Young Career Focus: Dr. Josep Cornella (Max-Planck-Institut für Kohlenforschung, Germany)

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. Josep Cornella (Max-Planck-Institut für Kohlenforschung, Germany).

Biographical Sketch

Dr. Josep (Pep) Cornella

Dr. Josep (Pep) Cornella studied chemistry at the University of Barcelona (Spain). His MSc studies in the Department of Organic Chemistry investigated the chemistry of allylboron reagents. After completing his Master's thesis in 2008, he moved to the United Kingdom to pursue doctoral studies in the group of Prof. Igor Larrosa at Queen Mary University of London (QMUL) where he focused on the use of aromatic carboxylic acids as aryl donors in metal-catalyzed decarboxylative reactions. In 2012, he received a Marie Curie Fellowship to pursue postdoctoral studies in the group of Prof. Ruben Martin at the Institut Català d'Investigació Química (ICIQ, Spain) where he focused on the development of Ni-catalyzed transformations for the activation of C–O bonds and carbon dioxide (CO_2) insertion. In 2015, he obtained a Beatriu de Pinós Fellowship to carry out further postdoctoral studies in the group of Prof. Phil S. Baran at The Scripps Research Institute, California (USA), where he developed novel transformations based on the concept of "redox-active esters" as radical coupling partners for Ni- and Fe-catalyzed cross-couplings.

In spring 2017, he was appointed as a Max Planck Group Leader in the Department of Organometallic Chemistry at the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr (Germany). He has been a Max Planck Research Group Leader (MPRGL) since the summer of 2017 at the same Institute, where he leads the Laboratory for Sustainable Homogeneous Catalysis, and was the recipient of the Thieme Chemistry Journals Award in 2017.

INTERVIEW

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

Dr. J. Cornella The main focus of our research group is the development of ***rapid***, ***practical*** and e***fficient*** methodologies for organic synthesis based on sustainable and cheap catalysts, towards more sustainable chemical processes. In addition to efficiency and practicality, we are highly interested in discovering new reactivity with the aim of unveiling novel transformations. More specifically, our group's interests are in the *fundamental understanding and application of catalytic processes* and the *development of simple reagents* for organic synthesis. We believe that these two approaches have enormous potential with potential impact across the chemical sciences.

SYNFORM *When did you get interested in synthesis?*

Dr. J. Cornella I was first fascinated by synthesis in my undergraduate courses at the Universitat de Barcelona, where I undertook the class "Síntesi Orgànica" with Prof. Albert Moyano. There, I discovered the beauty and fun of constructing molecules and the plethora of possibilities for connecting and disconnecting bonds. Then, during my PhD and postdoc I learned how metals and catalysis can influence such disconnections, ultimately leading to extremely straightforward methodologies. I was fascinated by the idea of using transition metals to dramatically shorten a synthesis that required several steps and a tremendous amount of effort, time and resources. With this idea in mind, we are trying to add another variable to the equation: sustainability. In addition to streamlining synthesis, we are also attempting to provide sustainable approaches to these processes. In our laboratory, this implies the design of simple and readily available reagents or earth-abundant metals as catalysts.

© Georg Thieme Verlag Stuttgart • New York – Synform **2019/02**, A22–A25 • Published online: January 18, 2019 • DOI: 10.1055/s-0037-1609819

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

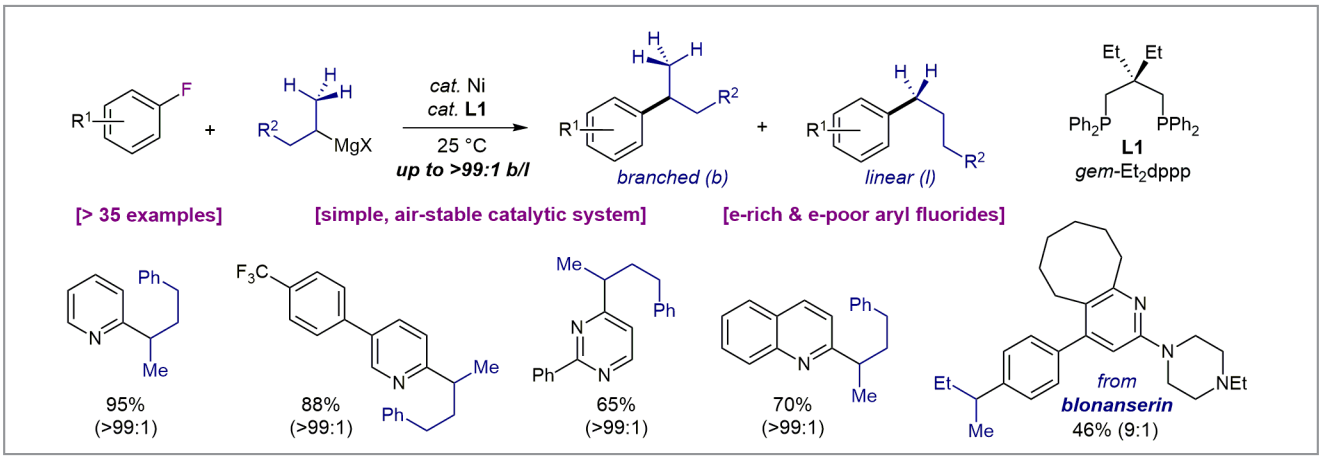
Dr. J. Cornella Organic synthesis is truly vivid and alive. More specifically, homogeneous catalysis has become an indispensable tool for organic synthesis. New methodologies to assemble molecular entities appear every day from researchers around the world at an incredible pace. Thousands of methods are published every year, thus highlighting the richness and wide interest in this area. However, it seems that these fast-growing and large number of efficient and available methods do not translate when looking at applications in industrial contexts. A recent report[1] from medicinal chemists revealed that industry relies mainly on a small and specific set of reactions to synthesize their libraries of compounds. Although many factors can contribute to this, a determining factor is that the methods of choice (namely Suzuki cross-coupling, amide bond formation, enantioselective hydrogenation, etc.) are those which are simple, robust, scalable and reliable, especially when applied in complex synthetic contexts. In this regard, our research group places particular emphasis on covering the largest chemical space possible when developing new strategies (presence of a large variety of heterocycles and sensitive functional groups) to be able to achieve the maximum translational potential possible.

SYNFORM *Your research group is active in the area of catalysis applied to organic synthesis. Could you tell us more about your research and its aims?*

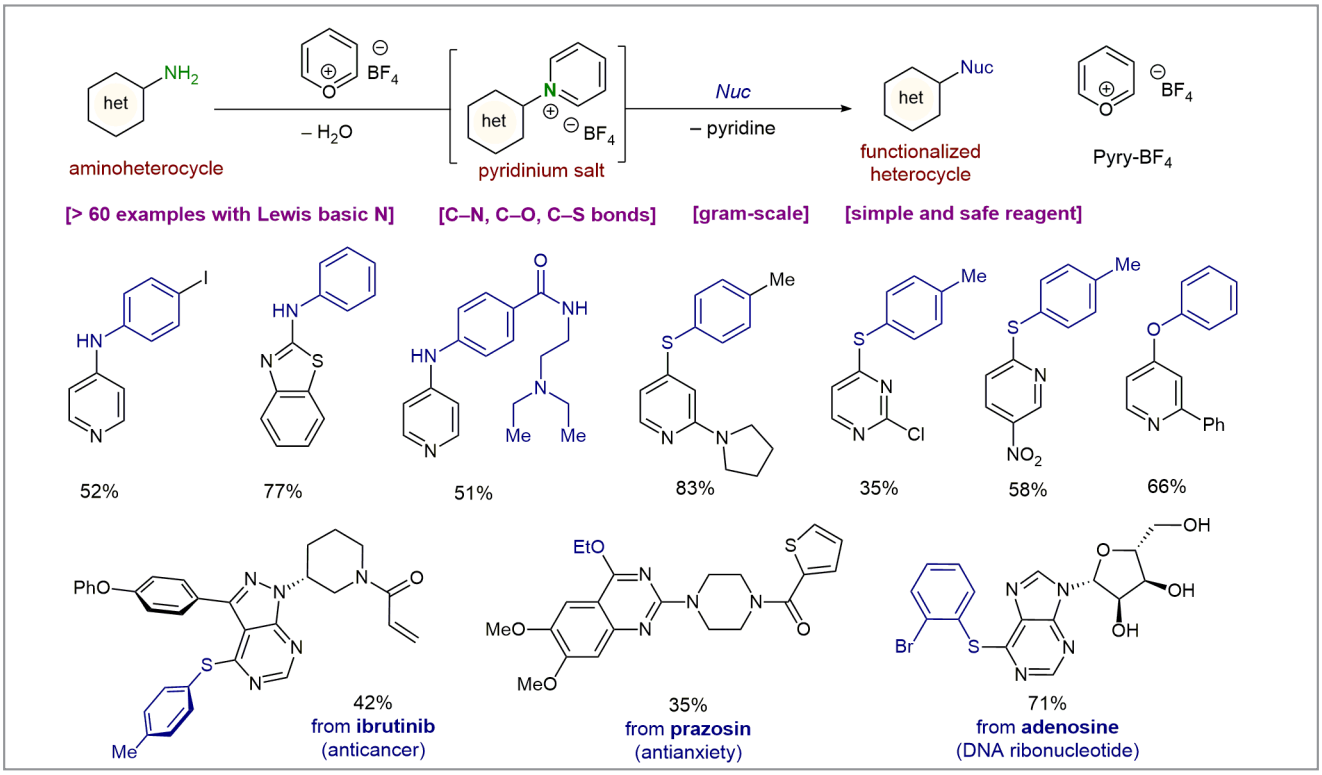
Dr. J. Cornella In particular, we are interested in developing methodologies based on cheap and abundant Ni salts for the decoration of heterocycles, which are of major importance in pharmaceutical and agrochemical settings. We have developed a methodology for the functionalization of C–F bonds with alkyl Grignard reagents in a regioselective fashion to construct new C–C bonds.[2] In addition to the activation of challenging and strong C–F bonds, we have identified a feature in the ligand (Thorpe–Ingold effect) that minimizes the formation of the commonly obtained by-products through β-hydride elimination/insertion events. This allows a rapid construction of non-planar structures which are of great interest to medicinal chemists to design and modify protein–drug interaction sites (Scheme 1).

Another area we are interested in is the development of practical reagents for organic synthesis. In this regard, we have recently developed a pyrylium reagent (Pyry-BF_4) which is capable of targeting amino groups C(sp^2)–NH_2, which are prevalent in a wide variety of chemical compounds. The reagent reacts preferentially with these functionalities, thus priming them for a simple and robust nucleophilic aromatic substitution (S_NAr).[3] Prior to our work, such reactivity was rather limited to the use of polyalkylated amines or diazo compounds, which are either explosive or unselective. The protocol developed by our group proceeds with extreme chemoselectivity and this permits the modification of C(sp^2)–NH_2 bonds in late-stage functionalization contexts as demonstrated by the successful modification of densely functionalized molecules such as ibrutinib (anticancer), prazosine (antianxiety) and adenosine (DNA-building material) (Scheme 2).

Another research line we are currently exploring is the study of the chemistry of low-valent elements. For example, we are interested in highly reduced species of Ni and their capabilities as catalysts. While the high oxidation states of

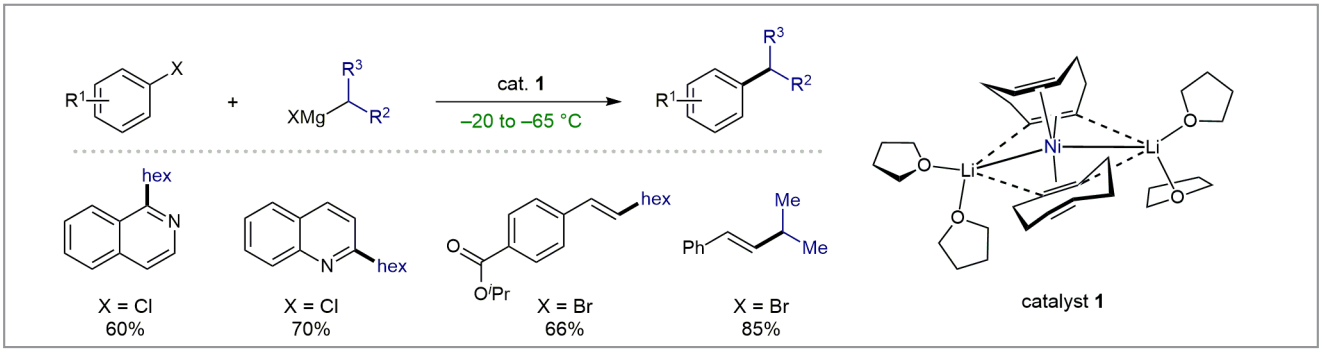


Scheme 1 Ni-catalyzed branch-selective alkylation of C–F bonds



Scheme 2 Development of a pyrylium reagent for the activation of C–NH_2 in aminoheterocycles

Ni – Ni(IV) to Ni(0) – are well-known in the literature, little is known about the highly reduced species of Ni in the context of cross-coupling. In traditional cross-couplings the electron density is provided by the ancillary ligand: we wondered what would happen if this process is reversed, and the electron density is mainly supplied by the metal center. Inspired by the seminal work from Jonas and Pörschke in the 1970s at MPI Kohlenforschung, we were able to identify a highly reduced Ni–Li–olefin complex [formally a Ni(-II)], which is capable of catalyzing Kumada–Corriu cross-couplings at cryogenic temperatures.[4] The unprecedented activity of this Ni(-II) complex at low temperatures allowed the coupling of moieties bearing sensitive functional groups, which would react with the Grignard at higher temperatures, such as esters and nitriles. Although preliminary studies point towards the possibility of a low-valent catalytic cycle involving Ni(-II) species to forge C–C bonds, details on a full mechanistic picture are still under investigation (Scheme 3).



Scheme 3 Formal Ni(-II) precatalyst for Kumada cross-coupling

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

Dr. J. Cornella The most important scientific contribution is always yet to come. However, I am very proud of the contributions we have made in such a short time. The discovery of a branch-selective alkylation of C–F bonds disclosed an unknown Thorpe–Ingold effect in the ligand which led to complete retention over isomerization. The catalytic activity of a formal Ni(-II) complex has led to a reconsideration of the role of the ligands in Kumada cross-coupling and the consideration of low-valent species involved in catalytic cycles. And finally, the development of the Pyry-BF_4 has permitted a safe, selective and scalable S_NAr into $C(sp^2)$–NH_2 bonds, which has been elusive to date. Although all these results have been small contributions to each particular field, I believe our continuous work in this area will open new vistas and I am convinced (as is every chemist) that great things to discover lie ahead of us.

REFERENCES

(1) D. G. Brown, J. Boström *J. Med. Chem.* **2016**, *59*, 4443–4458.
(2) (a) M. J. O'Neill, T. Riesebeck, J. Cornella *Angew. Chem. Int. Ed.* **2018**, *57*, 9103–9107. (b) M. J. O'Neill, J. Cornella *Synthesis* **2018**, *50*, 3974–3996. (c) M. J. O'Neill, J. Cornella *CHIMIA* **2018**, *72*, 601–605.
(3) D. Moser, Y. Duan, F. Wang, Y. Ma, M. J. O'Neill, J. Cornella *Angew. Chem. Int. Ed.* **2018**, *57*, 11035–11039.
(4) L. Nattmann, S. Lutz, P. Ortsack, R. Goddard, J. Cornella *J. Am. Chem. Soc.* **2018**, *140*, 13628–13633.