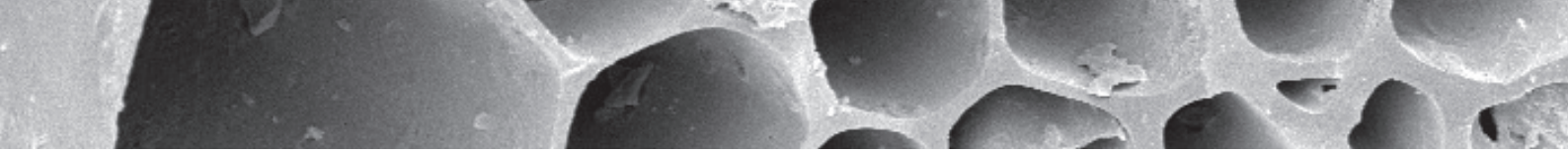
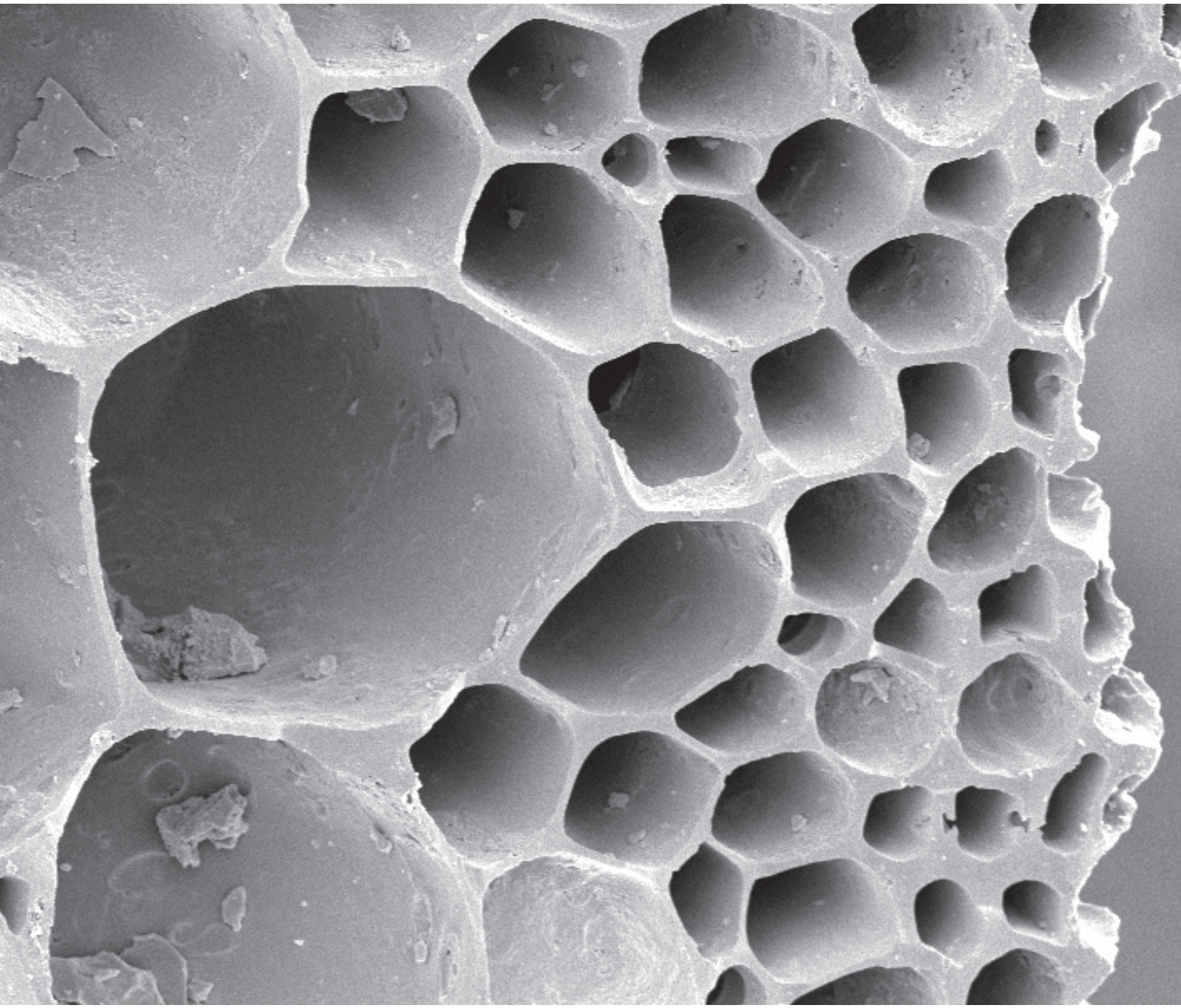
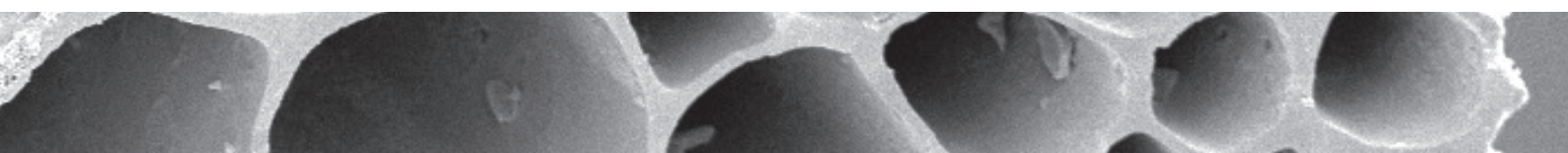


# CHEMISTRY
## in Sri Lanka



The Tri Annual Publication of
the Institute of Chemistry Ceylon

September 2019 Volume 36 No. 03



# Chemistry in Sri Lanka

ISSN 1012 - 8999

**The Tri-Annual Publication of the Institute of Chemistry Ceylon**

Founded in 1971, Incorporated by Act of Parliament No. 15 of 1972

Successor to the Chemical Society of Ceylon, founded on 25th January 1941

**Vol. 36 No. 3** **September 2019**



Theme for the year -

**Shaping Careers of Chemists Through Advancement of Chemical Technology**

Adamantane House, 341/22, Kotte Road, Welikada, Rajagiriya

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E mail : ichemc@sltnet.lk web page : www.ichemc.edu.lk

## Outline of our Institute

The Institute of Chemistry Ceylon is a professional body and a learned society founded in 1971 and incorporated by act of Parliament No. 15 of 1972. It is the successor to the Chemical Society of Ceylon which was founded in 1941. Over 50 years of existence in Sri Lanka makes it the oldest scientific body in the country.

The Institute has been established for the general advancement of the science and practice of Chemistry and for the enhancement of the status of the profession of Chemistry in Sri Lanka. The Institute represents all branches of the profession and its membership is accepted by the government of Sri Lanka (by establishment circular 234 of 9-3-77) for purposes of recruitment and promotion of chemists.

**Corporate Membership**
Full membership is referred to as corporate membership and consists of two grades: **Fellow (F.I.Chem.C.)** and **Member (M.I.Chem.C.)**

Application for non-corporate membership is entertained for four grades: Associate (former Graduate) (A.I.Chem.C.), Licenciate (L.I.Chem.C.), Technician (Tech.I.Chem.C.) and Affiliate Member.

**Revision of Membership Regulation**
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Those who have passed the DLTC examination or LTCC examination or have obtained equivalent qualification and are engaged in the practice of Chemistry (or chemical sciences) acceptable to the Council are entitled to the designation Tech.I.Chem.C.
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All corporate members (Members / Fellows) are entitled to vote and become Council/ Committee members whether Chartered Chemists or not.

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Any application for admission to the appropriate class of membership or for transfer should be made on the prescribed form available from the Institute Office.

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Fees should be payed on 1st of July every year and will be in respect of the year commencing from 1st July to 30th June

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## *CHEMISTRY IN SRI LANKA*

*Chemistry in Sri Lanka is a tri-annual publication of the Institute of Chemistry Ceylon and is published in January, May and September of each year. It is circulated among the members of the Institute of Chemistry and students of the Graduateship/DLTC course and libraries. The publication has a wide circulation and more than 750 copies are published. Award winning lectures, abstracts of communications to be presented at the annual sessions, review papers, activities of the institute, membership news are some of the items included in the magazine.*

*The editor invites from the membership the following items for publication in the next issue of the Chemistry in Sri Lanka which is due to be released in January 2020.*

- *Personal news of the members*
- *Brief articles of topical interests*
- *Forthcoming conferences, seminars and workshops*
- *Latest text books and monographs of interest to chemists*

*All publications will be subjected to approval of the 'Editorial and Publicity Committee' and the Council of the Institute of Chemistry Ceylon.*

*Further, prospective career opportunities for chemists, could be advertised in Chemistry in Sri Lanka at a nominal payment. The editor welcomes suggestions from the members for improvement of the publication.*

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## Guest Editorial

# My life with light

Dr. Tharushi A Perera

*Assistant Teaching Professor, Mercy College, Dobbs Ferry, NY 10522, USA*

I sincerely thank Dr. Ranmal Gunatilake, Hon. Editor, Institute of Chemistry Ceylon for the opportunity to address the Chemistry in Sri Lanka readers through the medium of this guest editorial. It is a real honor and pleasure for me. Herein, I would like to share with you the unprecedented results of my scientific research, life with light.

The ability to access the divergent reactivity of organic molecules by thermal or photochemical control was exquisitely described by Woodward and Hoffmann in a series of papers dating back to 1965. From this work, the so-called "Woodward–Hoffmann rules" established a distinction between the stereospecificity observed under thermal and photochemical control based on the topology of orbital interactions. In parallel to these findings, advances in quantum mechanics and molecular orbital theory helped to delineate the dichotomy between the structure and reactivity of the triplet and singlet ground-state carbenes. While the origin of triplet carbenes date back to the early 1800s when Dumas attempted to dehydrate methanol, the existence of singlet carbenes was first elucidated in the late 1950s by Breslow and Wanzlick (Figure 1).

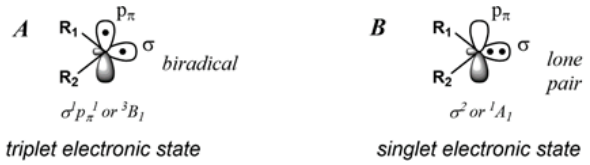


**Figure 1:** Electronic spin states of triplet (A) and singlet (B) carbenes.

Despite numerous modifications to the structure of singlet and triplet carbenes, there has been a minimal success in preparing isolable triplet analogs, or singlet carbenes that display triplet reactivity (Figure 2).

The discovery of thermal and photochemical control by Woodward and Hoffmann revolutionized how we understand chemical reactivity. Similarly, we were able to show the first example of a carbene that exhibits differing thermal and photochemical reactivity. When a singlet ground-state N,N′-diamidocarbene (DAC) 1 was photolyzed at 380 nm, excitation to a triplet state was observed. The triplet-state electronic structure was characteristic of the expected biradical σ1pπ1 spin configuration according to a combination of spectroscopic and computational methods. Surprisingly, the triplet state of 1 was found to engage a series of arenes in thermally reversible Büchner ring expansion reactions, marking the first examples where both cyclopropanation and ring expansion of arenes were rendered reversible.4 Not only are these photochemical reactions different from the known thermal chemistry of 1, but the reversibility enabled us to perform the first examples of photochemically induced arene exchange/expansion reactions at a single carbon center.

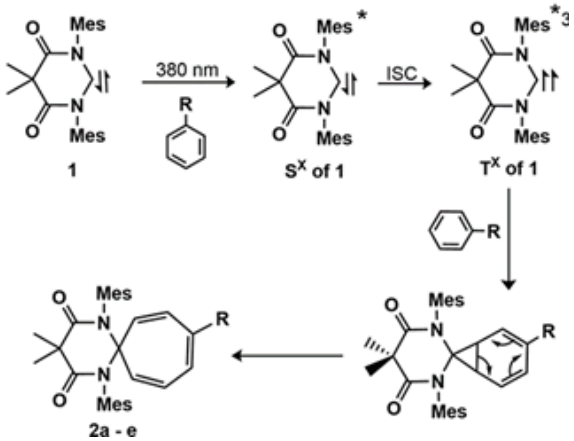


**Figure 2:** Proposed mechanism for the formation of 2a – 2e

We have revised the long-standing precept that stable, isolable carbenes exist as a singlet ground state whereas transient carbenes are typically regarded as triplet ground-state carbenes, showing that it is no longer

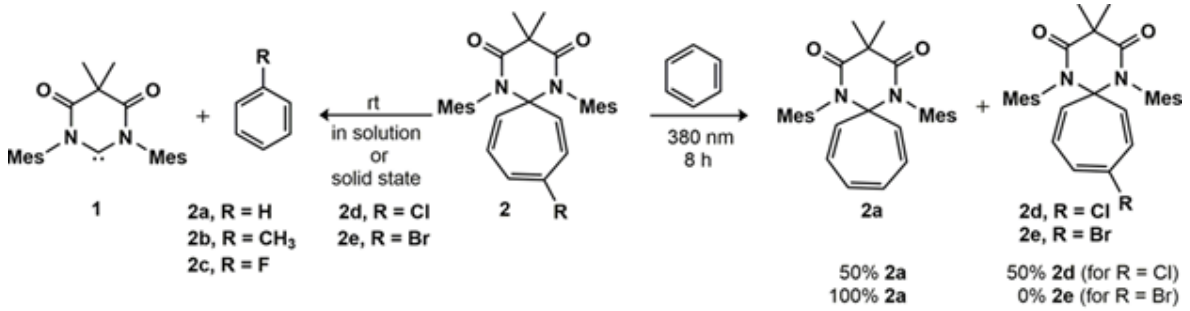


**Figure 3:** Reversibility of Büchner ring expansion reactions

valid. We reported that both spin states (and attendant reactivity) are accessible for the diamidocarbene 1. While 1 is isolated as a highly stable singlet electronic ground-state, carbene photolysis at 380 nm allows for the rapid conversion through intersystem crossing to an excited triplet state. The triplet excited state of 1 has been fully characterized through a combination of low-temperature spectroscopic measurements and computational analyses. These studies indicate that the excited state of 1 can be characterized as the expected spin-unpaired biradical structure, typical of triplet carbenes. The triplet excited state of 1 was also found to engage a series of aromatic compounds in the known Büchner ring expansion reaction to cleanly afford a single cycloheptatriene isomer in all cases (2a–2e) (Figure 3). Remarkably, the photochemical reaction of 1 with benzene or toluene provided drastically different products than the known thermal products (which forms the from C–H activation processes) reported by Bielawski. In this regard, we equate the two distinct reactivity profiles of 1 as photochemical and thermal control like what Woodward and Hoffmann described for pericyclic electrocyclization reactions.

Beyond the novelty of accessing the triplet excited state of DAC 1, the subsequent Büchner ring expansion reactions were found to exhibit unprecedented reversibility, even in the solid state for some derivatives. This unique feature provided the first examples where both cyclopropanation and ring expansion reactions were rendered reversible, enabling the ability to interconvert 2d or 2e into 2a through atom-economic, high-fidelity photochemical reactions. The surprising discoveries presented herein are likely to initiate new fundamental studies and expand the applications of stable carbenes. Similar to other reversible ring-forming reactions, such as the Diels–Alder reaction, reversible Büchner ring expansion processes may also find applications ranging from structurally dynamic materials to novel methodologies in organic synthesis as the cycloheptatriene motif is commonly found in biologically active molecules.

College of Chemical Sciences is home, a place very close to my heart. Whenever I think of CCS, it reminds me of three things: vibrant schedule, great friends and amazing teachers. Speaking of amazing teachers, Late Emeritus Prof. J N O Fernando, Prof. S P Deraniyagala, Mr. Mevan Pieris, Dr. Sisira Weliwegamage, Prof. S Sotheeswaran, Prof. S A Deraniyagala, Prof. H D Gunawardhana, Prof. M D P De Costa and Mr. M R M Haniffa are few of many teachers who have made a distinct impression in my mind. I'm forever grateful to them for their guidance, help, support and best wishes.

**References:**

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## Message from the President

Senior Professor Priyani A Paranagama
*President, Institute of Chemistry, Ceylon*
*Director, Institute of Indigenous Medicine, University of Colombo*
*Chair and Senior Professor, Department of Chemistry, University of Kelaniya*

It is an absolute honour for me to have been entrusted with the prestigious role of the President of the Institute of Chemistry Ceylon 2019/2020. I would like to express my sincere gratitude to my predecessor, Prof Sudantha Liyanage, for his outstanding leadership in steering the Institute to greater heights during his term as the President.

Chemistry being a part of many different aspects in everyday life, opens up a myriad of opportunities for someone who seeks a career in chemistry. Thus, "Shaping Careers of Chemists through Advancement of Chemical Technology" – the Council theme for 2019/2020 has been chosen with the vision of linking scientific discoveries and their applications in the industry.

Among the many goals I have set for the coming year, the International Conference on "Frontiers in Chemical Technology" takes precedence. The primary objective of this conference is to form a bridge between the industries and the scientists around the globe in order to propel the launch of scientific innovations in the world. The conference, being chaired by myself, will be held at the Galle Face Hotel, Colombo from 17$^{th}$ to 19$^{th}$ June, 2020 with the participation of scientists and enthusiastic young chemists from all over the world.

Female chemistry professionals play an essential role in enhancing and promoting uses of chemistry. Hence, the establishment of a Women Chemists Committee (WCC) in the Institute is another milestone I intend to achieve during my term as the President. The mission of such a committee is to attract, retain, develop, promote, and advocate for women to positively impact diversity, equity and inclusion in the society and the profession. Thereby it is intended to bring about the empowerment of women throughout the chemical enterprise.

The commencement of the BSc (Hons) Chemistry programme is another top priority goal in my activity plan for the year. We have already completed the Institutional Review process and are awaiting the comments of the Programme Review. As soon as the comments are received, we hope to work on them and implement any necessary changes to offer the BSc programme at the College of Chemical Sciences without any further delay.

I also hope to prompt the construction project for the new building at Malabe which will accommodate lecture halls, laboratory facilities, instrument centres and administrative offices of the Institute of Chemistry and will be serving a student population of over 1000. The laying of the foundation stone for the building is scheduled to take place in September and it is hoped that the actual construction work will begin soon after.

The development project in Dehiwela is another venture I plan to embark on during my term as the President of the Institute. This project is undertaken to generate funds for the Clodagh Nethsingha Foundation.

I am sure I will be able to succeed in achieving all of the above goals and more with the support and active contribution of the members of the Council and the Institute. I look forward to the 2019/2020 Council year and I hope that I leave the Institute in a place that is better than when I became President, by the end of my year.

# 48th Annual Sessions of the Institute of Chemistry Ceylon

Prof. Sudantha Liyanage, President, IChemC delivering the Presidential Address

Mr. Navin Adikarama, Chief Guest delivering his Address

Prof. Srianthie Deraniyagala receives the Yeoman Service Award

Mr. Sahan Jayasingha receives Special Service Award

Dr. Pamoda Ratnaweera delivering the Chandrasena Memorial Award Lecture

Winners of the All Island Chemistry Quiz 2018/19 - Mahamaya Girls' College, Kandy


Chemistry Olympiad Sri Lanka 2019 - winners with Officials

Participants

Participants

# Induction Ceremony of 82nd President and Annual Dinner of the Institute of Chemistry Ceylon

Lighting of the oil lamp by outgoing President Prof. Sudantha Liyanage

Introducing the new president by Snr. Prof. S. P. Deraniyagala

Prof. Priyani Paranagama being inducted as the 82nd President of the IChemC

Prof. Priyani Paranagama addressing the audience

Proposing the toast by Prof. Neelakanthi Gunawardena

Prof. Ajit M Abeysekera, Chief Guest delivering his address

Participants

Participants

# Forty Eighth Annual Sessions and Seventy Eighth Anniversary Celebrations 2019

## Presidential Address

Senior Professor Sudantha Liyanage, *PhD, C.Chem., F.I.Chem.C., F.PRISL, FRSC*
*Immediate Past President, Institute of Chemistry Ceylon*
*Dean of the Faculty of Technology, University of Sri Jayewardenapura*

'Chemistry' is a term that is often overlooked. It is quite seldom acknowledged as the essence of our being. Chemistry is similar to software, hardly anyone notices its existence as it makes tasks seamless. Chemistry too is of a similar nature, it is in the air we breath, the food we eat, it is very simply the soul of everyday life. Therefore, it is not surprising that in deafening silence a demand has arisen as the role chemical industries play in the society is immense. However, there is a severe gap in our struggle to move forward in the industry as Chemical education still has not stepped up to meet the desired standards in Sri Lanka.

One intricate measure of a country's development is the chemical industries that are established within the country and in that sense, Sri Lanka is quite poor. A common indicator used for this purpose is the sulphuric acid production per annum and in Sri Lanka, it is zero. If I am not mistaken, there was a sulfuric acid plant at Ranala about ten years ago. Unfortunately, due to the associated environmental and health issues, the plant was forced to close down. We even had our own caustic soda plant at Paranthan chemicals, Jaffna. It was functioning as a government-owned Industry and it was closed down due to the Civil war. Now the current Condition of it is they import bulk chemicals from India and other countries and distribute it amongst the chemical industries and Government organizations in Sri Lanka.

Thus, it is evident that the situation has not always been so bleak. I believe, Sri Lanka saw its peak in the chemical industries during a period from 1970 to 1977. However, the privatization of certain sectors, the civil war and the introduction of high-end technology that replaced manpower resulted in the move of the Chemical-based industries to the shadows if they were fortunate enough to be operational. Without a chemical production line, a country's economy would undoubtedly suffer and there would even be negative impacts on the labour force of a country.

Chemical industries fetch billions of dollars to a country. As it is such an intricate part of everything that surrounds us, the avenues we can venture into are diverse. If we are to play a role in the upliftment of Sri Lanka's economy, we have to promote different sectors of chemical industries in Sri Lanka. Even the existing industries function with minimum technology and with short production lines, they should strive to grow larger. It is disappointing to say that most of the government policies such as taxation aren't providing a favourable environment for the existence and growth of chemical industries in Sri Lanka. It is my belief that the government should actively participate in creating a healthier environment for the chemical industries in Sri Lanka to grow.

Addressing the readers as the past president of the Institute of Chemistry Ceylon, I am confident in assuring that the Sri Lankan society is strong enough to withstand the changes that are occurring globally. It is also a journey that the Sri Lankan society must welcome if it is to promote and secure upcoming industries.

For this to succeed the education and foundation that is given at the College of Chemical Sciences should be strong. It should provide aspiring young minds the necessary intellect to foresee and work towards a smarter and braver nation.

As an institution, we are responsible for nurturing keen minds. However, that is just one part of the equation.

The staff of an institute is the backbone of it. My mantra in the manner in which I led was to create a wholesome employer-employee relationship. As I said, chemistry is important and it resonates to create a better environment for our students.

During my time here, I have grown personally and professionally. It is my sincere hope that I have moulded IChemC with my aspirations of providing those keen with the education to change the trajectory of this nation.

Stepping down from my authority as the president of the IChemC, I wish everyone the best of luck and hope that one day Sri Lanka would grow to become the dream nation and that all scientists would collaboratively move towards achieving this goal.

~~*~~

## Chief Guest's Address

Mr. Navin Adikarama

*Chairman, Industrial Development Board of Ceylon*

Chemical industries have drastically impacted the lives of people. Unconsciously or consciously, all quotidian activities involve chemicals in one way or the other. In 2011, it was estimated that the world chemicals sales amounted to over $3500 billion. This means every man, woman, and child around the world, on average, uses $500 worth of chemicals a year. Of course, the main users of the chemicals are in the developed countries, with each person using approximately $1200 worth of chemicals annually. In 2017, India exported chemicals worth of about USD 3 billion and Singapore, chemicals that are of about USD 3.1 billion worth.

However, in Sri Lanka, we have an industrial sector that contributed to about 27% of the GDP and a manufacturing sector contributing approximately about 18.2%. What is unfortunate, is that there has been a decline observed in the contribution from chemical-related industries as much as 4.1% in 2018. This is challenging for Sri Lanka and the question arises, how can we overcome this challenge?

Become smart! The answer is as simple as that. Smart products, smart tax regimes, smart innovations, and products. Since long, educational systems in Sri Lanka has worked towards introducing well-qualified professionals in the stream of Chemistry to the global and local market. One such Institute that is worthy of commendation is the Institute of Chemistry Ceylon, a body that has been contributing to the development of branches related to science massively. The graduates that are produced from the Institute have a substantial role in contributing to the development of chemical-based industries. What is mainly needed for the development of these industries is access to raw materials, plentiful water supplies, good communications (road, rail and port facilities), and closeness to the customer for the products, reliable energy supplies, and the availability of skilled labor.

We all agree that technological advancements are for the holistic wellbeing of all humans. We must not forget that we have to hand over a well-established and developed country to our future generations which becomes an intricate responsibility of all members at the Institute of Chemistry Ceylon.

## Yeoman Service Award: Professor Srianthie Deraniyagala

Prof. Srianthie Deraniyagala graduated from the University of Colombo in 1978, with a First Class Honours degree in Chemistry. In 1979, she joined the Department of Chemistry, University of Colombo as an Assistant Lecturer and was promoted as a Senior Lecturer, Associate Professor, Professor and Senior Professor, the post she currently holds. She has 40 years of service at the University of Colombo.

She obtained her PhD in 1984 from Dalhousie University, Canada in the area of Bio-Organic Chemistry. She spent her sabbatical leave at Wesleyan University, USA working on beta-lactamases. Prof. Deraniyagala is a keen and active researcher, whose research focuses primarily on studying the bioactivity of medicinal plants. She has numerous publications both locally and internationally to her credit. She has also authored several books, monographs and book chapters.

Prof. Srianthie Deraniyagala has served the College of Chemical Sciences, Institute of Chemistry Ceylon as a visiting lecturer since way back in 1986. She was a visiting Senior Professor at the College from January 2015 to October 2015 and again from May 2018 to November 2018. In this capacity, in addition to conducting lectures and laboratory classes and supervising students in their research work, she was heavily involved in curriculum development.

She has served on numerous committees during her long association with the Institute. She has held key positions as; Editor, 1994/1995; Chairperson, Science Popularization Committee, 1995/1996; Assistant Treasurer 2005/2006; Chairperson, School Chemistry Programme 2005/2006; and Chairperson, Monograph Committee 2012 to date.

She has also served as a Member of several committees. Namely, the Academic Board from 1998 to date; Editorial & Publicity Committee, 1995 to 1999 and again in 2003/2004; Science Education Committee, 2002 to 2005; Training Seminars & Workshops Committee, 2008/2009; Building Project Committee, 2002 to 2005, Library Committee, 2004/2005; House & Finance Committee, 1994/1995, 2003 to 2006 and again in 2015/2016; and Social Affairs Committee, 1996 to 1999.

Prof. Srianthie Deraniyagala has contributed immensely to the upliftment of the programmes and activities conducted by the College of Chemical Sciences and the Institute of Chemistry Ceylon for over 30 years. In recognition of the valuable and dedicated service rendered by her, in an honorary capacity, the Council of the Institute of Chemistry Ceylon unanimously decided to award Professor Srianthie Ayoma Deraniyagala the Yeomen Service Award at the 48th Annual Sessions of the Institute of Chemistry Ceylon in 2019.

## Chemistry of the Cover

At present, biochar has gained immense research interest from scientists all around the world as it is a low cost carbonaceous adsorbent that can be used for soil and environmental remediation purposes. The adsorption process of biochar is dependent on the feedstock type, production conditions and any chemical or physical value additions that are incorporated on it. The above figure is a scanning electron micrograph of the surface of tea waste biochar.

The image was adapted from the recently published research article by Dr. Ranmal Gunatilake " Peiris, C.; Nayanathara, O.; Navarathna, C. M.; Jayawardhana, Y.; Nawalage, S.; Burk, G.; Karunanayake, A. G.; Madduri, S. B.; Vithanage, M.; Kaumal, M. N.; Mlsna, T. E.; Hassan, E. B.; Abeysundara, S.; Ferez, F.; Gunatilake, S. R., The influence of three acid modifications on the physicochemical characteristics of tea-waste biochar pyrolyzed at different temperatures: a comparative study. *RSC Advances* **2019**, *9* (31), 17612-17622."

## Chandrasena Memorial Award

Awarded for an exceptional research contribution of an original nature in the field of Organic Chemistry and/or related areas such as Biochemistry, Pharmacognosy, Molecular Biology and Bioactivity studies.

### Chandrasena Memorial Award - 2019

Dr. Pamoda Ratnaweera is a Senior Lecturer attached to the Department of Science and Technology at the Uva Wellassa University of Sri Lanka. She obtained her BSc Special Degree in Zoology with first-class honors and three gold medals having topped the batch at the University of Colombo in 2007. She got a Government HETC scholarship for her postgraduate studies and obtained her PhD in Natural Products Chemistry also from the University of Colombo, in 2015. Dr. Ratnaweera has served as a faculty member for over a decade at the Faculty of Applied Sciences, Uva Wellassa University, Sri Lanka. She also served as a Visiting Scientist at the Department of Chemistry, University of British Columbia, Canada, in 2012, 2014 and 2016. Dr. Ratnaweeera was the recipient of the prestigious General Research Committee Postgraduate Research Award of the Sri Lanka Association for the Advancement of Science (SLAAS) in 2016 and Vice Chancellor's Award for the most outstanding young researcher of the year 2017 by the Uva Wellassa University. Dr. Ratnaweera possess over 16 research publications in peer-reviewed indexed journals and two patents for her credit. She received Presidential Awards for her high-quality natural product research publications presented in some prestigious journals. Dr. Ratnaweera's research currently conducted at the Uva Wellassa University is funded by the National Science Foundation Sri Lanka and through a University research grant. Beside them, she has won the Royal Society Commonwealth Grant, UK in 2016 to work on a collaborative research project in a biosynthetic enzyme laboratory at the University of British Colombia, Canada.

# Novel and interesting antibiotic scaffolds from endophytic fungi of Sri Lankan origin

Pamoda B Ratnaweera

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Antibiotic resistance within a wide range of infectious agents is increasing steadily, causing a growing public health crisis in the world today. The World Health Organization (WHO) has reported infectious and parasitic diseases as a leading cause of death in the world, causing 15.6 % of all deaths in women and 16.7 % in men. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections have currently become a global pandemic in hospitals, long-term care facilities and community health settings.

The development of resistance by pathogens limits the useful lifespan of antibiotics, thus causing an urgent need for introduction of new compounds. The number of new antibiotics reaching the market has also decreased over the past 25 years. Scientists have found the antibiotics evolved from natural products can penetrate the barriers of target bacteria more successfully than antibiotics developed from synthetic approaches. Hence, the most appropriate method to address the antibiotic resistance of bacteria is to find new alternatives to the currently available broad spectrum antibiotics through exploitation of nature for novel compounds.

Fungal endophytes are a group of microorganisms which spend all or part of their life cycle inter and/or intra-cellularly colonizing the healthy tissues of a plant without causing any visible manifestation of disease symptoms. They are an innovative group of organisms that can produce a plethora of secondary metabolites that feature unique structural characteristics and fascinating biological activities. However, only a handful of plants on the earth have been studied so far for endophytic fungal metabolites. Therefore a worldwide scientific effort is currently under way in isolating fungal endophytes and their bioactive natural products for a better and healthier future.

Due to the vast number of plant species in the world,

creative and imaginative strategies are necessary to quickly narrow down the search for bioactive endophytes. This provides the best opportunities to isolate endophytes prone to produce novel bioactive products. According to Strobel, plants from distinct environmental settings and/or with an unconventional biology, are considered to be a promising source for isolating novel fungal endophytes as well as new secondary metabolites.

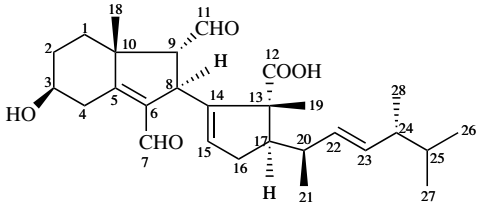
Sri Lanka is a relatively small island with a variety of climatic conditions and a high degree of biodiversity that may harbor endophytes with distinctive biosynthetic abilities. In the backdrop that effective and innovative antibiotics are needed to replace older ones, which are becoming obsolete due to drug resistant pathogenic bacteria, exploring the antibacterial producing capacity of endophytes becomes meaningful. So far, only a few Sri Lankan plants have been systematically investigated for the production of antibacterial substances by their fungal endophytes.

During our hunt of antibiotics and other bioactive compounds, endophytic fungi from various plants from different ecological settings in Sri Lanka were isolated, screened, the major bioactive secondary metabolites were purified using bioassay guided chromatographic techniques, isolated bioactive compounds were characterized using NMR and mass spectroscopic techniques and bio activities were evaluated. In the case of the novel compound solanioic acid, confirmation of correct structural/stereochemical assignments was acquired by X-ray crystallography, and semi-synthetic modifications while biogenesis pathway was investigated through stable isotope feeding experiments.

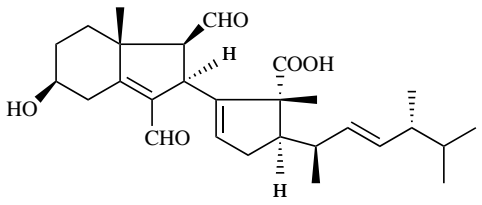
Investigation of weed plants commonly refereed as grasses and sedges led to the most interesting finding within our endophytic fungal research. Weed plants show vigorous and aggressive growth regardless of environmental or ecological conditions. They successfully grow in harsh and disturbed environments and have the ability to flourish despite insect, microbial or pathogenic attacks. These considerations led to the hypothesis that endophytic fungal populations inhibiting these plants, via the production of certain specific biologically active secondary metabolites, may contribute towards the hosts' ability to overcome biotic and abiotic stresses. This was supported by our recent isolation of the novel antibiotic solanioic acid which possesses a highly functionalized and rearranged steroidal carbon skeleton from *Rhizoctonia solani* isolated from the medicinal weed *Cyperus rotundus* (Kaladuru) common sedge in Sri Lanka.

Solanioic acid (**1**) has an unprecedented carbon skeleton that features a highly functionalized conjoint ring system which represents a new antimicrobial scaffold, with promising in vitro activity against the problematic human pathogen Methicillin resistant *Staphylococcus aureus* (MRSA, MIC: 1 μg $mL^{-1}$). It also showed activities against Gram positive *Bacillus subtilis* (MIC: 1 μg $mL^{-1}$), *Staphylococcus aureus* (MIC: 1 μg $mL^{-1}$) and the yeast *Candida albicans* (MIC: 16 μg $mL^{-1}$). The promising activity of this compound against MRSA warrants further investigation of solanioic acid as an antibacterial drug lead (Patent no.18450).

The culture feeding experiment with [1-$^{13}$C]-acetate, [2-$^{13}$C]-acetate and [1,2-$^{13}$C]-acetate showed that the steroid ring B contraction involved in the biogenesis of the unprecedented carbon skeleton of the solanioic acid involves cleavage of the C-5/C-6 bond. Besides, the [1-$^{13}$C]-acetate feeding study yielded not only solanioic acid but also its C-9 epimer (**2**). The isolation of 9-epi-solanioic acid suggests that first natural product formed by this pathway is 2, which have the normal C-9 steroid configuration. The 9-epi-solanioic acid is then either biosynthetically or spontaneously epimerized to solanioic acid which is the thermodynamically most stable epimer.



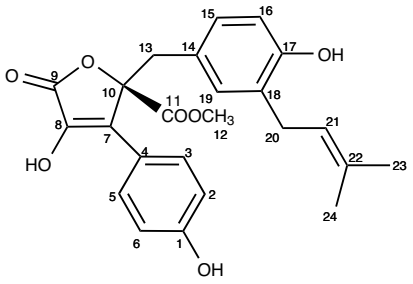

1




2

Apart from solanioic acid, Butyrolactone I (**3**) was isolated from the endophyte Trichoderma virens from the sedge Cyperus melanosperrmus and 9-epi viridol (**4**) from endophyitc Aspergillus terreus from Cyperus bulbosus. The MIC values of Butyrolactone I and 9-epi

viridol were in the range 128-256 μg $mL^{-1}$ against Gram-positive *B. subtilits*, *S. aureus*, MRSA and *Escherichia coli*.



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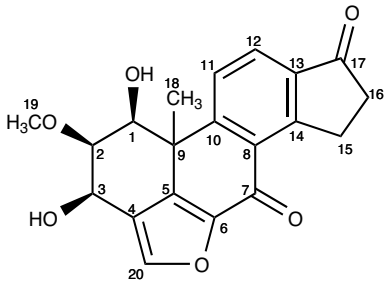
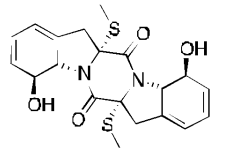


**4**

*Costus speciosus* (Tebu) is a traditional indigenous medicinal plant in Sri Lanka reputed to control diabetes. Three new thiodiketopiperazine derivatives, rostratazine A (**5**), rostratazine B (**6**) and rostratazine C (**7**) along with exserohilone (**8**) and boydine A (**9**) were isolated from the endophyte *Setosphaeria rostrata* obtained from Costus speciosus collected from a home garden. The compound 8 showed alpha-glucosidase inhibitory activity ($IC_{50}$ value 82 μg/mL) while 6 showed porcine pancreatic alpha amylase inhibitory activity ($IC_{50}$: 250 μg/mL).



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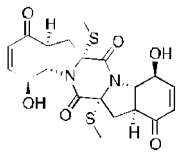

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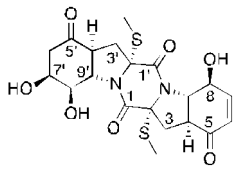

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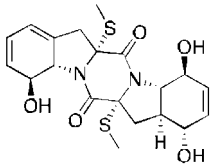

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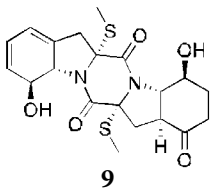
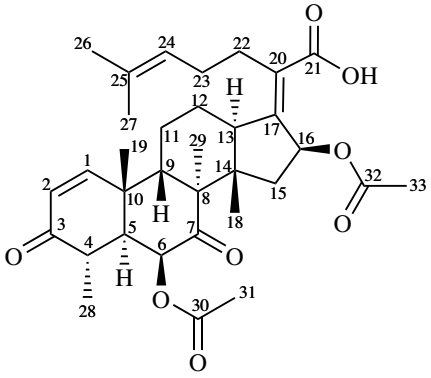


**9**

Rainforests due to their high species diversity and competition become potentially productive environments for discovery of novel molecular structures and biologically active metabolites. *Anoectochilus setaceus* (Wana raja) is an endemic endangered orchid traditionally used for snake bite poisoning. We isolated a nortriterpenoid, helvolic acid (**10**) from an endophytic *Xylaria* sp. obtained from the orchid *Anoectochilus setaceus* collected from Kanneliya rainforest Sri Lanka Helvolic acid reported antibacterial activity against Methicillin-resistant *Staphylococcus aureus* (MRSA, MIC 4 μg $mL^{-1}$) and *Bacillus subtilis* (MIC: 2 μg $mL^{-1}$).

*Opuntia dillenii* (Katu pathok) is an invasive cactus found in the South-Eastern province of Sri Lanka. Shipunov *et al*. have mentioned that in the host's invaded range, endophytes increase the competitiveness of the host by producing metabolites inhibitory to evolutionarily native plants. In our investigation endophytic *Fusarium* sp. isolated from the invasive cactus Opuntia dillenii yielded the antimicrobial secondary metabolite equisetin (**11**). Equisetin, is a tetramic acid derivative and it showed MIC values of 8 μg $mL^{-1}$ against *B. subtilis* and 16 μg $mL^{-1}$ against *S. aureus*. We proposed these biologically active substances may enhance the competitive ability of the host against microorganisms and perhaps increase its adaptability to withstand the biotic and harsh abiotic stress factors that assist in the successful establishment of *O. dillenii* to the detriment of native plants in the area.



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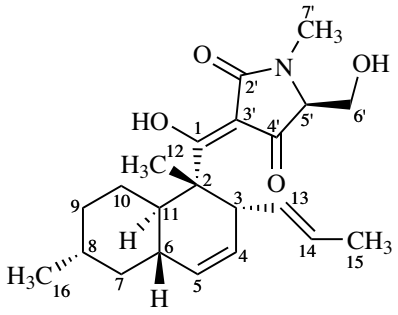
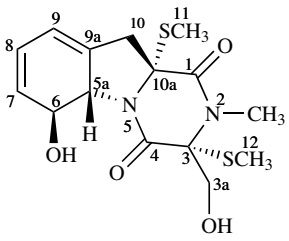


**11**

Mangrove associates are species mainly distributed in terrestrial or aquatic habitat but also occur in the mangrove ecosystem. According to Tomlinson criteria, mangrove associates are also distinguished from true mangroves by lacking aerial roots, vivipary and no physiological mechanism for salt exclusion. However, mangrove associates growing in the mangrove habitat also have to face the same extreme ecological conditions as the true mangroves. Therefore these mangrove associates also have the potential of producing bioactive natural products as the true mangroves. This is evident by our isolation of antimicrobial gliotoxin (**12**) (MIC: 0.13 μg $mL^{-1}$ against *B. subtilis*, 16 μg $mL^{-1}$ against *S. aureus*, 32 against MRSA and *E. coli* and 64 μg $mL^{-1}$ against Pseudomonas aeruginosa) and Bisdethiobis(methylthio) gliotoxin (**13**) from an extract of the endophytic fungus *Hypocrea virens* from the plant *Premna serratifolia* collected from mangrove habitat in Negombo.

*Calamus thwaitesii* is a vulnerable rattan species in Sri Lanka which is rapidly decreasing due to overexploitation for furniture industry. The endophytic Mycoleptodiscus species isolated from the leaves of C. thwaitesii resulted the alkaloid mycoleptodiscin B (**14**) which showed promising antimicrobial activities against *B. subtilis* (MIC: 0.5 μg $mL^{-1}$), S. aureus (MIC: 1 μg mL-1), MRSA (MIC: 32 μg $mL^{-1}$) and pathogenic fungus *Candida albicans* (MIC: 64 μg $mL^{-1}$). Though mycoleptodiscin B was previous reported to possess moderate cytotoxic activity our study was the first to report the antimicrobial activities of mycoleptodiscin B (Patent No. 18931)



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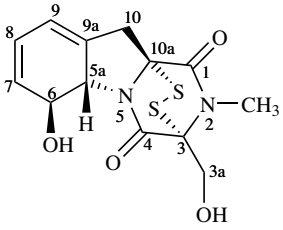
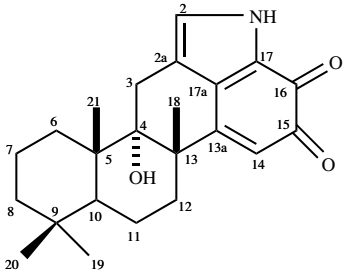


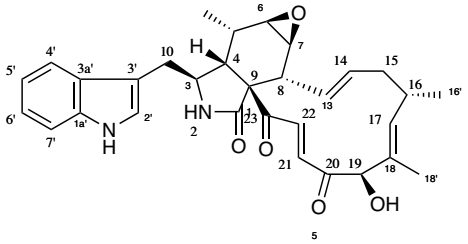
**13**



**14**

Inland fresh water bodies also are productive ecosystems in the world which house diverse microorganisms. Aquatic plants highly adapted to its environmental and ecological conditions also harbour endophytic fungi having bioactive metabolites. Our investigation of endophytic fungi of *Nymphaea nouchali* (Nil manel) led to the isolation of the known secondary metabolites chaetoglobosin A and C (**15, 16**) from *Chaetomium globosum*, with chaetoglobisn A showing good antibacterial activities (MIC: 16 μg $mL^{-1}$ against *B. subtilis*, 32 μg $mL^{-1}$ *S. aureus* and MRSA).

Except solanioic acid (**1**), 9-epi-solanioic acid (**2**) and rostratazines (**3-5**), other metabolites isolated through this extensive investigation turned out to be previously known compounds. However, in some instances the fungal source was new while the isolation of endophytic fungi from the host organisms and report of their antimicrobial activities turn out to be novel reports with some ecological implications. The investigations revealed that endophytic fungi from different, harsh and competitive environment settings are capable of producing a variety of bioactive compounds which confirm Strobel's rationale that host plant selection from unique and unusual ecological settings may lead to the discovery of novel chemical scaffolds.



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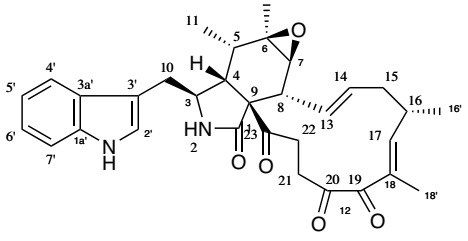

**16**

This study is a clear indication that the endophytes of unique Sri Lankan organisms is a fruitful source for isolating novel bioactive structures such as solanioic acid which will be useful antibacterial agents and encourages further investigations into this potentially

very productive field of study.

**Acknowledgements**

Research work was funded by the HETC grant UWU/O-ST/N3 and NSF grant RG2012/NRB/01. Greatly acknowledge Prof. Raymond Andersen, Department of Chemistry, University of British Columbia, Canada, for providing facilities for NMR spectral determinations. Valuable contributions of all other co-investigators are also acknowledged.

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## Guest Articles

# Nanopore: An Ostensibly Simple Sensor Stamping Single Molecule-Level Ohmic Readouts

Buddini I Karawdeniya & Nuwan Bandara

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Single-molecule/particle level analysis has surpassed the era of ensemble average studies and now faces grander challenges unique to each molecular class, for example, genomic sequencing with minimal financial foot-print been the most notable. The eventual goal of most of these efforts is to create a hand-held device that can read data on-site, upload it to a cloud, perform analysis and provide feedback in minutes while having an accuracy comparable or surpassing that of conventional instrumentation. Nanopore sensors have emerged at a time of demand with the promise to tackle a wide spectrum of biomolecules to cater fields such as biomedicine, mechanical engineering, pharmaceutical chemistry, physics, *etc*. A nanopore in its simplest definition is a nanoscale aperture spanning an impervious natural or solid-state membrane which separates two electrolyte reservoirs. The analyte is added to one chamber (cis) and driven across the nanopore in response to a voltage bias applied to the other chamber (trans). The transiting analyte perturbs the ionic-current of the open-pore generally causing a drop in the current (exceptions exist)—more formally termed an event—which bares molecular information characterized by the duration ($\Delta t$), depth ($\Delta I$) and inter-event duration ($\Delta f$). Charged molecules travel by electrophoresis (EP) and depending on the pH, the nanopore surface might have a net charge, generating an electroosmotic force (EO) that opposes or reinforces the electrophoretic force. Uncharged molecules may travel solely by electroosmosis. Manipulation and optimization of these forces (EP and EO) enable successful sensing.

The first demonstration of a nanopore to profile DNA was merely two decades ago using α-Hemolysin—a natural nanopore excreated by a bacteria—and since then, it has evolved into characterizing a plethora of biological and non-biological analytes—proteins, glycans, viruses, liposomes, exosomes, polymers. The focal point of nanopores since its inception has been on DNA sequencing. Natural pores were chosen because of their immaculate size, reproducibility and comparative dimensions of the sensing zone with nucleotide spacing being amongst other beneficial factors. Nanopore sensing is nondestructive, label-free and usually operate at a nM to pM concentration range at a bias of $\leq$ 1V, requiring only few microliters of the sample. While the technology associated with biological nanopores has expanded

into some commercial setups, sequencing the human genome still remains a challenge. With time, inevitably, many realized that confining nanopores to merely DNA sequencing limits its potential. Even though the natural nanopores are size reproducible, and the size of the sensing constriction is well suited for DNA sequencing, the inability to tune the size was a major drawback to profile other natural analytes. For example, an AAV virus is about ~25 nm in diameter, HIV is about ~100 nm in diameter, proteins are few nanometers in diameter whereas α-hemolysin has an aperture that is too small even for double-stranded DNA to translocate—thus limiting itself to a single-stranded DNA. The approach to profile proteins and branched molecules such as glycans were to denature and digest them respectively—the natural nanopore is unable to profile the pristine state of these molecules. So what is the solution?

To overcome the limitations of natural nanopores while preserving the best of it, solid-state nanopores (**SSN**) came to the picture in the early 2000s. These are nanopores fabricated through impervious solid membranes such as silicon nitride (**$SiN_x$**), glass and polymers like polycarbonate. The more abundantly used material is $SiN_x$ due to its robust, microfabrication compatible nature. The pores were initially milled using microscopy methods such as TEM (transmission electron microscope), FIB (focused ion beam microscope), SEM (scanning electron microscope) and HIM (helium ion microscope). The choice of microscope depends on the desired size of the nanopore: for smaller nanopores (<10 nm), TEM and HIM are preferred and for larger pore diameters, FIB is preferred. While TEM can be used to make pores with a larger diameter, it is time-consuming. Even though the nanopore is a simple sensor, the fabrication of it seemed complicated and requiring state-of-the-art instruments. This hampered the development of SSN greatly.

A little over 5 years ago, an overhead, time and cost-efficient method came into the picture called the controlled dielectric breakdown (CDB) to fabricate SSN. In simple, a high voltage (<1 V/nm) is applied across the membrane (both cis and trans contain 1 M KCl typically) until an abrupt increase in current is observed which is indicative of pore formation. Then smaller voltage pulses are applied until the pore size of interest is reached. A pore can be fabricated under 10 minutes and the circuitry needed for the CDB setup is cheap (<50$)—there are other costs associated with nanopore science that we have discussed at the end of this article. We note that there was enormous resistance in the nanopore field when CDB was introduced—such an invention should typically end up in a top-tier journal such as Nature, yet, the authors who demonstrated it first had to settle for a medium impact journal. However, as heavy users of CDB, we are delighted (even though we are not the inventors) to see that the use of CDB in the nanopore community is continuosly increasing. We introduced a method similar to CDB in 2018 where a Tesla coil lighter was used to fabricate nanopores—the slogan been don't smoke, make nanopores!

While nanopore fabrication protocols became simpler and faster, it attracted more attention for single-molecule sensing beyond genomics. The SSN was soon explored for other molecules and particles. Rigid nanoparticles could be discriminated by size and demonstrated significant size resolution as compared to classical methods like Dynamic Light Scattering (DLS) and TEM. Soon SSN was used for single-molecular analysis of proteins (without resorting to denaturing agents) which enabled the evaluation of a myriad of molecular information that natural nanopores could not harness, including, but not limited to, the folding-unfolding (e.g. voltage and temperature-induced), protein-receptor interactions and protein response to change of media (pH, salt, cations, etc.). In recent years SSN has been used for mechanical characterization of bio-nano particles like liposomes and viruses; i.e: rigidity, viscoelasticity, stiffness, etc. The big question is, why is it important? For starters, liposomes are widely used drug carriers and it has been shown that they can be eletro-deformed as they transit through a nanopore if a sufficiently high voltage is applied. The degree of deformation is speculated to be a function of the cargo content, thus in the future, we would see SSN discerning liposomes based on their packaging and playing a leading role in dose-related assaying. The membrane properties of the HIV virus change as it matures which can be used as a marker for its infectivity. This was successfully demonstrated by the group of Prof. Kim. The SSN continues to improve over the years with different protocols having been introduced to improve and custom tune the surface chemistry of the SSN. This

was done to minimize clogging, enhance current stability, and to improve the signal-to-noise. Protocols such as PDMS coating, silane thin films, gold thin films with thiol chemistry alongside the direct surface functionalization of organic moiteies by using hydrosilylation is also in use.

Recently, nanopores have been further challenged by a rather complicated class of biomolecules—polysaccharides—that have higher diversity in monomer composition, charge, and isomeric forms as compared to DNA or proteins.2 The sensing platform demonstrated astounding promise in profiling polysaccharides by discriminating heparin ( a commonly used anticoagulant drug) from the adulterant over sulfated chondroitin sulfate (OSCS). In 2008, there were over 100 deaths in the US due to a heparin batch being contaminated by OSCS and gone undetected by classical techniques.

A typical setup to perform nanopore experiments includes a low current amplifier, a digitizer (e.g. Digidata 1440A), asoftware (custom written or purchased) and a computer. The total cost would therefore be ~70,000$. There is only a handful of countries in the whole world that have nanopore expertise. In addition to genomics, both proteomics and glycomics have been tackled by this tiny sensor and currently presents great promise in -omics. Despite the robust nature and ability to be integrated into a handheld device, there are no successful SSN based devices in use just yet. Thus, there is a great opportunity to fill this void. Can Sri-Lanka afford this? The answer is a simple yes. Does Sri-Lanka have the expertise for this? Again the answer is a simple yes. The more pressing question, however, is, would Sri-Lanka be proactive and have a foothold in this evergrowing portion of molecular sensing anytime soon—we hope the answer will soon be a grand yes!

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# Drug Delivery Systems: A new Frontier in Nano-technology

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Nanotechnology is a recent advancement in science, defined as "Science, engineering, and technology conducted at the Nano scale" (National nanotechnology initiatives in USA). Applications of nanotechnology cover a vast range from basic material science, personal care applications, agriculture and medicine. Nanotechnology is used in the field of medicine for treatment, diagnosis, monitoring, genetic engineering and drug delivery.

More than 150 years ago, Michael Faraday who prepared gold particles in nanometer scale made the first breakthrough that would pave the way for major change in how medicine will be practiced in the future. Later, researchers conjugated these colloidal gold particles with antibodies to target specific staining known as immune-gold staining. This can be considered as the precursor of recent application for drug delivery in nanotechnology. In 1960s, Liposomes and polymer micelles were first prepared, however they were not referred as Nano-particles (NP) until 2000. In 1970s, NPs and dendrimers were first introduced. The successful development of micelles as drug delivery system (DDS) was reported in 1980. In 1990s, block co-polymers of polyethylene glycol (PEG), PEG-Polylysine were invented. The modern use of Nano-technology in drug delivery began when United States launched the national Nano-technology initiative.

**Role of Nano-technology in drug delivery**

DDS is defined by national institute of health in USA as, "Formulation of a device that enables the introduction of therapeutic substances in to the body and improves efficiency and safety by controlling the rate, time and place of release of drug in the body." Conventional DDSs have many drawbacks including poor bioavailability, side effects, low drug loading capacity, plasma fluctuation of the drug levels, low therapeutic effectiveness and lack of target delivery. Traditional DDS circulate drugs to the cells in the body non-selectively, which can lead to serious consequences such as side effects, multiple drug resistance (MDR) and reduced drug concentration at target location. For example, in cancer treatment the conventional drug delivery to the tumor cells can affect normal tissues causing nephrotoxicity, neurotoxicity and cardiotoxicity. These drawbacks have motivated on scientists to investigate more about new DDS.

How Nano-technology can overcome these drawbacks can be understood by discussing the mechanism of drug delivery using Nano-particles (NP). The process of drug delivery can be mainly divided as; the administration of the drug or therapeutic product; release of the active part of the drug and transport active ingredients across the biological membrane to the target site to perform action.

Use of Nano-technology in DDS includes delivery and targeting of pharmaceutical, therapeutical and diagnostic agents by the help of NPs to the cells. The drug-NP conjugate should be able to deliver drugs to the target site without degradation in gastrointestinal track and without reducing drug activity. Secondly it should attack the target cells without causing any harm to the other cells and also it should reduce side effects.

**How NPS improve drug delivery?**

The chemical and physical properties of NPs make them efficient DDSs that have the potential to improve the bioavailability, drug carrying capacity, stability for the drugs within the body, controlled release and targeted delivery (Figure 1).

Nano-technology increases bioavailability of drugs as a result of their special uptake mechanisms such as absorptive endocytosis and the ability to avoid degradation in the gastrointestinal track. The drug incorporated in to the NP is easily diffused through biological membranes. Drug-polymer attachment changes the drug solubility, hydrophobicity and permeability. The drug loading capacity can be increased by minimizing solubility, increasing ionic interactions between drug and matrix and by maximizing the absorption of drug load.

The NPs are also able to remain in the blood for long period. The drugs attached NP can avoid being attacked by the immune system by having a particle surface decorated with biodegradable, hydrophilic copolymers. Poly- glycolic acid (PGA), poly-lactic acid (PLA) and their co-polymers are widely used for decorating the

surface.

The self-controlling system of drug release helps to reduce the plasma fluctuation and minimize the side effects. Controlled drug releasing in particular sites can be controlled by different ways, 1) polymers are biodegradable and it is degraded in controllable manner to release drugs to the site 2) pores within the polymer can be altered so that the drug diffusion occurs more readily or slowly, 3) the distance of fusion and surface area of the NP can be altered by changing the size. Smaller size means larger surface area and drug release and dissolving becomes faster. The drugs are released by matrix via diffusion, swelling, erosion or degradation. The drug release is controlled by osmotic pressure, mechanical pumping and through electro kinetic transport.

Nano-technology based DDS provides drugs to target sites by their ligand attraction process. The NP surface can be decorated by ligands and these ligands can attach to the specific receptors in the surface of targeted cell by bio-recognition. The NPs enter the target cells by receptor mediated endocytosis. Inside the cell NPs are developed in to endosomes. Then endosomes merge with each other to form large endosomes or lysosomes. Finally therapeutic drugs can be released in response to enzymes or acidic pH with controllable manner by degradation of polymeric NP shell. Ultimately NPs in DDS enhance the ability to use highly toxic, poorly soluble, unstable drugs and maximizing patient comfort.

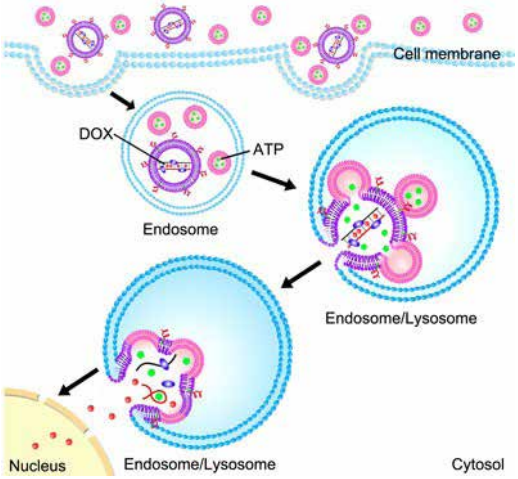


**Figure 1:** Targeted delivery of drugs by NPS

**Different types of NPs**

Above mentioned actions can be achieved by different types of NPs. There are mainly two types of NPs; organic NPs such as liposomes, Nano crystals, dendrimers, polymeric NPs and inorganic NPs such as metal NPs and silica (Figure 2).

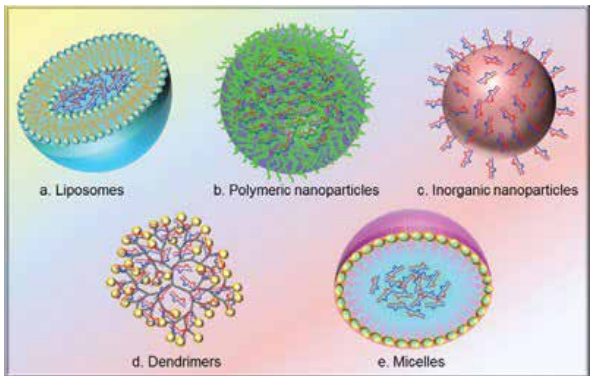


**Figure 2:** Different types of NPs

Liposomes are amphiphilic molecules that are able to carry both hydrophobic and hydrophilic drugs. The shape, surface, charge, size and functional groups in liposomes can be easily changed according to the drug and the target site. Drugs can be incorporated in to liposomes by encapsulation method (Figure 3). Liposomes are encapsulated with various drugs such as anticancer drugs, neurotransmitters, antibiotics and anti-inflammatory drugs. For instance Doxorubicin which is a highly toxic anticancer drug can be safely and accurately delivered directly to the tumor cells instead of accumulating in the heart and kidney.

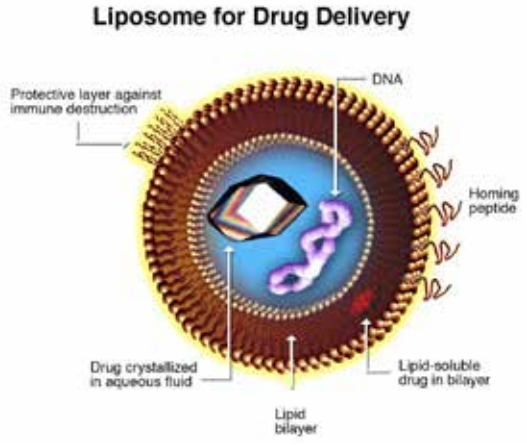


**Figure 3:** Liposomes as NP

The Nano crystals can reduce accumulation of carrier particles and directly incorporate the drug to the target site. Nano crystals have the ability to become stable in aqueous dispersion without any stabilizers. Dendrimers are synthetic polymers with well defined

size and structural branched chains. Drugs can be incorporated either to internal surface/core or surface by covalent bonds and it is decided by the drug and the target site.

The polymeric NPs can deliver drugs to the site of action with minimum toxic levels and it is hydrolysed inside the body to produce bio-degradable metabolite monomers like lactic acid and glycolic acid. Protein and peptide drugs can be conjugated with polymers such as PEG and it can prevent protein drug degradation in stomach and increase the half-life of drugs in plasma. The polymeric NPs with surface decorated with PEG and target ligands are capable of delivering highly toxic cancer drugs like Doxorubicin to target sites without harming healthy cells. In the treatment of Tuberculosis continuous and frequent drug supply to the cells can be achieved by NPs covered with PEG and attached with drugs such as Rifampicin (RMP), Isoniazid (INH)/Pyrazinamide (PZA). Polymeric NPs, nano gels, liposomes, micelles, dendrimers and protein NPs are being investigated for use in treatment of several ophthalmic conditions.

Metal Nano-particles (MNP) such as gold, silver, iron, platinum and ceramic, are used due to their optical, magnetic, electrical properties and size which leads to less solvent contamination and uniform distribution. In ophthalmology glaucoma can be treated with Nano-diamonds with drug (timolol maleate) embedded in contact lenses. Researchers attempt to reduce side effects of platinum used in cancer therapy by using gold NPs.

Silica Material such as Xerogels and Mesoporous silica NPs have higher biocompatibility, convenient functionalization and high porous matrix. Phenytoin, Cisplatin, Nifedipine, Doxorubicin, Metronidazole and Heparin are drugs incorporated with Xerogels. Mesoporous silica nanomaterial have high surface area for drug absorption. Anticancer drugs, antibiotics, heart disease drugs are delivered by mesoporous which controls drug release by diffusion method. Silica and magnetic NPs can be successfully used in bone regeneration.

**Future opportunities**

Most applications are still under research, animal testing or only at hypothesis level. Researchers try to improve blood circulation period of NPs by coating their surface with red cell membranes instead of PEG, design NPs with different shapes, ligands and drug particles, use photosensitive agents that accumulate in tumors, make blood vessels more porous to facilitate penetration by NPs, attach RNA to treat skin cancers and develop monoclonal antibodies and vaccines that are directed against tumors.

In future, Nano-technology based DDS can lead to further advancements in antitumor therapy, gene therapy and radiotherapy. Multi-functional NPs will ++++be capable of detecting malignant cell, deliver different drugs at the same time, visualize the location by imaging agents, killing cancer cells with minimum side effects and monitor and treat at the same time. NPs will be playing a crucial role in robotic surgery. The NPs can be combined with computer programmes to automate regulation of homeostasis such as blood glucose level and serum Calcium level. In immunology, NPs have the potential to act as powerful protectors against foreign particles.

**Conclusion**

Nano-technologies as DDSs are designed to improve the pharmacological and therapeutic properties of conventional drugs. Current application of NP based drug delivery focus on conditions such as malignancies, diabetics, heart diseases and central nervous system diseases. The NP based drug delivery can be further developed to cure challenging diseases like AIDS. In the future it may be possible to develop Nano-technology to treat different diseases at the same time by producing multifunctional Nano-particles.

The ultimate goal of NP drug delivery is to improve proper treatment, diagnostics and monitoring with improved performance, effectiveness, safety and patient adherence as well as reduction in the cost.

## Student Corner

# The Transistor

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Transistor the building block of the modern processor was invented by Physicists John Bardeen, Walter Brattain, and William Shockley in 1947 at Bell Laboratories, USA. Considering the importance of the invention, the inventors were awarded the Nobel Prize in Physics in 1956 . In the original patent application, the device was named as semiconductor amplifier and later it was renamed as the transistor abbreviating trans-resistor. Without the invention of the transistor, a computer with the capabilities of a typical desktop computer would have been of a size of a three storied building, and laptops/ mobile phone are just science fictions.

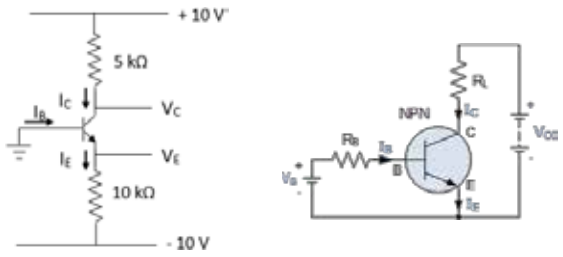
In general, there are two main types of transistor namely Bipolar Junction Transistors (BJTs) and Field Effect Transistors (FETs) that are in use today. The design of both transistor types is different from the original point contact transistor. Today, the semiconductor device manufacturing industry is capable of fabricating billions of transistors in a single silicon chip. For example, Qualcomm Snapdragon 850 System-on-chip (SOC) which is used by Android Flagships, contains over 5.3 billion transistors.

Let's take a glance at the action of a Bipolar Junction Transistor or BJT. BJTs are made by fabricating two pn junctions, side by side. This arrangement can be realized by having two n regions on either side of a central p region or vice versa. Hence, there can be two types of BJTs possible, which are called npn and pnp. The two pn junctions in a BJT can be biased in different modes namely, cutoff, active, and saturation. Active and cutoff modes are used when BJT is used as a switch, and when it is in active mode it works as a current amplifier. The current flow convention of an npn transistor is shown in Figure 1. Considering the conservation of current flow through the transistor, the following equation can be derived.

$$I_E = I_B + I_C \qquad [1]$$

When a transistor operates in active mode, the DC current gain (β) of the device is defined as IC/IB, and the ratio of the current at the Collector terminal to that at the Emitter terminal, IC/IE, is called α. Relationship between α and β can be derived with the help of the equation (1) as follows

$$\alpha=\beta/(\beta+1) \text{ or } \beta=\alpha/(1-\alpha)$$




A B

**Figure 1:** Circuit diagrams of use of npn transistor in common Emitter configuration. Note that standard convention of current flow is also marked

Table 1 gives a summary of the properties of the Si BJT in different modes of operation.

**Table 1**: Certain properties of BJT in different modes of operation

| | BE junction | BC junction | Currents | Voltages |
|---|---|---|---|---|
| Cutoff | Reverse biased | Reverse biased | $I_B=I_C=0$ | |
| Active | Forward biased | Reverse biased | $I_C = \beta I_B$ | $V_{BE} = 0.7$ V (for Si) |
| Saturation | Forward biased | Forward biased | $I_C < \beta I_B$ | $V_{BE} = 0.7$ V, $V_{CE}=0.1$ V (for Si) |

Common emitter configuration of the BJTs is the most widely used configuration due to its flexibility and high current and voltage gains.

Consider the example circuit given in Figure 1 (A), where the voltage at the emitter VE is given as −0.7 V and β=50. Let's find $I_E$, $I_C$, $I_B$ and $V_C$ assuming the device is in active mode.

**Analysis**

1. VE is given as -0.7 V. So the potential drop across 10 k resistor is (-0.7 – (-10) ) V = 9.3 V. Hence the current(IE ) through 10 k resistor is given by IE = 9.3 V / 10 k = 0.93 mA
2. Using $I_C = \alpha I_E$, $\alpha=\beta/(\beta+1)$
   $\alpha = 50/(50+1) = 50/51$
   $I_C = \alpha$ IE → $I_C = 50/51 \times 0.93$ mA = 0.912 mA
3. From equation 1 → $I_E = I_B + I_C$ → IB = $I_E - I_B$ = 0.93 – 0.912 = 0.18 mA
4. Since the current through the 5 k resistor is IC, the potential drop through the resistor can be written as, $(10 \text{ V} - V_C) = I_C \times RC = 0.912 \times 10^{-3}$ A × 5 kΩ = 4.56 V

   10 V – $V_C$ = 4.56 V → $V_C$ = 5.44 V

The example circuit given in Figure 1 (B), where $V_{CC}$ = 5 V, $V_B$ = 5 V, $R_B$ = 100 Ω, $R_L$ = 200 Ω, β = 100 and transistor operates in saturation mode. Let's find IB, $I_C$ and $V_C$.

1. Since the transistor is in saturation mode, $B_E$ junction is forward biased and $V_{BE}$ = 0.7 V (see Table 1). So, the potential at point B is 0.7 V. Hence the potential drop across the $R_B$ resistor is (5 V – 0.7 V) =4.3 V; So current though the resistor, $I_B$ = 4.3 V /100 Ω = 43 mA
2. Since transistor is in the saturation mode $V_{CE}$ = 0.1 V. So, the potential drop across the resistor $R_L$ is ($V_{CC}$ - $V_C$) = (5 V – 0.1 V) = 4.9 V. Hence current through the resistor RL , $I_C$ = 4.9 V/ 200 Ω = 245 mA

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# Chirality of Molecules


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Chirality is the existence of different configurations (three dimensional arrangements) of a substance with an identical chemical formula. The word **Chirality** is derived from the Greek word *chéri* meaning hand. A chiral object has a handedness, hence is not superimposable on its mirror image (Figure 1). These non-superimposable mirror images are called optical isomers or enantiomers. When an organic molecule has a tetrahedral centre, bonded to four different atoms or groups, it is called a chiral centre or a stereogenic centre.

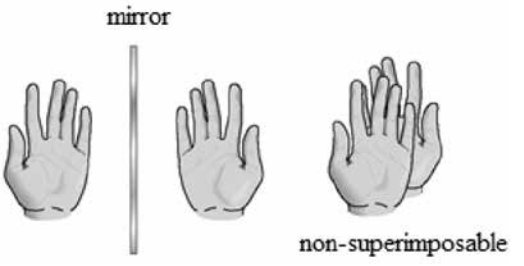


**Figure 1:** Left and right hands are mirror images, but they are not identical, or superimposable.

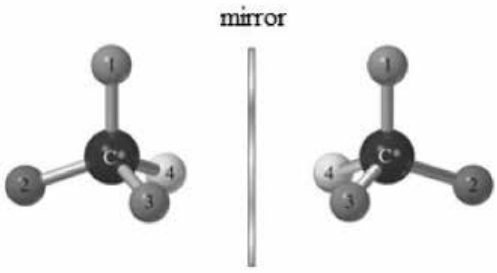


**Figure 2:** Ball-and-stick representation of an enantiomeric pair.

In contrast, achiral objects such as a plain round ball, a nail, etc. do not have handedness. The chirality of an object is related to its symmetry. If an object possesses a plane, a line or a point in or through it, about which a rotation or reflection leaves the object in a configuration, indistinguishable from the original, it must be achiral.

To distinguish one enantiomer from the other,

organic chemists Robert Sidney Cahn, Christopher Kelk Ingold, and Vladimir Prelog devised a naming system using a set of sequencing rules called Cahn-lngold-Prelog (CIP) priority rules. According to CIP priority rules, first, each atom bonded to the stereocenter is assigned a priority, based on atomic number. The higher the atomic number, the higher its priority. If identical atoms are attached to the stereogenic centre, then priorities are determined based on the atomic number of the next atom attached. If atoms are bonded to a double or triple bond, they are considered to be bonded to an equivalent number of similar atoms by single bonds. After the priorities are assigned, molecule must be oriented with the lowest priority group pointing away from the observer. After getting the correct view, draw a circular arrow from connecting substituents 1 to 2 to 3 from highest to lowest priority (ignore the substituent 4). If the arrow moves clockwise (right turn) then the configuration is called R. The R notation is originated from the Latin word rectus, meaning right. If the arrow moves counter-clockwise (left turn) then the configuration is S (derived from the Latin word sinister, meaning left). A stereogenic centre thus has two different designations, R or S, depending on the orientation of the substituents.

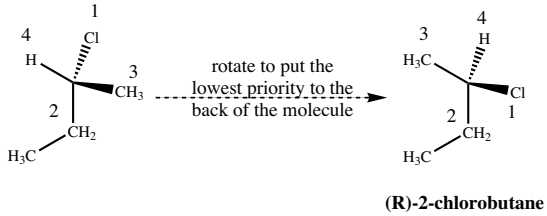


**Figure 3:** CIP nomenclature of 2-chlorobutane.

Molecules with more than one chiral (stereogenic) center can have enantiomers where all stereocentres are inverted and another type of stereoisomers which differ at least at one, but at less than all stereocentres. Therefore, they are not mirror images, not enantiomers of each other. They are called diastereomers. Molecules with multiple chiral centers may or may not be chiral. A meso compound is an achiral compound that has more than one chiral center and a plane of symmetry.

Chirality is an extremely important phenomenon in the pharmaceutical industry. Many drug molecules possess at least one chiral center, resulting enantiomers. Enantiomers have identical physical properties (such as solubility, melting point, boiling point) and chemical reactivities towards achiral reagents. However, they are differentiated by chiral environments such as receptors and enzymes. As a consequence, the enantiomers can have different physiological responses in the human body. One classic example of the effect of different enantiomers is thalidomide, where R-thalidomide is responsible for the therapeutic sedative effect and S-thalidomide has teratogenic properties.

**Prochirality**

An achiral center can be transformed into a chiral center by replacement of a "prochiral" substituent (usually hydrogen) with another substituent or by converting a $sp^2$ carbon into a chiral $sp^3$ carbon via an addition reaction.

Replacement of the H atoms in achiral 2-cyclohexylethanol would lead to a chiral R and S mixture as shown below. When the H atom is replaced by Deuterium to result the chiral compound R, then that H atom is called pro-*R*. When the Hydrogen is replaced by Deuterium to result the chiral compound S, then that H atom is called pro-*S* (Figure 4). These two hydrogens, HA and HB are called "heterotopic" (from Greek "'heteros'" = different and "topos" = place) and the carbon which the two hydrogens are attached is called "prochiral center".

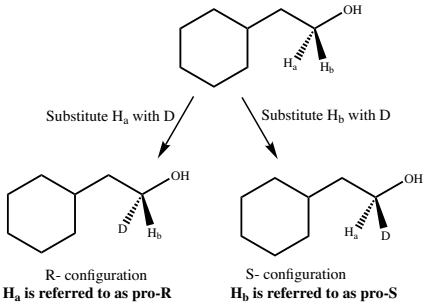


**Figure 4:** Pro-R and pro-S substituents.

Prochiral carbonyl carbon is a $sp^2$ hybridized carbon that is reacted with a nucleophile to form a $sp^3$ hybridized chiral carbon. The two sides of the carbonyl group (front and back) are referred to as "faces". When the priorities (according to the Cahn-Ingold-Prelog priority order) of three substituents of the carbonyl group are oriented clockwise (1 to 2 to 3) on the face we look at, it is called the *re* face (rectus face) and the face where the highest to lowest substituents are oriented in counterclockwise is referred to as the *si* face (sinister face). Nucleophiles may attack carbonyl groups from the *re* face or the *si*

face. The stereochemistry of the product (enantiomer) depends upon which face of the planar carbonyl group undergoes the nucleophilic attack and the priority of the incoming group (figure 5).

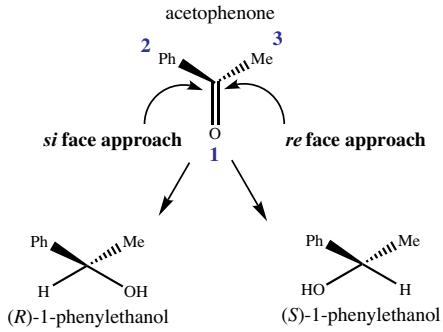


**Figure 5:** Hydride attack on carbonyl carbon from the re face or the si face.

In biological systems, the two 'identical' groups bound to a prochiral center of an incoming substrate molecule is differentiated since they occupy different regions in three-dimensional space. Similarly, the two planar 'faces' of a prochiral $sp^2$ - hybridized carbon is also recognized by the enzymes. One example is the NAD+ catalyzed oxidation of ethanol by yeast alcohol dehydrogenase. Studies with deuterium labelled substrates have shown that the oxidation of ethanol occurs with exclusive removal of the pro-R hydrogen from ethanol and with addition only to the re face of NAD+ (figure 6).

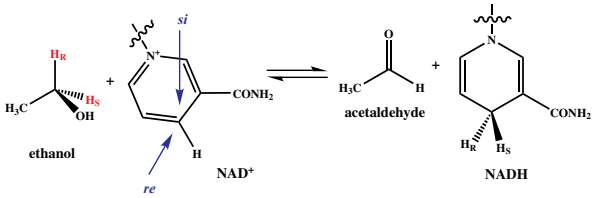


**Figure 6:** $NAD^+$ catalyzed oxidation of ethanol by yeast alcohol dehydrogenase.

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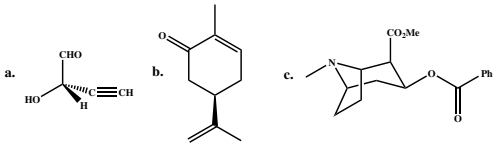
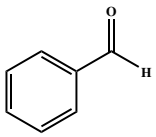
**Problems:**

1. Determine the configurations of the stereocentres of the following compounds using R/S nomenclature.




2. Which enantiomer is formed from attack of a methyl Grignard reagent on the si face of benzaldehyde?



# Chemistry Olympiad Sri Lanka and International Chemistry Olympiad 2019

Chemistry Olympiad Sri Lanka (COSL) is annually organized by the Institute of Chemistry Ceylon from 2017 onwards with the objectives of popularizing Chemistry among school students, and recognizing and rewarding talented Chemistry students in the country.

The third Chemistry Olympiad Sri Lanka (COSL) competition and training sessions were successfully held on 23rd and 24th May 2019 at the Institute of Chemistry headquarters, Adamantane House, Rajagiriya. Prior to the theory and practical examinations one-and-a-half day training sessions including Chemistry practical sessions covering organic, inorganic, analytical and physical chemistry were conducted by the lecturers of the College of Chemical Sciences, IChemC together with their fellow university academics. Twenty nine finalists who were selected from the results of the preliminary examination conducted by the National Chemistry Olympiad Committee in January 2019 at twelve Universities Island wide, and their teachers participated in the training sessions.

Most of the participants told us that this event was an unforgettable experience and not just a competition for them, and they enjoyed the practical sessions and encouraged their interest towards Chemistry.

Rathnayake Mudiyanselage Sugath Ravindu Sanwara from Ananda College, Colombo was the Gold medal winner of the COSL 2019. Thishanka Alahakoon from Dharmaraja College, Kandy and R. M. P. Akila Prabodha Rajapaksha from Bandaranayake College, Gampaha won the silver and bronze medals, respectively. In addition to the medals these three students were awarded scholarships to follow the Graduateship Examination in Chemistry conducted by the IChemC. Winners of the COSL competition received their medals and prices at the Annual Sessions of the IChemC held on 10th June 2019 at the Sri Lanka Foundation Institute.

The IChemC has been given the official status in 2016 to represent the International Chemistry Olympiad (IChO) competition by the IChO Steering Committee. Accordingly, the IChemC participated in the IChO representing Sri Lanka as observers for two consecutive years from 2018.

This year, Dr Ireshika De Silva, Secretary of the National Chemistry Olympiad Committee participated in the IChO 2019, which was held in Paris, France from 21st July to 30th July as a Scientific Observer representing Sri Lanka. Altogether 84 countries including 4 observing countries participated in the IChO 2019.

Dr Ireshika De Silva has got the opportunity to present the progress of conducting the National Chemistry Olympiad competition and future plans for participating in the IChO. The Steering committee was very happy about the progress made by Sri Lanka and successfully completing the two years as observing country. Hence, Sri Lanka would be eligible to participate a team in the IChO 2020 for the first time, which will be held in Turkey.

The Chemistry Olympiad Committee wishes to thank the IChemC sincerely for sponsoring the Chemistry Olympiad competitions, and sending Scientific Observers in 2018 and 2019.

Dr Ireshika De Silva and Dr. C.N. Ratnaweera

Chemistry Olympiad Sri Lanka

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