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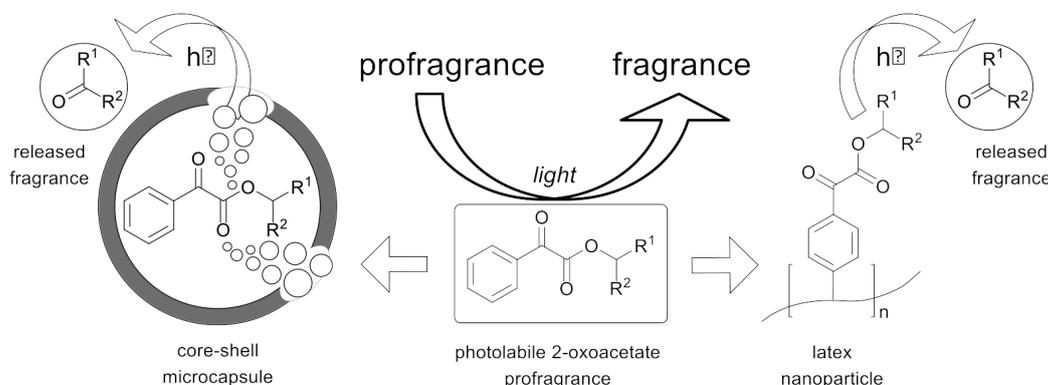
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Profragrance chemistry as interdisciplinary research area and key technology for fragrance delivery

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The performance of perfumed consumer articles is often judged on the duration of fragrance perception. To slow down the evaporation of highly volatile perfumery compounds, the development of non-volatile precursors, so-called profragrances, which release perfumery compounds by covalent bond cleavage during application, has become an important research area in the perfume industry [1]. Reaction conditions, which may serve as a trigger to deliver fragrances from their corresponding precursors, have to be mild to occur during the use of the respective consumer articles in an everyday life environment. Temperature variations, exposure to (day)light, the presence of oxygen or water (including changes in pH) and the action of enzymes have been identified as being suitable for this purpose.



The general concept of profragrance development and its interdisciplinarity, spanning from organic synthesis *via* analytical chemistry to various aspects of materials science, will be demonstrated at the example of light-sensitive delivery systems [2]. On exposure to ambient daylight, 2-oxoacetates degrade to form an aldehyde or ketone together with a molar equivalent of CO and/or CO₂. The compounds have been used as light-activated profragrances to control the release of volatile carbonyl compounds in functional perfumery. However, when stored in aqueous media, 2-oxoacetates (partially) hydrolyse, thus resulting in an undesired premature degradation of the precursors. To overcome this inherent hydrolytic instability, two different approaches, namely the copolymerisation of 2-oxoacetate monomers into latex nanoparticles [3] and the encapsulation of the profragrances into core-shell microcapsules [3,4], have been investigated (see Scheme). While the formation of CO and/or CO₂ as side-products of the photoreaction has no impact on the fragrance release from 2-oxoacetate monomers or polymers, we could demonstrate that the gas formation inside core-shell microcapsules generated an overpressure, which rapidly led to the extension or burst of the capsule wall and thus to an efficient fragrance release [4]. Both delivery systems fulfilled the expected requirements in terms of performance; photolabile 2-oxoacetates thus offer a broad range of applicability for the light-induced delivery of fragrances.

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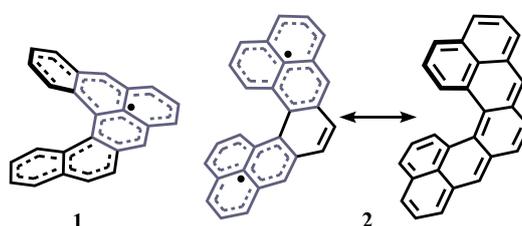
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Helically Chiral Open-Shell Polycyclic Aromatic Hydrocarbons

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The combination of chirality and magnetic properties integrated in a single molecule is scarce, but it is potentially useful for development of spintronic devices.^[1,2] The spin-delocalized chiral molecular systems are not only of fundamental value to obtain “three-dimensionally” delocalized spin structure but also of great interest to generate chiral magnets and access electron-spin qubit systems using a polarized photon. Helicenes, *ortho*-annulated polycyclic aromatics, possess a non-planar helically chiral π -conjugated structure. By creating a helicene system bearing one or more unpaired electrons, one should thus be able to combine (i) the magnetic properties, related to the non-zero spin of a molecule, and (ii) the chiroptical properties, stemming from the inherent chirality of the molecule.



We have designed and synthesized the first helically chiral phenalenyl hydrocarbons, radical **1** and biradicaloid **2**. The [5]helicene backbone gives rise to the inherent chirality and the phenalenyl substructure provides one unpaired electron. While compound **1** has an open-shell doublet ground state, compound **2** has a singlet ground state and a thermally accessible triplet excited state. We named^[3] compound **2** as “Cethrene” because of its “C”-shape and chirality. Cethrene can be represented by either a biradical or a quinoidal resonance form. At room temperature, cethrene gave a well-resolved EPR spectrum on account of population of the triplet state. The EPR signal intensity decreased upon decreasing the temperature and almost diminished at 200 K. The Bleaney Bower’s fit gave the singlet-triplet (S-T) energy gap of 5.6 kcal mol⁻¹, which is significantly smaller than that of its planar analog heptazethrene (8.9 kcal mol⁻¹), as a result of helical twist that gives rise to through-space antibonding and bonding interactions within the HOMO and the LUMO, respectively. The detailed synthetic strategy, structure-property relationship, chiroptical and magnetic properties, and the theoretical investigation of compounds **1** and **2** will be discussed during the presentation.

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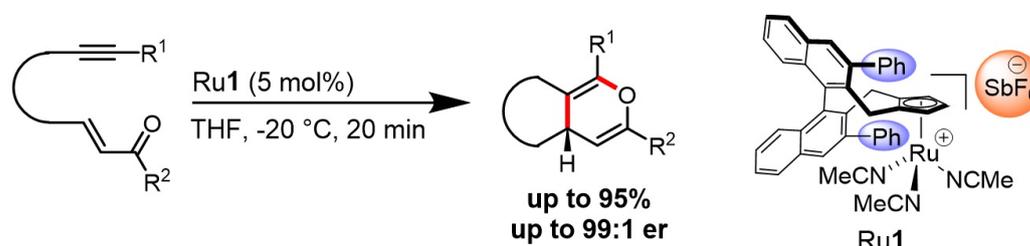
Chiral Ruthenium-cyclopentadienyl Complexes as Versatile Catalysts for Enantioselective Transformations

D. Kossler¹, N. Cramer¹

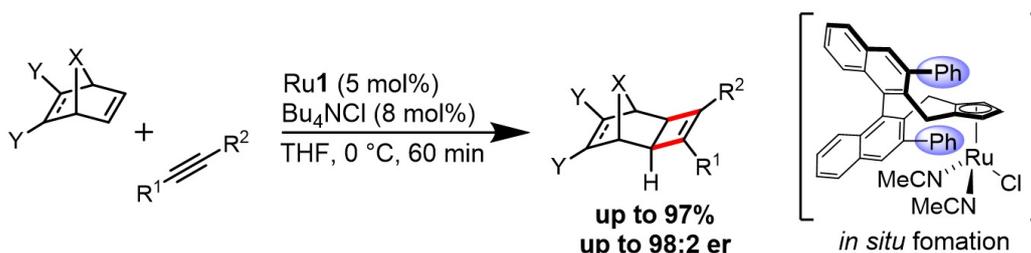
¹EPF Lausanne

The cyclopentadienyl (Cp) ligand is of fundamental importance for organometallic chemistry and as such found in countless transition-metal catalysts. Chiral versions of these catalysts often employed tethering strategies to the complexed metal, which goes to the expense of free coordination sites. Our group has developed chiral versions of these ligands, which keep the maximum number of coordination sites unoccupied and therefore available in the catalytic cycle.¹

Ruthenium catalyzed cycloisomerizations offer a rapid access to complex molecular frameworks in an atom economical fashion.² Therefore the cationic [CpRu(MeCN)₃]⁺PF₆⁻ complex found widespread application in organic synthesis. Recently we reported the synthesis of a set of chiral cationic Ru(II) catalysts bearing our chiral Cp^x ligands and their application in the formal [4+2] cyclization of yne-enones to the corresponding pyrans in high enantioselectivity.³



In the course of this project we discovered a considerably large influence of the counterion on the reactivity and selectivity of the transformation. We opted to explore these effects with particular emphasis on covalently binding anions, thus obtaining a chiral congener of the well-established neutral Cp*Ru(cod)Cl catalyst. This idea proved to be feasible and led to the development of an asymmetric version of the ruthenium catalyzed formal [2+2] reaction of strained bicyclic alkenes with internal alkynes to chiral *exo*-cyclic cyclobutenes.⁴



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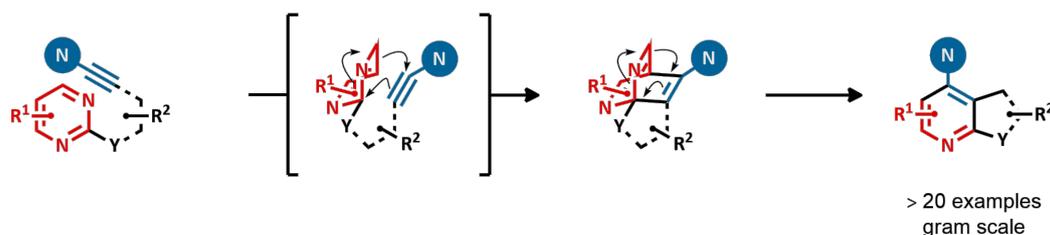
Inverse Electron-Demand [4 + 2]-Cycloadditions of Ynamides: AccesstoNovel Pyridine Scaffolds

G. Duret¹, R. Quinlan¹, R. E. Martin², B. Yin¹, P. Bisseret³, M. Neuburger⁴, V. Gandon⁵, N. Blanchard^{3*}

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Functionalized polycyclic aminopyridines are central to the chemical sciences, but their syntheses are still hampered by a number of shortcomings. These nitrogenated heterocycles can be efficiently prepared by an intramolecular inverse electron demand hetero Diels–Alder (ihDA) cycloaddition of ynamides to pyrimidines. This ihDA/rDA sequence is general in scope and affords expedient access to novel types of aminopyridinyl scaffolds that hold great promise in terms of exit vector patterns.

We report an efficient method to prepare various fused aminopyridines and spiro-amino pyridines through the first inverse electron demand hetero Diels–Alder cycloadditions of ynamides. [1] More than twenty original examples were obtained with good yields and the scale up of this method was efficiently obtained using flow chemistry. DFT calculations provide mechanistic insights suggesting that the overall process is favored both on kinetic and thermodynamic grounds.



We report an efficient method to prepare various fused aminopyridines and spiro-amino pyridines through the first inverse electron demand hetero Diels–Alder cycloadditions of ynamides. [1] More than twenty original examples were obtained with good yields and the scale up of this method was efficiently obtained using flow chemistry. DFT calculations provide mechanistic insights suggesting that the overall process is favored both on kinetic and thermodynamic grounds.

[1] Guillaume Duret, Robert Quinlan, Rainer E. Martin, Philippe Bisseret, Markus Neuburger, Vincent Gandon, Nicolas Blanchard *Org. Lett.*, **2016**, 18, 1610–1613.b

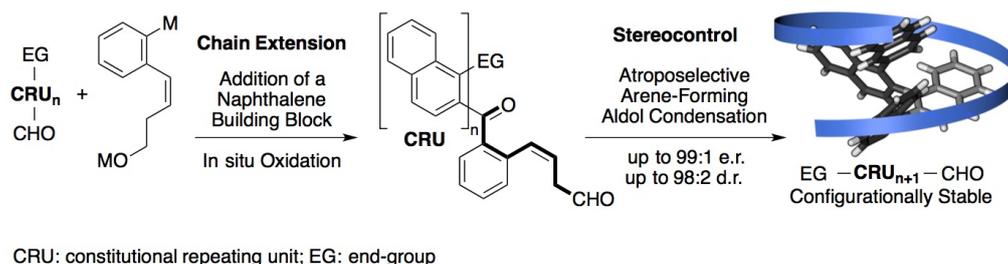
Stereoselective Arene-Forming Aldol Condensation: Synthesis of Configurationally Stable Oligo-1,2-naphthylenes

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Structurally well-defined oligomers play a fundamental role in the function of natural systems, such as peptides or DNA. Synthetic counterparts, e.g. truncated helicenes, are often characterized by a low configurational stability and typically pose a substantial synthetic challenge.

The presentation will outline our approach to the catalyst-controlled synthesis of oligo-1,2-naphthylenes. Based on the hindered rotation about the aryl-aryl single bonds, these oligomers show high configurational stability. For the efficient oligomer assembly, an building block addition approach was developed. An *in situ* double oxidation followed by a stereoselective arene-forming aldol condensation elongates the oligomer by one unit. The shape, such as the *P*-helix secondary structure is thereby transcribed from a chiral amine catalyst and excellent atropoenantio- and atropodiastereoselectivity of up to 99:1 was achieved.



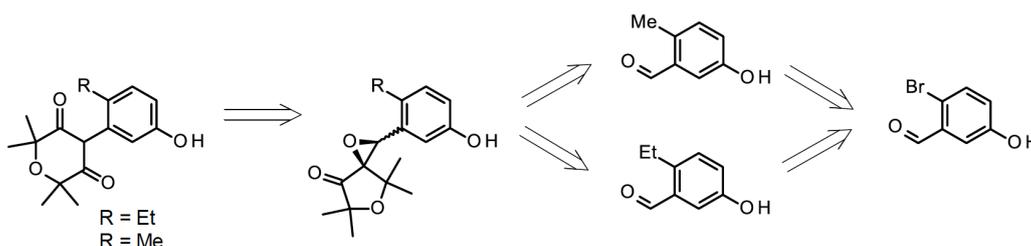
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Optimization of Manganese Coupling Reaction for Kilogram-scale Preparation of two Aryl-1,3-dione Building Blocks

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The inhibition of acetyl-CoA carboxylase (ACCCase) is one of the most commercially important modes of action for the control of grass weeds. To support our discovery program of new ACCCase-inhibiting carbocyclic aryl-1,3-diones an efficient synthesis of two building blocks was required.



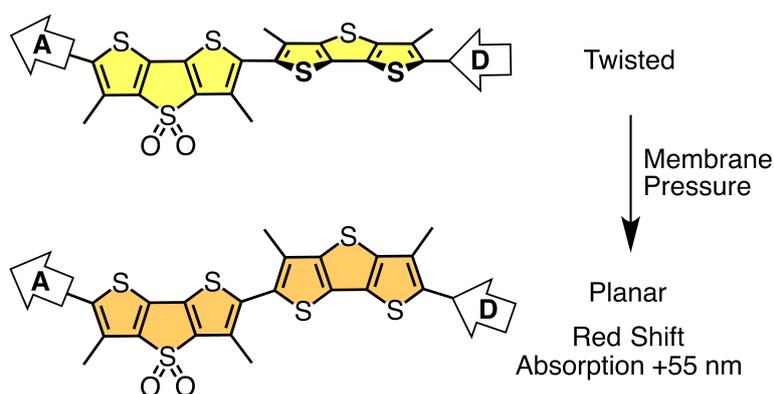
A concise kilogram-scale synthesis was developed employing manganese-catalysed cross coupling and semi-pinacol rearrangement/ring expansion.

Mechanosensitive Fluorescent Membrane Probes

Q. Verolet¹, S. Soleimanpour¹, M. Dal Molin¹, A. Colom¹, A. Roux¹, N. Sakai¹, S. Matile^{1*}

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The bilayer membrane characteristics such as lateral tension, fluidity and polarity are crucial parameters in many biological processes. Inspired by the lobster pigmentation and the origin of its impressive color variation after cooking, our group proposed a new class of fluorescent probes that exploits the combination of chromophore planarization and polarization to report on its environment [1]. The fluorescent push-pull probe is built with at least two aromatic moieties linked by a sigma bond. The sensitivity towards fluidity change arises from the flattening of the aromatic scaffold in the ground state induced by the passage to a more rigid environment. This planarization red shifts the absorption spectrum enough to discriminate the phase transition from L_d to S_o lipid bilayer membranes with the naked eye. Finally, a charged head is connected to the chromophore to control the internalization and the position of the probe inside the membrane. To maximize the mechanosensitivity and the fluorescence of the probe, a screening of the length, deplanarization [2], nature [3] and push-pull [4] of the aromatic moiety was accomplished.



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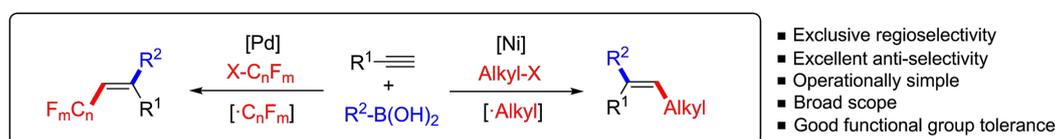
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Metal-Catalyzed Stereoselective Dicarbofunctionalization of Alkynes

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Intermolecular processes involving the regio- and stereoselective formation of two new C-C bonds across an alkyne are in high demand as they provide an efficient access to tri- and tetra-substituted olefins.^[1] In this context, single step procedures involving bench stable reagents and catalysts are still scarce.^[2] Here, we report two different metal-catalyzed three-component reactions of terminal alkynes with alkyl halides and organoboronic acids.^[3] In case of using palladium as a catalyst, perfluoroalkyl iodides were efficiently installed whereas the use of nickel enabled the incorporation of α -carbonyl derivatives or unactivated alkyl groups. These methods, which proceed via radical mechanisms, allow the preparation of the corresponding alkenes under mild conditions in a regiocontrolled manner with excellent anti-selectivities. In addition, the stability of all reaction partners makes these reactions operationally simple and widely applicable.



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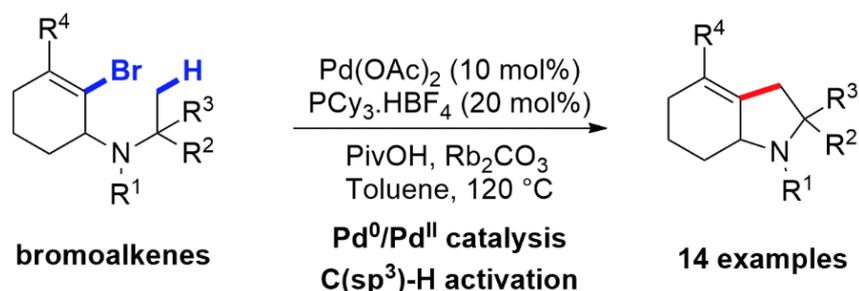
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Development and applications of C(sp³)-H Alkenylation

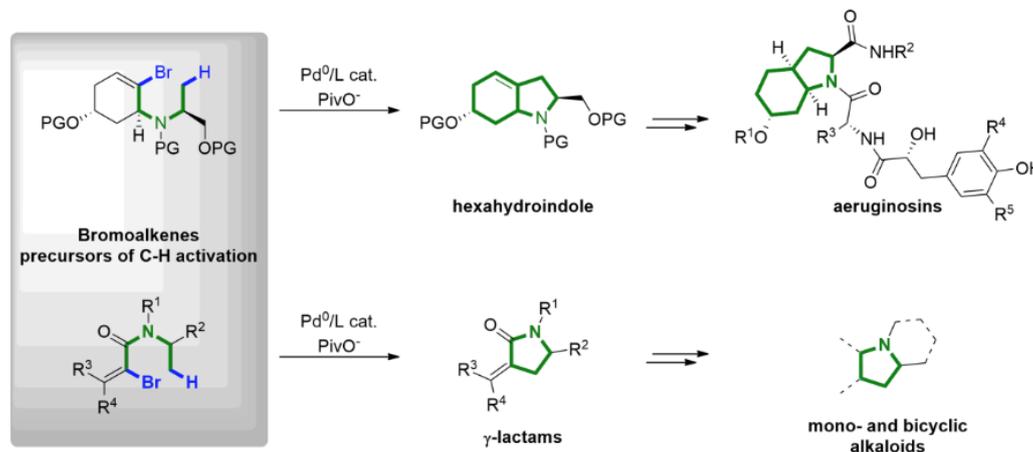
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In the last decade, the transition metal-catalyzed intramolecular activation of unactivated C-H bonds has emerged as powerful method to transform otherwise inert entities.¹ Within this field, we recently developed a straightforward access to hexahydroindoles by intramolecular C(sp³)-H alkenylation starting from bromoalkenes.²



In this communication, we will report access to alkaloids by use of this intramolecular C(sp³)-H alkenylation. Firstly, the combination of this methodology with a directed C(sp³)-H arylation allowed to achieve a divergent synthesis of aeruginosins.³ In a second part, the development of a modular C(sp³)-H alkenylation leading to γ -lactams,⁴ which are prevalent scaffolds found in numerous bioactive natural molecules, will be described.



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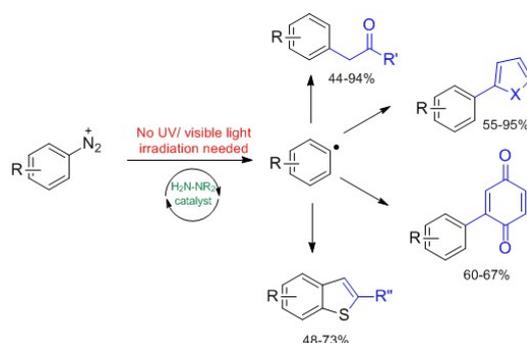
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A family of low molecular-weight, organic catalysts for reductive C-C and C-N bond formation

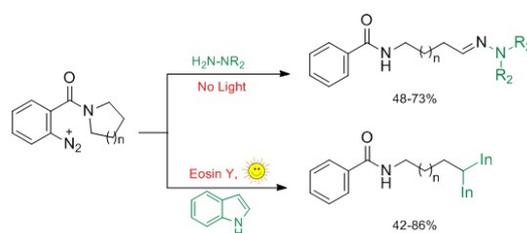
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Diazonium salts function as ideal sources of organic radicals that engage in several important transformations [1]. Recently, the use of photocatalysts in conjunction with a visible light source proved to be an efficient method for achieving different transformations with diazonium salts[2]. Our group has developed a family of low molecular-weight, organic catalysts that promote a range of C-C bond forming reactions of diazonium salts, and achieve so without the need for any metal adjuvant or irradiation with light[3]. These catalysts efficiently promote a range of transformations with competitive yields (Scheme 1)



We additionally report a metal-free, mild procedure for redox-neutral α -amino functionalization[4] with concomitant C-N[5] as well as C-C bond formation[6] (Scheme2).



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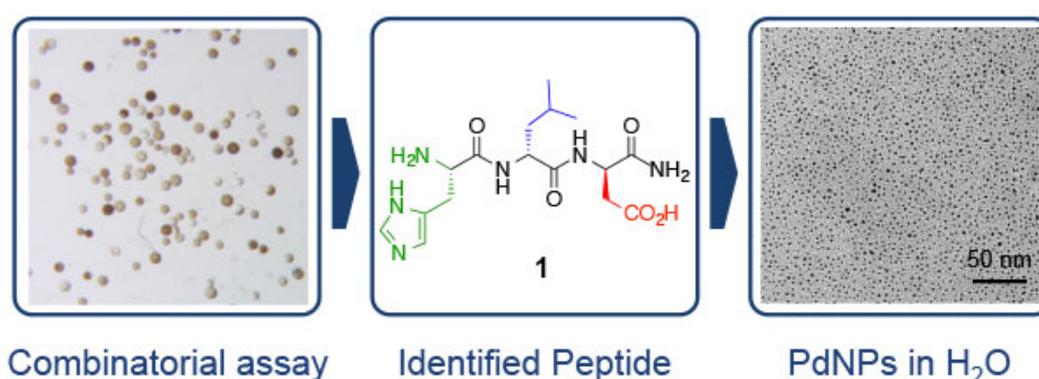
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Size-controlled nanoparticle formation in aqueous media with a thiol-free tripeptideS. Corrà¹, H. Wennemers¹¹ETH Zurich, Laboratorium für Organische Chemie, Vladimir-Prelog-Weg 3, 8093 Zürich

Nature uses interactions between metals and proteins for a variety of purposes ranging from catalysis to biomineralization. The modularity of peptides renders them attractive as additives for the formation of nanoparticles (NPs) and opens attractive avenues for the preparation of novel materials with specific functions and a broad range of applications.[1]

Our group has previously developed a combinatorial assay for the identification of peptides that control the formation of silver NPs within one-bead-one-compound libraries.[2] Now, we applied this combinatorial methodology for the identification of peptides that control the formation of palladium NPs and identified H-His-D-Leu-D-Asp-NH₂ (**1**) as an additive for the generation of highly stable, monodisperse, and water-soluble PdNPs with average diameter of 2.8 ± 0.8 nm. Tripeptide **1** proved to be applicable for the preparation of gold and platinum NPs with, again, excellent control over their size-distribution.[3]



Studies with close analogues of tripeptide **1** revealed the specific role of each amino acid in the sequence, His as surface-binding motif, D-Leu to build a hydrophobic shell, and D-Asp to provide water-solubility and additional stability by charge repulsion. Additional analyses provided insight into the structure of the peptidic self-assembled monolayer. These findings open interesting prospects for the formation of functionalized PdNPs.[3]

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