

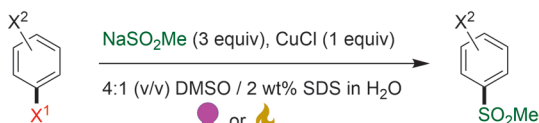
Synform

People, Trends and Views in Chemical Synthesis

2023/10

Copper-Enabled Photo-Sulfonylation of Aryl Halides Using Alkylsulfonates

Highlighted article by V. Mdluli, D. Lehnherr, Y.-h. Lam, Y. Ji, J. A. Newman, J. Kim



LEGEND
💡 365 nm, 35 °C 🔥 thermal, 35 °C

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Dear Readers,

In this October issue of SYNFORM we continue the series of interviews with the eminent Editors who form the Associate Board of our Open Access journal *SynOpen*, which has recently received a first and very positive Impact Factor (2022) of 2.5. The first is with Professor Martin Banwell, from the Institute for Advanced and Applied Chemical Synthesis (IAACS), Guangzhou (P. R. of China). In the second we get to know better Professor Irene Izzo, from the Department of Chemistry and Biology “A. Zambelli”, University of Salerno (Italy). The third interview is with Professor Vibha Tandon, from the Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi (India). A warm welcome to Martin, Irene and Vibha! We are very glad to have you on board in the Thieme Chemistry family!

The issue itself, however, begins with the Literature Coverage of a recent article by D. Lehnher (USA) and comes from the private sector. It describes a conceptually new method for synthesizing sulfones, which are important compounds used as functional group handles in synthetic intermediates and are often endowed of important bioactivity. Following that is a second Literature Coverage article reporting on a truly fascinating piece of research recently published in *Science* by A. Braunschweig (USA) about the effect of mechanical distortion of bonds and molecules on the acceleration of Diels–Alder reactions.

Enjoy your reading!



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If you have any questions or wish to send feedback, please write to Matteo Zanda at: synform@outlook.com

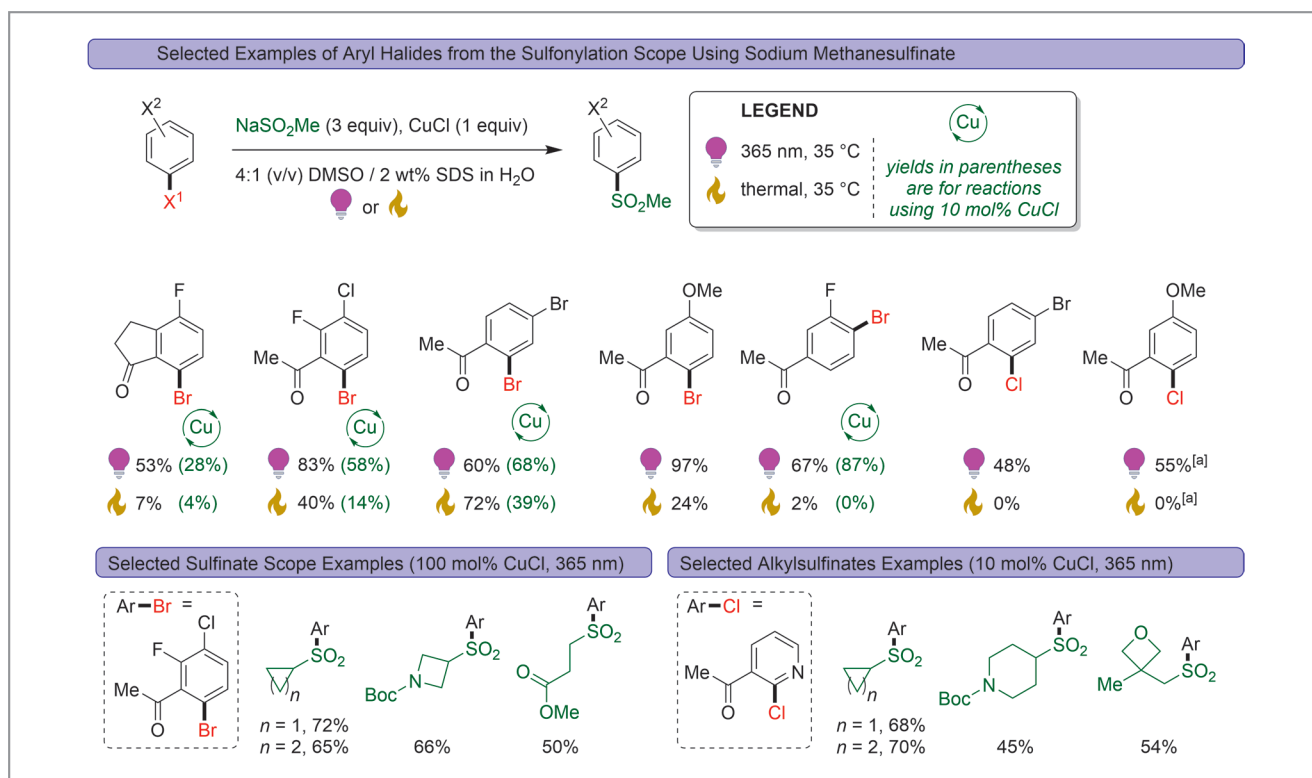
Copper-Enabled Photo-Sulfonylation of Aryl Halides Using Alkylsulfonates

Adv. Synth. Catal. **2023**, 365, in press; DOI: 10.1002/adsc.202300257

Sulfones are prevalent in synthetic organic chemistry, and can serve both as functional group handles in synthetic intermediates as well as structural features in bioactive targets. "Methods of synthesizing sulfones include oxidation of sulfides, metal-catalyzed cross-couplings of sulfonates, direct C–H functionalizations, and three-component couplings using SO₂ or its surrogate",¹ explained Dr. Dan Lehnher from the Process Research and Development department of Merck & Co., Inc. (Rahway, New Jersey, USA), whose group was interested in developing novel and efficient strategies for installing sulfonyl groups into organic molecules. "Both electrochemical and photochemical methods have been developed to access sulfones.² For example, Rueping,³ Molander⁴ and

Manolikakes⁵ have reported methods of cross-coupling sulfonate salts to aryl halides via metallaphotoredox leveraging a nickel catalyst and either an Ir- or Ru-photocatalyst."

Photochemistry enables access to highly reactive intermediates (e.g., open-shell intermediates), which has facilitated the development of many synthetic methods, achieving broad impact in organic synthesis. "The most widely used photocatalysts have traditionally been coordination complexes of d⁶ transition metals, especially iridium (Ir^{III}) due to their high photo- and redox-stability. However, iridium is rare and thus very expensive. Therefore, there are ongoing efforts in organic synthesis in shifting to earth-abundant metals, such as iron, cobalt, nickel, and copper, to enable sustainable catalysis. This



Scheme 1 All reactions run using arylhalide (1.0 mmol), NaSO₂Me (3.0 mmol), and CuCl (either 100 or 10 mol%) in 4:1 (v/v) DMSO / 2 wt% aq. sodium dodecylsulfate for 36 h. Photochemical conditions use the Penn PhD m2 Photoreactor (365 nm, 100% LED intensity, 400 rpm stir rate, 5200 rpm fan rate resulting in internal reaction temperature of 35 °C); thermal conditions are 35 °C hot plate (400 rpm stir rate). ^[a] 42 h instead of 36 h.

can be especially important when seeking the development of large-scale industrial processes,” said Dr. Lehnherr.

For this work, Dr. Lehnherr and his co-workers used copper(I) chloride to enable the photosulfonation of aryl halides with alkylsulfinate salts. Dr. Lehnherr told SYNFORM: “The copper-driven photosulfonation was inspired by a fundamentally different approach than previous methods, namely photoactivation of aryl halides to access non-planar triplet geometries.⁶ These non-planar triplet states allow access to the σ^* associated with a C–X bond, which is not accessible in the ground state, potentially facilitating nucleophilic aromatic substitution in the excited state (Figure 1, top). DFT calculations of the triplet geometries of some polyhalogenated arenes revealed energetically accessible non-planar geometries which featured an out-of-plane carbon–halide bond relative to the other carbon atoms of the arene (Figure 1, bottom). Furthermore, this carbon–halide bond was elongated, indicating a bond-weakening event.”

The authors’ success with this method was demonstrated with a substrate scope of >20 aryl halides (including heteroarenes) and >10 alkylsulfinate salts (Scheme 1). “Besides aryl bromides and aryl iodides, the sulfonation method can also utilize aryl chlorides, which is noteworthy as C–Cl are typically less reactive compared to C–Br and C–I bonds,” explained Dr. Lehnherr. He continued: “Regio- and chemo-selective sulfonation of polyhalogenated arenes under mild conditions was achieved, which is orthogonal to traditional cross coupling methods that typically require high reaction temperatures (80–100 °C) and can lack selectivity.” To illustrate the benefits of the photochemical activation approach (365 nm, 35 °C internal reaction temperature), the authors also characterized the yields under thermal conditions (35 °C, no light). Dr. Lehnherr remarked: “UV-vis and NMR spectroscopy provide mechanistic insight, including the evidence for in situ formation of CuSO_2Me when CuCl and NaSO_2Me are mixed in solution. X-ray crystallography was utilized to obtain structural confirmation when two potential regioisomeric products could be formed.” He concluded: “Overall, this sulfonation method provides complementarity to existing photochemical methods of cross-coupling sulfinate salts with aryl halides, as it works well with alkylsulfinate salts whereas previously reported methods are more developed for arylsulfinate salts.”^{3–5}

Matteo Farah

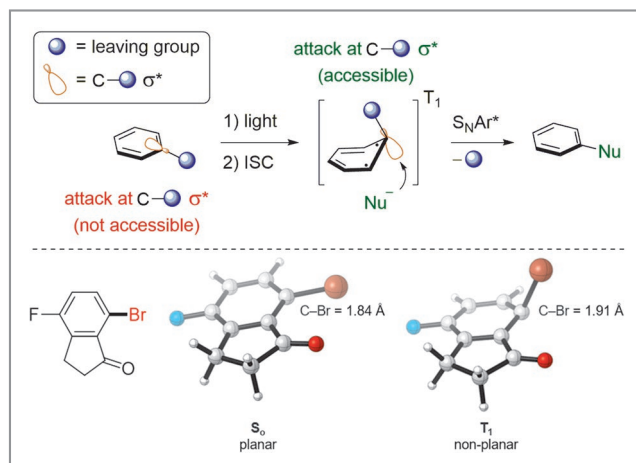


Figure 1 (Top) Strategic design for photo-sulfonation of non-planar triplets to access aryl-alkylsulfones. (Bottom) DFT computed ground state (S_0) and excited state triplet (T_1) geometries for a bromo-fluoroindanone derivative illustrating the change in geometry from planar to non-planar and the elongation of the C–Br bond.

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About the authors



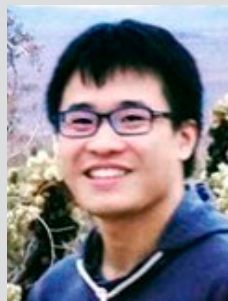
Dr. V. Mdluli

Velabo Mdluli obtained a Master of Science (Chemistry) at the University of Massachusetts Dartmouth (USA) in 2016, doing research with Professor David Manke working on the synthesis and characterization of tripodal ligands and their coordination to early transition metals. He then went on to do a Ph.D. in chemistry at Carnegie Mellon University (USA) with Professor Stefan Bernhard, working on tailoring the design of cationic iridium(III) complexes for photodriven hydrogen evolution and applications toward organic transformations. Velabo is currently an MRL postdoctoral researcher at Merck & Co., Inc., Rahway, NJ, USA working with Dr. Dan Lehnherr on the development of new photochemical and electrochemical synthetic methods.



Dr. D. Lehnherr

Dan Lehnherr received his B.Sc. degree from the University of Victoria (Canada), where he carried out undergraduate research on photochemistry topics in the laboratory of Professor Peter Wan. He obtained his Ph.D. from the University of Alberta (Canada) under the mentorship of Professor Rik R. Tykwinski (Chemistry) and Professor Frank A. Hegmann (Physics) developing conjugated organic materials for optoelectronic applications (e.g., photodetectors and thin film transistors) and dimeric pentacenes as a platform for investigating intramolecular singlet fission for solar cell technologies. He was an NSERC Postdoctoral Fellow at Harvard University (USA) with Professor Eric N. Jacobsen focusing on organocatalysis and reaction mechanism elucidation where he developed dimeric thiourea catalysts for cooperative anion-binding catalysis. Subsequently he carried out postdoctoral research at Cornell University (USA) with Professor William R. Dichtel, developing synthetic methods to foldamers and nanographenes and studying their properties. Since 2016 he has been in the Catalysis Group within Process Research and Development at Merck & Co., Inc., Rahway, NJ, USA. His research interests are at the intersection of reaction discovery, physical organic chemistry, computational chemistry, and new capabilities to enable the development of medicines.



Dr. Y-H. Lam

Yu-hong Lam completed his DPhil in organic synthesis under the guidance of Professor Veronique Gouverneur at the University of Oxford (UK). He pursued postdoctoral research in computational chemistry at UCLA (USA), working alongside Professor Ken Houk. He is currently a computational organic chemist working at Merck & Co., Rahway, NJ, USA. His research primarily revolves around leveraging computational chemistry techniques, encompassing both physics-based and machine learning-based approaches, to streamline pharmaceutical process research and development. He has co-authored over 40 research papers and reviews. He has played a key role as co-chair of the Computational Chemistry working group within the IQ Consortium, showcasing his leadership and expertise in advancing computational chemistry practices in pharmaceutical research.



Dr. Y. Ji

Yining Ji earned her B.Sc. degree from the University of Barcelona (Spain) before obtaining her Ph.D. at the same institution under the guidance of Professor Antoni Riera and Professor Xavier Verdaguer. Her doctoral work focused on the development of new asymmetric Pauson–Khand reactions. Following her Ph.D., she conducted postdoctoral research at the Scripps Research Institute (USA) with Professor Donna G. Blackmond, where she conducted in-depth mechanistic studies on catalytic reactions. In 2014, Yining Ji joined Merck & Co., Inc. in Rahway, NJ, USA. Her expertise is at the intersection of organic chemistry and physical organic chemistry. Yining made significant contributions to the field, co-authoring over 35 research papers and reviews. Her primary interest is in leveraging mechanistic principles to enhance the understanding, improvement, and discovery of organic chemistry, with a specific focus on streamlining pharmaceutical process research and development.

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*Dr. J. A. Newman*

Justin A. Newman received his B.A. with Honors in Chemistry from Knox College (USA) where he worked with Prof. Mary Crawford using gas-phase FTIR to determine atmospheric reaction rate constants. From there he received his PhD from Purdue University (USA) under the mentorship of Prof. Garth Simpson. His PhD work focused on the development of non-linear optical microscopy instrumentation and methodologies for probing

the crystallinity of a wide range of materials including small molecule pharmaceuticals and proteins. In 2016 he joined Merck & Co., Inc., Rahway, NJ, USA in the Materials Science group where his research is now focused on the physical characterization of drug substance and drug product solids. Since 2018 he has led a small team of crystallographers dedicated to solving crystal structures of small molecule organics.

*Dr. J. Kim*

Jungchul Kim received his M.S. from Sogang University, Seoul, South Korea under direction from Professor J. Kang, researching chiral ligand synthesis for asymmetric synthesis. He obtained his Ph.D. from Oregon State University (USA) under the mentorship of Professor James D. White, working on the total synthesis of natural products. He was a postdoctoral fellow at Ohio State University (USA) with Professor Leo A. Paquette where

he studied the asymmetric total synthesis of Spongistatin 1. He joined the department of process chemistry at Schering-Plough Research Institute (USA) in 2002 and is currently within Process Research and Development at Merck & Co., Inc., Rahway, NJ, USA. His primary research area is focused on commercial process development of new synthetic routes to pharmaceuticals.

Acceleration of Diels–Alder Reactions by Mechanical Distortion

Science **2023**, *380*, 1053–1058

This paper, authored by the group of Professor Adam Braunschweig at the City University of New York (USA), addresses one of the biggest challenges that has stood in the way of the ‘greening’ of organic chemistry, which is the heavy reliance of the chemical industry on solvents. According to Professor Braunschweig, organic solvents currently account for ~90% of chemical waste, and heating and cooling them is one of the reasons why chemical manufacturing uses ~37% of all manufacturing energy. “Mechanochemical reactions, where force is used to drive the reaction under solvent-free conditions, can eliminate a substantial amount of waste and energy usage in chemical manufacturing,” said Professor Braunschweig, adding: “Mechanochemistry, however, has not been widely adopted because the chemical community does not understand how force acts upon the transition state and why different products are observed under mechanochemical conditions vs. solvothermal conditions.” He explained: “The reason this has been so difficult to investigate is because it’s really hard to measure the force being applied to reactants, so no one really understood what happens to molecules. The few theories that existed couldn’t really explain different selectivities – why different products were sometimes observed under mechanochemical conditions – so they were incomplete. Here, we did some really complicated experiments using modified surfaces, nanoscopic tip-arrays, kinetics, etc., but the conclusions are really simple to understand: what we found is that pushing on molecules bends them. That’s it. But what’s really cool about that is that the bent molecules tend to follow a different reaction path than their unbent counterparts, because these new pathways may have lower activation barriers for the bent molecules but not the unbent molecules. In a nutshell, the consequences of this work are: chemists can now start investigating computationally how bending molecules may affect reactivity or they can understand previously unexplainable selectivities with this new paradigm.”

This research paper is a result of collaboration between an interdisciplinary team composed of experimental and computational chemists and mechanical engineers that are all part of the National Science Foundation’s Center for Mechanical Control of Chemistry (CMCC). The authors of this work believe that mechanochemistry has the chance to completely change how organic chemistry is carried out in the next twenty years, but it is currently in its infancy, and so it requires experts in both chemistry and mechanics to answer very basic questions

that have not yet been answered. “This paper is really answering the most basic question in mechanochemistry, what happens when you push on molecules with directional force?” said Professor Braunschweig. He continued: “As evidence of how much we have to learn about mechanochemical reactions, this most basic of questions had not yet been addressed adequately.”

To perform these studies, the authors used a modified Park Systems atomic force microscopy platform in the Braunschweig lab to control precisely the force and time applied between molecules on surfaces and molecules on the tips of polymer-pen arrays, which are elastomeric arrays with hundreds of individual tips. Professor Braunschweig explained: “Upon bringing the tips into contact with the surfaces, a nanoreactor is formed between the tips and the surfaces that confines the reactants under an applied force. The computer-controlled movement of the piezoactuators that hold the array provide precise control over force and reaction time. With these parallel arrays, we can test the effects of many values of force and time in a single printing experiment, which allows us to explore the effects of hundreds of different experimental conditions on reaction rates of Diels–Alder reactions in a single afternoon. As a result, we could test a series of Diels–Alder reactions and extract structure–activity relationships under applied load.”

Professor Braunschweig explained that the authors investigated the reaction kinetics of [4+2] Diels–Alder cycloaddition reactions between dienophiles and surface-confined diene monolayers to measure how force affects reaction rates. They chose pericyclic reactions because they proceed in concerted fashion without intermediates, which minimizes challenges in analyzing their kinetics. “The first and primary goal was to induce chemical reaction using mechanical compression and confirm the bond formation by characterizing the reaction outcome in different ways,” remarked Professor Braunschweig. He went on: “After establishing this method, we selected reactants that had a well-established order in reactivity in solution-based chemistry. The dienophiles were modified with fluorophores, so the reaction was analyzed by simply taking fluorescent images of the printed surfaces. Experiments were complemented with density-functional theory (DFT) calculations and finite element analysis modeling of the forces exerted between the tips and the surfaces.”

Professor Braunschweig told SYNFORM of two unexpected results that helped the authors understand what was really occurring in this system, and in mechanochemical reactions more generally. He explained: “The first surprise came when we were able to determine the activation volumes of these reactions. The activation volume is the dependence of the reaction rates on pressure. The activation volumes of Diels–Alder reactions under hydrostatic pressure – pressure applied in solution which presses on reactants from all sides equally – have been known for ~50 years. The activation volumes under uniaxial forces – where pressure is applied from one direction, as occurs in our system and other mechanochemical reactors – were approximately 1000 greater than in solution, which told us something unique was occurring under uniaxial stress.” This helped guide the authors’ calculations, which revealed another big surprise, which is that force acts by bending the molecules, and only a tiny amount of bending is needed to substantially accelerate the reaction. Professor Braunschweig said: “For example, to get a reduction in the activation barrier of ~4 kJ/mol under hydrostatic conditions requires ~150 MPa of pressure, whereas under mechanochemical conditions (uniaxial stress) the same 4 kJ/mol lowering of the activation barrier can be achieved at <1 MPa. This is like the force of gently pressing two fingers together.” Professor Braunschweig

concluded: “That was an incredible result to us, and it’s when we realized that we had discovered something profound.”

Mattias Fanak

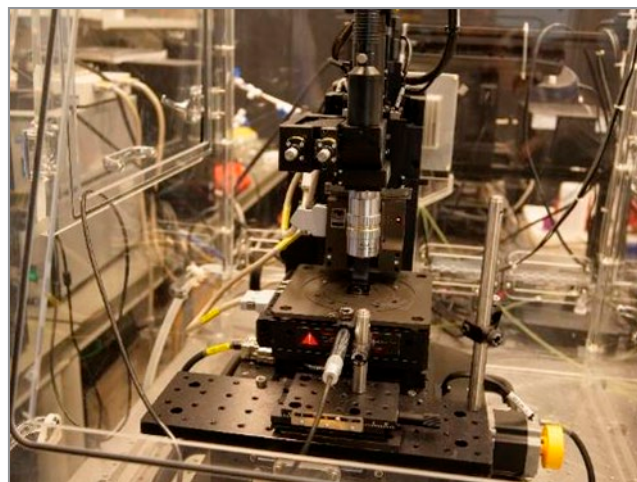


Figure 1 The printing platform is based on a customized atomic-force microscope equipped with a tilting stage, humidity chamber, and holder to accommodate massively parallel polymer pen arrays

About the authors



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Yerzhan S. Zholdassov received his B.S. in chemical technology at South Kazakhstan State University (Kazakhstan) in 2012 and M.S. in chemical technology at Russian State University of Oil and Gas (Russian Federation) in 2016. Currently he is a Ph.D. candidate at the City University of New York (USA) under the supervision of Prof. A. B. Braunschweig.



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Li Yuan is a Ph.D. candidate at the Department of Mechanical Engineering and Applied Mechanics, University of Pennsylvania (USA). He completed B.S. and M.S. in solid mechanics in Tsinghua University (China) in 2017 and 2020, respectively. Currently, he is specialized in frictional behavior, mechanical and electronic properties of 2D materials at the nanoscale.



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Ryan W. Kwok received his B.S. in chemistry at Hunter College of the City College of New York (USA). Currently he is a Ph.D student at CUNY (USA) and works under the supervision of Prof. M. Marianski and is specializing in density functional theory studies.

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Alejandro Boscoboinik received his M.S. in chemistry at the Universidad Nacional de San Luis (Argentina) in 2013. He completed his Ph.D. at the University of Wisconsin-Milwaukee (USA) in 2020. Subsequently, he joined Prof. R. Carpick as a postdoctoral fellow at UPenn (USA).



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Daniel J. Valles received his B.S. in chemistry at Stony Brook University (USA) and M.S. in chemistry at Brooklyn College of CUNY (USA). After completing his Ph.D. in 2021 with A. Braunschweig, he joined Geon Formulation Solutions company as a Scientist.



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Dr. R. W. Carpick

Robert W. Carpick received his B.Sc. in physics from the University of Toronto (Canada) in 1991, and his M.A. and Ph.D. in physics from the University of California at Berkeley (USA) in 1997 under the supervision of Dr. Miquel Salmeron. He spent two years as a postdoctoral appointee at Sandia National Laboratory (USA) in the Surface and Interface Science Department, and then the Biomolecular Materials and Interfaces Department where he worked under the supervision of Dr. Alan R. Burns. He joined UPenn (USA) in January 2007 after serving for 7 years on the faculty of the Engineering Physics Department at the University of Wisconsin-Madison.

Adam B. Braunschweig received his B.A. in chemistry at Cornell University (USA) in 2001 and his Ph.D. in organic chemistry at the University of California – Los Angeles (USA) in 2006. He is a Professor of Nanoscience and Chemistry at the Advanced Science Research Center of the City University of New York (USA), and his group studies surface reactions, antiviral development, mechanochemistry, and photocatalysis.

Editorial Board Focus: Prof. Martin Banwell (Institute for Advanced and Applied Chemical Synthesis, P. R. of China)

Background and Purpose. From time to time, SYNFORM portraits Thieme Chemistry Editorial Board or Editorial Advisory Board members who answer several questions regarding their research interests and revealing their impressions and views on the developments in organic chemistry as a general research field. This Editorial Board Focus presents Prof. Martin Banwell (Institute for Advanced and Applied Chemical Synthesis, P. R. of China) who joined the Associate Board of *SynOpen* with effect of January 2023.

Biographical Sketch



Prof. M. Banwell

Martin Banwell is an internationally renowned expert in organic chemistry. He is now the Dean of Institute for Advanced and Applied Chemical Synthesis (IAACS, P. R. of China) as well as a Master/PhD tutor, and his main study is the total synthesis of active natural products and research and development of new drugs. He was elected as an academician of the Australian Academy of Sciences in 2004, and he is also a fellow of the Royal Society of Chemistry and the Royal Australian Chemical Society, as well as an honorary fellow of the Royal New Zealand Chemical Society. He was a highest-level (Level-E2) tenure-track professor at the Australian National University. In 2018, he was awarded the Officer Medal by the Australian Federal Government, the highest level award for Australian citizens, for his contributions to scientific research. In 2021, he was awarded the Chinese Government Friendship award by Prime Minister Keqiang Li. Till now, he has published almost 400 SCI papers in journals like *Nature Chemistry*, *Accounts of Chemical Research*, and *Organic Letters*, and has been authorized for 13 international patents.

INTERVIEW

SYNFORM You are a leading researcher in the field of organic synthesis. Could you tell us more about the importance of that field and your current research activities?

Prof. M. Banwell I am an organic chemist focused on the total synthesis of biologically active natural products that can serve as leads for the development of new therapeutic agents. In a number of instances our studies also address the supply problems associated with developing natural products as drug entities.

SYNFORM Please comment on your role as an Associate Editor of *SynOpen*.

Prof. M. Banwell I am still fleshing out my role as a new Associate Editor of *SynOpen* but obviously wish to work to encourage my colleagues to submit papers to the journal and so make it all the more successful. I also anticipate developing a plan for a special issue of the journal devoted to marine natural products chemistry, especially as this applies to such activities in the South China Sea and the South Pacific.

SYNFORM Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?

Prof. M. Banwell I have recently been involved in establishing a new research institute based at Jinan University in Southern China that is concerned with chemical synthesis in its manifold forms – this entirely new entity is called the Institute for Advanced and Applied Chemical Synthesis or IAACS and will soon move into a dedicated new building on the Zhuhai campus of the University. While my research can be all-consuming at times, I am a keen swimmer, hiker, skier (downhill), traveler and bookworm.

Martin Banwell

Editorial Board Focus: Prof. Irene Izzo (Università degli Studi di Salerno, Italy)

Background and Purpose. From time to time, SYNFORM portraits Thieme Chemistry Editorial Board or Editorial Advisory Board members who answer several questions regarding their research interests and revealing their impressions and views on the developments in organic chemistry as a general research field. This Editorial Board Focus presents Prof. Irene Izzo (Università degli Studi di Salerno, Italy) who joined the Associate Board of *SynOpen* with effect of January 2023.

Biographical Sketch



Prof. I. Izzo

Irene Izzo received a Magna Cum Laude degree in chemistry in 1994 and a doctoral degree in chemistry from the University of Salerno (Italy) in 1998 (Dissertation title: "Synthesis of Biologically Active Marine Steroids and Cholestane Analogs." Thesis supervisor: Prof. Guido Sodano). In 1998 she received a post-doctoral fellowship, working at University "Louis Pasteur" of Strasbourg (France) in the Laboratoire de Stéréochimie (E.C.P.M.), tutored by Prof. Guy Solladié. Since March 2007 she has been an associate professor at the Department of Chemistry and Biology "A. Zambelli" of the University of Salerno. In 2008–2009 she was a visiting scientist at the Institute for Research in Biomedicine of Barcelona (Spain) in the group of Prof. Fernando Albericio. Since the academic year 2013–2014 she has been teaching in the second year of the "Chemistry and BioTechnology" (ChemBioTech Master) at the University of Strasbourg (France), organized by the École européenne de chimie, polymères et matériaux (ECPM) and the Strasbourg School for Biotechnology (ESBS), a course devoted to the Solid-Phase Synthesis of Biomacromolecules. She has also been Erasmus Departmental Coordinator since 2014. In 2018 she received the national Italian habilitation as full professor. Her field of research is the total synthesis and semisynthesis of bioactive natural products (mainly marine steroids and cyclopeptides) and their analogues. She is also involved in the synthesis of artificial ion channels and peptidomimetics, in particular cyclic peptoids. She is author of more than 90 articles, 4 book chapters and more than 90 communications to national and international congresses.

INTERVIEW

SYNFORM *You are a leading researcher in the field of organic synthesis. Could you tell us more about the importance of that field and your current research activities?*

Prof. I. Izzo The art of organic synthesis has been the basis for the scientific developments of the 21st century in several research fields: medicine, materials science and biology. Constantly we should be able to face new challenges to improve the quality of life in a global world and to make a fairer and more sustainable life for all citizens of our planet. Organic synthesis, in combination with other fields of chemistry, physics, engineering, biology and medicine, will be a fundamental tool in this context. I am interested in total synthesis of natural products (in prevalence of marine origin) and their analogues and in the design and synthesis of peptidomimetics with a macrocyclic structure (cyclic peptoids). Our aim is to obtain compounds which could be useful as bioactive agents, as environmentally safe catalysts, and as molecular scaffolds in materials science.

SYNFORM *Please comment on your role as an Associate Editor of SynOpen.*

Prof. I. Izzo I will involve women and young researchers as authors, promoting their contribution in a "fast, fair, and flexible" open access in different topics of organic synthesis.

SYNFORM *Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?*

Prof. I. Izzo I believe that to be a good scientist, you must open your mind to the social and cultural aspects of life, learning from cultures far from ourselves. That's why I love traveling and reading. Moreover, I am continually searching for the beauty of the world around us and I try to capture it with photography and drawing.

Mattia Fenu

Editorial Board Focus: Prof. Vibha Tandon (Jawaharlal Nehru University, India)

Background and Purpose. From time to time, SYNFORM portraits Thieme Chemistry Editorial Board or Editorial Advisory Board members who answer several questions regarding their research interests and revealing their impressions and views on the developments in organic chemistry as a general research field. This Editorial Board Focus presents Prof. Vibha Tandon (Jawaharlal Nehru University, India) who joined the Associate Board of *SynOpen* with effect of March 2023.

Biographical Sketch



Prof. V. Tandon

Vibha Tandon obtained her Ph.D. in 1991 in chemistry on the sequential synthesis of oligonucleotides using special protecting groups from Allahabad University (India). She carried out postdoctoral studies at the Department of Chemistry, IIT Kanpur (India) to develop synthetic methodology for oxidation of alkenes and sulfides using cobalt complexes as organometallic catalyst. Thereafter, in 2009, she joined Delhi University (DU, India) as an assistant professor at Dr. B.R. Ambedkar Centre for Biomedical Research, and later the same year moved to the Department of Chemistry, DU as an associate professor. Presently, she is a professor at the Special Centre for Molecular Medicine (SCMM), Jawaharlal Nehru University (JNU, India). She was Chairperson of the Research Coordination Committee of JNU, creating a number of Special Interest Groups at JNU and started a networking project. She served as Chairperson of SCMM from 2015 to 2017 and Chief proctor from 2016 to 2017. She was Chairperson of

the Women Scientists Program, Chemical Sciences Stream, of the Department of Science and Technology, Government of India from 2016 to 2021. Presently, she is Chairperson of the Biotechnology Career Advancement and Re-Orientation Programme (BioCARE) for women launched by the Department of Biotechnology, Ministry of Science and Technology, Government of India.

She has published 93 papers in international journals, and has to her credit four international and four Indian patents. Prof. Tandon has mentored 25 Ph.D. students and around 70 students for six-month projects. She has been teaching Masters and Ph.D. students for the last 25 years.

She was awarded a Royal Society Fellowship (2007-08) to work at Prof. Michael J. Gait's laboratory, MRC Cambridge, UK. She has been on a DAAD fellowship (2010-2011) and an INSA visiting fellowship (2011-12) to work in the Radiation Biology laboratory of Prof. George Iliakis at the Institute of Medical Radiation Biology at Essen (Germany); and a Fulbright Senior Research fellowship (2012-2013) to visit the Department of Cell Biology, Georgia State University (Atlanta, USA).

INTERVIEW

SYNFORM What is the focus of your current research activities?

Prof. V. Tandon My group's research interest over the last five years include: designing novel approaches to synthesize biologically active heterocyclic molecules for use in the treatment of cancer, bacterial infection, and neurodegenerative disease; development of operationally simple organocatalyzed stereoselective catalytic strategies for asymmetric synthe-

sis under mild conditions; investigation of metal-catalyzed cross-coupling and highly atom-economic C-C and C-N bond-forming domino reactions.

My group has carried out Brønsted acid/chiral phosphoric acid catalyzed regioselective synthesis of carboxamidation of indolyl alcohols using isocyanate esters. In addition, my lab established a Pd-catalyzed synthesis of multi-aryl 7-azaindoles using sequential arylation of 5-bromo-6-chloro-3-iodo-1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine. Four diverse aryl groups are installed in a chemoselective fashion providing a general method to synthesize sterically encumbered compounds and

extended 7-azaindoles. Three selective sequential arylations at C-3, C-5, and C-6 via Suzuki–Miyaura cross-coupling followed by direct C-2 arylation using a Pd catalyst and AgOTf as an additive are highlights of that work. Interestingly, the tetraaryl 7-azaindoles showed aggregate-induced emission (AIE) making them potentially useful as fluorophores in OLEDs, sensors, and bio-imaging tools.

Other than heterocyclic chemistry, my group is largely involved in translational research. We have two strong leads (novel molecules) in the pipeline to be developed as drugs: PPEF, an antibacterial agent against MDR bacterial strains, and DMA, a radioprotector against radiation therapy in cancer patients. We have shown that DMA, a benzimidazole, exerts radioprotection to normal cells during radiotherapy of tumor in patients. I deciphered that the Akt/PKB/GSK3 β /NF κ B pathway is selectively activated in normal cells in tumor-bearing mice, but not in tumor cells. The ICMR has approved DMA for product development as a radioprotector. DMA confers protection against Xerostomia, reduces radioresistance and causes increased survival in HNSCC. GMP synthesis and GLP grade safety pharmacology & toxicology IND enabling studies have been done on DMA by Intox Pvt. Ltd., Pune, and Eurofins–Advinus Pvt. Ltd., Bangalore, which was funded by ICMR. I am working closely with head and neck patients of Medanta Hospital, Gurgaon and GTB Hospital, Delhi.

My group has also developed an antibiotic candidate, PPEF, a small molecule targeting topoisomerase IA and III protein selectively in bacteria, but which does not act on gyrase. PPEF efficiently kills 640 multi-drug-resistant pathogenic strains of eleven Gram negative and Gram positive bacterial strains identified by the WHO as “Priority Pathogens”. PPEF covers PRIORITY 1. CRITICAL: 1. *Pseudomonas aeruginosa*, carbapenem-resistant; 2. Enterobacteriaceae, carbapenem-resistant, ESBL-producing; PRIORITY 2: HIGH 1. *Enterococcus faecium*, vancomycin-resistant; 2. *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant; 3. *Salmonella*, fluoroquinolone-resistant; PRIORITY 3: MEDIUM 1. *Streptococcus pneumoniae*, penicillin-non-susceptible; 2. *Shigella* spp., fluoroquinolone-resistant. Preclinical evaluation showed high efficacy of PPEF against MRSA in septicaemia mice model.

SYNFORM Please comment on your role as an Associate Editor of SynOpen.

Prof. V. Tandon My role will be to establish SynOpen as a journal which publishes original high-quality research in medicinal chemistry and to involve the scientific community with SynOpen so as to create faith in SynOpen. I will try to make SynOpen a journal of high repute in next few years.

SYNFORM Could you tell us something about yourself outside the lab, such as your hobbies or extra-work interests?

Prof. V. Tandon I am interested in gardening and landscaping, as well as counselling and working for girls and women to bring them back into mainstream society to earn enough to live with dignity.



Coming soon

— Literature Coverage

Design, Synthesis and Visible-Light-Induced Non-Radical Reactions of Dual-Functional Rh Catalysts

— Literature Coverage

Nickel-Catalysed Enantioselective Hydrosulfenation of Alkynes

— Literature Coverage

Suzuki–Miyaura Coupling of Aryl Nosylates with Diethanolamine Boronates

Further highlights

Synthesis Review: Exploring Chemical Modifications of Aromatic Amino Acid Residues in Peptides

(by M. S. Maji, B. Paul and co-workers)

Synlett Account: From Sweet Molecular Giants to Square Sugars and Vice Versa

(by P. Compain)

Synfacts Synfact of the Month in category “Metals in Synthesis”: Copper-Catalyzed Difluoroalkylation of Silyl-Enol Ethers

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