SYNFORM

People, Trends and Views in Synthetic Organic Chemistry

2008 / 05

THE INSIDE STORY

Chemistry in Singapore

SYNSTORIES

- Modular Syntheses of Polyene Natural Products via Iterative Cross-Coupling

CONTACT

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marketing@thieme-chemistry.com

Thieme Chemistry

Dear readers,

this new issue of **SYNFORM** presents an **INSIDE STORY** article dedicated to one of the most impressive examples of a fast-growing economy that is fully committed to the pursuit of an aggressive national research & development program: Singapore. This small country is becoming a major hub for research and education, and **SYNFORM** could not miss the chance to report on this sort of "paradise for scientists". This **INSIDE STORY** has been possible thanks to the generous collaboration of several people in Singapore, including Dr. Christina Chai, Dr. David Chen, Dr. Steven Collier, Professor Teck-Peng Loh, and others who accepted the invitation to provide valuable information and dedicate some of their precious time to **SYNFORM** during my recent trip to Singapore. The Singapore model is probably difficult to export to the Western world, and there are many reasons for that. However, more long-term investments in infrastructure, research and education are needed in Europe, and even in America; Singapore may represent an important stimulus in this direction and not just a competitor in the global world market.

The issue is completed by a **SYNSTORY** article on a new remarkable synthetic strategy – a modular approach to polyene natural products via iterative cross-coupling – developed by the group of Professor Martin D. Burke (USA).

Stay tuned to **SYNFORM**!

Matteo Zanda

Editor of **SYNFORM**

CONTACT ++++

If you have any questions or wish to send feedback, please write to Matteo Zanda at:
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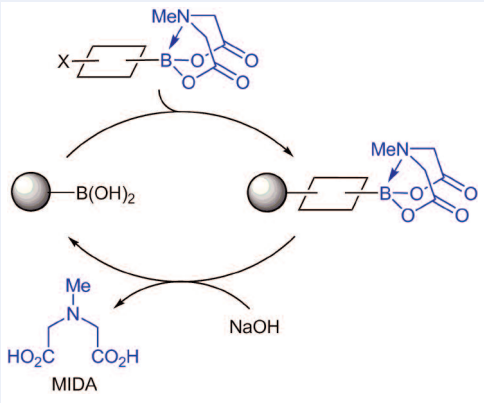

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Chemistry in Singapore

Background. I had a dream. A place where scientists can do excellent research without wasting their time and energy desperately looking for funding, because money is already there, available and ready to use. A place where new, modern, state-of-the-art research buildings and labs pop up everywhere like mushrooms. A place where science and research are considered a true national priority, where talented scientists are considered a national treasure. Well, this is not a dream – such a place actually exists and has a name: Singapore!

This small (about 700 km^2) and densely populated (almost 5 million people in 2007) island nation, formerly a British colony that declared independence from Malaysia in 1965, is becoming a major hub for world-class education and research, and is committed to long-term investments in infrastructure, research and education. Singapore is one of the fastest growing economies in the Asia-Pacific region and is fully committed to pursue an aggressive national research & development program. Thus, Singapore is striving to build a solid national research infrastructure and nurture home-grown talent, by supporting PhD studies, providing opportunities for post-doctoral training and exposing local students to foreign talent attracted to Singapore from the five continents by the competitive salaries and excellent facilities that are offered to live and work there. Very low criminality and a multi-ethnic, essentially English-speaking population represent added value in the global market of science and business. Actually, Singapore is progressively becoming a 'siren song' for scientists all over the world, an appeal that is really hard to resist, but, in contrast to the mythological sirens, the Singapore appeal is unlikely to lead to a bad result for those scientists who heed the call. Companies are also not immune to the 'Singa-siren', as demonstrated by the ever-increasing number of industrial clusters that are growing in places like the Singapore Science Park (www.singaporesciencepark.com) and elsewhere.

The Singapore skyline with the Mer Lion, symbol of the island nation

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The chemistry research labs of the new CBC building at NTU Singapore

The two main Singaporean universities, the National University of Singapore (NUS) and the Nanyang Technological University (NTU), are obviously the two main engines of the educational efforts. Chemistry is in a phase of strong expansion both at NUS (current Head of Chemistry Department is Professor Andy Hor Tzi Sum) and at NTU (current Head of the Division of Chemistry and Biological Chemistry is Professor Teck Peng Loh), which is particularly impressive for the latter. I had the chance to spend one week in the fantastic, 'jungle campus' of the NTU, to feel the vibrant atmosphere of the chemical sciences there, and to visit the impressive new Chemistry & Biological Chemistry building, which was opened in December 2007. The new CBC building is modeled after the new Oxford Chemistry building, reputed to have among the best safety features by industry standards in the western world. The cluster of new buildings, that include Physics and Mathematical sciences, can accommodate about 300 faculty and staff members, 500 PhD research students, and teaching facilities for 2,000 undergraduates.

A*STAR is the Agency for Science, Technology and Research of Singapore, and is part of the Ministry of Trade & Industry. The Institute of Chemistry and Engineering Sciences (ICES), directed by Dr. Keith Carpenter, was established as an autonomous national research institute under A*STAR in 2002, and is based on Jurong Island, a man-made island located southwest of the main island of Singapore. Organic chemistry is essential in many programs developed at ICES, such as the New Synthesis Techniques and Applications (NSTA), which is managed by Dr. Christina Chai and investigates areas pertaining to the synthesis of organic molecules for the pharmaceutical, fine and specialty chemical industries. In the southwest of Singapore, five of the seven buildings of the ultra-modern city of science, Biopolis, with its futuristic seven-tower complex linked by sky bridges, house the biomedical research institutes of A*STAR. The Helios building hosts the Chemical Synthesis Laboratory (CSL) directed by Professor K. C. Nicolaou, who has appointments both with Scripps Research Institute and the University of California, San Diego (USA), whereas Dr. David Chen was appointed as the principal investigator to oversee the operations of the laboratory. The CSL, which is operative since the beginning of 2005, represents a sort of extension of the world-renowned Nicolaou lab at Scripps, both in its research interests and its organization.

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In terms of industrial research, Singapore is also extremely aggressive in attracting companies, both pharmaceutical and chemical, with some very valuable assets, such as its well-trained and efficient work force, excellent infrastructure, a very supportive government, and a high-standard intellectual property protection system. Thus, Singapore is highly competitive in attracting companies in Asia, despite the presence of giants like India and China in the same area, who cannot offer the same set of attractive features, at least for the moment. Singapore is already hosting, at various levels, about 7,000 multinational companies having R&D centers, manufacturing or regional headquarter facilities. Among the big multinational companies, one should mention GlaxoSmithKline (GSK), that chose Singapore a long time ago and in 2007 opened a new Medicinal Chemistry Laboratory in Biopolis, the Novartis Institute for Tropical Diseases, and several large API production sites by Lonza, Pfizer, Schering-Plough, Novartis and a plethora of other companies, including a number of SMEs.

One of the very active companies in Singapore is Albany Molecular Research Inc. that is based in Science Park III. AMRI's Dr. Steven J. Collier (now at Codexis Singapore) explained that the company is now expanding its research facilities into new labs, close to the existing ones, to considerably increase its research work force in Singapore. According to Dr. Collier, Singapore is an ideal place for industrial research mainly because of its well-educated work force that is essentially English speaking, and the effective protection of intellectual property, in line with the highest international standards. Although Dr. Collier did not see significant drawbacks of doing research in Singapore, the fact that this is a 'far-away country' clearly has an impact in terms of connections with the rest of the 'developed' research world, particularly in terms of timely delivery of materials, reagents and products.

In line with the format of ***SYNFORM***'s ***INSIDE STORIES***, I met some of the key people mentioned above and conducted brief interviews with them about "Chemistry in Singapore".

Matteo Zanda

A view of the NTU campus

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INTERVIEW 1

*(Questions by M. Zanda (**SYNFORM**), answers by C. L. L. Chai)*

Question 1 | *What are the main fields of interest of ICES, particularly those related to organic chemistry?*

Answer 1 | The main interests are in the area of synthetic methodologies, total synthesis, medicinal chemistry, catalysis, polymer chemistry. The research that we do is not as academic as in some universities as our research should have some potential applications in industry.

Question 2 | *Why should a chemist go to ICES to undertake or continue a career in science?*

Answer 2 | We can offer an international environment and experience, excellent facilities, a chance to be exposed to research that is relevant to chemical and pharmaceutical applications, potential to commercialize inventions, improved job prospects if the chemist performs well in ICES due to exposure to multinational companies and start-ups in the biomedical field. One can also carry out interdisciplinary research easily, as Singapore is small and there are approximately 14 A*STAR institutions in different areas.

Question 3 | *What about the long-term career perspectives for a chemist in ICES?*

Answer 3 | We are on three-year contracts, renewable with good performance. For the staff, there is a good career track. Researchers can also gain experience in the other A*STAR research institutions and hence they can expand their skill sets. There are opportunities in management or as technical leaders.

BIOGRAPHICAL SKETCH

INTERVIEWED

Dr. Christina L. L. Chai (A*Star ICES)

Australian citizen.
Address: Institute of Chemical and Engineering Sciences, 1 Pesek Road, Jurong Island, 627833, Singapore
e-Mail: Christina_chai@ices.a-star.edu.sg

Education:
- PhD in organic chemistry from the Australian National University, Canberra, Australia (1990)
- BSc (Hons) from the University of Canterbury, Christchurch, New Zealand (1987)

Previous appointments:
Dyson Perrins Laboratory, University of Oxford (UK) – Violette and Samuel Glasstone Fellow (1990–1991); Joint appointee at Victoria University of Wellington (New Zealand) as a Lecturer in Chemistry and Research Fellow with Industrial Research Limited (IRL) (1991–1993); Joint appointee as Lecturer (Department of Chemistry)/Research Fellow (Research School of Chemistry), Australian National University (1994–1996); Senior Lecturer, Department of Chemistry, ANU (1996–2001); Associate Professor, Department of Chemistry, ANU (2001–2004); Honorary Adjunct position at Nanyang Technological University, Singapore (2005–present)

Current position:
Program manager/Principal scientist of the New Synthesis Techniques and Applications programme, Institute of Chemical and Engineering Sciences, Singapore

Research interests:
Development of new methodologies, catalysts and reagents in synthesis; Drug development and design; Synthesis of bioactive compounds; Biological mechanisms

Publications:
Over 65 journal publications, 1 book, 4 filed patents

Awards:
Violette and Samuel Glasstone Research Fellowship in Science (1990); Ian Potter Travel Award (1997); DAAD Fellowship (2001); Alexander von Humboldt Fellowship (2005–2006)

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INTERVIEW 2

*(Questions by M. Zanda (**SYNFORM**), answers by T. P. Loh)*

Question 1 | *Nurturing a home-grown talent pool is a priority for science and research in Singapore. What are the strategy and the contribution of NTU in this respect, particularly in the area of chemistry?*

Answer 1 | An aggressive outreach to cultivate interest in chemistry, to create an alumni spirit and a good environment for research and scholarships for locals, encourage research at a young age, and so on.

Question 2 | *What are the short-term and the long-term goals of NTU in the field of chemistry?*

Answer 2 | To recruit the best undergraduate and graduate students is certainly one of major goals. We need to recruit the best young faculty members from around the world, providing the best infrastructure for our faculty to excel. And we must be able to keep the best people here. But there is a rather long list of additional important goals:

- Networking for exchange to create global awareness of NTU.
- Recruiting world-class researchers, both young and already established 'star' professors.
- Providing the best infrastructure for doing first-class research: a new building with excellent safety features and all the necessary equipments has just been built.
- Creating a culture for doing vibrant research, what we want to achieve by inviting top researchers to come and give seminars and interact with our faculty and students, etc.

BIOGRAPHICAL SKETCH

INTERVIEWED

Professor Teck Peng Loh, (NTU Singapore)

- Fellow at the Institute of Advanced Study, Nanyang Technological University (Singapore) since 2007
- PhD, Harvard University (USA) in 1994
- Masters of Engineering (Chem), Tokyo Institute of Technology (Japan) in 1989
- Bachelor of Engineering (Chem), Tokyo Institute of Technology (Japan) in 1987

Teck Peng Loh, the Head of the Division of Chemistry & Biological Chemistry, joined Nanyang Technological University as Professor in February 2005. During his 11 years (1994–2005) at the National University of Singapore, he had risen through the ranks of Lecturer, Senior Lecturer, and Associate Professor to Professor in 2004. He was also the Program Leader of the Medicinal Chemistry program at NUS.

Teck Peng's research activities include green chemistry, asymmetric synthesis, the development of new synthetic methodology, and total synthesis of architecturally complex organic molecules with interesting biological activities. He also discovered many new concepts and methods for organic synthesis and completed the total syntheses of many complex molecules. To date, he has published 136 papers in international refereed journals, 102 conference papers, 5 book chapters, has a Hirsch index of 35 and a total number of 3437 citations.

Teck Peng Loh is the program leader of Medicinal Chemistry at National University of Singapore. He is a frequent plenary speaker or invited speaker at many international conferences. Recently, he was invited to join the Editorial Advisory Board of *Chemical Communications* to help shape one of the world's top chemistry journals. He also receives frequent invitations to write book chapters, review articles, and other manuscripts.

He was awarded the prestigious Japanese Government (Mombusho) scholarship from 1982–1989. In 1997, the National University of Singapore bestowed him the University Outstanding Researcher Award. He has been an Adjunct Professor of Soo Chow University (P. R. of China) and Tsukuba University (Japan) since 2002 and 2005, respectively. He was also a Visiting Professor at Columbia Medical School, Columbia University (USA) from 2002–2003.

Teck Peng Loh has been the Head of the Division of Chemistry & Biological Chemistry in SPMS since July 2005, working hard to set up a world-class chemistry department.

He has also received a number of teaching awards, including NUS Faculty Teaching Excellence Award (2002), NUS Excellent Teachers (2001), Meritorious Teaching Award (2000) and University Outstanding Teaching Award (1997). His professional appointments include: Advisory Board Member of ISCFC-07 held at NTU at the end of 2007, Advisory Board Member of Chemical Communications as coordinator of the "Asia Core Program", Honorary Secretary of Singapore National Institute of Chemistry, Chairman of the Singapore International Chemistry Conference (SICC-4), External Advisory Board Member of Singapore Polytechnic, External Examiner of Singapore Polytechnic (Diploma of Chemical Process Technology) since 2007, Co-Chairman of the ISCIC-6 & ISCOC-9 2006. He also has a seat on the Technical Committee on National Drinking Water Quality Standards and is a member of the SCBE Promotion and Tenure Committee.

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- Encouraging faculty to apply for external grants and to create start-up companies.
- As Singapore is a small country, we have to continue to publish to create international awareness, as well as to support established professors who have done well in Singapore, giving them the best support (graduate students, etc).
- Keeping the focus on synthetic chemistry.
- Encouraging staff to attend conferences as well as to organize international conferences, thus allowing faculty members to benchmark themselves with the best in the world.

We are aware of the need to showcase our work more. Government support is essential and we have to continue to stress the importance of chemistry for chemical and life sciences.

INTERVIEW 3

*(Questions by M. Zanda (**SYNFORM**), answers by D. Y.-K. Chen)*

Question 1 | *Why are K. C. Nicolaou and David Chen lending their name recognition to the chemistry in Singapore?*

Answer 1 | Having been involved in chemical synthesis over the years, apart from our roles as scientists, it is also our passion as educators to promote the arts and sciences of chemical synthesis to regions of the world where this discipline is still underdeveloped, or perhaps its full potential has not yet been tapped into. As scientists and educators, clearly, fame and name recognition is never on the top of the agenda, and simply having the opportunity to bring our passions to a wider audience is a priceless reward by itself. At the same time, it is important to focus on the quality of our research and to maintain at the world standard, such that Singapore, as a country, will be recognized for its strength in chemical synthesis in the days to come. Undeniably, this is an exciting time to be involved in scientific research in Asia, and the strong support and vision from the Singapore government makes the whole proposal even more enticing. Equally fulfilling is the opportunity to contribute to the Singapore economy by providing highly skilled synthetic chemists in this vibrant biomedical community, a rewarding exercise from both the academic and commercial perspectives.

Question 3 | *What would you say to a potential candidate to convince him/her to come to your institution in Singapore to undertake a career in science, particularly in chemistry?*

Answer 3 | We used to invite good candidates to come for a campus visit. It has one the best infrastructures in the world to do chemistry research. We have well-trained undergraduate students who can be potential graduate students – locals as well as students from this region. We can offer good start-up packages (NRF, NAP, division support). Moreover, Singapore is a multicultural country which welcomes foreign talent. English is the medium of instruction, and Singapore invests heavily in research, worth S$12 billion in the next five years. Last but not least, we can offer a good environment to do excellent research.

BIOGRAPHICAL SKETCH

INTERVIEWED

Dr. David Yu-Kai Chen
(A*Star CSL Biopolis)

Born on July 31, 1976, New Zealand citizen.
Address: Institute of Chemical and Engineering Sciences (ICES), Chemical Synthesis Laboratory@Biopolis (CSL@Biopolis), 11 Biopolis Way, The Helios Block #03–08, 138687, Singapore
e-Mail: david_chen@ices.a-star.edu.sg

Education and awards:
David got his PhD in organic synthesis (1998–2001) under the supervision of Dr. Ian Paterson at the University of Cambridge (UK) – Thesis title: "Total Synthesis of Spongistatin 1/Altohyrtin A and Siphonariid-Derived Marine Natural Products". He is the recipient of a number of awards, achievements, memberships, and appointments including membership of the Economic Development Board Chemistry Taskforce, Singapore (2005 to present) and the Adjunct Assistant Professorship at NTU Singapore (2005 to present).

Work experience:
Principal Investigator at the Chemical Synthesis Laboratory@Biopolis (CSL@Biopolis), Institute of Chemical and Engineering Sciences, A*Star, Singapore (March 2005 to present); Senior Research Chemist at Medicinal Chemistry, Merck Research Laboratory, specialized in drug discovery, lead identification and optimization (November 2003–February 2005); Post-doctoral research associate, The Scripps Research Institute (USA) under the supervision of Professor K. C. Nicolaou (January 2002–September 2003); Research assistant at Auckland Cancer Society Research Centre under the supervision of Professor William A. Denny (April–August 1998); He is coauthor of 24 publications in high-impact journals and has given more than 10 invited lectures.

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Question 2 | *What are the perspectives of your lab and group, as well as the long-term programs?*

Answer 2 | Chemical synthesis, to me, is an important fundamental science that will continue to play an indispensible role in any research discipline. We believe the synthesis of architecturally complex compounds serves a dual role, both in educating young scientists, and as catalyst for discovery in both chemistry and biology. The Chemical Synthesis Laboratory@Biopolis is currently focusing on a number of architecturally complex natural products endowed with promising therapeutic potentials. It is my intention to leverage off the discoveries made during our synthetic campaigns, both in chemistry and biology, to further expand our scientific capability into multiple dimensions. More specifically, this refers to designing new reactions, uncovering novel reactivities and chemical biology. Clearly, this is a multi-disciplinary activity where its success critically depends on strong collaborative efforts. However, one thing I wish to emphasize is that any new research direction should complement and not replace our existing capability in synthetic chemistry training. Synthetic chemistry will always serve as the foundation.

Question 3 | *How is, in your opinion, the current level and quality of chemical sciences in Singapore as compared with the most advanced countries, such as the USA, Japan, European Union?*

Answer 3 | Traditionally, chemical sciences in Singapore mainly refer to chemical engineering, where Singapore has a more established reputation. The synthetic chemistry in Singapore has tremendous potential and is an area we are eager to tap into. More specifically, universities have already demonstrated their capability in delivering young, promising chemists. At the same time, there is also a stronger emphasis placed on synthetic chemistry, clearly evident in both the development of infrastructure and recruitment of new faculty members. The issue in hand is moving beyond the fundamental training at bachelor and master level, and to be more competitive under research environments in comparison with the USA, UK and EU counterparts. This is exactly the area which Chemical Synthesis Laboratory@Biopolis is trying to address. Overall, we wish to serve as a catalyst to instigate more activities in high-level chemistry research and to provide a more competitive environment both locally in Singapore and on the world stage.

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Modular Syntheses of Polyene Natural Products via Iterative Cross-Coupling

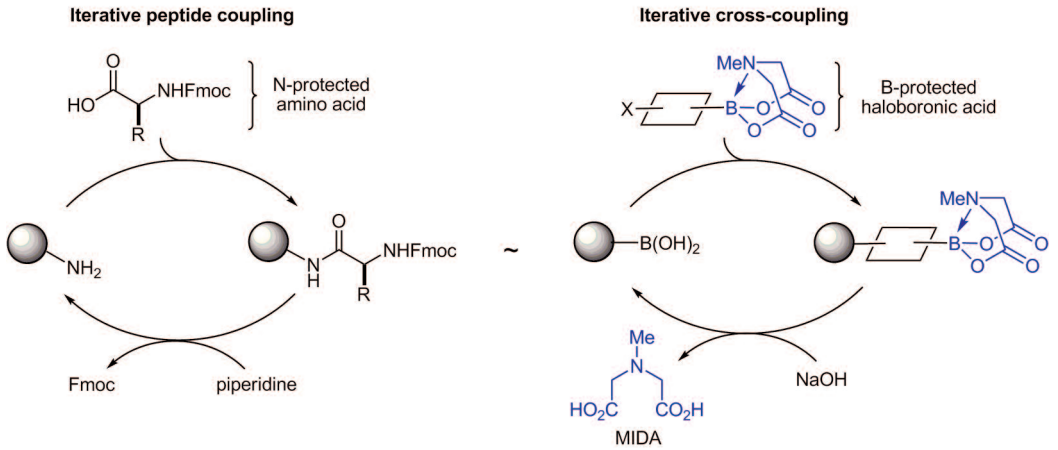
J. Am. Chem. Soc. **2008**, *130*, 466–468

Complex small molecules (natural products and drug-like compounds) have seemingly limitless potential to promote advances in science and medicine, but the degree to which this potential can be realized is ultimately a function of the simplicity, efficiency, and flexibility with which these types of compounds can be synthesized in the laboratory. In this regard, an inspiring benchmark can be found in the process of modern peptide synthesis in which the target molecules are made via the simple, iterative coupling of commercially available bifunctional amino acid building blocks. This process is now routinely automated and readily utilized not only by chemists, but also by biologists and physicists to promote discoveries across a wide range of disciplines.

In stark contrast, the laboratory synthesis of small molecules remains a relatively complex, arduous, and non-systematized process practiced almost exclusively by chemists with specialized background and training. A new synthesis strategy developed by the group of Professor Martin D. Burke from the Department of Chemistry, University of Illinois at Urbana-Champaign (USA) aims to dramatically change this. "Analogous to peptide synthesis," said Professor Burke, "we have discovered a way to synthesize complex small molecules using only one reaction (the Suzuki–Miyaura coupling) iteratively to bring together a collection of bifunctional *haloboronic acid* building blocks. Enabling this 'iterative cross-coupling' approach, graduate student Eric Gillis discovered (*J. Am. Chem. Soc.* **2007**, *129*, 6716) that the cheap and environmentally friendly ligand N-methyliminodiacetic acid (MIDA) can reversibly attenuate the reactivity of boronic acids towards cross-coupling. Moreover," continued Professor Burke, "Eric found that this ligand can be cleaved using very mild aqueous bases (alternative approaches for controlling the reactivity of boronic acids require harsh reagents that are incompatible with complex small molecules). Eric harnessed this new methodology to complete the first total synthesis of the natural product ratanhine, using only the Suzuki-Miyaura reaction to bring together a collection of easily synthesized, readily purified, and highly robust building blocks."

Like peptide synthesis, this simple approach is inherently modular and flexible, well-suited for combinatorial chemistry, and hopefully adaptable to automation. "*This latter goal is being intensely pursued in my laboratories at this time*," said Professor Burke. Moreover, thanks to a partnership with a major international chemical company, a large collection of these types of haloboronic acid building blocks will be commercially available worldwide within the next 6–8 months.

Analogous strategies for the synthesis of peptides and small molecules



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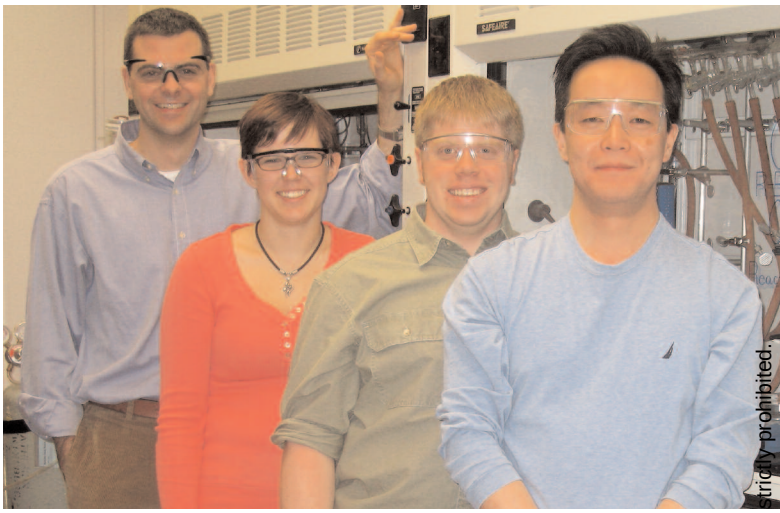
"We hope that this will facilitate the broad utilization of these reagents. In addition, we have received strong interest from the pharmaceutical industry and one major company has already begun using this approach in their drug-discovery efforts." he said.

Although it is certainly true that small molecules have tremendous structural diversity and do not so obviously lend themselves to this type of unified synthesis strategy, according to Professor Burke "it is interesting to note that most natural products are in fact biosynthesized via the iterative coupling of bifunctional building blocks (polyketides from acetate and/or propionate units, polyterpenes from isoprene building blocks, etc.). This is similar in many ways to the biosyntheses of their peptide, oligonucleotide, and oligosaccharide counterparts. In addition," noted Professor Burke, "most drug-like small molecules are comprised of different combinations of aryl, heteroaryl, and related types of units. Thus, there are certain types of 'building blocks' that appear over and over again in small molecules, and we feel that this inherent modularity can be harnessed to great effect."

A specific example of this can be found in the most recent communication from the Burke group which is subject of this ***SYNSTORY***. "In this paper, post-doctoral fellow Suk Joong Lee, graduate student Kaitlyn Gray, and undergraduate student James Paek disclosed their discovery that this iterative cross-coupling strategy can be applied to the synthesis of the notoriously challenging 'polyene' natural products," he said. "As we highlight in this article, polyenes represent an extremely broad and useful class of complex small molecules and the same 'haloalkenylboronic acid' building blocks could in theory be useful for making a wide variety of these types of compounds." However, polyenylboronic acids are notoriously unstable, which thus far has precluded their general utilization. "Overcoming this limitation," said Professor Burke, "we discovered a collection of bifunctional haloalkenyl MIDA boronates which are strikingly stable to purification and storage, and remarkably selective to a wide range of cross-coupling reactions. This stability is maintained in the resulting polyenyl MIDA-boronate ester intermediates – which is perhaps the most striking result from this work. For example," he continued, "we found that several of the corresponding boronic acids are so unstable that they cannot even be isolated, yet the MIDA boronates can be purified with silica gel chromatography and stored indefinitely as crystalline solids. In fact, some of these reagents have been stored on the bench-top under air for nearly two years now without any appreciable decomposition."

Thus, according to Professor Burke, the two things that make these polyene building blocks special are "first, their theoretical capacity for limitless iterative coupling (as opposed to more traditional 'lynchpin' reagents which only enable two coupling steps), and second, the striking stability of these reagents and the intermediate polyenylMIDAboronate esters, which is critical to their successful utilization. We demonstrate this utility with efficient syntheses of all-*trans*-retinal, β-parinaric acid, and half of the amphotericin B macrolide skeleton. To the best of our knowledge," he said, "the latter represents the longest polyene ever synthesized using the Suzuki–Miyaura reaction. In this paper we also describe the first triply metal selective (Zn vs. Sn and B) cross-coupling reaction, the first selective cross-coupling with a differentially ligated diboron reagent, and the first cross-couplings between polyenylchlorides and vinylboronic acids."



From left: Prof. M. D. Burke, K. Gray, E. Gillis and Dr. S. J. Lee

"We hope that these types of building blocks and methods will dramatically improve the way in which many natural products and other small molecules are synthesized in the laboratory," concluded Professor Burke. "In the long term, we are very optimistic that this iterative cross-coupling strategy can help make the process of complex small molecule synthesis as simple as possible."

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COMING SOON ▶▶ COMING SOON ▶▶

SYNFORM 2008/06 is available from May 21, 2008

In the next issues:

THE INSIDE STORY ▶▶▶▶

▶ **An Interview with Sir Jack Baldwin**

SYNSTORIES ■■■■

■ **Proline-Catalyzed Mannich Reactions of Acetaldehyde**
(Focus on an article from the current literature)

■ **An Enantioselective Organocatalytic Oxidative Dearomatization Strategy**
(Focus on an article from the current literature)

■ **Chiral Brønsted Acid Catalyzed Asymmetric Baeyer-Villiger Reaction**
(Focus on an article from the current literature)

FURTHER HIGHLIGHTS ++++

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Review on: Electrophilic Iodination of Organic Compounds Using Elemental Iodine or Iodides *(by S. Stavber et al.)*

SYNLETT
Account on: 1,7-Electrocyclizations of Azomethine Ylides – Scope and Synthetic Aspects *(by M. Nyerges et al.)*

SYNFACTS
Synfact of the Month in category "Polymer-Supported Synthesis": Suzuki–Miyaura Coupling Reaction Using Palladium Nanoparticles Immobilized on SPB

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