MEETING REPORT

Eleventh Frank Warren conference*

Frank L. Warren was one of the pioneers of natural product chemistry in South Africa (SA). The South African Chemical Institute (SACI), the official body of chemists in SA, has been organizing 'specialist' organic chemistry conferences since July 1961. The first one was held in the Giant's Castle area of Drakensberg. After Warren's death, the council of SACI decided to formalize these organic chemistry conferences which came to be known as the 'Frank Warren National Organic Chemistry Conferences'. The Frank Warren conference was first held in Pietermaritzburg in 1983. The eleventh conference marks the fiftieth anniversary of the 'specialist' organic conferences in SA. The objective of the conference was to discuss the latest discoveries in organic chemistry and drug discovery.

The conference had plenary lectures, key lectures and invited talks by eminent scientists. The special Warren Lecture was delivered by Michael Davies-Coleman (Rhodes University (RU), Grahamstown). There were student presentations in the competition for 'young chemist' award. Over 200 researchers, including a large number of chemists and scientists from academia and industry, attended the conference. The participants represented four continents giving the conference an international perspective.

In his welcome note, the chairperson Ross Robinson (University of KwaZulu-Natal (UKZN), Pietermaritzburg) highlighted the themes of the conference and gave a brief overview of the scientific programme. Deogratius Jaganyi (UKZN) presented a brief history of these conferences. Ivan Green (SACI) elaborated upon the objectives of SACI which was established almost a century ago (in 1912) and which is striving for the advancement of science and the practice of chemistry in SA.

Richard Taylor (University of York, York) delivered a talk on 'Serendipity in natural product synthesis: tales of the unexpected'. He explained some unexpected observations in the total synthesis of bioactive natural products such as oxazolomycins, dictyosphaeric acids, daphnezomines and grandisines (Figure 1). Charles DeKoning (University of the Witwatersrand (Wits), Johannesburg) spoke on novel methods for the synthesis of oxygen containing heterocycles. He explained some new methods for the construction of the isochroman nucleus and the total synthesis of oxygen containing heterocycles such as cardinalin-3, mengeferin and gilvocarcin-V. Anthony Barrett (Imperial College London, London) highlighted the recent advances in the total synthesis of antibiotic natural products. He affirmed that the 6-alkyl-2,4-dihydroxybenzoic acid unit occurs in numerous bioactive natural products particularly as macrocyclic lactone systems. He exemplified the antifungal agents from a marine fungus *Hypoxylon oceanicum* and a protein tyrosine kinase inhibitor radicicol.

The Baylis–Hillman reaction involves the tertiary amine or phosphine-catalysed reaction between activated alkenes and aldehydes to give multifunctional adducts. The reaction has been the subject of a number of reviews and has attracted considerable attention from chemists and is described in textbooks. In this context, Perry Kaye (RU) delivered a talk on the theoretical perspectives on the Baylis–Hillman reaction. He described a theoretical study at the B3LYP/6-31g + (d) level of the 1,4-diazabicyclo[2.2.2]octane-catalysed Baylis–Hillman reaction between methyl vinyl ketone and acetaldehyde. In his talk on discovery and surprises with natural products, Erick Carreira (ETH Zurich, Zurich) pointed out that natural products are ideal for research at the interface of chemistry, biology and medicine. He explained the nature and chemical characteristics of natural and artificial chlorosulpholipids and carbohydrates (sucrose – a natural carbohydrate and sucralose – an artificial chloroderivative of carbohydrates). Roger Hunter (University of Cape Town (UCT), Rondebosch) discussed the new methods in organic synthesis. He showed the different methodologies for improved construction of key functional groups and structural motifs such as 1-chlorobenzotriazole for one-pot coupling of different thiols to generate unsymmetrical disulphides via an *in situ* trapping step.

Garreth Arnott (University of Stellenbosch, Stellenbosch) spoke about the asymmetric synthesis of inherently chiral calix[4]arenes. He explained that they are supramolecular bowl-shaped compounds that can be readily synthesized by condensation of p-substituted phenols and formaldehyde. The three-dimensional shape facilitates their use as building blocks for a variety of applications such as receptors for anions, cations and neutral molecules. Henok Kinfe (University of Johannesburg, Johannesburg) talked about the selective O-glycoside synthesis from glycals by $Al(OTf)_3$-catalysed addition or ferrier rearrangement reactions. Rosa Klein (RU) gave a talk on the applications of solution state nuclear magnetic resonance (NMR) in the determination of the structure of organolithium aggregates. She explained that ^{13}C and ^{7}Li-NMR studies suggested a diversity in organolithiums formed in the metal-halogen exchange (MHE) reaction leading to a smorgasbord of products on subsequent electrophilic aromatic substitution with geranyl bromide. Johan Jordaan (North-West University (NWU), Potchefstroom) elucidated the chemistry of decacyclo[$10.7.2.0.^{1,2}.0.^{2,6}.0^{3,10}.0.^{4,9}.0^{7,11}.0^{14,20}.0.^{15,21}$] heneicosane-5,8,13,19-tetraone. He mentioned that Grubbs pre-catalysts are useful in ring closing metathesis, self metathesis, cross metathesis and ring opening metathesis polymerization.

Dennis Liotta (Emory University, Atlanta) gave a presentation on new therapies for treating cancer and inflammation. He explained that the combined efforts of chemists, pharmacologists and biochemists at Emory University have resulted in the successful development of novel and selective preclinical and clinical agents of biomedical interest. He revealed some success stories such as the identification of novel small molecules

*A report on the eleventh Frank Warren conference held at the University of KwaZulu-Natal, Pietermaritzburg, South Africa during 17–21 January 2010. The event was organized by the South African Chemical Institute.

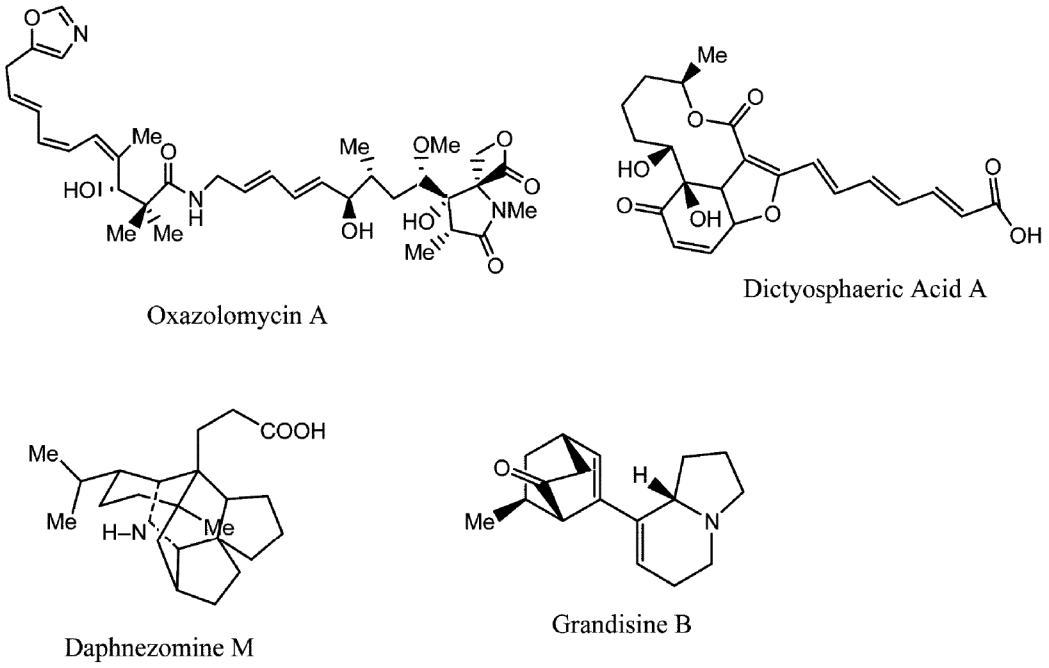

Figure 1. Bioactive natural products (Credit: Richard Taylor).

targeted to CXXR4 (sphingosine, sphinganine and ceramide) and NFkB (triptolide and its derivatives), both of which play significant roles in the progression of many types of cancers and inflammatory diseases. In her talk on the design of non-steroidal glucocorticoid receptor agonists, Hawa Diallo (EpiNova DPU, Stevenage) explained that inflammatory diseases such as rheumatoid arthritis, chronic obstructive pulmonary disease (COPD) and asthma have been treated for many years with glucocorticoid agonists and oral glucocorticoids like dexamethasone and prednisolone. She discussed the discovery of novel non-steroidal glucocorticoid receptor agonists by her group. Chris Edlin (iThemba Pharmaceuticals, Gauteng) gave a lucid presentation on breathing life into phosphodiesterase (PDE)-4 inhibitors. He explained that PDE-4 inhibitors are a class of drugs that can provide therapies for asthma and COPD and described some of the new strategies for developing inhaled drugs for these disorders.

The folate metabolism has been successfully targeted for both the prophylaxis and the treatment of malaria. *Plasmodium falciparum* (Pf) dihydrofolate reductase-thymidylate synthase (DHFR-TS) is a validated target for malaria chemotherapy. Amanda Rousseau (CSIR Biosciences (CSIR), Modderfontein) delivered a talk on novel anti-malarials targeting the folate metabolism. She revealed that her group has developed a novel series of compounds targeting the folate metabolism based on a design utilizing the crystal structures of wild type and mutant PfDHFR. This series of compounds have shown potent activity against a chloroquine/cyguanil resistant strain of *P. falciparum* (Gambian FCR-3 strain). Arina Lourens (CSIR) gave a presentation on the design and synthesis of potential IspF enzyme inhibitors. She narrated her group's experiences in the development of IspF enzyme inhibitors using pharmacophore generation and screening of ligands *in silico* against the pharmacophore and/or docking in the crystal structure of *E. coli* IspF-CDP. Ben Bezuidenhoudt (University of the Free State (UFS), Bloemfontein) discussed the conversion of pravastatin into an advanced intermediate in the synthesis of HMG-CoA reductase inhibitor BB-476. Owing to the multistep process with low overall yields (ca 2%) of the existing total synthetic procedure for BB-476, alternative routes for commercial access to this compound were investigated through pravastatin.

Carl Montague (LIFE lab, Durban) highlighted LIFE lab's requirement for medicinal chemistry skills in its human health portfolio. He explained that his lab is one of the four biotechnology innovation centres established by the Department of Science and Technology, serving as a vehicle to implement national biotechnology strategies. It was established in 2003 and has two portfolios – human health and bioprocessing. The human health portfolio focuses mainly on infectious diseases that are major health challenges in Africa, viz. HIV/AIDS, tuberculosis and malaria.

Michael Davies-Coleman, in the Warren Lecture, outlined the perspectives on the research on natural products. He titled this talk suitably as 'natural products research in South Africa – end of an era or an endless opportunity?' He explained that the pharmaceutical industry has been relying heavily on natural products or natural product-derived new chemical entities (NCEs) to fuel the drug discovery pipeline. He explored the current status of natural product research in SA with respect to first, the legacy of Frank Warren and other pioneers of natural product chemistry and second, South Africa's ability to respond to an emerging paradigm shift in global natural product research. Davies-Coleman offered several examples to suggest that there are endless opportunities for natural product research and potential for natural product drug discovery in the oceans of SA, one illustration was that of the pyrroloimi-

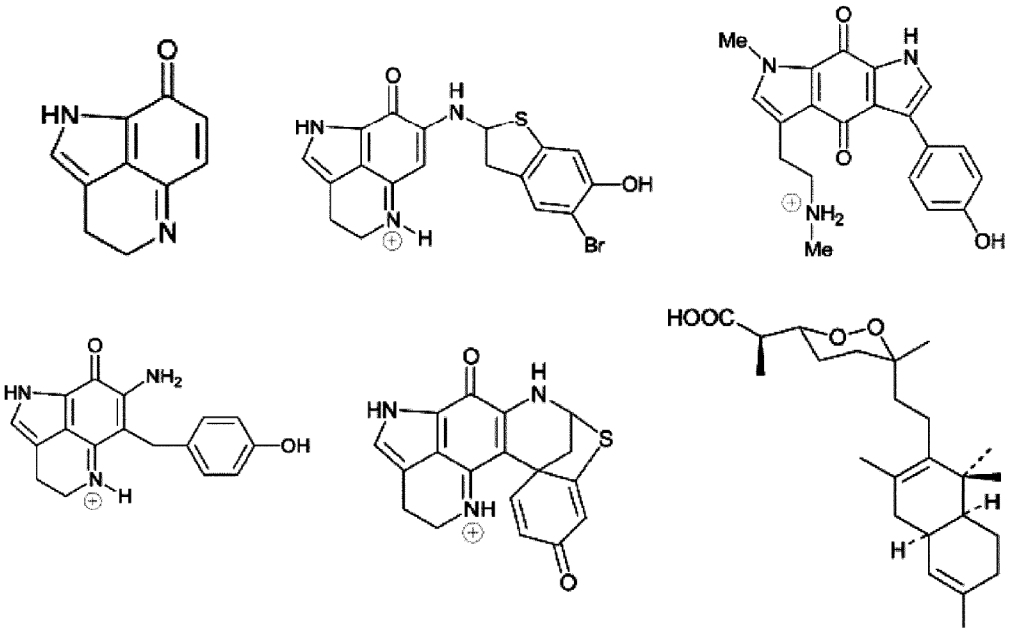

Figure 2. Pyrroloiminonquinone metabolites isolated from *Tsitsikamma* and *Strongylodesma* species (Credit: Michael Davies-Coleman).

noquinone metabolites isolated from endemic SA marine sponges of the genus *Tsitsikamma* and *Strongylodesma* species (Figure 2).

Ernest Giralt (University of Barcelona, Barcelona) delivered a talk on peptide design for protein-surface recognition. Jan van der Westhuizen (UFS) spoke on the photochemical synthesis of flavonoids and related compounds and Vosloo (NWU) lectured on the design and development of Grubbs-type complexes for use in alkene metathesis reactions. Stephen Pyne (University of Wollongong, New South Wales) gave a presentation on the structural revisions and total synthesis of polyhydroxylated pyrrolizidine alkaloids. Malose Mphahlele (University of South Africa, Pretoria) spoke on 4-substituted-2-aryl-3-iodoquinolines as substrates for the synthesis of polysubstituted and polynuclear quinoline derivatives.

Cedric McCleland (Nelson Mandela Metropolitan University, Port Elizabeth) delivered a talk on the computational studies on radical and radical-cation mediated cyclization reactions. Russell Barrow (Australian National University, Canberra) spoke on chemists with culture. Andrew Marston (UFS) presented on the isolation of acetylcholinesterase inhibitors (ACEI) from amaryllidaceae by high-speed counter-current chromatography. David Gammon (UCT) described the work on preparing unusual biologically-active branched sugars. Willem Otterlo (Wits) talked about small molecules in the field of chemical biology.

Overall, the conference highlighted the research being carried out in organic chemistry and drug design. Towards the end of the conference, it was announced that the next (twelfth) Frank Warren conference will be held at Rhodes University in 2012 under the leadership of Davies-Coleman.

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