in particular lignin, is proposed as a valid solution for the replacement of current non-renewable sources. However, the complex and irregular structure of this biopolymer difficult the obtention of target aromatic organic molecules. Most of the traditional lignin degradation catalytic methods use harsh conditions without reaching high levels of selectivity. However, in recent years photocatalysis in combination with earth-abundant metal catalyst has emerged as a promising methodology for the selective depolymerization of lignin under mild conditions.

Our goal for this communication is to present the aerobic oxidative bond cleavage of Lignin models catalysed by aminotriphenolate complexes of vanadio[1] under visible light at room temperature. Under these conditions, vicinal diols, β-1 and β-O-4 lignin models have been studied, affording high-value aromatic products as carbonyl compounds or phenols with high selectivity.



Scheme 1 – Photocatalytic aerobic C-C bond oxidative cleavage of lignin models.

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Green synthesis of 2-cyanopyrazine by gas phase ammoxidation using vanadium-containing catalysts

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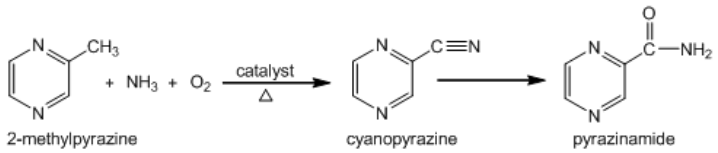
Heterogeneously catalyzed ammoxidation is an important industrial process for producing nitriles from olefins, alkyl aromatics and hetero aromatics in a continuous gas phase process [1]. This approach is also more eco-friendly, sustainable, economic, clean and green route for the synthesis of a large number of industrially important nitriles [1]. In particular, ammoxidation of 2-methylpyrazine (MP) to 2-cyanopyrazine (CP) is of special commercial significance, because the desired product CP is further used in the synthesis of pyrazinamide, an effective anti-tubercular drug (Scheme 1). Vanadium-containing materials are most promising catalysts for the ammoxidation of MP. In this contribution, we describe the application of novel metal vanadates as efficient catalysts for the ammoxidation of 2-methylpyrazine.



Scheme 1. Gas phase ammoxidation of MP to CP

Various bulk metal vanadate catalysts (M = Al, Fe, Cr, Nb, La and Bi) were synthesized according to the procedure described elsewhere [2]. NH_4VO_3 is used as a source of vanadium, while metal nitrates are used as precursors for all employed metals. In total, six different metal vanadates were prepared and tested. At first, the metal to vanadium atomic ratio was kept constant at 1 : 1. The prepared catalysts were initially dried at 110 °C for 16 h and then calcined under air flow in the temperature range from 500 to 600°C depending upon the type of metal vanadate. The catalysts were characterized by various techniques such as ICP-OES, BET-surface area, X-ray diffraction, FTIR, XPS etc. Catalytic tests were carried out in a fixed bed stainless steel reactor in the temperature range from 300 to 460°C. The products were collected in a cold trap and analyzed by Gas chromatograph equipped with FID and methanizer.

X-ray diffraction (XRD) patterns confirmed the formation of well crystalline orthovanadates in all the metal vanadate catalysts except $AlVO_4$. In case of $AlVO_4$, two crystalline phases were found such as V_2O_5 and $AlVO_4$ phase. BET surface

areas of these metal vanadates are found to vary in the range from <5m^2/g to ~35m^2/g, depending upon the nature of metal employed in metal vanadate catalyst. X-ray photoelectron spectroscopy (XPS) revealed the enrichment of vanadium in the near-surface-region, which again depends upon the type of metal present in metal vanadate catalyst. Catalytic tests showed that the conversion of MP (X-MP) is observed to increase continuously with increase in reaction temperature and reaching almost 100% conversion in the temperature range of 360 to 440°C, depending upon the catalyst composition. Among all, $AlVO_4$ was found to be highly active but less selective. $NbVO_5$ exhibited the best performance in terms of yield of CP (Y-CP=69%) followed by $LaVO_4$ (Y-CP=62%) at almost total conversion of MP. Furthermore, some additional products were also formed such as pyrazine (Py), pyrazinamide (PyA) and carbon oxides (CO_x). Based on the performance, optimization of Nb/V and La/V ratios was carried out in subsequent experiments. These results revealed that $LaVO_4$ catalyst with an optimised La : V ratio of 0.1 : 0.9 has improved the yield of CP significantly to 86% at nearly 100% conversion of MP. Additionally, the space-time-yield (STY) of CP was also enhanced further to ca. 525 $g_{CP}/kg_{cat}/h$, which is the highest value reported so far in the literature.

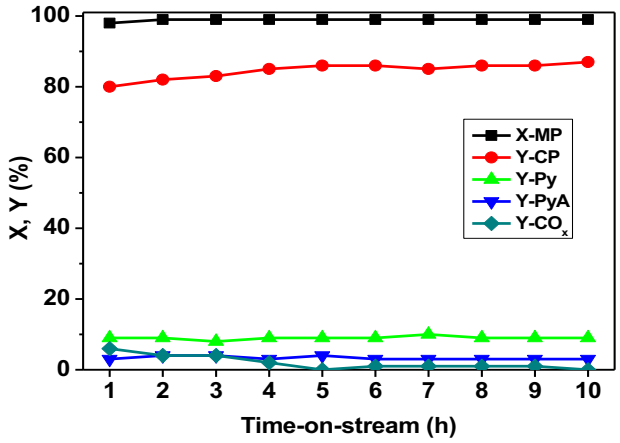


Fig. 1. Time-on-stream behaviour of $LaVO_x$ catalyst (La:V=0.1:0.9)

Results revealed that the nature of metal in a metal vanadate has shown strong influence on the surface V/M ratios and phase composition. Surface V/M ratios play a key role on the activity and selectivity. Tuning the surface composition is an important aspect for developing highly efficient catalysts. Optimization of La/V ratio remarkably improved the yield of CP with extremely high space-time-yields. Almost 100% conversion of MP with 86% yield of CP could be successfully achieved using an optimised $La_{0.1}V_{0.9}O_x$ catalyst in a gas phase continuous ammoxidation process.

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Protein metalation by vanadium compounds: structural studies

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The interaction with proteins plays a crucial role in uptake, transport, storage, toxicity and mechanism of action of metallodrugs.[1-2] Recently, details of interaction between several biological macromolecules and metal-based drugs are being revealed structurally.[3] Selected examples of recent crystallographic studies disclosing details of the protein metalation process by vanadium compounds will be presented.[4-7] The structural analysis allows to obtain crucial information to understand in more depth the molecular mechanisms at the basis of biological activity of the analyzed vanadium compounds and of the recognition by their specific biomolecular targets.

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Vanadium-based catalyst design guidelines using an explainable Machine Learning model for predicting epoxidation yields

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Vanadium complexes are commonly described as suitable catalysts for industrial epoxidation of small alkenes and allylic alcohols. Despite being a valuable chemical commodity, epoxide production depends on fossil-fuel feedstock, making this high revenue industry one of the largest carbon emitters[1]. To provide environmental and chemical sustainability, chemists turned to tunable vanadium catalyst design to streamline epoxidation feedstock consumption and energy optimization. But given the complexity of these mechanisms, time-consuming empirical approaches often cannot provide relevant mechanistic and kinetic information.

To address trial-and-error testing limitations, Data Science tools can estimate optimal catalyst chemical features correlated with high epoxidation yields[2]. By analyzing large volumes of raw epoxidation data, Machine Learning (ML) models use chemical descriptors encoding key structural information to outline physicochemical characteristics of optimal catalysts. These models can predict activities for molecules possessing similar descriptor values for the specific chemical space, thus generating new chemical entities. But the design of these epoxidation catalysts often fails because of the lack of computational libraries encoding relevant reaction parameters.

In this communication, we outline vanadium-based catalyst design guidelines using an explainable computational model for predicting epoxidation yields of allylic alcohols and alkenes. We showcase how we built an in-house *in silico* dataset of 273 epoxidation reaction with key vanadium-catalyst and experimental descriptors to feed a ML ensemble algorithm capable of predicting epoxidation yields with 91% accuracy (**Figure 1**). Using explainable feature correlation data over 90000 data-points, we were able to forecast vanadium catalyst and ligand features associated with high reaction yields with a maximum error of 4.1%. Ligand features of vanadium catalysts scaffolds $VOSO_4$, $VO(O\textit{i}Pr)_3$, and $VO(acac)_2$ were revealed to have higher importance in model accuracy, as elevated electronic and surface area descriptors disclosed higher prediction error trends. We argue this as an intuitive model framework capable of

revealing relevant chemical characteristics for catalyst design, towards automatic epoxidation reaction optimization.

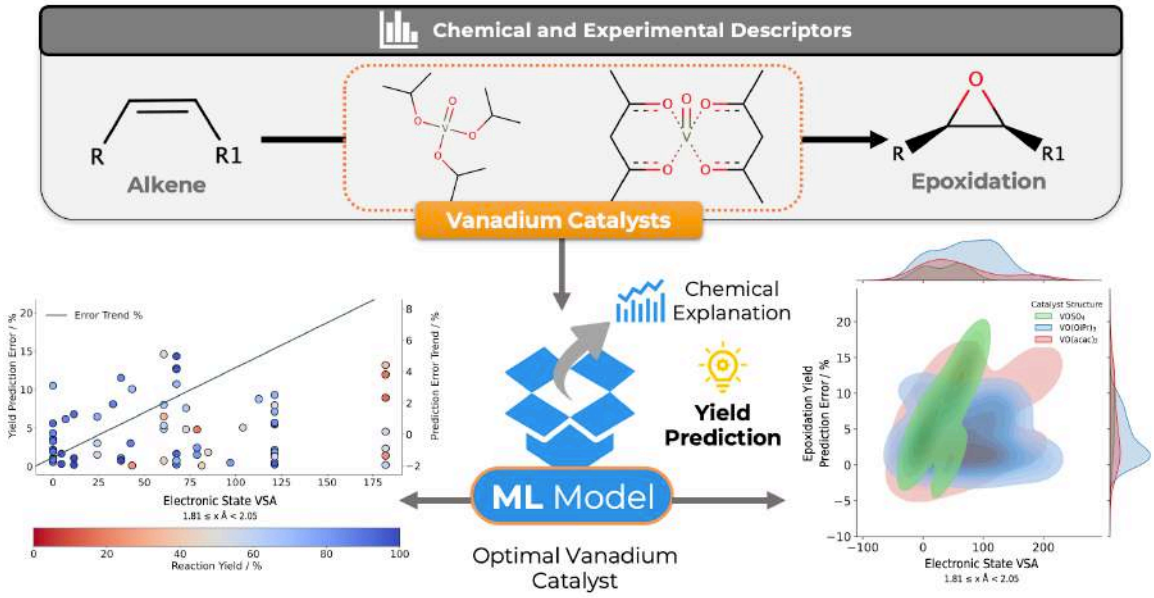

Figure 1 – Workflow for catalytic epoxidation yield model prediction using an explainable ML-based model.

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Increasing temperature sensitivity for ^{51}V NMR thermometers through ligand-to-metal charge transfer

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Designing molecules with variable-temperature magnetic resonance characteristics is vital to non-invasive imaging of temperature. Among many magnetic resonance characteristics, the chemical shift of a nucleus is a spectroscopic signature, where the resonant frequency directly reports as a probe on the local temperature. Toward better, higher sensitivity thermometers, molecular design can control and improve temperature sensitivity. The vanadium nucleus is of interest due to its wide chemical shift window, high natural abundance, and its relatively small quadrupolar moment among transition metal nuclei. Presented is a design route of amplifying temperature sensitivity of the ^{51}V chemical shift via ligand-to-metal charge transfer electronic structure design criteria. To test our hypothesis, the structural, electronic spectroscopy, and variable-temperature ^{51}V NMR spectroscopic properties of a series of complexes are reported: [VO(3-OEtHshed)(tbad)] (**1**, tbad = 3-(adamantyl)-5-(*tert*-butyl)-benzene-1,2-diol, 3-OEtHshed = (*E*)-2-ethoxy-6-(((2-((2-hydroxyethyl)amino)ethyl)imino)methyl)phenol), [VO(3-OEtHshed)(cat)] (**2**, cat = catechol), and derivatives. All complexes synthesized were characterized by ^{51}V, ^{1}H NMR, FT-IR, and UV-Vis spectroscopies. Multiple isomers are present in the solution ^{51}V spectra for complexes **1** and **2,** which are attributed to the catechol ligand. The influence of the catecholate ligand on electronic structure will be discussed and potential tuning of $\Delta\delta/\Delta T$ via ligand design will be presented.

Acknowledgements: The authors thank the National Science Foundation for support of this work (CHE-2047325) and Colorado State University.

Oxidovanadium(IV) complexes containing 8-hydroxyquinoline Schiff bases – synthesis, characterization and biological screening

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The growing recognition of vanadium's involvement in various biological processes has increasingly motivated research in the design of novel metal-based anticancer compounds.[1]

8-Hydroxyquinoline derivatives form stable complexes with different metal ions that also present interesting pharmacological profiles. In fact, recently published results obtained by our group with Zn(II)- and Cu(II)-complexes of 8HQ derivatives bearing piperidine/morpholine moieties indicated significant cytotoxicity (IC_{50} < 10 μM) in melanoma cells.[2] These results, together with our interest in developing new metallodrugs based on oxidovanadium(IV), prompted us to use the same Schiff bases (**L1**-**L3**) to prepare new vanadium species with potential biological activities (**Figure 1**).

The complexes were characterized by mass spectrometry, FTIR and UV–visible absorption spectroscopies as well as by single-crystal X-ray diffraction. Given that vanadium complexes are susceptible to undergo oxidation in air-exposed solutions, their stability in organic/aqueous media using UV-Vis spectroscopy was also determined.

Considering that the Cu(II)-complex with **L2** was the most promising one, **[V(IV)O(L2)$_2$]** was selected for an antiproliferative screening in both human and murine colon carcinoma/melanoma cells, and the results are comparable with related metal (Zn, Cu, Fe, Ni) compounds. This complex exhibited high antiproliferative properties towards all cell lines tested, particularly for the human cancer cell lines, with IC_{50} values < 10 μM, following a 48 h incubation period. Moreover, it demonstrated a higher cytotoxic potential than 5-fluorouracil (5-FU), which was used as a positive control. In addition, a synergistic effect was also observed when **[V(IV)O(L2)$_2$]** was combined with 5-FU. Ongoing *in vitro* studies are being conducted aiming to unravel the mechanism(s) of action.

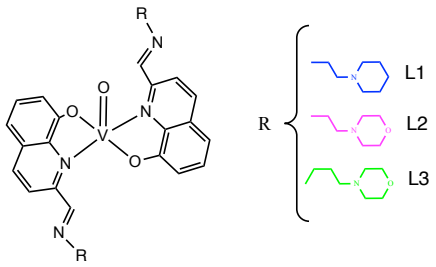

Figure 1 – General structure of the new oxidovanadium(IV) complexes.

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A comparative study of vanadium extraction from different concentrates by the salt roast-water leach process

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The salt roast-water leach process is widely applied to extracting vanadium from vanadium titanomagnetite (VTM) concentrates and metallurgical slags. In VTM ores vanadium as V^{3+} is typically found replacing Fe^{3+} in magnetite, though some V^{4+} is known to occupy the Ti^{4+} sites in ilmenite[1]. Under oxidizing conditions in the presence of sodium salts, vanadium is converted to water soluble sodium vanadate compounds such as $NaVO_3$. In the following leaching stage, these dissolve in water[2].

$V_2O_3 + Na_2CO_3 + O_{2(g)} \rightarrow 2\ NaVO_3 + CO_{2(g)}$

$NaVO_3 + H_2O \rightarrow Na^+_{(aq)} + H_2VO_4^-{}_{(aq)}$

After studying the application of the salt roast-water leach process to three VTM concentrates (VTM-A, VTM-B, weathered VTM) and one V/Fe concentrate (V-Mag), some general trends begin to emerge. Increasing the addition of sodium carbonate increases the amount of vanadium dissolving, up to a point. Higher sodium carbonate addition results in fusing, and the formation of water-soluble silicates. Sodium sulphate does not form soluble silica species but can be less effective for extracting vanadium than roasting with carbonate at the same temperature and salt addition.

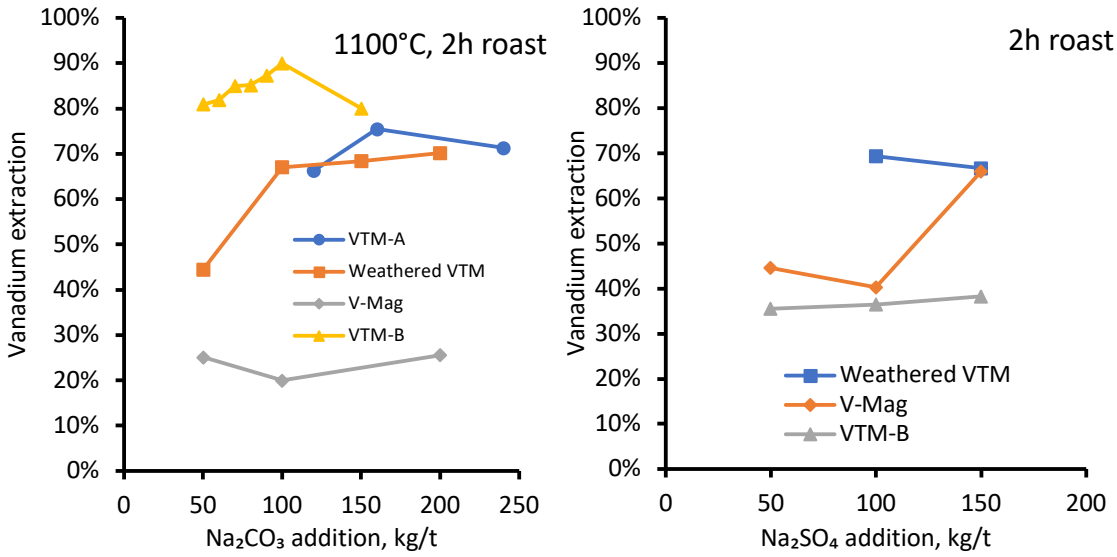

Figure 1 - Vanadium extracted by water leaching after roasting with different amounts of sodium carbonate (left) and sodium sulphate (right).

Roasting with sodium sulphate also requires higher (>1200°C) temperatures for effective vanadium extraction, compared to roasting with sodium carbonate which is effective at 1100°C[2]. This was most effective when applied to the weathered VTM material.

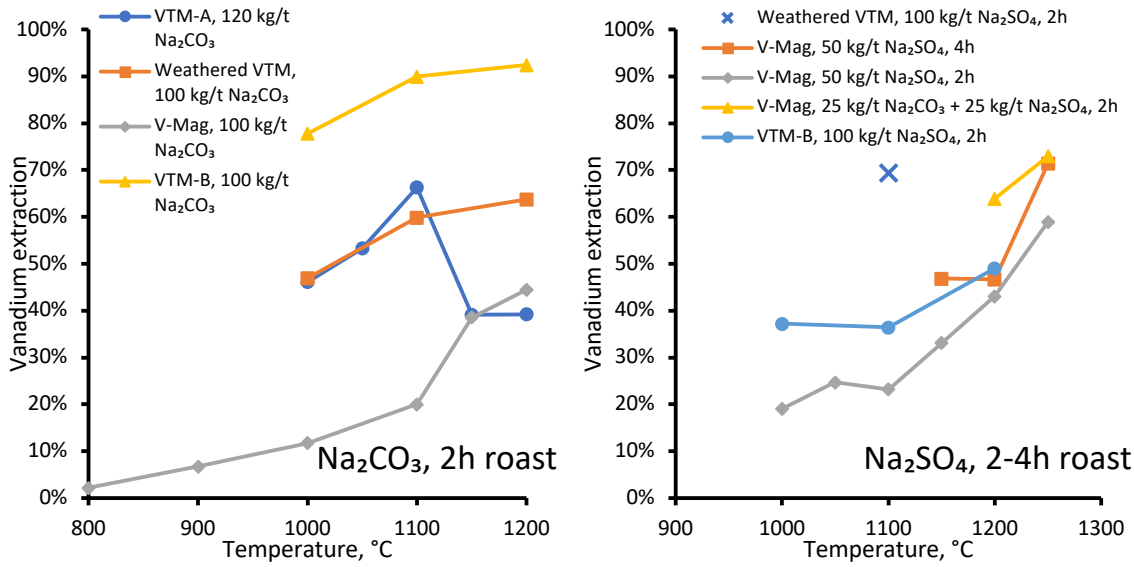

Figure 2 - Vanadium extracted by water leaching with sodium carbonate (left) and sodium sulphate (right) at different temperatures.

Roasting with sodium carbonate was effective for extracting vanadium from the VTM and weathered VTM samples, but not the V-Mag sample. For the V-Mag sample, roasting with a 50:50 mixture of Na_2CO_3/Na_2SO_4 was significantly more effective than the same total amount of either salt alone, with 14-22% more vanadium dissolving in the subsequent leach at a particular temperature and total salt dose. This mixed salt approach has been applied industrially in South Africa[3], and these results show that it can be effective for samples otherwise resistant to conversion by roasting with either sodium carbonate or sulphate alone.

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Electronic properties of polyoxovanadoborates and alkoxylated polyoxovanadates

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Polyoxometalates (POMs) are a family of molecular compounds derived from oxides and are formed principally by V, Nb, Mo, Ta, and W. Among the POMs, the polyoxovanadates (POVs) are a wide family of compounds that can be formed by vanadium and oxygen and by vanadium, oxygen, and a heteroatom such as boron. Polyoxovanadoborates (BVO) are also interesting for their magnetic properties. For example, the family of the $[V_{12}B_{18}O_{60}H_6]$ shows interesting properties in two different mixed-valence ratios ($V_{11}^{IV}V^{V}$ & $V_{10}^{IV}V_2^{V}$). The magnetic properties for the 11-electron species show a small ferromagnetism at low temperatures, which is suppressed by increasing the applied field. This behaviour is not observed for the 10-electron species. Magnetic and electronic properties of some $[V_{12}B_{18}O_{60}H_6]$ will be discussed.

The classic structures of POMs have been named by the scientists that discovered them. For example, the $[M_6O_{19}]^{n-}$ has been named the Lindqvist structure. The vanadium Lindqvist species $[V_6O_{19}]^{8-}$ has never been isolated in aqueous media because of the nature of the vanadium-oxygen bond of the structure. The form to obtain this structure is exchanging the oxido bridging ligands by alkoxido groups[1], giving rise to hexavanadate structures that can act as electron reservoirs[2]. These mixed-valence structures are very interesting from the molecular materials point of view due to their electronic properties. Also, the magnetic properties of the Lindqvist polyoxovanadate will be discussed.

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Synthesis of Functionalized Bottlebrush Polymers by *Cis*-specific Metathesis Polymerization by Vanadium-Alkylidene Catalysts

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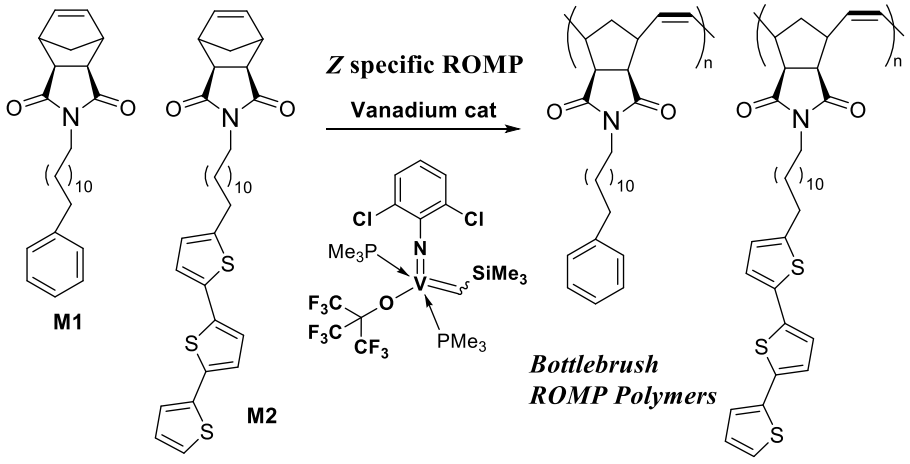
(Arylimido)vanadium(V)-alkylidene complexes containing perhalogenated phenoxide/alkoxide ligands have been known to exhibit high catalytic activities for ring-opening metathesis polymerization (ROMP) of cyclic olefins with thermal stability.[1] Bottlebrush polymers (BBPs) are promising materials owing to their controlled direction of side arms connected to the polymer main chain, and there are many reports for the synthesis by adopting (living) ROMP of norbornene macromonomers via grafting through approach using the ruthenium-carbene catalyst. However, the method still faces difficulties in control of *cis/trans* olefinic double bonds in the polymers, incomplete monomer conversion, and the catalyst decomposition. We thus herein report the stereospecific synthesis (exclusive *Z*-selective) of BBPs containing functionality at the side arms.

ROMP of *exo*-*N*-12-phenyldodecyl-norbornene-2,3-dicarboximide (M1), and *exo*-*N*-12-terthiophenyldodecyl-norbornene-2,3-dicarboximide (M2) using $V(CHSiMe_3)(N\text{-}2,6\text{-}Cl_2C_6H_3)[OC(CF_3)_3](PMe_3)_2$ gave the corresponding BBPs containing highly *cis* olefinic double bonds (**Scheme 1**); the highly *cis*-specific ROMPs could be achieved even at 50 ºC. The details will be introduced in the symposium.



Scheme 1 – Synthesis of *cis*-selective bottlebrush ROMP polymers.

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Alkali and alkaline-earth metal polyoxovanadates

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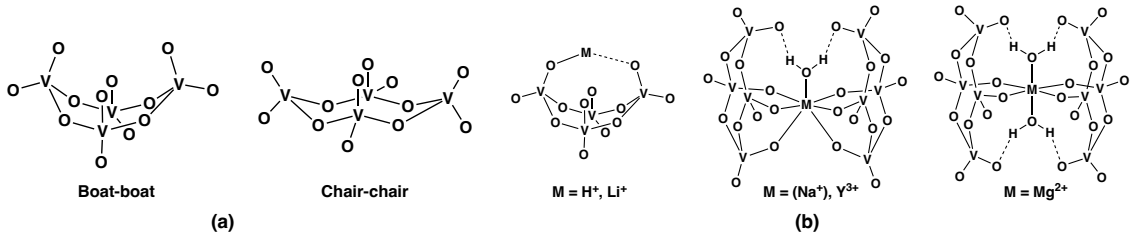
The speciation study of biologically relevant vanadate complexes with various organic ligands has been conducted to reveal the mechanism of biological activities of vanadium.[1] However, inorganic salts also interact with vanadates and potentially form a pure inorganic complex. Especially, when the salt concentration, for example NaCl concentration is more than 0.1 mol/dm^3 in the blood, is relatively high, the possibility of the formation of alkali and/or alkaline-earth metal vanadates should be investigated. We have previously investigated the coordination complexes of polyoxovanadates with various transition-metal cations and we have established the chemistry of all-inorganic coordination complex by a cyclic polyoxovanadate ring as a macrocyclic ligand.[2] From neutral to a weak alkaline condition, tetravanadates are one of the dominant species in solution. The cyclic tetravanadates have a 8-membered ring consisted by four vanadium and four oxygen atoms. The representative conformations of tetravanadates are boat-boat and chair-chair forms depicted in **Scheme 1**(a). The boat-boat conformation can bind a small cation such as a proton or a lithium cation at its saddle position through oxygen atoms to form inorganic salts as shown in **Scheme 1**(b). For the synthesis of the protonated form, a weak acid such as acetylacetone has to be used to prevent the further condensation reaction that is resulting the formation of decavanadates. The larger ionic radius cations form a sandwich type complex in chair-chair conformation with an additional coordination of a few water molecules in the pocket between two tetravanadates. The coordination mode of tetravanadates is either bidentate or tridentate mode. The coordinated water is supported by hydrogen bonds within a molecule, but EXAFS study indicates the dissociation equilibrium of water molecules in solution state. These complexes crystalized in a concentration of 0.2 mmol/dm^3 by using tetrabutyl ammonium cations and it may suggest that these types of species may also form in the blood when the vanadium concentration is high enough. In the case of sodium cation, two sodium ions are sandwiched between two tetravanadates.



Scheme 1 – (a) Conformations of tetravanadates, and (b) schematic structure drawings of alkali and alkali-earth metal polyoxovanadates. Dotted lines indicate hydrogen bonds.

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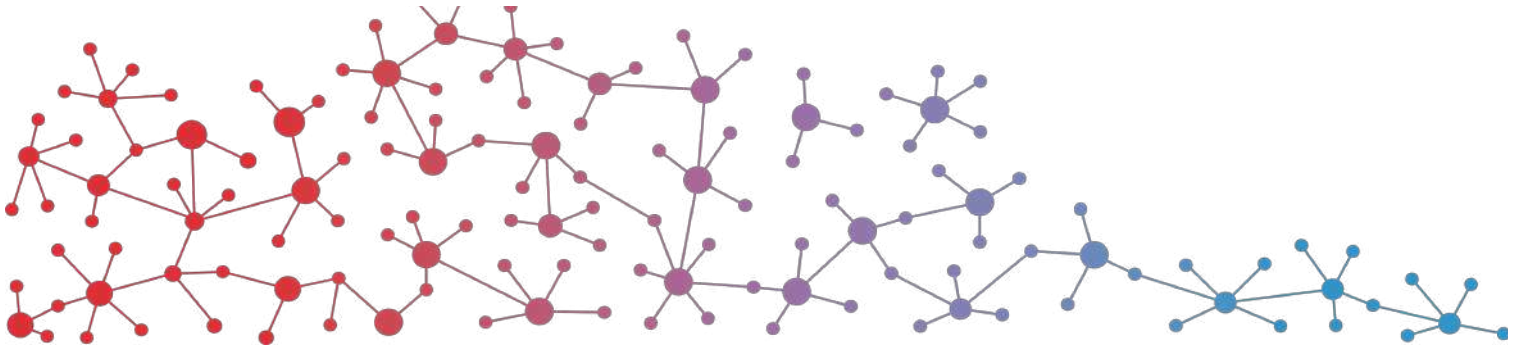

PC1	Increasing Hydrophobicity and Stability of Vanadium Schiff Base Catecholate Complexes with Adamantyl Substituted Catechol Ligands – Andrew Bates
PC2	Design and Modulation of Selectivity Towards Vanadium(V) and Uranium(VI) Ions: Coordination Properties and Affinity of Hydroxylamino-Triazine Siderophores – Angelos Amoiridis
PC3	Vanadium influence of natural extract antioxidant activity on neuroprotection – Athanasios Salifoglou
PC4	Vanadium and manganese speciation and its effect on mitochondrial reactive oxygen species formation – Connor C. Dolan
PC5	In Vitro, Oral Acute, and Repeated 28-Day Oral Dose Toxicity of a Mixed-Valence Polyoxovanadate Cluster – Debbie Crans
PC6	Vanadium(V) Pyridine-Containing Schiff Base Catecholate Complexes are Novel Lipophilic, Redox-Active and Selectively Cytotoxic in Glioblastoma (T98g) Cells – Debbie Crans
PC7	Guanidinium decavanadate as a small biomimetic model to understand decavanadate protein interactions through arginine side chains – Enrique González-Vergara
PC8	Complex formation of anticancer 8-hydroxyquinoline derivatives with oxidovanadium(IV): solution stability and structure – Éva A. Enyedy
PC9	Synthesis and Characterization of tri-isopropyl catechol and di-isopropyl catechol for use in Bioactive Vanadium (V) Schiff Base Complexes – Kameron Klugh
PC10	Oxovanadium(V)–Catalyzed Coupling Reaction of Alcohols with Silyl Enol Ethers via C-O Bond Cleavage – Kento Okabayashi
PC11	Early transition metal complexes supported by PNP pincer ligands – Luís G. Alves
PC12	Binding of oxidovanadium(IV) complexes $[V(IV)O(malt)_2]$ and $[V(IV)O(empp)_2]$ to lysozyme – Maddalena Paolillo
PC13	Vanadium(V) Complexes with Siderophore Vitamin E-Hydroxylamino-Triazine Ligands – Maria Loizou
PC14	Synthesis and characterization of heteropolyoxo-fluoro vanadium/copper compound and its redox properties for application as photoanode – Maria Michaelidou
PC15	Vanadium(IV) coordination compounds with picolinic acid derivatives – Mišel Hozjan
PC16	Development of Ring-Closing Metathesis Reactions by Vanadium(V)-Alkylidene Catalysts – Moe Unoki
PC17	Stability and Structure-Activity Relationship Analysis of Halogenated Vanadium Schiff-base Catecholate Complexes – Skyler Allen Markham
PC18	V-catalytic aerobic C-C bond cleavage of aliphatic 1,2-diols: thermal and photoinduced processes – William Bertoluzzo

Increasing hydrophobicity and stability of vanadium Schiff base catecholate complexes with adamantyl substituted catechol ligands

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Hydrophobic Schiff base catecholate non-innocent vanadium complexes have recently been reported to have in vitro efficacy against platinum-resistant glioblastoma (T98G) cell lines, which may make them suitable for chemotherapy against glioblastoma. Despite the limited hydrolytic stability of V(V) Schiff base catecholate complexes, a previous study has demonstrated that bulky hydrophobic substituents on the catecholate ligand increase hydrolytic stability of the complexes under the assay conditions. The study also found that related complexes had greater cytotoxicity against T98 human glioblastoma cells. To better understand the relationship between hydrolytic stability and observed cytotoxicity, we synthesized new catecholate ligands with bulky, aliphatic adamantyl substituents. In this work, we synthesized several novel V(V) catecholate analogs with adamantyl-substituted catecholate ligands. The hydrolytic stability of the complexes was then studied by UV-Vis spectroscopy under the assay conditions. Antiproliferative activities and stability for complexes were also evaluated in glioblastoma (T98G) cells. All complexes synthesized were characterized by ^{51}V, ^{1}H NMR, and UV-Vis spectroscopies. The impact of the catecholate ligand on the properties of the complexes will be discussed, as well as preliminary work in glioblastoma cell lines.

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Design and Modulation of Selectivity Towards Vanadium(V) and Uranium(VI) Ions: Coordination Properties and Affinity of Hydroxylamino-Triazine Siderophores

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Siderophores, are a family of organic substitutes that contain hard donor atoms such as N and O, exhibiting high affinity and selectivity towards hard metal ions, including trans-$U^{VI}O_2^{2+}$ and cis-$V^{V}O_2^{+}$. Therefore, such molecules can find applications in the removal of hard metal ions from the human body, radioactive waste, and seawater. A scientific challenge is the design of siderophore chelators with improved properties that enhance both selectivity and thermodynamic stability in their interaction with metal ions. Based on the strong binding and high selectivity demonstrated by the substitute 2,6-di-[hydroxy(methyl)amino]-4-morpholino-1,3,5-triazine H_2bihyat[1,2] for trans-$U^{VI}O_2^{2+}$, a new family of organic substitutes with two sites for complexation of hard metal ions was designed, characterized by the common feature of two 2,6-di-[hydroxy(methyl)amino]-1,3,5-triazine groups connected via 1,4-hydroquinone (**H_4qtn**), 1,4-phenylene diamine (**H_4pdl**), and ethylene diamine (**H_4enl**). The reaction of the new substitutes with trans-$U^{VI}O_2^{2+}$ and cis-$V^{V}O_2^{+}$ led to the isolation of dinuclear complexes.

The ability of the new organic molecules to bind hard metal ions compared to other hard donor-atom ligands such as dipicolinic acid, H_2bihyat, and CO_3^{2-} was examined by NMR, revealing that all three molecules are much stronger binders. The selectivity of the new molecules towards binding trans-$U^{VI}O_2^{2+}$ over cis-$V^{V}O_2^{+}$ increases at high pH, while overall, uranyl complexation is less favorable.

The formation of the heterometallic species of the form $U^{VI}O_2(\mu\text{-}O)V^{V}O_2$ influences the selectivity and dynamics of the reactions of these molecules in aqueous solutions that contain both metals. Additionally, the kinetics of the substitution of bound uranyl by vanadium species and vice versa were examined by NMR. Based on those studies, a

mechanism that describes the Uranyl – Vanadate exchange on the ligand's binding sites is proposed.

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Vanadium influence of natural extract antioxidant activity on neuroprotection

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Neurodegeneration is a neuronal cellular process, inflicting irreparable damage to neuronal cell tissues in human brain, ultimately leading to the debilitating pathological conditions exemplified through Alzheimer's, Parkinson's, and other diseases. Albeit difficult to remedy the neurological damage, inflicted upon hippocampal cells in the brain and reverse neurodegeneration, a number of approaches linked to appropriate handling of neurodegeneration, retardation, and potentially inhibition, averting neuronal cell demise have been invoked and proposed over the years as proactive actions. Key to such approaches is incorporation of antioxidants and/or antioxidant-containing materials of natural origin in the habitual consumption of food stuffs, health foods, and pharmaceutically-relevant substances in the human diet. To that end, plant extracts rich in antioxidants, including flavonoids, polyphenols, and other organic and inorganic components have come under scrutiny over the past decades. Poised to investigate the potential antioxidant capacity of naturally derived plant extracts in proactively promoting neuroprotection of the human brain, thus combating oxidative stress neuronal cell destruction,[1] research was launched in our lab on Cornus mas L. extracts known for their anticarcinogenic, anti-inflammatory and antiviral properties. Our goal was to uncover neuroprotective properties that the specific extracts might exhibit on neuronal tissues, thereby justifying their incorporation in the human diet. Key to that effort was the introduction of low molecular mass metal-organic factors of well-defined physicochemical profile, enhancing or synergistically invigorating the neuroprotective effects that might emerge. To that end, extensive in vitro work employing the specific plant extracts was pursued, with neuronal cell lines (N2a, SH-SY5Y) being used as model neuronal cultures, and the following aspects of the extracts investigated in depth: a) toxicity (viability, proliferation, migration, morphology), b) antioxidant properties (in the presence of hydrogen peroxide), and b) introduction of soluble vanadium(IV)-citrate

species to examine the potential assisting and/r enhancement effects that might have.

The results of the carried out experiments suggest that a) there is a concentration- and time-dependent relationship between the plant extracts examined and neuronal cell viability. In fact, the neuronal cells are viable in the presence of high concentrations of the extracts (up to 3 mg/ml), b) the antioxidant capacity of the extracts was found to be equally dependent on the concentration and time of exposure of the cells (up to 72 hours) and being capable of withstanding the oxidative stress activity of hydrogen peroxide in a pre-emptive and recovery mode, and c) the addition of V(IV)-citrate,[2] a well-defined binary metal-organic factor, was shown to exhibit supportive action to the plant extracts, thereby sustaining in a concentration dependent-fashion a favorable effect.

The physicochemical properties of V(V)-citrate, along with the biological profile of the examined plant extracts project the salient features of metal-organic contribution to the molecular interactions sustaining neuronal cell survival, thereby formulating atoxic and biochemically competent preparations of such plant extracts, with neuroprotective activity[3] averting neurodegeneration or retarding it over the span of human life.

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Vanadium and manganese speciation and its effect on mitochondrial reactive oxygen species formation

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Metals are associated with many complex biochemical processes and are found throughout the environment. While many metals can be essential, they can become toxic in high enough concentrations. The presence of metal ions has been associated with the oxidative stress balance in the body and the promotion of disease. Vanadium and manganese have been thought to be associated with neurodegenerative diseases, cancer, diabetes. Vanadium has been investigated in its ability to protect against these diseases through therapeutic complexes; however, they both have been indicated to promote disease when exposed to in excess. Many transition metals can exist in several oxidation states and vanadium and manganese offer an opportunity to study the differences caused by the speciation of two adjacent elements in the periodic table on reactive oxygen species (ROS) formation in mitochondria. $VOSO_4$, $NaVO_3$, $VO(acac)_2$, $MnCl_2$, and $Mn(acac)_2$ were tested for their ability to quench and generate ROS via fluorescence assays with vanadium species showing varying ability to quench hydrogen peroxide and manganese species showing no ability to quench hydrogen peroxide. These species were tested on heart mitochondria isolated from mice and results were obtained using high resolution O2K respirometry for their ability to produce mitochondrial ROS and their effect on ROS producing proteins in the electron transport chain. While showing wide variability, these studies showed differences in simple metal salts and a simple coordination complex, demonstrating the importance of speciation chemistry in effect on aerobic respiration.

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In Vitro, Oral Acute, and Repeated 28-Day Oral Dose Toxicity of a Mixed-Valence Polyoxovanadate Cluster

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Polyoxovanadates (POV) are a subgroup of polyoxometalates (POM), which are nanosized clusters. This manuscript describes the first toxicity evaluation of a mixed-valence polyoxovanadate, pentadecavanadate, $(Me_4N)_6[V_{15}O_{36}Cl]$, abbreviated as V15. Cytotoxicity experiments using peripheral blood mononuclear cells (PBMC), larvae *of Artemia salina Leach*, and in vivo oral acute and repeated 28-day doses in mice was carried out. The LC_{50} values in PBMC cells and *A. salina* were 17.5 Å $\pm$ 5.8 µmol L^{-1}, and 17.9 µg L^{-1}, respectively, which indicates high cytotoxic activity. The toxicity in mice was not observed upon acute exposure in a single dose, however, the V15 repeated 28-day oral administration demonstrated high toxicity using 25 mg/kg, 50 mg/kg and, 300 mg/kg doses. The biochemical and hematological analyses during the 28-day administration of V15 showed significant alteration of the metabolic parameters related to the kidney and liver, suggesting moderate toxicity. The V15 toxicity was attributed to the oxidative stress and lipid peroxidation, once thiobarbituric acid (TBAR) levels significantly increased. This is the first study reporting a treatment-related mortality in animals acutely administrated with a mixed valence POV. These results document the toxicity of this mixed-valence POV.

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Vanadium(V) Pyridine-Containing Schiff Base Catecholate Complexes are Novel Lipophilic, Redox-Active and Selectively Cytotoxic in Glioblastoma (T98g) Cells

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Two new series of complexes with pyridine-containing Schiff bases, [V^{V}O(SALIEP)L] and [V^{V}O(Cl-SALIEP)L] (SALIEP=N-(salicylideneaminato)-2-(2-aminoethylpyridine; Cl-SALIEP=N-(5-chlorosalicylideneaminato)-2-(2-aminoethylpyridine, L=catecholato(2-) ligand) have been synthesized. Characterization by ^{1}H and ^{51}V NMR and UV-vis spectroscopies confirmed that: 1) most complexes form two major geometric isomers in solution, and [V^{V}O(SALIEP)(DTB)] (DTB=di-tertbutylcatecholato(2-)) forms two isomers that equilibrate in solution; and 2) tert-butyl substituents were necessary to stabilize the reduced V^{IV} species (EPR spectroscopy and cyclicvoltammetry). The pyridine moiety within the Schiff base ligands significantly changed their chemical properties with unsubstituted catecholate ligands compared with the parent HSHED (N-(salicylideneaminato)-N'-(2-hydroxyethyl)-1,2-ethanediamine) Schiff base complexes. Immediate reduction to V^{IV} occurred for the unsubstituted-catecholato VV complexes on dissolution in DMSO. By contrast, the pyridine moiety within the Schiff base significantly improved the hydrolytic stability of [V^{V}O(SALIEP)(DTB)] compared with [V^{V}O(HSHED)(DTB)] in organic solvent and cell culture media. There was significant cellular uptake of the intact complex by T98g (human glioblastoma) cells and very good anti-proliferative activity (IC_{50} 6.7+0.9 μM, 72 h), which was five times higher than for the non-cancerous human cell line, HFF-1 (IC_{50} 34+10 μM). This made it a potential drug candidate for the treatment of advanced gliomas.

Project has been accepted for publication in Chemistry – A European Journals

Guanidinium decavanadate as a small biomimetic model to understand decavanadate protein interactions through arginine side chains

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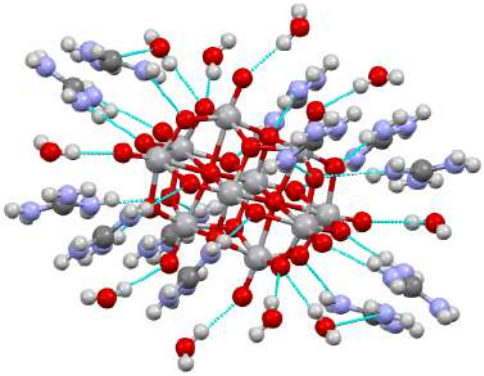
Thirty years ago, the crystal structure of a Guanidinium Decavanadate addition compound was described by Wang X. et al.[1]. Now the structure has been redetermined with better resolution, and it has been characterized by experimental and theoretical methods to understand its non-covalent interactions and serve as a biomimetic model for arginine bound to decavanadate ions in protein settings such as those found in TRMP4[2]. The guanidinium's capacity to interact with decavanadate through electrostatic interactions and extensive hydrogen bonds is presented in the figure. This study provides new knowledge and insights into the non-covalent intermolecular interactions between decavanadate anion $[V_{10}O_{28}]^{6-}$ and $(GG^{+})_n$ (Guanidinium Group, with n = 6 and 12) complexes using density functional theory (DFT) method. The non-covalent interactions presented by this compound are essential to understand the role of the hydrogen bonds and electrostatic interactions in proteins that have crystallized containing the decavanadate anion (V_{10}), contributing to understanding the reason for the behavior of this ion in contrast to the vanadate ion $(V_1)^{3-6}$.



Scheme 1. Decavanadate anion surrounded by Guanidinium cations (Mercury Presentation).

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Complex formation of anticancer 8-hydroxyquinoline derivatives with oxidovanadium(IV): solution stability and structure

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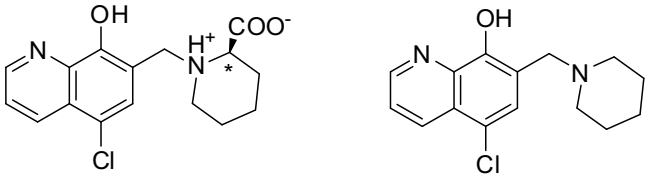
Chemotherapy remains a prevalent and effective therapeutic approach for a multitude of cancer types, despite limitations including serious side-effects and resistance. Multidrug resistance (MDR) of cancer cells against structurally different anticancer agents is a major problem often leading to unsuccessful chemotherapy outcomes. The 8-hydroxyquinoline (HQ) scaffold is a privileged structure in many biologically active compounds; numerous HQ derivatives display anticancer properties and certain representatives were reported to be effective against MDR[1].
The pharmacokinetic and pharmacodynamic properties of HQ derivatives can be fine-tuned via the modification of the basic structure using different substituents and/or metal complex formation. Thanks to the {*N*,*O*} chelating group, the HQs exhibit the capacity to form stable complexes with a diverse array of metal ions. Intracellular complex formation with endogenous metal ions is often reported as a significant contributing factor to the underlying mechanism of action. As the complexation can alter the physico-chemical properties such as size, charge, lipophilicity and solubility as well as the mechanism of action, numerous HQ complexes of nonessential metal ions were also developed such as tris(8-quinolinolato)gallium[2], half-sandwich organorhodium and organoruthenium compounds[3] or complexes of oxidovanadium(IV)[4,5].

The oxidovanadium(IV) complexes formed with 5-chloro-7-iodo-quinolin-8-ol[4] and other halogen- or differently substituted derivatives[5] have undergone evaluation against human cancer cell lines. These studies revealed significant cytotoxicity and preference for cancer cells over the normal cells. In our previous work[6], complexes bearing benzohydrazone HQ derivatives were developed and tested, revealing good cytotoxicity on melanoma and lung adenocarcinoma cancer cell lines. Based on our

solution speciation studies, these 2-substituted HQ ligands form mono- and bis-ligand complexes with oxidovanadium(IV) in different protonated states, and various coordination isomers were found due to the additional donor atoms of the benzohydrazone moiety. Moreover, the family of HQ-derived Mannich bases with alkylamine substituents at position 7 was identified to display MDR-selective toxicity[1], and amino acid hybrids with excellent aqueous solubility were also developed[3,7].

Herein the complex formation processes of two HQ-derived Mannich bases (**Scheme 1**) with oxidovanadium(IV) were studied using UV-visible spectrophotometric titrations to determine the formation constants of the complexes under strictly O_2-free conditions, and electron paramagnetic resonance spectroscopy was applied to confirm the speciation model and reveal the coordination modes. HQ and its water-soluble counterpart, HQ-5-sulfonate, were also involved for comparison. Preliminary data on the cytotoxic activity of the complexes will be presented as well.



HQCl-D-hPro **HQCl-pip**

Scheme 1 – HQ-derived Mannich bases studied in this work.

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Acknowledgements: This work was financially supported by the National Research, Development and Innovation Office–NKFIA (Hungary) through project TKP-2021-EGA-32 and the support of the 'Lendület' Programme (ELKH (Hungary), LP2019-6/2019) is also acknowledged.

Synthesis and characterization of tri-isopropyl catechol and di-isopropyl catechol for use in bioactive vanadium (V) Schiff base complexes

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Non-innocent Schiff base vanadium(V) catecholate complexes have been recently found to be promising agents for glioblastoma, an aggressive form of brain cancer. Several studies have shown that a subclass of vanadium Schiff base complexes, vanadium (V) catecholates, have proven that bulky hydrophobic substituents on the catecholate ligand increase hydrolytic stability and cytotoxicity in T98 glioblastoma cells.[1] Further investigation of varying the substituents on the catecholate ligands and the corresponding complexes is integral to the understanding of such anticancer and cytotoxic properties of vanadium (V) catecholate complexes. In this study, two catecholate ligands - novel 3,4,6-tri-isopropyl catechol and 3,5-di-isopropyl catechol - were synthesized and then used to make the Schiff base vanadium(V) catecholate complexes. The structure of the ligands and the complexes were confirmed by NMR spectroscopy. The ligands were further investigated by electrochemistry. The complexes were then tested in glioblastoma (T98g) cell lines, and the results were compared to those in normal cells.

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Oxovanadium(V)–Catalyzed Coupling Reaction of Alcohols with Silyl Enol Ethers *via* C-O Bond Cleavage

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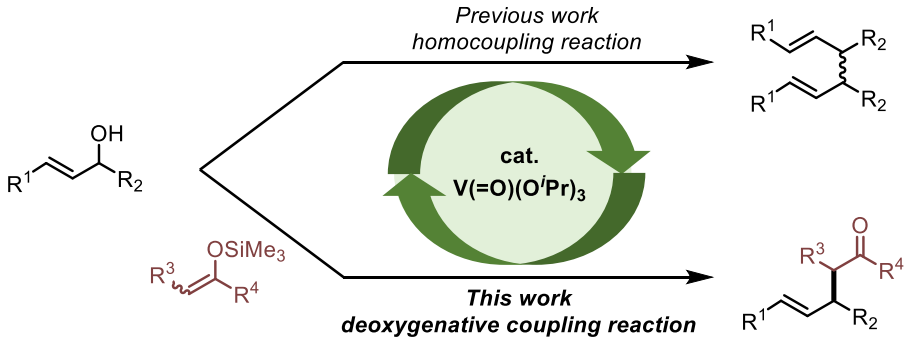
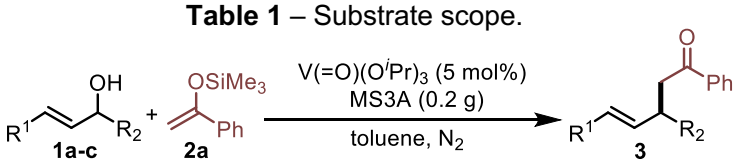
γ,δ-Unsaturated carbonyl compounds are important raw materials for pharmaceuticals and agrochemicals and as synthetic intermediates for natural products. Generally, γ,δ-unsaturated carbonyl compounds have been synthesized by Claisen rearrangement of allyl vinyl ethers. For the development of environmentally friendly methods, the direct synthesis of γ,δ-unsaturated carbonyl compounds from allyl alcohols is desired. Several examples have been reported for the direct alkylation of allyl alcohols with silyl enol ethers, but generally required precious catalysts and promoters. As far as we know, there is no direct synthesis of γ,δ-unsaturated carbonyl compounds by the oxovanadium-catalyzed coupling reaction of allyl alcohols with silyl enol ethers. Previously, our group reported the oxovanadium-catalyzed homocoupling reaction of allyl alcohols *via* C-O bond cleavage[1]. Inspired by this report, we tackled on the synthesis of γ,δ-unsaturated carbonyl compounds by the deoxygenative coupling reaction of allyl alcohols with silyl enol ethers[2].

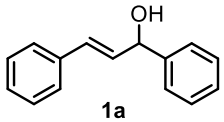
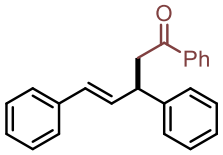
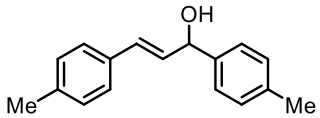
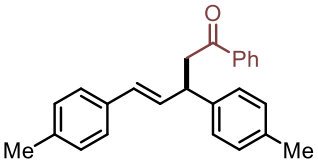
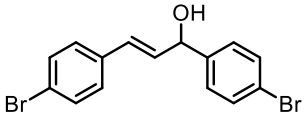
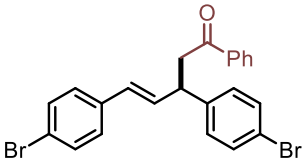


The reaction of 1,3-diphenylpropen-1-ol (**1a**) with silyl enol ether **2a** in the presence of $V(=O)(O^iPr)_3$ as a catalyst and MS3A as a dehydrating reagent was found to afford γ,δ-unsaturated carbonyl compound **3aa** in 85% isolated yield (**Table 1**, Entry 1). Therefore, a series of allyl alcohols **1** were used to confirm the substrate scope of this catalytic coupling reaction. Starting from **1b** bearing methyl group at *para*-

position, the desired product **3ba** was obtained in 51% isolated yield (Entry 2). Allyl alcohol **1c** with bromo substituent at *para*-position participated in this catalytic reaction to form the corresponding unsaturated carbonyl compound **3ca** in 46% isolated yield (Entry 3). In addition, it is worth nothing that a gram-scale coupling reaction of **1a** with **2a** was successfully proceeded to afford the desired product **3aa** in 82% isolated yield. Fortunately, this catalytic system could be applied to benzyl alcohol derivatives.

Table 1 – Substrate scope.



Entry	Substrate	Product	Isolated yield
1	 **1a**		**3aa**[a] 85%
2	 **1b**		**3ba**[b] 51%
3	 **1c**		**3ca**[b] 46%

[a] Reaction condition: **1a** (0.20 mmol), **2a** (0.20 mmol), V(=O)(O^{i}Pr)$_3$ (5 mol%), MS3A (0.2 g) in toluene (2.0 mL) under N_2 at 100 °C for 8 h.

[b] Reaction condition: **1** (0.20 mmol), **2a** (0.40 mmol), V(=O)(O^{i}Pr)$_3$ (5 mol%), MS3A (0.2 g) in toluene (2.0 mL) under N_2 at 150 °C for 24 h.

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Early transition metal complexes supported by PNP pincer ligands

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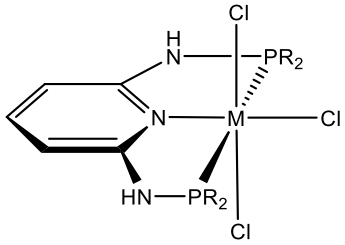
Pincer ligands have attracted tremendous interest over the last years because their mid to late transition metal complexes have shown important catalytic applications[1-5]. Conversely, the chemistry of early transition metal complexes supported by PNP pincer ligands has been scarcely reported[6-8]. We present and discuss herein the syntheses and structural features of Ti(III), V(III) and Mo(III) complexes supported by tridentate PNP pincer ligands based on 2,6-diaminopyridine of the type [(PNP)MCl_3] (**Scheme 1**).



Scheme 1 – [(PNP)MCl_3] complexes (M = Ti, V and Mo).

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Binding of oxidovanadium(IV) complexes $[V^{IV}O(malt)_2]$ and $[V^{IV}O(empp)_2]$ to lysozyme

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The presence of vanadium in biological systems, the number of physiological roles, the insulin-boosting action together with the antitumor and the antiparasitic properties have stimulated an intense research activity on this interesting metal and its compounds.[1,2] It is well-known that vanadium complexes (VCs) can regulate different enzymes, including kinases and phosphatases, normalize blood glucose and lipids and induce a modest recovery of insulin sensitivity in diabetic animals. In particular, V^{IV} compounds are more effective in reducing blood glucose than the V^{III} and V^{V} analogues.[3,4] However, the mechanism of action of VCs is still unclear. Indeed, none of those compounds entered the clinics yet.[1] The reason is the limited knowledge on their transformation in the body, on their biological targets and on the interaction mode with bioligands. Therefore, the interaction of the active species of VCs with biological macromolecules, such as proteins, is of great importance to deeply understand VCs potential pharmacological activity.[5,6] Among the most promising VCs, $[V^{IV}O(malt)_2]$ (malt = 3-hydroxy-2-methyl-4H-pyran-4-onato) (**Figure 1A**), and $[V^{IV}O(empp)_2]$ (Hempp = 1-methyl-2-ethyl-3-hydroxy-4(1H)-pyridinone) (**Figure 1B**), have shown a great biological activity.

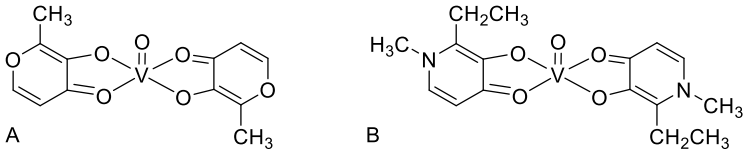

Figure 1 – A) $[V^{IV}O(malt)_2]$; B) $[V^{IV}O(empp)_2]$

The aim of this work has been to characterize, from a structural point of view, the interaction of $[V^{IV}O(malt)_2]$ and $[V^{IV}O(empp)_2]$ with the model protein hen egg white lysozyme (HEWL). The $[V^{IV}O(malt)_2]$/HEWL system showed non-covalent binding of *cis*-$[VO(malt)_2(H_2O)]$ and $[VO(malt)(H_2O)_3]^+$, and covalent binding of $[VO(H_2O)_{3\text{-}4}]^{2+}$, *cis*-$[VO(malt)_2]$ and other V-containing fragments to the side chains of Glu35, Asp48,

Asn65, Asp87, and Asp119 and to the C-terminal carboxylate.[7] For the $[V^{IV}O(empp)_2]$/HEWL system, the covalent binding of $[V^{IV}O(empp)(H_2O)]^+$ to the side chain of Asp48, and non-covalent binding of *cis*-$[V^{IV}O(empp)_2(H_2O)]$, $[V^{IV}O(empp)(H_2O)]^+$, $[V^{IV}O(empp)(H_2O)_2]^+$, and of an unusual trinuclear oxidovanadium(V) complex, $[V^{V}_3O_6(empp)_3(H_2O)]$, with accessible sites on the protein surface were observed.[8] The comparison between the binding modes of $[V^{IV}O(malt)_2]$ and $[V^{IV}O(empp)_2]$ to HEWL revealed similarities and differences related to the ligand structure, the stability of the $V^{IV}O^{2+}$ species, the possibility of formation of covalent and/or non-covalent bonds, and the stabilization of the adducts through secondary interactions (**Figure 2**). The oxidation of V^{IV} to V^{V} with formation of the trinuclear species $[V^{V}_3O_6(empp)_3(H_2O)]$ was detected in the $[V^{IV}O(empp)_2]$/HEWL system, while in the $[V^{IV}O(malt)_2]$/HEWL system, no similar adducts were found.[8]

The reactivity of $[V^{IV}O(malt)_2]$ and $[V^{IV}O(empp)_2]$ with HEWL could help in understanding of transport and mechanisms of action of vanadium, promoting the development of new compounds as potential therapeutic agents.

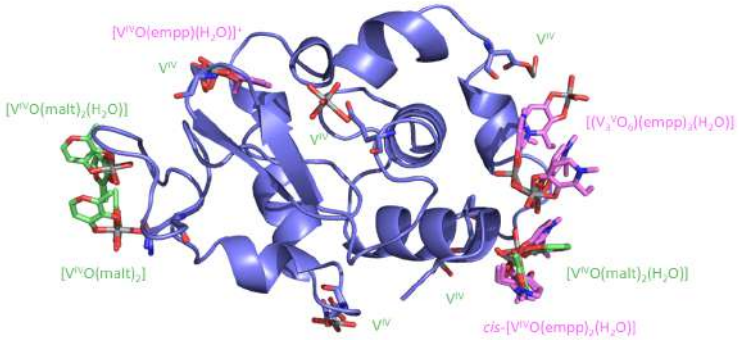

Figure 2 – Superimposition of the structures of the adducts formed by HEWL with $[V^{IV}O(malt)_2]$ and $[V^{IV}O(empp)_2]$.

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Vanadium(V) complexes with siderophore vitamin E-hydroxylamino-triazine ligands

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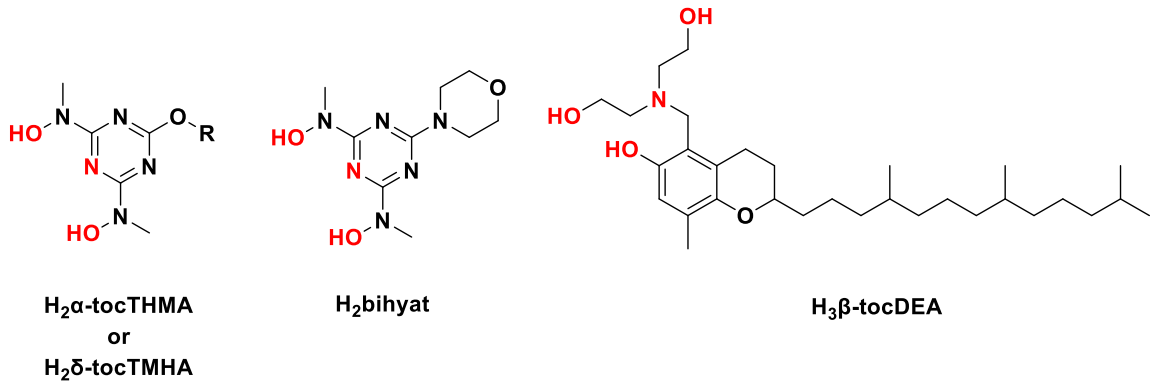
The understanding of the physiological role of vanadium ions in biological systems as well as the biological activity of vanadium compounds have been stimulated the interest of the scientific community towards the vanadium chemistry. Vanadium compounds exert antitumor effects through activation of apoptotic pathways, cell cycle arrest and the generation of ROS, inducing lower toxicity than anticancer platinum-based molecules. Recently, we reported the first study of the synthesis of complexes comprising tocopherol ligating to metals. The ligands in this study are β-tocopherols substituted with chelate groups in *o*-position derivatives (Scheme 1, H_3β-tocDEA), thus, enabling coordination of the metal ion from the phenolic oxygen. The [V^VO(β-tocDEA)] has been found to exhibit enhanced hydrolytic stability and cytotoxicity to cancer cells.

Here in, we have attached a siderophore moiety on the phenoxy oxygen of the chromanol, forming two new ligands, the 2,4-dichloro-6-(((R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)-1,3,5-triazine (**H_2α-tocTHMA**) and 2,4-dichloro-6-(((R)-2,8-dimethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl)oxy)-1,3,5-triazine (**H_2δ-tocTHMA**). The labile hydrogen atom of the hydroxy group has been replaced with the triazine moiety forming an inert ether bond and, thus, the new organic molecules will act as ligand owing lower antioxidant activity than free tocopherols. As chelate group for V^V we have chosen the siderophore hydroxylamino-triazine (Scheme 1), targeting to enhance the hydrolytic stability of the V^V complexes as much as possible. Although Fe^{III} forms with the H_2bihyat ligand stronger complexes than V^V, NMR and UV-vis spectroscopies evidence that the V^V in the complexes with the amphiphilic hydroxylamino-triazine ligands cannot be replaced by Fe^{III} ions. The V^V complexes of this study exhibiting a chromanol hydroxy group unavailable for coordination, present no significant toxicity to cells.



H_2α-tocTHMA or H_2δ-tocTMHA

H_2bihyat

H_3β-tocDEA

Scheme 1 - Hydroxylamino-triazine ligands and H_3β-tocDEA. RO- is α- or δ-tocopherol. The donor atoms for metal ion coordination are in red color.

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Synthesis and characterization of heteropolyoxo-fluoro vanadium/copper compound and its redox properties for application as photoanode

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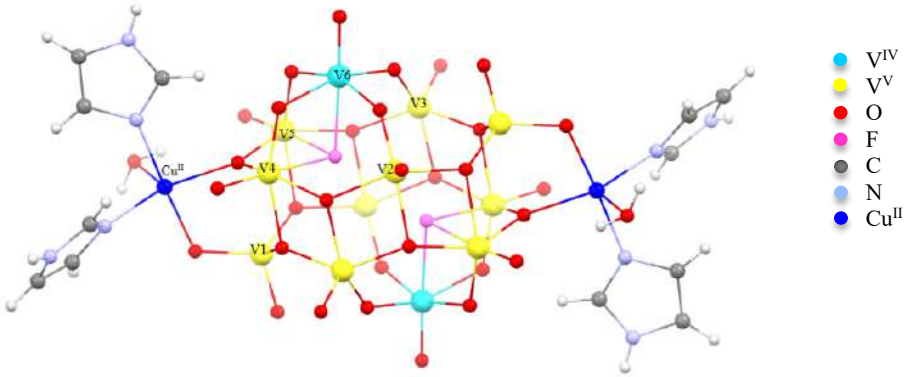
Vanadium polyoxometalates (POVs) present particular interest due to various properties. The variation of POVs complexes in their size, composition, charge and structure has led to many excellent but also different properties. They have stable structures and the charge of their anions can be adjusted according to their composition. Some of their properties are reversible redox action, catalytic action, conductivity. In addition, these compounds could give luminescence, magnetism, and others. Such rich properties make POVs present potential applications in many fields such as solar cells, photocatalytic hydrogen production, organic wastewater degradation, and photoelectrocatalysis.[1,2]

Incorporation of fluoride in the vanadium polyoxometalates results in new polyoxofluorovanadate clusters of novel structures with usually two oxygen centers substituted by fluorine atoms. This happens due to the changes in the charge or in the structure which affects the formation and stability of the various building blocks and the presence of vanadium species in aqueous solutions. Another important feature of polyoxofluorovanadate complexes is the stabilization of vanadium in oxidation state IV. This results in the formation of $V^{IV/V}$ mixed oxidation state complexes with interesting physical properties. Several mechanisms have also been proposed regarding the way the complexes are synthesized. Most polyoxofluorovanadate complexes have been synthesized in hydrothermal conditions, a method known for its complexity, however, in recent years other milder conditions have been tested which are equally efficient. There are only a few known polyoxofluorovanadate clusters that combines an extra transition metal and this field has a great potential of discovering new compounds with significant properties.[1,2]

A new heteropolyoxo-fluoro vanadium/copper **$[Him]_4[V^{V}_{10}V^{IV}_2Cu^{II}_2O_{12}(\mu\text{-}O)_{10}(\mu_3\text{-}O)_{10}(\mu_3\text{-}F)_2(im)_4(OH_2)_2]\cdot[OH_2]_4$** (**Scheme 1**), has been synthesized in one pot synthesis in ambient conditions, and redox properties have been determined by cyclic voltammetry (CV) and amperometry.



Scheme 1 - Crystallographic structure of the anion of the new compound.

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Vanadium(IV) coordination compounds with picolinic acid derivatives

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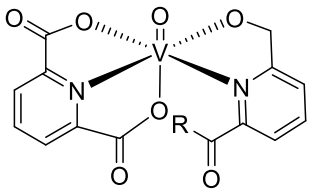
About twenty elements seem to be essential for the proper functioning of the human body, half of which are metals and the other half nonmetals. In addition to the metals already confirmed essential, the role of the others is also being studied. Vanadium is one of the metals that is the focus of interest. Although it is necessary for some animals, such as normal growth in rats, its role in the human body is still under controversy. The first evidence that vanadium might have a beneficial effect on the human body emerged when it was discovered at the turn of the 19. century that vanadium compounds could lower blood glucose levels[1]. Since then, vanadium compounds have been studied extensively for this purpose. The main reason for the bioactive effects of vanadium compounds is the similarity between vanadate (VO_4^{3-}) and phosphate (PO_4^{3-}) anions[2]. Both have similar coordination geometry, allowing vanadate to compete with phosphate for active sites that are dependent on phosphate. However, the important difference between the two is that vanadate binds to the active sites with stronger interactions, and subsequently can inhibit certain processes. Early results with simple inorganic vanadium species proved successful, showing good insulin-like effects in *in vitro* and *in vivo* assays[3]. Later, complexation of vanadium by ligands proved to be a great way to improve the efficacy of these putative anti-diabetic agents. In this context, a very promising compound turned out to be bis(ethylmaltolato)oxovanadium(IV), BEOV, which was also subject to clinical trials. In addition to BEOV, many other complexes have also been tested and are still under investigation. The main advantage of coordination compounds is that they offer the possibility of fine-tuning the following properties: biological activity, stability to avoid degradation prior to absorption, specificity and toxicity. Vanadium complexes with picolinic acid (pyridine-2-carboxylic acid) and its derivatives have shown promising insulin-mimetic activity[4], and we have also extended our research to the close analogue dipicolinic acid (pyridine-2,6-dicarboxylic acid) and its derivatives.

We have successfully prepared a variety of V^{IV} complexes with amide derivatives of picolinic acid. In each case, the V atoms are coordinated octahedrally by a dipicolinato ligand and an amide derivative of picolinic acid.



Scheme 1 – General scheme of prepared coordination compounds.

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Development of Ring-Closing Metathesis Reactions by Vanadium(V)-Alkylidene Catalysts

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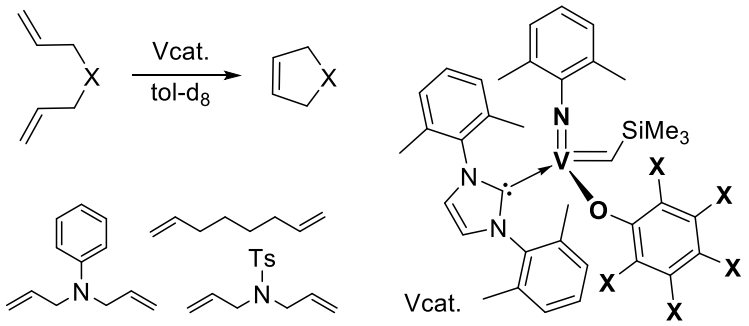
The (arylimido)vanadium(V)-alkylidene (carbene) complexes (**Scheme 1**) display promising capabilities especially for ring opening metathesis polymerization (ROMP) of cyclic olefins.[1-3] The perhalogenated phenoxide analogues, $V(CHSiMe_3)(N\text{-}2,6\text{-}Cl_2C_6H_3)(OC_6X_5)(PMe_3)_2$, enabled to proceed ROMP not only of norbornenes with high efficiency,[2a,b] but also low strained cyclic olefins.[2c] The perfluorinated alkoxides, $V(CHSiMe_3)(NAr)[OC(CF_3)_3](PMe_3)_2$, enabled to proceed *cis*-specific ROMP of norbornene even at 80 ºC,[2a,b] whereas c*is-syndiospecific* ROMP could be achieved by the NHC alkylidenes, $V(CHSiMe_3)(N\text{-}2,6\text{-}Cl_2C_6H_3)(OC_6X_5)(NHC)$ [NHC=1,3-bis-(2,6-dimethylphenyl)imidazol-2-ylidene].[3] *N*-Heterocyclic carbene (NHC) ligands are known to be effective for stabilization the NHC catalyst (shown in the **Scheme 1**) is highly active in ring-closing metathesis reactions (RCM). Since the catalyst performance (activity, selectivity) should be affected by the ligands employed, we will present the more details including the substrate scope. More detailed results will be introduced in the symposium.



Scheme 1. Ring-closing metathesis reaction by vanadium catalysts.

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Stability and Structure-Activity Relationship Analysis of Halogenated Vanadium Schiff-base Catecholate Complexes

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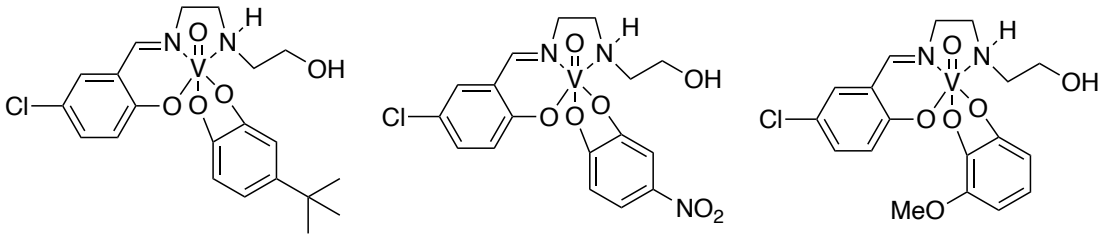
Non-innocent vanadium complexes are of interest to medicinal chemistry for their anticancer properties[1]. Because of this, new vanadium complexes are being synthesized with intent to use these complexes as anticancer therapeutics. Vanadium Schiff-base catecholate complexes have been shown to be highly reactive and have relatively short lifetimes[2,3]. Both properties make these complexes excellent candidates for intratumoral injection to treat glioblastoma cancer cells, as the release of less toxic decomposition products will result in a decrease in toxicity and likely kill less healthy cells in comparison to the complexes. Recent work in the Crans group has led to the development of chloro-substituted Schiff-base catecholate complexes, the [VO(Cl-Hshed)(X)] series, are highly active complexes with short lifetimes[3]. To further develop the understanding of these complexes, complexes using catechols with varying electron withdrawing and electron donating properties were synthesized and their procedures optimized. From this study, we were able to determine the significance of using sterically hindered catechols on both stability and biological activity. This study has led to the development of highly active complexes (about 10 times more active than current treatment cis-platin), currently patent-pending.



Scheme 1 – Selected sample of complexes from the [VO(Cl-Hshed)(X)] Series.

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V-catalytic aerobic C-C bond cleavage of aliphatic 1,2-diols: thermal and photoinduced processes

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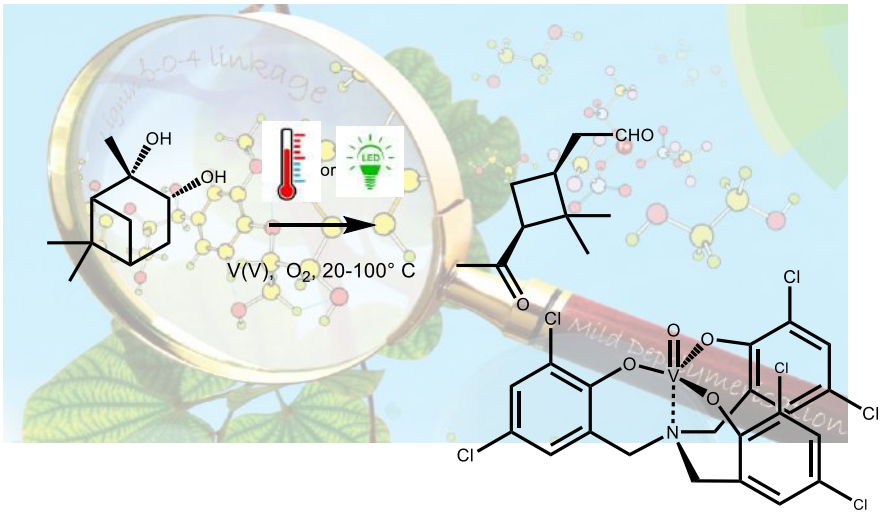
Currently, the majority of lignocellulosic biomass is valued for its holocellulose constituent, which is used to make pulp, paper, and bioethanol. The remaining lignin, which has the highest carbon content, is usually burned, and handled as waste. About 30% of the planet's non-fossil organic carbon is found in lignin. Lignin's main structural component is a polymer of randomly linked phenyl propane units connected by a wide variety of linkages. The three monolignol monomers, cumaryl alcohol, coniferyl alcohol, and sinapyl alcohol, which are all methoxylated to varying degrees, are the most prevalent precursors.[1]

This research group has developed, in the past years, a new methodology for the aerobic oxidative cleavage of 1,2-diols based on homogeneous catalysis with vanadium aminotriphenolates[2] that can be considered simple models of lignin. In this communication we will report the preliminary results obtained in the aerobic C-C-bond cleavage of cyclic 1,2-diols yielding bis-carbonyl derivatives using vanadium aminotriphenolates as catalysts both under thermal and photo-induced conditions. The two methodologies will be compared and the influences of different reaction parameters (temperature, solvent, wavelength, substrate) on the reaction course.



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