Deposition and arrangement of cellulose microfibrils during collenchyma cell development

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Cellulose serves as key load bearing biopolymer in plant cells, whose deposition and alignment is of vital importance to direct cell expansion, regulate cell growth rate and determine cell shape. However, a unified conclusion has not been drawn on how they change during plant development in order to maintain wall rigidity. In the current study, celery collenchyma, a representative of thickened primary walls, were used. We found that the cellulose microfibrils deposited more or less transversely regardless of developmental stages, but the cellulose microfibrils became more longitudinal orientated with formation of ordered herringbone patterns during growth, suggesting passive orientation of cellulose microfibrils could occur during plant growth.



Figure 1. AFM image of cellulose microfibrils in the outer surface of young collenchyma cells (A) and estimated cellulose microfibril angles distribution at different maturity (B) from small angle X-ray scattering.

- 1. Saxe, F., Eder, M., Benecke, G., Aichmayer, B., Fratzl, P., Burgert, I., & Rüggeberg, M. (2014). Measuring the distribution of cellulose microfibril angles in primary cell walls by small angle X-ray scattering. *Plant methods*, *10*, 25-32.
- 2. Leroux, O. (2012). Collenchyma: a versatile mechanical tissue with dynamic cell walls. *Annals of botany*, *110*, 1083-1098.

Total synthesis of ovafolinin A and B via a novel cascade cyclisation



Figure 1. Structures of ovafolinin A and B.^{1,2}

Ovafolinin A and B (**fig. 1**), isolated from *Lyonia ovalifolia* var. elliptica,¹ and also ovafolinin B from *Sinocalamus affinis*,² are lignans which contain a unique tetra- and pentacyclic benzoxepin-bridged aryl tetralin structure. We report the first total synthesis of these natural products utilising an acyl-Claisen rearrangement (**fig. 2**) to construct the lignan backbone with correct relative stereochemistry.



Figure 2. Acyl-Claisen rearrangement to form the disubstituted morpholine pent-4-enamide and subsequent overview of the synthetic route to (\pm) -ovafolinin A and B.

Furthermore, judicious use of bulky TBDPS protecting group placed reactive moieties in the correct orientation resulting in a cascade reaction forming the benzoxepin-bridged aryl tetralin from a linear precursor in a single step (**fig. 2**).



Figure 3. Overview of the synthesis of enantiopure ovafolinin A and B.

Following confirmation of the relative stereochemistry for ovafolinin A and B, a chiral synthesis was then devised to confirm the absolute stereochemistry. This chiral route utilised an Evan's chiral oxazolidinone to obtain a single enantiomer of the same key compound prior to cyclisation (**fig. 3**), resulting in the first synthesis of enantiopure ovafolinin A and B.

2. Xiong L, Zhu C, Li Y, Tian Y, Lin S, Yuan S, Hu J, Hou Q, Chen N, Yang Y, Shi J. J Nat Prod. 2011, 74, 1188–1200.

^{1.} Kashima K, Sano K, Yun YS, Ina H, Kunugi A, Inoue H. Chem Pharm Bull (Tokyo) 2010, 58, 191–194.

Smart Functionalized Catalytic Films for Water Purification

<u>Courtney Davy</u> Professor L. James Wright

As the world's population increases the industrial and agricultural activities intensify, therefore the availability of clean water is becoming a rapidly growing global problem. In these situations, the need for removal of trace contaminants such as pesticides, herbicides, active pharmaceutical ingredients and endocrine disrupters is particularly important.¹ None of the current methods used for water purification is ideal and finding efficient and cost effective methods to remove trace levels of organic pollutants is very difficult.^{1, 2} There is a clear need for an alternative system that will enable large volumes of water to be efficiently and simply treated to remove organic pollutants, especially those that are difficult to be removed by current methods.

The proposed new purification system is based on the creation of an innovative smart catalytic film (SCF) that will remove organic pollutants from water through a catalytic oxidation process that converts them to harmless products. The water will be purified as it simply runs across the film as shown in figure 1. Large volumes of water can be easily purified by the catalytic oxidative destruction of harmful pollutants without having to dose the entire water body with H_2O_2 .

The current research has looked into developing SCF using polychloromethylstyrene (PCMS). We have successfully functionalized the polymer film with molecular brushes and have adsorbed the oxidation catalyst (FeB^{*}) through irreversible non-covalent interactions (figure 2). Our research shows that the pollutant molecules can be oxidised by the activated FeB^{*} catalyst molecules and that the SCF can be used up to 50 times (depending on the molecular brush) until degradation of the catalyst occurs.



Figure 1: Schematic diagram of the overall purification system, incorporating smart catalytic films



Figure 2: Structure of Fe^{III}-TAML catalyst, FeB*

- 1. Dalrymple, O. K.; Yeh, D. H.; Trotz, M. A. Journal of Chemical Technology and Biotechnology 2007, 82, 121-134.
- 2. Khetan, S. K.; Collins, T. J.; *Chemical Reviews* **2007**, *107*, 2319-2364.

Poster 54

Use of peptide-drug conjugates systems as potential therapeutics for polycystic kidney disease (ADPKD)

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Autosomal dominant polycystic kidney disease (ADPKD) is characterised by progressive growth of bilateral renal cysts and gives rise to hypertension, renal pain and renal insufficiency. There are no efficient treatments available to cure ADPKD other than to alleviate the pain and symptoms of renal manifestation. Recently Auckland Cancer Society has identified a promising compound that shows broad spectrum of activity against numerous cancer cell lines¹. This compound has been modified by introducing a free thiol group to facilitate its conjugation with a peptide, which acts as a cargo carrier (figure 2). A number of analogues were also synthesised that can potentially be tested against used ADPKD. A reported kidney specific peptide sequence will be used as a cargo carrier peptide for kidney targeting². This kidney specific peptide was successfully conjugated to the thiolated compound (figure 2). This poster will highlight the synthesis of the peptide-drug conjugate and the synthesis of the other analogues.



Figure 1. Proposed peptide-conjugate system to target ADPKD



Figure 2. Successfully synthesised conjugate system with model compound

1. Gamage, S. A.; Brooke, D. G.; Redkar, S.; Datta, J.; Jacob, S. T.; Denny, W. A., Structureactivity relationships for 4-anilinoquinoline derivatives as inhibitors of the DNA methyltransferase enzyme DNMT1. *Bioorg Med Chem* **2013**, *21* (11), 3147-53.

2. Geng, Q.; Sun, X.; Gong, T.; Zhang, Z.-R., Peptide–drug conjugate linked via a disulfide bond for kidney targeted drug delivery. *Bioconjugate chemistry* **2012**, *23* (6), 1200-1210.

Exploring Obscure Wine Aroma Compounds – Thiols and Sesquiterpenes

Nina Duhamel

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The objective of our research is to further our knowledge of the compounds and chemical pathways giving rise to wine aroma. One part of the project focuses on thiols, in particular 3-mercapto hexanol (3MH), 3-mercapto hexylacetate (3MHA), and 4-mercaptomethyl-pentan-2-one (4MMP) which are known to be favourable wine aroma compounds.^{1,2} By investigating via which chemical pathways these are formed, the levels of these compounds can be manipulated via changes in viticulture or winemaking processes, resulting in increased quality of wine aroma.³ The three thiols 3MH, 3MHA, and 4MMP, along with the cysteinyl and glutathionyl adducts of 3MH, have all been synthesised with deuterium labels, for use as internal standards. Sulfonic acid derivatives of *trans*-2-hexenal have also been synthesised for investigation as possible thiol precursors.⁴ The second part of the project is the exploration of a class of compounds named sesquiterpenes, several of which have been identified in wines.⁵ We are carrying out the total synthesis of spirolepechinene,⁶ have performed deuterium labelling of commercially available sesquiterpenes, and subsequently developed a GCMS/MS method for the accurate quantification of 10 sesquiterpenes in grape. The method was then used to quantify sesquiterpene levels in a wide range of grape musts from the Trentino-Alto Adige region of Italy.



Figure 1. Key structures and representative precursors under investigation. Relative stereochemistry of spirolepechinene is highlighted, as is the position of deuterium labelling on caryophyllene oxide.

- 1. Tominaga, T., Baltenweck-Guyot, R., Des Gachons, C. P., Dubourdieu, D., *American Journal of Enology and Viticulture*. **2000**, *51*(2), 178-181.
- Swiegers, J. H., Capone, D. L., Pardon, K. H., Elsey, G. M., Sefton, M. A., Francis, I. L., Pretorius, I. S., *Yeast.* 2007, 24(7), 561-574.
- 3. Swiegers, J. H., Willmott, R., Hill-Ling, A., Capone, D. L., Pardon, K. H., Elsey, G. M., Pretorius, I. S., *Developments in food science*. **2006**, *43*, 113-116
- 4. Piano, F., **2013**. Studies on the Occurrence of Thiol Related Aromas in Wine (Doctoral dissertation, Università degli Studi di Milano).
- 5. Martin, D.; Toub, O.; Chiang, A.; Lo, B.; Ohse, S.; Lund, S.; Bohlmann, J. PNAS, 2009, 106, 7245-7250.
- 6. Eggers, M. D., Sinnwell, V., Stahl-Biskup, E., Phytochemistry. 1999, 51(8), 987-990.

Transformation of indoles by C-H borylation

Andrew Eastabrook Christy Wang, Emma Davison, Dr Jonathan Sperry

We will discuss the use of an iridium-catalysed borylation reaction as an enabling step in the conversion of indoles to indolequinones, biologically active heterocyclic motifs that usually rely on fragment based approaches for their preparation¹. Application of this borylation methodology in the synthesis of densely substituted, 2,3,5,7-tetrasubstituted indoles will also be presented².



1. Eastabrook, A. S.; Wang, C.; Davison, E. K.; Sperry, J. J. Org. Chem. 2015, 80, 1006.

a) Eastabrook, A. S.; Sperry, J. Aust. J. Chem. 2015, 68, 1810. b) Eastabrook, A. S.; Sperry, J. Synthesis. [Online early access]. DOI: 10.1055/s-0036-1589018 Published Online: May 8, 2017. https://www.thieme-connect.de/products/ejournals/html/10.1055/s-0036-1589018 (Accessed July 14, 2017)

Spectroscopic Studies of the chemistry of H4SiO4 Polymerization at the Aqueous-Magnetite Interface

<u>Nadia H. Elgaroshi</u>

Gordon Miskelly and Peter Swedlund

Iron oxides and oxyhydroxides (here in termed simply as iron oxides) are important phases that are widespread in the nature. Iron oxides often haver large surface areas which enable them to adsorb many dissolved ions or molecules influencing the chemistry of natural aquatic system¹. Silicic acid (H₄SiO₄) is ubiquitous in natural water systems as the result of weathering of silicate minerals² and has a high affinity for the surface of iron oxide . The interaction between H₄SiO₄ and iron oxide can involve sorption, polymerisation and precipitation and influences numerous properties of iron oxides such as the surface charge, phase stability and particle morphology³. In this study we use *in situ* ATR-IR to understand H₄SiO₄ sorption and polymerisation on the surface of magnetite. *In situ* ATR-IR spectra were measured over time as magnetite reacted with 1.6 mM H₄SiO₄ in 0.1 NaCl at pH 9. The spectra showed the oxidation state of the magnetite surface (FeCL₂/FeCl₃) as evident from the infra red band at 940 cm⁻¹ but when the magnetite surface had been oxidized to Fe^{III} due to the influence of SO₄⁻² which promote formation of goethite(FeOOH), the ATR-IR spectra showed a large amount of oligomeric and polymeric silicate species at 1010 cm⁻¹ and 1100 cm⁻¹ alternatively Figure 1. This was rationalised from the structure of the magnetite (111) face and the goethite (021) face.



Figure 1; ATR-IR absorbance spectra recorded as (a) fresh magnetite ($FeCl_2/FeCl_3$) and (b) oxidize magnetite ($FeSO_2/FeCl_3$) with H₄SiO₄.

1. Cornell, R. M.; Schwertmann., U., The iron oxides. VCH: New York 1996.

2. (a) Meng, Z. G.; Korfiatis, G. P.; Christodoulatos, C.; Bang, S., Treatment of arsenic in Bangladesh well water using a household co-precipitation and filtration system. *Water Research* **2001**, *35* (12), 2805-2810; (b) Urasa, I. T.,

Determination of arsenic, boron, carbon, phosphorus, selenium, and silicon in natural-waters by direct-current plasma atomic emission-spectrometry. *Analytical Chemistry* **1984**, *56* (6), 904-908.

3. Cornell, R. M.; Schwertmann, U., *The iron oxides : structure, properties, reactions, occurences and uses.* 2 ed.; Wiley-VCH: Weinheim, 2003.

Pt nanoparticles electrodeposited on to PEDOT-g-PAA brushes

Alissa Hackett

Duncan McGillivray, Jadranka Travas-Sejdic

Electrodeposition of metal nanoparticles is a simple and robust method of synthesizing nanoparticles on substrates. Conducting polymers (CPs) make ideal substrates for electrodeposition, providing a conductive, high surface area scaffold, while the deposited nanoparticles can enhance the optical and electrochemical properties of the CP.¹ The addition of polymer brushes grafted from CPs add another layer of customization, with the ability to add functionality, tune solubility, improve optical properties, or prevent non-specific binding in the case of sensing devices.² However, while numerous studies have been conducted using incorporation of metal nanoparticles in (conducting) polymer substrates or on to polymer brush-coated substrates, there is currently no published research into nanoparticle deposition on CP-brush substrates. Such materials could provide multiple avenues of tuning surface chemistry and physical properties to specific applications.

We have synthesised polyacrylic acid (PAA) brushes grafted on to a conducting PEDOT backbone to complex with Pt^{2+} ions, allowing them to be reduced electrochemically to Pt^{0} nanoparticles. The negatively charged PAA brushes are pH-sensitive and can also interact with positive charges on the (oxidized) CP backbone, leading to reversible swelling/collapse of the brushes based on the oxidation state of the CP and environmental pH. The Pt nanoparticles enhance the electroactivity and pH responsiveness of the film, leading to a range of applications such as (bio)sensing devices, catalysis, and electrically addressable substrates for cell culture.



Figure 1: Pt²⁺ complexing with PEDOT-g-PAA surface prior to being electrochemically reduced to Pt⁰ nanoparticles.

2. Strover, L. T.; Malmström, J.; Travas-Sejdic, J. The Chemical Record 2016, 16, 393-418.

^{1.} Patten, H. V.; Ventosa, E.; Colina, A.; Ruiz, V.; López-Palacios, J.; Wain, A. J.; Lai, S. C. S.; Macpherson, J. V.; Unwin, P. R. *Journal of Solid State Electrochemistry* **2011**, *15*, 2331-2339.

Improving speciation of metal based anticancer agents in serum samples *via* coated capillaries for CE-ICP-MS analysis

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Metal-based anticancer agents are known to interact with serum proteins after intravenous administration, particularly with the proteins albumin and transferrin, and the interaction is considered an important influence on their transportation, selectivity, and efficacy [1]. For platinum-based compounds this interaction is thought to decrease the active concentration, while for ruthenium it is proposed as a method of intracellular accumulation. A recent study with organoruthenium complexes and HCT116 tumour cells demonstrated that accumulation is not always correlated with cytotoxic activity [2].

We contrast the cytotoxicity and cellular accumulation rates of both cisplatin and RAPTA-C at 4, 24, 48 and 72 h time intervals, measuring both the intra- and extracellular metal concentration *via* ICP-MS and then determine speciation *via* CE–ICP-MS analysis. CE analysis using silica capillaries can be challenging due to protein interactions with the charged silanol groups [3]. We optimised a capillary coating method using poly(vinyl pyrrolidone) (PVP), which demonstrated considerable advantages compared with polybrene, for the efficient separation and detection of metal complex-protein adducts. The use of the internal standard tris(acetylacetonato)cobalt(III) further improved the reproducibility of electropherograms and detection limits.



Figure 1. Quantitative and speciation kinetic data collected from cellular uptake studies with RAPTA-C and cisplatin in HCT116 cancer cells as analyzed by ICP-MS and CE–ICP-MS analysis.

References:

- [1] Timerbaev, A. R., Hartinger, C. G., Aleksenko, S. S., Keppler, B. K., Chem. Rev. 2006, 106, 2224-2248.
- [2] Kubanik, M., Holtkamp, H., Söhnel, T., Jamieson, S. M. F., Hartinger, C. G., Organometallics 2015, 34, 5658-5668.
- [3] Groessl, M., Hartinger, C. G., Polec-Pawlak, K., Jarosz, M., Keppler, B. K., *Electrophoresis* 2008, 29, 2224-2232.

The total synthesis of sciodole, a biomimetic approach

Josh Homer Jonathan Sperry, Supervisor

Sciodole (1), isolated from the pungent fruit bodies of the mushroom species *Tricholoma sciodes*, is a bisindole derivative that presents a unique synthetic challenge; an N1-C7 bond not often seen in natural products.¹ Although indole alkaloids are commonly derived from tryptophan *in vivo*, the proposed structure suggests a partially reduced dimeric species of 5-methoxy-2,4-dimethylindole (2), a compound ultimately derived from lascivol (3).²



Figure 1. Proposed biosynthesis of sciodole.

The two fragments comprising sciodole will be synthesized separately. The aromatized fragment (2) will be constructed using a literature Nentitzescu indolisation³ followed by selective C4-functionalization. The partially reduced fragment (4) will be prepared from a pyrrole core via an oxidative intramolecular Heck coupling and stereoselective oxidation. The final step will involve a novel nucleophilic coupling of the two fragments, affording the natural product while retaining the desired stereochemistry.

- 1. Sterner, O. Nat. Prod. Lett. **1994**, 4(1), 9-14.
- 2. Eizenhofer, T.; Fugmann, B.; Sheldrickb, W. S.; Steffan, B.; Steglich, W. Liebigs Ann. Chem. 1990, 1115-1118.
- 3. Huang, Y.; Zhang, W.; Zhang, X.; Wang, J. *Res. Chem. Intermed.* **2010**, 36, 975-983.

Synthesis of the Tetracyclic Core of Integrastatins, Inhibitors of HIV-1 Integrase

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Integrastatin A (1) and B (2) were both isolated as racemic compounds from an unnamed fungal source (ATCC74478) and an endophytic *Ascochtya* species (ATCC74477).¹ These natural products have shown to exhibit potent inhibition of the strand-transfer reaction of recombinant HIV-1 integrase (IC₅₀ = 1.1μ M and 2.5μ M, respectively)¹ and thus are promising targets for the development of a novel anti-HIV therapy. The integrastatins are characterised by the unique [6.6.6.6]-tetracyclic skeleton, possessing a central [3.3.1]-dioxabicyclic core.²⁻⁵ Despite the distinguished molecular framework as well as the medicinal interest in these natural products, methods to effect a flexible and practical synthesis of the integrastatins have been underexplored.



Our current work aims to develop an efficient synthetic strategy for the tetracyclic core **3**, with the expectation that a successful synthesis would provide a valuable platform for the total synthesis of these natural products. The focus of this research is to construct the tetracyclic core **3** from its precursor **4**, which in turn would be derived from the addition of methyl group onto the lactone **5**, followed by an acid-catalysed intramolecular cyclisation. Addition of the anion of 1,3-dithiane **6** onto the acetophenone **7** would trigger concomitant intramolecular lactonisation to afford **5**.



- 1. Singh, S. B.; Zink, D. L.; Quamina, D. S.; Pelaez, F.; Teran, A.; Felock, P.; Hazuda, D. J. *Tetrahedron Lett* **2002**, *43*, 2351-2354.
- 2. Foot, J. S.; Giblin, G. M.; Taylor, R. J. Org Lett 2003, 5, 4441-4.
- 3. Ramana, C. V.; Nageswara Reddy, C.; Gonnade, R. G. Chem Commun (Camb) 2008, 27, 3151-3.
- 4. Tadross, P. M.; Bugga, P.; Stoltz, B. M. Org Biomol Chem 2011, 9, 5354-7.
- 5. More, A. A.; Ramana, C. V. Org Lett **2016**, *3*, 612-615.

Isolation and identification of vitamin D3 oxidation products in simulated whole milk powder by liquid chromatography mass spectrometry

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In a successful fortification program, the stability of micronutrients added to the food is one of the most important factors.¹ The added vitamin D3 is known to sometimes decline during storage of fortified milk powders, and oxidation through fatty acid lipoxidatoin is suspected as the likely cause.². Identification of vitamin D3 oxidation products (VDOPs) in natural foods is a challenge due to the low amount of their contents. Thus, the main objective of this study is to find a method to extract and to identify VDOPs in whole milk powder. The multi stage mass spectrometry (MSⁿ) spectra can help to propose plausible schemes for unknown compounds and their fragmentations.³ With the growth of combinatorial libraries, mass spectrometry (MS) has become an important analytical technique because of its speed of analysis, sensitivity and accuracy.⁴ This study has focused to identify the fragmentation rules for some VDOPs by incorporating MS data with *in silico* calculated MS fragmentation pathways (Mass Frontier). Diels-Alder derivatization was used to enhance the sensitivity and selectivity for mass spectrometry data collection. Finally, the confirmed PTAD derivatised target compounds were separated and analyzed using ESI(+)-UHPLC-MS/MS in multiple reaction monitoring (MRM) mode in model samples.



Figure 1. MRM chromatograms and structures of **a**) VD3-PTAD at 560 \rightarrow 298 (black) and pre-VD3-PTAD at 560 \rightarrow 383 (red), and **b**) VDOPs-PTAD at 576 \rightarrow 298 (green) and VDOPs-PTAD at 576 \rightarrow 314 (blue).

- 1. Spiro, A.; Buttriss, J. L. *Nutrition Bulletin* 2014, 39(4). 322-350.
- 2. Choe, E.; Min, D. B. Journal of Food Science 2005, 70(9), 142-159.
- 3. Fabre, N.; Rustan, I.; de Hoffmann, E.; Quetin-Leclercq, J. *Journal of the American Society for Mass Spectrometry* 2001, *12*, 707-715.
- 4. Klagkou, K.; Pullen, F.; Harrison, M.; Organ, A.; Firth, A.; Langley, G. J. *Rapid communications in mass spectrometry* 2003, *17*, 1163-1168.

Development of Anti-Cancer Organometallic Complexes with Bidentate N-Heterocyclic Carbenes Ligands

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Metallopharmaceuticals have flourished since the discovery of the antineoplastic properties of cisplatin.^{1,2} Despite their major impact as chemotherapeutic agents, their severe side effects as well as intrinsic or acquired resistance required resistance call for the development of novel platinum and non-platinum compounds.^{3,4}

In the last decade, a vast number of organoruthenium compounds were synthesised and tested for their tumour-inhibiting properties. Specifically half-sandwich "piano-stool" Ru(II)-arene complexes were developed to have unique features such as the ability to form specific interaction with biomolecules and revealed promising anticancer activity. The "aromatic seat" plays a key role in stabilizing the ruthenium centre in its oxidation state +II and also provides a hydrophobic character which facilitates the passive transport through the cell membrane. The remaining ligands, with a broad variety of pharmacological properties, can be considered as the legs of the chair and can be mono- or polydentate with mostly halide(s) incorporated as leaving group(s) (Figure 1).^{5,6}

N-Hetrocyclic carbenes (NHCs) have strong σ -donor properties and are able to form stable complexes with transition metals which make them good option to develop new potent anticancer drugs.⁷ We prepared a series of novel Ru(II)-NHC complexes and their antiproliferative properties were assayed against different human cancer cell lines.



Figure 1. General structure of Ru(II)-Bidentate NHC complexes and the molecular structure of selected examples

References:

- 1. Van Rijt, S. H.; Sadler, P. J., Drug Discov. T. 2009, 14, 1089-1097.
- 2. Jakupec, M. A.; Galanski, M.; Arion, V. B.; Hartinger, G. g.; Keppler, B. K., Dalton Trans. 2008, 183-194.
- 3. Bergamo A.; Sava G., Dalton. Trans.2007, 13, 1267–1272.
- 4. Fricker SP., Dalton. Trans. 2007, 43, 4903–4917.
- 5. Gasser, G.; Ott, I.; Metzler-Nolte, N., J. Med. Chem. 2010, 54, 3-25.
- 6. Nazarov, A. A.; Hartinger, C. G.; Dyson, P. J., J. Organomet. Chem. 2014, 751, 251-260
- 7. Oehninger, R. Rubbiani and I. Ott, Dalton Trans, 2013, 42, 3269-3284

Synthesis of Boron Porphyrinoids

<u>Aaron Tay</u> Penelope J. Brothers, David C. Ware

In the past two decades, the Brothers' research group has synthesised boron porphyrins and corroles by inserting boron into their N_4 cores using boron halides yielding rich chemistry for both the boron and the ligands.^{1,2} As an extension of this work, new classes of porphyrinoids have been investigated for boron coordination: calixphyrins and porphyrazines.^{3,4}

A series of mono and diboron calixphyrins (Calix) have been synthesised using BF_3 , BCl_3 and $PhBCl_2$ as the boron sources. Due to the presence of both dipyrrin and dipyrromethane bonding sites, structural isomers have been isolated. The reaction with $PhBCl_2$ in the presence of $N(^{i}Pr)_2Et$ results in the unexpected reduction of the calixphyrin ligand. The insertion of boron into porphyrazines (Pz) has been achieved using BCl_3 and $PhBCl_2$. The reaction with BCl_3 forms an air- and moisture-sensitive intermediate which can be converted into the stable $B_2OF_2(Pz)$ using BF_3 as the fluorine source. The reaction with $PhBCl_2$ forms two diboron products, PhBOBPh(Pz) and PhBOBOH(Pz).

The structural similarities of boron porphyrinoids with BODIPYs as well as the tripyrrolic subporphyrinoids lead to the possibility that these new classes of compounds could have a potentially wide range of applications.



Figure 1: Crystal structure of B2OF2(Calix)



Figure 2: Crystal structure of B₂OF₂(Pz)

- 1. Brothers, P. J. Inorg. Chem. 2011, 50, 12374-12386.
- 2. Brothers, P. J. Chem. Commun. 2008, 2090-2102.
- 3. Sessler, J. L.; Zimmerman, R. S.; Bucher, C.; Kral, V.; Andrioletti, B. Pure Appl. Chem. 2001, 73, 1041-1057.
- 4. Fuchter, M. J.; Zhong, C.; Zong, H.; Hoffman, B. M.; Barrett, A. G. M. Aust. J. Chem. 2008, 61, 235-255.

In-depth electrochemical investigation into reproducibility of mixed self-assembled monolayers formed from different deposition methodologies

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The controlled and reproducible production of functionalised surfaces is vitally important for the development of reliable transducers for biosensors. Surface modification of gold electrodes is often performed using self-assembled monolayers (SAMs) of alkanethiols with reactive end groups (e.g. amines, carboxylic acids and azides). The physical properties of these SAMs can be tuned by incorporation of a diluent adsorbate that is hydrophobic or hydrophilic in nature.¹

In this work aminoferrocene and ethynylferrocene have been used as electroactive probes to investigate the use of carbodiimide coupling² and azide-alkyne Huisgen cycloaddition reactions to functionalise self-assembled monolayers on gold surfaces. Two SAM deposition methodologies were investigated: chemisorption from dilute solutions of thiol terminated adsorbate species in ethanol and *in* situ base catalysed deprotection and self-assembly of mixed monolayers from thioacetyl-terminated adsorbate species.³

Mixed monolayers formed from both methodologies with either carboxylic acid or azide functionality and with either hydrophobic or hydrophilic diluent species were electrochemically probed to characterise the reproducibility of the modified surfaces. The two attachment chemistries where also probed for efficiency and reproducibility of both ferrocene and ssDNA oligomer capture agent attachment to the surface.



Figure 1. (A) A schematic example of one of the conditions tested in this work. (B) A typical cyclic voltammogram of ferrocene attached to the electrode surface by azide-alkyne Huisgen cycloadditon

1. Ronkainen, N. J.; Halsall, H. B.; Heineman, W. R., Electrochemical biosensors. *Chem. Soc. Rev.* **2010**, *39*, 1747-1763.

2. Booth, M. A.; kannappan, K.; Hosseini, A.; Partridge, A., In-Depth Electrochemical Investigation of Surface Attachment Chemistry via Carbodiimide Coupling. *Langmuir* **2015**, *31*, 8083-8041.

3. (a) Tour, J. M.; Jones, L., II; Pearson, D. L.; Lamba, J. J. S.; Burgin, T. P.; Whitesides, G. M.; Allara, D. L.; Parikh, A. N.; Atre, S., Self-Assembled Monolayers and Multilayers of Conjugated Thiols, α, ω -Dithiols, and Thioacetyl-Containing Adsorbates. Understanding Attachments between Potential Molecular Wires and Gold Surfaces. *J. Am. Chem. Soc.* **1995**, *117*, 9529-34; (b) Inman, C. E.; Reed, S. M.; Hutchison, J. E., In Situ Deprotection and Assembly of S-Tritylalkanethiols on Gold Yields Monolayers Comparable to Those Prepared Directly from Alkanethiols. Langmuir **2004**, *20*, 9144-9150.

Synthetic studies towards the indole alkaloids kottamides A-E

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Novel chemical structures offer interesting and challenging synthetic targets with those that are bioactive having the additional advantage of providing an ideal platform for the development of new drug leads. The research presented herein concentrates on the total synthesis of the kottamides A-E **1**-**5** (Figure 1) which are novel metabolites isolated from the marine ascidian *Pycnoclavella kottae* in New Zealand. Such compounds show appreciable bioactivity particularly against leukaemia cell lines, displaying inhibitory concentrations as low as 14 μ M.^{1,2} A key step in the synthesis is identified as a ruthenium catalysed hydroamidation which is utilised to selectively install a *cis*-enamide bridge³ linking the highly substituted imidazolone rings for kottamides A-D **1**-**4** and the uncommon 1,2-dithiolane ring for kottamide E **5** to respective bromine substituted indole fragments. Additionally a series of analogues will be completed by allowing substitution of a range of different amide coupling partners such as those derived from amino acids Ala, Phe and Met to name a few. The substitution pattern of bromine on the aromatic ring will also be a point of investigation.



Figure 1. *cis*-Enamide containing indole alkaloids kottamides A-E **1-5** and the synthesis of kottamide E **5** and related analogues.

- 1 Copp, B.R., Appleton, D.R., Page, M.J., Lambert, G., & Berridge, M.V. *J. Org. Chem.*, **2002**, 67(15), 5402-5404.
- 2 Baker, D.D., & Alvi, K.A. Curr. Opin. Biotech., 2004, 15(6), 576-583.
- 3 Dickson, E., Copp, B.R., & Barker, D. *Tetrahedron Lett.*, **2013**, *54*(38), 5239-5242.

Synthesis of 2-formylpyrroles using a Maillard approach: Elucidation of the bioactive pharmacophore in traditional Chinese medicines

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2-Formyl pyrrole compounds have been isolated from a variety of plants with traditional medicinal uses. Among these compounds are the acortatarin family of natural products, which inhibit the production of reactive oxygen species.¹ This bioactivity has application in the treatment of diabetic nephropathy; the most common cause of chronic kidney failure.² This project aims to explore the activity of the 2-formyl pyrrole pharmacophore via library synthesis and SAR studies.



Figure 1: Maillard-type reaction to access 2-formyl pyrrole natural products.

Our group has developed a Maillard-type reaction to synthesise 2-formyl pyrrole natural products and their analogues.^{3–5} This Maillard reaction allows for the divergent synthesis of 2-formyl pyrrole compounds from a single dihydropyranone intermediate **1**. Complexity is derived from the amine coupling partners, which have been prepared from amino acids and other chiral pool compounds. Herein we present details of the total synthesis and compound library work for SAR bioactivity assays.

- 1. Tong, X.-G.; Zhou, L.-L.; Wang, Y.-H.; Xia, C.; Wang, Y.; Liang, M.; Hou, F.-F.; Cheng, Y.-X. Org. Lett. **2010**, *12* (8), 1844–1847.
- 2. Van Buren, P. N.; Toto, R. Adv. Chronic Kidney Dis. 2011, 18 (1), 28–41.
- 3. Yuen, T.-Y.; Eaton, S. E.; Woods, T. M.; Furkert, D. P.; Choi, K. W.; Brimble, M. A. *Eur. J. Org. Chem.* **2014**, *2014* (7), 1431–1437.
- 4. Woods, T. M.; Kamalov, M.; Harris, P. W. R.; Cooper, G. J. S.; Brimble, M. Org. Lett. 2012, 14 (22), 5740–5743.
- 5. Geng, H. M.; Stubbing, L. A.; Li-yang Chen, J.; Furkert, D. P.; Brimble, M. A. *Eur. J. Org. Chem.* **2014**, *2014* (28), 6227–6241.