

**RMIT Applied Chemistry CHEM1108 Honours Research Projects
2004**

Title: FLUORIDE PROFILES IN TEETH (CR1)

Supervisor: Assoc. Prof. Colin Rix (Phone 9925 2628, email colin.rix@rmit.edu.au)

Consultant : Professor John Clement (Dental Hospital, University of Melbourne)

Background:

The teeth and bones of most mammals consist essentially of hydroxy-apatite ($3\text{Ca}_3(\text{PO}_4)_2 \cdot \text{Ca}(\text{OH})_2$) in a collagen matrix. Fluoride can be partly incorporated into such biominerals by OH substitution according to the following equation:



to produce fluor-apatite ($n < 0.1$) and it has been reported that Shark's teeth are almost pure fluor-apatite ($n = 1$).

Although bulk analyses for fluoride are useful, a more informative analysis in solid samples is given by a fluoride depth profile.

Fluoride profiles in "normal" human teeth are well documented. However, our aim is to measure fluoride profiles in "abnormal" teeth from individuals suffering genetic disorders and also those with fluorosis.

Finally, to our knowledge, there is only a paucity of data regarding fluoride profiles in fish teeth, and so the current investigation is intended to include a survey of this neglected area.

Aims : The aims of this project are:

1. To develop a reliable analytical procedure for the determination of fluoride profiles in hard tissue such as teeth and bones.
2. To apply the analytical method to the accurate measurement of fluoride profiles in teeth from a variety of human and fish sources.

Research Plan:

Establish a reliable analytical procedure for measuring fluoride profiles using a micro-drilling technique, in combination with fluoride and calcium analyses. This will require accurate analyses of the chemical composition of enamel and dentine, using suitably sectioned teeth.

Use the analytical protocol developed to determine accurate fluoride profiles in a variety of solid biological tissues, especially teeth.

Special requirements : Fluoride selective ion electrode and autoanalyser (provided by supervisor)

Metal Adsorption and Complex Formation in Biopolymers using a Quartz Crystal Microbalance (CRDM1)

Assoc. Prof. Colin Rix : phone 9925 2628, email colin.rix@rmit.edu.au

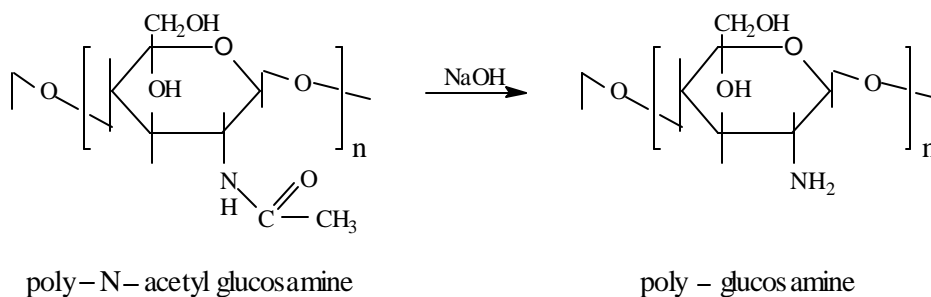
Prof. David Mainwaring : phone 9925 2125, email david.mainwaring@rmit.edu.au

Department of Applied Chemistry

This study will focus on kinetic studies of the binding of metal cations from solution to the important biopolymer *chitosan*. It will principally involve time studies of adsorption and complex formation onto thin films of chitosan at different temperatures, that is the determination of isotherms at different temperatures. This can provide the energetics of metal uptake, eg information about activation energy, enthalpy and entropy, as well as information on the role of diffusion mechanisms.

The Bio-Polymer

Chitosan is a non-toxic, polyamino-carbohydrate derived from the natural product, chitin (which is found in crustacean shells) via the following reaction :



Chitosan is a generic name used to describe chitin which has been 60-95% deacetylated.

The presence of free amino-groups in chitosan enable it to behave as a polyamine metal-binding ligand. In addition, the amino-groups can undergo reactions typical of primary amines, and so chemical modification is possible to produce polymers with selective binding properties.

Systems to be studied:

Chitosan films with copper and silver ionic solutions at various electrolyte concentrations will be studied initially. Subsequently, the surface area of the chitosan film may increased to provide higher adsorption areas.

Techniques to be employed:

Quartz crystal microbalances (QCM) are widely used to obtain information on the chemical sensitivity and selectivity of chemically active films which have been deposited on the surface of the quartz crystal. Simple quartz crystal microbalances have become very useful for determining surface

reactions that range from inorganic systems to biological systems such as immunoassays, where the mass loading simply relates to the shift in the oscillating frequency. In well controlled systems, gravimetric loading can be determined as a function of time and temperature.

More recently, it has been shown that the mass effect is not the only effect to influence QCMs. Rather a second factor, the change in film rigidity plays an important role and is capable of giving information on the changing film properties during an experiment. Since our previous research into metal ion binding on chitosan has indicated mechanisms of metal ion cross-linking, the measurement of this second effect, simultaneously with mass uptake will provide information on the evolving microstructure of the biopolymer as the isotherm proceeds. Since both measurements are made independently, these may be uncoupled and a detailed description of the process obtained.

References : Will be provided as necessary.

**Title : Preparation of Mixed Ligand Organometallic Derivatives
of Group VI Metal Carbonyls (CRJH1)**

Supervisors : **Dr Colin Rix** Phone 9925-2628, email colin.rix@rmit.edu.au
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Instruments/Techniques used : n.m.r., ESMS & FTIR .

Skills : An interest in synthetic organometallic chemistry.

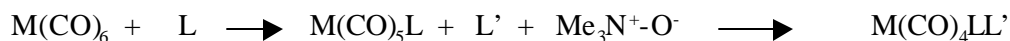
Background : The chemistry of Group VI metal carbonyl derivatives with phosphines (PR_3), phosphites ($P(OR)_3$), arsines (AsR_3) and aromatic amines is well developed, and we have made contributions in this area. However, mixed ligand compounds of the carbonyls is relatively unexplored. Thus, we intend to examine the physico-chemical properties of these compounds, especially with regard to their chemical behaviour. In addition, we plan to investigate the usefulness of Electro-Spray Mass Spectrometry as applied to these type of compounds, since the utility of this technique is not a well developed area.

Project Aims : This project aims to use a variety of nitrogen, phosphorus and arsenic ligands to prepare some metal carbonyl derivatives of Mo and W using several different synthetic routes. Various physical techniques such as n.m.r. , Electro-Spray Mass Spectrometry and i.r. spectroscopy will be used to identify and characterize the products of the reactions.

If time permits, a mono-cyclic phosphite will also be prepared and used to synthesise some metal complexes.

Project Description :

Reactions with metal hexacarbonyls :





These reactions have the potential to produce well-defined mixed-ligand complexes such as phosphine/phosphite, phosphite/arsine, etc, the chemistry of which is relatively unexplored.

References : Will be provided as necessary.

A Comparison of Chemometric Methods for the Analysis of Spectroscopic Data (JH1)

Key Words spectroscopy, mixtures,

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Aim

To compare a variety of chemometric techniques, including classical and modern regression and neural networks, for the calibration of infrared and UV/Visible spectra of complex mixtures.

Introduction

Using infrared or UV/Visible spectroscopy to analyse mixtures with very similar spectra is a challenging problem which lends itself well to analysis by chemometric methods. Use of PCs and recent software has meant these techniques have become more accessible to the analytical chemist. This means all the data from the spectrum, not just a few wavelengths, can be used in calculations. Modern techniques like Partial Least Squares and Principal Component Regression can sort out meaningful information from noise even where the components in the mixture have very similar spectra. These methods have proved very useful in the analysis of polymer spectra and hydrocarbon mixtures (such as xylenes), for example.

Another modern technique that is becoming popular is neural network analysis. In this technique a 'learning network' is trained using known mixtures. Neural networks are models of biological structures consisting of linked neurons. A neuron consists of multiple inputs and a single output. The neuron can be modified by assigning a weight to each input. The assigning of the weights is referred to as 'training' the network. While software is available to do the training there are a number of parameters that need to be set which can affect the training so, unlike regression methods, tuning of the method is necessary to obtain the best results.

Methods

Xylenes are a good model mixture set to study the effectiveness of modelling techniques. The infrared and UV spectra of each component are very similar. The spectra will initially be measured. Software such as Minitab and chemometric software such as Scan can be used to apply the regression methods. The neural network analysis will make use of an Excel ad-on called “Neuralyst”.

Other model sets of data that may be studied include polymer mixtures and colourimetric analysis of metals in solution

A Study of the Measurement of Oxygen Demand in Waste Streams (JHBM1)

Key Words oxygen demand, BOD, COD

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Aim

To study the reliability of measurements of Oxygen Demand in waste streams

Introduction

The measurement of Oxygen Demand (OD) in waste streams is extremely important in assessing the potential of this waste to pollute natural waters. The most commonly used technique to measure OD is Biochemical Oxygen Demand (BOD). Despite the lack of precision of this technique discharge limits are often expressed as BOD limits. The aim of this project is to do a comprehensive study of the variability associated with the BOD method, using samples of waste from commercial sources, and BOD with Chemical Oxygen Demand (COD) and Total Organic Carbon (TOC) measurements.

Methods

The BOD of waste samples will be measured, using DO meters to measure Dissolved Oxygen, and compared to measuring the DO by the Winkler method. The use of OxiTop bottles to directly record BOD will also be checked. COD will be measured using the closed reflux method. Statistical methods will be used to quantify the sources of variability

A Study of Natural Organic Matter in Aquatic Systems using 3-D Fluorescence Mapping (JHPCI)

Key Words natural organic matter, fluorescence

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Aim

To study Natural Organic Matter in aquatic systems, using the technique of 3-D fluorescence mapping

Introduction

Natural Organic Matter (NOM) affects pH and alkalinity of natural waters, trace metal chemistry and bioavailability, degradation and transportation of hydrophobic organic materials, formation of disinfection by-products during water treatment and heterotrophic production in blackwater ecosystems. Accordingly, NOM has received attention in a wide variety of disciplines.

The aim of this project is to study NOM using 3-D fluorescence mapping. Variation in 3-D maps would be investigated to see if these maps can characterise the sites and help to identify the source of the NOM and also identify industrial organic contaminants.

An important consideration is the effects of metal complexation to NOMs and consequent changes in the 3-D maps. This can be linked to the degree to which NOMs can mobilise metals.

Methods

Fluorescence spectra are usually measured by either fixing the excitation wavelength and measuring the emission spectrum or fixing the emission wavelength and measuring the excitation spectrum.

When measuring the 3-D spectra a series of emission spectra are recorded over a range of excitation wavelengths and these spectra used to create a contour plot of the 3-D surface. The 3-D maps of a variety of natural water samples, as well as humic fractions from soils, tannins from vegetation etc will be measured and differences between the maps investigated. Cluster analysis techniques will be applied to further investigate differences between samples. The influence of metals on the 3-D maps will also be carried out.

The Synthesis of Substituted Arylphosphonic Acids and their Application to Crystal Engineering (KLCR1_2004)

Key Words supramolecular chemistry, metal organophosphonates, phosphonic acids

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Advisor: Dr Jonathan White (School of Chemistry, Melbourne University)

Aim

Include a brief but succinct statement of the aim. You could have several sub-points.

Introduction

This section should describe the context of the project, with some background information. Explain why it may be important to do the project.

Please keep this first section, including methods to one page, so that the total project proposal can be kept to one two sided sheet.

Methods

Description of experimental methods expected to be used in the project.

PTO to page two; this should be printed on the back of page one.

Crystal Engineering of Metal-Substituted Organophosphonate Materials (KLCRAF1_2004)

Key Words supramolecular chemistry, metal organophosphonates, phosphonic acids

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Advisor: Dr Jonathan White (School of Chemistry, Melbourne University)

Aim

The aim of this synthetic inorganic-organic project is: to explore the driving forces behind the structural assembly of metal-substituted organophosphonate materials; to understand the nature and strength of the supramolecular interactions (eg. Hbonding, π - π overlap) within the molecules; and to investigate the effects of changing certain chemical features of the molecule, upon the structure type of the ultimate product(s).

Introduction

Crystal engineering is a relatively new field of chemical research concerned with controlling or predicting the type of structures that can be formed from a given ligand. Not only can such techniques be used to generate new materials with specific properties, but it can also result in a better understanding of solid-state topochemically governed reactions. Phosphonic acids have been shown to form extremely strong hydrogen bonds as the basis of their solid-state structures,¹⁻⁵ however, the use of organic phosphorus acids as a building block for supramolecular complexes has only just begun. Research in this area has traditionally concentrated on metal organophosphonates, an extensive class of organic-inorganic hybrid materials, which can adopt a wide variety of motifs: *clusters*,⁶ *networks*,⁷ and *lamellar-type (layered) complexes*.⁸

Our Group has recently produced a series of novel, supramolecular, heterocyclic adducts of copper(II) organophosphonates, by hydrothermal reaction of univalent copper complexes,⁹ $[\text{Cu}(\text{D})_2]\text{X}$ (where D = 1,10-phenanthroline (*phen*) or 2,2'-bipyridyl (*2,2'-bipy*) and X = Cl, Br, I or NCS), with organophosphonic and organosulphonic acids, with the aim of determining the effect of the organic acid, amine or 'X' upon the ultimate structure of the complexes.

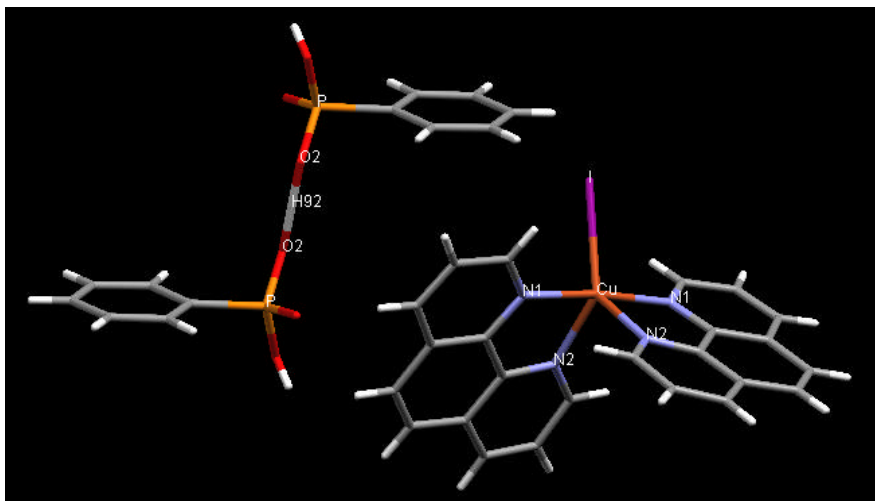


Fig. 1 Molecular unit of iodobis(*phen*)copper(II) phenylphosphonate(**3**)

Compounds **1-4**, $[\text{CuX}(\text{phen})_2][\text{C}_6\text{H}_5\text{P}(\text{O})(\text{OH})_2][\text{C}_6\text{H}_5\text{P}(\text{O})_2(\text{OH})]$, where X = Cl (**1**), Br (**2**), I (**3**) (**Fig. 1**), and NCS (**4**), are ionic in nature and possess a monoclinic structure, with the copper(II)-halide bond lying along a two-fold crystallographic axis. The crystals exhibit an alternating, lamellar structure in which one-dimensional ‘ribbons’ of $[\text{CuX}(\text{phen})_2]^+$ cations are interleaved with two-dimensional ‘sheets’ of $[\text{C}_6\text{H}_5\text{P}(\text{O})(\text{OH})_2][\text{C}_6\text{H}_5\text{P}(\text{O})_2(\text{OH})]^-$ dimers (**Fig.2**). The ribbons are associated through π - π bonding of the heterocyclic rings, and the acid sheets through a combination of π - π bonding of the aromatic rings, and hydrogen-bonding between the P=O and P-OH of neighbouring acid dimers. Analogous derivatives have also been prepared by the reaction of $[\text{Cu}(\text{phen})_2]\text{Br}$ with benzylphosphonic acid (**5**), $[\text{Cu}(2,2'\text{-bipy})_2]\text{I}$ with phenylphosphonic acid (**6**) and $[\text{Cu}(\text{phen})_2]\text{I}$ with phenylsulphonic acid (**7**).

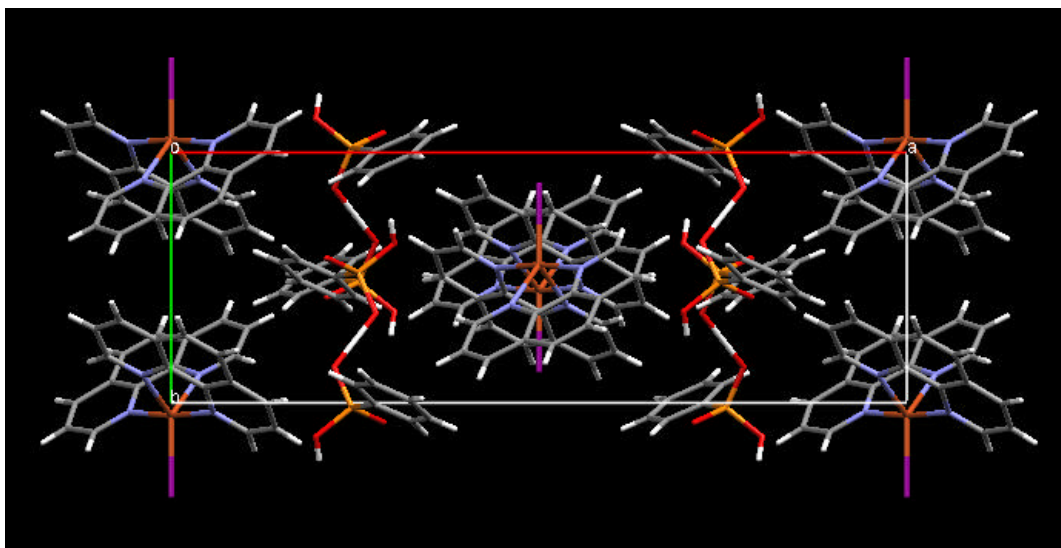


Fig.2 Crystal packing diagram of (**3**), viewed along the *c*-axis.

Program of Work

In this study we wish to further investigate the assembly of transition metal-substituted organophosphonate materials, in particular the strength/flexibility of the hydrogen-bonded acid-dimer linkage. The student will begin by preparing compounds (1) and (4) to gain experience in synthetic and characterisation techniques. Then, with the aid of literature search, and previous chemical, crystallographic and modelling data, synthetic routes to new materials containing different metals, acids, amines or 'X' substituents will be designed, and attempts made to prepare and characterise these 'target' materials. This project will run in parallel with a PhD program involving mathematical modelling of the 'target' phosphonate materials, and enabling direct comparison of synthetic and theoretical outcomes.

Any chemicals, autoclaves, synthesis ovens, required for this project will be made available from the *Solid State Materials Group*' supplies. These chemicals are in stock, and little external purchasing will be required in the initial stages of the project. The student will also require access to facilities and training in FTIR, UV/vis, TGA/DTA, Powder and Single Crystal X-ray techniques (RMIT/Melbourne), and AAS/ICP throughout the later stages of the project. The student will be expected to attend and occasionally contribute to research group meetings, and will work closely with the postgraduate students involved in this area.

References

1. Sharma, C.V.K., Hessheimer, A.J. and Clearfield, A. (2001) *Polyhedron*, 20, 2095.
2. Sharma, C.V.K., Clearfield, A., and Zhang, B. (2001) *Chem. Mater.*, 13, (10) 3099.
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8. G. Cao, H. Lee, V.M. Lynch and T.E. Mallouk, *Inorg. Chem.*, 1988, **27**, 2781.
9. R. Clarke, K. Latham, C. Rix, M. Hobday and J. White (2003) *Dalton Trans.*, submitted.

C-Glycosidation by the Wittig Rearrangement (PMcK1)

Key Words C-glycosides; carbohydrates; Wittig rearrangement

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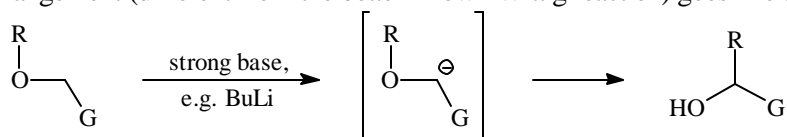
Aim

To use the Wittig rearrangement to make C-glycosides of six-membered rings

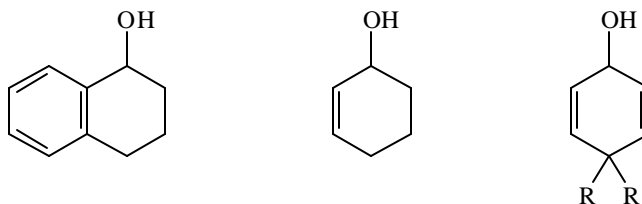
Introduction

C-Glycosides are compounds in which a sugar is attached to another organic bit by a carbon-carbon bond. Many C-glycosides have anti-cancer or anti-viral or anti-bacterial properties, but they are very difficult to synthesise. The other organic bit is very often aromatic or quinonoid.

The Wittig rearrangement (different from the better-known Wittig reaction) goes like this:

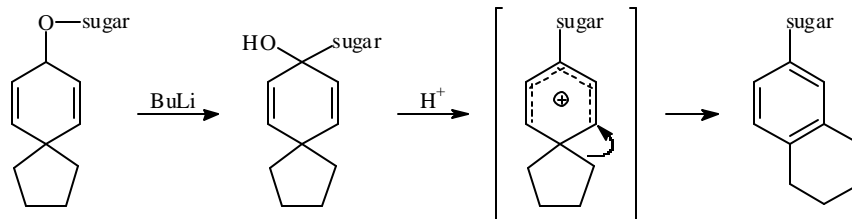


where G is preferably aromatic or vinyl. The mechanism seems to involve radical dissociation. This reaction has been used by Nakai¹ to produce benzylic and allylic C-glycosides from the easily made O-glycosides, by using a silyl-protected sugar as the R group. This project seeks to extend this reaction to make C-glycosides in which the sugar is attached to a six-membered ring, using O-glycosides of alcohols like these:



These are conveniently made by borohydride reduction of the corresponding ketones.

The third type is interesting, because acid causes the OH to be lost, creating a cation that rearranges by 1,2 migration of an R group, producing an aromatic compound. This could be very useful:



The alcohols will be converted into silylated O-glycosides of a reference sugar (glucose) using literature procedures, and these subjected to the Wittig rearrangement. The products will be isolated, chromatographed, and their structures determined by ir, nmr, and ms.

1. K. Tomoke, H. Yamamoto, T. Nakai, *J. Am. Chem. Soc.*, 1996, **118**, 3317

Methods

Organic synthesis; preparative chromatography; nmr; ir; gc/ms.

Five Carbons from Four: The Morpholine/Manganese Dioxide Reaction (PMcK2)

Key Words organic reaction; reaction mechanism; morpholine; manganese dioxide; oxidation

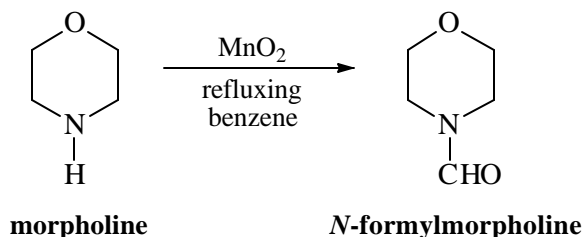
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Aim

- (i) To explore the structural requirement(s) for substrates for the morpholine/manganese dioxide reaction;
- (ii) To determine the coproducts;
- (iii) To determine the stoichiometry as accurately as possible.

Introduction

We have observed the following very strange reaction:



What happens in this reaction is a mystery. Not even the coproducts are known. Investigations so far have shown:

- (i) The reaction occurs similarly for *some* similar cyclic secondary amines;
- (ii) The yield based on morpholine is about 25–30%;
- (iii) No gases are evolved, and no other products can be found in the benzene; but some, not yet well characterized, coproducts are found strongly adsorbed to the solid manganese dioxide;
- (iv) The MnO_2 stoichiometry seems to be one mole of MnO_2 used per mole of *N*-formylmorpholine produced, at least if morpholine is in excess.

These areas need further investigation.

Methods

Organic synthesis; volumetric analysis; Soxhlet extraction; gas chromatography; nmr; ir; gc/ms.

Title Hydrazonates (PMcK3)

Key Words hydrazonate; reaction; Michael acceptor; drug synthesis; C-glycoside

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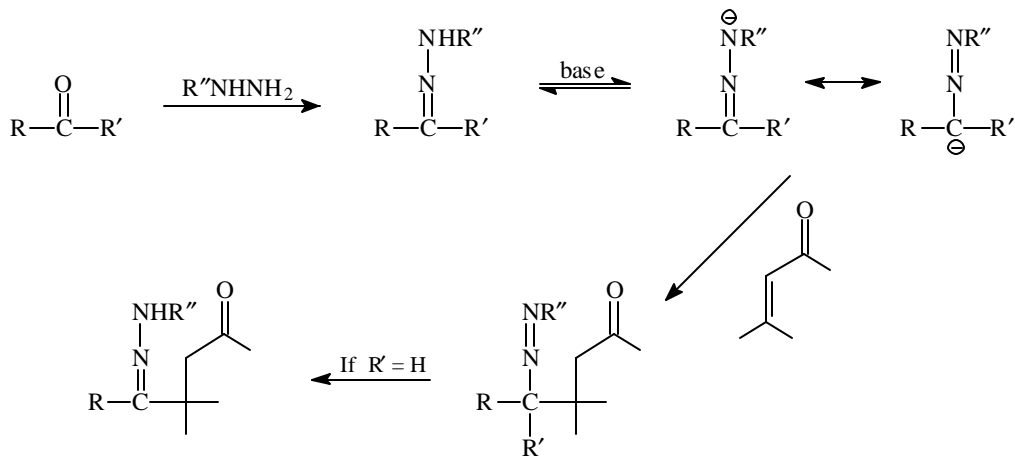
Aim

To explore the base-catalysed reactions of hydrazones with Michael acceptors.

Introduction

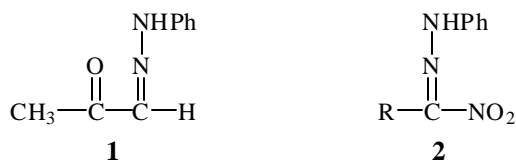
We have been looking at possible new reactions that might help in the synthesis of C-glycosides—compounds containing a sugar attached to other organic bits by a carbon-carbon bond. Some C-glycosides have very interesting antibiotic, anti-viral and anti-cancer properties, but they are hard to synthesise because of the fragility of sugars.

Carbonyl derivatives of sugars such as oximes and hydrazones are easily made, and we have been investigating potential nucleophilicity of oxime anions at carbon. Molecular calculations, however, suggest that hydrazone anions might be more reactive. In this project we'll look at the reaction of hydrazones with Michael acceptors in the presence of base:



Of course the hydrazone anion is nucleophilic at nitrogen also, but reaction with Michael acceptors at nitrogen should be reversible.

The project will find suitable base, solvent, temperature and time combinations for the reaction of model hydrazones with a Michael acceptor. It will include hydrazones with electron-withdrawing groups conjugated with the $C=N$, for example (1) and the apparently unknown (2), whose synthesis will be explored. Calculations suggest such hydrazones will react more easily still.



Methods

Organic synthesis; preparative chromatography; nmr; ir; gc/ms.

Diels-Alder Synthesis of Paulomycin Analogues (PMcK4)**Key Words** organic synthesis; antibiotics; paulomycin; Diels-Alder

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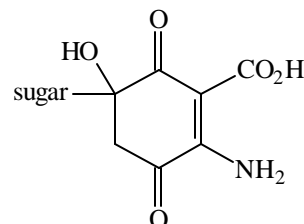
Aim

To synthesize paulomycin analogues containing simple sugars.

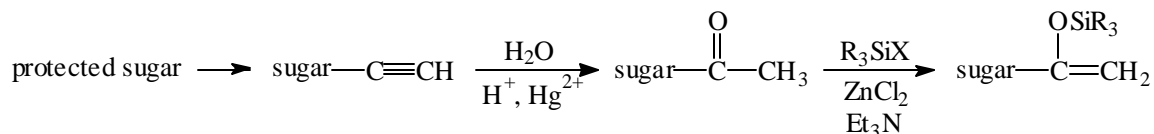
Introduction

Paulomycin is a natural antibiotic isolated from strains of the microorganism *Streptomyces paulus*. It has low toxicity and is active against a variety of bacteria, including *Staphylococcus aureus* ('golden staph') strains that are resistant to other antibiotics. This is very important, since multiply-resistant golden staph is now endemic, and is the principal cause of post-operative wound infection.

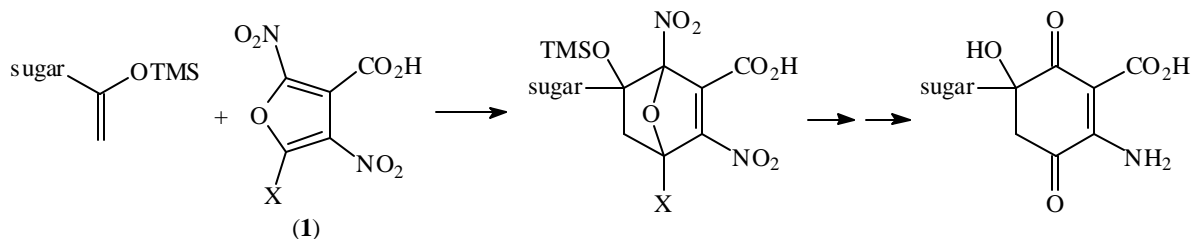
Paulomycin has the form shown on the right. The sugar is a very complex disaccharide. (There are actually several paulomycins, which differ slightly in the sugar part.) The requirements in the sugar for activity are not known; this project will use a simple model sugar. Note that the sugar is attached to the rest of the molecule by a carbon-carbon bond. This project will explore an approach to the synthesis of the above type of compound, using a Diels-Alder reaction with inverse electron demand. Two previous Honours projects are available to build on.



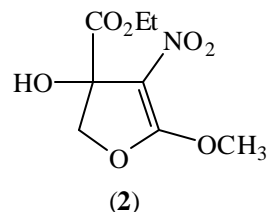
Electron-rich sugar-containing dienophiles will be prepared by means of alkyne chemistry:



An ethynyl sugar has already been prepared and only needs to be converted to the oxyalkene. This will be reacted with suitable electron-deficient dienes of the form (1):



Considerable progress has been made towards the synthesis of **1**: we have prepared a furan of the form **2**, which, however, is very resistant to E1 dehydration. Other dehydration methods need to be explored and the second nitro group added.



Methods

Organic synthesis; nmr; ir; gc/ms. Molecular modelling may be useful.

Thionitrites: a potent functional group? (PMcK5)

Key Words Thionitrite; vasodilator

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Aims

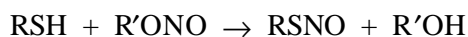
1. To investigate optimum methods of preparation of thionitrites;
2. To prepare samples of representative primary, secondary and tertiary thionitrites from pure thiols and compare their stabilities;
3. To obtain and analyse n.m.r., infra-red, ultraviolet/visible and mass spectra of these thionitrites, and thereby establish their structures and the relationships between structures and spectroscopic properties.

Introduction

Thionitrites are compounds of the general structure R–S–N=O. They are somewhat unstable (those with tertiary R are most stable), decomposing to RSSR and nitric oxide NO. NO is a neurotransmitter, and is part of the sequence of events that dilates blood vessels. Thionitrites are both natural and potential artificial sources of NO. They may therefore be medicinally useful in the treatment of angina, baldness and impotence, especially as their low polarity would aid absorption through the skin.

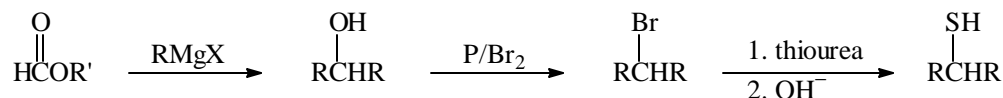
Nevertheless, the chemistry of thionitrites has been little explored, and even spectroscopic data is very thin on the ground. One curious observation in the literature is that tertiary thionitrites are green, and primary ones are red. We have found that all thionitrites are bichromic—in low concentration or thin layers they look green, in high concentration or thick layers they look red. Tertiary ones look green at higher concentrations than primary ones. The n.m.r. properties are also unusual and need further investigation.

It is claimed in the literature that thionitrites are most easily made from thiols RSH and NO₂. The claimed stoichiometry is not consistent with our observations, and we have found that ‘thionitrites’ prepared by this method contain large amounts of disulphide RSSR. Preliminary work suggests that a much better results are obtained using alkyl nitrites:



We shall use ethyl nitrite, b.p. 17°, which can easily be prepared in quantity.

Thiols—mainly large ones, to reduce (but not eliminate) smells—will be purified and carefully characterised. A few thiols, especially secondary ones, will be prepared (see e.g. the scheme below). Several different thionitrite preparation procedures will be trialled to determine which gives the purest and most stable product. Spectra will be run; sometimes this will require rapid working.



Methods

Organic synthesis; nmr; ir; uv; gc/ms.

Synthesis of Cochineal Waxes (PMcK6)

Key Words organic synthesis; natural products; wax; cochineal; chemotaxonomy

Supervisor Peter McKay
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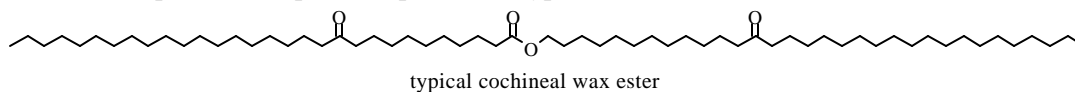
Aim

To synthesise reference samples of cochineal wax esters for comparison with biological samples.

Introduction

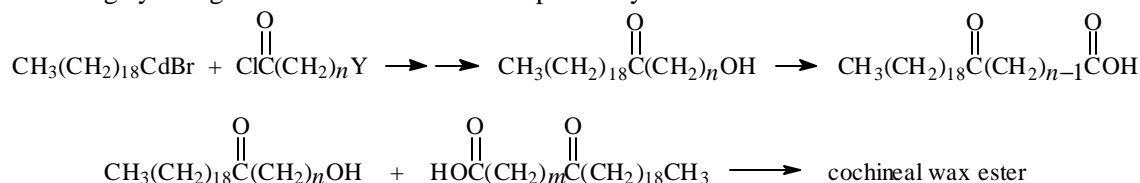
The cochineal insect is a fascinating scale insect that lives on prickly pear. It provides a fast red dyestuff, which was formerly used to dye cloth and is still used as a food dye.

There are several 'wild' species of the cochineal insect, and one 'domesticated' species, of unknown origin, which needs human care to survive, but produces copious dyestuff. The wild species are hard to distinguish, but we have shown that the wax they secrete—which, unusually, is often only one or two compounds—is species-dependent. A typical structure is:

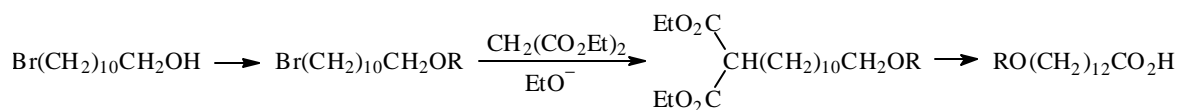


Structures from different species give interesting insights into the relationships between the species.

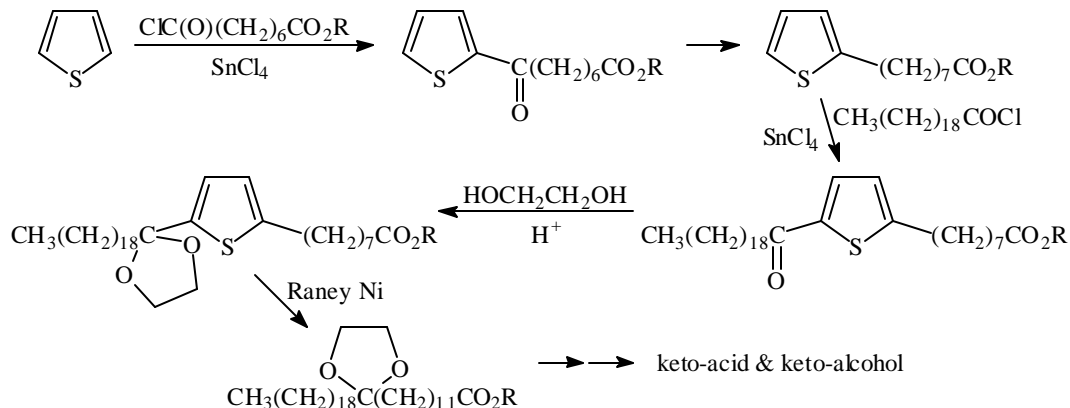
This work however needs reference compounds of known structure. Making these is not trivial, since steric hindrance is significant in long chain compounds, and recrystallisation does not always purify them. High-yielding reactions must be used. One possibility is



This will require producing a 13-oxy tridecanoic acid from commercial 11-bromoundecanol:



An alternative route uses thiophene technology:



Methods

Organic synthesis; nmr; ir; gc/ms.

Synthesis of Tryptamines (TR1)

Key Words tryptamine derivatives, organic synthesis, microwave synthesis.

Supervisor Trevor Rook

Cosupervisor Jim Pearson

Room 3.2.23

Organisation Victoria Forensic Science Centre

Telephone 9925 3361

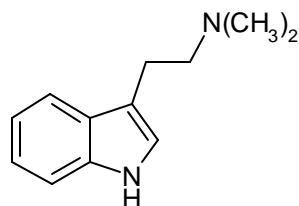
E-mail trevor.rook@rmit.edu.au

Aim

The aim of this project is to synthesise and fully characterise a range of tryptamine derivatives for the Victoria Forensic Science Centre.

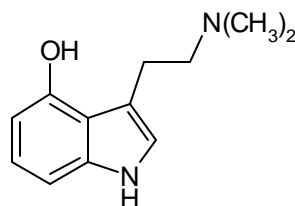
Introduction

Tryptamines are an important class of bioactive compounds based on the indole backbone and a number have hallucinogenic properties. Natural products included in this class are LSD and psilocybin; as well there are a number of synthetic analogues. The forensic science laboratory of the Victoria Police - Victoria Forensic Science Centre - is interested in obtaining a range of these synthetic compounds as analytical standards. These are all known compounds, hence the project will explore new synthetic methods for their production. This will include adaptation of existing methods and development of entirely new synthetic procedures. In particular, the use of microwave methods will be explored.



CR/jc. Fluoride:ww2

N,N-dimethyltryptamine



4-Hydroxy-N,N-dimethyltryptamine

Title **Synthesis of Benzylpiperazines (TR2)****Key Words** benzylpiperazine derivatives, organic synthesis, microwave synthesis.**Supervisor** Trevor Rook

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Cosupervisor Jim Pearson

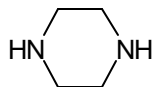
Organisation Victoria Forensic Science Centre

Aim

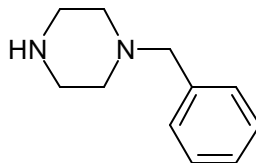
The aim of this project is to synthesise and fully characterise a range of piperazine derivatives for the Victoria Forensic Science Centre.

Introduction

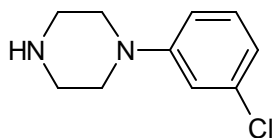
Piperazine derivatives are a relatively new class of compounds that have come onto the illicit drugs market overseas. Benzylpiperazine is considered to have effects very similar to ecstasy. The forensic science laboratory of the Victoria Police - Victoria Forensic Science Centre - is interested in obtaining a range of these synthetic compounds as analytical standards. These are all known compounds; hence the project will explore new synthetic methods for their production. This will include adaptation of existing methods, and development of entirely new synthetic procedures. In particular, the use of microwave methods will be explored.



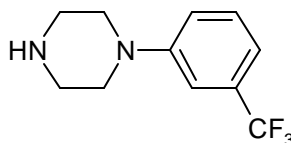
piperazine



benzylpiperazine



3-chlorophenylpiperazine



3-trifluoromethylphenylpiperazine

Methods

Organic synthesis and characterisation.

Title: Development of a Three-Dimensional Separation Technique – On-line Hyphenated HPLC-GC × GC (PM01)

Key Words GC×GC; Capillary GC; Normal-phase HPLC; Reversed-Phase HPLC; cryogenic modulation; high resolution; Fast GC

Supervisor Professor Philip Marriott
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Aim

To implement and investigate a new Three-Dimensional Separation method based initially on normal-phase HPLC separation in combination with comprehensive two-dimensional gas chromatography (GC×GC). To test applications of this new approach by studying and quantifying key molecular separations tasks that can be achieved by using class separation in HPLC with ultra-high resolution GC×GC.

Introduction

Over the past 5 years, the RMIT ACROSS (Australian Centre for Research on Separation Science) group has been developing a technique invented in this Department, called cryogenic modulation. Two advanced operational modes called comprehensive two-dimensional gas chromatography (GC×GC) and targeted multidimensional gas chromatography (TMDGC) have been the primary research areas. Recent studies in petrochemical and essential oil analysis suggest that we can still search for even greater separation power. The use of HPLC will allow some degree of class separation of complex samples prior to the final finish of GC×GC. In this way, we expect to be able to realise even greater separation power for ultra-high resolution chemical separation. The logical development of a new instrumental technique involves demonstration of fundamental operational principles, evaluation of its scope and limitations, and perhaps most of all to promote and achieve widespread acceptance. It is also important to apply the technique to as wide a range of analytical studies as possible. Previous HPLC-GC studies have addressed petrochemicals, essential oils and fatty acids/triglycerides. Our HPLC-GC×GC applications will be directed to these areas, with a view to develop general principles of the technique. The aim is to generate publishable basic, analytical performance and applications studies of the technique.

**Title: New Methods for Amino Acid Analysis by using
Comprehensive Two-Dimensional Gas Chromatography
(GCxGC) (PM02)**

Key Words GCxGC; Capillary GC; Amino Acid analysis; cryogenic modulation; high resolution; Fast GC

Supervisor Professor Philip Marriott co-Supervisors Dr Danielle Ryan; Dr Craig Trenerry
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Aim

To investigate the application of GCxGC to the analysis of amino acids derivatives in a range of materials, from consumer products to natural products.

Introduction

The analysis of amino acids (AAs) is a topical and important subject. Amino acids are basic nutritional compounds which are the fundamental building blocks of proteins. Many foods contain amino acids, and increasingly AAs are found in nutritional supplements, as so called 'health foods'. Many consumer products also contain naturally-derived AAs, for instance in beer, and other foods. It is of interest to determine the daily intake of such nutrients in the typical diet. Traditionally, chromatographic methods are used for the analysis of amino acids. Both GC and HPLC are employed for this speciation task. For the former, derivatisation is required before suitable analysis can be conducted, but GC analysis does allow high resolution separation and importantly GC/MS methods to be used. HPLC is used as an alternative method. For detection sensitivity and specificity, derivatisation is also needed – either post- or pre-column. Without HPLC/MS, identification remains uncertain. We have developed a new technique of comprehensive two-dimensional gas chromatography, which offers greater sensitivity and separation power, and we wish to start this method for routine and high-efficiency AA analysis. By using GCxGC hyphenated with our time-of-flight mass spectrometer, we should be able to screen AAs in a range of samples. A new simplified derivatisation process will be employed for preparation of the AA samples. The outcomes of this project will firstly be publishable methods for GCxGC analysis of AAs, and applications involving AA assays in a range of natural products.

***Title:* Comprehensive Two-Dimensional Gas Chromatography for Forensic Analysis of Chiral Drugs in the Racing Industry (PM03)**

Key Words GCxGC; Capillary GC; Drug analysis; cryogenic modulation; high resolution; Fast GC

Supervisor Professor Philip Marriott co-Supervisor Dr Paul Wynne (RASL)
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Aim

To study advanced separation methods for the enantioselective analysis of a variety of drugs by using comprehensive two-dimensional gas chromatography. To undertake a study of real sample analysis of alkaloids from plants, and metabolite formation *in vivo* using enantioseparation to deduce chiral ratios in selected drugs

Introduction

We have demonstrated the use of comprehensive two-dimensional gas chromatography (GCxGC) for the analysis of drugs of interest to the racing industry, and prolintane metabolites in dog urine. More recently drug screening in toxicological samples has been studied, again by using GCxGC. We wish to now extend these studies by investigating chiral separations of these drugs. Whilst enantioseparations are not routinely performed for routine drug testing, there is an increasing research interest in analysis of the chiral forms of drugs, since they often have quite different (toxicological) activities. Further interest lies in the different rates of metabolism of the chiral forms, since this usually is strongly correlated with isomeric structure. In this study, we wish to develop GCxGC and GCxGC/TOFMS methods for routine analysis of chiral drugs. Once the fundamental separation performance has been established, we will then select typical studies of drugs e.g. extracted from plants or from animal metabolic studies using samples available from RASL, to provide demonstration of the utility of the method for chiral recognition of drugs. This project builds upon our previous studies, but also links with a current research program in development of chiral selectors for enhanced separation of target enantiomeric separations.

***Title:* Time-of-Flight Mass Spectrometry Technology for Fast GC and Comprehensive Two-Dimensional Gas Chromatography (PM04)**

Key Words GCxGC; Capillary GC; Fast GC; TOFMS

Supervisor Professor Philip Marriott co-supervisor Robert Shellie
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Aim

To study methods available with time-of-flight mass spectrometry for qualitative and quantitative analysis by using fast gas chromatography and the advanced separation technique of comprehensive two-dimensional gas chromatography (GCxGC). To develop two-dimensional separation maps for analysis of essential oils in GCxGC-FID and GCxGC-TOFMS.

Introduction

Whilst comprehensive two-dimensional gas chromatography (GCxGC) is a powerful separation method, there is an underlying need to provide an additional dimension of identification of compounds by using mass spectral acquisition. The most appropriate MS technology for the fast chromatography peaks generated in GCxGC is time-of-flight (TOF) MS. An additional advantage of TOFMS is its unique spectral deconvolution performance for overlapping peaks. One of our main application areas for GCxGC is essential oil analysis. One of the complications of MS for these samples is that many components have similar mass spectra. Thus we often require both peak retention, and MS matching to give improved identification. By using two dimensions of separation (GCxGC), we improve significantly the power of GC to separate and give better retention information to match with component identity. TOFMS can then be added to further confirm peak identity.

Since TOFMS also allows deconvolution, it is important to develop an understanding of this procedure, and so we will also study fast gas chromatography for essential oil analysis, and evaluate the power of fast GC-TOFMS for routine analysis and identification. This can then be contrasted with GCxGC-TOFMS as an analytical tool. Quantitative measurements will also be of interest, and so this must be included in overall evaluation of the methods.

This project builds upon our previous studies on, GCxGC-FID, GCxGC-TOFMS and GCxGC-quadrupole MS, and will provide our laboratory with improved understanding of the applicability of TOFMS methods to various analytical tasks.

If time allows, we shall also include development of 'retention maps', or GC/GC/MS libraries for essential oils.

Title: The direct separation of the diastereoisomers and enantiomers of the fungicide triadimenol and related compound triadimefon by capillary electrophoresis (PM05)

Key Words Capillary Electrophoresis (CE); HPLC; Fungicide analysis; HPLC/MS

Supervisor Professor Philip Marriott co-supervisor Dr Craige Trenerry, (State Chemistry Laboratory – now Primary Industries Research Group (PIRG) of the DPI)

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Aim

The target compounds are fungicides used in crop production. This project will study the analytical methods for analysis of mixtures of these compounds, and their residues in various products, such as grapes. An important aspect will be to develop procedures for separation of their isomers, in order to be able to study metabolism of the fungicides.

Introduction

Triadimefon is optically active (2 isomers) and triadimenol has 2 pairs of diastereoisomers. This project will study separation of the two compounds by CE, including their isomers, followed by the separation of the optical isomers isolate residues in grape marc (incurred and spiked) and other matrices extracted by SPE methods. This will allow determination of the total fungicide content, and also the optical isomer speciation. The CE methods will be compared with total fungicide content data obtained by GC and/or LCMSMS.

The preferential isomer breakdown of the two compounds with time in the environment, will be an additional study that given time will be an important indicator of mechanisms into persistence of the different isomers under environmental conditions.

The project is intended to include field trials in conjunction with the Institute at Mildura on wine extracts.

Methods for extraction of typical fungicides are available, and also separation procedures for these compounds by using HPLC, GC and CE. Chiral separations have been reported, but not for both of the target compounds, nor in matrices that will be investigated here.

. ***Title***: Extraction and analysis of Nitrofuran residues from foods and animal produce by using Liquid Chromatography methods (PM06)

Key Words HPLC; Pesticide analysis; HPLC/MS

Supervisor Professor Philip Marriott co-supervisor Dr Nigel Simpson (Varian Inc)
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Aim

The target compounds are pollutants that occur especially in shellfish and shrimp, and as toxicants their presence in food must be identified in situations where they are likely to be in the environment. This project will implement and develop methods for the extraction and analysis of the target pollutants in various matrices, and attempt to identify metabolites.

Introduction

The broad area of proposed research is extraction and analysis by LC (and LC/MS if available) of Nitrofurans residues from foods and animal produce. The scientific goal is to produce a method or methods that demonstrate good extraction by Solid-Phase Extraction (SPE) and separation by Liquid Chromatography.

Solid phase extraction techniques will be optimized to permit maximum extraction performance towards the residues, whilst minimizing co-extracted impurities.

HPLC will be based on reversed-phase methods, and will employ a range of detection methods – UV-vis, fluorescence and diode array, and hopefully Mass Spectrometry. Again, optimized separation performance and validated separation will be an aim.

The educational goal would be to provide contemporary experience in an area of current interest in the global analytical chemistry world.

The opportunity to collaborate with industry on the project design, and subsequently the writing of research results for publication in a scientific journal or promotion at technical conferences, depending on the completeness and quality of data generated, will be a second goal.

Varian Inc will provide the SPE and HPLC columns required to complete this work and will co-mentor the student undertaking the research. Varian will assist in obtaining standards and will support purchase of solvents for the separation stage.

If the outcomes of the project permit preparation of a technical note for the use by Varian in their product literature, results will be provided to Varian to permit this to be done.

Title Alcohol and aldehyde concentrations in commercial transport vehicles. (TENP1)

Key Words ethanol fuels, buses, formaldehyde

<i>Supervisor</i>	Terry Elms	<i>Cosupervisor</i>	Nichola Porter
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Aim

The aim of this project is to assess the exposure of bus drivers to formaldehyde as a result of exhaust fumes from different types of fuels.

Introduction

With the move to reducing air pollution, some vehicles, including buses, are now running on ethanol based fuels. However, one of the problems associated with this type of fuel is the production of formaldehyde. This project will investigate the levels of formaldehyde to which passengers and bus drivers are subjected. The formaldehyde method will need to be validated before sampling air on buses

Methods

The first part of the project will be to set up the methods for measuring formaldehyde. This will be followed by sampling experiments, in which monitors will be placed in the cabins of consenting bus drivers. It is anticipated that the student will use GC analysis for these experiments.

Title VOC Emissions from New Vehicles. (NPJH1)

Key Words car interiors, indoor air quality, VOCs

Supervisor	Jeff Hughes	Cosupervisors	Terry Elms/Nichola Porter
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E-mail		E-mail	terry.elms@rmit.edu.au

Aim

The aim of this project is to determine the major contributing products found in the materials used in the interior of new vehicles which contribute to the “new car” smell.

Introduction

Everyone is familiar with the “new car” smell. Previous work has shown that the levels of VOCs in new cars can be very high, exceeding the limits recommended for indoor air¹. In 2003, a second project was conducted to determine the sources of these compounds. While some compounds were identified, others need elucidation and correlating with compounds actually found inside the new vehicles

Methods

Initially materials will be obtained from a car manufacturer and subjected to different temperatures. The emissions will be collected using head space solid phase extraction methods. Once the techniques have been validated, they will be used to measure compounds found inside a new vehicle on a warm day. SPME and GC-MS will be the two main methods used for this project.

¹ Taavi Hunt VOC Emissions Form New Cars, Honours Thesis, Department of Applied Chemistry, RMIT 2002.

Title Variation of flavinoids in grapes during the growing season (NPTE1)

Key Words wine, grapes, flavonoids, sunlight, shade, GC-MS

Supervisor	Nichola Porter	Cosupervisor	Terry Elms
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E-mail	nichola.porter@rmit.edu.au	E-mail	terry.elms@rmit.edu.au

Aim

The aim of this project is to establish the techniques required to measure a number of chemicals important for the flavour of wine and their variation during the growing season.

Introduction

Flavonoids are important chemicals in the make up of wine; they add flavour, colour and antioxidants. They also influence the mouth feel of the wine. They can be divided into three groups anthocyanins, flavonols and flavans

Anthocyanins are largely responsible for the red colour of wine and are usually found only in the skin of red grapes. Flavonols are less intensely coloured and tend to be yellow. They add bitterness to the flavour of the wine and it is believed they also act as a sun screen for the plant. Flavans also add bitterness to the flavour wine but they are involved in the formation of phenolic polymers, which tend to add astringency.

The combination of these compounds has a significant influence on the quality of the wine. The concentration of these compounds will vary with time of year and may vary with levels of sunlight. Consequently, the effect of shade may have a significant influence. This project will set up the techniques for measuring these compounds and will apply the techniques to grapes grown with and without shade in a vine yard close to Melbourne.

Methods

The method of analyses will require extraction techniques followed by GC-MS

Title Emissions from wood mulch (NP1)

Key Words wood, mulch, VOC, analysis, GC-MS

Supervisor	Nichola Porter	Cosupervisor	Ian Galbally
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Telephone	9925 7187	Telephone	
E-mail	nichola.porter@rmit.edu.au	E-mail	

Aim

The aim of this project is to monitor the emissions from wood mulch over time and identify the main emission products.

Introduction

When plants are cut, they emit an array of chemicals. Some of these chemicals are to defend the plant from pest attack, while others are involved in the healing process. These and other compounds give rise to the characteristic smells, which arise from cut grass and mulched wood. Some of the VOCs emitted contribute to photochemical smog. It has been estimated that in peak mowing season that these emissions contribute up to a third of the total VOC emissions²

In a project just completed on *Grevillea Robusta*³, a number of compounds were identified by GC-MS using sorbent tubes and canisters to collect the emissions. The project to be conducted in 2004 will investigate another species. Results from head space solid phase extraction will be compared with extraction via thermal desorption tubes.

For the most part, the project will be conducted at the CSIRO in Aspendale where the chambers for collecting the emissions have already been set up.

Methods

The chosen species will be mulched and placed into chambers designed at the CSIRO for this type of analysis. The method of analyses will require extraction techniques followed by GC-MS

Title Terrestrial Natural Products – Chemical Investigation of Australian flora (SU1)

Either the Chemical Investigation of *Helichrysum diosmifolium*

or

The Chemical Investigation of the Western Australian Banksia, *Leptophylla* subspecies *melletica*

² www.dar.csiro.au/publications/Galbally_2002a.pdf Air Pollution And The Smell Of Cut Grass Wayne Kirstine, Ian Galbally and Martin Hooper accessed 6/12/03

³ Fedele Rosemary, Biogenic Emissions from *G. robusta* Mulch, Honours Thesis, Department of Applied Chemistry RMIT, 2003

Key Words natural products, extraction, isolation, purification, characterisation, structural elucidation, biological activity

Supervisor Dr Sylvia Urban
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Aim

The project scope is to carry out the extraction of an Australian plant specimen. The selection includes either *Helichrysum diosmifolium* or *Leptophylla* subspecies *melletica*, both of which display some biological activity. The ultimate aim is to isolate and purify both the biological active secondary metabolite(s) as well as any other interesting natural products.

Introduction

The focus of the Marine and Terrestrial Natural Product Chemistry (MATNAP) Group is directed towards the area of isolation and structural elucidation of novel natural products. Once secondary metabolites have been identified the emphasis shall be to evaluate these for any biological activity. The overall aim of the group is to study natural products for potential applications as new pharmaceuticals (drug discovery) or agrochemicals or indeed other applications.

In this project you will have a choice to investigate either the Australian plant, *Helichrysum diosmifolium*, collected from the Mornington Peninsula in December 2002 or the Western Australian banksia *Leptophylla* subspecies *melletica*, collected 22 km north of Eneabba in June, 2003. A biological evaluation of the crude extract of both plant specimens indicated that both possess some anti-microbial, anti-tumour and anti-viral activities. Chemical investigation will begin by performing an extraction of the plant material, followed by isolation via chromatographic purification (bench columns and HPLC) of secondary metabolites. This will be followed by a full characterisation and structural elucidation of all isolated compounds, involving standard analytical techniques as well as 1D and 2D NMR spectroscopy. All natural product(s) isolated will be re-screened for biological activity to confirm the bioactivity of the crude extract.



Helichrysum diosmifolium
 (photo by S. Urban)



Banksia *Leptophylla* subspecies *melletica*
 (photo by S. Urban)

The project would be best suited to a person that enjoys the challenge of working in an exciting area of chemistry, the use of analytical instruments, the challenge of NMR interpretation of a complete unknown and the reward of isolating a novel natural product, which will justify a journal publication.

Methods

Solvent extractions, column chromatography and HPLC will be applied for extraction and purification. For characterisation of natural products IR, UV, mass spectrometry and NMR spectroscopy will be employed. Chemical degradations, further NMR experiments, molecular modelling and possible synthesis for structure confirmation may be applied.

Title Marine Natural Products – An Investigation of the algae, *Laurencia* sp.(SU2)

Key Words natural products, extraction, isolation, purification, characterisation, structural elucidation, biological activity

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Aim

The project scope is to carry out the extraction of two marine algae of the *Laurencia* sp. Biological evaluation of the two *Laurencia* sp., indicated that both displayed significant biological activity. Following initial investigations (including a comparison of chemical constituents), one of the two algae will be selected for large-scale extraction. The ultimate aim will be to isolate and purify both the biological active secondary metabolite(s) as well as any other interesting natural products.

Introduction

The focus of the Marine and Terrestrial Natural Product Chemistry (MATNAP) Group is directed towards the area of isolation and structural elucidation of novel natural products. Once secondary metabolites have been identified the emphasis shall be to evaluate these for any biological activity. The overall aim of the group is to study natural products for potential applications as new pharmaceuticals (drug discovery) or agrochemicals or indeed other applications.

In this project you will initially investigate two southern Australian marine algae, *Laurencia filiformis* var. *heteroclauda* and *Laurencia elata*, collected intertidally from St Paul's beach Sorrento in January 2003. A biological evaluation of the crude extract of this plant specimen indicated that both possessed significant anti-microbial, anti-tumour and anti-viral activities. Chemical investigation will begin by performing a small-scale extraction of both algae to carry out a secondary metabolite investigation and comparison study. Following from this analysis one of the algae will be selected for a large-scale extraction followed by isolation via chromatographic purification (bench columns and HPLC) of secondary metabolites. This will be followed by a full characterisation and structural elucidation of all isolated compounds, involving standard analytical

techniques as well as 1D and 2D NMR spectroscopy. All natural product(s) isolated will be re-screened for biological activity to confirm the bioactivity of the crude extract.



Laurencia sp. (Photo by S. Urban)

The project would be best suited to a person that enjoys the challenge of working in an exciting area of chemistry, the use of analytical instruments, the challenge of NMR interpretation of a complete unknown and the reward of isolating a novel natural product, which will justify a journal publication.

Methods

Solvent extractions, column chromatography and HPLC will be applied for extraction and purification. For characterisation of natural products IR, UV, mass spectrometry and NMR spectroscopy will be employed. Chemical degradations, further NMR experiments, molecular modelling and possible synthesis for structure confirmation may be applied.

Title Mass Spectrometry of Natural Products – An Investigation of the Phenoxazone Pigments of the Orange-Rot Fungus, *Pycnoporus cinnabarinus* (SU3)

Key Words mass spectrometry, natural products, extraction

Supervisors Dr Peter Cullis and Dr Sylvia Urban
Department of Applied Chemistry

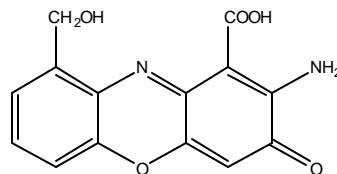
Telephone 9925 3363 and 9925 2635

E-mail peter.cullis@rmit.edu.au and sylvia.urban@rmit.edu.au

Aim

The project scope will involve small-scale extraction, isolation and structural characterisation of compounds produced from the orange-rot fungus, *Pycnoporus cinnabarinus*. The fungus is known to produce phenoxazone pigments and the possible presence of cinnabarin (1) has been established in this specimen.¹ The ultimate aim of this project is to use various mass spectrometry techniques such as electrospray mass

spectrometry and LC/MS to confirm the presence of the phenoxazone pigments and to possibly identify the presence of additional phenoxazone analogues.



(1)

Pynoporus cinnabarinus (Photo by S. Urban)

Introduction

Polypore fungi that form orange bracket-shaped reproductive bodies (basidiocarps) on dead wood are known as the orange rot fungus. In this project you will investigate the pigments associated with the orange-rot fungus, Pynoporus cinnabarinus (kingdom: fungi; phylum: Basidiomycota; class: Basidiomycetes; order: Polyporales; family: Polyporaceae; genus: Pynoporus). In the past, the fungus has also been referred to as Trametes cinnabarina, a 'shelf' fungus. The constituents of T. cinnabarina, have been only minimally characterised to date, but it is known that the fungus contains organic germanium at 800-2000 parts per million (ppm).² In this project, various small-scale extractions of the fungus will initially be carried out as the phenoxazone pigments associated with the orange-rot fungus are notoriously insoluble in most organic solvents and in water. Following on from this the aim

Title Chemical and Biological Investigation of the marine sponge, *Latrunculia* sp. (SU4)

Key Words natural products, extraction, isolation, purification, characterisation, structural elucidation, biological activity

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Aim

The project scope is to carry out the extraction of the Victorian marine sponge, *Latrunculia* sp., which has been selected on the basis of the ability for the crude extract to inhibit neuronal nitric oxide synthase (n-NOS).^{1,2} The ultimate aim is to isolate and purify both the biological active secondary metabolite(s) as well as any other novel/interesting natural products. The project forms the basis of a joint collaboration between the Marine and Terrestrial Natural Product Chemistry (MATNAP) Group at RMIT University and the Australian Institute of Marine Science (AIMS). The shared interest includes:

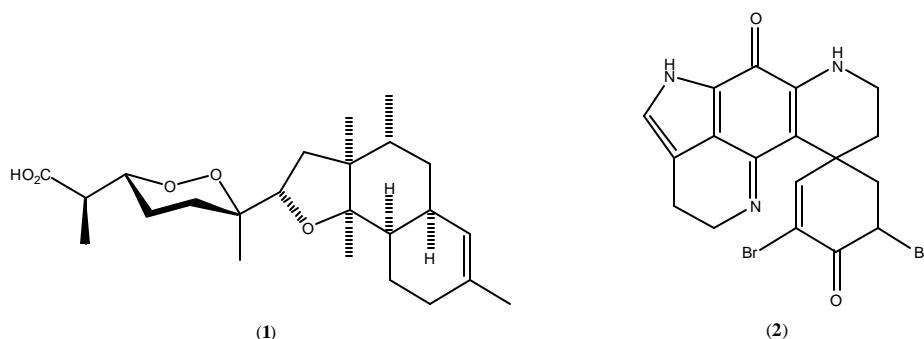
- 1) To expand a marine bio-resources library to enhance national opportunity in biodiscovery
- 2) To conduct collaborative research with the goal of isolating novel chemistry



Latrunculia sp. (Photo provided by AIMS)

Introduction

Trunculins such as trunculin F (**1**) and Contrunculins have been previously isolated from a Victorian sponge, *Latrunculia*.³ Discorhabdins such as discorhabdin C (**2**) have been isolated from the same genus of sponge collected in New Zealand waters,⁴ and *Prianos* collected from Japan.⁵ These compounds are proving useful as anti-tumour and immunomodulatory agents, as well as inhibitors of neurodegenerative processes.⁶



Groweiss *et al* noted that collections of the same species of *Latrunculia* from different spots of the Gulf of Eilat and the Gulf of Suez yielded slightly different chemistry.⁷ The impact the environment may have on the chemistry produced by the sponge is of great interest and may provide a raft of novel chemistry. In this project the Bioactives Research Team within the Marine Biotechnology Group at AIMS is interested in comparing the chemistry of samples from the same genus collected in both tropical and temperate waters. n-NOS is a critical enzyme involved in the maintenance of cellular health. Excessive stimulation, however, produces an abundance of free radical nitric oxide that can be detrimental to the cell. The goal is to identify novel chemistry that act as n-NOS inhibitors. These have the potential to be used as leads for therapeutic drugs, such as in the treatment of stroke victims.^{8,9}

The project would be best suited to a person that enjoys the challenge of working in an exciting area of chemistry, the use of analytical instruments, the challenge of NMR interpretation of a complete unknown and the reward of isolating a novel natural product, which will justify a journal publication.

Methods

Full taxonomy will be provided by AIMS. Solvent extractions, column chromatography and HPLC will be applied for extraction and purification. For characterisation of natural products IR, UV, mass spectrometry and NMR spectroscopy will be employed. AIMS will also provide access to their Biomolecular Analysis Facility and any additional databases. will be to detect and confirm the presence of the phenoxazone pigments such as cinnabarin by:

1. Atmospheric pressure ionisation (API) mass spectrometry (ESI/MS and APCI MS)
2. Matrix Assisted Laser Desorption Ionisation (MALDI) MS
3. LC separation followed by MS techniques developed above
4. An MS/MS study primarily using MALDI post source decay (PSD) to elucidate the structures of the phenoxazones
5. To determine if any novel phenoxazones are present (possible structures), possibly with the aid of other spectroscopic techniques

Methods

Extractions involving various organic solvents, water, acid and base. HPLC and mass spectrometry will be employed. There is also a possibility of using GC/MS for this study.

