Young Career Focus: Professor Jaideep Saha (Centre of Biomedical Research, India)

Background and Purpose. SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Professor Jaideep Saha (Centre of Biomedical Research, India).

Biographical Sketch

Prof. J. Saha

Jaideep Saha obtained his B.Sc. (Hons) in Chemistry from S.A. Jaipuria College, Calcutta University (India) in 2003 and his M.Sc. (Chemistry) from IIT Madras (India) in 2005. He pursued his doctoral studies with Prof. Mark W. Peczuh at the University of Connecticut (USA) where he worked in synthetic method development for the synthesis of unnatural carbohydrates and phosphine-catalyzed transformations. He was a research intern at Boehringer-Ingelheim Pharmaceutical Inc. CT (USA) in the chemical development department, where he worked with Dr. Chris Senanayake and Dr. Daniel Fandrick. After completing his PhD in 2012, he moved to the University of Pittsburgh (USA) as a post-doctoral fellow to work with Prof. Peter Wipf (2012–2013). He worked on medicinal chemistry projects and synthesized selective small-molecule inhibitors of NOX-2 enzyme. At that time he was also a Vascular Medicine Institute Fellow at the school of medicine. For his second post-doc, he moved to the University of Oxford (UK) as a Marie-Curie Post-doctoral Fellow in 2013 to work with Prof. Stuart Conway, where he developed small-molecule probes for targeting hypoxia. In December 2016, he began his independent career at the Centre of Biomedical Research (India) as an Assistant Professor, later promoted to Associate Professor (2019), where his group is involved in the development of new synthetic methodologies and the preparation of compounds for application in medicinal chemistry and drug discovery.

Recently he was awarded the Thieme Chemistry Journals Award (2022). He has been inducted as an early career advisory board member of *Bioorganic & Medicinal Chemistry* and *Bioorganic & Medicinal Chemistry Letters* (2022). He is also the recipient of a Marie-Curie Fellowship (2013), an INSPIRE faculty award from Department of Science and Technology, India (2013), a Dr. K. S. Krishnan Research Fellowship, BRNS India (2015), and a Discovery Early Career Research Award (DECRA) by ARC in 2017.

INTERVIEW

SYNFORM *What is the focus of your current research activity?*

Prof. J. Saha Our current research activities have several overlapping themes, all of which are directed to synthetic method development using various catalytic approaches or radical-based chemistry. We are particularly interested in using strained organic molecules as synthons in our methodologies. These compounds can be stipulated for various strain-release-driven transformations or functionalizations and thus can deliver very interesting scaffolds which are otherwise not very easy to synthesize. For the last couple of years, we have been using several of them, including donor–acceptor cyclopropanes or vinyl cyclopropanes, aziridines, (aza)-bicyclobutanes, propellanes, etc. Depending on the activation modalities – i.e., whether metal or Lewis acid activation or radical conditions are used – these molecules can be engaged in many exciting transformations. Besides this, we are also actively working on exploiting azaoxyallyl cations or similar types of reactive intermediates in developing new synthetic transformations. In the same vein, we have become interested in developing ways to intercept the reactive intermediates that are generated during different chemical transformations; for example, oxypentadienyl cation is known to form during the course of the Piancatelli rearrangement or Nazarov reaction. We look for strategies that can intercept the original manifold and this can be achieved by taming the reactive intermediate involved. Such an exercise can give access to new reactivity, which can be translated into unconventional synthetic transformations.

In a nutshell, our motivation and goals behind all the research endeavors in our laboratory is to unfold new reactivity, develop sustainable chemical transformations and ultimately to leverage our findings in various contexts of medicinal chemistry and chemical biology.

 Synform **2023/02**, A40–A42 • Published online: January 17, 2023 • DOI: 10.1055/s-0040-1720585

SYNFORM *When did you get interested in synthesis?*

Prof. J. Saha It first struck me when I was studying for my bachelor's degree in chemistry (B.Sc.) at college. While I had to take all types of chemistry courses, organic chemistry became my favorite subject in no time. I was fascinated by the principles of organic synthesis, its mechanisms and the concept of chirality. I became even more passionate when I started my M.Sc. dissertation project in carbohydrate synthesis, with the late Prof. Loganathan at Indian Institute of Technology Madras in 2004. It was my first opportunity to work in an organic chemistry research lab.

From that point on, I began to appreciate the power of organic synthesis and it was very thrilling for me that with smart retrosynthetic logic and well-articulated design plans, synthetic chemists can synthesize complex natural products, including oligomeric carbohydrates, in the lab.

After completing my M.Sc., I decided to pursue doctoral studies in the field of synthetic organic chemistry and I entered the Ph.D. program at the University of Connecticut, USA with Prof. Mark W. Peczuh. I spent the most rewarding and most memorable time in graduate school in the process of becoming a trained organic chemist. After finishing my Ph.D., I pursued two consecutive post-doctoral studies in different areas of organic synthesis as I wanted to expand my expertise more into the applied areas.

I was fortunate that I came across some excellent teachers and mentors (Prof. Loganathan, Prof. Mark Peczuh, Prof. Peter Wipf, Prof. Stuart Conway, Prof. Amy Howell) who inspired and motivated me at different stages of my career and those were the push for which, today, I am one of the practitioners of this wonderful scientific discipline.

SYNFORM *What do you think about the modern role and prospects of organic synthesis?*

Prof. J. Saha In my opinion, organic synthesis is one of the most creative and important scientific disciplines which has had a great impact on human life and society on various fronts ranging from medicines, agrochemicals, cosmetics, and vitamins to materials, energy fuels and polymers. Over time, this field has undergone a massive transformation and now its role in enabling science and technology is truly remarkable as many allied disciplines – such as chemical biology, biotechnology, materials science and nanotechnology – benefit enormously from the discoveries of organic synthesis. A great example to cite in this very context would be the 2022 Noble Prize in Chemistry, that highlights the impact of click chemistry and biorthogonal chemistry in several cross-disciplinary research areas.

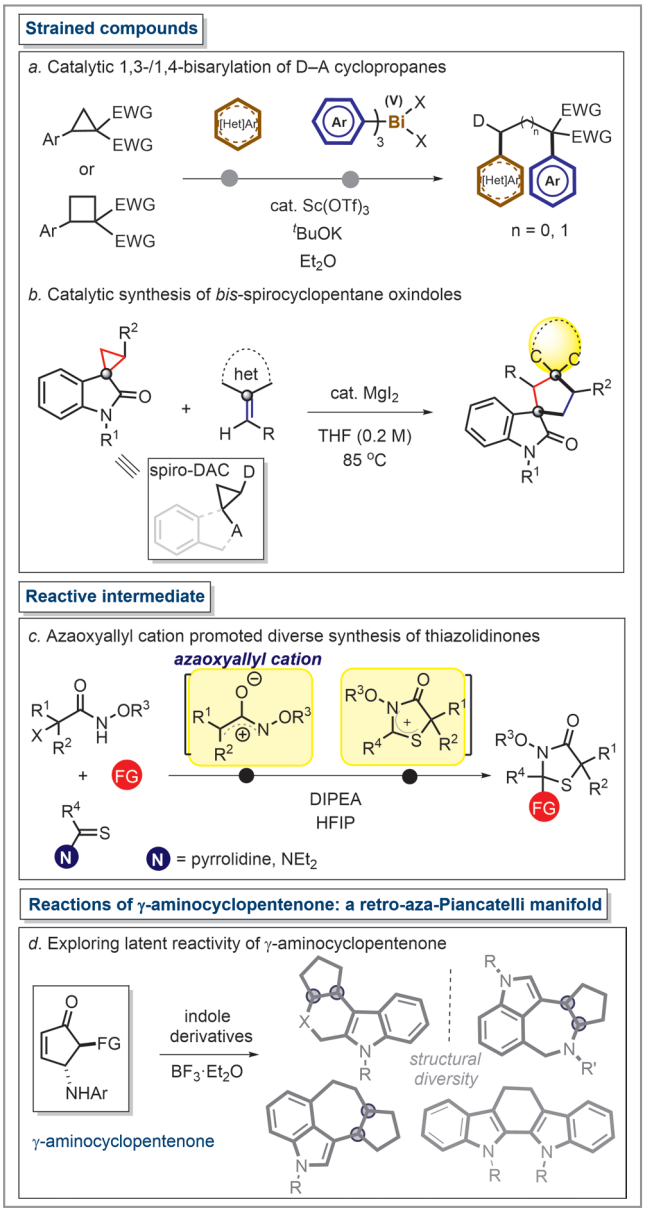
Since organic synthesis is, at its core, about practicing the means to create new chemical bonds involving carbon atoms, the development of creative and sustainable organic transformations will always be the essence of this field. However, it is also of paramount interest to extend the skillset of organic synthesis to interdisciplinary domains in order to foster new innovations and discoveries, especially in human health and medicine.

SYNFORM *Could you tell us more about your group's areas of research and your aims?*

Prof. J. Saha Broadly speaking, we use various strained organic molecules or reactive intermediates and develop useful synthetic methodologies, and we particularly focus on nitrogen heterocycles or scaffolds that have medicinal relevance (Scheme 1). The reason we became interested in exploring strained compounds, or those that can form reactive intermediates, is their rich and diverse pool of reactivity which can be tapped for new synthetic transformations. For example, we have explored the reactivity of donor–acceptor (D–A) cyclopropanes/cyclobutanes for ring-opening 1,3-/1,4-bisfunctionalization reactions and through such a strategy we were able to incorporate two distinct functional groups on the resulting acyclic system in tandem (*J. Org. Chem.* **2019**, *84*, 710–725; *Org. Lett.* **2020**, *22*, 5115–5120). Further, we were able to append the "strain" to the oxindole ring and show the use of such an oxindole-activated D–A cyclopropane in a de novo synthesis of spirocyclopentane oxindole frameworks with an all-carbon quaternary center (*Chem. Commun.* **2019**, *55*, 7069–7072).

Developing the azaoxyallyl cation promoted transformation is another active area of research in our group. We found this transient intermediate particularly fascinating as it can be generated under extremely mild conditions (metal-free), yet the scope of the transformation is truly diverse and valuable. We have shown this chemistry can be tactically used for preparing some very important classes of heterocycles and other important compounds (*Org. Lett.* **2019**, *21*, 5848–5852; *J. Org. Chem.* **2022**, *87*, 613–627). These include morpholines, thiazolidinones, six-membered saturated S,N- and Se,N-heterocycles and organic peroxides. Structure–reactivity relationship of this transient intermediate always made us curious and recently we uncovered a distinct reactivity pattern when an α-aryl group is present. Such a system is suitably poised to undergo an intramolecular nucleophilic N-arylation [Ar(Csp^2)–N cyclization] step, leading to oxindoles (*Chem. Eur. J.* **2022**, *28*, e202201208). There are other exciting ongoing projects based on this theme.

 Synform **2023/02**, A40–A42 • Published online: January 17, 2023 • DOI: 10.1055/s-0040-1720585



Scheme 1 Selected work from the research group

In the same vein, we are interested in those organic transformations that proceed through reactive intermediates. Our interests lie in tweaking of the normal manifold of those reactions (basically we look to intercept the underlying reactive intermediate with different trapping agents) and forging new and elusive chemical transformations. We have explored the Piancatelli rearrangement and Nazarov reaction and so far, we have contributed to some very interesting developments in this context (*Angew. Chem. Int. Ed.* **2021**, *60*, 8808–8812; *Chem. Commun.* **2022**, *58*, 2504–2507).

I should also point out that sometimes we become actively engaged in projects that are purely curiosity-driven, even when we do not possess the core competence or prior experience in those areas. In my experience, such projects always teach us new chemistry, irrespective of the outcomes.

In the next couple of years, we are planning to be more engaged in developing synthetic transformations based on radical chemistry. Besides the new objectives, we like to employ our favorite "strained compounds" or reactive intermediate in such regimens.

SYNFORM *What is your most important scientific achievement to date and why?*

Prof. J. Saha Within the first two to three years of my independent research career at CBMR Lucknow, the world was hit by the COVID-19 pandemic. It is not so hard to imagine how it could have impacted any early career researcher to stay on the track of ongoing research projects. Therefore, each of the research projects that we were able to pursue or even complete during that uncertain time stands for an important scientific achievement to me and to our research group. I also believe that as we are a young research group, all of us are in the process of constant learning and every time we cross a milestone, we celebrate it as one of the most important scientific achievements in that time point. However, if I still have to choose one, I would like to talk about the work in particular that we had published in 2021 (*Angew. Chem. Int. Ed.* **2021**, *60*, 8808–8812). This study revealed an unexpected latent nucleofugal reactivity of the γ-aminocyclopentenone system, which was leveraged to gain access to many functionalized indole derivatives and indole–alkaloid-like structures, more in the fashion of diversity-oriented synthesis. Most importantly, the starting material used in this study was the end product of an aza-Piancatelli rearrangement and mechanistically the transformation indicated the feasibility of a retro-aza-Piancatelli manifold, which is unprecedented in the context of this venerable name reaction.

  • Published online: January 17, 2023 • DOI: 10.1055/s-0040-1720585