

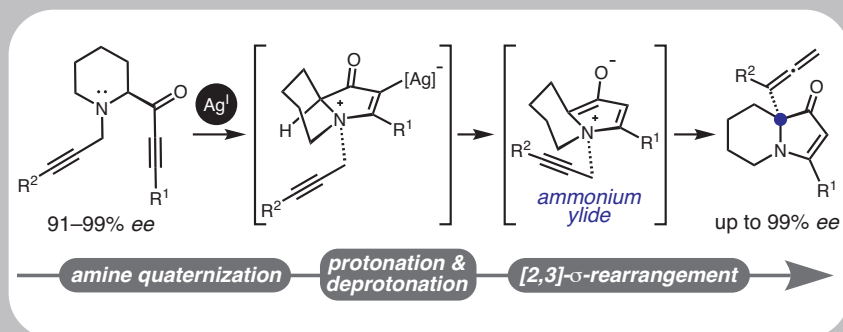
# Synform

People, Trends and Views in Chemical Synthesis

2021/04

## Lewis Acid Catalyzed Domino Generation/ [2,3]-Sigmatropic Rearrangement of Ammonium Ylides to Access Chiral Azabicycles

Highlighted article by S. Xi, J. Dong, H. Chen, Q. Dong,  
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## Dear Readers,

What I am missing the most right now - professionally speaking - is an ACS conference. I know, not everyone is a fan of ACS meetings. They are so huge, dispersive, with tens of parallel sessions scattered in those mammoth conference centres. One sometimes has to walk easily half an hour to move from one lecture to another and it's just impossible to attend all the interesting stuff that's going on; it's way too much, too big, too hectic. But it's so exciting to meet all those people in one place, so nice to see all those volunteers keenly helping out and keeping everything under control, those buses frantically carrying thousands of attendees back and forth from hotels to the meeting venue all day long. I love the 8 o'clock American coffee before starting the first lecture, wandering around in those massive and freezing corridors with all that excessive air conditioning that dries you out in a matter of minutes, so that you have to keep drinking massive amounts of coffee to survive. I am missing even the once feared and hated intercontinental flight and the stressful US border check... and obviously I am missing the stellar science that goes on in an ACS meeting, from the hidden gems presented in small rooms to the sponsored talks given by chemistry superstars in massive ballrooms, the buzzing atmosphere and all the meetings and discussions going on everywhere, all day long, from 7 am to 10 pm. I just can't wait for the next ACS meeting in person!!! Meanwhile we are fortunate enough that we can still enjoy the stellar chemistry of this new issue of SYNFORM, which starts with a groundbreaking *Science* paper on the modification of polyethylene chains by Susannah Scott (USA). The next article unravels the potential of photocatalysis applied to lignan biosynthesis as reported by Jean-Philip Lumb (Canada). The third article is a very informative Young Career Focus interview with Anat Milo (Israel), while the honour and

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duty of closing the issue in style is on the shoulders of Yu Lan and Min Zhang (P. R. of China) with their novel entry to chiral azabicycles from ammonium ylides.

Enjoy your reading!!



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## New Uses for Recycled Carbon: Converting Waste Polyethylene into Alkylaromatics

*Science* **2020**, *370*, 437–441

Polyethylene is the world's most widely used and produced polymer, highly valued for its lightness and strength. It is a key component of countless everyday items, such as plastic bags, bottles, caps, lids, pipes, containers, as well as many that are lesser-known, such as wire and cable insulation, woven fabrics and yarns, and wear-resistant artificial hip and knee joints. Although polyethylene itself is not directly harmful, being rather inert and essentially non-toxic, it makes up a significant portion of human-generated litter and environmental pollution; furthermore, the original source for its production is largely ethylene obtained from energy-intensive fossil fuel processing, which also represents a major environmental issue.

"The synthetic polymer industry is nearly 150 years old, but mass production really started to take off about 60 years ago and has been growing exponentially ever since," said Professor Susannah Scott, from the University of California, Santa Barbara (USA). "Polymer chemists learned how to tailor material properties by modulating both the molecular-level microstructure and the macromolecular entanglements using just carbon and hydrogen (and the occasional heteroatom), creating an industry which is now one of the largest non-energy uses for fossil carbon."

Professor Scott explained that the widespread adoption of plastic, driven by its low cost of production and robustness,<sup>1</sup> has led to increasingly visible pollution of the natural environment. Only a small fraction of used plastic is destined for mechanical recycling into polymer-based products, due to challenges in recovery and cleaning and degradation of properties during reprocessing. In some countries, incineration keeps most plastic out of landfills, but the process recovers far less energy than was invested in making the plastics. Conventional routes to feedstock recycling target monomers which can be repolymerized. "This is thermodynamically feasible for condensation polymers but not for addition polymers, of which the polyolefins such as polyethylene and polypropylene constitute the majority of plastic waste," said Professor Scott. "Alternative approaches involving hydrogenolysis can convert polymers into smaller molecules at lower temperatures due to the strong exothermicity of the reaction,<sup>2</sup> but require a relatively expensive co-reactant (H<sub>2</sub>) and generate low-value paraffins as products. Such reactions may not provide

the necessary economic driving force to motivate polyolefin recycling, since the products can be obtained more cheaply (and potentially with a smaller environmental footprint) in alternative ways."

At the onset of this project, Professor Scott's group was inspired by a report on the depolymerization of polyethylene in which the homogeneous Ir-catalyzed dehydrogenation of polyethylene and *n*-hexane was coupled with Re-catalyzed olefin metathesis at 175 °C.<sup>3</sup> Professor Scott said: "We initially attempted to conduct a solvent-free analogue of this reaction using two heterogeneous catalysts (Pt/Al<sub>2</sub>O<sub>3</sub> and ReOx/Al<sub>2</sub>O<sub>3</sub>) and a low-molecular-weight polyethylene. It proceeded smoothly at 280 °C over the course of 24 hours to generate a hydrocarbon liquid with much-reduced molecular weight. However, a control reaction involving only the dehydrogenation catalyst revealed that the metathesis catalyst is not required. Indeed, depolymerization over Pt/Al<sub>2</sub>O<sub>3</sub> in the absence of solvent gave a similar liquid. However, the orange color suggested the presence of polyaromatic chromophores. Further spectroscopic analysis by field desorption mass spectrometry revealed that alkylbenzenes are major products, with smaller amounts of higher polyaromatic hydrocarbons that contribute the visible color."

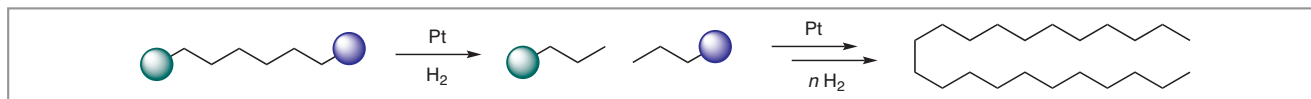
Since the formation of alkylaromatics is strongly endothermic at moderate reaction temperatures, the key to their formation is the coupling of aromatization with hydrogenolysis, which provides an internal source of energy. "The tandem reaction therefore benefits from having a macromolecular carbon source; much shorter hydrocarbon chains such as those found in crude oil cannot engage in the necessary reaction balancing," explained Professor Scott. She continued: "Control experiments with C<sub>30</sub>H<sub>62</sub> failed to produce significant amounts of alkylaromatics, presumably because the shorter hydrocarbon chains are not an effective H<sub>2</sub> sink."

Professor Scott noted: "The aromatic fraction is predominantly dialkylbenzenes, which can be sulfonated to form anionic surfactants. These materials resemble the linear alkylbenzene sulfonates, which are biodegradable surfactants manufactured from fossil fuels."

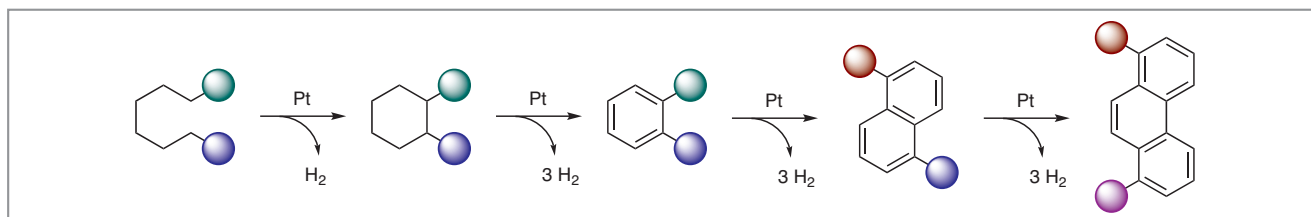
"Future work will involve increasing the catalytic activity, increasing the alkylaromatic yield, and tuning the product distribution to favor particular molecular weights," said Pro-

fessor Scott, who concluded: "For industrial application, the tolerance of the catalyst to impurities in post-consumer plastic waste must be optimized, and the ability to conduct the reaction in a continuous fashion must be developed."

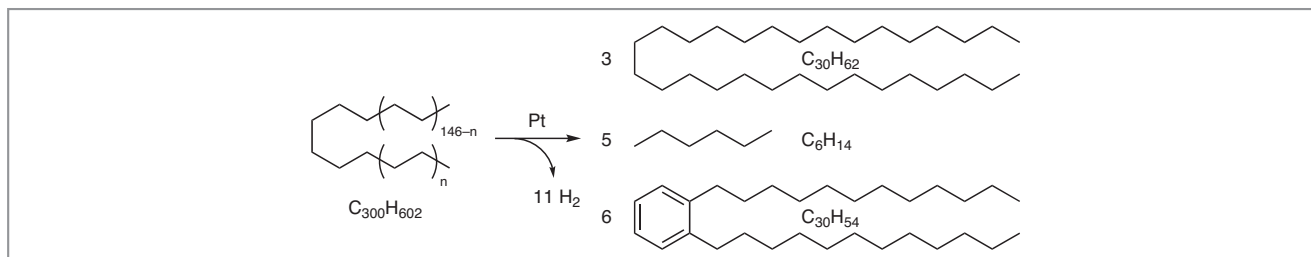
*Mattes Fenske*



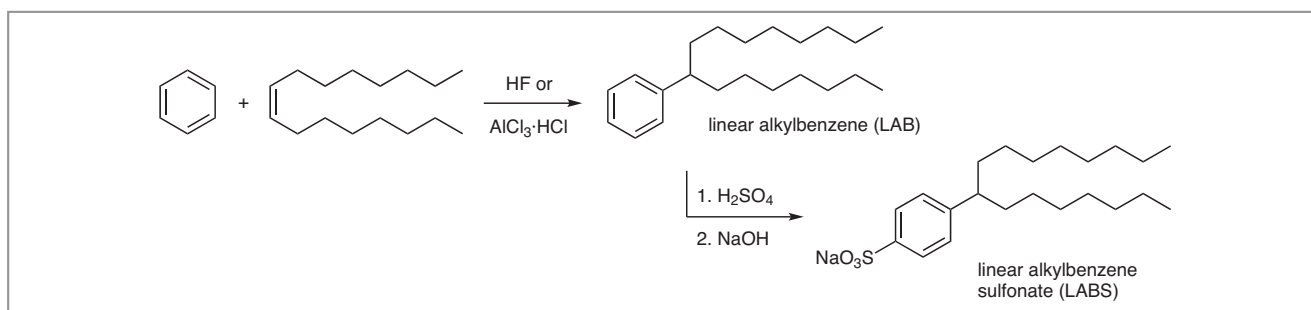
**Scheme 1** Exothermic



**Scheme 2** Endothermic



**Scheme 3** Tandem hydrogenolysis/aromatization



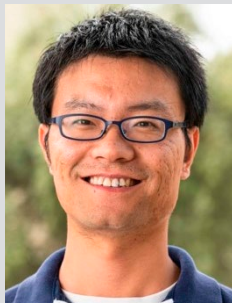
**Scheme 4** Conventional manufacturing of alkylbenzene sulfonates

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*Prof. M. Abu-Omar*

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*Prof. S. Scott*

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## Mimicking Oxidative Radical Cyclizations of Lignan Biosynthesis Using Redox-Neutral Photocatalysis

*Nat. Chem.* **2021**, *13*, 24–32

Dibenzocyclooctadiene (DBCOD) lignans are complex natural products isolated from medicinal plants of the Schisandraceae family. For many years, extracts of these plants have been used throughout Eastern Europe and Asia for their wide-ranging health benefits, which have included anti-viral and anti-oxidant activities and perhaps most importantly, hepatoprotection. With the increased use of pharmaceuticals throughout much of Asia, interest has grown in small molecules that can alleviate drug-induced liver toxicity, and in this regard, preliminary clinical trials using extracts from *Schisandra chinensis* and *Schisandra sphenanthera* have shown promising results. The group of Professor Jean-Philip Lumb at McGill University (Montreal, Canada) has been interested in these natural products.

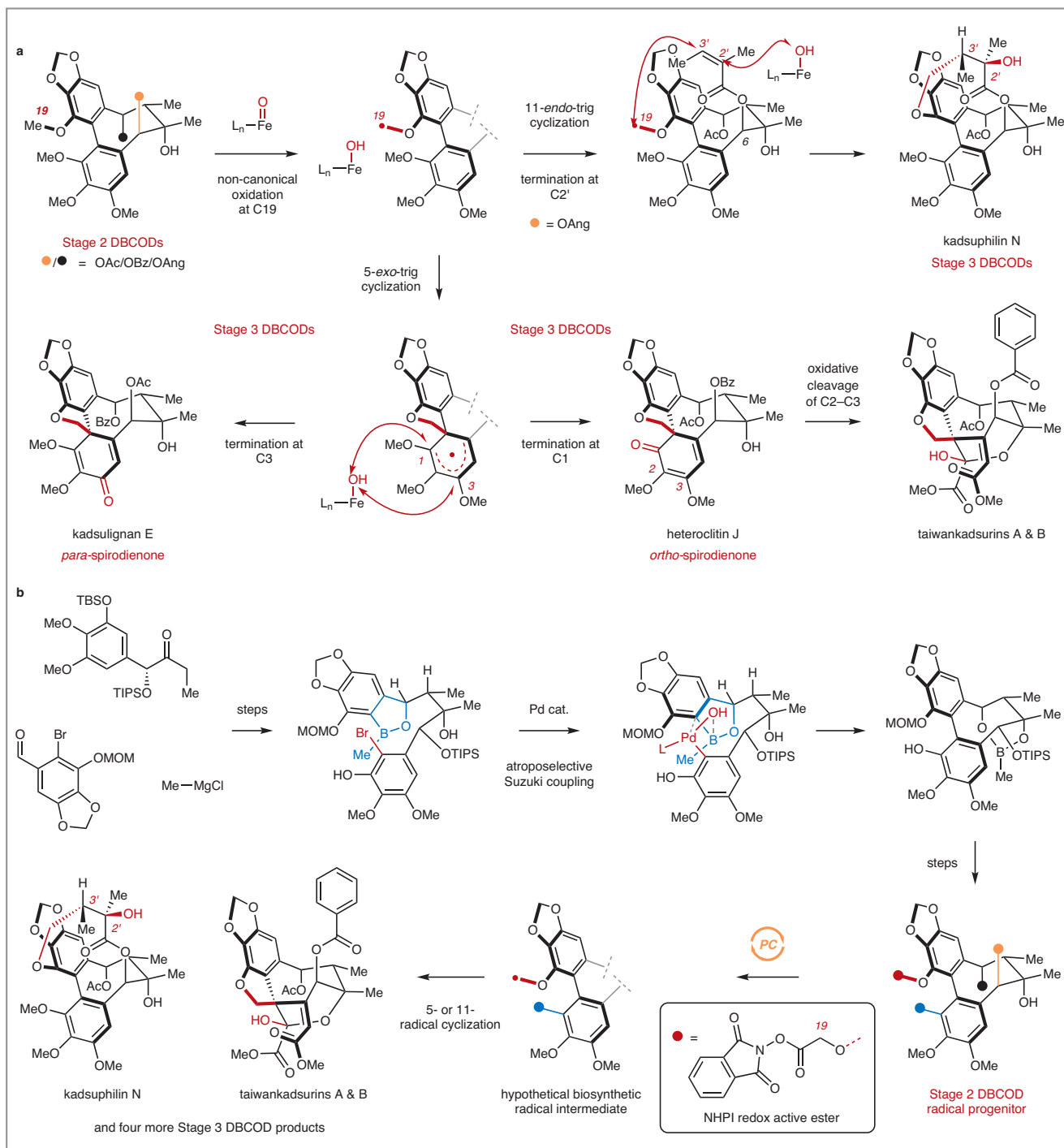
“While many DBCODs have been known since the early 1970s, the most complex members, which we call ‘Stage 3 DBCODs’ in our work, have not been previously synthesized,” explained Professor Lumb. He continued: “Stage 3 members contain a very high oxygen content embedded within intricate, polycyclic structures (Scheme 1a). This is perhaps best exemplified by the taiwankadsurins and kadsuphilin N, which comprise uniquely bridged ring systems surrounding an 8-membered carbocyclic core. Their complexity, coupled with their poor availability from natural sources, has limited detailed biological studies, and little is known about how these natural products exert their beneficial effects.”

Biosynthetically, DBCODs are products of an oxidative pathway that transforms relatively simple phenyl propane units into increasingly intricate structures (Scheme 1a). Professor Lumb said: “The pathway includes Stage 1 members that possess the characteristic 8-membered ring of the family in a fully saturated form. Stage 2 members are then generated by sequential C–H oxygenations around this core that install benzylic esters and a 3° alcohol. While little is known about the orchestration of these oxidations, they are most likely performed by iron oxygenases, following a canonical mechanism of C–H abstraction and rebound. This is the most common mechanism of cytochrome P450s and non-heme oxygenases, and involves the recombination of a substrate-centered radical and the enzyme’s Fe-(III)-OH. Rebound is typically very fast, and occurs with rate constants between  $10^7$  to  $10^{11}$  s<sup>-1</sup>.”

Professor Lumb explained that to arrive at Stage 3 DBCODs, an unusual, non-canonical C–H oxidation must take place, in which intermediate substrate-centered radicals isomerize prior to rebound. In the DBCODs, this isomerization involves a transannular radical cyclization that generates the 11-membered marcolactone of kadsuphilin N, or a 5-membered spirocyclization that breaks aromaticity to produce the taiwankadsurins. “Under normal circumstances, these radical cyclizations would be much slower than rebound, raising questions about how the associated enzymes avoid canonical hydroxylation in order to promote these challenging C–C bond formations,” remarked Professor Lumb. He continued: “Relatively little is known about non-canonical enzymes and their unique mechanisms for C–H oxidation, and by comparison to their canonical cousins, relatively few conditions exist for their mimicry in the lab.”

In order to explore the chemistry and biochemistry of Stage 3 DBCODs, the group designed a strategy to mimic their characteristic non-canonical biosynthesis that hinged on late-stage radical cyclizations (Scheme 1b). “The use of radicals in complex molecule synthesis has seen a resurgence in recent years that is largely driven by the ever-expanding toolbox of chemoselective reaction conditions for their formation. In our case, we benefited immensely from modern photocatalytic tools in order to generate the hypothetical biosynthetic radicals,” remarked Professor Lumb. He continued: “We then watched as they selected between downstream transformations, including the 5- and 11-membered-ring cyclizations that ultimately led to the Stage 3 targets. Despite their complexity, we could perform these cyclizations on good scales and in high yields, leading to hundreds of milligrams of some family members.”

“Before arriving at the key, photocatalytic step, we needed to develop an asymmetric and scalable route to the Stage 2 DBCOD framework that would afford us the flexibility to access multiple Stage 3 members (Scheme 1b),” said Professor Lumb, who added: “To do so, we developed an atroposelective, Pd-catalyzed cyclization to install the key 8-membered ring that forms the tetra-*ortho*-substituted biaryl bond with very high diastereocontrol. Given the well-known difficulties of forming biaryl bonds stereoselectively, we think that the lessons learned from our optimization studies could be more



**Scheme 1** (a) Biosynthetic hypothesis for the generation of Stage 3 dibenzocyclooctadiene (DBCOD) lignans from Stage 2 progenitors involves late-stage non-canonical oxidations to create the 11-membered macrolactone in kadsuphilin N or the 5-membered spirocycle in taiwankadsurins. (b) Our synthetic strategies combine early-stage diastereo- and atroposelective assemblies of simple building blocks, and late-stage biomimetic radical cyclizations using photo-redox catalysis.

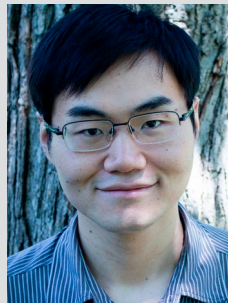


broadly useful in other synthetic contexts. Here, it provided multiple grams of Stage 2 DBCODs that could sustain our late-stage discovery efforts.”

Professor Lumb concluded: “We hope that our work will call attention to the fascinating chemistry of these natural products, and that it will help to unravel the mechanisms by which they exert their beneficial biological effects. We also hope that our work will inspire complementary efforts to capitalize on Nature’s biosynthetic blueprint, and explore non-canonical branches of oxidative metabolism.”



### About the authors



*Dr. Z. Huang*

**Zheng Huang** was born in China and received his BSc degree from the University of Science and Technology of China (P. R. of China) in 2013. He completed his PhD in 2020 under the supervision of Professor Jean-Philip Lumb at McGill University (Canada), and is currently a postdoctoral fellow in the same group. His research is focused on aerobic catalysis and biomimetic total synthesis of complex natural products.



*Prof. J.-P. Lumb*

**Jean-Philip Lumb** obtained his B.A. from Cornell University (USA) in 2002, before moving to the University of California, Berkeley (USA) to pursue a PhD with Professor Dirk Trauner. He was then a postdoctoral fellow at Stanford University (USA) working with Professor Barry Trost, before beginning his independent career at McGill University (Canada) in 2011. The Lumb research group focuses on bio-inspiration and catalysis in order to develop efficient and flexible syntheses of complex natural products.

## Young Career Focus: Dr. Anat Milo (Ben-Gurion University, Israel)

**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 Dr. Anat Milo (Ben-Gurion University, Israel).

### Biographical Sketch



Dr. A. Milo

**Anat Milo** received her B.Sc./B.A. in Chemistry and Humanities from the Hebrew University of Jerusalem (Israel) in 2001, M.Sc. from UPMC Paris (France) in 2004 with Berhold Hasenknopf, and Ph.D. from the Weizmann Institute of Science (Israel) in 2011 with Ronny Neumann. Her postdoctoral studies at the University of Utah (USA) with Matthew Sigman focused on developing physical organic descriptors and data analysis approaches for chemical reactions. In October 2015, she returned to Israel and joined the Department of Chemistry at Ben-Gurion University, where her research group develops experimental, statistical, and computational strategies for identifying molecular design principles in catalysis with a particular focus on stabilizing and intercepting reactive intermediates by second-sphere interactions.

### INTERVIEW

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

**Dr. A. Milo** My research group integrates experimental, computational, and statistical methods to design and construct modular catalyst libraries and provide strategies for discovering and optimizing selective catalytic reactions. We also develop physical-organic analysis methods for exposing structure–activity and structure–selectivity relationships within reaction manifolds. These methods entail: (1) obtaining reaction outputs, such as rate, enantio-, regio-, or chemo-selectivity of experimental libraries; (2) correlating the reaction outputs with molecular descriptors of different reaction components (catalyst, substrate, directing group, solvent) for the concurrent interrogation of mechanistic hypotheses and optimization of catalytic processes; and (3) combining advanced data visualization, multidimensional mathematical modelling, and computational chemistry in order to reveal trends within complex datasets. This strategy serves to predict reaction outcomes, advance mechanistic understanding, and accelerate the development of new efficient catalytic systems. Predicting *a priori* which catalyst structure would be optimal for a given reaction remains the Holy Grail in the field of catalyst design, particularly in complex catalytic systems involving multiple components. By preparing catalyst libraries that provide access to focused yet diverse experimental datasets and synergistically combining statistical and computational methods to study these datasets, our approach aims to uncover general design principles for catalyst design.

**SYNFORM** *When did you get interested in synthesis?*

**Dr. A. Milo** My interest in synthesis was ignited during my M.Sc., mentored by Prof. Berni Hasenknopf at Pierre and Marie Curie University (UPMC, Paris 6). Our aim was to tether an

organic moiety to an inorganic polyoxometalate cluster and at the end of my M.Sc., after a multistep synthesis, I only had a few milligrams of product. Looking back, I was not a proficient synthetic chemist to say the least, but I did realize the value of being able to prepare your own objects of study. As a result, during my Ph.D. studies, I spent an extensive amount of time honing my synthetic skills. I was lucky enough to have been trained by an extremely talented senior Ph.D. student, Maxym Vasylyev, who taught me how to plan reactions, dry solvents, use a Schlenk line, and generally, how to think like a synthetic chemist.

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

**Dr. A. Milo** Our society, and with it the chemical industry, has always been defined by two orthogonal developments, communication and automation. Both will gain more traction in my opinion due to the world pandemic we are living through, as we witness the advantages provided by modern communication and automation of work processes. We now also have the means to automate many of the tasks that were once reserved for highly skilled synthetic chemists, such as reaction design, conditions screening, reaction optimization, product purification, etc. This has, on the one hand, democratized the discovery process and made it easier to access starting materials and drug leads, which can then also be automatically tested in biological assays. On the other hand, it may seem that these advancements have stripped synthetic chemists of their traditional roles. This observation may be true to some extent, however, as I see it, merely preparing compounds is not our calling as chemists. Our role was and remains the invention of new more efficient, sustainable processes, and we now have more means at our disposal to do so at an increased pace.

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

**Dr. A. Milo** My group's main research focus currently is establishing a straightforward and systematic strategy for modifying organocatalyst structures in the reaction vessel by combining highly modular catalytic systems with mathematical modelling techniques to facilitate the discovery and prediction of secondary-sphere design principles.<sup>1-4</sup> This methodology provides a tunable handle for the nuanced recognition of substrates by their geometry and electronic properties, thus enabling the discovery and optimization of organocatalytic systems. Traditionally, optimizing the reac-

tivity and selectivity of catalytic reactions is accomplished by modifying reaction conditions and catalyst structures in a rational and incremental manner. For example, the classical strategy for optimizing selectivity is founded on steric biasing by installing units that impart repulsion and leave only one of the quadrants of the catalyst available for an approaching substrate.<sup>5-8</sup> Nonetheless, the application of non-covalent interactions has been gaining traction in recent years because they offer a powerful handle for controlling reactivity and selectivity through transition-state stabilization rather than destabilization of undesired pathways.<sup>9-18</sup> Although these interactions are considered weak, their influence at a distance, through networks of interacting molecular units, such as those comprising the secondary sphere, cannot be overstated.<sup>16,19,20</sup> The significant advantage of our approach stems from the development of mathematical models to predict optimal secondary-sphere modifiers for diverse organocatalyst and substrate classes. Curation and systematic analysis of these models serve to construct a conceptual framework for the rational design and fruitful incorporation of orthogonal secondary-sphere modifiers into countless organocatalytic systems. The modularity and predictability of these organocatalyst libraries make them easily adaptable to new substrates and reactions without the need for an elaborate synthetic effort. Ultimately, this research program aims to transform organocatalyst development by providing a highly modular platform for their design, preparation, mechanistic elucidation, optimization, and performance prediction.

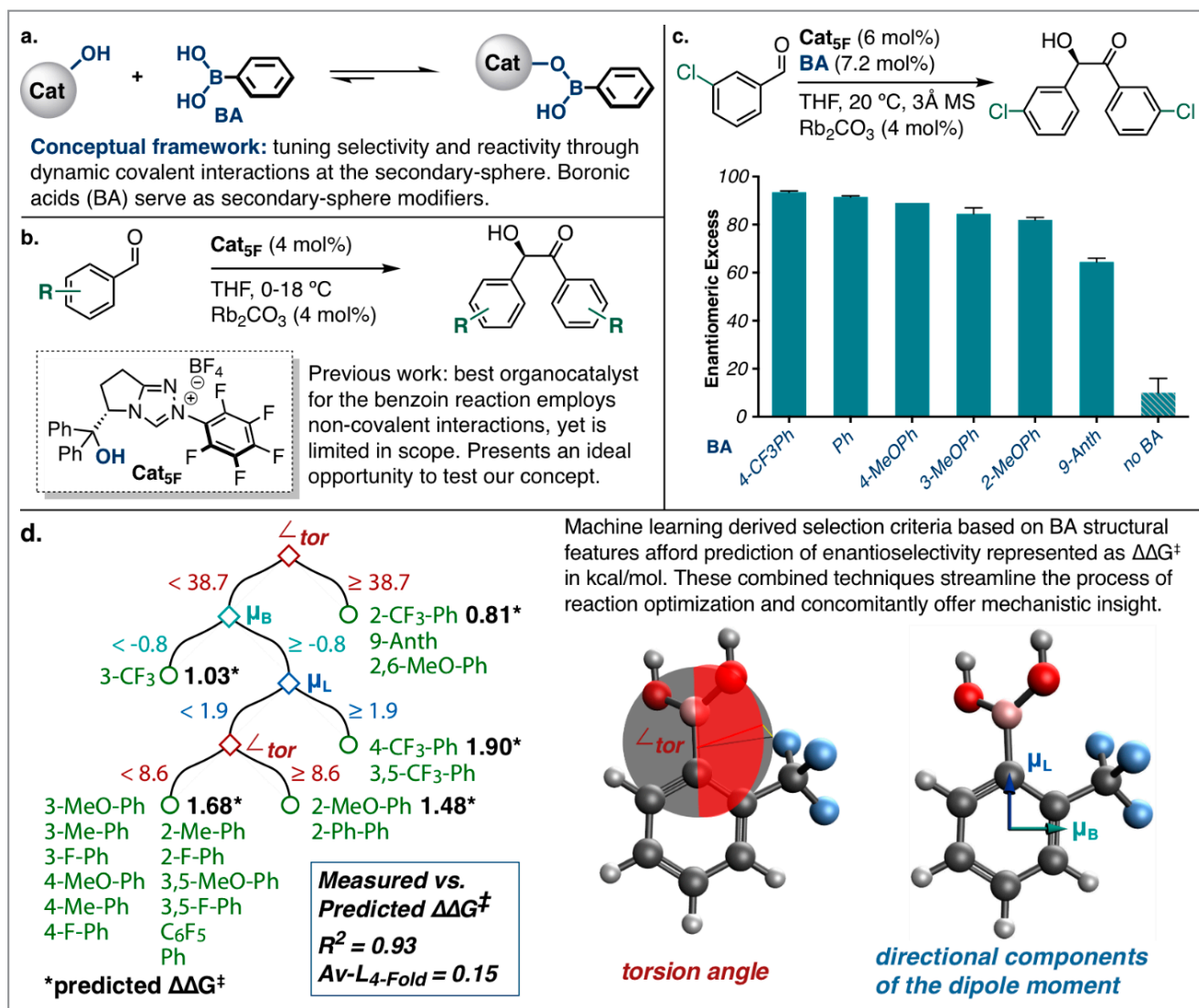
**SYNFORM** *What is your most important scientific achievement to date and why?*

**Dr. A. Milo** Our group has provided a proof-of-concept for the ability of secondary-sphere modifiers to provide a handle for the optimization of organocatalytic reactions.<sup>4</sup> The secondary-coordination sphere was first described more than a century ago in the context of organometallic complexes as groups that are not directly bonded to a metal, but are coordinated to its ligands.<sup>21,22</sup> This definition has since been expanded to any moiety in the molecular microenvironment of coordination compounds that influences the orientation and electronic properties of their ligands by introducing non-covalent interactions, such as hydrogen bonding, electrostatic forces, and hydrophobic effects.<sup>23-25</sup> Although it is now well established that such interactions have a fundamental effect on reactivity and selectivity in enzymatic catalysis,<sup>26-28</sup> metal-mediated processes and transition-metal chemistry,<sup>23-25,29-33</sup> there is a scarcity of studies explicitly incorporating secondary-sphere modifiers into organocatalytic systems. We

define the secondary sphere in the context of organocatalysis as moieties that are not covalently bonded to an active site, yet are located in proximity to it, and are closely involved in its mechanism of action through dynamic or non-covalent interactions. These interactions control the geometry and electronic properties of the reaction intermediates and transition state(s). Our proof-of-concept of this approach was focused on dynamic-covalent binding between boronic acids (BAs) and

catalysts with available hydroxy groups (see Figure 1). The binding mode of the modifier was orthogonal to catalytic activity, avoiding catalyst inhibition. Likewise, the modifier was located in close proximity to the active site and possessed the capacity for dynamic and non-covalent interactions that guided reactivity and selectivity.

*Mattes female*



**Figure 1** (a) Modifying catalyst structures in the reaction vessel by forming dynamic boronic ester bonds *in situ* under catalytically relevant conditions. (b) Catalytic system developed by Zeitler and Connon containing a hydroxy group that is involved in enantioselectivity-controlling non-covalent interactions.<sup>34</sup> (c) Comparison of the enantioselectivity obtained in the benzoin condensation using several BA modifiers with a challenging model substrate containing an electron-withdrawing group, 3-chlorobenzaldehyde. (d) Mathematical model for reactions with 3-chlorobenzaldehyde as substrate and different BAs: decision tree based on the mean standard error decrease at each node provides a prediction of enantioselectivity. Goodness-of-fit represented by  $R^2$  and the average L (predictive loss) value of a 4-fold validation performed 500 times on randomized sets.

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## Lewis Acid Catalyzed Domino Generation/[2,3]-Sigmatropic Rearrangement of Ammonium Ylides to Access Chiral Azabicycles

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The *N*-fused azabicyclic structure with a bridgehead quaternary center in fused 5/*X* (*X* = 5, 6, 7) rings is one of the most ubiquitous bicyclic structural frameworks. This motif is also the central structural unit found in a large number of therapeutics and natural products. Professor Min Zhang, from Chongqing University (P. R. of China), whose group has a long-standing interest in the total synthesis of complex natural products, explained that – from the chemistry viewpoint – the development of efficient reactions to construct such bicyclic ring systems remains a daunting challenge for organic chemists, presumably because of the problems associated with quaternary stereogenic center installment, as well as the inefficiency of bicyclic framework construction.<sup>1</sup> “Among the existing strategies to build this type of bicyclic skeleton, many are focused on the generation of the bridgehead quaternary stereogenic center and the bicyclic framework in multi-step ways, whereas efficient methods capable of combining these two events in one step are still very limited,” said Professor Zhang.

[2,3]-Sigmatropic rearrangement of ammonium ylides is one of the most efficient approaches for synthesizing complex nitrogenous compounds.<sup>2,3</sup> During the rearrangement, a new stereogenic carbon center can be stereoselectively created by chiral induction of the neighboring chiral ammonium nitrogen atom through a concerted five-membered-ring transition state. “The most common way to generate the ammonium ylides for the rearrangement requires two separate steps: quaternization of a tertiary amine, then deprotonation of the resulting quaternary ammonium salt with a strong base.<sup>2,3</sup> The harsh reaction conditions needed for the preparation and deprotonation of the quaternary ammonium salts, as well as the problems associated with purification of ammonium salts, limit the application scope of this type of reaction,” explained Professor Zhang.

Recently, a collaborative effort between the group of Professor Zhang and that of Professor Yu Lan uncovered a Lewis acid catalyzed domino generation/[2,3]-sigmatropic rearrangement of ammonium ylides, by which *N*-fused azabicyclic skeletons featuring various ring systems (5/*X*, *X* = 5, 6, 7) and bridgehead quaternary stereogenic centers were constructed simultaneously (Scheme 1). “The ammonium ylides were generated under mild reaction conditions by using a  $\pi$ -Lewis acid silver salt as the catalyst without a strong

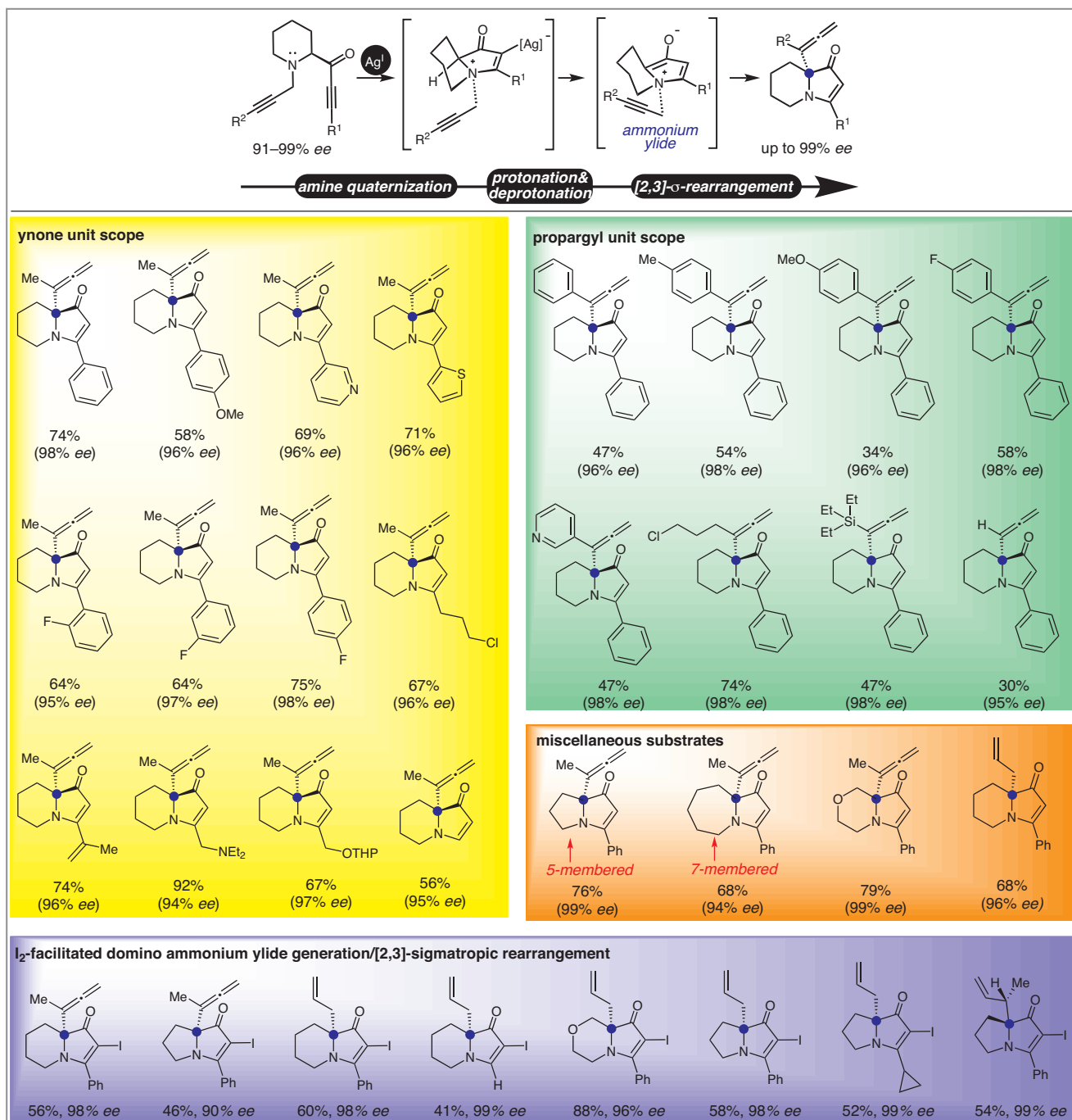
base, which is a requisite in traditional approaches to these compounds,<sup>4</sup>” said Prof. Zhang. He continued: “This protocol is compatible with racemization-prone substrates and consequently the chirality information originating from the chiral amino acids is efficiently transferred, furnishing a series of *N*-fused azabicycles in high enantiomeric purity (up to 99% ee).” Combined with density functional theory (DFT) calculations, the experimental results revealed that: 1) the reaction process involves four steps: tertiary amine quaternization, water-assisted protonation and deprotonation, and propargylic or allylic [2,3]-sigmatropic rearrangement; 2) protonation of the C–Ag bond largely increases the acidity of the C2–H and occurs prior to its deprotonation. “Both events were assisted by the residual water in the reaction system, which leads to the generation of ammonium ylides under mild conditions, without the involvement of strong bases, thus resulting in almost no chirality erosion,” remarked Prof. Zhang. Following on the success of using a silver salt as the catalyst, and as an extension of this protocol, replacing the silver catalyst with a stoichiometric amount of I<sub>2</sub> generated the corresponding iodinated *N*-fused azabicycles with more handles for further synthetic elaboration.<sup>5</sup> Prof. Zhang concluded: “Considering the easy accessibility of the chiral precursors, this method represents a new mild way to generate ammonium ylides, and provides a new efficient method to construct *N*-fused azabicycles with a bridgehead quaternary center in various ring sizes.”

*Min Zhang*

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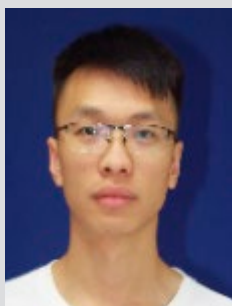


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