21st International Congress for Heterocyclic Chemistry

Program and Abstract Book

The University of New South Wales

15th - 20th July 2007

21st International Congress for Heterocyclic Chemistry

The University of NSW

Sydney, Australia

15-20 July, 2007

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All information correct at time of printing and is subject to change

On behalf of the International Society of Heterocyclic Chemistry (ISHC) it is my great pleasure to welcome all the delegates and their guests to the 21st International Congress of Heterocyclic Chemistry. This conference is the largest international meeting of heterocyclic chemists and attracts delegates from all around the globe. I trust that you will enjoy the antipodean environment at this 21st ICHC Congress that we are very honoured to host for the first time in Australia.

Every two years the International Society of Heterocyclic Chemistry holds an International Congress on Heterocyclic Chemistry providing a forum for its members to network and share their recent research findings in the broad field of heterocyclic chemistry. The scientific program assembled is outstanding and comprises a combination of plenary and keynote addresses, with parallel sessions including invited addresses and contributed oral presentations, and two large poster sessions. In addition the ISHC Senior Prize in Heterocyclic Chemistry (sponsored by Pfizer) will be presented to Professor KC Nicolaou (Scripps Research Institute) and the ISHC Katritzky Junior Award in Heterocyclic Chemistry (sponsored by GlaxoSmithKline) will be presented to Professor David MacMillan (Princeton).

David Black, Roger Read, Kate Jolliffe, and all of the members of the local organizing committee have spent many hours preparing to make this 21st ICHC conference a success. I trust you will enjoy the feast of heterocyclic chemistry they have arranged for you this week at the same time enjoying the spectacular city of Sydney. I wish all delegates a memorable time both scientifically and socially.

MA Brimble

Professor Margaret Brimble
President International Society of Heterocyclic Chemistry
21st ICHC, Sydney, 2007

Dear Delegates and Accompanying Persons,

It gives us great pleasure to welcome you to the 21st International Congress for Heterocyclic Chemistry at the University of New South Wales in Sydney, Australia as this is the first time in the history of the Congress that it has come to this part of the world.

Together with the Conference Secretary, Dr Kate Jolliffe, and the Organising Committee, we have done our best to put together an exciting, stimulating, and currently relevant programme. We have been greatly encouraged by your acceptance to participate, and by the high quality of the scientific contributions. We refer here to the world leaders in heterocyclic chemistry and to the younger graduate students who will become the future leaders.

We have more than 400 delegates from more than 40 countries, and they will contribute 11 plenary and award lectures, 9 keynote lectures, 10 invited lectures, 72 oral presentations, and 280 posters. All aspects of heterocyclic chemistry will be on display, and this will emphasise the widespread importance of the area. In particular, the applications of heterocyclic compounds to human health will be highlighted through the industrial presentations, and we thank all our sponsors for their important contributions.

Throughout the week, we look forward to many opportunities for stimulating interactions. To this end, a relaxed and typically Australian social program has been arranged. We also trust that you will be able to extend your visit to enjoy the city and its environs.

We do hope that you will enjoy your stay in Sydney, from both the chemical and social points of view and once again offer our warmest welcome.

Professor David Black
Conference Co-Chair

Associate Professor Roger Read
Conference Co-Chair

Delegate, Speaker & Poster Information

All enquiries should be directed to the Registration Desk located in the Clancy Auditorium Foyer

Registration Desk
The Registration Desk will be open during the following hours:

Sunday 15 July	3.30pm – 5.30pm
Monday 16 July	7.00am – 5.30pm
Tuesday 17 July	7.30am – 5.30pm
Wednesday 18 July	7.30am – 1.00pm
Thursday 19 July	7.30am – 5.30pm
Friday 20 July	7.30am – 1.00pm

Internet Lounge
The Internet Lounge is sponsored by Sigma-Aldrich and is located in the Green Room, off the Clancy Auditorium Foyer. Three terminals are available for delegates to keep in contact with their offices. The Internet Lounge will be open from 7.30am – 5.00pm each day.

Speakers' Preparation Room
The Speakers' Preparation room is located in the Green Room, off the Clancy Auditorium Foyer, near the Registration Desk and will be open during the following hours:

Sunday 15 July	3.30pm – 5.30pm
Monday 16 July	7.30am – 1.30pm
Tuesday 17 July	7.30am – 12.30pm
Wednesday 18 July	7.30am – 11.30am
Thursday 19 July	7.30am – 12.30pm
Friday 20 July	7.30am – 11.30am

Speakers are required to check in their presentations as early as possible. An AV technician will be available to assist with your requirements.

Poster Sessions
Poster sessions will be held in the Mathews Pavilions during the following times ONLY:

Monday 16 July	5.00pm – 7.00pm
Tuesday 17 July	5.00pm – 7.00pm

Delegates presenting posters are required to have their poster up by 9.30am on the morning of their presentation. I.e. Monday poster presenters to have posters up by Monday 9.30am.

Posters are to be taken down after the session and removed from the Pavilions. No responsibility will be taken for posters left behind.

Poster positions are numbered 1-140 and you have been issued with your numbers. If you need to check your number and day of presentation, please see the Registration Desk

Committees

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Prof. David Black	Vice-President
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Dr. Stanley Lang	Treasurer

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The ICHC 21 Sydney Organising Committee gratefully acknowledges the support of our sponsors and exhibitors.

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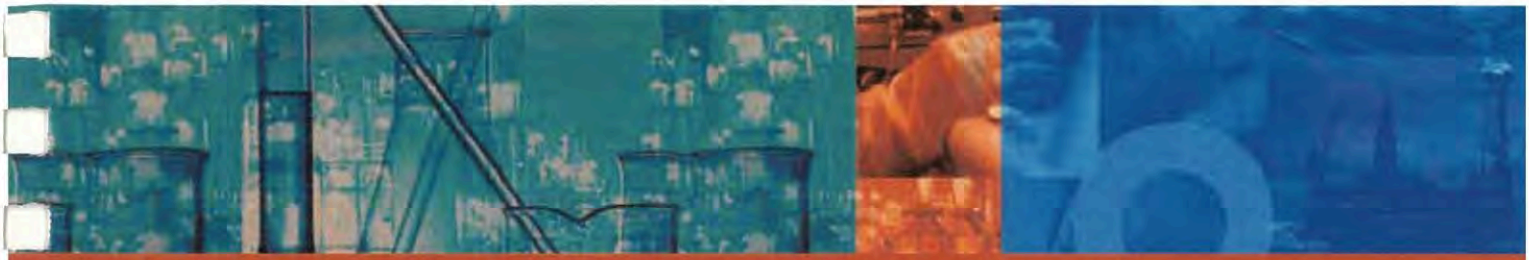

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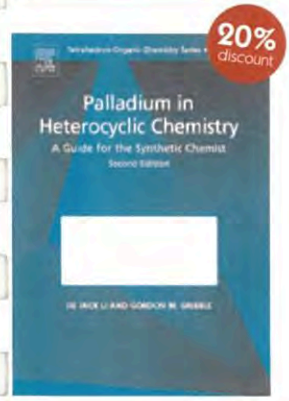

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A Guide for the Synthetic Chemist

Edited By: Jie Jack Li and Gordon W Gribble

Palladium chemistry, despite its immaturity, has rapidly become an indispensable tool for synthetic organic chemists. Recently, the number of applications of palladium chemistry to the syntheses of heterocycles has grown exponentially. These developments highlight the need for a monograph dedicated solely to the palladium chemistry in heterocycles and this book provides a comprehensive explanation of the subject.

Hardback 165 X 240 mm 658 pages ISBN: 978-0-08-045116-9 October 2006 £110.00 €175 $160US

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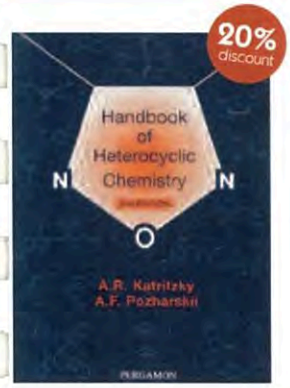

HANDBOOK OF HETEROCYCLIC CHEMISTRY

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By A.R. Katritzky and A.F. Pozharskii

An indispensable resource for graduate students and researchers alike, The Handbook of Heterocyclic Chemistry, 2nd Edition, is illustrated throughout with thousands of clearly drawn chemical structures and contains over 1500 chemical figures and reactions. The highly systematic coverage given to the subject makes this one of the most authoritative single-volume accounts of modern heterocyclic chemistry available.

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Paperback 152 X 229 mm 760 pages ISBN-13: 978-0-08-042989-2 October 2000 £47.99 €70.95 $82.95US

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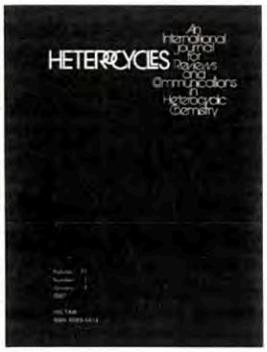

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Programme at a Glance

Date & Time	Clancy Foyer	Clancy Auditorium	Green Room	Mathews Pavilions	Mathews A	Mathews B	Mathews C	Mathews D	Leighton Hall
SUNDAY 15th JULY									
12.00pm - 5.00pm				Exhibitor's Set Up					
3.30pm - 5.00pm	Registration	ISHC Executive Committee Meeting	Speakers' Prep Room						
5.30pm - 7.00pm									Welcome Reception
MONDAY 16th JULY									
9.00am - 9.30am	Registration Desk	Conference Opening	Speakers' Prep Room	Exhibition Open					
9.30am - 10.30am		Prof. Scott Denmark							
Morning Tea - 10.30am - 11.00am - Mathews Pavilions									
11.00am - 12.00pm	Registration Desk	Prof. Masahiro Murakami	Speakers' Prep Room	Exhibition Open					
12.00pm - 12.30pm		Prof. Alan Rowan							
Lunch - 12.30pm - 1.30pm - Mathews Pavilions									
1.30pm - 2.00pm	Registration Desk	Prof. Rajender Varma	Speakers' Prep Room	Exhibition Open					
2.00pm - 2.30pm		Ms Keller Barnhardt							
2.30pm - 3.00pm		Prof. Nicholas Leadbeater							
Afternoon Tea - 3.00pm - 3.30pm - Mathews Pavilions									
3.30pm - 3.50pm	Registration Desk		Speakers' Prep Room	Exhibition Open	Prof. Margaret Brimble	Dr Shinji Yamada	Prof. Anna Maria Almerico	Dr Naoki Kakusawa	
3.50pm - 4.10pm					Prof. Tomasz Janecki	Dr Phillipe Belmont	Prof. Hamish McNab	Dr Alan Aitken	
4.10pm - 4.30pm					Prof. CK Chu	Prof. Jayanta Ray	Prof. Wahid Basyouni	Prof. Masayuki Sato	
4.30pm - 4.50pm					Prof. Colin Suckling	Prof. Dennis Taylor	Prof. Mitsuji Yamashita	Dr Craig Hutton	
5.00pm - 7.00pm				Poster Session					

TUESDAY 17th JULY

Date & Time	Clancy Foyer	Clancy Auditorium	Green Room	Mathews Pavilions	Mathews A	Mathews B	Mathews C	Mathews D	Leighton Hall
9.00am - 10.00am	Registration Desk	Prof. Takuzo Aida	Speakers' Prep Room	Exhibition Open					
10.00am - 10.30am		Dr Toshiaki Mase							
Morning Tea - 10.30am - 11.00am - Mathews Pavilions									
11.00am - 12.00pm	Registration Desk	Dr Dave Tschaen	Speakers' Prep Room	Exhibition Open					
12.00pm - 12.30pm		Dr Naresh Kumar							
Lunch - 12.30pm - 1.30pm - Mathews Pavilions									
1.30pm - 2.00pm	Registration Desk		Speakers' Prep Room	Exhibition Open	Dr Andrew Katsifis	Prof. Maxwell Crossley	Dr Takeaki Naito	Prof. Pierre Vogel	
2.00pm - 2.20pm					Assoc. Prof. Mark Rizzacasa	Prof. Steven Langford	Dr Palli Thordarson	Prof. Mikhail Khusainov	
2.20pm - 2.40pm					Prof. Norbert de Kimpe	Dr Kazunori Tsubaki	Prof. Jean Jacques Vanden Eynde	Prof. Stephen Hashmi	
2.40pm - 3.00pm					Dr Maud Reiter	Dr Andrew Try	Dr Jonathan Morris	Mr Dinesh Garud	
Afternoon Tea - 3.00pm - 3.30pm - Mathews Pavilions									
3.30pm - 3.50pm	Registration Desk		Speakers' Prep Room	Exhibition Open	Dr Yasuyuki Kita	Dr Zaharah Aiyub	Prof. Peter Scammells	Prof. Colin Raston	
3.50pm - 4.10pm					Prof. Martin Banwell	Dr Craig Francis	Dr Gunnar Westman	Dr Andrew Whiting	
4.10pm - 4.30pm					Prof. Valentine Nenajdenko	Dr Max Dang	Dr Martine Demeunynck	Prof. Peter Gaertner	
4.30pm - 4.50pm					Prof. Hiroaki Sasai	Dr John Ryan	Prof. John Bremner	Dr Ashok Dongamanti	
5.00pm - 7.00pm				Poster Session					

WEDNESDAY 18th JULY									
Date & Time	**Clancy Foyer**	**Clancy Auditorium**	**Green Room**	**Mathews Pavilions**	**Mathews A**	**Mathews B**	**Mathews C**	**Mathews D**	**Leighton Hall**
9.00am - 10.00am	Registration Desk	Prof. K.C. Nicolaou	Speakers' Prep Room	Exhibition Open					
10.00am - 10.30am		Prof. Thomas Carell							
Morning Tea - 10.30am - 11.00am - Mathews Pavilions									
11.00am - 12.00pm	Registration Desk	Prof. David MacMillan	Speakers' Prep Room	Exhibition Open					
12.00pm - 12.30pm		Prof. Hisao Nishiyama							
Lunch - 12.30pm - 1.15pm - Clancy Foyer									
Captain Cook Harbour Cruise - 1.00pm - 5.30pm									

THURSDAY 19th JULY

Date & Time	Clancy Foyer	Clancy Auditorium	Green Room	Mathews Pavilions	Mathews A	Mathews B	Mathews C	Mathews D	Leighton Hall
9.00am - 10.00am	Registration Desk	Prof. Mikiko Sodeoka	Speakers' Prep Room	Exhibition Open					
10.00am - 10.30am		Dr Phillip Gale							
Morning Tea - 10.30am - 11.00am - Mathews Pavilions									
11.00am - 12.00pm	Registration Desk	Prof. Thorsten Bach	Speakers' Prep Room	Exhibition Open					
12.00pm - 12.30pm		Prof. Cynthia Burrows							
Lunch - 12.30pm - 1.30pm - Mathews Pavilions									
1.30pm - 2.00pm	Registration Desk		Speakers' Prep Room	Exhibition Open	Prof. Lutz Tietze	Dr David Chen	Dr Roderick Bates	Prof. Gary Weisman	
2.00pm - 2.20pm					Prof. Chris Willis	Dr Tom Goodwin	Prof. Mary Garson	Prof. Hiyoshizo Kotsuki	
2.20pm - 2.40pm					Dr Eric Kantchev	Prof. Tamas Patonay	Dr Satoshi Yokoshima	Dr Dieter Kaufmann	
2.40pm - 3.00pm					Prof. Rainer Streubel	Prof. Yikang Wu	Dr Jason Smith	Miss Maria Matveenko	
Afternoon Tea - 3.00pm - 3.30pm - Mathews Pavilions									
3.30pm - 3.50pm	Registration Desk		Speakers' Prep Room		Prof. Akio Kamimura	Dr Peter Rutledge	Dr Matthew Todd	Prof. Stephen Pyne	
3.50pm - 4.10pm					Assoc. Prof. Patrick Perlmutter	Mr Daniel Obando	Prof. Gyorgy Hajos	Dr Romano Orru	
4.10pm - 4.30pm					Dr Karl Hemming	Miss Gemma Ferguson	Prof. Pavel Stuzhin	Dr Stanislav Radl	
4.30pm - 4.50pm					Prof. Chrisato Mukai	Dr Pedro Joseph-Nathan	Dr Daniel Tyson	Prof. Zhi-Tang Huang	
5.00pm - 5.30pm							ISHC Business Meeting		
Congress Dinner - 7.30pm - 10.30pm - Dockside, Darling Harbour									

FRIDAY 20th JULY									
Date & Time	**Clancy Foyer**	**Clancy Auditorium**	**Green Room**	**Mathews Pavilions**	**Mathews A**	**Mathews B**	**Mathews C**	**Mathews D**	**Leighton Hall**
9.00am - 10.00am	Registration Desk	Prof. Rick Danheiser	Speakers' Prep Room	Exhibition Open					
10.00am - 10.30am		Prof. Ferenc Fülöp							
Morning Tea - 10.30am - 11.00am - Mathews Pavilions									
11.00am - 12.00pm	Registration Desk	Prof. Shengming Ma	Speakers' Prep Room						
12.00pm - 1.00pm		Prof. Andrew Holmes							
1.00pm - 1.15pm		22 ICHC Presentation							
1.15pm - 1.30pm		Closing Ceremony							

ISHC General Business Meeting

GENERAL BUSINESS MEETING OF THE ISHC

Venue: Mathews Theatre C at UNSW

Date: Thursday July 19th, 2007

Time: 5.00pm to 5.30pm

AGENDA

1. Apologies
2. Election Results
3. Amendments to the Constitution and by-laws.
4. Report of State of the Society (Stan Lang)
5. Financial matters – dues
6. 21st ISHC in Sydney (2007)
7. 2009 22nd ISHC in Canada (2009)
8. 2011 23rd ISHC in Europe (2011)
9. Awards
10. Progress in Heterocyclic Chemistry
11. ISHC website
12. Other business

Daily Programme

Sunday, 15 July 2007

Registration

Clancy Auditorium Foyer — **3.00pm – 5.30pm**

ISHC Executive Committee

Clancy Auditorium Stage — **3.30pm – 5.00pm**

Welcome Reception

Scientia Building - Leighton Hall — **5.30pm – 7.00pm**

Monday, 16 July 2007

Opening Ceremony

Clancy Auditorium **9.00am – 9.30am**

9:00am *Professor David Black, The University of New South Wales, AUSTRALIA*

9.05am *Professor Mike Archer, Dean, Faculty of Science, The University of New South Wales, AUSTRALIA*

9:10am *Her Excellency Professor Marie Bashir AC, CVO, The Governor of NSW, AUSTRALIA*

9:20am *The Hon. Verity Firth MP, Minister for Science & Medical Research, AUSTRALIA*

Plenary Speaker

Clancy Auditorium **9.30am – 10.30am**

Chaired by Professor Margaret Brimble, University of Auckland, NEW ZEALAND

9:30am Cycloadditions of 2-Azoniaheterodienes: An Enabling Technology for the Synthesis of Natural & Non-Natural Products
Professor Scott Denmark, University of Illinois, USA

Morning Tea

Mathews Pavilions **10.30am – 11.00am**

Plenary and Keynote Speakers

Clancy Auditorium **11.00am – 12.30pm**

Chaired by Dr Thomas Goodwin, Hendrix College, USA

11:00am Transition Metal Catalyzed Approaches to Silole Synthesis
Professor Masahiro Murakami, Kyoto University, JAPAN

12.00pm Mechanistic Aspects of Threading of Polymers in Processive Rotaxane Catalysts
Professor Alan Rowan, Radboud University of Nijmegen, NETHERLANDS

Lunch

Mathews Pavilions **12.30pm – 1.30pm**

Microwave Session

Clancy Auditorium **1.30pm – 3.00pm**

Chaired by Dr Darryl McConnell, Boehringer Ingelheim Austria GMBH, AUSTRIA

1:30pm Greener Synthesis of Heterocyclic Compounds using Microwave Irradiation
Professor Rajender Varma, U.S Environmental Protection Agency, USA

2:00pm Advancements in Microwave Technology
Ms Keller Barnhardt, CEM Corporation, USA

2:30pm Expanding the Scope of Microwave -Promoted Chemistry
Professor Nicholas Leadbeater, University of Connecticut, USA

Afternoon Tea

Mathews Pavilions **3.00pm – 3.30pm**

Contributed Oral Presentations

Mathews Theatre A **3.30pm – 4.50pm**

Chaired by Dr Professor Yasuyuki Kita, Osaka University, JAPAN

3:30pm Synthetic Studies towards the Spirolide Family of Shellfish Toxins
Professor Margaret Brimble, University of Auckland, NEW ZEALAND

3:50pm Synthesis of 2-Alkylidene-1-Oxoheterocycles as Promising Anticancer Agents
Professor Tomasz Janecki, Technical University of Lodz, POLAND

Monday, 16 July 2007 cont...

4:10pm Practical Synthesis of (-)-Carbocyclic Cytosine (Carbodine) and its In Vitro and In Vivo Antiviral Activity Against Venezuelan Equine Encephalitis (VEE) Virus
Professor C.K. Chu, The University of Georgia, USA

4:30pm Heterocyclic DNA Minor Groove Binders: Synthesis, Physicochemical Properties & Biological Activity of Alkene Linked Compounds
Professor Colin Suckling, University of Strathclyde, SCOTLAND

Contributed Oral Presentations

Mathews Theatre B **3.30pm – 4.50pm**

Chaired by Professor Norbert De Kimpe, Ghent University, BELGIUM

3:30pm Photodimerization Reaction of 4-Styrylpiridines: The Role of a Cation-π Interaction in the Stereoselectivity
Dr Shinji Yamada, Ochanomizu University, JAPAN

3:50pm Heterocycles Synthesis via Benzannulation, Aminobenzannulation & Heterocyclization Reactions
Dr Philippe Belmont, CNRS and University of Lyon, FRANCE

4:10pm Ceric Ammonium Nitrate (CAN) Mediated Stereoselective Decarboxylative Hydroxylation/Alkoxylation & Oxidation of N-aryl-γ-Lactam Carboxylic Acids
Professor Jayanta Ray, Indian Institute of Technology, INDIA

4:30pm 1,2-Dioxines - Ignored Starting Materials for Chemical Synthesis
Professor Dennis Taylor, The University of Adelaide, AUSTRALIA

Contributed Oral Presentations

Mathews Theatre C **3.30pm – 4.50pm**

Chaired by Professor John Bremner, University of Wollongong, AUSTRALIA

3:30pm Benzothieno-Triazolo-Pyrimidine: A New Class of Potential DNA-Binders
Professor Anna Maria Almerico, Department Farmacochimico, Tossicologico e Biologico, ITALY

3:50pm Heteroindoxyls
Professor Hamish McNab, The University of Edinburgh, SCOTLAND

4:10pm Synthesis & Plant-growth Regulating Properties of some new Purine Derivatives
Professor Wahid Basyouni, National Research Centre, EGYPT

4:30pm Preparation of 2,3-Bromides and 2,3-Epoxides of Phospholanes as Analogues of Phospha Sugars & Their Important Biological Activities
Professor Mitsuji Yamashita, Shizuoka University, JAPAN

Contributed Oral Presentations

Mathews Theatre D **3.30pm – 4.50pm**

Chaired by Professor Pierre Vogel, Ecole Polytechnique Federale de Lausanne, SWITZERLAND

3:30pm Rhodium Catalyzed 1,4-Conjugated Addition of Sb-aryl-1,5-Azastibocines to α,β-Unsaturated Carbonyl Compounds
Dr Naoki Kakusawa, Hokuriku University, JAPAN

3:50pm Synthetic Applications of Chiral 1,3-Dioxolan-4-ones
Dr *Alan Aitken, University of St Andrews, SCOTLAND*

4:10pm Synthesis of 4-Fluoroazolinones
Professor Masayuki Sato, University of Shizuoka, JAPAN

4:30pm Substituent Effects in the Stereoselectivity of the Petasis Reaction
Dr Craig Hutton, University of Melbourne, AUSTRALIA

Poster Session

Mathews Pavilions **5.00pm – 7.00pm**

Tuesday, 17 July 2007

Plenary and Keynote Speakers

Clancy Auditorium **9.00am – 10.30am**

Chaired by Professor Martin Banwell, Australian National University, AUSTRALIA

9:00am Functional Soft Materials by Programmed Molecular Assembly
Professor Takuzo Aida, The University of Tokyo, JAPAN

10:00am A General & Practical Synthesis of Benzthiazoles
Dr Toshiaki Mase, Banyu Pharmaceutical Company, JAPAN

Morning Tea

Mathews Pavilions **10.30am – 11.00am**

Plenary and Keynote Speakers

Sponsored by Department of State & Regional Development - NSW First for Business

Clancy Auditorium **11.00am – 12.30pm**

Chaired by Dr Stan Lang, Valeant Pharmaceuticals International, USA

11:00am The Synthesis of Novel Drug Candidates
Dr Dave Tschaen, Merck, USA

12:00pm Biommetic Fouling Control: Development of Novel Antimicrobial Agents
Dr Naresh Kumar, Biosignal and The University of New South Wales, AUSTRALIA

Lunch

Mathews Pavilions **12.30pm – 1.30pm**

Invited Lectures and Contributed Oral Presentations

Mathews Theatre A **1.30pm – 3.00pm**

Chaired by Professor Rainer Streubel, University of Bonn, GERMANY

1:30pm Novel Heterocyclic Radiopharmaceuticals for Imaging Cancer, Neurodegeneration & Inflammation
Dr Andrew Katsifis, ANSTO Radiopharmaceuticals & Industrials, AUSTRALIA

2:00pm Total Synthesis of the Potent Anticancer 1,4-Dioxanes (–)-Episil Vestrol & (–)-Silvestrol
Associate Professor Mark Rizzacasa, The University of Melbourne, AUSTRALIA

2:20pm Synthesis of Natural Pyranonaphthoquinones & Related N-Containing Natural Products
Professor Norbert De Kimpe, Ghent University, BELGIUM

2:40pm Application of Iminium-Activation Technologies Towards the Total Synthesis of Frondosin B.
Dr Maud Reiter, Princeton University, USA

Invited Lectures and Contributed Oral Presentations

Mathews Theatre B **1.30pm – 3.00pm**

Chaired by Professor Sally Brooker, University of Otago, NEW ZEALAND

1:30pm Porphyrin-based Compounds that Mimic Aspects of Photosynthetic Reaction Centres
Professor Maxwell Crossley, The University of Sydney, AUSTRALIA

2:00pm On the Chemistry of 1,4,5,8-Naphthalenediimides
Professor Steven Langford, Monash University, AUSTRALIA

2:20pm Colorimetric Recognition of Spermidine & Spermine Based on Phenolphthalein Derivatives
Dr Kazunori Tsubaki, Kyoto University, JAPAN

2:40pm Tröger's Base Analogues as NLO Chromophores
Dr Andrew Try, Macquarie University, AUSTRALIA

Tuesday 17, July 2007 cont...

Invited Lectures and Contributed Oral Presentations

Mathews Theatre C **1.30pm – 3.00pm**

Chaired by Professor Dr. Lutz Tietze, GAU-Göttingen, GERMANY

1:30pm Heterocycle Synthesis via Radical Reaction
Professor Takeaki Naito, Kobe Pharmaceutical University, JAPAN

2:00pm Photocatalytic Reduction of NAD+
Dr Palli Thordarson, The University of Sydney, AUSTRALIA

2:20pm Synthetic Routes to Novel Bisbenzimdazoles as Potential Drug Candidates
Professor Jean Jacques Vanden Eynde, University of Mons-Hainaut, BELGIUM

2:40pm Development of Pyrrolopyrimidines as Inhibitors of ATP-Binding Proteins
Dr Jonathan Morris, University of Adelaide, AUSTRALIA

Invited Lectures and Contributed Oral Presentations

Mathews Theatre D **1.30pm – 3.00pm**

Chaired by Professor Jan Bergman, Karolinska Institute, SWEDEN

1:30pm The Use of Sultines in the Asymmetric Synthesis of Polypropionate Antibiotics
Professor Pierre Vogel, Ecole Polytechnique Federale de Lausanne (EPFL), SWITZERLAND

2:00pm Reactions of 2H-1,2,3-diazaphospholes with Bifunctional Nucleophilic Reagents: Theoretical and Experimental Investigation
Professor Mikhail Khusainov, Kazan State Technological University, RUSSIAN FEDERATION

2:20pm Gold Catalysis as an Efficient Tool for the Synthesis of Heterocycles
Professor Stephen Hashmi, Universität Heidelberg, GERMANY

2:40pm An Efficient Synthesis of Selenapenams & Selenacephems Using Key Intermediate 4-(2-Trimethylsilylethylseleno)Azetidinone
Mr Dinesh Garud, Gifu University, JAPAN

Afternoon Tea

Mathews Pavilions **3.00pm – 3.30pm**

Contributed Oral Presentations

Mathews Theatre A **3.30pm – 4.50pm**

Chaired by Professor Chris Willis, University of Bristol, UNITED KINGDOM

3:30pm Total Synthesis of (±)-γ-Rubromycin
Dr Yasuyuki Kita, Graduate School of Pharmaceutical Sciences, Osaka University, JAPAN

3:50pm New Processes for the Synthesis of Biologically Relevant Heterocycles
Professor Martin Banwell, Australian National University, AUSTRALIA

4:10pm New Advances in Synthesis of Polyannulated Thiophenes
Professor Valentine Nenajdenko, MSU, RUSSIAN FEDERATION

4:30pm Bifunctional Chiral Organocatalysts for the Enantiselective Aza-Morita-Baylis-Hillman Reaction
Professor Hiroaki Sasai, The Institute of Scientific & Industrial Research, Osaka University; JAPAN

Tuesday 17, July 2007 cont...

Contributed Oral Presentations

Mathews Theatre B **3.30pm – 4.50pm**

Chaired by Professor Colin Suckling, University of Strathclyde, SCOTLAND

3:30pm Synthesis & Fluorescence Characteristics of 2-N-Methylanilinopyridine & 2-N-Ethylanilinopyridine: Effect of Transition Metal
Dr Zaharah Aiyub, University of Malaya, MALAYSIA

3:50pm N,N-Dialkyl-N'-Chlorosulfonyl Chloroformamidines in the Synthesis of Novel Heterocycles
Dr Craig Francis, CSIRO Molecular & Health Technologies, AUSTRALIA

4:10pm Discovery of Novel Benzimidazole Phosphonates as Non-Nucleotide AMP-Mimetics to Inhibit FBPASE with In Vivo Efficacy in Rats
Dr Max Dang, Metabasis Therapeutics Inc, USA

4:30pm Application of Azomethine Ylide Chemistry to the Preparation of Seven-membered Ring Heterocycles: 1,3-Benzodiazepin-5-ones
Dr John Ryan, CSIRO, AUSTRALIA

Contributed Oral Presentations

Mathews Theatre C **3.30pm – 4.50pm**

Chaired by Professor Mary Garson, The University of Queensland, AUSTRALIA

3:30pm Improved Synthetic Approaches Toward 5'- and N6 Functionalised Adenosine Derivatives
Professor Peter Scammells, Monash University, AUSTRALIA

3:50pm Synthesis & DNA-binding Studies of Cyanine Dyes
Dr Gunnar Westman, Chalmers University of Technology, SWEDEN

4:10pm Synthesis of Guanidino Substituted Acridines, Precursors of Cytotoxic Quinone-Imine-Methide Intermediates
Dr Martine Demeunynck, Departemente Chimie Moleculaire, FRANCE

4:30pm Pharmacophore-based Design and Synthesis of a New Inhibitor of the NorA Bacterial Efflux Pump
Professor John Bremner, The University of Wollongong, AUSTRALIA

Contributed Oral Presentations

Mathews Theatre D **3.30pm – 4.50pm**

Chaired by Dr Alan Aitken, University of St Andrews, SCOTLAND

3:30pm Rotating Surfaces in Facilitating Chemical Transformations
Professor Colin Raston, The University of Western Australia, AUSTRALIA

3:50pm Synthesis & Green Applications of Organic, Bifunctional Catalysts: Boronic Acid Functionalized Nitrogen Heterocycles
Dr Andrew Whiting, Durham University, UNITED KINGDOM

4:10pm Metal Containing Imidazolium Ionic Liquids as Efficient & Recyclable Catalysts in C-C-Bond Formation
Professor Peter Gaertner, Vienna University of Technology, AUSTRIA

4:30pm Environmental Benign Synthesis of Some Novel Biodynamic Heterocycles & Their Biological Activity
Dr Ashok Dongamanti, Osmania University, INDIA

Poster Session

Mathews Pavilions **5.00pm – 7.00pm**

Wednesday, 18 July 2007

Plenary and Keynote Speakers

Clancy Auditorium **9.00am – 10.30am**

Chaired by Professor Margaret Brimble, University of Auckland, NEW ZEALAND

9:00am Total Synthesis of Complex Heterocyclic Natural Products
Professor K.C. Nicolaou, The Scripps Research Institute and University of California, USA

10:00am Synthesis of Modified Nucleosides for Metal Deposition in and Around DNA
Professor Thomas Carell, Ludwig-Maximilians Universitat, GERMANY

Morning Tea

Mathews Pavilions **10.30am – 11.00am**

Plenary and Keynote Speakers

Clancy Auditorium **11.00am – 12.30pm**

Chaired by Professor Jeffrey Aube, The University of Kansas, USA

11:00am New Catalysis Concepts
Professor David MacMillan, Princeton University, USA

12:00pm Chiral Phenyl-Bis(Oxazoline) as an Efficient Auxiliary for Asymmetric Catalysis
Professor Hisao Nishiyama, Nagoya University, JAPAN

Lunch

Please pick up your lunch and board the buses for the Harbour Cruise

Clancy Auditorium Foyer **12.30pm – 1.15pm**

Captain Cook Harbour Cruise

Tickets Required

Gate 9 – High Street **12.30pm – 5.30pm**

Buses will pick up from Gate 9 from 12.30pm. Please make your way to the bus as soon as possible after picking up your lunch.

Thursday, 19 July 2007

Plenary and Keynote Speakers

Clancy Auditorium **9.00am – 10.30am**

Chaired by Professor Johannes Fröhlich, Vienna University of Technology, AUSTRIA

9:00am Enantioselective Synthesis of Heterocyclic Compounds based on Palladium Enolate Chemistry
Professor Dr Mikiko Sodeoka, RIKEN (The Institute of Physical and Chemical Research), JAPAN

10:00am Heterocyclic Cleft Shaped Receptors for Molecular Recognition & Transport
Dr Phillip Gale, University of Southampton, UNITED KINGDOM

Morning Tea

Mathews Pavilions **10.30am – 11.00am**

Plenary and Keynote Speakers

Clancy Auditorium **11.00am – 12.30pm**

Chaired by Professor Kiyoshi Tomioka, Kyoto University, JAPAN

11:00am Total Synthesis of Heterocyclic Natural Products
Professor Thorsten Bach, Technischen Universität München, GERMANY

12:00pm Guanine Oxidation Leading to Hydantoins: From Organic Synthesis to Biology
Professor Cynthia Burrows, University of Utah, USA

Lunch

Mathews Pavilions **12.30pm – 1.30pm**

Invited Lectures and Contributed Oral Presentations

Mathews Theatre A **1.30pm – 3.00pm**

Chaired by Professor Peter Matyus, Semmelweis University, HUNGARY

1:30pm Enantioselective Synthesis of Vitamin E & Heterocycles Using Domino Pd-Catalyzed Transformations
Professor Lutz Tietze, GAU-Göttingen, GERMANY

2:00pm Stereocontrolled Syntheses of Functionalised Tetrahydropyrans
Professor Chris Willis, University of Bristol, UNITED KINGDOM

2:20pm Practical, One-Pot, Three-Component Synthesis of N-Heterocylic Carbene (NHC)-Ligated Palladacycles & Their Use as Well-defined Precatalysts for Pd-Mediated Cross-coupling Reactions
Dr Eric Assen B. Kantchev, Institute of Bioengineering and Nanotechology, SINGAPORE

2:40pm Phosphorus Heterocyclic Chemistry: New Structures & Reactions
Professor Rainer Streubel, University of Bonn, GERMANY

Invited Lectures and Contributed Oral Presentations

Mathews Theatre B **1.30pm – 3.00pm**

Chaired by Professor Girolamo Cirrincione, University of Palermo, ITALY

1:30pm Synthetic Investigation of Haplophytine – Architecturally Complex Hetero-Dimeric Indole Alkaloid
*Dr David Chen, A*Star - Institute of Chemical and Engineering Sciences, SINGAPORE*

2:00pm Prospecting for Pheromones: Heterocycles from Elephants & Maned Wolves
Professor Tom Goodwin, Hendrix College, USA

2:20pm Palladium-Catalyzed Cross-Coupling Reactions in the Field of Chromonoids & Flavonoids
Professor Tamás Patonay, University of Debrecen, HUNGARY

2:40pm Enantioselective Synthesis of Some Natural Lactones
Professor Yikang Wu, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, CHINA

Thursday 19, July 2007 cont...

Invited Lectures and Contributed Oral Presentations

Mathews Theatre C **1.30pm – 3.00pm**

Chaired by Professor Peter Scammells, Monash University, AUSTRALIA

1:30pm N,O-Heterocycles as Synthetic Intermediates
Dr Roderick Bates, Nanyang Technological University, SINGAPORE

2:00pm Novel Furanoterpene Metabolites from Marine Organisms
Professor Mary Garson, The University of Queensland, AUSTRALIA

2:20pm A Practical Synthesis of Oseltamivir
Dr Satoshi Yokoshima, University of Tokyo, JAPAN

2:40pm Regio & Chemoselective Reactions of Pyrrole: Towards Selectively Substituted Pyrroles & Pyrrolidine Analogues
Dr Jason Smith, University of Tasmania, AUSTRALIA

Invited Lectures and Contributed Oral Presentations

Mathews Theatre D **1.30pm – 3.00pm**

Chaired by Associate Professor Mark Rizzacasa, University of Melbourne, AUSTRALIA

1:30pm Cross-bridged Tetraamine Ligands - Synthesis & Radiopharmaceutical Applications
Professor Gary Weisman, University of New Hampshire, USA

2:00pm Proline-catalyzed Asymmetric Aldol Reactions. Enantioselective Total Synthesis of Biologically Active Natural Products
Professor Hiyoshizo Kotsuki, Kochi University, JAPAN

2:20pm Nitrohaloalkenes - Valuable Building Blocks for the Directed Synthesis of Persubstituted Heterocycles
Professor Dieter Kaufmann, Clausthal University of Technology, GERMANY

2:40pm Chemoenzymatic Total Syntheses of ent-Lycoricidine & Various Analogues from Bromobenzene
Miss Maria Matveenko, Australian National University, AUSTRALIA

Afternoon Tea

Mathews Pavilions **3.00pm – 3.30pm**

Contributed Oral Presentations

Mathews Theatre A **3.30pm – 4.50pm**

Chaired by Professor Dr. Ernst Schaumann, Clausthal University of Technology, GERMANY

3:30pm Stereoselective Michael Addition of Amides & Lactams to Nitroalkenes
Professor Akio Kamimura, Yamaguchi University, JAPAN

3:50pm The First Enantioselective Total Synthesis of the Pervilleines and their 8-Oxa analogues, potent MDR reversal agents for cancer and HIV
Associate Professor Patrick Perlmutter, Monash University, AUSTRALIA

4:10pm New Routes to Analogues of the Indolizidine, Homotropane & Pyrrolobenzodiazepine Natural Products
Dr Karl Hemming, University of Huddersfield, UNITED KINGDOM

4:30pm Studies of Ring-Closing Mode: Exo-Trig versus Endo-Dig
Professor Chisato Mukai, Kanazawa University, JAPAN

Thursday 19, July 2007 cont...

Contributed Oral Presentations

Mathews Theatre B **3.30pm – 4.50pm**

Chaired by Professor Anna Maria Almerico, University of Palermo, ITALY

3:30pm N-Heterocyclic Scaffolds for Iron-mediated Hydrocarbon Oxidation
Dr Peter Rutledge, The University of Sydney, AUSTRALIA

3:50pm Synthesis & Antifungal Activity of Bispyridinium Compounds
Mr Daniel Obando, The University of Sydney, AUSTRALIA

4:10pm A_1 Adenosine Receptor Allosteric Enhancers as Cardioprotective Agents
Miss Gemma Ferguson, Victorian College of Pharmacy, Monash University, AUSTRALIA

4:30pm Absolute Configuration of Heterocyclic Natural Products by Vibrational Circular Dichroism
Dr Pedro Joseph-Nathan, CINVESTAV-IPN, MEXICO

Contributed Oral Presentations

Mathews Theatre C **3.30pm – 4.50pm**

Chaired by Dr Malcolm McLeod, The University of Sydney, AUSTRALIA

3:30pm Azamacrocycle Complexes for Biomedical Applications
Dr Matthew Todd, The University of Sydney, AUSTRALIA

3:50pm New Dimroth Rearrangement of Aminoisoquinolinium Salts
Professor Gyorgy Hajos, Institute of Biomolecular Chemistry, HUNGARY

4:10pm Porphyrazines with Annulated Heterocycles: Theoretical Aspects & Experimental Facts
Professor Pavel Stuzhin, Ivanovo State University of Chemical Technology, RUSSIAN FEDERATION

4:30pm Highly Substituted Anthracene Bisimide Derivatives: Synthesis & Optical Properties
Dr Daniel Tyson, Ohio Aerospace Institute, USA

Contributed Oral Presentations

Mathews Theatre D **3.30pm – 4.50pm**

Chaired by Professor Gary Weisman, University of New Hampshire, USA

3:30pm Exploiting the Borono-Mannich Reaction in Bioactive Alkaloid Synthesis
Professor Stephen Pyne, The University of Wollongong, AUSTRALIA

3:50pm Atom Efficient & Diversity Orientated Multicomponet Reactions for the Synthesis of Valuable Heterocycles
Dr Romano Orru, Vrije University, THE NETHERLANDS

4:10pm Recent Advances in Utilization of Vicarious Nucleophilic Substitution (VNS) Products in the Synthesis of Indoles
Dr Stanislav Radl, Zentiva, CZECH REPUBLIC

4:30pm Heterocyclic Ketene Aminals: Versatile Synthons for the Synthesis of Novel Heterocycles
Professor Zhi-Tang Huang, Institute of Chemistry, The Chinese Academy of Sciences, CHINA

ISHC Business Meeting

Mathews Theatre C **5.00PM – 5.30PM**

Congress Dinner

Buses depart from Hotels at 6.45pm

Dockside, Darling Harbour **7.30pm – 10.30pm**

Friday, 20 July 2007

Plenary and Keynote Speakers

Clancy Auditorium **9.00am – 10.30am**

Chaired by Professor Mohsen Daneshtalab, Memorial University of Newfoundland, CANADA

9:00am New Cycloaddition & Annulation Strategies for the Synthesis of Heterocyclic Compounds
Professor Rick Danheiser, Massachusetts Institute of Technology, USA

10:00am The complexity of the Ring-Chain Equilibrium of 1,3-(X-N)- Heterocycles
Professor Ferenc Fülöp, University of Szeged, HUNGARY

Morning Tea

Mathews Pavilions **10.30am – 11.00am**

Plenary and Keynote Speakers

Clancy Auditorium **11.00am – 1.00pm**

Chaired by Professor Marco Ciufolini, University of British Columbia, CANADA

11:00am Heterocycles Based on the Chemistry of Alkylidenecyclopropanes and (Aza-)Cyclopropenes
Professor Shengming Ma, Shanghai Institute of Organic Chemistry, CHINA

12:00pm The Dipolar Cycloaddition Route to Piperidine Alkaloids
Professor Andrew Holmes, The University of Melbourne, AUSTRALIA

22 ICHC Presentation

Clancy Auditorium **1.00pm – 1.15pm**

Professor Mohsen Daneshtalab, Memorial University of Newfoundland, CANADA

Closing Ceremony

Clancy Auditorium **1.15pm – 1.30pm**

Professor David Black, The University of New South Wales, AUSTRALIA

Monday 16th July
Keynote & Plenary Speaker Abstracts

CYCLOADDITIONS OF 2-AZONIAHETERODIENES: AN ENABLING TECHNOLOGY FOR THE SYNTHESIS OF NATURAL AND NON-NATURAL PRODUCTS

Scott E. Denmark

Department of Chemistry, University of Illinois, Urbana, IL 61801, USA

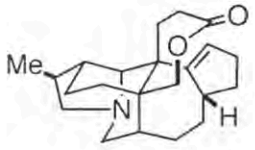
The tandem [4+2] / [3+2] cycloaddition of nitroalkenes has evolved into a powerful, complexity-generating transformation. With the ability to create up to four new bonds, four rings, and six stereogenic centers, rich with functionality, this reaction has already demonstrated great potential for the synthesis of stereochemically complex alkaloids.[1]

This lecture will highlight recent advances in the application of this tandem cycloaddition to the synthesis of a number of nitrogen-containing target structures that represent different research objectives. First, progress toward the total synthesis of daphnilactone B, a member of the daphniphyllum class of terpene alkaloids will be described. The approach to this molecule features a highly stereoselective nitroalkene cycloaddition that sets vicinal quaternary stereogenic centers.[2]

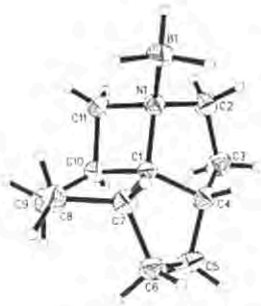
Second, the use of the tandem [4+2]/[3+2] cycloaddition, operating in the spiro mode, has allowed a general synthesis of 1-azafenestranes, a novel class of strained molecules that show significant planarizing distortion at the central carbon atom. Synthetic, structural and computational studies on this class of compounds will be described.[3]

Third, the fused-mode tandem [4+2]/[3+2] cycloaddition provides ready access to an azatricyclic framework that serves as a platform for the generation of chiral quaternary ammonium salts that are being optimized and evaluated for their potential as enantioselective phase transfer catalysts for a variety of anionic reactions.

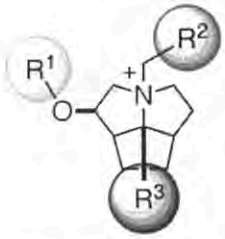
Finally, extension of the scope of 2-azoniadienes that are capable of [4+2]/[3+2] cycloaddition will be described in the synthesis, transformations, and the structural/computational analysis of *N*-vinyl nitrones.[4]



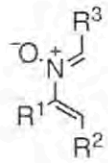
daphnilactone B



cis, trans, cis, cis
[4.5.5.5]-1-azafenestrane



chiral ammonium salt



N-vinyl nitrone

References:

1. Denmark SE, Cottell JJ. Nitronates. In *The Chemistry of Heterocyclic Compounds: Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, Padwa A, Pearson WH, Eds.; Wiley-Interscience: New York, 2002; pp 83-167.
2. Denmark SE, Baiazitov RY. *Org. Lett.* 2005; *7*, 5617-5620.
3. Denmark SE, Montgomery JI, Kramps LA. *J. Am. Chem. Soc.* 2006; *128*, 11620-11630.
4. Denmark SE, Montgomery JI. *J. Org. Chem.* 2006; *71*, 6211-6220.

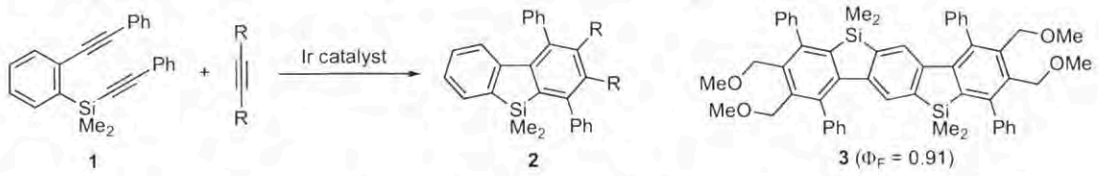
TRANSITION METAL CATALYZED APPROACHES TO SILOLE SYNTHESIS

Masahiro Murakami

Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Katsura, Kyoto 615-8510, Japan

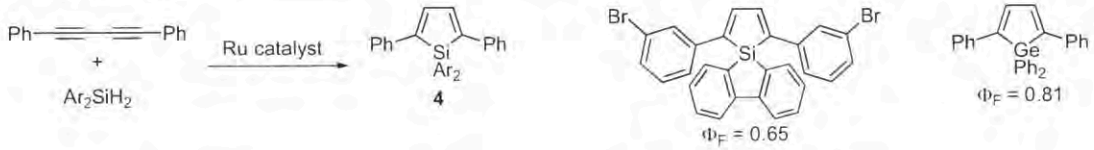
Siloles (silacyclopentadienes) are members of an intriguing class of silicon-based π-conjugated molecules that possess unique photophysical and electronic properties owing to their low-lying LUMO associated with $\sigma^*-\pi^*$ conjugation.[1] For example, high electron-transporting performances have been reported for some of siloles. There are several methods reported for the syntheses of the silole derivatives. However, the reactions necessitate cyclization step under strongly basic and/or reducing conditions, which require special precaution and limit the presence of sensitive functional groups. It is, therefore, highly desired to develop a new method for the synthesis of silole skeletons. Transition metal catalyzed reactions often proceed under mild conditions and allow preinstallation of various functionalities. This lecture will describe the results of our studies on the synthesis of silole derivatives by transition metal catalyzed cyclization reactions.

Silicon-bridged 1,6-diynes **1** underwent [2+2+2] cycloaddition with alkynes in the presence of an iridium(I)–phosphine catalyst to afford densely substituted silafluorene derivatives **2**.[2] Extended silafluorene skeletons were constructed by the [2+2+2] cycloaddition of tetraynes. Ladder-type silafluorene **3** has high fluorescence quantum yield (Φ_F) of 91%.



1 **2** **3** (Φ_F = 0.91)

Dihydrosilanes undergo double *trans*-hydrosilylation with 1,3-diynes in the presence of a cationic ruthenium catalyst to afford 2,5-disubstituted siloles **4**.[3] In particular, 9-silafluorene is a good hydrosilylating agent to produce spiro-type siloles in good yield. Diphenylgermane also reacted with the 1,3-diynes to give germoles in high yield. Some of the produced metalloles exhibited high quantum efficiency. These reactions offer a general method for the synthesis of 2,5-diarylmetalloles having various functional groups from readily available starting materials.



Φ_F = 0.65 Φ_F = 0.81

Other transition metal-catalyzed reactions forming silole skeletons will also be discussed.

References:

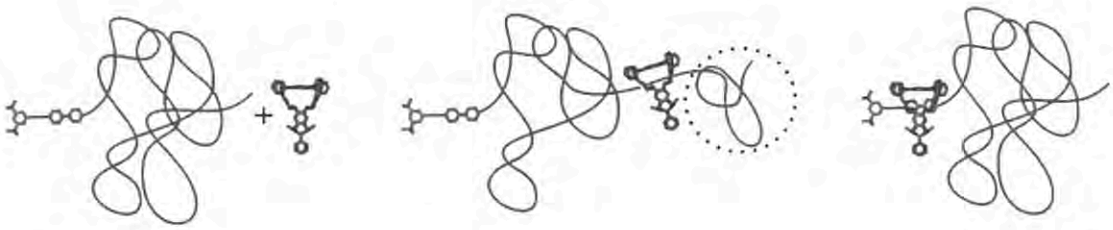
(1) Yamaguchi, S., Tamao, K. *J. Chem. Soc., Dalton Trans.* **1998**; 3693-3702.
(2) Matsuda, T., Kadowaki, S., Goya, T., Murakami, M. *Org. Lett.*, **2007**; 9, 133-136.
(3) Matsuda, T., Kadowaki, S., Murakami, M. *Chem. Commun.*, **2007**; 2627-2629.

MECHANISTIC ASPECTS OF THREADING OF POLYMERS IN PROCESSIVE ROTAXANE CATALYSTS

Ruud G.E. Coumans, Joost Clerx, Pilar Hidalgo Ramos, Alexander B.C. Deutman, Johannes A.A.W. Elemans, Roeland J.M. Nolte, **Alan E. Rowan**

Institute for Molecules and Materials, Radboud University Nijmegen, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands. Email: A.Rowan@science.ru.nl

Natural processive enzymes, such as λ-exonuclease or DNA polymerase III, operate by threading a DNA strand in a pseudo-rotaxane topology and subsequently slide along the chain performing several rounds of catalysis before they dissociate.[1] These highly efficient biocatalysts have inspired us to develop the first example of a synthetic processive rotaxane catalyst:[2] manganese porphyrin-containing macrocycle was threaded onto a polybutadiene strand and mimicked the catalytic action of a natural processive enzyme by catalyzing the epoxidation of the double bonds of the polymer while sliding along its chain.



In order to investigate this threading in more detail a series mono functionalized polymers was synthesized which contain a blocking N,N'-dialkyl-4,4'-bipyridinium trap at one side of the polymer chain and an open end at the other side.[3] The macrocycles are unable to slip over the blocking group and therefore they have to traverse the whole polymer chain before they reach the bipyridine trap which quenches the fluorescence of the macrocycle. Fluorescence emission studies revealed that the kinetics of threading followed a second order process and that the rate of threading was found to dependent on the polymer length with a length-dependent barrier of 61 J/nm which increases to 93 J/nm when a larger more flexible macrocycle was used.

The thermodynamics of threading revealed that for all polymers $\Delta H^{\ddagger}_{on}$ was positive and $\Delta S^{\ddagger}_{on}$ strongly negative with the absolute value of $\Delta S^{\ddagger}_{on}$ increasing with polymer length. These results are supportive of the nucleation mechanism proposed by Muthukumar,[4] resembling the transportation of DNA through the opening in a virus particle.

These studies have provided direct evidence that macrocyclic compounds can readily thread onto polymeric chains and slide along. The time needed to reach the blocked end of the polymer is related to polymer length, and the rate-limiting step involves a barrier of entropic origin in which a certain part of the open end of the polymer has to stretch and unfold. Recent studies describing how this threading rate can be controlled using a metallated porphyrin-containing macrocycle, will also be discussed.[5]

[1]. Wang, J.; Sattar, A.; Wang, C. C.; Karam, J. D.; Konigsberg, W. H.; Steitz, T. A. *Cell* **1997**, *89*, 1087.
[2]. Thordarson, P.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Nature* **2003**, *424*, 915.
[3]. Coumans, R. G. E.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19647.
[4]. Muthukumar, M. *Phys. Rev. Lett.* **2001**, *82*, 3188.
[5]. Hidalgo Ramos, P.; Coumans, R. G. E.; Deutman, A. B. C.; Smits, J. M. M.; de Gelder, R.; Elemans, J. A. A. W.; Nolte, R. J. M.; Rowan, A. E. *J. Am. Chem. Soc.* **2007**, *129*(17) 5699.

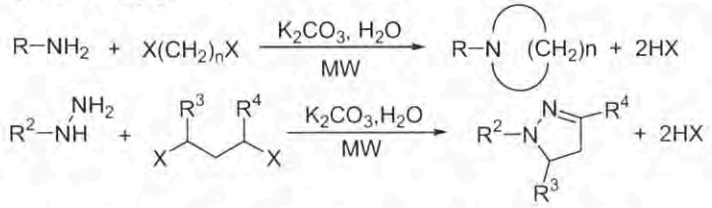
GREENER SYNTHESIS OF HETEROCYCLIC COMPOUNDS USING MICROWAVE IRRADIATION

Rajender S. Varma

Sustainable Technology Division, National Risk Management Research Laboratory, U.S. Environmental Protection Agency, 26 West Martin Luther King Drive, MS 443, Cincinnati, Ohio 45268, USA. Fax: 1-513-569-7677; E-mail: Varma.Rajender@epa.gov

An introduction of our interest in the microwave-assisted greener synthesis of a variety of heterocyclic compounds will be presented. It involves microwave (MW) exposure of neat reactants (undiluted) catalyzed by the surfaces of recyclable mineral supports, such as alumina, silica, clay, or their 'doped' versions, for the rapid one-pot assembly of heterocyclic compounds, such as flavonoids, related benzopyrans and quinolone derivatives [1]. The strategy to assemble oxygen- and nitrogen-heterocycles from *in situ* generated reactive intermediates via enamines [2] or using hypervalent iodine reagents [3] will be described. Examples of multicomponent reactions that can be adapted for rapid parallel synthesis include solventless synthesis of dihydropyrimidine -2(1H)-ones (Biginelli reaction) [4], imidazo[1,2-a]annulated pyridines, pyrazines, and pyrimidines (Ugi reaction) [5].

Organic synthesis in aqueous media [6] is rapidly gaining importance in view of the fact that the use of many toxic and volatile organic solvents, particularly halogenated hydrocarbons, contributes to pollution. Water is relatively benign [7] and has been utilized in combination with MW irradiation for the *N*-alkylation of amines by alkyl halides in the presence of aqueous NaOH [8]. This nucleophilic substitution chemistry can be manipulated using microwaves to generate cyclic amines *via* double *N*-alkylation of primary amines by dihalides or tosylates [9]. The protocol circumvents running multi-step reactions to assemble *N*-aryl azacycloalkanes, isoindoles, etc. and avoids the use of expensive metal catalysts in building aryl C-N bonds; functional groups such as carbonyl, ester, hydroxyl, etc. remain unaffected under these mild reaction conditions. The approach is also extended to hydrazines thus providing access to dihydropyrazoles (Scheme) [9].



R, R^1, R^2 = H, alkyl, aryl; R^3, R^4 = H, alkyl; X = Cl, Br, I, TsO.

Scheme Microwave-assisted synthesis of nitrogen heterocycles

References:

[1] (a) Varma RS *Green Chem.* 1999, *1*, 43-55. (b) Varma RS *J. Heterocycl. Chem.* 1999, *36*, 1565-1571. (c) Varma RS *Organic Synthesis using Microwaves and Supported Reagents in Microwaves in Organic Synthesis*; Loupy A (ed.) 2nd Edn. Chapt. 8, Wiley-VCH: Weinheim, 2006, pp 362-415; (d) Varma RS *Microwave Technology - Chemical Synthesis Applications: Kirk-Othmer Encyclopedia of Chemical Technology*, 5th Ed., Vol. 16, John Wiley & Sons, Inc., New York, 2006, pp 538 -594.

[2] Varma RS; Dahiya R. *J. Org. Chem.* 1998, *63*, 8038-8041.

[3] Varma RS; Kumar D; Liesen PJ *J. Chem. Soc. Perkin Trans. 1*, 1998, 4093-4096.

[4] Kappe CO; Kumar D; Varma RS *Synthesis*, 1999, 1799-1803.

[5] Varma RS.; Kumar D *Tetrahedron Lett.* 1999, *40*, 7665-7669.

[6] (a) Wei W; Keh CCK.; Li CJ.; Varma, RS *Clean Tech. & Environ. Policy* 2005, *7*, 62-69. (b) Skouta R; Varma RS; Li CJ *Green Chem.* 2005, *7*, 571-575.

[7] Varma RS *Organic Chem. Highlights*, Clean Chemical Synthesis in Water, Feb. 1, 2007, URL: http://www.organic-chemistry.org/Highlights/2007/01February.shtm

[8] Ju Y; Varma RS *Green Chem.* 2004, *6*, 219-221.

[9] (a) Ju Y; Varma RS *Tetrahedron Lett.* 2005, *46*, 6011-6014. (b) Ju Y; Varma RS *Org. Lett.* 2005, *7*, 2409-2411. (c) Ju Y; Varma RS *J. Org. Chem.* 2006, *71*, 135-141.

ADVANCEMENTS IN MICROWAVE TECHNOLOGY

E. Keller Barnhardt, Grace S. Vanier, T. Michael Barnard

CEM Corporation, Matthews, NC, USA

Microwave chemistry has made phenomenal strides over the past two decades. Once considered a method best suited for high temperature and high pressure reactions quickly and efficiently, microwave chemistry has evolved into a technique that can be used across the entire range of organic transformations. The use of microwave energy is not limited to high temperature / high-pressure reactions. It is a highly efficient energy source capable of performing otherwise challenging reactions in a very short period of time. This presentation will focus on the recent developments surrounding microwave chemistry, including, but not limited to the use of gaseous reagents, advanced microwave synthesis techniques, and the ability to perform larger scale reactions.

EXPANDING THE SCOPE OF MICROWAVE-PROMOTED CHEMISTRY

Nicholas E. Leadbeater

Dept of Chemistry, University of Connecticut, 55 N. Eagleville Road, Storrs, CT 06269 USA

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In this lecture, up-to-the-minute results from ongoing programs in the area of microwave-promoted chemistry will be presented. Topics covered will be:

- New method development for organic chemistry – in particular for reactions involving reactive gases.
- The scale-up of reactions for process chemistry – assessing batch and continuous processing.
- Development of tools for in-situ reaction monitoring including Raman spectroscopy and digital camera observation.
- Exploration of the use of microwave irradiation in bioscience applications.

Keeping with the overall theme of the conference, examples of heterocycle synthesis will be showcased, where possible, in each of the general areas covered in the lecture.

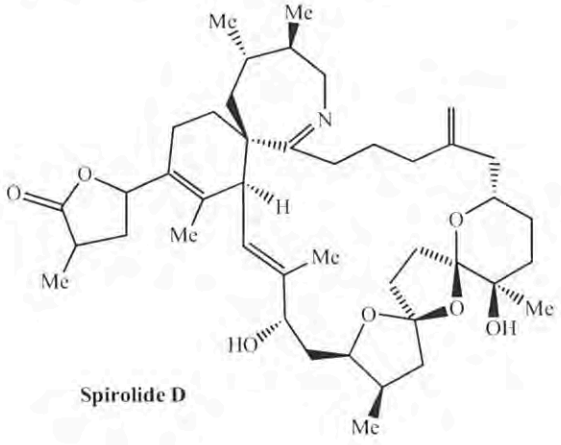
Monday 16th July
Mathews Theatre A
Contributed Oral Presentations

SYNTHETIC STUDIES TOWARDS THE SPIROLIDE FAMILY OF SHELLFISH TOXINS

Margaret A. Brimble, Kai Meilert, Karsten Koerber and Patrick O'Connor

Department of Chemistry, The University of Auckland, 23 Symonds St., Auckland, New Zealand

The spirolides A-D[1] comprise a family of pharmacologically active macrocycles found in the polar lipid fraction obtained from the digestive glands of contaminated mussels (Mytilus edulis), scallops (Plactopecten magellanicus) and toxic plankton from the eastern coast of Nova Scotia. The spirolides contain a novel 6,5,5-spiroacetal ring system and a unique 6,7-spiroimine unit embedded in a macrocylic structure. No total synthesis of the spirolides has been reported to date. The synthesis of the 6,5,5-bis-spiroacetal moiety of the spirolides using an iterative radical oxidative cyclization strategy will be presented[2] together with our initial studies towards the spiroimine unit of these complex macrolides.



Spirolide D

References:

[1] Hu, T, Curtis, JM, Oshima, Y, Quilliam, MA, Walter, JA, Watson-Wright, WM, Wright, J L. *J. Chem. Soc., Chem. Commun.*, 1995; 2159-2161.

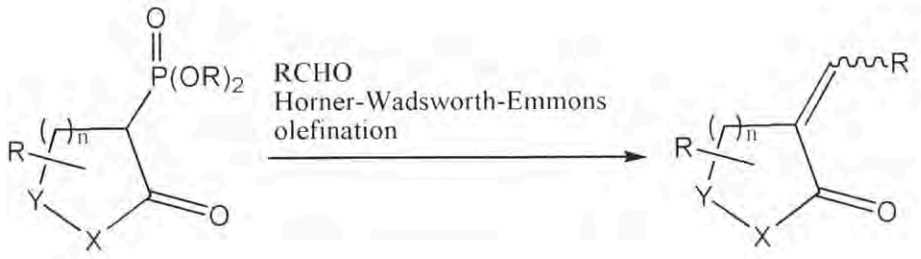
[2] Meilert, K, Brimble, MA. *Org. Biomol. Chem.*, 2006; 4, 2184-2192.

SYNTHESIS OF 2-ALKYLIDENE-1-OXOHETEROCYCLES AS PROMISING ANTICANCER AGENTS

Tomasz Janecki

Institute of Organic Chemistry, Technical University of Lodz, Zeromskiego 116, 90-924 Lodz, Poland (e-mail: tjanecki@p.lodz.pl)

Compounds containing α-alkylidenelactone and lactam skeletons are a well recognized group of natural and synthetic products which very often show strong anticancer activity [1]. Numerous methods of the synthesis of these compounds have been corroborated so far [2]. One, very promising group of these methods employs organophosphorus reagents for the introduction of the alkylidene moiety onto lactone or lactam rings *via* the Wittig type reaction [3].
Recent efforts in our laboratory have resulted in a significant development of this method to the synthesis of α-alkylidenelactones and lactams as well as other 2-alkylidene-1-oxoheterocycles 2. More specifically, we developed several synthetic approaches to the 2-phosphoryl-1-oxoheterocycles 1 which are excellent Horner-Wadsworth-Emmons reagents and, when applied to the olefination of various aldehydes, provide access to 3-alkylidenedihydrofuran-2(3*H*)-ones, 3-alkylidenepyrrolidin-2-ones, 4-alkylideneisoxazolidin-5-ones, 4-alkylideneisoxazolidin-3-ones or 4-alkylpyridazin-3(2*H*)-ones [4]. These approaches and chemistry discovered in the course of their development will be discussed.



1 **2**

n = 1,2; X = O, NR; Y = CH_2, O, NR

Furthermore, the relationship between the structure and cytotoxic activity of the synthesized compounds, which are promising anticancer agents, will also be addressed.

References:
[1] Hoffmann HMR., Rabe J. *Angew. Chem.,Int. Ed. Engl.*, 1985; 24, 94-110
[2] GowriSankar S., Lee ChG., Kim JN. *Tetrahedron Lett.*, 2004; 45, 6949-6953 and references therein
[3] Janecki T. *Targets in Heterocyclic Systems – Chemistry and Properties*, Attanasi O. A., Spinelli D., Eds., Italian Chemical Society, 2006, Vol. 10, in press
[4] Albrecht A., Kedzia J., Koszuk JF., Warzycha E., Janecki T. *Tetrahedron Lett.*, 2006; 47, 2353-2355; Janecki T., Wasek T., Rozalski M., Krajewska U., Studzian K., Janecka A. *Bioorg. Med. Chem. Lett.*, 2006; 16, 1430-1433; Janecki T., Blaszczyk E., Studzian K., Janecka A., Krajewska U., Rozalski M. *J. Med. Chem.*, 2005; 48, 3516-3521 and references therein

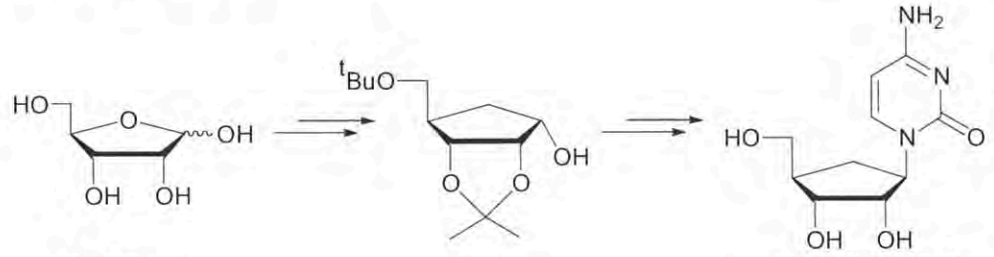
PRACTICAL SYNTHESIS OF (-)-CARBOCYCLIC CYTOSINE (CARBODINE) AND ITS IN VITRO AND IN VIVO ANTIVIRAL ACTIVITY AGAINST VENEZUELAN EQUINE ENCEPHALITIS (VEE) VIRUS

C. K. Chu,[2*] J. R Rao,[1] J. G. Julander,[2] R and. W. Sidewell[2]

[1]*The University of Georgia College of Pharmacy, Athens, GA, 30602 and* [2]*Utah State University Institute Antiviral Research, Logan, UT 84322 USA*

Natural as well as synthetic carbocyclic nucleosides are well known for their interesting biological activities, including antitumor as well as antiviral activities against a wide variety of RNA and DNA viruses. The carbocyclic analogue of cytosine (carbodine 2) was previously prepared as a racemic mixture and has been shown to possess significant antitumor (lymphoid leukemia L1210 in mice) and antiviral activities against human influenza type A virus, measles, vesicular stomatitis virus and herpes simplex viruses (HSV-1 and HSV-2). These interesting biological properties of carbodine, prompted us to synthesize enantiomerically pure (-)-carbodine (2) for biological evaluations. Herein, we report an efficient and practical synthesis of (-)-carbodine (2) as well as its antiviral activities against VEE and yellow fever virus.

The key intermediate, chiral cyclopantanol 1, was achieved from a chiral enone by a 1,4-addition reaction in a multi-gram scale. The cyclopentanol intermediate 1 was reacted with protected cytosine under Mitsunobu reaction conditions, however, it provided only O-alkylated product instead of the desired N-alkylated product. Therefore, the desired heterocycle, cytosine was constructed by the linear approach to afford the target nucleoside, (-)-carbodine (2) in a gram scale. The (-)-carbodine (2) showed potent antiviral activity against Venezuelan equine encephalitis virus (TC-83 virus strain, EC_{90} 0.3 μM) with the high selective index >333 and yellow fever virus (17D virus strain, EC_{90} 2.2 μM) in Vero cells (Supported by NIH AI 056540 and NO1-AI-30048).

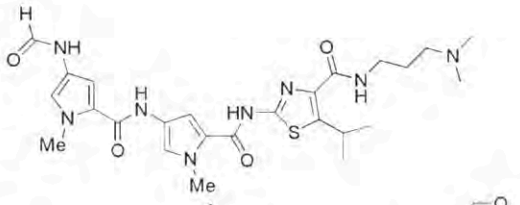


HETEROCYCLIC DNA MINOR GROOVE BINDERS: SYNTHESIS, PHYSICOCHEMICAL PROPERTIES, AND BIOLOGICAL ACTIVITY OF ALKENE LINKED COMPOUNDS

Colin J Suckling[a], Roger D Waigh[b], Simon P Mackay[b], John Parkinson[a], Abedawn I Khalaf[a], Nahoum Anthony[b], Elizabeth Ellis[b], Iain S Hunter[b], Curtis G Gemmell[c], David Breen[a], and Gavin Donoghue[a].

a. WestCHEM Research School, Department of Pure & Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow, G1 1XL, Scotland.
b. Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow, G4 0NR, Scotland.
c. Division of Infection and Immunity, IBLS, University of Glasgow, Glasgow Royal Infirmary, 84 Castle Street, Glasgow, G4 0SF, Scotland.

Heterocyclic DNA minor groove binders (MGBs) have been widely studied as potential therapeutic agents but the structural components have typically been limited to heterocyclic amino acids linked by amide bonds 1 [1]. From the point of view of biological activity, cell penetration is important and consequently, more lipophilic compounds might be more effective. We and others have shown that branched alkyl groups as substituents on the heterocyclic monomers can provide significant increases in antibacterial activity [2] and high selectivity of binding to specific DNA sequences [3]. An extension of this argument would be to replace the amide link with an isosteric alkene. Recently, we have synthesised a number of such compounds (e.g. 2) and have found them to have exceptional antibacterial activity *in vitro* and *in vivo* [4]. This paper will outline the synthetic routes, which are especially challenging when the alkene links two pyrrole units. In addition, to aid the preparation of libraries of compounds for testing, we have developed a new synthetic route for the preparation of a variety of tail groups (analogues of the morpholinoethyl group in 2) involving phosphorus (III) bisimidates that are activated for nucleophilic displacement late in the synthesis.



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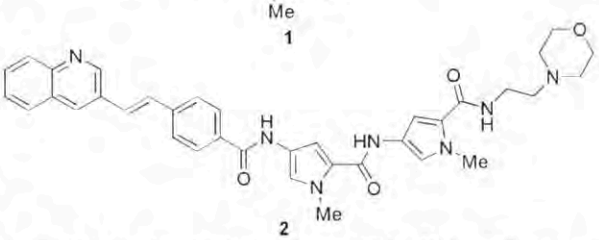


2

The biological activity of these compounds poses interesting physicochemical questions relating to their access to target sites and their binding to DNA. Physicochemical properties of individual MGBs, especially pK_a of the tail group appear to be significant, and the increased hydrophobic character produced by the alkene promotes self association of MGB molecules in solution. Both properties are relevant to DNA binding and we have studied the thermodynamics of binding of alkene containing MGBs in comparison with purely amide linked MGBs in a short oligonucleotide by NMR and isothermal calorimetry. In both cases, binding is strong with K_Ds in the 10 - 100 nM range. Consistent with this information are data from T_m measurements in which binding of an MGB causes an increase in the T_m of a decamer by 10°C. The salient physicochemical properties of our MGBs will be reviewed.

1. Suckling CJ. *Expert Opinion on Therapeutic Patents*, 2004: 14, 1693-1724.
2. Anthony NG, Fox KR, Johnston BF, Khalaf AI, Mackay SP, McGroarty IS, Parkinson JA, Skellern GG, Suckling CJ, Waigh RD. *Bioorg. Med. Chem. Letters*, 2004: 14, 1353-1356.
3. Khalaf AI, Waigh RD, Drummond AJ, Pringle B, McGroarty IS, Skellern GG, Suckling CJ. *J. Med. Chem.* 2004: 47, 2133-2156.
4. Khalaf AI, Waigh RD, Suckling CJ. UK patent application 0619325.4.

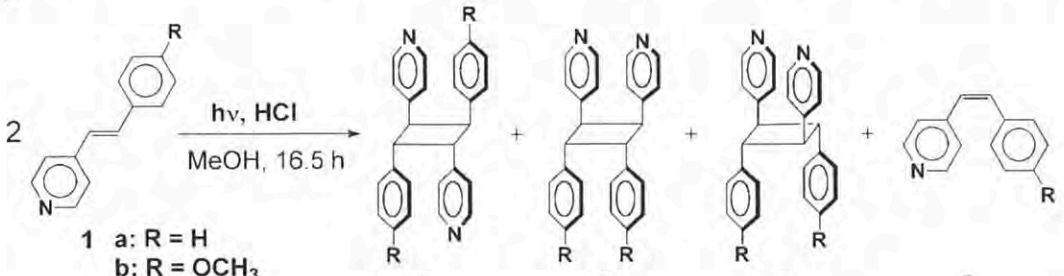
Monday 16th July
Mathews Theatre B
Contributed Oral Presentations

PHOTODIMERIZATION REACTION OF 4-STYRYLPIRIDINES: THE ROLE OF A CATION-π INTERACTION IN THE STEREOSELECTIVITY

Shinji Yamada, Naoko Uematsu and Mai Sugawara

Department of Chemistry, Ochanomizu University, Bunkyo-ku, Tokyo 112-8610, Japan

It has been reported that the dimerization of 4-styrylpyridine in acidic media produced *syn* head-to-tail adduct as a major product (1). However, no explanation has been given for the stereoselectivity. In the course of our continuing effort addressed towards the development of the utility of cation-π interaction as a new conformation-controlling tool for organic molecules (2), we were interested in the stereoselective dimerization of 4-styrylpyridines. In this presentation, we describe that intermolecular cation-π interaction plays a key role on the regio- and stereoselectivities of [2+2]-photodimeization reactions of *trans*-4-styrylpyridines **1a-c**.



trans-4-Styrylpyridines (**1a-c**) in 1.66 M of methanol solution was irradiated with a 450W high-pressure mercury lamp. The [2+2]-photodimerization of **1a** proceeded to afford three isomeric dimers (**2a**-**4a**) and *cis*-isomer (**5a**). At the neutral condition, **5a** was produced as a major product. On the other hand, in the presence of conc. HCl, *syn* head-to-tail adduct **2a** was produced as a major product. Table 1 clearly shows HCl dependence on the product distribution. The yield of **2a** increases as the amount of HCl increases, strongly suggesting the existence of the cation-π interaction in the HCl salt. In the acidic media, the substrates would form a molecular dimer by cation-π interactions as shown in Figure 1. Consequently, *syn* head-to-tail dimer **2a** was selectively produced. The substituent effect on the product distribution also supported this explanation.

Table 1. Photocycloaddition of **1a**

conc.HCl (eq.)	ratio of products (%)				
	2a	**3a**	**4a**	**5a**	**1a**
0	17.0	11.1	11.2	41.9	18.9
1	54.5	5.6	5.6	26.3	10.2
3	59.9	13.5	13.2	9.5	4.0
5	63.7	8.3	14.1	9.3	4.6
10	68.3	6.7	13.3	8.0	3.7

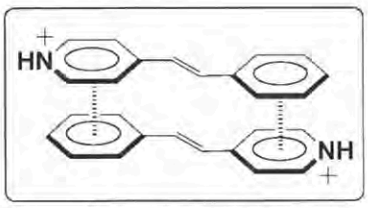


Figure 1. Plausible molecular dimer

References:

(1) (a) Li, X. H.; Wu, L. Z.; Zhang, L. P.; Tung, C. H. *Org. Lett.* 2002; 4, 1175-1177. (b) Quina, F. H.; Whitten, D. G. *J. Am. Chem. Soc.* 1977; 99, 877-883.

(2) (a) Yamada, S.; Morita, C. *J. Am. Chem. Soc.* 2002; 124, 8184-8185. (b) Yamada, S.; Misono, T.; Tsuzuki, S. *J. Am. Chem. Soc.* 2004; 126, 9862-9872. (c) Yamada, S.; Yamamoto, J.; Ohta, E. *Tetrahedron Lett.* 2007; 48, 855-858.

HETEROCYCLES SYNTHESIS VIA BENZANNULATION, AMINOBENZANNULATION AND HETEROCYCLIZATION REACTIONS.

Philippe Belmont

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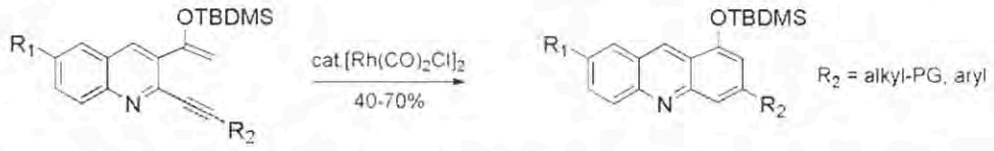
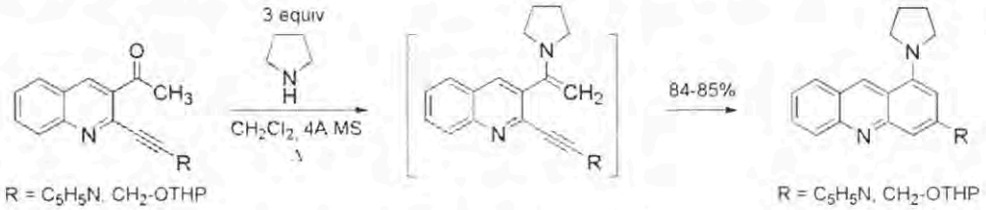
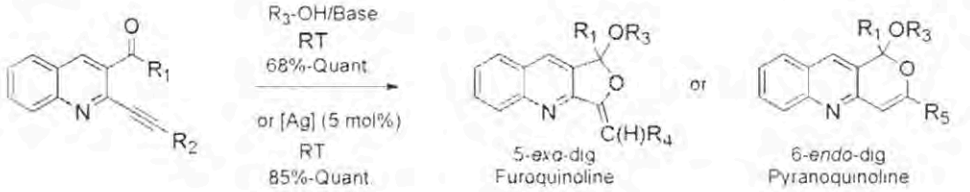
The first methodology is inspired from a naphthalene synthesis developed previously with silyl-enol-ethers units [1]. The key quinoline intermediates are substituted with a TBDMS-enol-ether and protected functionalized alkynes (PG). The cyclization step is a rhodium-catalyzed benzannulation [2] yielding the desired poly-substituted acridine derivatives:



Herndon [3] reported a powerful method allowing the access to aminonaphthalenes thanks to the dual role of a palladium catalyst. In relation to that work, we recently disclosed a pyrrolidine triggered metal-free aminobenzannulation reaction [4]. Indeed, when pyrrolidine and powdered 4Å molecular sieves (4Å MS) were used together, the enamine synthesis and the aminobenzannulation step took place subsequently. Thus, we obtained very smoothly new 1-aminoacridines derivatives, even bearing a sensitive protective group (tetrahydropyranyl, THP). This methodology is being generalized on other heterocyclic cores.



Finally, an efficient 5-*exo*-dig or 6-*endo*-dig cyclization was observed when alkynyl-quinolines bearing a carbonyl group were submitted to a mixture of an alcohol (alkyl-OH, diol, amino-alcohol) with an inorganic base (potassium carbonate) [5]. The same cyclization process was also possible as a more general silver-catalyzed heterocyclization method [6].
The dihydrofuroquinoline derivatives formed are structurally related to the well-known furoquinoline alkaloids family. The scope and limitations of this reaction have also been studied with diverse bases or silver catalysts and various alkynyl, alcohol and carbonyl derivatives.



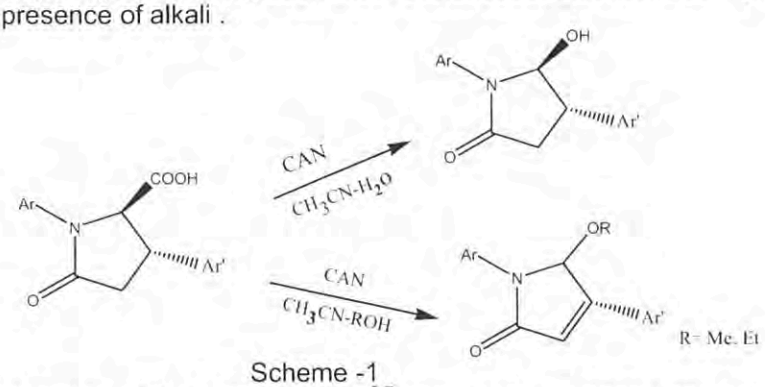
References:
[1] Dankwardt J.W. *Tetrahedron Lett.* 2001; 42, 5809-5812.
[2] Belmont P., Andrez J.-C., Allan C.S.M. *Tetrahedron Lett.* 2004; 45, 2783-2786.
[3] Herndon J.W., Zhang Y., Wang K. *J. Organomet. Chem.* 2001; 634, 1-4.
[4] Belmont P., Belhadj T. *Org. Lett.* 2005; 7, 1793-1795.
[5] Godet T., Bosson J., Belmont P. *Synlett* 2005; 2786-2790.
[6] Godet T., Vaxelaire C., Michel C., Milet A., Belmont P. *Chem. Eur. J.* 2007; in press.

CERIC AMMONIUM NITRATE (CAN) MEDIATED STEREOSELECTIVE DECARBOXYLATIVE HYDROXYLATION/ALKOXYLATION & OXIDATION OF N-ARYL-γ-LACTAM CARBOXYLIC ACIDS

Gopa Barman, Pranab Haldar and Jayanta K. Ray*

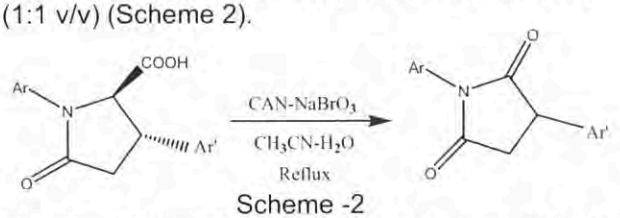
Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India
jkray@chem.iitkgp.ernet.in

A number of high valent metals e.g. Pb (IV), Co (III), Ag (II), Mn (III), and Ti (III) have been used as oxidative decraboxylating agents, but all of these reagents have several drawbacks. Ceric Ammonium Nitrate (CAN) has emerged as a versatile one-electron oxidant for carbon-hetero atom bond formation reactions.[1,2] In connection with our interest on chemo selective functional group transformations[3,4] of γ-lactam derivatives, we were interested in exploring CAN mediated reactions toward the decarboxylative hydroxylation/alkoxylation of 1,4-diarylpyrrolidin-2-one-5-carboxylic acids at room temperature in organo-aqueous solvent (Scheme 1).Not only we got decarboxylative hydroxylation/alkoxylation with several substrates, but also highly stereo-selective dehydration in presence of alkali .



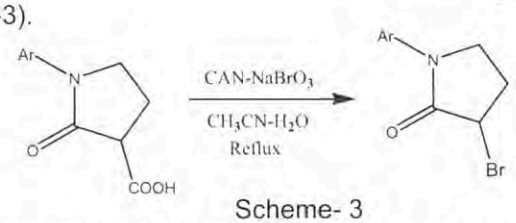
Scheme -1

Next, the combination of CAN and $NaBrO_3$[6,7] provided a general one-pot method for the conversion of 1,4– diaryl δ-lactam carboxylic acid to 1,3-diaryl succinimide in refluxing acetonitrile-water (1:1 v/v) (Scheme 2).



Scheme -2

Interestingly, when we performed the same reaction with N-aryl-2-oxo-pyrrolidine-3-carboxylicacids as the substrate, we observed decarboxylative bromination as the major product (Scheme-3).



Scheme- 3

Mechanistic and spectroscopic details will be presented.

References:

1. Nair, V.; Panicker, S. B.;Nair,L.G.; George, T. G.;Augustine, A. *Synlett* 2003, 156-165.
2. Tranhanovsky, W.S.; Cramer,J.; Brixius,D W. *J. Am. Chem. Soc.* 1974, 96, 1077-1081.
3. Haldar,P and Ray,J.K. Organic Letters 2005,7, 4341-4343.
4. Haldar,P ; Guin,J and Ray, J.K. *Tetrahedron Letters* 2005, 46,1071-1074.
5. Haldar,P. and Ray, J.K. *Tetrahedron Letters* 2003, 44, 8229-8231.
6. Molander, A.G. *Chem. Rev* 1992, 92, 29-68.
7. Ganin E. and Amer, I. *Synthetic Communication* 1995, 25(20), 3149-3154.

1,2-DIOXINES – IGNORED STARTING MATERIALS FOR CHEMICAL SYNTHESIS!

Dennis K. Taylor

The University of Adelaide
School of Chemistry and Physics

1,2-Dioxines are also commonly know as endoperoxides and are clearly under-utilised starting materials for chemical synthesis. We have been exploring the chemistry of these useful precursors over the last decade and this presentation will highlight a range of new chemical transformation that we have invented to make useful precursors for the ready construction of bioactive natural and non-natural products. Examples will include the preparation of cyclopropanes, gamma-lactones, rare sugars, pyrans, furans and epoxy ketones.

Monday 16th July
Mathews Theatre C
Contributed Oral Presentations

BENZOTHIENO-TRIAZOLO-PYRIMIDINE
A NEW CLASS OF POTENTIAL DNA-BINDERS

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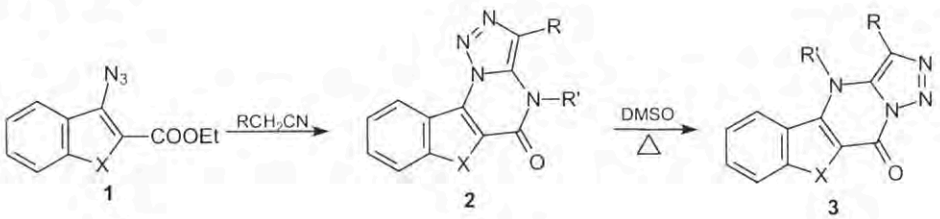
DNA recognition by small molecules is a fundamental problem in drug design because cytotoxic agents that interfere with these processes can modulate transcription, protein binding and expression of specific genes. Derivatives which combine DNA intercalating ability with minor groove binding are in the focus of many studies. In this light and in connection with our ongoing researches in the field [1], we report herein our more recent findings on isosters of indolo-triazolo-pyrimidines of type 2 (X=NMe). The synthetic access to new class of tetracycles 2 (X=S), benzothieno[2,3-e][1,2,3]triazolo[1,5-a]pyrimidine, derivatives of this hitherto unknown ring system, was provided by domino reaction of substituted acetonitriles (R=Ph, CN, COOEt) and azido heterocycles under basic conditions. These last through the azido moiety can act as a 1,3-dipolar compound in cycloaddition reactions with dipolarophiles. The intermediate is an 1-heterocyclyl-triazole which bears an amino group susceptible of further reactions. In fact, in the presence of a vicinal carboxylate function, cyclizes originating the pyrimidine third ring. The nature of the substrate, the reaction conditions and the bond-forming economy (two rings formation in sequence) can widely influence the nature of the reaction products [2]. Dimroth rearrangement on compounds 2 (X=S, R=Ph) led to the linear tetracycle of type 3.



All the new derivatives 2 and 3 possess physical-chemical properties suitable for DNA intercalation, as evidenced by preliminary screening tests carried out *in silico* by using docking procedure to selected DNA fragments. Both polycycles are also susceptible of further decoration by introducing on the pyrimidine nitrogen chains suitable for binding with DNA grooves. By analogy with indole derivatives, in which the presence of suitable chains [R'=$(CH_2)_3$COOEt, $(CH_2)_3$COOH, $(CH_2)_3$CONH$(CH_2)_2$imidazol-4-yl] modulated the cytotoxic activity and DNA binding capability [3], the same type of chains were introduced in compounds 2 and 3.
Antiproliferative activity and interaction with calf thymus DNA of the new compounds is under investigation.

References:
[1] a) Lauria A, Patella C, Diana P, Barraja P, Montalbano A, Cirrincione G, Dattolo G, Almerico AM *Heterocycles*, 2003, 60, 2669-2675. b) Lauria A, Patella C, Diana P, Barraja P, Montalbano A, Cirrincione G, Dattolo, G, Almerico AM *Tetrahedron Lett.*, 2006, 47, 2187–2190.
[2] a) Lauria A, Diana P, Barraja P, Almerico AM, Cirrincione G, Dattolo G, *J. Heterocycl. Chem.*, 2000, 37, 747-750. b) Lauria A, Diana P, Barraja P, Montalbano A, Cirrincione G, Dattolo G, Almerico AM, *Tetrahedron*, 2002, 58, 9723-9727.
[3] Lauria A, Patella C, Dattolo, G, Almerico AM *J. Med. Chem.*, submitted.

HETEROINDOXYLS

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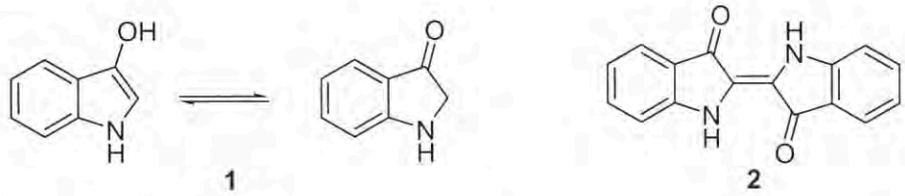
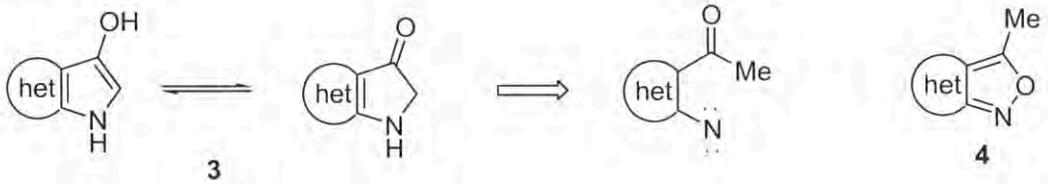
Indoxyl [3-hydroxyindole, or indol-3-(2*H*)-one) 1 is a fundamental heterocyclic system that is of importance as the reduced monomer of indigo 2, a dye which has been in use for at least 4,000 years.[1]



1 2

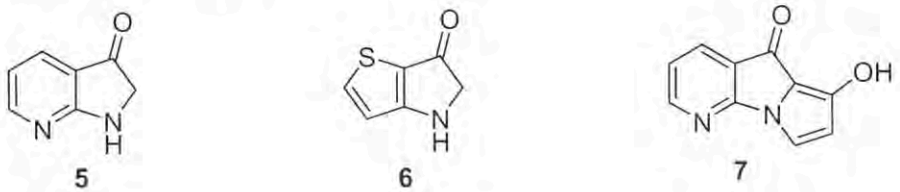
Despite this venerable history, nothing is known of the synthesis or properties of indoxyls in which the fused benzene ring is replaced by a heterocycle 3. In this paper, we will show how highly reactive heteroindoxyls 3 can be made under flash vacuum pyrolysis (FVP) conditions using a key cyclisation step involving nitrene insertion. The role of fused isoxazole intermediates 4 in these reactions will also be discussed;[2] temperature-conversion plots of the FVP process allows conditions to be established which maximise the preparative yields of 3 and 4.



3 4

Specific heteroindoxyls which will be considered include the fused pyridine analogue 5 and the fused thiophene 6. By analogy with the chemistry of indoxyl 1 itself, preliminary studies of the properties of 5 and 6 have been carried out and these results will also be reported, including:

- Tautomerism
- Oxidative dimerisation to indigo analogues
- Reactions of the pyrrolone ring at the 2-position
- Reactions of the pyrrolone ring at the nitrogen atom
- Cyclisation reactions, including the novel two-step formation of the fused hydroxypyrrolizinone 7



5 6 7

1. For example, Allen, RLM, *Colour Chemistry*, Nelson, London, 1971.
2. *c.f.* Dyall, LK, Suffolk, PM, Dehaen, W, L'abbe, G, *J. Chem. Soc., Perkin Trans. 2*, 1994; 2115-2119.

SYNTHESIS AND PLANT-GROWTH REGULATING PROPERTIES OF SOME NEW PURINE DERIVATIVES.

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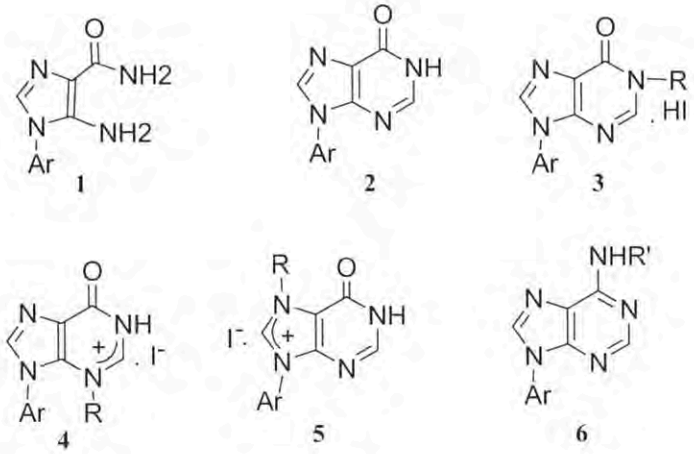
Purine and its derivatives have successfully been employed in many biological directions. Many 6-substitutedaminopurine derivatives have been reported to have useful plant-growth regulating properties. Therefore, the present work deals with the synthesis and plant-growth regulating activity of some new purine derivatives.

Treatment of the 5-amino-1-aryl-1*H*-imidazole-4-carboxamide 1 with ethyl chloroformate / DMF reagent mixture afforded 9-aryl-1,9-dihydro-6*H*-purin-6-one 2. Upon reacting the latter product with alkyl iodides the 7-alkyl purinium iodide salts 3 were obtained rather than the expected products of type 4 or 5. Furthermore, the 6-substitutedaminopurine derivatives 6 were synthesized when treating product 2 with phosphoryl chloride followed by reaction with 1^{ry} amines.

Plant-growth regulating effects for selected examples from the synthesized products 6 were reported.



PREPARATION OF 2,3-BROMIDES AND 2,3-EPOXIDES OF PHOSPHOLANES AS ANALOGUES OF PHOSPHA SUGARS AND THEIR IMPORTANT BIOLOGICAL ACTIVITIES

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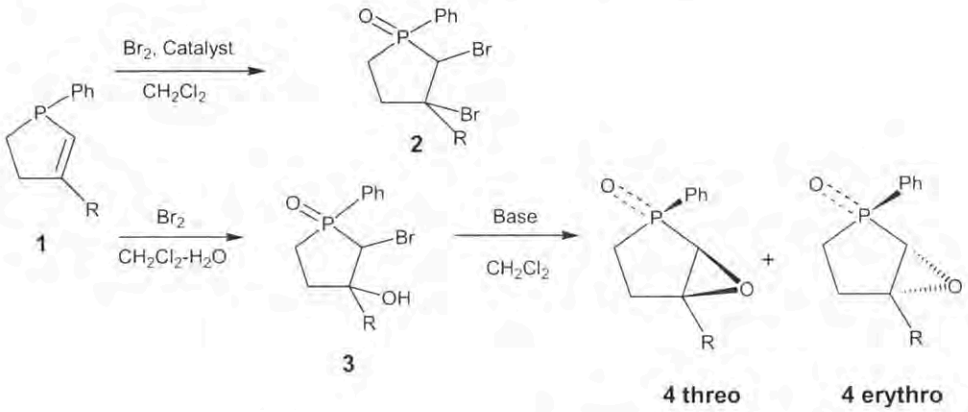
Sugar derivatives, whose oxygen atom in the hemiacetal ring is replaced by a carbon, nitrogen, or sulphur atom, are called as pseudo sugars. The characterization of pseudo sugars from naturally occurring products, such as *carba*, *aza*, or *thia* sugars, or chemically prepared products are well investigated and many of them are found to be biologically active sugars. On the other hand, phospha sugars which have a phosphorus atom in the sugar ring are not yet found in the nature and the synthesis and characterization of them are not so well studied.

Previous methodologies for the preparation of phospha sugars used entirely sugar starting materials, however, we are challenging to develop novel synthetic routes from heterocyclic compounds, mainly, 2- or 3-phospholene derivatives. Here we will report a new reaction to prepare 2,3-epoxyphospholanes (1, 2) and 2,3-dibromophospholanes as analogues of phospha sugars and their biological activities.

Treatment of 3-methyl-1-phenyl-2-phospholene 1-oxide (1) with bromine in DCM in the presence of catalyst or in aqueous organic media gave 2,3-dibromo-3-methyl-1-phenylphospolane 1-oxide (2) 2-bromo-3-hydroxy-3-methyl-1-phenylphospholane 1-oxideor (3). Bromide 3 was converted into 2,3-epoxy-3-methyl-1-phenylphospholane 1-oxide (4 threo and 4 erythro).



The characterization of 2,3-dibromide 3 and 2,3-poxide 4 was firstly investigated to reveal that they have important biological activities.

References:

(1) Yamashita, M.; Valluru, K. Reddy; Lakonda, N. Rao; Buchammagari, H.; Maeda, M.; Suzuki, K.; Totsuka, H.; Takahashi, M.; Oshikawa, T. *Tetrahedron Lett.* 2003, 44, 2339-2341.
(2) Totsuka, H.; Maeda, M.; Valluru, K. Reddy; Takahashi, M.; Yamashita, M. *Heterocyclic Commun.* 2004, 10, 295-300.

Monday 16th July
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Contributed Oral Presentations

RHODIUM CATALYZED 1,4-CONJUGATED ADDITION OF *Sb*-ARYL-1,5-AZASTIBOCINES TO α,β-UNSATURATED CARBONYL COMPOUNDS

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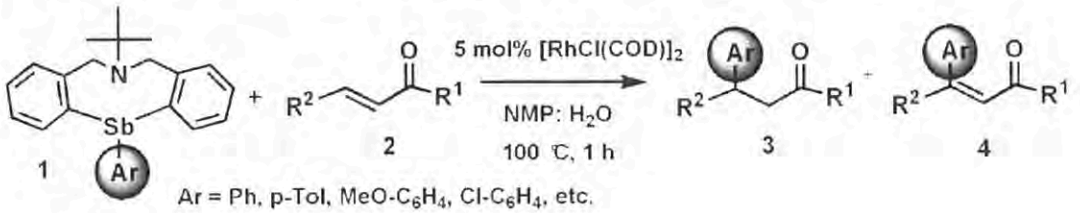
Recent development of the chemistry on main group elements has disclosed the versatile structures and reactivities of the compounds containing typical heavier elements. These properties are often unprecedented in conventional chemistry of lower elements such as carbon, nitrogen and oxygen. And they can be developed into a variety of practical synthetic methodologies.

Taking advantage of these characters of heavier elements, we have investigated utilization of organoantimony compounds as new organic synthetic reagent. One of our recent findings on 1,5-azastibocine (1) has revealed the presence of hypervalency of *Sb* atom and elongation of *Sb-C* bond by intramolecular *N-Sb* non-bonding interaction. Because of the *N-Sb* interaction, 1 was found to be excellent transmetallating agent. For example, Pd-catalyzed cross-couplings of 1,5-azastibocines with various organic halides proceeded quickly at room temperature under mild condition.[1,2] These results stimulated us to apply 1 to 1,4-conjugate addition to α,β-unsaturated carbonyl compounds.

First, suitable catalyst for the 1,4-conjugated addition was surveyed. Reaction of 1 and methyl vinyl ketone (2, H^1 = Me, H^2 = H) was conducted with various transition metal catalysts in aqueous dioxane. Palladium catalysts such as $Pd(OAc)_2$, $PdCl_2$, $PdCl_2(PPh_3)_2$ gave Heck-type adduct (4) in moderate yields as major product, whereas rhodium catalysts such as $[RhCl(cod)]_2$, $[Rh(OH)(cod)]_2$, $RhClO_4(nbd)$, $RhBF_4(cod)$ afforded the expected adduct (3) predominantly. The catalyst of choice was revealed to be $[RhCl(cod)]_2$ in terms of yield of 3 and the product selectivity. Under this catalyst, 3 was formed exclusively in 83 % yield.

Next, suitable solvent was screened. In dipolar aprotic solvents (DMF, TMU, NMP), the reaction completed more quickly than in etheral solvents (dioxane, THF, dimethoxyethane) and protic solvent (ethanol). In aqueous condition, 1,4-conjugated adduct (3) was formed selectively and the reaction in aqueous NMP completed efficiently (80 % yield) in short time (1 h). However, in dehydrated NMP, formation of Heck-type adduct (4) was observed in 9 % yield as well as 1,4-adduct (3) in 74 % yield. The reaction was applicable to a wide range of α, β-unsaturated ketones and esters. We also demonstrated that these α, β-unsaturated substrates underwent 1,4-conjugated addition with various *Sb*-aryl-1,5-azastibocines.

Under the same reaction condition, methyl vinyl ketone also underwent 1,4-conjugated addition with non-activated Ar_3Sb. However, the reaction required much longer time (24 h). The result indicated that non-bonding *N-Sb* interaction in 1 contributed to activation of aryl group on 1 and reduction of reaction time.



References:

1.Kakusawa, N; Tobiyasu, Y; Yasuike S; Yamaguchi K; Seki, H; Kurita, J. *Journal of Organomet. Chem.* 2006; 691, 2953-2968.

2. Kakusawa, N; Kurita, J. *Heterocycles* 2006; 68, 1335-1348.

SYNTHETIC APPLICATIONS OF CHIRAL 1,3-DIOXOLAN-4-ONES

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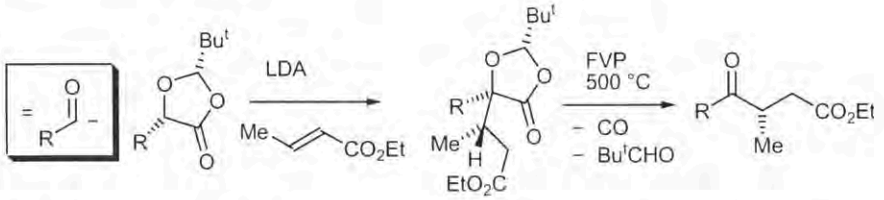
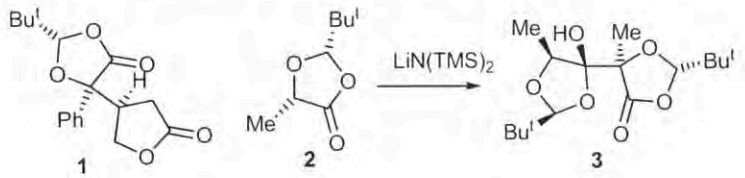
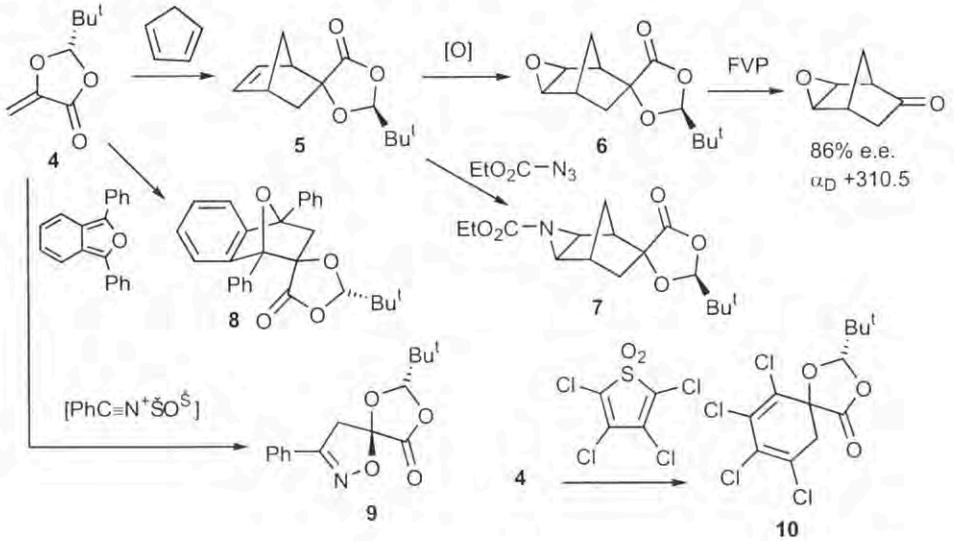
Some time ago we showed that chiral 1,3-dioxolan-4-ones derived from α-hydroxy acids such as mandelic or lactic acid could act as acyl anion equivalents by alkylation and then fragmentation under FVP conditions with loss of pivalaldehyde and CO.[1]



Later this was extended to a wider range of electrophiles including nitrostyrenes and butenolide which gave product 1.[2] When the lactic acid derived compound 2 is treated with base in the absence of an electrophile an unusual self-addition occurs to afford 3.



More recently we have prepared a number of chiral Diels Alder adducts from the methylene dioxolanone 4 which may act as a chiral ketene equivalent after pyrolytic fragmentation. A variety of cycloadducts have been formed as shown. Attempted pyrolytic fragmentation of 5 simply led to cycloreversion but this could be prevented by conversion to the epoxide 6 or aziridine 7. Pyrolysis of epoxide 6 then gave the chiral ketone in good e.e. The nitrile oxide adduct 9 appears to be the first 1,3-dipole adduct of 4 and the unusual tetrachloro compond 10 has also been obtained. The structures and absolute configurations of 7, 8 and 9, as well as 1 and 3 have all been confirmed by X-ray diffraction.



References:

1 Aitken, R.A., Thomas, A.W., *Synlett*, 1998; 102-104.

2 Aitken, R.A., McGill, S.D., Power, L.A., *Arkivoc*, 2006; vii, 292-300.

SYNTHESIS OF 4-FLUOROAZOLINONES

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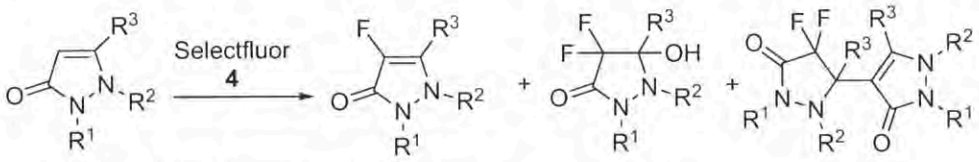
There is a strongly increasing interest in fluorine-containing biologically active compounds for potential application as pharmaceuticals and agrochemicals. This is due to the fact that introduction of fluorine into organic molecules often leads to improved biological activities of the parent compound. As represented by antipyrine, azolinones are potential scaffold for biologically active compounds. However, only scattering data are available for fluorination of pyrazolin-5-ones at the 4-position. Here we report electrophilic fluorination of pyrazolin-5-ones 1, isoxazolin-5-ones 2 and isoxazolin-3-ones 3 at the 4-position by Selectfluor 4.

1. Pyrazolin-3-ones

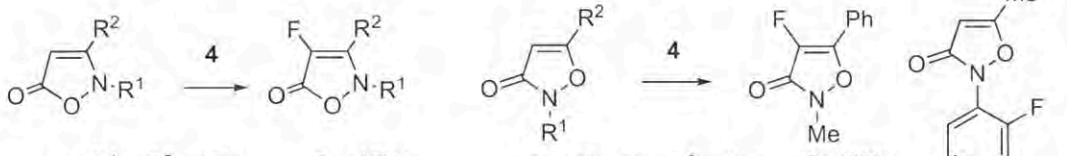
Treatment of pyrazolinones 1a~e with Selectfluor (4, 1 equiv.) in acetonitrile gave 4-fluoro derivative 5a~e together with 4,4-difluoro-5-hydloxy compounds 6a~e and dimeric compound 7a,b, respectively.



1a~e	R^1	R^2	R^3	5 (%)	6 (%)	7 (%)
a	Ph	Me	Me	13	19	15
b	Ph	Me	Ph	32	32	13
c	Ph	Ph	Me	24	32	-
d	Me	Me	Ph	9	32	-
e	Me	Me	Me	8	7	-

2. Isoxazolin-5-ones and isoxazolin-3-ones

Fluorination of isoxazolin-5-ones 2a,b with Selectfluor gave 4-fluoro compound 8a,b in good yields. Isoxazolin-3-ones 3 were less reactive than 2; on treatment with Selectfluor, 3a gave 4-fluoro compound 9a in low yield and 5-methyl-2-phenylisoxazolin-3-one 3b afforded not 4-fluoro compound but 2-(2-fluorophenyl) compound 10 in 39% yield.



2a (R^1 = R^2 = Me) **8a** (46%)
2b (R^1 = Me, R^2 = Ph) **8b** (72%)

3a (R^1 = Me, R^2 = Ph) **9a** (30%)
3b (R^1 = Ph, R^2 = Me)

10 (39%)

3. Discussion

The results indicate pyrazolinones are the most reactive and isoxazolin-3-one are the least reactive in the electrophilic fluorination at the 4-position. The relative reactivity is rationalized by electromeric effect in the β-heteroatom-substituted enone system involved in the heterocycles. Nitrogen is more electron donating than oxygen leading to the reactivity order of 1 > 2 > 3 at the 4-position. Correlation of HOMO energy level with the observed reactivity of these azolinones is also discussed.

SUBSTITUENT EFFECTS IN THE STEREOSELECTIVITY OF THE PETASIS REACTION

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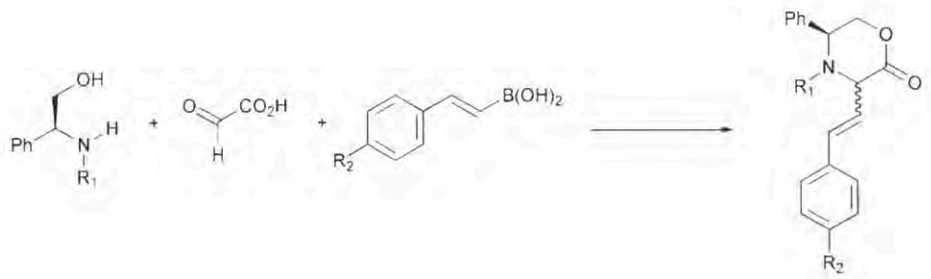
The Petasis reaction, or boronic acid Mannich reaction, involves the three-component coupling of an amine, aldehyde and organoboronic acid, and has developed over the last few years into a powerful synthetic tool.[1] One of the most important uses of the Petasis reaction is the synthesis of α-amino acids using glyoxylic acid as the aldehyde component. A wide range of aryl- and vinyl-boronic acids have been employed in such reactions, allowing the production of a wide variety of arylglycine and vinylglycine derivatives.[2,3] The use of chiral amines enables the stereoselective production of α-amino acid derivatives.

We have observed that the nature of the substituents on the amine and styrenylboronic acid components has a drastic effect on the stereoselectivity of the Petasis reaction. Our results and their interpretation in terms of the reaction mechanism will be discussed.



References:
1 Southwood TJ, Curry MC, Hutton CA. *Tetrahedron*, 2006; 62, 236-242.
2 Petasis NA, Zavialov IA. *J. Am. Chem. Soc.*, 1997; 119, 445-446.
3 Petasis NA, Goodman A, Zavialov IA. *Tetrahedron*, 1997; 53, 16463-16470.

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MP01

SYNTHESIS OF ZANTHOXYLINE AND RELATED COMPOUNDS

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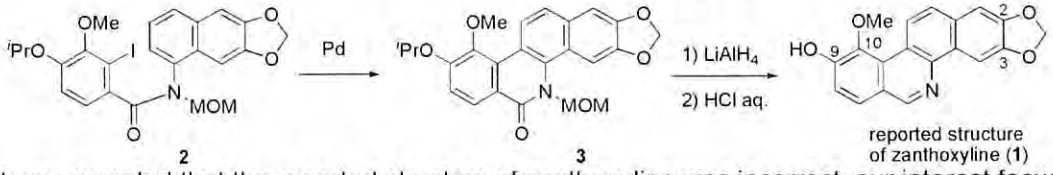
Zanthoxyline (1) is a benzo[*c*]phenanthridine alkaloid that was isolated from *Zanthoxylum rhoifolium* in 1997, which possesses four oxygen functional groups at the 2, 3, 9, and 10 positions.[1] This substituent pattern is a very rare case in the class of natural benzo[*c*]phenanthridines. In order to investigate the detailed biosynthetic pathway of this material, we suggested that its chemical synthesis was necessary.

We have studied the palladium-mediated intramolecular biaryl coupling reaction of benzanilide derivatives, and this technique has been used for the total synthesis of various types of natural benzo[*c*]phenanthridine alkaloids.[2] Thus, we envisioned that the same strategy could also be useful for the synthesis of 1.

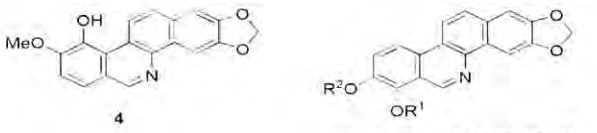
Our approach involves the intramolecular biaryl coupling reaction as the key reaction of benzonaphthamide 2 which could be prepared from the corresponding benzoic acid and naphthylamine through a simple condensation. After the pentacyclic compound 3 was successfully prepared, reduction with $LiAlH_4$ and concomitant treatment with aqueous HCl afforded the objective compound 1. Surprisingly, the spectral data of the synthetic 1 did not resemble the reported ones.



2 3 reported structure of zanthoxyline (**1**)

Since it was revealed that the reported structure of zanthoxyline was incorrect, our interest focused on the determination of the correct structure of the compound. We considered that compound 4 would be plausible, which has almost the same structure as the reported zanthoxyline except for the substituent groups at the 9 and 10 positions. Thus, we similarly synthesized compound 4 by through the intramolecular biaryl coupling reaction. However, the spectral data of the synthetic product was again not identical to the reported ones.

We also prepared decarine (5) and isodecarine (6). The comparison of these data will be presented, and the correct structure of the reported zanthoxyline will also be discussed.



4

decarine (**5**): R^1= Me; R^2= H
isodecarine (**6**): R^1= H; R^2= Me

References:
[1] Moura NF., Ribeiro HB., Machado ECS., Ethur EM., Zanatta N., Morel AF. *Phytochemistry*, 1997; 46, 1443-1446.
[2] Harayama T. *Heterocycles*, 2005; 65, 697-713; and references cited therein.

MP02

SYNTHESIS, PHOTOPHYSICAL AND ELECTROCHEMICAL PROPERTIES OF NOVEL CONJUGATED DONOR-ACCEPTOR MOLECULES BASED ON PHENOTHIAZINE AND BENZIMIDAZOLE

Xiao-Hang Zhang, Seonho Kim, Suh Jin Lee, Han-Ill Lee, In Su Lee, Sung Ik Yang,* Kwang-Hyun Ahn*

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Two series of new organic fluorophores, asymmetrical 3-(benzimidazol-2-yl)-10-hexyl-10H-phenothiazine and symmetrical 3,7-bis(benzimidazol-2-yl)-10-hexyl-10H-phenothiazine as well as their derivatives with variable substituents at the 1 position of benzimidazole subunit have been synthesized. Electronic absorption and electrochemistry measurements reveal that the five-membered heteroaromatic rings directly bonded to the phenothiazine facilitate maximal coplanarity across the whole molecules which were also verified by the optimized molecular geometry. On the other hand, the photoluminescence spectra indicate the emission is resulted from charge-transfer excited state. Various substituents to the acceptor moieties can allow a fine-tuning of the LUMO levels of the molecules without significantly affecting the HOMO energy levels. The method provides a new route for designing ambipolar molecules whose energy levels are well-matched with the Fermi levels of the electrodes to facilitate the electron or hole injection/transfer in OLED devices.

MP03

SYNTHETIC APPLICATIONS OF A CHIRAL 5-METHYLENE-1,3-DIOXOLAN-4-ONE

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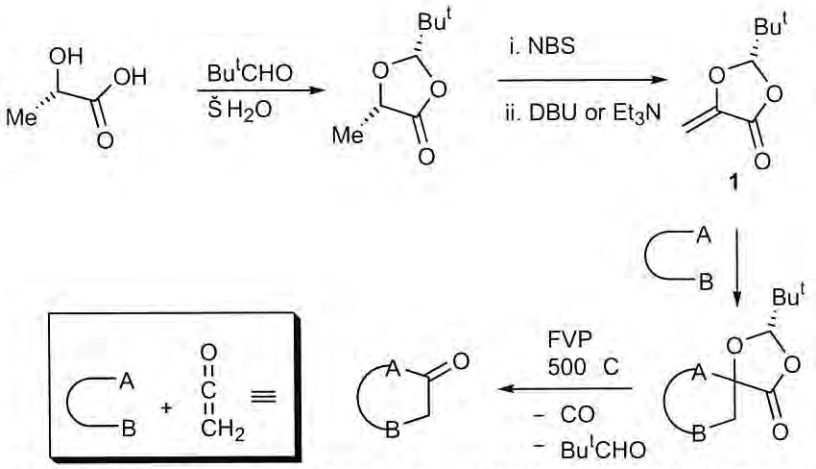
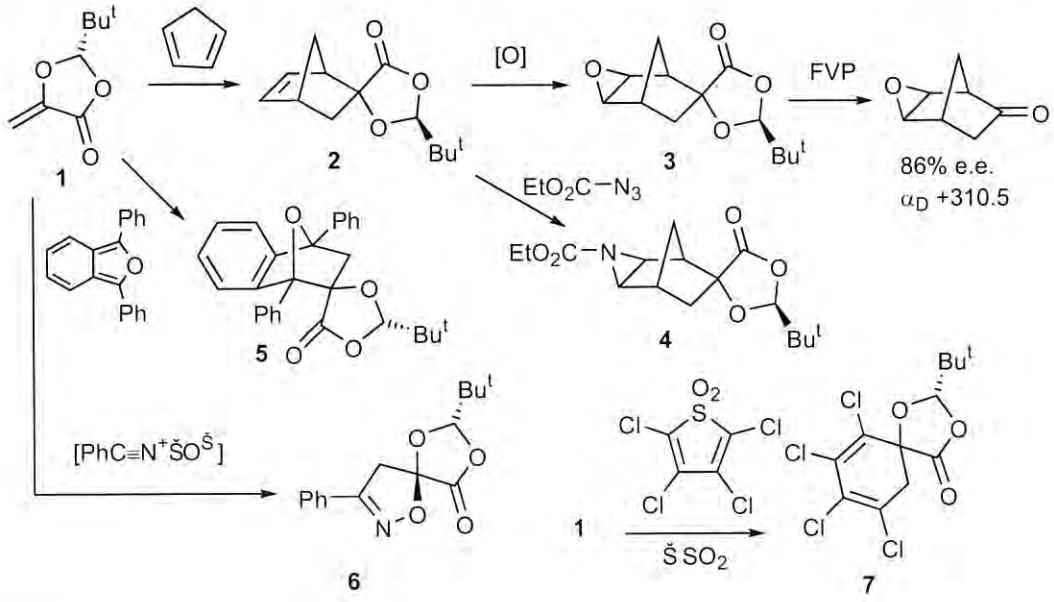
The methylenedioxolanone 1 is readily prepared as shown from *S*-lactic acid and contains a reactive double bond susceptible to cycloaddition reactions. We have examined in detail various Diels Alder, and more recently 1,3-dipolar, cycloadditions. Since the adducts may decompose thermally under FVP conditions with loss of Bu^tCHO and CO, this makes 1 a chiral ketene equivalent.[1]



A variety of cycloadducts have been formed as shown. Attempted pyrolytic fragmentation of 2 simply led to cycloreversion but this could be prevented by conversion to the epoxide 3 or aziridine 4. Pyrolysis of epoxide 3 then gave the chiral ketone in good e.e. The nitrile oxide adduct 6 appears to be the first 1,3-dipole adduct of 1 and the unusual tetrachloro compond 7 has also been obtained. The structures and absolute configurations of 4, 5 and 6 have been confirmed by X-ray diffraction.



References:

1 Aitken, R.A., McGill, S.D., Power, L.A., *Arkivoc*, 2006; vii, 292-300.

MP04

NEW RADICAL CYCLISATION APPROACHES TO FUSED-RING INDOLES AND QUINOLINES

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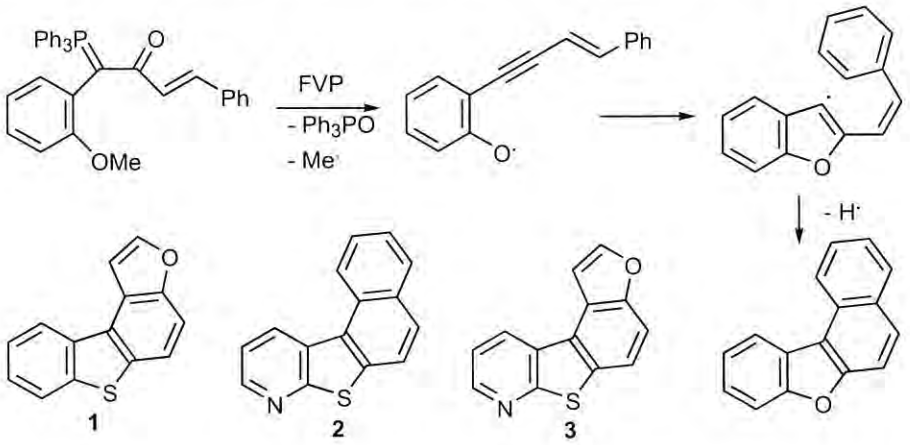
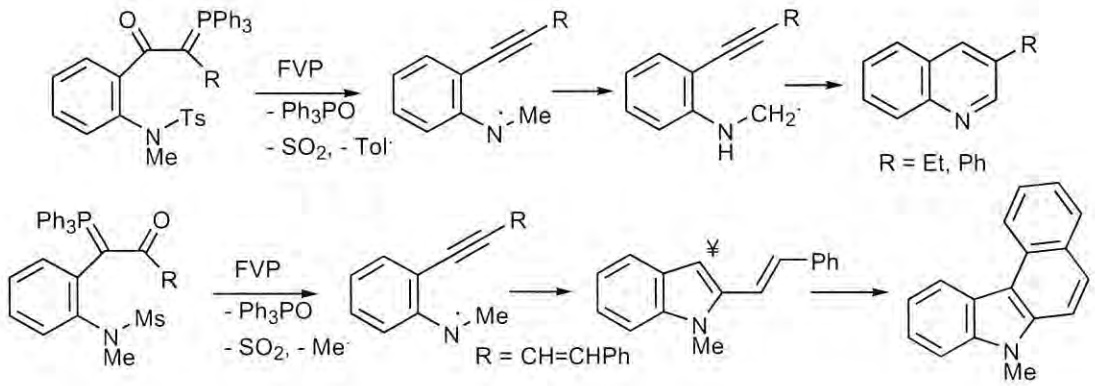
Some time ago we described tandem cyclisation resulting in formation of benzonaphthofurans when stabilised phosphorus ylides bearing an ortho methoxy group were subjected to flash vacuum pyrolysis.[1] As shown below this involves, formation of an alkyne, cyclisation of a phenoxy radical and subsequent cyclisation of the resulting benzofuryl radical. Later the scope of this approach was extended greatly to include (i) methylthio as well as methoxy groups leading to ring-fused thiophenes, (ii) heterocyclic starting components leading to products such as **1-3**, (iii) inclusion of substituents at various positions and (iv) use of naphthyl ylides leading to pentacyclic products.[2]



In more recent work, we have started to examine ylides with an ortho nitrogen function as a route to indoles. Preliminary results have shown that in some cases the desired indole and indeed benzo[*c*]carbazole formation occurs but in others an unexpected cyclisation leads to 3-substituted quinolines as shown.



References:

1 Aitken, R.A., Burns, G., Morrison, J.J., *J. Chem. Soc., Perkin Trans. 1*, 1998; 3937-3941.

2. Garnett, A.N., PhD Thesis, University of St Andrews, 2000.

MP05

NEW APPROACHES TO THE ELUSIVE 1,4-OXAZINES

Kati M. Aitken and R. Alan Aitken*

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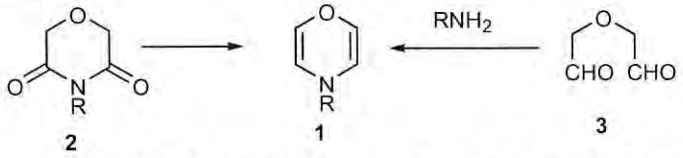
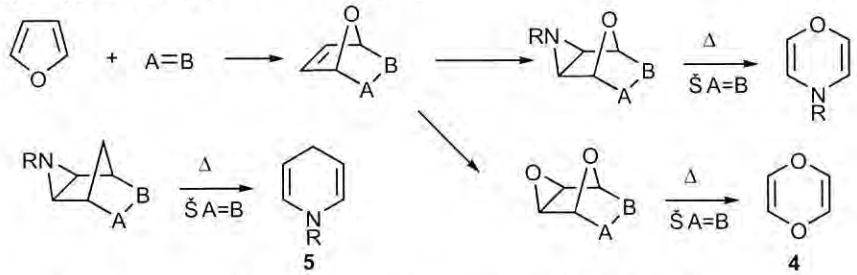
There are currently few routes to simple monocyclic 1,4-oxazines 1 and the parent compound (R = H) remains unknown.[1] Routes involving deoxygenation of the oxazinediones 2, analogous to the successful preparative route for 1,4-thiazine, were unsuccessful,[2] as were some approaches based on the oxydialdehyde 3.



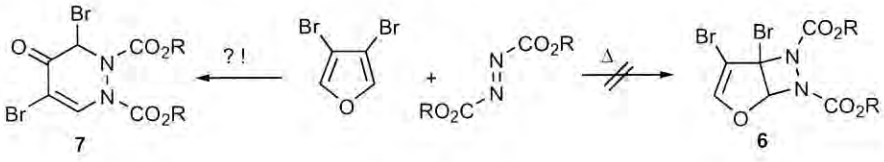
2 1 3

The new Diels Alder - retro Diels Alder approach shown below is inspired by our preparation of 1,4-dioxin 4 where A=B was maleic anhydride,[3] but also follows the much earlier work of Meyers on synthesis of dihydropyridines 5 where A=B was N_2.[4]

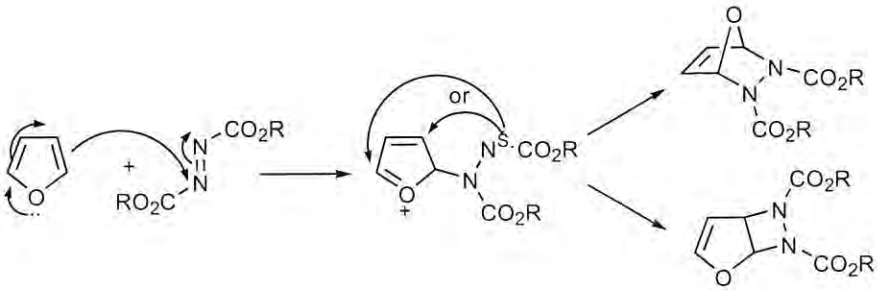


5 4

The latest results will be presented including the interesting finding that azo diesters, which might be expected to react with furans to give either the apparent [2+2] adducts (e.g. 6) or the [4+2] adducts, actually give the most unexpected tetrahydropyridazinone 7 (!). How this relates to the [2+2] adduct formation which has only been reported in an isolated case before,[5] or to the [4+2] process will be discussed.



7 6



References:

1 Aitken, K.M., Aitken, R.A., *Comp. Heterocycl. Chem. III*, 2008; Vol. 7, Chapter 6, in press.
2 Aitken, R.A., Farrell, D.M.M., Kirton, E.H.M., *Khim. Geterotsikl. Soedin.*, 2001; 1678-1683.
3 Aitken, R.A., Cadogan, J.I.G., Gosney, I., *J. Chem. Soc., Perkin Trans. 1*, 1994; 927-931.
4 Stout, D.M., Takaya, T., Meyers, A.I., *J. Org. Chem.*, 1975; 40, 563-569.
5 Zefirov, N.S., Dudinov, A.A., *Zh. Org. Khim.*, 1967; 3, 411.

MP07

THE ACIDITIES OF SOME 1-SUBSTITUTED-1*H*-BENZOTRIAZOLE DERIVATIVES

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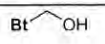
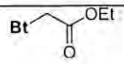
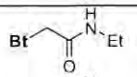
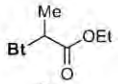
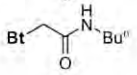
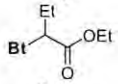
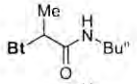
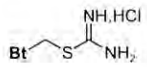
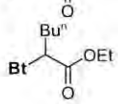
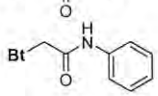
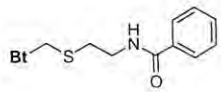
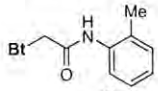
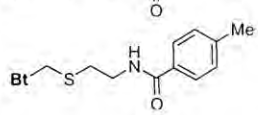
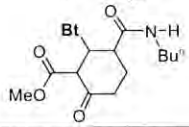
In this study, we present an experimental and theoretical study for the estimation of pK_a values of some 1-substituted-1*H*-benzotriazole derivatives in aqueous solution by spect-roscopic, semi empirical and ab initio methods. The following 1*H*-benzotriazole derivatives were prepared according to the methods in the literature [1-8]. The experimental pK_a values of benzotriazole derivatives, examined, were measured by UV spectroscopic method. The theoretical pK_a values of benzotriazole derivatives have been calculated in aqueous solution (ε=78.4) by means of semi empirical and ab initio methods.

Table 1

Compounds					
1		7		11	
2		8		12	
3		9		13	
4		10		14	
5				15	
6				16	

References:

[1] Liu, Qing-Xiang; Xu, Feng-Bo; Li, Qing-Shan; Zeng, Xian-Shun; Leng, Xue-Bing; Zhang, Zheng-Zhi. *Chinese Journal of Chemistry*, 2002, 20(9), 878-883.
[2] Gaylord, N.G.; Kay, D. J., *Journal of Organic Chemistry*, 1958, 23 1574-5.
[3] Su, Weike; Yang, Bibo; Li, Yongshu, *Journal of Chemical Research, Synopses,* 2002, 11, 542-543.
[4] Katritzky, Alan R.; Serdyuk, Larisa; Xie, Linghong., *Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry,* 1998, 6, 1059-1064.
[5] Katritzky, Alan R.; Wu, Jing., *Synthesis*, 1994, 6, 597-600.
[6] Zhang, Xin-Ming; Xie, Xiao-juan; Tao, Gui-de; Tong, Xiao-tian, *Anhui Shifan Daxue Xuebao, Ziran Kexueban*, 2001, 24(2),136-7, CAN: 136:279397.
[7] Katritzky, Alan R.; Ghiviriga, I; Oniciu, D. C.; Soti, F., *Journal. of Heterocyclic Chemistry,* 1996, 33(6), 1927-34.
[8] Sparatore, F.; La Rotonda, M. I.; Caliendo, G.; Novellino, E.; Silipo, C.; Vittoria, A., *Farmaco, Edizione Scientifica* 1988, 43(1), 29-47.

MP08

AN ACYL-CLAISEN APPROACH TO THE COMPLEX TETRAHYDROFURAN LIGNAN MANASSANTIN B – A POTENT HIF-1 INHIBITOR

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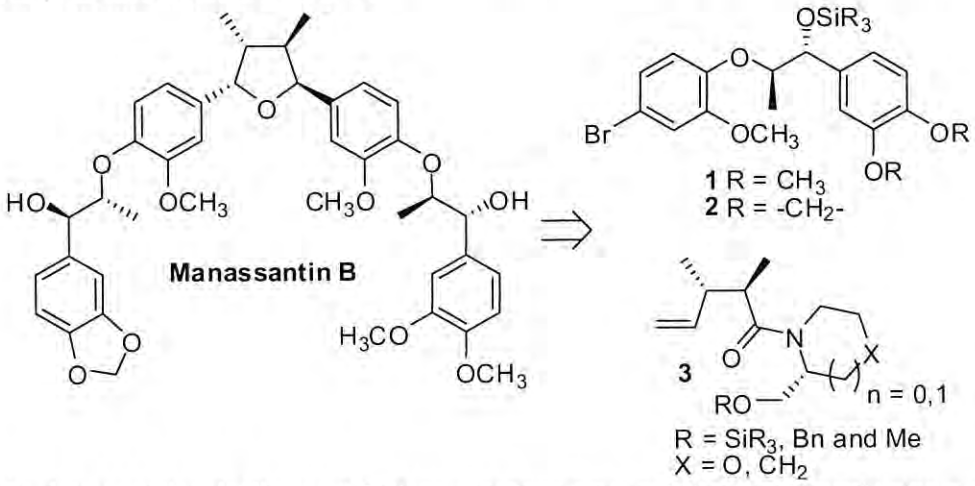
Department of Chemistry, University of Auckland,

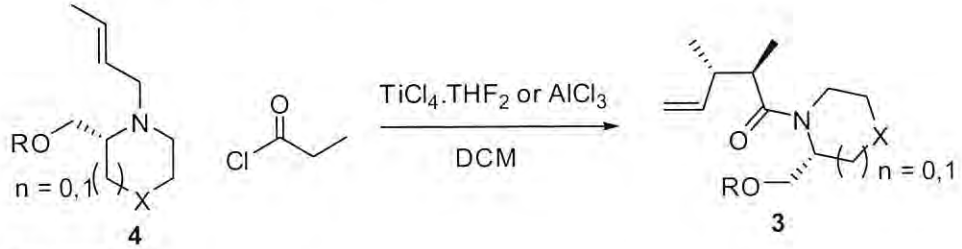
23 Symonds St, Auckland, New Zealand

Manassantin B is a complex tetrahydrofuran dineolignan, isolated in minute amounts from *Saururus chinensis*, a herb used safely for hundreds of years throughout China and Korea in folk medicine to treat diseases such as oedema, jaundice and inflammation.[1] Manassantin B has recently been found to selectively inhibit hypoxic activation of HIF-1 (IC_{50} = 3 nM), making it one of the most potent inhibitors of HIF-1 activation known,[2] but unlike other potent HIF-1 inhibitors manassantin B is not highly cytotoxic and acts by a currently unknown mechanism.[2] Manassantin B has also been shown to inhibit other transcription factors related to tumour survival.[3]

Our highly convergent synthetic strategy to Manassantib B ulitizes the addition of the diaryl bromide 1 and 2 to amide 3. The chirality of this amide is achieved by using an acyl-Claisen rearrangement of crotyl-substituted heterocycle 3.



To date enantioselective acyl-Claisen reactions have only been achieved using a combination of α-oxygenated acid chlorides and chiral Lewis acids.[4] We have been attempting to further develop this reaction to allow the use of any acid chloride by incorporating chiral piperidines and morpholines 4. Our synthetic studies towards the synthesis of Manassantin B and other dineolignans utilizing this methodology will be presented.



References:
1. Rao KV, Alvarez FM. *Tetrahedron Lett.*, 1983; 24, 4947-4950.
2. Hodges TW, Hossain CF, Kim Y, Zhou Y, Nagle DG. *J. Nat. Prod.* 2004; 67, 767-771.
3. Hwang BY, Lee J, Nam JB, Hong Y, Lee JJ. *Phytochemistry*, 2003; 64, 765-771.
4. Yoon TP, MacMillan DWC. *J. Am. Chem. Soc.* 2001; 123, 2911-2912.

MP09

SYNTHESIS OF 1,4-BENZOQUINONYL SUBSTITUTED TETRATHIAFULVALENES

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Department of Chemistry, Riga Technical University, Azenes St. 14/24, LV-1048, Latvia
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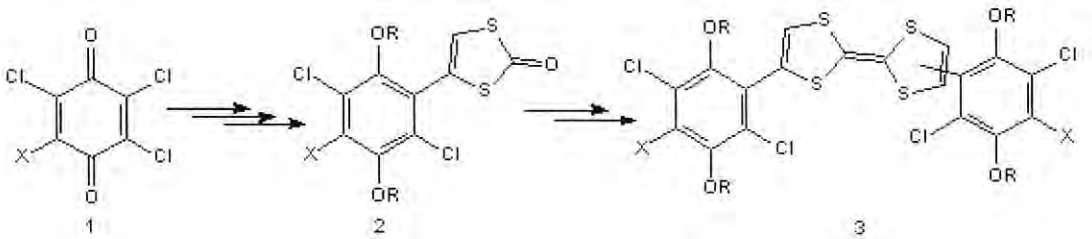
Great interest in the chemistry of benzoquinones is created by their high reactivity and very wide range of their practical application. Quinonoid compounds are used as electron accepting components in the synthesis of charge transfer complexes and ion radical salts aiming to prepare materials for molecular electronics. Our interest in quinone chemistry led us to develop methodologies for the synthesis of mono- and bisheteroarylsubstituted benzoquinones (1 - 4). Although tetrathiafulvalene (TTF) and its derivatives have been extensively studied for more than 30 years as π-electron donors in intermolecular charge-transfer materials, the intriguing potential of TTF as a donor in an intramolecular sense has only recently been developed. We have elaborated a method that would allow access to donor-acceptor dyads in which the donor (TTF) and acceptor (benzoquinone) fragments connected *via* C-C bond. The heteroarylsubstituted hydroquinone derivatives **2** were prepared according to the protocol summarized in (3, 4). Donor-acceptor dyads, acceptor-donor-acceptor triads and extended TTF derivatives can be received on the basis of **2**. Different protection (R = Me, Ac, Bn) of hydroxyl groups was examined. The synthesis of TTF derivatives **3** proceed upon treatment of 2-oxo-1,3-dithiole derivatives **2** with triethyl phosphite (under heating or MW-irradiation) in toluene or solvent-free conditions. The following removal of a protective groups and oxidation will be discussed.



X= Cl or hetaryl
R = H, Me, Ac, Bn

References:
(1) Valters R., Karlivans G., Gulbis J., Utinans, M., Bace A. *Phosphorus, Sulfur, and Silicon*, 1994, 95-96, 457-461.
(2) Batenko N. G., Karlivans G. A., Valters R. E. *Chem. Heterocycl. Comp.*, 2005, 41, 691-717.
(3) (3)Karlivan G. A., Valter, R. E., Gulbis, Yu. V. *Chem. Heterocycl. Comp.*, 1998, 34, 907-911.
(4) Batenko N. G., Karlivans G. A., Valters R. E. *Heterocycles*, 2005, 65, 1569-1576.

European Social Fund is gratefully acknowledged for financial support.

MP10

SYNTHESIS OF TETRAMIC ACID ANALOGUES AS POTENTIAL HIV-INTEGRASE INHIBITORS

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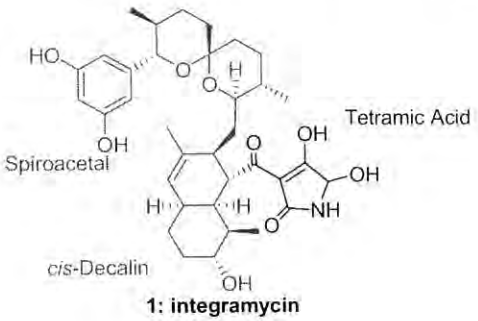
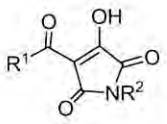
[a] *School of Chemistry, University of Sydney, Sydney, NSW, 2006, Australia.*
[b] *Eskitis Institute for Cell and Molecular Therapies, Griffith University, Brisbane, QLD, 4111 Australia.*

The Human Immunodeficiency Virus (HIV) has become a major global health concern. With over 40 million people infected and the continual emergence of resistant strains of the virus, there is a pressing need for new HIV treatments. [1] Integramycin (**1**) is a potent inhibitor of HIV-integrase and a promising lead for the development of novel anti-HIV drugs. [2] Little is known about the mode of action of integramycin, and hence we aim to systematically investigate the structural requirements for the anti-integrase activity of this complex natural product.



1: integramycin



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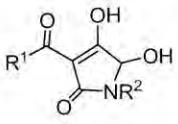

3

Current work towards the tetramic acid segment of **1** has centred on the synthesis of a number of maleimide derivatives of the general form **2**, from the coupling and subsequent cyclisation of β-oxocarbamides with oxalyl chloride. Regioselective reduction of the maleimide derivatives yields the corresponding tetramic acids **3**. [3] Careful selection of R groups will allow control of pharmacokinetic properties and lead to the collection of preliminary SAR data for this class of compounds. This in turn will aid in the rational design of new potential therapeutic agents.

References:
[1] UNAIDS/WHO AIDS 2004 Report on the Global AIDS Epidemic.
http://www.unaids.org/bangkok2004/report.html
[2] Singh, S. B.; Zink, D. L.; Heimbach, B.; Glenilloud, O.; Teran, A.; Silverman, K.; Lingham, R.; Felock, P.; Hazuda, D. *Org. Lett.* 2002, *4*, 1123-1126.
[3] Issa, F.; Fischer, J.; Turner, P.; Coster, M. J. *J. Org. Chem.* 2006, *71*, 4703-4705.

MP12

SYNTHESIS OF NEW HETEROPOLYFLUORENES

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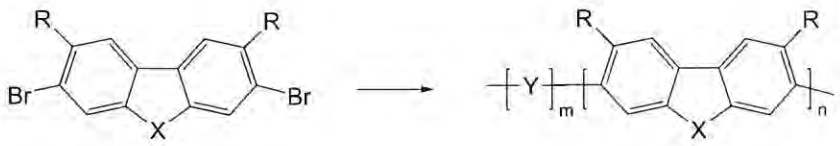
[a]*Departamento de Engenharia Quimica e Biológica, Centro de Química Estrutural, Instituto Superior Técnico, Avenida Rovisco Pais, P-1049-001 Lisboa, Portugal.*
[b]*Makromolekulare Chemie and Institut für Polymertechnologie, Bergische Universität Wuppertal, Gauss-Str. 20, D-42097 Wuppertal, Germany.*

Heteropolyfluorenes (HPFs) 1 have emerged as a new class of polymers for commercial applications. Some examples regarding their potencial as conjugated polymers for optical and electronic devices have been recently investigated.[1,2] In HPFs, the substituition of the sp^3 hybridized carbons at position 9 of fluorene by other atoms can result in particular interactions between the heteroatom and the π-conjugated polyphenylene-like framework. Starting from 2,7-dibromo-9-heterofluorenes 2 new structures of functional conjugated polymeric materials based on HPFs are reported.



2 **1**

X= B-Ar, Si-R_2 ...
Y= fluorenes ...

References:

1. Chan KL., McKiernan M., Towns C., Holmes AB. *J. Am. Chem. Soc.* 2005; 127, 7662-7663. 2. Chen RF., Fan QL., Zheng C., Huang W. *Org. Lett.* 2006; 8, 203-205.

MP13

NEW APPROACHES TO THE FORMATION OF CHIRAL HETEROCYCLIC CARBONATES BY ENANTIOSPECIFIC ADDITION OF CARBON DIOXIDE TO EPOXIDES

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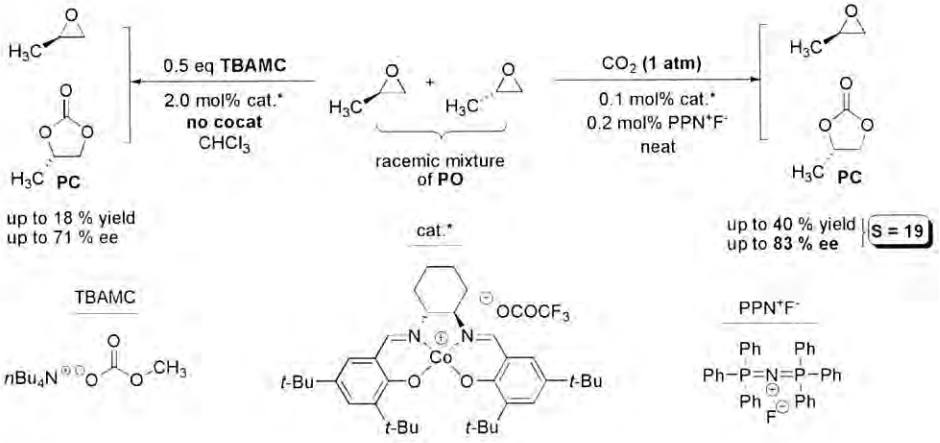
phone: 0221/470 3293

Keywords: epoxides, cyclic carbonates, carbon dioxide, asymmetric catalysis, kinetic resolution

The kinetic resolution of racemic epoxides, especially of propylene oxide (PO), with carbon dioxide as the reagent represents an attractive method because it provides on the one hand enantiopure epoxide and on the other hand synthetically useful optically active heterocyclic carbonate.[1] The latter are valuable building blocks for polymeric materials such as polycarbonates, masked 1,2-diols, and pharmaceutical/fine chemicals.[2]
In this context, new and improved binary catalyst systems were developed to generate cyclic carbonates, especially propylene carbonate (PC), already at atmospheric CO_2-pressure. Unprecedented selectivity for this reaction was achieved with a Co^{III}(salen)-trifluoracetyl complex as catalyst and bis(triphenyl-phosphoranylidene) ammonium halides (PPN^+X^-) as cocatalyst, affording e.g. propylene carbonate in 40 % yield and 83 % ee
(selectivity factor = 19).[3]



In addition, propylene carbonate was prepared for the first time by kinetic resolution of PO using 0.5 eq of tetrabutylammonium methyl carbonate (TBAMC) as CO_2-source. With TBAMC as "activated CO_2", enantioselectivities up to 71 % ee were obtained.
The remaining enantiopure epoxides are themselves a particularly important class of chiral heterocyclic intermediates because of their versatile reactivity.[4]

References:

[1] Lu, X.-B.; Liang, B.; Zhang, Y.-J.; Tian, Y.-Z.; Wang, Y.-M.; Bai, C.-X.; Wang, H.; Zhang, R. *J. Am. Chem. Soc.* 2004, *126*, 3732-3733.
[2] Shaikh, A. A. G.; Sivaram, S. *Chem. Rev.* 1996, *96*, 951.
[3] Berkessel, A.; Brandenburg, M. *Org. Lett.* 2006, *8*, 4401.
[4] Besse, P.; Veschambre, H. *Tetrahedron* 1994, *50*, 8885.

MP14

PREPARATION OF ORGANIC-INORGANIC MATERIALS FOR PHOTOINDUCED ELECTRON-TRANSFER

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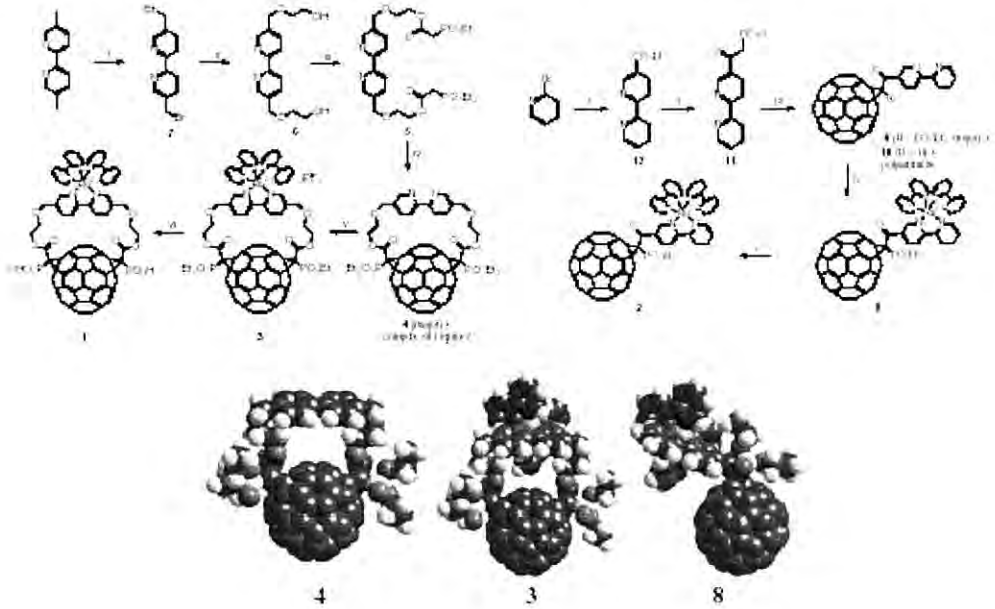
The conversion of solar light into useful chemical energy is a goal that in principle may artificially be achieved by the rational design of the appropriate arrangement of components in the solid state. Nevertheless, even though the preparation of solid structures is more and more in the side of designing
and predictive principles conceptually similar to those used in solution chemistry,1 we are still far from this accomplishment. However, the use of layered inorganic salts in which organic structures (i.e. electron-donor and acceptor systems) can be orderly deposited either by weak interactions or covalent
bonds, a widespread technique to prepare tailored solids with coveted properties,2 may be applied to approaching this end. Our recent work in the chemistry of metal phosphonates thus prompted us to prepare, and hereby describe, the dyad systems **1** and **2** (Figure 1),3 with the aim that their PO3 groups
could be appropriate anchoring points to the suitable inorganic matrix. In this way the charge-transfer process would probably benefit of a polar, solid and rigid environment, conditions that seem to be paramount in the achievement of long-lived charge-separated states.



References
1 Dey, A.; Kirchner, M. T.; Vangala, V. R.; Desiraju, G. R.; Mondal, R.; Howard, J. A. K. *J. Am. Chem. Soc.* **2005**, *127*, 10545.
2 Brunet, E.; Huelva, M.; Vázquez, R.; Juanes, O.; Rodríguez-Ubis, J.C. *Chem. Eur. J.* **1996**, *12*, 1578. Brunet, E.; de la Mata, M. J.; Juanes, O.; Rodriguez-Ubis, J. C. *Chem. Mater.* **2004**, *16*, 1517. Brunet, E.; de la Mata, M. J.; Juanes, O.; Rodriguez-Ubis, J. C *Angew. Chem., Int. Ed.* **2004**, *43*, 619-621. Brunet, E. *Chirality* **2002**, *14*, 135. Brunet, E.; Alhendawi H. M. H.; Cerro C., de la Mata M. J., Juanes O., Rodríguez-Ubis J. C. *Angew. Chem. Int. Ed.* **2006**, *45*, 6918. Brunet, E.; Alonso, M.; de la Mata, M. J.; Fernandez, S.; Juanes, O.; Chavanes, O.; Rodriguez-Ubis, J. C. *Chem. Mater.* **2003**, *15*, 1232.
3 For recent examples of dyad systems see: Clifford, J.N.; Accorsi, G.; Cardinali, F.; Nierengarten, J-F.; Armaroli, N.; *C.R.Chimie*, **2006**, *9*, 1005. Zhou, Z.; Sarova, G.H.; Zhang, S.; Ou, Z.; Tat, F.T.; Kadish, K.M.; Echegoyen, L.; Guldi, D.M.; Schuster, D.I.; Wilson, S.R. *Chem. Eur. J.* **2006**, *12*, 4241.

MP15
SYNTHETIC STUDIES TOWARDS THE CDE-RING OF PECTENOTOXIN-2

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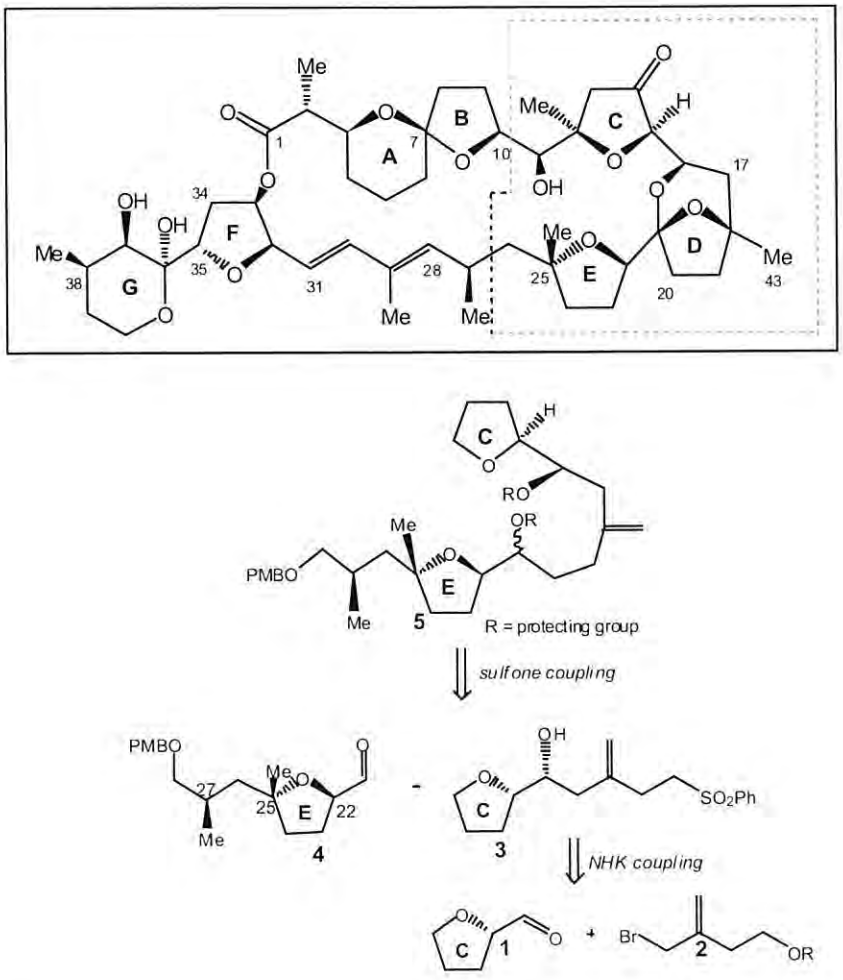
The pectenotoxins (PTX) are a family of 12 marine natural products comprising a 40-carbon macrolide ring containing a spiroacetal, three substituted tetrahydrofurans and 19 (or 20 for PTX11) stereocentres.[1] PTX2 is the most potent member of the PTX family – exhibiting activity against human lung, colon and breast cancer cell lines with LC_{50}'s in the nanomolar range.[2] We report our synthetic studies towards the CDE fragment of PTX2. The construction of the E ring relied on the use of a chiral pool reagent for the establishment of the C-27 stereocentre. The stereocentre at C-25 was constructed using a stereocontrolled Grignard reaction whilst the *trans* fused tetrahydrofuran E ring was formed by the iodoetherification of a terminal olefin. Coupling of the model C ring 3 and E ring 4 fragments was accomplished using a sulfone alkylation. The CD ring fragment 3 was made by a Felkin Ahn controlled Nozaki-Hiyama-Kishi (NHK) -type coupling of allylic bromide 2 to the model C-ring aldehyde 1.



References:

1. Sasaki K, Wright JLC, Yasumoto T. *J. Org. Chem*, 1998; 63, 2475-2480.
2. Jung LH, Sim CJ, Lee CO. *Journal of Natural Products*, 1995; 58, 1722-1726.

MP16

UNDERSTANDING THE CONFORMATIONAL BEHAVIOUR OF 1,1'-BIS(1,2,3,4-TETRAHYDROISOQUINOLINE) DERIVATIVES IN RESPONSE TO CHANGES IN PH

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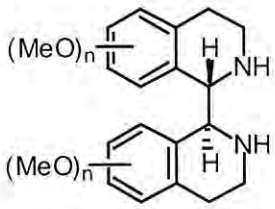
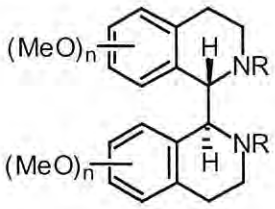
Secondary and tertiary alkylamine bisisoquinoline derivatives, *eg* **1** and **2** respectively, exhibit free rotation about their central C1-C1' bridging bonds but they do have preferred conformations in which they exist at ambient temperature in the solid and solution states. The secondary and tertiary amine classes appear to respond differently in the way they modify their preferred conformations to changes in the pH of the medium. This behaviour has importance in applications of the molecules as cooperative binding ligands.



1



2 (R = alkyl)

Evidence will be provided to show that both groups undergo sequential monoprotonation and then diprotonation, which drives the conformational changes, but that secondary amine derivatives participate in strong internal hydrogen bonding situations that yield a relatively stable bridged species of well defined stereochemistry, reminiscent of covalent, methylene bridged derivatives. Changes in the conformation of the nitrogen heterocyclic rings have also been inferred.

MP17

TOWARDS CATCH AND RELEASE 1,1'-BISISOQUINOLINE DERIVATIVES

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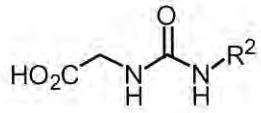
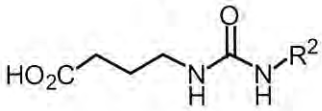
A new class of ureidyl bis-tetrahydroisoquinoline derivatives 1 has been designed and synthesised as potential catch and release agents for organic synthesis. The system is modelled on an analogous dendrimer-bound ureidylamine group of compounds developed by Meijer,[1,2] but is unique in having an ethylenediamine core as part of a bis-tetrahydroisoquinoline template that exhibits conformational mobility. The preferred ground state structures of analogues with various N-alkyl tether lengths, thio- or oxo-urea groups, and distal N-aryl or N-adamantyl substituents were determined and the binding of representative examples with ureidyl acids 2 and 3 was assessed. Optimal binding (catch) appears to take place when R^1 = adamantyl and R^2 = phenyl. There was no advantage in the use of thiourea derivatives in the isoquinoline partner and the tether lengths of both bis-isoquinoline and the ureidyl acid partners were not critical. Evidence will be presented that suggests the association between ureidyl amines and ureidyl acids is reasonably tolerant of the methylene linker chain length and can be influenced by changes in neutral organic solvents (release).

1

R^1 = aryl, adamantyl
X = O, S
n = 1 – 4



2



3

R^2 = Ph, adamantyl

References:

1. D. d. Groot, B. F. M. d. Waal, J. N. H. Reek, A. P. H. J. Schenning, P. C. J. Kamer, E. W. Meijer and P. W. N. M. v. Leeuwen, *J. Am. Chem. Soc.*, 2001, *123*, 8453-8458.
2. R. Chen, R. P. J. Bronger, P. C. J. Kamer, P. W. N. M. Leeuwen and J. N. H. Reek, *J. Am. Chem. Soc.*, 2004, *126*, 14557-14566.

MP19

EXPLORATION OF THE PETASIS REACTION TO GENERATE HIGHLY FUNCTIONALISED AMINO ACIDS

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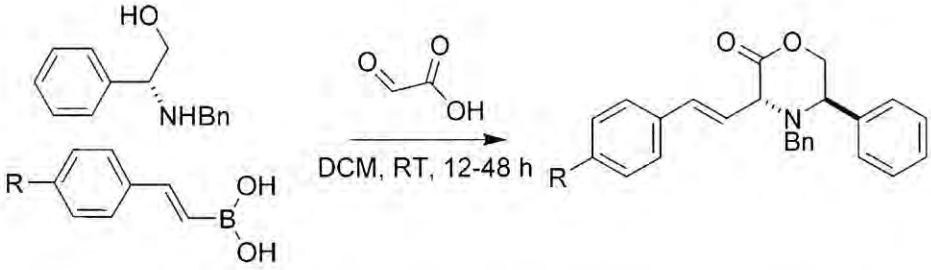
School of Chemistry, Bio21 Molecular Science and Biotechnology Institute, University of Melbourne, Australia



Highly functionalised biologically active cyclic peptides are increasingly being used as therapeutic agents. Vancomycin and cyclosporin have been in clinical use for several decades, while more recently semi-synthetic analogues of the echinocandin class of cyclic peptides have been approved for use as anti-fungal agents.

Synthetic or semi-synthetic preparation of these complex cyclic peptides must address methods for the stereocontrolled preparation of the functionalised amino acid residues. The problem of creating the highly functionalised amino acids present in these peptides has been investigated using the Petasis reaction.

References:

Southwood, TJ.; Curry, MC; Hutton, CA. *Tetrahedron* 2006, *62*, 236-242.

MP20

A SIMPLE AND HIGH-YIELDING SYNTHESIS OF β-CARBOLINES AND THEIR FURTHER ELABORATION INTO EXTENDED FUSED HETEROCYCLIC RING SYSTEMS

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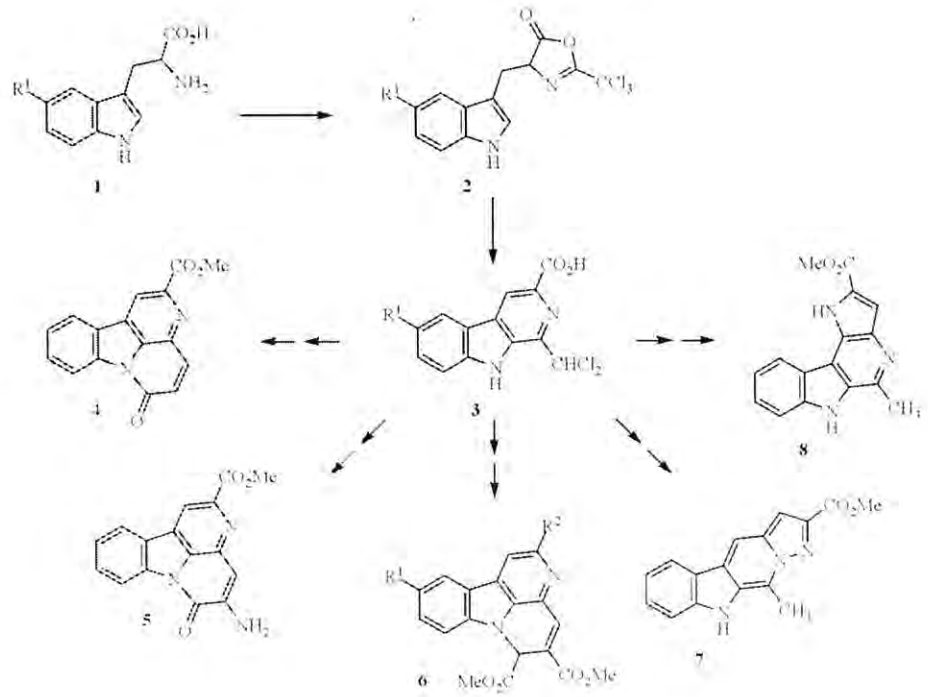
We have utilized a previously reported procedure for the preparation of **β**-carbolines,[1] with modification to prepare in high yield and simplicity synthetically useful **β**-carbolines 3 (R=H, OMe), via the isolable oxazolone 2.[2] The two-step procedure requires no purification procedures and provides **β**-carbolines 3 from readily available tryptophan 1 (R=H) or derivatives of tryptophan in high yield. The **β**-carbolines 3 so prepared have been further elaborated into various extended fused heterocyclic ring systems such canthin-6-ones 4 and 5, canthines 6 (R^2=CHO, CO_2Me), pyrazolo[1',5':1,6]pyrido[3,4-b]indoles 7 and pyrrolo[4',5':5,6]pyrido[3,4-b]indoles 8.[3]



References:
[1] Bergman, J., Lidgren, G., Gogoll, A. *Bull. Soc. Chim. Belg.*, 1992; 101, 643-660.
[2] Condie, GC and Bergman, J. *Eur. J. Org. Chem.*, 2004; 1286-1297.
[3] Condie, GC and Bergman, J. *J. Heterocyclic Chem.*, 2004; 41, 531-540.

MP21

A SYNTHETICALLY FLEXIBLE APPROACH TO FUNCTIONALISED BICYCLIC PYRIDONES.

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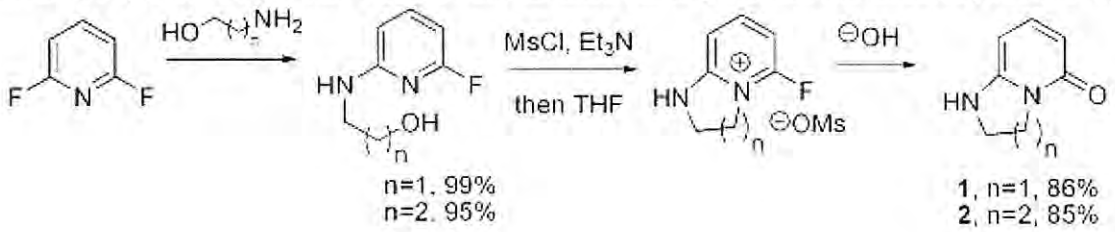
Bicyclic pyridones 1 and 2 are of interest as potential drug scaffolds. Substituted compounds based on these scaffolds have been reported as analgesics and anti-inflammatory agents.[1]
Previous routes to compounds containing 1 and 2 introduce substituents at an early point of the synthesis, limiting the range of variants available. Our aim is to provide a synthetically flexible route to compounds, based around 1 and 2, to allow diverse arrays to be generated.

A route to parent compounds 1 and 2 from common starting material 2,6-difluoropyridine is reported.



Directed ortho-metallation of 2,6-difluoropyridine can be used to introduce synthetically flexible groups, such as boronic acids or halogens.[2] Boronic acid 3 can be used to form substituted compounds, based on 2, via an early stage Suzuki coupling. However, more usefully, iodine can be carried through the cyclisation, either at the C3/C5 position or (by halogen-dance) at C4 position, to give intact iodinated scaffolds 4 and 5 which can be further functionalised via Suzuki coupling. The use of scaffolds 4 and 5 has the potential to be applied to a range of C-C and C-heteroatom bond forming processes to generate substituent diversity at a late stage.

References:
[1] Kubo, K., Ito, N., Souzu, I., Isomura, Y., Homma, H. and Murakami, M., Yamanouchi Pharmaceutical Co. Ltd., Japan, 1981, US 4,288,438.
[2] Schlosser M. and Rausis T., *Eur. J. Org. Chem.* 2004, 1018-1024.

MP24

SYNTHESIS OF DIMERIC FLAVONOIDS

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Over last few years flavonoids have received considerable attention on account of their medicinal properties. Many natural flavonoids exist as dimers, in which two flavonoid molecules are coupled together at various positions. These dimeric flavonoids have been shown to possess a wide range of physiological and biological properties including antioxidant, anticancer, anti-inflammatory and antiviral activities.

A range of dimeric flavonoids have been synthesized and details of the variety of dimerization methodologies will be presented.

MP25

MICROWAVE ASSISTED SYNTHESIS OF SOME NOVEL HETEROCYCLIC COMPOUNDS

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Heterocyclic compounds form the largest classical division of organic chemistry and have immense importance biologically, industrially and indeed to the functioning of any developed human society. Both heterocycles and medicines are interconnected in the recent era. Most of the modern drugs contain heterocyclic nucleus. The biological properties of heterocycles in general make them one of the prime interests of the pharmaceutical as well as biotechnological industries. A perusal of literature has revealed that heterocyclic compounds are found to exhibit anti-fungal, anti-bacterial,anti-viral,anti-parasitic, anti-tubercular,anti-inflammatory and anti-diabetic activities.

Currently the prime interest is to associate research in chemistry with environmental protection. Among the number of procedures recommended, Green Chemistry is one which involve, eco-friendly reagents and catalysts, selected media such as water, ionic liquids or solvent free reactions and non-classical modes of activation such as microwaves .The popularity of microwave assisted synthesis is rapidly growing during last few decades. This unconventional chemical laboratory technique is safe, energy efficient and environment friendly. Inorganic solid supports have made a landmark as the reactions can be performed in dry media or solvent free condition. Further the usage of solid support in conjugation with microwave assisted synthesis leads to high yield and remarkable rate enhancement.

As a part of our on going programme towards the non-conventional approach to the experimental set-up of organic reactions, the concept of microwave organic reaction enhancement chemistry has been adopted for the rapid and efficient synthesis of some novel heterocyclic compounds. All the compounds synthesized in the present investigation were screened for their biological activity and characterized by their analytical and spectral data such as IR, UV, NMR & Mass.

References:
1. Michael JP *Nat.Prod.Rep.* 2001;18, 543-559
2.Witt A, Bergman J, 2003; 7 659

MP26

SYNTHESIS OF 3,5-BIS(3'-INDOLYL)ISOXAZOLES, ANALOGUES OF MARINE ALKALOID NORTOPSENTIN

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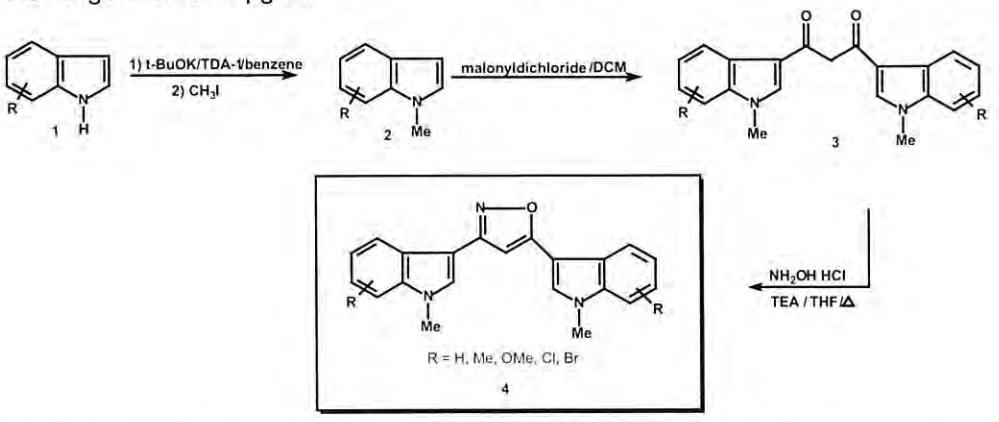
Marine indole alkaloids have emerged as an important class of compounds because of their high degree of biological activities including antimicrobial, antiviral and antitumor properties. Nortopsentins A-C, having a characteristic 2,4-bis(3'-indolyl)imidazole skeleton, exhibited *in vitro* cytotoxicity against P388 cells (IC_{50} 1.7-7.8 μg/ml) and antifungal activity against *Candida albicans*. Their N-indolyl methylated derivatives showed significant improvement in P388 activity compared with that of the parent compounds (IC_{50} 0.34-0.90 μg/ml).[1,2]
Due to the interesting biological activities, different analogues of the marine Nortopsentins have been reported. Thus many bis(indolyl)alkaloids, in which the imidazole moiety of Nortopsentin was replaced by thiazole, pirymidine, pyrazine and pyrazinone rings, were designed and synthesized. These analogues possessed strong inhibitory activity against a broad range of human tumor cell lines (GI_{50} <0.01-89.4 μM).[3-7]
We have recently reported the syntheses and antitumor activities of 2,5-bis(3'-indolyl)thiophenes [8] and 3,5-bis(3'-indolyl)pyrazoles [9] which showed antiproliferative activity in the micromolar range. In our attempts to search for novel antitumor compounds, we designed new analogues with further modification of indole alkaloids to get more potent and selective agents. Thus we planned to synthesize a new series of bis-indolyl-5-membered heterocycles in order to verify the influence of the central heterocyclic ring on the antineoplastic activity.
Here, we report the synthesis of 3,5-bis(3'-indolyl)isoxazoles in which an isoxazole central ring substitutes the imidazole moiety of Nortopsentin. Indole derivatives (**1**) were converted into the corresponding N-methyl derivatives (**2**) using potassium *t*-butoxide, TDA-1 as catalyst and methyl iodide in dry benzene. A Friedel-Crafts reaction of the N-methylindoles (**2**) with malonyldichloride in dichlorometane yielded the desired symmetrical 1,3-diketones of type (**3**) which were converted into the corresponding 3,5-bis(3'-indolyl)isoxazoles (**4**) using hydroxylamine hydrochloride in refluxing TEA/THF. All bis-indolyl-isoxazoles (**4**) tested in a panel of 12 human tumor cell lines showed IC_{50} values in the range 11.4-57.7 μg/ml.



[1] Alvarez M.; et al. *Heterocycles*, 1991 ; 32, 1391-1429; [2] Sakem S.; et al. *J. Org. Chem.* 1991 ; 56, 4304-4307; [3] Gu X. ; et al. *Bioorg. Med. Chem. Lett.* 1999; 8, 569-572; [4] Jiang B.; et al. *Bioorg. Med. Chem.* 2000; 8, 363-371; [5] Jiang B.; et al. *Bioorg. Med. Chem.* 2001; 9, 1149-1154; [6] Jiang B.; et al. *Bioorg. Med. Chem.* 2001; 11, 475-477; [7] Xiong W.; et al. *Bioorg. Med. Chem. Lett.* 2001; 9, 1773-1780 ; [8] Diana P.; et al. *Bioorg. Med. Chem. Lett.* 2007; in press; [9] Diana P.; et al. *Bioorg. Med. Chem. Lett.* 2007; submitted.

MP27

SYNTHESIS, CHARACTERIZATION AND SPECTRAL ANALYSIS OF NEW NEODYMIUM(III), LANTHANUM(III) AND CERIUM(III) COMPLEXES OF 3,3'-(3,4,5-TRIMETHOXYBENZYLIDENE)-BIS(4-HYDROXYCOUMARIN)

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Complexes of neodymium(III), lanthanum(III) and cerium(III) with 3,3'-(3,4,5-trimethoxybenzylidene)-bis(4-hydroxy-2H-1-benzopyran-2-one) (H2L) were synthesized by reaction of the water soluble salts of the corresponding metals and the ligand, in amounts equal to metal : ligand molar ratio of 1:1. The complexes were prepared by adding an aqueous solution of neodymium(III), lanthanum(III) and cerium(III) salts to an aqueous solution of the ligand, which is converted beforehand in water soluble salt (Na2L) by adding dilute solution of sodium hydroxide. The corresponding complexes of the biscoumarin were characterized by different physicochemical methods – elemental analysis, IR-, 1H- and 13C- NMR- spectroscopies and mass spectral data. The spectral data of synthesized complexes were interpreted on the basis of comparison with the spectra of the free ligand. This analysis showed that in the Nd(III), La(III) and Ce(III) complexes the ligands coordinated to the metal ion through both deprotonated hydroxyl groups. On the basis of the v(C=O) red shift observed, participation of the carbonyl groups in the coordination to the metal ion was also suggested.

Keywords: biscoumarins, neodymium(III), lanthanum(III) and cerium(III) complexes, elemental analysis, IR-, 1H-NMR-, 13C-NMR- and Mass- spectra.

References:
[1] Grussner AG. *Jubilee Vol. Emil Barell*, 1946; (238-252).
[2] Desnoyers PD, Binovic KB. *Therapie*, 1967; 22(1), (207-218).
[3] Mitra AKM, De AD, Karchaudhuri NK, Misra SKM, Mukhopadhyay AKM. *J. Ind. Chem. Soc.*, 1998; 75(9), (526-528).
[4] Kostova IK, Manolov IM, Konstantinov SK, Karaivanova MK. *Eur. J. Med. Chem.*, 1999; 34(1), (63–68).
[5] Manolov IM, Kostova IK, Konstantinov SK, Karaivanova MK. *Eur. J. Med. Chem.*, 1999; 34(10), (853–858).
[6] Perola EP, Xu KX, Kollmeyer TMK, Kaufmann SHK, Prendergast FGP, Pang Y-PP. *J. Med. Chem.*, 2000; 43(3), (401-408).
[7] Griffith RG, Chanphen RC, Leach SPL, Keller PAK. *Bioorg. & Med. Chem. Lett.*, 2002; 12(4), (539-542).
[8] Keller PAK, Birch CB, Leach SPL, Tyssen DT, Griffith RG. *J. Mol. Graph. & Mod.*, 2003; 21(5), (365-373).
[9] Khan KMK, Iqbal SI, Lodhi MAL, Maharvi GMM, Perveen SP, Choudhary MIC, Atta-Ur-Rahman, Chohan ZHC, Supuran CTS. *J. Enz. Inh. & Med. Chem.*, 2004; 19(4), (367-371).
[10] Kostova IK, Manolov IM, Momekov GM. *Eur. J. Med. Chem.*, 2004; 39(9), (765–775).
[11] Raleva SR, Savov AS, Froloshka LF, Dundarova DD, Manolov IM, Argirova RA. *Biotechn. & Biotechn. Equip.*, 2005; 19(2), (11-17).
[12] Kostova IK, Momekov GM, Tzanova TT, Karaivanova MK. *Bioinorg. Chem. & Appl.*, 2006; 2006, (9 p.).
[13] Manolov IM, Raleva SR, Genova PG, Savov AS, Froloshka LF, Dundarova DD, Argirova RA. *Bioinorg. Chem. & Appl.*, 2006; 2006, (7 p.).

MP30

UNNATURAL AMINO ACIDS WITH HETEROCYCLIC SIDE-CHAINS AS NOVEL SUBSTITUENTS FOR OPIOID PEPTIDES

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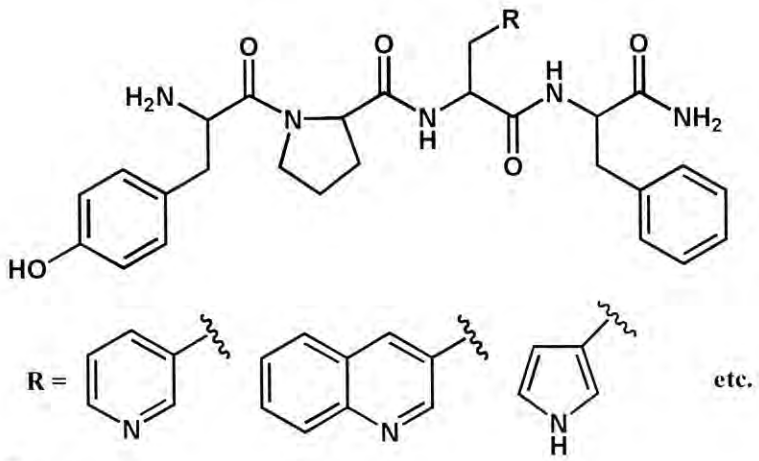
Centrally acting opiates, such as morphine, are the most frequently used analgesics for the relief of severe pain, though they suffer a number of well-known side-effects, including tolerance and physical dependence. Endomorphin-1 (Tyr-Pro-Trp-Phe-NH_2) and endomorphin-2 (Tyr-Pro-Phe-Phe-NH_2) are endogenous opioid peptides [1] that act as agonists at the same μ opioid receptor as morphine, but they are thought to inhibit pain without some of the undesired side-effects of plant opiates. This observation encouraged extensive studies on the possible use of endomorphins as analgesics instead of morphine. However, peptides in general have a limited *in vivo* efficacy, as they are easily degraded by different proteases [2]. Various chemical modifications, such as substitution of natural amino acids by their D-isomers or by unnatural amino acids, are being developed in order to enhance enzymatic stability of opioid analogs [3].
It has been established earlier that aromatic amino acid in position 3 of endomorphins plays a key role in the interaction of these peptides with opioid receptors [4]. In the present study a series of new endomorphin analogs, modified in position 3 by introducing unnatural amino acids with heterocyclic side-chains, was synthesized (Figure).



Figure

The correlation between electronic and steric properties of the new amino acid residues and the in vitro affinity of the obtained analogs at the μ-opioid receptor as well as their stability against enzymatic degradation has been determined.

References:
[1] Zadina JE., Hackler L., Ge LJ., Kastin AJ. Nature, 1997; 386, 499-502.
[2] Stone LS., Fairbanks CA., Laughlin TM., Nguyen HO., Bushy TM., Bessendorf MW. Neuroreport, 1997; 8, 3131-3135.
[3] Janecka A., Fichna J., Janecki T. Curr. Topics Med. Chem., 2004; 4, 1-17.
[4] Fichna J., do-Rego J., Costentin J., ChungNN., Schiller PW., Kosson P., Janecka A. Biochem. Biophys. Res. Commun., 2004; 320, 531-536.

MP31

N,N'-DIALKENYL-2,3- AND 3,4-THIOPHENEDICARBOXAMIDES AS SUBSTRATES FOR RING CLOSING METATHESIS REACTION

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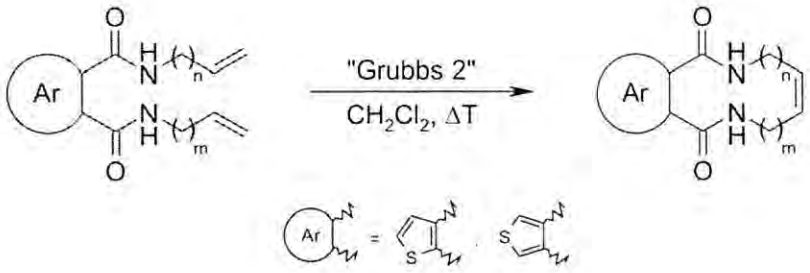
Ring closing metathesis reaction (RCM) is an established procedure for synthesis of carbo- and heterocycles [1]. Our group investigates the suitability of several carboxylic acid derivatives to be substrates for RCM. Prior works [2] showed that e.g. phthalic acid diamides are useful substrates for RCM. As being precursors for potential diazamacrocyclic ligands, these RCM products are of further interest.



Scheme 1: RCM of N,N'-dialkenyl thiophenedicarboxamides

Within our work we developed optimized syntheses for N,N'-dialkenyl substituted thiophenedicarboxamides, both for the 2,3 and 3,4 substitution pattern. These carboxamides were tested as substrates for RCM using Grubbs catalyst 2nd generation (Scheme 1). The influence of the alkenyl chain length (n,m = 1...3) on the success of the RCM is shown. In case of the formation of cyclized products, the E/Z ratio of the newly formed C-C double bond is given. Scope and limitations of the entire protocol will be dicussed.

References:

[1] Grubbs R.H. (Ed.) *Handbook of Metathesis Volume 1;* Wiley-VCH: Weinheim, 2003.

[2] a) Horkel, E. Diploma Thesis, Vienna University of Technology, 2004.
b) Horkel, E.; Hametner, C.; Fröhlich, J. *11thBDSHC Book of Abstracts*, 2005, PO-34

MP32

THE EFFECT OF PEG GROUP LENGTH ON THE APPLICATION OF PEG-GRAFTED POLYSTYRENE RESINS IN SOLID PHASE ORGANIC SYNTHESIS

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Poly(styrene-oxyethylene) graft copolymers (PS-PEG), e.g. Tentagel resins are known to be advantageous for the usage in solid phase organic synthesis (SPOS). The flexible PEG grafts provide a solution-like environment and produce a polymer that swells in both non-polar and polar solvents. In addition they provide good quality gel-phase ^{13}C NMR spectra [1], which are used for non-destructive on-resin analysis. The main drawback of such resins is the low degree of substitution resulting from the high content of PEG (about 68 units).

In a preliminary work of our group [2] we found a strong correlation between the graft lengths and the line widths in gel-phase ^{13}C NMR spectra. We observed a kind of extreme value regarding the improvement of the line shape. By grafting a PEG chain with only 8 units, it was possible to obtain results similar to Tentagel.

In our strategy we substituted the long PEG chain against shorter monodisperse oligo(oxyethylene) tethers (n=2-12 units) with the idea of increasing the loading and minimizing the PEG signal in the gel-phase spectra. Therefore a series of novel polystyrene-oligo(oxyethylene) graft copolymers has been synthesized and examined concerning their applicability for solid phase organic reactions in polar solvents. We compared the results with reaction sequences made on the commercially available Tentagel resin.

On the one hand we selected a Heck coupling reaction on solid phase as an example, because of the necessity of a polar solvent mixture (DMF/TEA). On the other hand we tested the ability of our resin to perform as a support in a solid phase synthesis of Hydantoin [3]. The four-step reaction sequence was selected because it involves a variety of reactions and reagents in different solvents.

In our work we present and discuss the comparability of the NMR spectroscopic analysis with the observed reaction abilities.

References:

[1] Braunshier C., Hametner C. *QSAR Comb. Sci.* 2007; in press.
[2] Braunshier C., Hametner C., Fröhlich J. *J. Mex. Chem. Soc.* 2006; 50, Special Issue 1, IUPAC ICOS-16, 169.
[3] Kita R., Svec F., Fréchet M. J. *J. Comb. Chem.* 2001; 3, 564-571.

MP33

ORDERED NANOPOROUS SCAFFOLDS VIA SELF-ASSEMBLING ORGANIC BUILDING BLOCKS

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Considerable effort has been devoted to the creation of ordered arrays of nanopores on a variety of surfaces. Potential applications for such materials include highly efficient solar cells, real-time electrochemical sensors, miniaturised hard disks, continuous flow reactors, catalytic supports, and drug delivery devices. Self-assembling organic 'building blocks' provide direct access to these complex multi-scale nanostructured materials i.e. a bottom-up approach. We have utilized the self-organising attributes of supramolecular discotic liquid crystals and the reversibility of hydrogen bonding interactions to construct ordered nanoporous thin films on various surfaces.

Gallic acid derivative 1 and benzotri(imidazole) 2 bind in non-polar solvents to form, respectively, a 3:1 supramolecular complex 1.2 via complementary H-bonds [1] (Fig 1). Thin films (~120 nm thick) were prepared by spin-coating solutions (2.25 % w/v in $CHCl_3$) of complex 1.2 onto various substrates such as microscope slides and indium tin oxide (ITO). Slow cooling of these films from the isotropic phase provided a homeotropically aligned (or face-on) hexagonal columnar mesophase between 27.0 and 84.5 °C (as determined by differential scanning calorimetry (DSC)). Cross-linking of the supramolecular discotic mesophase by photopolymerisation of methacrylate ester groups, which were incorporated during synthesis, provided a rigid polymer matrix [2]. Initial etching studies in which the benzotri(imidazole) cores 2 are removed from the polymer matrix have proved encouraging with films remaining stable to the etching conditions. Further characterisation of the ordered nanoporous scaffolds is currently ongoing.

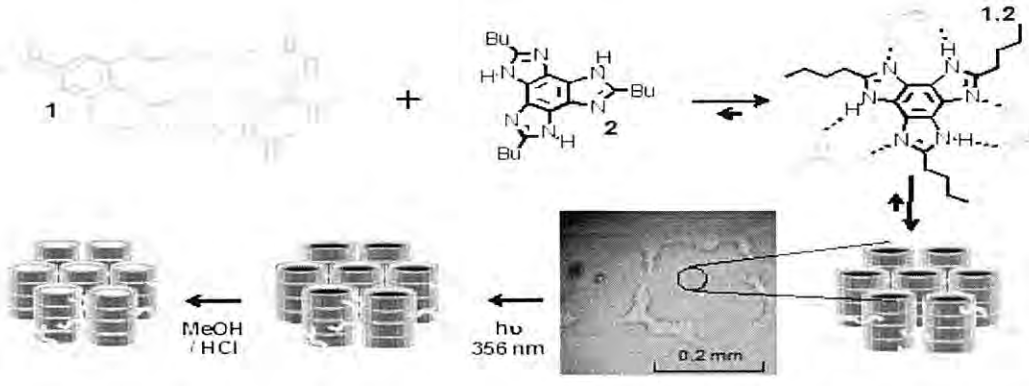

Figure 1: Gallic acid 1 binds with core 2 affording 3:1 complex 1.2 respectively. This complex forms a columnar hexagonal phase as evidenced by DSC and the homeotropic domains with dendritic texture shown in the micrograph. Face-on aligned thin films are photocrosslinked and core 2 is subsequently etched yielding nanoporous scaffolds.

References:
[1] Lee HK., Chang YJ., Oh NK., Zin, WC., Kim, K. *Angew. Chem. Int. Ed.*, 2001; 40, 2669-2670, [2] Mueller A., O'Brien DT. Chem. Rev., 1995; 95, 229-2260,

MP35

HIGH SPEED PREPARATION OF FUNCTIONALIZED QUINOLONES AND BISQUINOLONES *VIA* TRANSITION METAL-MEDIATED PROTOCOLS

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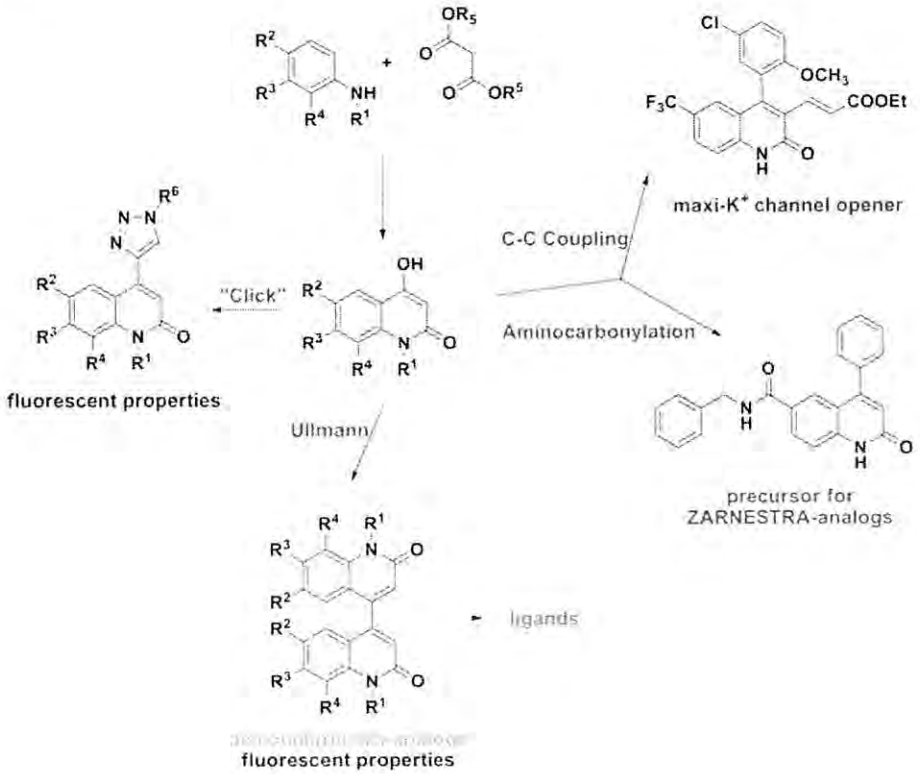
Substituted quinoline-2(1H)-ones (carbostyrils) are ubiquitous subunits in compounds with synthetic as well as natural origin and widely used in the todays medicinal and pharmaceutical research as potential drug candidates. In addition, being push-pull systems, specific carbostyrils are expected to possess fluorescent properties, making them valuable tags with diverse analytical applications.
Here we report on the synthesis of various functionalized quinoline-2(1H)-ones which posses biological activity and/or have fluorescent properties. All quinoline-2(1H)-ones were synthesized starting from easy obtainable 4-hydroxyquinolones[1], via microwave promoted C-C coupling reactions (Suzuki[2,3], Heck[3], Ullmann[2]), involving Pd(0)- or Ni(0)-species as catalysts. Microwave induced 1,3-cycloaddition ("click") process led to the formation of triazol-containing carbostyrils, which were investigated for their fluorescent properties.



References:
[1] Razzaq, T.; Kappe, CO. *Tetrahedron Lett.*, 2007; in press.
[2] Hashim, J.; Glasnov, TN.; Kremsner, JM.; Kappe, CO. *J. Org. Chem.*, 2006; 71, 1707.
[3] Glasnov, TN.; Stadlbauer, W.; Kappe, CO. *J. Org. Chem.*, 2005; 70, 3864.

MP36

SYNTHESIS OF C6-OXYGENATED 3-AZABICYCLONONANES - AE RING ANALOGUES OF METHYLLYCACONITINE

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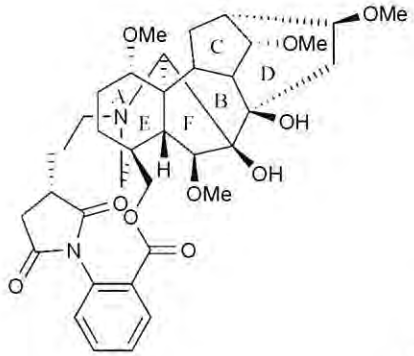
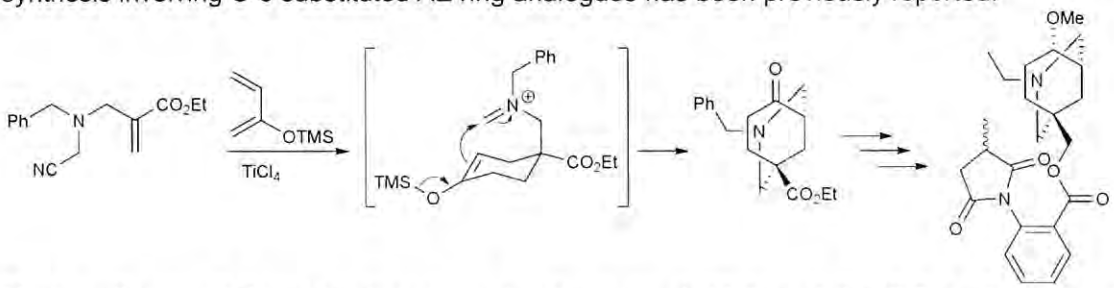
The hexacyclic norditerpenoid Delphinium alkaloid methyllycaconitine (MLA) 1 is a selective antagonist of the α-7 neuronal nicotinic acetylcholine receptor, a target for drug development in the treatment of Alzheimer's Disease.[1] 3-Azabicyclo[3.3.1]nonanes such as 2 mimic the AE rings of MLA 1 and contain both a homocholine motif in the piperidine E ring[2] and oxygenated substitution at C-6 of the cyclohexane A ring.



MLA **1**

AE Ring Bicyclic Analogue of MLA **2**

Recent studies involving the acetylcholine binding protein of the snail Lymnea stagnalis (L-AChBP), a functional and structural mimic of the nAChRs, have produced crystal structures that indicate positive interactions between the ligand binding domain of the receptor and these motifs,[3] however only one synthesis involving C-6 substituted AE ring analogues has been previously reported.[4]



Most syntheses of 3-azabicyclononanes involve oxo-substitution at the C-9 position, however this requires additional transformations before the methylsuccinimidoanthranilate moiety can be appended. The reaction of an α-cyanoamine with a silyl enol ether catalysed by titanium tetrachloride has been reported[5] as a one-pot synthesis of 6-oxo-3-azabicyclononanes. The synthesis of AE ring bicyclic analogues such as 2 having 6S* methoxy substitution utilising this method is herein presented.

References:
1. Paterson D, Nordberg A. *Prog. Neurobiol.* 2000; 61, 75-111.
2. Lind RJ, Hardick DJ, Blagbrough IS, Potter BVL, Wolstenholme AJ, Davies ARL, Clough MS, Early FGP, Reynolds SE, Wonnacott S. *Insect Biochem.* 2001; 31, 533-542.
3. Hansen SB, Sulzenbacher G, Huxford T, Marchot P, Taylor P, Bourne Y. *The EMBO Journal* 2005; 24, 3635-3646.
4. Barker D, Lin DH-S, Carland JE, Chu CP-Y, Chebib M, Brimble MA, Savage GP, McLeod MD. *Bioorg. Med. Chem.* 2005; 13, 4565-4575.
5. Yang T-K, Hung S-M, Lee D-S, Hong A-W, Cheng C-C. *Tet. Lett.* 1989; 30, 4973-4976.

MP37

AN ASYMMETRIC BIRCH ALKYLATION APPROACH TO THE SPIROIMINE UNIT OF THE SPIROLIDES

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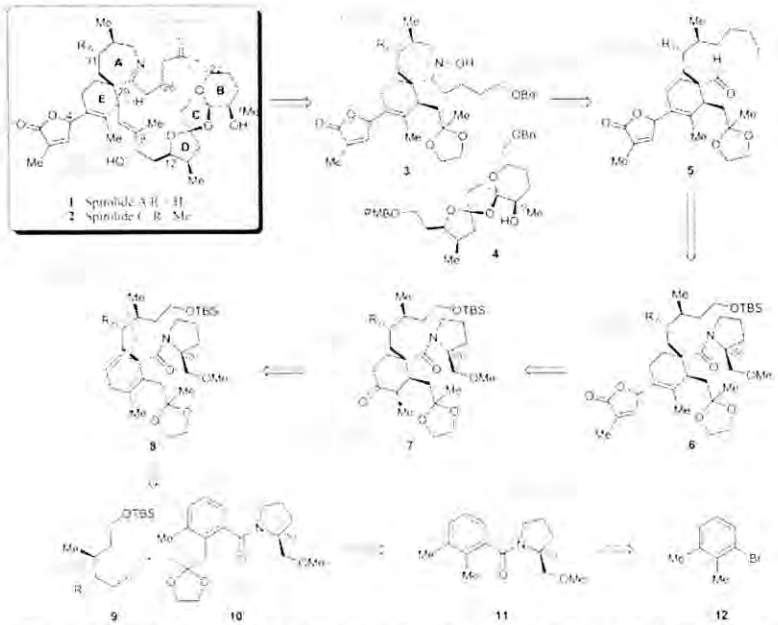
Spirolides A-D are a new class of marine toxins containing a novel 6,5,5-bis-spiroacetal ring system (ring B, C, D) and an unusual 7,6-spirocyclic imine moiety (ring A, E). The spirolides were isolated from the digestive glands of contaminated mussels (*Mytilus edulis*), scallops (*Placopectenmagellanicus*) and toxic planton from the eastern coast of Nova Scotia, Canada, they have also been isolated from the culture of a toxic clone of the dinoflagellate *Alexandrium ostenfeldii*.[i] The spirolides activate L-type calcium channels and also act as muscarinic acetylcholine receptor antagonists,[ii] thus giving access to lead compounds for the treatment of cardiovascular disorders. The spiroimine moiety is thought to be the activate pharmacophore in these marine biotoxins.[iii] This study provides a novel synthetic approach to the spiroimine A, E ring making use an asymmetric variant of the Birch reductive alkylation[iv,v] to access the quaternary C29 stereocentre. The chiral pyrrolidine derived benzamide 9 can be reductively alkylated with chiral iodine 10. Further steps include allylic oxidation and amide directed hydrogenation. Methodology for the formation of bicyclic imine ring has been established by our research group on a model system. Once completed the spiroimine fragment 3 will be coupled to the 5,5,6-spiroketal 4, previously reported by our research group,[vi] via S_N2 sulfone alkylation and Nozaka-Hiyama-Kishi (NHK) coupling.



[i] Hu, T., Burton, I. W., Cembella, A. D., Curtis, J. M., Quilliam, M. A., Walter, J. A. and Wright, J. L. C. *J. Nat. Prod.*, 2001, 64, 308-312.
[ii] Gill, S., Murphu, M., Clause, J., Richard, D., Quilliam, M., MacKinnon, S., LaBlanc, P., Mueller, R. and Pulido, O. *Neurotoxicology*, 2003, 24, 593-604.
[iii] Stewart, M., Blunt, J. W., Munro, M. H. G., Robinson, W. T. and Hannah, D. J. *Tetrahedron Lett.*, 1997, 38, 4889-4890
[iv] Schultz, A. G., Macielag, M., Podhorez, D. E. and Suhadolnik, J. C. *J. Org. Chem.*, 1988, 53, 2456-2464.
[v] Schultz, A. G. *Chem. Comm.*, 1999, 1263-1271.
[vi] Meilert, K. and Brimble, M. A. *Org. Lett.*, 2005, 7, 3479-3500.

MP39

SYNTHESIS OF CYCLIC POLYGLYCEROLS

Masahiro Hamada, Takahiro Kawagishi, Tatsuro Kiyoto, Kimio Yoshikawa, Noriyuki Nakajima.

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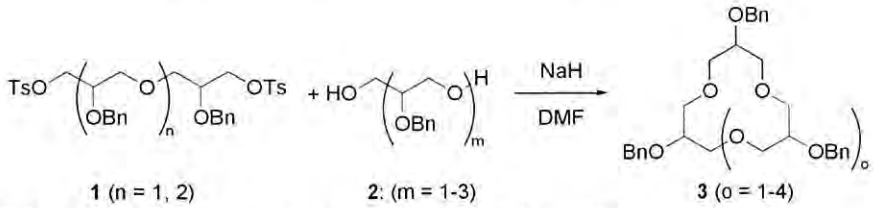
Polygrycerols are oligomers of glycerol (glycerin). Although polyglycerols is readily available in bulk quantities by industrial manufacture, the reaction requires drastic conditions, including high temperature and alkaline media. Therefore, commercially available polyglycerols are very complicated oligomeric mixtures and undefined molecular composition with difficult characterization. We therefore focused our attention on the synthesis of single and fine structure of highly cyclic polyglycerols as an authentic standard. In this presentation, we report about a synthesis of cyclic polyglycerols by intramolecular cyclization.
We first tried 1:1 condensation of ditosylates 1 and diols 2. But in all cases, the desired cyclic products 3 were given in very low yield (up to 19%, Scheme 1).

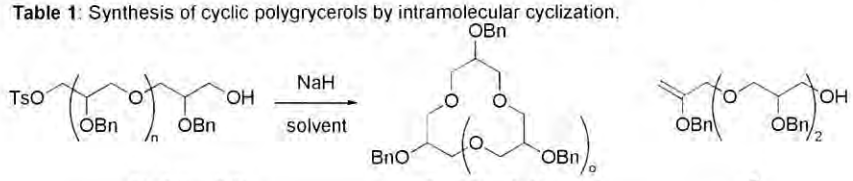


1 (n = 1, 2) **2**: (m = 1-3) **3** (o = 1-4)

Scheme 1: Synthesis of cyclic glycerols by intermolecular coupling.

The by-product of coupling of triglycerol ditosylate and triglycerol was linear hexaglycerol 4d, which was treated with NaH in DMF at 80 °C for 2 days to obtain cyclic hexaglycerol 3d in 70% yield (Table 1, entry 4). On the base of this result, we tried intramolecular cyclization of polygrycerol monotosylate. When the monotosylates 4a-c were treated with NaH in DMF at 80°C for 2 days, 12-, 16-, and 20-membered cyclic benzyl glycerols (3a, 3b, and 3c) were obtained in 38%, 38%, and 54% yields, respectively (Table 1, entries 1-3). To increase the yield of cyclic trigrycerol, we modified the experimental procedure (Table 1, entries 5-7), that is, a solution of triglycerol monotosylate 4a in solvent was added dropwise to a mixture of NaH in hot solvent over 3 h, and then the mixture was refluxed for 22 h. In the result, the desired product 3a was given in 30-60% yields. Furthermore, a vinyl ether 5, which was obtained by a β-elimination of tosyl group, was given as a by-product. THF was better solvent in this procedure (entry 7).

Table 1: Synthesis of cyclic polygrycerols by intramolecular cyclization.



4a-d (n = 2-5) **3a-d** (o = 1-4) **5**

Entry	Substrate	Solvent	Temp.	Time	**3** (yield)	**5** (yield)
1	**4a** (n = 2)	DMF	80 °C	2 d	**3a** (o = 1, 38%)	—
2	**4b** (n = 3)	DMF	80 °C	2 d	**3b** (o = 2, 38%)	—
3	**4c** (n = 4)	DMF	80 °C	2 d	**3c** (o = 3, 54%)	—
4	**4d** (n = 5)	DMF	80 °C	2 d	**3d** (o = 4, 70%)	—
5	**4a** (n = 2)	DMF	80 °C	22 h	**3a** (o = 1, 35%)	43%
6	**4a** (n = 2)	toluene	reflux	22 h	**3a** (o = 1, 30%)	—
7	**4a** (n = 2)	THF	reflux	22 h	**3a** (o = 1, 60%)	26%

References:

Kawagishi T. Yoshikawa K. Ubukata M. Hamada M. Nakajima N. *Heterocycles*, 2006; 69, 107-111.

MP40

SYSTEMATICAL STUDY OF STILLE & SUZUKI CROSS-COUPLING REACTIONS IN 4- & 5-POSITION OF 2-PHENYLTHIAZOLES AND –OXAZOLES

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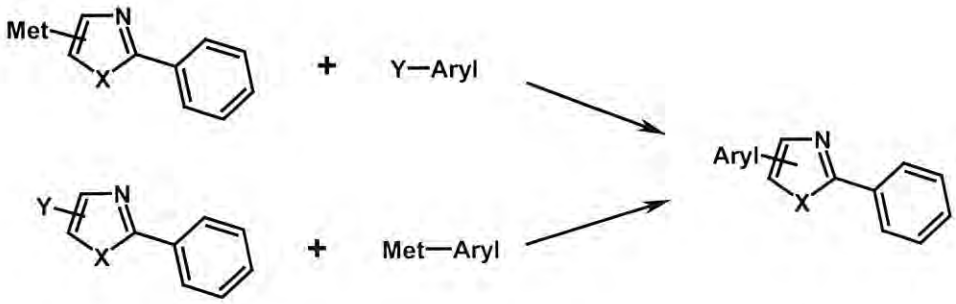
Substituted thiazoles and oxazoles are both interesting building blocks and frequently encountered structural motifs in a variety of natural products and synthetic bioactive compounds useful as pharmaceuticals or in plant protection. Beside of traditional cyclization strategies complex structures are often available *via* application of metal-catalyzed cross-coupling reactions. The Stille as well as the Suzuki reaction have proven to be very versatile methods as they both show high tolerance towards various functional groups. Compared to other cross-coupling reactions (e.g. Negishi) the required metal organyls are stable and easy to handle.

Within this contribution we present a systematical study of the cross-coupling capability of the 4- and 5-position of 2-phenylthiazoles and –oxazoles. The influence of the position of the halogen (Br *vs.* I) as well as of the metal in the corresponding coupling partners was investigated. While Stille reagents are well known boronic acids of thiazoles and oxazoles turned out to be unstable. Therefore, we developed a facile method for the synthesis of corresponding boronic acid esters for subsequent Suzuki coupling reactions.
4-Halo-compounds, which are not accessible *via* direct halogenation, were synthesized from 5-substituted derivatives by application of the halogen dance reaction to these heterocyclic systems for the first time in our group. Pronounced differences were encountered when homocyclic coupling partners were replaced by some heterocyclic systems.



X= S, O
Y= I, Br
Met = $SnBu_3$, $B(OR)_2$

MP41

GOLD-CATALYSED REACTIONS OF ALKYNYLETHERS AND ALKYNYLAMINES

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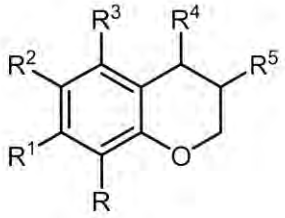
Gold-catalysed reactions have become a hot spot in catalysis research.[1] In particular the interaction of the gold catalyst with alkynes has been a driving force for the field.[2] We now used alkynylethers and alkynylamines for the synthesis of dihydrobenzofurans 1, chromanes 2, dihydroindols 3 and tetrahydroquinolines 4.

1



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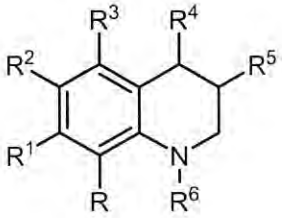
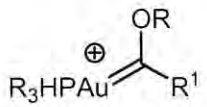


4

The efforts to stabilize organometallic intermediates (like gold carbenoids of type 5) in these heterocyclisation reactions by the additional donor atoms will also be reported.



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References:
1) Hashmi ASK, Hutchings G, *Angew. Chem.*, 2006; 118, 8064–8105; *Angew. Chem. Int. Ed.*, 2006; 45, 7896–7936.
2) Hashmi ASK, *Gold Bull.*, 2003; 36, 3–9.

MP42

SYNTHESIS OF THE FG RINGS OF THE PECTENOTOXINS.

Amanda Heapy, Margaret Brimble and Thomas Wagner

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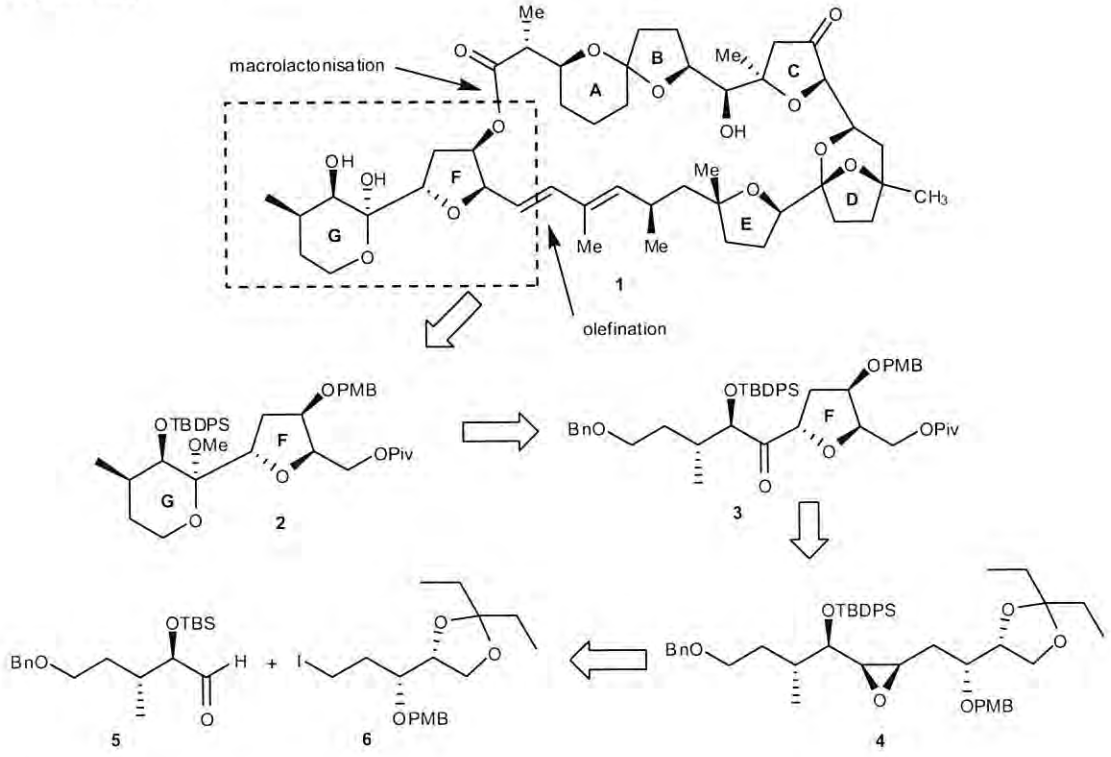
The pectenotoxins (PTX) are a family of 14 (PTX-1-14) polyether macrolides isolated from scallops (*Patinopecten yessoenis*).[1] The PTX family of toxins contain a complex macrolide framework comprising a spiroacetal, three substituted tetrahydrofurans and 19 (or 20 in PTX-11 and PTX-13) stereogenic centres. The PTXs have been implicated in the occurrence of diarrhetic shellfish poisoning, are hepatotoxic and exhibit selective cytotoxicity against several cancer cell lines[2] thus prompting their total synthesis.[3] The work reported herein continues on from the successful synthesis of the ABC ring of PTX undertaken in this group.[4] We report our synthesis of the FG subunit 2 of PTX-2 1. The G ring is installed by simultaneous deprotection of benzyl ether 3 followed by 6-*exo-trig* cyclisation of the resultant alcohol onto ketone 3. The F ring is constructed by 5-*exo-tet* cyclisation of a masked δ-hydroxy epoxide 4, itself available via stereocontrolled epoxidation of a (*Z*)-olefin precursor. The olefin is in turn constructed via (*Z*)-selective Wittig reaction of aldehyde 5 with the phosphonium salt derived from iodide 6. The key stereocentres in intermediates 5 and 6 are then established using Sharpless asymmetric epoxidation and Sharpless asymmetric dihydroxylation, respectively.



References:

1. T. Yasumoto T., M. Murata , Y. Oshima, G. K. Sano and J Matsumoto, *Tetrahedron*, 1985, 41, 1019-1025.
2. K. Fladmark, M. H. Serres, N.L. Larsen, T. Yasumoto, T. Aune and S.O. Doskeland, *Toxicon*, 1998, 36, 1101-1114.
3. For an invited comprehensive review on Synthetic Studies Towards the Pectenotoxins see: R. Halim and M. A. Brimble., *Org. Biomol. Chem.*, 2006, DOI: 10.1039/b611531b.
4. R. Halim, M. A. Brimble, J. Merten. *Org. Biomol. Chem.*, 2006, 7, 1387-1399.

MP43

CASCADE REARRANGEMENTS OF PHOTOCHEMICALLY FORMED OXETANES, ENABLING ACCESS TO A NOVEL FUSED RING SYSTEM.

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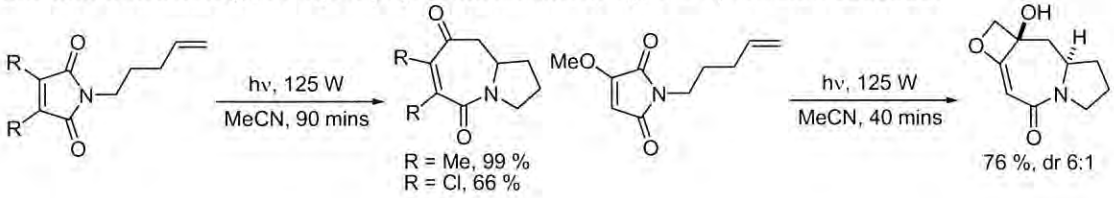
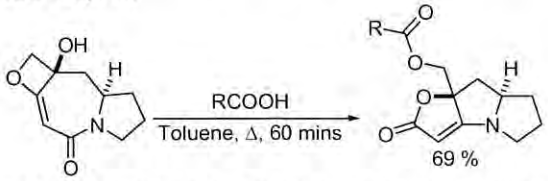
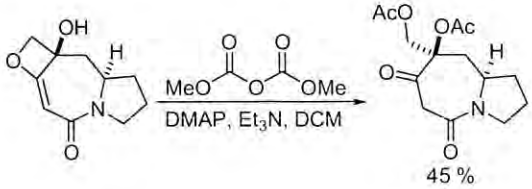
The [5+2] cyclisation has been developed[1] as a simple route to fused azepines. Steric bulk (R = Me, Cl) has been found to be a requirement to prevent undesired intermolecular side reactions. The use of alkoxy groups as a "blocking group" greatly accelerated the reaction, and resulted in formation of oxetane functionality *via* a [5+2] cyclisation/Norrish Type II cyclisation cascade.[2]

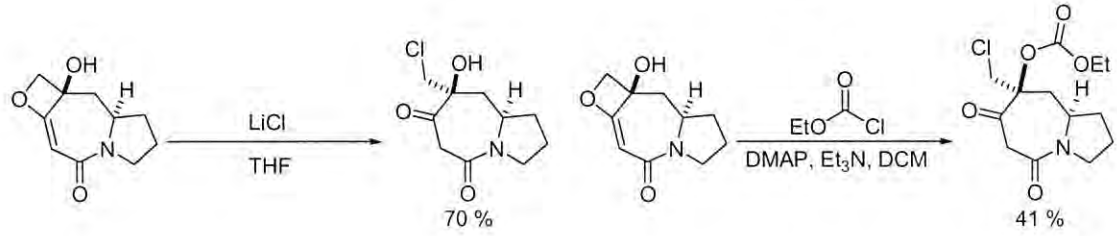


Such oxetane fused azepine systems have been found to undergo a remarkable rearrangement under mildly nucleophilic acidic conditions. While these yields are only moderate, this does provide a rapid route into this novel fused tricycle.



This rearrangement has been found to tolerate a wide variety of acid nucleophiles and a range of substitutions on the oxetane and azepine cores. Some alcohols were also found to undergo rearrangements. Mechanistic studies have isolated compounds similar to proposed intermediates on the rearrangement pathway, while various halogen nucleophiles were also found to cause ring opening.





References:

(1) (a) Booker-Milburn, K.I.; *Tetrahedron Lett*, 1998; 39, 7423-7426 (b) Booker-Milburn, K.I.; *J.Org.Chem.*, 2005; 70, 7558-7564 (c) Booker-Milburn, K.I.; *J.Org.Chem.*, 2007; 72, 1449-1457

(2) Booker-Milburn, K.I.; *Org.Lett.*, 2004; 6, 1481-1484

MP44

ASYMMETRIC SYNTHESIS OF 3-ALKOXYOXINDOLES BY α-ARYLATION OF AMIDE ENOLATES

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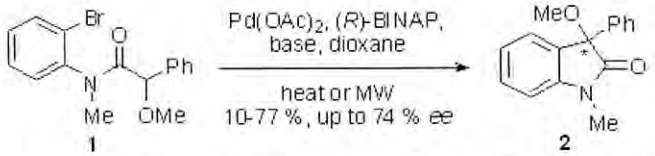
University of Leeds, United Kingdom

The palladium-catalyzed α-arylation of amide enolates could be developed into a general route to access chiral 3-hydroxy-substituted oxindoles. In oxindoles, the best level of chiral induction to date achieved by Hartwig *et al*, while impressive at 76% *ee*, still remains of limited synthetic usefulness.[1] We have theorized that one source of the hitherto modest chiral induction is the formation and interconversion of two possible geometric enolate isomers that upon arylation by Pd(0) in a chiral environment would give rise to two different enantiomers of the product. The nature of the substrates leading to the relevant compounds gives rise to the possibility of controlling the enolate configuration by chelation to an oxaphilic counter ion.

After probing the reaction conditions for a small number of protected 3-hydroxyoxindole substrates (unprotected substrate failed to deliver oxindole), we proceeded to conduct asymmetric investigations on a model compound 1 using optically active BINAP as a ligand. It was found that the simple transition to a chelating base improved the enantiomeric excess, as hoped.



1 2

The sensitivity of the reaction conditions and the apparent instability of the anilide substrates lead us to try and shorten the reaction times first by increasing the temperature, then by applying microwave conditions. We were pleased to see that the level of chiral induction increased using more efficient and homogenous microwave heat transfer. It was found that the conversion of the substrate and the chirality of the product 2 both depended greatly on reaction temperature.

In hope of finding a way around the limited yields of the BINAP-mediated arylation while keeping the reaction temperature at a minimum, a selection of bidentate phosphine ligands was screened. A more electron-rich, commercially available BINAP-analogue saw a slight increase in both yield and *ee*. Work is currently ongoing to extend the screening of ligands to encompass *N*-heterocyclic carbenes and more electron-donating bidentate ligands, investigate the properties of alternative chelating counter ions and expand the scope of the reaction conditions to more diverse substrates.

In summary we have shown that α-arylation can be performed on a model substrate with BINAP as a ligand in modest yields but with, for BINAP, high *ee*. It seems very likely that optimisation of ligand properties and other conditions would promote better yields and even better *ee*.

References:

1. Hartwig J. F., Lee S. *J. Org. Chem.* 2001; 66, 3202-3215.

MP45

SYNTHETIC STUDIES OF AZASPIRENE ANALOGUES HAVING A SPIRO RING SKELETON

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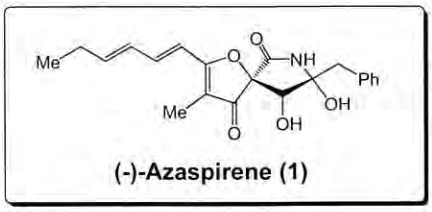
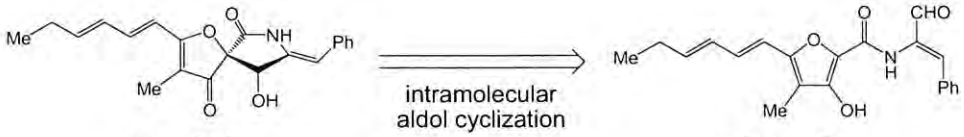
(-)-Azaspirene (1), an inhibitor of angiogenesis, was isolated from the fungus *Neosartorya* sp. by Osada and co-workers in 2002[1] and its asymmetric synthesis was reported recently by Hayashi et al.[2] and by Tadano et al.[3] We have designed its retrosynthetic pathway to a spiro intermediate 2 via intramolecular aldol cyclization of furanol intermediate 3 and have studied the synthesis and the isomerization reactions of (5*S**, 9*S**)-8, an analogue of 2, for the synthesis of azaspirene analogue 9.

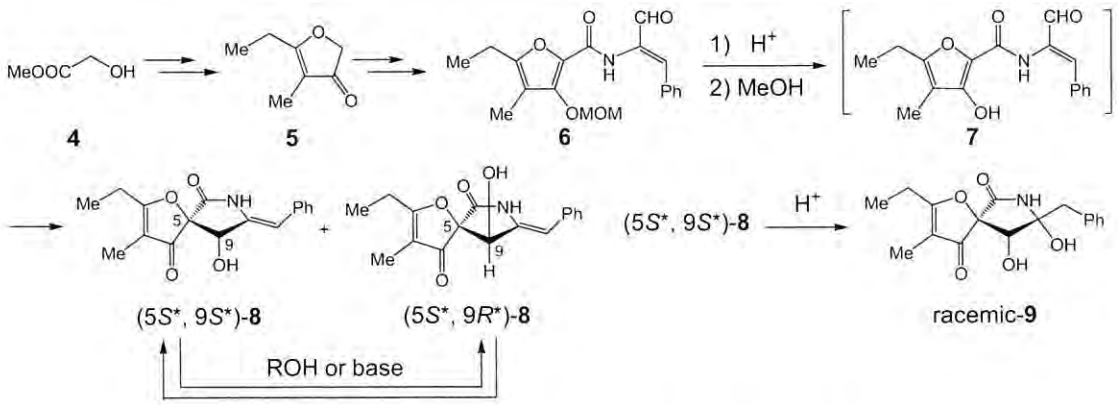


(-)-Azaspirene (1)



racemic-**2** furanol **3**

We have accomplished the synthesis of 9 via isomerization of furanol 7 (Scheme 1). Initially, we synthesized aldehyde 6 via furanone 5, which was further transformed into a 1/2 mixture of spiro compounds (5*S**, 9*S**)-8 and (5*S**, 9*R**)-8 by removal of a MOM group in acidic media. Interestingly, isomerization of 8 in methanol reached equilibrium to give the ratio of 2/1 with predominant formation of the desired (5*S**, 9*S**)-8 and the following stereoselective hydration afforded the racemic azaspirene analogue 9. The spiro intermediates, (5*S**, 9*S**)-8 and (5*S**, 9*R**)-8, were found to isomerize themselves under basic conditions or in the presence of alcohol. The spiro intermediates 8 showed a similar behaviour to azaspirene precursor 2 and the isomerization rates are dependent on alcohols or bases.



Scheme 1. Synthesis of racemic azaspirene analogue 9

References:
1) Asami Y., Kakeya H., Onose R., Yoshida A., Matsuzaki H., Osada H. *Org. Lett.*, 2002; 4, 2845-2848.
2) Hayashi Y., Shoji M., Yamaguchi J., Sato K., Yamaguchi S., Mukaiyama T., Sakai K., Asami Y., Kakeya H., Osada H. *J. Am. Chem. Soc.*, 2002; 124, 12078-12079.
3) Aoki S., Oi T., Shimizu K., Shiraki R., Takao K., Tadano K. *Bull. Chem. Soc. Jpn.*, 2004; 77, 1703-1716.

MP46

DISCOVERY OF 2-IMINOBENZIMIDAZOLES AS A NEW CLASS OF TRYPANOTHIONE REDUCTASE INHIBITORS BY HIGH-THROUGHPUT CHEMICAL SCREENING

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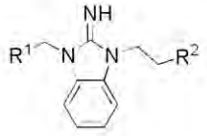
Parasitic protozoa of the family Trypanosomatidae are the causative agent of many significant tropical diseases including African trypanosomiasis, Chagas disease and Leishmaniasis. Current drugs on the market have severe limitations including administration difficulties, long treatment regimes, life-threatening side effects, and increasing incidence of drug resistance.[1,2,3] The intracellular reducing environment of trypanosomatids is maintained by a unique thiol redox system where the glutathione/glutathione reductase (GR) couple found in mammalian cells is replaced by a polyamine-glutathione adduct trypanothione/ trypanothione reductase (TR) couple. TR is a key enzyme of the parasite antioxidant defence,[4] does not occur in the mammalian host, and has been found to be essential for all trypanosomatids currently studied.[5]

A high-throughput screening campaign of a library of 100,000 lead-like compounds identified nine novel chemical classes of TR inhibitors. A prominent class were the 2-iminobenzimidazoles.[6] The essential pharmacophore of this class of compounds has been identified by the synthesis and biological investigation of a series of analogues. Further biological testing revealed that members of this new class of TR inhibitors have potent trypanocidal activity against *Trypanosoma brucei rhodesiense*, do not inhibit closely related human glutathione reductase and have low cytotoxicity against mammalian cells. This chemical series has significant potential for further development as a new class of therapeutics for trypanosome mediated diseases.



(I)
R^1 = aryl containing group
R^2 = basic amine group

References:

1. Fairlamb AH. Trends Parasitol., 2003; 19, 488-494.
2. Paulino M., et. al. Mini-Rev. Med. Chem., 2005; 5, 499-519.
3. Croft SL, Sundar S, Fairlamb AH. Clin. Microbiol. Rev., 2006; 19, 111-126.
4. Dumas C. et. al. EMBO J., 1997; 16, 2590-2598.
5. Schmidt A, Krauth-Siegel RL. Curr. Top. Med. Chem., 2002; 2, 1239-1259.6. Holloway GA, Baell JB, Fairlamb AH, Novello PM, Parisot JP, Richardson J, Watson KG, Street IP. Bioorg. Med. Chem. Lett., 2007; 17, 1422-1427.

MP48

ATROPISOMERS OF 2-ARYLINDOLINES

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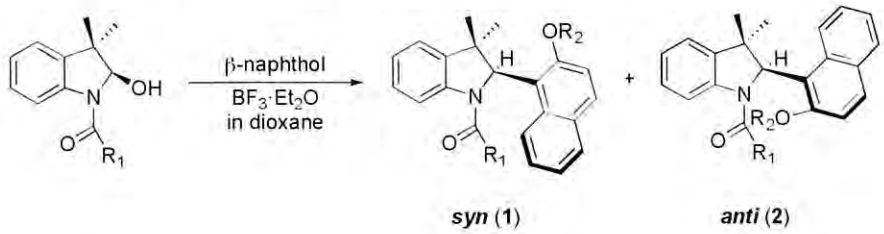
Atropisomers have attracted continuous attention from both theoretical and biological points of view, although there are few examples of isolation of a pair of atropisomers. We found that a pair of atropisomers of the 2-arylindolines were easily synthesized and isolated. As a result, twenty one pairs of stable diastereomeric atropisomers caused by restricted rotation around the Csp^3-Csp^2 bond of [2-(2-hydroxy- or 2-methoxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydroindol-1-yl](substituted-phenyl)methanones (1, 2) and 1-[2-(2-hydroxynaphthalen-1-yl)-3,3-dimethyl-2,3-dihydroindol-1-yl]alkan-1-ones (1, 2) and [2-(3-bromo-6-hydroxy-2,4-dimethylphenyl)-3,3-dimethyl-2,3-dihydroindol-1-yl](4-nitrophenyl)methanones were isolated (Scheme 1). The conformational analyses of the atropisomers were performed based on the X-ray crystallographic structures and ^{1}H-NMR spectral data. It became clear that rotation around the C2-naphthyl bond is restricted at room temperature, whereas the >NCO-Ar bond rotates freely.



Scheme 1

Secondly, the rotation barriers and the intra- and intermolecular interactions of atropisomers of 2-arylindolines were assessed by isomerization reaction in various solvents, ^{1}H-NMR spectral data, and X-ray crystallographic structures. As a result, an index of the rotation barrier is estimated to be ca. 26-28kcal/mol for isolable atropisomer. In addition, the existence of π···π interaction, >N···OH hydrogen bond, C-H···OH hydrogen bond, CH_3···π interaction, and edge to face interaction has been found as intra- and intermolecular weak interaction forces (Figure 1).

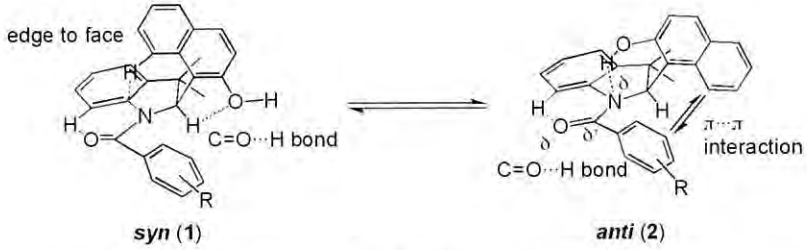


Figure 1. Weak Intramolecular Interactions in Restricted Rotation

Finally, the ground-state and transition-state structures for restricted rotation of 1 are calculated by semiempirical MO (PM3, PM5, AM1), *ab initio* (HF/3-21G) and DFT (B3LYP/6-31G*) methods. As a result, the DFT calculations are entirely consistent with the observed experimental results. Based on the DFT-calculated geometries, the intramolecular weak interactions in the restricted rotation are analyzed.

References:
Ito F., Moriguchi T., Yoshitake Y., Eto M., Yahara S., Harano K., *Chem. Pharm. Bull.*, 2003; 51, 688-696.

MP49

SmI_2-INDUCED RADICAL SPIROCYCLIZATION REACTION BETWEEN AROMATIC RINGS

Hiroki Iwasaki,[1] Toru Eguchi,[1] Nozomi Tsutsui,[1] Hiroaki Ohno[2] and Tetsuaki Tanaka[1]

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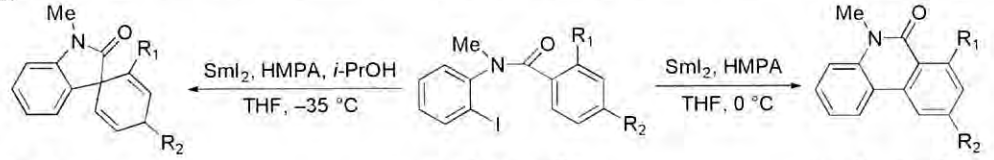
Aryl radical addition onto an aromatic ring has become an important tool in organic synthesis. The traditional method relies upon heavy metal-mediated oxidative radical arylation of arenes through the cation radical intermediates, which is a useful procedure for the biaryl coupling of electron-rich arenes. Recently, intramolecular reductive radical arylation using Bu_3SnH or other hydrogen sources has been extensively studied.

Synthesis of spirocycles has attracted a great deal of attention due to their unique molecular structure and diverse biological activities. In our ongoing study on samarium(II)-mediated cyclization reaction onto an aromatic ring, we found that treatment of *N*-methylbenzanilide derivative 1a with SmI_2 and HMPA in the presence of *i*-PrOH gave spirocycle 2a in 89% yield. In contrast, when the reaction of 1b was conducted in the absence of *i*-PrOH, the biaryl coupling product 3b was selectively obtained in 60% yield.[1]



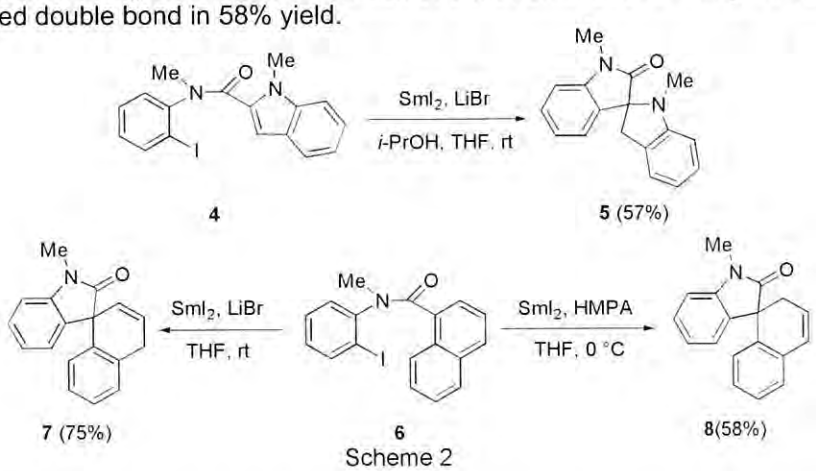
2a: R^1 = Me, R^2 = H
2b: R^1 = H, R^2 = Me

1a: R^1 = Me, R^2 = H
1b: R^1 = H, R^2 = Me

3a: R^1 = Me, R^2 = H
3b: R^1 = H, R^2 = Me

Scheme 1

We also investigated samarium(II)-mediated intramolecular biaryl coupling reaction of various aryl radical precursors such as indole and naphthalene derivatives. The spirocyclization onto indole ring proceeded in 57% yield by using LiBr as an additive instead of HMPA. It was also revealed that treatment of 6 with SmI_2 and LiBr in the absence of *i*-PrOH selectively gave spirocycle 7 with an isolated double bond in 75% yield, while the reaction of 6 with SmI_2 and HMPA gave spirocycle 8 having a conjugated double bond in 58% yield.



4

5 (57%)

7 (75%)

6

8(58%)

Scheme 2

The results with these substrates as well as scope and limitations of this transformation will be presented.

References:
1 Ohno H.; Iwasaki H.; Eguchi T.; Tanaka T. *Chem. Commun.* 2004; 2228-2229.

MP52

SELECTIVE MODIFICATION OF NEOMYCIN B USING THE MITSUNOBU REACTION

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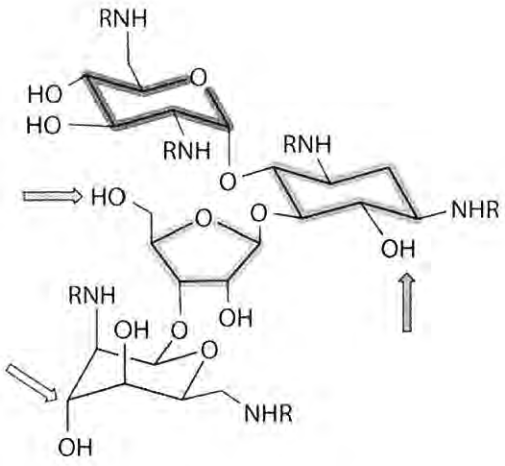
[†]*Eskitis Institute, Griffith University, Nathan, QLD 4111 Australia*
**Institute for Glycomics, Griffith University, Gold Coast, QLD 9726 Australia*



Aminoglycoside antibiotics are widely used for the treatment of a variety of infections including tuberculosis and pneumonia in particular. Despite the broad-spectrum efficacy of these natural amino sugars, the use of these drugs is restricted due to their toxicity, poor oral bioavailability and poor cell permeability. Consequently, semi-synthetic analogues of this class of compounds are attractive targets for medicinal chemists.

The aminoglycoside antibiotic neomycin B has been converted into several novel building blocks that can be used for the specific modification of three of the four ring systems. Under carefully controlled conditions, the Mitsunobu reaction can be used to selectively dehydrate the *ido* ring to give the *talo* epoxide, not a tricyclic aziridine-azetidine structure as has been claimed previously. Subsequently however, under more forcing conditions, the 2-deoxy streptamine ring undergoes Mitsunobu dehydration to give an aziridine. An unusual remote neighbouring group effect was observed. When the primary hydroxyl of the ribose ring was blocked, aziridine formation on the deoxystreptamine ring did not occur. A possible explanation is suggested involving formation of a cyclic phosphorane intermediate which either stabilizes the all-axial conformation of the deoxystreptamine required for aziridine ring formation or facilitates transfer of the triphenylphosphinoxy leaving group from the primary hydroxyl of ribose to the secondary hydroxyl of the deoxystreptamine. Both the epoxide and epoxide-aziridine neomycin building blocks can be ring-opened with azide, and subjected to "click" type chemistry with terminal alkynes to generate a series of new neomycin analogues. For example, we have attached a cholesterol moiety to neomycin B, as it has recently been demonstrated that mycobacteria enter the macrophage by way of a cholesterol-dependent mechanism. These reactions can all be carried out without recourse to *O*-protecting groups.

MP53

A METHOD FOR THE CONNECTION OF NATURAL COMPOUNDS WITH HETEROCYCLES VIA REACTIVE PRECURSORS

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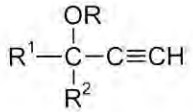
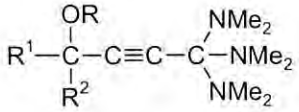
[b]*Universität Stuttgart, Institut für Organische Chemie, Pfaffenwaldring 55, D-70569 Stuttgart, Germany*

From natural occurring ketones can be prepared alkoxy-alkynes 1, 2 by ethynylation and subsequent alkylation of the resulting carbinosl at the oxygen. The alkynes 1, 2 can be transformed into the orthoamide-derivatives 3, 4 in a one step reaction.

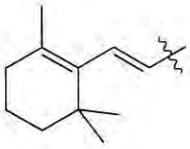


1 , 2



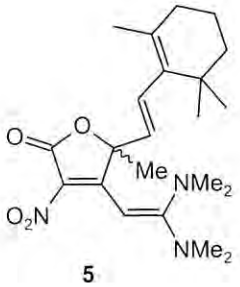
3 , 4	**a**	**b**
R	Me	Me_3Si

1 , 3 : R^1 = Me, R^2 =



2 , 4 : R^1-R^2 =

From the orthoamide 3b and ethyl nitroacetate and from 3a and 3-indyolylacetonitrile can bey prepared the heterocyclic compounds 5 and 6. The camphor derived orthoamide 4b reacts with benzamidine to give the pyrimidine derivative 7. In the reaction of 4a with cyanoacetamide is pyridones 8.



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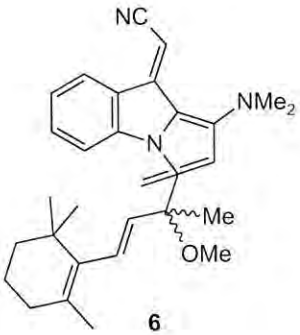

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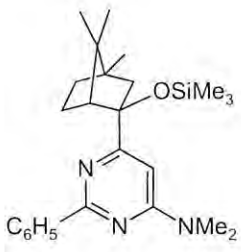

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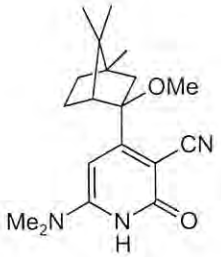

8

MP54

A ONE POT SYNTHESIS OF SOME 3-SUBSTITUTED TETRONIC ACIDS

Karen E. Jarvis and Andris J. Liepa

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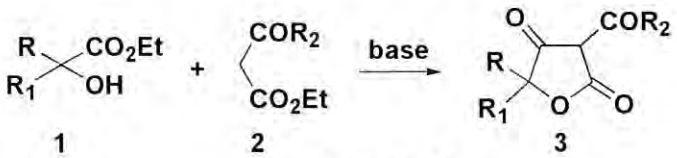
Derivatives of tetronic acids 3 are widely found in nature, for example, in sponges and fungal and lichen metabolites.[1] They are also known for their insecticidal,[2] antifungal,[3] antibiotic,[4] anti-inflammatory,[5] analgesic,[6] anticoagulant[7] and antiepileptic[8] activities. More recently, these compounds have been reported as anti-HIV-1 protease inhibitors[9] and anticancer agents.[10]

In the last hundred years, literature methods for preparing tetronic acids typically require a number of steps involving protection and activation.

This poster reports a simple, one pot synthesis of 3-substituted tetronic acids 3 from hydroxy esters 1 and acyl acetates 2 in the presence of organic amines or sodium alkoxides (Scheme 1), without the need for any protection and deprotection.



Scheme 1

The key feature of this reaction is the use of inexpensive, readily available starting materials *via* a one pot methodology.

The susceptibility of ester substituents in the 3- position to nucleophilic attack is also discussed.

References:

1. Krepski, LR, *Tetrahedron Lett.* 1985, *26*, 981.
2. Ibi A, Yaniguchi E, Maekawa K, *Agric. Biol. Chem.*, 1979, *43*, 1641.
3. Luk K, Readshaw SA, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1641.
4. Ley SV, Trudell ML, Wadsworth DJ, *Tetrahedron*, 1991, *47*, 8285.
5. Foden FR, McCormick J, O'Mant DM, *J. Med. Chem.*, 1975, *18*, 19.
6. Dal Pozzo A, Dansi A, Neneghini E, *Bull. Chim. Farm.*, 1974, *113*, 280.
7. d) Witiak D, Kokrady SS, Patel ST, Akbar H, Feller DR, Newmann HAI, *J. Med. Chem.*, 1982, *25*, 90.
8. Zhang CL, Chatterjee SS, Stein U, Heinemann U, *Naunyn-Schmideberg's Arch. Pharmacol.*, 1992, *345*, 85.
9. Roggo BE, Petersen F, Delmendo R, Jenny HB, Peter HH, Roesel J, *J. Antibiot.*, 1994, *47*, 136.
10. Poli G, Giambastiani G, *J. Org. Chem.*, 2002, *67*, 9456.

MP55

TOTAL SYNTHESIS OF 3A-HYDROXYPYRROLO[2,3-*B*]INDOLINE ALKALOID, ALLINE

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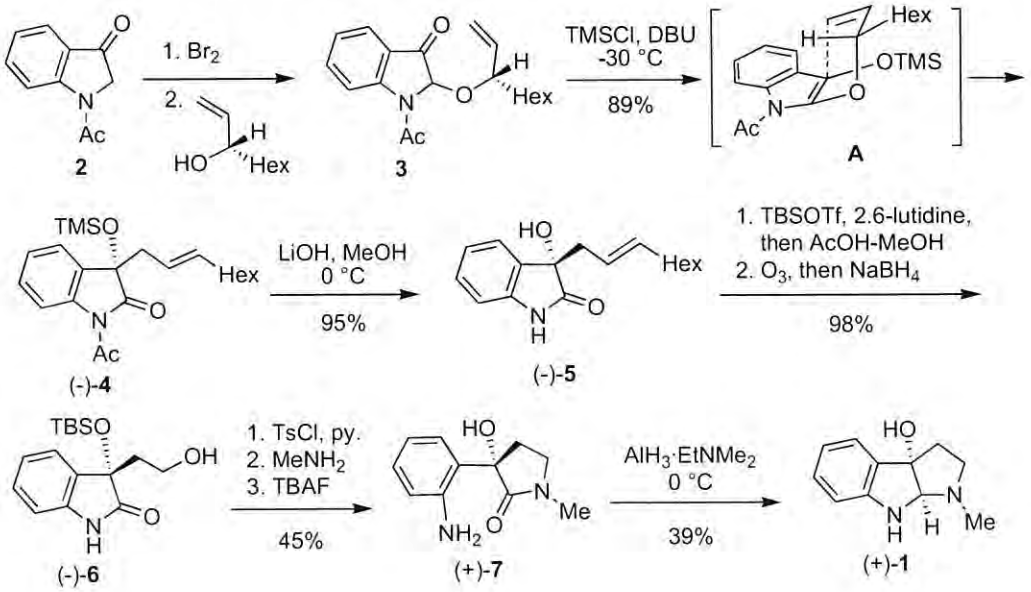
A number of 3a-hydroxy-pyrrolo[2,3-*b*]indoline alkaloids possessing interest biological activities have been isolated natural sources. Alline (1) was isolated from *Allium odora*, [1a] *A. senescens* and *A. anisoprodium*. [1b] The racemic compound 1 was synthesized by photosensitized oxidation of tryptamine prior to its isolation, [2] but its absolute configuration has been not determined yet. We presumed the absolute configuration of 1 ($[\alpha]_D$ +136.3°) [1a] to be 3a*S*,8a*R* by comparing with the specific rotation of (-)-physostigumine [3] and others, and tried the synthesis of (3a*S*,8a*R*)-1 via silyl-enolization/Claisen rearrangement of (3'*S*)-2-(1'-nonen-3'-yloxy)indolin-3-one 3.[4]

The indolin-3-one 3 was readily available by bromination of 1-acetylindolin-3-one 2 followed by substitution with (3*R*)-1-nonen-3-ol (99 %ee). Silyl-enolization/Claisen rearrangement of 3 took place smoothly at -20 °C via a chair-like transition state A to give (-)-3-(2'-nonenyl)-3-silylroxyindolin-2-one 4 (86 %ee). Hydrolysis of 4 with LiOH and *O*-TBS-silylation of (-)-5 followed by ozonolysis and $NaBH_4$-reduction produced the alcohol (-)-6 in high yield. *O*-Tosylation of (-)-6, substitution with methylamine and desilylation with TBAF provided (+)-1,3-aminoalcohol 7. Reduction of (+)-7 with $AlH_3{\cdot}EtNMe_2$ at 0 °C proceeded with cyclization to give alline (3a*S*,8a*R*)-(+)-1, of which the spectral data were identical with those of natural [1a] and synthetic products.[2] Since the optical rotation of both synthetic 1 and natural alline indicated dextrorotary, it is shown that natural alline (1) has also 3a*S*,8a*R*-configuration.



References:

1. (a) Tashkhodzhaev B, Samikov K, Yagudaev MR, Antsupova TP, Shakirov R, Yunusov SY, *Khim. Prirod. Soed.* 1985, 687-691. (b) Samikov K, Shakirov R, Antsupova TP, Yunusov SY, *Khim. Prirod. Soed.* 1986, 383.
2. Nakagawa M, Yoshikawa K, Hino T, *J. Am. Chem. Soc.* 1975, *97*, 6496-6501.
3. Marino JP, Bogdan S, Kimura K, *J. Am. Chem. Soc.* 1992, *114*, 5566-5572.
4. Kawasaki T, Takamiya W, Okamoto N, Nagaoka M, Hirayama T, *Tetrahedron Lett.*, 2006, 47, 5379-5382.

MP56

NEW AND SAFE FORMULATION OF HETEROCYCLIC DRUG ALONG WITH AMINO ACID: A MECHANISTIC APPROACH

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L- Tyrosine is a conditionally essential amino acid. In addition to being involved in protein synthesis. L-Tyrosine is a precursor for the synthesis of the Catecholamines epinephrine, norepinephrine and dopamine. Hydrochlorothiazide [6-chloro-3, 4-dihydro-2H-1, 2, 4-benzothiadiazine-sulfonamide1, 1-dioxide] is a sulphur and nitrogen containing heterocyclic having diuretic and antihypertensive activity. This belongs to the thiozolidine family, and shows the substitution reaction in the ring. It affects the distal renal tubular mechanism of electrolyte reabsorption. Hydrochlorothiazide increases excretion of sodium and chloride in approximately equivalent amounts. The present study has been made in two separate steps. In first step, solubility, dissolution and kinetic oxidation of drug by Vanadium (V) has been studied to understand the metabolic conversion in biological system. The first step is followed along with tyrosine in second step. The λ_{max} of drug was found at 272 nm. In the presence of 0.05% SLS drug shows complete dissolution within 30 min. In second case drug was oxidized with V(V) and kinetic parameters were obtained. Drug shows higher oxidation rate in the presence of amino acid. Activation parameters for overall reaction have been computed. Michaelis-Menton type of kinetics has been proposed.

MP57

SELECTIVE ALKYNYLATION OF BENZOTRIAZOLE USING ALKYNYLIODONIUM SALTS

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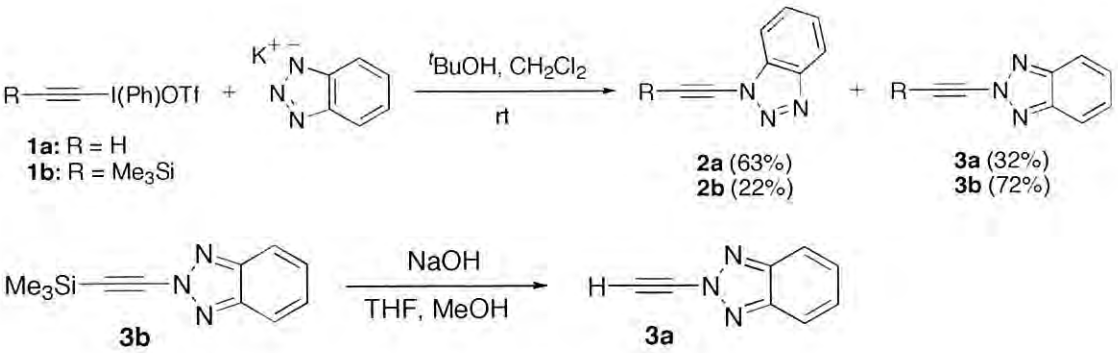
Some alkynyliodonium salts act as an alkynylating agent. A direct *N*-alkynylation of benzotriazole is generally difficult because the direct substitution at the triple bond of alkynes is a high energy process. Previously we have found that alkynylation of benzotriazole takes place selectively at the 1 position in the reaction with alkynyliodonium salts.[1] Here we report a regioselective alkynylation of benzotriazole using alkynyliodonium salts. By using this method, we have succeeded in the preparation of parent 1- and 2-ethynylbenzotriales.

Reaction of ethynyl(phenyl)iodonium triflate **1a** with benzotriazole ion in *tert*-BuOH and CH_2Cl_2 gave 1-ethynylbenzotriazole **2a** as a major product (63%). Although 2-ethynylbenzotriazle **3a** was formed in 32% yield, it was reasonably stable but partly decomposed during purification. Unexpectedly, the reaction of (trimethylsilylethynyl)iodonium triflate **1b** with benzotriazole ion gave 2-(trimethylsilylethynyl)benzotriazole **3b** as a major product (72%). Treatment of **3a** with NaOH in THF and MeOH gave pure 2-ethynylbenzotriazole **3a**. Thus, we have prepared 1- and 2-ethynylbenzotoriazoles **3a** and **3b** regioselectively.

Reactions of other substituted alkynyliodonium salts will be presented.



References:

1. Kitamura, T.; Tashi, N.; Tsuda, K.; Fujiwara, Y. *Tetrahedron Lett.*, 1998; 39, 3787-3790; Kitamura, T.; Tashi, N.; Tsuda, K.; Chen, H.; Fujiwara, Y. *Heterocycles*, 2000; 52, 303-312.

MP58

SYNTHETIC STUDY OF PHOTOCHEMICALLY REMOVABLE PROTECTING GROUPS

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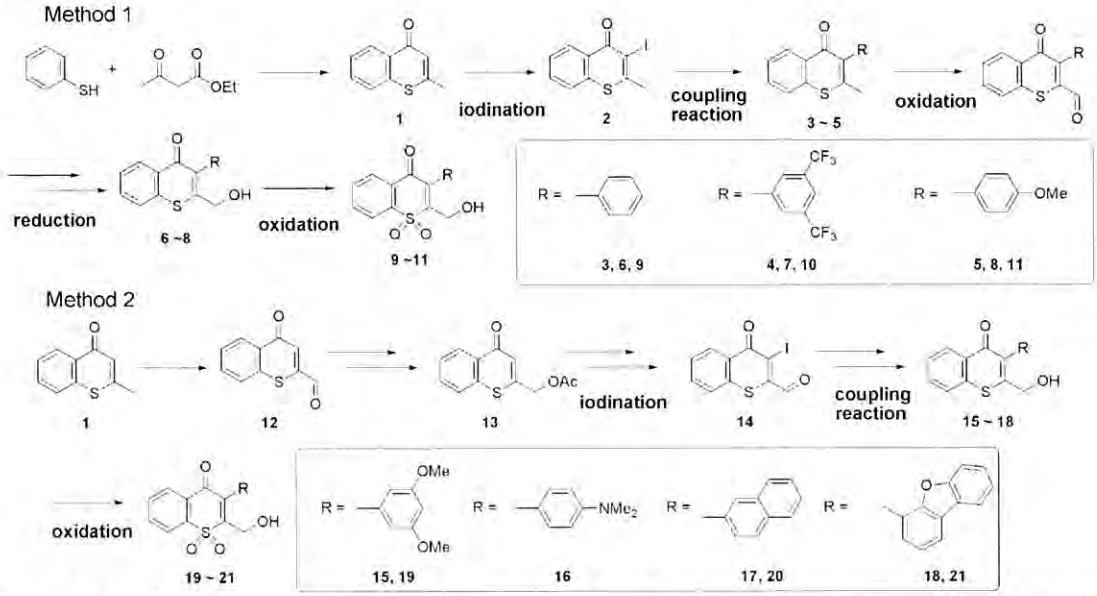
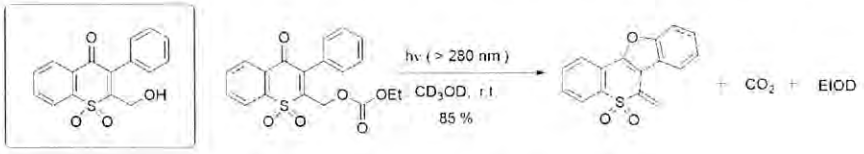
Photochemically removable protecting reagents have great potential in both synthetic and biological chemistry. The study of this type of protection has been increasing because of recent advances in solid-phase synthesis and combinatorial chemistry. For example, these protective groups are used to synthesize DNA microarray.[1] However the complete deprotection of the photolabile groups require a long period of irradiation. To overcome this problem, we envisaged a new efficient photolabile group, requiring a shorter deprotection time. Thiochromone derivatives contain a sulfur atom with a π conjugated system which expands over the bicyclic skeltone. This characteristic nature is similar to a coumaline compound, which has photodeprotection properties. To investigate the suitability of thiochromone compounds as candidates for photolabile groups, we designed and synthesized 11 series of thiochromone derivatives (scheme 1). Thiochromone compounds 6-8 were prepared from commercially available thiophenol and ethyl acetoacetate. Next oxidation of 6 -8 by *m* – CPBA gave sulfone derivatives 9 – 11 (Method 1). Thiochromone derivatives 15 – 18, 19 – 21 were prepared by another method (Method 2).

Scheme 1



We found that thiochromone derivatives were sensitive as photodeprotecting groups. NMR analysis showed that sulfone derivatives released EtOH after irradiation whith an ultra high-pressure mercury lamp (λ> 280 nm). However photodeprotection of corresponding sulfide derivatives did not occur, except for *p*-dimetylamino derivatives. Synthesis of thiochromone compounds as candidates for photolabile groups, including examination of the mechanism of photoreaction, are now in progress.



Reference:

1) McGall, G. H. et al, *J. Am. Chem. Soc.* 1997, *119*, 5081-5090

MP59

MOLECULAR REARRANGEMENT OF 1-SUBSTITUTED 9b-HYDROXY-3,3a,5,9b-TETRAHYDRO-1*H*-IMIDAZO[4,5-*c*]QUINOLINE-2,4-DIONES

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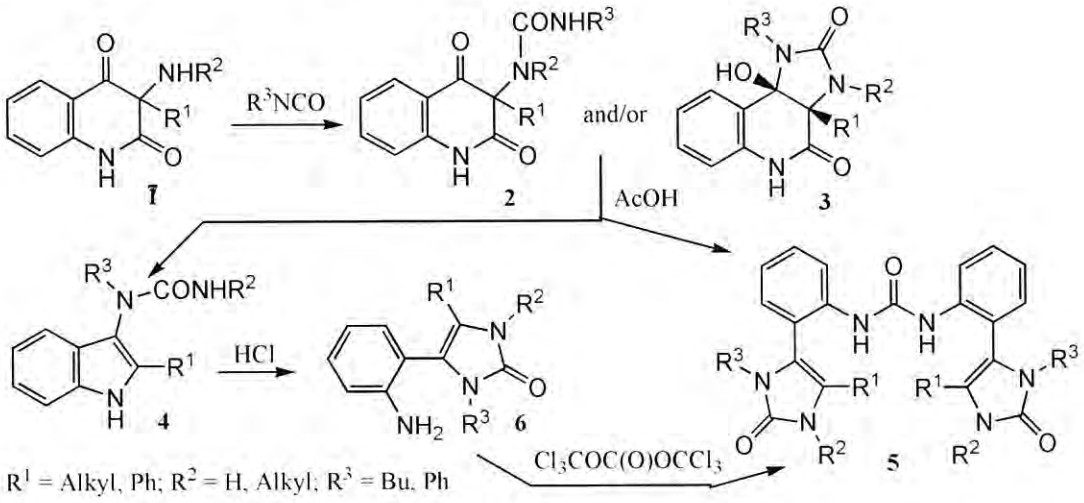
Recently, reaction of 3-amino-1*H*,3*H*-quinoline-2,4-diones with urea in boiling acetic acid has been described [1,2]. In dependence on the character of substitution in the starting compounds, four different types of rearranged compounds were obtained. Suggested reaction mechanism of this rearrangement [1,2] was confirmed by the synthesis and rearrangement of supposed reaction intermediates [3,4].
Continuing in this topic, we have prepared analogous 3′-substituted ureido derivatives 2 and their cyclic isomers 3 by the reaction of 1 with isocyanates [5]. In this communication, we describe the molecular rearrangement of these compounds.
Two types of reaction products have been isolated from the reaction of compounds 2 and 3 in boiling acetic acid: 3-ureidoindoles 4 and/or 1,3-diarylureas 5.



By the action of hydrochloric acid, the first of them rearrange to give 1,3-dihydroimidazol-2-ones 6. The structure of 1,3-bis[2-(2-oxo-2,3-dihydro-1*H*-imidazol-4-yl)-phenyl]-ureas (5) was confirmed by their synthesis from 6 and triphosgene. The proposal of the reaction mechanism of described reactions will be discussed.

Acknowledgements: This study was supported by the Ministry of Education of the Czech Republic (Grant No. MSM 7088352101) and The Czech Science Foundation (Grants No. 203/05/2106 and 203/07/0320).

References:

[1] Klásek A, Kořistek K, Lyčka A.Holčapek M. *Tetrahedron*, 2003; 59, 1283-1288.
[2] Klásek A, Kořistek K, Lyčka A., Holčapek M. *Tetrahedron* 2003; 59, 5279-5288.
[3] Klásek A., Lyčka A,; Holčapek M, Hoza I. *Tetrahedron* 2004; 60, 9953-9961.
[4] Klásek A., Lyčka A, Holčapek M, Kovář M, Hoza I. *J. Heterocyclic Chem.*2006; 43, 1251-1260.
[5] Klásek A, Lyčka A, Holčapek M, Hoza I. *J. Heterocyclic Chem.*2006, *43*, 203-211.

MP60

DIRECT CONSTRUCTION OF BICYCLIC HETEROCYCLES BY PD(0)-CATALYZED TANDEM CYCLIZATION OF PROPARGYLIC BROMIDES

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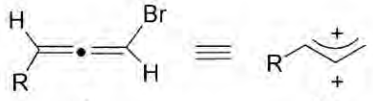
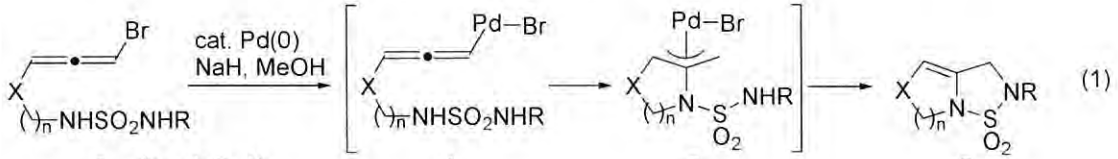
The development of efficient method for formation of carbon-nitrogen bonds constitutes an important area in organic chemistry. Such amination reactions have recently been greatly expanded including intramolecular reactions. Recently, we reported palladium(0)-catalyzed synthesis of medium-sized heterocycles based on our recent discovery that bromoallenes **1** can act as allyl dication equivalents **2** in the presence of a palladium catalyst and alcohol (Fig 1).[1-2] To apply and expand this novel reactivity of bromoallenes to synthesis of other useful heterocycles, we planned a preparation of cyclic sulfamides, an important class of compounds with pharmacological and chemical potentiality, by intramolecular diamination of bromoallenes containing a sulfamide functionality as dual nucleophilic moieties. As we expected, we found that tandem cyclization of various bromoallenes **3** directly affords bicyclic sulfamides **6** containing five- to eight-membered rings through η^3-allylpalladium intermediate **5** (eq 1).[3-4]



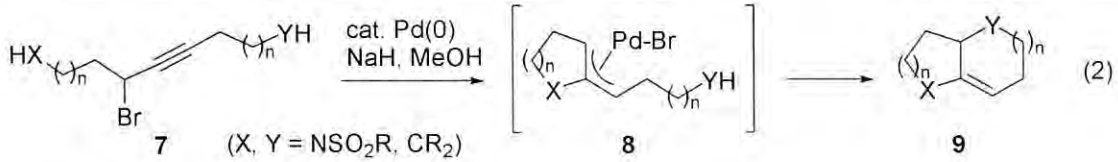
1 **2**

Fig.1 Allyl Dication Equivalents



3 (n = 1, 3, 4) **4** **5** **6** (1)

It is also well known that propargylic compounds are important substrates in synthetic organic chemistry. They possess similar reactivities to bromoallenes forming allenylpalladium complexes by oxidative addition to Pd(0) species. In this study, we planned tandem cyclization of bromoallenes and propargylic bromides having two nucleophilic moieties on each terminal carbon. Due to the difficulty in preparation of this type of bromoallenes, we investigated reactions of propargylic bromides **7** and succeeded in synthesizing bicyclic heterocycles **9** in the presence of palladium(0) through η^3-allylpalladium intermediate **8** (eq 2). The detail results of this novel tandem reaction will be presented.



7 (X, Y = NSO_2R, CR_2) **8** **9** (2)

References:
1) Ohno H.; Hamaguchi H.; Ohata M.; Tanaka T. *Angew. Chem., Int. Ed.*, 2003; *42*, 1749-1753.
2) Ohno H.; Hamaguchi H.; Ohata M.; Kosaka S.; Tanaka T. *J. Am. Chem. Soc.* 2004; *126*, 8744-8754. 3) Hamaguchi H.; Kosaka S.; Ohno H.; Tanaka T. *Angew. Chem., Int. Ed.*, 2005; *44*, 1513-1517. 4) Hamaguchi H.; Kosaka S.; Fujii N.; Ohno H.; Tanaka T. *Chem. Eur. J.*, 2007; *13*, 1692-1708.

MP61

NEW 1,2,3-DITHIAZOLE CHEMISTRY

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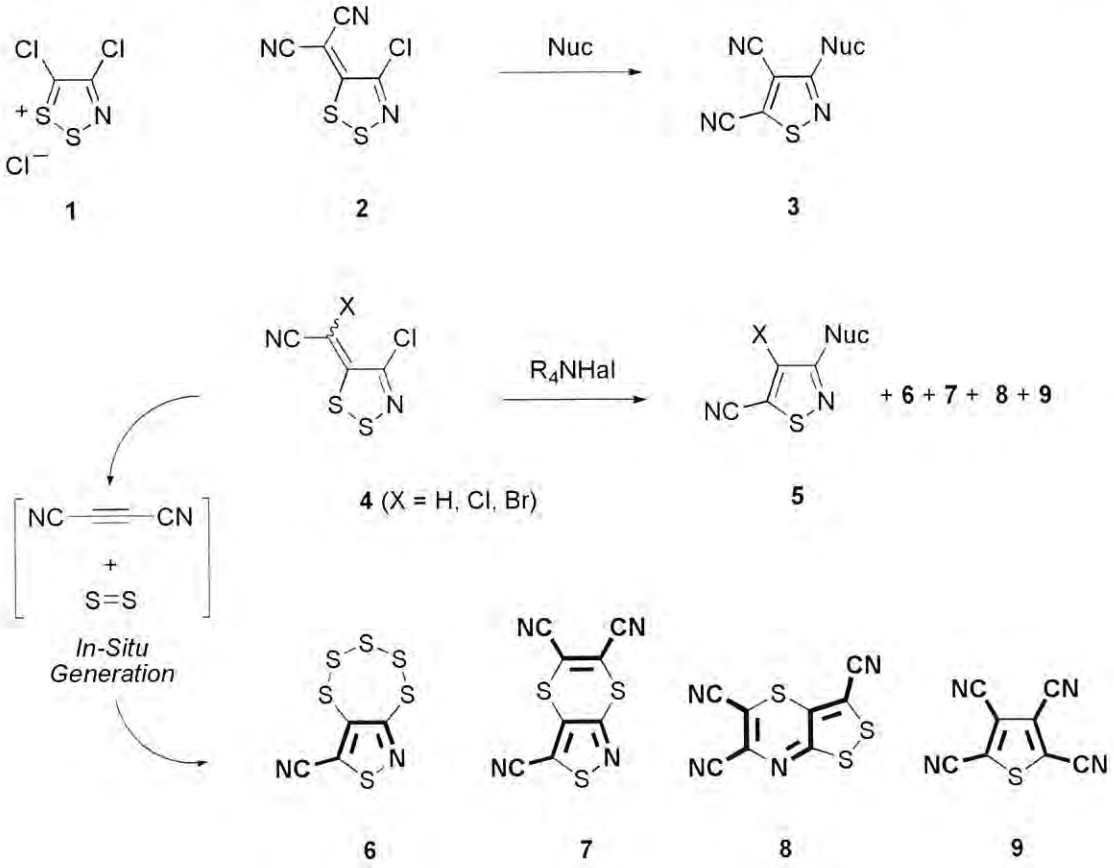
Treatment of 4,5-dichloro-1,2,3-dithiazolium chloride 1 (Appel salt) with malononitrile gave 2-(4-chloro-5*H*-1,2,3-dithiazole-5-ylidene)-propanedinitrile 2 which is readily transformed to isothiazole-4,5-dicarbonitriles 3 in the presence of nucleophiles or anhydrous HBr. During an investigation of the reaction mechanism and the overall scope of this transformation the dithiazolacetonitriles 4 (X = H, Cl, Br) were prepared and investigated with tetraalkylammonium halides. These compounds gave complex reaction mixtures from which only traces to moderate yields of the desired isothiazole-4,5-dicarbonitriles 5 could be isolated. Isolation and characterization of the by-products identified the presence of compounds 6 – 9. These can formally be obtained *via* multi-component cycloadditions between dicyanoacetylene and diatomic sulfur both of which could possibly be generated from the starting dithiazolacetonitrile itself. Treatment of dithiazolacetonitrile 4 (X = H) with triethylamine gave only compounds 6 – 9 and no trace of the desired isothiazole-4,5-dicarbonitrile 5. Further investigation of this reaction could lead to a convenient route for *in-situ* generation of dicyanoacetylene or substituted acetylenemonocarbonitriles from the readily available Appel salt 1.



1 2 3 4 (X = H, Cl, Br) 5 6 7 8 9

MP64

STUDIES TOWARDS THE TOTAL SYNTHESIS OF (±)-SELAGINOIDINE

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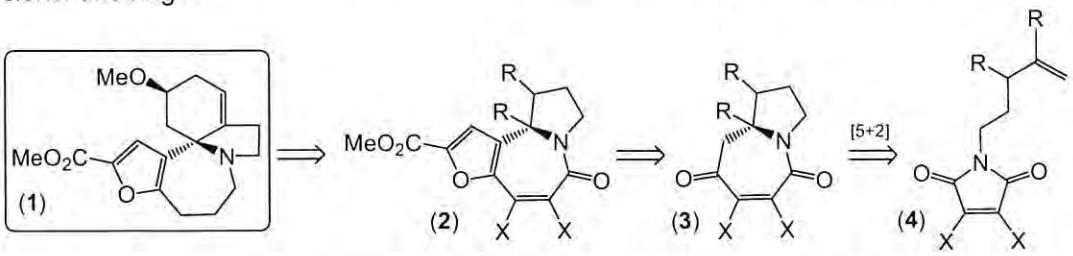
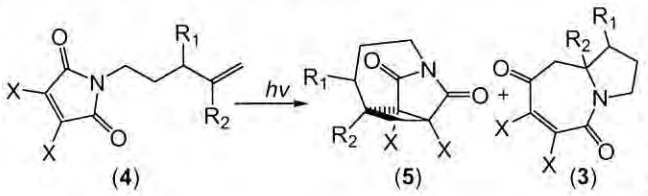
School of Chemistry, University Of Bristol, Bristol, BS8 1TS, UK.

(±)-Selaginoidine (1) is a member of the homoerythrina alkaloid family, a group that display a variety of pharmacological effects.[1] This poster describes the application of a [5+2] photocycloaddition[2] reaction in a synthetic strategy, aimed at completing the first total synthesis of Selaginoidine (1).

It was envisioned that (±)-Selaginoidine (1) could be accessed from the product of a [5+2] photocycloaddition (3), utilising appropriate R groups as handles for further elaboration to complete the cyclohexene ring.



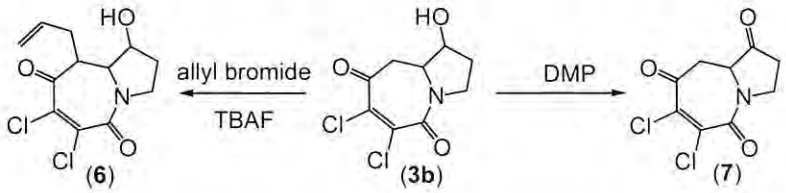
At the outset various *N*-alkenyl maleimides (4) were synthesised and following irradiation with UV light resulted in [5+2] (2) and [2+2] (3) photocycloadducts.



Examples

	X	R_1	R_2	Yield % (**5**)	Yield % (**3**)
a	Me	$=CH(CH_2)_3-$		56	0
b	Cl	OH	H	0	75
c	Me	$=CH_2$	$(CH_2)_2OTBS$	40	22

The optimal yield for the [5+2] reaction was achieved for 4b, providing alcohol 3b in a 75% yield. Maleimide 4b could be prepared easily on a multigram scale in a 3 step process from acrolein.



Alkylation of 3b proved challenging, requiring a range of bases to be screened. It was eventually prepared under mild conditions through alkylation upon allyl bromide with catalytic amounts of TBAF. Oxidation of 3b was also carried out in a 73 % yield.

I have developed a fast route to a key intermediate towards the synthesis of (±)-Selaginoidine (1). Current work is focussed on completing the synthesis of the final two rings.

References:

1. Tsuda, Y.; Sano, T. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: San Diego, CA, 1996; Vol. 48, p 249.
2. Booker-Milburn, K. I.; *Eur. J. Org. Chem.*, 2001, 1473.

MP65

INTER- AND INTRAMOLECULAR PALLADIUM-CATALYZED ALLYL CROSS-COUPLING REACTIONS USING IN SITU GENERATED ALLYLINDIUM FROM ALLYL ACETATES WITH INDIUM AND INDIUM TRICHLORIDE

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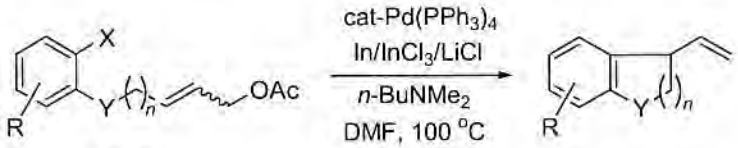
Inter- and intramolecular palladium-catalyzed allyl cross-coupling reactions using in situ generated allylindium from the reaction of allyl acetates with indium and indium trichloride in the presence of Pd(0) catalyst and *n*-$BuNMe_2$ in DMF were successfully demonstrated. Allylindiums in situ generated from reductive transmetalation of π-allylpalladium(II) complexes, in which were obtained from a variety of allyl acetates in the presence of Pd(0) catalyst, with indium and indium trichloride could be effective nucleophilic coupling partners in Pd-catalyzed cross-coupling reactions. A variety of allyl acetates such as 1-buten-3-yl acetate, crotyl acetate, and 2-methyl allyl acetate in cross-coupling reactions afforded the corresponding allylic compounds in good yields. Various electrophilic cross-coupling partners such as aryl iodides and vinyl bromides and triflates participate in these reactions. Not only intermolecular but also intramolecular Pd-catalyzed cross-coupling reactions work equally well to produce the desired allylic coupling products in good yields.



n = 1, 2, 3

X = Br, I, OTf

Y = $C(CO_2Et)_2$, $CHCO_2Et$, NTs, CH_2ONBoc, $CH_2C(CO_2Et)_2$
$CH_2C(SO_2Ph)_2$, $CH_2C(CN)_2$, $CH_2C(CO_2Et)(SO_2Ph)$

References:

1. Lee PH, Seomoon D, Lee K, Kim S. Kim H, Kim H, Shim E, Lee M, Lee S, Kim M, Sridar M. *Adv. Synth. Catal.* 2004; 346, 1641-1645.
2. Lee PH, Seomoon D, Lee K, Kim H. *Chem. Eur. J.* 2007; 13, in press.

MP66

THE INDIUM-MEDIATED SELECTIVE INTRODUCTION OF ALLENYL AND PROPARGYL GROUPS AT THE C4-POSITION OF 2-AZETIDINONES AND THE $AuCl_3$-CATALYZED CYCLIZATION OF 4-ALLENYL-2-AZETIDINONES

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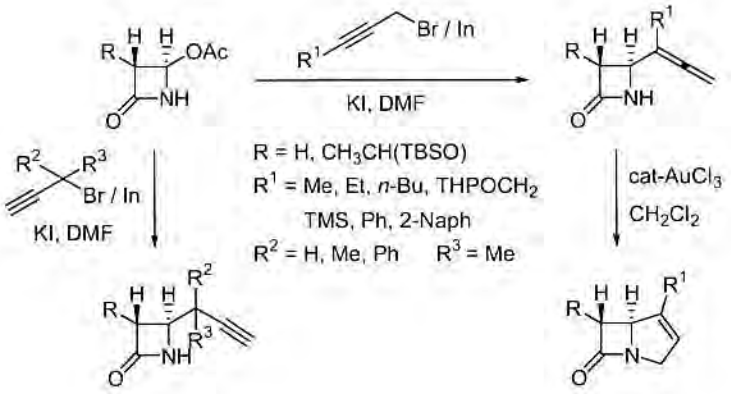
Reaction of 4-acteoxy-2-azetidinones with organoindium reagents generated in situ from indium and γ-substituted propargyl bromides in the presence of KI in DMF selectively produced 4-allenyl-2-azetidinones in good to excellent yields. α-Substituted propargyl bromides and indium selectively gave 4-propargyl-2-azetidinones. 4-(1'-Substituted allenyl)-2-azetidinones were treated with 5 mol% gold trichloride in dichloromethane to produce the bicyclic β-lactams in good yields.



References:
Lee PH, Kim H, Lee K, Kim M, Noh K, Kim H, Seomoon D. *Angew. Chem. Int. Ed.* 2005; 44, 1840-1843.

MP67

PALLADIUM-CATALYZED ALLYL CROSS-COUPLING REACTIONS OF IN SITU GENERATED ALLYLINDIUM REAGENTS WITH ORGANIC ELECTROPHILES

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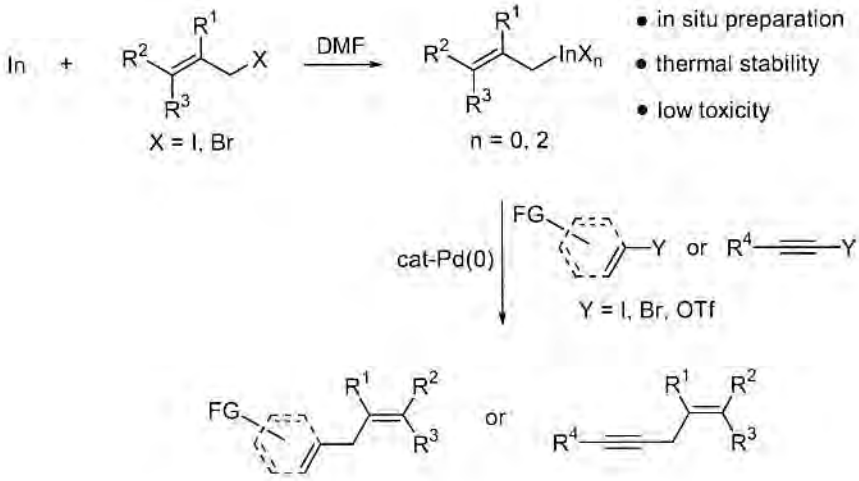
Inter- and intramolecular palladium-catalyzed allyl cross-coupling reactions using in situ generated allylindium from allyl halides with indium were successfully demonstrated. In situ generated allylindiums could be effective nucleophilic coupling partners in Pd-catalyzed cross-coupling reactions. A variety of allyl halide such as allyl iodide, allyl bromide, crotyl bromide, prenyl bromide, geranyl bromide, and 3-bromocyclohexene in cross-coupling reactions afforded the corresponding allylic compounds in good yields. Stereochemistry of double bond is retained for the allylic cross-coupling reaction. Various electrophilic cross-coupling partners such as aryl and vinyl halides, dibromoolefin, alkynyl iodide, and aryl and vinyl triflates participate in these reactions. The presence of various substituents such as *n*-butyl, ketal, acetyl, ethoxycarbonyl, nitrile, *N*-phenyl amide, nitro, and cholride group on the aromatic ring of electrophilic coupling partners showed little effect on efficiency of the reactions. The present conditions work equally well not only intermolecular but also intramolecular Pd-catalyzed cross-coupling reactions. This method provides efficient synthetic method for the introduction of allyl group to sp^2- and *sp*-hybridized carbon, which can be easily further functionalized. The present method complements existing synthetic methods as a result of advantageous features such as easy preparation and handling, thermal stability, high reactivity and selectivity, operational simplicity, and low toxicity of allylindium reagents.



References:

1. Lee PH, Sung SY, Lee K. *Org. Lett.* 2001; 3, 3201-3204.
2. Lee K, Lee, J. Lee PH. *J. Org. Chem.* 2002; 67, 8265-8268.

MP68

NTERNAL ALKENE HYDROAMINATIONS CATALYZED BY ZIRCONIUM (IV) COMPLEXES AND ASYMMETRIC HYDROAMINATIONS CATALYZED BY YTTRIUM(III) COMPLEXES

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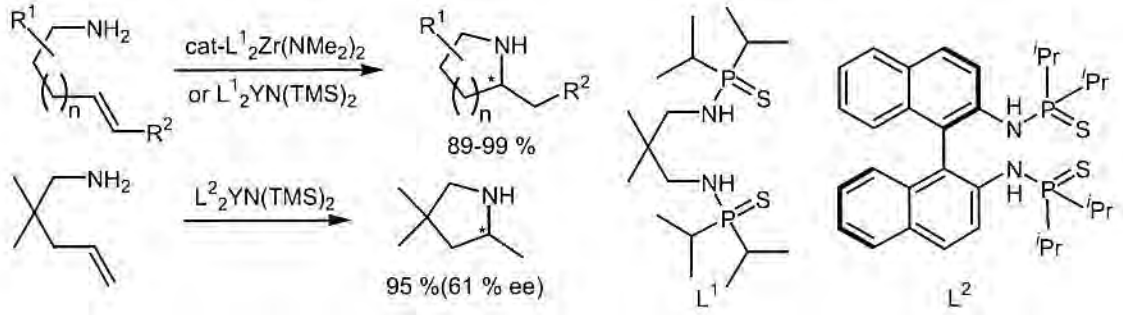
The neutral Zr(IV) complex obtained from NPS proligand and zirconium *via* elimination of dimethylamine has been shown to be an effective precatalyst for intramolecular alkene hydroaminations that provide cyclic amines in good to excellent yields. A variety of chiral ligands were prepared for asymmetric internal alkene hydroaminations. Treatment of aminoalkene with 5 mol% precatalyst derived from metalation of (*R*)-binaphthyl diamine-based NPS ligand to $Y[N(TMS)_2]_3$ produced 2,4,4-trimethylpyrrolidine in 95% yield (61% ee).



References:
1. Kim H, Lee PH, Livinghouse T. *Chem. Commun.* 2005, 5205-5207.
2. Kim H, Kim YK, Shim JH, Kim M, Han M, Livinghouse T, Lee PH. Lee PH, *Adv. Synth. Catal.* 2006; 348, 2609-2618.
3. Kim H, Livinghouse T, Shim JH, Lee SK, Lee PH. *Adv. Synth. Catal.* 2006; 348, 701-704.

MP69

THE SERENDIPITOUS SYNTHESIS OF 6-HYDROXYISATINS

Julie M. Locke,[a] Kara L. Vine,[b] Marie Ranson,[b] Stephen G. Pyne,[a] and John B. Bremner[a]

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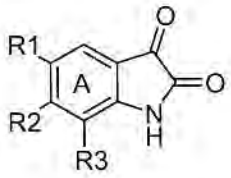
Isatin and its derivatives form a large family of compounds that exhibit a wide range of biological properties including cytotoxic and antineoplastic activities.[1] Previous work in our group has shown that the *in vivo* cytotoxicity (IC_{50}) of isatin (1a) against a number of human cancer cell lines improves with increasing bromination of ring A[2] (1b-d) and is also significantly enhanced by *N*-alkylation.

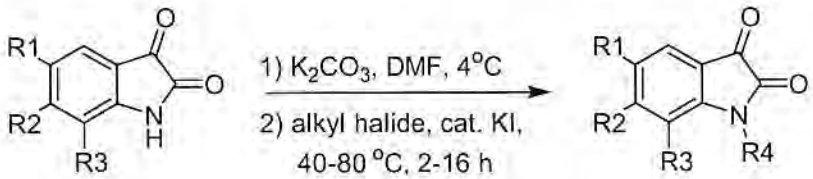


1

Cytotoxicity of Isatin Derivatives:

Compound	R1	R2	R3	IC_{50} (μM)[3]
1a	H	H	H	565
1b	Br	H	H	64.5
1c	Br	Br	H	11.6
1d	Br	Br	Br	6.7

The synthesis of *N*-alkylated isatins from 1 can be accomplished using the straightforward method shown below.[4] This poster will discuss the synthesis and cytotoxic activities of some 6-hydroxy-*N*-alkylisatin derivatives (2, R2 = OH) that form as side-products from an unanticipated S_NAr reaction occurring under relatively mild conditions.



1 **2**

References:
1. Da Silva, JFM, Garden, SJ, Pinto, AC, *J Brazil. Chem. Soc.*, 2001, 12(3), 273-324.
2. Vine, KL, Locke, JM, Ranson, M, Pyne, S, Benkendorff, K, Bremner, JB, *Bioorg. Med. Chem.*, 2007, 15, 931-938.
3. The cytotoxicity of isatins against U937 (human monocyte-like, histiocytic lymphoma) cells determined using dose-response curves. The alues shown are a mean of triplicate of at least two independent experiments.
4. Torres, JC, Pinto, AC, Garden, SJ, Tetrahedron, 60, 2007, 9889-9900.

MP70

ASYMMETRIC BENZYLATION WITH PLANAR-CHIRAL PHASE-TRANSFER CATALYSTS HAVING A DIBENZ[*E,G*]ISOINDOLINIUM UNIT

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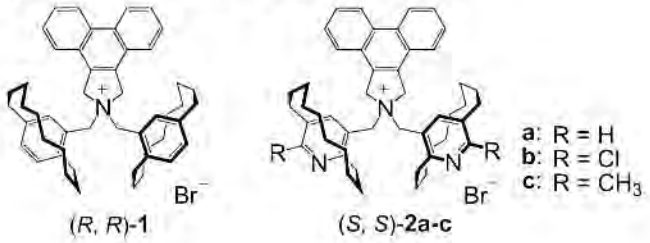
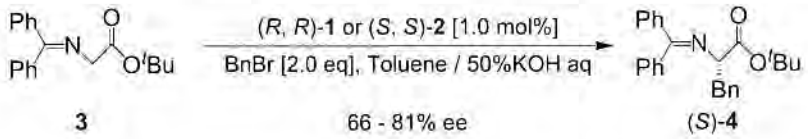
Asymmetric alkylation of glycine derivatives has been regarded as a representative reaction to evaluate efficiency of phase-transfer catalysis with various organocatalysts. A number of chiral quaternary ammonium salts have been developed thus far to demonstrate usefulness of such enantioselective reagents represented by cinchona alkaloid catalysts[1)] and binaphthyl-modified spiro-type catalysts.[2)] However planar-chiral phase-transfer catalysts have not been reported yet in literature, although planar-chiral compounds have been widely used as potent chiral derivatizing agents.

We have previously designed planar-chiral phase-transfer catalysts (PTCs) having pyridinophane and cyclophane moieties on a 2,3-dihydro-1*H*-benz[*d,e*]isoquinoline unit and have demonstrated that catalytic asymmetric benzylation of glycine derivative 3 proceeded to give the corresponding phenylalanine derivative 4 with moderate enantioselectivity (up to 69% *ee*). For exploring further effective catalysts, we have synthesized novel planar-chiral PTCs incorporating either two planar-chiral cyclophanes or pyridinophanes on a nitrogen atom of dibenz[*e,g*]isoindoline such as catalyst 1 or 2. Planar-chiral PTCs (*R, R*)-1 and (*S, S*)-2a-c were synthesized from dibenz[*e,g*]isoindoline by the reaction with two equiv amounts of bromomethyl-substituted [10]paracyclophane or [10]parapyridinophanes. The catalytic phase-transfer reaction with the cyclophane catalyst, (*R, R*)-1, effected asymmetric benzylation of 3, which afforded the product (*S*)-4 with moderate enantiomeric excess of 66% *ee*. On the other hand, reactions of the pyridinophane-type catalysts, (*S, S*)-2a-c, showed higher enantioselectivitles of 71-81% *ees* in the asymmetric benzylation reactions. These results indicate that the planar-chiral cyclophanes and pyridinophanes on a dibenz[*e,g*]isoindolinium moiety are potentially useful chiral catalysts for enantioselective PTC reactions.





Scheme 1. Catalytic asymmetric benzylation with (*R, R*)-**1** and (*S, S*)-**2a-c**

References:

1) Jew S., Jeong B. Yoo M., Huh H., Park H. *Chem. Commun.*, 2001; 1244-1245.

2) Kitamura M., Shirakawa S., Maruoka K. *Angew. Chem. Int. Ed.*, 2005; 44, 1549-1551.

MP71

OXIDATIVE ALKYLAMINATION OF AZINES VIA NUCLEOPHILIC AROMATIC SUBSTITUTION OF HYDROGEN USING $AgPy_2MnO_4$ AS OXIDANT.

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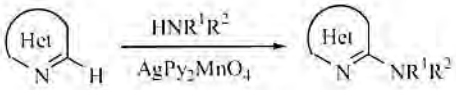
Benjamin J. Van der Veken and Bert U. W. Maes

Organic Synthesis, Department of Chemistry, University of Antwerp, Groenenborgerlaan 171, B-2020 Antwerp, Belgium

The interest in nucleophilic aromatic substitution of hydrogen seriously increased in the last decades due to the important advantage that this methodology does not require any preliminary introduction of a good leaving group into the aromatic substrate [2]. While oxidative amination of azines with KNH_2 / NH_3 / $KMnO_4$ or NH_3 / $KMnO_4$ is well studied, the corresponding oxidative alkylamination with alkylamine / $KMnO_4$ has remarkably received only little attention. Interestingly, the majority of the limited number of published examples on oxidative alkylamination deal with methylamination. Reports on the use of other alkylamines are surprisingly scarce. Our laboratory discovered that the oxidative alkylamination of several azines including 3-nitropyridine, quinazoline and 1,3,5-triazine proceeds with a wide range of primary and secondary alkylamines via nucleophilic substitution of hydrogen when $AgPy_2MnO_4$ is used as oxidant [3,4]. While for some substrates (e.g. 3-nitropyridine) and alkylamines $KMnO_4$, the standard oxidant for oxidative amination, gives moderate to good results it is completely useless for reactions with other substrates (e.g. quinazoline). $AgPy_2MnO_4$ seems to be a general and superior oxidant for oxidative alkylamination on all the azines studied, independent of the alkylamine used. Based on DFT calculations and ^1H NMR measurements theoretical insight has been gained for the difference in performance between $KMnO_4$ and $AgPy_2MnO_4$ on the different substrates.



HNR^1R^2 = primary or secondary alkylamine

[1] On leave from the Southern Federal University Russian Federation. [2] Chupakhin ON, Charushin VN, van der Plas HC, *Nucleophilic Aromatic Substitution of Hydrogen*, Academic Press, San Diego, 1994. [3] Gulevskaya, AV; Maes, BUW; Meyers, C; Herrebout, WA; Van der Veken, BJ, *Eur. J. Org. Chem.* 2006; 5305-5314. [4] Gulevaskaya, A; Maes, BUW; Meyers, C, *Synlett* 2007; 71-74.

MP72

SYNTHESIS OF 5,6,11,12-TETRAHYDRODIBENZO[*b,f*][1,5]DIAZOCINES AND THEIR REACTIONS WITH ALDEHYDES AND KETONES TO GIVE FUNCTIONALISED TRÖGER'S BASE ANALOGUES

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Due to its concave shape and chiral nitrogens, Tröger's base (TB) (Fig. 1) is of great interest in areas such as host-guest chemistry,[1] molecular tweezers[2] and catalysis.[3] We foresee that access to a diverse range of functional groups on the bridge of TB will be most useful for the development of these potential applications. Hence, we would like to report the preparation of several TB analogues bearing different functional groups attached to the bridge, an area of TB research which has been given little attention.[4-6]

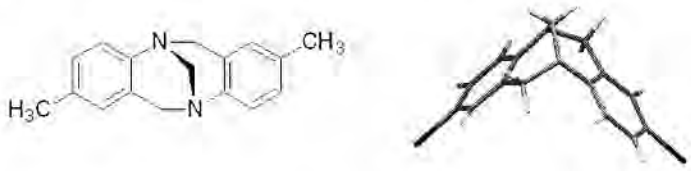
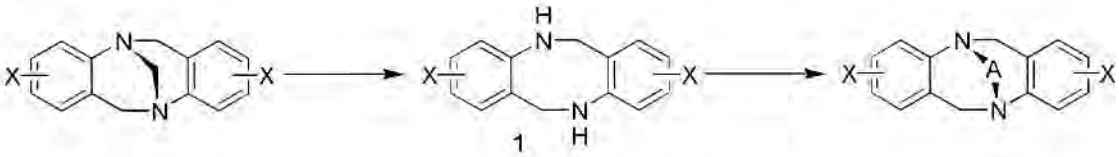


Figure 1. A representation of Tröger's base and a 3D representation of a 2,8-dibromo analogue illustrating the cavity.

The general synthetic approach used here for making alterations to the bridging unit of TB is outlined in Scheme 1 and a very efficient approach for the synthesis of 5,6,11,12-tetrahydrodibenzo[*b,f*][1,5]diazocines (1) has been employed.[7] With the aid of microwave chemistry a number of TB molecules bearing bridges derived from sterically hindered ketones have also been prepared.



Scheme 1

Introduction of new bridges derived from chiral aldehydes has been used to aid resolution of the TB analogues through the generation of diastereomers.

References:

(1) Goswami S.; Ghosh K.; Dasgupta S. *J. Org. Chem.* 2000, *65*, 1907-14.
(2) Harmata M. *Acc. Chem. Res.* 2004, *37*, 862-873.
(3) Herrmann W.; Kuhn F.; Mattner M.; Artus G.; Geisberger M.; Correia.; J. *J. Organomet. Chem.* 1997, *538*, 203-209.
(4) Cooper F. C.; Partridge M. W. *J. Chem. Soc.*, 1955, 991-4.
(5) Greenberg A.; Molinaro N.; Lang M. *J. Org. Chem.* 1984, *49*, 1127-1130.
(6) Johnson R. A.; Gorman R. R.; Wnuk R. J.; Crittenden N. J.; Aiken J. W. *J. Med. Chem.* 1993, *36*, 3202-3206.
(7) Harmata M.; Kahraman M. *Tetrahedron: Asymmetry* 2000, *11*, 2875-2879.

MP74

A NEW ADENINE RECEPTOR: DESIGN, SYNTHESIS AND CHARACTERISATION

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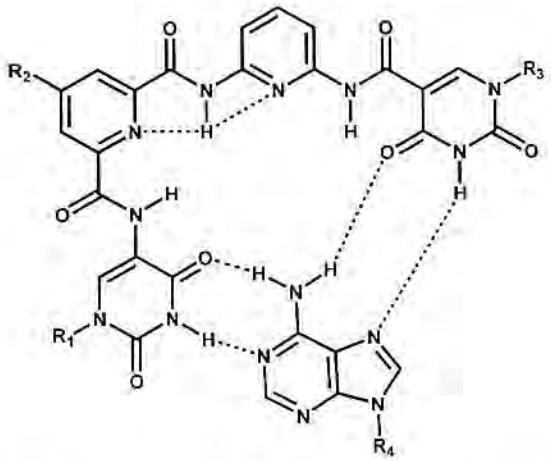
Precise recognition of nucleobases is essential for biologically significant functions such as genome duplication, protein synthesis and signal transduction. Heterocycles with multiple hydrogen bonding sites have gained much attention for their utility in host-guest chemistry. A new planar adenine receptor[1, 2] has been designed and synthesized to simultaneously bind the Watson-Crick and Hoogsteen sites.

A DNA sequence is called "sense", if its sequence is copied by these enzymes and then translated into protein. The sequence on the opposite strand is complementary to the sense sequence and is therefore called the "antisense" sequence. Antisense DNA oligomers can enter the cell where they can pair with, and so inactivate, complementary mRNA sequences. Insertion of this new receptor into an oligonucleotide is expected to improve the antisense effect. [3]

Insight into the complementary binding of Adenine in non-polar solvent and in oligonucleotide will be discussed.



Adenine Base non-covalently bonded via Watson Crick and Hoogsteen Bonds to the receptor

References:

1. Deslongchamps G., Galan A., de Mendoza J., Rebek J., *Angew. Chem.* 1992, 104, 58-61
2. Hisamatsu Y, Hasada K, Wasada-Tsutsui Y., *Chem. Eur. J.* 2006, 12, 7733-7741
3. Wagner RW., Flanagan WM. *Mol. Med. Today* 1997,31-38

MP75

TOTAL SYNTHESIS OF LUOTONIN A AND 14-SUBSTITUTED ANALOGUES

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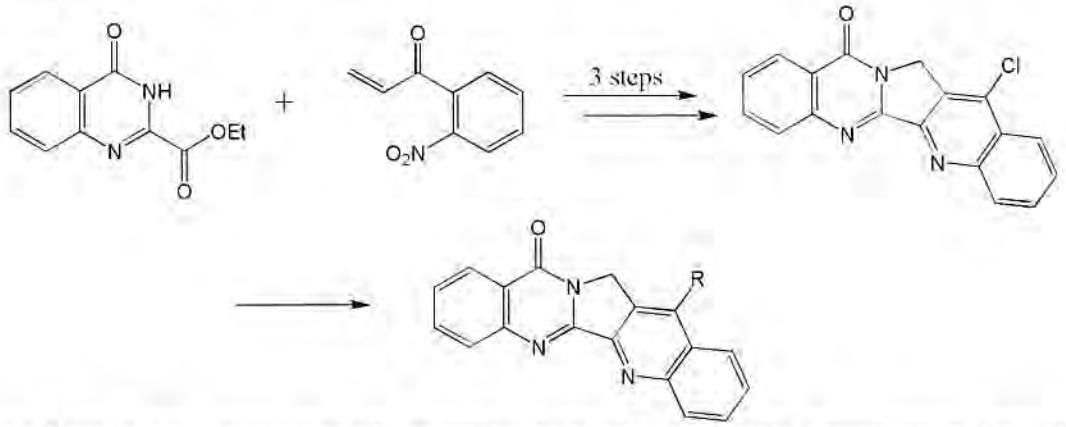
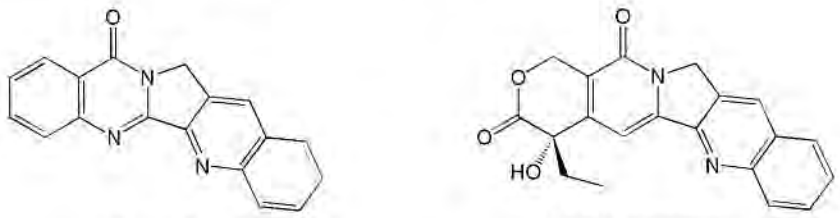
Department of Biosciences and Nutrition
Unit of Organic Chemistry

A new and practical synthetic route for the preparation of luotonin A has been developed in a four step procedure with a 79 % overall yield. Coupling of the known compounds ethyl 4-oxo-3,4-dihydroquinazoline-2-carboxylate and 1-(2-nitrophenyl)prop-2-ene-1-one generated 14-chloroluotonin A in three steps. Several new 14-substituted luotonin A analogues were prepared using 14-chloroluotonin A as the key intermediate.



Luotonin A has a close association with another natural product, namely, camptothecin. Both of these compounds display topoisomerase I inhibition, but biological uptake is limited, due to poor solubility.[1] Analogues of camptothecin are currently used as treatments for colorectal cancer and several other compounds are in clinical trials against other cancers.[2]



luotonin A

20-(*S*)-camptothecin

Synthetic techniques for producing luotonin A compounds are currently limited to a few described routes.[3] Our new method allows an efficient route to the preparation of the 14-substituted analogues of luotonin A.

References:

[1] Ma Z.-Z; Hano Y; Nomura T and Chen Y-J, *Heterocycles*, 1997, 46, 541-546; M. E. Wall, M. Wani C, Cook C. E, Palmer K. H, McPhail A. T and Sim G. A, *J. Am. Chem Soc.*, 1966, 88, 3888-90.
[2] Soepenberg O, Sparreboom A and Verweij J, Clinical Studies of Camptothecin and Derivatives, in *The Alkaloids*, Cordell G. A, Ed.; Vol 60, p 1-50, Elsevier, Amsterdam, 2003.
[3] Ma Z.-Z; Hano Y; Nomura T and Chen Y.-J, *Heterocycles*, 2005, 65, 2203-2219, and refs. therein; Bowman W. R, Elsgood M. R. J, Stein T and Weaver G. W, *Org. Biomol.Chem.*, 2007, 5, 103-113; Michael J. P. *Nat. Prod. Rep.*, 2007, 24, 223-246, and refs. therein.

MP77

SYNTHESIS OF CRYPTOSANGUINOLENTINE BY REACTION OF INDOLE-2,3-DICARBOXYLIC ANHYDRIDE WITH ANILINES

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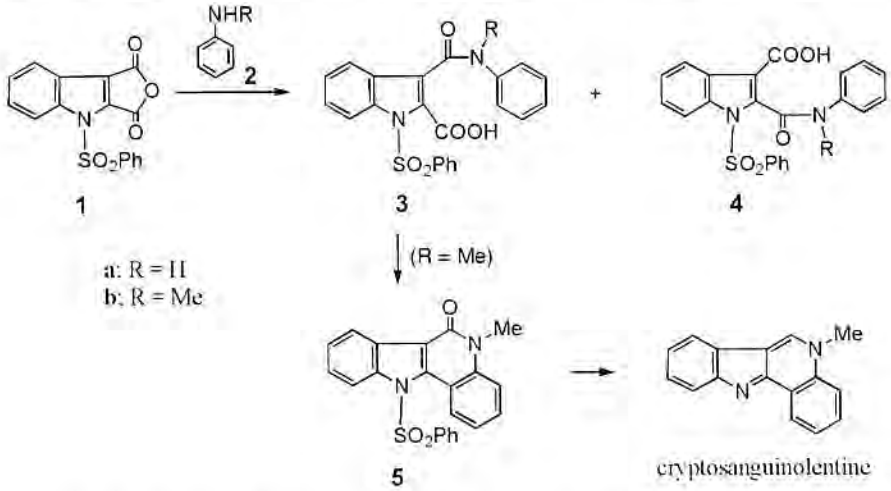
Cryptosanguinolentine (isocryptolepine), isolated from a West African plant *Cryptolepis sanguinolentia* in 1996,[1] is a member of indoloquinoline alkaloids (benzo-γ-alkaloids), which showed antiplasmodial properties. Molina reported a useful synthesis of cryptosanguinolentine by Red-Al reduction of benzo-γ-carbolinone derivative, which was prepared from cyclization of azide compound, but some difficulties faced in preparation of benzo-γ-carbolinone derivative by using azide compound.[2] Mérour showed an excellent synthesis of benzo-γ-carbolinone derivatives by Heck cycliztion of *N*-(2-iodophenyl)indole-3-carboxamide prepared from indole-3-carboxylic acid and 2-iodoaniline.[3] Recently, we have shown that indole-2,3-dicarboxylic anhydride (1) was a useful synthon in the synthesis of olivacine[4] and caulersin.[5] Here, we report a synthesis of cryptosanguinolentine by reaction of indole-2,3-dicarboxylic anhydride with anilines.

Reaction of 1-(benzenesulfonyl)indole-2,3-dicarboxylic anhydride (1) with aniline (2a, R = H) at room temperature gave 2-carbamoylindole-3-carboxylic acid (4a) as a sole product, but 3-carbamoylindole-2-carboxylic acid (3a) was not found. However, Treatment of 1 with *N*-methylaniline (2b, R = Me) in dichloromethane afforded a mixture of 3-carbamoylindole-2-carboxylic acid (3b) and 2-carbamoylindole-3-carboxylic acid (4b) (3b : 4b = 2 : 3), but in acetonitrile 2b was isolated as a major product (3b : 4b = 3 : 1). Decarboxylative Heck-type cyclization of 3b was performed by treatment with $Pd(OCOCF_3)_2$ (20 mmol%)[6] and Ag_2CO_3 in DMSO and DMF at 80°C to give a mixture of 11-benzenesulfonyl-5-methylindolo[3,2-*c*]-quinoline (5) and the corresponding decarboxylation product in 45% and 24% yields, respectively. 5 could be converted by reduction with $LiAlH_4$ in hot dioxane to cryptosanguinolentine in high yield.



References

1) Sharaf, M. H. M.; Schiff, P. L.; Tackie, A. N.; Phoebe, C. H.; Martin, G. E.; *J. Heterocycl. Chem.*, 1996, *33*, 239-243.
2) Fresneda, P. M.; Molina, P. M.; Delgado, *Tetrahedron*, 2001, *57*, 6197-6702.
3) Mouladdib, A.; Joseph, B.; Hasnaoui, A. Mérour, J. *Synthesis*, 2000, 549-556.
4) Miki, Y.; Tsuzaki, Y.; Hibino, H.; Aoki, Y. *Synlett.*, 2004, 2206-2208.
5) Miki, Y.; Aoki, Y.; Miyatake, H.; Minematsu, T.; Hibino, H., *Tetrahedron Lett.*, 2006, *47*, 5215-5218.
6) Tanaka, D; Myers, G., *Org. Lett.*, 2004, *6*, 433-436.

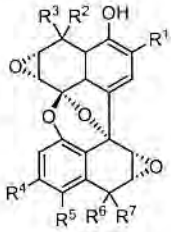
MP78

SYNTHETIC STUDIES ON BISNAPHTHOSPIROKETAL ANTIBIOTICS, SPIROXINS

Kazuyuki Miyashita,[1,2] Chizuru Moriyama,[1] Shigeaki Fujiyoshi,[1] Takayuki Sakai[1] and Takeshi Imanishi[1]

1 Graduate School of Pharmaceutical Sciences, Osaka University
2 Faculty of Pharmacy, Osaka Ohtani University

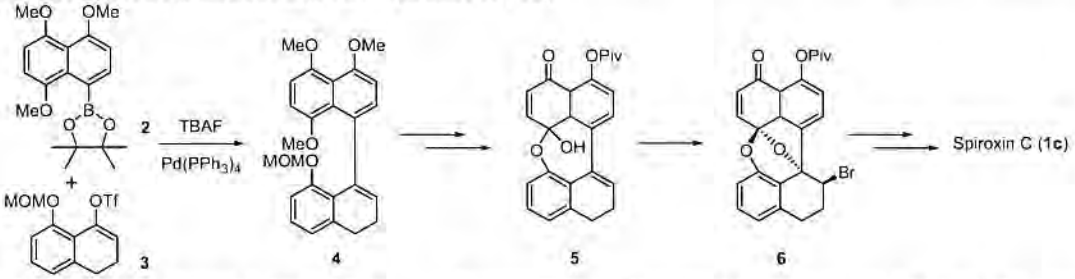
Spiroxins A-E (1a-e) were obtained from fungus isolated from a soft orange coral collected in Vancouver Island, Canada in 1999, and were shown to have a unique bisnaphthospiroketal structure as a basic skeleton. A major component, spiroxin A (1a) was reported to show antibacterial and antitumor activities, the mechanism of which was suggested to be due to its single-stranded DNA cleavage activity. We were interested in and started synthetic study on these natural products. Here, we show total synthesis of racemic spiroxin C (1c) and synthetic study of spiroxin A (1a).



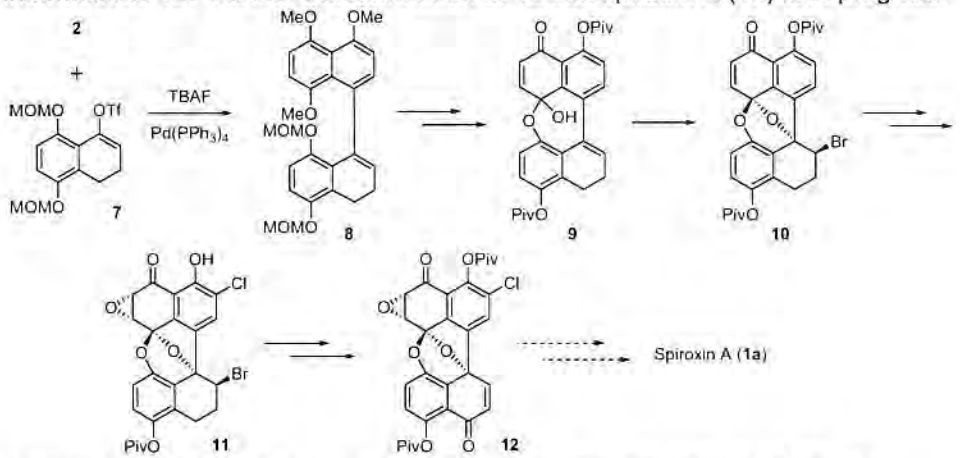
Spiroxins (1)

A (**a**): R^1 = Cl, R^2,R^3 = O, R^4 = H, R^5 = OH, R^6,R^7 = O
B (**b**): R^1 = Cl, R^2,R^3 = O, R^4 = Cl, R^5 = OH, R^6,R^7 = O
C (**c**): R^1 = H, R^2,R^3 = O, R^4 = R^5 = H, R^6,R^7 = O
D (**d**): R^1 = H, R^2 = OH, R^3 = R^4 = R^5 = H, R^6,R^7 = O
E (**e**): R^1 = Cl, R^2,R^3 = O, R^4 = Cl, R^5 = OH, R^6 = OH, R^7 = H

Total synthesis of racemic spiroxin C[1] At first, we found that Suzuki-Miyaura cross-coupling reaction of 2 with 3 in the presence of TBAF was effective for the synthesis of binaphthyl derivative 4. After several steps, bromoetherification of 5 successfully furnished 6 having the desired basic skeleton, which was transformed into spiroxin C (1c).



Synthetic study on racemic spiroxin A Encouraged by the results above, we applied the synthetic strategy to the synthesis of spiroxin A (1a). Employing 7 having an oxygen function at the suitable position, binaphthyl 8 was obtained by the same Suzuki-Miyaura cross-coupling reaction. After transformation into hemiacetal 9, bromoetherification proceeded similarly to yield 10, Regioselective introduction of chlorine was also successfully carried out to afford 11, which was converted into a key intermediate 12. Further transformation of 12 into spiroxin A (1a) is in progress.



References: 1) Miyashita, K.; Sakai, T.; Imanishi, T. *Org. Lett.* 2003, 5, 2683-2686.

MP79

ANTI-ULCER SCREENING AND TOXICITY TEST FOR SCHIFF BASE OF INDOLE DERIVATIVES

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[2]Department of Molecular Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.

Schiff base compounds were synthesized from indole derivatives via refluxing in acidic ethanol for two hours. Metal complexes of those ligands were also synthesized from Cu (II), Zn (II) and Ni (II) in basic ethanol and they were refluxed for five hours. These ligands and complexes are characterized via several spectroscopic means to ensure the purity and structures. Anti-ulcer screening on high and low doses (250mg/kg and 62.5mg/kg, respectively) was done on six albino Sprague-Dawley rats that had been induced ulcer by absolute ethanol. The ulcer lesion area of the stomachs were identified and counted. Toxicity test was carried out for 28 day involving the negative control, high dose, low dose and positive control which was given current anti-ulcer drug.

References:

Liss, R.H., Letourneau, R.J. & Schepis, J.P. Digestive Diseases and Sciences, 1986; 31, 108S-114S.
Kamel, G., Akila, G., Smain, A. & Seddik, K. Pharmacological Research, 1999; 39, 151-156.
Jamal, A., Javed, K., Aslam, M. & Jafri, M.A. Journal of Ethnopharmacology, 2006; 103, 149-153.
Tan, P.V., Nditafon, N.G., Yewah, M.P., Dimo, T. & Ayafor, F.J. Journal of Ethnopharmacology, 1996; 54, 139-142.
Gul, W. & Hamann, M.T. Life Sciences, 2005; 78, 442-453.
Higashio, Y. & Shoji, T. Applied Catalysis A: General, 2004; 260, 251-259.

MP80

AN ASSESSMENT OF METHODS FOR PREDICTING THE ABSORPTION AND FLUORESCENCE WAVELENGTHS OF HETEROCYCLIC DYES

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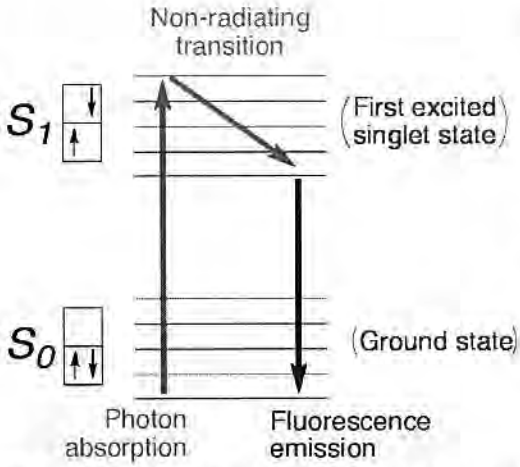
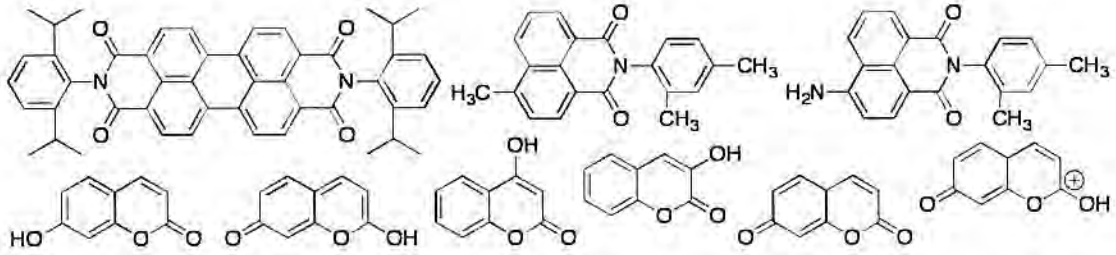


There is a growing demand for fluorescent dyes for use in basic research areas such as genomics, proteomics and medical diagnosis. Ideally, these dyes have high extinction coefficients, large Stokes shifts, and high fluorescence quantum yields. Using computations we are not only able to predict the absorption maxima of dyes, but we can also predict fluorescence emission maxima. Hence we can design new dye moities, identifying compounds that have the desired optical properties without the need to enter into a tedious process of trial and error in the laboratory.

Therefore, starting with a selection of model systems (see Figure inset) that may serve as design leads for the development of novel fluorophores for biotechnology applications, we are conducting a broad computational exploration of industrially important fluorescent dyes and stains. However, as an initial step, the accuracy of several electronic structure methds (*e.g.*, density functional theory, wave function theory, semi-empirical theory) has been assessed when applied to the prediction of dye absorption and fluorescence wavelengths. Herein, we report our preliminary findings using TD-DFT.



MP81

FACILE ROUTES TO 1,2,4-TRIAZOLO-[3,4-b][1,3,4]THIADIAZINES AND 1,2,4-TRIAZINO-[3,4-b][1,3,4] THIADIAZINE BY HETEROPOLYACIDES

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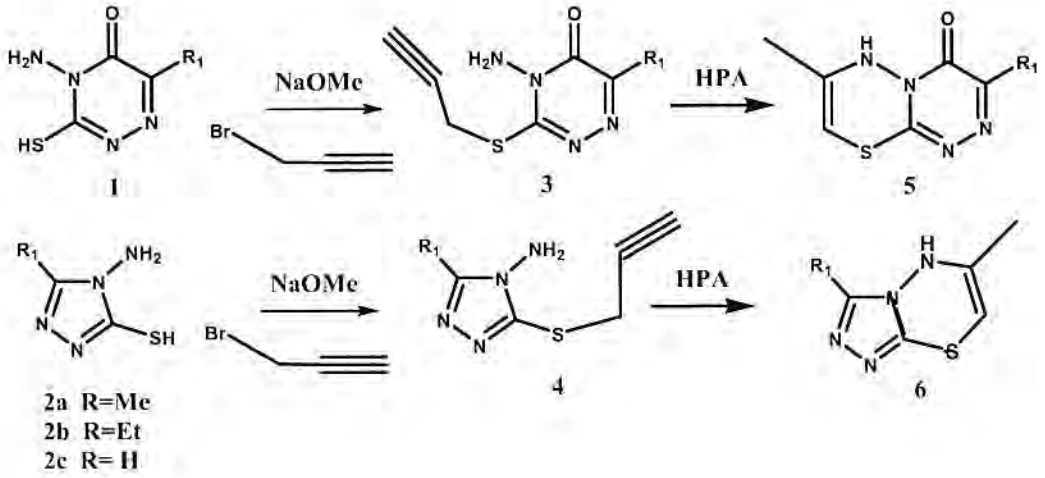
1,2,4-triazolo[3,4-b][1,3,4]thiadiazines and 1,2,4-triazino[3,4-b][1,3,4]thiadiazines constitute two classes of compounds interesting from view points of chemical reactivity [1] and biological activity[2]. Due to their importance, the synthesis of these compounds have interested for discovery of improved protocols towards milder and high yielding approaches. We have recently reported the preparation of 1,2,4- triazolo[3,4-b][1,3,4]thiadiazines by refluxing 4 in dimethylsulfoxide for 5 min and in presence of Lithium hydride as a base by 60% yiled [3]. We have also described The use of Pd-salt for catalyzed intramolecular cyclization and functionalization of acetylenes [4]. Armed with these experiences, we have reported cyclization of compound 3 with a catalytic amount of $PdCl_2(PhCN)_2$ by reflux in acetonitrile for 6 hours (40% yield)[5] . In continuation of our attempts to develop selective and preoperatively useful methodology, based on using various heteropolyacids as green catalysts in various organic reactions [6], here in we wish to report a rapid and convenient method for synthesis of these compounds. Our findings indicate that heteropolyacids HPA catalysts are effective for synthesis of 1,2,4-triazolo[3,4-b][1,3,4]thiadiazines and 1,2,4-triazino[3,4-b][1,3,4]thiadiazines with high yield.



References:
[1] a) F. P. Invidiata, G. Furno, L. Lampronti, D. J. Semoni, *Heterocyclic Chem.* 2001, 34, 1255-1258. b) N. D. Heindel, J. R. Reid, *Org. Prep. Proced. Int.*, 1981, 13, 123-135 (CA 9543055). c) V. K. Chadha, *J. Indian Chem. Soc.*, 1978, 55, 817-819.
[2] a) F. P. Invidiata, S. Grinaudo, P. Grammanco, L. Grammanco, *Farmaco*,, 1991, 46, 1489-1492. b) A. M. M. E. Omar, O, M. Aboulmafe, *J. Heterocyclic Chem.*, 1986, 23, 1339.
[3] M. M. Heravi, M. Rahimizadeh, M. Seyf, A. Davoodnia and M. Ghassemzadeh, *Phosphorus, Sulfur and Silicon*, 167, 211 (2000).
[4] M. M. Heravi and Bakavoli, , *J. Chem. Res.*, 11, 480 (1995).
[5] M. M. Heravi and P. Khosrofar, *J. Sci. I. R. Iran*, 7(2), 86(1996).
[6] a) M. M. Heravi, F. Derikvand, F .F. Bamoharram, J. Mol. Catal. A Chem. 242 (2005) 173; b) M. M. Heravi, R. Motamedi, N. Seifi, F. F. Bamoharram, J. Mol. Catal. A Chem.249(2006) 1; c) M. M. Heravi, R. Motamedi, N. Seifi, F. F. Bamoharram, Catal.Commun Inpress(2006); d) F. F.Bamoharram, M. M. Heravi, M. Roshani, A. Gharib, M. Jahangir, Appl. Catal. A: Gen. 302 (2006) 42; e) F. F.Bamoharram, M. M. Heravi, M. Roshani, N.Tavakoli, J. Mol. Catal., A: Chem. 252 (2006) 219; f) M. M. Heravi, F. Derikvand, F. F.Bamoharram, J. Mol. Catal. A Chem.253 (2006) 16. g) M. M. Heravi, Kh. Bakhtiari, F. F. Bamoharram, Catal.Commun., 7(2006) 499.

MP82

REGIO-SELECTIVITY IN CYCLIZATION OF C^2-SUBSTITUENTS ON INDOLES : CYCLIZATION TO 6- OR 7- MEMBERED RING

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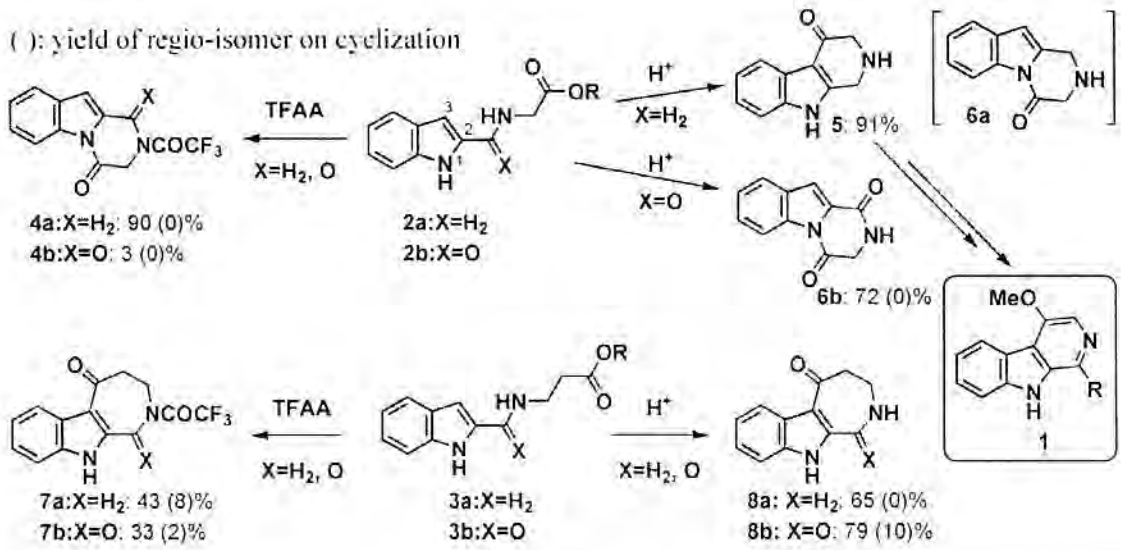
Recently, α- or β- fused pyridoindole and azepinoindole derivatives were reported as interesting biologically active compounds. We have developed[1] the synthesis of 4-oxygenated β-carbolines 1 using C^3-selective cyclization of the C^2-substituent of N^1-unprotected indole 2a. On the course of the study, we have found[2] that the substrate 2b cyclized to N^1-position. The regio-selectivity of the cyclization seemed to depend on the substrate structures and the reaction conditions.
In this poster, we will present the precise studies of the regio-selectivity of the cyclization of 2 to 6-membered ring (pyridoindole) and 3 to 7-membered ring (azepinoindole). Treatment of 2a,b with TFAA gave N^1-cyclized products 3a,b as main products in each case. On the other hand, acid (CH_3SO_3H or PPA) treatment of 2b also gave N^1-cyclized product 6b as a main product, whereas the reaction of 2a,b under the same condition gave C^3-cyclized product 5 as a main product. The unexpected formation of 5 should be explained as follows. The N^1-cyclized product 6a was clearly obtained on TLC in the initial stage of the reaction and then disappeared. Thus, 6a was once formed kinetically, and then the rearrangement occurred thermodynamically to to give 5.
On the 7-membered ring closure system, the substrates 3a,b gave C^3-cyclized products 7a,b and 8a,b as main products in each case (with TFAA or acids).
We will discuss these interesting regio-selectivity in cyclization between 6- and 7-memberd ring systems and the reaction mechanisms.



References:
(1) Suzuki, H.; Adachi, M.; Ebihara, Y.; Gyoutoku, H.; Furuya, H.; Murakami, Y.; Okuno, H. *Synthesis*, 2005; 28-32.
(2) Suzuki, H.; Shinpo, K.; Yamazaki, T.; Niwa, S.; Yokoyama, Y.; Murakami, Y. *Heterocycles*, 1996; 42, 83-86.

MP83

A NEW SYNTHETIC ROUTE TO (±)-HIRUSTENE AND (±)-1-DESOXYHYPOPHILIN USING SAMARIUM(II)-INDUCED SEQUENTIAL REACTIONS

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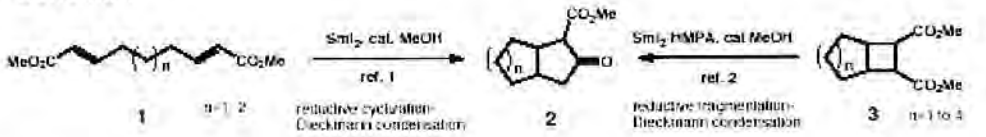
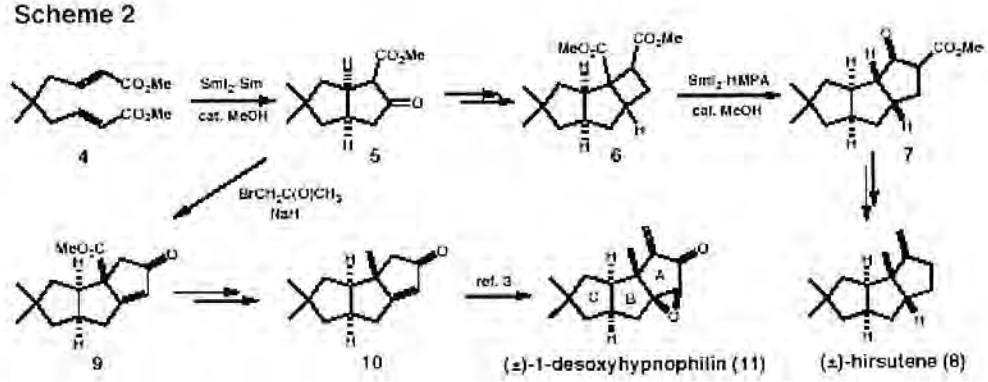
Samarium(II) iodide (SmI2) is effective reagent for the formation of C-C bond and considerable attention has been focused on various types of SmI2-induced reactions. During the studies on SmI2-promoted intramolecular cyclizations, two kinds of efficient reactions for the production of bicyclic ketones were found: 1) a sequential reductive cyclization-Dieckmann condensation of bis-α,β-unsaturated esters **1** with SmI2 in the presence of catalytic amount of methanol to provide cyclopentanone **2** (n=1, 2); 1 2) a ring expansion reaction of 1,2-cyclobutanedicarboxylate **3** with SmI2-HMPA to provide **2** (n=1 to 4)2 (Scheme 1). We choose hirsutene as a synthetic target, which is typical member of triquinane sesquiterpene, to show the synthetic utility of these reactions. Here we wish to describe a new synthetic route to (±)-hirsutene which involves SmI2–induced sequential reactions, **4** to **5** and **6** to **7**, as key steps as shown in Scheme 2. (±)-1-Desoxyhypnophilin (**11**) was also synthesized from common precursor **5** via rapid transformation of **5** into triquinane ring system **9** and reductive conversion of **9** into **10**.

Scheme 1



Scheme 2



1) Shinohara, I., Okue, M., Yamada, Y., Nagaoka, H. *Tetrahedron Lett.* **2003**; *44*, 4649-4652.
2) Shinohara, I., Nagaoka, H. *Tetrahedron Lett.* **2004**; *45*, 1495-1498.
3) Harrowven, D. C., Lucas, M. C., Howes, P. D. *Tetrahedron* **2001**, *57*, 9157-9162.

MP84

SYNTHESIS AND EVALUATION OF BITHIENYLPYRIDINES AS ANALYTICAL REAGENTS FOR FLUOROMETRIC DETERMINATION

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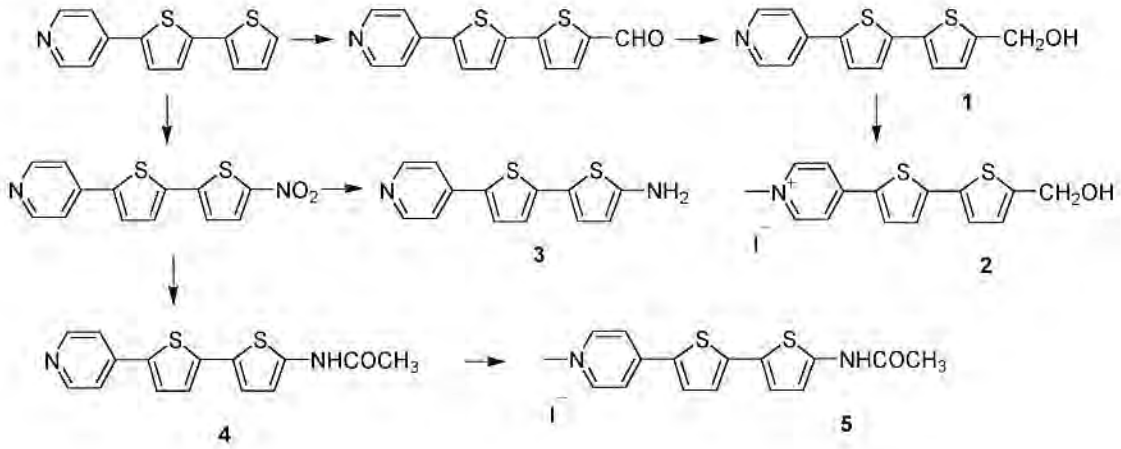
5'-(4-Pyridyl)-2-(5,2'-bithienyl)methanol (1), 5'-[4-(1-methylpyridinio)]-2-(5,2'-bithienyl)methanol iodide (2), and 4-(5-amino-2,2'-bithienyl-5'-yl)pyridine (3) were synthesised as new fluorescent labeling reagents for capillary electrophoresis of carboxylic acids as follows.



Reagents 1 and 2 reacted with carboxylic acids in the presence of DCC under microwave irradiation for 6 min to give the stable and strongly fluorescent corresponding esters. In the case of reagent 1, the esters of six fatty acids (acetic, butylic, hexanoic, octanoic, decanoic, and dodecanoic acids) were satisfactorily separated and were sensitively detected at 450 nm with excitation at 360 nm. Linear detection ranges and detection limits of these acids were 6.9×10^{-7} —5.0×10^{-5} M and 6.9×10^{-7}—5.0×10^{-6} M (S/N =3), respectively. In the case of reagent 2, the esters of eighteen fatty acids (formic, acetic, propionic, butylic, pentanoic, hexanoic, heptanoic, octanoic, nonionic, decanoic, undecanoic, dodecanoic, tridecanoic, tetradecanoic, pentadecanoic, hexadecanoic, heptadecanoic, and octadecanoic acids) were satisfactorily separated and were sensitively detected at 520 nm with excitation at 400 nm. Linear detection ranges and detection limits of these acids were 3.0×10^{-8}—5.0×10^{-5} M and 3.0×10^{-8}—2.8×10^{-7} M (S/N =3), respectively.
Reagent 3 reacted with carboxylic acids and aldehydes in the presence of DCC under microwave irradiation for 6 min to give the corresponding stable and strongly fluorescent esters and Schiff's bases. Linear detection ranges and detection limits of eight fatty acids (butylic, hexanoic, octanoic, decanoic, dodecanoic, tetradecanoic, hexadecanoic, and octadecanoic acids) were 9.4×10^{-8}—5.0×10^{-6} M and 9.4×10^{-8}—3.0×10^{-7} M (S/N =3), respectively.
The synthesis and fluorescence properties of the other some bithienylpyridine derivatives including compounds 4 and 5 will be discussed.

MP85

FACILE ONE-POT SYNTHETIC ROUTES TO FUSED TETRAHYDROPYRIMIDINES

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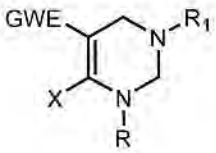
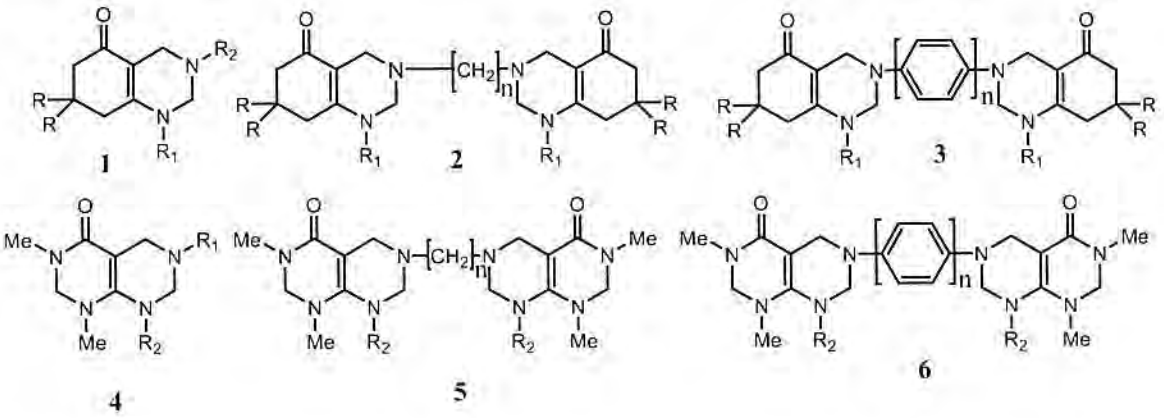
Analogues of 5-Nitro-1,2,3,4-tetrahydropyrimidines[1,2] are known to possess potential insecticidal & pestcidal properties. However, 1,2,3,4-tetrahydropyrimidines having other electron withdrawing groups in position 5 of the ring were not known in the literature and hence their bioactivities remained unexplored. Prompted by these facts, we have reported facile one-pot synthetic strategies for novel tetrahydropyrimidines[3-6] of the following type.



In the present oral presentation, we would like to disclose short-cut syntheses of hitherto unreported fused & bis-fused tetrahydropyrimidines of general formula 1, 2, 3, 4, 5 & 6, biological properties of which are under investigation.



References:

1. Urbanska HD, Kartitzky AR & Urbanski T, *Tetrahedron*, 1969, 25, 1617-1628.
2. Sone M, Tominaga Y, Matsuda Y & Kobayashi G, *Yakugaku Zassi*, 1977, 97, 262.
3. Karim K, Kishore K & Vishwakarma JN, *J Heterocyclic Chem*, 2003, 40, 901-903.
4. Chanda K, Dutta MC, Karim E & Vishwakarma JN, *J Heterocyclic Chem*, 2004, 41, 627-631.
5. Dutta MC, Chanda K & Vishwakarma JN, *J Heterocyclic Chem.*, 2005, 42, 121-123.
6. Chanda K, Dutta MC, Hellissey P & Vishwakarma JN, *J Heterocyclic Chem*, 2005 42, 975-978.

MP86

ONE-POT SYNTHESIS OF INDOLIZINE AND 2-AZAINDOLIZINE DERIVATIVES BY OXIDATION OF 2-CYANOMETHYL- AND 2-AMINOMETHYL-PYRIDINES

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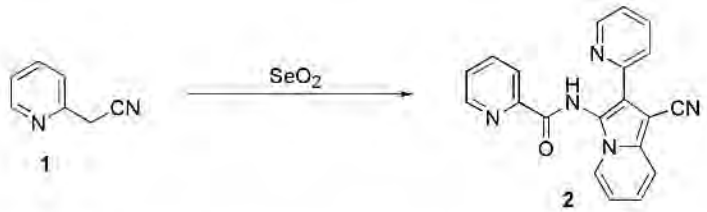
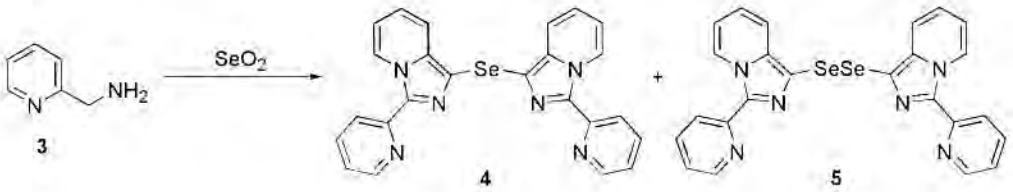
Indolizine and 2-azaindolizine skeletons are much interesting because of their possible utilities as pharmaceutics and as ligands for the development of new catalysts. Recently, we have investigated the oxidation reaction of 2-aminometylpyridine for the synthesis of 2,3,5,6- tetra-(2-pyridyl)pyrazine where the molecular oxygen was used as oxidant.[1] During the course of studying the work, we have found that selenium dioxide is a convenient oxidant for synthesizing heterocyclic skeletons such as indolizine and 2-azaindolizine.
When 2-cyanomethylpyridine (1) was reacted with two equivalents of selenium dioxide, indolizine derivative (2) was obtained as colorless crystals.



When 2-aminomethylpyridine (3) was reacted with excess amounts (3 eq.) of selenium dioxide, 2-azaindolidine derivatives, (4) and (5), were obtained. Especially, diselenide (5) is interesting since symmetrical diheterocyclic diselenides are used in biomimetic studies on anti-thyroid drugs and thyroid hormone synthesis.[2]



Complexation of (2), (4), and (5) were also carried out, and their structures were determined on the data of X-ray structural analysis.

References:
1) Okamoto Y., Ogura K., Kinoshita T. Polyhedron, 1984; 3,635-638. Ogura K., Kurasawa Y., Yamaguchi Y., Okamoto Y. *Heterocycles*, 2003; 59, 283-291.
2) Roy G., Nethaji M., Mugesh G. *J. Am. Chem. Soc.*, 2004; 126, 2712-2713.

MP89

EFFICIENT SYNTHESIS OF 1,3-DISUBSTITUTED 1,2-DIHYDROISOQUINOLINES BY CARBOPHILIC LEWIS ACID-CATALYZED TANDEM NUCLEOPHILIC ADDITION AND CYCLIZATION OF *ORTHO*-ALKYNYLARYALDIMINES

Shingo Obika,[a] Hideki Kono,[a] Yoshizumi Yasui,[a] Reiko Yanada[b] and Yoshiji Takemoto[a,*]

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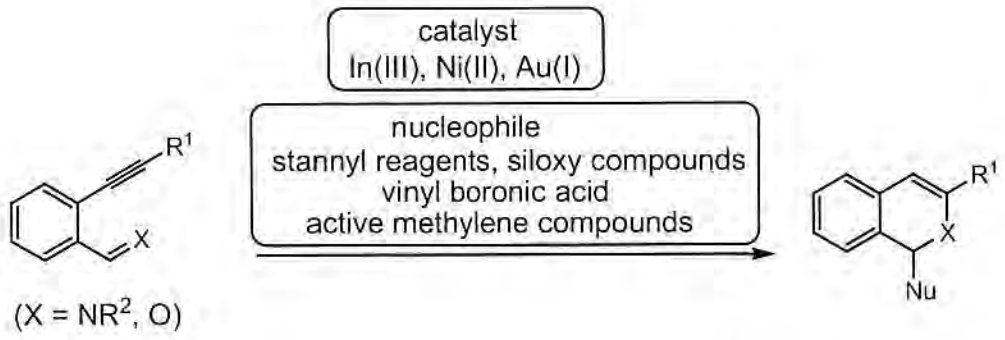
Dihydroisoquinoline is known a useful skeleton in organic synthesis and many total syntheses of natural alkaloids have been achieved using the 1,2-dihydroisoquinolines as synthetic intermediates. Consequently, a number of elegant approaches for the synthesis of the 1,2-dihydroisoquinolines have been developed and Reissert-type reaction of isoquinoline derivatives is one of the representative methods for 1-substituted 1,2-dihydroisoquinolines. In contrast to 1-substituted 1,2-dihydroisoquinolines, there are yet a few convenient methods for 3-substituted and 4-substituted 1,2-dihydroisoquinolines, because most of the reported methods for the aimed compounds require multi-step process.

Based on these backgrounds, our interest was directed towards the concise construction of 3-substituted 1,2-dihydroisoquinoline ring system. In this presentation, we described the convenient synthesis of such dihydroisoquinolines using soft Lewis acid-catalyzed tandem nucleophilic addition and cyclization reaction of *ortho*-alkynylarylaldimine. In this reaction, carbophilic Lewis acid catalysts such as In(III), Ni(II), and Au(I) were found to nicely activate the C-C triple bond and promote 6-*endo* mode cyclization accompanied with introduction of various nucleophiles into the C1 position. Furthermore, this method was also applicable to the synthesis of 1*H*-isochromenes via the same tandem reaction of 2-alkynylarylaldehydes.



References:
1) Yanada, R.; Obika, S.; Kono, H.; Takemoto, Y. *Angew. Chem. Int. Ed.* 2006, *45*, 3822-3825.

MP91

ASYMMETETRIC SYNTHESIS OF *anti*-1,2-AMINO ALCOHOLS: A FORMAL SYNTHESIS OF (-)-SWAINSONINE AND TOWARDS THE TOTAL SYNTHESIS OF HYACINTHACINE B_3

Christopher W. G. Au and Stephen G. Pyne

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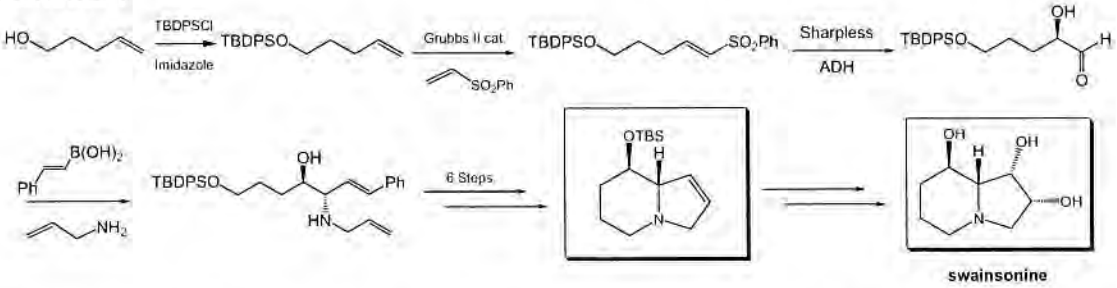
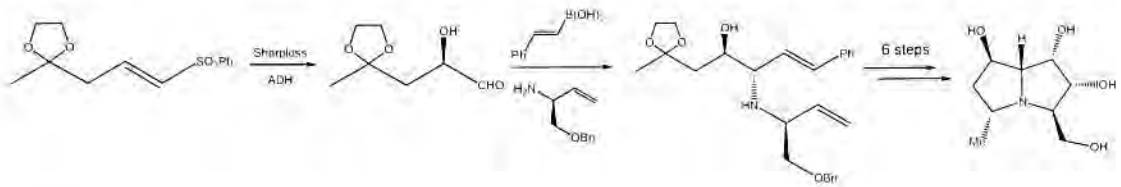
Chiral α-hydroxy aldehydes generated *in situ* by the ADH reaction of vinyl sulfones undergo a borono-Mannich reaction with β-styrenyl boronic acid and primary amines to give *anti*-1,2-amino alcohols in high enantiomeric purities (83-95% ee). This new method allows much more rapid access to these valuable chiral building blocks that has been used in a short formal synthesis (10 synthetic steps from 4-penten-1-ol) of (-)-swainsonine (Scheme 1).[1]

Scheme 1



The methodology developed in the above scheme is currently applied to the synthesis of the natural product target hyacinthacine B_3, a polyhydroxylated pyrrolizidine alkaloid isolated from bulbs of *Muscari armeniacum* (Scheme 2).[2]

Scheme 2



References

1. Au, C. W. G.; Pyne, S. G. *J. Org. Chem.* 2006, *71*, 7097-7099.
2. Asano, N.; Kuroi, H.; Ikeda, K.; Kizu, H.; Kameda, Y.; Kato, A.; Adachi, I.; Watson, A. A.; Nash, R. J.; Fleet, G. W. J. *Tetrahedron Asymmetry* 2000, *11*, 1-8.

MP92

TOWARDS THE TOTAL SYNTHESIS OF THE STEMONA ALKALOID OXYPROTOSTEMONINE

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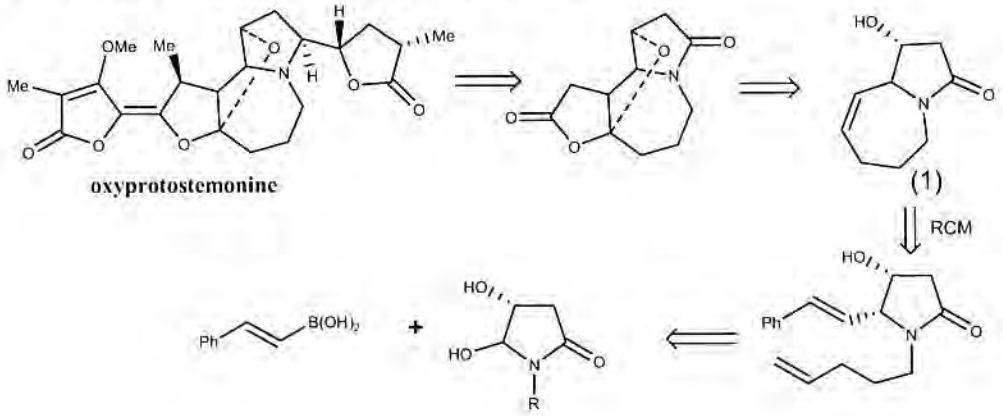
Stemona alkaloids are isolated from the Stemonaceae family of plants. Roots and rhizomes of these plants are used in Chinese and Japanese traditional medicine as an anti-cough remedy and for their antiparasitic properties.[1,2] Oxyprotostemonine, a Stemona alkaloid, was isolated from the roots of *Stemona curtisii* by the Pyne group in 2003. It was also determined to have very good lavicidal activity on mosquito larvae.[3] A flexible, convergent synthetic approach to oxyprotostemonine and its simpler analogues will allow to do further biological tests. Our retrosynthetic plan is shown below involves addition of a vinylboronic acid to a *N*-acyliminium ion and ring closing metathesis as the key steps to construct the pyrrolo[1,2-*a*]azepine core (1).



References:

1. H. Greger,*Planta Med.* 2006, *72*, 99-113.
2. R. A. Pilli *et. al., Nat. Prod. Rep.* 2000, *17*, 117-127.
3. P. Mungkornasawakul, S. G. Pyne *et. al. J. Nat. Prod.* 2004, *67*, 675-677.

MP93

SYNTHESIS OF 2-EPI- UNIFLORINE A

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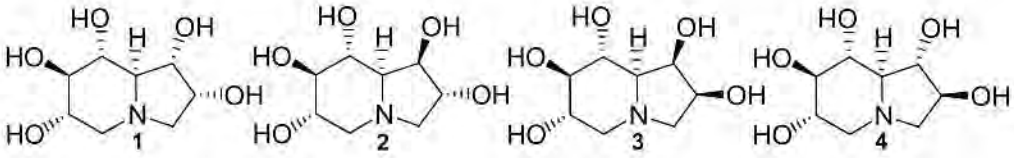
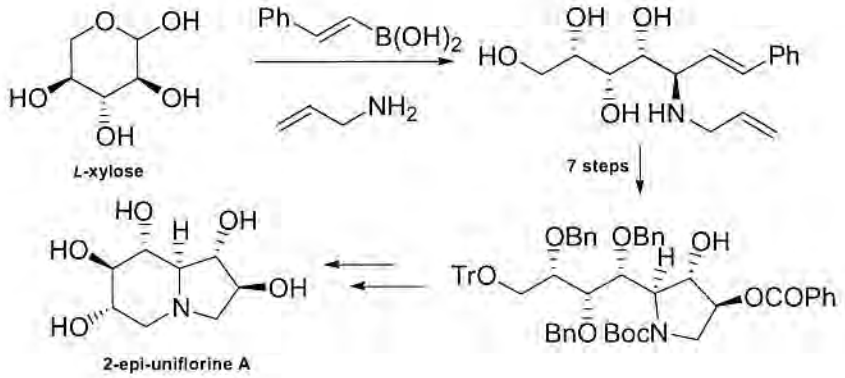
Uniflorine A, a polyhydroxylated indolizidine alkaloid, was isolated in 2000 from the leaves of the tree *Eugenia uniflora* L. This compound inhibits the α-glucosidases maltase and sucrase with IC_{50} values of 12 and 3.1 μM, respectively. The structure of unflorine A was deduced from NMR analysis to be that shown as structure 1.[1] The total synthesis of Putative uniflorine A was completed in 2004. The spectral and physical data of the material did not match that reported for natural product. Therefore we concluded that the proposed structure of uniflorine A is incorrect.[2] In order to elucidate the correct structure of Uniflorine A we are focusing on the synthesis of the 4 possible 1,2-diol stereoisomers of 1, namely, 1-4.



In 2005, 1-epi-uniflorine A 2 and 1,2-diepi-uniflorine A 3 were synthesized, their NMR data did not match with that of the natural product.[3] This poster reports on our progress toward the synthesis of 2-epi-uniflorine A 4 starting from *L*-xylose as illustrated below in Scheme 1.



References:

1. Matsumura, T.; Kasai, M.; Hayashi, T.; Arisawa, M.; Momose, Y.; Arai, I.; Amagaya, S.; Komatsu, Y. *Pharm. Biol.* 2000, *38*, 302-307.
2. Davis, A. S.; Pyne, S. G.; Skelton, B. W.; White, A. H. *J. Org. Chem.* 2004, *69*, 3139-3143.
3. Zhiming, Z.; Song, L.; Mariano, P. S. *Tetrahedron.* 2005, *61*, 8888-8894.

MP94

SYNTHESIS OF THE PYRIDO [1, 2-*a*] AZEPINE CORE; METHODOLOGIES TOWARDS THE TOTAL SYNTHESIS OF THE *STEMONA* ALKAOLIDS

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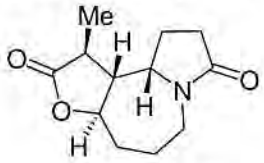
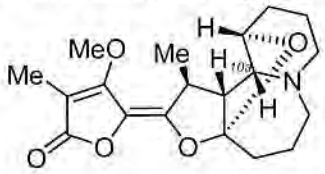
Stemona alkaloids are a unique class of natural products exclusively isolated from the monocotyledonous family Stemonaceae mainly distributed in S.E. Asia and have many interesting biological properties including insect anti-feedant and repellent activity and have potential pharmaceutical applications.[1] The common structural feature is represented by a pyrrolo [1,2-a] azepine nucleus 1 and more recently in 2003 was discovered the pyridoazepine class 2 formed, it is thought, by homologation of the pyrrolidine ring to a piperidine based carbocycle.[2]

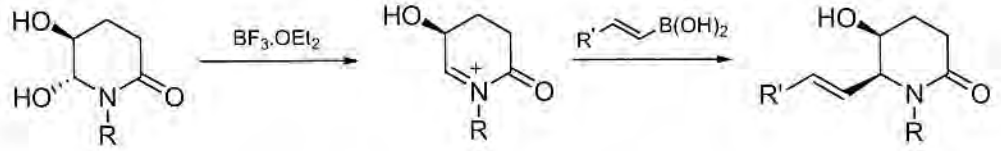


stemoamide 1



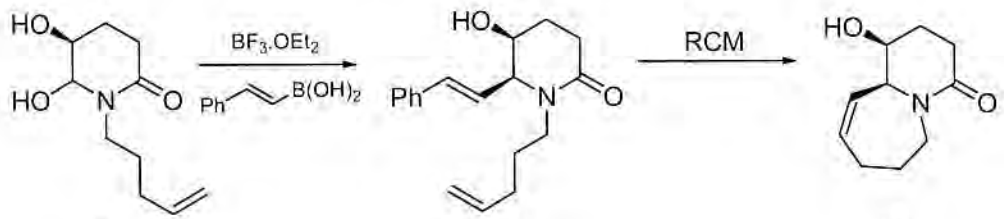
stemocutisine 2

Our efforts towards the total synthesis of the pridoazepine class alkaloids utilises an intermediate acyliminium ion 4 formed from a precursor hemi-aminal 3 and initiated by $BF_3.OEt$.[2,3] Subsequent diastereoselective nucleophilic attack by a vinylagous boron species, typically a boronic acid, yields the desired product 5 in good yield and with good to exceptional diastereoselectivity. This method represents an efficient means to introduce the required asymmetry at the *10a* position on the carbocycle core.



3 **4** **5**

Application of this methodology to the appropriate system 6 has led to the synthesis of the pyridoazepine core 8 *via* RCM of the *bis*-olefin 7.



6 **7** **8**

1. Greger H. *Planta. Med.*, 2006; 72, 99-113.
2. Mungkornasawakul P, Pyne SG., Jatisaienr A, Supyen D., Lie W, Ung AT., Skelton BW. and White AH., *J. Nat. Prod.*, 2003; 66, 980-982.
3. Batey RA., MacKay DB. and Santhakumar V., *J. Am. Chem. Soc.*, 1999, 121, 5075-5076.

MP95

SYNTHETIC STUDIES TOWARDS CRISAMICIN A

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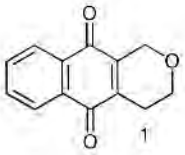
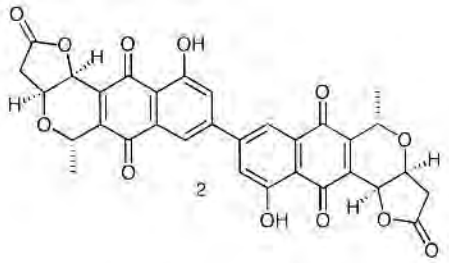
Isolated from bacterial and fungal sources, pyranonaphthoquinone antibiotics exhibit a wide range of biological activities including antibacterial, antiviral and anticancer activities.[1] While structural variation is present within the pyranonaphthoquinone family, each pyranonaphthoquinone contains a common naphtha[2,3-*c*]pyran-5,10-dione ring system 1. Dimeric pyranonaphthoquinone crisamicin A 2 was isolated from a Philippino mud sample containing the fungus *Micromonospous purpureochromogenes* and displays antibacterial activity against Gram-positive bacteria as well as exhibits antitumor, antiviral and immunomodulatory properties.[2]

The Hauser-Kraus annulation consists of the Michael addition of a stabilized phthalide anion onto an appropriate Michael acceptor, followed by a tandem intramolecular Claisen condensation and subsequent aromatization to afford dihydroquinones.[3,4] Utilizing a dimeric phthalide, double Hauser-Kraus annulation should offer a facile route to the dimeric crisamicin A 2.



1



2

References:

1 Brimble MA, Duncalf LJ, Nairn MR. *Nat. Prod. Rep.* 1999; 16, 267-81.

2 Nelson RA, Pope Jr. JA, Luedemann GM, McDaniel LE, Schaffner CP. *J. Antibiotics* 1986; 39, 335-44.

3 Hauser FM, Rhee RP. *J. Org. Chem.* 1978; 43, 178-80.

4 Kraus GA, Sugimoto H. *Tetrahedron Lett.* 1978; 2263-2266.

MP96

SYNTHESIS AND CHARACTERIZATION OF NEW HETEROCYCLIC NITROGEN-SULPHUR PROLIGANDS

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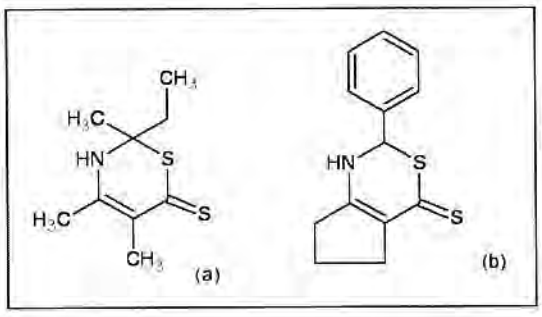
Organic compounds synthesis, especially heterocyclic synthesis with nitrogen and sulfur heteroatoms, constitute a field of interest for Coordination Chemistry, because of their use as potential ligands. The nitrogen-sulfurated quelating agents molecular architecture is guided towards the synthesis of [NS]1-, [N2S2]2- and particularly in this case [S2]2- ligands type which are widely used in metallobiomolecules biomimetic, in homogeneous catalysis,, electrochemistry and in medicine.

The first heterocyclic proligand synthetized was the 2-ethyl-2,4,5-trimethyl-2,3-dihydro-2H-1,3-thiazine-6-thione, this was done refluxing butanone with carbon disulphide in ammonium hydroxide media, the product is generated though simple condensation reactions.

Similar heterocyclic derivatives have been synthetized using a transimination reaction, this is the case of the 2-phenyl-1,5,6,7-tetrahydrocyclopenta[d][1,3]-thiazine-4(2H)-thione which is generated from N-bencelidenaniline and 2-amino-1-cyclopenten-1-dithiocarboxilic acid both dissolved in acetonitrile, in this reaction first the aniline unit is replaced followed by an spontaneous cyclation to produce the quelating agent.

Both heterocyclic proligands are obtained as yellow solids characterized by FTIR, UV-Vis, NRM-1H and 13C, mass spectrometry and x-rays powder diffraction. Their chelating capacity have been tried, obtaining metal complexes of the type: [M(S2)2] (M = Cu(II), Ni(II) and Co(II)).



Heterocyclic proligandos synthetized: (a) 2-ethyl-2,4,5-trimethyl-2,3-dihydro-2H-1,3-thiazine-6-thione and (b) 2-phenyl-1,5,6,7-tetrahydrocyclopenta[d][1,3]-thiazine-4(2H)-thione.

References:
Takeshima T. *J. Org Chem*, 1968, 34, 730-735.
Fontal B. *J. Heterocycles Chem.*, 2001, 38, 5, 1223-1225
Bordás P. *J. Org. Chem.*, 1972, 37,1727-1729.
Mondal S. K. *Inorg. Chem.*, 1978, 191, 17-21.

MP97

APPLICATION OF AZOMETHINE YLIDE CHEMISTRY TO THE PREPARATION OF FIVE-MEMBERED RING HETEROCYCLES

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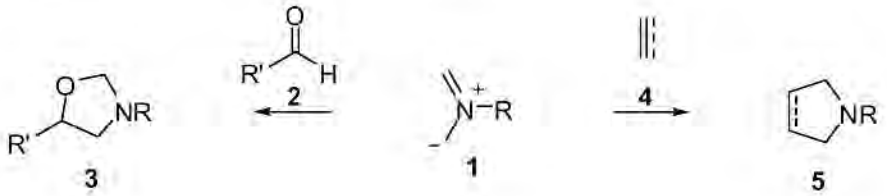
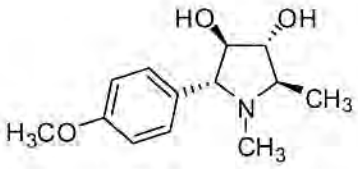
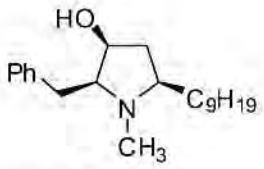
[B] *School of Chemistry, University of Tasmania, Private Bag 75, Hobart, Tasmania 7001, Australia*

Azomethine ylides undergo a wide variety of [3+2] cycloaddition reactions to give five-membered ring products.[1] Herein, we report the scope and limitations of the reactions of an azomethine ylide 1 with aldehydes 2 to give isoxazolidines 3.[2,3] We also report investigations of the utilisation of azomethine ylide chemistry in the synthesis of the a range of pyrrolidine targets 5 including pyrrolidine alkaloids (-)-Codonopsinine an antibiotic isolated from *Codonopsis clematidea*,[4] and)+)-Preussin an antifungal agent isolated from *Aspergillus ochraceus*.[5]





(-)-Codonopsinine



(+)-Preussin

References:

1. Eberbach W. *Science of Synthesis*, 2004; 27, 441-498; Harwood LM., Vickers RJ. *Chemistry of Heterocyclic Compounds*, 2002, 59, 169-252.
2. Ryan JH, Spiccia N, Wong, LSM. *Southern Highlands Conference on Heterocyclic Chemistry*, Moss Vale, (2006).
3. Padwa A., Dent W. *J. Org. Chem.* 1987, 52, 235.
4. Yoda H, Nakajima T, Takabe K. *Tetrahedron Lett.* 1996, 37, 5531-5534.
5. Schwartz RE, Liesch J, Hensens O, Zitano L, Honeycutt S, Garrity G, Fromtling RA, Onishi J, Monaghan R. *J. Antibiot.* 1988, 41, 1774-1779.

MP98

INHIBITORS OF FARNESYL PYROPHOSPHATE SYNTHASE (FPPS) AS NEW ANTIPARASITIC AGENTS

Carl S. Rye, Georgina Holloway, Katrina Billington, John Parisot, Caroline Miles, Keith Watson, Jonathan Baell, and Ian Street

The Walter and Eliza Hall Institute of Medical Research, Biotechnology Centre

Farnesyl pyrophosphate synthase (FPPS) is an enzyme that catalyses the condensation of C_5 alcohols to form the C_{10} and C_{15} products geranyl diphosphate and farnesyl diphosphate, respectively. It is an essential enzyme in a variety of parasites that cause diseases such as American trypanosomiasis (Chagas disease), African trypanosomiasis, and Leishmania. Thus, it represents an attractive target for drug development.

Current drugs for these parasites are generally quite toxic, have a wide range of unpleasant side effects, and are often ineffective on all stages of the associated diseases. Unfortunately, large pharmaceutical companies are generally not interested in taking on a project that mainly affects poor, third world countries.

With a funding collaboration from The Special Programme for Research and Training in Tropical Diseases (TDR), we have conducted a high throughput screening campaign for small molecules that inhibit FPPS and have found several compounds that are highly active against this enzyme, as well as the target parasites *in vitro*. Medicinal chemistry is currently in progress to develop these hits into lead candidates, and hopefully new treatments for the associated diseases.

MP99

ENANTIOSELECTIVE CYCLOPROPANATION REACTIONS WITH PLANAR-CHIRAL PYRIDINIUM YLIDES

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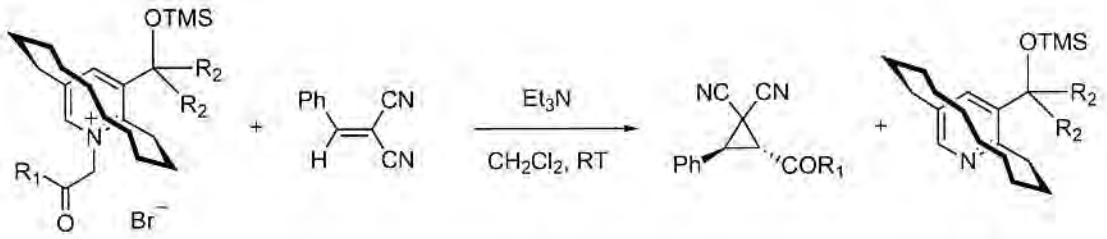
Chiral pyridinium ylides are attracting molecules that undergo enantioselective[1] and diastereoselective[2] cyclopropanation reactions with methylidenemalononitrile derivatives. We have been studying the enantioselective cyclopropanation with planar-chiral pyridinium ylides having a [10]parapyridinophane skeleton[3] and the reactions of such ylides generated *in situ* from the corresponding pyridinium salt (*S*)-1az (R_1 = Ph; R_2 = *n*-Bu) afforded optically active cyclopropane 2a with up to 73% *ee*. Then, we have designed planar-chiral pyridinium salts (*S*)-1bx-z bearing a bulky *tert*-butoxy group as precursors of the corresponding ylides for seeking higher enantioselectivity in their cyclopropanation reactions.

Initially, we examined the reaction of the pyridinium ylide generated from (*S*)-1bx (R_1 = *t*-BuO; R_2 = Me) in the presence of triethylamine with benzalmalononitrile at room temperature. The desired cyclopropanation proceeded efficiently to give *trans*-cyclopropnane 2b in 89% yield with 89% *ee* as well as planar-chiral pyridinophane 3x and its desilylated form in almost quantitative yield. Further improvement of the enantioselectivity was observed in the reaction with (*S*)-1by and (*S*)-1bz (R_2 = Ph and *n*-Bu, respectively) incorporating more bulky C-3 substituent groups locating at the opposite side beyond an oligomethylene bridge of the planar-chiral units. The "*remote stereocontrole effects*" appeared in the reactions of (*S*)-1by-z to increase the enantiomeric excess of the cyclopropane 2b to 93% *ee*. The present results indicate that the bulky *tert*-butoxy group on the pyridinium moiety works very efficiently for the improvement of enantioselectivity in cyclopropanation reactions of benzalmalononitrile.



1az: R_1 = Ph, R_2 = *n*-Bu
1bx: R_1 = *t*-BuO, R_2 = Me
1by: R_1 = *t*-BuO, R_2 = Ph
1bz: R_1 = *t*-BuO, R_2 = *n*-Bu

2a: Up to 73% *ee*
2b: 89-93% *ee*

3x-z

References:

1) Yamada S.; Yamamoto J.; Ohta E. *Tetrahedron Lett.* 2007, 48, 855-858.
2) (a) Kojima S.; Fujimoto K.; Itoh Y.; Hiroike K.; Murakami M.; Ohkata K. *Heterocycles* 2006, 67, 679-691. (b) Kojima S.; Hiroike K.; Ohkata K. *Tetrahedron Lett.* 2004, 45, 3565-3568. (c) Kojima S.; Fujimoto K.; Shinohara Y.; Shimizu M.; Ohkata K. *Tetrahedron Lett.* 2000, *41*, 9847-9851.
3) Kanomata N.; Sekine K.; Yamashita S. *Pacifichem* 2005, ORGN1768.

MP100

SYNTHESIS AND PROPERTIES OF AZULENOPENTATHIEPINS AND THEIR DERIVATIVES

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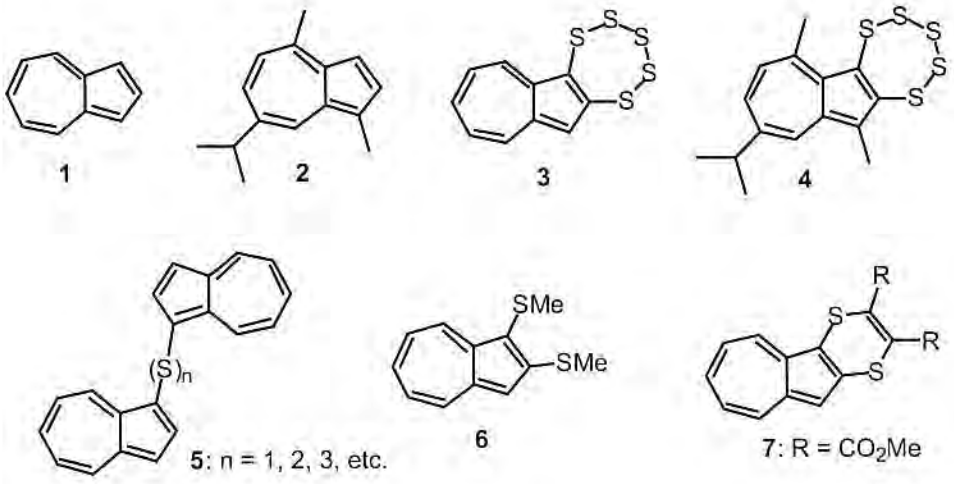
Azulenes are one of the interesting classes in non-benzenoid aromatics and their chemical, physical and biological properties are of interest in connection with benzenoid aromatics. However, synthetic methods of azulenes with sulfur atoms have not been much investigated [1,2]. We report herein the synthesis and properties of azulenopentathiepins 3, 4 and their derivatives.

Although reaction of azulene 1 with elemental sulfur (S_8) in 1,2,4-trichlorobenzene under thermal conditions afforded only a mixture of bis(azulyl)sulfides 5 (n = 1, 2, 3, etc.) with black precipitates, the reaction in boiling pyridine yielded novel azulene-based cyclic pentasulfide (azulenopentathiepin) 3 as bluish green powder (14 % yield). Treatment of guaiazulene 2 under the same conditions gave a trace amount of guaiazulenopentathiepin 4; the reactivity seemingly decreased by steric hindrance of the methyl group(s). The use of *N,N'*-dithiobis(phthalimide) as the sulfurating agent improved the yield of 4 to 5 %.

Electrochemical properties of azulenopentathiepins 3 and 4 were investigated by CV measurement. Each voltammogram showed an irreversible wave. The first reduction potentials (E_1^{red}) of 3 and 4 were nearly equal to those of azulenes 1 and 2, respectively (E_1^{red}: 1; -1.93V, 2; -2.03V, 3; -2.09V, 4; -2.12V). On the other hand, their electron donation ability was slightly smaller than that of 1 and 2 (E_1^{ox}: 1; +0.64V, 2; +0.40V, 3; +0.97V, 4; +0.79V).

Transformation of azulenopentathiepin 3 into azulene derivatives with sulfur atoms was investigated. Reduction of 3 with $NaBH_4$ generated bis(thiolate), which was methylated by iodomethane to give 1,2-bis(methylthio)azulene 6 (63 % yield). Reaction of 3 with PPh_3 in the presence of DMAD afforded dithiin 7 (54 % yield).



References:

[1] Replogle LL. Arluck RM. and Maynard JR. *J. Org. Chem.*, 1965; 30, 2715-2718.

[2] Asao T. Ito S. and Morita N. *Tetrahedron Lett.*, 1989; 30, 6345-6348.

MP101

A NOVEL (3+2+N) ROUTE TO PIPERIDINES

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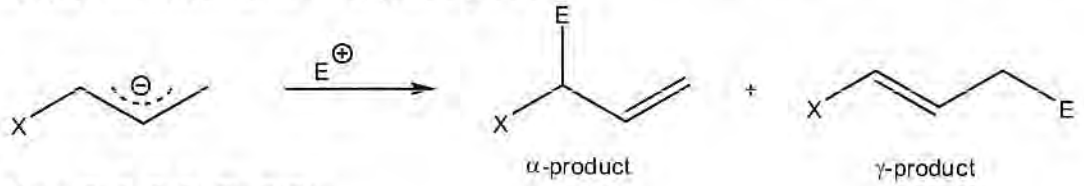
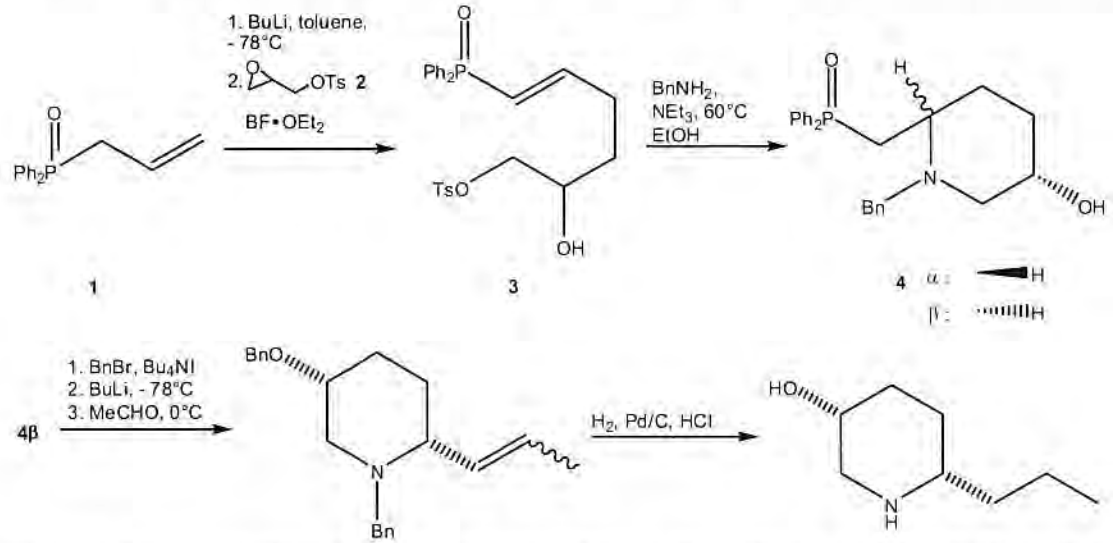
ernst.schaumann@tu-clausthal.de

Hetero-substituted allyl anions are useful synthetic building blocks, though the regioselectivity in the reaction with electrophiles may pose a problem:[1]



X e.g. PhS, R_3Si, $Ph_2P(O)$

Thus, the reaction of deprotonated allylphosphine oxides [X=$Ph_2P(O)$] with epoxides in DME yields 2:1 to 1:2 mixtures of α- and γ-adducts.[2] Interestingly, the regioselectivity is shifted almost exclusively to the **γ**-adduct if toluene is used as solvent. The resulting unsaturated alcohols can be used in various synthetic transformations. In particular, use of epoxytosylate 2 as electrophile gives ready access to the monotosylated diol 3 which, by addition of benzylamine, cyclizes to piperidine 4 in high yield, though with low diastereoselectivity (α/β 1,3:1). The stereoisomers can be separated and the 4**β** isomer easily be taken to the alkaloid pseudoconhydrine (see Scheme).



In conclusion, a piperidine synthesis from an allyl anion (C_3 synthon), an epoxide (C_2 synthon), and a primary amine is demonstrated.

References:
1. Katritzky AR, Piffl M, Lang H, Anders E *Chem. Rev.*, 1999; 99, 665-722
2. Ergüden JK, Schaumann E *Synthesis*, 1996; 707-710

MP102

TOTAL SYNTHESIS OF THE MARINE NATURAL PRODUCT CLAVOSOLIDE D

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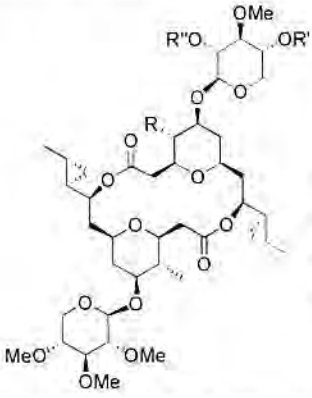
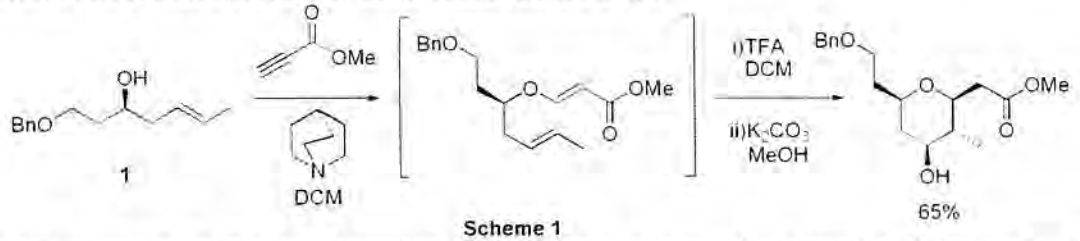
The clavosolides A-D are a family of unusual diolides isolated from the marine sponge *Myriastra clavosa* found in the Phillipines[4] and represent challenging synthetic targets.



	R	R'	R''
Clavosolide A	-Me	-Me	-Me
Clavosolide B	-Me	-Me	H
Clavosolide C	-Me	H	-Me
Clavosolide D	H	-Me	-Me

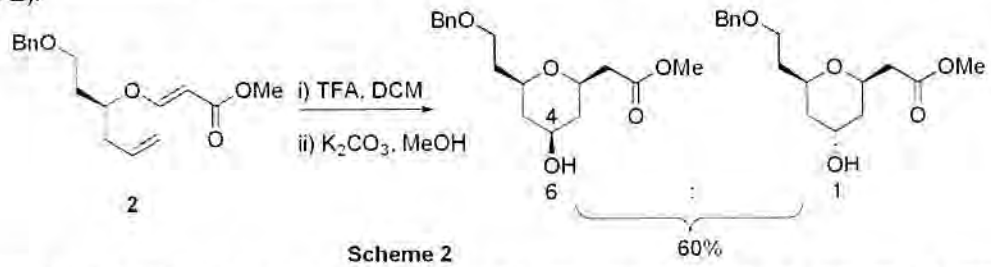
Although clavosolides A-C were found to be non-cytotoxic, the biological properties of clavosolide D are yet to be tested, due to the small quantity of material isolated.
Total synthesis of clavosolide D will allow confirmation of the proposed structure and provide material for the evaluation of any biological properties.

The Prins cyclisation has been established as a valuable tool for the stereoselective synthesis of substituted tetrahydropyrans.[5] Access to the tetra-substituted tetrahydropyran core of the clavosolides was achieved in a rapid and efficient manner via conversion of chiral homoallylic alcohol **1** into the appropriate enol ether and subsequent trifluoroacetic acid promoted Prins cyclisation in a one pot process (Scheme 1)[6].



Scheme 1

A similar approach to the tri-substituted tetrahydropyran core of clavosolide D by cyclisation of homoallylic enol ether **2** led to the formation of C-4 epimers in a still synthetically useful 6:1 ratio (Scheme 2).



Scheme 2

β-Selective glycosidation, side chain elaboration and macrolactonisation are required to complete the total synthesis.

References:
[4] (a) Rao, MR, Faulkner, DJ. *J. Nat. Prod.*, 2002; 65, 386-388; (b) Erickson, KL, Gustafson, KR, Pannell, LK, Beutler, JA, Boyd, MR. *J. Nat. Prod.*, 2002; 65, 1303-1306.
[5] Barry, CS, Crosby, SR, Harding, JR, Hughes, RA, King, CD, Parker, GD, Willis, CL. *Org. Lett.*, 2003; 5, 2429-2432.
[6] (a) Barry, CS, Bushby, N, Charmant, JPH, Elsworth, JD, Harding, JR, Willis, CL. *Chem. Commun.*, 2005; 5097-5099. (b) Barry, CS, Elsworth, JD, Seden, PT, Bushby, N, Harding, JR, Alder, RW, Willis, CL. *Org. Lett.*, 2006; 8, 3319-3322.

MP103

CONVENIENT SYNTHESIS OF POLYSUBSTITUTED PYRIDINES THROUGH [4+2] CYCLOADDITION OF ISOTELLURAZOLES WITH ACETYLENIC DIENOPHILES

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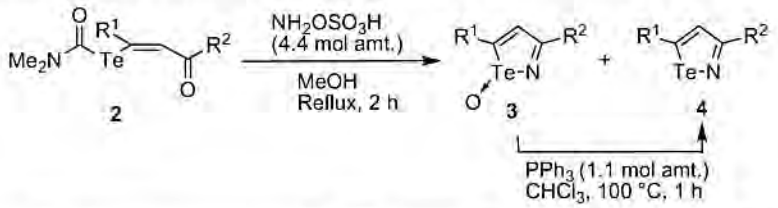
One-pot treatment of bis(*N,N*-dimethylcarbamoyl) ditelluride (1) with $NaBH_4$ and propynone derivative afforded β-(*N,N*-dimethylcarbamoyltelllurenyl)alkyl ketones 2 in moderate yields, and the products were converted into the corresponding isotellurazole *Te*-oxides 3 by treating with hydroxylamine *O*-sulfonic acid. The ring closure of was assumed to proceed through intramolecular nucleophilic substitution on the nitrogen atom of oxime sulfonates by the attack of *in situ* generated chalcogen nucleophiles. Deoxygenation of isotellurazole *Te*-oxides 3 were successfully carried out by treating Ph_3P.[1,2]

Table 1. Syntheses of Isotellurazole *Te*-Oxides (3) and Isotellurazoles (4).[a]

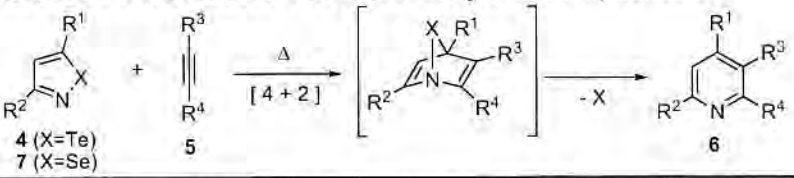


Substrate			Yield / %		Yield / % of Deoxygenation [b]	
R^1	R^2	2	3	4	3 to 4	$Ph_3P=O$
C_6H_5	CH_3	2a	79 (3a)	4 (4a)	91 (4a)	quant.
C_6H_5	C_6H_5	2b	86 (3b)	trace (4b)	94 (4b)	quant.
C_6H_5	*p*-ClC_6H_4	2d	74 (3d)	0	89 (4d)	quant.

[a]All reactions were carried out under an Ar atmosphere. [b]Carried out in a sealed tube.

Subsequent treatment of isotellrazoles 4 with an acetylenic dienophiles 5 bearing an electron-withdrawing substituent, i.e. dimethyl acetylenedicarboxylate (DMAD), methyl propiolate, even at R.T. afforded polysubstituted pyridines 6 in highly regioselective manner *via* hetero-Diels-Alder reaction and subsequent extrusion of elemental tellurium. Similar conversion of isoselenazole 7a into pyridine 6a just required refluxing temperature in toluene for a long time, and the synthetic utility of the pathway from 4 into 6 is just presented.

Table 2. Synthesis of Polysubstituted Pyridines 6 through Hetero-Diels-Alder Reaction of Isotellurazoles 4 with Electron-deficient Acetylenic Compounds 5.



Isochalcogenazole			Acetylenic Dienophile (5)		Solvent	Temp	Time	Yield of 6
R^1	R^2	X	R^3	R^4		/ °C	/ h	/ %
C_6H_5	CH_3	Se	COOMe	COOMe	Toluene	Reflux	24	83 (6a)
C_6H_5	CH_3	Te	COOMe	COOMe	CH_2Cl_2	R.T.	12	91 (6a)
C_6H_5	CH_3	Te	COOMe	H	CH_2Cl_2	R.T.	24	79 (6a')
C_6H_5	CH_3	Te	COOMe	C_6H_5	Toluene	Reflux	24	24 (6a'')

References:
1) Lucchesini, F., Bertini, V. *Synthesis*, 1983; 824-827.
2) Shimada, K. et al., *Bull. Chem. Soc. Jpn.*, 2007; *80*, 567-577.

MP104

SYNTHESES OF CALYSTEGINES AND TROPANES VIA *ENDO*-SELECTIVE INTRAMOLECULAR NITRONE-ALKENE CYCLOADDITION OF HEPT-6-ENOSES

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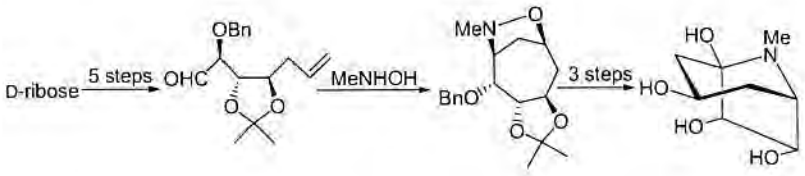
The effect of blocking groups and stereochemistry of the substituents on the regio- and stereoselectivity in intramolecular nitrone-alkene cycloaddition (INAC)[1,2] of hept-6-enoses are reported.

With *N*-alkyl hydroxylamine, hept-6-enoses containing a *cis*-acetonide blocking group, underwent an INAC reaction to give *cis*-fused bicyclo[4.3.0] isoxazolidines exclusively whereas those containing a 2,3-*O*-*trans*-diacetal blocking group gave a mixture of *cis*-, *trans*-fused isoxazolidines and bridged isoxazolidines.[3]

Now, high yielding *endo*-selective INAC reactions of hept-6-enoses controlled by a *trans*-acetonide to give bridged bicyclo[4.2.1] isoxazolidines exclusively are realized for the first time. The cycloadducts were readily transformed into alkaloids, calystegines and tropanes.[4]



References:
(1) Koumbis, A. E.; Gallos, J. K. *Curr. Org. Chem.* 2003, 585-628.
(2) Shing, T. K. M.; Elsley, D. A.; Gillhouley, J. G. *J. Chem. Soc., Chem. Commun.* 1989, 1280-1281.
(3) Shing, T. K. M.; Wong, A. W. F.; Ikeno, T. and Yamada, T. *J. Org. Chem.* 2006, 71, 3253-3263.
(4) Shing, T. K. M.; Wong, W. F.; Ikeno, T. and Yamada, T. *Org. Lett.* 2007, 9, 207-209.

MP107

KINETIC AND OXIDATIVE STUDY OF SULPHUR-NITROGEN CONTAINING HETEROCYCLIC DRUG HYDROCHLOROTHIAZIDE

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Hydrochlorothiazide [6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-sulfonamide1,1-dioxide] is a sulphur and nitrogen containing heterocyclic having diuretic and antihypertensive activity. This belongs to the thiozolidine family, and shows the substitution reaction in the ring. It affects the distal renal tubular mechanism of electrolyte reabsorption. Hydrochlorothiazide increases excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium and bicarbonate. The oral administration of HCTZ shows diuresis after 2 hours. The maximum is occurred at about 4 hours. The completion of circulation has been completed between 6-12 hours. The present study has been done in two separate steps. In first step, study of dissolution and in the second step kinetic study of oxidation by V(V) to understand the metabolic conversion in biological system has been explored. The λ_{max} of drug was found at 272 nm. In the presence of 0.05% SLS drug shows complete dissolution within 30 min. In second case drug was oxidized with V(V) and kinetic parameters were obtained. The rate was found to be first order in [V(v)] , [Drug] and [H^+] respectively. Activation parameters for overall reaction have been computed. Michaelis-Menton type of kinetics has been proposed.

The present study will be helpful to understand the metabolism of HCTZ.

MP108

A KINETIC APPROACH TO UNDERSTAND THE METABOLISM OF SULPHUR AND NITROGEN CONTAINING HETEROCYCLIC DRUG HYDROCHLOROTHIAZIDE

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Department of Chemistry, Dr.H.S.Gour University, Sagar,M.P.
India

Hydrochlorothiazide [6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-sulfonamide1,1-dioxide (HCTZ)] is a nitrogen and sulphur containing heterocyclic compound. It belongs to the thiozolidine family, and shows the substitution reactions in the ring. It is the benzothiadiazide derivative with diuretic and antihypertensive nature. It affects the distal renal tubular mechanism of electrolyte reabsorption. Hydrochlorothiazide increases excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium and bicarbonate. The oral administration of HCTZ shows diuresis after 2 hours. The maximum is occurred at about 4 hours. The completion of circulation has been completed between 6-12 hours. The present study has been done in two separate steps. In first step, study of dissolution and in the second step kinetic study of oxidation by V(V) to understand the metabolic conversion in biological system has been explored. The λ_{max} of drug was found at 272 nm. In the presence of 0.05% SLS drug shows complete dissolution within 30 min. In second case drug was oxidized with V(V) and kinetic parameters were obtained. The rate was found to be first order in [V(v)] , [Drug] and [H^+] respectively. Activation parameters for overall reaction have been computed. Michaelis-Menton type of kinetics has been proposed.

MP109

2-AMINOQUINOLINE DERIVATIVES AS TEC SH3 DOMAIN LIGANDS

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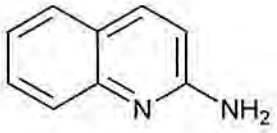
Src Homology 3 (SH3) domains are small, protein-protein interaction domains present in a variety of proteins that mediate a range of cellular signalling pathways.[1] Many of these pathways, when deregulated, lead to diseases such as osteoporosis and cancer, making SH3 domains appealing targets for the development of potential therapeutics.[2, 3]

Using the Tec-SH3 domain as a model system we have identified 2-aminoquinoline 1 as a lead compound with moderate binding affinity (K_d = 125 μM). The synthesis of acetal substituted 2-aminoquinolines, such as 2, has increased the affinity of this compound by 6-fold.[4, 5]



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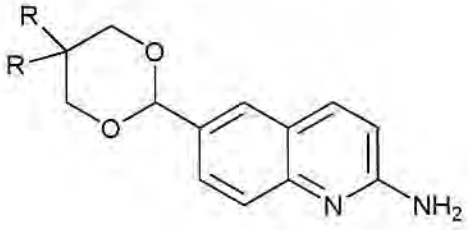
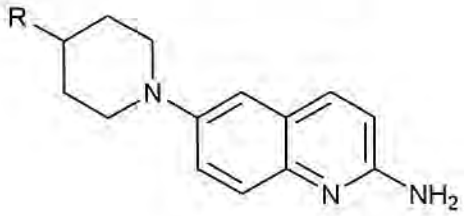


2

Our most recent investigations have involved further investigation of heterocyclic substituents at the 6-position. Compounds, such as 3 and 4, have been prepared via Buchwald-Hartwig amination of an appropriate quinolylhalide with saturated nitrogenous heterocycles.



3

4

Preliminary results have shown that the above-mentioned 6-substituted 2-aminoquinolines bind to the Tec-SH3 domain with improved affinity relative to the lead compound 1. It is expected that further exploration of ligands of this type will lead to further improvements in binding affinity.

References:

1. Ren, R., Mayer, B.J., Cicchetti, P. and Baltimore, D., *Science*, 1993, 259, 1157-1161.
2. Vidal, M., Gigoux, V., Garbay, C., *Crit. Rev. Oncol. Hematol.*, 2001, 40, (2), 95-193.
3. Mayer, B. J., *J. Cell Sci.*, 2001, 114, 1253-1263.
4. Inglis, S. R., Stojkoski, C., Branson, K.M., Cawthray, J.F., Fritz, D., Wiadrowski, E., Pyke, S.M., Booker, G.W., *J. Med. Chem.*, 2004, 47, 5405-5417.
5. Inglis, S. R., Jones, R.K., Fritz, D., Stojkoski, C., Booker, G.W., Pyke, S.M., *Org. Biomol. Chem.*, 2005, 3, 2543-2557.

MP112

APPROACHES TO THE STEREOSELECTIVE SYNTHESIS OF AE ANALOGUES OF METHYLLYCACONITINE.

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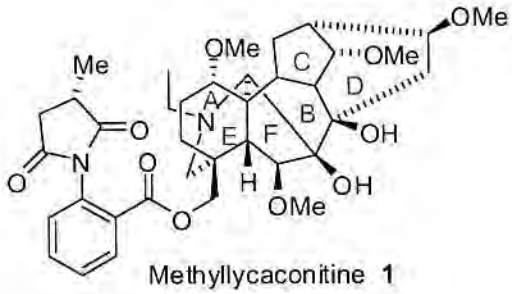
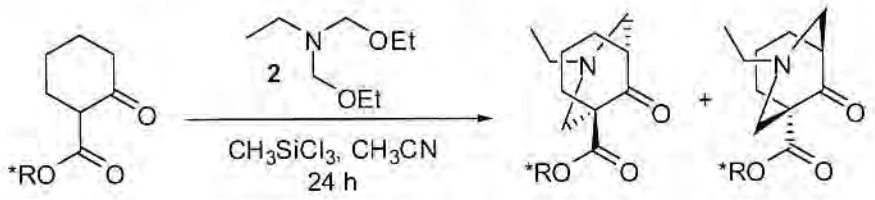
23 Symonds St, Auckland, New Zealand

Methyllycaconitine (MLA) 1 is a potent, highly selective antagonist of the α7 neuronal acetylcholine receptor (nAChR).[1] To date, no total synthesis of MLA has been reported, however syntheses of E, AE, ABE, AEF, ABDE and ABDF ring subunits of MLA have been prepared[2]. With the exception of the E ring analogues, all previous syntheses of MLA substructures have been carried out without stereocontrol. Current work is focused on developing an enantioselective synthesis of the AE azabicyclo[3.3.1]nonane ring system of MLA by incorporating a chiral auxiliary into the precursor required for the key double Mannich reaction. The availability of enantiopure MLA subunits would allow further probing of the mechanism for binding of such compounds to the receptor.



Methyllycaconitine **1**

A double Mannich reaction utilizing *N,N*-bis(ethoxymethyl)alkylamines such as 2 has been reported as the most efficient means of synthesizing azabicyclo[3.3.1]nonanes.[3] The effect of incorporating various chiral auxiliaries into the double Mannich precursors will be reported.



R* = Chiral auxiliary

References:

1. Albuquerque, EX; Pereira, EFR; Arpad, M; Eisenberg, HM; Maelicke, A; Alkondon, M. *Behav. Brain Res.* 2000, *113*, 131-141
2. Goodall, KJ; Barker, D; Brimble, MA. *Synlett*, 2005, *12*, 1809-1827.
3. Brocke, C; Brimble, MA; Lin, DSH; McLeod, MD. *Synlett*, 2004, *13*, 2359-2363.

MP113

SYNTHESIS, SPECTRAL AND ACID-BASE PROPERTIES OF β-PHENYL SUBSTITUTED 1,2,5-THIA(SELENA)DIAZOLOPORPHYRAZINES: INFLUENCE OF NUMBER AND POSITION OF FUSED HETEROCYCLES

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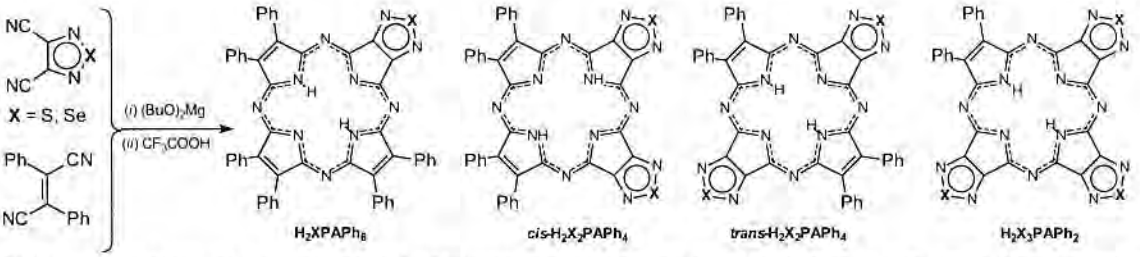
Fusion of 1,2,5-thia(selena)diazole rings by porphyrazine macrocycle endows it with peculiar physico-chemical properties in the solid state and in solution [1]. Following our recent reports on the low-symmetry 1,2,5-thia(seleno)diazolobenzoporphyrazines [2], we have prepared, isolated and characterized a complete series of β-phenyl substituted 1,2,5-thia(seleno)diazoloporphyrazines with varied number and location of annulated heterocycles:



Effect annulation of 1,2,5-thia(selena)diazole moieties on the UV-VIS spectra have been analyzed as being due to the changes in the dimension and symmetry of the porphyrazine π-chromophore on the basis of MO perturbation theory and semiempirical calculations. The lesser involvement in the conjugation of the 4d orbitals of Se than the 3d orbitals of S results in the bathochromic shift of the Q-band in the Se-containing species as compared to the corresponding S-analogues.

Consecutive annulation of 1,2,5-thia(selena)diazole rings increases the acidity of the internal pyrrolic NH-groups, which are easily deprotonated in the presence of $(NBu_4)OH$ in CH_2Cl_2 solution. At the same time basicity of *meso*-nitrogen atoms of the porphyrazine macrocycle decreases in the order H_2XPAPh_6 > *cis*-$H_2X_2PAPh_4$ > *trans*-$H_2X_2PAPh_4$ > $H_2X_3PAPh_2$ in which Se-analogues have slightly higher basicity in comparison to the corresponding S-analogues.

Acknowledgement. This work was supported by Russian Foundation of Basic Research (grants No. 05-03-32921 and 06-03-81022)

References:

1. Donzello MP, Ercolani C, Stuzhin PA. *Coord. Chem. Rev.*, 2006; 205, 1530-1561.
2. (a) Kudrik EV; Bauer EM, Ercolani C, Chiesi-Villa A, Rizzoli C, Gaberkorn A, Stuzhin PA, *Mendeleev Communications* 2001, 45-47. (b) Donzello MP, Ercolani C, Gaberkorn AA, Kudrik EV, Meneghetti M, Marcolongo G, Rizzoli C, Stuzhin PA, *Chem. Eur. J.*, 2003; 9, 4009-4024. (c) Gaberkorn AA, Donzello MP, Stuzhin PA, *Russ. J. Org. Chem.* 2006, 42, 929-935. (d) Gaberkorn AA, Popkova IA, Stuzhin PA, Ercolani C., *Russ. J. Gen. Chem.* 2006; 76, 1494-1503.

MP114

1,4-DIAZEPINOTRIBENZOPORPHYRAZINES: SYNTHESIS, STRUCTURE AND ACID-BASE PROPERTIES

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[b]Dipartimento di Chimica Universita di Roma "La Sapienza", P-le A. Moro, 5, I-00185 Roma Italy, e-mail: claudio.ercolani@uniroma1.it
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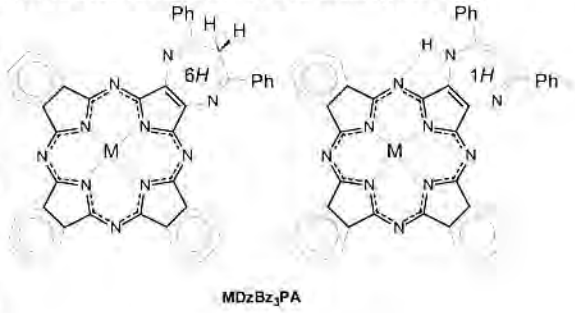
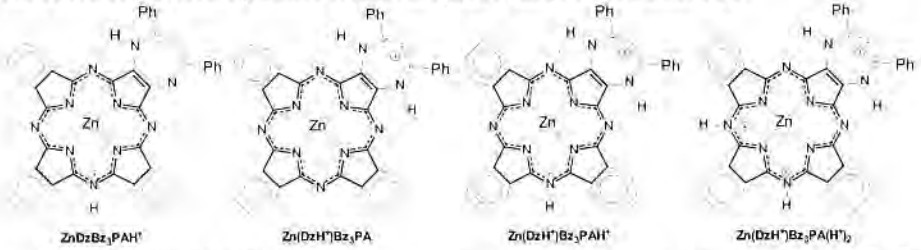
Porphyrazines with four annulated 1,4-diazepine rings (MDz_4PA) exhibit unusual spectral and other physico-chemical properties due to the strong electronic interaction between central tetrapyrrolic macrocycle and peripheral heterocycles [1]. Using mixed co-cyclotetramerization of 5,6-diphenyl-1,4-diazepino-2,3-dicarbonitrile with an excess of phthalodinintrile in the presence of lithium *n*-butoxide in *n*-butanol we have prepared the dilithium derivative of 1,4-diazepino[2,3-*b*]tribenzo[*g,l,q*]porphyrazine, Li_2DzBz_3PA, which was hydrolysed to the free base H_2DzBz_3PA and converted the Zn(II) complex, $ZnDzBz_3PA$, by treatment with Zn(II) acetate in pyridine. Unlike tetradiazepinoporphyrazines MDz_4PA [1], no doublets of the diastereotopic CH_2 protons - characteristic feature of the 6*H*-tautomer - could be observed over wide temperature range in the ^1H NMR spectra of $MDzBz_3PA$. Instead singlet of the NH proton at ca 11.3 ppm evidences in favour of the 1*H* tautomeric form of the diazepine ring.

Presence of several basic centers in $MDzBz_3PA$ – four porphyrazine *meso*-nitrogen atoms and diazepine N-atom(s) - determines complex behavior of $MDzBz_3PA$ in acid media. Basic properties have been studied using spectrophotometric and ^1H NMR titrations in binar media with increasing acidity and different polarity – C_6H_6-CH_3COOH-H_2SO_4, CH_2Cl_2-CF_3COOH-H_2SO_4 and DMSO-CF_3COOH. In the case of Zn(II)-complex $ZnDzBz_3PA$ *meso*-N-atoms are more basic than the diazepine N-atoms and the *meso*-protonated cation $ZnDzBz_3PAH^+$ is formed first. In CH_2Cl_2-CF_3COOH media equilibrium between this cation and the diazepinium cation $Zn(DzH^+)Bz_3PA$ is observed.



$MDzBz_3PA$



$ZnDzBz_3PAH^+$ $Zn(DzH^+)Bz_3PA$ $Zn(DzH^+)Bz_3PAH^+$ $Zn(DzH^+)Bz_3PA(H^+)_2$

In 70-80% CF_3COOH these monocations are converted in the "mixed" dication $Zn(DzH^+)Bz_3PAH^+$, and then in the presence of H_2SO_4 to the trication $Zn(DzH^+)Bz_3PA(H^+)_2$. In the case of the free base H_2DzBz_3PA the basicity of the diazepine N-atoms appears to be higher than that of the *meso*-N atoms. Experimental pK_{ai} values determined in the different media are discussed in comparison with the theoretical values of proton affinity calculated by semiempirical AM1 method.

Acknowledgements. This work was initiated in the University "La Sapienza" (Rome), facilitated by the scientific agreement with Ivanovo State University of Chemical Technology and additionally supported by the Russian Foundation of Basic Research (No. 06-03-81022).

References:

1. Donzello M.P., Ercolani C., Stuzhin P.A., Chiesi-Villa A., Rizzoli C. *Eur. J. Inorg. Chem.* 1999; 2075-2084.
2. Donzello M.P., Dini D., D'Arcangelo G., Ercolani C., Zhan R., Ou Z., Stuzhin P.A., Kadish K.M. *J. Am. Chem. Soc.* 2003; 125, 14190-14204.

MP115

ENCAPSULATING ANIONS IN HETEROCYCLIC LIGAND BASED METALLOSUPRAMOLECULAR ASSEMBLIES

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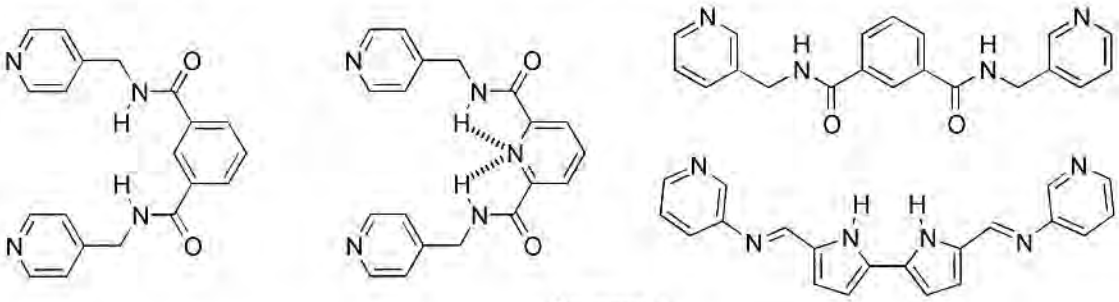
Over the last decade enormous strides have been made towards establishing the self-assembly criteria for the formation of metallo-supramolecular assemblies.[1] Against this backdrop of success in synthesis, the focus has shifted to investigating, controlling and advancing the properties of these assemblies for new applications.[2] Apace with the development of metallo-supramolecular chemistry, the area of anion recognition chemistry has also risen to the scientific fore over the last ten years atop the realisation of the widespread prevalence and implications of anions in many areas.[3]

We are interested in preparing highly selective and strong binding receptors for anion guests by combining specific recognition motifs for targeting anions with the encapsulating properties, size exclusion phenomena and self-assembly features of metallo-supramolecular assemblies. To this end we have prepared a number of heterocyclic ligands that incorporate a central hydrogen bond donor region and two exterior heterocyclic transition metal binding sites (Scheme 1). We are pursuing investigations into anion templated assemblies of these heterocyclic ligands targeting polygonal metallo-macrocyclic assemblies (triangles, squares etc) and polyhedral cage-type assemblies.



Scheme 1.

For reactions involving selected amide ligands with silver(I) metal salt precursors we have been unable to satisfactorily overcome robust ligand-ligand hydrogen bonding interactions, which has led to the observance of coordination networks in the solid state. New ligands are being pursued that circumvent this outcome. Utilising pre-organised palladium precursors has given control over the formation of the desired assemblies.

References:

[1] Leininger, S., Olenyuk, B., Stang, PJ. *Chem. Rev.* 2000; 100, 853-908; Holliday, BJ., Mirken, CA. *Angew. Chem. Int. Ed.* 2001; 40, 2022-2043; Hamilton, TD., MacGillivray, LR. *Cryst. Growth Des.* 2004; 4, 419-430.

[2] Amijs, CHM., van Klink, GPM., van Koten, G. *Dalton Trans.* 2006; 308-327.

[3] Beer, PD., Gale, PA. *Angew. Chem. Int. Ed.* 2001; 40, 486-516; Gale, PA. (guest editor) *Coord. Chem. Rev.* 2006; 250, issues 23 & 24.

MP116

THE FIRST TOTAL SYNTHESIS OF POTENT ANTI-MRSA BROMOMETHYLTHIOINDOLES MC 7 AND MC 8.

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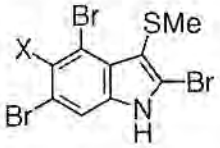
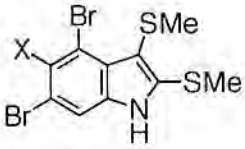
Kamei *et al.*[1] isolated bromomethylthioindoles MC 5-8 from marine algae as the most active anti-MRSA substances. We have interested in the total synthesis of these compounds from the view point of its activities and the chemistry of the alkylthiolation of indoles. We have applied the following our new observations to the total synthesis of MC 5-8.

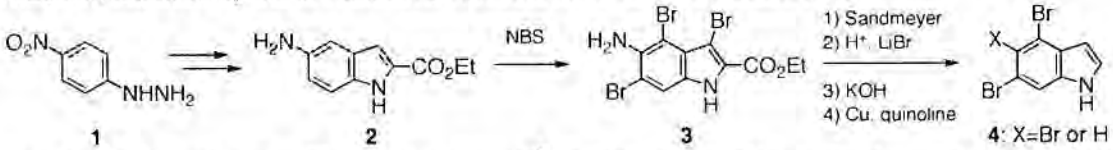


MC 5: X=H
MC 7: X=Br

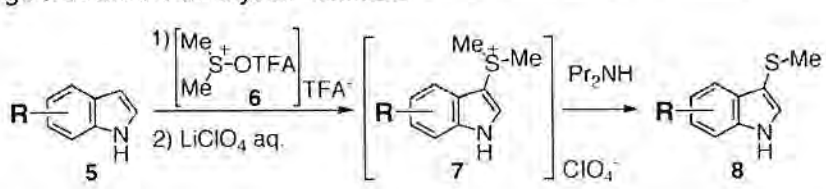


MC 6: X=H
MC 8: X=Br

1. Regioselective synthesis of C^4-C^6 poly-brominated indoles 4.
The 4,5,6-tri- and 4,6-dibromoindoles 4 were synthesized *via* bromination of 2, and Sandmeyer reaction, followed by the C^3-selective *non*-reductive *de*-bromination of 3.

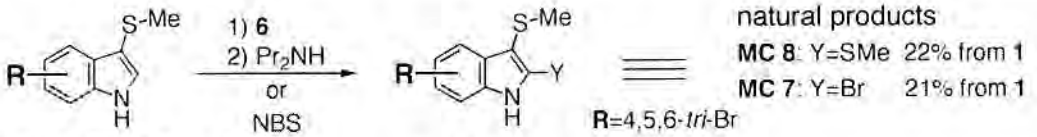


2. Introduction of methylthio group into C^3-position of indoles without using stinky thiols[2]. We developed a new synthetic method for 3-methylthioindoles 8 from unprotected indoles 5 using DMSO-TFAA complex 6 *via* dimethylsulfonium salt 7. The salt 7 was *de*-methylated by refluxing in Pr_2NH to give desired 3-methylthioindoles 8.



R	Yield (%) of **8**
H	89
5-NO_2	84
5-Me	91
2-CO_2Et	75
4,5,6-*tri*-Br	**99**

3. Electrophilic substitution at C^2-position of 3-methylthioindoles 8[2].
Introduction of the methylthio or bromo group at the C^2-position of 3-methylthioindoles 8 was achieved by DMSO-TFAA complex 6 or NBS *via* the electrophilic substitution at C^2-position.



8: **R**= 5-NO_2, 1-Ts, 4,5,6-*tri*-Br
9: Y=SMe, Br

natural products
MC 8: Y=SMe 22% from **1**
MC 7: Y=Br 21% from **1**

Consequently we achieved the first total synthesis of the anti-MRSA natural products MC 7 and MC 8 in good yields. The synthesized MC 7 and MC 8, as well as some synthetic intermediates showed potent anti-MRSA and anti-VRE activities. The total synthesis of MC 5 and MC 6 is now in progress.

References:
(1) Horikawa, M.; Noro, T.; Kamei, Y. *J. Antibiot.* 1999; *52*, 186-189.
(2) Suzuki, H.; Mori, Y.; Kasahara, Y.; Sawada, K.; Hamashima, T.; Kamei, Y.; Okuno, H.; 233rd ACS National Meeting No. 196, 2007 (Chicago)

MP118

ASYMMETRIC SYNTHESIS OF PIPERIDINE DRIVATIVES BY USING THIOUREA-CATALYZED ASYMMETRIC MICHAEL ADDITION OF ACTIVATED METHYLENE COMPOUNDS TO -UNSATURATED IMIDES

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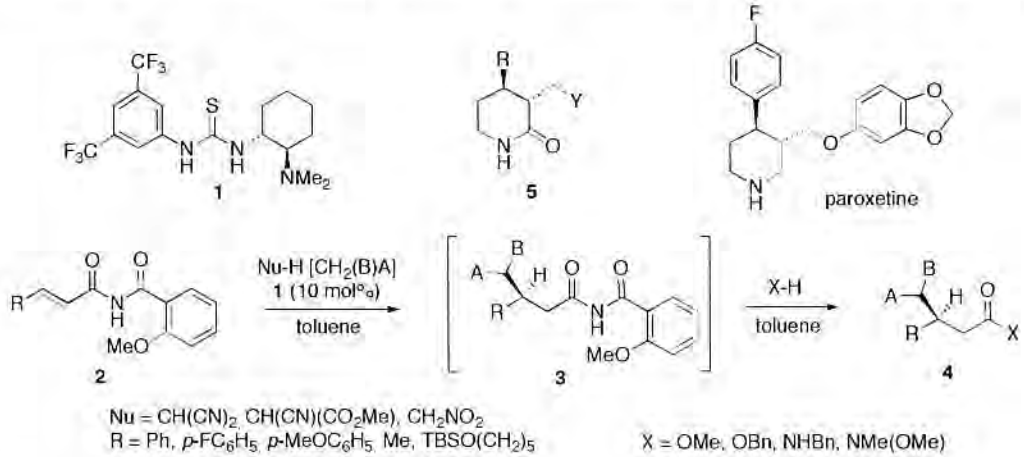
Piperidine moiety, as an important structural component of several key biomolecules and natural products, has been widely employed in the design of biologically active compounds. Therefore, considerable effort has been directed toward the synthesis of such heterocycle. As a part of our ongoing study on developing novel and efficient asymmetric reactions using bifunctional thiourea catalysts,[1,2] we investigated thiourea-catalyzed asymmetric Michael addition of activated methylene compounds to α,β-unsaturated carboxylic acid derivatives for the synthesis of chiral 3,4-disubstituted piperidines. In this presentation, we will present the details of the organocatalytic enantioselective Michael reactions of different nucleophiles with various α,β-unsaturated imides.[3]

Although we had already reported that the bifunctional thiourea-catalyzed Michael reactions of 1,3-dicarbonyl compounds such as methyl malonate and β-keto esters with nitroalkenes proceeded with high enantioselectivity of up to 93% ee,[1] the same reaction with α,β-unsaturated acid derivatives gave no addition products. To extend the synthetic utility of bifunctional thiourea 1 in the asymmetric reaction, we undertook screening of proper Michael acceptors other than nitroalkenes by using malononitrile. Further examination revealed that *N*-alkenoyl-2-methoxybenzamide 2 was the best substrate among the corresponding benzamide derivatives bearing different substituents on the aromatic ring. Indeed, several activated methylene compounds such as malononitrile, methyl α-cyanoacetate, and nitromethane could be employed as a nucleophile to give the Michael adducts 3 in good to excellent yields with up to 93% ee. The results of spectroscopic experiments clarified that this enhanced reactivity was attributed to intramolecular hydrogen-bonding interaction between the N-H of the imide and the methoxy group of the benzamide moiety. Thus, the key to success of the catalytic enantioselective Michael addition is dual activation of the substrate by both intramolecular hydrogen-bonding in the imide and intermolecular hydrogen-bonding with thiourea 1 as well as the activation of a nucleophile by the tertiary amine of the bifunctional thiourea. We also discuss about the reaction mechanism and synthetic application of the Michael adducts 3 into more versatile compounds 4 and 5.



References:

1) Okino, T.; Hoashi, Y.; Furukawa, T.; Xu, X.; Takemoto, Y. *J. Am. Chem. Soc.* 2005, *127*, 119-125; Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* 2003, *125*, 12672-12673.
2) Okino, T.; Nakamura, S.; Furukawa, T.; Takemoto, Y. *Org. Lett.* 2004, *6*, 625-627.
3) Y. Hoashi, T. Okino, Y. Takemoto,, *Angew. Chem. Int. Ed.*, 2005, *44*, 4032-4035; Inokuma, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* 2006, *128*, 9413-9419.

MP119

SYNTHESES AND THERMAL REACTIONS OF HETEROCYCLIC SULFIDES AND SULFOXIDES HAVING SEVERAL SUBSTITUENTS ON β-POSITION

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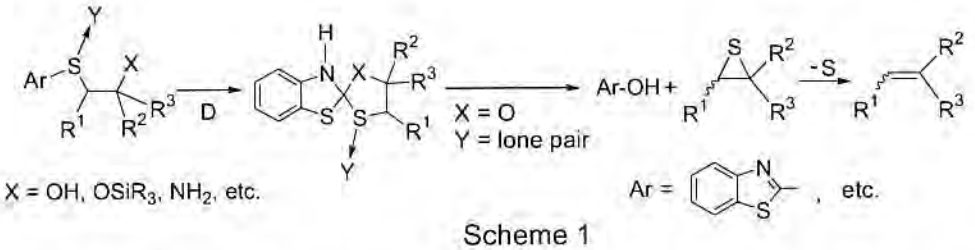
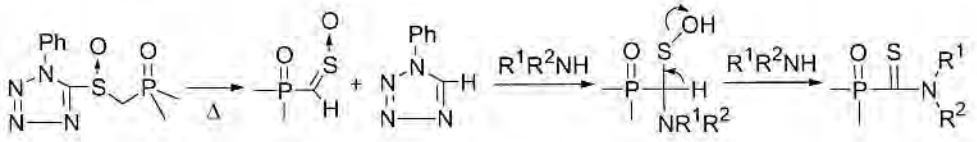
Previously, the authors have reported that β-phenacyl sulfoxides bearing several heteroaromatics, such as 2-*N*-oxypyridiyl, 2-benzothiazolyl, 5-(1-methyl)-1,2,3,4-tetrazolyl, and 5-(1-phenyl)-1,2,3,4-tetrazolyl groups, undergo thermolytic reactions to afford the corresponding thioaldehydes or sulfines, depending on the nature of heteroaromatics.[1), 2)] Further, the authors have studied the thermolysis of β-hydroxysulfides[3)] bearing several heterocycles to afforded the corresponding substituted olefins and hydroxy heteroaromatics in excellent yields, respectively. From the results of the formation of sulfur-oxygen exchange product, i.e., hydroxy heteroaromatics, and other mechanistic studies, the olefin product was considered to be formed *via* the five-membered spiro intermediates (Scheme 1).



Scheme 1

This time the thermolysis of β-hydroxy sulfoxides bearing benzothiazole has been also examined. The formation of bis[2-(2-benzothiazoloxy)ethyl] disulfide seems to suggest that the thermolysis proceeded *via* the initial formation of the spiro-intermediate to form [2-(2-benzothiazoloxy)ethyl]-1-sulfenic acid, which was converted to the disulfide consecutively. We have also studied the thermolysis of β-oxyphosphosulfoxide bearing several heteroaromatics.[4)] In their thermolyses in the presence of several amines, phosphincarbothioamide were formed in good yield. This result suggests that sulfine containing phosphine oxide derivatives is formed as the reaction intermediate. The details will be present and discussed.



Scheme 2

References:

1) Morita, H.; Takeda, M.; Kamiyama, H.; Yoshimura, T.; Fujii, T.; Ono, S.; Shimasaki, C. *J. Org. Chem.* 1997, *62*, 9018.

2) Morita, H.; Takeda, M.; Kamiyama, H.; Yoshimura, T.; Fujii, T.; Ono, S.; Shimasaki, C. *J. Org. Chem.* 1999, *64*, 6730.

3) Morita, H.; Yamada, N.; Mizuochi, M. *Tetrahedron* 2007 in press.

4) Morita, H.; Takeda, M.; Fujii, T.; Yoshimura, T.; Shimasaki, C. *Tetrahedron Lett.* 1999, *40*, 2327.

MP120

THE THERMOLYSIS OF *DISPIRO*-1,2,4-TRIOXANES TO PRODUCE MACROLIDES

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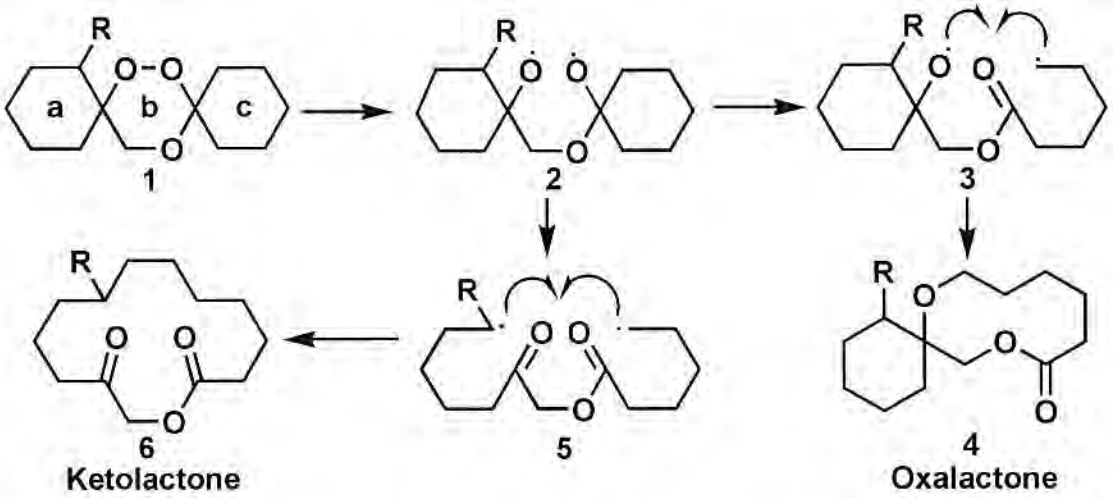
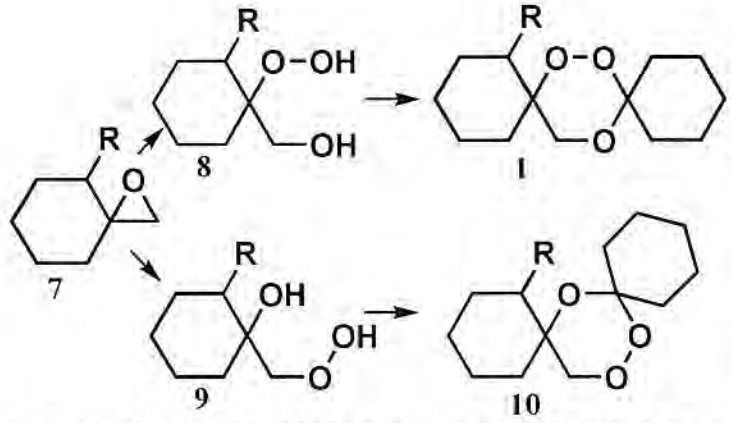
Heriot-Watt University, Edinburgh, Scotland, EH144AS

Macrolides with complex substitution patterns have a wide range of pharmaceutical applications, including as antibiotics, anti-tumour agents and anti-HIV agents. In addition structurally simple macrolides are also components of natural musks or fragrances. Thermolysis of *dispiro*-1,2,4-trioxanes (1) offers a potentially convenient synthetic route to macrolides as outlined in Scheme 1.



Scheme 1 However, the thermolysis of trioxane (1, R=H) produced a mixture of fragmented products and the oxalactone (4). In contrast, thermolysis of *dispiro*-1,2,4-trioxanes (1, R=OMe) produced the 14-membered macrolide (6, R=OMe) as the major isolable product in high yield. This synthetic route has produced a number of novel macrolides in high yield from *dispiro*-1,2,4-trioxanes. Investigation of the mechanism by DFT calculations predicts the rate of opening of ring a is significantly slower than that of ring c and so is the key step that determines the product obtained. In addition, varying the nature of the R group dramatically lowers the barrier to opening of a.

The Synthesis of novel *dispiro*-1,2,4-trioxane structures



1,2,4-Trioxane rings hold anti-malarial properties first seen in the Chinese herb qinghaosu. *Dispiro*-1,2,4-trioxanes 1 can be prepared by acid catalysed perhydrolysis of an epoxide 7 to give 8 followed by condensation of 8 with a ketone. The use of $MoO_2(acac)_2$ as a catalyst instead of acid in the ring opening of epoxide 7 results in the formation of hydroperoxide 8 and unusually its novel isomer 9. Interestingly isomer 9 was only obtained with $MoO_2(acac)_2$, specific R groups and extended reaction times. Condensation of a cyclic ketone into 9 results in the formation of a series of novel dispiro-1,2,4-trioxanes 10.

MP121

INVESTIGATION OF THE USE OF α-METHYL PROLINE DERIVATIVES AS ORGANOCATALYSTS

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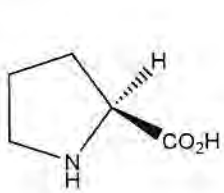
Among the increasing number of organic chiral catalysts within the growing field of asymmetric organocatalysis, *(S)*-proline (1) has gained significant attention for its ability to catalyse three major reactions, namely the Mannich reaction, the aldol reaction and the Michael addition enantioselectively.

In contrast to *(S)*-proline, *(S)*-2-methylproline (2) has only been used as an organocatalyst in a few isolated examples.[1-3] One example is the efficient and stereoselective catalysis of the intramolecular α-alkylation of aldehydes where *(S)*-2-methylproline (2) proved to be a better organocatalyst than *(S)*-proline (1).[3]

Recently, *(S)*-proline tetrazole (3) has also emerged as a better organocatalyst than *(S)*-proline (1). It has greater compatibility with organic solvents[4-6] and better efficiency, and stereoselectivity has been observed in Mannich reactions, nitro-Michael reactions, aldol reactions and α-oxidations of ketones.[4-7] Thus, by combining the advantages of the tetrazole functionality and the potential benefit from the presence of a methyl group at C-2 of the proline ring, we envisage that *(S)*-2-methylproline tetrazole (4) represents a novel organocatalyst with potential use as an efficient and enantioselective organocatalyst.

The use of *(S)*-2-methylproline (2) and *(S)*-2-methylproline tetrazole (4) will be investigated in the aldol and other reactions, and the results compared with the use of existing organocatalysts reported in literature.



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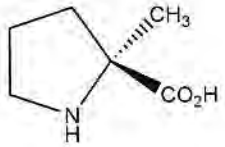

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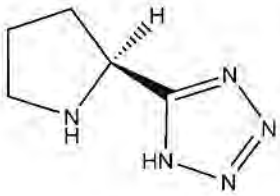

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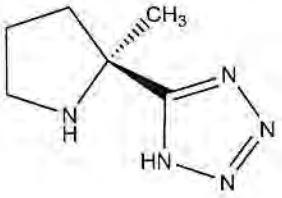

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References:

1. Sakthivel, K.; Notz, W.; Bui, T.; Barbas III, C. *J. Am. Chem. Soc.*, 2001; 123, 5260-5267.
2. Engqvist, M.; Casas, J.; Sunden, H.; Ibrahem, I.; Cordova, A. *Tetrahedron Lett.* 2005; 46, 2053-2057.
3. Vignola, N.; List, B. *J. Am. Chem. Soc.* 2004; 126, 450-451.
4. Hartikka, A.; Arvidsson, P. *Tetrahedron: Asymmetry* 2004; 15, 1831-1834.
5. Cobb, A.; Shaw, D.; Longbottom, D.; Gold, J.; Ley, S. *Org. Biomol. Chem.* 2005; 3, 84-96.
6. Cobb, A.; Shaw, D.; Ley, S. *Synlett* 2004; 3, 558-560.
7. Torri, H.; Nakadai, M.; Ishihara, K.; Saito, S.; Yamamoto, H. *Angew. Chem. Int. Ed.* 2004; 43, 1983-1986.

MP122

SYNTHESIS OF POTENT ANTITUMOR SAPONIN OSW-1 AND ITS ANALOGUES

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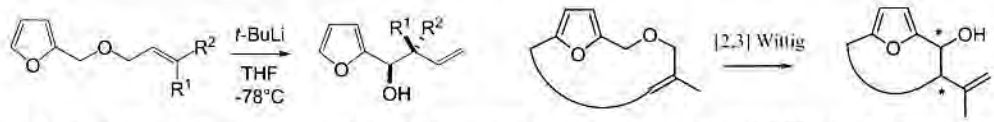
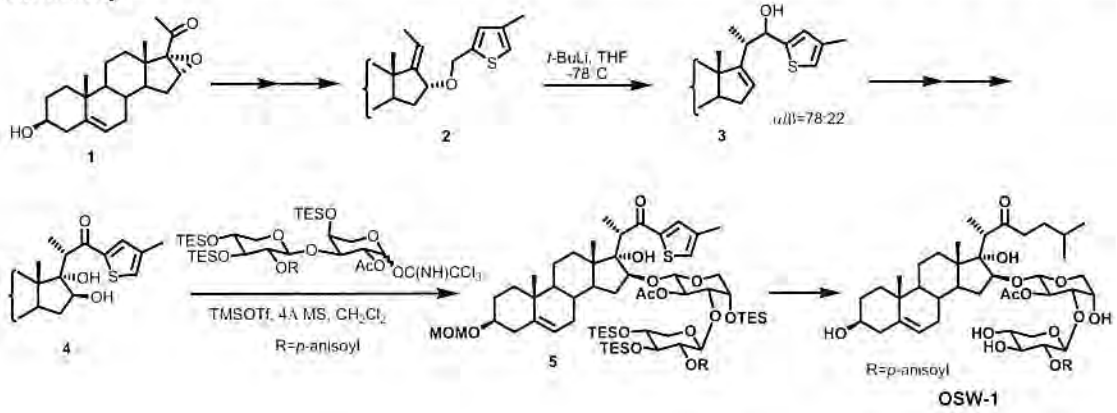
OSW-1, an acylated cholestane diglycoside, has been isolated from the bulbs of *Ornithogalum saundersiae* (Liliaceae) by Sashida, Mimaki and co-workers in 1992. OSW-1 exhibited extremely potent cytotoxic activity against various human malignant tumor cells. Its cytotoxic activities are from 10- to 100-fold more potent than some well-known anticancer agents in clinical use, such as mitomycin C, adriamycin, cisplatin, camptothecin, and taxol. Much attention has been paid on the synthesis of OSW-1 and its congeners.

We recently described the Wittig rearrangement of allyl furfuryl ethers leading to 2-furylmethanol derivatives.[1] A major advantage of this Wittig rearrangement is that the α-oxy-carbanion, deprotonated preferentially by BuLi, proceeded via 2,3-sigmatropic rearrangement to give stereoselectively homoallylic alcohols. We have succeeded in the synthesis of 2,5-bridged furanocycles containing α-isopropenyl alcohol moiety at the C(2) and C(3) positions, a common structure of furanocyclic diterpenes such as kallolide A and bipinnatin J, based on the Wittig rearrangement of cyclic allylic furfuryl ether.[2]



Thus, we intended to synthesize an extremely potent antitumor saponin OSW-1 and its analogues by means of the Wittig rearrangement of allylic thiophenemethyl ether for the construction of (20*S*)-22-hydroxy steroidal side chain.

Wittig rearrangement of 17*E*(20)-ethylidene-16α-thiophenemethyloxy steroid 2, prepared from commercially available epoxy ketone 1, afforded (20*S*)-22-hydroxy steroid 3 in 59% yield. Introduction of trans diol functionality at the C(16) and C(17) positions was carried out by usual methods to give 16β, 17α-diol 4. Glycosylation of the accepter 4 with disaccharide imidate, synthesized by the known protocol, proceeded smoothly under the promotion of TMSOTf to give the desired β-glycoside 5. Removal of all protecting groups followed by desulfurization furnished OSW-1. Synthesis of designed analogues of OSW-1 and further study of a structure-activity relationship are on the way in our laboratory.



OSW-1

References:

1. Tsubuki, M.; Kamata, T.; Okita, H.; Arai, M.; Shigihara, A.; Honda, T. *Chem. Commun.* 1999, 2263-2264.
2. Tsubuki, M.; Takahashi, K.; Honda, T. *J. Org. Chem.* 2003, *68*, 10183-10186.